School of Physiotherapy and Exercise Science

An Investigation of People with Persistent Low Back Pain and High Pain-Related Fear

Joao Paulo Torres Caneiro

This thesis is presented for the Degree of
Doctor of Philosophy
of
Curtin University

June 2018

Author's Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

Human Ethics: The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007) – updated March 2014. The research study received ethics approval from the Curtin University Human Research Ethics Committee (EC00262), Approval Number #HR157/2015.

Joao Paulo Torres Caneiro

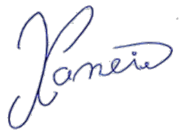
Date: 18th June 2018

Statement of Contributors

The candidate, Joao Paulo Caneiro, was responsible for all aspects of the research presented in this thesis, including study design, data collection, data analysis, interpretation, and reporting of results. The following supervision team also contributed to the research design and some aspects of analysis, interpretation and writing/editing:

- Professor Peter O'Sullivan (*Principal Supervisor*) [i]
- Professor Anne Smith (*Co-Supervisor*) [i]
- Professor Ottmar Lipp (*Co-Supervisor*) [ii]
- Professor Steven J. Linton (*Associate Supervisor*) [iii]
- Professor G. Lorimer Moseley (*Associate Supervisor*) [iv]

Further details of author contributions to each study are reported in the methods sections of the individual studies.



Date: 18th June 2018

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Abstract

Introduction

Persistent low back pain (LBP) that is associated with high pain-related fear is disabling. The personal impact is multi-factorial, affecting many aspects of people's lives. Various approaches have been proposed to manage this disorder, leading to a substantial increase in health care costs. However, disability related to persistent LBP continues to increase, with current interventions failing to make meaningful changes to individuals who live with this condition. Modern pain science proposes that pain is an implicit protective mechanism influenced by a complex interaction of multiple factors across the biopsychosocial spectrum. This multidimensional interplay varies between and within people over time, making pain a complex and individual experience. The fear avoidance model proposes that pain that is interpreted as a sign of threat is underpinned by negative pain-related cognitions and emotions driving protective behaviours, avoidance and disability. However, how these factors interplay in people with pain-related fear is not well understood. Furthermore, understanding how changes in these factors relate to reductions in disability over the course of an intervention may provide insight in the processes of change in people with persistent LBP and high pain-related fear.

Therefore, the aims of this doctoral thesis were: 1) To investigate implicit evaluations of danger and physiological responses to images of people bending and lifting with a flexed lumbar spine (round-back), in people with persistent LBP reporting different levels of self-reported fear of bending. 2) To determine the current state of evidence concerning the effectiveness (reduction in disability, pain and pain-related fear) of behavioural interventions intentionally designed for people with persistent LBP and high pain-related fear. 3) To evaluate temporal changes in pain-related fear (generic fear beliefs and specific fear of bending) and pain (pain expectancy and experience related to bending with a round-back) in a person with persistent LBP and high pain-related fear undergoing a Cognitive Functional Therapy intervention. In addition, to explore qualitative factors underlying the process of change using repeated clinical interviews. 4) (i) To evaluate temporal changes in outcome (disability) and factors that underlie treatment response (potential mediators from cognitive and emotional dimensions) during a Cognitive Functional Therapy intervention in four people with persistent LBP and high pain-related fear. (ii) To evaluate how changes in potential mediators related to changes in disability at different timepoints during the intervention.

Study 1

Methods: This study used an exploratory cross-sectional experimental design. *Sample*: A convenience sample of 44 people (54% female) with persistent LBP, who differed in self-reported fear of bending with a round-back. *Procedure:* Participants completed a picture-viewing paradigm with pleasant, neutral and unpleasant images, and images of people bending and lifting with a flexed lumbar spine ('round-back') to assess physiological responses (eye-blink startle modulation, skin conductance). They also completed an implicit association test (IAT) and an affective priming task (APT). Both assessed implicit associations between (i) images of people bending/lifting with a flexed lumbar spine posture ('round-back' posture) or bending/lifting with a straight lumbar spine posture ('straight-back' posture), and (ii) perceived threat (safe vs dangerous).

Results: All participants displayed an implicit association between words meaning 'danger' and images of bending and lifting with a round-back (IAT (0.5, CI [0.3; 0.6]; $p < 0.001$) and APT (24.2, CI [4.2; 44.3]; $p = 0.019$)). This implicit association was unrelated to self-reported fear of bending (IAT ($r = -0.24$, 95% CI [−0.5, 0.04], $p = 0.117$) and APT ($r = -0.00$, 95%CI [−0.3, 0.3], $p = 0.985$)). Furthermore, levels of self-reported fear of bending were not associated with eye-blink startle ($F(3, 114) = 0.7$, $p = 0.548$) or skin conductance responses ($F(3, 126) = 0.4$, $p = 0.780$) to pictures of bending/lifting.

Discussion: These results support that self-reported pain-related fear may be more cognitively driven; in which an unhelpful pain schema may influence avoidance behaviour, and a physiological fear response may only occur when the person is exposed to the task itself. This provides insight to the understanding of the relationship between pain and fear of movement.

Study 2

Methods: A prospectively registered (PROSPERO CRD42016037175) systematic review following the PRISMA statement was conducted. *Search*: two reviewers conducted the search in five electronic databases; articles published to February 2018. *Inclusion*: RCTs and SCEDs of interventions targeting adults (≥18 years) with persistent LBP (≥3 months) and high pain-related fear (TSK≥38/68, PASS-20≥68/100, or PCS≥24/52, either in

isolation or combined with a more specific measure of fear of movement - e.g. PHODA>50/100). *Selection*: two reviewers independently examined titles and abstracts using Covidence. *Outcomes*: disability, pain and fear (converted to 0-100 scale) at posttreatment (< 3months), short-term (3 to < 6 months) and medium-term (6 to 12 months). *Methodological quality*: the Cochrane Risk of Bias Tool and PEDro scale (RCTs); and Risk of Bias In N-of-1 Trials scale (SCEDs) were used to assess methodological quality of the studies. *Data analysis*: For RCTs, meta-analysis compared change in disability, pain and fear between groups. For SCEDs, narrative synthesis of outcomes was performed.

