The effectiveness and experiences of pain science education for adults with chronic musculoskeletal pain

Volume 1

James Alexander Watson

A thesis submitted in partial fulfilment of the requirement of Teesside University for the degree of Doctor of Philosophy

December 2022

Abstract

Chronic musculoskeletal pain (CMP) affects approximately ¼ of adults worldwide and is considered an urgent global public health concern. CMP negatively impacts the quality of life of the individual in addition to a large societal financial burden. Pain science education (PSE) is an increasingly popular and potentially promising intervention to support individuals with CMP. The primary aim of this thesis was to investigate the effectiveness and experiences of PSE for adults with CMP. To address this research aim a multiphase mixed-methods research design was used. This included; a mixed-methods systematic review and meta-analysis of PSE; a systematic review and meta-analysis of the inter-individual differences in response to PSE; and a quasi mixed-methods feasibility study of a PSE informed pain management programme (PMP). The findings of the mixed-methods systematic review found PSE interventions do not produce clinically meaningful improvements in pain and disability but do produce clinically meaningful improvements in kinesiophobia and pain catastrophising in the short and medium term, respectively. There were tendencies for greater effects where PSE was combined with other interventions and it was proposed combining PSE with a PMP may be particularly fruitful. The qualitative component suggested that PSE interventions can facilitate pain reconceptualisation in some individuals and this may enhance their ability to cope with their condition. Some, but not all participants underwent pain reconceptualisation which raised the question whether PSE may be effective for some but not others, implying individual differences in response to PSE. The second systematic review investigated inter-individual differences in disability responses to PSE in people with CMP. There was insufficient evidence for the notion of clinically important inter-individual differences but given the small number of studies included further work is needed to draw any firm conclusions. The qualitative component of the feasibility study identified the potential of conceptual change theory as a framework for exploring and developing pain reconceptualisation. The first systematic review generated two synthesised findings comprised of several key principles, such as allowing the patient to tell their story, that may enhance the patient experience and effectiveness of PSE. The findings from these primary and secondary studies informed the development of a protocol for a pilot multi-site, single blind, parallel group randomised controlled trial (RCT) investigating the effectiveness of a PSE informed PMP for adults with CMP. The protocol will seek to meet these key principles when delivering the PSE. This is an important next step to explore if delivering PSE in this proposed optimal manner is effective for improving outcomes in people with CMP. Collectively, this thesis has developed the understanding of the effectiveness and experiences of PSE for adults with CMP and provided fruitful research avenues to further this understanding.

Copyright and Disclaimer

Acknowledgements

Reflecting on the support I have had from family, friends, colleagues and mentors throughout my Ph.D. I'm struck with an overwhelming sense of gratitude and I'm not sure how I can fully reflect this in words. Here goes…

When I first commenced my Ph.D., a colleague remarked that I have the 'Dream Team' for a supervisory team. The past 7 years have proven this colleague absolutely right! Prof. Cormac Ryan, Prof. Denis Martin and Prof. John Dixon, I am immensely grateful for your ongoing support, guidance, wisdom and humour throughout this process, you have helped shape me into a better thinker, and person. Thank you, John, for your regular support early on in my journey, and for continuing that support into your retirement! Thank you, Denis, for teaching me to think deeply about the words I use to accurately convey my findings, and their meaning. I hope to one day be able to pick out the key question / meaning as clearly and precisely as you. Thank you, Cormac, for always being available when I have needed you, for providing feedback on my work with a super human turnaround time without sacrificing on quality. I've come across few people in life as warm, kind and eternally positive as you. I hope to continue our work together for years to come!

To my best friends Dom and Rob, and partner Steph thank you for your friendship and the great memories we have shared over the years, you've helped recharge my batteries to allow me to keep driving my Ph.D. forward. Thank you for talking through my various Ph.D. ideas and problems and thank you for encouraging me to prioritise getting me Ph.D. done!

Thank you to Teesside University and all my collaborators who have given their time and expertise. In particular Prof Greg Atkinson for your statistical expertise!

Thank you to my participants who gave their time and shared their stories, and those who facilitated recruitment, without you this work would not have been possible.

Finally, thank you to all my family for their constant support providing me with stable, secure, deeply grounded roots that have enabled me to develop broad wings. Sharon, thank you for your ongoing support. Dad, I'm in awe of how hard you work. Thank you for teaching me hard work creates opportunities and for your weekly guidance and wisdom. Mum, thank you for guiding me to find my values and passions, and for modelling how to live with integrity. Dave, thank you for your support and guidance, and for your eye for detail.

Abbreviations

BPS	British Pain Society
CI	Confidence interval
CLBP	Chronic lower back pain
CMP	Chronic musculoskeletal pain
FAM	Fear Avoidance Model
HCP	Health care professional
JBI	Joanna Briggs Institute
MCID	Minimal clinically important difference
MOM	Mature Organism Model
NICE	National Institute for Health and Care Excellence
NHS	National Health Service
OMERACT	Outcome Measures in Rheumatology
PI	Prediction interval
PMP	Pain management programme
PSE	Pain science education
RCT	Randomised controlled trial
SD	Standard deviation
SDir	Standard deviation for individual response
SIGN	Scottish Intercollegiate Guidelines Network

Outputs from this thesis

Publications

Watson, J.A., Ryan, C.G., Cooper, L., Ellington, D., Whittle, R., Lavender, M., Dixon, J., Atkinson, G., Cooper, K. and Martin, D.J., 2019. Pain neuroscience education for adults with chronic musculoskeletal pain: a mixed-methods systematic review and meta-analysis. *The Journal of Pain*, 20(10), pp.1140-e1. Cited 197 times as of 21/11/2022.

Watson, J.A., Ryan, C.G., Atkinson, G., Williamson, P., Ellington, D., Whittle, R., Dixon, J. and Martin, D.J., 2021. Inter-individual differences in the responses to pain neuroscience education in adults with chronic musculoskeletal pain: A systematic review and meta-analysis of randomized controlled trials. *The Journal of Pain*, 22(1), pp.9-20. Cited 14 times as of 21/11/2022.

Conference Presentations

November 2020: Oral presentation. Title: How should we deliver pain neuroscience education? Physiotherapy UK Conference 2020, Focused Symposium Speaker.

Blogs

January 2020. Title: Translating Research for Practice: PNE and Chronic Musculoskeletal Pain. Available at: https://ppa.csp.org.uk/content/translating-research-practice-pne-chronic-musculoskeletal-pain

Contribution to other work

King, R., Robinson, V., Elliott-Button, H.L., **Watson, J.A.,** Ryan, C.G. and Martin, D.J., 2018. Pain Reconceptualisation after Pain Neurophysiology Education in Adults with Chronic Low Back Pain: A Qualitative Study. *Pain Research and Management*. Cited 44 times as of 21/11/2022.

@

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction

1.1 Introduction

Chronic musculoskeletal pain (CMP) affects 27.5% of adults worldwide (Zimmer *et al.*, 2021) and is considered "*an urgent global public health concern"* (Hartvigsen *et al.*, 2018). In addition to the negative impact on the individual's quality-of-life (Breivik *et al.*, 2006; Tüzün, 2007a) there is a large societal financial burden associated with CMP. Annual healthcare costs for patients with chronic low back pain (CLBP) are double those of matched controls (Hong, *et al.*, 2013). In the United Kingdom, indirect costs for osteoarthritis and rheumatoid arthritis are estimated to be £14.8 billion (Oxford Economics, 2010). The total cost of CMP is likely to be much higher.

Interventions which encourage and empower patients to self-manage are recommended for individuals with CMP (Gifford, 1998; Frost *et al.*, 2004; NICE, 2020a; NICE, 2020b; NICE, 2021). Education is a key component of this approach with the premise that the better an individual understands their condition, the more empowered they will feel and the better they will be able to manage it (Gifford, 1998; Robinson *et al.*, 2016). There has been some disagreement within the literature regarding the use of education for the treatment of CMP (Ainpradub *et al.*, 2016; Hurley *et al.*, 2016). Ainpradub *et al.*, (2016) in a meta-analysis concluded that education should not be recommended for the treatment of non-specific low back and neck pain. However, the majority of the studies included in this meta-analysis used biomedical education which focus on *protecting* a *damaged* back. Several studies have suggested that biomedical education has limited efficacy and may, inadvertently, have a negative effect (Maier-Riehle and Härter, 2001; Moseley, 2004; Moseley, Nicholas and Hodges, 2004).

Hurley *et al.*, (2016) argue it is the *type* of education that is important. Since the conception of the biopsychosocial approach to healthcare there has been a growth in the use of biopsychosocial education. One branch of biopsychosocial education which has become increasingly popular amongst researchers and clinicians is pain science education (PSE) – an educational approach which "*aims to change someone's understanding of what pain actually is, what function it serves, and what biological processes are thought to underpin it"* (Moseley, and Butler, 2015, p.808). The core objective is to reconceptualise an individuals' understanding of pain from "*pain is a marker of tissue damage or disease* to *pain is a perceived need to protect body tissue"* (Moseley and Butler, 2015, p.808). This new conception is thought

to be less threatening and thus facilitates the participation in other biopsychosocial based interventions (Moseley and Butler, 2015). PSE has been shown to be statistically significantly ($P < 0.05$) superior to biomedical education for improving self-reported disability, pain attitudes, pain catastrophising and physical performance tests in individuals with CMP (Moseley, Nicholas and Hodges, 2004). Thus, it appears that the *type* of education may be important when considering whether education is effective or not.

Just as Hurley *et al.*, (2016) argue that it is the type of education that is important, Stofflett and Stoddart, (1994) stress the importance of *how* that education is delivered (the pedagogical approach). They demonstrate greater conceptual understanding following a conceptual change pedagogy compared to a traditional didactic approach. Conceptual change pedagogy focuses on existing knowledge and knowledge structures, rather than just learning new information (Vosniadou, 2008). This seems particularly relevant within the field of pain management where individuals bring with them existing knowledge about pain to their clinical interactions. Where needed PSE aims to shift pain conception from pain is "a marker of tissue damage or disease" to pain is a "perceived need to protect body tissue" (Moseley and Butler 2015 p.807). Posner *et al.*, (1982) outlined four conditions for conceptual change; 1) dissatisfaction with the existing conception 2) Intelligibility of the new concept i.e., it must be understandable 3) Plausibility of the new concept i.e. it must appear likely, and 4) Fruitfulness i.e. the practical usefulness of the new concept. The employment of these four conditions may be useful when designing PSE interventions to optimise their ability to facilitate pain reconceptualisation. However, prior to designing PSE interventions informed by these conditions there is a need to explore the role, if any, they have in the process of pain reconceptualisation. To date there is no published literature that has explored the role of the conditions for conceptual change in the process of pain reconceptualisation.

Conceptual change theory refers to learning that challenges and shapes existing knowledge and knowledge structures, rather than just learning new information (Vosniadou, 2008). Given that the core objective of PSE is to shift pain conception from pain is "a marker of tissue damage or disease" to pain is a "perceived need to protect body tissue" (Moseley and Butler 2015 p.807) the use of conceptual change theory would seem appropriate to inform the optimisation of PSE delivery. Conceptual change theory has previously been utilised to inform the development of science education (Stofflett and Stoddart, 1994) which has clear overlap with trying to deliver PSE.

PSE was first introduced by Louis Gifford (Gifford, 1998) in his seminal paper *Pain, the Tissues and the Nervous System: A conceptual model* where he outlined his Mature Organism Model.

Moseley, (2002) applied these principles within a study which combined PSE with physiotherapy to treat patients with CLBP. The educational approach was then integrated into a manual, Explain Pain (Butler and Moseley, 2003; Butler and Moseley, 2013) and has taken many formats including one-on-one intensive sessions (Moseley, 2002; Moseley, 2004; Moseley, Nicholas and Hodges, 2004), small group tutorial-type sessions (Moseley, 2003) large group seminars lasting up to three hours (Pires, Cruz and Caeiro, 2015), booklets (Louw *et al.*, 2014), story books (Gallagher, McAuley and Moseley, 2013) and via email (Louw, 2014a).

PSE has often been investigated as a stand-alone intervention instead of within a multimodal approach for which it was intended (Moseley and Butler, 2015). Several studies have gone part of the way to integrating PSE into a multimodal approach by combining it with physiotherapy (Moseley, 2002), motor control training (Moseley, 2003) and aquatic exercise (Pires, Cruz and Caeiro, 2015) all with promising results. Ryan *et al.*, (2010) somewhat counterintuitively found that PSE alone was associated with better outcomes than the combination of PSE and exercise classes. They were delivered as separate interventions. During the exercise class participants could have been exposed to patients and/or therapists with a 'biomedical' view of pain. Subsequently, the information learned from PSE may have been diluted by attending the exercise class. These studies highlight the additive effect of combining PSE with another intervention but also emphasise the importance of carefully integrating PSE into the intervention it is combined with in order not to inadvertently dilute the effect. Two reviews have emphasised the importance of combining PSE with other biopsychosocial interventions (Yun, 2017; Wood and Hendrick, 2019) finding larger effects in studies where this was conducted. Despite most studies investigating PSE alone, several systematic reviews have shown promising results for the use of PSE when treating CMP, however these reviews all have significant limitations which will be discussed in the literature review of this thesis (See Chapter 3) (Louw *et al.*, 2011; Clarke, Ryan and Martin, 2011; Louw *et al.*, 2016; Cuenda-Gago and Espejo-Antunez, 2017; Tegner *et al.*, 2018; Wood and Hendrick, 2019).

Building on a growing quantitative evidence base that began more than 20 years ago, more recently there has been an increase in the number of qualitative studies exploring PSE. This literature has sought to explore patients' experiences of PSE and how it has influenced their understanding of pain and management of their condition. However, the qualitative literature on PSE can also be criticised for the focus on PSE as a sole intervention. Three of the four qualitative studies (all undertaken by the Research group at Teesside University) have been a 2-hour PSE session (King, *et al.*, 2016; Robinson *et al.*, 2016; King, *et al.*, 2018). These

qualitative studies have shown promising results for PSE where they found 'partial and patchy' levels of reconceptualisation. Considering the relatively short length of the intervention and the didactic lecture style delivery these studies demonstrate the potential of PSE to facilitate reconceptualisation. Wijma *et al.*, (2018) was the first qualitative study to explore PSE in combination with other biopsychosocial interventions. Patients were offered PSE over multiple sessions +/- physiotherapy +/- psychology +/- medication. Despite the increase in qualitative research within the field of PSE to date there has been no qualitative synthesis of these studies. A synthesis of qualitative data can be used to provide further depth to the analysis of quantitative data (Sandelowski, Docherty and Emden, 1997).

A pain management programme (PMP) is the recommended treatment for CMP where there is a significant impact on quality-of-life, physical, psychological, and social function (The British Pain Society, 2013). A PMP is implemented by an interdisciplinary team according to broadly cognitive behavioural principles with the aim of improving the physical, emotional and social components of health and function. A variety of methods are used in PMP for directly and indirectly producing behaviour change with education having a central role (The British Pain Society, 2013). Given that PSE was developed with the intent to be delivered in combination with other biopsychosocial based interventions, integrating PSE with a PMP would seem logical and appropriate. However, only one conference abstract (Von Bertouch, McAuley and Moseley, 2011) has explicitly combined PSE with a PMP. The PSE group showed superior outcomes over education based on the Back Book (Roland *et al.*, 2002) for pain, function, pain knowledge, and work status. However, there are several methodological limitations in this study that are discussed in the literature review of this thesis (See Chapter 3).

The primary aim of this thesis was to investigate the effectiveness and experiences of PSE for adults with CMP.

1.2 Outline of chapters

This thesis consists of eight interlinked chapters outlined below:

Chapter 2: Background

This chapter defines CMP, provides a brief overview of its aetiology, provides an overview of its prevalence and socioeconomic impact, and introduces PSE, its origins and underlying theoretical approach.

Chapter 3: Literature review

This chapter critically reviews the evidence for PSE as an intervention for adults with CMP and highlights the gaps that exist within the current literature.

Chapter 4: Theoretical Perspective

This chapter outlines pragmatism, the theoretical perspective used as the framework for this thesis and why it is appropriate for a mixed-methods approach.

Chapter 5: Pain science education a mixed-methods systematic review and meta-analysis

A mixed methods review comprised of a segregated synthesis of quantitative and qualitative literature to investigate the clinical effectiveness, and patients' experience of, PSE for people with CMP.

Review questions were: 1) How effective is PSE as an intervention for the management of adults with CMP? *2)* What are the perceptions of PSE in adults with CMP? Question 2 is delineated into the following three objectives: a) To explore patient experiences of participating in PSE. b) To explore their perceptions of its effectiveness. c) To explore how it influenced their understanding of pain. The Joanna Briggs Institute Reviewers Manual 2017 (Aromataris and Munn, 2017) was used to direct the methods of this mixed-methods systematic review and meta-analysis. A protocol for the review was registered on Prospero (CRD42017068436).

Chapter 6: Inter-individual differences in response to pain science education a systematic review and meta-analysis

A systematic review and meta-analysis was conducted applying a novel statistical method for the field of pain to calculate the true inter-individual variation in outcome in response to PSE for adults with CMP. A protocol for the review was registered on Prospero (CRD42017068436).

Chapter 7: Quasi mixed-methods feasibility study of a PSE informed PMP

A quasi mixed-methods QUALITATIVE + quantitative study was conducted on a National Health Service PSE informed PMP based in the North East of England. The study aimed to

explore the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology; to explore the role of the conditions for conceptual change in the process of pain reconceptualisation; to explore the relationship between the degree of pain reconceptualisation and changes in clinical outcomes; to undertake preliminary work to look at the metrics to inform a pilot RCT investigating the effectiveness of a PSE informed PMP. The final aim had three objectives; to investigate recruitment procedures and rates of recruitment; to investigate the appropriateness of outcome measures used within the trial; to investigate the appropriateness of the eligibility criteria. The trial was registered on ClinicalTrials.gov (NCT03152604).

Chapter 8: Discussion and conclusions

The aim of this chapter was to draw together the work of the previous chapters to demonstrate the novel contribution of this thesis and make recommendations for research, policy and practice.

Chapter 2: Background

2.1 Introduction

This chapter defines CMP, provides a brief overview of its prevalence, aetiology and consequences, introduces PSE, its origins and underlying theoretical approach.

2.2 Definition of terms

Pain is defined by the International Association for the Study of Pain as "*An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage"* (Raja *et al.*, 2020). Musculoskeletal pain is that which arises in muscle, bone, joints or tissue in the body (Booth *et al.*, 2017). Chronic pain, is defined as pain *which lasts beyond the time that tissue healing would normally be expected to have occurred, often taken as ≥3 months* (The British Pain Society, 2013). Thus, CMP is pain that arises in muscle, bone, joints or tissue in the body lasting beyond 3 months (The British Pain Society, 2013; Booth *et al.*, 2017).

2.3 Prevalence of CMP

In the United Kingdom (UK) approximately 5 million adults develop chronic pain each year with only two thirds resolving (Donaldson, 2008). Recently conducted systematic reviews have estimated the prevalence of CMP. A systematic review of UK prevalence, including 19 studies with a combined sample of 139,933 participants, estimated that between 33% and 50% of the UK population have CMP (Fayaz *et al.*, 2016). Elzahaf *et al.*, (2012) compared the prevalence of CMP in '*developing*' and '*developed*' countries as rated on the Human Development Index. Nineteen studies which encompassed 65 surveys were included with a sample of 182,019 participants. Due to insufficient reliable data the prevalence of CMP in developing countries was "*uncertain"*. Following sensitivity analysis that removed two large studies global prevalence was estimated as 28%, lower than the that estimated by Fayaz *et al.* (2016). The estimate of Elzahaf *et al* aligns with the work of Zimmer *et al.,* (2021) who estimated adult global prevalence as 27.5%. It is unclear why this discrepancy in prevalence estimates between the reviews occurred. One reason may be that Elzahaf *et al.* (2012) and Zimmer *et al.,* (2021) included studies from around the world with Fayaz *et al.* (2016) only including UK studies. It is possible that due to sociocultural differences the prevalence of CMP is higher

within the UK compared to other countries. Another explanation could be differences in the reliability of chronic pain coding between the UK and other countries, particularly those that are less developed. There were some similarities between the reviews reporting CMP to be more prevalent in women, and in older people (Fayaz *et al.* 2016; Elzahaf *et al.* 2012; Zimmer *et al.*, 2021).

2.4 Impact on the individual

Findings from the Global Burden of Disease Study 2017 showed that musculoskeletal disorders such as low back pain, neck pain and other musculoskeletal disorders all feature in the top 11 causes of years lived with disability (James *et al.*, 2018). Musculoskeletal disorders were the leading cause of years lived with disability in the United Kingdom, representing 30.5% of the total (Murray *et al.*, 2013). Thus, individuals with CMP spend more time disabled by their disease relative to other conditions. CMP negatively impacts individuals in several ways, including, but not limited to reduced physical activity, sleep disturbance, falls, fatigue, anxiety, depression, fear of movement and loss of friends. These can all result in reduced quality of life (Harris, Morley and Barton, 2003; Tüzün, 2007b; Molton and Terrill, 2014). Chronic pain can lead to loss of role in both professional and personal life. In a study looking at adjustment to chronic pain, participants reported a mean loss of 3.38 roles (Harris, Morley and Barton, 2003). In a survey on the impact of chronic pain in Europe, 19% of participants had lost their job and 13% had changed jobs due to their pain (Breivik *et al.*, 2006). This loss or change in professional role can impact on how the individual views themselves, having a negative perception of self, feeling ashamed and experiencing a loss of masculinity in the case of men (Bailly *et al.*, 2015). Results from a systematic review of studies (n=54) exploring self and identity in chronic pain found an association with negative evaluations of self and poorer psychological status. It is important to highlight that most of the studies were rated as "*weak quality"* (n=25) with the majority of the studies cross-sectional in design. Thus, the strength of the findings are limited. In summary, chronic pain negatively impacts individuals across several domains ultimately reducing their quality of life.

2.5 Socioeconomic impact of CMP

There is a large financial burden placed on society due to CMP. Some costs are incurred directly by the health care system. Musculoskeletal conditions cost NHS England £5 billion a year (Department of Health and Social Care, 2012). In the UK chronic pain accounts for 4.6 million GP appointments each year (Belsey, 2002) with £584 million spent on prescriptions for pain (Donaldson, 2008). Annual healthcare costs for patients with chronic low back pain are

double those of matched controls (£1,074 vs £516) (Hong *et al*., 2013). Maniadakis and Gray, (2000) estimated direct health care costs to the UK due to low back pain were £500 million. Looking beyond the direct costs, there are also indirect costs to the economy due to CMP. In the UK in 2021 over 23 million days a year were lost at work due to musculoskeletal conditions (Office for National Statistics, 2022). Twenty years ago, Maniadakis and Gray, (2000) estimated indirect costs due to LBP as between £6.6 billion and £12.3 billion. More recent evidence estimate the indirect cost for osteoarthritis and rheumatoid arthritis as £14.8 billion (Oxford Economics, 2010). Given the huge financial burden of CMP to society it is important that interventions used in the management of patients with CMP are evidenced based and cost-effective.

2.6 Aetiology of CMP

2.6.1 Introduction

The French philosopher Rennes Descartes believed that pain was representational in that its intensity was directly proportional to the level of tissue damage. He proposed that when sufficiently stimulated, physical tubes spanning from bodily tissues to the brain were tugged, releasing animal spirits causing pain and a motor withdrawal response (Descartes, 1972). Three and a half centuries later, (Wall, 1979b) refuted the theory that pain's role was to signal damage, highlighting that the presence and intensity of pain was too poorly related to the level of damage for this to be true. Rather he proposed that pain indicated a bodily state where recuperation and recovery should be commenced to keep the individual from aggravating existing injuries. Without pain to motivate recuperation Wall proposed that individuals would seek to gratify their other needs over healing (Wall, 1979b; Wall, 2000). This, Wall proposed, explained painless injury. In life-threatening situations, limiting movement can be detrimental to the survival of the individual and thus safety is prioritised over healing.

Building on the work of Wall, Klein, (2015) proposed that pain is a homeostatic sensation motivating individuals to protect their body (Klein, 2015). Pains of potential damage motivate individuals to act in such a way that avoids damage, thus protecting the body. Pains of actual damage motivate individuals to protect an injury to aid healing. Pain can thus be viewed as an adaptive experience associated with the perception of actual or potential damage to the self, which promotes the survival of the organism (Raja et al. 2020; Klein, 2015; Wall, 1979a). Experimental evidence provides some support to these proposals where credible indications of safety to body tissue can decrease pain and credible indications of threat to body tissue can increase pain (Moseley and Arntz, 2007; Büchel *et al.*, 2014; Anchisi and Zanon, 2015;

Moseley and Butler, 2015). Tabor *et al.,* (2017, p.3) propose this "*clearly points to the notion that pain results when the immediate objective of the organism is bodily protection….. the experience of pain can be modelled as a perceptual experience reflecting unconscious optimal estimates about the state of the world, which includes the body, and our best course of action within it."*

The aetiology of CMP can be viewed from an *enactive* approach. Here pain is viewed as "*a relational and emergent process of sense-making through a lived body that is inseparable from the world that we shape and that shapes us"* (Stilwell and Harman, 2019, p. 1). Enactivism stemmed from the fusion of embodied cognition and phenomenology. *"Embodied Cognition holds that an agent's (person's) cognition (incorporating thoughts and feelings) is deeply dependent upon features of their physical body; that is, when aspects of the agent's body beyond the brain play a significant causal or physically constitutive role in cognitive processing*" (Thacker, 2015 p. 6). Whilst *"Phenomenology is the study of structures of consciousness as experienced from the first-person point of view* (Smith, 2018).

The Mature Organism Model (MOM) (Gifford, 1998), Thacker, (2015) argues, is a model of pain grounded within enactivism. The MOM states the organism's central nervous system continuously 'samples ⇒ scrutinises ⇒ responds ⇒ resamples' information internally and externally (Figure 2.1). Internal sampling includes information coming from the body and also information stored within the central nervous system. External sampling includes information from the environment perceived via the senses. Responses (outputs) can be changes in physiology and behaviour, involving activity within the organism's systems e.g., motor, sympathetic, immune and endocrine. The MOM clearly incorporates the '5E' enactive approach to pain outlined by Stilwell and Harman (2019) who built upon Gallagher's '4E' approach for thinking about the mind through the addition of 'emotive' (Rowlands, 2010). The 5E's are (1) embodied, (2) embedded, (3) enacted, (4) emotive and (5) extended. They are outlined here; Embodied (defined above), embedded (perception is based upon our background and current context), enacted (perception is not simply a representation of the world, rather an active, embodied process of sense making), emotive (the cognitive, bodily and environmental elements of emotion are fused in an embodied form of sense making) and extended (objects, institutions, society and culture are an additional part of cognition influencing perception) (Thacker, 2015; Stilwell and Harman, 2019). Thacker, (2015 p.7) also states that with a small conceptual shift the MOM can also align with arguably the "*hottest*" topic in the neurosciences, predictive coding (here termed predictive processing) (Clark, 2015) (Figure 2.2).

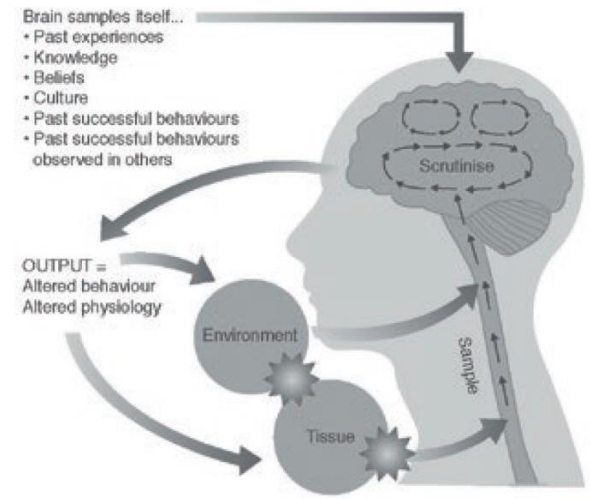


Figure 2.1 The mature organism model

Legend: *This figure shows the mature organism model by Gifford, (1998). Reproduced with permission, see Appendix 24.*

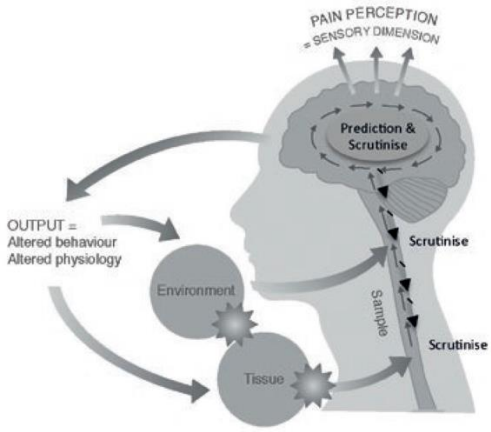


Figure 2.2 The mature organism model explained with predictive coding

Legend: *"A small conceptual shift easily aligns the MOM with the concept of predictive coding. Here, higher levels of the nervous system continuously "output" predictions (solid downward arrows) of the activity of lower levels of the nervous system. Scrutinising the differences between inputs and predictions occurs at all levels of the nervous system and results in the upward flow of error signals (ascending arrows). These error signals update the prediction until there are no more errors – resulting in the perception of pain. (Thacker, 2015 p.8). Reproduced with permission see Appendix 24.*

Gifford (1998) purported the view that somatosensory processing begins with an input that is scrutinised and produces an output e.g. pain perception. In contrast, predictive processing views somatosensory processing, and perception in general, as beginning with a prediction of the afferent sensory data based upon what the nervous system expects to receive given what

it has learned about the world and the current context (termed priors). In MOM terminology the nervous system 'scrutinises ⇒ responds ⇒ samples ⇒ re-scrutinises'. In essence, predictive processing views (pain) perception as an inference. The concept of perception as an inference is not new dating back to the 19th century philosopher Helmholtz (Von Helmholtz, 1867). With the emergence of Bayesian inferences, *perception as an inference* has been provided a computational basis (Yuille and Kersten, 2006). In the context of perception, bayesian inference is a form of probabilistic reasoning that accounts for both prior knowledge and current sensory data. Both are weighted using their precision (inverse-variance). Precision can also be described as the level of uncertainty. Less precision = more uncertainty = lower weight allocated. Greater precision = less uncertainty = greater weight allocated. For example, where there is low precision in current sensory data, this sensory data will be weighted low, with a greater relative weight assigned to prior knowledge to inform perception (Knill and Pouget, 2004; Kersten, Mamassian and Yuille, 2004; Franklin and Wolpert, 2011; Nour and Nour, 2015; Clark, 2015). *"Bayesian perceptual inference thus uses prior expectations to constrain the interpretation of incoming sensory data." (*Nour and Nour, 2015 p. 5). With this model of perception, it becomes understandable how *"…an abnormality in perception may arise from an abnormality in one's beliefs about the world, and vice versa"* (Fletcher and Frith, 2009 p.6).

If predictive processing is correct, the nervous system is hierarchically organised and generative whereby higher levels "output" prediction (or model) activity of lower levels. Continuously and concurrently the prediction is compared (scrutinised) across multiple levels of the nervous system against the actual afferent sensory data. At each level of the nervous system, higher levels "output" predictions to lower levels whilst lower levels "input" *prediction error* to higher levels. Prediction error is the difference between what the higher level of the nervous system expects to receive (the prediction) and what it actually receives (afferent sensory data). Only the prediction error ascends the levels of the nervous system (Clark, 2015; Lupyan and Clark, 2015; Tabor *et al.*, 2017). There is an attempt at every level of the nervous system to address the discrepancies between predictions and afferent sensory data through prediction error minimisation. This can be brought about by changing the input or changing the output. Prediction error can be minimised by keeping the predictions from higher levels constant and changing the afferent sensory data to match the prediction (changing the input). Thus, predicting these non-actual sensory states can be seen as self-fulfilling prophecies that are brought about through the *action* one takes to engage the world. Some prediction error cannot be resolved by action. It must be minimised by higher levels of the nervous system updating their prediction (changing the output) so that they better reflect the afferent sensory data. It is worth highlighting that the point of updating the predictive model (i.e., learning) is to

connect one with the world in such a way that enables one to select better actions. Perception is thus deeply *action oriented* (Clark, 2015). This is illustrated by this quote from Clark (2015, p.138):

"…actions flow from percepts that predict sensory signals some of which entrain actions that recruit new percepts. As we engage the world with our senses, percepts and action recipes now co-emerge, combining motor prescriptions with rolling efforts at knowing and understanding. Action, cognition, and perception are thus continuously co-constructed, simultaneously rooted in the cascading predictions that constitute, test, and maintain our grip upon the world."

Prediction error shapes our model of the world, in the short term (inferences) and long term (learning). Therefore, it is important to know the reliability of these error signals. For example, does the afferent sensory data not match the prediction made because it contains information that disproves our hypothesis (for example, we hear a lion but see a mouse), or because the sensory data is too noisy (we hear a lion but only see a cloud of dust). The former should cause us to update our beliefs (a roaring mouse!), the latter should not (Den Ouden, Kok and De Lange, 2012). Prediction errors are purported to be weighted by their reliability (termed precision) with less weight put on less reliable sensory data and more weight put on more reliable sensory data (Feldman and Friston, 2010; Hohwy, 2012). Attention is the dimension of the generative model that weights the prediction error. When attending towards something, the deviation from the prediction (prediction error) is weighted greater than when not attending (Den Ouden, Kok and De Lange, 2012; Feldman and Friston, 2010). fMRI studies investigating visual attending have shown that attending towards a category expands cerebral representations of that category, and of semantically-related but unattended categories, and reduces representations of semantically-dissimilar categories (Çukur *et al.*, 2013). Attending allows our system to bias selected sensory channels during multimodal processing and alter the balance between higher level predictions and lower level afferent sensory data. Under the right circumstances, higher level predictions are capable of influencing lower levels in ways that can significantly alter (modulate) the ascending sensory data (Clark, 2015; Den Ouden, Kok and De Lange, 2012). *"Attention, action, and perception are now joined in mutually supportive, self-fueling loops."* (Clark, 2015 p.83).

2.6.2 Acute pain described using the MOM encompassing predictive processing

Acute pain will be briefly outlined using the MOM encompassing predictive processing with the example of a small lumbar erector muscle tear whilst picking a box up off the floor. Acute pain is usually associated with tissue damage (or potential damage) resulting from injury, illness, surgery or acute inflammation (International Association for the Study of Pain, 2010). The organism *scrutinises* itself and what it has learned about the current context (it's priors) and *responds* by outputting a prediction of the afferent sensory data it expects to receive. In this case, in the moments before sustaining a lumbar erector tear where the organism's sensory channels have not registered damage (or potential damage), higher levels of the nervous system will *respond* by outputting a prediction of a healthy body under little risk of damage. The organism then *samples* itself and the environment to access the accuracy of its prediction. This occurs across multiple levels of the nervous system continuously and concurrently. The organism will use the full array of its sensory repertoire to sample if any damage has occurred (or potentially may occur). The focus here will be on sampling from nociceptors with an awareness that there will be concurrent sampling from a range of sensory channels e.g., visual, auditory, proprioceptive, smell etc. The information from these other sensory channels will be used by the organism to contextualise the meaning of the nociception. Nociceptors are free nerve endings in peripheral tissues and include fast conducting myelinated A∂ fibres that are activated by mechanical and thermal stimuli, and slow conducting non-myelinated C-fibres that are activated by high threshold mechanoreceptors. In the presence of inflammation C-fibres respond to mechanical, thermal and chemical stimuli (Moseley and Butler, 2017). Upon damage to the lumbar erector muscle, tissues and immune cells release a variety of pro-inflammatory chemicals sometimes collectively known as the 'inflammatory soup'. This includes (but is not limited to) bradykinin, prostaglandin, serotonin, nerve growth factor and tumour necrosis factor (Gifford, 2014; Moseley, and Butler, 2017; Chapman and Vierck, 2017). The combination of damage and inflammation will stimulate the mechanical and chemical receptors respectively on the nociceptors causing them to depolarize sending an action potential up their axon. Activation of nociceptors further increases inflammation through the release of substance P that activates mast cells resulting in vasodilation. This facilitates migration of more immune cells into the area such as macrophages and neutrophils which further secrete pro-inflammatory chemicals adding to the 'inflammatory soup'. The presence of inflammatory soup lowers the threshold for firing of nociceptors resulting in an increase in peripheral input to the central nervous system (Gifford, 2014; Moseley and Butler, 2017; Chapman and Vierck, 2017).

A∂ and C-fibers terminate at laminae I-II of the dorsal horn of the spinal cord and thus will ascend the afferent sensory data to here (Gifford, 2014; Porth, 2015). The nociceptors release neurotransmitters such as glutamate and other amino acids to transmit the afferent sensory

data to the second order neuron (or second sampler). The second order neuron can be nociceptor specific or a wide dynamic range fiber that is able to receive input from a variety of inputs including non-nociceptive data. The second order neurons will *sample* the incoming afferent sensory data and *scrutinize* this against the prediction from higher levels of the nervous system. The increased afferent sensory barrage from nociceptors in the lumbar erectors will register as a prediction error (the prediction was a healthy back) and will therefore be passed up to higher levels of the nervous system. The second order neurons transmit to the thalamus, periaqueductal grey and parabrachial areas which are involved in inhibitory or faciliatory pathways (Fornasari, 2012; Gifford, 2014). Higher levels of the nervous system are able to influence lower levels in a way that can alter (modulate) the ascending sensory data (Clark, 2015; Den Ouden, Kok and De Lange, 2012). Depending on the context, this modulation may result in facilitation or inhibition of nociception by the thalamus, periaqueductal grey and parabrachial areas which are themselves influenced by higher (and lateral) levels of the nervous system. The exact areas of the nervous system that are 'higher' (and lateral) are not fully understood and is beyond the scope of this thesis to discuss. They are however likely to be widely distributed across the brain and vary between individuals (Clark, 2015; Moseley and Butler, 2017).

Upon receiving the nociceptive prediction error from lower levels of the nervous system, higher levels of the nervous system will scrutinise the nociceptive information in addition to its other priors (including prediction error from other sensory channels, the predictions from higher (and lateral) levels based upon past experiences, knowledge, beliefs, culture, past successful behaviours, past successful behaviours observed in others and more) responding by generating a predictive model in an enacted process of sense making. This model represents, based upon all the information (embodied, embedded, enacted, emotive and extended) a model which entrains actions and perceptions that are mostly likely (as predicted by the organism) to result in the most advantageous ways to engage the world in the current context (Tabor *et al.,* 2017; Clark, 2015; Stilwell and Harman 2019). Having sustained a small tear to the lumbar erectors the predictive model is likely to output a prediction of sensory signals, some of which entrain actions that coordinate the organism's body in such a way as to protect the organism i.e., pain perception, dropping the box and increase in trunk muscle activity for protective guarding (Klein, 2015; Tabor *et al.,* 2017; Clark, 2015). Concurrent responses may include communicative behaviours such as facial expressions conveying pain, screaming, crying and groaning, and/or safety behaviours avoiding moving their back, specifically lumbar flexion and supporting their back with their hands. These responses are likely to be useful in the initial days following the injury to facilitate healing and recruit social support to aid survival (Gifford, 2014).

If the context in which the injury occurred is changed such that it is not advantageous to the organism's survival to be in pain at that time (as predicted by the organism), this will likely change the response of the nervous system regarding pain perception and ensuing behaviours (Wall, 1979b; Wall 2000; Gifford, 2014; Klein, 2015; Tabor *et al.,* 2017; Stilwell and Harman 2019). In this second example, the individual sustains the same injury as in the previous example (small lumbar erector muscle tear) whilst picking a box up off the floor, but this time they're moving the box out the way of a door to escape from an approaching attacker. In the moments before lumbar erector injury where the organism's sensory channels have not registered damage from nociceptors in the back, higher levels of the nervous system will *respond* by outputting a prediction of a healthy body, however in contrast to the previous example, under huge risk of damage by the approaching attacker. Part of the response from the organism's nervous system is likely to bring about responses from the motor, sympathetic, endocrine and immune systems resulting in the 'flight or fight' response. This includes (but not limited to) an elevated heart rate and respiratory rate, increase in muscle tone and pupil dilation (Sapolsky, 2004). Another response will be to produce *actions* that will result in survival i.e., quickly moving the box out the way of the door at all costs. Whilst the organism perceives potential damage from the attacker, it is not advantageous to produce pain as this would almost certainly reduces chances of survival. The organism will *sample* itself and the environment to access the accuracy of its prediction. This occurs across multiple levels of the nervous system continuously and concurrently. The organism will use the full array of its sensory repertoire to sample if any damage (or potential damage) has occurred. Nociceptors will be activated by the lumbar erector muscle tear and amplified by the inflammatory soup. An important point to highlight is that the immune response here will likely be attenuated by greater sympathetic activity in the body preceding the injury, with the individual attempting to escape from the attacker (Sapolsky, 2004; Gifford, 2014). This will result in less inflammatory soup to sensitise the nociceptors ultimately resulting in less afferent sensory barrage ascending to the dorsal horn of the spinal cord compared to the previous example (with the exact same injury, without the attacker in pursuit). This is an example of embodied cognition at work. The nociceptors will ascend the (attenuated) nociception to laminae I-II of the dorsal horn of the spinal cord stimulating the release of excitatory neurotransmitters (Porth, 2015; Gifford, 2014). As in the previous example, the nociceptor specific second order neuron will sample and scrutinize this signal against the prediction from higher levels. The increased (but attenuated) afferent sensory barrage from nociceptors in the back will register as a prediction error (the prediction was a healthy back) and will therefore be passed up to higher levels of the nervous system including to the thalamus, periaqueductal grey and parabrachial areas, and then higher levels still (Fornasari, 2012; Gifford, 2014).

Upon receiving the nociceptive prediction error from lower levels of the nervous system, higher levels of the nervous system will scrutinise the nociceptive information in addition to its other priors and respond by generating a predictive model. This model represents, based upon all the information (embodied, embedded, enacted, emotive and extended) a model which entrains actions and perceptions that are mostly likely (as predicted by the organism) to result in the most advantageous ways to engage the world in the current context (Clark, 2015; Klein, 2015; Tabor et al. 2017; Stilwell and Harman 2019). With an attacker approaching, escaping them is likely to be prioritised over the threat of the lumbar erector muscle tear. If pain perception was a dimension of the model outputted by the organism, the organism's ability to escape the attacker would be greatly reduced, and with it the chance of survival. The model will therefore likely be comprised of outputs that do not attend to the nociceptive information coming from the back. This means the deviation from the prediction (increased nociceptive barrage from the back) will be weighted as low (Den Ouden, Kok and De Lange, 2012; Feldman and Friston, 2010). Furthermore, by not attending, the balance between higher level predictions and lower level sensory data is likely to be weighted in favour of higher level predictions (a healthy body, for now, escape from that attacker!). Thus, the organism may respond by outputting a model which leads the thalamus, periaqueductal grey and parabrachial areas to respond by releasing inhibitory neurotransmitters at the dorsal horn where the primary nociceptors terminate (Clark, 2015; Den Ouden, Kok and De Lange, 2012; Gifford, 2014). This will decrease the nociceptive afferent barrage ascending from the second order neuron, to higher levels, bringing the afferent sensory data more in line with the higher level prediction (changing the input). This may allow high levels of the nervous system to allocate more resources to other responses which may be more relevant to the organism's survival e.g., running away and processing visual data regarding possible escape routes.

2.6.3 The transition from acute to chronic pain using the MOM, predictive processing and the fear avoidance model

The MOM encompassing predictive processing will now be used in addition to the fear avoidance model to describe the transition from acute to chronic pain.

This section will follow on from the first example given in section 2.6.2, where an individual sustained a small tear to their lumbar erector (*without* being chased by an attacker), which has resulted in pain perception and the adoption of safety and communicative behaviours. The damaged lumbar erector muscle will stimulate increased inflammation in the area increasing for between two to three days post injury and starting to reduce at approximately

two weeks. Over this time the sustained levels of inflammation bring about changes to local peripheral nerves such as C, A∂ and Aß fibers. The changes include decreased threshold potential of receptors and increased number of receptors on the membrane of peripheral nerves. This is termed peripheral sensitization and results in an increase in input to the central nervous system (Gifford, 2014; Moseley and Butler, 2017).

The increase in afferent barrage from the sensitized peripheral nerves (C, A∂ and Aß fibers) located around the damaged lumbar erector bombards the nociceptor specific and wide dynamic range second order neurons in the dorsal horn leading to an increase in excitatory neurotransmitters such as glutamate and asparate being released. The excitatory neuropeptide substance P is also released which leads to a cascade of chemical reactions inside the second order neurons ultimately inhibiting receptors for inhibitory neurotransmitters on the second order neuron, termed disinhibition. The cascade of chemical reactions from substance P also results in mg++ being ejected from NMDA receptors which activates inactive receptors on the second order neuron. Furthermore, the increase in activity activates previously dormant synapses that the nociceptor specific second order neurons have with sensory fibers such as Aß fibers which now can input into the nociceptor specific pathway. The second order neurons also release nitric oxide which diffuses back onto the pre-synaptic neuron stimulating it to release even more excitatory neurotransmitters. The second order neuron will also make more ion channels and receptors for the post synaptic membrane, upregulate the level of neurotransmitter production, and the number of synapses between the first and second order neuron increase. This all results in 'wind up' like phenomena. This excitability state can become so heightened that second order neurons can become spontaneously active, firing without any peripheral input (Gifford, 2014; Moseley and Butler, 2017).

Whilst these peripheral and peripheral-central changes are taking place, higher levels of the nervous system will be continuously scrutinising ⇒ responding ⇒ sampling ⇒ re-scrutinising. The increased prediction error from lower levels (increasing nociceptive barrage from the back) will be scrutinised along with other priors such as other sensory prediction error, past experiences, knowledge, beliefs, culture, past successful behaviours, past successful behaviours observed in others and more (Clark, 2015; Gifford 2014). Widespread erroneous beliefs around pain are likely to lead to a response from friends and family for the individual to '*be careful, that looks bad*' and may lead the individual to go and seek care from a healthcare professional (Buchbinder *et al.*, 2018). Many negative pain beliefs originate from meeting healthcare professionals (Darlow *et al.*, 2012; Bunzli *et al.*, 2015). In spite of MRI results correlating poorly with levels of pain and disability (Steffens *et al.*, 2014) and national

guidelines advising against routine imaging, rates are high (Buchbinder *et al.,* 2018). The results of these scans can be iatrogenic and may be made worse by the language healthcare professionals use (Webster *et al.*, 2013; Stewart and Loftus, 2018). In this example, after receiving their scan the individual was told '*their spine is like a digestive biscuit! They must be very careful not to damage it further*'. These messages serve as credible evidence of danger with the individuals' nervous system likely responding by outputting a model which attends to the nociceptive prediction error coming from the back. This may lead to the thalamus, periaqueductal grey and parabrachial areas to stop any inhibition and increase excitation at the dorsal horn of the spinal cord, further amplifying the nociceptive afferent barrage. This may contribute to the perception of back pain and the adoption of other protective behaviours (Tabor *et al.,* 2017; Fornasari, 2012; Gifford, 2015). By attending to the nociceptive afferent barrage over time, the previously dominant model of 'a healthy back with no pain' is likely to be updated to 'a damaged painful back' (Tabor *et al.,* 2017; Clark, 2015).

The fear avoidance model (FAM) is useful here when explaining how acute pain can develop into chronic pain. The FAM was first proposed by Letham et al. (1983) and has been updated several times (Lethem *et al.*, 1983; Vlaeyen *et al.*, 1995; Vlaeyen and Linton, 2000; Asmundson, Norton and Vlaeyen, 2004; Leeuw *et al.*, 2007; Vlaeyen, Crombez and Linton, 2016). The model explains how negative affect and threatening illness information can fuel catastrophising, leading to fear of pain, and ultimately disability. Asmundson et al. cited in Leeuw et al. (2007) modified the work of Vlaeyen and Linton, (2000) through the inclusion of anxiety, which is differentiated from fear (Figure 2.3). Fear motivates defensive and escape behaviour in the presence of a threat, in this case pain or harm. Anxiety is a more future orientated state creating hypervigilance that leads to avoidance of behaviour that is perceived as threatening i.e., that which may cause pain or harm (Leeuw et al. 2007). However, clinically the difference between fear and anxiety is less evident and more recently published models omit the separate pathway for anxiety (Vlaeyen, Crombez and Linton, 2016). The most contemporary FAM (Vlaeyen, Crombez and Linton, 2016) proposes that if the threat value of the pain is low, the individual will likely prioritise engagement in valued life goals, leading to approach and recovery. Where the threat value of pain is high, driven through a harm representation of pain (*your back is painful because it's crumbling like a digestive biscuit*), as is the case in the example given in the above paragraph, the individual will likely prioritise pain control and thus lead to a cycle of fear-avoidance-interference-negative affect-pain. This process will likely lead to disuse and deconditioning of the individual leading them to become more vulnerable, and thus more in need of greater activation of protective responses such as pain and avoidance (Gifford, 2014).

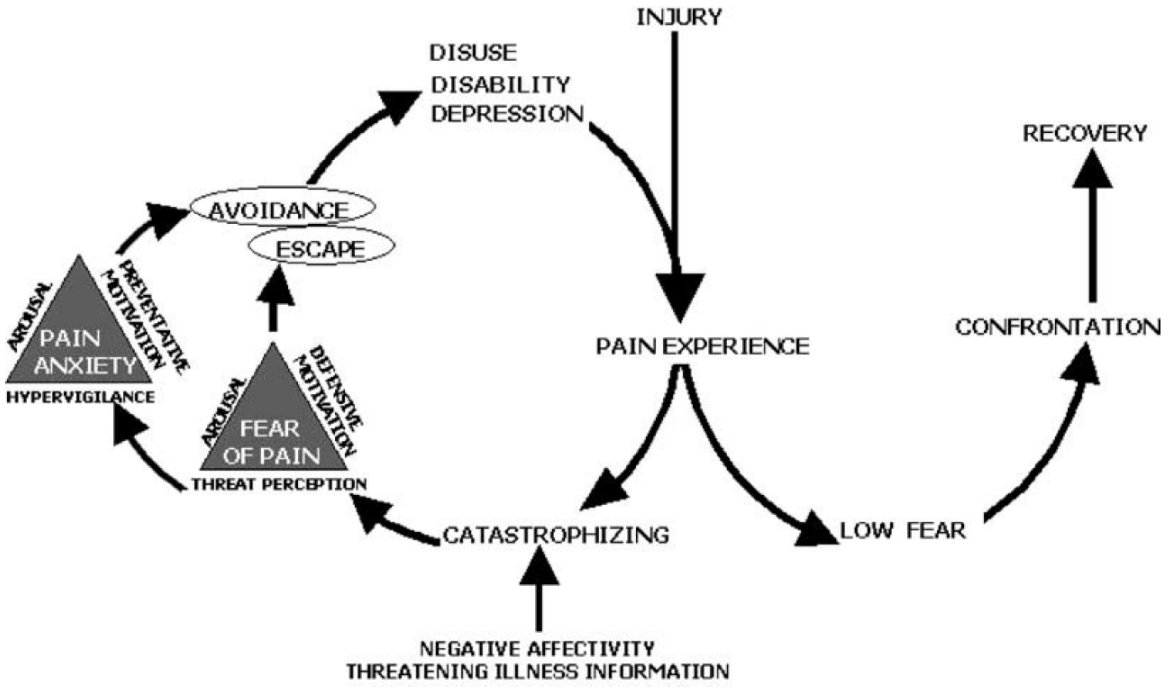


Figure 2.3 The fear-avoidance model of chronic pain

Legend: *This figure shows the fear-avoidance model of chronic pain based on the fear-avoidance model of Vlaeyen and Linton (2000) and the fear-anxiety-avoidance model of Asmundson et al. (2004) cited in Leeuw et al. (2007). Reproduced with permission see Appendix 25.*

2.7 Treatments for chronic musculoskeletal pain

2.7.1 Introduction

The Royal College of Anaesthetists produced Core Standards for Pain Management Services in the UK, advocating biopsychosocial management. These standards have been endorsed by the professional societies/associations of general practitioners, nurses, psychologists, pharmacists, physiotherapists and occupational therapists. The British Pain Society (BPS), Scottish Intercollegiate Guidelines Network (SIGN), and The National Institute for Health and Care Excellent (NICE) all advocate a biopsychosocial approach to the management of chronic pain within their clinical guidelines as detailed in Table 2.1.

Table 2.1 Overview of current guidelines for the management of chronic pain

Give recommendation for	**Guideline**
Education	SIGN, 2013; BPS, 2013; NICE, NG59; NICE, CG177; NICE, NG193
Physical therapies	SIGN, 2013; BPS, 2013; NICE, NG59; NICE, CG177; NICE, NG193
Pharmacological therapies	SIGN, 2013; NICE, NG59; NICE, CG177; NICE, NG193
Psychological therapies	SIGN, 2013; BPS, 2013; NICE, NG59; NICE, NG193
Complementary therapies	SIGN, 2013; NICE, NG193
Combined multi-disciplinary therapies	SIGN, 2013; BPS, 2013; NICE, NG59

Legend: *BPS, British Pain Society. NICE NG, National Institute for Clinical Excellence Guideline. NICE CG, National Institute for Clinical Excellence Clinical Guideline SIGN, Scottish Intercollegiate Guidelines Network. Clinical guideline references:*

- *SIGN, 2013* (Scottish Intercollegiate Guideline Network, 2013)
- *BPS, 2013* (The British Pain Society, 2013)
- *NICE, NG59* (NICE, 2020)
- *NICE, CG177* (NICE, 2020)
- *NICE, NG193* (NICE, 2021)

Education is included in recommendations from SIGN, NICE and BPS perhaps unsurprisingly as it plays an important part of the management of most long-term conditions. The better an individual understands their condition, the more empowered they will feel and the better they will be able to self-manage (Gifford, 1998; Robinson et al., 2016; (Morgan, *et al.*, 2017).

Disagreement in the literature exists regarding the use of education for the treatment of CMP (Ainpradub et al., 2016; Hurley et al., 2016). In the conclusions of their meta-analysis Ainpradub et al., (2016) state that education should not be recommended for the treatment of non-specific low back and neck pain. However, Hurley et al., (2016) highlight that the majority of the studies included in this meta-analysis used biomedical education that focused on *protecting* a *damaged* back. Several studies have suggested that biomedical education has limited efficacy and may, inadvertently, have a negative affect (Maier-Riehle and Harter, 2001; Moseley, 2004; Moseley et al., 2004).

Hurley et al., (2016) advocate that it is the type of education that is important. Since the conception of the biopsychosocial approach to healthcare there has been a growth in the use of biopsychosocial education. One branch of biopsychosocial education which has become increasingly popular amongst researchers and clinicians is pain science education (PSE) (Moseley and Butler, 2015)

2.7.2 What is pain science education?

Pain science education (PSE) is an educational approach grounded in the biopsychosocial model with the core objective to reconceptualise pain perception from pain is *"a marker of tissue damage or disease"* to pain is *a "perceived need to protect body tissue"* (Moseley and Butler 2015 p.807). Alternative names for PSE used within the literature include; explain pain (Butler and Moseley, 2003; Moseley and Butler 2015; Moseley and Butler 2017); therapeutic neuroscience education (Zimney, Louw and Puentedura, 2014); pain neurophysiology education (Moseley, Nicholas and Hodges, 2004); pain neuroscience education (Louw et al. 2016); and pain biology education (Ryan et al. 2010).

PSE was first introduced by Louis Gifford (Gifford, 1998) in his seminal paper *Pain, the Tissues and the Nervous System: A conceptual model* where he outlined his Mature Organism Model. Gifford, (1998, p33) states *"On-going pain states are best explained to patients in terms of an altered sensitivity state as a result of altered information processing throughout the system, and not solely a result of damaged and degenerating tissues. This helps patients accept the notion that hurt does not necessarily equate with harm - which leads on to the positive message that carefully graded increases in physical activity mean stronger and healthier tissues."* Moseley, (2002) applied these principles combining PSE with physiotherapy to treat patients with chronic low back pain. The approach was then integrated into a manual for patients and clinicians "*Explain Pain"* (Butler and Moseley, 2003) where Butler and Moseley explicitly ground the approach within conceptual change theory. Conceptual change learning is focused on challenging existing knowledge rather than solely learning new information (Sniadou, 2013). Those in pain are not a 'blank slate', bringing with them beliefs and knowledge about their pain, thus conceptual change learning would appear a logical approach in which to ground PSE. "Explain Pain" was updated a decade later (Butler and Moseley, 2013). In 2017 a clinician specific manual "Explain pain supercharged" was published to facilitate in-depth pain knowledge required to deliver PSE successfully (Butler and Moseley, 2017). Moseley and Butler, (2015 p.807) describe PSE as "*a range of educational interventions which aim to change someone's understanding of what pain actually is, what function it serves, and what biological processes are thought to underpin it"*. Moseley (2007

p.169) outlined four key concepts important for pain reconceptualisation "*(i) that pain does not provide a measure of the state of the tissues; (ii) that pain is modulated by many factors from across somatic, psychological and social domains; (iii) that the relationship between pain and the state of the tissues becomes less predictable as pain persists; and (iv) that pain can be conceptualised as a conscious correlate of the implicit perception that tissue is in danger."* (Moseley, 2007).

PSE has been delivered in several formats including one-on-one intensive sessions (Moseley, 2002; Moseley, 2003; Moseley, 2004, Moseley, Nicholas and Hodges, 2004), small group tutorial-type sessions (Moseley, 2003), large group seminars (Pires, Cruz and Caeiro, 2015), booklets (Louw et al., 2014), story books (Gallagher et al., 2013), via email (Louw, 2014b) and online courses (Retrain Pain Foundation, 2019). The duration of PSE varies from 0.5 hours (Louw et al. 2014) to 3 hours (Pires, Cruz and Caeiro, 2015), delivered over single (Louw et al. 2014) or multiple (Téllez-García *et al.*, 2015; Malfliet *et al.*, 2018) sessions. PSE has often been investigated alone, (Moseley, 2004; Meeus *et al.*, 2010; Van Oosterwijck *et al.*, 2013; van Ittersum *et al.*, 2014) however PSE was always intended to be part of a multimodal approach (Gifford, 1998; Moseley and Butler, 2015). Some studies have combined PSE with other interventions including physiotherapy (Moseley, 2002), motor control training (Moseley, 2003) and aquatic exercise (Pires, Cruz and Caeiro, 2015) with promising results.

There are methods within PSE that are used including, but not limited to, the use of metaphors (Butler and Moseley, 2003; Retrain Pain Foundation, 2019), the Protectometer (Moseley and Butler, 2015), and the twin peaks model (Butler and Moseley, 2003). Metaphors include comparing pain to a fire alarm, with chronic pain becoming an overly sensitive fire alarm going off with just one lit candle (Retrain Pain Foundation, 2019). The Protectometer is a tool for patients to identify various things in their life that the brain may see as credible evidence of safety, termed SIMs (Safety in Me), or credible evidence of danger, termed DIMs (Danger in Me). The categories include things they feel, hear, smell, taste or touch, thoughts and beliefs, the people in their lives, the places they go, the things they say, and the things they think (Moseley and Butler, 2015). The twin peaks model is used to illustrate graded exposure where patients identify their 'basecamp' in their 'sore, but safe zone'. This approach is purported to establish more consistent levels of activity which can then be gradually increased over time, instead of avoiding activity due to fear of pain and or damage, or boom busting where high levels of activity and followed by very low levels of activity due to significant exacerbations of pain ultimately reducing physical conditioning levels and negatively impacting on mood (Butler and Moseley, 2003).

2.7.3 How pain science education might work

The purported mechanism of effect central to PSE is pain reconceptualisation, defined as *"the acquisition of a new, less threatening understanding about the nature of one's pain*" (King et al. 2016 p.1389). This understanding encompasses the four pillars outlined by (Moseley, 2007). This new conception is hypothesised to change the threat value associated with a range of sensory inputs shifting the prediction of the state of the world, and thus the most advantageous response, from that which results in pain, to that which does not (Moseley and Butler, 2015). This can be explained using the MOM encompassing predictive processing. If the individual with pain achieves pain reconceptualisation, this is the equivalent of changing the *priors* of knowledge and beliefs about pain. Thus, when the individual's nervous system scrutinises its priors (including but not limited to past experiences, knowledge, beliefs, culture, past successful behaviours, past successful behaviours observed in others) it is likely to respond differently.

By changing the knowledge and beliefs priors to align with the four pillars of reconceptualisation outlined by Moseley (2007) the response may be to output a model which predicts low levels of nociception coming from the back, and also assigns a low weight to any nociception coming from this area. Thus, by not attending to the nociception and predicting lower levels, responses at lower levels of the neuronal hierarchy may be to bring about these changes. The thalamus, periaqueductal grey and parabrachial areas may output predictions that bring about the release of inhibitory neurotransmitters at the dorsal horn of the spinal cord, and reducing any faciliatory neurotransmitters released. This will reduce the level of nociception ascending the nervous system. Furthermore, by reducing the firing rate of first and second order neurons, peripheral sensation may reduce and the *wind up* of the central nervous system ultimately reducing pain perception.

Through the lens of the FAM, by PSE reducing the threat value of pain the individual is more likely to prioritise engagement in valued life goals over pain control. This means they will approach painful and previously feared activities, leading to recovery (Vlaeyen, Crombez and Linton, 2016). Furthermore, the patient may be more open to active interventions such as exercise, where previously this would have been avoided due to fear of pain, thus promoting recovery.

PSE usually includes pacing and graded exposure, such as the twin peaks model in the Explain Pain manual (Butler and Moseley, 2003). Importantly, this goes some way in showing

the patient *how* to engage in their valued life goals/exercise whilst avoiding the Boom-Bust, and fear avoidance cycles. By enabling individuals to establish more consistent levels of activity and minimise flares of symptoms, this may promote recovery.

This subsection (2.7.3) has outlined some of the potential hypothesis as to how PSE might work through the lens of some of the eminent models within the pain sciences. A common theme throughout all these models is that PSE works by changing the meaning of the individuals pain. The change in meaning of the pain changes the output of the system which could be behavioural and/or perceptual in nature. Ultimately there are several different hypotheses as to how PSE might work and current evidence base does not allow definitive explanations to be made.

2.8 Conclusion

Chapter 2 has defined chronic pain, outlined its impact to the individual and to society. It has also explored the aetiology of chronic pain from an enactive perspective using the MOM, predictive processing and FAM to explore acute pain, and its transition to chronic pain. Treatments for CMP have been briefly outlined with particular attention towards educational interventions, specifically PSE. The MOM, predictive processing and the FAM have then been used to describe how PSE might work. One important question which has not been addressed is how effective PSE is for adults with CMP which shall be the focus of the following chapter.

Chapter 3: Literature review

3.1 Introduction

In the previous chapter, CMP was defined, its aetiology, prevalence and socioeconomic impact outlined, and PSE was introduced outlining its origins and underlying theoretical approach. The aim of this chapter is to review the evidence for PSE as an intervention for adults with CMP and highlight the gaps that exist within the current literature that this thesis seeks to address. Understanding the current gaps within the literature will provide important context and direction for subsequent chapters.

3.2 Search strategy

A series of wide scoping searches was conducted rather than a targeted systematic search in order to find relevant literature in keeping with the aim of this chapter. The searches were based on the following key search terms: chronic musculoskeletal pain, chronic pain, pain neuroscience education, pain neurophysiology education, explain pain. These are the different terms commonly used to describe PSE in the literature. Boolean operators OR and AND were used to increase the sensitivity of the search by combing key search terms (Mc Elhinney *et al.*, 2016). Searches were conducted regularly between 2015-2021 with no date limiters using the following electronic databases; AMED, CINAHL, MEDLINE and google scholar. The search was supplemented by hand searching the references lists, and citied-by lists, of relevant articles.

3.3 How effective is PSE as an intervention for adults with CMP?

PSE was first introduced by Louis Gifford (Gifford, 1998) in his seminal paper *Pain, the Tissues and the Nervous System: A conceptual model* where he outlined his Mature Organism Model. Four years later Moseley, (2002) applied these principles within an RCT which compared PSE plus physiotherapy versus usual care as directed by their general practitioner for the treatment of CLBP (n=57). The physiotherapy component included two sessions per week for four weeks, comprising of passive treatments such as spinal mobilisation/manipulation and soft tissue massage, but not electrophysical modalities. Participants in this group also were given a standardised home-exercise programme for specific trunk muscle training to be undertaken on two occasions per week and completed indefinitely. Compliance was not assessed. The PSE component entailed weekly one hour sessions for four weeks delivered in a one-to-one seminar format. Participants also completed a PSE workbook over ten days. The control

groups' treatment included physical exercises, weekly manipulation, medications, and analgesic injections. At one month follow up the PSE plus physiotherapy group showed a mean reduction in pain of 1.5/10 points (95% CI: 0.7 to 2.3) and disability of 3.9/18 (95% CI: 2.0 to 5.8) greater than control (P = <0.01 for both). At one year follow up the PSE plus physiotherapy group maintained a greater mean reduction in pain of 1.9/10 points for pain (95% CI: 1 to 2.8) and disability of 3.9/18 points (95% CI: 2.3 to 5.8) than control (p < 0.025 for both). In addition, the PSE plus physiotherapy group had a mean of 9.6 (95% CI: 6.9 to 11.9) fewer health care visits than the control group (P < 0.001). The results from this RCT provided preliminary evidence that PSE plus physiotherapy has efficacy for reducing pain and disability in the short and long term, and reducing health care visits when compared to usual care for the management of CLBP. A key limitation of this work was that due to the design of this study, the effect of the PSE component could not be delineated from that of the physiotherapy interventions (PSE plus physiotherapy versus usual care). Thus, improvements in the intervention group could not be solely attributed to PSE. Another limitation was the specific content and delivery style of the PSE was poorly explained meaning it would be very difficult to replicate.

In 2003, the educational approach used by Moseley (2002) was integrated into a manual, *Explain Pain* (Butler and Moseley, 2003; Butler and Moseley, 2013) which is arguably the gold standard text for PSE and allowed the PSE approach used by Moseley (2002) to be replicated by several RCTs exploring the efficacy of PSE underpinned by this manual (Moseley, Nicholas and Hodges 2004; Meeus et al. 2010; Ryan et al. 2010; Von Bertouch, McAuley and Moseley, 2011; van Ittersum et al. 2013; Van Oosterwijck et al. 2013; Gallagher, McAuley and Moseley 2013; Louw et al. 2014; Pires, Cruz and Caeiro, 2015; Téllez-García et al. 2015; Wälti, Kool and Luomajoki, 2015; Louw et al. 2016; Malfliet et al. 2018. With the quantitative evidence base rapidly growing, there was a need to rigorously summarise the evidence on PSE, which led to a number of groups undertaking systematic reviews investigating the effectiveness of PSE. In December 2011 the first systematic review on PSE was published (Louw et al. 2011) concluding that there was "*compelling*" evidence for PSE to improve pain, disability, catastrophising, and physical performance. Since that first review almost 10 years ago, there have been a number of quantitative PSE reviews published (Clarke, Ryan and Martin, 2011; Moseley and Butler, 2015; Louw et al. 2016; Yun, 2017; Tegner et al. 2018; Wood and Hendrick, 2019). Broadly these reviews aimed to investigate the effectiveness of PSE. The findings of these reviews are mixed with some authors concluding the evidence for PSE is "compelling" (Louw et al. 2011) and others concluding that PSE alone was not a viable intervention for long-lasting improvements in pain and disability (Moseley and Butler, 2015). Whilst the more contemporary reviews include more studies than earlier reviews, similarly to

the early reviews they all have several methodological limitations. A summary of each review, its key findings and the gaps in the literature they leave are outlined in Table 3.1.

Table 3.1 Summary of Pain Science Education Reviews.

Review	**Number of studies (Number of participants)**	**Type of review (Non-systematic, systematic, +/- Meta-analysis)**	**Key findings**	**Limitations and gaps**
Louw et al. (2011)	8 (401)	Systematic review	Concluded there is "*compelling"* evidence for PSE to improve pain, disability, catastrophising, and physical performance.	• Lack of registered protocol. • Inclusion of non-RCT designs. • No meta-analysis • Conflict of interest as AL is an author of PSE books. • No qualitative component
Clarke, Ryan and Martin, (2011)	2 (122)	Systematic review and meta-analysis	The random effects meta-analysis showed the mean pain reduction in the short-term of PSE to be 5 mm greater on the 100-mm VAS (95% CI: 0 to 10) than control.	• Lack of registered protocol. • Meta-analysis up did not meet the criterion of ≥5 studies to ensure the power of the meta-analysis is greater than that of the individual (Jackson and Turner, 2017) • Both studies within the review were co-authored by authors of PSE books and thus there is a conflict of interest. • Homogeneous sample (CLBP) • No qualitative component

Moseley and Butler, (2015)	n/a	Narrative review	Concluding that the evidence suggests that PSE alone is not a viable intervention for long-lasting improvements in pain and disability.	• Lack of registered protocol. • No meta-analysis • Conflict of interest as LM is an author of PSE books. • No qualitative component
Louw et al. (2016)	13 (734)	Systematic review	Concluded that there is "*strong"* evidence that PSE positively effects pain, disability, psychosocial factors, movement, health care utilisation, and pain knowledge.	• Lack of registered protocol. • No meta-analysis • Conflict of interest as AL is an author of PSE books. • No qualitative component
Yun, (2017)		Systematic review and meta-analysis	"Findings within this meta-analysis reveal that pain neurophysiology education combined in adjunct to therapeutic interventions has a greater treatment effect size when compared to therapeutic interventions alone."	• Unpublished doctoral thesis. • Lack of registered protocol. • Meta-analysis up did not meet the criterion of ≥5 studies to ensure the power of the meta-analysis is greater than that of the individual studies (Jackson and Turner 2017). • Homogeneous sample (CLBP) • No qualitative component

Tegner et al. (2018)	7 (300)	Systematic review and meta-analysis	*"The main result of this review was moderate quality evidence that [PSE] has an effect on pain relief for patients with CLBP just after intervention. The review found low quality of evidence that [PSE] has an effect on disability just after the intervention and on pain and disability at 3-month follow-up. For the TSK, there was a nonsignificant effect, with low to very low quality of evidence."*	• Lack of registered protocol. • Meta-analysis for kinesiophobia at 4 weeks follow up and disability and kinesiophobia at 3 month follow up did not meet the criterion of ≥5 studies to ensure the power of the meta-analysis is greater than that of the individual studies (Jackson and Turner 2017). • Homogeneous sample (CLBP) • The inclusion of 3 RCTs raises questions over the validity of the review in being able to delineate the effect of PSE from other interventions (Moseley, 2002; Ryan et al. 2010; Wälti, Kool and Luomajoki, 2015). Moseley, (2002) compared PSE plus physiotherapy versus usual care, Ryan et al. (2010) compared PSE alone versus PSE plus exercise group, Wälti, Kool and Luomajoki, (2015) compared PSE plus sensory and motor retraining versus usual care physiotherapy. None of these studies are able to conclude that the effects were due to the addition of PSE over the other interventions received. • No qualitative component
Wood and Hendrick, (2019)	8 (615)	Systematic review and meta-analysis	*"This study provides moderate quality evidence for the use of PSE as an adjunct to*	• Lack of registered protocol. • Meta-analysis investigating the effect of PSE on pain catastrophising and kinesiophobia in the short-term,

			usual physiotherapy interventions in the improvement of disability and pain scores in CLBP in the short-term. We are uncertain whether PSE may improve long-term pain and disability."	disability and pain in the long-term, and the effect of PSE plus an intervention for disability in the short-term did not meet the criterion of ≥5 studies to ensure the power of the meta-analysis is greater than that of the individual studies. • Homogeneous sample (CLBP) • The inclusion of 2 RCTs raises questions over the validity of the review in being able to delineate the effect of PSE from other interventions (Moseley, 2002; Wälti, Kool and Luomajoki, 2015). Moseley, (2002) compared PSE plus physiotherapy versus usual care, Wälti, Kool and Luomajoki, (2015) compared PSE plus sensory and motor retraining versus usual care physiotherapy. These studies are unable to conclude that the effects were due to the addition of PSE over the other interventions received. • Inclusion of a study (Werner *et al.*, 2016) with a mean duration of pain <2 months despite the inclusion criteria stating duration of pain ≥3 months. • No qualitative component

Legend: *CLBP, chronic low back pain. PSE, pain science education. TSK, Tampa scale for kinesiophobia. RCT, randomised controlled tria*l. AL, Adrian Louw.