Results: This study included three RCTs (total n=167) and 7 SCEDs (total n=34, range 2 to 6 participants). All RCTs scored ‘moderate to high’ risk of bias; two studies were rated as ‘fair quality’ and one was rated as ‘high quality’. Meta-analysis was possible for posttreatment data only. RCTs provide ‘average quality’ evidence that exposure-based interventions are more effective than wait-list control for disability (MD= -8.8; CI [-17.47, -0.13]; p=0.05) and fear (MD= -8.48; CI [-13.16, -3.8]; p=0.0004), but the effects size is small and less than minimal clinically important change. There was no evidence for superiority of exposure-based over activity-based interventions for disability, pain or fear. All SCEDs had moderate risk of bias, and were rated as low to moderate quality. SCEDs provide evidence that exposure-based interventions are effective in reducing disability and fear, and low quality evidence of its superiority over activity-based interventions. Pain reduction was only reported in SCEDs, and only for half of the sample.

Discussion: Behavioural interventions for people with persistent LBP and high pain-related fear are moderately effective in reducing disability and fear, but only modestly effective on pain. Surprisingly, the widely held assumption that exposure-based interventions are the treatment of choice for this group is only very weakly supported by existing literature. Behavioural interventions for people with persistent LBP and high pain-related fear could be optimized by enhancing their capacity to target and affect change in pain.

Study 3

Methods: This study used a single-case report design with repeated measures over 18 months. This study evaluated temporal changes in pain-related fear, pain expectancy and

experience related to bending with a round-back. *Sample*: n=1; the participant was a retired manual worker with a twenty-five years' history of LBP and high pain-related fear. *Measures:* Self-report appraisals of bending in relation to fear, pain expectancy and experience during bending scored on a Numeric Rating Scale (NRS), Orebro Musculoskeletal Screening (OMPSQ), TAMPA Kinesiophobia Scale. Clinical interviews at 6, 12 and 18-month follow-ups were used to explore qualitative factors underlying this process of change. *Intervention:* An individualised exposure-based behavioural intervention (Cognitive Functional Therapy) to target key drivers of persistent LBP, and delivered over six sessions in a three-month period.

Results: The person experienced reduction in pain-related fear, pain expectancy and experience related to bending with a round-back; and substantial changes in pain-related fear (TSK: 47 to 33/68) and risk profile (OMPQ: 61 to 36/100). Clinical interviews revealed the key aspects that helped him achieve independence were: learning new behaviours that led to a new experience of control over pain, and a mindset change to a biopsychosocial understanding of LBP that made sense; this process was underpinned by a strong therapeutic alliance with the physiotherapist.

Discussion: Although the outcomes must be considered within the limitations of a single case report, this design enabled frequent and in-depth repeated assessment to elucidate elements of change over time. However, several other cognitive (e.g. self-efficacy) and emotional (e.g. distress) factors that could have mediated change were not evaluated.

Study 4

Methods: This study used a three-phases (A-B-A'/B') replicated single-case experimental design was employed to evaluate how changes in potential mediators related to changes in disability at different timepoints over the course of an intervention. *Phases*: A (8-week baseline), B (12-week intervention), and A' (12-week follow up with a criterion-based booster B'). *Sample*: n=4; adults (≥18 years old) with persistent LBP (≥6 months); pain intensity ≥4/10 on numerical rating scale (NRS); and high pain-related fear (≥40/68 TSK and ≥7/10 specific fear of bending and lifting with a flexed lumbar spine - pictorial NRS scale). *Measures*: Weekly assessment of outcome (disability) and proposed mediators (cognitive and emotional factors); and standardised outcome measures at single timepoints (pre-post). *Intervention*: Cognitive Functional Therapy delivered weekly over three months. *Assessment of treatment effect*: visual and statistical analysis (conservative dual-control, and non-overlap Tau-U). Ass*essment of temporal association between changes in disability and proposed mediators*: a series of cross-lag correlation analyses adjusted for autocorrelation using Simulation Modelling Analysis.

Results: Visual and statistical analysis indicated that all participants (n=4) undergoing Cognitive Functional Therapy demonstrated reductions in disability and proposed mediators. Cross-lag correlation analysis determined that, for all participants, changes in most of the proposed mediators (pain, pain controllability, and fear) were most strongly associated with changes in disability at lag zero, indicating that changes occurred concomitantly and not before changes in disability. Importantly, there was individual variability of the pattern and temporal process of change.

Discussion: This early temporal relationship between potential mediators and the outcome, with changes occurring immediately or soon after the first treatment session was an important and novel finding of this study. This study demonstrated how change unfolded uniquely for each individual, highlighting that the process of change is as individual as the experience of pain. These results lend support to a complex systems model of understanding the therapeutic change process in persistent LBP in people with high pain-related fear.

Conclusion

This doctoral thesis adds knowledge to the current understanding of the relationship between pain, fear and disability, providing a view that people with persistent LBP and pain-related fear may hold an unhelpful pain schema. This pain schema may be conceptualized as an unhelpful response to a threatening experience. This body of work has identified that current behavioural interventions have limited effectiveness for pain reduction, and that targeting pain control may provide an opportunity for optimization of exposure-based interventions for the treatment of people with persistent LBP and high pain-related fear.

The process of change is complex, individual and variable as is the experience of LBP. The results of this thesis indicate that pain-related cognitions, emotions and behaviours are part of a pain schema, and when this schema is disrupted it appears that all components change simultaneously; rather than in a linear sequential manner. These results support a complex systems framework for the understanding of clinical change. Although speculative, interventions may be more effective when targeting all aspects of the schema in an integrated manner, rather than its individual components. A *safety learning model* is proposed as a theoretical framework to understand the disruption to a person's pain schema.

Graphical abstract

AN INVESTIGATION OF PEOPLE WITH PERSISTENT LOW BACK PAIN & HIGH PAIN-RELATED FEAR

Author: **JP. Caneiro** | *Supervisor:* P. O'Sullivan | *Co-supervisors:* A. Smith; O. Lipp | *Assoc. supervisors:* SJ, Linton; GL. Moseley

AIMS of THESIS

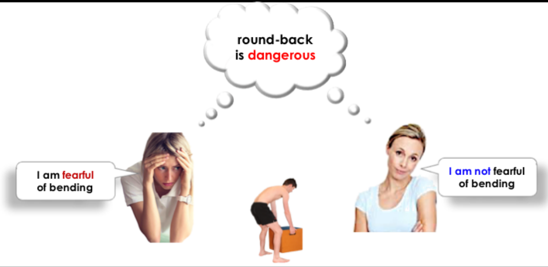
(i) To understand how people with persistent LBP and pain-related fear evaluate danger implicitly,

(ii) To determine the current state of evidence concerning the effectiveness of behavioural interventions in reducing disability, pain and fear in people with persistent LBP and high pain-related fear, and

(iii) To understand the process of change and the factors underlying treatment response in people with persistent LBP and high pain-related fear undergoing Cognitive Functional Therapy.

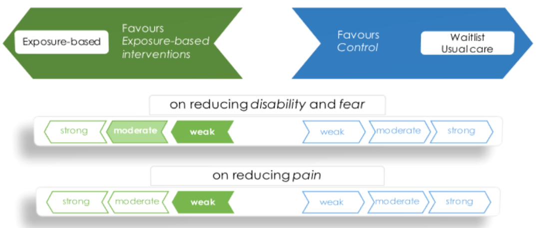
STUDY 1

- People with persistent LBP fear bending with a round-back even if they say they don't
- Viewing a threat was not sufficient to elicit a physiological defensive response
- Pain-related fear is not a phobia; rather it is an unhelpful pain schema developed in response to a threatening experience



STUDY 2

Effectiveness of exposure-based behavioural interventions

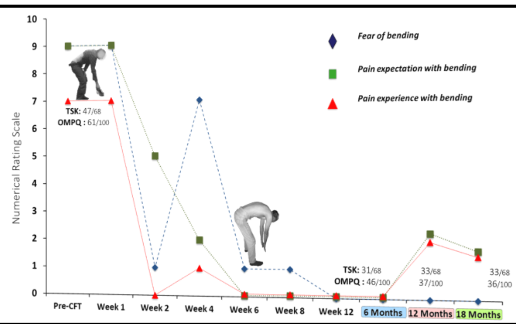


Superiority of exposure-based vs. activity-based behavioural interventions

Surprisingly, the widely-held assumption that exposure is the treatment of choice for people with persistent LBP and high pain-related fear is poorly supported.

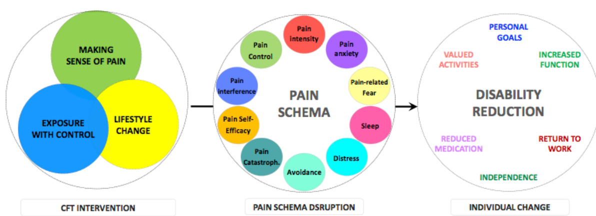
STUDY 3

- Evaluation of changes in pain-related fear and pain over 18months; including clinical interviews
- *New behaviour* linked to perceived pain control
- *Mindset change* related to de-threatening of radiology and behavioural learning
- *Therapeutic alliance* related to good communication
- Insight to factors related to change in pain-related fear



STUDY 4

- Single-case experimental design to evaluate the process change at an individual level
- Change is complex, multifactorial and individual
- Pain experience, pain control and fear changed concomitantly to disability, suggesting a pain schema disruption
- Safety learning is proposed as a change mechanism



CONCLUSIONS

(i) People with persistent LBP and pain-related fear may hold an unhelpful pain schema.

(ii) Pain-related cognitions, emotions and behaviours are part of a pain schema, and when this schema is disrupted it appears that all components change simultaneously; rather than in a linear sequential manner.

(iii) These results support a complex systems framework for the understanding of clinical change.

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This journey would have not been the same, if at all existent, without the enormous and humbling support from my wonderful wife **Raphaela**. Your love gives me strength!

Because of all this support, my PhD has been a magnificent experience. Thank you!

Dedication

This thesis was built upon many hours of work. Hours which were constantly supported by my family. To them, I dedicate this work.

My beautiful wife *Raphaela*, my soul mate, thank you for your unconditional love and support during this journey. I am greatly appreciative of all the sacrifices that you made! *Que Deus continue abençoando a nossa linda família. Te amo ainda mais do que ontem!*

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My mother *Nadia*, for inspiring me to dream beyond the limits of my perceived limitations, for guiding me towards the adventure of learning, and for helping me to understand my place in the world. Thank you for making my education possible, even when it seemed impossible to you!

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My second family, which I acquired through the love of my wife, *César & Angélica*. Your availability and ongoing support caring for our little Noah has been invaluable. Thank you for being there for us!

To those who live in pain, and whose journeys are challenging and fulfilled with suffering; may your stories be heard, your goals understood and your lives lived!

List of publications

Chapter 3

Caneiro JP, O'Sullivan P, Smith A, Moseley GL, Lipp OV. "Implicit evaluations and physiological threat responses in people with persistent low back pain and fear of bending" *Scandinavian Journal of Pain*. 2017 Oct; 17:355-366. DOI: 10.1016/j.sjpain.2017.09.012

Chapter 5

Caneiro JP, Smith A, Rabey M, Moseley GL, O'Sullivan P. "Process of Change in Pain-Related Fear: Clinical Insights from a Single Case Report of Persistent Back Pain Managed with Cognitive Functional Therapy" *Journal of Orthopaedic & Sports Physical Therapy*. 2017 Sep;47(9):637-651. DOI: 10.2519/jospt.2017.7371.

List of submissions

Chapter 4

Caneiro JP, Ng L, O'Sullivan P, Moseley GL, Bunzli S, Smith A. "Behavioural interventions for people with chronic low back pain and high pain-related fear: a systematic review of their effectiveness in reducing disability, pain and fear" – under review by the *Clinical Journal of Pain*.

Chapter 6

Caneiro JP, Smith A, Linton SJ, Moseley GL, O'Sullivan P. "How does change unfold? An evaluation of the process of change in four people with persistent low back pain and high pain-related fear managed with Cognitive Functional Therapy: a replicated single-case experimental design study" – under review by *Behaviour Research and Therapy*.