In summary, the evidence for the effectiveness of PSE for adults with CMP based upon existing systematic review/meta-analysis is mixed. Furthermore, there are several gaps present in the systematic reviews investigating PSE for adults with CMP which need to be addressed. Firstly, future reviews should register a protocol to minimise the risk of reporting bias. Second, future meta-analysis should only be performed where pooled data includes the minimum five recommended studies to ensure sufficient statistical power (Jackson and Turner 2017). Third, future reviews should isolate the effect of PSE by only including studies that compare (i) PSE to true control (or usual care), (ii) concomitant studies, where PSE has been delivered in addition to another intervention where that other intervention has been received by both groups, or (iii) head-to-head studies where PSE has been compared to another active intervention. Fourth, to date, no PSE meta-analysis has been performed on a sample of heterogeneous CMP. Fifth, despite the increase in qualitative research within the field of PSE to date there has been no qualitative synthesis of these studies. Qualitative methods look beyond effectiveness, exploring a person's lived experience so that a deeper insight into their understanding of a phenomenon is achieved. This includes patients' experiences of receiving an intervention, in this case PSE (Magilvy and Thomas, 2009). This approach can allow the exploration of how the intervention works, the facilitators and barriers to the intervention, and identify how it might be enhanced from the patients perceptive (Barbour, 2000; Lockwood *et al.*, 2017). Furthermore, guidance for undertaking systematic reviews published by the Centre for Reviews and Dissemination at the University of York emphasise the increasing recognition of the contribution qualitative research can have, helping to develop an understanding of the people, practices and policies behind interventions and mechanisms (Centre for Reviews and Dissemination, 2009). Future reviews should address this gap by synthesising the qualitative literature. The more recent emergence of qualitative studies provides the opportunity to undertake such a mixed-methods review. Mixed-methods reviews attempt to maximise the ability of their findings to inform policy and practice through the inclusion of diverse forms of evidence (Lizarondo *et al.*, 2020).This section has outlined the evidence on the effectiveness of PSE for adults with CMP and highlighted the gaps within the literature. It is also important to explore if PSE is more effective for some types of individuals with CMP. Considering the significant gaps in the literature outlined in this section, this thesis will aim to undertake a segregated synthesis of the current quantitative and qualitative literature to investigate the clinical effectiveness, and patients' experience of, PSE for people with CMP.

3.4 Is PSE more effective for some types of individuals with CMP?

In the previous section the effectiveness of PSE was discussed from the perspective of the average effect on the CMP population. Research in the field of pain management has focused

almost exclusively on mean intervention effects (Furlan *et al.*, 2006; Searle *et al.*, 2015; Kamper *et al.*, 2015). In an analysis published in the British Medical Journal some have questioned such a focus and concluded we should be *"…casting aside our slavish reliance on the average, and asking what works for whom in what circumstance…"* (Moore *et al.*, 2013 p.3.) By focusing on mean intervention effects important inter-individual differences in response to pain management interventions could have been obfuscated. Such response heterogeneity is particularly important within the context of precision medicine, an increasingly popular field which encompasses 'tailor-made' therapies based on the patient's individual response to a given intervention (Senn, Rolfe and Julious, 2011). This individualised approach to medicine aims to improve the quality of care and reduce costs (Spear, Heath-Chiozzi and Huff, 2001).

The potential importance of a tailored approach to PSE has been highlighted by the research group at Teesside University in a series of three qualitative studies (Robinson et al. 2016; King et al. 2016; King et al. 2018). In these studies, the relevance of PSE to the individual (i.e., how tailored the material is to that individual) appeared to be an important factor in the success of PSE. Where PSE was perceived as relevant by the patient, they reported greater perceived benefit. The opposite was found where PSE was not perceived as relevant (Robinson et al. 2016; King et al. 2016; King et al. 2018). This qualitative work suggests that some people might respond better than others to PSE. If this is the case, PSE could be targeted to certain individuals or groups, however no one has tested if some people respond to PSE better than others using appropriate quantitative methodology as reported by authors outside of the field of PSE and indeed outside the field of pain (Hopkins, 2015; Atkinson and Batterham, 2015; Williamson, Atkinson and Batterham, 2017; Williamson, Atkinson and Batterham, 2018; Atkinson, Williamson and Batterham, 2019). Thus, there is a need to address this gap within the literature, which this thesis will seek to do.

The group for Outcome Measures in Rheumatology (OMERACT) in their publication "*Optimal Strategies for Reporting Pain in Clinical Trials and Systematic Reviews: Recommendations from an OMERACT 12 Workshop*" endorsed the use of sample responder counts to complement the quantification of mean treatment effects (Busse *et al.*, 2015). Moore *et al.,* (2013) also advocate the use of these responder counts for measuring analgesic success or failure. Sample responder counts entail quantifying how many patients in each intervention group change above or below a pre-set threshold. Unfortunately, this approach does not provide any information about response heterogeneity to a given intervention in the context of precision medicine. In fact, these responder counts lack statistical power and may merely reflect within-subject random variation between timepoints and/or group differences in mean

change (Senn, 2005; Snapinn and Jiang, 2007; Senn, 2016a; Senn, 2018). Furthermore, the dichotomisation (responder or non-responder) also creates problems adjusting for baseline differences between study groups (See Atkinson, Williamson and Batterham, 2019 for a comprehensive review). These sample responder counts tell us little about whether different people respond to different degrees to the same intervention, which is one of the fundamental questions in precision medicine. Should any inter-individual differences be falsely identified using the above-mentioned methods, any follow-up analysis to explore potential moderators of the intervention effect to explain the individual differences in response are therefore unwarranted (Atkinson and Batterham, 2015; Atkinson, Williamson and Batterham, 2019). Subsequent follow-up studies on the same participants would be a waste of resource and potentially unethical if no true inter-individual differences in response existed to explain.

Despite the above mentioned issues regarding sample responder counts, they have made their way into national pain guidelines in the United Kingdom and Canada (Busse *et al.*, 2015; NICE, 2016), analgesic medication pain research (Moore *et al*., 2013) and research on PSE (Pires, Caeiro and Cruz, 2016; Werner *et al.*, 2016). There is a need to address this inappropriate growing trend in the literature regarding the use of sample responder counts for exploring individual responses.

Inter-individual differences in response can be quantified appropriately by comparing the SDs of the baseline-to-follow-up changes between the experimental and control groups (Atkinson and Batterham, 2015; Cortés *et al.*, 2018). The difference between these SDs represents the SD for individual responses (SDir) which quantifies the individual variability in treatment response *per se*. The SD of the mean change score solely for the intervention group comprises treatment response variance *in addition to* the random variability in measurements between the baseline and follow-up timepoints. The SD of the changes in the control group represents this random variability in measurements between baseline and follow up – the random within-subjects variance component and measurement error.

In summary, previous research in the field of pain management has focused on mean treatment effects which could have obfuscated important individual differences in response to interventions. Sample responder counts used for investigating individual differences in response have been advocated within the literature by OMERACT and used in Canadian and United Kingdom national pain guidelines. However, this approach tells us little about whether different people respond to different degrees to the same intervention, which is the fundamental question in precision medicine. This approach has several issues including lacking statistical power, problems adjusting for baseline differences between study groups,

and finally may merely reflect within-subject random variation between time points and/or group differences in mean change. To date, there has been no investigation of 'true' individual response variation of the effect of PSE, or indeed any pain management intervention. This represents an important gap within the literature. If individual differences are observed, then true predictors of individual response could potentially be truly identified, then PSE could be tailored to the individual optimising its effect. This is an important question and a significant gap in the literature that this thesis aims to address.

3.5 Should PSE be delivered alone or in addition to another intervention?

Several studies have investigated the effect of PSE as a stand-alone intervention with promising results when delivered to a population with CMP (Moseley, Nicholas and Hodges 2004; Meeus et al. 2010; van Ittersum et al. 2013; Van Oosterwijck et al. 2013; Gallagher, McAuley and Moseley 2013; Malfliet et al. 2018). However, the authors of the PSE manual have made the argument that PSE was always intended to be delivered alongside another interventions (Moseley and Butler, 2015). In the main, studies that have investigated the effect of PSE combined with other interventions including physiotherapy (Moseley, 2002), motor control training (Moseley, 2003), sensory and motor retraining (Wälti, Kool and Luomajoki, 2015), and aquatic exercise (Pires, Cruz and Caeiro, 2015) have found promising results suggesting combining PSE with another intervention may have an additive effect. In contrast Ryan et al., (2010) compared PSE alone versus PSE plus group exercise for the treatment of CLBP (n = 38). The exercise group comprised of six weekly sessions lasting 40-55 minutes. The PSE was a one off 2.5-hour one-to-one session. Counterintuitively, PSE alone was associated with better outcomes than the combination of PSE and exercise classes. The authors postulated that because interventions (The PSE component and the exercise component) were delivered in isolation, without any joined up thinking between them, during the exercise class participants could have been exposed to patients and/or therapists with a 'biomedical' view of pain. Subsequently, messages delivered during the PSE session may have been diluted due to their attendance at the exercise class, and negatively impacted their pain beliefs. This study emphasised the importance of carefully integrating PSE into the intervention it is combined with in order not to inadvertently dilute the effect. With several studies showing promising results for PSE alone, and in combination with other interventions there was a need to undertake a review of the literature to explore what was more effective.

Moseley and Butler, (2015) in their narrative review concluded that the evidence suggests that PSE alone is not a viable intervention for long-lasting improvements in pain and disability. A recent doctoral thesis supports the work of Moseley and Butler, (2015). Yun, (2017) conducted

a systematic review and meta-analysis and found that when combining PSE with another therapeutic intervention greater treatment effects are seen when compared to the therapeutic intervention alone. The findings of these two reviews appear to suggest that combining PSE with other interventions may lead to more favourable outcomes.

In theory combining PSE with another intervention should provide more favourable outcomes. Indeed, PSE was always intended to be delivered in combination with other biopsychosocial based interventions (Moseley and Butler, 2015). However, this has not been explored in depth within the literature and is an important gap that this thesis will address.

Given that PSE was intended to be delivered in combination with other biopsychosocial based interventions, integrating PSE with a pain management programme (PMP) would seem logical and appropriate. A PMP is arguably the most comprehensive, multimodal intervention within the field of pain management. Within PMPs a variety of methods are used to directly and indirectly produce behaviour change such as cognitive and behavioural therapy, learning and conditioning processes, skills training, physical exercise and education. Patients practice the skills learned on the programme and integrate them into their daily routines in order to become an expert in their application (The British Pain Society, 2013). A PMP is implemented by an interdisciplinary team according to broadly cognitive and behavioural principles with the aim of improving the physical, emotional and social components of health and function in individuals with CMP (The British Pain Society, 2013).

However, to date, only one conference abstract (Von Bertouch, McAuley and Moseley, 2011) has explicitly combined PSE with a PMP. In this RCT, PSE plus PMP was compared against education based on the Back Book (Roland et al. 2002) plus PMP for the treatment of CMP (n = 64). More than half of the participants had CLBP. Both groups received an intensive four-week PMP. The education (PSE or back book) consisted of 2 x 1.5-hour group sessions, a manual which was to be completed during the PMP and facilitated group discussion about the education at the end of each week of the PMP. The authors were contacted about the duration of the 'facilitated discussion' and reported *"it was longer than 10 min and less than one hour"* (personal communication). Primary Outcomes of pain and self-reported function were assessed at four timepoints; pre-treatment, post-treatment, 6 months and 12 months. Pain intensity was measured using the visual analogue scale (VAS) and function was measured using the patient-specific functional scale (Stratford *et al.*, 1995). Pain improved over time for both groups (main effect of time, $F(3,186) = 52.97$, $p < 0.001$) with greater reductions observed in the PSE group (main effect of group, $F(1,62) = 11.24$, $p = 0.001$), mainly driven by 6 and 12 month follow up data (time x group interaction, $F(3,186) = 8.73$, $p < 0.001$). The mean decrease

in pain was greater in the PSE group compared to the back book group at 6 and 12 month time points (mean ± SD: 5.2 ± 2.2 vs 2.0 ± 2.0; interaction $p<0.01$). Similarly to pain, function improved over time (main effect of time, $F(3,186) =185.9$, $p <0.001$), and was greater in the PSE group. However there was not a significant interaction between group and time (time x group interaction, $F(1,62) = 3.11$, $p = 0.08$). The secondary outcomes, including pain biology knowledge and catastrophising showed statistically significantly greater improvements in the PSE group at post treatment and follow-ups ($p<0.05$). The PSE group also showed superior outcome for work status. The results of Von Bertouch, McAuley and Moseley, (2011) suggest that combined PSE plus PMP achieved better health outcomes than the back book plus PMP. However, there were several methodological limitations in this study which should be highlighted. 1) Lorimer Moseley is a co-author of the book Explain Pain (Butler and Moseley, 2003) for which the PSE material used in Von Bertouch, McAuley and Moseley, (2011) was based, thus there is a risk of bias in favour of the PSE group. While Moseley has appropriately fully acknowledged this conflict of interest, a significant body of literature has demonstrated that a conflict of interest can influence RCT outcome. Groups that have a potential conflict of interest tend to publish research which have more positive findings than those produced by neutral groups (Kjaergard and Als-Nielsen, 2002; Lexchin *et al.*, 2003). 2) Function was assessed using self-report questionnaires, which is in keeping with previous PMP studies (Chipchase and Hill, 2012) however, this provides information which may not necessarily reflect the real capability of the patients' performance (Smeets *et al.*, 2006). 3) The study was unpublished and thus lacks the scrutiny of a published article. 4) The study was done in Australia and may not generalise to the United Kingdom. 5) The control intervention was an intervention specifically for back pain (Back Book) and thus the appropriateness of this as an intervention for a sample with heterogeneous musculoskeletal pain is questionable.

Due to the limitations outlined above there is a need for an RCT based in the United Kingdom to investigate the efficacy of a PSE informed PMP that is conducted by a group that has no financial interest in PSE, will select an appropriate control intervention more suited to heterogeneous musculoskeletal pain, and uses objective measures of function. However, prior to undertaking an RCT, the Medical Research Council state that during the development and evaluation of a complex intervention (in this case a PSE informed PMP), it is important to undertake preliminary work, to investigate the components of RCT methodology prior to a full-scale trial (Craig *et al.*, 2008). These components include recruitment procedures and rates of recruitment, the appropriateness of outcome measures used, and the appropriateness of eligibility criteria. This thesis will address these issues by undertaking this preliminary work.

Another criticism of Von Bertouch, McAuley and Moseley, (2011) is that they only used a quantitative approach. There is a need to better understand how PSE works. PSE is proposed to work via pain reconceptualisation, whereby there is a shift in pain conception from pain means damage, towards pain means perceived need to protect tissues influenced by somatic, psychological and social domains (Moseley, 2007). Von Bertouch, McAuley and Moseley, (2011) assessed pain reconceptualsation using self-report questionnaires including the Survey of Pain Attitudes (Jensen and Karoly, 1987), Pain catastrophising scale (Sullivan, Bishop and Pivik, 1995) and the Biology of Pain questionnaire (Catley, O'Connell and Moseley, 2013) which whilst accepted as valid questionnaires in their own right they lack sufficient scope to explore the extent of reconceptualisation central to PSE (Robinson et al., 2016). Qualitative methods allow the exploration of a person's lived experience (first-hand insights and perceptions from someone who has experience of the phenomenon of interest) so that a deeper insight into their understanding of a phenomenon is achieved (Magilvy and Thomas, 2009). Qualitative interviews provide a richer, more in depth analysis of issues than self-report questionnaires helping to uncover personal, complex and often conflicting beliefs (Pope and Mays, 1995). This is illustrated in a qualitative study by King et al. (2018) where a participant was interviewed before and after a single PSE session - a participant was asked about the cause of their back pain after PSE:

". . .it is the new nerve in sending the messages up. . ." (King et al. (2018 P.4, Participant 1 post))

They appeared to have taken on board elements of PSE demonstrated by the use of neuroscience language "new nerve", referring to neuroplasticity: However, this language was used in combination with more structural explanations:

"I know I've got sclerosis of my lower back...whether the arthritis is starting to affect it more I don't know." (King et al. (2018 P.5, Participant 1 post)

In a similar early study by the same group, a quote from King et al. (2016) demonstrates the richness that qualitative analysis can yield. Here, participant K appears to understand the concepts presented in PSE, however they seemed unwilling or unable to apply them to her pain:

"You have your signals going, your brain is assessing what's going on and essentially the pain response may not be proportionate to the underlying whatever. And I suppose I understand that but whether it's that I'm not willing to accept it or whether it's that I can't bear to accept it

*. . . I just, I can't believe that there's not something [structural] there. Something must have happened, there must be a reason. [Participant K Post-PSE]" (*King et al. 2016 p. 1391).

In this case it seems likely that the participant would have been able to correctly answer some of the questions on the pain biology quiz (Catley, O'Connell and Moseley, 2013) whilst still holding a belief that their pain meant damage. Quantitative measures like the pain biology quiz are not able to capture these nuanced and contradictory conceptions which can be more elucidated by qualitative methods (Magilvy and Thomas, 2009; Robinson et al., 2016). To the authors knowledge, there are only four qualitative studies published on PSE (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018; King et al. 2018). Three of the studies were published by the research group at Teesside University exploring the experiences of a 2-hour group based PSE intervention with all three studies broadly finding the same themes. These included 1) degrees of reconceptualisation; 2) personal relevance; 3) importance of prior beliefs; 4) perceived benefit of PSE (Robinson et al. 2016; King et al. 2016; King et al. 2018). These studies can be criticised as they only explore PSE delivered in isolation. Thus, there is a need to explore the extent and nature of pain reconceptualisation using qualitative methodology where PSE has been delivered as part of a multimodal intervention.

Wijma et al. (2018) addressed this partially by exploring PSE delivered over multiple sessions +/- physiotherapy +/- psychology +/- medication. However, only 5/15 participants were given PSE plus two or more of either physiotherapy, psychology or medication. With 2/3 of participants not receiving multi-modal treatment there is a gap within the literature to date exploring the perceptions and experiences of adults with CMP who have received PSE fully integrated with a truly multi-modal intervention like a PMP. The use of qualitative methods would facilitate an in depth exploration of how adults with CMP understanding of their own pain is influenced by a PSE informed PMP.

In summary, the PSE literature shows that PSE alone can be beneficial for individuals with CMP for improving pain, disability and psychosocial outcomes, however reviews of the literature point to greater effects when PSE is combined with other interventions. Theoretically a PMP seems appropriate and logical as a multimodal intervention to be delivered alongside PSE. PSE should be integrated carefully into the PMP in order not to inadvertently dilute the effect. Only one study (Von Bertouch, McAuley and Moseley, 2011) has investigated the effect of a PSE informed PMP however there are several methodological limitations and there is a need to conduct preliminary work prior to a full scale RCT. This preliminary work should include a qualitative component to explore the extent and nature of pain reconceptualisation following a PSE informed PMP. Furthermore, relationship between the degree and nature of

pain reconceptualisation and changes in clinical outcomes should be explored to further the understanding of how benefit occurs. This thesis will address the gaps outlined in this section by undertaking a quasi mixed-methods study of a PSE informed PMP.

There is a need to better understand how PSE works. PSE is proposed to work via pain reconceptualisation, whereby there is a shift in pain conception from pain means damage, towards pain means perceived need to protect tissues influenced by somatic, psychological and social domains (Moseley, 2007). To date no research has attempted to better understand how pain reconceptualisation as assessed qualitatively translates into clinical benefits. Therefore there is a need to explore the relationship between the degree of pain reconceptualisation and changes in clinical outcomes.

3.6 Optimising PSE using conceptual change science

As discussed in the previous section, PSE could be enhanced by combining/integrating it with another intervention. However, it could also potentially be enhanced by optimising the format that PSE is delivered. This could potentially be achieved by drawing on conceptual change theories. Conceptual change learning refers to learning that challenges and shapes existing knowledge and knowledge structures, rather than just learning new information (Vosniadou, 2008). Given that the core objective of PSE is to shift pain conception from pain is *"a marker of tissue damage or disease"* to pain is a *"perceived need to protect body tissue"* (Moseley and Butler 2015 p.808) the use of conceptual change theory would seem appropriate to inform the optimisation of PSE delivery. Posner, et al. (1982) outlined four conditions for conceptual change; 1) dissatisfaction with the existing conception 2) Intelligibility of the new concept i.e., it must be understandable 3) Plausibility of the new concept i.e. it must appear likely, and 4) Fruitfulness i.e. the practical usefulness of the new concept. The PSE intervention used in three previous qualitative studies (Robinson et al. 2016; King et al. 2016; King et al. 2018) was partially informed by these conditions. Robinson et al. (2016 p.60) report "*The PSE session, as delivered here, addressed some but not all of these steps to a greater or lesser extent*.". Conceptual change strategies are purported to inform PSE (Moseley and Butler, 2015), and a recent PSE manual targeted at clinicians (Moseley and Butler, 2017) recommends the use of conceptual change theory in PSE delivery. Recommendations to use conceptual change theory when delivering PSE may be warranted to optimise PSE interventions, however to date no research has explored the role of the conditions for conceptual change in the process of pain reconceptualisation. This is a gap in the literature that this thesis will address.

3.7 Conclusion

Conclusions from quantitative reviews on PSE are mixed but largely in support of PSE as an intervention to treat CMP. There are a variety of limitations in these previous reviews outlined above and thus there is a need for a comprehensive mixed-methods systematic review and meta-analysis on PSE for the treatment of CMP. Furthermore, there is a need for an additional systematic review and meta-analysis which investigates individual response variation of the effect of PSE which has not been adequately explored in previous literature. PSE has been used to treat CMP alone and in combination with other interventions. Combining PSE with a PMP appears to be a logical and promising choice. Prior to undertaking a full scale RCT evaluating the effectiveness of a PSE informed PMP the Medical Research Council (Craig et al. 2008) advise undertaking preliminary work to investigate the viability of the components of RCT methodology. Finally, the use of conceptual change theory has been recommended to optimise PSE delivery, however first there is a need for research to explore the role of the conditions for conceptual change in the process of pain reconceptualisation. This thesis will undertake this work using a variety of study designs. The findings can be used to develop a protocol for pilot RCT investigating the effectiveness of a PSE informed PMP.

3.8 Aims of thesis

The primary aim of this thesis was to investigate the effectiveness and experiences of PSE for adults with CMP.

The sub aims of this thesis were:

- To undertake a segregated synthesis of the current quantitative and qualitative literature to investigate the clinical effectiveness, and patients' experience of, PSE for people with CMP. (Chapter 5)

- To conduct a systematic review and meta-analysis of the available research to quantify the 'true' inter-individual variation in pain, disability and psychosocial outcomes in response to PSE in adults with CMP. (Chapter 6)

- To explore the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology. (Chapter 7)

- To explore the role of the conditions for conceptual change in the process of pain reconceptualisation. (Chapter 7)

- To explore the relationship between the degree of pain reconceptualisation and changes in clinical outcomes. (Chapter 7)

- To explore the feasibility of undertaking a pilot RCT investigating the effectiveness of a PSE informed PMP. (Chapter 7)
    a. To investigate recruitment procedures and rates of recruitment.
    b. To investigate the appropriateness of outcome measures used within the trial.
    c. To investigate the appropriateness of the eligibility criteria.

Chapter 4: Theoretical Perspective and Methodology

4.1 Introduction

The primary aim of this thesis was to investigate the effectiveness and experiences of PSE for adults with CMP. This chapter presents the theoretical perspective and methodology employed to address the primary thesis aim. The aim of this chapter was not to engage in extensive philosophical debate over the superiority of one paradigm over another. The purpose of this chapter is to make the author's philosophical assumptions clear from the outset, enabling the reader to meaningfully understand the research detailed in this thesis.

4.2 Theoretical perspective: Pragmatism

Research in health science has traditionally consisted of two distinct perspectives which hold contrasting views on how knowledge is created (Morgan, 2007). These perspectives determine the kind of knowledge researchers look for and how they interpret that knowledge (Creswell & Clark, 2017). The constructivist paradigm that informs qualitative methodology holds the assumption that knowledge can only be seen through individuals and their subjective views (McCann and Clark, 2003). The positivist paradigm that informs quantitative methodology holds the assumption that there is an objective reality distinct from subjective perceptions which can be understood by objective evaluation free from subjective bias (Andrew and Halcomb, 2009). Both qualitative and quantitative methodologies have historically been used in isolation and integrating the approaches has been extensively debated often referred to in the literature as the 'paradigm wars' (Creswell and Clark, 2017; Tashakkori, Johnson and Teddlie, 2020). In more recent years the value of combining quantitative and qualitative approaches has been increasingly recognised with mixed methods emerging as 'the third research paradigm' (Onwuegbuzie, Johnson and Turner, 2007; Creswell and Clark, 2017). I explored two theoretical perspectives which are commonly adopted within mixed methods research to approach this thesis, pragmatism and critical realism (Shannon-Baker, 2016).

Critical realism (Bhaskar, 1975) , views there being an objective reality that exists without the interference of human beings, and without human beings this reality would still exist. It differentiates objective reality, and socially developed knowledge, arguing that the objective reality that we live in is socially constructed by individuals (Denzin and Lincoln, 2011). Whilst this objective reality exists and we can gain access to it, reality itself can never be completely

understood (Baert, 2005). As reality can never be completely understood critical realism advocates using multiple methods to facilitate a critical examination of the problem from multiple perspectives to enhance understanding of reality as much as possible (Bhaskar, 1975). This makes it a relevant theoretical perspective for mixed methods research. Critical Realism is 'fallibilist' viewing knowledge as rarely absolute, accepting that with further inquiry or the use of different methods amendments or complete rejections can be made (Benton and Craib, 2017).

Whilst I could have taken the theoretical perspective of critical realism, I felt pragmatism was a better fit for me as a person, and a researcher. My personal purpose is learning how to live well and sharing that with the world. My hope is that by learning more about how to live well and sharing that with others I can facilitate people to make practical changes to their lives that allow them to live a better life. A theoretical perspective that focused on practical changes and real world impact seemed to be a good fit for me, which is why I chose to take pragmatism as my theoretical perspective.

Pragmatism is "a vague, ambiguous, and overworked word" (Rorty, 1982 p.160). The lack of a strict definition of pragmatism stems from its relative youth as a philosophy, first cited a little over 100 years ago. The absence of a universal definition highlights it as a living philosophy, still working itself out (Talisse and Aikin, 2008 p.3). Pragmatism was first proposed by Charles Sanders Peirce as an intuitive methodological principle for conducting philosophical inquiry. Peirce viewed many traditional positions in philosophy, particularly metaphysics as meaningless because they perpetuated inquiry that did not have any practical usefulness. He hoped that his new method for conducting philosophy would clear the road of inquiry of 'meaningless gibberish' leaving 'a series of problems capable of investigation by the observational methods of the true sciences' (Talisse and Aikin, 2008 p.11). Peirce outlined his pragmatic maxim in 'How to Make our Ideas Clear':

"Consider what effects, which might conceivably have practical bearings, we conceive the object of our conception to have. Then, our conception of those effects is the whole of our conception of the object." (Peirce, 1992 p.132).

There have been numerous contributors to pragmatism, most notably William James and John Dewey who sparked a movement towards pragmatism as a philosophy (Talisse and Aikin, 2008 p. 24). Peirce, James and Dewey sharply disagreed about the scope of pragmatism, leading to some stark differences in philosophical thought. These differences were so great that Peirce in 1905 renounced the term pragmatism and renamed his philosophy

pragmaticism, a term “ugly enough to be safe from kidnappers” (Talisse and Aikin, 2008 p.3-6). It is beyond the scope of this thesis to delve into the intricacies of each founder’s version of pragmatism. Instead a general overview, of Pragmatism, from my own perspective, shall be given to ensure the reader understands the philosophical assumptions that underpin this thesis. The work of Dewey has made a more significant contribution to my view of pragmatism.

Dewey described pragmatism as the systematic exploration of what he called the logic and ethics of scientific inquiry philosophy (Morgan, 2013). Dewey argues that whilst reality exists apart from human experience, it can only be come upon though human experience. Thus, the pragmatists epistemology is that all knowledge is based on experience, with all knowledge viewed as social knowledge (Morgan, 2013 p.39). Pragmatists agree that research occurs in a social, historical and political context (Creswell and Poth, 2016 p. 28). Fallibilism is endorsed by pragmatism, viewing knowledge, meaning and research conclusions as rarely absolute, accepting that with further inquiry amendments or complete rejections can be made (Onwuegbuzie, et al., 2007). Dewey coined the term warranted beliefs instead of universal truths to reflect pragmatisms fallibilistic assumptions (Morgan, 2013 p.26). Pragmatism gives preference to action over philosophising (Onwuegbuzie, et al., 2007). It places great emphasis on the real world practical implications that conducting research has, seeing inquiry that will ultimately have no practical value as useless (Talisse and Aikin, 2008 p.10-11; Creswell & Poth, 2016 p. 28). The emphasis on practical usefulness is the main reason I chose pragmatism over critical realism as I felt it better aligns with my personal purpose. The focus on real world impact informed the development of the sub aims of this thesis particularly in Chapter 5 that will conduct a mixed-methods systematic review and meta-analysis to investigate the clinical effectiveness, and patients’ experience of, PSE for people with CMP, and Chapter 7 that will undertake preliminary work to look at the metrics to inform a pilot RCT investigating the effectiveness of a PSE informed PMP. Pragmatism gives central importance to the research question. It enables researchers to select the best method(s) to address this question, rather than being limited by a research paradigms commitment to a limited set of methods (Creswell & Poth, 2016 p. 28). This makes it a particularly compatible philosophy for mixed-methods research (Morgan, 2013 p.14).

4.3 Multiphase Mixed-Methods Design

From a pragmatic theoretical perspective the research question is central to determining the methods used. Where a question is best answered through the use of mixed methods pragmatism views qualitative and quantitative methods as compatible (Tashakkori, Johnson and Teddlie, 2020; Creswell & Poth, 2016 p. 28). A question that aims to investigate

effectiveness is best addressed through quantitative approaches whilst a question that aims to investigate *experiences* is best addressed through qualitative approaches (Bishop, 2015). Within the context of this thesis, the primary research question is *'to investigate the effectiveness and experiences of PSE for adults with CMP'.* This question therefore demands a mixed methods design.

Bishop (2015) outlines various typologies of mixed-methods research designs that have been proposed by various authors. Bishop (2015 p.4) highlights that these typologies are best *"… used as a source of inspiration to develop tailor-made designs that provide the best possible fit to one's research questions*." rather than seen as off-the-shelf designs to fit to one's research question. The mixed-methods design that was used as a source of inspiration for this thesis is the *multiphase* mixed-methods design (Creswell and Plano Clark, 2017). In this design, mixed-methods are used in multiple studies concurrently or sequentially to address the overall research question. Figure 4.1 illustrates this design within this thesis.

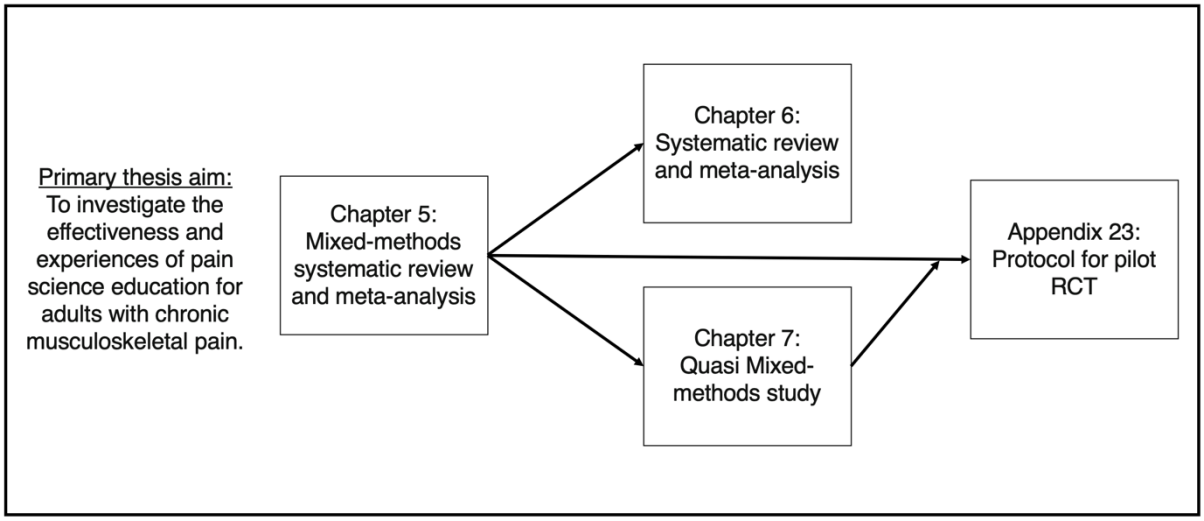


Figure 4.1 Multiphase research design of the thesis

Legend: *This figure illustrates the multiphase research design of this thesis informed by Creswell and Plano Clark (2017).*

4.4 Conclusion

In conclusion pragmatism is a theoretical perspective that aligns with my personal purpose and focuses on real world impact. Pragmatism gives central importance to the research question which enables the selection of the best methods to address the research question.

The primary aim of this thesis was to investigate the effectiveness and experiences of PSE for adults with CMP. Multiple methods in multiple studies conducted both sequentially and concurrently were deemed by the research team to best address this research aim. This design is described as a *multiphase mixed-methods design* (Creswell and Plano Clark, 2017).

Chapter 5: Pain science education a mixed-methods systematic review and meta-analysis

Note: This chapter has been published, and cited 197 times as of 21/11/2022.

Watson, J.A., Ryan, C.G., Cooper, L., Ellington, D., Whittle, R., Lavender, M., Dixon, J., Atkinson, G., Cooper, K. and Martin, D.J., 2019. Pain neuroscience education for adults with chronic musculoskeletal pain: a mixed-methods systematic review and meta-analysis. *The Journal of Pain*, 20(10), pp.1140-e1.

The mixed-methods systematic review presented in the chapter was conducted using Joanna Briggs Institute (JBI) methodology for mixed-methods systematic reviews (Lizarondo et al. 2020). JBI is a research and development centre collaborating internationally with over 70 centres aiming to improve global healthcare outcomes by promoting the synthesis, transfer and utilisation of evidence (Aromataris and Munn, 2017). Most systematic reviews to date have either synthesised quantitative or qualitative evidence. JBI mixed-methods reviews aggregate qualitative findings that provide understanding of the human experience with quantitative findings about the effectiveness of interventions (Lizarondo et al. 2020). The inclusion of diverse forms of evidence may enhance the usefulness of reviews to decision-makers (Bressan et al., 2016) and attempt to maximise the ability of their findings to inform policy and practice (Lizarondo et al. 2020).

J.W. led the development of this review contributing 80% to the overall body of work. Furthermore, J.W. led on every sub-component or the work. The other 20% of the review was developed by several academics from Teesside University and other institutions. Table 5.1 lists those involved and the tasks they conducted.

Table 5.1 Contribution of authors to mixed-methods review

Name/Job title/Employer/Role in the review	Tasks completed
James Watson Ph.D. Student Teesside University	Development of review questions Development and registration of mixed-methods protocol Formulation of search strategy Sifting of all search results and retrieval of full texts Reviewed full text for inclusion

Lead Author	Assessment of methodological quality of included qualitative and quantitative papers Data extraction from qualitative and quantitative papers Contacted study authors for missing information Preparation of quantitative data for meta-analysis Analysis of quantitative and qualitative data Meta-aggregation of quantitative and qualitative findings Preparation of review for comments and distribution to co-authors Updated review and submitted for publication
Dr. Cormac Ryan Reader in Physiotherapy Teesside University Co-author	Development of review questions Contributed to development of mixed-methods protocol Assessment of methodological quality of included papers Analysis of qualitative papers Commented on and made changes to review draft
Dr. Lesley Cooper Research assistant Teesside University Co-author	Data extraction from qualitative papers Assessment of methodological quality of qualitative papers Analysis of qualitative papers Commented on and made changed to review draft
Dominic Ellington Senior Physiotherapist North Tees and Hartlepool NHS Foundation Trust Co-author	Assisted with sifting of search results Reviewed full texts for inclusion Commented on and made changed to review draft
Robbie Whittle Senior Physiotherapist North Tees and Hartlepool NHS Foundation Trust Co-author	Assisted with sifting of search results Reviewed full texts for inclusion Commented on and made changed to review draft

Michael Lavender Highly Specialist Clinical Psychologist North Tees and Hartlepool NHS Foundation Trust Co-author	Data extraction from quantitative papers Reviewed and approved paper for publication
Prof. John Dixon Professor of Applied Physiology and Rehabilitation, and the Associate Dean (Research & Innovation) Teesside University Co-author	Development of review questions Contributed to development of mixed-methods protocol Assessment of methodological quality of qualitative papers (3rd Reviewer) Commented on and made changes to review draft
Prof. Greg Atkinson Professor of Health Sciences and Biostatistics Research Teesside University Co-author	Contributed to development of mixed-methods protocol Preparation of quantitative data for meta-analysis Analysis of quantitative data Commented on and made changes to review draft
Prof. Kay Cooper Clinical Professor of Allied Health Professions Robert Gordon University Co-author	Assessment of methodological quality of qualitative papers Analysis of qualitative papers Commented on and made changes to review draft
Prof. Denis Martin	Development of review questions Contributed to development of mix-methods protocol Assessment of methodological quality of included quantitative papers (3rd reviewer)

Professor of Rehabilitation and Director of the Centre for Rehabilitation Sciences Teesside University Co-author	Analysis of qualitative papers Commented on and made changes to review draft

5.1 Introduction

Chronic musculoskeletal pain (CMP) is considered "*an urgent global public health concern"* (Hartvigsen et al 2018) and affects 27.5% of adults worldwide (Zimmer *et al.*, 2021). There is a large societal financial burden associated with CMP. In the United Kingdom, estimated indirect costs for osteoarthritis and rheumatoid arthritis are estimated to be £14.8 billion (Oxford Economics, 2010). The total cost of CMP is likely to be much higher. Furthermore, CMP negatively impacts on individual's quality of life (Breivik et al. 2006; Tüzün, 2007).

Research and clinical guidelines recommend interventions that encourage and empower people with CMP to self-manage (Gifford, 1998; Frost *et al.*, 2004; NICE, 2020a; NICE, 2020b; NICE, 2021). Education is fundamental to this approach with the premise that the better an individual understands their condition, the more empowered they become and the better able they are to self-manage (Gifford, 1998; Robinson et al., 2016). Given the biopsychosocial nature of CMP, an educational approach grounded in the biopsychosocial model would seem an appropriate form of education for people with this condition. An increasingly popular form of biopsychosocial education is pain science education (PSE), which has the overarching aim of facilitating individuals to reconceptualise their pain as less threatening. Alternative names for PSE used within the literature include; explain pain (Butler and Moseley, 2003; Moseley and Butler 2015; Moseley and Butler 2017); therapeutic neuroscience education (Zimney, Louw and Puentedura, 2014); pain biology education (Ryan et al., 2010); and pain neurophysiology education (Clarke et al. 2011).

In recent years, there has been an increase in the number and quality of PSE reviews. This reflects the rapidly growing quantitative evidence base in the area. Many of these reviews show promising results for PSE (Louw et al., 2011; Clarke et al., 2011; Moseley and Butler, 2015; Louw et al., 2016; Cuenda-Gago and Espejo-Antunez, 2017; Yun, 2017; Tegner et al. 2018; Wood and Hendrick, 2019). The most recent review published in English on PSE in heterogeneous CMP concluded that the current evidence supports the use of PSE for improving function, pain, psychosocial factors, movement, health care utilisation, and pain

knowledge (Louw et al., 2016). Two recent meta-analysis on patients with CLBP broadly support these findings for pain and disability but not psychosocial factors (Wood and Hendrick, 2019; Tegner et al. 2018). However, neither had a registered protocol and few of the individual analyses pooled the recommended five or more studies (Jackson and Turner 2017). Additionally, both included studies where the effect was not clearly attributable to PSE e.g., PSE + Intervention A Verses Intervention B. To date no published review has conducted a meta-analysis on PSE in heterogeneous CMP.

In addition to a growth in the quantitative literature, in 2016 the first qualitative study on PSE was published (Robinson et al., 2016). Previous reviews of the literature have focused solely on quantitative studies (Louw et al., 2011; Clarke et al., 2011; Geneen *et al.*, 2015; Moseley and Butler, 2015; Louw et al., 2016; Cuenda-Gago and Espejo-Antunez, 2017; Yun, 2017). The emergence of qualitative studies provides the opportunity to undertake a mixed-methods review. Mixed-methods reviews attempt to maximise the ability of their findings to inform policy and practice through the inclusion of diverse forms of evidence (Lizarondo et al. 2020). This mixed methods review aimed to undertake a segregated synthesis of quantitative and qualitative literature to investigate the clinical effectiveness, and patients' experience of, PSE for people with CMP.

5.2 Review question/objectives

Review questions were:
How effective is PSE as an intervention for the management of adults with CMP?

What are the perceptions of PSE in adults with CMP? Question 2 is delineated into the following three objectives:
To explore patient experiences of participating in PSE.
To explore their perceptions of its effectiveness.
To explore how it influenced their understanding of pain.

5.3 Methods

The protocol for this review was published on PROSPERO (CRD42017068436).

The Joanna Briggs Institute Reviewers Manual (Lizarondo et al. 2020) was used to direct the methods of this mixed-methods systematic review and meta-analysis.

5.3.1 Inclusion criteria

- Studies including adults (≥18 years) who have CMP (including chronic lower back pain, chronic neck pain, osteoarthritis or rheumatoid arthritis, in addition to those who suffer non-specific or widespread musculoskeletal pain conditions).
- Diagnosis of CMP was consistent with the British Pain Society definition *(chronic pain, which lasts beyond the time that tissue healing would normally be expected to have occurred, often taken as ≥3 months (The British Pain Society, 2013).*
- Quantitative studies using a RCT design that (i) compared the intervention with no treatment (true control) or usual care (ii) concomitant studies where PSE was delivered in addition to another intervention where that other intervention was received by both groups and (iii) head-to-head studies where PSE was compared to another active intervention.
- Studies reporting the following objective and subjective measures - primary outcomes: pain; any validated measure of pain (numeric rating scale/visual analogue scale). Disability; any validated measure of disability (e.g., Roland Morris Disability Questionnaire). Secondary outcomes: any validated measure, which investigates the individuals' physical and/or psychosocial wellbeing.
- Qualitative studies that explored the experiences and perceptions of adults with CMP who had received PSE.

5.3.2 Exclusion criteria

- Studies that included participants with non-musculoskeletal pain such as cancer pain, visceral pain or post stroke pain.
- Studies published in a language other than English as translation services were not available.

5.3.3 Search strategy and selection of studies

A three-step search strategy was used to identify both published and unpublished studies. An initial limited search of MEDLINE and CINAHL was undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used. A second search using all identified keywords (Pain AND (Physiology OR Neurophysiology OR Neuroscience OR Biology) AND Education) and index terms was then undertaken across all included databases (The Cochrane Library, AMED, CINAHL Complete, MEDLINE, PsycINFO, PEDro, Scopus, EMBASE, Education Resources Information Centre (ERIC), Web of Science, clinicaltrials.gov, dissertations indexed with ProQuest Dissertations and Theses Global and EThOS) from 2002-

25 July 2017 and updated on 14 June 2018. This timeframe was selected as the first PSE study was published in 2002 (Moseley 2002). Finally, the reference lists and citing articles of all key identified articles were searched for additional studies. (Appendix 1 which provides the full search strategy).

Upon completion of the above search, all citations were exported into EndNote (Thomson Reuters, UK). Duplicates were removed by J.W. using methods outlined by (Bramer *et al.*, 2016). Microsoft Excel was used to create a study screening sheet including titles and abstracts which were assessed for suitability against the inclusion and exclusion criteria. All citations were independently screened by two authors (J.W. & D.E. or R.W.). Disagreements were resolved through discussion or a third reviewer (D.E. or R.W.). J.W. retrieved the full text articles marked as 'include' or 'uncertain'. J.W. & D.E. or R.W read the full text, again assessing suitability for inclusion against the inclusion/exclusion criteria. Disagreements were resolved through discussion or a third reviewer (D.E. or R.W.). Full texts deemed not to meet the criteria were rejected and the rationale recorded (see Appendix 2).

5.3.4 Assessment of methodological quality

Quantitative articles selected for critical appraisal were independently assessed by two reviewers (J.W., C.R.) for methodological validity using the Cochrane tool for assessing risk of bias (Higgins *et al.*, 2011). Disagreements were resolved by discussion or a third reviewer (D.M.).

Selected qualitative articles were independently assessed by two reviewers (L.C. and either J.W or K.C.) for methodological validity using the standardized critical appraisal instrument from the Joanna Briggs Institute, the Qualitative Assessment and Review Instrument (The Joanna Briggs Institute, 2018). L.C. and K.C. have undergone The Joanna Briggs Institute Comprehensive Systematic Review Training Program. As J.W. co-authored 1 of the qualitative studies (King et al., 2018), he did not review this article. Disagreements were resolved by discussion or a third reviewer (K.C. or J.D.)

Where there was insufficient information to make a decision regarding any aspect of the critical appraisal the original authors were contacted via email requesting further information by J.W.

5.3.5 Data extraction

5.3.5.1 Stage 1

Two reviewers (J.W., M.L.) independently extracted the quantitative data using JBI-SUMARI (Munn, 2016) including details about the interventions, populations, study methods and outcomes of relevance to the review question/objectives.

Qualitative data were extracted independently (J.W., L.C.) using JBI-SUMARI (Munn, 2016). The data extracted included specific details about the phenomena of interest, populations, study methods and outcomes of relevance to the review question/objectives. Where possible verbatim data from research participants was extracted to illustrate each finding. Where this was not provided in the source papers the authors description of the theme was extracted.

Two reviewers (J.W., L.C.) read each qualitative study several times to develop their understanding of the key themes presented. They discussed the key themes related to the objectives of the review and agreed the level of theme for data extraction would be at the theme level for three articles (Robinson et al. 2016; King et al. 2016; King et al. 2018) and at the sub-theme level from one paper (Wijma et al. 2018). This was because the sub-theme level from Wijma et al. (2018) was judged to be equivalent to the theme level of the first three papers. Three studies provided verbatim data from research participants for all themes which were used to illustrate each finding (Robinson et al. 2016; King et al. 2016; King et al. 2018). Wijma et al. (2018) used a mixture of verbatim data from research participants and a synopsis of what was said by research participants written by researchers. A mixture of these were used to illustrate their findings. J.W. and L.C. independently extracted findings and illustrations, comparing their results afterwards to ensure consensus. Findings were rated according to their quality using JBI levels of credibility, see table 5.2.

Table 5.2 Joanna Briggs Institute levels of credibility and definitions

Level of credibility	Definition
Unequivocal	Findings accompanied by an illustration that is beyond reasonable doubt and therefore not open to challenge
Credible	Findings accompanied by an illustration lacking clear association with it and therefore open to challenge
Unsupported	Findings not supported by data

Legend: *This table describes the JBI levels of credibility and definitions (Lockwood et al. 2017)*

5.3.5.2 Stage 2

The results of each single-method synthesis included in the mixed-methods review was extracted in numerical, tabular or textual format. Syntheses of quantitative data consisted of appropriate elements of the meta-analysis forest plot. For qualitative data, it consisted of appropriate elements of the QARI-view table.

5.3.6 Data synthesis

This review employed a parallel-results convergent design (Hong, *et al.*, 2017) where the quantitative and qualitative evidence were analysed and presented separately (Stage 1 of data synthesis), otherwise known as a segregated design (Sandelowski, Voils and Barroso, 2006). The synthesised findings yielded from each separate analysis were complementary as they addressed different aspects of PSE. The final stage of the mixed-methods synthesis (stage 2) was configuration, where the complementary findings were juxtaposed and organised into a line of argument (Sandelowski, Voils and Barroso, 2006; Sandelowski *et al.*, 2012).

Further details of stage 1 data synthesis for each single-method synthesis:

The primary statistics extracted from each quantitative study were mean changes in pain, disability, pain catastrophising and kinesiophobia for intervention and control groups, in addition to the associated standard deviations (SDs) of these changes. When a SD of change was not reported, and could not be obtained by contacting the authors, it was either calculated from other information given such as standard error, or estimated from the baseline and follow

up SDs, according to methods described in the Cochrane handbook (Deeks, Higgins and Altman, 2011). Where there was uncertainty a robust data set was used.

Where possible, treatment effect sizes were pooled in a meta-analysis using comprehensive meta-analysis (CMA) software version 3, and double data entry was carried out for all results. Pooled effects sizes (and associated 95% confidence intervals) were quantified in a weighted fashion using the inverse variance approach. I-squared and Tau-squared statistics were used to quantify heterogeneity, and the sources of any heterogeneity were explored using metaregression. The 95% prediction intervals (representing the likely range for the pooled mean effect size in a future similar RCT) were also calculated according to the methods reported by (IntHout *et al.*, 2016). The tau statistic is a SD that describes the typical variability of the mean effect between studies (Higgins, 2008). Where statistical pooling was not possible, the findings were presented in narrative form including tables and figures to aid in data presentation wherever appropriate.

Qualitative research findings were pooled using JBI SUMARI software (Munn, 2016). This involved the aggregation or synthesis of findings to generate a set of statements that represent that aggregation. This was achieved by assembling the findings (level 1 findings) rated according to their quality and categorising these findings based on their similarity of meaning (level 2 findings). These categories were then subjected to a meta-synthesis generating a single comprehensive set of synthesized findings (level 3 findings). Where textual pooling was not possible, the findings were presented in a narrative form (Lizarondo et al. 2020).

5.3.7 Quality of evidence

The Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach (Guyatt *et al.*, 2008) was used to rate the overall quality of quantitative evidence for each outcome. A team of international guideline developers created the GRADE approach to provide a comprehensive, pragmatic, transparent and explicit system to rate the quality of evidence and strength of recommendations (Guyatt et al., 2008). The GRADE approach has been adopted by leading groups including British Medical Journal, Cochrane and the Joanna Briggs Institute. Submission of a GRADE Summary of Findings table is mandatory for many peer-reviewed scientific journals.

A Summary of findings tables facilitate ease of knowledge translation for clinicians and patients, providing clear evidence regarding the effectiveness and risks associated with specific interventions. Information regarding the quality of that evidence is also given,

classifying primary and secondary outcomes, into one of four levels of quality; high, moderate, low or very low quality (Table 5.3). Evidence from RCTs is rated as high quality, with the confidence in the evidence being downgraded when the studies used for the recommendation have issues with risk of bias, inconsistency, indirectness, imprecision and publication bias (Guyatt et al., 2008).

Table 5.3 GRADE Quality of evidence and definitions

Level of quality	Descriptor
High quality	Further research is very unlikely to change our confidence in the estimate
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low quality	Any estimate of effect is very uncertain

Legend: *This table describes the GRADE Quality of evidence and definitions (Guyatt et al., 2008)*

Based on the principles of GRADE the ConQual approach was developed by a working group of researchers with experience in conducting qualitative reviews from the JBI (Munn *et al.*, 2014). The approach easily provides clinicians with information regarding the quality of synthesised findings from a qualitative review. Factors that increase or decrease the confidence in qualitative findings were considered. Confidence was defined as "*the belief, or trust, that a person can place in the results of research"* (Munn et al. 2014 p.3). Credibility and dependability were the two main factors that increased confidence in qualitative findings. (Guba and Lincoln, 1989) originally proposed credibility and dependability as the qualitative equivalents of reliability and internal validity, respectively. Credibility is defined as the fit between the original data and the researcher's interpretations. Dependability refers to the findings being replicable and consistent.

The credibility of each finding is assessed by the fit between the illustration taken from the original data to support the finding and the researchers' interpretations. The scale of credibility is shown in Table 5.2 above.

The dependability of each finding is assessed by questions 2-4, 6 and 7 of the critical appraisal instrument (Lockwood et a. 2017). They are listed below:

2. *Is there congruity between the research methodology and the research question or objectives?*
3. *Is there congruity between the research methodology and the methods used to collect data?*
4. *Is there congruity between the research methodology and the representation and analysis of data?*
6. *Is there a statement locating the researcher culturally or theoretically?*
7. *Is the influence of the researcher on the research, and vice-versa, addressed?*

Qualitative studies are initially rated as high quality, with the findings from each study downgraded according to their credibility and dependability. Downgrading for credibility is considered when all findings included in a synthesised finding have not been ranked as unequivocal. Downgrading for dependability occurs when the five questions above have not been met.

In this review L.C. and J.W. critically appraised all included qualitative studies except for King et al. (2018) which L.C. and K.C. appraised as J.W. is a co-author. L.C. and J.W. or K.C. independently determined the dependability and credibility. A ConQual summary of qualitative findings is shown in the results section.

5.4 Results

5.4.1 Data collection

Following removal of duplicates, 12,137 publications were identified during the initial searches outlined above. Based on information given in the title, abstract and subject headings J.W. and a second reviewer (D.E. or R.W.) assessed all references for relevance to the review. Sixty-three potentially relevant full texts were retrieved and evaluated against the inclusion criteria by J.W. and D.E. or R.W.. No further studies were found by checking the reference lists or citing articles. Forty-three quantitative, two qualitative and one mixed-methods publication were excluded at this stage. See document, Appendix 2 for a list of excluded publications and reasons for exclusion. Figure 5.1 details the PRISMA flow diagram.

For the quantitative component of the review,13 publications reporting data from 12 RCTs were included (Moseley, Nicholas and Hodges, 2004; Meeus et al. 2010; Von Bertouch, McAuley and Moseley, 2011; Van Oosterwijck et al., 2013; Gallagher, McAuley and Moseley, 2013; van Ittersum et al. 2014; Louw et al. 2014; Louw et al. 2016; Pires, Cruz and Caeiro, 2015; Téllez-García et al. 2015; Lluch *et al.*, 2018; Bodes *et al.*, 2018; Malfliet et al. 2018). For the qualitative component of the review, 4 publications reporting 4 studies were included (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018; King et al. 2018).

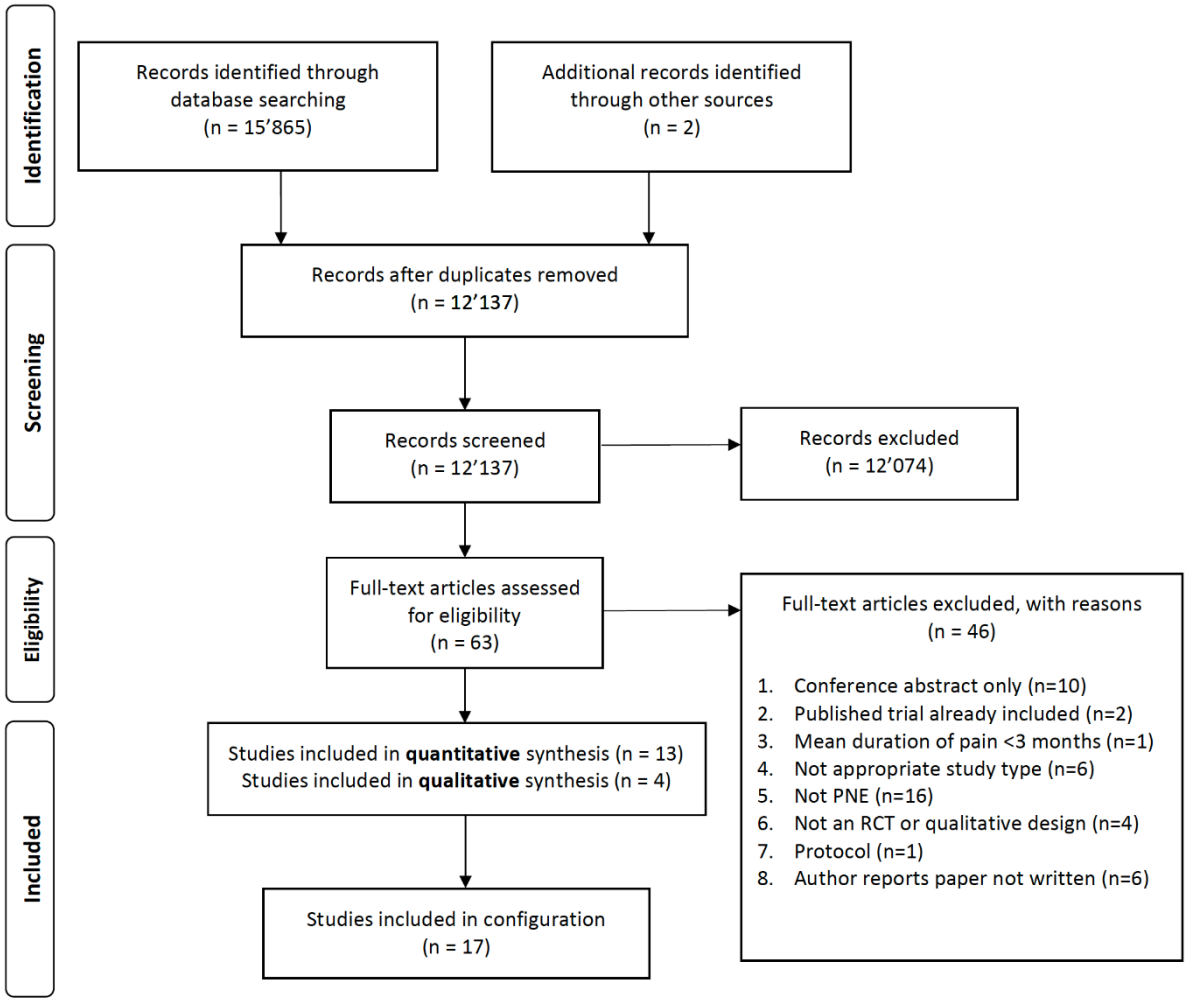


Figure 5.1 PRISMA flow diagram

Legend: *This figure shows the PRISMA flow diagram of the search and study selection process. Adapted from* (Moher *et al.*, 2009).

5.4.2 Methodological quality

5.4.2.1 Quantitative studies

Thirteen publications from 12 RCTs were critically appraised. Quality scores ranged from 1-6 out of 7; seven RCTs scored ≥5. Seven authors were contacted to provide additional information regarding study methods, with only one not responding (Moseley, Nicholas and Hodges, 2004; Von Bertouch, McAuley and Moseley, 2011; Gallagher, McAuley and Moseley 2013; van Ittersum et al. 2013; Pires, Cruz and Caeiro, 2015; Téllez-García et al. 2015; Louw et al. 2016). The critical appraisal was updated accordingly for the six that replied. Table 5.4, Figures 5.2 and 5.3 present the results of the critical appraisal.

Table 5.4 Critical appraisal of quantitative studies

Study	Score /7	Score /7 as a Percentage
Bodes 2018	4	57%
Gallagher 2013	5	71%
Lluch 2018	5	71%
Louw 2014/16	3	43%
Malfliet 2018	6	86%
Meeus 2010	5	71%
Moseley 2004	5	71%
Pires 2015	3	43%
Téllez-Garcia 2015	2	29%
van Ittersum 2013	1	14%
Van Oosterwijck 2013	5	71%
Von Bertouch 2011	5	71%

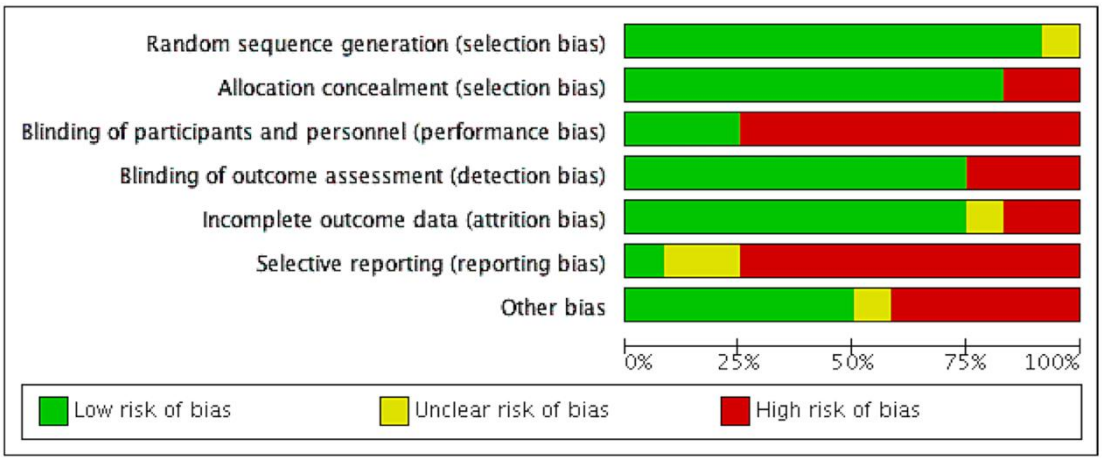


Figure 5.2 Risk of bias graph.

Legend: *Review authors' judgements about each risk of bias item presented as percentages across all included studies. Produced by using RevMan software (Review Manager. Version 5.3. Copenhagen: The Nordic Cochrane Centre. The Cochrane Collaboration, 2014).*

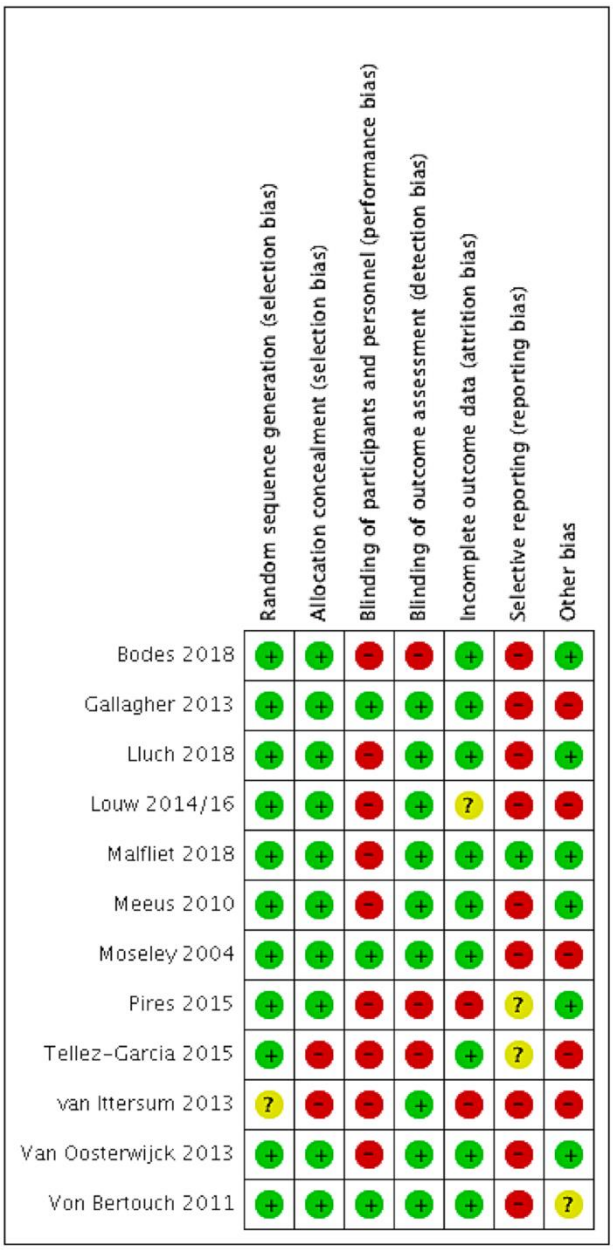


Figure 5.3 Risk of bias summary.

Legend: *Review authors' judgements about each risk of bias item for each included study. Produced by using RevMan software (Review Manager. Version 5.3. Copenhagen: The Nordic Cochrane Centre. The Cochrane Collaboration, 2014).*

5.4.2.2 Qualitative studies

Four publications were appraised. Quality scores ranged from 4-9 /10. One study scored 4/10 (King et al. 2018). They failed to make explicit their philosophical or methodological perspective, merely stating their method, theoretical thematic analysis. Thus, questions 1-5 were marked as unclear. L.C. and K.C. were of the opinion that because this study was applied qualitative research it therefore does not require alignment with one particular philosophy or methodology and that the study was of sound methodological quality with appropriate methods applied. Table 5.5 presents the results of the critical appraisal.

Table 5.5 Critical appraisal of qualitative studies

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Total
Robinson et al. 2016	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
King et al. 2016	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Wijma et al. 2018	U	Y	Y	Y	Y	N	N	Y	U	Y	6
King et al. 2018	N	U	U	U	U	Y	N	Y	Y	Y	4
%	0%	75%	75%	75%	75%	75%	50%	100%	75%	100%	

Legend: *Y = yes; N = No; U = Unclear*

5.4.3 Summary of findings table and ConQual table

The GRADE Summary of Findings table was created by J.W. with input from C.R. using GradePro (Table 5.6). The table includes the primary outcomes of pain and disability, together with the secondary outcomes of pain catastrophising and kinesiophobia. The ConQual summary of findings table includes the credibility and dependability of the synthesised findings from the qualitative component of the review (Table 5.7)

Table 5.6 Summary of findings

PSE compared to control for treatment of adults with chronic musculoskeletal pain						
Patient or population: treatment of adults with chronic musculoskeletal pain **Setting**: **Intervention**: PSE **Comparison**: Control						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	**Risk with PSE**				
Pain score in the short term assessed with a 100-mm VAS from 0 to 100 (higher is worse)	The mean pain score in the short term was **-15.17** mm	The mean change in pain score in the short term in the intervention group was 5.91 mm lower (13.75 lower to 1.93 higher) than the control group	-	524 (9 RCTs)	⨁⨁◯◯ LOW a,b,c,d,e,f,g,h	Lower score indicates lower pain. A change of less than 10mm is considered not clinically important. PSE may result in little to no difference in pain score in the short term.
Pain score in the medium term assessed with a 100-mm VAS from 0 to 100 (higher is worse) follow-up: range, 3−6 months	The mean pain score in the medium term was **-17.63** mm	The mean change in pain score in the medium term in the intervention group was 6.27 mm lower (18.97 lower to 6.44 higher) than the control group	-	457 (7 RCTs)	⨁◯◯◯ VERY LOW a,d,e,f,g,h,i,j	Lower score indicates lower pain. A change of less than 10mm is considered not clinically important. The evidence is very uncertain about the effect of PSE on pain score in the medium term.
Change in disability score in the short term assessed with: Validated measure of disability converted to percentage Scale from: 0 to 100 (higher is worse)	The mean change in disability score in the short term was **-12.84** units	The mean change in disability score in the short term in the intervention group was 4.09 units lower (7.72 lower to 0.45 lower) than the control group	-	644 (10 RCTs)	⨁⨁⨁◯ MODERATE b,c,d,e,f,g,h,k	Lower score indicates lower disability. A change of less than 10 units is considered not clinically important. PSE probably results in a small possibly unimportant effect in disability score in the short term.

Table 5.6 Summary of findings

PSE compared to control for treatment of adults with chronic musculoskeletal pain						
Patient or population: treatment of adults with chronic musculoskeletal pain **Setting**: **Intervention**: PSE **Comparison**: Control						
Outcomes	**Anticipated absolute effects**[*] (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	**Risk with PSE**				
Change in disability score in the medium term assessed with: Validated measure of disability converted to percentage Scale from: 0 to 100 (higher is worse) follow up: range 3 months to 6 months	The mean change in disability score in the medium term was **-13.09** units	The mean change in disability score in the medium term in the intervention group was 8.14 units lower (15.60 lower to 0.68 lower) than the control group	-	457 (7 RCTs)	⨁⨁⨁◯ MODERATE b,d,e,f,g,h,j,k	Lower score indicates lower disability. A change of less than 10 units is considered not clinically important. PSE probably results in a small possibly unimportant effect in disability score in the medium term.
Change in pain catastrophising score in the short term assessed with: Pain catastrophising scale from: 0 to 52 (higher is worse)	The mean change in pain catastrophising score in the short term was **-2.82** units	The mean change in pain catastrophising score in the short term in the intervention group was 3.33 units lower (6.01 lower to 0.65 lower) than the control group	-	598 (9 RCTs)	⨁⨁⨁◯ MODERATE b,d,e,f,g,h,j,k	Lower score indicates lower pain catastrophising. A change of less than 5.2 units is considered not clinically important. PSE probably results in a small possibly unimportant effect in pain catastrophising score in the short term.
Change in pain catastrophising score in the medium term (MT PCS) assessed with: Pain catastrophising scale from: 0 to 52 (higher is worse) follow up: range 3 months to 6 months	The mean change in pain catastrophising score in the medium term was **-4.39** units	The mean change in pain catastrophising score in the medium term in the intervention group was 5.26 units lower (10.59 lower to 0.80 higher)	-	375 (6 RCTs)	⨁⨁⨁◯ MODERATE b,d,e,f,g,h,j,k	Lower score indicates lower pain catastrophising. A change of less than 5.2 units is considered not clinically important. PSE probably reduces pain catastrophising score in the medium term slightly.

Table 5.6 Summary of findings

PSE compared to control for treatment of adults with chronic musculoskeletal pain						
Patient or population: treatment of adults with chronic musculoskeletal pain **Setting**: **Intervention**: PSE **Comparison**: Control						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	**Risk with PSE**				
Change in kinesiophobia score in the short term assessed with: Tampa Scale for Kinesiophobia converted to percentage Scale from: 25 to 100 (higher is worse)	The mean change in kinesiophobia score in the short term was **-4.06** units	The mean change in kinesiophobia score in the short term in the intervention group was 13.55 units lower (25.89 lower to 1.21 lower)	-	372 (7 RCTs)	⨁⨁⨁◯ MODERATE d,e,f,g,h,j,k,l	Lower score indicates lower kinesiophobia. A change of less than 10 units is considered not clinically important. PSE probably reduces kinesiophobia score in the short term slightly.
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval						
GRADE Working Group grades of evidence **High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect **Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different **Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect **Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect						

Explanations

a. Some concern regarding reporting bias and allocation concealment.

b. Some variation is size of the effect, however mostly in the same direction.

c. Good overlap of the confidence intervals.

d. Significant P value.

e. I-Squared above 50%

f. Tau-Squared higher than point estimate.

g. Sample of chronic musculoskeletal pain comparing PSE against control using an appropriate outcome measure.

h. Sample size above 300. Below the criterion (10%) for appreciable harm.

i. Large variation in size of the effect, going in both directions.

j. Poor overlap between the confidence intervals.

k. The majority of the weight comes from low risk studies. Although there was some concern over blinding of participants and personnel, this predominantly came from lack of blinding of personnel, which is normal for such studies.

l. Some variation in the size of the effect, all going in the same direction.