Appendix A

Caneiro JP, O'Sullivan P, Lipp OV, Mitchinson L, Oeveraas N, Bhalvani P, Abrugiato R, Thorkildsen S, Smith A. "Evaluation of implicit associations between back posture and safety of bending and lifting in people without pain" – ***accepted*** for publication by the *Scandinavian Journal of Pain*.

Appendix B

Caneiro JP, O'Sullivan P, Smith A, Ovrebekk I, Tozer L, Williams M, Teng ML, Lipp OV. "Physiotherapists have an implicit danger bias to bending and lifting with a round-back posture" – under review by *Musculoskeletal Science & Practice*.

List of presentations

Invited speaker

"The process of change in low back pain and pain-related fear". Western Australian Symposium of the Australian Physiotherapy Association 2018, 12th May, Perth WA, Australia.

"Fear-avoidance". Education seminar by the Australian Pain Society - Supporting Multidisciplinary Pain Management in Australia Vision. All people will have optimal access to pain prevention and management throughout their life, 2018, 7th June Perth WA, Australia.

"Cognitive Functional Therapy: what do we know about it?" Australian Physiotherapy Association Event, 2015 14th December Perth WA, Australia.

Oral presentations

Caneiro JP, O'Sullivan P, Smith A, Moseley GL, Lipp OV. "Bending and lifting with a round-back is perceived as dangerous! Implicit attitudes of people with back pain irrespective of fear". WCPT 2017, 4th July, Cape Town, South Africa

Caneiro JP, Smith A, Rabey M, Moseley GL, O'Sullivan P. "Cognitive Functional Therapy promotes change in highly fearful patient with persistent low back pain". APA 2015, 5th June, Sydney NSW, Australia.

Poster presentation

Caneiro JP, Smith A, Linton SJ, Moseley GL, O'Sullivan P. "How does change unfold? An evaluation of the process of change in four people with persistent low back pain and high pain-related fear managed with Cognitive Functional Therapy: a replicated single-case experimental design study" 2018 IASP, 15th September, Boston, USA

Caneiro JP, Ng L, O'Sullivan P, Moseley GL, Bunzli S, Smith A. "Behavioural interventions for people with chronic low back pain and high pain-related fear: a systematic review of their effectiveness in reducing disability, pain and fear" 2018 IASP, 15th September, Boston, USA

Caneiro JP, O'Sullivan P, Smith A, Ovrebekk I, Tozer L, Williams M, Teng ML, Lipp OV. "Physiotherapists have an implicit bias to bending and lifting with a round-back being perceived as dangerous". WCPT 2017, 4th July, Cape Town, South Africa

Caneiro JP, Smith A, Rabey M, Moseley GL, O'Sullivan P. "Process of change in pain-related fear. Clinical insights from a single-case of persistent back pain managed with Cognitive Functional Therapy". Exposure Therapies - CHAMP Orebro University, 2017 9th June, Orebro, Sweden.

Co-authored publications

O'Sullivan PB, **Caneiro JP**, O'Keeffe M, Smith A, Dankaerts W, Fersum K, O'Sullivan K. Cognitive Functional Therapy: An Integrated Behavioural Approach for the Targeted Management of Disabling Low Back Pain. Physical Therapy Journal. 2018 May 1;98(5):408-423. DOI: 10.1093/ptj/pzy022.

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Hainline B, Turner JA**, Caneiro JP**, Stewart M, Lorimer Moseley G. Pain in elite athletes-neurophysiological, biomechanical and psychosocial considerations: a narrative review British journal of sports medicine (2017) 51 17 1259 – 1264. DOI: 10.1136/bjsports-2017-097890.

Ng L, **Caneiro JP**, Campbell A, Smith A, Burnett A, O'Sullivan P." Cognitive functional approach to manage low back pain in male adolescent rowers: a randomised controlled trial. British journal of sports medicine (2015) 49 17 1125 – 1131. DOI: 10.1136/bjsports-2014-093984

Letters to the Editor

Palsson TS, **Caneiro JP**, Hirata RP, Griffin D, Gibson W, Travers MJ. Commentary: Trunk Muscle Activity during Drop Jump Performance in Adolescent Athletes with Back Pain. Frontiers in Physiology. 2018 Apr 16;9:298. DOI: 10.3389/fphys.2018.00298.

Caneiro JP, Smith A, O'Sullivan K, O'Keeffe M, Dankaerts W, Fersum K, Gibson W, Wand BM, O'Sullivan P. " RE: ""Low back pain misdiagnosis or missed diagnosis: Core principles"" (Monie AP, Fazey PJ, Singer KP. Manual Therapy 22 (2016) 68-71 Musculoskelet Science Practice (2017) 28 e1 - e2. DOI: 10.1016/j.math.2016.09.006

O'Sullivan P, **Caneiro JP**, O'Keeffe M, O'Sullivan K. Regarding the complexity of Low back Pain. Journal of Orthopaedic & Sports Physical Therapy (2017) 47 2 126 – 127. DOI: 10.2519/jospt.2017.0202

O'Sullivan P, **Caneiro JP**, O'Keeffe M, O'Sullivan K. Regarding Unravelling the complexity of Low back Pain. Journal of Orthopaedic & Sports Physical Therapy (2017) 47 3 219 – 220. DOI: 10.2519/jospt.2017.0202

Book Chapter

Caneiro JP, O'Sullivan P. Cognitive Functional Therapy: reabilitação do atleta com dor lombar PROFISIO Programa de Atualização em Fisioterapia Esportiva e Traumato-Ortopedica (2016) 2 5 39-90

Prizes, Awards & Appointments

Australian Physiotherapy Association WA branch Award of Excellence 2018 for Contribution as an *Emergent Researcher*.

Elsevier Prize 2018 for the Doctoral student publishing the best article in a Scientific Journal – Curtin University

Appointed as an *Associate Editor* for the British Journal of Sports Medicine, 2018

Appointed as an Associate Editor for Body In Mind science translation website, 2016

Professional engagement

Caneiro JP. Lower back pain within an Individual's context. In Touch – Musculoskeletal Physiotherapy Australia Association magazine, 2017 Issue 1.

Caneiro JP, Ng L, O'Sullivan P. "A person-centred approach to back pain in sport". Sports Medicine Australia magazine 2016, volume 34 Issue 1.