Table 5.7 ConQual summary of findings

Systematic Review title: Pain neuroscience education for adults with chronic musculoskeletal pain: a mixed-methods systematic review				
Population: adults with chronic musculoskeletal pain				
Phenomena of interest: the perceptions of PSE in adults with chronic musculoskeletal pain including 1) their experiences of participating in PSE 2) their perceptions of its effectiveness 3) explore how it influenced their understanding of pain.				
Synthesised finding	Type of research	Dependability	Credibility	ConQual score
A comprehensive assessment allowing the patient to tell their own story should be undertaken to ensure they feel heard. This will also facilitate the identification of their prior understanding and beliefs. PSE can then be delivered in a manner relevant to that patient. In addition, patients clarifying their story to a healthcare professional may raise their awareness of the biopsychosocial nature of pain, promoting readiness to engage with PSE.	Qualitative	Downgrade 1 level*	Downgrade 1 level**	Low
Achieving pain reconceptualisation can enhance patients' ability to cope with their condition. To promote pain reconceptualisation PSE should be delivered by health care professionals (HCPs) skilled in PSE delivery and facilitation of group, or one-to-one interactions with, and between, patients and other HCPs. Progress towards reconceptualisation should be monitored throughout, tailoring concepts that have not been accommodated to ensure relevance of PSE to the individual.	Qualitative	Downgrade 1 level*	Downgrade 1 level**	Low

**Downgraded one level as whilst two studies scored perfectly on dependability, the other two studies scored 3 and 1. The mean dependability score was 3.5.*

*** Downgraded one level due to a mix of unequivocal and equivocal findings.*

5.4.4 Description of quantitative studies

A summary of all publications are presented in Table 5.8

The diagnosis of CMP differed across the 12 RCTs, the most prevalent being CLBP (n = 5) (Moseley, Nicholas and Hodges 2004; Pires, Cruz and Caeiro, 2015; Téllez-García et al. 2015; Bodes et al. 2018; Malfliet et al. 2018), lumbar radiculopathy (n = 1) (Louw et al. 2014/16), heterogeneous pain (n = 2) (Von Bertouch, McAuley and Moseley, 2011; Gallagher, McAuley and Moseley 2013), chronic fatigue syndrome with chronic widespread pain syndrome (n = 1) (Meeus et al. 2010), fibromyalgia (n = 2) (van Ittersum et al. 2013 Van Oosterwijck et al. 2013) and knee osteoarthritis (n = 1) (Lluch et al. 2018). There was a total of 755 participants in the sample of 12 included RCTs with the number of participants ranging from 12-120 (Téllez-García et al. 2015; Malfliet et al. 2018). All studies included more women than men ranging from 7% male to 46% male (van Ittersum et al. 2013; Louw et al. 14/16). The mean age of participants ranged from 37 to 70 years (Téllez-García et al. 2015; Lluch et al. 2018). The mean baseline pain across all studies ranged from 43/100 to 79/100 (Pires, Cruz and Caeiro, 2015; Bodes et al. 2018).

Studies were conducted in a range of locations including private rehabilitation clinics (n = 2) (Moseley, Nicholas and Hodges 2004; Bodes et al. 2018) and University facilities (n = 3) (Van Oosterwijck et al. 2013; Bodes et al. 2018; Malfliet et al. 2018). Studies were conducted in several countries including the USA, Europe and Australia (Meeus et al. 2010; van Ittersum et al. 2013; Van Oosterwijck et al. 2013; Malfliet et al. 2018; Louw et al. 2014/16). The duration of educational intervention ranged from 0.5 hours (Meeus et al. 2010; Van Oosterwijck et al. 2013; Louw et al. 2014/16) to 3 hours (Von Bertouch, McAuley and Moseley, 2011; Pires, Cruz and Caeiro, 2015). Written information was the main intervention for two studies (Gallagher, McAuley and Moseley 2013; van Ittersum et al. 2013). Participants were given 3 and 6 weeks respectively to read and absorb the information.

PSE was delivered in single and multiple sessions. We defined ‘multiple’ as having a PSE contact with a member of the study team on more than one occasion via face-to-face, telephone or email. Written information alone was defined as 1 contact, however supporting leaflets/materials were not included when given in addition to face-face. PSE was delivered in a single session by four studies (Moseley, Nicholas and Hodges 2004; Meeus et al. 2010; Gallagher, McAuley and Moseley 2013; Louw et al. 2014/16), and over multiple sessions in eight studies (Von Bertouch, McAuley and Moseley, 2011; van Ittersum et al. 2013; Van

Oosterwijck et al. 2013; Pires, Cruz and Caeiro, 2015; Téllez-García et al. 2015; Lluch et al. 2018; Bodes et al. 2018; Malfliet et al. 2018).

Table 5.8 Characteristics of included quantitative studies

Study	Methods	Sample size (baseline)/ gender/ mean age in years	Participants	Intervention(s)	Duration of educational intervention	Control	Authors conclusions/notes	Setting/country
Moseley, Nicholas and Hodges 2004	RCT	N = 58 43% M 43.5	LBP of >6 months duration. Baseline pain as mean % = 59.5% Duration of pain in mean (SD) months = 29.5 (12)	3h individual PSE, with 20m break. 10 section workbook with 3 questions at end of each section. To be completed over 10 days.	PSE 2.67h Control 2.67h	3h individual Back education, with 20m break. 10 section workbook with 3 questions at end of each section. To be completed over 10 days.	PSE results in some normalisation of pain cognitions and physical performance but not self-perceived disability. Doubts raised about suitability of structural pathology based education.	Private rehabilitation clinics Unknown
Von Bertouch 2011	RCT	N = 64 33% M 42.4	All chronic pain patients >50% CLBP Baseline pain as mean % = 64% Duration of pain in mean months = unknown	2x 1.5h Group PSE + PMP. Manual to be completed during PMP. Facilitated discussion about PSE at end of each week of PMP.	PSE 3h Control 3h	2x 1.5h Group Back book + PMP. Manual to be completed during PMP. Facilitated discussion about PSE at end of each week of PMP.	n/a	Unknown Unknown

Meeus et al. 2010	RCT	N = 48 17% M 40.3	CFS diagnosed according to the 1994 Centers for Disease Control and Prevention criteria for CFS (Fukuda *et al.*, 1994) . Patients also had chronic widespread pain diagnosed according to The American College of Rheumatology 1990 criteria (Wolfe *et al.*, 1990) Baseline pain as mean % = Unknown Duration of pain in mean months = unknown	0.5h individual PSE	PSE 0.5h Control 0.5h	0.5h individual pacing and self-management education	PSE led to improved scores on the Neurophysiology of Pain Test. PSE had immediate effects on ruminating about pain. No therapy effect for pain thresholds found.	Chronic fatigue clinic. Brussels Belgium.

van Ittersum et al. 2013	RCT	N = 105 7% M 46.7	Fibromyalgia diagnosed according to The American College of Rheumatology 1990 criteria (Wolfe et al. 1990). 18-65 years of age. Baseline pain as mean % = 71.5% Duration of pain in mean months = unknown	Written PSE + 1 phone call for motivation/questions +/- 2x phone calls/emails for further clarification/questions	Unknown	Written Relaxation exercises + 1 phone call for motivation/questions +/- 2x phone calls/emails for further clarification/questions	Written PSE alone is not effective for changing the impact of the illness on daily life, pain catastrophising, or illness perceptions in fibromyalgia patients.	Specialised centres for chronic pain and chronic fatigue. Belgium.
Van Oosterwijck et al. 2013	RCT	N = 30 13% M 45.9	Fibromyalgia diagnosed according to The American College of Rheumatology 1990 criteria (Wolfe et al. 1990). 18-65 years of age.	0.5h individual PSE. PSE leaflet. 1x telephone call (unknown duration) to answer questions about the leaflet, motivate to read leaflet and encourage application of material to life.	PSE 0.5h Control 0.5h	0.5h individual Self-management techniques. Leaflet about activity management. 1x telephone call (unknown duration) to answer questions about the leaflet, motivate to read leaflet and encourage	Fibromyalgia patients can understand and remember PSE. PSE resulted in less worrying in the short-term, and long term improvements in vitality, physical functioning, mental health, and general health perceptions. No significant changes	University facilities. Brussels, Belgium.

			Baseline pain as mean % = 61.3% Duration of pain in mean (SD) months = 136 (71)			application of material to life.	established in pain catastrophising, hypervigilance, or kinesiophobia. Pain pressure thresholds were unchanged. A positive effect on endogenous pain inhibition at 3 month follow up was found.	
Gallagher, McAuley and Moseley 2013	RCT	N = 79 39% M 43.5	18-75 years of age with pain that had been sufficient to disrupt their activities of daily living for more than the previous 3 months. Baseline pain as mean % = 65% Duration of pain in mean (SD) months = 28 (19.5)	80-page booklet divided into 11 sections - Metaphors and stories to help understand the biology of pain	Unknown	80-page booklet divided into 11 sections - Advice about managing pain (The back book and Manage your pain)	Written material using metaphors to explain key biological concepts increased knowledge of pain biology and decreased catastrophic thought processes about pain and injury when compared to material that presented biopsychosocial advice for pain management.	Book with metaphors so participants home? Unknown

Pires, Cruz and Caeiro, 2015	RCT	N = 62 35% M 51	Low back pain >3 months duration +/- leg pain. 18-65 years of age. Baseline pain as mean % = 42.9% Duration of pain in mean (SD) months = unknown	2x 1.5h Group PSE. 12 sessions of aquatic exercise over 6 weeks. 30-50m each session.	PSE 3h Control 3h	12 sessions of aquatic exercise over 6 weeks. 30-50m each session.	PSE is a clinically effective addition to aquatic exercise. The addition of PSE resulted in statistically significant reduction in pain intensity at 3 month follow up. No statistically significant differences were found for pain intensity at 6 weeks follow up or functional disability at either follow up.	Outpatient clinic. Portugal
Louw et al. 2014/16	RCT	N = 67 46% M 49.6	Patients with lumbar radiculopathy, scheduled for lumbar surgery. 18-65 years of age. Baseline pain as mean % = 48.4% Duration of pain in mean (SD) months = 3 (7.5)	0.5h individual PSE. PSE booklet "your nerves are having back surgery" & Lumbar surgery + usual care	PSE 0.5h Control 0	Lumbar surgery alone + usual care	Providing a single PSE session to patients prior to lumbar surgery results in significant reduction in healthcare costs 3-years after lumbar surgery.	7 Clinical sites in the United States of America.

Tellez-Garcia et al. 2015	RCT	N = 12 33% M 36.5	Chronic non-specific low back pain ≥3 months defined as pain symptoms localised below costal margin and over the gluteus area. 18-65 years of age. Without referral into lower extremity >1 year. ≥4 points on RMDQ. Not received physio past 6 months. At least 1 active trigger point reproducing their symptoms diagnosed according to criteria outlined by (Travell and Simons, 1992)	2 x 0.5h individual PSE. + written information about PSE as homework Trigger point-dry needling, 1x per week for 3 weeks.	PSE 1h Control 0	Trigger point-dry needling, 1x per week for 3 weeks.	Trigger point dry needling is effective for improving pain, disability, kinesiophobia and widespread pressure pain sensitivity at short term in individuals with mechanical LBP. The inclusion of PSE exerts a greater impact for decreasing kinesiophobia.	Unknown Unknown

			Baseline pain as mean % = 65% Duration of pain in mean (SD) months = 18 (8.5)					
Lluch et al. 2018	RCT	N = 54 37% M 70.3	Symptomatic knee osteoarthritis (Diagnosed according to the American College of Rheumatology criteria (Altman *et al.*, 1986) of >3 months duration and scheduled to undergo total knee replacement. Baseline pain as mean % = 58% Duration of pain in mean (SD) months = 93 (67.8)	Individual PSE 1x 50-60m & 3 x 20-30m + read Explicano el dolor (Butler, 2010) Knee joint mobilisations once a week for 4 week, 3 sets of 10. Self-mobilisations 4 sets 20 reps per day. 2 months Total knee replacement 1 month after finishing education and mobilisations.	PSE 2.17h Control 2.17h	Individual Biomedical education 1x 50-60m & 3 x 20-30m. Knee joint mobilisations once a week for 4 week, 3 sets of 10. Self-mobilisations 4 sets 20 reps per day. Total knee replacement 1 month after finishing education and mobilisations.	A preoperative treatment for people with knee osteoarthritis combining PSE with knee joint mobilisations did not produce any additional benefits in knee pain and disability and central sensitisation measures when compared with that combining biomedical education with knee joint mobilisation. Superior effects were observed in the PSE and knee joint mobilisation group for psychosocial variables related to pain catastrophising and kinesiophobia.	Orthopaedic surgery service of a hospital. Spain.

Bodes et al. 2018	RCT	N = 56 27.3% M 47	Nonspecific CLBP for ≥6 months 20-75 years of age Baseline pain as mean % = 79% Duration of pain in mean (SD) months = Unknown	Therapeutic exercise – including motor control exercises for the lumbar spine, stretches, and aerobic exercise. To be completed daily. Group (4-6 patients) PSE 2x 30 to 50 minutes plus a leaflet.	PSE 1.33h Control 0	Therapeutic exercise – including motor control exercises for the lumbar spine, stretches, and aerobic exercise. To be completed daily.	A program of PSE combined with therapeutic exercise is more effective in reducing pain, disability, and pain catastrophizing compared with therapeutic exercise alone in patients with CLBP.	Private clinic and university. Spain.
Malfliet et al. 2018	RCT	N = 120 39.2% M 39.8	Nonspecific chronic spinal pain (neck and lower back) at least 3 days/week for at least 3 months since the first symptoms. 18-65 years of age Baseline pain as mean % = 50.65	3 PSE sessions 1. 0.5-1h group (maximum of 6 patients). Information booklet provided at the end. 2. ~0.63h Home-based online e-learning module containing 3 explanatory videos and questions about pain.	PSE 1.88h Control 1.88h	3 biomedical education sessions 1. 0.5-1h group (maximum of 6 patients). Information booklet provided at the end. 2. ~0.63h Home-based online e-learning module containing 3 explanatory videos	PSE, and not neck/back school education, is able to improve kinesiophobia, beliefs regarding the negative impact of the illness on quality of life and functional capacity, and beliefs regarding the chronicity of pain and the time scale of illness symptoms. However, none of the educational programs of this study was able to decrease the	University hospitals in Ghent and Brussels, Belgium.

			Duration of pain in mean (SD) months = 82 (143.25)	3. 0.5 Individual. Focus on patients personal needs following difficulties with session 2. Focus on the application of knowledge to participant's life.		3. 0.5 Individual. Focus on patients personal needs following difficulties with session 2. Focus on the application of knowledge to participant's life.	participant's perceived disability due to pain. Nevertheless, as kinesiophobia in particular is generally considered to be a strong predictor and mediator of chronic pain, PSE is preferred as education approach for people with nCSP.	

Legend: *Characteristics of included quantitative studies. Abbreviations: LBP, low back pain; CLBP, chronic low back pain; nCSP, non-specific chronic spinal pain; PSE, pain neuroscience education; PMP, pain management programme; CFS, chronic fatigue syndrome; RMDQ, Roland Morris Disability Questionnaire; SD, standard deviation.*

5.4.5 Description of qualitative studies

A summary of all publications are presented in Table 5.9. Three of the four qualitative studies included participants with heterogeneous CMP (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018). The remaining study included participants whose primary complaint was CLBP (+/- leg symptoms) (King et al., 2018). Three studies were carried out in the UK in an NHS Pain Clinic by the same research group (Robinson et al. 2016; King et al. 2016; King et al., 2018). The other was carried out in the Netherlands (Wijma et al. 2018) in participants' own homes (n = 14) or a physiotherapy practice (n = 1).

All studies used individual semi-structured interviews with open questions to collect data. Two conducted repeat interviews (King et al. 2016; King et al., 2018). One study also conducted using a focus group made up of healthcare professionals (n = 6) to discuss, optimise, and verify the theory constructed from the patient interviews (Wijma et al. 2018). Interviews in all studies were audio-recorded and transcribed verbatim. Data was analysed using a range of qualitative techniques including interpretive phenomenological analysis (Robinson et al. 2016; King et al. 2016), grounded theory (Wijma et al. 2018), and theoretical thematic analysis. (King et al., 2018).

Included studies provided data regarding the (i) experiences of participating in PSE for patients with CMP (ii) the extent, and nature of patient's reconceptualisation of their CMP following PSE. (iii) experiences of patients with CMP who recently received PSE in a transdisciplinary setting.

Table 5.9 Characteristics of included qualitative studies

Study/Country	Methodology/Methods	Participants	Phenomenon of interest	Findings
Robinson et al. 2016 UK	Interpretive phenomenological analysis. Semi-structured individual interviews using open questions, post only.	N = 10 adults with chronic musculoskeletal pain recruited from an NHS Pain Clinic. Mean age = 48.5 years (Range = 28-64) 60% Male.	Following a single 2h group PSE session: to explore the experience of PSE for people with chronic pain and to gain insight into their understanding of	Three themes emerged: perceived relevance for the individual participant; perceived benefits for the individual participant; and

		Mean duration of pain = 9.2 years (Range = 2-32). 3 unemployed, 3 employed, 1 self-employed, 1 retired, 1 sick-leave.	their pain after PSE.	evidence of reconceptualisation. Within these themes there were examples of positive and negative experiences, the latter manifesting as lack of relevance, lack of benefit and lack of evidence of reconceptualisation. An interlinking narrative was the importance of relevance.
King et al. 2016 UK	Interpretive phenomenological analysis. Semi-structured individual interviews using open questions, pre and post.	N = 7 adults with chronic musculoskeletal pain recruited from an NHS Pain Clinic. Mean duration of pain = 9.7 years (Range = 2-26 years).	Following a single 2h group PSE session: to investigate the degree and nature of people's reconceptualisation of their own chronic pain following PSE.	Themes described variable degrees of reconceptualisation, including none; people's beliefs about their pain before PSE as barriers to or facilitators of reconceptualisation; and the influence of reconceptualisation on clinical benefits of PSE.
Wijma et al. 2018 The Netherlands	Grounded Theory. Semi-structured interviews using open questions.	Interviews N = 15 recruited from a transdisciplinary	Explore the experiences of patients with chronic pain who recently received	Several topics and subthemes emerged. The pre-PSE phase, in which

	Focus group with healthcare professionals	outpatient treatment centre. Mean age = 47 (Range 18-62) 47% Male Mean duration of pain = 7 years (Range = 23-0.5) Focus group 6 members of Transcare: one general practitioner, two psychologists, two physiotherapists, and one researcher. 50% Male Mean age = 46 years (Range = 37-57) Mean experience = 22 years (Range = 16-34) Two had higher professional education with postgraduate qualification. Two had a university postgraduate qualification. Two had a university postgraduate qualification and PhD.	PSE in a transdisciplinary setting.	respondents met the healthcare professionals during a board intake. The second topic, a comprehensible PSE, comprised of understandable explanation, and the interaction between the physiotherapist and psychologist. The third topic involved the outcomes of PSE, with the subthemes awareness, finding peace of mind, and fewer symptoms. The final topic, scepticism, contained doubt towards the diagnosis and PSE, disagreement with diagnosis and PSE, and PSE can be confronting.
King et al. 2018 UK	Theoretical thematic analysis.	N = 12 adults (≥18 years) and had a primary complaint of chronic (>6 months	Following a single 2h group PSE session: to investigate the	The *a priori* themes – degrees of reconceptualisatio

	Semi-structured individual interviews using open questions, pre and post.	duration) lower back pain (+/- leg symptoms) of a neuro/musculoskeletal origin. Recruited from an NHS Pain Clinic. Mean age = 48 years (Range = 25-72). 42% Male. Mean duration of pain = 10 years 4 months (Range = 8 months-26 years). 3 unemployed, 6 employed, 3 retired. Participants ranged from holding no qualifications to holding a BSc (Hons) degree.	extent, and nature, of people's reconceptualisation of their CLBP following PSE.	n, personal relevance, importance of prior beliefs and perceived benefit of PSE – were all clearly identifiable within the data and did indeed provide a good description of participants' accounts. One participant reported distress during the session which is the first reporting of an adverse event associated with PSE in the literature.

5.4.6 Deviations from original protocol

In addition to the two primary outcome measures of pain and disability, there were several outcome measures, which under our protocol were classified as secondary outcome measures including; 12 validated psychosocial outcome measures; four physical performance outcome measures; and three objective outcome measures of pain pressure threshold. A summary can be seen in document Appendix 3.

Jackson and Turner (2017) recommend only pooling data where there are no less than five studies to ensure that the power from a random-effects meta-analysis is greater than that of the individual studies. Thus, only pain, disability, pain catastrophising, and kinesiophobia met this criterion and could be pooled. The decision was made to only report results for those measures that met this criterion to keep the review focussed and coherent. Thus, pain, disability and pain catastrophising were pooled in the short (<3 months) and medium term (≥3-6 months). Kinesiophobia was pooled in the short term only. Where pooling was not appropriate for the included outcomes, it was presented narratively.

5.5 Findings of the review

5.5.1 Quantitative component

Data was classified under three time points including short-term (<3 months), medium-term (≥3-6 months) and long-term (≥12 months) (Clarke et al. 2011).

5.5.1.1 Primary outcome: Pain

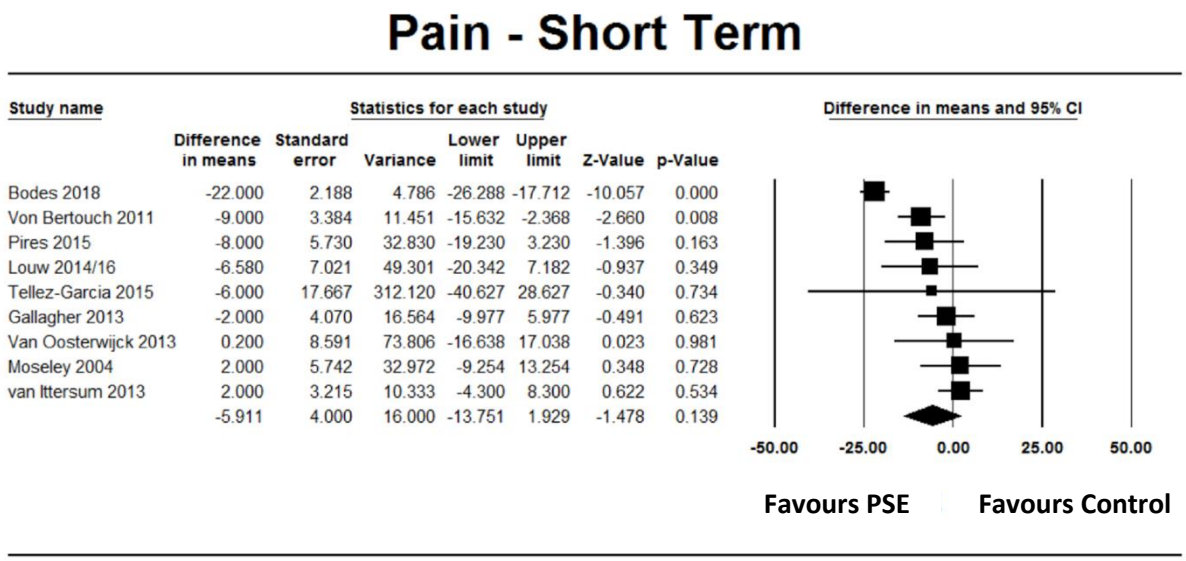
Ten RCTs collected data on pain. A variety of outcome measures were used to collect pain data including 0-10 numerical rating scales (NRS) by four studies (Gallagher, McAuley and Moseley 2013; Louw et al. 2014/16; Téllez-García et al. 2015; Bodes et al. 2018); 100mm visual analogue scales (VAS) by three studies (Moseley, Nicholas and Hodges 2004; Von Bertouch, McAuley and Moseley, 2011; Pires, Cruz and Caeiro, 2015); the Medical Outcomes Short-Form 36 Health Status Survey (SF-36), for which the category 'bodily pain' was used by one study (Van Oosterwijck et al. 2013); the Fibromyalgia impact questionnaire, for which the 0-10 NRS was used by one study (van Ittersum et al. 2013); and The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) by one study (Lluch et al. 2018).

Three studies assessed pain using pain pressure thresholds (Lluch et al. 2018; Van Oosterwijck et al. 2013; Meeus et al. 2010). However, it was inappropriate to pool this data with the questionnaires from other studies.

Data was available for nine RCTs for which pain was assessed in the short term, and seven in the medium term. All pain outcomes were converted into a 100mm VAS to allow pooling, with a higher percentage indicating more pain (Busse et al. 2015).

5.5.1.1.1 Short-term

The random effects pooled results across all PSE interventions vs control in nine studies (Moseley, Nicholas and Hodges 2004; Von Bertouch, McAuley and Moseley, 2011; Gallagher, McAuley and Moseley 2013; Van Oosterwijck et al. 2013; van Ittersum et al. 2013; Téllez-García et al. 2015; Pires, Cruz and Caeiro, 2015; Louw et al. 2014/16; Bodes et al. 2018) (n = 524 participants) showed the mean pain reduction of PSE to be 5.91 mm greater on the 100mm-VAS (95% CI: -13.75 to 1.93) than control (P = 0.139; low-quality evidence; Figure. 4). The 95% prediction interval for the mean effect was -31.51 to 19.69. Heterogeneity was considerable (I^2 = 85.22, tau = $\pm$ 10.36).



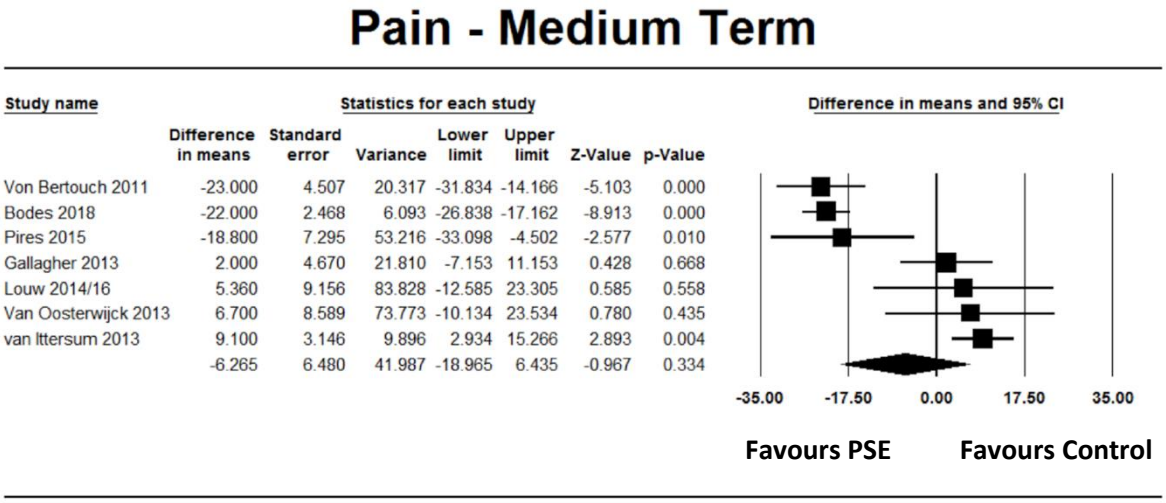
Model		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	9	-10.237	1.347	1.814	-12.877	-7.597	-7.601	0.000	54.133	8	0.000	85.222	107.245	79.064	6251.063	10.356
Random	9	-5.911	4.000	16.000	-13.751	1.929	-1.478	0.139								

Figure 5.4 Forest plot of PSE versus control in the short term; primary outcome pain.

Legend: *A P-value of 0.000 reflects the precision of the meta-analysis software output. These P-values should be interpreted as P < 0.0005.*

5.5.1.1.2 Medium-term

The random effects pooled results across all PSE interventions vs control in seven studies (Von Bertouch, McAuley and Moseley, 2011; Gallagher, McAuley and Moseley 2013; Van Oosterwijck et al. 2013; van Ittersum et al. 2013; Pires, Cruz and Caeiro, 2015; Louw et al. 2014/16; Bodes et al. 2018) (n = 457 participants) showed mean pain reduction of PSE to be 6.27 mm greater on the 100-mm VAS (95% CI: -18.97 to 6.44) than control (P = 0.334; very low quality evidence; Figure 5). The 95% prediction interval for the mean effect was -48.67 to 36.14. Heterogeneity was considerable (I^2 = 92.81, tau = ± 16.07).



Model		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	7	-9.715	1.572	2.472	-12.797	-6.634	-6.179	0.000	83.436	6	0.000	92.809	258.273	202.556	41028.873	16.071
Random	7	-6.265	6.480	41.987	-18.965	6.435	-0.967	0.334								

Figure 5.5 Forest plot of PSE versus control in the medium term; primary outcome pain.

Legend: *A P-value of 0.000 reflects the precision of the meta-analysis software output. These P-values should be interpreted as P < 0.0005.*

5.5.1.1.3 Long-term

Only two studies reported on pain in the long term and thus were not pooled. Von Bertouch, McAuley and Moseley, (2011) compared PSE plus PMP vs Back book education plus PMP, with both groups showing decreases from baseline of 53mm and 22mm on 100mm VAS respectively.

Louw (2014/16) compared PSE plus lumbar surgery vs lumbar surgery alone, with both groups showing decreases from baseline at 12 months for leg pain of 3.7 and 3.3 points on 0-10 NRS for the PSE and control groups respectively (P > 0.075). At 36 months, the groups showed reductions from baseline of 3.4 and 3.7 points for the PSE and control groups respectively (P = 0.028).

5.5.1.2 Primary outcome: Disability

Eleven RCTs collected data on disability. A variety of outcome measures were used including the Roland Morris Disability Questionnaire (RMDQ) by three studies (Moseley, Nicholas and Hodges 2004; Téllez-García et al. 2015; Bodes et al. 2018); the Oswestry Disability Index (ODI) by two studies (Louw et al. 2014/16; Téllez-García et al. 2015); the Patient Specific Functional Scale (PSFS) by three studies (Von Bertouch, McAuley and Moseley, 2011; Gallagher, McAuley and Moseley 2013); The Pain Disability Index by one study (Malfliet et al. 2018); the Medical Outcomes Short-Form 36 Health Status Survey (SF-36), for which the category 'physical functioning' was used by one study (Van Oosterwijck et al. 2013); the Fibromyalgia impact questionnaire, for which 'physical functioning' was used by one study (van Ittersum et al. 2013); the Quebec Back Pain Disability Scale by one study (Pires, Cruz and Caeiro, 2015); the WOMAC by one study (Lluch et al. 2018).
Disability data were available for 10 RCTs in the short term, and seven in the medium term. All measures of disability were converted into a score /100 to facilitate pooling, with a higher score indicating greater disability.

5.5.1.2.1 Short-term

The random effects pooled results across all PSE interventions vs control in ten studies (Moseley, Nicholas and Hodges 2004; Von Bertouch, McAuley and Moseley, 2011; Gallagher, McAuley and Moseley 2013; Van Oosterwijck et al. 2013; van Ittersum et al. 2013; Téllez-García et al. 2015; Pires, Cruz and Caeiro, 2015; Louw et al. 2014/16; Bodes et al. 2018; Malfliet et al. 2018) (n = 644 participants) showed mean disability reduction of PSE to be 4.09/100 (95% CI: -7.72 to -0.45) greater than control (P = 0.028; moderate quality evidence; Figure 6). The 95% prediction interval for the mean effect was −15.42 to 7.25. Heterogeneity was considerable (I^2 = 86.17, tau = ± 4.65). Téllez-García et al. (2015) collected two disability outcome measures (RMDQ and ODI). Following discussion, we chose to use the ODI within the analysis and undertook a sensitivity analysis replacing the ODI with the RMDQ. This had no statistically or clinically significant effect on the results.

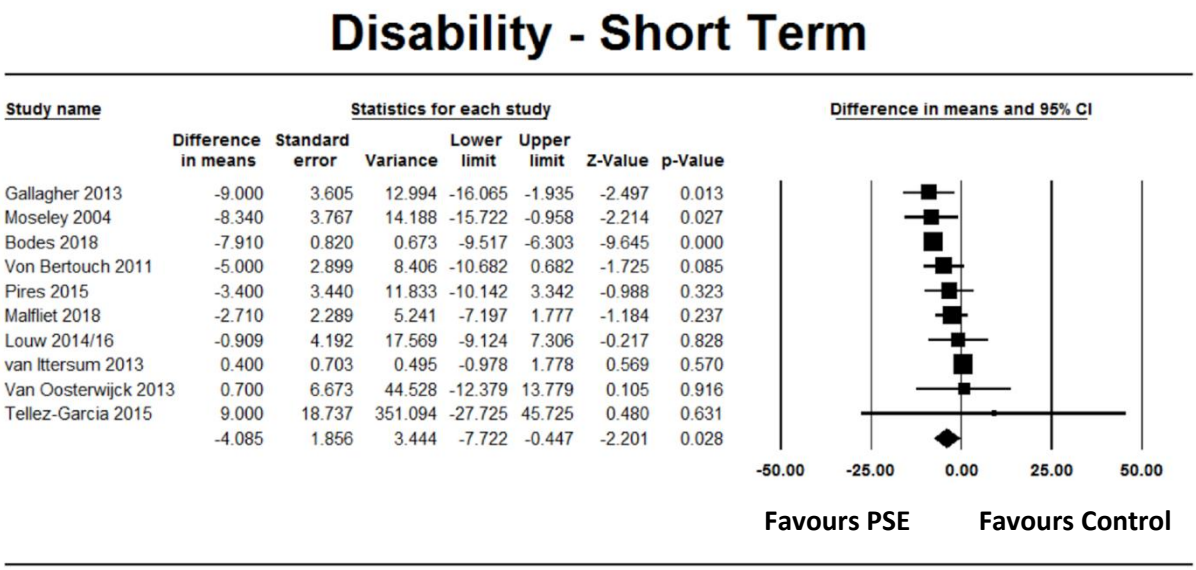
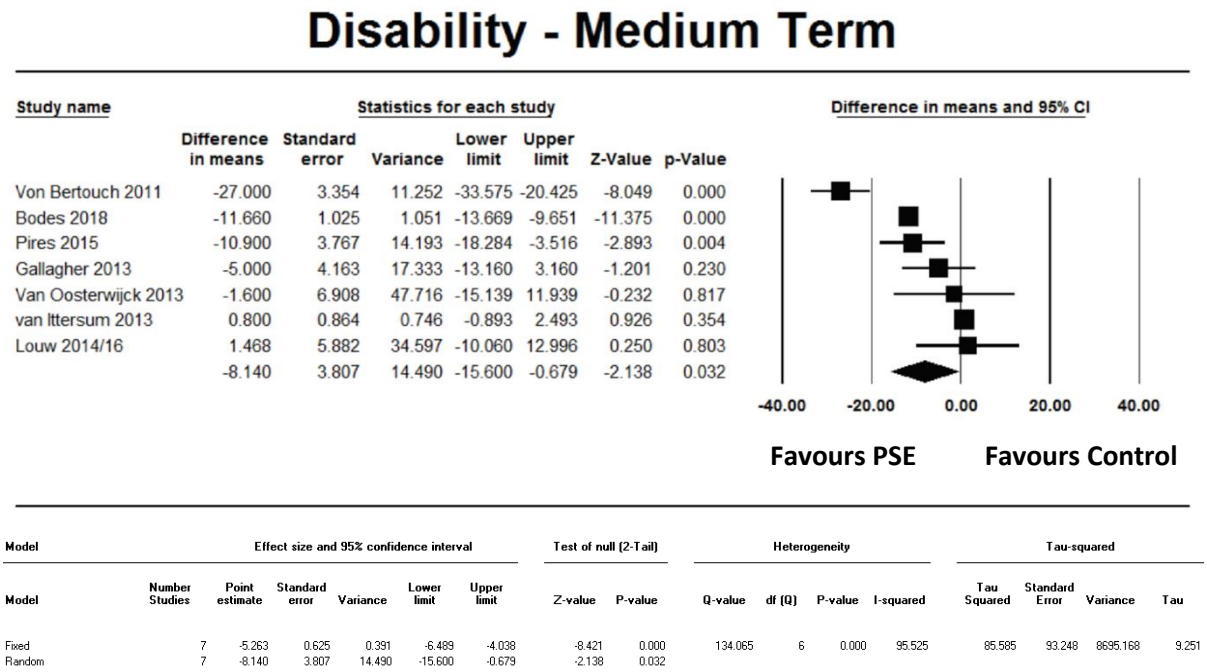


Figure 5.6 Forest plot of PSE versus control in the short term; primary outcome disability.

Legend: *A P-value of 0.000 reflects the precision of the meta-analysis software output. These P-values should be interpreted as P < 0.0005.*

5.5.1.2.2 Medium-term

The random effects pooled results across all PSE interventions vs control in seven studies (Von Bertouch, McAuley and Moseley, 2011; Gallagher, McAuley and Moseley 2013; Van Oosterwijck et al. 2013; van Ittersum et al. 2013; Pires, Cruz and Caeiro, 2015; Louw et al. 2014/16; Bodes et al. 2018) (n = 457 participants) showed mean disability reduction of PSE to be 8.14/100 (95% CI: -15.60 to -0.68) greater than control (P = 0.032; moderate quality evidence; Figure 7). The 95% prediction interval for the mean effect was −32.62 to 16.34. Heterogeneity was considerable (I^2 = 95.53, tau = ± 9.25).



Model		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	7	-5.263	0.625	0.391	-6.489	-4.038	-8.421	0.000	134.065	6	0.000	95.525	85.585	93.248	8695.168	9.251
Random	7	-8.140	3.807	14.490	-15.600	-0.679	-2.138	0.032								

Figure 5.7 Forest plot of PSE versus control in the medium term; primary outcome disability

Legend: *A P-value of 0.000 reflects the precision of the meta-analysis software output. These P-values should be interpreted as P < 0.0005.*

5.5.1.2.3 Long-term

Only two studies reported on disability in the long term and thus were not pooled. Von Bertouch, McAuley and Moseley, (2011) compared PSE plus a PMP vs Back book education plus a PMP, with both groups showing decreases from baseline of 6.3 and 5.1 points /10 on the PSFS respectively. There was no between groups comparison presented in this study. Louw (2014/16) compared PSE plus lumbar surgery vs lumbar surgery alone, with both groups showing decreases for disability of 19 and 23 points on 0-100 ODI respectively at 12 months follow up. The effect of group did not reach statistical significance (P > 0.075). At 36 months, the groups showed reductions of 21 and 22 points, respectively. The effect of group did not reach statistical significance (P = 0.317). There were no significant differences between year 1 and 3 (P = 0.761).

5.5.1.3 Secondary outcome: Pain Catastrophising

Ten RCTs collected data on pain catastrophising. (Moseley, Nicholas and Hodges 2004; Von Bertouch, McAuley and Moseley, 2011; Van Oosterwijck et al. 2013; van Ittersum et al. 2013;

Meeus et al. 2010; Gallagher, McAuley and Moseley 2013; Louw et al. 2014/16; Lluch et al. 2018; Bodes et al. 2018; Malfliet et al. 2018). All studies used the Pain Catastrophising Scale (PCS). PCS datum for one study was not available and could not be provided by the author on request (Von Bertouch, McAuley and Moseley, 2011).

5.5.1.3.1 Short-term

The random effects pooled results across all PSE interventions vs control in nine studies (Moseley, Nicholas and Hodges 2004; Van Oosterwijck et al. 2013; van Ittersum et al. 2013; Meeus et al. 2010; Gallagher, McAuley and Moseley 2013; Louw et al. 2014/16; Lluch et al. 2018; Bodes et al. 2018; Malfliet et al. 2018) (n = 598 participants) showed mean pain catastrophising reduction of PSE to be 3.33 points /52 on the PCS (95% CI: -6.01 to -0.65) greater than control (P = 0.015; moderate quality evidence; Figure 8). The 95% prediction interval for the mean effect was −12.61 to 5.96. Heterogeneity was considerable (I^2 = 97.62, tau = ± 3.79).

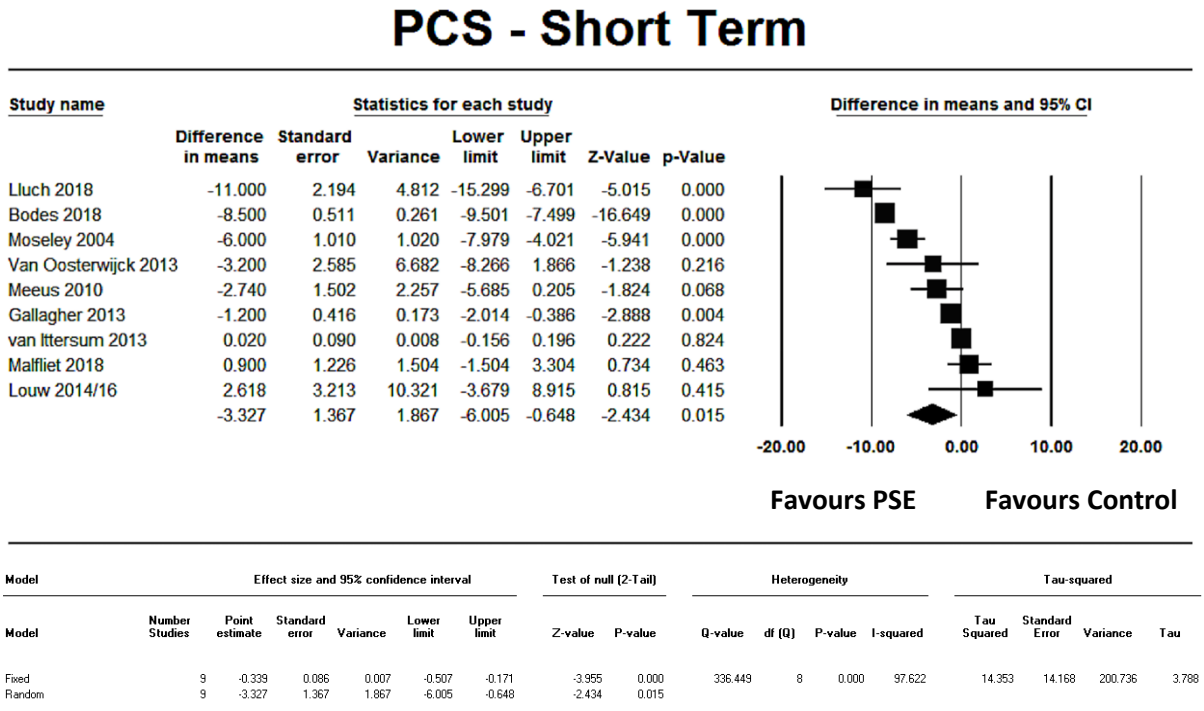
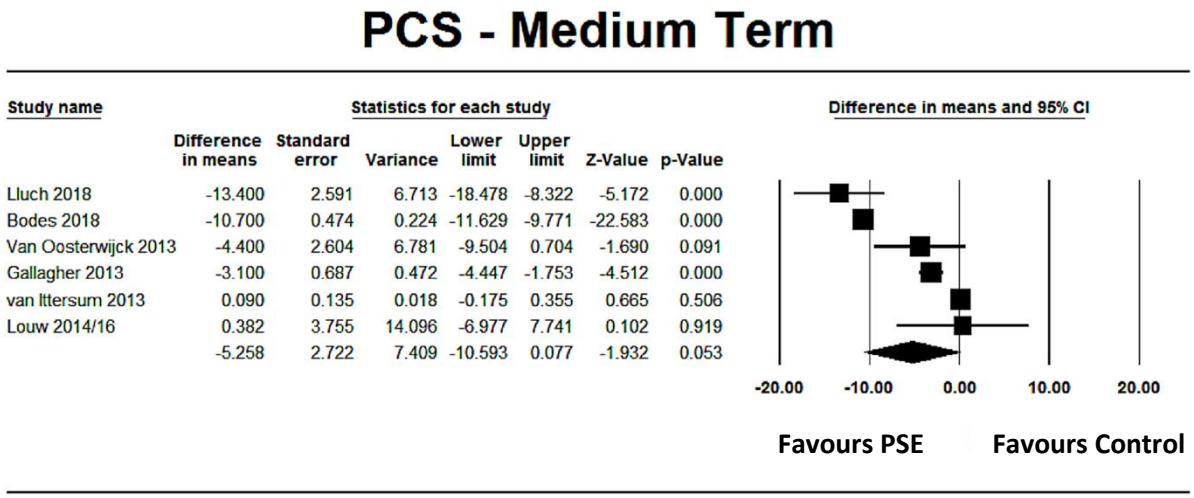


Figure 5.8 Forest plot of PSE versus control in the short term; secondary outcome pain catastrophizing.

Legend: *A P-value of 0.000 reflects the precision of the meta-analysis software output. These P-values should be interpreted as P < 0.0005.*

5.5.1.3.2 Medium-term

The random effects pooled results across all PSE interventions vs control in six studies (Van Oosterwijck et al. 2013; van Ittersum et al. 2013; Gallagher, McAuley and Moseley 2013; Louw et al. 2014/16; Lluch et al. 2018; Bodes et al. 2018) (n = 375 participants) showed mean pain catastrophising reduction of PSE to be 5.26 points out of 52 on the PCS (95% CI: -10.59 to 0.08) greater than control (P = 0.053; moderate quality evidence; Figure 9). The 95% prediction interval for the mean effect was −23.01 to 12.49. Heterogeneity was considerable (I^2 = 99.03, tau = ± 6.35).



Model		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	6	-0.844	0.128	0.016	-1.094	-0.594	-6.622	0.000	516.556	5	0.000	99.032	40.276	44.456	1976.356	6.346
Random	6	-5.258	2.722	7.409	-10.593	0.077	-1.932	0.053								

Figure 5.9 Forest plot of PSE versus control in the medium term; secondary outcome pain catastrophizing.

Legend: *A P-value of 0.000 reflects the precision of the meta-analysis software output. These P-values should be interpreted as P < 0.0005.*

5.5.1.3.3 Long-term

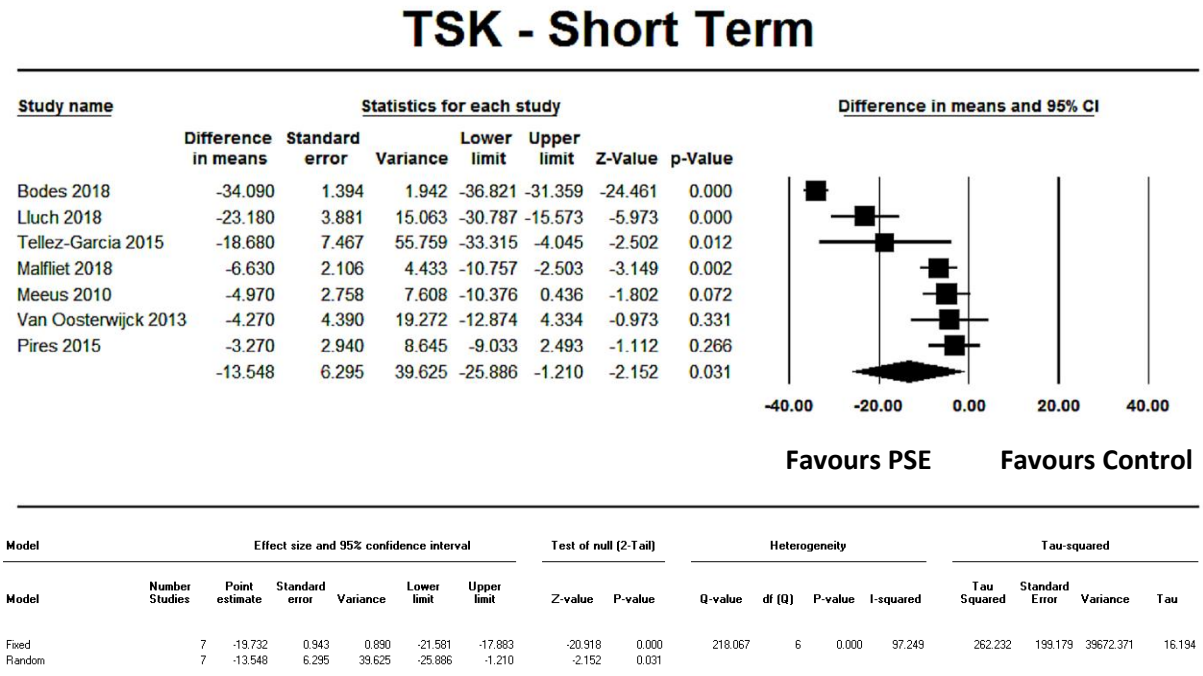
Only one study reported on pain catastrophising in the long term (Louw 2014/16) comparing PSE plus lumbar surgery vs lumbar surgery alone, with both groups showing decreases for pain catastrophising of 12.3 and 13.3 points on 0-52 PCS respectively at 12 months follow up. The statistical significance of this is unknown. At 36 months, the groups showed reductions of 15.0 and 19.3 points respectively. The statistical significance of this is unknown.

5.5.1.4 Secondary outcome: Kinesiophobia

Seven RCTs collected data on Kinesiophobia (Meeus et al. 2010; Van Oosterwijck et al. 2013; Pires, Cruz and Caeiro, 2015; Téllez-García et al. 2015; Lluch et al. 2018; Bodes et al. 2018; Malfliet et al. 2018). All studies used the Tampa Scale for Kinesiophobia (TSK), with three studies using the 17-item version (TSK-17) (Van Oosterwijck et al. 2013; Téllez-García et al. 2015; Malfliet et al. 2018); one study using the 17-item chronic fatigue syndrome version (TSK-CFS) (Meeus et al. 2010); one study using the 13-item version (TSK-13) (Pires, Cruz and Caeiro, 2015); and two studies using the 11-item version (TSK-11) (Lluch et al. 2018; Bodes et al. 2018). TSK data was converted into a percentage to allow pooling, with a higher percentage indicating greater kinesiophobia.

5.5.1.4.1 Short-term

The random effects pooled results across all PSE interventions vs control in seven studies (Meeus et al. 2010; Van Oosterwijck et al. 2013; Pires, Cruz and Caeiro, 2015; Téllez-García et al. 2015; Lluch et al. 2018; Bodes et al. 2018; Malfliet et al. 2018) (n = 372 participants) showed mean reduction in kinesiophobia of PSE to be 13.55% on the TSK (95% CI: -25.89 to -1.21) greater than control (P = 0.03; moderate quality evidence; Figure 10). The 95% prediction interval for the mean effect was −56.06 to 28.96. Heterogeneity was considerable (I^2 = 97.25, tau = ± 16.19).



Model		Effect size and 95% confidence interval					Test of null (2-Tail)		Heterogeneity				Tau-squared			
Model	Number Studies	Point estimate	Standard error	Variance	Lower limit	Upper limit	Z-value	P-value	Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
Fixed	7	-19.732	0.943	0.890	-21.581	-17.883	-20.918	0.000	218.067	6	0.000	97.249	262.232	199.179	39672.371	16.194
Random	7	-13.548	6.295	39.625	-25.886	-1.210	-2.152	0.031								

Figure 5.10 Forest plot of PSE versus control in the short term; secondary outcome kinesiophobia.

Legend: *A P-value of 0.000 reflects the precision of the meta-analysis software output. These P-values should be interpreted as P < 0.0005.*

5.5.1.4.2 Medium-term

Four studies investigated kinesiophobia. Van Oosterwijck et al. (2013) compared PSE vs Self-management advice, with both groups showing decreases from baseline at 3 months of 3 and 1 points respectively on 17-68 TSK-CFS. The exact P value was not provided however the authors did report it was not statistically significant. Pires et al. (2015) compared PSE plus aquatic therapy to aquatic therapy alone, with both groups showing decreases from baseline at 3 months of 5 and 3 points respectively on 13-52 TSK-13. This was not statistically significant. Lluch et al. (2018) compared PSE plus knee joint mobilisations and total knee replacement to biomedical education plus knee joint mobilisations and total knee replacement with both groups showing reductions from baseline at 5 months of 13 and 3 points on the 11-44 TSK-11. This reached statistical significance (P < 0.01) in favour of PSE. Bodes et al. 2018 compared PSE plus therapeutic exercise to therapeutic exercise alone with both groups showing reductions from baseline at 3 months of 13 and 4 points on 11-44 TSK-11. This reached statistical significance in favour of PSE; P = <.01.

5.5.1.4.3 Long-term

No studies looked at kinesiophobia in the long term.

5.5.1.5 Exploration for heterogeneity

Possible sources of heterogeneity (Publication bias, study quality, age, %male, baseline pain, duration of pain, PSE alone or PSE + intervention and duration of education) were explored using metaregression analyses (See document Appendix 4).

For pain in the short and medium term, all covariates were not significant (P > 0.05) except for PSE alone or PSE plus an intervention ((P = 0.02; coefficient = -13.7829 for short term) (P < 0.01; coefficient = 28.7171 for medium term)).

For disability in the short term all covariates were not significant (P > 0.05). For disability in the medium term all covariates were not significant (P > 0.05), except for PSE alone or PSE plus an intervention (P < 0.01; coefficient = -15.2197) and duration of education (P = 0.03; coefficient = -7.0841).

For PCS in the short term all covariates were not significant (P > 0.05) except for PSE alone or PSE plus an intervention (P < 0.01; coefficient = -7.6528). For PCS in the medium term, all covariates were not significant (P > 0.05), except for PSE alone or PSE plus an intervention (P < 0.01; coefficient = -9.7706) and duration of education (P < 0.01: coefficient = -6.8079).

For TSK in the short term all covariates were not significant (P > 0.05) except for baseline pain (P < 0.01; coefficient = -0.8468).

The Eggers' regression intercept was not significant (P > 0.05) for all outcomes at all timepoints indicating there was no evidence of publication bias. Cochrane recommend only using a funnel plot to investigate publication bias where there are at least ten studies to ensure the power of the test is high enough to distinguish chance from real asymmetry (Sterne, Egger and Moher, 2011). Therefore a funnel plot was only created for disability in the short term as this was the only outcome and timepoint where n = 10.

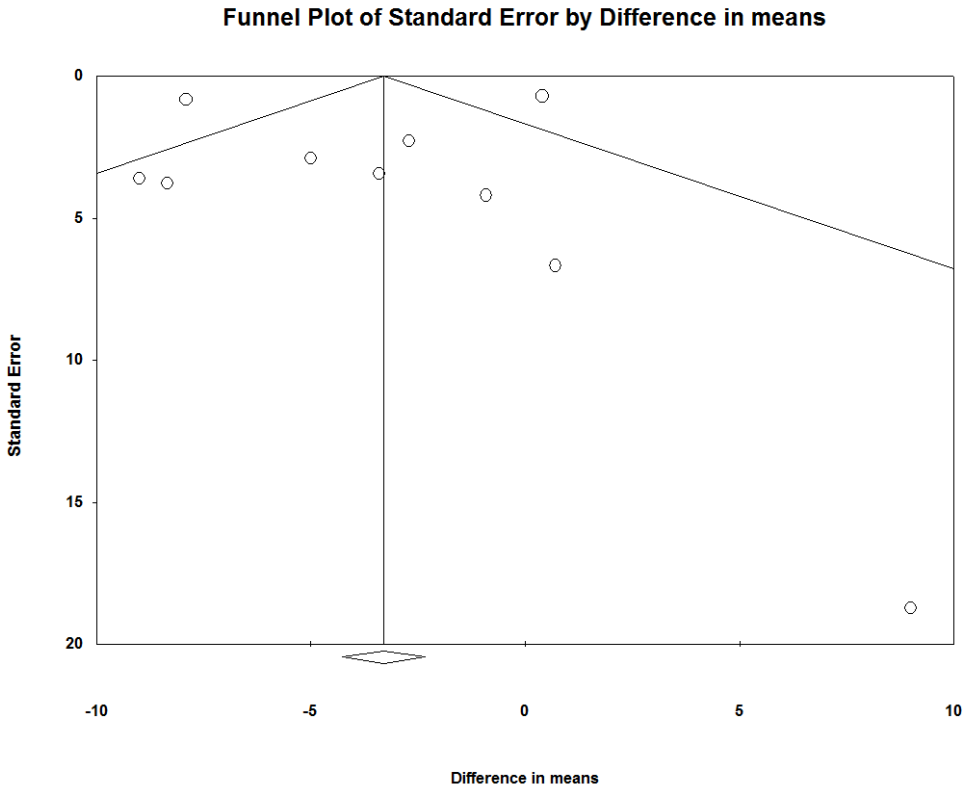


Figure 5.11 Funnel plot showing publication bias for studies used in the short term disability meta-analysis.

A funnel plot is a scatter plot of the effect estimates from individual studies against some measure of precision, in this case standard error. Asymmetry of a funnel plot is not solely cause by reporting bias, with heterogeneity and chance also potentially having an effect

(Sterne et al. 2011). The funnel plot shown in Figure 5.11 is asymmetrical largely due to Téllez-García et al. (2015). One possible reason for this asymmetry is the low sample size (n = 12) resulting in a low measure of precision (Standard error = 18.74). Sterne et al. (2011) recommend that where small studies tend to lead to lower estimates of benefit than larger studies, publication bias can probably be excluded. Téllez-García et al. (2015) suggested that PSE had a negative effect on disability in the short-term which contrasts to the findings of 7/9 of the included studies, all of which had a greater sample size. Finally, Eggers test was not significant (P = 0.776) indicating no evidence of publication bias.

5.5.2 Qualitative component

Two synthesised findings were generated from 23 study findings extracted from four studies (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018; King et al. 2018). Findings were illustrated using direct participant quotes and authors' descriptions, therefore they were assigned a mix of unequivocal and credible levels of credibility. The study findings, illustrations and levels of credibility are presented in Table 5.10.

Table 5.10 Qualitative findings with illustrations and levels of credibility

Robinson et al. (2016)	
Finding	**Perceived relevance for the individual participant (U)**
Illustration	No it wasn't [relevant to me] ... because I'd already tried all the things that he said. Participant G. P.58
Finding	**Perceived benefits for the individual participant (U)**
Illustration	"I began to think well am I losing my mind? Honestly. And then when he was going through things, and that's me that, yeah, that's me that ... I thought God it's not me going crazy, you know it was brilliant." P.58
Finding	**Evidence of reconceptualisation (U)**
Illustration	"Because you assume if you're in constant pain its damage to the nerves and something you're doing is aggravating it and just what's causing the constant pain rather than it being (reinjured) and it was explained about the heightened sensitivity. [Cause of the pain] "I believe it's the damage to the disc in my spine" P.59
King et al. (2016)	
Finding	**Varying degrees of reconceptualisation (U)**

Illustration	"Basically I've got a build-up of chemicals around the nerves in the damaged area, I can't remember exactly, I think its cortisone, I can't remember? but basically what it's doing it's exciting the nerve but at the same time it's clinging to the gates on the bottom of your nerves so it's not allowing them to shut properly, so my brain's reacting by saying what the hell's going on. So therefore it's creating more gates, creating more branches of nerves, to try to understand all of the information. And if I've understood it alright this is basically hyper exiting it more so they're in a constant state of excitement . . . It was just really interesting because like I say it was something that I was vaguely aware of but not in that much detail" [Participant J Post-PSE]. "It's degenerative and it's not going to get, you know, I'm not going to get younger or anything." [Participant E Post-PSE]. P.1391
Finding	**Prior beliefs as facilitators of and barriers to reconceptualisation (U)**
Illustration	Participant K actively resisted letting go of her prior beliefs. She seemed able to understand the concepts in PSE but was unwilling or unready to apply them to her pain. "You have your signals going, your brain is assessing what's going on and essentially the pain response may not be proportionate to the underlying whatever. And I suppose I understand that but whether it's that I'm not willing to accept it or whether it's that I can't bear to accept it . . . I just, I can't believe that there's not something [structural] there. Something must have happened, there must be a reason." [Participant K Post-PSE]. P.1391
Finding	**The influence of reconceptualisation on clinical benefit (U)**
Illustration	"It also reassured me that I wasn't going barmy . . . it [PSE] explained that I'm not. What I am experiencing is real and it explained why, without something necessarily being wrong . . . things like the sensitivity is a kind of new thing that no one had offered before" [Participant B Post-PSE]. P.1391
King et al. (2018)	
Finding	**Personal relevance (U)**
Illustration	"…at the time things that she was explaining did make sense and how, you know, things just triggered and how it all moves around your body and your mind and everything…I could relate to it, I could relate to it." P7 post P.5
Finding	**Degrees of reconceptualisation (U)**
Illustration	"…any slight jarring, or anything like that, and it sends my back into spasm, which is like just basically creating a protective shell and it's so used to doing it it's on hypersensitive and I think that's generally why my pain is, and it's just not switching off…(Interviewer: What causes that hypersensitivity?) …I think

	that's all those too much chemicals in my body." P4 post "The reason why I'm in pain? Because of my impingement..." P9 post P.4-5
Finding	**Importance of prior beliefs (U)**
Illustration	Participant 11 was actively opposed to any alternative explanation – indeed she had walked out of a previous consultation when the clinician enquired about social issues. "…all she wanted to know about was my personal life and I walked out because I said I'm not here about anything other than a crash…" P11 pre P.6
Finding	**Perceived benefit of PSE (U)**
Illustration	"…when I was walking quite briskly I just slowed down. I thought, oh calm down you've got plenty of time to get there…where before I would have just carried on…" P7 post P.6
Wijma et al. (2018)	
Finding	**A broad intake (C)**
Illustration	...Because the intake was elaborate, it made them feel that they were able to tell their complete story.... They were confronted with their problems, symptoms and functional limitations for three consecutive hours. During the intake the respondents felt the need to clarify their symptoms to both the healthcare professionals and themselves. By doing this, some already came to an increased awareness and better understanding of their complaints, symptoms, and contributing factors… P.5
Finding	**The healthcare professionals (U)**
Illustration	"I was able to tell from my own perspective how something feels, because I felt heard. I felt I was taken seriously. And when I get that feeling, the other one (healthcare professionals) can get a clearer image of me" Helen. P.5
Finding	**Understandable explanation (U)**
Illustration	"They explained it very well, because at the general practitioner I got a blue booklet about chronic pain. About nerves and how it all works. That your body is actually a burglar alarm set incorrectly. That one I remember, when people ask me how I am doing and what was discovered, I tell them that. It [the metaphor] appeals to the imagination". Wendy. P.6
Finding	**Interaction between the physiotherapist and psychologist (C)**
Illustration	It was noticed by the respondents that there was interplay between the physiotherapist and psychologist during the session.... It made respondents feel like they kept an eye on them, checked if the provided information was understood, and reflected on the respondents' thoughts and emotions.

	Respondents mentioned that this facilitated the understanding of Pain Neuroscience Education and enhanced the translation to the respondent's daily self-management. P.7
Finding	**Awareness (C)**
Illustration	The Pain Neuroscience Education initiated a process of awareness in which the respondents' gained more insight in their symptoms and how to cope with their condition. P.7
Finding	**Consciousness of their body (C)**
Illustration	...they learned how to use their body more appropriately, being more conscious of tense postures and the positive influence of relaxation. Respondents mentioned that they learned to express their limits, even though it is difficult not to cross their boundaries. P.7
Finding	**Gaining self-control (U)**
Illustration	"I think that (the education of) Transcare is good for awareness in that you don't have to think 'Oh, I'm in pain and I can't do anything'. It's about taking more responsibility yourself. (...) Whether physically or mentally". Walt. P.7
Finding	**Finding peace of mind (U)**
Illustration	"And now I found some peace of mind. Like, well, stop searching. There is, so far, nothing more to do (...) So, well, a bit of peace of mind. Some clarity". Helga "The reassurance is, at least that's how I interpreted it, that there is pain but no damage. And that I don't know, I don't know if there is no damage. I'm still in doubt". Rene. P.7
Finding	**Fewer symptoms (C)**
Illustration	Some had fewer symptoms.... Some said it was too early in the process for symptom reduction. Others did not have fewer symptoms but were better able to handle them. P.7
Finding	**Doubt towards the diagnosis and Pain Neuroscience Education (U)**
Illustration	"Look we still have some distrust, but that's because we were sent away by several doctors in the past with the message 'Learn to live with it'. You know. Transcare says, we know what is going on, that's it. We just hope that they are right". John. P.8
Finding	**Disagreement with the diagnosis and Pain Neuroscience Education (C)**
Illustration	They found Pain Neuroscience Education comprehensible but did not recognise it as applicable to themselves. They believed in a physical cause rather than a co-psychological cause for their symptoms. P.8

Finding	**Pain Neuroscience Education can be confronting (C)**
Illustration	They felt the way central sensitisation was explained to them was too confronting and Pain Neuroscience Education should be given more carefully. P.8
Finding	**Insight into symptoms (C)**
Illustration	... they gained insight into the way their behaviour, emotions, and perceptions influenced their pain. Respondents mentioned that they became aware of the influence of previous events on pain... P.8

Legend: *The qualitative findings with illustrations and levels of credibility are shown. Credibility is defined as the fit between the original data and the researcher's interpretations. Credibility is graded as; Unequivocal (U) where the findings are accompanied by an illustration that is beyond reasonable doubt and therefore not open to challenge; Credible (C) where the findings are accompanied by an illustration lacking clear association with it and therefore open to challenge; and Unsupported (U) where the findings are not supported by the data. (Lockwood et al. 2017).*

Findings were grouped according to similarity of concept in categories by J.W. and L.C. independently. They both then discussed their categories and co-created five categories, see Table 5.11. K.C. reviewed the categories to ensure they were grounded in the findings.

Table 5.11 Qualitative Categories with descriptions

Pain Reconceptualisation
The degree to which patients understood the causes and underlying mechanisms driving their pain varied ranging from low i.e., remained biomedical, partial and patchy i.e. some language consistent with the contemporary understanding of pain mixed with some language consistent with the biomedical model, and finally high i.e. where their language reflected a shift in pain beliefs towards the contemporary understanding of pain.
Importance of prior beliefs
The more prior beliefs are entrenched in a biomedical understanding/tissue damage understanding the more difficult it is to shift towards a biopsychosocial understanding.
Patients perceptions of important elements of PSE sessions
Patients identified being able to tell their own story, feeling heard, the quality of the teaching and interactions between, and with the deliverers to be important elements of the PSE sessions. Patients reported that PSE can be confronting and should be delivered more carefully to minimise this.

Importance of relevance
It is important that patients are able to relate the information being delivered to their own circumstance. Failure to do this may result in reduced benefit and understanding of their own pain.
New understanding following PSE can enhance active/helpful coping
Patients reported feeling better able to cope with their symptoms. They reported feeling validated, being more accepting of their condition and their limitations. They reported increased physical activity, body awareness and use of skills such as pacing and relaxation. Not all reports were positive. Some doubted key messages while others felt it was too early to tell if PSE had been beneficial for them.

Legend: *PSE, Pain science education.*

The five categories were then subjected to a meta-synthesis generating a single comprehensive set of two synthesized findings by J.W., L.C., C.R. and D.M.. K.C. reviewed the synthesised findings to ensure they were grounded in the categories.

Synthesised finding 1: A comprehensive assessment allowing the patient to tell their own story should be undertaken to ensure they feel heard. This will also facilitate the identification of their prior understanding and beliefs. PSE can then be delivered in a manner relevant to that patient. In addition, patients clarifying their story to a healthcare professional may raise their awareness of the biopsychosocial nature of pain, promoting readiness to engage with PSE.

A meta-aggregative flow chart showing how the findings were combined to form categories and synthesised finding 1 is shown in Figure 5.12.

Synthesised finding 2: Achieving pain reconceptualisation can enhance patients' ability to cope with their condition. To promote pain reconceptualisation PSE should be delivered by health care professionals (HCPs) skilled in PSE delivery and facilitation of group, or one-to-one interactions with, and between, patients and other HCPs. Progress towards reconceptualisation should be monitored throughout, tailoring concepts that have not been accommodated to ensure relevance of PSE to the individual.

A meta-aggregative flow chart showing how the findings were combined to form categories and synthesised finding 1 is shown in Figure 5.13.

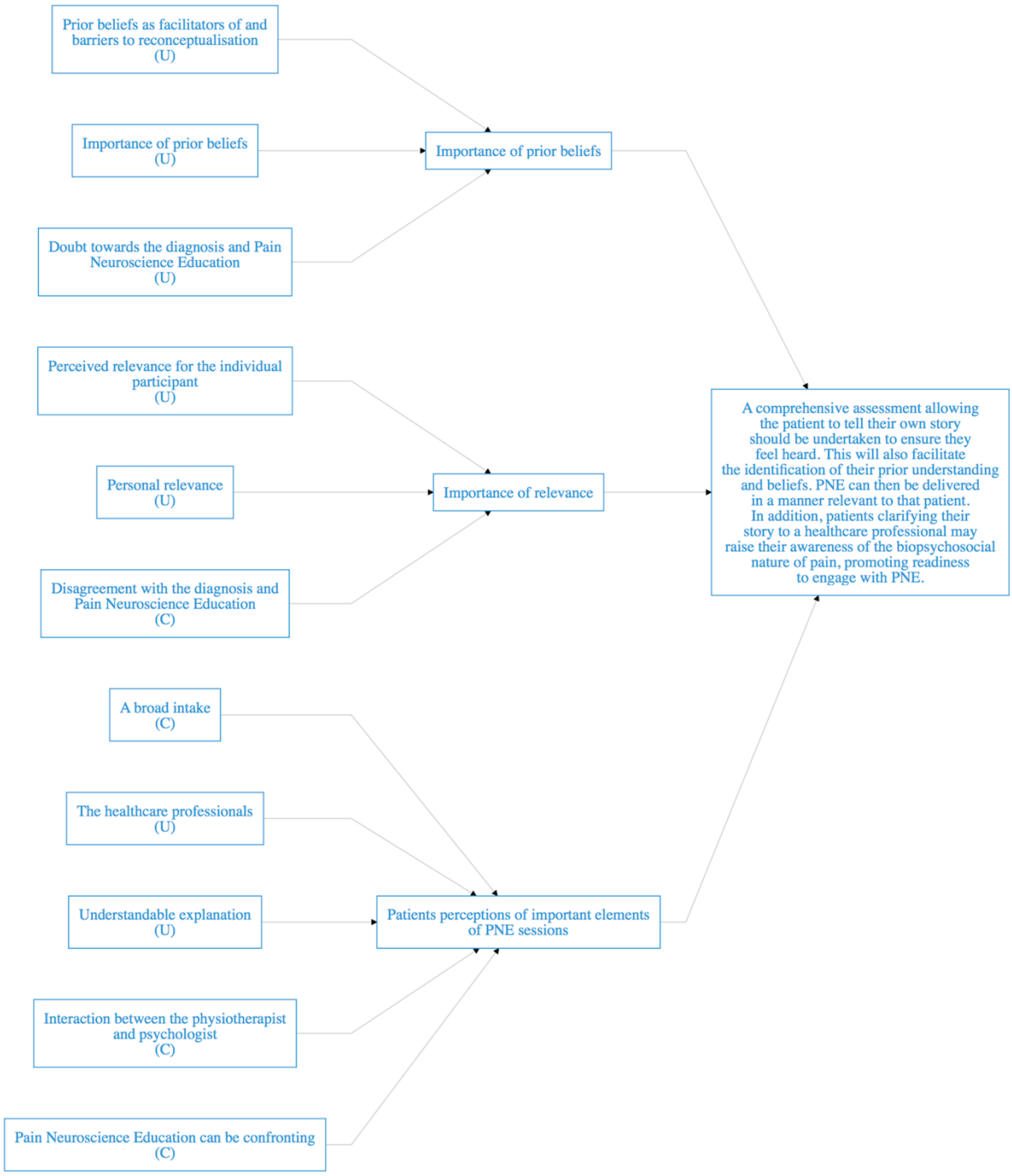


Figure 5.12 Synthesised finding 1 meta-aggregative flow chart

Legend: *The qualitative findings with their levels of credibility are shown, linked to the categories and finally the synthesised finding. Credibility is graded as; Unequivocal (U) where the findings are accompanied by an illustration that is beyond reasonable doubt and therefore not open to challenge; Credible (C) where the findings are accompanied by an illustration lacking clear association with it and therefore open to challenge; and Unsupported (U) where the findings are not supported by the data. (Lockwood et al. 2017).*

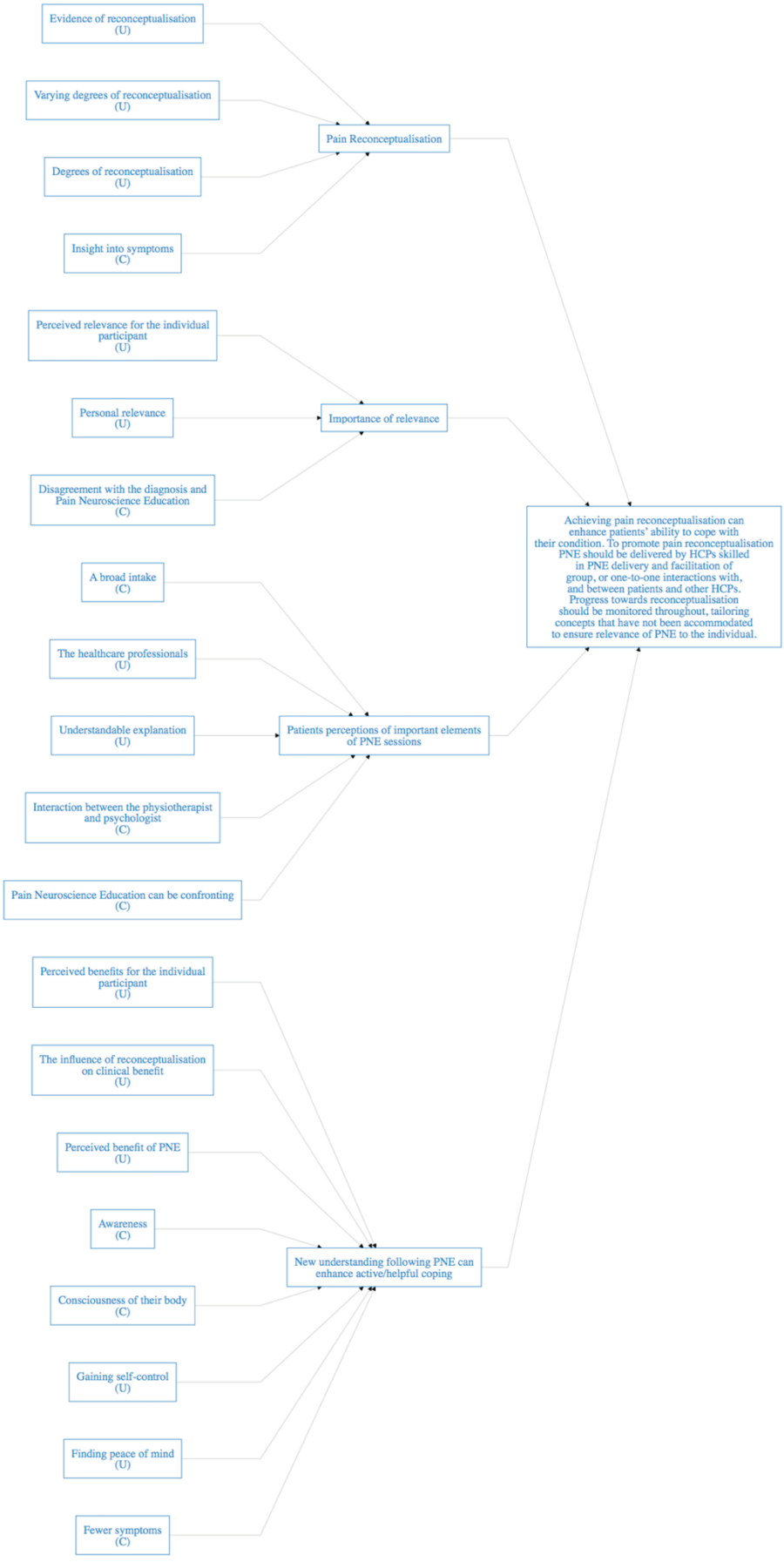


Figure 5.13 Synthesised finding 2 meta-aggregative flow chart

Legend: *The qualitative findings with their levels of credibility are shown, linked to the categories and finally the synthesised finding. Credibility is graded as; Unequivocal (U) where the findings are accompanied by an illustration that is beyond reasonable doubt and therefore not open to challenge; Credible (C) where the findings are accompanied by an illustration lacking clear association with it and therefore open to challenge; and Unsupported (U) where the findings are not supported by the data. (Lockwood et al. 2017).*

5.6 Discussion

This mixed methods review aimed to undertake a segregated synthesis of quantitative and qualitative studies to investigate the clinical effectiveness, and patients' experience of, PSE for people with CMP. Data from 12 RCTs (n = 755 participants) demonstrated that PSE can reduce pain, disability, pain catastrophising and kinesiophobia in the short-to-medium term. Data from four qualitative studies (n = 50 participants) identified several key components important for enhancing the patient experience of PSE such as allowing the patient to tell their own story. These components can enhance pain reconceptualisation, which appears to be an important process to facilitate patients' ability to cope with their condition.