Ng L, **Caneiro JP,** O'Sullivan P. "Managing rowers with back pain" In Motion – Australian Physiotherapy Association magazine 2016 Issue 1.

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List of Abbreviations

ACT	Acceptance and Commitment Therapy
APT	Affective Priming Task
BDI	Beck Depression Inventory
BPI	Brief Pain Inventory
CBT	Cognitive Behaviour Therapy
CCBT	Contextual Cognitive Behavioural Therapy
CCD	Changing Criterion Design
CFT	Cognitive Functional Therapy
CLBP	Chronic Low Back Pain
CPAQ	Chronic Pain Acceptance Questionnaire;
CSM	Common Sense Model
CSQ	Coping Strategies Questionnaire
DBT	Dialectical behaviour therapy
FAM	Fear-avoidance model
GA	Graded Activity
GEXP	Graded Exposure in vivo
HADS	Hospital Anxiety Depression Scale
IAT	Implicit Association Test
MAAS	Mindful Attention Awareness Scale
MBD	Multiple Baseline Design
MCIC	Minimal Clinically Important Change
MDC	Minimal Detectable Change
MPI	Multidimensional Pain Inventory
MPQ	McGill Pain Questionnaire
OMPQ	Orebro Musculoskeletal Questionnaire
PAIRS	Pain and Impairment Relationship Scale
PCL	Pain Cognition List
PCS	Pain Catastrophizing Scale
PDI	Pain Disability Index
PHODA	Photograph Series of Daily Activities
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSEQ	Pain Self-Efficacy
PVAQ	Pain vigilance and Awareness Questionnaire
QBPDS	Quebec Back Pain Disability Scale
RCT	Randomized Controlled Trial
RMDQ	Roland Morris Disability Questionnaire
SCED	Single Case Experimental Design
SCR	Skin Conductance Response
SF-MPQ	Short Form McGill Pain Questionnaire
SMD	Standardised Mean Difference
TAU	Treatment As Usual
TSK	Tampa Scale of Kinesiophobia
VAS	Pain intensity
WLC	Waitlist Control

Chapter 1 Introduction of Thesis

"*Fear of pain is more disabling than pain itself*"
(p.2821, Waddell 1996)

Pain is an individual experience that is dependent on an implicit evaluation of threat to the person's body (Tabor et al. 2016; Wallwork et al. 2016; Moseley and Butler 2016). This evaluation considers the interaction of multiple interrelated systems that maintain a person's health homeostasis (Lotze and Moseley 2015; Brodal 2017). Fundamentally, perceptions of threat to the body and/or to one's ability to pursue their values and goals urge protective responses such as pain and avoidance to restore homeostasis (Vlaeyen 2015). These protective responses are effective, precise and may be helpful in the context of acute tissue damage and pathology (e.g. fracture; disc prolapse with neural compromise). However, when protection persists beyond healing time or in the absence of tissue damage, this response is no longer precise or helpful and it is thought to influence the persistence of pain, affecting a person's daily functioning (Vlaeyen, Crombez, and Linton 2016; Vlaeyen, Morley, and Crombez 2016; O'Sullivan et al. 2016; Moseley and Vlaeyen 2015). Accordingly, modern pain science understands persistent low back pain (LBP) as a protective response that is unhelpful and sensitive to any perceived signs of threat, which often represent a 'false alarm' of an overprotected system (O'Sullivan et al. 2016; Moseley and Butler 2016).

Over the last 25 years, LBP became the number one cause of disability worldwide (Hartvigsen et al. 2018). Persistent disabling LBP has a significant impact at a personal and public health level with the costs associated with this condition being greater than cancer and diabetes combined (Abajobir et al. 2017; Hoy et al. 2014). A lack of understanding of the cause of LBP, the perceived adverse consequences of having LBP, and the inability to control pain or to get better despite following the advice ('rules') received from various health care practitioners, can result in an experience that is unpredictable and frightening (Bunzli, Smith, Schutze, et al. 2015). Not surprisingly, people with persistent LBP describe the experience as having their 'lives on hold' (Bunzli, McEvoy, et al. 2013). Among those with persistent LBP, people with associated high levels of pain-related fear are greatly affected (Bunzli et al 2015), commonly reporting greater levels of disability (Zale et al. 2013; Crombez et al. 1999), pain severity (Kroska 2016; Sullivan et al. 2009), work absenteeism (Martel, Thibault, and Sullivan 2010; Braden et al. 2008), and less physical (Sullivan et al. 2009) and social (Thibault et al. 2008) participation than people with persistent LBP and lower levels of pain-related fear. This, highlights the inherent complexity, as well as the social and health economic burden attributed to this challenging group of patients.

The fear-avoidance model (FAM) describes how pain that is interpreted as threatening, leads to a process whereby negative pain-related cognitions and emotions drive a vicious cycle of protective behaviours, avoidance and disability. Conversely, it proposes that when pain related tasks are gradually confronted without fear this leads to recovery (Vlaeyen and Linton 2000). Grounded on this model and based on traditional behavioural interventions (Fordyce 1976), exposure-based interventions emerged in the field of pain to manage people with pain-related fear (Vlaeyen et al. 2001). Although initial investigations of exposure for the management of people with persistent LBP and pain-related fear were promising (Boersma et al. 2004; de Jong et al. 2005; Vlaeyen, De Jong, Onghena, et al. 2002; Vlaeyen et al. 2001; Vlaeyen, de Jong, Geilen, et al. 2002), later randomized controlled trials failed to reproduce the results of the original studies (Leeuw et al. 2008; Woods and Asmundson 2008; Linton et al. 2008). However, because fear reduction is the key principle underlying exposure, there is a widely held notion that exposure-based interventions are the 'gold standard' for the treatment of pain-related fear. Remarkably, not many studies have targeted people specifically with *high* pain-related fear.