An improvement in clinical outcomes of 10% has been proposed as a minimally clinically important difference (MCID) in the recent NICE guidelines for back and radicular pain (NICE, 2016). Pooled data showed a reduction in pain and disability in favour of PSE ranging from 4 to 8 out of 100 units, which are likely of little clinical benefit. In contrast, pooled data showed a reduction in pain catastrophising in favour of PSE of 5.26 units (CI: -10.59 to 0.08) in the medium term (A change of 5.2 units [10%] is considered clinically meaningful) and a reduction in kinesiophobia of 13.55 out of 100 units (CI: -25.89 to -1.21) in the short term. Thus, in the short to medium term clinically meaningful improvements were seen in these psychosocial outcome measures.

Previous narrative reviews have concluded that there is '*compelling*' and '*strong*' evidence that PSE positively effects pain and disability (Louw et al 2011; Louw et al 2016), which contrasts with our findings likely due to the differences in methodological approach and the inclusion of a number of additional studies not published at the time of those previous reviews (Lluch et al 2018; Bodes et al. 2018; Malfliet et al. 2018). Moseley and Butler (2015) were more reserved in the conclusions of their narrative review stating that *alone PSE is not a viable intervention for improving pain and disability*. This is broadly in keeping with our findings.

Our findings for short-term pain relief (-5.91/100mm) are similar in magnitude to the effect reported by Clarke et al. (2011) (-5/100mm) and Wood and Hendrick, (2018) (-0.73/10). In contrast, Tegner et al. (2018) reported an improvement above the MCID (-1.03/10), which is more in keeping with previous narrative reviews (Louw et al 2011; Louw et al 2016). Our findings for pain relief in the medium-term (-6.27/100mm) also differ from Tegner et al. (2018) who found a clinically relevant effect (-1.09/10). Our findings for short-term disability (-4.09/100 units) show smaller effects compared to Wood and Hendrick, (2018) (-2.28/24) and Tegner et al. (2018) (-1/10). In contrast, our findings for medium-term disability (-8.14/100 units) are similar in magnitude to Tegner et al. 2018 (-0.82/10).

Previous narrative reviews have reported favourable findings for PSE reducing pain catastrophising (Clarke et al. 2011; Louw et al 2011; Louw et al 2016). Our findings in part support this previous work finding PSE to produce a clinically meaningful improvement in pain catastrophising in the medium-term, though not the short-term. It may be that in the case of certain psychosocial measures there is a time lag in the effect. We can only hypothesise as to why this lag may occur though it may be that a period of reflection and experimentation with the knowledge gained from PSE is needed to facilitate pain reconceptualisation and/or clinical improvements.

For kinesiophobia previous narrative reviews have reported inconclusive findings with mixed results (Louw et al 2011; Louw et al 2016) and no clear conclusions made. This differs to our work where we found PSE to have a greater effect on kinesiophobia than any other measure investigated in the short term (-13.55%). This is likely due to the inclusion of three recently published studies (Lluch et al 2018; Bodes et al. 2018; Malfliet et al. 2018), two of which found PSE to have a particularly large beneficial effect for kinesiophobia. Our findings for kinesiophobia in the short-term are greater than that of Tegner et al. (2018) (-5.73/68) and Wood and Hendrick (2018) (-4.72/52).

The current work builds on the three previous meta-analysis on PSE (Clarke et al. 2011; Wood and Hendrick, 2019; Tegner et al. 2018). First, we registered a protocol prior to commencing the review, published on PROSPERO (CRD42017068436). Second, this is the first meta-analysis where the pooled data included the minimum five recommended studies to ensure sufficient statistical power (Jackson and Turner 2017). Third, the current work could isolate the effect of PSE through the inclusion of studies that compared (i) PSE to true control (or usual care), (ii) concomitant studies, where PSE has been delivered in addition to another intervention where that other intervention has been received by both groups, (iii) head-to-head studies where PSE has been compared to another active intervention. Finally, the current

review meta-analysed data from studies' whose samples included heterogeneous CMP. This is the first meta-analysis to be performed on this sample in PSE. The second, third and final points may also go some way in explaining the differences in pooled effects found between the current and past reviews (Clarke et al. 2011; Wood and Hendrick, 2019; Tegner et al. 2018).

There was substantial heterogeneity between studies. To explore this heterogeneity a series of meta-regressions were undertaken. Greater effects for pain (short and medium-term), disability (medium-term) and pain catastrophising (short and medium-term) were seen when PSE was combined with another intervention compared to PSE delivered in isolation. The steepness of the slopes indicated that the unit improvements in pain and disability for combined interventions was clinically relevant. Similarly, greater effects for disability (medium-term) and pain catastrophising (medium-term) were seen when longer durations of PSE were delivered. However, the slopes of the meta-regressions were shallow, indicating that the unit improvements in these outcomes for longer duration interventions are small and of questionable clinical relevance. Our findings are in keeping with Wood and Hendrick (2018) and a recent doctoral thesis meta-analysis reporting PSE combined with another therapy to be more effective than PSE alone for pain and disability in individuals with CLBP (Wood and Hendrick 2018; Yun, 2017). This finding is also in agreement with two previous narrative reviews (Moseley and Butler, 2015; Louw et al 2016). However, the combination of PSE with other interventions should be done in a co-ordinated way to ensure that patients do not get mixed-messages potentially reducing the effectiveness of PSE (Ryan et al. 2010).

The results of our meta-regressions are in line with previous reviews within the field of PSE (Wood and Hendrick 2018; Yun, 2017; Moseley and Butler, 2015; Louw et al 2016 and Ryan et al. 2010) suggest that PSE may be most effective when integrated with other active interventions rather than alone. Furthermore, PSE was always intended to be part of a multimodal approach (Gifford, 1998; Moseley and Butler, 2015). Interestingly, out of the studies included within our meta-analysis Von Bertouch et al. (2011) demonstrated the greatest mean difference between groups for both primary outcomes at the medium term (Pain -23/100, disability -27/100) where they compared PSE plus a pain management programme (PMP) to Back Book based education plus a PMP. Arguably, a PMP is the most comprehensive, multimodal intervention within the field on pain management. A variety of methods are used in PMPs for directly and indirectly producing behaviour change including methods based on cognitive and behavioural therapy, learning and conditioning processes, skills training, physical exercise and education. Patients practice the skills learned on the program and integrate them into their daily routines in order to become an expert in their

application (The British Pain Society, 2013). A PMP is implemented by an interdisciplinary team according to broadly cognitive behavioural principles with the aim of improving the physical, emotional and social components of health and function in individuals with CMP (The British Pain Society, 2013). Given that where there is significant impact on physical, psychological and social function, PMP based on cognitive behavioural principles are recommended for those with CMP (The British Pain Society, 2013), it is perhaps unsurprising that combing PMP and PSE produced the largest effects out of all studies for the primary outcomes. Theoretically they should be naturally facilitative.

There are a number of methodological issues regarding Von Bertouch et al. (2011) which should be highlighted. 1) Lorimer Moseley is a co-author of the book Explain Pain (Butler and Moseley, 2003) for which the PSE material used in Von Bertouch et al. (2011) was based, thus there is a risk of bias in favour of the PSE group. Groups that have a potential conflict of interest tend to publish research which has more positive findings than those produced by neutral groups (Kjaergard and Als-Nielsen, 2002; Lexchin et al., 2003). 2) Function was assessed using self-report questionnaires, which is in keeping with previous PMP studies (Chipchase and Hill, 2012) however, this provides information which may not necessarily reflect the real capability of the patients' performance (Smeets et al., 2006). 3) Pain reconceptualsation was assessed using self-report questionnaires including the Survey of Pain Attitudes (Jensen et al., 1987), Pain catastrophising scale (Sullivan et al., 1995) and the Biology of Pain questionnaire (Moseley, 2003), which whilst accepted as valid questionaries in their own right they lack sufficient scope to explore the extent of reconceptualisation central to PSE (Robinson et al., 2016). Qualitative methods allow the exploration of a person's lived experience (first-hand insights and perceptions from someone who has experience of the phenomenon of interest) so that a deeper insight into their understanding of a phenomenon is achieved (Magilvy and Thomas, 2009). Qualitative interviews provide a richer, more in depth analysis of issues than a self-report questionnaire helping to uncover personal, complex and often conflicting beliefs (Pope and Mays, 1995). Three out of four qualitative studies included within the qualitative component of this review explored PSE alone (Robinson et al. 2016; King et al. 2016; King et al. 2018). The remaining study explored PSE within a transdisciplinary setting. Here PSE was offered +/- psychology, +/- physiotherapy, +/- medication. Ryan et al. (2010) highlight the importance of delivering interventions in a co-ordinated way to ensure that patients do not get mixed-messages potentially reducing the effectiveness of PSE. It is unclear if PSE was co-ordinated in this way.

There appears to be a gap within the literature exploring a PSE integrated with a PMP using qualitative methods. The use of qualitative methods would facilitate an in depth exploration of

the mechanisms by which a PSE informed PMP works, the facilitators of and barriers to the intervention, and identify potential areas to improve it (Barbour, 2000). Furthermore, there is a need to test this intervention rigorously using objective measures of function in addition to patient reported outcome measures under randomised controlled trial conditions to inform clinical practice. This also needs to be conducted by a research group that has no financial interest in PSE. The Medical Research Council state that during the development and evaluation of a complex intervention (in this case a PSE informed PMP), it is important to undertake feasibility work, to investigate the components of RCT methodology prior to a full-scale trial (Craig *et al.*, 2008). Chapter 7 will undertake a mixed-method feasibility study aiming to develop a feasible research protocol for a mixed-methods RCT investigating the efficacy and experiences of a PSE informed PMP.

The two synthesised findings were split into principles to facilitate the mixed-methods analysis. See Table 5.12.

Table 5.12 Principles of synthesised findings

Synthesised finding	Principles
1	**S1a)** A comprehensive assessment allowing the patient to tell their own story ensuring they felt heard. **S1b)** Identification of prior understandings and beliefs to facilitate the delivery of PSE in a manner relevant to the patient. **S1c)** A comprehensive assessment allowing the patient to clarify their story to a HCP to raise their awareness of the biopsychosocial nature of pain.
2	**S2a)** PSE delivered by a HCP skilled in PSE delivery **S2b)** PSE delivered by a HCP skilled in facilitation of group, or one-to-one interactions with, and between patients and other HCPs **S2c)** Progress towards reconceptualisation was monitored throughout tailoring concepts that have not been accommodated to ensure relevance of PSE to the individual. **S2d)** Achieving pain reconceptualisation can enhance patients' ability to cope with their condition

Legend: *S1, Synthesised finding 1. S2, Synthesised finding 2. HCP, Health care professional. PSE, Pain science education.*

The key principles shown in Table 5.12 may be important for enhancing the patient experience of PSE. Principle S1a emphasises the importance of undertaking *a comprehensive assessment allowing the patient to tell their own story ensuring they felt heard*. This finding is supportive of previous qualitative research that has explored the conceptions of patients with low back pain (n = 17) about their encounters in the health care system (Holopainen *et al.*, 2018). In this study the patients' initial physiotherapy appointments were recorded and they were later shown the video sequence that they were involved in and were invited to reflect on their experience. Participants it was important when the HCP gave them "*time to tell their story, even when it went a little off topic"*, and found it unhelpful when the HCP did not listen to them (Holopainen et al. 2018 p. 272).

It was difficult to discern if the principles identified within the qualitative work were used by the included individual RCTs given the information provided. Only two principals were identified across the RCTs (S2a and S2c). Principal S2a was identified in 6 RCTs where the skill of the PSE deliverer was described using terms such as 'experienced' (Bodes et al. 2018; Lluch et al 2018; Moseley et al. 2004), 'with clinical experience' (Malfliet et al. 2018), and 'specially trained' (Van Oosterwijck et al. 2013; Bertouch, McAuley and Moseley, 2011). Whilst we interpreted these terms all to mean skilled in PSE delivery, we accept that it is possible that a HCP could be 'specially trained', 'experienced' or have 'clinical experience' and still not be 'skilled' in the delivery of PSE. Four RCTs monitored pain reconceptualisation throughout PSE, tailoring concepts not understood to the individual (principal S2c). Pain reconceptualisation was monitored via participant questions in two RCTs (Tellez-Garcia et al. 2015; Malfliet et al. 2018), whilst the two other RCTs used questionnaires (Lluch et al. 2018; Van Oosterwijck et al 2013).It is unclear if the principles identified as important for optimising PSE within the qualitative component of this review were used within the included RCTs. Thus, it is possible that the included RCTs are underestimating the potential effect of PSE delivered well.

The qualitative synthesis suggests that PSE is helpful for coping with CMP when pain reconceptualisation is achieved (S2d). Our meta-analysis found PSE to produce clinically significant reductions in kinesiophobia (short-term) and pain catastrophising (medium-term). Although not a direct measure of pain reconceptualisation, they do provide an insight into how an individual understands their pain, and how threatened they feel because of it. We can infer that one of the ways PSE is helpful for coping is by reducing the threat value of pain. This less

threatening and fearful state of being (reduced fear of movement and reduced catastrophic thinking) may change a patients' priority away from pain control towards pursuit of valued life goals, breaking the cycle of fear-avoidance-interference-negative affect-pain illustrated by the fear-avoidance model of pain (Vlaeyen, Crombez and Linton, 2016). Furthermore, the patient may be more open to active interventions such as exercise, where previously this would have been avoided due to fear of pain, thus promoting recovery.

PSE usually includes pacing and graded exposure, such as the twin peaks model in the Explain Pain manual (Butler and Moseley, 2003). Importantly, this goes some way in showing the patient *how* to engage in their valued life goals/exercise whilst avoiding the Boom-Bust cycle. It is likely that working out how to engage in valued life goals/exercise will be challenging for patients, and thus may take time before progress is made in this domain. This is in part reflected in the quantitative component of this review where disability approached clinical significance in the medium term, but not the short term. As patients begin to master the skills of pacing and graded exposure, their engagement in valued life goals/exercise may increase, with associated decreases in perceived disability.

The quantitative component of our review focused on the mean intervention/treatment effect. This focus on mean intervention effect whilst common in research on pain interventions (Searle, et al. 2015; Kamper et al. 2015; Furlan et al. 2006), could have obfuscated important inter-individual differences in response to PSE (King, Neil A. *et al.*, 2008; Williamson, Atkinson and Batterham, 2018). The quantitative component of this review suggests there is a variety of responses to PSE with wide 95% CI and 95% prediction intervals (PI) for all outcomes suggesting PSE may produce clinically important changes for some patients and not others. Short term pain 95% CI: -13.75 to 1.93, 95% PI -31.51 to 19.69; medium term pain 95% CI: -18.97 to 6.44, 95% PI: -48.67 to 36.14; short term disability 95% CI: -7.72 to -0.45, 95% PI: −15.42 to 7.25; medium term disability 95% CI: -15.60 to -0.68, 95% PI: −32.62 to 16.34; short term pain catastrophising 95% CI: -6.01 to -0.65, 95% PI: −12.61 to 5.96; medium term pain catastrophising 95% CI: -10.59 to 0.08, 95% PI: −23.01 to 12.49; and short term kinesiophobia 95% CI: -25.89 to -1.21, 95% PI: −56.06 to 28.96. The qualitative component of this review suggests that PSE, through reconceptualisation can enhance patients ability to cope with their condition (principle S2d) but this may not work for everyone alluding to the possibility of individual differences in response to PSE. However, clinically relevant inter-individual response variation should first be conducted using appropriate methodology (Atkinson and Batterham 2015; Williamson, Atkinson and Batterham, 2017; Williamson, Atkinson and Batterham, 2018; Atkinson, Williamson and Batterham 2019) to confirm if such inter-individual responses truly exist. If individual differences are present, and predictors of individual

response are identified, then PSE could be tailored to the individual optimising its effect (Williamson et al. 2018). The next chapter in this thesis (Chapter 6) aims to conduct a systematic review and meta-analysis of the available research to quantify the 'true' inter-individual variation in pain, disability and psychosocial outcomes in response to PSE.

Since the date of the search for Chapter 5 (14/06/2018) to 12/09/2022, via regular searches of the literature, JW is aware of the publication of two RCTs but no qualitative studies that would have met the inclusion criteria for this review (Saracoglu *et al.*, 2020; Khosrokiani *et al.*, 2022). Khosrokiani et al. (2022) compared the effectiveness of PSE (n = 40) versus biomechanics education (n = 40) for adults with chronic non-specific neck pain. In line with the findings of Chapter 5 for kinesiophobia, Khosrokiani et al. (2022) found statistically significantly (p = <0.05) greater effects in the PSE group with a small effect size (Cohen's d= 0.34; 95% confidence interval [CI] 0.11–0.51) compared to the biomechanics group. Also in line with Chapter 5 there was no statistically significant difference between groups for pain intensity. The findings of Khosrokiani et al. (2022) add confidence to the findings of Chapter 5.

Saracoglu et al. (2020) compared the effectiveness of three groups in adults with chronic lower back pain 1) PSE + manual therapy + home exercise (n = 20); 2) Manual therapy + home exercise (n = 19); 3) Home exercise (n = 18). Group 1 & 2 but not 3 meet the criteria for Chapter 5 with group 1 & 2 being concomitant in design (where PSE was delivered in addition to another intervention where that other intervention was received by both groups). In line with the findings of Chapter 5, at 3 months post intervention Saracoglu et al. (2020) found statistically significantly (p = <0.05) greater beneficial effects at 3 months post intervention in the group with PSE for Kinesiophobia (Tampa Scale for Kinesiophobia [17-68] 4.63 (1,47 to 7,80) p < .001*). Furthermore, in alignment with Chapter 5 there was no significant difference between groups at 3 months for disability ((Back performance scale [0-15] 0.35 (−1,13 to 1,83) p = .88); Oswestry disability index [0-100] 1.91 (−3,46 to 7,29) p = .67)). These findings add confidence to the findings of Chapter 5.

In contrast to Chapter 5, Saracoglu et al. (2020) found statistically significantly (p = <0.05) greater beneficial effects for the PSE group for pain intensity (Numerical pain rating scale [0-10] Mean Difference (95% CI) 1.39 (0,27 to 2,51) p = .01*). The dose of PSE in Saracoglu et al. (2020) was 4 x ~45 minutes delivered in a one-one format. There was tentative suggestion within the findings of Chapter 5 that greater effects may occur where PSE is delivered over a longer duration. Furthermore there is evidence that PSE is more effective where it is delivered one-one compared to group delivery (Moseley, 2003). The dose and one-one delivery of PSE

in Saracoglu et al. (2020) may explain the beneficial effects of PSE for pain intensity which contrasts to the findings of Chapter 5.

One could argue there is a need to update Chapter 5 given the new publications. However the Cochrane Collaboration who are arguably the world leader in health related systematic reviews do not routinely update their systematic reviews within 7 years of publication, and there is evidence that when such updates are undertaken they rarely lead to changes in conclusions (Bashir, Surian and Dunn, 2018). This chapter published in a high impact journal (Watson *et al.*, 2019) in its current form demonstrates competence in critical review of quantitative and qualitative literature and has provided novel contributions to the evidence base fulfilling the requirements of a Ph.D.. Given the significant resource that would be required to formally update the review, and the evidence suggesting an update is unlikely to change its conclusions, an update is not considered necessary at this point and is beyond the scope of this thesis but would be considered for post-doctoral work.

5.7 Strengths and Limitations

One limitation of this review was that it did not look at economic outcomes such as cost effectiveness. A recent RCT on acute low back pain (and thus not eligible for this review) by (Traeger *et al.*, 2019) found PSE to reduce health care utilisation at 3 months (but not 12 months) compared to control. Louw et al. (14/16) and Moseley (2002) found PSE to reduce healthcare usage within a CMP sample and therefore may be a cost-effective intervention, an important consideration given the large financial burden associated with CMP.

The heterogeneity of design, participants, outcome measures, delivery methods and comparators could be considered a limitation of this review. Some may question the validity of pooling such data. However, by reporting I^2 and Tau we have been transparent about the statistical heterogeneity and we have explored the heterogeneity using meta-regression.

Another limitation was that only studies published in English were eligible for inclusion as no facility for translation was available. Thus, important data from non-English studies may have been missed.

Lack of response and/or inadequate reporting in the original studies resulted in the SD of change being estimated for four RCTs reporting on pain and disability, five studies reporting on pain catastrophising and three studies reporting on kinesiophobia. While this is accepted Cochrane review practice it is still an estimation.

The quantitative component of this review focused on the mean intervention/treatment effect. There seemed to be a wide variety of responses to PSE with wide 95% CI and 95% prediction intervals (PI) for all outcomes suggesting PSE may produce clinically important changes for some patients and not others. The focus on mean intervention effect in this review could have obfuscated important inter-individual differences in response to PSE (King et al. 2008; Williamson et al. 2018). The qualitative component of this review suggests that PSE can enhance patients ability to cope with their condition (principle S2d) but this may not work for everyone alluding to the possibility of individual differences in response to PSE. There is a need to test this more robustly and Chapter 6 will look to address this limitation by investigating the Inter-individual differences in the responses to pain science education in adults with chronic musculoskeletal pain.

There was a paucity of qualitative studies with three of those coming from our group. The studies from our group were assessed for quality by members of the review team who were not authors on those original qualitative studies to minimise bias.

5.8 Implications for policy and practice

The qualitative component of this review identified several important components for optimising the patient experience such as the need for a skilled clinician to deliver the intervention with expertise in group facilitation and/or one-to-one interactions. These have implications not just for how PSE should be delivered but also for the training of the education provider. The quantitative findings also provide useful direction for how PSE could be delivered to enhance effectiveness such as delivering longer total durations of PSE and combining PSE with other interventions.

5.9 Implications for research

Given the apparent additional effects of longer durations of PSE and delivering PSE in combination with other interventions, future research should explore the dosage response to PSE and combinations with other interventions to provide guidance on the development of optimal interventions. Our findings highlight that combining PSE with a PMP may be a particularly fruitful avenue to explore. Future research should investigate the effectiveness of a PSE informed PMP. There is also a need for a qualitative study to explore the extent and nature of pain reconceptualisation following a PSE informed PMP. Furthermore, mixed-methods research is needed to explore if there is a relationship between the extent and nature

of pain reconceptualisation and changes in clinical outcomes. In addition, the qualitative component of this review has identified a number of components which optimise the patient experience. Quantitative studies are needed to explore what influence optimising these components have on patient outcomes. More studies investigating cost-effectiveness are needed. There is a need for more RCTs to investigate the long-term effectiveness of PSE.

5.10 Conclusions

This mixed-methods review undertook a segregated synthesis of quantitative and qualitative studies to investigate the clinical effectiveness, and patients' experience of, PSE for people with CMP. Electronic databases were searched for studies published between 01/01/2002 and 14/06/2018. Twelve randomised controlled trials (n = 755) that reported pain, disability and psychosocial outcomes and four qualitative studies (n = 50) that explored patients experience of PSE were included. The meta-analysed pooled treatment effects for PSE vs control had low clinical relevance in the short-term for pain (-5.91/100; 95% confidence interval [CI], -13.75 to 1.93) and disability (-4.09/100; 95%CI -7.72 to -0.45) and the medium-term for pain (-6.27/100; 95%CI -18.97 to 6.44) and disability (-8.14/100; 95%CI -15.60 to -0.68). The treatment effect of PSE for kinesiophobia was clinically relevant in the short-term (-13.55/100; 95%CI -25.89 to -1.21) and for pain catastrophising in the medium-term (-5.26; 95%CI -10.59 to 0.08). Meta-synthesis of 23 qualitative findings resulted in the identification of two synthesized findings that identified several key components important for enhancing the patient experience of PSE such as allowing the patient to tell their own story. These components can enhance pain reconceptualisation, which appears to be an important process to facilitate patients' ability to cope with their condition. The quantitative component of this review focused on the mean intervention/treatment effect which could have obfuscated important inter-individual differences in response to PSE (King et al. 2008; Williamson et al. 2018). The wide 95% CI and 95% PI for all outcomes suggests PSE may produce clinically important changes for some patients and not others. Furthermore the qualitative component of this review alluded to the possibility of individual differences in response to PSE, with principle S2d highlighting that PSE can enhance patients ability to cope with their condition, but this may not work for everyone. Therefore future research needs to investigate possible inter-individual differences in response to PSE which will be undertaken in the next chapter of this thesis.

Chapter 6: Inter-individual differences in response to pain science education a systematic review and meta-analysis

Note: This chapter has been published, and cited 14 times as of 21/11/2022.

Watson, J.A., Ryan, C.G., Atkinson, G., Williamson, P., Ellington, D., Whittle, R., Dixon, J. and Martin, D.J., 2021. Inter-individual differences in the responses to pain neuroscience education in adults with chronic musculoskeletal pain: A systematic review and meta-analysis of randomized controlled trials. *The Journal of Pain*, 22(1), pp.9-20.

This chapter brought a novel method to pain science for calculating inter-individual differences in response to a treatment. This is conducted within the context of a systematic review and meta-analysis on PSE. The chapter highlighted how using erroneous methods for calculating inter-individual differences can drastically change conclusions when compared to appropriate methods. The protocol was published on PROSPERO (CRD42017068436).

J.W. led the development of this review contributing 80% to the overall body of work. Furthermore J.W led on every sub-component of the work. The other 20% of the review was developed by several academics from Teesside University and other institutions. Table 6.1 lists those involved and the tasks they conducted.

Table 6.1 Contribution of authors to mixed-methods review

Name/Job title/Employer/Role in the review	Tasks completed
James Watson Ph.D. Student Teesside University	Development of review questions Development and registration of protocol Formulation of search strategy Sifting of all search results and retrieval of full texts Reviewed full text for inclusion

Lead Author	Assessment of methodological quality of included qualitative and quantitative papers Data extraction Contacted study authors for missing information Preparation of quantitative data for analysis Analysis Preparation of review for comments and distribution to co-authors Updated review and submitted for publication
Prof. Cormac Ryan Professor of Rehabilitation Teesside University Co-author	Development of review questions Contributed to development of protocol Assessment of methodological quality of included papers Analysis Commented on and made changes to publication draft and chapter
Prof. John Dixon Professor of Applied Physiology and Rehabilitation, and the Associate Dean (Research & Innovation) Teesside University Co-author	Development of review questions Contributed to development protocol Commented on and made changes to publication draft and chapter
Prof. Greg Atkinson Professor of Health Sciences and Biostatistics Research Teesside University	Contributed to development of protocol Preparation of quantitative data Analysis Commented on and made changes to publication draft

Co-author	
Dominic Ellington Senior Physiotherapist North Tees and Hartlepool NHS Foundation Trust Co-author	Assisted with sifting of search results Reviewed full texts for inclusion Commented on and made changes to publication draft
Robbie Whittle Senior Physiotherapist North Tees and Hartlepool NHS Foundation Trust Co-author	Assisted with sifting of search results Reviewed full texts for inclusion Commented on and made changes to publication draft
Dr Philip Williamson Research associate Teesside University Co-author	Contributed to development of protocol Preparation of quantitative data Analysis Commented on and made changes to publication draft
Prof. Denis Martin Professor of Rehabilitation and Director of the Centre for Rehabilitation Sciences Teesside University Co-author	Development of review questions Contributed to development of protocol Assessment of methodological quality of included quantitative papers (3rd reviewer) Commented on and made changes to publication draft and chapter

6.1 Introduction

Pain science education (PSE) is an educational approach used in the management of chronic pain. PSE aims to reconceptualise an individuals' understanding of their pain as less threatening to facilitate rehabilitation (Moseley, 2007). Since its inception PSE has become increasingly popular in clinical practice (Moseley and Butler, 2015). Chapter 5 of this thesis conducted a mixed-methods systematic review and meta-analysis on the effectiveness of PSE for adults with chronic musculoskeletal pain (CMP) (Watson et al. 2019). Quantitatively there was no evidence to indicate that PSE results in clinically important changes over control for pain or disability. In contrast there was moderate quality evidence that PSE produces small clinically important changes over control for pain catastrophising and kinesiophobia. The qualitative component of the review, specifically synthesised finding 2d highlighted that achieving some degree of pain reconceptualisation following PSE can enhance peoples' ability to cope with their condition, but this may not work for everyone.

One question that arose during Chapter 5 was whether PSE may be effective for some types of people, implying that there may be some individual differences in response to PSE (Watson et al. 2019). The quantitative component of Chapter 5 focused on the mean intervention/treatment effect. This focus on mean intervention effect whilst common in research on pain intervention (Furlan et al. 2006; Kamper et al. 2015; Searle, et al. 2015), could have obscured important inter-individual differences in response to PSE (King et al. 2008; Williamson et al. 2018). Such response heterogeneity is particularly important within the context of precision medicine, an increasingly popular field which encompasses 'tailor-made' therapies based on the person's individual response to a given intervention (Senn, Rolfe and Julious, 2011). This individualised approach to medicine aims to improve the quality of care and reduce costs (Spear, Health-Chiozzi and Huff, 2001). The potential importance of a tailored approach has been highlighted by some of the qualitative studies on PSE from Teesside University. The relevance of PSE to the individual (i.e., how tailored the material is to that individual) appears to be an important factor in the success of PSE (Robinson et al. 2016; King et al. 2016; King et al. 2018; Watson et al. 2019). Where PSE was reported to be relevant, people reported greater perceived benefit. The opposite was found where PSE was deemed not relevant (Robinson et al. 2016; King et al. 2016; King et al. 2018). The latter is illustrated by participant 12 from King et al. (2018) who did not undergo any pain reconceptualsation and did not find the session relevant to them;

". . .I didn't get the chance to explain what my problems were. . .it was about pain in general but it wasn't targeted at myself or anybody specific, it was just like everybody." (King et al. 2018 p. 5 Participant 12 post PSE)

Some researchers (Pires et al. 2016) have attempted to complement the quantification of mean treatment effects with a quantification of how many people in each intervention group change above or below a pre-set threshold, termed sample responder counts. Pires et al. (2016) used this method to investigate the effect of PSE plus aquatic exercise compared to aquatic exercise alone. The proportion of patients who experienced a greater than 50% reduction in pain was calculated. The proportion of patients meeting the 50% threshold in the PSE + exercise group raised from 47% at 3 weeks to 70% at 12 weeks. This proportion raised from 25% to 34% in the exercise alone group. The authors concluded that *"Individual response analysis showed that the patients receiving EDU+EXE achieved an early response to pain, had higher response rates at all the endpoints and were also more likely to achieve a sustained response over time compared to those receiving EXE only."* (Pires et al. 2016). The authors go on to advocate for future studies to investigate patient-level responses in addition to mean treatment effects to enhance clinical decisions.

Crucially though, there are several problems with the approach of responder counting used by Pires et al. (2016). Firstly, and most fundamental with sample responder counting in a parallel groups RCT is the 'counterfactual'. It is not possible to identify which individual is a responder in the treatment group, because it is not known what would have happened to that individual if, they had been in the control group (Senn, 2016b). Furthermore, counting the number of people who respond in a sample is compromised by random within-subject variation between time points. The individual differences in this within subject variation can be particularly misleading within the context of responder counts. There are always some individuals who show a large degree of random variability between baseline and follow up time points, whilst others have relatively little. Those individuals where this variability is large in the positive direction results in these individuals categorised as responders, and those in the negative direction as adverse responders. Where an individual has relatively little random variability these individuals are categorised as non-responders. Counting the number of responders in the experimental and control group could be proposed as rectifying this problem, however this is also misleading. In their hypothetical study, Atkinson, Williamson and Batterham, (2019) used a simulated data set where the sample had no individual differences in treatment response. Despite no treatment response heterogeneity being present at all, the method of responder counting resulted in differences in the number of responders, non-responders, and adverse responders between groups. The only factor that was different was the mean group difference. This suggests that responder counts may merely reflect differences in group mean response rather than individual differences in response, and thus are not appropriate to explore response heterogeneity within the context of precision medicine. Another problem with responder counting is reduced statistical power relative to an analysis

on the original scale. Snappin and Jiang, (2007) showed that to ensure statistical power of 90% the sample size requirements for responder analysis was approximately 60% higher compared to using mean difference. In summary responder counting lacks statistical power and may merely reflect within-subject random variation between timepoints and/or group differences in mean change (Atkinson, Williamson and Batterham, 2019). These sample responder counts tell us little about whether different people respond to different degrees to the same intervention, which is one of the fundamental questions in precision medicine. Should any inter-individual differences be falsely identified using the above-mentioned methods, any follow-up analysis to explore potential moderators of the intervention effect to explain the individual differences in response are therefore unwarranted (Atkinson and Batterham, 2015; Atkinson, Williamson and Batterham, 2019). Subsequent follow-up studies on the same participants is a waste of resources, and potentially unethical, if no true inter-individual differences in response exist to explain.

Inter-individual differences in response can be quantified by comparing the SDs of the baseline-to-follow-up changes between the experimental and control groups (Atkinson and Batterham, 2015; Cortés et al., 2018). The difference between these SDs represents the SD for individual responses (SDir) which quantifies the individual variability in treatment response *per se*. The SD of the mean change score solely for the intervention group comprises treatment response variance *in addition to* the random variability in measurements between the baseline and follow-up timepoints. The SD of the changes in the control group represents this random variability in measurements between baseline and follow up – the random within-subjects variance component and measurement error.

The qualitative analysis from Chapter 5 highlighted that PSE may be effective for some people but not for others implying that true inter-individual differences in response to PSE may exist which could be explored to facilitate appropriate targeting of PSE to those most likely to benefit (Watson et al. 2019). However, clinically relevant inter-individual response variation should first be conducted using appropriate methodology (Atkinson and Batterham 2015; Williamson, Atkinson and Batterham, 2017; Williamson, Atkinson and Batterham, 2018; Atkinson, Williamson and Batterham 2019) to confirm the presence of such inter-individual responses. If individual differences are observed, and predictors of individual response are identified, then PSE could be tailored to the individual optimising its effect (Williamson et al. 2018).

To date, there has been no investigation of ‘true’ individual response variation of the effect of PSE, or indeed any pain management intervention. Therefore, this chapter aimed to conduct a systematic review and meta-analysis of the available research to quantify the ‘true’ inter-

individual variation in pain, disability and psychosocial outcomes in response to PSE in adults with CMP.

6.2 Methods

The protocol for the systematic review was published on PROSPERO (CRD42017068436). The analysis of inter-individual differences is presented here in detail to ensure the background and rationale for this novel method within the field of pain is adequately reported. A detailed account of the full review-methods was detailed in Chapter 5 and been published (Watson et al. 2019) but a brief summary is provided below.

6.2.1 Inclusion and Exclusion Criteria

6.2.1.1 Inclusion criteria

- Studies including adults (≥18 years) who have CMP consistent with the British Pain Society definition (chronic pain, that lasts beyond the time that tissue healing would normally be expected to have occurred, often taken as ≥3 months) (The British Pain Society, 2013).
- RCTs that (i) compared the intervention with no treatment (true control) or usual care (ii) concomitant studies where PSE was delivered in addition to another intervention where that other intervention was received by both groups and (iii) head-to-head studies where PSE was compared to another active intervention.
- Studies reporting either pain and/or disability and/or psychosocial wellbeing.
- The SD of the changes for the intervention and control groups must have been included within the publication, have been available from the author upon request, or could be calculated from other information given such as the standard error. This is an additional criterion that was not included in the registered protocol.

6.2.1.2 Exclusion criteria

- Studies that included participants with non-musculoskeletal pain such as cancer pain, visceral pain or post stroke pain.

6.2.2 Search Strategy

Pre-identified keywords (Pain AND (Physiology OR Neurophysiology OR Neuroscience OR Biology) AND Education) and index terms were searched across all included databases (The Cochrane Library, AMED, CINAHL Complete, MEDLINE, PsycINFO, PEDro, Scopus, EMBASE, Education Resources Information Centre (ERIC), Web of Science, clinicaltrials.gov, dissertations indexed with ProQuest Dissertations and Theses Global and EThOS) from 2002-25 July 2017, and updated on 14 June 2018.

After removing duplicates, the title and abstracts were screened by two authors and disagreements were resolved through discussion or a 3rd reviewer. The full-text was obtained for all records that could potentially fit the criteria. Upon reading the full-texts those deemed not to meet the inclusion criteria were rejected. See Appendix 5 for a list of excluded publications and reasons for exclusion.

6.2.3 Deviation from protocol

In Chapter 5 (Watson et al. 2019) when the SD of change was not reported, and could not be obtained by contacting the authors, it was either calculated from other information given such as standard error, or estimated from the baseline and follow up SDs, according to methods described in the Cochrane handbook (Higgins, Deeks and Altman, 2011). Where there was uncertainty regarding the validity of baseline, follow up and change score SDs from included studies we opted not to use this data to inform our calculations to estimate the SD of change scores. Instead, we used a robust data set of individuals with CMP where we were confident in the validity of the baseline, follow up and change score SDs. However, for the current review, given that to calculate the true inter-individual differences in response to an intervention the SD of the mean change score is of central importance (Atkinson and Batterham 2015), it would be inappropriate to estimate the SD of the change or use a robust data set. Thus, an additional criterion for inclusion was created for the current review where the SD of the changes for the intervention and control groups must have been published in the article, available upon request by the author, or could be calculated from other information given, such as the standard error.

6.2.4 Assessment of methodological quality and data extraction

Articles selected for critical appraisal were independently assessed by two reviewers using the Cochrane tool for assessing risk of bias (Higgins *et al.,* 2011). Two reviewers independently extracted the data using JBI-SUMARI (Munn, 2016) including details about the

interventions, populations, study methods and outcomes of relevance to the review question/objectives. The Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach (Guyatt et al. 2008) was used to rate the overall quality of quantitative evidence for each outcome. The summary of findings tables created using GradePro are presented in Table 6.2 and 6.3.

6.2.5 Meta-analysis

To contextualise the results for individual response variance we conducted a random-effects meta-analysis for the mean difference in disability across the included studies using a restricted maximum likelihood (REML) model combined with the Knapp-Hartung method. This method uses quantiles of the t distribution to calculate a confidence interval for the average effect instead of the standard normal distribution in the more conventional methods (Van Aert and Jackson, 2019). The Knapp-Hartung method has been shown to be superior to the DerSimonian-Laird method where there is a small number of studies (<20) and heterogeneity is present (IntHout, Ioannidis and Borm, 2014). We then extracted the standard deviation of the changes in disability for both control (C) and PSE (I) groups. The true individual response variance (intervention minus control) was then calculated by $\sqrt{(SD_I^2-SD_C^2)}$ (Hopkins, 2015). The standard error (SE) for this variance was then calculated using the equation: $SE = \sqrt{[2(SD_I^4/DF_I + SD_C^4/DF_C)]}$, where DF_I and DF_C are the degrees of freedom of the standard deviation in the PSE group and the control groups (Hopkins, 2015). A negative value for the individual response variance for the confidence intervals or prediction intervals implies greater variability in the changes in disability in the control versus PSE group.

The individual response variances and their SEs were meta-analysed using an REML model combined with Knapp-Hartung method. It's important to highlight that the variances are unbiased, whereas the SD is not, and deriving a SE for the SD for individual responses is also problematic. Thus, we synthesised the individual response variances instead of the SDs for individual responses. The point estimate for the pooled individual response variance were derived together with a 95% CI to express its uncertainty. The point estimate and CIs were then square rooted to convert to an SD metric. If the lower limit was negative, the sign was ignored, the square root taken, and the sign re-applied. This approach is consistent with the 'no bound' option in SAS/STAT® software, which permits negative variances (SAS Institute Inc. 2017. SAS/STAT 14.3 User's Guide. Cary, NC: SAS Institute Inc.).

Using the methods of Swinton et al. (2018) the proportion of responders in the population of interest within each included RCT was estimated. To estimate this, the observed mean change score and true individual response variance are needed for each RCT. Normal variance is assumed. The total area of any probability distribution is equal to one, thus the estimate of the proportion of response can be obtained by calculating the area of the derived normal distribution that lies beyond the minimally clinically important difference (MCID). An MCID of 10% was used in recent NICE guidelines for back and radicular pain (NICE, 2016). The calculation estimating the proportion of response was performed via an online calculator (Rice University:, 2019). The proportion of response was estimated for the intervention and control groups for all RCTs and has been used to demonstrate the difference in results, and thus conclusion that could be made if researchers erroneously ignored the control group data.

The tau statistic (τ) was used to quantify between-study heterogeneity – a SD that describes the typical variability of the mean effect between studies (Higgins, 2008; Borenstein *et al.*, 2017). A 95% prediction interval was calculated using the tau and the SE for the pooled mean effect to quantify the expected range of true effects in future similar studies (IntHout et al. 2016). Stata (StataCorp. 2019. Stata Statistical Software: Release 16. College Ststion, TX: StataCorp LLC.) was used to conduct all statistical analysis.

6.3 Results

6.3.1 Data collection

Following removal of duplicates, 12,136 publications were identified (Figure 6.1). Fifty-seven full text articles were screened. Forty-nine articles were excluded at this stage. See Appendix 5 for a list of excluded publications and reasons for exclusion. Thus, six publications reporting five RCTs were included (Gallagher, McAuley and Moseley, 2013; Louw et al. 2014/16; Malfliet et al. 2018; Pires, Crus and Caeiro, 2015; van Ittersum et al. 2014). The included studies encompassed a total of 428 participants (I = 212, C = 216). Table 6.5 provides further details regarding the studies.

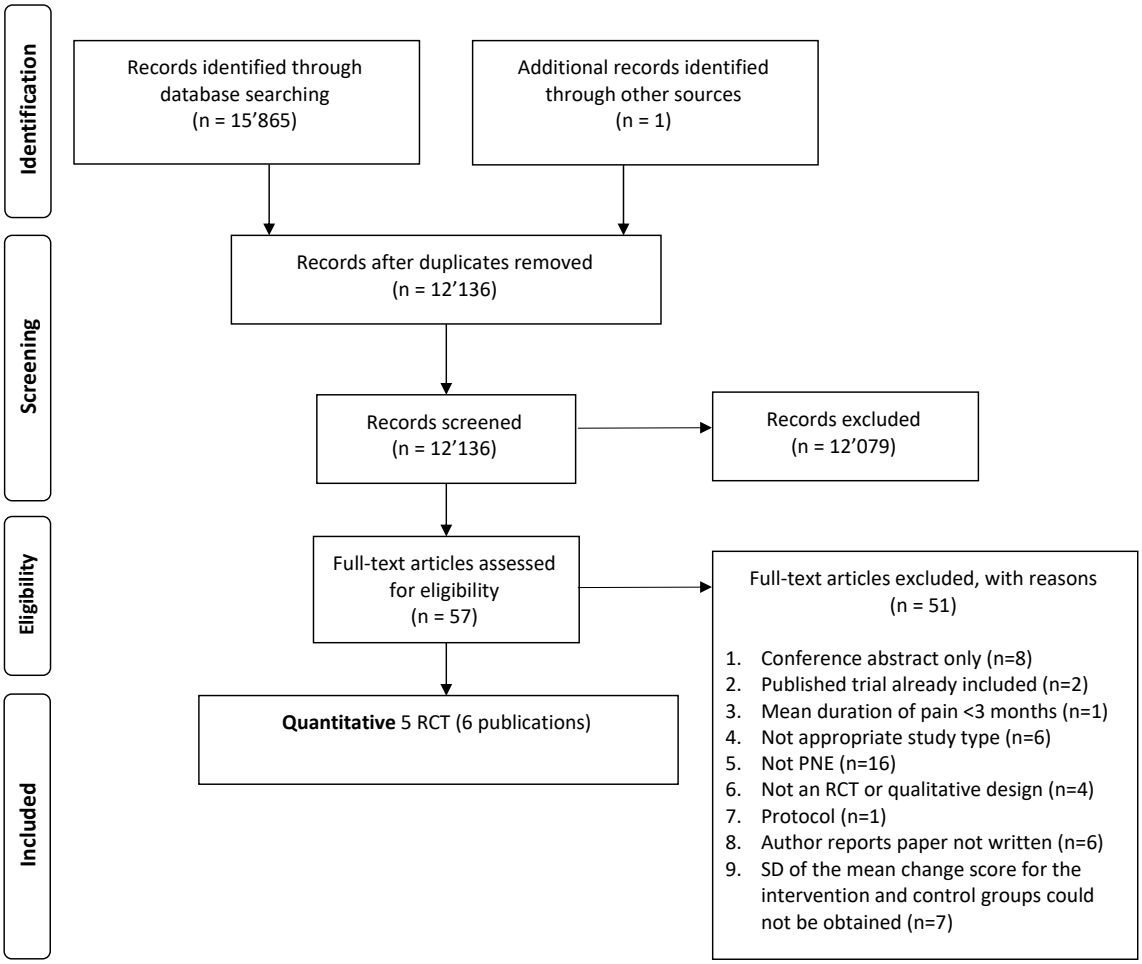


Figure 6.1 PRISMA flow diagram

Legend: *This figure shows the PRISMA flow diagram of the search and study selection process. Adapted from Moher et al. (2009).*

6.3.2 Methodological quality

Quality scores ranged from 1-6 out of 7 (Table 6.2). There was a high risk of performance bias due to lack of blinding of participants and personnel (Figure 6.2 and 6.3 produced by using RevMan software (Review Manager. Version 5.3. Copenhagen: The Nordic Cochrane Centre. The Cochrane Collaboration, 2014).

Table 6.2 Critical appraisal of quantitative studies

Study	Score /7	Percentage
Gallagher 2013	5	71%
Louw 2014/16	3	43%
Malfliet 2018	6	86%
Pires 2015	3	43%
van Ittersum 2013	1	14%

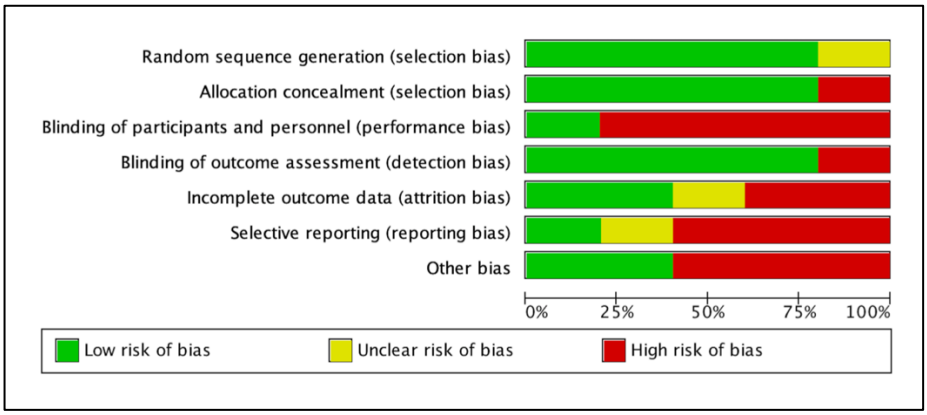


Figure 6.2 Risk of bias graph.

Legend: *Review authors' judgements about each risk of bias item presented as percentages across all included studies. Produced by using RevMan software (Review Manager. Version 5.3. Copenhagen: The Nordic Cochrane Centre. The Cochrane Collaboration, 2014).*

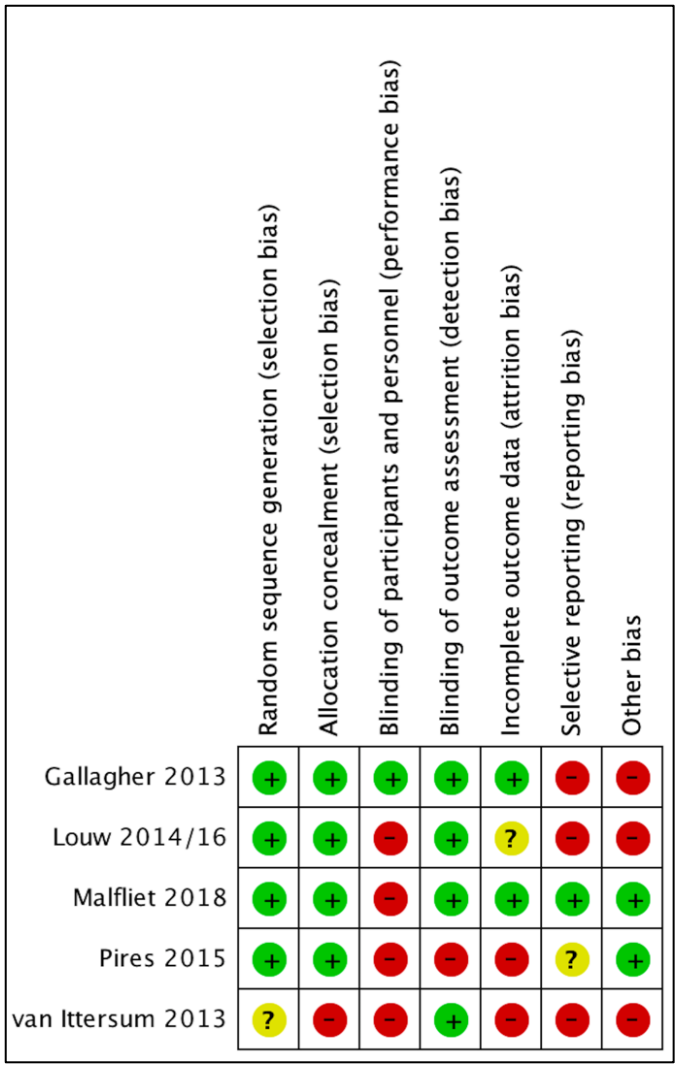


Figure 6.3 Risk of bias summary.

Legend: *Review authors' judgements about each risk of bias item for each included study. Produced by using RevMan software (Review Manager. Version 5.3. Copenhagen: The Nordic Cochrane Centre. The Cochrane Collaboration, 2014).*

6.3.3 Summary of findings tables'

The GRADE Summary of Findings tables' were created by J.W. with input from C.R. using GradePro (Table 6.3 and 6.4). The tables' include the primary outcomes of disability.

Table 6.3 Summary of findings

PSE compared to control for treatment of adults with chronic musculoskeletal pain						
Patient or population: treatment of adults with chronic musculoskeletal pain **Setting**: **Intervention**: PSE **Comparison**: control						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	**Risk with PSE**				
Change in disability score in the short term. (ST Disability) assessed with: Validated measure of disability converted to percentage Scale from: 0 to 100 (worse)	The mean change in disability score in the short term. was **-8.63** units	mean **2.26 units lower** (6.49 lower to 1.97 higher)	-	428 (5 RCTs)	⊕◯◯◯ VERY LOW a,b,c,d,e,f,g,h	PSE may reduce/have little to no effect on change in disability score in the short term. but the evidence is very uncertain.
*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval						
GRADE Working Group grades of evidence **High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect **Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different **Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect **Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect						

Explanations

a. A large proportion of the weight came from a study where there was concern over selection bias, performance bias, attrition bias, reporting bias and other bias. There was concern with most studies over performance bias which whilst normal of these types of studies may still impact the results.

b. Some variation is size of the effect, however the difference between studies does not reach a clinically meaningful difference

c. Good overlap of the confidence intervals.

d. I-Squated above 50%

e. Tau-Squared higher than point estimate.

f. Sample of chronic musculoskeletal pain comparing PSE against control using an appropriate outcome measure.

g. Has over 400 participants but imprecise due to prediction interval including null effect and clinically important benefit.

h. A comprehensive search was conducted on electronic databases and trials registries. References lists and citing articles of included studies were searched to identify any further articles.

Table 6.4 Summary of findings

Do inter-individual differences in disability change in response to PSE exist in adults with chronic musculoskeletal pain?				
Patient or population: treatment of adults with chronic musculoskeletal pain **Setting**: **Intervention**: PSE **Comparison**: control				
Outcomes	**Estimated absolute inter-individual difference in response** (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Inter-individual variability in disability change in the short term. SD_{IR} assessed with: Validated measure of disability converted to percentage Scale from: 0 to 100 (worse)	mean **7.36 units** (3.93 lower to 11.12 higher)	428 (5 RCTs)	⊕◯◯◯ VERY LOW [a,b,c,d,e,f,g]	Little evidence of "true" variation in peoples' response to PSE for disability, but the evidence is very uncertain.
CI: Confidence interval				
GRADE Working Group grades of evidence **High certainty:** We are very confident that the true difference in response lies close to that of the estimate of the difference in response **Moderate certainty:** We are moderately confident in the difference in response estimate: The true difference in response is likely to be close to the estimate of the difference in response, but there is a possibility that it is substantially different **Low certainty:** Our confidence in the difference in response estimate is limited: The true difference in response may be substantially different from the estimate of the difference in response **Very low certainty:** We have very little confidence in the difference in response estimate: The true difference in response is likely to be substantially different from the estimate of difference in response				

Explanations

a. A large proportion of the weight came from a study where there was concern over selection bias, performance bias, attrition bias, reporting bias and other bias. There was concern with most studies over performance bias which whilst normal of these types of studies may still impact the results.

b. Some variation in size of the effect, however the difference between studies does not reach a clinically meaningful difference

c. Good overlap of the confidence intervals.

d. Tau-Squared higher than point estimate.

e. Sample of chronic musculoskeletal pain comparing PSE against control using an appropriate outcome measure.

f. While the analysis includes over 400 participants this lack precision due to the very wide prediction interval including both a clinically important positive effect and clinically important negative effect.

g. No evidence of publication bias. Sample sizes ranged from 62-120. A comprehensive search was conducted on electronic databases and trials registries. References lists and citing articles of included studies were searched to identify any further articles.

6.3.4 Description of quantitative studies

A summary of all publications are presented in Table 6.5

The diagnosis of CMP differed across the 5 RCTs, the most prevalent being CLBP (n = 2) (Pires, Cruz and Caeiro, 2015; Malfliet et al. 2018). Other diagnosis include lumbar radiculopathy (n = 1) (Louw et al. 2014/16), heterogeneous pain (n = 1) (Gallagher, McAuley and Moseley 2013), and fibromyalgia (n = 1) (van Ittersum et al. 2013). There was a total of 428 participants in the sample of 5 included RCTs with the number of participants ranging from 62-120 (Pires, Cruz and Caeiro, 2015; Malfliet et al. 2018). All studies included more women than men ranging from 7% male to 46% male (van Ittersum et al. 2013; Louw et al. 14/16). The mean age of participants ranged from 40 to 51 years (Malfliet et al. 2018; Pires, Cruz and Caeiro, 2015). The mean baseline pain across all studies ranged from 43/100 to 72/100 (Pires, Cruz and Caeiro, 2015; van Ittersum et al. 2013).

Studies were conducted in a range of locations including specialised centres for chronic pain/fatigue (n = 1) (van Ittersum et al. 2013), outpatient clinics (n = 1) Pires, Cruz and Caeiro, 2015) and University facilities (n = 1) (Malfliet et al. 2018). Most studies were conducted in Europe (n = 3) (Pires, Cruz and Caeiro, 2015; van Ittersum et al. 2013; Malfliet et al. 2018), with one in the United States of America (Louw et al. 14/16) and the other unknown (Gallagher, McAuley and Moseley 2013). The duration of educational intervention ranged from 0.5 hours (Louw et al. 2014/16) to 3 hours (Pires, Cruz and Caeiro, 2015). Written information was the main intervention for two studies (Gallagher, McAuley and Moseley 2013; van Ittersum et al. 2013). Participants were given 3 and 6 weeks respectively to read and absorb the information.

PSE was delivered in single and multiple sessions. We defined ‘multiple’ as having a PSE contact with a member of the study team on more than one occasion via face-to-face, telephone or email. Written information alone was defined as 1 contact, however supporting leaflets/materials were not included when given in addition to face-face. PSE was delivered in a single session by two studies (Gallagher, McAuley and Moseley 2013; Louw et al. 2014/16), and over multiple sessions in three studies (van Ittersum et al. 2013; Pires, Cruz and Caeiro, 2015; Malfliet et al. 2018).

Table 6.5 Characteristics of included studies

Study	Methods	Sample size (baseline)/ gender/ mean age in years	Participants	Intervention(s)	Duration of educational intervention	Control	Authors conclusions/notes	Setting/country
van Ittersum et al. 2013	RCT	N = 105 7% M 46.7	Fibromyalgia diagnosed according to The American College of Rheumatology 1990 criteria (Wolfe et al. 1990) 18-65 years of age. Baseline pain as mean % = 71.5%	Written PSE + 1 phone call for motivation/questions +/- 2x phone calls/emails for further clarification/questions	Unknown	Written Relaxation exercises + 1 phone call for motivation/questions +/- 2x phone calls/emails for further clarification/questions	Written PSE alone is not effective for changing the impact of the illness on daily life, pain catastrophising, or illness perceptions in fibromyalgia patients.	Specialised centres for chronic pain and chronic fatigue. Belgium.

			Duration of pain in mean months = unknown					
Gallagher, McAuley and Moseley 2013	RCT	N = 79 39% M 43.5	18-75 years of age with pain that had been sufficient to disrupt their activities of daily living for more than the previous 3 months. Baseline pain as mean % = 65% Duration of pain in mean (SD) months = 28 (19.5)	80-page booklet divided into 11 sections - Metaphors and stories to help understand the biology of pain	Unknown	80-page booklet divided into 11 sections - Advice about managing pain (The back book and Manage your pain)	Written material using metaphors to explain key biological concepts increased knowledge of pain biology and decreased catastrophic thought processes about pain and injury when compared to material that presented biopsychosocial advice for pain management.	Unknown Unknown
Pires, Cruz and Caeiro, 2015	RCT	N = 62 35% M 51	Low back pain >3 months duration +/- leg pain. 18-65 years of age.	2x 1.5h Group PSE. 12 sessions of aquatic exercise over 6 weeks. 30-50m each session.	PSE 3h Control 3h	12 sessions of aquatic exercise over 6 weeks. 30-50m each session.	PSE is a clinically effective addition to aquatic exercise. The addition of PSE resulted in statistically	Outpatient clinic. Portugal

			Baseline pain as mean % = 42.9% Duration of pain in mean (SD) months = unknown				significant reduction in pain intensity at 3-month follow up. No statistically significant differences were found for pain intensity at 6 weeks follow up or functional disability at either follow up.	
Louw et al. 2014/16	RCT	N = 67 46% M 49.6	Patients with lumbar radiculopathy, scheduled for lumbar surgery. 18-65 years of age. Baseline pain as mean % = 48.4% Duration of pain in mean (SD) months = 3 (7.5)	0.5h individual PSE. PSE booklet "your nerves are having back surgery" & Lumbar surgery + usual care	PSE 0.5h Control 0	Lumbar surgery alone + usual care	Providing a single PSE session to patients prior to lumbar surgery results in significant reduction in healthcare costs 3-years after LS.	7 Clinical sites in the US.
Malfliet et al. 2018	RCT	N = 120 39.2% M 39.8	Non-specific chronic spinal pain (neck and lower back) at	3 PSE sessions 4. 0.5-1h group (maximum of 6 patients).	PSE 1.88h Control 1.88h	3 biomedical education sessions 4. 0.5-1h group (maximum of 6	PSE, and not neck/back school education, is able to improve kinesiophobia, beliefs regarding the	University hospitals in Ghent and

			least 3 days a week for at least 3 months since the first symptoms. 18-65 years of age Baseline pain as mean % = 50.65 Duration of pain in mean (SD) months = 82 (143.25)	Information booklet provided at the end. 5. ~0.63h home-based online e-learning module containing 3 explanatory videos and questions about pain. 6. 0.5 Individual education. Focus on patients' personal needs following difficulties with session 2. Focus on the application of knowledge to participants life.		patients). Information booklet provided at the end. 5. ~0.63h Home-based online e-learning module containing 3 explanatory videos 6. 0.5 Individual. Focus on patients' personal needs following difficulties with session 2. Focus on the application of knowledge to participants life.	negative impact of the illness on quality of life and functional capacity, and beliefs regarding the chronicity of pain and the time scale of illness symptoms. However, none of the educational programs of this study were able to decrease the participants perceived disability due to pain. Nevertheless, as kinesiophobia is generally considered to be a strong predictor and mediator of chronic pain, PSE is preferred as the educational approach for people with non-specific chronic spinal pain.	Brussels, Belgium.

Legend: *Randomized controlled trial, RCT. Male, M. Characteristics of included studies. PSE, Pain science education. SD, Standard deviation. RCT, Randomised controlled trial*

6.3.5 Mean group difference in response to PSE meta-analysis

Jackson and Turner, (2017) recommend only pooling data where the number of studies is ≥5 to ensure adequate statistical precision. Disability was the only outcome measured consistently in all five included studies, thus the analysis focused solely on this outcome.

The pooled mean group difference in pre/post changes in disability (intervention minus control) was -2.26 units /100 (95% CI: -6.49 to 1.97). See Figure 6.4. Between study heterogeneity in mean treatment effect was observed (τ = 2.49; 95% CI: 0.48 to 4.51). The prediction interval revealed that, were investigators to undertake a future trial, the 95% plausible range for mean disability change versus control would be -11.56 to 7.04 units /100.

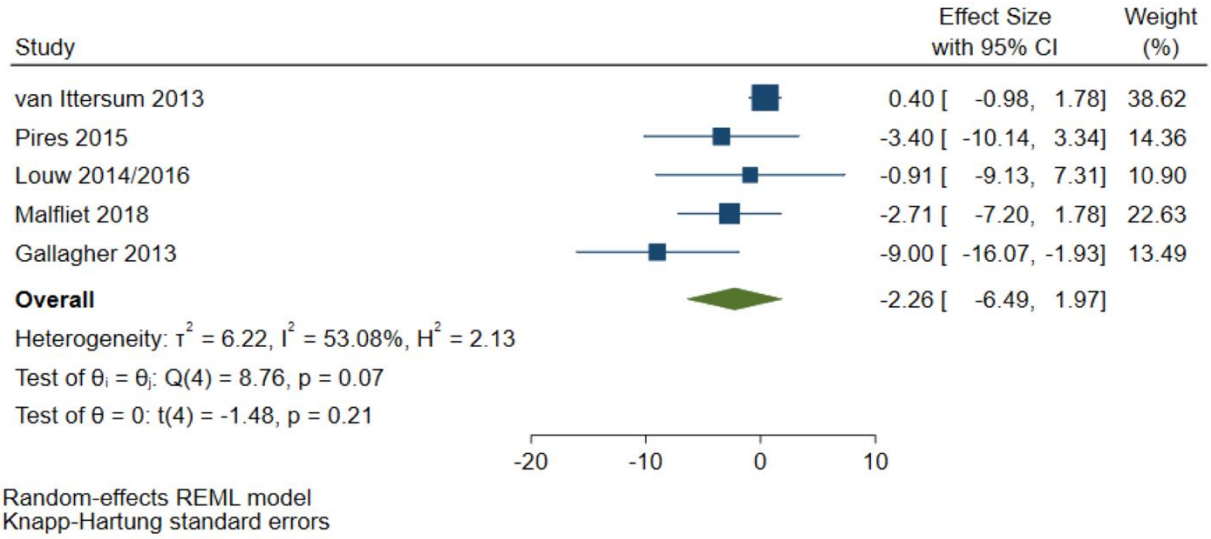


Figure 6.4 Forest plot of PSE versus control in the short term; mean difference of disability between groups.

6.3.6 Inter-individual differences in response to PSE meta-analysis

The pooled point estimate for the inter-individual variability in disability change in response to PSE (SD_{IR}) was 7.36 units /100 (95% CI: -3.93 to 11.12). Substantial between-study heterogeneity was observed (τ = 6.55). The 95% prediction interval for true inter-individual responses was -10.20 to 14.57. Appendix 6 provides a step by step guide for the calculations here.

Using the methods of Swinton et al. (2018) the proportion of responders in the population of interest within each included RCT was estimated (Table 6.6). The threshold reduction in

disability for clinical relevance was set at -10/100, in keeping with recent NICE guidelines for back and radicular pain (NICE, 2016).

Table 6.6 Proportions of responders

Study	Mean Change (PSE)	SD (PSE)	% Responders (PSE)	Mean change (Con)	SD (Con)	% Responders (Con)	Mean treatment effect (PSE-Con)	SD for true Ind diffs	% Responders based on SDir
van Ittersum et al. 2013	0.7	4.2	0	0.3	2.9	0	0.4	3.0	0
Pires, Cruz and Caeiro, 2015	-11.1	15.8	53	-7.7	10.6	41	-3.4	11.7	29
Louw et al. 2014/16	-12.0	18.5	54	-11.1	13.8	53	-0.9	12.3	23
Malfliet et al. 2018	-1.1	13.8	26	1.6	11.2	15	-2.7	8.1	18
Gallagher, McAuley and Moseley 2013	-36	17	94	-27.0	15.0	87	-9.0	8	45

Legend: *Proportions of responders. PSE, Pain science education. Con, Control. SD, Standard deviation. SDir, Standard deviation for individual responses.*

6.4 Discussion

Chapter 6 details a systematic review and meta-analysis of the literature aiming to quantify the control-group adjusted inter-individual variation in pain, disability and psychosocial outcomes in response to PSE in adults with CMP. Several potential studies did not report the

SD of the mean change, and this information could not to be obtained upon request meaning the analysis was restricted to disability.

The inter-individual difference in disability change in response to PSE, as indicated by the SDir of 7.36 /100 units, did not reach the criterion for clinical significance (10 /100 units). Therefore, there is insufficient evidence at present for the existence of inter-individual differences in people's response to PSE over and above random within-subjects variability between baseline and follow-up observations. Although this finding, seems at odds with previous qualitative study findings from the research group at Teesside University (Robinson et al. 2016; King et al. 2016; King et al. 2018), that qualitative work focused upon patient experience rather than attempting to objectively quantify inter-individual differences. Considering the upper 95% CI (11.12 /100 units) and wide 95% prediction interval -10.20 to 14.57 of the SDir, any inferences regarding "true" inter-individual responses are unclear. Given the small number of included studies, the wide prediction intervals are unsurprising and this illustrates the importance of statistical power in any analysis of response heterogeneity (Atkinson and Batterham, 2015; Atkinson, Williamson and Batterham, 2019).

Therefore, it is apparent that more high quality RCTs are needed that sufficiently report relevant data. Researchers and reviewers of academic journals should ensure that the means and standard deviations of the change scores in all treatment groups are reported. This will provide the information required to include the study within meta-analyses of both individual responses and mean effect of treatment.

It is worth highlighting that the very common act of simply looking at the intervention group 'responders' (Table 6.6) would have falsely led researchers in three studies (Pires, Cruz and Caeiro, 2015; Louw et al. 2014/16; Malfliet et al. 2018) to conclude that substantial response heterogeneity was present with 26% to 54% of participants 'responding'. This may have led to follow-up analyses to explore potential moderators which may be unwarranted and a waste of resources. Furthermore, any follow-up studies on the same participants may be unethical if there are no true individual differences in response present to explain (Atkinson and Batterham, 2015). As previously outlined simply looking at the intervention group findings falls down due to the 'counterfactual' (Senn, 2016b). Moreover, counting the number of people who change above or below a threshold is compromised by random within-subject variation between time points and measurement error (Atkinson, Williamson and Batterham, 2019). One could propose to count the responders in the experimental and control group to rectify this problem.

Table 6.6 details the percentage of 'responders' in the control group. A researcher may conclude a substantial response heterogeneity in two studies (Pires, Cruz and Caeiro, 2015; Louw et al. 2014/16) with 41% and 53% of participants in the control group 'responding'. Contrasting with less response heterogeneity in the other studies 0%, 15% and 87% (van Ittersum et al. 2013; Malfliet et al. 2018; Gallagher, McAuley and Moseley, 2013). However simply counting the number of responders in both groups is misleading as highlighted by Atkinson, Williamson and Batterham, (2019) whos' findings illustrate that differences in the proportion of responders may simply reflect differences in mean group difference, rather than response heterogeneity. They advocate the methods outlined by Swinton et al. (2018), using the SDir, which was the only method that reflected the true response heterogeneity present in the manufactured data set used by Atkinson, Williamson and Batterham, (2019). Moreover, the SDir is less sensitive to differences in group mean and also removes the compromise of random within-subject variation between time points and measurement error present when simply looking at the % of responders in the intervention group. The % of responders based on the SDir are shown in Table 6.6. The % of responders based on the SDir compared to the responders solely in the intervention group are lower in four of the studies (Pires, Cruz and Caeiro, 2015; Louw et al. 2014/16; Gallagher, McAuley and Moseley, 2013; Malfliet et al. 2018). Conclusions of the presence of response heterogeneity in these four studies would be likely with the % of responders ranging from 18-45% (Pires, Cruz and Caeiro, 2015; Louw et al. 2014/16; Gallagher, McAuley and Moseley, 2013; Malfliet et al. 2018). The likely conclusion of response heterogeneity in four studies differs from three studies when looking solely at the intervention group and two studies looking at the control group.

Whilst exploring response heterogeneity using the % of responders based on the SDir is an improvement for the above mentioned reasons over solely looking at the % of responders in the intervention group, or comparing the % of responders between the intervention and control groups, there are still issues with this approach. Converting measurements on a continuous scale into a binary (responder / non-responder) variable leads to poorer statistical power and leads to problems adjusting for baseline differences between study groups (Senn, 2005; Snappin and Jang, 2007). All three approaches used to inform Table 6.6 all have limitations as outlined above, and all would have likely led to researchers of most studies to conclude response heterogeneity to PSE is present. These conclusions differ from the response heterogeneity meta-analysis conducted in this chapter, that there is insufficient evidence at present for the existence of inter-individual differences in people's response to PSE given the pooled SDir of 7.36 /100 units did not reach the criterion for clinical significance (10 /100 units). The difference in findings and thus conclusions likely come from the current study using appropriate methodology to investigating individual differences in response (Atkinson and

Batterham, 2015; Atkinson, Williamson and Batterham, 2019; Swinton et al. 2018).

This is the first systematic review and meta-analysis to employ the method of calculating true inter-individual differences in response to an intervention within the field of the pain sciences (Swinton *et al.*, 2018). Given the huge global burden of chronic pain, and the limited efficacy of current treatment options for matching peoples' individual responses to treatments, appropriate methodology needs to be applied across the pain field. This will hopefully lead to improved quality of care, reduced costs (Spear, Health-Chiozzi and Huff, 2001) and ultimately improve the quality of life of people with pain.

6.5 Strengths and Limitations

Only five studies were eligible for this review which meant that only disability data could be analysed and the inter-individual differences in response to PSE for other outcomes are unknown. Six studies that were otherwise eligible, were excluded because they did not report the appropriate data needed to conduct an inter-individual differences meta-analysis and this data was not available upon email request. There is no reason to believe that authors would withhold this data and thus it is assumed these studies are missing at random. Only studies published in English were eligible for inclusion as no facility for translation was available. Thus, important data from non-English studies may have been missed.

The nature of the comparison group will influence the calculation of the inter-individual difference. In the case of usual care comparisons and other intervention comparisons, if these have inherent variability in response within them, beyond random variability (noise) of a true no intervention control, this may mask the degree of interindividual variability seen within the PSE (intervention of interest) group. Thus, this could have influenced the findings. Nevertheless, in the case of intervention vs usual care, if there are true individual differences in the responses to the novel component(s) of the intervention under study, then this should, in theory, manifest itself in a larger change variance in the intervention group vs the usual care group.

6.6 Conclusion

This is the first study to investigate “true” inter-individual differences in response within the field of pain. By this, it means a quantification of response heterogeneity that takes into account the individual differences in baseline to follow-up change that can be observed in the

comparator groups, and are attributable to random fluctuation in pain scores over time. The review included five randomised controlled trials (n=428) in which disability outcomes were reported. Using a random effects meta-analysis, the pooled SD (95% CI) for control group-adjusted response heterogeneity to PSE was 7.36 units /100 (95% CI: -3.93 to 11.12). Therefore these findings provide little evidence at present of 'true' variation in peoples responses to PSE regarding disability, but the evidence is GRADED as 'very low' certainty and thus the evidence is 'very uncertain'. Furthermore, given the wide 95% confidence and prediction intervals any inferences made regarding true individual variation in peoples' response to PSE are unclear. Moreover, given the small number of studies included in the analysis further work is warranted before firm conclusions can be drawn. Future studies should not explore which factors may explain which people will benefit from PSE until such time as the existence of inter-individual differences has been confirmed using appropriate methodology. This recommendation is extended to all pain interventions. Whilst future research needs to explore if inter-individual differences in response to PSE exist, it is also important to explore how best to deliver PSE to optimise both individual and group effects. The findings of Chapter 5 were suggestive that combining PSE with a PMP may be a fruitful avenue to explore and Chapter 7 shall undertake preliminary work on this combined intervention.

Chapter 7: Quasi mixed-methods feasibility study of a pain science education informed pain management programme

J.W. led the development of this quasi mixed-methods study contributing 90% to the overall body of work. The other 10% of the study was developed by several academics from Teesside University and other institutions. Table 7.1 lists those involved and the tasks they conducted.

Table 7.1 Contribution of authors to Chapter 7

Name/Job title/Employer/Role in the review	Tasks completed
James Watson Ph.D. Student Teesside University Lead Author	Development of review questions Development and registration of protocol Data collection Interview transcription Data analysis Wrote up the study Updated manuscript based on co-author comments
Prof. Cormac Ryan Professor of Rehabilitation Teesside University Co-author	Development of review questions Contributed to development of protocol Data analysis Commented on and made changes to review draft
Prof. John Dixon Professor of Applied Physiology and Rehabilitation, and the Associate Dean (Research & Innovation) Teesside University Co-author	Development of review questions Contributed to development of protocol Commented on and made changes to review draft
Prof. Denis Martin	Development of review questions

Professor of Rehabilitation and Director of the Centre for Rehabilitation Sciences Teesside University Co-author	Contributed to development of protocol Commented on and made changes to review draft
Dr Rebecca McNaughton Senior Lecturer Teesside University Co-author	Development of review questions Contributed to development of protocol Data analysis
Ms Victoria Robinson Clinical Specialist Physiotherapist South Tees Hospitals NHS Foundation Trust Co-author	Participant recruitment Data collection (part of routine care delivered as part of NHS role)
Mr Neil Goodenough Clinical Specialist Physiotherapist South Tees Hospitals NHS Foundation Trust Co-author	Participant recruitment Data collection (part of routine care delivered as part of NHS role)

7.1 Introduction

The purported mechanism of effect central to PSE is pain reconceptualisation, defined as *"the acquisition of a new, less threatening understanding about the nature of one's pain*" (King et al. 2016 p1389). This understanding encompasses the four pillars of contemporary pain science outlined by Moseley (2007) *(1) Pain does not provide a measure of the state of the tissues; (2) Pain is modulated by many factors across somatic, psychological and social domains; (3) The relationship between pain and tissue becomes less predictable as pain persists; and (4) pain can be conceptualised as a conscious correlate of the implicit perception that tissue is in danger.* A shift in understanding towards these four pillars is hypothesised to change the threat value associated with a range of sensory inputs shifting the prediction of the state of the world, and thus the most advantageous response. The four pillars are in alignment with what people with pain value learning about pain from PSE (Leake *et al.*, 2021).

To date there are only a small number of qualitative studies that explore the extent and nature of pain reconceptualisation following PSE (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018; King et al. 2018). However, in these studies, either all participants (Robinson et al. 2016; King et al. 2016; King et al. 2018) or the majority of participants (Wijma et al. 2018) did not receive PSE delivered as part of a truly multi-modal intervention like a PMP. This is important as PSE was always intended to be delivered as part of a multi-modal approach (Moseley and Butler, 2015). Furthermore, the process of exploring reconceptualisation in previous qualitative studies was not explicitly aligned to the pillars of contemporary pain science outlined by Moseley (2007). Thus some aspects of reconceptualisation may have been overlooked or not explored in sufficient depth. Therefore, Chapter 7 will address these gaps in the literature by using qualitative methodology to explore the extent and nature of pain reconceptualisation using the framework of the pillars of contemporary pain science following a PSE informed PMP.

Whilst pain reconceptualisation is purported to be the mechanism of effect central to PSE, little work has been done to map the degree of pain reconceptualisation to the degree of clinical benefit as assessed through patient reported outcome measures and objective measures. This is an important gap within the literature and needs to be explored.

The delivery of PSE is not usually linked to any educational theory approach. As such it is difficult to know what is the best way to deliver it to optimise outcomes. The UK Medical Research Council advocate using theory to inform the development of complex interventions (Craig et al. 2008). Using theory informed delivery could help to identify what components

might be most useful and thus the intervention could be adapted to harness the impact. Conceptual change theory refers to learning that challenges and shapes existing knowledge and knowledge structures, rather than just learning new information (Vosniadou, 2008). Given that the core objective of PSE is to shift pain conception from pain is *"a marker of tissue damage or disease"* to pain is a *"perceived need to protect body tissue"* (Moseley and Butler 2015 p.807) the use of conceptual change theory would seem appropriate to inform the optimisation of PSE delivery. Conceptual change theory has previously been utilised to inform the development of science education (Stofflett and Stoddart, 1994) which has clear overlap with trying to deliver PSE. Posner et al. (1982) outlined four conditions for conceptual change: (1) dissatisfaction with the existing conception (2) Intelligibility of the new concept i.e., it must be understandable (3) Plausibility of the new concept i.e. it must appear likely, and (4) Fruitfulness i.e. the practical usefulness of the new concept. Understanding if the conditions for conceptual change have a role in pain reconceptualisation may provide a clear framework within which to optimise the delivery for future clinical practice and research studies. Chapter 7 will seek to address this gap within the literature by using Framework analysis (Ritchie et al., 2014) to explore the role of the conditions for conceptual change in the process of pain reconceptualisation.

The findings of the mixed-methods systematic review and meta-analysis on pain science education detailed earlier in this thesis (Chapter 5) highlighted that combining PSE with a PMP may be a particularly fruitful avenue to explore (Watson et al. 2019). There is a need for an RCT to investigate the effectiveness of a PSE informed PMP for adults with CMP. However prior to undertaking an RCT, the Medical Research Council state that during the development and evaluation of a complex intervention (in this case a PSE informed PMP), it is important to undertake preliminary work to investigate the components of RCT methodology prior to a full-scale trial (Craig et al. 2008). This chapter will also seek to undertake important preliminary work to inform the design of a future feasibility study by looking at recruitment procedures and rates of recruitment, the appropriateness of outcome measures and the appropriateness of eligibility criteria.

7.2 Aims

1) To explore the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology (see section 7.4.2).

2) To explore the role of the conditions for conceptual change in the process of pain reconceptualisation (see section 7.4.3).

3) To explore the relationship between the degree of pain reconceptualisation and changes in clinical outcomes (see section 7.4.4).

4) To explore the feasibility of undertaking a pilot RCT investigating the effectiveness of a PSE informed PMP (see section 7.4.5).

a. To investigate recruitment procedures and rates of recruitment.
b. To investigate the appropriateness of outcome measures used within the trial.
c. To investigate the appropriateness of the eligibility criteria.

7.3 Methods

7.3.1 Ethical approval and permission

Ethical approval to carry out the study was granted by Teesside University School of Health and Social Care Research Governance and Ethics Committee (Study Number: 177/16) (appendix 7) and the Health Research Authority Research Ethics Committee (Study Reference:16/NE/0409) (appendix 8).

This study was registered on ClinicalTrials.gov on 03/05/2017, Unique Protocol ID: 177/16.

7.3.2 Design

A pre-planned same sample parallel quasi mixed methods study involving a single group pre-test post-test design was used. The primary component of this study is qualitative and the quantitative component is supplementary, and thus could be described as a QUALTATIVE + quantitative study (Tashakkori, Johnson and Teddlie, 2020).

This study is a quasi mixed methods design as whilst there are quantitative and qualitative components, there is not an overarching umbrella question that would be illustrative of a true mixed methods design. Instead there are aims that are best addressed through qualitative (1 and 2) and quantitative means (4). It could be argued that aim 3 is truly mixed methods in nature however given the relative weight to aims 1-2, and the lack of integration of qualitative and quantitative approaches within the study as a whole, quasi mixed methods is a more accurate description of this study than mixed methods (Tashakkori, Johnson and Teddlie, 2020). The COREQ guidelines were used to guide this methods section to ensure transparency with the research methods used, facilitating the possibility of study duplication in future (Tong, Sainsbury and Craig, 2007).

7.3.3 Eligibility

To be eligible to participate in this study potential participants had to; Have capacity to give informed consent, be ≥18 years of age, had a duration of pain ≥6 months, and have been referred to the pain management programme at James Cook University Hospital. Participants were excluded if they had; Pain arising from a non-musculoskeletal origin such as cancer pain, visceral pain or post stroke pain, had worsening neural signs, had ever been treated by the interviewer (JW), or did not speak English due to lack of provision for translation within this study.

7.3.4 Setting, recruitment and participants

Convenience sampling was used in the current study with all patients who were selected to receive a pain management programme at James Cook University Hospital as part of their routine care were invited to take part in this study. Individuals were selected to receive the pain management programme during a multidisciplinary team meeting. At this meeting, the patient was approached by a health care professional who was not part of the research team minimising the risk of researcher coercion. That individual provided the potential participant with a basic overview of the project, a participant information sheet (appendix 9) and consent form (appendix 10). The potential participant was asked if they were happy for their contact details to be passed on to a researcher so that they may be contacted about the study once they had had an opportunity to read the information provided. If the potential participant did not wish to participate, then they continued with their usual care. If the potential participant was happy for their details to be passed on they were asked for written consent to do so

(appendix 11). Their contact details were then be passed to the researcher (JW) who contacted them by telephone approximately one week later.

At the beginning of the study there were a number of patients on a waiting list to attend the pain management programme who had already undergone the multidisciplinary team meeting. These potential participants were sent a letter (appendix 12) to inform them about the study and inviting them to contact researcher if they wish to participate in the study.

When the researcher contacted the potential participant (or they contacted the researcher) the researcher discussed the project with the potential participant who had an opportunity to ask any questions they had about the study to ensure they were fully informed. If following the telephone call the potential participant decided they did not wish to participate they continued their usual care. If the potential participant decided they would like to participate in the study, then a time and date was arranged for them to come to Teesside University approximately one week before the start of their usual care pain management programme. This was the first of two face to face contacts with the participant as part of the study. The staff running the pain management programme were blinded as to which patients agreed to participate in the study until the end of the pain management programme in order to avoid this information influencing their treatment. Usual care was in no way affected by patient's participation (or not) in this study.

Where the aim of a qualitative study is to understand common experiences and perceptions a sample of 12 participants has been proposed (Guest, Bunce and Johnson, 2006). This is in line with the sample sizes of previous PSE studies (Robinson et al. 2016; Wijma et al. 2018; King et al. 2018). Therefore this study aimed to recruit a convenience sample of 12 participants.

7.3.5 Intervention

As part of their routine care participants completed an NHS run PSE informed PMP. The PMP was ran in groups of up to 14 patients with heterogeneous chronic pain conditions. It consisted of 8 weekly 3 hour sessions with a week break halfway through. The sessions covered a range of topics including pain science education, compassion, gait re-education, mindfulness, emotional anatomy, graded exposure and activity pacing, posture, thoughts and emotions, communication, neck and shoulder balance, nerve glides and flare up management. Central to the PMP was PSE which attempted to help patients reconceptualise their pain so that they might manage it better. The PMP as a whole was delivered by a multidisciplinary team of pain

specialist physiotherapists, pain specialist occupational therapist and cognitive behavioural therapists. Each session was delivered by at least two clinicians of different professions.

7.3.6 Data collection

All data collected which was not otherwise collected as part of routine care by the NHS pain clinic took place at Teesside University, Constantine Building, Human Performance Laboratory. To ensure informed consent, when participants first attended Teesside University, they were provided with another copy of the participant information sheet, which was discussed with them followed by the opportunity to ask any further questions before being invited to complete the consent form. Everyone who gave written informed consent was allocated a three-digit unique study number which was written on a copy of their participant information sheet. Participants were instructed to keep this form to facilitate withdrawal. The researcher created one Coding Sheet (appendix 13) as a single hard copy which linked participants to their unique study number and was held in a secure cabinet in Professor Ryan's office. All data collected was recorded under the unique ID number only. The coding sheet was held until the last withdrawal date following which it was destroyed fully anonymising the data.

7.3.6.1 Demographic information

Demographic and baseline information was recorded by JW using standardized documentation (appendix 14). Demographic data included: Gender, ethnicity, Height (cm), Weight (kg), Age (years), BMI, first three digits of postcode, estimated number of health care contacts in the previous 1 month about their pain, working status allocated to one of five categories 1 – normal, 2 – normal hours reduced duties, 3 – normal duties reduced hours, 4 – reduced duties reduced hours, 5 – not working (Von Bertouch, McAuley and Moseley, 2011).

7.3.6.2 Outcome measures

Several patient reported outcome measures were collected as part of routine care on the first and last session of the PSE informed PMP (see appendix 15). Additional patient reported outcome measures (see appendix 16) and some objective measures were administered when participants attended the laboratory at Teesside University. Further details are provided below:

7.3.6.2.1 Patient reported outcome measures

Quality of life

The EQ-5D-5L and EQ VAS was collected as a measure of health related quality of life (Janssen *et al.*, 2013). The EQ-5D-5L was developed from the EQ-5D-3L in an attempt to improve the instruments sensitivity and reduce ceiling effects (Herdman *et al.*, 2011). The EQ-5D-5L consists of the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D-5L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has five levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The EQ VAS records self-rated health on a 20 cm vertical, 0-100 visual analogue scale with endpoints labelled 'the best health you can imagine' and 'the worst health you can imagine' (Herdman *et al.,* 2011). The convergent validity between the EQ-5D-5L and the WHO-5 items were assessed using Spearman rank order coefficients with all items significantly correlating ($p < 0.001$) (Janssen *et al.,* 2013). Feng et al. (2021) in their systematic review of 99 studies from 32 countries found the EQ-5D-5L to be a valid and reliable measure of quality of life. The test re-test reliability was rated as excellent defined as an Intraclass correlation 0.75–1.00 in 8/9 studies that measured this. The other study found an Intraclass correlation of 0.70 (Feng *et al.*, 2021). A minimally clinically important difference (MCID) of 0.03 was used by NICE in their recently published low back pain guidelines (NICE, 2016).

Kinesiophobia

The Tampa Scale of Kinesiophobia-17 (TSK-17) is a validated measure of an individual's fear of movement defined as an "*irrational and debilitating fear of physical movement resulting from a feeling of vulnerability to painful injury or re-injury*" (Kori, Miller and Todd, 1990). The original questionnaire contains 17 Likert-scale items ranging from 1 (strongly disagree) to 4 (strongly agree). The total score ranges from 17-68 with higher scores representing higher levels of fear of movement. In the current study the 11 item version was used, Tampa Scale of Kinesiophobia-11 (TSK-11) which uses the same Likert-scale range, giving a total score range from 11-44. The 11 item version has been validated against the original scale with a highly significant positive correlation was observed between the change scores on the TSK-17 and TSK-11 ($r=0.93$, $P<0.001$) (Woby *et al.*, 2005). Both measures demonstrate good internal consistency (TSK-17: $\alpha = 0.76$; TSK-11: $\alpha = 0.79$) and test–retest reliability (TSK-17: Intraclass correlation = 0.82, Standard error of measurement = 3.16 ; TSK-11: Intraclass

correlation = 0.81, Standard error of measurement = 2.54) (Woby et al., 2005). An MCID was unable to be identified.

Pain self-efficacy

The Pain self-efficacy questionnaire (PSEQ) is a validated questionnaire for the in a chronic pain population (Nicholas, 2007). Self-efficacy is defined as a resilient self-belief system in the face of an obstacle such as pain (Bandura, 1977). PSEQ contains ten likert-scale items covering a range of domains including work, socialising, enjoyment, coping and household jobs. The scoring ranges from 0 (not at all confident), to 6 (completely confident) on each item. The total score is calculated by adding all scores together giving a range between 0-60 where higher scores indicate high levels of self-efficacy. The PSEQ has demonstrated very high internal reliability using Cronbach's α (α = 0.92) (Asghari and Nicholas, 2001). The test– retest reliability was high (r = 0.73; p < 0.001) calculated using Pearson correlation comparing baseline to 3 months (Asghari & Nicholas, 2001). The validity of the PSEQ has been assessed by calculating its correlation with other validated measures. As would be expected significant negative correlations were observed between the PSEQ and the impact of pain on daily life (Self-report version of Sickness Impact Profile r = -0.60, p <0.001; Significant-other report version of Sickness Impact Profile r = -0.48, p <0.001), total number of medications used (r = -0.45, p <0.001), unhelpful coping strategies and beliefs (catastrophising subscale of the Coping Strategies Questionnaire r = -0.55, p <0.001; and the Pain Beliefs Questionnaire r = -0.74, p <0.001) and mood (Beck Depression Inventory r = -0.59, p <0.001; State version of State-Trait Anxiety Inventory r = -0.49, p <0.001) (Nicholas, 2007). An MCID was unable to be identified.

Psychological distress

The CORE-10 was used to assess participants degree of psychological distress (Barkham *et al.*, 2013). The CORE-10 contains ten likert-scale items with the end points 'Not at all' and 'Most or all of the time'. For half the items 'Not at all' scores '0' and 'Most or all of the time' scores '4'. For the other half this scoring is inverted. The total score is calculated by adding all the scores and dividing by the number of questions answered to get a mean.

The internal reliability is high (α = 0.92). The CORE-10 is also strongly correlated with the Clinical Outcomes in Routine Evaluation-Outcome Measure (CORE- OM) at 0.94 in a clinical

sample and 0.92 in a non-clinical sample (Barkham et al., 2013). An MCID was unable to be identified.

Pain severity and impact on functioning

The brief pain inventory (Short form) was used to assesses the severity of pain and its impact on functioning. The brief pain inventory (Short form) is the most contemporary and widely used iteration of the brief pain inventory (Cleeland, 2009). It was derived from the Wisconsin Brief Pain Questionnaire (Daut, Cleeland and Flanery, 1983) which was adapted to the brief pain inventory (long form)(Cleeland, and Ryan, 1994) before being condensed into the short from. The short form has front and back body diagrams, four pain severity items and seven pain interference items rated on a 0-10 scale. Lower scores on each item represent lower pain severity or pain interference. The internal reliability (Cronbach alpha) is high ranging from 0.80 to 0.87 for the four pain severity items and from 0.89 to 0.92 for the seven interference items (Cleeland, 2009). The test-retest reliability of the pain severity items is high with correlations ranging from 0.83 to 0.88. Correlations are higher for the interference items ranging from 0.83 to 0.93 (Mendoza et al., 2006). The brief pain inventory (short form) shows moderate convergent validity (r = 0.66, P < 0.001) for the interference items against the Owestry Disability Index (Song et al. 2016). An MCID was unable to be identified.

Pain catastrophising

The pain catastrophising scale (PCS) is a validated measure of pain catastrophising defined as *"an exaggerated negative mental set brought to bear during actual or anticipated painful experience"* (Sullivan *et al.*, 2001). The PCS asks participants to indicate the degree to which they have certain thoughts or feelings during a pain experience, rated on a 5-point scale with the end points (0) not at all and (4) all the time. There are 13-items and the total score is calculated by summing the scores giving a range of 0-52 with higher scores indicating higher levels of pain catastrophising. Sullivan et al., (1995) found the PCS to have good internal consistency (α = 0.87) supported by (Osman *et al.*, 1997) (α = 0.93). The PCS has been shown to significantly correlate to the fear of pain questionnaire *(r* = .80, *p* < .01), Beck Depression Inventory *(r* = .26, *p* < .05), State-Trait Anxiety Inventory—Trait *(r* = .32, *p* < .05), negative affectivity *(r* = - .32, *p* < .05), and pain intensity *(r* = - .46, *p* < .01) providing some construct validity Sullivan et al., (1995). An MCID was unable to be identified.

Pain science knowledge

The 12-item revised neurophysiology of pain questionnaire (RNPQ) was used to assess knowledge of pain neurophysiology. Responses are marked yes, no or undecided. One point is awarded for correct answers. No points are awarded for 'undecided'. Scores range from 0-12, with higher scores indicating greater knowledge of pain neurophysiology. The RNPQ has good test-retest reliability (intraclass correlation = >0.97) (Catley et al 2013). An MCID was unable to be identified.

7.3.6.2.2 Objective outcome measures

The use of objective measures builds on the work of the only previous study exploring the effects of a PSE informed PMP who only used self-reported measures of function (Von Bertouch, McAuley and Moseley, 2011). Whilst using self-report questionnaires is in keeping with previous pain management programme studies (Chipchase and Hill, 2012), this information may not necessarily reflect the real capability of the patients' performance (Smeets et al., 2006). Therefore there was a need to use valid and reliable objective measures of function.

Repeated sit-to-stand

The repeated sit-to-stand test is a measure of physical performance. Participants were required to stand up from the chair and return to a sitting position as quickly as possible five times. The time taken was recorded. The test was repeated, and the average time take for the two trials used to enhance reliability as recommended by Simmonds et al. (1998) who found the test re-test reliability to be only moderate with a intraclass correlation coefficient of 0.45. In contrast the interrater reliability was excellent with an intraclass correlation coefficient of 0.99. This test was significantly moderately correlated with self-reported disability as measured using the Roland and Morris Disability Questionnaire 0.45 $p < 0.01$ (Simmonds *et al.*, 1998). A MCID of 6 seconds for the repeated sit-to-stand test has been estimated for an individual with chronic musculoskeletal pain (Benaim *et al.*, 2019).

Fifty-foot walk at fastest speed

The Fifty-foot walk at fastest speed test is a measure of physical performance. Participants walked 25 feet, turned around and walked to the start line as quickly as possible. The time taken was recorded. This test shows high interrater reliability and test-retest reliability with an

intraclass correlation coefficient of 0.98 and 0.95 respectively. This test was significantly moderately correlated with self-reported disability as measured using the Roland and Morris Disability Questionnaire 0.43 $p < 0.01$ (Simmonds et al., 1998). An MCID was unable to be identified for this test.

7.3.6.3 Interview

After the questionnaires and objective measures had been collected participants were invited to participate in an interview to discuss their understanding of their pain. This was the first of two semi-structured, face-to-face interviews. Qualitative interviews can explore issues in more depth than a questionnaire and can help elucidate the complex, often conflicting personal beliefs people hold (Pope and Mays, 1995). This makes qualitative interviews particularly appropriate for exploring the extent and nature of a complex phenomenon like pain reconceptualisation. It is important to have a balance within the interview between the research agenda and participants viewpoints to be expressed (Barbour, 2020). Semi-structured interviews allow an interview schedule to be used ensuring relevant areas are discussed, whilst also being flexible to allow new topics of interest to be explored (Bryman, 2016). New information which may not have been considered by the researcher have the potential to emerge from semi-structured interviews (Offredy and Vickers, 2013). Thus semi-structured interviews are appropriate to explore the extent and nature of pain reconceptualisation pre to post a PSE informed PMP. The aim of the semi-structured interviews was to get insight into the extent and nature of pain reconceptualisation pre to post a PSE informed PMP from a range of people with a range of profiles and therefore data saturation was not sought. This is in line with the approach used in King et al. (2016).

An interview guide (appendix 17) was adapted from a guide used in previous research exploring pain reconceptualisation following a single PSE session (King et al. 2018). The researcher (JW) used the guide flexibly to explore the apriori themes whilst allowing topics to be discussed as they emerged and the conversation to flow naturally.

To enhance the credibility of the findings approximately two weeks after each interview, JW telephoned all participants to conduct member checks. This entailed describing extracts from the interview and allowing the participant the opportunity to verify if the researcher had made an appropriate interpretation of the interview. Giving participants the opportunity to discuss the researchers' interpretation of their experiences reinforces that the knowledge produced by the study is co-constructed (Doyle, 2007). All participants could be contacted with the average

duration of the telephone call lasting approximately 10 minutes. All participants agreed with the interpretation of the account and therefore no amendments were made.

7.3.6.4 Post-intervention data collection

Post intervention data collection took place approximately 2 weeks after participants completed the PMP. Participants completed the exact same battery of tests that they completed in the pre-intervention measurement session. The second semi-structured, face-to-face interviews used the same questions as the first interview, plus questions about changes in their beliefs about their pain (see appendix 17).

7.3.7 Quantitative data analysis

For the continuous variables within this study when assessing pre and post group scores the median and interquartile ranges were used as the sample (n = 8) was not large enough to determine if the data was normally distributed. Individual participant change scores were calculated to partially address aim three of this chapter, *to explore the relationship between the degree of pain reconceptualisation and changes in clinical outcomes* (see results subsection 7.4.4). The MCID was used to determine if the individual had undergone a clinically meaningful change based on their pre score. Where there is no specific MCID an improvement in clinical outcomes of 10% has been proposed as a MCID in the recent NICE guidelines for back and radicular pain (NICE, 2016). This criterion was also used in Chapter 5 of this thesis and will also be used for Chapter 7. To highlight the data are presented here to provide the reader with context only within this exploratory study. It would not be appropriate to infer any mechanism of effect of the intervention on the clinical outcomes used within this study as there was no control group. Any change between pre and post scores could be due to within-subject random variation between timepoint. A future RCT would be needed to investigate any possible effects of a PSE informed PMP. The quantitative data was analysed using the descriptive statistics function on Microsoft Excel for Mac Version 16.52.

To investigate recruitment procedures the recruitment rate was calculated for both recruitment methods i.e. via letter to those on the waiting list, or at multidisciplinary team meeting by a healthcare professional. The recruitment rate was calculated by: (Number of potential participants invited to participate / number of participants recruited) x 100. The recruitment procedure method that yields a higher recruitment rate will inform the recruitment procedure

for the future pilot RCT protocol. The dropout rate will also be calculated to inform the feasibility of undertaking a pilot RCT. The dropout rate was calculated by: (Number of participants who withdrew / Number of recruited participants at baseline) x 100. The above methods will in part address aim 4 of this chapter.

7.3.8 Qualitative data analysis

Framework analysis was used to analyse the qualitative data within this study (Ritchie, *et al.*, 2014). Framework analysis is a systematic and transparent method enhancing the credibility of the analysis (Srivastava and Thomson, 2009). The Framework method is flexible allowing a deductive and inductive approach to analysis (Gale *et al.*, 2013). This was appropriate for this study as it allowed the use of apriori themes including the four pillars of contemporary pain science outlined by Moseley (2007), and the four conditions for conceptual change outlined by Posner, et al. (1982) to be explored, whilst also allowing topics not considered by the researcher to emerge (Ritchie, Jane and Spencer, 2002a). Moseley's, (2007) four pillars of contemporary pain science are *(1) Pain does not provide a measure of the state of the tissues; (2) Pain is modulated by many factors across somatic, psychological and social domains; (3) The relationship between pain and tissue becomes less predictable as pain persists; and (4) pain can be conceptualised as a conscious correlate of the implicit perception that tissue is in danger.* Collecting data on these apriori themes would address aim one of this chapter and allow the exploration of the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology (see results subsection 7.4.2). Posner's, (1982) four conditions for conceptual change are (1) dissatisfaction with the existing conception (2) Intelligibility of the new concept i.e., it must be understandable (3) Plausibility of the new concept i.e. it must appear likely, and (4) Fruitfulness i.e. the practical usefulness of the new concept. Collecting data on these apriori themes would address aim two of this chapter and allow the exploration the role of the conditions for conceptual change in the process of pain reconceptualisation (see results subsection 7.4.3).

The hallmark of framework analysis is the production of matrices that distil the data and facilitate analysis (Ritchie, Jane and Spencer, 2002b). These matrices would be a helpful, and novel method to explore the extent and nature of pain reconceptualisation following a PSE informed PMP (King et al. 2016).

7.3.8.1 Familiarisation

During familiarisation the researcher immersed themselves in the data, gaining a comprehensive overview, noting any topics or issues of interest (Ritchie et al., 2014). The full transcript was listened to in full three times and read four times, noting down recurrent themes relevant to the aims of the study. The transcripts were returned to throughout the analysis providing important context to the data. The iterative nature of framework analysis is one of the benefits to this type of approach (Richie and Spencer, 2002a).

7.3.8.2 Constructing an initial thematic framework

During the familiarisation stage JW reflected on the four pillars of contemporary pain science outlined by Moseley (2007) and the four conditions for conceptual change outlined by Posner et al. (1982). Therefore, to address aim two of this chapter, *to explore the role of the conditions for conceptual change in the process of pain reconceptualisation*, JW needed to assess if an individual's concept of the four pillars of contemporary pain science had evidence for the presence of the conditions for conceptual change outlined by Posner et al. (1982).

For the purposes of coding data to minimise duplication rather than having separate themes for the 4 pillars of contemporary pain science and the four conditions for conceptual change it was determined that the data was best captured under the theme 'concept of pain'. This would include the subthemes of all 4 pillars of contemporary pain science. At later stages of analysis, the summaries created from the data coded under the four pillars of contemporary pain science could then be reanalysed to determine the evidence for the presence of 3/4 conditions for conceptual change including dissatisfaction with current conception, intelligibility of new concept, and plausibility of the new concept.

In contrast to the other three conditions the fourth condition of conceptual change, the fruitfulness of the new conception, relates to the individual's perception of the practical usefulness of the new concept, which is subtly distinct from the concept itself. JW determined that the fruitfulness of the concept was not captured by coding under the 4 pillars of contemporary pain science, and thus warranted inclusion as a standalone theme to ensure this chapter was able to explore the role of fruitfulness in the process of pain reconceptualisation as a whole. A key aspect of Framework analysis is the use of priori knowledge or themes as part of the thematic framework (Ritchie and Spencer, 2002a). In keeping with this, Fruitfulness was subdivided into two themes previously identified by the

research group at Teesside University (Robinson et al., 2016; King et al., 2016; King et al., 2018), Relevance, and Perceived benefits.

Whilst the researcher was open to new themes other than the merger of the themes outlined above to form theme 1 'Concept of Pain' no other themes were identified. Figure 7.1 shows the thematic framework. Figure 7.2 shows the descriptions of each theme to help the reader understand the kind of evidence that was interpreted as aligned to each theme. This was also used throughout the analysis to help guide the researchers (JW, CR) to appropriately code the participant data to each theme. The descriptions are not a strict criterion or an exhaustive list as there was an element of interpretation of the data by the researchers in keeping with the qualitative design of this study

Thematic framework

Theme 1 Concept of pain

- Pillar 1 - Pain does not provide a measure of the state of the tissues
- Pillar 2 – Pain is modulated by many factors across somatic, psychological and social domains
- Pillar 3 - The relationship between pain and tissue becomes less predictable as pain persists
- Pillar 4 - Pain can be conceptualised as a conscious correlate of the implicit perception that tissue is in danger

Theme 2 - Fruitfulness

- Sub-theme 1 Personal relevance of PSE
- Sub-theme 2 Perceived benefit of PSE

Figure 7.1 Thematic framework.

Legend: *This figure provides the thematic framework which is a hierarchy of themes and subthemes that relate to the aims of the study. PSE, Pain Science Education.*

Description of themes in thematic framework	
Theme	Description
CP-P1 Pain does not provide a measure of the state of the tissues	Awareness that pain does not provide a measure of the state of the e.g. *I don't think there is a relationship between pain and tissue state*

CP-P2 Pain is modulated by many factors across somatic, psychological and social domains	Somatic	Awareness of the central (e.g., *My brain amplifies my pain more than it needs to)* and peripheral mechanisms *(e.g. I think it's my nerves being too hyper)* mechanisms involved in pain.
	Psychological	Awareness of the role of attention (e.g., *I know being depressed and worked up makes my pain much worse because basically I give pain my attention*), anxiety (e.g. *How you deal with things emotionally has an impact on the pain. My pain is worse when I'm stressed*) & expectation (e.g. *If I think it's going to hurt it's more likely to hurt)* with the common denominator of their effect on pain seeming to be the evaluative context, or meaning of the pain (e.g. *My brain thinks every ceiling is a threat until I establish there are no holes or loose tiles, so if my brain thinks that's a threat it goes into protection mode*)
	Social	Awareness of the role of context on pain (e.g., *Social aspects of things do make the pain better*)
CP-P3 The relationship between pain and the state of the tissues becomes less predictable as pain persists		Awareness that the relationship between pain and tissue state becomes weaker. (*e.g., When initially got pain was injured, not sure at what point the tissues had healed because pain stayed. Thinks probably nothing wrong with tissues now, thinks tissues are probably quite healthy.)*
CP-P4 Pain can be conceptualised as the conscious correlate of the implicit perception that tissue is in danger		Awareness that it is not the state of the tissues or the actual threat to the tissues that determines pain, it is the unconscious perceived level of threat (e.g., *My pain is*

	related to level of danger my brain thinks is in my back)
Perceived relevance of PSE	Evidence that the individual found pain science education relevant to them was typically seen 1) When talking about their pain, use of first person singular e.g. I or my 2) clear statements discussing relevance '*I could* relate' 3) suggestions for improvements related to lack of personalised care 'I did get a chance to explain'
Perceived benefits of PSE	Evidence that the individual found PSE beneficial was typically seen by statements that they had 1) improved coping, 2) functional improvements, 3) a better understanding of their situation. Sometimes participants made explicit statements about PSE not being of benefit e.g., 'more interesting than useful'

Figure 7.2 Description of themes in thematic framework.

Legend: *This figure provides the thematic framework which is a hierarchy of themes and subthemes that relate to the aims of the study. The descriptions of the themes are provided to help the reader understand the kind of evidence that was interpreted as aligned to each theme. These descriptions are not a strict criterion or an exhaustive list as there was an element of interpretation of the data by the researchers in keeping with the qualitative design of this study. CP, Concept of pain. PSE, Pain Science Education.*

7.3.8.3 Indexing and Sorting

Indexing and sorting was conducted in NVivo 12 software (QSR International Pty Ltd., 2018). During indexing JW applied the thematic framework to the transcripts, coding the location of themes and subthemes. Sorting was performed automatically via NVivo12 (QSR International Pty Ltd., 2018), where all the data marked under a specific theme or subtheme during the indexing stage was collated, allowing data with similar content to be viewed together in what is termed a thematic set (Ritchie et al., 2014).

7.3.8.4 Reviewing data extracts

JW then reviewed the thematic sets to ensure they were coherent. A lack of coherence may have required subdivision or merger of themes. This was not necessary as the thematic sets were coherent.

7.3.8.5 Data summary and display

Framework analysis makes large amounts of data manageable through the production of framework matrices (Bowling and Ebrahim, 2005). JW constructed a matrix for each theme. The first column in the matrix was for participant case identification. The other columns were for the themes. Each participant case was assigned a row, which was kept consistent across matrices to facilitate ease of comparison. Once the matrices had been made JW began writing useful summaries by asking the question "*What, in essence, is each person saying about a particular theme?*" (Ritchie et al. 2014 p. 283).

When writing the summary Ritchie et al., (2014) emphasise the importance of maintaining the context, language and voice of the participant, however, they do not provide a detailed plan of how to do this. To make useful summaries for such a large volume of data manageable an approach was devised, partially informed by the 'description' sub stage of the 'abstraction and interpretation' stage of framework analysis.

Within the description sub stage, the researcher identifies the 'elements', succinct statements that reflect what is being said whilst maintaining the context, language and voice of the participant (Ritchie et al., 2014). To do this, JW created a table (See below Table 7.1 as an example and Appendix 18 for the full data). The table has participant quotes in the first column along with an identifier so the quote is easily located within the interview transcripts. JW analysed the quotes, condensing them into elements. The second column has the detected element along with an identifier so that the element can be tracked back to the participant quote during the later stages of analysis.

Table 7.2 – An example of 'Appendix 18 – Quotes to Elements', which shows the process of identifying the elements within participant quotes.

Subtheme 1: Pain does not provide a measure of the state of the tissues
P137 Post

Data summaries	Detected elements	
Q So if we go through the causes one by one just to explore why they cause pain, the first one was hyper mobility, so why does that cause pain? R Because you're stretching all your muscles, tendons and nerves all the time, they never fully relaxed, they're always taught so the only time you're not doing that is say when your laid flat on your back you're not pulling then around. P137 Post L112-117	CP-P1-P137postE1:	Hypermobility causes pain because muscles, tendons and nerves are stretched
Q Okay, cool. Erm, what does your pain tell you about the health of your tissues? R Errrrr, that it's rubbish, but erm yeah. Yeah it it basically says that the pain is basically there, it's like, it's always there but I don't necessarily see it as a bad thing, sometimes it can be a good thing. So sometimes it's just healthy tissues and it shows that they're working. And if they weren't in pain, I'd be a bit more worried, cose I'm so used to them always sparking with pain. But I think, I I don't	CP-P-1-P137postE2:	Pain means tissue health is rubbish
	CP-P-1-P137postE3:	Pain not necessarily a bad thing, sometimes it's just healthy tissues and it shows they're working
	CP-P-1-P137postE4:	I don't know what to think about the tissues cose I've been told so many different things by the pain clinic and others.

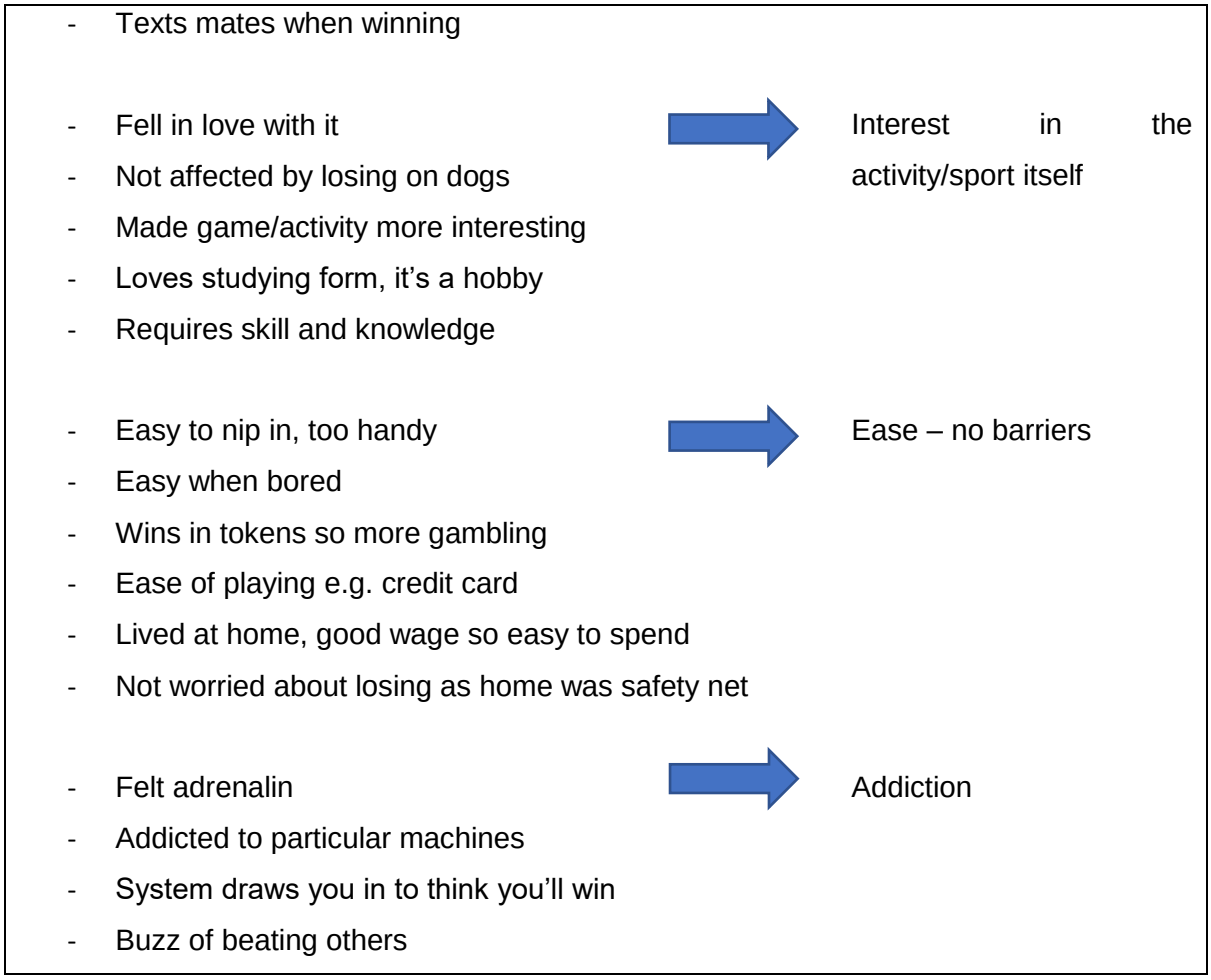
know really what to think about the tissues in general because when you get told so many different things I'm still working it out. You know from what the pain clinic have said and other things coming together. P137 Post L186-194		
R I don't think the tissues are damaged, I just think they're very sensitive. And I think once they desensitise a little bit, it will be slightly better. That's what I think it is, I think it's all to do with sensitivity. P137 Post L202-204	CP-P-1-P137postE5:	I don't think tissues are damaged, I think they're very sensitive

***Legend**: Q, Interviewer. R, Response from participant.* P137 Post L202-204, Participant 137 Post Intervention Line 202-204. CP-P1-P137postE4, *Concept of Pain-Pillar 1 Pain does not provide a measure of the state of the tissues-Participant 137 Post Intervention Element 4.*

In the methods outlined by Ritchie et al., (2014) after identifying the elements, they are then grouped together into 'dimensions' to capture the key aspects of the theme. See Table 7.3 for what this traditional approach would look like, partially reproduced from Ritchie et al., (2014 p. 314).

Table 7.3 An example of creating dimensions from elements

A Detected elements across the data set for 'the gambling experience'	B Key dimensions
- Family were playing them - Family member taught them to gamble - Would play with friends after drinks	With friends or family



Legend: *This was partially reproduced from Ritchie et al., (2014 p. 314)*

The current study deviated at this point in the analysis from that prescribed by Ritchie et al., (2014). The goal was not to capture the key aspects of the theme, rather, the goal of this step was to capture a useful summary of each participants knowledge and belief of each theme at each timepoint. Ritchie et al., (2014, p.286) *"appreciate that researchers may need to adapt the process within the context of any particular study".*

To create useful summaries the elements were input into a table (See below *Table 7.4* as an example and 'Appendix 19 – Elements to Useful summaries' for the full data) and analysed by 1) aggregating elements into one if they had the same meaning; 2) combining elements to form a longer sentence or paragraph which succinctly reflected the participants knowledge or beliefs about the theme. The analysis had an additional step for Theme 1, Sub-theme 2 'Pain is modulated by many factors across somatic, psychological and social domains' owing to its' multidimensional nature. Sub-theme 2 has three domains including somatic, psychological and social. Before steps 1 and 2 outlined in the paragraph above, the elements for sub-theme 2 were grouped into these domains to facilitate the development of the useful summaries.

Table 7.4 An example of 'Appendix 19 – Elements to Useful Summaries', which shows the process of grouping elements by similarity of meaning into 'Useful Summaries'.

Elements		Useful summaries
CP-P1-P137postE4:	I don't know what to think about the tissues cose I've been told so many different things by the pain clinic and others.	CP-P1-P137postS1: I don't know what to think about the tissues cose I've been told so many different things by the pain clinic and others.
CP-P1-P137postE2:	Pain means tissue health is rubbish	CP-P1-P137postS2: Pain means tissue health is rubbish. I'm probably wrong but I've been told, and it feels like, pain is caused by stretched and compacted muscles and tendons which damages them.
CP-P1-P137postE1:	Hypermobility causes pain because muscles, tendons and nerves are stretched	
CP-P1-P137postE6:	Use of walking stick causes physical pain because stretches and squashes muscles and tendons which damages them	
CP-P1-P137postE7:	Probably wrong but told and feels like pain caused by compacted muscles which damages them	
CP-P1-P137postE9:	Doesn't think tissues are damaged cose they're constantly healing, they're just sensitised	CP-P1-P137postS3: I don't think my tissues are damaged cose they're constantly healing, they're just sensitised because tissue damages takes longer to heal for me.
CP-P1-P137postE11:	Tissue damage takes longer to heal which is why nerves and body are sensitive	
CP-P1-P137postE3:	Pain not necessarily a bad thing, sometimes it's just healthy tissues and it shows they're working	CP-P1-P137postS4: Pain not necessarily a bad thing, sometimes it's just healthy tissues and it shows they're working. I don't think my tissues are damaged, I think they're over sensitised so I feel more pain.
CP-P1-P137postE5:	I don't think tissues are damaged, I think they're very sensitive	
CP-P1-P137postE8:	Thinks tissues are over sensitised so feels more pain	

CP-P1-P137postE10:	Doesn't think tissues are damaged, they're just more sensitive	

Legend: *CP-P1-P137postE4, Understanding Pain-Subtheme 1 Pain does not provide a measure of the state of the tissues-Participant 137 Post Intervention Element 4. CP-P1-P137postS1, Understanding Pain-Subtheme 1 Pain does not provide a measure of the state of the tissues-Participant 137 Post Intervention Useful Summary 1.*

After a useful summary of each theme for each participant at each timepoint was completed these summaries were input into a framework matrix called the Matrix of Useful Summaries, see 'Appendix 20 –Matrix of Useful Summaries' for the full data and Table 7.5 below which provides an extract of Appendix 20. This allowed each theme for each participant at each timepoint to be viewed. This marked the end of the data management stage

Table 7.5 An example of 'Appendix 20 – Matrix of Useful Summaries', which shows useful summaries of multiple themes, allowing ease of analysis.

Case	**Pillar 1: Pain does not provide a measure of the state of the tissues**	**Pillar 3: The relationship between pain and the state of the tissues becomes less predictable as pain persists**	**Pillar 4: Pain can be conceptualised as the conscious correlate of the implicit perception that tissue is in danger**
P137 Pre	Pain means my tissue health is probably not great. I know my pain is physical. I've been told my pain is definitely caused by fibromyalgia, osteoarthritis, hypermobility, nerve damage and a crumbling spine because bone grinds on bone which was a big deal to accept. Pain also caused by tissues being overstretched which I think damages them. When I get knee pain it means knee damage every time. CP-P1-P137preS1	Cause of knee pain was initially due to damage when kneecap snapped 7 years ago and the cause of knee pain now is still due to damage as it's not fully healed. CP-P3-P137preS1:	Pain is not related to the level of danger my brain thinks is in my body cose it's not to do with the brain, it's more to do with muscles, nerves and tissues. Cose you can trick your brain into doing all kinds of stuff. I have a fear of spiders, if one walked in my brain would overtake my body and I'd be out of the room. That's why it's more to do with the tissues and physical aspects. Obviously, I don't

			know, but I have a feeling going by my body. CP-P4-P137preS1:
P137 Post	I don't know what to think about the tissues cose I've been told so many different things by the pain clinic and others. CP-P1-P137postS1: Pain means tissue health is rubbish. I'm probably wrong but I've been told and it feels like pain is caused by stretched and compacted muscles and tendons which damages them. CP-P1-P137postS2: I don't think my tissues are damaged cose they're constantly healing, they're just sensitised because tissue damages takes longer to heal for me. CP-P1-P137postS3: Pain not necessarily a bad thing, sometimes it's just healthy tissues and it shows they're working. I don't think my tissues are damaged, I think they're over sensitised so I feel more pain. CP-P1-P137postS4:	Broke kneecap 7 years ago which was the start of pain, I don't think the tissues are damaged now cose they're constantly healing, they're just sensitive. CP-P3-P137postS1:	Pain is not related to the level of danger my brain thinks is in my body cose the brain only reacts to what the spinal cord and nerves tell it, plus in my own mind I'm not in any danger, I could be happily doing something not in any danger and still be in pain. Pain's maybe related to how worried my body is about state of tissue but that's not the brain, it's cose my body is sensitive. CP-P4-P137postS1:

Legend: *CP-P1-P137postS1, Understanding Pain-Subtheme 1 Pain does not provide a measure of the state of the tissues-Participant 137 Post Intervention Useful Summary 1.*

The second stage of framework analysis is 'abstraction and interpretation' which generated the findings from the analysis. During this stage the researcher viewed the data as a whole using the framework matrices (Appendix 20 –Matrix of Useful Summaries) developed in the 'data management' stage and looked for patterns and explanations to describe and interpret the data. Ritchie et al., (2014) outline several steps to analyse the data to create more abstract, higher order themes. Ritchie et al. (2014 p. 286) emphasise that not all researchers will undertake each step of the analysis, some may choose to remain at a more descriptive level with much depending on the aims of the study. Within the context of the aims of this study it was deemed more appropriate to keep the data at a more descriptive level of analysis, keeping

the findings closer to the participants voice which was important considering the aims of this chapter.

To facilitate aim one of this chapter, the exploration of the extent and nature of pain reconceptualisation following the PSE informed PMP JW categorised the useful summaries of the sub-themes of understanding of pain to their degree of alignment with contemporary pain science as outlined by Moseley, (2007) and described in Figure 7.2. This categorisation was informed by previous work by the research group at Teesside University where the evidence for the degree of reconceptualisation was categorised as “Strong”, “Partial and patchy”, and “No evidence” (King et al. 2018). The useful summaries displayed in Appendix 20 – Matrix of Useful Summaries. The degree of alignment to contemporary pain science was categorised by JW using the following descriptors of “Strong”, “Partial” and “Little or no” outlined in Figure 7.3. JW categorised a participants alignment to contemporary pain science as “Strong”, where there was clear and consistent evidence of pain beliefs aligned to contemporary pain science; “Partial”, where there was some evidence of pain beliefs aligned to contemporary pain science and some evidence of pain beliefs aligned to the biomedical model; and “Little or no”, where there was clear and consistent evidence of pain beliefs aligned to the biomedical model with very limited or no evidence of pain beliefs aligned to contemporary pain science. These categories are to help JW guide the reader to discern a pattern, or observe different patterns within individuals alignment to contemporary pain science and the degree of pain reconceptualisation. It is important to highlight that these categories are not truly discrete and that alignment to contemporary pain science and the degree of pain reconceptualisation is more of a spectrum.

Categorisation of alignment to contemporary pain science	Description
Strong	Clear and consistent evidence of pain beliefs aligned to contemporary pain science.
Patrial	Some evidence of pain beliefs aligned to contemporary pain science and some evidence of pain beliefs aligned to the biomedical model.
Little or no	Clear and consistent evidence of pain beliefs aligned to the biomedical model with very limited or no evidence of pain beliefs aligned to contemporary pain science.

Figure 7.3 Grading of alignment ***to contemporary pain science.***

Legend: *This figure shows the grading system used to categorise alignment to contemporary pain science as "Strong", "Partial" or "Little or no".*

The categorisations made by JW using Figure 7.3 were all verified by CR. Disagreements were resolved through discussion or with a 3rd researcher. The outcome of each categorisation and the rationale for each categorisation is shown in *Appendix 21 - Degree of alignment of participants understanding of pain to contemporary pain science* in keeping with the transparent nature of framework analysis. Table 7.6 below shows an extract of Appendix 21. The table includes a column for participant cases and a separate column for each of the four pillars of contemporary pain science (Moseley, 2007). This allows the degree to which each participants' understanding of pain was aligned to each pillar of contemporary pain science to be viewed pre and post a PSE informed PMP.

Table 7.6 An extract of Appendix 21

	Theme 1 Understanding Pain			
Case	**Pillar 1** **Pain does not provide a measure of the state of the tissues**	**Pillar 2** **Pain is modulated by many factors across somatic, psychological and social domains**	**Pillar 3** **The relationship between pain and the state of the tissues becomes less predictable as pain persists**	**Pillar 4** **Pain can be conceptualised as the conscious correlate of the implicit perception that tissue is in danger**
P137 pre	Little or no – clear pain = damage	Partial – evidence of awareness of peripheral sensitisation, but does not think pain is modulated by psychological or social domains.	Little or no – clearly no change in relationship	Little or no – more to do with tissues than brain
P137 post	Partial – They're unsure, some pain = damage,	Partial – Discusses peripheral sensitisation in greater detail than pre.	Strong – initially pain caused by damage,	Little or no – brain only reacts to what the nerves tell it.

	and also pain ≠ damage	Acknowledges psychological factors (Stress and attention) can modulate pain. Discuss how if they don't exercises they feel more stressed, which releases chemicals which makes them more sensitive. Denies depression impacts their pain. No evidence of the role of the social domain.	now not damaged, sensitive	

Legend: *This table shows an extract of 'Appendix 21 Degree of alignment of participants understanding of pain to contemporary pain science' which displays the degree to which each participants 'Understanding of Pain' was aligned to contemporary pain science, graded from "Strong", where there was clear and consistent evidence of pain beliefs aligned to contemporary pain science; "Partial", where there was some evidence of pain beliefs aligned to contemporary pain science and some evidence of pain beliefs aligned to the biomedical model; and "Little or no", where there was clear and consistent evidence of pain beliefs aligned to the biomedical model with very limited or no evidence of pain beliefs aligned to contemporary pain science.*

P137 pre, Participant 137 Pre intervention. P137 post, Participant 137 Post intervention.

To facilitate exploration of the patterns and explanations within the data during the abstraction and interpretation stage, a condensed version of Appendix 21 was created called Table 7.12 (See results and discussion subsection 7.4.2 for the complete table or Table 7.7 provided below for an example). The outcome of the categorisations for the degree of alignment of participants understanding of pain to contemporary pain science categorised and justified by JW (verified by CR) outlined above in Appendix 21 were transferred in a condensed format to Table 7.12. Given the rationale for the decision to categorise alignment to contemporary pain science was clearly recorded in Appendix 21, this rationale was not duplicated in Table 7.12. The advantage of presenting this data in a condensed format was to ensure that Table 7.12 could be easily viewed as a whole to facilitate the exploration of patterns and explanations within the data. Importantly for aim one of this chapter, *to explore the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology,* participants alignment to contemporary pain science at the pre and post timepoints could also be easily viewed. This allowed any change along the continuum outlined in Figure 7.3 of "Strong", "Partial" and "Little or no" to be seen. To further highlight if any change in alignment to contemporary pain science had occurred pre to post the PSE informed PMP a traffic light

system was used. One green dot  indicated a shift towards contemporary pain science by one category along the “Little to no”, “Partial” and “Strong” continuum i.e., moving from “little to no” to “Partial”, and thus indicative of the presence of pain reconceptualisation. Two green dots  indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from “little to no” to “Strong”, and thus indicative of the presence of strong pain reconceptualisation. One orange dot  indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot  indicated a shift away from contemporary pain science by one category along the “Little to no”, “Partial” and “Strong” continuum i.e., moving from “Strong” to “Partial”, and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots  indicated a large shift away from contemporary pain science by two categories along the continuum i.e., moving from “Strong” to “Little or no”, and thus indicative of the presence of strong anti-pain reconceptualisation. In addition, the traffic light system was also used in the first column to display the overall change in alignment to contemporary pain science including all four pillars of contemporary pain science. This is equivalent to the overall degree of pain reconceptualisation. To calculate overall degree of pain reconceptualisation the number of green, amber and red dots were combined with the total shown in the post participant row in the first column. The total number of green dots across all four subthemes was included in the overall degree of reconceptualisation. The number of red dots present across all four subthemes resulted in the equivalent number of green dots being removed from the overall score I.e., one red dot and one green dot cancel each other out. Amber dots neither add or minus the number of green or red dots. Where there was overall no change an amber dot was shown to reflect no overall degree of reconceptualisation.

Table 7.7 A table showing an extract of Table 7.12

Case, timepoint and overall degree of reconcept-ualisation	**Understanding of pain**			
	Pillar 1 **Pain does not provide a measure of the state of the tissues**	**Pillar 2** **Pain is modulated by many factors across somatic, psychological and social domains**	**Pillar 3** **The relationship between pain and the state of the tissues becomes less**	**Pillar 4** **Pain can be conceptualised as the conscious correlate of the implicit perception**

			predictable as pain persists	**that tissue is in danger**
P137 pre	Little or no	Partial	Little or no	Little or no
P137 post 	Partial 	Partial 	Strong 	Little or no 

Legend: *This table shows an extract of Table 7.12 - The degree to which each participants 'Understanding of Pain' was aligned to contemporary pain science, graded from "Strong", where there was clear and consistent evidence of pain beliefs aligned to contemporary pain science; "Partial", where there was some evidence of pain beliefs aligned to contemporary pain science and some evidence of pain beliefs aligned to the biomedical model; and "Little or No", where there was clear and consistent evidence of pain beliefs aligned to the biomedical model with very limited or no evidence of pain beliefs aligned to contemporary pain science. A traffic light system was used to display a change in alignment to contemporary pain science from pre to post the PSE informed PMP. One green dot*  *indicated a shift towards contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial", and thus indicative of the presence of pain reconceptualisation. Two green dots*  *indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from "little to no" to "Strong", and thus indicative of the presence of strong pain reconceptualisation. One orange dot*  *indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot*  *indicated a shift away from contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "Strong" to "Partial", and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots*  *indicated a large shift away from contemporary pain science by two categories along the continuum i.e., moving from "Strong" to "Little or no", and thus indicative of the presence of strong anti-pain reconceptualisation. In addition, the traffic light system was also used in the first column to display the overall change in alignment to contemporary pain science including all four pillars of contemporary pain science. This is equivalent to the overall degree of pain reconceptualisation. To calculate overall degree of pain reconceptualisation the number of green, amber and red dots were combined with the total shown in the post participant row in the first column. The total number of green dots across all four subthemes was included in the overall degree of reconceptualisation. The number of red dots present across all four subthemes resulted in the equivalent number of green dots being removed from the overall score I.e., one red dot and one green dot cancel each other out. Amber dots neither add or minus the number of green or red dots. Where there was overall no change an amber dot was shown to reflect no overall degree of reconceptualisation.*

P137 pre, Participant 137 Pre intervention. P137 post, Participant 137 Post intervention.

Using Table 7.12 JW wrote a narrative summary of the findings exploring the extent and nature of pain reconceptualisation following a PSE informed PMP thus addressing aim 1 of this chapter (see result and discussion subsection 7.4.2). The narrative summary was supported with extracts from the useful summaries generated in the data management stage. By using the useful summaries rather than direct quotes, the author was able to convey the participants

beliefs more fully and coherently without including large extracts from the interview transcripts. Some could argue that this reduces the credibility of the findings (Munn et al. 2014) as direct quotes are not used, however this is mitigated by the transparent and accessible flow from useful summary to interview transcript.

The next step was to address aim 2 of this chapter, *to explore the role of the conditions for conceptual change in the process of pain reconceptualisation* (see result and discussion subsection 7.4.3). The conditions for conceptual change outlined by Posner et al. 1982 are; 1) dissatisfaction with the existing conception 2) Intelligibility of the new concept i.e., it must be understandable 3) Plausibility of the new concept i.e. it must appear likely, and 4) Fruitfulness i.e. the practical usefulness of the new concept. To explore the role of the conditions for conceptual change in the process of pain reconceptualisation the strength of the evidence for the presence of Posner's conditions needed to be ascertained. The approach to grading the strength of the evidence for the presence of Posner's conditions is outlined in Table 7.8.

Table 7.8 Shows the grading system used to assign the strength of evidence for the four conditions for conceptual change

Condition for conceptual change	Question	Little or no evidence	Partial evidence	Strong evidence
Dissatisfaction with the biomedical model	Does the participant show some dissatisfaction with the biomedical model?	The participant shows no or very limited evidence of dissatisfaction with the biomedical model *"Pain means my tissues are damaged"*	The participant shows some evidence that they are dissatisfied with the biomedical model *"I have no idea how pain works"*	The participant shows clear dissatisfaction with the biomedical model *"pain does not provide a measure of the state of tissues"*
Intelligibility of concept	Does the participant understand this concept?	The participant shows no or very limited evidence they understands the concept	The participant shows some evidence they understand the concept "My alarm system is more sensitive so I can	The participant shows clear evidence they understand the concept *"I can see how a sensitive alarm system leads to increased pain*

		"Pain means my tissues are damaged"	feel tissue damage more than others"	*levels despite tissues being intact"*
Plausibility of concept	Does the participant believe this concept?	The participant shows no or very limited evidence they believe the concept *"Whilst I understand how having a sensitive alarm system could result in pain without damage, I don't believe this is the case with me, I have real pain"*	The participant shows some suggestion they believe the concept *"I guess my alarm system being more sensitive could mean I have pain without damage"*	The participant shows clear evidence they believe the concept *"I believe that because my alarm system is more sensitive I have pain without damage"*
Fruitfulness of concept	Does the participant believe the concept has made their life better in a way they can see?	The participant shows no or very limited evidence the concept helps them *"This did not help me manage my pain any better"*	The participant shows some evidence the concept helps them "Whilst I have a better understanding of my pain and the things that effect it, my pains worse if not better"	The participant shows clear evidence the new concept helps them *"Now I understand I have pain because of a sensitive alarm system I'm less afraid to move, I've been gradually increasing my activity levels and I'm feeling better for it"*

Legend: *Table 7.8 shows the grading system used to assign "Little or no" evidence, "Partial" evidence, and "Strong" evidence for the four conditions for conceptual change outlined by Posner et al. (1982). Example participant quotes are used to provide further context to the grading system.*

The grading of the strength of the evidence for the conditions for conceptual change were made by JW using the grading system outlined in Table 7.8. These gradings were all verified by CR. Disagreements were resolved through discussion or with a 3rd researcher. The outcome of each grade was recorded in Appendix 22 – 'Posner et al 1982 conditions within Useful summaries' in keeping with the transparent nature of framework analysis. Table 7.9 below shows an extract of Appendix 22. It includes a column for each theme, and each themes' respective useful summary for the associated case/timepoint. The next four columns

are for the grading (using the grading system outlined in Table 7.8) and rationale for the strength of evidence for the presence of the four conditions for conceptual change outlined by Posner et al., (1982).