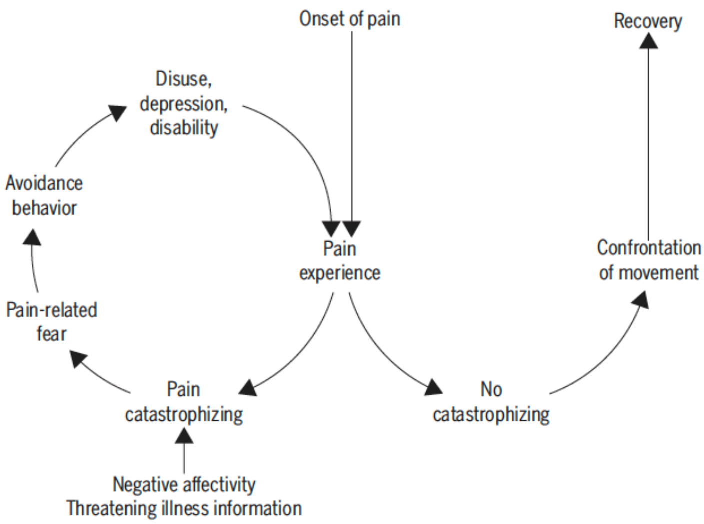

Figure 1.1 The fear-avoidance model (Vlaeyen & Linton 2000)

Although pain-related fear is one of the strongest modifiable predictors of disability in people with LBP (Zale and Ditre 2015; Wertli, Rasmussen-Barr, Weiser, et al. 2014), the process by which pain-related fear is modified to reduce disability is unclear. Attempts to validate the sequential interaction between pain-related cognitive and emotional factors proposed by the fear-avoidance model have not supported the linear nature assumed by this model (Pedler et al.

2018; Wideman et al. 2013; Bergbom, Boersma, and Linton 2012; Wideman, Adams, and Sullivan 2009). Furthermore, how these factors unravel in the treatment process remains poorly understood. Recently, prospective qualitative data investigating pathways of change in people with persistent LBP and high pain-related fear suggests that the process of recovery may vary between people, and that a key component of this process related to the perception of gaining control over pain (Bunzli et al. 2016). However, this and how change unravels over the course of treatment has not been quantitatively evaluated in people with persistent LBP and high pain-related fear.

Understanding how changes in cognitive and emotional factors relate to reduction in disability over the course of an intervention may provide insight in understanding processes of change in people with persistent LBP and high pain-related fear. This may have clinical implications by identifying what factors need targeting and when they should be targeted in the treatment process. Furthermore, this knowledge may inform future intervention trials and potentially indicate possible avenues to optimize existing behavioural interventions.

In consideration of the challenges posed to the current understanding and management of people with persistent LBP and *high* pain-related fear, the body of work presented in this doctoral thesis aims to better understand how individuals with persistent disabling LBP and high pain-related fear evaluate danger at an implicit level; how effective behavioural interventions are for this group; and how the process of change unfolds at an individual level.

1.1 Structure of thesis

This thesis is comprised of seven chapters and two appendices.

Chapter 1 provides an introductory overview of the problem that is persistent disabling low back pain (persistent LBP), its relationship with pain-related fear and current gaps in the understanding and management of people with persistent LBP and high pain-related fear.

Chapter 2 provides a review of the scientific literature regarding the impact of persistent LBP and pain-related fear, how to manage it and how to evaluate it at an individual level. The chapter concludes by summarizing the gaps in the literature.

Chapter 3 describes a cross-sectional experimental study investigating implicit evaluations and physiological responses to threat in people with persistent LBP with a range of self-reported fear levels. This study was published in the *Scandinavian Journal of Pain*, and it will be presented in its published format.

Chapter 4 reports a systematic review of the literature on the effectiveness of behavioural interventions to promote reduction in disability, pain and fear, in people with persistent LBP and high pain-related fear. This study was submitted to the *Clinical Journal of Pain*, and it will be presented in its submitted format.

Chapter 5 presents a single case report with repeated measures (self-report and clinical interviews) over 18 months to gain insight to the process of change in pain-related fear. This study was published in the *Journal of Orthopaedic & Sports Physical Therapy*, and it will be presented in its published format.

Chapter 6 describes a replicated single-case series to evaluate the process of change in people with persistent LBP and high pain-related fear. This study was submitted to the *Behaviour Research & Therapy Journal*, and it will be presented in its submitted format.

Chapter 7 presents the discussion of the main findings of this thesis. A *safety learning* model is proposed to understand the process of disruption of a person's pain schema. The chapter concludes by describing the strengths and limitations of this body of work, future research directions and the concluding remarks of this thesis.

The appendices present two parallel studies that aimed to answer questions that emerged from the experimental study in Chapter 3.

Appendix A reports a cross-sectional experimental study that evaluated implicit associations between back posture and safety of bending and lifting in people without pain. Furthermore, this study also analysed the participant's qualitative descriptions of the safest lifting posture. This study has been *accepted* for publication by the *Scandinavian Journal of Pain*, and it will be presented in its submitted format.

Appendix B reports a cross-sectional experimental study that evaluated implicit associations between images of bending and lifting with a round-back and words representing danger, in physiotherapists that manage musculoskeletal conditions. This study was submitted to the *Musculoskeletal Science & Practice Journal*, and it will be presented in its submitted format.

Chapter 2 Literature review

The aim of this chapter is to review the scientific literature regarding: (i) the burden of persistent disabling LBP (ii) how pain-related fear relates to persistent disabling LBP, (iii) how pain-related fear is assessed clinically and experimentally, (iv) the current management of people with persistent LBP and pain-related fear, (v) the role of an individualised multidimensional intervention for persistent LBP that can be utilised for people with high pain-related fear, and (vi) what factors underlie treatment response of current approaches. Finally, it will discuss how changes over time at an individual level are best evaluated.

2.1 SECTION 1: Low Back Pain

2.1.1 The global burden of low back pain

Low back pain (LBP) remains one of the most prevalent and costly health problems and has been estimated to affect 632 million people worldwide (Maher, Underwood, and Buchbinder 2016; Buchbinder et al. 2013). According to the Global Burden of Disease Project, LBP has the highest global impact in terms of years lived with disability in both developed and developing countries (Abajobir et al. 2017; Hoy et al. 2014; Vos, Flaxman, et al. 2012). While most people with LBP pain improve rapidly, for many it becomes a persistent (often termed 'chronic', with pain lasting > 3months) and highly disabling condition (Kongsted et al. 2016), with studies reporting that 42% to 75% of people do not recover from an episode within a year (Itz et al. 2013; Scheele et al. 2013) . Those people reporting more painful or disabling LBP episodes comorbid with poor general health are more likely to seek care. The resultant societal costs of persistent disabling LBP (persistent LBP) are enormous, exceeding that of cancer and diabetes combined (Hartvigsen et al. 2018; Hoy et al. 2014).

The personal impact of persistent LBP is multi-factorial, and it extends beyond function, pervading many aspects of people's lives (Froud et al. 2014). It has been reported that people with persistent LBP describe this impact as having their "lives on hold," whereby they don't understand their pain problem, have few or none active strategies to manage it, and eventually lose their ability to do the things in life that they value (Bunzli, McEvoy, et al. 2013). This disengagement is commonly associated with escalating fear, distress, disability, and depression (O'Sullivan et al. 2016; Vlaeyen, Crombez, and Linton 2016; Bunzli, Watkins, et al. 2013).
Various approaches to manage persistent LBP have been proposed, leading to a substantial increase in health care costs (Gore et al. 2012; Deyo et al. 2009). However, disability related to persistent LBP continues to increase (Buchbinder et al. 2018; Hartvigsen et al. 2018; Foster et al. 2018; Maher, Underwood, and Buchbinder 2016; Deyo et al. 2009), with current interventions often failing to make meaningful changes to individuals who live with this condition (Foster et al. 2018; O'Sullivan et al. 2016).

2.1.2 The complex, multidimensional, individual nature of persistent LBP

Modern pain science supports persistent LBP as an emergent protective response produced by the interaction of neuro (Wand et al. 2011; Gatchel et al. 2007), immune (Grace et al. 2014; Marchand, Perretti, and McMahon 2005), endocrine (Generaal et al. 2016; Vachon-Presseau et al. 2013; Gatchel et al. 2007), and motor (van Dieen et al. 2018; Karos et al. 2017; van Dieen, Flor, and Hodges 2017; Hodges and Smeets 2015) systems, in response to the person's actual or perceived threat to their body, lifestyle and/or social context that may disrupt their homeostasis (Moseley and Butler 2016; Tabor et al. 2016; O'Sullivan et al. 2016). Fundamentally, the multiple and interrelated influences of all factors and systems (neuro, immune, endocrine) that can modulate a person's pain experience is here defined as a complex system (Brown 2009) – the *person's system*.

A *person's system* is modulated by a varying interplay of multidimensional factors including, physical (i.e. loading exposure and demands as well as levels of conditioning) (van Dieen, Flor, and Hodges 2017; Dankaerts et al. 2009; O'Sullivan 2005), psychological (i.e. cognitions and emotions) (Vlaeyen, Crombez, and Linton 2016; Pinheiro et al. 2016; Zale et al. 2013), psychophysiological (i.e. sympathetic arousal; HPA axis regulation) (Klyne et al. 2018; Elsenbruch and Wolf 2015; Glombiewski et al. 2015), sensory (i.e. bodily sensations, tissue sensitivity) (Rabey, Beales, et al. 2015; Rabey, Slater, et al. 2015; O'Sullivan et al. 2014) , social (i.e. socioeconomic, cultural, work, home environment, and stress) (Hestbaek et al. 2008; Hoogendoorn et al. 2000) , lifestyle (i.e. sleep, activity levels) (Kelly et al. 2011; Shiri et al. 2010b; Bjorck-van Dijken, Fjellman-Wiklund, and Hildingsson 2008), comorbid health (i.e. mental health, obesity) (Pinheiro et al. 2016; Shiri et al. 2010a) and non-modifiable factors (i.e. genetics, sex, life stage, culture) (Bartley and Fillingim 2013; Battie, Videman, and Parent 2004).

These multiple and interrelated interactions change over time and context (Bunzli et al. 2017; Wiech 2016), influencing tissue sensitivity and pain perception through inflammatory processes, neuro-immune-endocrine changes, altered body awareness, distress and overprotective behavioural responses to pain that shape a person's pain experience (George and Bishop 2018; Rabey et al. 2017b; Moseley and Butler 2016; Tabor et al. 2016; Elsenbruch and Wolf 2015; Marchand, Perretti, and McMahon 2005; Gatchel et al. 2007). Therefore, persistent LBP can be understood as an emergent response of a *person's system* in which the dynamic interplay and the relative contribution from each factor is variable, interrelated, and fluctuates temporally, making persistent LBP a unique experience to each individual (Brodal 2017; O'Sullivan et al. 2016; Brown 2009) - **Figure 2.1**.

Accordingly, people may present different sensitivity profiles (Fillingim 2017; Rabey, Beales, et al. 2015; Rabey et al. 2016). For instance, an individual may present with pain that is localized and consistently provoked and relieved with specific postures, movements or functional tasks (proportionate mechanical stimulus-pain response). This pain presentation may be considered to have features of primarily peripherally-mediated nociceptive processes (Hodges and Smeets 2015; O'Sullivan 2005), and/or associations between movement-related threat perceptions and nociceptive processing at a cortical level (Moseley and Vlaeyen 2015). In contrast, another person may present disproportionate mechanical stimulus-pain response patterns. This pain sensitivity profile is characterized by pain that is more widespread, and may be associated with pain sensitivity to pressure, cold, movement and loading, likely reflecting primarily central nervous system amplification of nociceptive inputs (Rabey et al. 2016; Rabey, Beales, et al. 2015; O'Sullivan et al. 2014). For others, pain may be spontaneous and/or not clearly reproducible with clinical examination, potentially indicating that central pain mechanisms likely dominate (Backryd et al. 2018; Rabey et al. 2016). Considering the large variability and multiple interactions within a person's system , not all patients will present with a clear pain presentation, in fact many will present with a mixed pattern of pain mechanisms (Backryd et al. 2018; Fillingim 2017; Rabey, Beales, et al. 2015).

Understanding the complex multidimensional interactions associated with a person's persistent LBP presentation may provide an opportunity for individualized management (O'Sullivan et al 2018).