***Table 7.9** A table showing an example of Appendix 22*

Case	Theme		Useful Summary	Evidence of Dissatisfaction	Evidence of Intelligibility	Evidence of Plausibility	Evidence of Fruitfulness
P137 Pre	Pillar 1		Pain means my tissue health is probably not great. I know my pain is physical. I've been told my pain is definitely caused by fibromyalgia, osteoarthritis, hypermobility, nerve damage and a crumbling spine because bone grinds on bone which was a big deal to accept. Pain also caused by tissues being overstretched which I think damages them. When I get knee pain it means knee damage every time. CP-P1-P1	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	Little or no fruitfulness – They did not find the claim that mood can impact on pain relevant to their experience 'for me it didn't make a blind bit of difference' R-P137preS1 No data available for perceived benefits.
	Pillar 2	Somatic	I think your brain takes your pain receptors in different parts of your body and precipitates them all over the place. Fibromyalgia stretches and makes nerves react 24/7 CP-P2-P137preS1	Partial dissatisfaction – some awareness of sensitivity CP-P2-P137preS1	Partial intelligibility – Awareness of some central and peripheral mechanisms and the concept of sensitivity. CP-P2-P137preS1	Partial plausibility – appears to find the concept likely CP-P2-P137preS1	
		Psychological	I've been told depression can make pain worse but I don't think psychological symptoms effect my pain because I've always suffered from depression so for me there wasn't any correlation between my depression and pain. It's more the effects of pain that's psychologically wearing CP-P2-P137preS2	Little or no dissatisfaction	Partial intelligibility – they are aware that their mood can impact on pain in general but do not think it affects their pain CP-P2-P137preS2. No	Little or no plausibility – they are actively opposed to psychological factors affecting their pain. Their experience of having a really good	

			Emotional factors don't affect my pain cose I could be having a really good day, feeling really good but still be in pain, that's how I know emotions don't affect my pain CP-P2-P137preS3 You can trick your brain into doing all kinds of stuff e.g., Has fear of spiders and if one walked in their brain would overtake body and they'd be out of the room. That's why it's not to do with the brain, it's more to do with the tissues and physical aspects rather than psychological. CP-P2-P137preS4		mention of the evaluative context or meaning of pain.	day and still being in pain is used as evidence against psychological factors impacting upon pain CP-P2-P137preS3	
		Social	Social factors have nothing to do with my pain CP-P2-P137preS5	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 3		Cause of knee pain was initially due to damage when knee cap snapped 7 years ago and the cause of knee pain now is still due to damage as it's not fully healed. CP-P3-P137preS1:	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Pain is not related to the level of danger my brain thinks is in my body cose it's not to do with the brain, it's more to do with muscles, nerves and tissues. Cose you can trick your brain into doing all kinds of stuff. I have a fear of spiders, if one walked in my brain would overtake body and I'd be out of the room. That's why it's more to do with the tissues and physical aspects. Obviously I don't know, but I have a feeling going by my body. CP-P4-P137preS1:	Partial dissatisfaction - Whilst the example they provide about how "…you can trick your brain into doing all kinds of stuff…." Where their "…brain would overtake body…" would seem to provide	Little or no intelligibility - Whilst the example they provide about how "…you can trick your brain into doing all kinds of stuff…." Where their "…brain would overtake body…" would seem to provide	Little or no plausibility - "…it's more to do with muscles, nerves and tissues…". CP-P4-P137preS1:	

			evidence in favour of ST4, counter intuitively they use this example as evidence that "…it's more to do with muscles, nerves and tissues…". They show some very partial dissatisfaction "…Obviously I don't know know…" CP-P4-P137preS1	evidence in favour of ST4, counter intuitively they use this example as evidence that "…it's more to do with muscles, nerves and tissues…". CP-P4-P137preS1:		
	Relevance	I've always suffered from depression so for me it didn't make a blind bit of difference [to my pain]. R-P137preS1				
	Perceived benefit	No data				
P137 Post	Pillar 1	I don't know what to think about the tissues cose I've been told so many different things by the pain clinic and others. CP-P1-P137postS1: Pain means tissue health is rubbish. I'm probably wrong but I've been told and it feels like pain is caused by stretched and compacted muscles and tendons which damages them. CP-P1-P137postS2:	Partial dissatisfaction – they hold conflicting views on if pain provides a measure of tissue state reporting "I don't know what to think about the tissues cose I've been told so many different things" CP-P1-P137postS1:	Partial intelligibility – they are aware of being oversensitive and thus pain not relating to tissue state "I don't think my tissues are damaged, I think they're over sensitised so I feel more pain" CP-P1-P137postS3:	Partial plausibility – there is evidence that they find this conception likely "I don't think my tissues are damaged, I think they're over sensitised so I feel more pain" CP-P1-P137postS3:	Strong fruitfulness – strong relevance and benefits Strong relevance – Use of first person when discussing pain, clear statements discussing relevance

			I don't think my tissues are damaged cose they're constantly healing, they're just sensitised because tissue damages takes longer to heal for me. CP-P1-P137postS3: Pain is not necessarily a bad thing, sometimes it's just healthy tissues and it shows they're working. I don't think my tissues are damaged, I think they're over sensitised so I feel more pain. CP-P1-P137postS4:	They report "Pain means tissue health is rubbish." But also that "I'm probably wrong" CP-P1-P137postD2: and later state "I don't think my tissues are damaged, I think they're over sensitised so I feel more pain" CP-P1-P137postS3:	Not full as they also state "Pain means tissue health is rubbish" CP-P1-P137postS2: The following summary shows partial understanding in that they name tissue sensitivity, however they suggest that this stems from their tissues taking longer to heal from damage. "I don't think my tissues are damaged cose they're constantly healing, they're just sensitised because tissue damages takes longer to heal for me. CP-P1-P137postS3:	However they're also not sure "I don't know what to think about the tissues cose I've been told so many different things" as they also think "Pain means tissue health is rubbish." But also that "I'm probably wrong" CP-P1-P137postS2:	Strong benefits – activity pacing, reduced length of flare ups, made feel as if not "insane" – however suggestions that this reinforced need to seek care, motivating them to go to A&E/urgent care if their pain flared. They were more confident and more positive. Furthermore their understanding of pain has given them some awareness of how to help manage their pain – "If you can stop the nerves, the pain receptors being produced as much so they reduce that will help with my pain." CP-P2-P137postS1
	Pillar 2	Somatic	Personally does not think tissues are damaged, I think the tissues are very sensitive so you feel more pain.	Strong dissatisfaction – they outline pain cause	Partial intelligibility – They outline peripheral	Strong plausibility – the use of	

			It's like your whole body is open, they haven't got any inhibitors so I need to dull the pain receptors. The PMP has taught me pain is to do with the tissues, more to do with the nerves. I didn't know your body over produces them so it makes you more sensitive. If you can stop the nerves, the pain receptors being produced as much so they reduce that will help with my pain. CP-P2-P137postS1 Somatic and Psyc: If I don't do my exercise, yoga or meditate I don't feel as centred in myself, which means I'm more sensitive to everything going on around me. When you're stressed it releases negative toxins in your body and stops the release of serotonin. That makes you feel down and makes all the pain worse, it makes you more sensitive to everything else around you CP-P2-P137postS2	by sensitivity not damage "Personally does not think tissues are damaged, I think the tissues are very sensitive so you feel more pain." CP-P2-P137postS1	changes in more detail than pre discussing over producing nerves, and inhibitors to dull the nerves "…they haven't got any inhibitors so I need to dull the pain receptors... I didn't know your body over produces them so it makes you more sensitive." CP-P2-P137postS1	"personally" suggests they find the concept likely CP-P2-P137postS1	
		Psychological	Somatic and Psyc: If I don't do my exercise, yoga or meditate I don't feel as centred in myself, which means I'm more sensitive to everything going on around me. When you're stressed it releases negative toxins in your body and stops the release of serotonin. That makes you feel down and makes all the pain worse, it makes you more sensitive to everything else around you CP-P2-P137postS2	Partial dissatisfaction – holds contradictory beliefs from that aligned with contemporary pain science "Getting stressed makes my pain worse" CP-P2-P137postS4 to a belief	Partial intelligibility – they report mood ("Getting stressed makes my pain worse" CP-P2-P137postS4) and attention ("You have to train the brain to ignore pain" CP-P2-P137postS7) impact on	Partial plausibility – they are clearly more open to psychological factors impact on their pain "Getting stressed makes my pain worse" CP-P2-P137postS4. They still make sense of	

			Less stress makes it easier to focus on things that make the pain go away like light yoga and exercise CP-P2-P137postS3 Getting stressed makes my pain worse CP-P2-P137postS4 I think depression sometimes can affect pain but not for me as I've always suffered with depression before I had pain. I'm on medication for low mood which makes me feel numb so that's why I can go low mood doesn't affect my pain because the low mood part has already been inhibited. CP-P2-P137postS5 Depression and anxiety don't affect my pain cose I can have a fantastic day and still be in pain CP-P2-P137postS6	more in line with the biomedical model "Depression and anxiety don't affect my pain cose I can have a fantastic day and still be in pain" CP-P2-P137postS6	pain. But also report mood don't affect their pain CP-P2-P137postS6. No mention of the evaluative context or meaning of pain.	their experience of having a fantastic day but still being in pain as evidence against psychological factors impacting on their pain. CP-P2-P137postS6. They also discuss in CP-P2-P137postS5 how they feel that being on how by being on anti-depressants inhibits the low mood aspect and because they're still in pain this is evidence against psychological factors impacting their pain.	
	Social	No data	No data	No data	No data	
Pillar 3		Broke kneecap 7 years ago which was the start of pain, I don't think the tissues are damaged now cose they're constantly healing, they're just sensitive. CP-P3-P137postS1:	Strong dissatisfaction – outlines pain initially due to damage however 7 years later pain is cause by	Strong intelligibility – outlines pain initially due to damage however 7 years later pain is cause by	Strong plausibility – "…I don't think the tissues are damaged now cose they're constantly healing,	

			sensitivity as tissues are constantly healing CP-P3-P137postS1	sensitivity as tissues are constantly healing CP-P3-P137postS1	they're just sensitive." CP-P3-P137postS1:	
	Pillar 4	Pain is not related to the level of danger my brain thinks is in my body cose the brain only reacts to what the spinal cord and nerves tell it, plus in my own mind I'm not in any danger, I could be happily doing something not in any danger and still be in pain. Pain's maybe related to how worried my body is a about state of tissue but that's not the brain, it's cose my body is sensitive. CP-P4-P137postS1:	Little or no dissatisfaction - believes that pain is down to the tissues, not the brains evaluation of threat "…the brain only reacts to what the spinal cord and nerves tell it…" CP-P4-P137postS1:	Little or no intelligibility - believes brain is a passive receiver "…brain only reacts to what the spinal cord and nerves tell it…" CP-P4-P137postS1:	Little or no plausibility – they use their experience of " I could be happily doing something not in any danger and still be in pain." As evidence against pillar 4 reducing it's plausibility	
	Relevance	I don't think the tissues are damaged, I just think they're very sensitive. I think once they desensitise a bit, it will be slightly better. That's what I think it is, I think it's all to do with sensitivity. R-P137postS1 If I don't meditate I get stressed which makes everything else that little bit more heightened including my pain. R-P137postS2 I see my mood and pain as separate, cose I'm on medication for my mood which makes me feel kind of numb, plus can have a fantastic day and still be in pain. R-P137postS3				

		I never thought about the baseline, how that can stop a flare up, now I'm putting that into practice and it's helping. R-P137postS4 [Was it relevant to you] Yeah, yeah. They change it slightly each time, so it was more relevant, and I thought that was really good. R-P137postS5 Well for me I went in there with, you know I'd tried all sorts I thought I'm not going to come out with anything here. I went in there and they showed me something new I was like wow, it was like, quite a big impact on me. It was like wait a minute this is something completely different. R-P137postS6		
	Perceived benefit	I went in there with, you know I'd tried all sorts I thought I'm not going to come out with anything here. I went in there and they showed me something new I was like wow, it was like, quite a big impact on me. It was like wait a minute this is something completely different. B-P137postS1 First thing they do is teach you about baselines. I know I can attempt it in my own way, by doing less and coping with the baseline rather than throwing myself into it everything. I still have the same amount of flare		

		ups but they're not as long, so they're reducing which is fantastic. B-P137postS2 I just thought the whole course in itself was really educational. It wasn't just here's your pain, deal with it, it was more of trying to explain it. When someone is trying to help you understand where the pain comes from and that it's not just your brain and yes the pain is real and the pain isn't just in your head and you're not making it up, it makes you a bit more, well positive. B-P137postS3 It made me feel like I was not insane. With this constant having this pain in my back. I was thinking oh it's just me being paranoid, there is absolutely nothing there. But it's like right you're not being paranoid, go and get the ibuprofen gel on, or put some lavender oil, burn some and it will help you to relax and that will help everything to heal. So I know now if it [my pain] goes worse and I need to go to the hospital I'm not going to be paranoid I'll get to the hospital and get seen. Rather than just plodding on with it. B-P137postS4 It's made me feel a bit more confident, less anxious that I was doing the wrong thing and now I'm doing the		

		right thing, that I can make it slightly better. B-P137postS5		

Legend: *Table 7.9 shows an extract of Appendix 22 – 'Posner et al 1982 conditions within Useful summaries', which shows how the role of Posner et al. 1982 conditions for conceptual change in the process of pain reconceptualisation were explored. The first column is for case/timepoint identification. The second column is for the themes and subthemes for which useful summaries were generated. The third column contains the useful summary for the associated theme, case and timepoint. The fourth column is for the strength of evidence, and supporting evidence for the presence of the four conditions for conceptual change outlined by Posner et al., (1982) and graded using the criteria outlined in Table 7.8 ranging from "Little or no" evidence, "Partial" evidence, and "Strong" evidence. 'No data' is used where the theme was not discussed within the interview.*

B-P137postS1 stands for: Perceived benefit subtheme Participant 137 Post intervention Useful Summary 1.

CP-P1-P137postS1 stands for: Understanding Pain-Subtheme 1 Pain does not provide a measure of the state of the tissues-Participant 137 Post Intervention Useful Summary 1.

To aid in the exploration of the role of Posner et al. (1982) conditions for conceptual change in the process of pain reconceptualisation, a condensed version of Appendix 22 was created called Table 7.13 (See results and discussion subsection 7.4.3 for the complete table or Table 7.10 provided below for an example). The strength of evidence gradings for the conditions for conceptual change graded and justified by JW (Verified by CR) were transferred from *Appendix 22 – Posner et al. 1982 conditions within useful summaries* in a condensed format to Table 7.13. The advantage of presenting this data in a condensed format was to ensure that Table 7.13 could be easily viewed as a whole. This was important for aim two of this chapter, *to explore the role of the conditions for conceptual change in the process of pain reconceptualisation* (see results and discussion subsection 7.4.3). This allowed any change along the continuum of the grades of the evidence for the presence of the conditions for conceptual change detailed in Table 7.8 of "Strong", "Partial" and "Little or no" to be seen. In line with the traffic light approach to display the change in alignment to contemporary pain science, a traffic light system was used to display a change in the strength of evidence for the presence of Posner's conditions for conceptual change within the useful summaries pre to post the PSE informed PMP. One green dot  indicated a strengthening in evidence for the conditions of conceptual change by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial". Two green dots  indicated a strengthening by two categories along the continuum i.e., moving from "little to no" to "Strong". One orange dot  indicated there was no meaningful change in the evidence for the conditions of conceptual change. One red dot  indicated a weakening in the evidence for the conditions of conceptual change by one category along the continuum i.e., moving from "Strong" to "Partial". Two red dots  indicated a weakening by two categories along the continuum i.e., moving from "Strong" to "Little or no".

Table 7.13 was used to explore the role of Posner et al. (1982) conditions for conceptual change in the process of pain reconceptualisation. JW then wrote a narrative summary of the findings, supported with extracts from the useful summaries generated in the data management stage thus addressing aim 2 of this chapter (see subsection 7.4.3).

Table 7.10 A table showing an example of Table 7.13

Case	Theme		Evidence of Dissatisfaction	Evidence of Intelligibility	Evidence of Plausibility	Evidence of Fruitfulness
P137 Pre	Pillar 1		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	Little or no fruitfulness
	Pillar 2	Somatic	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Psychological	Little or no dissatisfaction	Partial intelligibility	Little or no plausibility	
		Social	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 3		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	
P137 Post	Pillar 1		Partial dissatisfaction	Partial intelligibility	Partial plausibility	Strong fruitfulness
	Pillar 2	Somatic	Strong dissatisfaction	Partial intelligibility	Strong plausibility	
		Psychological	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Social	No data*	No data	No data	
	Pillar 3		Strong dissatisfaction	Strong intelligibility	Strong plausibility	
	Pillar 4		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	

Legend: *Table 7.10 shows an extract of Table 7.13 from the results section (7.4) which shows the grading of the strength of the evidence for the presence of Posner's conditions for conceptual change within the useful summaries. The first column is for case/timepoint identification. The second column is for the*

themes and subthemes for which useful summaries were generated. The second column as in Table 7.12 includes a traffic light system to display a change in alignment to contemporary pain science from pre to post the PSE informed PMP. One green dot  *indicated a shift towards contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial", and thus indicative of the presence of pain reconceptualisation. Two green dots*  *indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from "little to no" to "Strong", and thus indicative of the presence of strong pain reconceptualisation. One orange dot*  *indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot*  *indicated a shift away from contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "Strong" to "Partial", and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots*  *indicated a large shift away contemporary pain science by two categories along the continuum i.e., moving from "Strong" to "Little or no", and thus indicative of the presence of strong anti-pain reconceptualisation.P137 pre, Participant 137 Pre intervention. P137 post, Participant 137 Post intervention. The next four columns are for the strength of evidence, and supporting evidence for the presence of the four conditions for conceptual change outlined by Posner et al., (1982) and graded using the criteria outlined in Table 7.8 ranging from "Little or no" evidence, "Partial" evidence, and "Strong" evidence. A traffic light system was used to display a change in the strength of evidence for the presence of Posner's conditions for conceptual change within the useful summaries pre to post the PSE informed PMP. One green dot*  *indicated a strengthening in strength by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial". Two green dots*  *indicated a strengthening in strength by two categories along the continuum i.e., moving from "little to no" to "Strong". One orange dot*  *indicated there was no meaningful change in the strength of evidence. One red dot*  *indicated a weakening in strength by one category along the continuum i.e., moving from "Strong" to "Partial". Two red dots*  *indicated a weakening in strength by two categories along the continuum i.e., moving from "Strong" to "Little or no". 'No data' is used where the theme was not discussed within the interview. In addition, the traffic light system was also used in the first column to display the overall change in alignment to contemporary pain science including all four pillars of contemporary pain science. This is equivalent to the overall degree of pain reconceptualisation. To calculate overall degree of pain reconceptualisation the number of green, amber and red dots were combined with the total shown in the post participant row in the first column. The total number of green dots across all four subthemes was included in the overall degree of reconceptualisation. The number of red dots present across all four subthemes resulted in the equivalent number of green dots being removed from the overall score I.e., one red dot and one green*

dot cancel each other out. Amber dots neither add or minus the number of green or red dots. Where there was overall no change an amber dot was shown to reflect no overall degree of reconceptualisation.

Whilst this methods section has outlined a linear structure for how the analysis was conducted, in reality this was an iterative process, moving between the stages, and adjusting the method to ensure the aims of the study were met. The four pillars of contemporary pain science (Moseley, 2007) neatly map onto the 1-3 conditions of conceptual change theory (Posner et al. 1982). When exploring the role of the fourth condition, fruitfulness, in the process of pain reconceptualisation it became clear that it was very challenging, if not impossible, to consistently and transparently assign the aspects of fruitfulness to one particular pillar of contemporary pain science (Moseley, 2007). The following useful summary for perceived benefit by P249 outlines this issue;

"What you need to do is make a few little steps don't do the full thing just do a few little. The next week add a few more little ones in, and the week after again until you're coping with it fine."

B-P249postS1

This summary clearly demonstrates perceived benefit and thus fruitfulness, however it would take a large assumption to attribute this benefit to an understanding of one specific pillar of contemporary pain science e.g., Pillar 1, Pain does not provide a measure of the state of the tissues. In contrast due to the generality of the benefit it could be argued that this benefit may have been obtained by an understanding across multiple pillars of contemporary pain science and thus used multiple times as evidence of fruitfulness. This would have resulted in large amounts of repetition. Therefore, the exploration of the role of fruitfulness for pain reconceptualisation was conducted at the participant level, rather than at the level of each pillar of contemporary pain science. This was facilitated in Appendix 22 by the two domains of fruitfulness (Relevance and Perceived benefits) having their own row containing their respective useful summaries. The fruitfulness column where the categorisation of the strength of evidence for the presence of fruitfulness would be assigned and justified was expanded to span all the rows of useful summaries (All 4 pillars of contemporary pain science, relevance and perceived benefit). This allowed any evidence of fruitfulness present in the useful summaries of the four pillars of contemporary pain science to be recorded as well as the addition of relevance and benefits recorded under the respective themes.

7.3.9 Mixed Methods data analysis

The mixed methods analysis addressed aim 3 of this chapter, to explore the relationship between the degree of pain reconceptualisation and changes in clinical outcomes (see results subsection 7.4.4). To address aim 3 the results from subsection 7.4.2 that explored the extent

and nature of pain reconceptualisation and the findings from the quantitative analysis outlined in subsection 7.3.7 that detailed using the MCID to determine if a clinically meaningful change had occurred were combined into table format (See table 7.18 and 7.19 in subsection 7.4.4). The first colum in this table was for the participant case. The colour of the cell that details the participant case ID reflected the overall degree of reconceptualisation detailed in table 7.12, subsection 7.4.2. Green, where overall the participant had undergone reconceptualisation. Orange, where overall the participant had not changed i.e. no reconceptualisation. Red, where overall the participant had undergone anti-reconceptualisation i.e. less evidence of alignment to the pillars of contemporary pain science. The colour of the cell containing the result of the change in clinical outcome score differed depending on if the minimal clinically important difference for that outcome was reached. Green indicated an improved score which reached the MCID, orange indicated the MCID was not reached in the positive or negative direction, and red indicated a worsened score which reached the MCID. JW and CR then independently reviewed the tables and looked for any pattern between the extent and nature of pain reconceptualisation and change in clinical outcomes, which would be apparent by the colour of the pain reconceptualisation matching the colour of the change in clinical outcome.

To explore the appropriateness of the outcome measures used within the study JW informally sought feedback from participants after completion of the measure and documented in field notes where the measure was deemed inappropriate, stating the reason. An informal thematic analysis was conducted on the reasons stated by participants for any inappropriate outcome measures. The number of reports of a measures inappropriateness was calculated by counting the number of participants who mentioned this. Where arising these reasons were discussed by JW, CR and DM, and may inform the selection of outcomes used in future pilot work. To explore the appropriateness of the eligibility criteria used within the study JW documented in field notes where it was deemed that a participant is inappropriate for inclusion in the study but was not excluded based upon the criteria. The reason were discussed by JW, CR and DM, and may inform the criteria used in future pilot work. The above methods in part addressed aim 4 of this chapter.

7.4 Results

The results section will be split into five sub-sections, the first outlining participant details followed by a section dedicated to addressing each of the chapters four aims:

- **Subsection 7.4.1** – Participant details
- **Subsection 7.4.2 -** An exploration of the extent and nature of pain reconceptualisation following a pain science education informed pain management programme using qualitative methodology
- **Subsection 7.4.3 -** The exploration of the role of the conditions for conceptual change in the process of reconceptualisation.
- **Subsection 7.4.4** - An exploration of the relationship between the degree of pain reconceptualisation and change in clinical outcomes.
- **Subsection 7.4.5 -** Preliminary work to look at the metrics to inform a pilot randomised controlled trial investigating the effectiveness of a pain science education informed pain management programme

7.4.1 Participant details

Eight people volunteered to participate in this study all of whom were of white British ethnicity, of these three were men and five were female. The mean age in years (SD) was 51.2 (17.3) and ranged from 26 to 74. The mean height in cm (SD) was 167.1 (14.7) and ranged from 151 to 187.5. The mean weight in kg (SD) was 88.8 (23.8) and ranged from 51.5 to 130. The mean BMI (SD) was 31.3 (4.7) and ranged from 22.6 to 33.5. The mean duration of pain in years (SD) was 17.8 (14.8) and ranged from 6 to 45. The highest education level was O levels in two participants, A levels in one participant, with the rest achieving BSc level. Mean number of attendances (SD) at the PSE informed PMP was 6.4 (2) and ranged from 8 to 2. Participant demographic information is shown in Table 7.11

Table 7.11 Participant Demographic Information

ID	Age (years)	Height (cm)	Weight (kg)	BMI	Ethnicity	Gender	Duration of pain (Years)	Highest Ed Level	Attendance /8
137	34	155.5	81	33.5	White British	Female	6	A levels	7
249	26	156.5	82	33.5	White British	Female	17	BSc	2
344	66	187.5	130.2	37	White British	Male	45	O levels	8
403	74	178.5	82.6	25.9	White British	Male	11	BSc	6
451	54	180	104.4	32.2	White British	Male	34	BSc	8
717	37	175.5	104.4	33.9	White British	Female	3.5	BSc	6
890	53	151	51.5	22.6	White British	Female	20	O levels	6
929	66	152	74	32	White British	Female	6	BSc	8
Mean (SD)	51.2 (17.3)	167.1 (14.7)	88.8 (23.8)	31.3(4.7)		5/8 Female	17.8 (14.8)		6.4 (2)

Legend: *BMI, Body mass index. cm, centre meter. Ed, Education. Kg, Kilogram.SD, Standard deviation.*

7.4.2 An exploration of the extent and nature of pain reconceptualisation following a pain science education informed pain management programme using qualitative methodology

The aim of this subsection was to address aim one of this chapter, *to explore the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology*.

To facilitate exploration of the patterns and explanations within the data during the abstraction and interpretation stage, Table 7.12 was created.

Table 7.12 The degree to which each participants 'Concept of Pain' was aligned to contemporary pain science

Case, timepoint and overall degree of reconcept-ualisation	Concept of pain			
	Pillar 1 **Pain does not provide a measure of the state of the tissues**	**Pillar 2** **Pain is modulated by many factors across somatic, psychological and social domains**	**Pillar 3** **The relationship between pain and the state of the tissues becomes less predictable as pain persists**	**Pillar 4** **Pain can be conceptualised as the conscious correlate of the implicit perception that tissue is in danger**
P137 pre	Little or no	Partial	Little or no	Little or no
P137 post	Partial	Partial	Strong	Little or no
P249 pre	Partial	Strong	Strong	Strong
P249 post	Partial	Strong	Strong	Strong
P344 pre	Partial	Little or no	Little or no	Little or no
P344 post	Little or no	Partial	Little or no	Little or no
P403 pre	Little or no	Partial	Little or no	Partial
P403 post	Partial	Partial	Little or no	Partial
P451 pre	Little or no	Little or no	Little or no	Little or no
P451 post	Little or no	Little or no	Little or no	Little or no
P717 pre	Partial	Strong	Little or no	Strong
P717 post	Strong	Strong	Strong	Strong
P890 pre	Little or no	Little or no	Little or no	Little or no
P929 pre	Strong	Strong	Strong	Strong

Legend: *Table 7.12 - The degree to which each participants 'Understanding of Pain' was aligned to contemporary pain science, graded from "Strong", where there was clear and consistent evidence of pain beliefs aligned to contemporary pain science; "Partial", where there was some evidence of pain beliefs aligned to contemporary pain science and some evidence of pain beliefs aligned to the biomedical model; and "Little or No", where there was clear and consistent evidence of pain beliefs aligned to the biomedical*

model with very limited or no evidence of pain beliefs aligned to contemporary pain science. A traffic light system was used to display a change in alignment to contemporary pain science from pre to post the PSE informed PMP. One green dot  *indicated a shift towards contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial", and thus indicative of the presence of pain reconceptualisation. Two green dots*  *indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from "little to no" to "Strong", and thus indicative of the presence of strong pain reconceptualisation. One orange dot*  *indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot*  *indicated a shift away from contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "Strong" to "Partial", and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots*  *indicated a large shift away contemporary pain science by two categories along the continuum i.e., moving from "Strong" to "Little or no", and thus indicative of the presence of strong anti-pain reconceptualisation. In addition, the traffic light system was also used in the first column to display the overall change in alignment to contemporary pain science including all four pillars of contemporary pain science. This is equivalent to the overall degree of pain reconceptualisation. To calculate overall degree of pain reconceptualisation the number of green, amber and red dots were combined with the total shown in the post participant row in the first column. The total number of green dots across all four subthemes was included in the overall degree of reconceptualisation. The number of red dots present across all four subthemes resulted in the equivalent number of green dots being removed from the overall score i.e., one red dot and one green dot cancel each other out. Amber dots neither add or minus the number of green or red dots. Where there was overall no change an amber dot was shown to reflect no overall degree of reconceptualisation.*
P137 pre, Participant 137 Pre intervention. P137 post, Participant 137 Post intervention.

The theme *Concept of Pain* was comprised of the sub-themes of the four pillars of contemporary pain science defined by Moseley, (2007): *(1) Pain does not provide a measure of the state of the tissues; (2) Pain is modulated by many factors across somatic, psychological and social domains; (3) The relationship between pain and tissue becomes less predictable as pain persists; and (4) pain can be conceptualised as a conscious correlate of the implicit perception that tissue is in danger.*

7.4.2.1 Alignment of participants to contemporary pain science pre PSE informed PMP

The findings shown in Table 7.12 show 5 out of 8 participants (P137, P344, P403, P451, P890) pre intervention predominantly held beliefs in alignment with the biomedical model. The predominantly biomedical pain beliefs seen in participants within this study is in keeping with public surveys exploring pain beliefs across several countries, including the UK (Moffett *et al.*, 2000; Ihlebæk and Eriksen, 2003; Goubert, Crombez and De Bourdeaudhuij, 2004; Darlow *et*

al., 2014). In a UK based survey nearly two thirds of respondents incorrectly believed that back pain was usually caused by a slipped disc or trapped nerve (Moffett et al. 2000). The widespread misconception that pain relates to the state of the tissues was replicated in Norway where ~50% of respondents believed imaging can identify the cause of pain, ~50% believed back pain is caused by injury and heavy lifting and ~60% believed everyone with back pain should have an x-ray (Ihlebæk and Eriksen, 2003).

The above survey findings are in keeping with qualitative research exploring peoples pain beliefs (Lin *et al.*, 2013; Stenberg, Fjellman-Wiklund and Ahlgren, 2014; Darlow *et al.*, 2015). Lin et al. (2013) in a qualitative study exploring the pain beliefs of Aboriginal Australians with CLBP (n=32) more than half of participants believed there was a structural cause of their back pain;

"Well I got told by [medical specialist] that it might be a trapped nerve or, that was before I had my first MRI, and then they said no you've got lower lumbar ... and as I said it's just bone crunchin' on bone" (R5: 42-year-old man with highly disabling CLBP)
Lin et al. (2013, p.4)

Darlow et al. (2015) also found strong biomedical beliefs during their thematic analysis with participants with acute (n=12) and chronic (n=11) back pain. All participants within this study regarded the cause of their back pain to be from physical injury, damage, or dysfunction. Many also believed that back pain meant they had not adequately protected their back;

> *"I suspect it's probably from lifting something in the incorrect manner ... I haven't done anything [else] overly strenuous in the last week" (ALBP09)*
>
> Darlow et al. (2015, p.845)

All participants within the current study had previously received a 90 minute PSE intervention as part of their usual care before attending the PSE informed PMP. The extent and nature of reconceptualisation following this 90 minute PSE intervention has previously been explored by the research group at Teesside University and is detailed in their publications (Robinson et al. 2016; King et al. 2016; King et al. 2018). In all three studies post intervention there was heterogeneity regarding the degree of reconceptualisation with some participants undergoing strong degrees of reconceptualisation, some undergoing more partial and patchy reconceptualisation, and some not undergoing reconceptualisation at all. The heterogeneity in the degree of reconceptualisation was mirrored by the heterogeneity in alignment to

contemporary pain science (Robinson et al. 2016; King et al. 2016; King et al. 2018). The participants within the current study show similar heterogeneity in their alignment to contemporary pain science at the pre interview (before the PSE informed PMP) having recently attended a 90 minute PSE intervention. The similarity of the participants concept of pain within the current study pre intervention compared to previous survey studies, previous qualitative studies, and previous qualitative PSE studies increases confidence in the findings of the current study.

7.4.2.2 The overall degree of pain reconceptualisation following PSE informed PMP

When viewing all four pillars of contemporary pain science three participants (P137, P403, P717) showed evidence of pain reconceptualisation and were classified as 'pain reconceptualisors', represented by green and orange dots. The other three participants showed no overall change and were classified as 'non-reconceptualisors' represented by all orange dots (P249, P451) or orange dots with an equal number of red and green dots (P344).

It is important to highlight that being classified as a 'reconceptualisor' does not mean that the individual fully reconceptualised such that their alignment to contemporary pain science was strong in all four pillars. It merely means their alignment to contemporary pain science was strengthened overall post intervention compared to pre. Only one reconceptualisor (P717) was graded as strong in their alignment to all four pillars at the post interview with the other reconceptualisors (P137, P403) alignment to contemporary pain science graded as a mixture of strong, partial and little or no. Furthermore being classified as a non-reconceptualsor does not mean that pain reconceptualisation did not occur in any pillar of contemporary pain science. One participant (P344) underwent pain reconceptualisation in pillar 2 from little or no to partial, and simultaneously underwent anti-pain reconceptualision in pillar 1 moving from partial to little or no. Pillars 3 and 4 alignment to contemporary pain science was unchanged. These findings are illustrative that undergoing pain reconceptualisation in one pillar of contemporary pain science isn't always paired with reconceptualisation in the other pillars. Furthermore these findings emphasise that pain reconceptualisation is very much on a spectrum. Whilst I have tried to capture points on that spectrum by grading alignment to contemporary pain science from little or no, partial, and strong, in reality pain reconceptualisation is a continuous phenomenon. I have put the qualifiers in to help guide the reader to discern a pattern but it is important to highlight that these categories are not truly discrete.

The findings from the current study that some people who receive a PSE informed PMP undergo pain reconceptualisation, whilst others do not is in keeping with previous qualitative studies exploring pain reconceptualisation following PSE (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018; King et al. 2018). Wijma et al. (2018) conducted semi-structured interviews and focus groups, analysing the data using Grounded Theory. Grounded Theory involves using data collected in the field with conceptual thinking to build theory rather than theory or hypothesis testing (Corbin and Strauss, 2014; Khan, 2014). Wijma et al., 2018 constructed a theoretical framework from the data of constructs influencing the experience of Pain Neuroscience Education in patients with non-specific chronic pain. One aspect of this theoretical framework was 'Scepticism'. This included the sub-themes 'Doubt about the diagnosis and explanation' and 'Disagreement about the diagnosis and explanation' with some participants completely rejecting the messages delivered by PSE, indicative of the absence of pain reconceptualisation. In contrast, within the topic of 'Outcomes of Pain Neuroscience education', one sub-theme, 'Finding peace of mind' demonstrated that some participants accepted the messages of PSE which they found to be reassuring;

"*And now I found some peace of mind. Like, well, stop searching. There is, so far, nothing more to do. (…) So, well, a bit of peace of mind. Some clarity*".
(Wijma et al., 2018, p.7, Helga)

The findings of the quantitative literature are broadly in support of the narrative emerging from the qualitative literature that pain reconceptualisation can occur following PSE (Watson et al. 2019). In the quantitative aspect of Chapter 5, the meta-analysed pooled treatment effect for PSE versus control had clinical relevance in the short term for kinesiophobia (−13.55/100; 95% CI, −25.89 to −1.21) and for pain catastrophizing in the medium term (−5.26/52; 95% CI, −10.59 to .08). Although kinesiophobia and pain catastrophising are not direct measures of pain reconceptualization, they do provide an insight into how an individual understands their pain and how threatened they feel because of it. Therefore improvements in these measures are suggestive of the occurrence of pain reconceptualisation.

The authors of previous qualitative studies have suggested that delivering PSE over multiple sessions (Robinson et al. 2016) and in combination with other active interventions such as exercise (King et al. 2018) may facilitate pain reconceptualisation. Reviews of the PSE literature are also broadly supportive of these suggestions. The conclusions of Moseley and Butler, (2015) in their narrative review, and Yun, (2017) in their systematic review and meta-analysis both emphasised the importance of combining PSE with other active interventions. This was also supported by the findings of Chapter 5 of this thesis (published Watson et al.

2019) where greater effects for pain catastrophising in the medium term were seen when PSE was delivered for longer durations. However the slopes of the meta-regressions were shallow and of questionable clinical relevance. Greater improvements in pain catastrophising in the short and medium term were seen when PSE was combined with another intervention, with the slopes of the meta-regressions indicating clinical relevance. Given the previous PSE research one might have expected to see a more marked strength in participants degree of pain reconceptualisation in the current study compared to previous qualitative work that only used a single 90 minute PSE intervention. The pattern of pain reconceptualisation following the PSE informed PMP emerging from this chapter was similar to that of previous qualitative research. In contrast to the previous PSE research to date, this chapter provides no evidence to suggest that there may be a difference in the degree of pain reconceptualisation following a brief PSE intervention compared to a more intensive PSE combined with a PMP.

Why then may the findings from this chapter in part contradict the previous PSE research that suggest greater effects where PSE is delivered over longer durations and combined with other interventions? The small sample of participants for whom pre and post data was available may have obfuscated a possible pattern. Another explanation could be the samples used. Whilst the current study recruited from the same NHS Pain Clinic as in previous qualitative studies (Robinson et al. 2016; King et al. 2016; King et al. 2018), the current study recruited at a different point in the care pathway. Previous studies recruited individuals who were referred through to the 90 minute PSE intervention offered to most participants who attended the NHS Pain Clinic. The current study recruited participants who after attending the 90 minute PSE intervention were referred through to the PMP which is offered only to those individuals who are determined to have a higher level of clinical need. Therefore, it is possible that the current study recruited individuals who had subtle but important differences compared to previous studies, thus despite receiving PSE over a longer duration and combined with a PMP the degree of pain reconceptualisation seen was similar. As previous studies did not administer any patient reported outcome measures it is difficult to compare their samples with the current study to provide any evidence for or against the above hypothesis. Limited demographic data was collected, and thus a comparison of the duration of pain can be made. The mean duration of pain in years (SD) was visibly higher in the current study 17.8 (14.8) compared to Robinson et al. (2016) 9.2 (10), King et al. (2016) 9.7 (9.8), and King et al. (2018) 9.7 (8.6). Recently published data evaluating the North East of England Regional Back Pain and Radicular Pain Pathway suggests that duration of pain at baseline is of clinical importance (Jess *et al.*, 2021). Individuals who had a shorter duration of pain (<3months) demonstrated statistically ($P<0.05$) larger improvements than individuals who had a greater duration of pain (≥12 months) and in some cases surpassed the threshold for clinical relevance. The results of Jess et al. (2021)

may be less relevant within the context of the PSE qualitative studies discussed here as the duration of 30/31 participants from Robinson et al. (2016), King et al. (2016) and King et al. (2018) had a duration of pain ≥12 months, mirrored by the current study where 8/8 participants had a duration of pain ≥12 months. It is possible that as the duration of pain increases beyond 12 months the differences in clinical outcomes reported by Jess et al. (2021) become less important e.g., 4 years to 14 years may be less important than 3 months to ≥12 months.

Another possible explanation for the current chapters lack of alignment with previous PSE research suggesting greater effects where PSE is delivered over longer durations and combined with other interventions comes from Ryan et al. (2010) who explored the effect of PSE alone versus combined PSE and group exercise (n=38). Counterintuitively, PSE alone was associated with better outcomes. The authors postulated that as the PSE and group exercise interventions were not delivered in a joined up manner, the participants could have been exposed to other participants and/or therapists biomedical view of pain. Their findings emphasised the importance of carefully integrating PSE with other interventions in order to not inadvertently dilute the effect. The intervention used within the current study was a PSE informed PMP delivered in a NHS Pain Clinic. When JW observed the intervention it was apparent that PSE was integrated throughout most of the PMP, with clinicians referring back to the messages of PSE throughout. However there were some elements of the PMP that could be argued were more in alignment with the biomedical model than contemporary pain science. One session in particular focused on good posture and alignment during activities of daily living such as lying, sitting, standing and walking. The walking component of the PMP was discussed by four participants (P137, P249, P403, P717) and posture by one participant (P451). Three participants were particularly enthusiastic about the *correct* way to walk which they have integrated into their life;

"Well walking is one of them cose in [The PMP one of the facilitators] erm showed us the African women walking with 2 stone on her head and no hands etcetera and just wiggling the hips and things like that erm, you don't obviously the general public and obviously I didn't realise there is a correct and an incorrect way of walking erm but clearly there is, as you say if a skinny woman can pout 2 stone on her head and in not move when she's walking along is incredible"

Participant 403 Post L506-510

"Erm the physio side of it brilliant… I've been using different techniques for walking, and you know and things like that to try and alleviate the pain…"

Participant 717 Post L409-411

Interestingly all three participants who spoke positively about the walking component of the programme also underwent pain reconceptualisation which suggests that receiving some biomedical information about walking may not prevent pain reconceptualisation. Furthermore, the one participant who spoke negatively about the walking component did not reconceptualise. They did not find the walking component as relevant to them;

Interviewer: *"So it wasn't relevant to you because, there was a lot of mobility in the [programme]?"*

P249: *"Yeah there was a lot more of it to do with mobility issues and how you walk and how you run, and what kind of exercises you should do and things like that, but for me it wasn't that that I needed it was well how do I cope with the pain…"*
Participant 249 Post L1067-1072

These findings suggest that the lack of pain reconceptualisation in three of the participants may not be due to some biomedical messages within the PMP. There may be other factors which impact on the degree and nature of reconceptualisation which will be explored later within this chapter.

Another possible reason for the current chapters lack of alignment with previous PSE research about greater effects where PSE is delivered over longer durations and combined with other interventions is possible ceiling effects. All individuals within the current study had already attended a single brief 90 minute session of PSE and it is possible that some may have already undergone pain reconceptualisation creating a possible ceiling effect for greater degrees of reconceptualisation. The 90 minute session may have realigned the 'low hanging fruit' of erroneous concepts of pain, leaving only the harder to reach concepts. Ceiling effects appear to be present for P929, P249 and P717 pre PSE informed PMP who had "strong" alignment to contemporary pain science for four, three and two of the four pillars respectively. P249 and P929 explicitly talk about the single PSE intervention impacting on their understanding of their pain;

"…that's only because I've been to that [Explain pain session]. Previously I would have said there's something wrong, how can my shoulders and my back, you know there's something wrong but now I think I'm probably, my tissues quite healthy"
Participant P929 pre L754-757

“So it, it shouldn’t still be there now, that should be healed, whatever was injured would be healed by now, erm so we need to completely try and rewire the brain to know that that isn’t in pain anymore, that’s not injured, that’s that’s over a done with, and er that’s what my 8 week course is supposed to tell me a bit more about cose unfortunately I’ve only had the er one explain pain session”

Participant P249 pre L795-799

"...I’d already learnt it, was like erm the explain pain clinic all over again”

Participant P249 post L1017

Despite the possible impact of ceiling effects on the degree of pain reconceptualisation having attended a single 90 minute PSE session, three participants (P137, P403, P717) underwent pain reconceptualisation after attending a further PSE informed PMP. This raises an interesting question, does embedding PSE at multiple stages of the care pathway facilitate greater degrees of pain reconceptualisation? This question warrants further study.

In contrast to participants P137, P403, P717, Participant P451 had “little or no” alignment to contemporary pain science at the pre and post interview suggesting that both the single 90 minute PSE and the combined PSE and PMP did not produce any pain reconceptualisation. This raises the question are some individuals not suited to group based intervention and instead require much more personalised intervention to achieve any degree of pain reconceptualisation?

In summary, when viewing the degree of pain reconceptualisation across all four pillars of contemporary pain science the pattern emerging about extent and nature of pain reconceptualisation following a PSE informed PMP appears to mirror the pattern seen following a single brief PSE intervention. Therefore, in contrast to previous PSE research to date there is no evidence emerging to suggest that there may be a difference in the degree of pain reconceptualisation following a single brief PSE compared to where PSE is delivered over longer durations and combined with other interventions. Possible explanations for the absence of evidence for this possible pattern could include differences in the sample with the current study possibly having more complex pain presentations, and possible ceiling effects. This subsection has raised two questions which warrant further study:

- Does embedding PSE at multiple stages of the care pathway facilitate greater degrees of pain reconceptualisation?
- Are some individuals not suited to group based intervention and instead require much more personalised intervention to achieve any degree of pain reconceptualisation?

The sections below explore the change of participants concept of pain for each of the four pillars of contemporary pain science pre and post a PSE informed PMP.

7.4.2.3 The degree of reconceptualisation for pillar 1 - Pain does not provide a measure of the state of the tissues

Where participants displayed evidence that they believed pain provided a measure of the state of their tissues, this was interpreted as their concept of pain more heavily grounded in the biomedical model. Where participants displayed evidence their concept of pain did not provide a measure of the state of their tissues, this was interpreted as a concept of pain in alignment with pillar 1 of contemporary pain science.

For three participants (P137, P403, P717) there was clear movement towards the concept that their pain did not provide a measure of the state of their tissues compared to their pre interview, indicative of the presence of pain reconceptualisation. Participant P137 started from a position of “Little to no” alignment to contemporary pain science in the pre interview. This was reflected by their consistent and explicit statements indicating their pain means damage;

“When I get knee pain it means knee damage every time.”
CP-P1-P137preS1

After the PSE informed PMP there was a clear shift in their language bringing them more in line with contemporary pain science;

“I don’t think my tissues are damaged, I think they’re over sensitised so I feel more pain.”
CP-P1-P137postS4.

Interestingly, and in line with previous qualitative studies on PSE by the research group at Teesside University (Robinson et al. 2016, King et al. 2016, King et al. 2018), P137 simultaneously held contradictory concepts about the relationship between pain and tissue state following the intervention. Their language was both in line with contemporary pain science as above, and in line with the biomedical model;

"Pain means tissue health is rubbish. I'm probably wrong but I've been told and it feels like pain is caused by stretched and compacted muscles and tendons which damages them."
CP-P1-P137postS2.

Contradictory messages about the relationship between pain and tissue state, in addition to their interpretation of their pain sensation appears to have resulted in them holding contradictory conceptions. This has left them confused about the relationship between pain and tissue state;

"I don't know what to think about the tissues cose I've been told so many different things by the pain clinic and others."
CP-P1-P137postS1

Therefore their concept of pain for pillar 1 of contemporary pain science after the PSE informed PMP is best described as "Partial". The impact of contradictory messages conveyed to P137 emphasise the importance of consistency of message across the healthcare system about the relationship between pain and tissue state. Public and professional health campaigns that promote pain beliefs more in line with contemporary pain science may be important in addressing this issue. Buchbinder et al. (2018 p. 2384) in their landmark publication series on low back pain emphasised that society needs to;

"*Address widespread misconceptions in the population and among health professionals about the causes, prognosis, and effectiveness of different treatments for low back pain, and deal fragmented and outdated models of care"*

In 2020 Buchbinder et al. (2020 p. 6) provide an update to their publication and state;

"Widespread and inaccurate beliefs about low back pain in the population and among health professionals should be challenged, and a focus put on reducing the impact of low back pain on people's lives rather than seeking medical treatment for a "cure" "

Suman et al. (2020) show that changing public and professional beliefs is possible in their systematic review (n=18) of the effectiveness of mass media campaigns for the management of low back pain concluding;

"*Mass media campaigns for LBP appear effective for improving beliefs of the general public and health care providers, making beliefs more in line with current evidence and self-management principles.*"
Suman et al. (2020 p.27)

There appears to be growing consensus within the literature that inaccurate pain beliefs amongst the public and health professionals need to be addressed (Buchbinder et al. 2018; Buchbinder et al. 2020) and the account of P137 provides further weight to this argument (CP-P1-P137postS1). Furthermore there is promising evidence that public health campaigns that seek to address inaccurate pain beliefs can be successful in changing such beliefs (Suman *et al.*, 2021).

Two participants (P249, P451) showed no obvious pain reconceptualisation regarding their belief about the relationship between pain and tissue state. P249 pre displayed partial alignment to contemporary pain science for pillar 1. Similar to P137 post described above, P249 pre conveyed how contradictory evidence between what they have been told (or conceptually 'know') and what their body tells them leads to a conflicted and changing belief about the relationship between their pain and tissue state. They describe that this conflict becomes more salient when pain severity is high.

"I used to think there was a relationship between pain and tissue state but I've been told by so many specialists there is nothing wrong with my tissues, so I guess there is not. When my pains really sore it makes me think something is wrong. I think if I had a scan my tissues would look normal but they don't feel normal, it feels like there is damage but I don't think there really is."
CP-P1-P249preS2

After the PSE informed PMP their account showed no significant change;

"I don't think there is a relationship between pain and tissue state because in 16 years of pain I've not had any proof anything is wrong with the tissues, even if it feels like there is but in that moment when the pain is severe I'm thinking of my god what's wrong."
CP-P1-P249postS4

The account of P249 suggests that some individuals may place their first person subjective experience, in this case pain perception "***feeling"*** like tissue damage, at a higher level of

evidence compared to something that they are told or conceptually know i.e., their tissues are normal.

Notably one participant (P344) showed movement away from contemporary pain science, towards a biomedical concept of pain for pillar 1 after the PSE informed PMP indicative of a kind of anti-pain reconceptualisation. Whilst their account pre intervention was heavily grounded in the biomedical model;

"I think the cause of my pain is crushed vertebrae and disc related which is not self-repairing otherwise I would not be getting pain signals."

CP-P1-P344preS1

There was some dissatisfaction with this conception reflecting the "partial" nature of pillar 1 of their concept of pain;

"Couldn't say pain was the tissues because pain intensity varies so much"

CP-P1-P344preS4

However after the PSE informed PMP their account conveyed their certainty for the relationship between pain and tissue state;

"There is a relationship between pain and tissue state because if there wasn't damage you wouldn't feel pain. The pain is too real for there to be nothing wrong with the tissues. Pain's been in same place since injuries so that's 100% causing the pain."

CP-P1-P344postS1

The shift away from contemporary pain science and towards a biomedical concept of pain despite receiving education designed to do the opposite is particularly notable and is the first recorded case of this within the PSE literature.

There are several reports of public health education interventions engendering 'boomerang effects' whereby "*a strategic message generates the opposite attitude or behaviour than was originally intended*" (Byrne and Hart, 2009 p.4). These boomerang effects have been observed in attempts to reduce smoking (Wolburg, 2006) , reduce heavy alcohol consumption (Wechsler *et al.*, 2003), and reduce drug abuse (Rosenbaum and Hanson, 1998).

Psychological reactance theory (Brehm and Brehm, 2013) has been used to help explain the boomerang effect and may be at least partially helpful elucidating the anti-reconceptualisation seen in P344 pillar 1. The foundational principal of psychological reactance theory is that individuals cherish their freedom, choice and autonomy. When something is perceived by the individual to threaten their freedom the result may be psychological reactance (Brehm and Brehm, 2013). Psychological reactance is "*the motivational state that is hypothesized to occur when a freedom is eliminated or threatened with elimination*" (Brehm and Brehm, 2013 p.37). In a more contemporary model of psychological reactance, 'An Intertwined Process Cognitive-affective Model' by Dillard and Shen, (2005), reactance is comprised of "*an intermingling of negative cognition and anger*" (Dillard and Shen, 2005, p. 160). The cognitive component was operationalised as counter-arguing, for example criticisms of the message source or thoughts expressing disagreement with the message. The anger component was measured using a 5-point response scale anchored at 0 = "none of this feeling" and 4 = "a great deal of this feeling." (Dillard and Shen, 2005).

In the case of P344 they were hoping for a 'magic bullet' to cure their pain;

"…throughout my life I've been hoping they were going to invent this magic bullet erm, medi, medicinal bullet that would stop the pain or find some way of being able to operate on it and fix it…"

Participant 344 Post L509-511

Despite having had their pain for many years and receiving multiple interventions for their pain P344 still held expectations that the healthcare system would be able to help improve their pain;

"prior to going on the course I always had expectations that I would go and see my GP and they would say right we will try this and that would really help… going on the course has made me realise that that's not going to happen either"

Participant 344 Post L519-522

During the PSE informed PMP their belief and hope for a cure for their pain was threatened leaving them feeling angry;

"I'm still angry with the fact that it's never going to go away, and there's anger that there is no one to blame it's there, there's no body I can blame it's your fault I've got it, or it's your fault I can't get rid of it I know it's there, I know it's there…"

Participant 344 Post L519-522

Through the lens of psychological reactance theory, the hope of P344 that a magic bullet can cure their pain, and restore their freedom may have been perceived as under threat by the messages delivered in PSE. If pain does not provide a measure of tissue state then a surgery or medication to 'fix' their problem is less likely, as is the hope of being pain free ultimately putting the life they had planned under threat. This threat may have resulted in anger and explicit counter arguments the message delivered by PSE regarding the relationship between pain and the state of the tissues;

"There is a relationship between pain and tissue state because if there wasn't damage you wouldn't feel pain. The pain is too real for there to be nothing wrong with the tissues. Pain's been in same place since injuries so that's 100% causing the pain."
CP-P1-P344postS1

Therefore the Intertwined Process Cognitive-affective Model of psychological reactance proposed by Dillard and Shen, (2005) appears to be a good fit to explain the boomerang effect seen in P344 regarding pillar 1.

The boomerang effect has been seen in two studies by the research group at Teesside university (King et al. 2016; King et al. 2018). Contrary to P344 who underwent anti-reconceptualisation following PSE, the participants in the previous studies simply had their biomedical concept of pain reinforced. This was most salient for Participant E in King et al. (2016) who had read Explain Pain (Butler and Moseley, 2013) and attended the same 90 minute PSE intervention twice. Despite this, and in complete contradiction to the messages of multiple PSE interventions they reported PSE reinforced their belief that pain was directly linked to damage;

"It's degenerative and it's not going to get, you know, I'm not going to get younger or anything." [Participant E Post-PNE]
King et al. (2016 p.1391)

"Very much clearer . . . My understanding. I think when I went through it the first time I came out a bit bamboozled with it all. But having bought the book [Explain Pain, 2003] as well and read some of it, I think that really helps. But it solidifies sort of where I was going or trying to go." [Participant E Post-PNE]
King et al. (2016 p.1391)

The authors of these studies (King et al. 2016; King et al. 2018) suggest that the reinforcement of biomedical beliefs following PSE could be due to some form of confirmation bias. Confirmation bias can be defined as *"the seeking or interpreting of evidence in ways that are partial to existing beliefs, expectations, or a hypothesis in hand"* (Nickerson, 1998) P.175). Confirmation bias fits as an explanation of the boomerang effect following PSE where the participant was grounded in the biomedical model pre intervention, as was the case for the two previous studies (King et al. 2016; King et al. 2018). In contrast P344 was partially aligned to contemporary pain science pre intervention and thus it seems less plausible that P344 would interpret the messages delivered by PSE to fit with the biomedical model as their beliefs are already at least partially contrary to the biomedical model. Therefore the Intertwined Process Cognitive-affective Model of psychological reactance appears to be a better fit to explain the boomerang effect seen in P344 (Dillard and Shen, 2005).

7.4.2.4 The degree of reconceptualisation for pillar 2 - Pain is modulated by many factors across somatic, psychological and social domains

Pillar 2 of contemporary pain science is comprised of three domains. Evidence of central and peripheral mechanisms involved in pain was interpreted as evidence in understanding of the somatic domain. Evidence of the role of attention, anxiety, expectation and meaning of the pain was interpreted as evidence in understanding of the psychological domain. Evidence of the impact of social and environmental context on pain was interpreted as evidence in understanding the social domain.

Whilst P344 was the only participant to show movement away from contemporary pain science towards the biomedical model pillar 1, contrastingly they were the only participant to show greater reconceptualisation in pillar 2 moving from "Little or no" contemporary pain science understanding to "Partial". Pre intervention, whilst they discussed pain receptors and the brain having a role in pain they did not discuss central and peripheral mechanisms leading to sensitivity;

"As far as I'm aware there must be pain receptors sending signals somewhere to the brain to tell you you've got pain so stop doing it but I don't know if that's true. I don't know if that's the tissues sending signals to the brain saying stop or just the brain. The brain is obviously receiving signals to say you've got pain and the more it goes on the worse it gets. There must be something like that happening for my brain to tell me my pain is getting worse."

ST2-P344preS2

Furthermore they believed psychological and social domains don't modulate pain;

"I would say emotions cannot affect my pain, if I'm happy it doesn't get any better, or if I'm snappy it doesn't get any worse."
ST2-P344preS4

"No social factors affect my pain."
ST2-P344preS5

After the PSE informed PMP there was some suggestion of the role of the brain releasing chemicals which impact on gateways modulating pain reflecting a shift in the somatic domain;

"Pain is caused by endorphins and all the rest of it omitted from my brain for different reasons and gateways where the brain lets so much through. Medication is supposed to shut these gateways off so the receptors aren't sending the signals that you have pain."
ST2-P344postS2

There was also a shift in the psychological domain relating to attention;

"Basically you need something to take your mind away from the pain more than anything."
ST2-P344postS4

But not emotions;

"I don't think emotions make my pain worse or better."
ST2-P344postS3

Or the social domain;

"I don't think social factors change my pain."
ST2-P344postS6

The concurrent anti-reconceptualisation in pillar 1 and reconceptualisation in pillar 2 of participant 344 demonstrates that pain reconceptualisation is a non-linear, multi-dimensional process and provides support for the granular approach to exploring the extent and nature of

reconceptualisation taken in this study, using qualitative methods and all four pillars of contemporary pain science (Moseley, 2007).

For pillar 2 all other participants (P137, P249, P403, P451, P717) for whom post data was available showed no change. Two participants (P249, P717) displayed evidence of a concept in line with pillar 2 pre the intervention being assigned “Strong”. The qualitative categorisation process was not sensitive enough to elucidate a further strengthening in evidence of alignment to contemporary pain science in those individuals graded as “Strong” at the pre interview, thus creating a ceiling effect.

“They said my brain is still receiving that there is pain in my back. I was told we need to completely rewire the receptors and brain to know that my back isn’t in pain anymore, that it’s not injured. I think pain is more to do with my brain than the actual thing hurting.”
ST2-P249preS2

“I know being depressed and worked up makes my pain much worse because basically I give pain my attention.”
ST2-P249preS7

“When you’re stressed you seem to focus on the things that are wrong and then your body is trying to protect them so there’s more receptors and your brain is picking up that there’s more so you seem to feel more than what’s actually there.”
ST2-P717preS4

“Yeah social factors can make my pain worse, the family stress me out and that can make the pain worse.”
ST2-P717preS10

7.4.2.5 The degree of reconceptualisation for pillar 3 - The relationship between pain and tissue becomes less predictable as pain persists

Where participants displayed evidence that as pain persists it’s less likely due to tissue damage, it was interpreted as a belief in line with pillar 3. Where participants displayed evidence suggestive that their pain means damage regardless of the length of time they have had it, it was interpreted as a belief not aligned to pillar 3.

Six participants at the pre interview displayed little or no evidence of alignment to pillar 3 of contemporary pain science. A biomedical concept of pain for pillar 3 was demonstrated in keeping with the other qualitative literature exploring pain beliefs of individuals with chronic pain, where the majority of participants believed there was a structural cause of their pain (Lin et al. 2013; Darlow et al. 2015). This improves the confidence that the initial pain beliefs of participants within this study are in keeping with that of previous studies exploring pain beliefs.

Two participants (P137, P717) showed the only evidence of strong reconceptualisation within the study reflective of movement by two categories (from "little or no" to "strong") for the concept of pain that the relationship between pain and tissues becomes less predictable as pain persists. Before the PSE informed PMP P137 clearly felt their knee cap was still damaged from a prior injury 7 years ago;

"Cause of knee pain was initially due to damage when knee cap snapped 7 years ago and the cause of knee pain now is still due to damage as it's not fully healed."

CP-P3-P137preS1

After the intervention, they outline how 7 years on their knee cap will have healed but is just more sensitive;

"Broke kneecap 7 years ago which was the start of pain, I don't think the tissues are damaged now cose they're constantly healing, they're just sensitive."

CP-P3-P137postS1

All other participants (P249, P344, P403, P451) showed no evidence of a shift in their concept of pain post intervention compared to pre. One of these participants (P249) displayed evidence of a "strong" alignment to contemporary pain science for pillar 3 pre the intervention and thus there may be a ceiling effect here.

"Told pain from injury to coccyx which happened as a kid so injury would have healed by now so shouldn't be feeling pain but the brain still receives there's pain which is why it hurts. I need to completely rewire receptors and brain to know my back isn't in pain or injured anymore."

CP-P3-P249preS1

It was not possible to draw comparisons between the degree of pain reconceptualsation seen in previous qualitative PSE studies for pillar 3 due to previous studies exploring understanding of pain more broadly rather than the granular approach taken in this study.

7.4.2.6 The degree of reconceptualisation for pillar 4 - pain can be conceptualised as a conscious correlate of the implicit perception that tissue is in danger.

Evidence for a concept of pain aligned to pillar 4 was where participants displayed evidence they understood that it is not the state of the tissues or the actual threat to the tissues that determines pain, it is the unconscious perceived level of threat as determined, unconsciously, by the nervous system.

It is notable that pillar 4 of contemporary pain science was unchanged (orange dots) for all participants. This raises an interesting question, is pillar 4 the most resistant pillar to change? If so what are the reasons for this? There could be several reasons in addition to the point above outlining it is perhaps the most difficult concept to understand. Other reasons could include healthcare professionals not giving it enough time or focus during PSE, or whether it is simply the most intransigent to change, or all of the reasons provided. Given that individuals with pain find "*conceptualising pain as a heightened protective response that could be lessened*" as a valuable lesson from PSE (Leake et al. 2021 p.1), facilitating pain reconceptualisation for pillar 4 which closely aligns with this may be important to ensure perceived benefit of PSE.

Another reason for the lack of pain reconceptualisation could be possible ceiling effects. Two participants (P249, P717) already displayed evidence of a "strong" understanding of contemporary pain science for pillar 4 at the pre interview and thus a ceiling effect may have occurred.

"I think if my brain didn't worry so much about being in danger the pain wouldn't be as high."
CP-P4-P249preS4

"Pain is related to the level of danger my brain thinks is in my tissues cose that's what the receptors are for, to send to your brain messages. But just cose my brain thinks it's in danger doesn't mean it is."
CP-P4-P717preS1

As with pillar 3, it was not possible to draw comparisons between the degree of pain reconceptualsation seen in previous qualitative PSE studies for pillar 4 due to previous studies exploring understanding of pain more broadly rather than the granular approach taken in this study (Robinson et al. 2016; King et al., 2016; King et al. 2018).

7.4.3 The exploration of the role of the conditions for conceptual change in the process of reconceptualisation.

Subsection 7.4.3 aims to explore the role of Posner et al. (1982) conditions for conceptual change in the process of reconceptualisation. The rationale and justification for the grading of the presence of the evidence for the conditions for conceptual change is outlined in Appendix 22 - Posner et al. (1982) conditions within Useful Summaries. Table 7.13 below is a condensed version of appendix 22 to facilitate the exploration of the role of the conditions for conceptual change in the process of pain reconceptualisation.

Table 7.13 shows the grading of the strength of the evidence for the presence of Posner's conditions for conceptual change within the useful summaries.

Case	Theme		Evidence of Dissatisfaction	Evidence of Intelligibility	Evidence of Plausibility	Evidence of Fruitfulness
P137 Pre	Pillar 1		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	Little or no fruitfulness
	Pillar 2	Somatic	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Psychological	Little or no dissatisfaction	Partial intelligibility	Little or no plausibility	
		Social	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 3		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	
P137 Post	Pillar 1		Partial dissatisfaction	Partial intelligibility	Partial plausibility	Strong fruitfulness
	Pillar 2	Somatic	Strong dissatisfaction	Partial intelligibility	Strong plausibility	
		Psychological	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Social	No data*	No data	No data	
	Pillar 3		Strong dissatisfaction	Strong intelligibility	Strong plausibility	

	Pillar 4		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
P249 Pre	Pillar 1		Strong dissatisfaction	Partial intelligibility	Partial plausibility	Partial fruitfulness
	Pillar 2	Somatic	Strong dissatisfaction	Strong intelligibility	Partial plausibility	
		Psychological	Partial dissatisfaction	Strong intelligibility	Partial plausibility	
		Social	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
	Pillar 3		Strong dissatisfaction	Strong intelligibility	Strong plausibility	
	Pillar 4		Strong dissatisfaction	Partial intelligibility	Partial plausibility	
P249 Post	Pillar 1		Strong dissatisfaction	Strong intelligibility	Partial plausibility	Strong fruitfulness
	Pillar 2	Somatic	Strong dissatisfaction	Strong intelligibility	Strong plausibility	
		Psychological	Strong dissatisfaction	Strong intelligibility	Strong plausibility	
		Social	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
	Pillar 3		Strong dissatisfaction	Partial intelligibility	Strong plausibility	
	Pillar 4		Strong dissatisfaction	Partial intelligibility	Strong plausibility	
P344 Pre	Pillar 1		Partial dissatisfaction	Partial intelligibility	Partial plausibility	No data
	Pillar 2	Somatic	Partial dissatisfaction	Partial intelligibility	Partial plausibility	

		Psychological	Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	
		Social	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 3		Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Strong dissatisfaction	Partial intelligibility	Partial plausibility	
P344 Post	Pillar 1		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	Little or no fruitfulness
	Pillar 2	Somatic	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Psychological	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Social	Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 3		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Partial dissatisfaction	Partial intelligibility	Partial plausibility	
P403 Pre	Pillar 1		Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	No data
	Pillar 2	Somatic	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Psychological	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Social	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 3		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	

	Pillar 4		Strong dissatisfaction	Partial intelligibility	Strong plausibility	
P403 Post	Pillar 1		Partial dissatisfaction	Partial intelligibility	Partial plausibility	Strong fruitfulness
	Pillar 2	Somatic	Partial dissatisfaction	Partial intelligibility	Little or no plausibility	
		Psychological	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Social	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
	Pillar 3		Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Partial dissatisfaction	Partial intelligibility	Little or no plausibility	
P451 Pre	Pillar 1		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	No data
	Pillar 2	Somatic	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Psychological	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
		Social	Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 3		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
P451 Post	Pillar 1		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	Little or no fruitfulness
		Somatic	Partial dissatisfaction	Partial intelligibility	Partial plausibility	

	Pillar 2	Psychological	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
		Social	Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 3		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
P717 Pre	Pillar 1		Partial dissatisfaction	Partial intelligibility	Partial plausibility	Partial fruitfulness
	Pillar 2	Somatic	Partial dissatisfaction	Strong intelligibility	Partial plausibility	
		Psychological	Strong dissatisfaction	Strong intelligibility	Strong plausibility	
		Social	Partial dissatisfaction	Partial Intelligibility	Partial plausibility	
	Pillar 3		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Strong dissatisfaction	Strong intelligibility	Strong plausibility	
P717 Post	Pillar 1		Strong dissatisfaction	Strong intelligibility	Partial plausibility	Strong fruitfulness
	Pillar 2	Somatic	Strong dissatisfaction	Strong intelligibility	Strong plausibility	
		Psychological	Strong dissatisfaction	Strong intelligibility	Strong plausibility	
		Social	Partial dissatisfaction	Partial intelligibility	Partial plausibility	

	Pillar 3 🟢🟢		Partial evidence 🟢	Partial intelligibility 🟢	Little to no plausibility 🟡	
	Pillar 4 🟡		Strong dissatisfaction 🟡	Strong intelligibility 🟡	Strong plausibility 🟡	
P890 Pre	Pillar 1		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	No data
	Pillar 2	Somatic	No data	No data	No data	
		Psychological	Partial dissatisfaction	Partial intelligibility	Partial plausibility	
		Social	No data	No data	No data	
	Pillar 3		Little or no dissatisfaction	Little or no intelligibility	Little or no plausibility	
	Pillar 4		Partial dissatisfaction	Little or no intelligibility	Little or no plausibility	
P929 Pre	Pillar 1		Strong dissatisfaction	Strong intelligibility	Strong plausibility	Strong fruitfulness
	Pillar 2	Somatic	Strong evidence	Partial intelligibility	Partial plausibility	
		Psychological	Strong dissatisfaction	Strong intelligibility	Strong plausibility	
		Social	Partial dissatisfaction	Partial Intelligibility	Partial plausibility	
	Pillar 3		Strong dissatisfaction	Strong intelligibility	Strong plausibility	
	Pillar 4		Strong dissatisfaction	Strong intelligibility	Strong plausibility	

Legend: *Table 7.13 shows the grading of the strength of the evidence for the presence of Posner's conditions for conceptual change within the useful summaries. The first column is for case/timepoint identification. The second column is for the themes and subthemes for which useful summaries were generated. The second column as in Table 7.12 includes a traffic light system to display a change in alignment to contemporary pain science from pre to post the PSE informed PMP. One green dot* 🟢 *indicated a shift towards contemporary pain science by one category along the "Little to no", "Partial" and "Strong"*

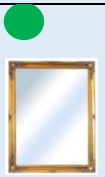
continuum i.e., moving from "little to no" to "Partial", and thus indicative of the presence of pain reconceptualisation. Two green dots  *indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from "little to no" to "Strong", and thus indicative of the presence of strong pain reconceptualisation. One orange dot*  *indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot*  *indicated a shift away from contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "Strong" to "Partial", and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots* *indicated a large shift away contemporary pain science by two categories along the continuum i.e., moving from "Strong" to "Little or no", and thus indicative of the presence of strong anti-pain reconceptualisation.P137 pre, Participant 137 Pre intervention. P137 post, Participant 137 Post intervention. The next four columns are for the strength of evidence, and supporting evidence for the presence of the four conditions for conceptual change outlined by Posner et al., (1982) and graded using the criteria outlined in Table 7.8 ranging from "Little or no" evidence, "Partial" evidence, and "Strong" evidence. A traffic light system was used to display a change in the strength of evidence for the presence of Posner's conditions for conceptual change within the useful summaries pre to post the PSE informed PMP. One green dot*  *indicated a strengthening in strength by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial". Two green dots*  *indicated a strengthening in strength by two categories along the continuum i.e., moving from "little to no" to "Strong". One orange dot*  *indicated there was no meaningful change in the strength of evidence. One red dot*  *indicated a weakening in strength by one category along the continuum i.e., moving from "Strong" to "Partial". Two red dots*  *indicated a weakening in strength by two categories along the continuum i.e., moving from "Strong" to "Little or no". In addition, the traffic light system was also used in the first column to display the overall change in alignment to contemporary pain science including all four pillars of contemporary pain science. This is equivalent to the overall degree of pain reconceptualisation. To calculate overall degree of pain reconceptualisation the number of green, amber and red dots were combined with the total shown in the post participant row in the first column. The total number of green dots across all four subthemes was included in the overall degree of reconceptualisation. The number of red dots present across all four subthemes resulted in the equivalent number of green dots being removed from the overall score i.e., one red dot and one green dot cancel each other out. Amber dots neither add or minus the number of green or red dots. Where there was overall no change an amber dot was shown to reflect no overall degree of reconceptualisation.*

'No data' is used where the theme was not discussed within the interview.

The role of each of Posner's conditions for conceptual change in the process of reconceptualisation for each pillar of contemporary pain science have been explored below by condensing Table 7.13 into four tables (Table 7.13, 7.14, 7.15, 7.16), one for each pillar of contemporary pain science.

7.4.3.1 Role of Posner et al. conditions for conceptual change in the process of reconceptualisation for pillar 1, pain does not provide a measure of the state of the tissues

Table 7.14 Shows the degree of pain reconceptualisation for pillar 1 and the change in strength of the evidence for the conditions for conceptual change.

Case and timepoint	Reconceptualisation for pillar 1 of contemporary pain science	Evidence for the conditions for conceptual change Posner et al. 1982			
		Evidence of Dissatisfaction	Evidence of Intelligibility	Evidence of Plausibility	Evidence of Fruitfulness
P137 Post	Pillar 1 				
P249 Post	Pillar 1 				
P344 Post	Pillar 1 				

P403 Post	Pillar 1 🟢	🟡	🟢	🟢	🟢🟢
P451 Post	Pillar 1 🟡	🟡	🟡	🟡	🟡
P717 Post	Pillar 1 🟢	🟢	🟢	🟡	🟢
Participant total	Pillar 1	5/6 participants mirrored	5/6 participants mirrored	5/6 participants mirrored	4/6 participants mirrored

Legend: *Table 7.14 shows the degree of pain reconceptualisation for pillar 1 and the change in strength of the evidence for the conditions for conceptual change. The first column is for case and time point identification. In the second column a traffic light system was used to grade the degree of reconceptualisation. One green dot* 🟢 *indicated a shift towards contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial", and thus indicative of the presence of pain reconceptualisation. Two green dots* 🟢🟢 *indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from "little to no" to "Strong", and thus indicative of the presence of strong pain reconceptualisation. One orange dot* 🟡 *indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot* 🔴 *indicated a shift away from contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "Strong" to "Partial", and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots* 🔴🔴 *indicated a*

large shift away from contemporary pain science by two categories along the continuum i.e., moving from "Strong" to "Little or no", and thus indicative of the presence of strong anti-pain reconceptualisation. The third to sixth columns are for the change in strength of evidence for the presence of the four conditions for conceptual change outlined by Posner et al., (1982). A traffic light system was used to display a change in the strength of evidence for the presence of Posner's conditions for conceptual change. One green dot  *indicated a strengthening in strength by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial". Two green dots*  *indicated a strengthening in strength by two categories along the continuum i.e., moving from "little to no" to "Strong". One orange dot*  *indicated there was no meaningful change in the strength of evidence. One red dot*  *indicated a weakening in strength by one category along the continuum i.e., moving from "Strong" to "Partial". Two red dots*  *indicated a weakening in strength by two categories along the continuum i.e., moving from "Strong" to "Little or no". Where the degree of reconceptualisation mirrored the change in strength of the condition for conceptual change i.e., matching coloured dots, a mirror*  *was input into the corresponding cell. This displayed where the change in evidence for each condition for conceptual change mirrored the degree of pain reconceptualisation. The number of participants that displayed a mirroring for each condition of conceptual change was included in the bottom row.*

Pillar 1 of contemporary pain science is *pain does not provide a measure of the state of the tissues*. Table 7.14 illustrates the degree of reconceptualisation in pillar 1 largely mirrored the change in strength of the evidence for the conditions for conceptual change. Every participant displayed mirroring in at least two conditions. Two participants (P451, P137) showed mirroring in all four of the conditions whilst three participants (P344, P403, P717) showed mirroring in three conditions.

Those individuals who underwent pain reconceptualisation for pillar 1 represented by more green dots (P137, P403, P717) showed greater presence of the conditions for conceptual change post intervention represented by mostly green dots with some orange dots. The inverse was seen where anti-reconceptualisation was observed, represented by a red dot. In this case the evidence for the presence of conditions for conceptual change post intervention was weaker represented by mostly red dots (P344). One of the two individuals (P451) who showed no pain reconceptualisation (orange dot) showed exact mirroring in all four conditions for conceptual change (all orange dots). While the findings of the remaining participant (P249) mapped less well than the other five participants. The evidence for two conditions (dissatisfaction and plausibility both assigned orange dots) mirrored the absence of pain reconceptualisation (orange dot). The other two conditions increased in strength (green dots). Post intervention P249 had a very good understanding of pillar 1 reflected by their strong intelligibility;

"The PMP confirmed there's no tissue damage and the role of the brain and receptors which helped loads. When the chair gently touched my back it wasn't enough to cause any damage, it just felt like it did because my receptors and brain screamed."

CP-P1-P249postS5:

The above summary also demonstrates their strong dissatisfaction with the biomedical model. Furthermore P249 showed strong fruitfulness from the reassurance their new understanding that 'there's no tissue damage' provided. Despite P249's strong intelligibility, dissatisfaction and fruitfulness post intervention, their partial alignment to contemporary pain science for pillar 1 was unchanged (orange dot). The importance of their partial plausibility may in part explain this. Both pre and post intervention P249 describe that although they don't think pain provides a measure of the state of the tissues, when their pain becomes really severe, they start to doubt this belief;

"I don't think there is a relationship between pain and tissue state because in 16 years of pain I've not had any proof anything is wrong with the tissues, even if it feels like there is but in that moment when the pain is severe I'm thinking of my god what's wrong."
CP-P1-P249postS4:

This account powerfully illustrates how at times of high pain severity the plausibility of nearly two decades of proof of no tissue damage and their strong understanding that pain does not provide a measure of the state of the tissues are doubted. This account raises the question does high pain severity reduce the plausibility that pain does not relate to the state of the tissues?

The findings of P249, P403, P717 shows that it is not the case that if an individual demonstrates a strengthening in the evidence for one or more conditions of conceptual change by default they will also show a strengthening in the remaining conditions. Conversely the findings of P344 show the reverse, it is not the case that if an individual shows a weakening in the evidence for presence of one or more of the conditions for conceptual change they will not by default show a weaking in the remaining conditions.

The findings of this subsection are illustrative that at least for some people, where pain reconceptualisation occurs the evidence for the presence of the conditions for conceptual change increases in strength. The inverse is also true, where anti-pain reconceptualisation occurs the evidence for the presence of the conditions for conceptual change decreases in strength. Where pain reconceptualisation or anti-pain reconceptualisation does not occur i,e., the alignment to contemporary pain science was unchanged, the evidence for the presence of the conditions for conceptual change are also largely unchanged. No one condition for conceptual change appeared to mirror more or less than another with five participants displaying mirroring for dissatisfaction, intelligibility and plausibility and four participants displaying mirroring for fruitfulness. The evidence for the conditions for conceptual change appears to, at least in part, be independent of the change in evidence for the other conditions for conceptual change. Overall, there is nothing in these findings to suggest that Posner et al. (1982) conditions for conceptual change have no role in the degree of reconceptualisation.

This subsection 7.4.3.1 has raised an question which warrant further study:

- Does high pain severity reduce the plausibility that pain does not relate to the state of the tissues?

7.4.3.2 Role of Posner et al. conditions for conceptual change in the process of reconceptualisation for pillar 2, Pain is modulated by many factors across somatic, psychological and social domains.

Table 7.15 Shows the degree of pain reconceptualisation for pillar 2 and the change in strength of the evidence for the conditions for conceptual change.

Case	Reconceptualisation at pillar 2 of contemporary pain science	Evidence for the conditions for conceptual change Posner et al. 1982			
		Evidence of Dissatisfaction	Evidence of Intelligibility	Evidence of Plausibility	Evidence of Fruitfulness
P137 Post	Pillar 2				
P249 Post	Pillar 2				
P344 Post	Pillar 2				
P403 Post	Pillar 2				

P451 Post	Pillar 2				
P717 Post	Pillar 2				
Participant total	Pillar 2	4/6 participants mirrored	5/6 participants mirrored	4/6 participants mirrored	1/6 participants mirrored

Legend: *Table 7.15 shows the degree of pain reconceptualisation for pillar 2 and the change in strength of the evidence for the conditions for conceptual change. The first column is for case and time point identification. In the second column a traffic light system was used to grade the degree of reconceptualisation. One green dot indicated a shift towards contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial", and thus indicative of the presence of pain reconceptualisation. Two green dots indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from "little to no" to "Strong", and thus indicative of the presence of strong pain reconceptualisation. One orange dot indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot indicated a shift away from contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "Strong" to "Partial", and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots indicated a large shift away from contemporary pain science by two categories along the continuum i.e., moving from "Strong" to "Little or no", and thus indicative of the presence of strong anti-pain reconceptualisation. The third to sixth columns are for the change in strength of evidence for the presence of the four conditions for conceptual change outlined by Posner et al., (1982). A traffic light system was used to display a change in the strength of evidence for the presence of Posner's conditions for conceptual change. One green dot indicated a strengthening in strength by one category along the "Little to no",*

"Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial". Two green dots  *indicated a strengthening in strength by two categories along the continuum i.e., moving from "little to no" to "Strong". One orange dot*  *indicated there was no meaningful change in the strength of evidence. One red dot*  *indicated a weakening in strength by one category along the continuum i.e., moving from "Strong" to "Partial". Two red dots*  *indicated a weakening in strength by two categories along the continuum i.e., moving from "Strong" to "Little or no". Where the degree of reconceptualisation mirrored the change in strength of the condition for conceptual change i.e., matching coloured dots, a mirror*  *was input into the corresponding cell. This displayed where the change in evidence for each condition for conceptual change mirrored the degree of pain reconceptualisation. The number of participants that displayed a mirroring for each condition of conceptual change was included in the bottom row.*

Pillar 2 of contemporary pain science is *pain is modulated by many factors across somatic, psychological and social domains*. Table 7.15 illustrates the degree of reconceptualisation in pillar 2 of contemporary pain science largely mirrored the change in strength of the evidence for conditions dissatisfaction (4 participants), intelligibility (5 participants) and plausibility (4 participants). In contrast to the other conditions, only one participant (P451) displayed mirroring for the fruitfulness condition. This raises an interesting question about the possibility of different contributions of the conditions for conceptual change in the process of pain reconceptualisation for pillar 2.

Five participants displayed mirroring between the degree of reconceptualisation and at least one condition. One participant (P451) showed mirroring in four of the conditions whilst two participants (P403, P717) showed mirroring in three conditions, one participant (P249) showed mirroring in two conditions, and one participant (P137) showed mirroring in one condition. Participant P344 was the only participant to not show any mirroring.

There was a common theme between P137 and P451 regarding the plausibility of psychological factors impacting on their pain. Interestingly they both used their experience of being in a great mood and still being in pain as evidence against the conception that psychological factors modulate pain.

"Emotional factors don't affect my pain cose I could be having a really good day, feeling really good but still be in pain, that's how I know emotions don't affect my pain"
CP-P2-P137preS3

"No emotions cannot affect my pain, I know this cose I got back pain lifting a root out in the garden on a beautiful autumn day in the garden, no anxiety, no emotion, I was very very happy but still got pain."
ST2-P451preS2

Interestingly P137 at the pre interview conceptually understood that mood can impact on pain, but they did not think it impacted their pain suggestive of a lack of relevance.

"I've been told depression can make pain worse but I don't think psychological symptoms effect my pain because I've always suffered from depression so for me there wasn't any correlation between my depression and pain. It's more the effects of pain that's psychologically wearing"
CP-P2-P137preS2

They rationalise that psychological factors don't impact on their pain as they have always suffered from depression, but not always suffered from pain so think there is no correlation between their depression and pain. Their interpretation of their experience reduces both the plausibility and fruitfulness (in the perceived relevance domain) of the conception that mood impacts on their pain. Following the intervention P137 is more open to the conception that psychological factors can modulate their pain, demonstrating more relevance than in the pre interview.

"Getting stressed makes my pain worse."

CP-P2-P137postS4

However in contradiction to the above, they go on to state that psychological factors don't impact on their pain. They again use their experience of being in a great mood but still being in pain, and their experience of having depression before pain as evidence against the conception that psychological factors can modulate their pain. P137 further rationalises their belief that psychological factors don't impact on their pain as they're on anti-depressants which in their view should remove the mood component. They interpret still having pain without the mood component as further evidence that psychological factors don't modulate their pain.

"Depression and anxiety don't affect my pain cose I can have a fantastic day and still be in pain"

CP-P2-P137postS6

"I think depression sometimes can affect pain but not for me as I've always suffered with depression before I had pain. I'm on medication for low mood which makes me feel numb so that's why I can go low mood doesn't affect my pain because the low mood part has already been inhibited."

CP-P2-P137postS5

The findings from P137 and P451 demonstrate the power of how an individual makes sense of their first person subjective experience in the formation of pain beliefs. The findings of P137 emphasises that people can weight the interpretation of their first person subjective experience at a higher level of evidence to that which they have been told, particularly when there is a lack of perceived relevance between the proposed conception and what they have been told. Such findings raise the question should health care professionals not simply tell individuals key concepts of PSE i.e., 'mood can impact on your pain', but rather explore with

the individual how they are interpreting their experience to guide their beliefs? Could involving individuals in the sense making process facilitate them to better understand and believe in, the conception? This approach may be particularly useful for those individuals whose conceptions, as in P137 and P451 are logical but crucially erroneous i.e., the belief that mood doesn't modulate pain because they can have a great day and still be in pain. Careful questioning could be used to gain a greater view of the context which may highlight other contributing factors to their experience and lead to a different interpretation. This approach is consistent with cognitive functional therapy which is increasingly popular within contemporary physiotherapy practice and integrates traditional physiotherapy rehabilitation with foundational cognitive and behavioural interventions (O'Sullivan *et al.*, 2018).

In the case of P137 their great day was spending all day at the beach with their family. This day involved a well above normal time standing and walking which for an individual who is significantly deconditioned unsurprisingly resulted in a flare of symptoms. With this understanding the simplistic interpretation that because they can be in a great mood and still in pain, mood does not impact on pain, may be weighted less when using their experience to guide their beliefs. Further questioning around the relationship between mood and pain may have then revealed, as in the case post PSE, that stress can increase their pain. This may increase the plausibility and relevance of conceptions that are in alignment with contemporary pain science and may facilitate pain reconceptualisation.

There is growing consensus that depression increases the risk of future episodes of pain (Pinheiro *et al.*, 2015; Bondesson *et al.*, 2018). In a recently published large (n = 504,365) cohort study in Sweden a bidirectional relationship between pain and depression was found. The incidence rate ratio for developing pain after mental illness was 2.02 (95% CI = 1.98–2.06) compared to without mental illness. There was an increased risk of equal magnitude for developing mental illness after pain 2.18 (95% CI = 2.14–2.22) compared to without pain (Bondesson et al. 2018). These findings are clearly in alignment with the second pillar of contemporary pain science that *pain is modulated by many factors across somatic, psychological and social domains* (Moseley, 2007). The reasoning of P137 and P451 raises the question would explaining the difference between state and trait depression/anxiety help individuals undergo pain reconceptualisation in pillar 2?

It is possible to improve the mood (or state) of a depressed individual using a distraction task (Joormann, Siemer and Gotlib, 2007). However this transient change in state does not itself change their diagnosis of depression, and therefore unlikely to weaken the bidirectional relationship that exists between depression and pain (Bondesson et al. 2018). Similarly a

history of smoking increases the risk of developing lung cancer but stopping for a few days is unlikely to impact that risk (Godtfredsen *et al.*, 2002; O'Keeffe *et al.*, 2018).

The findings of P137, P249, P344, P403 and P717 show that it is not the case that if an individual demonstrates a strengthening in the evidence for one or more conditions of conceptual change by default they will also show a strengthening in the remaining conditions.

The findings of this subsection show the degree of reconceptualisation in pillar 2 of contemporary pain science largely mirrors the change in strength of the evidence for dissatisfaction, intelligibility and plausibility. Where there is the absence of pain reconceptualisation the strength of the evidence for the conditions for conceptual change is largely unchanged. The evidence for the conditions for conceptual change appears to, in part, be independent of the change in evidence for the other conditions for conceptual change. Overall, there is nothing in these findings to suggest that Posner et al. (1982) conditions for conceptual change have no role in the degree of reconceptualisation however there is a possible pattern emerging that fruitfulness may have less of a role in the process of pain reconceptualisation for pillar 2.

Finally this subsection 7.4.3.2 raised some interesting questions:

- Do different conditions for conceptual change contribute to different degrees to the process of pain reconceptualisation for pillar 2?
- Should health care professionals not simply tell individuals key concepts of PSE i.e., 'mood can impact on your pain', but rather explore with the individual how they are interpreting their experience to guide their beliefs?
- Could involving individuals in the sense making process facilitate them to better understand and believe in, the conception?
- Could explaining the difference between state and trait depression/anxiety help individuals undergo pain reconceptualisation in pillar 2?

.

7.4.3.3 Role of Posner et al. conditions for conceptual change in the process of reconceptualisation for pillar 3, The relationship between pain and the state of the tissues becomes less predictable as pain persists.

Table 7.16 Shows the degree of pain reconceptualisation for pillar 3 and the change in strength of the evidence for the conditions for conceptual change.

Case and timepoint	Reconceptualisation at each pillar of contemporary pain science	Evidence for the conditions for conceptual change Posner et al. 1982			
		Evidence of Dissatisfaction	Evidence of Intelligibility	Evidence of Plausibility	Evidence of Fruitfulness
P137 Post	Pillar 3 🟢🟢	🟢🟢 	🟢🟢 	🟢🟢 	🟢🟢 
P249 Post	Pillar 3 🟡	🟡 	🔴	🟡 	🟢
P344 Post	Pillar 3 🟡	🔴	🟡 	🟡 	🟡 
P403 Post	Pillar 3 🟡	🟢	🟡	🟡	🟢🟢

					
P451 Post	Pillar 3				
P717 Post	Pillar 3				
Participant total	Pillar 3	4/6 participants mirrored	5/6 participants mirrored	5/6 participants mirrored	4/6 participants mirrored

Legend: *Table 7.16 shows the degree of pain reconceptualisation for pillar 3 and the change in strength of the evidence for the conditions for conceptual change. The first column is for case and time point identification. In the second column a traffic light system was used to grade the degree of reconceptualisation. One green dot*  *indicated a shift towards contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial", and thus indicative of the presence of pain reconceptualisation. Two green dots*  *indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from "little to no" to "Strong", and thus indicative of the presence of strong pain reconceptualisation. One orange dot*  *indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot*  *indicated a shift away from contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "Strong" to "Partial", and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots*   *indicated a large shift away from contemporary pain science by two categories along the continuum i.e., moving from "Strong" to "Little or no", and thus*

indicative of the presence of strong anti-pain reconceptualisation. The third to sixth columns are for the change in strength of evidence for the presence of the four conditions for conceptual change outlined by Posner et al., (1982). A traffic light system was used to display a change in the strength of evidence for the presence of Posner's conditions for conceptual change. One green dot  *indicated a strengthening in strength by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial". Two green dots*  *indicated a strengthening in strength by two categories along the continuum i.e., moving from "little to no" to "Strong". One orange dot*  *indicated there was no meaningful change in the strength of evidence. One red dot*  *indicated a weakening in strength by one category along the continuum i.e., moving from "Strong" to "Partial". Two red dots*  *indicated a weakening in strength by two categories along the continuum i.e., moving from "Strong" to "Little or no". Where the degree of reconceptualisation mirrored the change in strength of the condition for conceptual change i.e., matching coloured dots, a mirror*  *was input into the corresponding cell. This displayed where the change in evidence for each condition for conceptual change mirrored the degree of pain reconceptualisation. The number of participants that displayed a mirroring for each condition of conceptual change was included in the bottom row.*

Pillar 3 of contemporary pain science is *the relationship between pain and tissue becomes less predictable as pain persists* Table 7.16 illustrates the degree of reconceptualisation in pillar 3 largely mirrored the change in strength of the evidence for the conditions for conceptual change. Every participant displayed mirroring in at least 2/4 conditions. Two participants (P137, P451) showed mirroring in 4/4 of the conditions whilst two participants (P344, P717) showed mirroring in 3/4 conditions. No one condition for conceptual change appeared to mirror more or less than another with five participants displaying mirroring for intelligibility and plausibility and four participants displaying mirroring for dissatisfaction and fruitfulness.

The two participants who underwent pain reconceptualisation for pillar 3 represented by more green dots showed greater presence of the conditions for conceptual change post intervention represented by all green dots (P137) or mostly green dots with one orange dot (P717). The remaining four participants (P249, P344, P403, P451) underwent no reconceptualisation (orange dots). Out of the non-reconceptualisors P451 showed the greatest mirroring with all four conditions for conceptual change unchanged (orange dots). Two participants (P249, P344) showed a large rather than exact mirroring however their presentation was different. P344 showed no change in 3 out of 4 conditions (orange dots) and a weakening in evidence for the remaining condition (red dot). P249 has a more varied pattern with 2 out of 4 conditions unchanged (orange dots), 1 out of 4 weakening (red dot) and 1 out of 4 strengthening (green dot). The final participant P403 showed more partial mirroring with their absence of reconceptualisation mirrored by 2 out of 4 conditions for conceptual change (orange dots). The remaining conditions did not mirror this with both increasing in strength (one green dot each).

The findings of P249, P403, P717 shows that it is not the case that if an individual demonstrates a strengthening in the evidence for one or more conditions of conceptual change by default they will also show a strengthening in the remaining conditions. Indeed P249 showed a strengthening of fruitfulness whilst simultaneously showing a weakening of intelligibility. Similarly the findings of P344 show the reverse, it is not the case that if an individual shows a weakening in the evidence for presence of one of the conditions for conceptual change they will not by default show a weaking in the remaining conditions.

The findings of this subsection are illustrative that where pain reconceptualisation occurs the evidence for the presence of the conditions for conceptual change increases in strength. Where pain reconceptualisation or anti-pain reconceptualisation does not occur i.e., the alignment to contemporary pain science is unchanged, the evidence for the presence of the conditions for conceptual change are also largely unchanged. No one condition for conceptual

change appeared to mirror more or less than another with five participants displaying mirroring for intelligibility and plausibility and four participants displaying mirroring for dissatisfaction and fruitfulness. The evidence for one condition for conceptual change can alter independent of the other conditions of conceptual change. As with pillar 1 and 2 overall there is nothing in these findings to suggest that Posner et al. (1982) conditions for conceptual change have no role in the degree of reconceptualisation.

7.4.3.4 Role of Posner et al. conditions for conceptual change in the process of reconceptualisation for pillar 4, Pain can be conceptualised as the conscious correlate of the implicit perception that tissue is in danger

Table 7.17 Shows the degree of pain reconceptualisation for pillar 4 and the change in strength of the evidence for the conditions for conceptual change.

Case	Reconceptualisation at each pillar of contemporary pain science	Evidence for the conditions for conceptual change Posner et al. 1982			
		Evidence of Dissatisfaction	Evidence of Intelligibility	Evidence of Plausibility	Evidence of Fruitfulness
P137 Post	Pillar 4				
P249 Post	Pillar 4				
P344 Post	Pillar 4				
P403 Post	Pillar 4				

					
P451 Post	Pillar 4				
P717 Post	Pillar 4				
Participant total	Pillar 4	3/6 participants mirrored	6/6 participants mirrored	4/6 participants mirrored	2/6 participants mirrored

Legend: *Table 7.17 shows the degree of pain reconceptualisation for pillar 4 and the change in strength of the evidence for the conditions for conceptual change. The first column is for case and time point identification. In the second column a traffic light system was used to grade the degree of reconceptualisation. One green dot indicated a shift towards contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial", and thus indicative of the presence of pain reconceptualisation. Two green dots indicated a large shift towards contemporary pain science by two categories along the continuum i.e., moving from "little to no" to "Strong", and thus indicative of the presence of strong pain reconceptualisation. One orange dot indicated the evidence reflected no meaningful change in pain beliefs, and thus indicative of the absence of pain reconceptualisation. One red dot indicated a shift away from contemporary pain science by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "Strong" to "Partial", and thus indicative of the presence of a kind of anti-pain reconceptualisation. Two red dots indicated a large shift away from contemporary pain science by two categories along the continuum i.e., moving from "Strong" to "Little or no", and thus indicative of the presence of strong anti-pain reconceptualisation. The third to sixth columns are for the change in strength of evidence for the*

presence of the four conditions for conceptual change outlined by Posner et al., (1982). A traffic light system was used to display a change in the strength of evidence for the presence of Posner's conditions for conceptual change. One green dot 🟢 *indicated a strengthening in strength by one category along the "Little to no", "Partial" and "Strong" continuum i.e., moving from "little to no" to "Partial". Two green dots* 🟢🟢 *indicated a strengthening in strength by two categories along the continuum i.e., moving from "little to no" to "Strong". One orange dot* 🟡 *indicated there was no meaningful change in the strength of evidence. One red dot* 🔴 *indicated a weakening in strength by one category along the continuum i.e., moving from "Strong" to "Partial". Two red dots* 🔴🔴 *indicated a weakening in strength by two categories along the continuum i.e., moving from "Strong" to "Little or no". Where the degree of reconceptualisation mirrored the change in strength of the condition for conceptual change i.e., matching coloured dots, a mirror*  *was input into the corresponding cell. This displayed where the change in evidence for each condition for conceptual change mirrored the degree of pain reconceptualisation. The number of participants that displayed a mirroring for each condition of conceptual change was included in the bottom row.*

Pillar 4 of contemporary pain science is *pain can be conceptualised as a conscious correlate of the implicit perception that tissue is in danger*. Table 7.17 illustrates the degree of reconceptualisation for pillar 4 is largely mirrored by the change in evidence for conditions dissatisfaction (3 participants), intelligibility (6 participants) and plausibility (4 participants). In contrast, only two participants (P344, 451) displayed mirroring for the fruitfulness condition. This provides further support for the question raised when viewing pillar 2 about the possibility of different contributions of the conditions for conceptual change in the process of pain reconceptualisation.

Every participant displayed mirroring in at least one condition. P451 showed mirroring in all four conditions for conceptual change. The findings of P717 and P344 showed a large rather than exact mirroring pattern. Both participants showed no change in strength for intelligibility and plausibility (orange dots). P717 also showed no change in dissatisfaction, whilst P344 showed no change in fruitfulness. The remaining condition for P717 strengthened (green dot) and P344 weakened (red dot). Viewing all conditions for conceptual change for P344 and P717 three out of four conditions remained the same (orange dots) which largely mirrors with the lack of pain reconceptualisation (orange dot). The lack of reconceptualisation seen in P137 is also largely mirrored by the change in strength of the evidence for the conditions for conceptual change. However P137 showed a slightly different pattern to P344 and P717 with two conditions for conceptual change unchanged, one condition getting stronger (green dot), and one condition getting weaker (red dot). Similar to P137, two conditions for conceptual change for P249 were unchanged (orange dots), however the other two got stronger (green dots).

The findings of P403 show the least degree of mirroring between the conditions for conceptual change and pain reconceptualisation with only one condition mirroring (intelligibility). In contrast to the unchanging alignment to contemporary pain science indicative of the absence of pain reconceptualisation (orange dot) P403 showed a noticeable weakening in strength of evidence for plausibility (two red dots) and dissatisfaction (one red dot) and a noticeable strengthening in the evidence for fruitfulness (two green dots).

Of particular note for pillar 4, the intelligibility condition was unchanged (orange dots) in all participants mirroring the lack of pain reconceptualisation (orange dots) observed. Perhaps this is unsurprising as conceptually pillar 4 is arguably the most difficult to grasp and thus the intelligibility condition may be more heavily weighted. The importance of intelligibility is demonstrated in the account of P403 where their lack of understanding of pillar 4, reflected by

their classification of partial intelligibility appears to account for their weakening of dissatisfaction and a significant weakening of plausibility.

Pre intervention P403's intelligibility for pillar 4 was partial. They had some awareness that the brain plays a role in pain perception but this was incomplete;

"…Clearly it's got to be the brain, no other part of the body would tell me that I'm in pain other than the brain, not sure why."
CP-P4-P403preS1:

Their use of 'Clearly' suggested strong plausibility for their conception. After the PSE informed PMP whilst they still appear to understand that the brain has a role in pain perception, they are much more confused about pillar 4;

"I'm utterly confused about how the brain works…"
CP-P4-P403postS1

Their account of pillar 4 following the intervention shows their partial degree of intelligibility. Rather than the brain perceiving threat to the body and creating pain to protect the body, they believe the brain tries to protect the body from pain;

"…Finds strange how brain recognises attack of pain and tries to protect the body from the pain because that's not my experience…"
CP-P4-P403postS1

The lack of alignment between the concept and their experience, driven from a lack of intelligibility then appears to negatively impact on the plausibility and relevance of the conception;

"…I've never found the brain actually defends me from pain because my pain is permanent every waking moment. The PMP says the brain has the capacity to see something is wrong and acts to protect it, I don't accept it, it's not doing anything for me. The part of the brain that deals with threat of pain, the threat of harm to your body is not working in my case because I'm getting no relief from the pain. Part of my brain supposedly should be protecting my body, but it's not, it should be relieving the pain but it's not."
CP-P4-P403postS1

The account of P403 illustrates the interrelated nature of the conditions for conceptual change and raises the question is intelligibility important to ensure the plausibility and relevance of pillar 4?

The findings of P137, P249, P403, P717 shows that it is not the case that if an individual demonstrates a strengthening in the evidence for one or more conditions of conceptual change by default they will also show a strengthening in the remaining conditions. Indeed P137 and P403 showed a strengthening of fruitfulness whilst simultaneously showing a weakening of one or more other conditions for conceptual change. Similarly the findings of P344 show the reverse, it is not the case that if an individual shows a weakening in the evidence for presence of one of the conditions for conceptual change they will not by default show a weaking in the remaining conditions.

The findings of this subsection are illustrative that where pain reconceptualisation or anti-pain reconceptualisation does not occur i.e., the alignment to contemporary pain science is unchanged, the evidence for the presence of the conditions for conceptual change are also largely unchanged. This subsection also raised an interesting question, is intelligibility important to ensure the plausibility and relevance of pillar 4? The evidence for the conditions for conceptual change appears to in part be independent of the change in evidence for the other conditions for conceptual change. Overall, there is nothing in these findings to suggest that Posner et al. (1982) conditions for conceptual change have no role in the degree of reconceptualisation for pillar 4 however similar to pillar 2, there is a possible pattern emerging that fruitfulness may have less of a role in the process of pain reconceptualisation for pillar 4.

7.4.3.5 Summary of the exploration of the role of the conditions for conceptual change in the process of reconceptualisation.

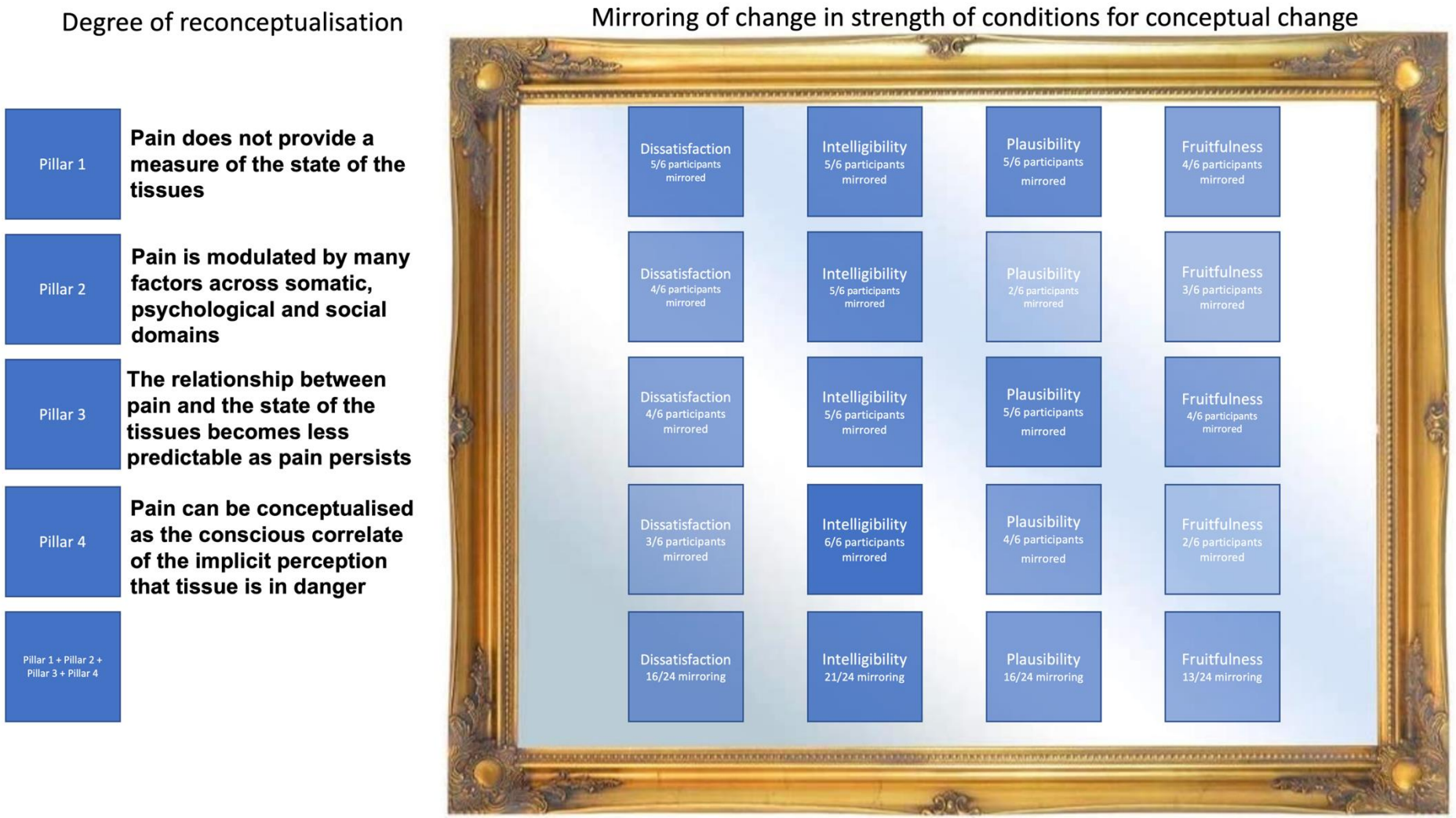


Figure 7.4 Master Mirror

Legend: *Shows the total mirroring scores for the degree of reconceptualisation for each pillar of contemporary pain science and each condition of conceptual change. These scores come from the totals from Tables 7.13, 7.14, 7.15, 7.16. This facilitates the exploration of the role of the conditions for conceptual change in the process of pain reconceptualisation. The total number of times the degree of reconceptualisation matched the change in strength of the evidence for the conditions for conceptual change was also presented in the bottom row.*

Figure 7.4 (Master Mirror) presents the total mirroring scores for each pillar of contemporary pain science and each condition of conceptual change to allow the mirroring between the two to be more easily seen across all pillars and conditions. The total number of times the degree of reconceptualisation mirrored the change in strength of the evidence for the conditions for conceptual change was also presented. These scores come from the totals from Tables 7.13, 7.14, 7.15, 7.16. Figure 7.4 facilitated aim two of this chapter, *to explore the role of the conditions for conceptual change in the process of pain reconceptualisation.* The change in strength of the evidence for Intelligibility mirrored the degree of reconceptualisation 21/24 occasions, dissatisfaction and plausibility mirrored the degree of reconceptualisation 16/24 occasions and fruitfulness mirrored the degree of reconceptualisation 13/24 occasions. There is nothing in these findings to suggest that Posner et al. (1982) conditions for conceptual change have no role in process of pain reconceptualisation. There is the emergence of a possible pattern that the conditions for conceptual change have a role in the process of pain reconceptualisation. A key finding of this chapter is that it could be of real value to more thoroughly investigate the role of the conditions for conceptual change in the process of pain reconceptualisation. This is an important area for future study as if the generic model of conceptual change proposed by Posner et al. (1982) is a good fit with the discipline specific area of pain reconceptualisation it warrants future research to explore if the conditions outlined by Posner et al. (1982) could be used to optimise PSE. This includes interventions aimed at changing pain beliefs of health care professionals and those with lived experience of chronic pain.

An interesting question raised when viewing the role of the conditions for conceptual change in the process of pain reconceptualisation for pillar 2 and 4 was there may be different contributions of each condition. Viewing Figure 7.4 (Master Mirror) this possible pattern emerges again with intelligibility (21/24) visibly mirroring the degree of reconceptualisation more compared to fruitfulness (13/24). This raises the question does intelligibility contribute more to pain reconceptualisation than fruitfulness? This possible pattern emerging may in fact be an artifact of methodology used for the analysis. In contrast to the other conditions, fruitfulness was explored at the participant level rather than at the level of each pillar of contemporary pain science. This decision was made as it became apparent that it was impossible to isolate the evidence for fruitfulness to any one specific pillar of contemporary pain science. Comparing fruitfulness at the participant level to the degree of reconceptualisation for each pillar of contemporary pain science could plausibly reduce the mirroring between the two. It may be more appropriate to analyse the mirroring between the degree of reconceptualisation seen at the participant level to the change in evidence for fruitfulness which is also at the participant level. At this level of analysis mirroring between the

degree of reconceptualisation and the evidence for fruitfulness is seen in five participants (P717, P451, P403, P344, P137). Three participants (P137, P403, P717) underwent overall pain reconceptualisation (green dots) which was mirrored by a strengthening in the evidence for fruitfulness (green dots). Two participants (P344, P451) underwent no overall pain reconceptualisation (Orange dots) which was mirrored by no overall change in the evidence for fruitfulness (orange dots). P249 who did not undergo any pain reconceptualisation (orange dot) in contrast had a strengthening in the evidence for fruitfulness (green dot). It is worth nothing that P249 may have had some level of a ceiling effect as at their pre interview they were graded as strong alignment to 2-4 pillars of contemporary pain science, and partial for pillar 1.

Previous PSE qualitative studies have also found a possible link between how fruitful an individual perceives the messages of PSE and the degree of reconceptualisation and clinical benefit (Robinson et al. 2016; King et al. 2016; King at al. 2018). Fruitfulness in the current study was assessed by answering the question *Does the participant believe the concept has made their life better in a way they can see?* Fruitfulness was deemed to be encompassed by two subthemes, including *Personal relevance of PSE,* and *Perceived benefit of PSE*. The importance of fruitfulness emerged in Robinson et al. (2016) where eight participants who found the PSE information personally relevant also found PSE to be of benefit. Of these eight participants who showed evidence of fruitfulness four showed some evidence of pain reconceptualisation. A similar pattern emerges about the potential importance of fruitfulness in the process of reconceptualisation in the other PSE qualitative studies (King et al. 2016; King at al. 2018). The findings of the current chapter pointing to a possible mirroring between fruitfulness and the degree of reconceptualisation is in line with the previous PSE literature to date and adds confidence to the findings of the current work.

The evidence for one condition for conceptual change can alter independent of the other conditions of conceptual change. The evidence for one condition for conceptual change could strengthen whilst the others remained the same or weakened. The reverse is also true.

In summary of these findings there is nothing to suggest that Posner et al. (1982) conditions for conceptual change have no role in process of pain reconceptualisation. A possible pattern emerging is that the degree of reconceptualisation mirrors the change in strength of the conditions for conceptual change. There is no evidence that any one of the conditions for conceptual change are more or less important in the process of pain reconceptualisation. Future work should use quantitative methods to assess if the conditions for conceptual change

have a role in the process of pain reconceptualisation, and if one or more of the conditions are more predictive than another.

7.4.4 An exploration of the relationship between the degree of pain reconceptualisation and change in clinical outcomes

The aim of this subsection was to address aim three of this chapter, *to explore the relationship between the degree of pain reconceptualisation and changes in clinical outcomes.*

When viewing all four pillars of contemporary pain science participants could be categorised into two groups, 'reconceptulisors' and 'non reconceptulisors'. Three participants (P137, P403, P717) are categorised as reconceptulisors represented by green and orange dots in Table 7.12. Three participants are categorised as non-reconceptulisors represented by all orange dots (P249, P451) or orange dots with an equal number of red and green dots (P344) in Table 7.12.

The pre and post intervention individual participant scores for all outcomes are provided in Table 7.18 and Table 7.19. The colour of the case identified relates to whether the participant is categorised as a reconceptualisor (green) or a non-reconceptualisor (orange). The colour of their corresponding outcome measure scores indicates if the minimal clinically important difference was reached, green indicates an improved score which reached the MCID, orange indicates the MCID was not reached in the positive or negative direction, and red indicates a worsened score which reached the MCID.

The data set within the current study does not show a discernible pattern between the degree of pain reconceptualisation and changes in clinical outcomes. For the participants who qualitatively were categorised as a reconceptualisor (P137, P403, P717) there was no clear improvement in the quantitative measures in comparison to those who showed no degree of pain reconceptualisation (P249, P344, P451). It is important to highlight that this is simply an exploratory study and therefore it is not appropriate to draw any strong conclusions from these findings. It is absolutely necessary that more people would be needed for a pattern to emerge and any future work should take this into consideration.

The absence of a discernible pattern between the degree of pain reconceptualisation and changes in clinical outcomes pre to post PSE raise the question is there a potential lag effect for pain reconceptualisation to translate into improved clinical outcomes? These findings are

consistent with previously published audit data by Lee et al. (2016). They found that an initial (4 weeks post intervention) improvement in pain biology knowledge was significantly associated with later (6 and 12 months post intervention) reduction in pain intensity (total effect = -2.20, 95% CI = -2.96 to -1.44) (Lee *et al.*, 2016). The link between change in understanding and clinical outcomes may take some time before any link becomes identifiable, if indeed such a link exist. This narrative is in part consistent with the results from chapter 5 of this thesis (Watson et al. 2019) where PSE was found to produce clinically significant reductions in kinesiophobia (short-term) and pain catastrophising (medium-term), with disability approaching clinical significance in the medium-term but not short-term. Viewing this through the lens of the fear avoidance model (Vlaeyen, Crombez and Linton, 2016) the less threatening and fearful state of being (reduced fear of movement and reduced catastrophic thinking) may change a patients' priority away from pain control towards pursuit of valued life goals. This may break the cycle of fear-avoidance-interference-negative affect-pain. Furthermore, the patient may be more open to active interventions such as exercise, where previously this would have been avoided due to fear of pain, thus promoting recovery. Importantly PSE usually includes principles of pacing and graded exposure (Butler and Moseley, 2003) which show the patient *how* to engage in their valued life goals/exercise. Working out how to engage in valued life goals/exercise is likely to be challenging for patients and thus may take time before improvements in disability are achieved. As patients begin to master the skills of pacing and graded exposure, their engagement in valued life goals/exercise may increase, with associated decreases in perceived disability and improvements in physical performance. In summary there is nothing in the data from the current work to point towards pain reconceptualisors having improved clinical outcomes compared to non-reconceptualisors. The existing theories and evidence base suggest that there may be a potential lag effect which raises the question if future PSE studies should include a long term follow up to allow for any potential lag effects in pain reconceptualisation translating into improved clinical outcomes to be captured?

Table 7.18 Showing pre and post individual participant scores of the Brief Pain Inventory (Short Form).

Case	Mean change in											
						Interference in (High = worse)						
	NRS Pain Worst past 24h	NRS Pain Least past 24h	NRS Pain Average past 24h	NRS Pain Now past 24h	Relief provided by treatment as a % (high = better)	General activity	Mood	Walking ability	Work	Relationships	Sleep	Enjoyment of life
	MCID = +/-1/10 (NICE, 2016).				MCID = +/-10/100 (NICE, 2016).	MCID = +/-1/10 (NICE, 2016).						
P137	-2	+2	+3	0	+10	-1	0	+1	0	-1	-1	-3
P249	-2	-3	-1	-1	-20	+2	0	+3	0	0	0	0
P344	-2	-2	-2	-1	0	0	-3	-5	-1	-3	-2	-1
P403	0	+4	0	+1	0	0	-3	+3	-2	-2	0	0
P451	0	+1	-1	+2	0	+1	0	-1	-1	0	-1	-3

P717	0	0	+1	0	+30	0	0	+3	0	0	0	-1

Legend: *Item 1, 2 and 7 of the Brief Pain Inventory (Short Form) not included here.*

The colour of the case identified relates to the presence (or not) of pain reconceptualisation. Green indicates pain reconceptualisation occurred. Orange indicates the absence of pain reconceptualisation. The colour of the outcome measures indicates if the minimal clinically important difference was reached, green indicates an improved score which reached the MCID, orange indicates the MCID was not reached in the positive or negative direction, and red indicates a worsened score which reached the MCID.

NRS, numerical rating scale. 24h, 24 hours. SD, Standard deviation. MCID, Minimally clinically important difference. ST, Sub-theme.

Table 7.19 Showing pre and post individual participant scores of all other quantitative outcomes.

Case	Mean change in										
	Health contact past 1 month High = worse	**Working status**	**STS Test Time High = worse**	**50ft Walk test High = worse**	**PCS (0-52) High = worse**	**NPQ (0-12) Low = worse**	**CORE-10 (0-40) High = worse**	**TSK-11 (11-44) High = worse**	**EQ-5D-5L High = worse**	**EQ-VAS Low = worse**	**Attendance /8**
			MCID = +/- 6 seconds (Benaim et al. 2019)	MCID = post score +/-10% of pre test score (NICE, 2016).	MCID = +/- 5.2/52 (NICE, 2016).	MCID = +/- 1.2/12 (NICE, 2016).	MCID = +/- 4/40 (NICE, 2016).	MCID = +/- 4.4/44 (NICE, 2016).	MCID = +/- 0.03 (NICE, 2016).	MCID = +/- 10/100 (NICE, 2016).	
P137	+1	No change	+13.7	+8.8	+11	-1	Missing	+3	+0.117	+15	7
P249	-1	No change	-6.0	-2.2	-3	-1	Missing	Missing	Missing	Missing	2
P344	0	No change	-1.6	-0.9	-18	0	0	-4	+0.056	0	8
P403	+1	Less	-4.0	+0.2	-14	-1	-5	-11	+0.074	-5	6
P451	+1	No change	-3.6	+1.6	+4	+1	-2	-4	+0.170	+5	8
P717	-1	More	-0.9	-0.3	-16	+1	Missing	Missing	Missing	Missing	6

Legend: *The colour of the case identified relates to the presence (or not) of pain reconceptualisation. Green indicates pain reconceptualisation occurred. Orange indicates the absence of pain reconceptualisation. The colour of the outcome measures indicates if the minimal clinically important difference was reached, green indicates an improved score which reached the MCID, orange indicates the MCID was not reached in the positive or negative direction, and red indicates a worsened score which reached the MCID.*

SD, Standard deviation. STS Test, Repeated sit to stand test at fastest speed. 50ft Walk Test, 50ft walk test at fastest speed. PCS, Pain catastrophising scale. NPQ, Revised Neurophysiology of Pain Questionnaire. TSK-11, Tampa scale of kinesiophobia 11 Item.

7.4.5 Preliminary work to look at the metrics to inform a pilot randomised controlled trial investigating the effectiveness of a pain science education informed pain management programme

The aim of this subsection is to explore the feasibility of undertaking a pilot RCT investigating the effectiveness of a PSE informed PMP. This will include:

a. To investigate recruitment procedures and rates of recruitment.
b. To investigate the appropriateness of outcome measures used within the trial.
c. To investigate the appropriateness of the eligibility criteria.

7.4.5.1 Participants, recruitment rates and procedures, eligibility criteria

A total of 95 patients at the pain clinic were invited to take part from April 2017 to December 2018 (21 months). The study recruited 8 participants. This is a recruitment rate of 8.4%. Six participants completed the study. Two participants dropped out of the study after the intervention had been received. One participant dropped out due to a worsening in their health not related to their pain condition. The other participant was not able to be contacted. Thus the dropout rate for this study was 25%.

A sample size of 70 has been recommended for pilot studies (Teare *et al.*, 2014). Based upon a recruitment rate of 8.4% and a dropout rate of 25% approximately 1150 potential participants would need to be invited to take part in a future pilot study where the same recruitment methods were employed. Given the relatively small numbers of patients who attended the pain management programme within NHS Pain Clinic used in this current study (95 over 21 months), to invite the number of potential participants to meet the recommended sample size (1150) for a future pilot study over a similar 21 month timeframe approximately 12 sites (1150 / 95) would be needed.

At the beginning of the study there were 18 patients on a waiting list to attend the pain management programme who had already undergone the multidisciplinary team meeting where most potential participants were approached about participation in the study. These patients' were sent a letter (appendix 12) to inform them about the study and inviting them to contact researcher if they wish to participate in the study. No participants were recruited using this method and therefore any future study should not recruit using this method and should consider more innovative ways to engage with this group.

The researchers felt that all participants who were included were appropriate for the study and there were no instances where the potential participant recruiter felt someone was appropriate for the study but was excluded due to failure to meet the eligibility criteria. Therefore, the eligibility criteria used within the current study appears to be appropriate to use within a future pilot study.

7.4.5.2 Quantitative Outcomes

The factor that led to incomplete data sets for outcomes collected as part of routine care were where the participant was DNA (did not attend) for the first or last session of the pain management programme. The main factor that led to incomplete data sets for outcomes collected at Teesside University was where participants could not be contacted to arrange post data collection. These reasons accounted for the majority of incomplete data.

For the measures administered at Teesside University by JW, difficulties were informally documented in field notes and will be briefly outlined here. For the Pain Catastrophising scale a common mistake from participants was to 'tick' the boxes rather than assign a number. All the measures, including the physical performance measures were acceptable to the participants and no complaints were raised when informal feedback was sought by JW from the participants about the completion of the outcome measures/physical performance tests.

All of the measures used within this study were appropriate to use within future pilot work. Future work should mitigate against the risk of incomplete data sets due to participants not attending the first of the pain management programme by sending the outcomes to participants in the post along with their appointment letter. The letter will encourage them to complete the outcomes in the week before they are due to attend the programme and bring them to the first session that they attend. To improve post intervention data collection any participants who do not attend the last session should be sent a post intervention data collection pack in the post with a pre-paid return envelope.

The time taken to complete each outcome for the study was recorded by JW for the measures administered at Teesside University, and by the clinical team for the measures administered at the NHS pain clinic. The mean duration of completion is detailed in table 7.20.

Table 7.20 Showing the mean duration for participants to complete each outcome.

Outcome	**Approximate duration required for completion**
Demographic data	10 minutes
The Pain Catastrophising Scale	5 minutes
Neurophysiology of pain questionnaire	5 minutes
Repeated sit to stand	5 minutes
Fifty-foot walk at fastest speed	5 minutes
Brief Pain Inventory (Short-form)	5 minutes
EQ-5D-5L and EQ-VAS	3 minutes
Tampa Scale for Kinesiophobia - 11	5 minutes
CORE-10	5 minutes

The pre and post intervention group scores for all outcomes are provided in Table 7.21. These data are presented here to provide the reader with some context only.

Table 7.21 Showing pre and post group scores of all quantitative outcomes

Quantitative measure		**Pre Median (IQR)**	**Post Median (IQR)**
NRS Pain Worst past 24h (0-10) High = worse		8.5(4)	7(3)
NRS Pain Least past 24h (0-10) High = worse		4(3.5)	3.5(3)
NRS Pain Average past 24h (0-10) High = worse		6.5(2.5)	6(3)
NRS Pain Now (0-10) High = worse		6.5(4.5)	5.5(5)
Relief provided by treatment as a % (high = better)		35(60)	30(40)
Interference (0-10) in: High = worse	General activity	8(2)	7.5(2)
	Mood	7.5(6)	4.5(4)
	Walking ability	7.5(4)	7(7)
	Work	9(2.5)	7.5(4)
	Relationships	6(5)	3.5(6)
	Sleep	9(2.5)	8.5(4)

	Enjoyment of life	9.5(3)	6.5(7)
Working status*	Normal duties	0	16.7
	Normal hours reduced duties	12.5	0
	Normal duties reduced hours	0	0
	Reduced duties reduced hours	25	16.7
	Not working	62.5	66.7
Repeated sit to stand test at fastest speed High = worse		17.1(14.5)	14.4(4.7)
Health contact past 1 month High = worse		3(3.5)	2(2)
50ft walk test at fastest speed. High = worse		13.4(7.1)	12.9(3.8)
Pain catastrophising scale (0-52) High = worse		28.5(9)	22.5(20)
Revised Neurophysiology of Pain Questionnaire (0-12) Low = worse		7(1.5)	7(1)
CORE-10 (0-40) High = worse		17(13)	12(unable to calculate due to limited data)
Tampa scale of kinesiophobia 11 Item (11-44) High = worse		42(10)	39.5(5)
EQ-5D-5L High = worse		0.16(0.63)	0.16(0.61)
EQ-VAS Low = worse		30(30)	40(15)

Legend: *SD, Standard deviation. STS Test, Repeated sit to stand test at fastest speed. 50ft Walk Test, 50ft walk test at fastest speed. PCS, Pain catastrophising scale. NPQ, Revised Neurophysiology of Pain Questionnaire. TSK-11, Tampa scale of kinesiophobia 11 Item. NRS, numerical rating scale. 24h, 24 hours.*

**Working status is presented as a percentage of participants in each category.*

7.5 Reflexivity

Reflexivity "*means turning of the researcher lens back onto oneself to recognize and take responsibility for one's own situatedness within the research and the effect that it may have on the setting and people being studied, questions being asked, data being collected and its interpretation*" (Berger, 2015) p. 220). In order for the reader to understand the researchers positionality in relation to the current study, in keeping with reflexivity, some information about the researchers will be given. Four of the researchers (JW, CR, VR, NG) have experience of using PSE clinically. Three of these (JW, VR, NG) are delivering PSE working in NHS pain management services within the North East of England. One researcher (CR) is delivering PSE to healthcare professionals, people with pain and the general public as part of their role in a public health campaign. All four researchers who have experience of delivering PSE (JW, CR, VR, NG) believe that it is a clinically useful intervention; however, they have no vested interest in the outcome of this study. JD, DM and RM have no experience of delivering PSE clinically and are neutral regarding its clinically utility. Their involvement was from a research methods perspective. JW conducted all interviews in this study. Whilst having six years clinical experience discussing pain with individuals with chronic pain in a therapeutic context, he had no prior experience undertaking interviews for qualitative research. As the researcher plays a significant role in the research process, his lack of interview experience within an academic context will have influenced the results. For some topics at some timepoints there was no data available to inform the degree of reconceptualisation, or the evidence for the presence of the conditions for conceptual change. It is possible that a more experienced interviewer may have facilitated more depth of discussion and more skilled questioning may have brought out these concepts in more detail. However, given the interviews were semi-structured, by default some areas will be explored more than others.

None of the participants were actively or historically involved in a therapeutic relationship with the interviewer (JW). JW had never met any of the participants before and participants knew him only as a researcher at Teesside University, not as a practicing physiotherapist. This relationship between JW and participants was established with the aim of minimising the likelihood of socially desirable responses from participants. It is possible that participants repeated the concepts and ideas from the PSE informed PMP in their interviews rather than true reconceptualisation about their pain. However, the semi-structured nature of the interviews allows the researcher to probe participants understanding of their pain.

7.6 Discussion

This quasi mixed-methods study conducted in Chapter 7 has a number of key findings that are novel contributions to the evidence base. This is the first study to date to explore the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology (see section 7.4.2). Following the PSE informed PMP three participants underwent pain reconceptualisation, and three participants underwent no reconceptualisation, broadly mirroring the variable degrees of reconceptualisation seen in previous research (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018; King et al. 2018). This was in part unexpected given the PSE literature to date has suggested delivering PSE in addition to other active interventions, particularly a PMP potentially results in greater effects (Moseley and Butler, 2015; Yun, 2017; Watson et al. 2019). Possible reasons for the absence of evidence for this pattern seen in previous PSE research were discussed. Section 7.4.2 raised two questions which warrant further study:

- Does embedding PSE at multiple stages of the care pathway facilitate greater degrees of pain reconceptualisation?
- Are some individuals not suited to group based intervention and instead require much more personalised intervention to achieve any degree of pain reconceptualisation?

Chapter 7 is the first study to date to explore the role of Posner et al. (1982) conditions for conceptual change in the process of pain reconceptualisation (see section 7.4.3). There is nothing in these findings to suggest that Posner et al. (1982) conditions for conceptual change have no role in process of pain reconceptualisation. There is the emergence of a possible pattern where the degree of reconceptualisation for the pillars of contemporary pain science (Moseley, 2007) mirrors the change in strength of the conditions for conceptual change (Posner et al. 1982). Section 7.4.3 also raised some questions which warrant further study:

- Does high pain severity reduce the plausibility that pain does not relate to the state of the tissues?
- Do different conditions for conceptual change contribute to different degrees to the process of pain reconceptualisation for pillar 2?
- Should health care professionals not simply tell individuals key concepts of PSE i.e., ‘mood can impact on your pain’, but rather explore with the individual how they are interpreting their experience to guide their beliefs?
- Could involving individuals in the sense making process facilitate them to better understand and believe in, the conception?
- Could explaining the difference between state and trait depression/anxiety help individuals undergo pain reconceptualisation in pillar 2 of contemporary pain science?

- Is intelligibility important to ensure the plausibility and relevance of pillar 4 of contemporary pain science?

This was also the first study to explore the relationship between the degree of pain reconceptualisation assessed qualitatively and changes in clinical outcomes (see section 7.4.4). The findings showed no discernible pattern between the degree of pain reconceptualisation and changes in clinical outcomes.

This study undertook important preliminary work to inform the development of a protocol (appendix 23) for a pilot RCT to investigate the effectiveness of a PSE informed PMP (see section 7.4.5). Conducting this pilot RCT is the next step in this body of work and the intention is to undertake this work as part of a post-doctorate.

7.6.1 Strengths and limitations

The most obvious strength of the current study was its quasi mixed-methods design. This allowed the study to answer a broader and more complete range of questions producing a more complete novel contribution of knowledge to inform theory and practice (Johnson and Onwuegbuzie, 2004).

The credibility and dependability are important strengths of the current study. Credibility evaluates if there is a good 'fit' between the original data and the authors interpretation (Tobin and Begley, 2004). The current study has provided a clear and transparent audit trail from participant transcripts, to elements, to useful summaries, to categorisation of alignment to contemporary pain science, and the evidence of the presence of the conditions for conceptual change (See appendices 7.2-7.6). Therefore, each finding can be traced back to the data meaning supporting the credibility of the findings is unequivocal, i.e., beyond reasonable doubt and not open to challenge (Munn et al. 2014).

Dependability evaluates if the research process is logical, tracible and clearly documented (Schwandt, 2014). To be logical the research methods should be appropriate to answer the research question, and in alignment with the chosen methodology (Munn et al. 2014). Five questions from the JBI- Qualitative Assessment and Review Instrument (JBI-QARI) have been specifically identified as relating to the concept of dependability (Hannes, Lockwood and Pearson, 2010). The questions are;

1. Is there congruity between the research methodology and the research question or objectives?
2. Is there congruity between the research methodology and the methods used to collect data?
3. Is there congruity between the research methodology and the representation and analysis of data?
4. Is there a statement locating the researcher culturally or theoretically?
5. Is the influence of the researcher on the research, and vice-versa, addressed?

Methodology is "*the strategy, plan of action, process or design lying behind the choice and use of particular methods and linking the choice and use of the methods to the desired outcomes.*" (Crotty, 2003 p.3). The methodology used within the current study is a contemporary version of Framework Analysis (Ritchie et al., 2014) which has previously been used to explore participant beliefs within the context of pain management (May, 2007; Cooper, Smith and Hancock, 2009) and is congruent with the objectives of this chapter. The methods used in this chapter to collect data include semi-structured interviews. This is both in keeping with previous research which used framework analysis (Cooper, Smith and Hancock, 2009; May, 2007) and in keeping with methods advocated by Ritchie et al., (2014). Thus there is congruence between the research methodology and methods. The representation and analysis of data is congruent with framework analysis as the data has been organised and condensed into the framework matrices advocated by Ritchie et al., (2014). A statement locating the researchers within this study theoretically and the influence of the researcher on the research, and vice-versa has been made (See section 7b.4.4 Reflexivity).

Another strength of the current work is the collection of data before and after the intervention which allowed the change in participants understanding of contemporary of pain science to be explored. This allowed for greater insight into the changes in pain beliefs than would be obtained by only interviewing after PSE as done by Robinson et al. (2016).

Previous research has called for studies that explore pain reconceptualisation using qualitative methods following PSE delivered as part of a comprehensive multimodal package of care (Robinson et al. 2016; King et al. 2018). The current study fulfils these calls and addresses an important gap within the literature by exploring pain reconceptualisation following a PSE informed PMP, rather than shorter, more uni-modal interventions (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018; King et al. 2018).

Furthermore, the current study builds on the work of Von Bertouch, McAuley and Moseley, (2011) who while assessing pain reconceptualisation following a PSE informed PMP, they did so using self-report questionnaires including the Survey of Pain Attitudes (Jensen et al., 1987), Pain catastrophising scale (Sullivan et al., 1995) and the Biology of Pain questionnaire (Moseley, 2003). Whilst accepted as valid questionnaires in their own right they lack sufficient scope to explore the extent of reconceptualisation central to PSE (Robinson et al., 2016). Qualitative methods allow the exploration of a person's lived experience (first-hand insights and perceptions from someone who has experience of the phenomenon of interest) so that a deeper insight into their understanding of a phenomenon is achieved (Magilvy and Thomas, 2009). The current study is the first of its kind to use qualitative methods to explore pain reconceptualisation following a PSE informed PMP addressing an important gap within the literature.

This study was the first study to explore how objective measures of function change following a PSE informed PMP. This is important as self-report measures of function that were used by Von Bertouch, McAuley and Moseley, (2011) whilst in keeping with previous pain management programme studies (Chipchase and Hill, 2012) provides information that may not necessarily reflect the real capability of the patients' performance (Smeets et al., 2006) and is an important strength of the current study.

One final strength of the study was the broad age range from 26 years (P249) to 74 years (P403) and broad duration of pain 3.5 years (P717) to 45 years (P344) ensuring the qualitative study sample is broad enough to collect a range of experiences.

There are also limitations to the current study which are important to consider. The transferability of the findings which *"refers to the generalisability of inquiry"* (Tobin and Begley, 2004 p.392) needs to be considered. The sample was demographically limited comprising white British people living in the North East of England. Research suggests that culture can influence several factors related to an individual's pain experience including but not limited to their pain intensity and tolerance, pain beliefs, emotional responses, how pain is communicated, and pain catastrophising (Peacock and Patel, 2008; Sharma, Abbott and Jensen, 2018). Thus, caution should be taken in transferring the results of the current study to other patient groups owing to the cultural differences that can impact on pain experience and pain beliefs.

The evidence of the presence of the conditions for conceptual change and the degree of pain reconceptualisation were both categorised into "little or no", "partial", and "strong". Whilst

categorising the evidence makes the material more digestible and accessible to the reader, the sensitivity of the analysis is reduced and some of the more nuanced differences within each category displaying the variation in responses are lost.

Another limitation of this study is that it did not recruit the intended sample size of 12, recruiting eight participants, with only six completing the study. Therefore, it is possible that this study may have missed out on important data that may have generated novel themes. However (Morgan,. *et al.*, 2002) found that the majority of new themes within the data are obtained within the first six interviews. This is supported by Guest, Bunce and Johnson (2006) who found that 70% of the identified themes were found in the first six interviews.

A limitation of the current study is that it only explored pain reconceptualisation at one step of the care pathway. Pain management and making sense of pain is an ongoing process and due to the lack of long-term follow-up in this study, the ongoing process of sense making was not captured.

7.6.2 Suggestions for future work

There is the emergence of a possible pattern where the degree of reconceptualisation for the pillars of contemporary pain science (Moseley, 2007) mirrors the change in strength of the conditions for conceptual change (Posner et al. 1982) which warrants further study. Future work should attempt to further explore the role of the conditions for conceptual change in the process of pain reconceptualisation. In addition to the exploration of the role of all conditions in the process of pain reconceptualisation, this chapter raised other more specific questions regarding the conditions of conceptual change; Is intelligibility important to ensure the plausibility and relevance of pillar 4? Could explaining the difference between state and trait depression/anxiety help individuals undergo pain reconceptualisation in pillar 2? Does high pain severity reduce the plausibility that pain does not relate to the state of the tissues? All of these questions warrant further exploration. This exploration could include the use of quantitative methods to attempt to quantify the relationship between the two. Whilst there are several questionnaires which are validated to measure pain knowledge and beliefs (Morgan *et al.*, 2002; Pate *et al.*, 2022) to the authors knowledge there is currently no validated questionnaire to evaluate the presence of the conditions for conceptual change. Therefore, future work could look to develop a questionnaire to measure the presence of the conditions for conceptual change quantitatively. Careful preliminary work to develop this questionnaire will be needed to ensure appropriate validity and reliability. Alternatively, a mixed methods

approach could be employed utilising the methodology developed in chapter 7 to qualitatively assess the evidence for the presence of the conditions for conceptual change. These qualitative findings could then be 'quantitatized' which could allow for a quantitative analysis to be conducted. Quantitizing is the process of transforming coded qualitative data into quantitative data (Tashakkori, Johnson and Teddlie, 2020). If the possible pattern between the potential mirroring of the degree of reconceptualisation and the conditions for conceptual change is verified by this future work the next step in a research programme could explore how/if conceptual change theory could be used to optimise pain reconceptualisation during PSE interventions.

The framework for designing scientific educational programmes outlined by Stofflett and Stoddart, (1994) could be a useful starting point. Their five-step approach aimed to facilitate conceptual change by ensuring Posner et al. (1982) conditions for conceptual change were satisfied. Step one would involve identifying the learners' misconceptions about their understanding of their pain. This could be achieved by administering a preassessment. The pain quiz which has been developed and revised to assess change in knowledge of pain science information could be a useful starting point for this preassessment (Catley, O'Connell and Moseley, 2013). The learners' misconceptions could be written on a board allowing the teacher to focus the instruction and facilitate the learners dissatisfaction of these misconceptions. The second step could entail exploring the pillars of contemporary pain science (Moseley, 2007) using guided discovery methods. Virtual reality has been shown to modulate pain intensity and could be a useful tool to facilitate guided discovery of pain beliefs (Li *et al.*, 2011). Through exploration the pillars of contemporary pain science may become intelligible and plausible to the learners, while providing counter experiences to their misconceptions, facilitating dissatisfaction. The third step could entail a discussion of the learners' findings, with the teacher guiding them using Socratic questioning towards scientifically accepted explanations. This step strengthens intelligibility and plausibility. The fourth step could involve the teacher referring back to the misconceptions written on the board, and asking the learners to explain if they are still acceptable, providing their rationale in relation to the previous experiments and discussion. This step strengthens dissatisfaction with existing conceptions. If learners retain their misconceptions the teacher can return to step 2 or 3. This will strengthen the intelligibility and plausibility of contemporary pain science while strengthening dissatisfaction of the learners' misconceptions. The final step could involve the learners' providing examples of how their new understanding of pain relates to their own pain experience, and what pain management strategies they would like to try based on their new understanding, facilitating fruitfulness of the conception.

This chapter found no discernible pattern between the degree of pain reconceptualisation and changes in clinical outcomes (see section 7.4.4). The existing theories and evidence base suggest that there may be a potential lag effect (Vlaeyen, Crombez and Linton, 2016; Lee et al. 2016; Chapter 5 - Watson et al. 2019). Future PSE studies should include a long term follow up to allow for any potential lag effects in pain reconceptualisation translating into improved clinical outcomes to be captured. Furthermore the degree and nature of pain reconceptualisation should be captured across multiple steps of the care pathway i.e., Timepoint 1: before 90 minute PSE intervention; Timepoint 2: after 90 minute PSE intervention/before PSE informed PMP; Timepoint 3: after PSE informed PMP. This would help address one question raised in chapter 7; Does embedding PSE at multiple stages of the care pathway facilitate greater degrees of pain reconceptualisation?

Chapter 7 raised the question; Are some individuals not suited to group-based intervention and instead require much more personalised intervention to achieve any degree of pain reconceptualisation? Future work should first explore if any inter-individual differences in response to group-based PSE exist using the methods outlined in Chapter 6 of this thesis. If inter-individual differences are identified further analysis can explore the reasons for this.

The findings from P137 and P451 were illustrative of the power of how an individual makes sense of their first-person subject experience in the formation of pain beliefs which raised two questions that warrant further study; Should health care professionals not simply tell individuals key concepts of PSE i.e., ‘mood can impact on your pain’, but rather explore with the individual how they are interpreting their experience to guide their beliefs? Could involving individuals in the sense making process facilitate them to better understand and believe in, the conception?

Combining PSE with a PMP was highlighted by Chapter 5 of this thesis (Watson et al. 2019) as a particularly fruitful avenue to explore as a treatment for individuals with CMP. In line with recommendations by the Medical Research Council (Craig et al. 2008), this chapter undertook important preliminary work to inform the development of a pilot study prior to an RCT to investigate the effectiveness of a PSE informed PMP for adults with CMP. Appendix 23 details the proposed pilot study which would be the logical next step as part of this research programme. The results from section 7.4.5 regarding recruitment procedures and rates of recruitment, the appropriateness of outcome measures and the appropriateness of eligibility criteria, have informed the development of the pilot study. The outcome measures and eligibility criteria used in the preliminary work conducted in chapter 7 do not need to be repeated in future pilot work. However, given future pilot work will include an intervention and

control group the recruitment procedures and rates of recruitment may differ when compared to the single group design of chapter 7 and thus will be re-evaluated in any future pilot work. The single group nature of chapter 7 did also not allow for randomisation procedures and the appropriateness of the control group to be evaluated and thus would need to be assessed in any future pilot work. The appropriateness and acceptability of the control group would also need to be assessed. The Medical Research Council (Craig et al. 2008) also advocate the investigation of the clinical effectiveness of the intervention, and to estimate effect sizes for outcome measures to inform future sample size calculations. The preliminary work conducted in this chapter did not have a sufficient sample size for these calculations to be performed and therefore the future pilot RCT will aim to conduct this work.

7.6.3 Implications for practice

Pain reconceptualisation appears to have been impaired for P137 where contradictory information has been received about the relationship between their pain and the state of their tissues. Many pain beliefs held by patients originate from their interactions with healthcare professionals (Darlow et al. 2012; Bunzli et al. 2015). These erroneous pain beliefs can lead to fear and disability as illustrated by the fear avoidance model of pain (Vlaeyen, Crombez and Linton, 2016). Evidence from a recently published systematic review and meta-analysis of RCTs suggests that biopsychosocial education can improve healthcare professionals' attitudes by 11.3% (95% confidence interval: 2.2–20.4%, *P* = .02), knowledge by 18.8% (12.4–25.3%, *P* = .01), and clinical behaviour (OR = 2.4, 0.9–5.9, *P* = .06). Health services involved in the care of individuals with chronic pain conditions should ensure their staff have a contemporary understanding of pain science facilitated through the delivery of biopsychosocial education so that clear and consistent messages about the multidimensional nature of pain are provided to patients.

7.7 Conclusion

Chapter 7 was a pre-planned single arm parallel quasi mixed methods study involving a pre-test post-test design. There were four aims to this study. The first aim explored the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology (see section 7.4.2). The degree of pain reconceptualisation following a PSE

informed PMP was variable with some, but not all participants undergoing pain reconceptualisation. This mirrors the pattern of reconceptualisation seen following a single brief PSE intervention, which contrasts to the previous PSE research to date that suggest greater degrees of reconceptualisation are achieved when PSE is delivered over longer durations and combined with other interventions. The second aim explored the role of the conditions for conceptual change in the process of pain reconceptualisation (see section 7.4.3). There was no evidence to suggest that Posner et al. (1982) conditions for conceptual change do not have a role in the process of pain reconceptualisation, and there was the emergence of a possible pattern that they might have a role. Further, the findings did not suggest that any one of the conditions for conceptual change was more or less important in the process of pain reconceptualisation. The third aim explored the relationship between the degree of pain reconceptualisation and changes in clinical outcomes (see section 7.4.4). This study found no discernible pattern between the degree of pain reconceptualisation and changes in clinical outcomes. The final aim explored the feasibility of undertaking a pilot RCT investigating the effectiveness of a PSE informed PMP (see section 7.4.5). This study had a recruitment rate of 8.4% and a dropout rate of approximately 25%. The eligibility criteria and outcome measures used within the current study appeared to be appropriate to use within a future pilot study. These findings informed the development of a protocol for a pilot RCT investigating the effectiveness of a PSE informed PMP (see appendix 23).

Chapter 8: Discussion and conclusions

8.1 Overview

The aim of this final chapter is to summarise the main findings of the studies in this thesis, to highlight the novel contributions this thesis has made to the scientific literature, to discuss the strengths and limitations of the thesis, and outline the implications of this thesis for practice and future research.

The primary aim of this thesis was to investigate the effectiveness and experiences of PSE for adults with CMP. Despite the number of reviews investigating the effectiveness of PSE there were several methodological limitations which were outlined in Chapter 3 and 5 that needed to be addressed. Therefore Chapter 5 aimed to undertake a segregated synthesis of the current quantitative and qualitative literature to investigate the clinical effectiveness, and patients' experience of PSE for people with CMP. This mixed-methods review detailed in Chapter 5 included four qualitative studies (n = 50) that explored patients' experience of PSE and twelve RCTs (n = 755) that reported pain, disability and psychosocial outcomes. The qualitative component of the review conducted a meta-synthesis of 23 qualitative findings and resulted in two synthesized findings that identified several key principles important for enhancing the patient experience of PSE such as principle S1a) that advocates for *A comprehensive assessment allowing the patient to tell their own story ensuring they feel heard*. This principle is in line with previous qualitative research where participants felt it was important for HCP to give them "*time to tell their story, even when it went a little off topic"*, and found it unhelpful when the HCP did not listen to them (Holopainen et al. 2018 p. 272). If principle S1a, and the other principles generated by Chapter 5 are met, the experience and effectiveness of PSE for adults with CMP may be enhanced. With the information available it was difficult to discern if these principles were used by the RCTs included in this review, with only two principles being clearly identified; S2a) *PSE delivered by a HCP skilled in PSE delivery*; and S2c) *Progress towards reconceptualisation was monitored throughout tailoring concepts that have not been accommodated to ensure relevance of PSE to the individual*. These principles were identified in six (Bodes et al. 2018; Lluch et al 2018; Moseley et al. 2004; Malfliet et al. 2018; Van Oosterwijck et al. 2013; Bertouch, McAuley and Moseley, 2011) and four (Tellez-Garcia et al. 2015; Malfliet et al. 2018; Lluch et al. 2018; Van Oosterwijck et al 2013) RCTs respectively. It is possible that previous RCTs have not delivered PSE in a manner as to optimise its effect which may in part explain the poor effects seen for the primary outcomes of the meta-analysis.

The quantitative component of Chapter 5 conducted a meta-analyses on the pooled treatment effects for PSE vs control. The primary outcomes of pain in the short-term (-5.91/100; 95% confidence interval [CI], -13.75 to 1.93) and medium-term (-6.27/100; 95%CI -18.97 to 6.44), and disability in the short-term (-4.09/100; 95%CI -7.72 to -0.45) and medium-term (-8.14/100; 95%CI -15.60 to -0.68) did not reach the predetermined MCID of 10% for clinical significance. These findings are in contrast to previous narrative reviews on PSE that concluded there is '*compelling*' and '*strong*' evidence that PSE positively effects pain and disability (Louw et al 2011; Louw et al 2016). Similarly, they contrast to previous meta-analysis where pain relief was above the MCID in the short (-1.03/10) and medium-term (-1.09/10) (Tegner et al. 2018). The findings for short-term pain relief (-5.91/100mm) are more in line with the effects reported by Clarke et al. (2011) (-5/100mm) and Wood and Hendrick, (2018) (-0.73/10). The effects seen in Chapter 5 for short-term disability (-4.09/100 units) are smaller than previous reviews by Wood and Hendrick, (2018) (-2.28/24) and Tegner et al. (2018) (-1/10), which contrasts to the effects seen in medium-term disability (-8.14/100 units) that are similar to Tegner et al. (2018) (-0.82/10).

Contrary to Chapter 5's primary outcomes, the secondary outcomes of kinesiophobia and pain catastrophising did reach the predetermined MCID of 10% for clinical significance in the short-term (-13.55/100; 95% CI: -25.89 to -1.21) and medium-term (-5.26/52; 95% CI: -10.59 to 0.08) respectively. The findings for kinesiophobia are greater than previous reports from the meta-analysis of Tegner et al. (2018) (-5.73/68) and Wood and Hendrick (2018) (-4.72/52), likely attributable to the fact that three RCTs that Chapter 5 included were published after these reviews were completed. Two of these RCTs found particularly large effects for kinesiophobia in the PSE group (Lluch et al 2018; Bodes et al. 2018; Malfliet et al. 2018). Previous narrative reviews support the findings of Chapter 5 for pain catastrophising, all finding favourable effects for PSE (Clarke et al. 2011; Louw et al 2011; Louw et al 2016). This consistent finding increases the confidence in these results.

An important limitation of Chapter 5 was the focus on the mean treatment effect which could have obfuscated important inter-individual differences in response to PSE (King et al. 2008; Williamson et al. 2018). Synthesised finding principle S2d, highlighted that PSE can enhance patients' ability to cope with their condition, but this may not work for everyone. This finding in combination with the wide 95% confidence intervals and 95% prediction intervals seen across all four outcomes in the meta-analysis suggested PSE may produce clinically important changes for some patients and not others. Therefore Chapter 6 (Watson *et al.*, 2021) attempted to address this limitation by aiming to conduct a systematic review and meta-

analysis of the available research to quantify the 'true' inter-individual variation in pain, disability and psychosocial outcomes in response to PSE in adults with CMP. Due to insufficient data the review was only able to analyse data for disability from five RCTs (n=428). The inter-individual difference in disability change in response to PSE, as indicated by the standard deviation for the individual response (SDir) of 7.36 /100 units was below the criterion for clinical significance (10 /100 units). Therefore, Chapter 6 concluded that there was insufficient evidence at present for the existence of inter-individual differences in people's response to PSE over and above random within-subjects variability between baseline and follow-up observations. Considering the upper 95% CI (11.12 /100 units) and wide 95% prediction interval -10.20 to 14.57 of the SDir, any inferences regarding "true" inter-individual responses are unclear. The lack of, and unclear findings regarding individual responses are not supportive of the only previous PSE study to explore individual responses who found a greater number of responders where PSE was combined with exercise compared with exercise alone (Pires et al. 2016). However as outlined in Chapter 6 there are several problems with the method of responder counting used in this study. Responder counting lacks statistical power and may merely reflect within-subject random variation between timepoints and/or group differences in mean change (Atkinson, Williamson and Batterham, 2019). Thus the findings of Pires et al. (2016) tells us little about whether different people respond to different degrees to PSE which is one of the fundamental questions in precision medicine. Chapter 6 was the first study to use appropriate methodology (Atkinson and Batterham, 2015) to explore if different people respond to different degrees to PSE.

The meta-regression conducted in Chapter 5 found clinically relevant greater effects for pain (short and medium-term), disability (medium-term) and pain catastrophising (short and medium-term) when PSE was combined with another intervention compared to PSE delivered in isolation. These findings are supportive of two previous narrative reviews (Moseley and Butler, 2015; Louw et al 2016), the work of Wood and Hendrick (2018), and a recent doctoral thesis meta-analysis (Yun, 2017) that all found greater effects where PSE was delivered in combination with another intervention. Indeed, PSE was always intended to be delivered as part of a multimodal approach (Gifford, 1998; Moseley and Butler, 2015). Arguably the most comprehensive, multimodal intervention within the field on pain management for CMP is a PMP and is endorsed by the British Pain Society (The British Pain Society, 2013). Interestingly, the work of Von Bertouch, McAuley and Moseley, (2011) who compared a PSE informed PMP to a back book informed PMP demonstrated the greatest mean difference between groups for both pain (-23/100) and disability (-27/100) out of all the RCTs included within Chapter 5's meta-analysis. This provided further rationale that a combined PSE and PMP may be a fruitful intervention to optimise the effects of PSE for adults with CMP. However

there were several methodological limitations of Von Bertouch, McAuley and Moseley, (2011) that are discussed in the literature review of this thesis (See Chapter 3) that needed to be addressed by an RCT. Prior to undertaking an RCT, the Medical Research Council state that during the development and evaluation of a complex intervention (in this case a PSE informed PMP), it is important to undertake preliminary work to investigate the components of RCT methodology prior to a full-scale trial (Craig et al. 2008). Chapter 7 sought to address some of the limitations of Von Bertouch, McAuley and Moseley, (2011) aiming to undertake preliminary work to look at the metrics to inform a pilot RCT investigating the effectiveness of a PSE informed PMP. This preliminary work was used to inform the development of a protocol (appendix 23) for a pilot RCT investigating the effectiveness of a PSE informed PMP.

One important limitation of Von Bertouch, McAuley and Moseley, (2011) was the sole use of quantitative measures to evaluate the presence of pain reconceptualisation. Whilst accepted as valid questionnaires and widely used in the PSE literature, the research group at Teesside University has shown that individuals with CMP can hold contradictory conceptions about their pain. Whilst at one level those with CMP can understand tissue hypersensitivity suggestive of pain reconceptualisation;

". . .it is the new nerve in sending the messages up. . ."

(King et al. (2018 P.4, Participant 1 post)

At the same time when questioned about the cause of their pain their responses are clearly grounded in the biomedical model;

"I know I've got sclerosis of my lower back...whether the arthritis is starting to affect it more I don't know."

(King et al. (2018 P.5, Participant 1 post)

These findings indicate that whilst an individual can take on board some of the messages of PSE, and plausibly correctly answers some questions from a pain quiz (Catley, O'Connell and Moseley, 2013), their underlying pain beliefs may still be heavily grounded in a biomedical model. Qualitative methodology is better suited to explore such a complex phenomenon as an individuals understanding of their own pain experience (Magilvy and Thomas, 2009). Whilst previous research had explored the extent and nature of pain reconceptualisation following a single PSE session using qualitative methodology (Robinson et al. 2016; King et al. 2016; King et al. 2018), there was a need to replicate this approach where PSE was delivered in combination with a PMP. Thus Chapter 7 was the first study to date that aimed to explore the

extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology. The findings mirrored previous PSE qualitative studies (Robinson et al. 2016; King et al. 2016; Wijma et al. 2018; King et al. 2018) where some participants underwent pain reconceptualisation, whilst others did not. With most of the PSE literature, including the findings from Chapter 5 showing greater effects where PSE was delivered in addition to another intervention, these findings were in part surprising. Chapter 7 discussed possible reasons for the lack of an apparent dose response such as the small sample size of participants who completed both pre and post data collection (n = 6), differences in the sample compared to previous studies (for example, visibly higher mean duration of pain Chapter 7's sample), and the presence of some biomedical messages delivered within the PMP which may have diluted the effect of PSE.

There was also a need to better understand PSE from a theory and mechanisms perspective. The purported mechanism of effect central to PSE is pain reconceptualisation, defined as *"the acquisition of a new, less threatening understanding about the nature of one's pain*" (King et al. 2016 p.1389). A shift in understanding is hypothesised to change the threat value associated with a range of sensory inputs shifting the prediction of the state of the world, and thus the most advantageous response. There was a need to explore reconceptualisation itself as a mechanism for improved clinical outcomes. Given Chapter 7 was exploring the degree of pain reconceptualisation qualitatively following an intervention which theory and previous evidence suggest could provide a large degree of clinical benefit, there was a good opportunity to explore the relationship between the degree of pain reconceptualisation and changes in clinical outcomes. Surprising Chapter 7 found no discernible pattern between the degree of pain reconceptualisation assessed qualitatively and changes in clinical outcomes was observed. These findings are contrary to one of the principles of the synthesised findings generated in Chapter 5, *S2d) Achieving pain reconceptualisation can enhance patients' ability to cope with their condition*. One might expect that if pain reconceptualisation enhances an individual's ability to cope with their condition, an improvement in some/several clinical outcomes would be seen. It is possible that the clinical outcomes used in Chapter 7 did not capture the specific domain that may help people cope with their condition. Alternatively it may be that it takes time for any changes in understanding of pain to result in changes in clinical outcomes. Therefore due to this potential lag effect, the lack of long-term follow up may be why a relationship between the degree of pain reconceptualisation and changes in clinical outcomes was not observed. Moreover the small sample may have obfuscated a relationship if one exists to find.

There is increasing awareness of the need for interventions to be grounded in theory reflected in the UK Medical Research Council framework for evaluating and designing complex interventions (Craig et al. 2008) and the intervention mapping framework for designing health promotion programmes (Fernandez *et al.*, 2019). Conceptual change theory is one educational theory that seems particularly relevant to the context of pain reconceptualisation. Conceptual change theory refers to learning that challenges and shapes existing knowledge and knowledge structures, rather than just learning new information (Vosniadou, 2008). Public surveys exploring pain beliefs across several countries, including the UK consistently show the general public have a predominantly biomedical understanding of pain (Moffett et al. 2000; Goubert, Crombez and De Bourdeaudhuij, 2004; Ihlebæk and Eriksen, 2003; Darlow et al. 2014). These public surveys are supported by the findings of qualitative studies exploring individuals pain beliefs (Lin et al. 2013; Stenberg et al. 2014; Darlow et al. 2015). Given that the core objective of PSE is to shift pain conception from pain is *"a marker of tissue damage or disease"* to pain is a *"perceived need to protect body tissue"* (Moseley and Butler 2015 p.807) the use of conceptual change theory would seem an appropriate theory to inform PSE. Exploring the role of Posner et al. (1982) conditions for conceptual change in the process of pain reconceptualsation may elucidate the proposed mechanisms involved in pain reconceptualisation and also may provide some insight into how better pain reconceptualisation could be brought about. Chapter 7 was the first study to date to explore the role of Posner et al. (1982) conditions for conceptual change in the process of pain reconceptualisation. There is nothing in these findings to suggest that Posner et al. (1982) conditions for conceptual change have no role in process of pain reconceptualisation. A possible pattern emerged where the degree of reconceptualisation for the pillars of contemporary pain science (Moseley, 2007) mirrored the change in strength of the conditions for conceptual change (Posner et al. 1982). There is a need for future work to assess this possible pattern.

Given part of the primary aim of this thesis was to investigate the effectiveness of PSE for adults with CMP there is a need to undertake an RCT evaluating a PSE informed PMP. However prior to undertaking an RCT the Medical Research Council highlight that when developing and evaluating a complex intervention (in this case a PSE informed PMP), preliminary work is required to investigate the components of RCT methodology prior to a full-scale trial (Craig et al. 2008). Chapter 7 started this preliminary work by investigating recruitment procedures and rates of recruitment, the appropriateness of outcome measures and the appropriateness of eligibility criteria. These findings have been used to inform the development of a protocol for a pilot RCT investigating the effectiveness of a PSE informed

PMP (appendix 23). Conducting this pilot RCT is the next step in this body of work and the intention is to undertake this work as part of a post-doctorate.

8.2 Contribution to knowledge

- Chapter 5 of this thesis conducted the first mixed-methods systematic review on PSE. This included several contributions to knowledge including;
    - The first qualitative synthesis of the PSE literature. This generated two synthesised findings which provide a novel contribution in that they are the first attempt to guide practice and research on how to deliver PSE to optimise the patient experience rather than asking questions of effectiveness.
    - The first quantitative synthesis of the literature with a registered protocol prior to commencing the review.
    - The first meta-analysis using a sample of individuals with heterogeneous CMP.
    - The first quantitative synthesis where every meta-analysis used pooled data that met the recommended five studies to ensure sufficient statistical power (Jackson and Turner 2017). This meta-analysis found PSE to produce clinically meaningful improvements in kinesiophobia and pain catastrophising in the short and medium-term respectively. This finding has been cited in a UK based pain focussed public health campaign (www.flippinpain.co.uk).
- Chapter 6 of this thesis conducted the first systematic review and meta-analysis to employ the method of calculating true inter-individual differences in response to an intervention within the field of PSE and the broader pain field. Chapter 6 found insufficient evidence for the existence of inter-individual differences in people's response to PSE over and above random within-subjects variability between baseline and follow-up observations. The wide CI and PI of the SDir mean any inferences regarding "true" inter-individual responses are unclear.
- Chapter 7 of this thesis conducted the first exploration of the extent and nature of pain reconceptualisation following a PSE informed PMP using qualitative methodology. When viewing pain reconceptualisation as a whole rather than the more granular level of each pillar of contemporary pain science, three participants underwent pain reconceptualisation, and three participants underwent no reconceptualisation.
- Chapter 7 of this thesis conducted the first exploration of the role of the conditions for conceptual change in the process of pain reconceptualisation. This study found no evidence to suggest that Posner et al. (1982) conditions for conceptual change have no role in the process of pain reconceptualisation. This study found the emergence of

a possible pattern where the degree of reconceptualisation for the pillars of contemporary pain science (Moseley, 2007) mirrors the change in strength of the conditions for conceptual change (Posner et al. 1982).

- Chapter 7 found no evidence that any one of the conditions for conceptual change (Posner et al. 1982) are more or less important in the process of pain reconceptualisation.
- Chapter 7 is the first study to explore the relationship between the degree of pain reconceptualisation assessed qualitatively and changes in clinical outcomes. The findings showed no discernible pattern between the degree of pain reconceptualisation and changes in clinical outcomes, however further work is needed.
- The thesis has produced findings that have informed the development of a novel protocol for a pilot multi-site, single blind, parallel group randomised controlled trial aiming to investigate the effectiveness of a pain science education informed pain management programme for adults with chronic musculoskeletal pain (see appendix 23).

8.3 Strengths and limitations of the thesis

The main strengths and limitations of the individual studies in this thesis have been set out in the relevant chapters. The purpose of this section is to outline the strengths and limitations of the thesis as a whole.

The main strength of this thesis was its use of multiple methods to address the overall thesis aim of investigating the effectiveness and experiences of PSE for adults with CMP. The thesis employed both primary and secondary data analysis which used both quantitative and qualitative approaches. This allowed the thesis to answer a broader and more complete range of questions producing a more complete novel contribution to inform practice and research (Johnson and Onwuegbuzie, 2007). Another strength is that all the main projects within this thesis had a registered protocol prior to the start of the project ensuring the risk of reporting bias was minimised. All contributors to this thesis have no conflict of interest regarding PSE. Compared to neutral groups, those that have a potential conflict of interest tend to publish research which has more positive findings (Kjaergard and Als-Nielsen, 2002; Lexchin et al., 2003).

One limitation of this thesis is that it focused on adults with CMP. Therefore, the findings of this thesis cannot be generalised to children and adolescents, or adults with other chronic pain conditions. Another limitation of this thesis is that it only included studies that were published

in English and only included participants that spoke in English who lived in the North East of England. Studies have suggested that an individual's culture can influence several factors related to their pain experience including but not limited to their pain intensity and tolerance, pain beliefs, emotional responses, how pain is communicated, and pain catastrophising (Peacock and Patel, 2008; Sharma, Abbott and Jensen, 2018). Therefore, by excluding data from non-English studies, non-English speaking people with pain and people living outside of the North East of England, caution should be taken when attempted to transfer and generalise the findings from this thesis to individuals from other cultures.

8.4 Recommendations for clinical practice

Chapter 5 of this thesis found moderate certainty of evidence that PSE is effective for reducing kinesiophobia and pain catastrophising in the short and medium-term respectively. Therefore, it is recommended that PSE is used to support individuals with CMP who have pain related fear and worry. Chapter 5 of this thesis generated two synthesised findings which identified a number of principles for optimising the experience of PSE such as monitoring progress towards pain reconceptualisation and the need for a skilled clinician to deliver the intervention. Clinicians should attempt to satisfy these principles when delivering PSE in an attempt to optimise patient experience of the intervention, and its effectiveness. Furthermore, clinicians should deliver PSE in combination with other active interventions as meta-regression conducted in Chapter 5 showed tendencies for clinically meaningful greater effects when compared to PSE alone.

8.5 Recommendations for future research

Future research should build on this thesis by investigating the effectiveness and experiences of PSE for children, adolescents and adults with all types of chronic pain not just musculoskeletal pain. Future reviews should not exclude studies based upon the language it is published in.

Future studies should not exclude participants based upon their spoken language. The United Kingdom has a culturally diverse population and it is widely acknowledged that ethnic minorities have poorer health and barriers to accessing healthcare (Szczepura, 2005). High-quality research is the foundation for an evidence-based approach to healthcare (Willis, Isaacs and Khunti, 2021). Research has shown that cultural differences impact on various important domains regarding an individuals' pain experience (Peacock and Patel, 2008; Sharma, Abbott and Jensen, 2018). Therefore it is crucial to ensure diversity within future

study samples to ensure future research is generalisable and transferable to benefit all of society, and does not perpetuate existing health inequalities (Oh *et al.*, 2015).

There were some tentative suggestions within the data from Chapter 5 that greater effects were seen when PSE was delivered over a longer duration. The slopes of the meta-regression were shallow which reflects an effect that is not clinically meaningful. Future research is needed to explore a possible dose response of PSE which may inform how the intervention can be optimised.

There also appears to be greater effects seen where PSE is delivered in combination with other interventions (Chapter 5; Moseley and Butler, 2015; Louw et al 2016; Wood and Hendrick, 2018; Yun, 2017). Indeed, PSE was always intended to be delivered in combination with other interventions (Gifford, 1998; Moseley and Butler, 2015). Future research should explore what combination of interventions should be delivered with PSE to optimise patient outcomes. Some may argue this raises important questions as to what PSE actually is. In their review Moseley and Butler, (2015) acknowledge there have been misconceptions about what PSE is, and they attempt to provide clarification. They state that PSE is *"a range of educational interventions that aim to change one's understanding of the biological processes that are thought to underpin pain" (*Moseley and Butler, 2015 p. 807). There is a clear attempt to differentiate PSE *"…from cognitive behavioral therapy and educational components of early multidisciplinary pain management programs…",* and to highlight *"…that [PSE] is not behavioral or cognitive advice…".* They go onto outline that a common misconception about PSE is that it *"is teaching people how to manage their pain, similar to, for example, coping skills training, relaxation training, goal setting, or problem solving skills"* (Moseley and Butler, 2015 p.809). Rather they clarify that PSE *"is teaching people about the biological processes underpinning pain. [PSE] does not include instruction on strategies or skills with which to reduce the impact of pain on one's life. [PSE] draws on instructional design and multimedia principles to present pain biology information.".* Thus PSE is ultimately an educational approach to teach someone about contemporary pain science which does not include other cognitive or behavioural pain management strategies. Furthermore, this conclusion appears to align with the description of the PSE intervention in the first published PSE RCT;

"Each subject participated in a one-hour education session, once per week for four weeks. The education session was in a one-to-one seminar format, was conducted by an independent therapist, and focused on the neurophysiology of pain with no particular reference to the lumbar spine. In addition, the subjects completed a short workbook which consisted of one

page of revision material and three comprehension exercises per day for 10 days." (Moseley, 2002 p.298)

Some confusion perhaps arises as arguably the most commonly used PSE manual (Butler and Moseley, 2013) includes the behavioural advice of activity pacing and graded exposure. Is this component part of PSE, or something to be delivered alongside PSE? i.e., PSE + activity pacing and graded exposure. Moreover, there has been an increase in what one could argue are PSE informed approaches (O'Sullivan et al. 2018; Ashar et al. 2021). Perhaps attempting to move the field on owing to the evidence that points to PSE alone does not provide clinically meaningful improvements in pain or disability (Chapter 5 and Watson et al. 2019), and the findings that PSE needs to be carefully integrated with other interventions to avoid diluting the messages of PSE (Ryan et a. 2010). These studies utilising PSE informed approaches (O'Sullivan et al. 2018; Ashar et al. 2021) whilst clearly containing PSE, to a greater or lesser extent in that there is an explicit attempt to shift someone's understanding of their pain to align with contemporary pain science, crucially are distinct from PSE as the PSE is integrated within a package of cognitive and behavioural approaches (Moseley and Butler, 2015; O'Sullivan *et al.*, 2018; Ashar *et al.*, 2022). Ultimately where the clinician has themselves undergone pain reconceptualisation these PSE informed approaches more likely reflect what is happening in clinical practice in that PSE would be delivered within a package of cognitive and behavioural approaches, as was always the intended use of PSE (Gifford, 1998; Moseley and Butler, 2015). Thus future research should investigate the effectiveness of these PSE informed interventions. However, future research should not neglect the optimisation of PSE itself as better parts make can make a better whole. This thesis has highlighted several fruitful research avenues to optimise PSE including the use of the synthesised findings from chapter 5. The optimisation of PSE may facilitate the optimisation of PSE informed approaches and this warrants further research. The findings from this thesis suggest that enhancing PSE using the synthesised findings and integrating this into a PMP may be a particularly fruitful avenue of research.

There have been calls to develop a core outcome set to be used within pain therapies clinical trials to allow comparison between clinical trials. To address this (Kaiser *et al.*, 2018) conducted a 3-stage consensus study using a mixed-methods approach that involved an international, multi-professional panel (individuals with lived experience, pain medicine specialist physicians, physiotherapists, psychologists and methodological researchers). The panel agreed on eight domains that should be collected in future clinical trials including; pain intensity and pain frequency, physical activity (including activities such as household chores), emotional wellbeing, health related quality of life, satisfaction with social roles and activities,

productivity (including work related activities both paid and unpaid), participant's perception of treatment goal achievement. The collection of these domains are endorsed by the British Pain Society in their in press guidelines for pain management programmes (The British Pain Society, 2022). The BPS also advocate the collection of; health-care utilisation, patient experience of the programme (both quantitative and qualitative), and process outcomes (monitoring concordance of the programme with best practice). Future research should seek to collect data on these domains to allow comparison of trials, and ultimately allow research to better guide practice to improve the effectiveness and patient experience of interventions for chronic pain.

Chapter 7 found nothing to suggest that Posner et al. (1982) conditions for conceptual change have no role in process of pain reconceptualisation with the emergence of a possible pattern where the degree of reconceptualisation may mirror the change in strength of the conditions for conceptual change. Furthermore there was no evidence that any one of the conditions for conceptual change are more or less important in the process of pain reconceptualisation. Future work should use quantitative methods to assess if the conditions for conceptual change have a role in the process of pain reconceptualisation, and if one or more of the conditions are more predictive than another. If further work shows support that Posner et al. (1982) conditions for conceptual change play a role in the process of pain reconceptualisation further work could explore if PSE interventions that have been designed to satisfy these conditions are more effective. The five-step approach outlined by Stofflet and Stoddart, (1994) for designing scientific education could be a useful framework here.

There is a need for more RCTs and qualitative studies to investigate the long-term effectiveness of PSE. As highlighted in Chapter 5 as a limitation, the lack of long-term follow up may have obfuscated the presence of any potential lag effects. On the other hand, any diminishing effects over time were also not able to be captured. The collection of long-term outcome data is endorsed by the British Pain Society (The British Pain Society, 2022). Given that chronic pain is a long-term condition it is important for future research to capture the effects of the intervention over a greater span of the condition to allow healthcare professionals, healthcare systems and those with lived experience to be more informed about the merits of the interventions that are on offer. This is in alignment with the national commitment of the National Health Service to promote shared decision making (Leng *et al.*, 2017). Research shows that those who are supported to make an informed decision about their care by a healthcare professional have better a better experience (Weingart *et al.*, 2011), better outcomes (Coulter and Collins, 2011) , and experience less regret about their decisions (Aning, Wassersug and Goldenberg, 2012).

8.6 Conclusions

The primary aim of this thesis was to investigate the effectiveness and experiences of PSE for adults with CMP. The findings of this thesis suggest that achieving pain reconceptualisation can enhance patient's ability to cope with their condition. PSE interventions appear to facilitate some patients to undergo pain reconceptualisation, however this is not the case for all. Even for those who do undergo pain reconceptualisation, their degree of pain reconceptualisation does not map to changes in other clinical outcomes. One possible reason for this lack of discernible pattern may be a lag effect between reconceptualisation and clinical benefit. Furthermore, PSE interventions do not produce clinically meaningful improvements in pain and disability in the short or medium-term. In contrast PSE does produce clinically meaningful improvements in kinesiophobia and pain catastrophising in the short and medium term respectively. It is possible that these positive changes in kinesiophobia and catastrophising over a longer duration may begin to translate to changes in behaviour, with associated changes in longer term pain and disability, however there is a paucity of long-term studies to evidence this.

PSE may not currently be being delivered in research and clinical practice in such a manner as to optimise its' ability to promote pain reconceptualisation and other clinical benefits. This thesis has identified a number of principles from the synthesised findings that may optimise the patient experience and may optimise the effectiveness of PSE. As was always intended (Gifford, 1998) PSE should be delivered in combination with other active interventions. A PMP is a logical active intervention to be used in combination with PSE and this warrants further study. This combined PSE informed PMP should be enhanced by ensuring the principles generated from the synthesised findings are met. Doing this may optimise the effectiveness and experiences of PSE for adults with CMP reducing the individual and societal burden of CMP. However, future research is needed to explore if delivering PSE in this proposed optimal manner is effective for improving outcomes in people with CMP.

Reference List

Ainpradub, K. *et al.* (2016) 'Effect of education on non-specific neck and low back pain: a meta-analysis of randomized controlled trials', *Manual Therapy,* 22, pp. 31-41.

Altman, R. *et al.* (1986) 'Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee', *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology,* 29(8), pp. 1039-1049.

Anchisi, D. and Zanon, M. (2015) 'A Bayesian perspective on sensory and cognitive integration in pain perception and placebo analgesia', *PloS One,* 10(2), pp. e0117270.

Aning, J.J., Wassersug, R.J. and Goldenberg, S.L. (2012) 'Patient preference and the impact of decision-making aids on prostate cancer treatment choices and post-intervention regret. ', *Curr Oncol.*

Aromataris, E. and Munn, Z. (2017) 'Joanna Briggs Institute reviewer's manual', *The Joanna Briggs Institute*.

Asghari, A. and Nicholas, M.K. (2001) 'Pain self-efficacy beliefs and pain behaviour. A prospective study', *Pain,* 94(1), pp. 85-100.

Ashar, Y.K. *et al.* (2022) 'Effect of pain reprocessing therapy vs placebo and usual care for patients with chronic back pain: a randomized clinical trial', *JAMA Psychiatry,* 79(1), pp. 13-23.

Asmundson, G.J., Norton, P.J. and Vlaeyen, J.W. (2004) 'Fear-avoidance models of chronic pain: an overview', *Understanding and Treating Fear of Pain,* , pp. 3-24.

Atkinson, G. and Batterham, A.M. (2015) 'True and false interindividual differences in the physiological response to an intervention', *Experimental Physiology,* 100(6), pp. 577-588.

Atkinson, G., Williamson, P. and Batterham, A.M. (2019) 'Issues in the determination of 'responders' and 'non-responders' in physiological research', *Experimental Physiology,* 104(8), pp. 1215-1225.

Baert, P. (2005) *Philosophy of the social sciences: Towards pragmatism.* Polity.

Bailly, F. *et al.* (2015) 'The impact of chronic low back pain is partly related to loss of social role: a qualitative study', *Joint Bone Spine,* 82(6), pp. 437-441.

Bandura, A. (1977) 'Self-efficacy: toward a unifying theory of behavioral change.', *Psychological Review,* 84(2), pp. 191.

Barbour, R. (2000) 'The role of qualitative research in broadening the 'evidence base'for clinical practice', *Journal of Evaluation in Clinical Practice,* 6(2), pp. 155-163.

Barkham, M. *et al.* (2013) 'The CORE-10: A short measure of psychological distress for routine use in the psychological therapies', *Counselling and Psychotherapy Research,* 13(1), pp. 3-13.

Bashir, R., Surian, D. and Dunn, A.G. (2018) 'Time-to-update of systematic reviews relative to the availability of new evidence', *Systematic Reviews,* 7(1), pp. 1-8.

Belsey, J. (2002) 'Primary care workload in the management of chronic pain. A retrospective cohort study using a GP database to identify resource implications for UK primary care', *Journal of Medical Economics,* 5(1-4), pp. 39-50.

Benaim, C. *et al.* (2019) '"Minimal clinically important difference" estimates of 6 commonly-used performance tests in patients with chronic musculoskeletal pain completing a work-related multidisciplinary rehabilitation program', *BMC Musculoskeletal Disorders,* 20(1), pp. 1-9.

Benton, T. and Craib, I. (2017) *Philosophy of social science: The philosophical foundations of social thought.* Bloomsbury Publishing.

Berger, R. (2015) 'Now I see it, now I don't: Researcher's position and reflexivity in qualitative research', *Qualitative Research,* 15(2), pp. 219-234.

Bhaskar, R. (1975) 'Feyerabend and bachelard: two philosophies of science', *New Left Review,* (94), pp. 31.

Bishop, F.L. (2015) 'Using mixed methods research designs in health psychology: An illustrated discussion from a pragmatist perspective', *British Journal of Health Psychology,* 20(1), pp. 5-20.

Bodes, G.P. *et al.* (2018) 'Pain neurophysiology education and therapeutic exercise for patients with chronic low back pain: a single-blind randomized controlled trial', *Archives of Physical Medicine and Rehabilitation,* 99(2), pp. 338-347.

Bondesson, E. *et al.* (2018) 'Comorbidity between pain and mental illness–evidence of a bidirectional relationship', *European Journal of Pain,* 22(7), pp. 1304-1311.

Booth, J. *et al.* (2017) 'Exercise for chronic musculoskeletal pain: a biopsychosocial approach', *Musculoskeletal Care,* 15(4), pp. 413-421.

Borenstein, M. *et al.* (2017) 'Basics of meta-analysis: I2 is not an absolute measure of heterogeneity', *Research Synthesis Methods,* 8(1), pp. 5-18.

Bowling, A. and Ebrahim, S. (2005) *Handbook of health research methods: investigation, measurement and analysis.* McGraw-Hill Education (UK).

Bramer, W.M. *et al.* (2016) 'De-duplication of database search results for systematic reviews in EndNote', *Journal of the Medical Library Association: JMLA,* 104(3), pp. 240.

Brehm, S.S. and Brehm, J.W. (2013) *Psychological reactance: A theory of freedom and control.* Academic Press.

Breivik, H. *et al.* (2006) 'Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment', *European Journal of Pain,* 10(4), pp. 287-333.

Bryman, A. (2016) *Social research methods.* Oxford university press.

Buchbinder, R. *et al.* (2018) 'Low back pain: a call for action', *The Lancet,* 391(10137), pp. 2384-2388.

Büchel, C. *et al.* (2014) 'Placebo analgesia: a predictive coding perspective', *Neuron,* 81(6), pp. 1223-1239.

Bunzli, S. *et al.* (2015) 'Beliefs underlying pain-related fear and how they evolve: a qualitative investigation in people with chronic back pain and high pain-related fear', *BMJ Open,* 5(10), pp. e008847.

Busse, J.W. *et al.* (2015) 'Optimal strategies for reporting pain in clinical trials and systematic reviews: recommendations from an OMERACT 12 workshop', *The Journal of Rheumatology,* 42(10), pp. 1962-1970.

Butler, D.S. and Moseley, G.L. (2003) *Explain Pain.* 1st edn.

Butler, D.S. and Moseley, G.L. (2013) *Explain Pain 2nd Edn.* Noigroup publications.

Byrne, S. and Hart, P. (2009) 'The 'Boomerang'Effect: A Synthesis of Findings and a Preliminary Theoretical Framework.', *Annals of the International Communication Association,* 33(1), pp. 3-37. doi: 10.1080/23808985.2009.11679083.

Catley, M.J., O'Connell, N.E. and Moseley, G.L. (2013) 'How good is the neurophysiology of pain questionnaire? A Rasch analysis of psychometric properties', *The Journal of Pain,* 14(8), pp. 818-827.

Centre for Reviews and Dissemination (2009) *Systematic Reviews. CRD's guidance for undertaking reviews in health care.* York: CRD, University of York.

Chapman, C.R. and Vierck, C.J. (2017) 'The transition of acute postoperative pain to chronic pain: an integrative overview of research on mechanisms', *The Journal of Pain,* 18(4), pp. 359. e1-359. e38.

Chipchase, L. and Hill, P. (2012) 'The long-term effectiveness of pain management programs: A systematic review and meta-analysis', *Journal of Pain Management,* 5(3), pp. 215.

Clark, A. (2015) *Surfing uncertainty: Prediction, action, and the embodied mind.* Oxford University Press.

Clarke, C.L., Ryan, C.G. and Martin, D.J. (2011) 'Pain neurophysiology education for the management of individuals with chronic low back pain: A systematic review and meta-analysis', *Manual Therapy,* 16(6), pp. 544-549.

Cleeland, C. (2009) 'The brief pain invnetory user guide. The University of Texas MD.

Cleeland, C.S. and Ryan, K. (1994) 'Pain assessment: global use of the Brief Pain Inventory.', *Annals, Academy of Medicine, Singapore.*

Cooper, K., Smith, B.H. and Hancock, E. (2009) 'Patients' perceptions of self-management of chronic low back pain: evidence for enhancing patient education and support', *Physiotherapy,* 95(1), pp. 43-50.

Corbin, J. and Strauss, A. (2014) *Basics of qualitative research: Techniques and procedures for developing grounded theory.* Sage publications.

Cortés, J. *et al.* (2018) 'Does evidence support the high expectations placed in precision medicine? A bibliographic review', *F1000Research,* 7.

Coulter, A. & Collins, A. (2011) *Making shared decision-making a reality.* Available at: https://www.kingsfund.org.uk/sites/files/kf/Making-shared-decision-making-a-reality-paper-Angela-Coulter-Alf-Collins-July-2011_0.pdf.

Craig, P. *et al.* (2008) 'Developing and evaluating complex interventions: the new Medical Research Council guidance', *Bmj,* 337.

Creswell, J.W. and Clark, V.L.P. (2017) *Designing and conducting mixed methods research.* Sage publications.

Creswell, J.W. and Poth, C.N. (2016) *Qualitative inquiry and research design: Choosing among five approaches.* Sage publications.

Crotty, M.J. (2003) 'The foundations of social research: Meaning and perspective in the research process', *The Foundations of Social Research,* , pp. 1-256.

Cuenda-Gago, J.D. and Espejo-Antunez, L. (2017) 'Effectiveness of education based on neuroscience in the treatment of musculoskeletal chronic pain', *Revista De Neurologia,* 65(1), pp. 1-12.

Çukur, T. *et al.* (2013) 'Attention during natural vision warps semantic representation across the human brain', *Nature Neuroscience,* 16(6), pp. 763-770.

Darlow, B. *et al.* (2015) 'Easy to harm, hard to heal: patient views about the back', *Spine,* 40(11), pp. 842-850.

Darlow, B. *et al.* (2012) 'The association between health care professional attitudes and beliefs and the attitudes and beliefs, clinical management, and outcomes of patients with low back pain: a systematic review', *European Journal of Pain,* 16(1), pp. 3-17.

Darlow, B. *et al.* (2014) 'Cross-sectional survey of attitudes and beliefs about back pain in New Zealand', *BMJ Open,* 4(5), pp. e004725.

Daut, R.L., Cleeland, C.S. and Flanery, R.C. (1983) 'Development of the Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases', *Pain,* 17(2), pp. 197-210.

Deeks, J.J., Higgins, J.P. and Altman, D.G. (2011) 'Chapter 16: special topics in statistics', *Cochrane Handbook for Systematic Reviews of Interventions.UK: The Cochrane Collaboration.*

Den Ouden, H.E., Kok, P. and De Lange, F.P. (2012) 'How prediction errors shape perception, attention, and motivation', *Frontiers in Psychology,* 3, pp. 548.

Denzin, N.K. and Lincoln, Y.S. (2011) *The Sage handbook of qualitative research.* sage.

Department of Health and Social Care (2012) *England level programme budgeting data 2010-11.* Available at: https://www.gov.uk/government/publications/2003-04-to-2010-11-programme-budgeting-data.

Descartes, R. (1972) 'Treatise of man, trans. TS Hall', *Harvard University.*

Dillard, J.P. and Shen, L. (2005) 'On the nature of reactance and its role in persuasive health communication', *Communication Monographs,* 72(2), pp. 144-168.

Donaldson, L. (2008) *On the state of public health: annual report of the Chief Medical Officer.* Department of Health.

Doyle, S. (2007) 'Member checking with older women: A framework for negotiating meaning', *Health Care for Women International,* 28(10), pp. 888-908.

Elzahaf, R.A. *et al.* (2012) 'The prevalence of chronic pain with an analysis of countries with a Human Development Index less than 0.9: a systematic review without meta-analysis', *Null,* 28(7), pp. 1221-1229. doi: 10.1185/03007995.2012.703132.

Fayaz, A. *et al.* (2016) 'Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies', *BMJ Open,* 6(6), pp. e010364.

Feldman, H. and Friston, K.J. (2010) 'Attention, uncertainty, and free-energy', *Frontiers in Human Neuroscience,* 4, pp. 215.

Feng, Y. *et al.* (2021) 'Psychometric properties of the EQ-5D-5L: a systematic review of the literature', *Quality of Life Research,* 30(3), pp. 647-673.

Fernandez, M.E. *et al.* (2019) 'Intervention mapping: theory-and evidence-based health promotion program planning: perspective and examples', *Frontiers in Public Health,* 7, pp. 209.

Fletcher, P.C. and Frith, C.D. (2009) 'Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia', *Nature Reviews Neuroscience,* 10(1), pp. 48-58.

Fornasari, D. (2012) 'Pain mechanisms in patients with chronic pain', *Clinical Drug Investigation,* 32(1), pp. 45-52.

Franklin, D.W. and Wolpert, D.M. (2011) 'Computational mechanisms of sensorimotor control', *Neuron,* 72(3), pp. 425-442.

Frost, H. *et al.* (2004) 'Randomised controlled trial of physiotherapy compared with advice for low back pain', *Bmj,* 329(7468), pp. 708.

Fukuda, K. *et al.* (1994) 'The chronic fatigue syndrome: a comprehensive approach to its definition and study', *Annals of Internal Medicine,* 121(12), pp. 953-959.

Furlan, A.D. *et al.* (2006) 'Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects', *Cmaj,* 174(11), pp. 1589-1594.

Gale, N.K. *et al.* (2013) 'Using the framework method for the analysis of qualitative data in multi-disciplinary health research', *BMC Medical Research Methodology,* 13(1), pp. 1-8.

Gallagher, L., McAuley, J. and Moseley, G.L. (2013) 'A randomized-controlled trial of using a book of metaphors to reconceptualize pain and decrease catastrophizing in people with chronic pain', *The Clinical Journal of Pain,* 29(1), pp. 20-25.

Geneen, L.J. *et al.* (2015) 'Effects of education to facilitate knowledge about chronic pain for adults: a systematic review with meta-analysis', *Systematic Reviews,* 4(1), pp. 1-21.

Gifford, L. (2014) 'Aches and Pains.

Gifford, L. (1998) 'Pain, the tissues and the nervous system: a conceptual model', *Physiotherapy,* 84(1), pp. 27-36.

Godtfredsen, N.S. *et al.* (2002) 'Smoking reduction, smoking cessation, and mortality: a 16-year follow-up of 19,732 men and women from The Copenhagen Centre for Prospective Population Studies', *American Journal of Epidemiology,* 156(11), pp. 994-1001.

Goubert, L., Crombez, G. and De Bourdeaudhuij, I. (2004) 'Low back pain, disability and back pain myths in a community sample: prevalence and interrelationships', *European Journal of Pain,* 8(4), pp. 385-394.

Guba, E.G. and Lincoln, Y.S. (1989) *Fourth generation evaluation.* Sage.

Guest, G., Bunce, A. and Johnson, L. (2006) 'How many interviews are enough? An experiment with data saturation and variability', *Field Methods,* 18(1), pp. 59-82.

Guyatt, G.H. *et al.* (2008) 'GRADE: an emerging consensus on rating quality of evidence and strength of recommendations', *Bmj,* 336(7650), pp. 924-926.

Hannes, K., Lockwood, C. and Pearson, A. (2010) 'A comparative analysis of three online appraisal instruments' ability to assess validity in qualitative research', *Qualitative Health Research,* 20(12), pp. 1736-1743.

Harris, S., Morley, S. and Barton, S.B. (2003) 'Role loss and emotional adjustment in chronic pain', *Pain,* 105(1-2), pp. 363-370.

Hartvigsen, J. *et al.* (2018) 'What low back pain is and why we need to pay attention', *The Lancet,* 391(10137), pp. 2356-2367.

Herdman, M. *et al.* (2011) 'Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L)', *Quality of Life Research,* 20(10), pp. 1727-1736.

Higgins, J.P. (2008) 'Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified', *International Journal of Epidemiology,* 37(5), pp. 1158-1160.

Higgins, J.P. *et al.* (2011) 'The Cochrane Collaboration's tool for assessing risk of bias in randomised trials', *Bmj,* 343.

Hohwy, J. (2012) 'Attention and conscious perception in the hypothesis testing brain', *Frontiers in Psychology,* 3, pp. 96.

Holopainen, R. *et al.* (2018) 'From "non-encounters" to autonomic agency. Conceptions of patients with low back pain about their encounters in the health care system', *Musculoskeletal Care,* 16(2), pp. 269-277.

Hong, J. *et al.* (2013) 'Costs associated with treatment of chronic low back pain: an analysis of the UK General Practice Research Database', *Spine,* 38(1), pp. 75-82.

Hong, Q.N. *et al.* (2017) 'Convergent and sequential synthesis designs: implications for conducting and reporting systematic reviews of qualitative and quantitative evidence', *Systematic Reviews,* 6(1), pp. 1-14.

Hopkins, W.G. (2015) 'Individual responses made easy', *Journal of Applied Physiology,* 118(12), pp. 1444-1446.

Hurley, J. *et al.* (2016) 'Effect of education on non-specific neck and low back pain: a meta-analysis of randomized controlled trials', *Manual Therapy.*

Ihlebæk, C. and Eriksen, H.R. (2003) 'Are the``myths"of low back pain alive in the general Norwegian population?', *Scandinavian Journal of Public Health,* 31(5), pp. 395-398.

International Association for the Study of Pain (2010) *Mechanisms of Acute Pain.* International Association for the Study of Pain.

IntHout, J. *et al.* (2016) 'Plea for routinely presenting prediction intervals in meta-analysis', *BMJ Open,* 6(7), pp. e010247.

IntHout, J., Ioannidis, J. and Borm, G.F. (2014) 'The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method', *BMC Medical Research Methodology,* 14(1), pp. 1-12.

Jackson, D. and Turner, R. (2017) 'Power analysis for random-effects meta-analysis', *Research Synthesis Methods,* 8(3), pp. 290-302.

James, S.L. *et al.* (2018) 'Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017', *The Lancet,* 392(10159), pp. 1789-1858.

Janssen, M.F. *et al.* (2013) 'Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study', *Quality of Life Research,* 22(7), pp. 1717-1727.

Jensen, M.P. and Karoly, P. (1987) 'Notes on the Survey of Pain Attitudes (SOPA): original (24-item) and revised (35-item) versions', *Arizona State University, Tempe, AZ.*

Jess, M. *et al.* (2021) 'Does duration of pain at baseline influence longer-term clinical outcomes of low back pain patients managed on an evidence-based pathway?', *Spine,* 46(3), pp. 191-197.

Joormann, J., Siemer, M. and Gotlib, I.H. (2007) 'Mood regulation in depression: Differential effects of distraction and recall of happy memories on sad mood.', *Journal of Abnormal Psychology,* 116(3), pp. 484.

Kaiser, U. *et al.* (2018) 'Developing a core outcome domain set to assessing effectiveness of interdisciplinary multimodal pain therapy: the VAPAIN consensus statement on core outcome domains', *Pain,* 159(4), pp. 673-683. doi: 10.1097/j.pain.0000000000001129 [doi].

Kamper, S.J. *et al.* (2015) 'Multidisciplinary biopsychosocial rehabilitation for chronic low back pain: Cochrane systematic review and meta-analysis', *Bmj,* 350.

Kersten, D., Mamassian, P. and Yuille, A.L. (2004) 'Object perception as Bayesian inference'.

Khan, S.N. (2014) 'Qualitative research method: Grounded theory', *International Journal of Business and Management,* 9(11), pp. 224-233.

Khosrokiani, Z. *et al.* (2022) 'Comparison the Effect of Pain Neuroscience and Pain Biomechanics Education on Neck Pain and Fear of Movement in Patients with Chronic Nonspecific Neck Pain During the COVID-19 Pandemic', *Pain and Therapy,* 11(2), pp. 601-611.

King, N.A. *et al.* (2008) 'Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss', *International Journal of Obesity,* 32(1), pp. 177-184.

King, R. *et al.* (2018) 'Pain reconceptualisation after pain neurophysiology education in adults with chronic low back pain: A qualitative study', *Pain Research and Management,* 2018.

King, R. *et al.* (2016) 'An exploration of the extent and nature of reconceptualisation of pain following pain neurophysiology education: A qualitative study of experiences of people with chronic musculoskeletal pain', *Patient Education and Counseling,* 99(8), pp. 1389-1393.

Kjaergard, L. and Als-Nielsen, B. (2002) 'Association between competing interests and authors' conclusions: epidemiological study of randomised clinical trials published in the BMJ', *Bmj,* 325(7358), pp. 249.

Klein, C. (2015) *What the body commands: The imperative theory of pain.* MIT Press.

Knill, D.C. and Pouget, A. (2004) 'The Bayesian brain: the role of uncertainty in neural coding and computation', *Trends in Neurosciences,* 27(12), pp. 712-719.

Kori, S.H., Miller, J.A. and Todd, D.D. (1990) 'Kinesiophobia: a new view of chronic pain behavior', *Pain Manage,* 3, pp. 35-43.

Leake, H.B. *et al.* (2021) 'What do patients value learning about pain? A mixed-methods survey on the relevance of target concepts after pain science education', *Pain,* 162(10), pp. 2558-2568.

Lee, H. *et al.* (2016) 'Does changing pain-related knowledge reduce pain and improve function through changes in catastrophizing?', *Pain,* 157(4), pp. 922-930.

Leeuw, M. *et al.* (2007) 'The fear-avoidance model of musculoskeletal pain: current state of scientific evidence', *Journal of Behavioral Medicine,* 30(1), pp. 77-94.

Leng, G. *et al.* (2017) 'National commitment to shared decision making', *Bmj,* 359.

Lethem, J. *et al.* (1983) 'Outline of a fear-avoidance model of exaggerated pain perception—I', *Behaviour Research and Therapy,* 21(4), pp. 401-408.

Lexchin, J. *et al.* (2003) 'Pharmaceutical industry sponsorship and research outcome and quality: systematic review', *Bmj,* 326(7400), pp. 1167-1170.

Li, A. *et al.* (2011) 'Virtual reality and pain management: current trends and future directions', *Pain Management,* 1(2), pp. 147-157.

Lin, I.B. *et al.* (2013) 'Disabling chronic low back pain as an iatrogenic disorder: a qualitative study in Aboriginal Australians', *BMJ Open,* 3(4), pp. e002654.

Lizarondo, L. *et al.* (2020) 'Chapter 8: Mixed methods systematic reviews', in Aromataris, E. and Munn, Z. (eds.) *JBI Manual for Evidence Synthesis.* Adelaide: Joanna Briggs Institute.

Lluch, E. *et al.* (2018) 'Preoperative pain neuroscience education combined with knee joint mobilization for knee osteoarthritis', *The Clinical Journal of Pain,* 34(1), pp. 44-52.

Lockwood, C. *et al.* (2017) 'Chapter 2: Systematic reviews of qualitative evidence', in Aromataris, E. and Munn, Z. (eds.) *Joanna Briggs Institute reviewer's manual [Internet].* Adelaide: The Joanna Briggs Institute.

Louw, A. (2014a) 'Therapeutic neuroscience education via e-mail: a case report', *Physiotherapy Theory and Practice,* 30(8), pp. 588-596.

Louw, A. (2014b) 'Therapeutic neuroscience education via e-mail: a case report', *Physiotherapy Theory and Practice,* 30(8), pp. 588-596.

Louw, A. *et al.* (2011) 'The effect of neuroscience education on pain, disability, anxiety, and stress in chronic musculoskeletal pain', *Archives of Physical Medicine and Rehabilitation,* 92(12), pp. 2041-2056.

Louw, A. *et al.* (2014) 'Preoperative pain neuroscience education for lumbar radiculopathy: a multicenter randomized controlled trial with 1-year follow-up', *Preoperative Pain Neuroscience Education for Lumbar Radiculopathy: A Multicenter Randomized Controlled Trial with 1-Year Follow-Up.*

Louw, A. *et al.* (2016) 'The efficacy of pain neuroscience education on musculoskeletal pain: a systematic review of the literature', *Physiotherapy Theory and Practice,* 32(5), pp. 332-355.

Lupyan, G. and Clark, A. (2015) 'Words and the world: Predictive coding and the language-perception-cognition interface', *Current Directions in Psychological Science,* 24(4), pp. 279-284.

Magilvy, J.K. and Thomas, E. (2009) 'A first qualitative project: Qualitative descriptive design for novice researchers', *Journal for Specialists in Pediatric Nursing,* 14(4), pp. 298-300.

Maier-Riehle, B. and Härter, M. (2001) 'The effects of back schools–a meta-analysis', *International Journal of Rehabilitation Research,* 24(3), pp. 199-206.

Malfliet, A. *et al.* (2018) 'Blended-learning pain neuroscience education for people with chronic spinal pain: randomized controlled multicenter trial', *Physical Therapy,* 98(5), pp. 357-368.

Maniadakis, N. and Gray, A. (2000) 'The economic burden of back pain in the UK', *Pain,* 84(1), pp. 95-103.

May, S. (2007) 'Patients' attitudes and beliefs about back pain and its management after physiotherapy for low back pain', *Physiotherapy Research International,* 12(3), pp. 126-135.

Mc Elhinney, H. *et al.* (2016) 'Sensitivity and specificity of electronic databases: The example of searching for evidence on child protection issues related to pregnant women', *Evidence Based Midwifery,* 14(1), pp. 29-34.

McCann, T.V. and Clark, E. (2003) 'Grounded theory in nursing research: Part 1–Methodology'.

Meeus, M. *et al.* (2010) 'Pain physiology education improves pain beliefs in patients with chronic fatigue syndrome compared with pacing and self-management education: a double-blind randomized controlled trial', *Archives of Physical Medicine and Rehabilitation,* 91(8), pp. 1153-1159.

Moffett, J.A.K. *et al.* (2000) 'Public perceptions about low back pain and its management: a gap between expectations and reality?', *Health Expectations,* 3(3), pp. 161-168.

Moher, D. *et al.* (2009) 'Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement', *Annals of Internal Medicine,* 151(4), pp. 264-269.

Molton, I.R. and Terrill, A.L. (2014) 'Overview of persistent pain in older adults.', *American Psychologist,* 69(2), pp. 197.

Moore, A. *et al.* (2013) 'Expect analgesic failure; pursue analgesic success', *Bmj,* 346.

Morgan, D.L. (2007) 'Paradigms lost and pragmatism regained: Methodological implications of combining qualitative and quantitative methods', *Journal of Mixed Methods Research,* 1(1), pp. 48-76.

Morgan, D.L. (2013) *Integrating qualitative and quantitative methods: A pragmatic approach.* Sage publications.

Morgan, H.M. *et al.* (2017) 'We need to talk about purpose: a critical interpretive synthesis of health and social care professionals' approaches to self-management support for people with long-term conditions', *Health Expectations,* 20(2), pp. 243-259.

Morgan, M.G.*et al.* (2002) *Risk communication: A mental models approach.* Cambridge University Press.

Moseley, G.L. (2003) 'Joining forces–combining cognition-targeted motor control training with group or individual pain physiology education: a successful treatment for chronic low back pain', *Journal of Manual & Manipulative Therapy,* 11(2), pp. 88-94.

Moseley, G.L. (2004) 'Evidence for a direct relationship between cognitive and physical change during an education intervention in people with chronic low back pain', *European Journal of Pain,* 8(1), pp. 39-45.

Moseley, G.L. (2007) 'Reconceptualising pain according to modern pain science', *Physical Therapy Reviews,* 12(3), pp. 169-178.

Moseley, G.L. and Arntz, A. (2007) 'The context of a noxious stimulus affects the pain it evokes', *Pain®,* 133(1-3), pp. 64-71.

Moseley, G.L. and Butler, D.S. (2015) 'Fifteen years of explaining pain: the past, present, and future', *The Journal of Pain,* 16(9), pp. 807-813.

Moseley, G.L. and Butler, D.S. (2017) *Explain pain supercharged.* NOI.

Moseley, G.L., Nicholas, M.K. and Hodges, P.W. (2004) 'A randomized controlled trial of intensive neurophysiology education in chronic low back pain', *The Clinical Journal of Pain,* 20(5), pp. 324-330.

Moseley, L. (2002) 'Combined physiotherapy and education is efficacious for chronic low back pain', *Australian Journal of Physiotherapy,* 48(4), pp. 297-302.

Munn, Z. (2016) 'Software to support the systematic review process: the Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information (JBI-SUMARI)', *JBI Evidence Synthesis,* 14(10), pp. 1.

Munn, Z. *et al.* (2014) 'Establishing confidence in the output of qualitative research synthesis: the ConQual approach', *BMC Medical Research Methodology,* 14(1), pp. 1-7.

Murray, C.J. *et al.* (2013) 'UK health performance: findings of the Global Burden of Disease Study 2010', *The Lancet,* 381(9871), pp. 997-1020.

NICE (2016) *Low back pain and sciatica in over 16s: Assessment and management DRAFT. (NICE guideline NG59).*

NICE (2020a) 'Low back pain and sciatica in over 16s: assessment and management NICE guideline [NG59]'.

NICE (2020b) 'Osteoarthritis: care and management (Clinical guideline [CG177]).

NICE (2021) 'Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain
NICE guideline [NG193]'.

Nicholas, M.K. (2007) 'The pain self-efficacy questionnaire: taking pain into account', *European Journal of Pain,* 11(2), pp. 153-163.

Nickerson, R.S. (1998) 'Confirmation bias: A ubiquitous phenomenon in many guises', *Review of General Psychology,* 2(2), pp. 175-220.

Nour, M.M. and Nour, J.M. (2015) 'Perception, illusions and Bayesian inference', *Psychopathology,* 48(4), pp. 217-221.

O'Keeffe, L.M. *et al.* (2018) 'Smoking as a risk factor for lung cancer in women and men: a systematic review and meta-analysis', *BMJ Open,* 8(10), pp. e021611.

O'Sullivan, P.B. *et al.* (2018) 'Cognitive functional therapy: an integrated behavioral approach for the targeted management of disabling low back pain', *Physical Therapy,* 98(5), pp. 408-423.

Office for National Statistics (2022) *Sickness absence in the UK labour market.* Available at: https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/employmentandemployeetypes/datasets/sicknessabsenceinthelabourmarket.

Offredy, M. and Vickers, P. (2013) *Developing a healthcare research proposal: An interactive student guide.* John Wiley & Sons.

Oh, S.S. *et al.* (2015) 'Diversity in clinical and biomedical research: a promise yet to be fulfilled', *PLoS Medicine,* 12(12), pp. e1001918.

Onwuegbuzie, A.J., Johnson, B.R. and Turner, L.A. (2007) 'Toward a definition of mixed methods research', *Journal of Mixed Methods Research,* 1(2), pp. 112-133.

Osman, A. *et al.* (1997) 'Factor structure, reliability, and validity of the Pain Catastrophizing Scale', *Journal of Behavioral Medicine,* 20(6), pp. 589-605.

Oxford Economics (2010) *The economic costs of arthritis for the UK economy.* Oxford: Oxford Economics.

Pate, J.W. *et al.* (2022) 'The Concept of Pain Inventory for Adults (COPI-Adult): Assessing Knowledge and Beliefs Regarding Pain Science Education', *The Clinical Journal of Pain,* 38(1), pp. 32-40.

Peacock, S. and Patel, S. (2008) 'Cultural influences on pain', *Reviews in Pain,* 1(2), pp. 6-9.

Peirce, C.S. (1992) *The essential Peirce: selected philosophical writings.* Indiana University Press.

Pinheiro, M.B. *et al.* (2015) 'Symptoms of depression and risk of new episodes of low back pain: a systematic review and meta-analysis', *Arthritis Care & Research,* 67(11), pp. 1591-1603.

Pires, D., Caeiro, C. and Cruz, E. (2016) 'Individual patient responder analysis of the effectiveness of a pain neuroscience education programme in chronic low back pain', *International Federation of Orthopaedic Manipulative Physical Therapists (IFOMPT) Conference.*

Pires, D., Cruz, E.B. and Caeiro, C. (2015) 'Aquatic exercise and pain neurophysiology education versus aquatic exercise alone for patients with chronic low back pain: a randomized controlled trial', *Clinical Rehabilitation,* 29(6), pp. 538-547.

Pope, C. and Mays, N. (1995) 'Qualitative research: reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research', *Bmj,* 311(6996), pp. 42-45.

Porth, C.M. (2015) 'Disorders of special sensory function: vision, hearing, and vestibular function', *Essentials of Pathophysiology: Concepts of Altered Health States.4th Ed.Philadelphia, PA: Wolters Kluwer,* 975.

Posner, J.G. *et al.* (1982) 'Accommodation of a scientific conception: Toward a theory of conceptual change', *Accommodation of a Scientific Conception: Toward a Theory of Conceptual Change.*

Raja, S.N. *et al.* (2020) 'The revised IASP definition of pain: concepts, challenges, and compromises', *Pain,* 161(9), pp. 1976.

Retrain Pain Foundation (2019) *Retrain Pain Foundation.* Available at: https://www.retrainpain.org.

Rice University: (2019) *Online Statistics Education: A Multimedia Course of Study.* Available at: http://onlinestatbook.com/2/calculators/normal_dist.html (Accessed: 02/09/2019).

Ritchie, J. *et al.* (2014) 'Qualitative research practice: A guide for social science students and researchers. Sage Publications'.

Ritchie, J. and Spencer, L. (2002a) 'Qualitative data analysis for applied policy research', in 'Qualitative data analysis for applied policy research'*Analyzing qualitative data.* Routledge, pp. 187-208.

Ritchie, J. and Spencer, L. (2002b) 'Qualitative data analysis for applied policy research', in 'Qualitative data analysis for applied policy research'*Analyzing qualitative data.* Routledge, pp. 187-208.

Robinson, V. *et al.* (2016) 'A qualitative exploration of people's experiences of pain neurophysiological education for chronic pain: the importance of relevance for the individual', *Manual Therapy,* 22, pp. 56-61.

Roland, M.*et al.* (2002) *The back book: The best way to deal with back pain.* TSO.

Rorty, R. (1982) *Consequences of pragmatism: Essays, 1972-1980.* U of Minnesota Press.

Rosenbaum, D.P. and Hanson, G.S. (1998) 'Assessing the effects of school-based drug education: A six-year multilevel analysis of project DARE', *Journal of Research in Crime and Delinquency,* 35(4), pp. 381-412.

Rowlands, M.J. (2010) *The new science of the mind: From extended mind to embodied phenomenology.* Mit Press.

Ryan, C.G. *et al.* (2010) 'Pain biology education and exercise classes compared to pain biology education alone for individuals with chronic low back pain: a pilot randomised controlled trial', *Manual Therapy,* 15(4), pp. 382-387.

Sandelowski, M., Docherty, S. and Emden, C. (1997) 'Qualitative metasynthesis: Issues and techniques', *Research in Nursing & Health,* 20(4), pp. 365-371.

Sandelowski, M., Voils, C.I. and Barroso, J. (2006) 'Defining and designing mixed research synthesis studies', *Research in the Schools: A Nationally Refereed Journal Sponsored by the Mid-South Educational Research Association and the University of Alabama,* 13(1), pp. 29.

Sandelowski, M. *et al.* (2012) 'Mapping the mixed methods–mixed research synthesis terrain', *Journal of Mixed Methods Research,* 6(4), pp. 317-331.

Sapolsky, R.M. (2004) *Why zebras don't get ulcers: The acclaimed guide to stress, stress-related diseases, and coping.* Holt paperbacks.

Saracoglu, I. *et al.* (2020) 'The short-term effects of neuroscience pain education on quality of life in patients with chronic low back pain: a single-blinded randomized controlled trial', *European Journal of Integrative Medicine,* 33, pp. 101046.

Schwandt, T.A. (2014) *The Sage dictionary of qualitative inquiry.* Sage publications.

Scottish Intercollegiate Guideline Network (2013) *SIGN 136: Management of chronic pain: A national clinical guideline.* Edinburgh: Scottish Intercollegiate Guideline Network.

Searle, A. *et al.* (2015) 'Exercise interventions for the treatment of chronic low back pain: a systematic review and meta-analysis of randomised controlled trials', *Clinical Rehabilitation,* 29(12), pp. 1155-1167.

Senn, S. (2005) 'Dichotomania: an obsessive compulsive disorder that is badly affecting the quality of analysis of pharmaceutical trials', ISI The Hague, The Netherlands.

Senn, S. (2016a) 'Mastering variation: variance components and personalised medicine', *Statistics in Medicine,* 35(7), pp. 966-977.

Senn, S. (2018) 'Statistical pitfalls of personalized medicine.', *Nature,* 563(7733), pp. 619–621.

Senn, S., Rolfe, K. and Julious, S.A. (2011) 'Investigating variability in patient response to treatment–a case study from a replicate cross-over study', *Statistical Methods in Medical Research,* 20(6), pp. 657-666.

Shannon-Baker, P. (2016) 'Making paradigms meaningful in mixed methods research', *Journal of Mixed Methods Research,* 10(4), pp. 319-334.

Sharma, S., Abbott, J.H. and Jensen, M.P. (2018) 'Why clinicians should consider the role of culture in chronic pain', *Brazilian Journal of Physical Therapy,* 22(5), pp. 345.

Simmonds, M.J. *et al.* (1998) 'Psychometric characteristics and clinical usefulness of physical performance tests in patients with low back pain', *Spine,* 23(22), pp. 2412-2421.

Smeets, R.J. *et al.* (2006) 'The usability of six physical performance tasks in a rehabilitation population with chronic low back pain', *Clinical Rehabilitation,* 20(11), pp. 989-997.

Smith, D.W. (2018) *The Stanford Encyclopedia of Philosophy.* Available at: https://plato.stanford.edu/archives/sum2018/entries/phenomenology.

Snapinn, S.M. and Jiang, Q. (2007) 'Responder analyses and the assessment of a clinically relevant treatment effect', *Trials,* 8(1), pp. 1-6.

Sniadou, S.V. (2013) 'Conceptual change in learning and instruction: The framework theory approach', in 'Conceptual change in learning and instruction: The framework theory approach'*International handbook of research on conceptual change.* Routledge, pp. 23-42.

Spear, B.B., Heath-Chiozzi, M. and Huff, J. (2001) 'Clinical application of pharmacogenetics', *Trends in Molecular Medicine,* 7(5), pp. 201-204.

Srivastava, A. and Thomson, S.B. (2009) 'Framework analysis: a qualitative methodology for applied policy research'.

Steffens, D. *et al.* (2014) 'Does magnetic resonance imaging predict future low back pain? A systematic review', *European Journal of Pain,* 18(6), pp. 755-765.

Stenberg, G., Fjellman-Wiklund, A. and Ahlgren, C. (2014) ''I am afraid to make the damage worse'–fear of engaging in physical activity among patients with neck or back pain–a gender perspective', *Scandinavian Journal of Caring Sciences,* 28(1), pp. 146-154.

Sterne, J., Egger, M. and Moher, D. (2011) 'Addressing reporting biases. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1. 0 (updated March 2011). The Cochrane Collaboration, 2011', *Available from Handbook.Cochrane.Org.*

Stewart, M. and Loftus, S. (2018) 'Sticks and stones: the impact of language in musculoskeletal rehabilitation', *Journal of Orthopaedic & Sports Physical Therapy,* 48(7), pp. 519-522.

Stilwell, P. and Harman, K. (2019) 'An enactive approach to pain: beyond the biopsychosocial model', *Phenomenology and the Cognitive Sciences,* 18(4), pp. 637-665.

Stofflett, R.T. and Stoddart, T. (1994) 'The ability to understand and use conceptual change pedagogy as a function of prior content learning experience', *Journal of Research in Science Teaching,* 31(1), pp. 31-51.

Stratford, P. *et al.* (1995) 'Assessing disability and change on individual patients: a report of a patient specific measure', *Physiotherapy Canada,* 47(4), pp. 258-263.

Sullivan, M.J., Bishop, S.R. and Pivik, J. (1995) 'The pain catastrophizing scale: development and validation.', *Psychological Assessment,* 7(4), pp. 524.

Sullivan, M.J. *et al.* (2001) 'Theoretical perspectives on the relation between catastrophizing and pain', *The Clinical Journal of Pain,* 17(1), pp. 52-64.

Suman, A. *et al.* (2021) 'A systematic review of the effectiveness of mass media campaigns for the management of low back pain', *Disability and Rehabilitation,* 43(24), pp. 3523-3551.

Swinton, P.A. *et al.* (2018) 'A statistical framework to interpret individual response to intervention: paving the way for personalized nutrition and exercise prescription', *Frontiers in Nutrition,* 5, pp. 41.

Szczepura, A. (2005) 'Access to health care for ethnic minority populations', *Postgraduate Medical Journal,* 81(953), pp. 141-147.

Tabor, A. *et al.* (2017) 'Pain: a statistical account', *PLoS Computational Biology,* 13(1), pp. e1005142.

Talisse, R.B. and Aikin, S.F. (2008) *Pragmatism: a guide for the perplexed.* A&C Black.

Tashakkori, A., Johnson, R.B. and Teddlie, C. (2020) *Foundations of mixed methods research: Integrating quantitative and qualitative approaches in the social and behavioral sciences.* Sage publications.

Teare, M.D. *et al.* (2014) 'Sample size requirements to estimate key design parameters from external pilot randomised controlled trials: a simulation study', *Trials,* 15(1), pp. 1-13.

Tegner, H. *et al.* (2018) 'Neurophysiological pain education for patients with chronic low back pain', *The Clinical Journal of Pain,* 34(8), pp. 778-786.

Téllez-García, M. *et al.* (2015) 'Neuroscience education in addition to trigger point dry needling for the management of patients with mechanical chronic low back pain: a preliminary clinical trial', *Journal of Bodywork and Movement Therapies,* 19(3), pp. 464-472.

Thacker, M. (2015) 'Louis Gifford–revolutionary: the Mature Organism Model, an embodied cognitive perspective of pain', *Psychother.Priv.Pract,* 152, pp. 4-9.

The British Pain Society (2013) *Guidelines for Pain Management Programmes for adults.*

The British Pain Society (2022) *Guidelines for Pain Management Programmes for adults.*

The Joanna Briggs Institute (2018) *Critical Appraisal Tools.* Adelaide: The Joanna Briggs Institute.

Tobin, G.A. and Begley, C.M. (2004) 'Methodological rigour within a qualitative framework', *Journal of Advanced Nursing,* 48(4), pp. 388-396.

Tong, A., Sainsbury, P. and Craig, J. (2007) 'Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups', *International Journal for Quality in Health Care,* 19(6), pp. 349-357.

Traeger, A.C. *et al.* (2019) 'Effect of intensive patient education vs placebo patient education on outcomes in patients with acute low back pain: a randomized clinical trial', *JAMA Neurology,* 76(2), pp. 161-169.

Travell, J.G. and Simons, D.G. (1992) *Myofascial pain and dysfunction: the trigger point manual.* Lippincott Williams & Wilkins.

Tüzün, E.H. (2007a) 'Quality of life in chronic musculoskeletal pain', *Best Practice & Research Clinical Rheumatology,* 21(3), pp. 567-579.

Tüzün, E.H. (2007b) 'Quality of life in chronic musculoskeletal pain', *Best Practice & Research Clinical Rheumatology,* 21(3), pp. 567-579.

Van Aert, R.C. and Jackson, D. (2019) 'A new justification of the Hartung-Knapp method for random-effects meta-analysis based on weighted least squares regression', *Research Synthesis Methods,* 10(4), pp. 515-527.

van Ittersum, M.W. *et al.* (2014) 'Written pain neuroscience education in fibromyalgia: a multicenter randomized controlled trial', *Pain Practice,* 14(8), pp. 689-700.

Van Oosterwijck, J. *et al.* (2013) 'Pain physiology education improves health status and endogenous pain inhibition in fibromyalgia: a double-blind randomized controlled trial', *The Clinical Journal of Pain,* 29(10), pp. 873-882.

Vlaeyen, J.W., Crombez, G. and Linton, S.J. (2016) 'The fear-avoidance model of pain', *Pain,* 157(8), pp. 1588-1589.

Vlaeyen, J.W. *et al.* (1995) 'The role of fear of movement/(re) injury in pain disability', *Journal of Occupational Rehabilitation,* 5(4), pp. 235-252.

Vlaeyen, J.W. and Linton, S.J. (2000) 'Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art', *Pain,* 85(3), pp. 317-332.

Von Bertouch, L., McAuley, J.H. and Moseley, G.L. (2011) 'Explaining pain before a multidisciplinary pain management programme improves long term pain and disability outcomes', *Proceedings of the Australian Pain Society 31st annual scientific meeting, Darwin, Australia.*

Von Helmholtz, H. (1867) *Handbuch der physiologischen Optik: mit 213 in den Text eingedruckten Holzschnitten und 11 Tafeln.* Voss.

Vosniadou, S. (2008) *International handbook of research on conceptual change.* Routledge New York.

Wall, P.D. (1979a) 'On the relation of injury to pain the John J. Bonica Lecture', *Pain,* 6(3), pp. 253-264.

Wall, P.D. (1979b) 'Three phases of evil: the relation of injury to pain', *Brain and Mind,* (69), pp. 293.

Wall, P.D. (2000) *Pain: The science of suffering.* Columbia University Press.

Wälti, P., Kool, J. and Luomajoki, H. (2015) 'Short-term effect on pain and function of neurophysiological education and sensorimotor retraining compared to usual physiotherapy in patients with chronic or recurrent non-specific low back pain, a pilot randomized controlled trial', *BMC Musculoskeletal Disorders,* 16(1), pp. 1-11.

Watson, J.A. *et al.* (2021) 'Inter-individual differences in the responses to pain neuroscience education in adults with chronic musculoskeletal pain: A systematic review and meta-analysis of randomized controlled trials', *The Journal of Pain,* 22(1), pp. 9-20.

Watson, J.A. *et al.* (2019) 'Pain neuroscience education for adults with chronic musculoskeletal pain: a mixed-methods systematic review and meta-analysis', *The Journal of Pain,* 20(10), pp. 1140. e1-1140. e22.

Webster, B.S. *et al.* (2013) 'Iatrogenic consequences of early magnetic resonance imaging in acute, work-related, disabling low back pain', *Spine,* 38(22), pp. 1939.

Wechsler, H. *et al.* (2003) 'Perception and reality: a national evaluation of social norms marketing interventions to reduce college students' heavy alcohol use.', *Journal of Studies on Alcohol,* 64(4), pp. 484-494.

Weingart, S.N. *et al.* (2011) 'Hospitalized patients' participation and its impact on quality of care and patient safety', 23(3), pp. 269-277.

Werner, E.L. *et al.* (2016) 'Cognitive patient education for low back pain in primary care: a cluster randomized controlled trial and cost-effectiveness analysis.', *Cognitive Patient Education for Low Back Pain in Primary Care: A Cluster Randomized Controlled Trial and Cost-Effectiveness Analysis,* 41(6), pp. 455-462.

Wijma, A.J. *et al.* (2018) 'What is important in transdisciplinary pain neuroscience education? A qualitative study', *Disability and Rehabilitation,* 40(18), pp. 2181-2191.

Williamson, P.J., Atkinson, G. and Batterham, A.M. (2017) 'Inter-individual responses of maximal oxygen uptake to exercise training: a critical review', *Sports Medicine,* 47(8), pp. 1501-1513.

Williamson, P.J., Atkinson, G. and Batterham, A.M. (2018) 'Inter-individual differences in weight change following exercise interventions: a systematic review and meta-analysis of randomized controlled trials', *Obesity Reviews,* 19(7), pp. 960-975.

Willis, A., Isaacs, T. and Khunti, K. (2021) 'Improving diversity in research and trial participation: the challenges of language', *The Lancet Public Health,* 6(7), pp. e445-e446.

Woby, S.R. *et al.* (2005) 'Psychometric properties of the TSK-11: a shortened version of the Tampa Scale for Kinesiophobia', *Pain,* 117(1-2), pp. 137-144.

Wolburg, J.M. (2006) 'College students' responses to antismoking messages: Denial, defiance, and other boomerang effects', *Journal of Consumer Affairs,* 40(2), pp. 294-323.

Wolfe, F. *et al.* (1990) 'The American College of Rheumatology 1990 criteria for the classification of fibromyalgia', *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology,* 33(2), pp. 160-172.

Wood, L. and Hendrick, P.A. (2019) 'A systematic review and meta-analysis of pain neuroscience education for chronic low back pain: Short-and long-term outcomes of pain and disability', *European Journal of Pain,* 23(2), pp. 234-249.

Yuille, A. and Kersten, D. (2006) 'Vision as Bayesian inference: analysis by synthesis?', *Trends in Cognitive Sciences,* 10(7), pp. 301-308.

Yun, J. (2017) *A comparison of pain neurophysiology education with therapeutic interventions versus therapeutic interventions alone on pain and function in individuals with chronic low back pain: a meta-analysis.*

Zimmer, Z. *et al.* (2021) 'A global study of pain prevalence across 52 countries: examining the role of country-level contextual factors', *Pain (Amsterdam),* Publish Ahead of Print doi: 10.1097/j.pain.0000000000002557.

Zimney, K., Louw, A. and Puentedura, E.J. (2014) 'Use of Therapeutic Neuroscience Education to address psychosocial factors associated with acute low back pain: a case report', *Physiotherapy Theory and Practice,* 30(3), pp. 202-209.