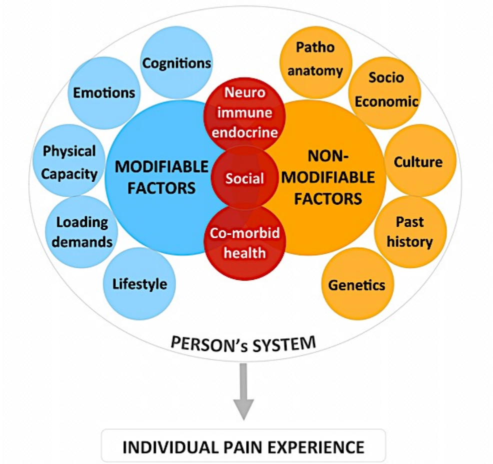

Figure 2.1 Illustration of a person's pain experience emerging from the complex, multidimensional interaction of factors.

Note: Some factors such as socio-economic and patho-anatomy may be non-modifiable (e.g. disability retirement; spondylolisthesis) or modifiable (e.g. sick leave; modic changes, disc prolapse) depending on the individual's context and clinical presentation.

2.2 SECTION 2: Pain-related fear

2.2.1 What is pain-related fear, and how it relates to persistent LBP?

Fear is the anticipatory emotional response to a specific and imminent threat (Rachman 1998). Fear may protect the person from danger because it activates defensive behaviours associated with the fight or flight response (LeDoux 2014; Vlaeyen et al. 2012; Cannon 1929). *Pain* is currently conceptualized as a sign of potential bodily threat that may require protection (Tabor et al. 2016; Wallwork et al. 2016; Moseley and Butler 2016). When the threat is coming from within the body such as in the case of LBP, people may fear the causes and consequences they assume to be associated with their pain (Kroska 2016; Bunzli, Smith, Watkins, et al. 2015). Patients may report fear of 'interoceptive stimuli' (e.g. sensations such as feeling 'unstable', feeling a 'crack', or feeling a 'sharp' or 'hot' pain), 'proprioceptive stimuli' (e.g. pain-provoking activities, movements), and 'exteroceptive stimuli' (e.g. threatening information about their body and consequences of pain received from health care encounters, imaging scans, media, family and friends). These stimuli may be interpreted as a sign of damage (e.g. "I will damage my disc") or further suffering and further functional loss (e.g. fear to become unable to play with kids, work, become wheelchair-bounded) (Bunzli, Smith, Watkins, et al. 2015). Thus, *pain-related fear* is not an unitary construct (Bunzli, Smith, Watkins, et al. 2015), and can be defined as a cognitive and emotional response to an evaluation that the body is in danger and needs protecting (Vlaeyen, Crombez, and Linton 2016). Accordingly, avoidance (e.g. not performing a movement and/or activity) and/or protective behaviour (e.g. bracing while performing a movement) is a common sense protective response to reduce or prevent unwanted pain experiences (Kroska 2016). This protective response may be adaptive (helpful) in the context of acute tissue damage and pathology (e.g. fracture). However, when protection persists beyond the normal healing times or in the absence of pathology, this response is considered mal-adaptive (unhelpful) and impacts on the person's daily functioning, limiting positive experiences and further sustaining pain and disability (Vlaeyen, Crombez, and Linton 2016; Bunzli, Smith, Schutze, et al. 2015).

Pain-related fear mediates the pathway to disability in persistent LBP (Lee et al. 2015). High levels of pain-related fear have been identified as a predictor of increased disability levels and poorer outcomes in people with persistent LBP (George and Beneciuk 2015; Wertli, Rasmussen-Barr, Weiser, et al. 2014; Zale et al. 2013). Favourably, pain-related fear is one of the strongest modifiable predictors of disability in people with LBP (Zale and Ditre 2015; Bunzli, Smith, Schutze, et al. 2015), suggesting that reduction of pain-related fear may influence the reduction of disability (Wertli, Rasmussen-Barr, Weiser, et al. 2014; Wideman, Adams, and Sullivan 2009).

2.2.2 The fear-avoidance model

The prevailing model that explains the pathway to disability associated with persistent LBP is the fear-avoidance model (FAM) (Vlaeyen and Linton 2012; Crombez et al. 2012; Vlaeyen and Linton 2000). The concept underpinning the fear-avoidance model was first described by Lethem et al (1983)(Lethem et al. 1983) and Slade et al (1983)(Slade et al. 1983), and later further developed by Vlaeyen & Linton (2000) (Vlaeyen and Linton 2000), who introduced it as a model to describe the cascade of events that can occur when pain is perceived as threatening. According to the fear-avoidance model, the meaning assigned to pain influences the person's experience and response to pain; for instance, when pain is appraised as a threat, the person perceives a lack of control over pain and its possible (catastrophic) consequences (Vlaeyen and Linton 2012; Crombez et al. 2012; Vlaeyen and Linton 2000). This unpredictability of pain creates an expectation that future actions will cause pain, resulting in fear and avoidance of activities that do or might provoke pain and/or damage (Vlaeyen, Crombez, and Linton 2016; Moseley and Vlaeyen 2015; Crombez et al. 2012). The fear-avoidance model presented in **Figure 1.1** illustrates how disability, distress and physical disuse develop as a result of learning avoidance behaviours (protective and safety-seeking behaviours) elicited by pain that is perceived as threatening (Vlaeyen, Crombez, and Linton 2016; Vlaeyen and Linton 2012; Vlaeyen and Linton 2000).

2.2.2.1 Fear acquisition through a learning perspective

Fear acquisition has been well documented in the literature through associative learning (Pearce and Hall 1980), which occurs when a neutral stimulus (conditioned stimulus) is paired with an aversive one (unconditioned stimulus), resulting in the conditioned stimulus acquiring motivational properties and eliciting responses similar to the unconditioned stimulus. Specifically, acquisition of movement-related fear has been demonstrated by Meulders et al (2011) using a differential conditioning paradigm. Their results suggest that fear of movement and avoidance behaviour can be acquired as a direct experience through an associative learning process (Meulders, Vansteenwegen, and Vlaeyen 2011). Using the same paradigm, the authors found that similar responses were elicited by the mere intention to perform a painful movement, preceding the actual performance of the movement (Meulders and Vlaeyen 2013). Recently, it was demonstrated that fear of touch can be acquired through associative learning, eliciting self-reported and physiological fear responses (indexed by skin conductance and eye-blink startle) when the context is unpredictable (Biggs et al. 2017). Pain-related fear can also be acquired by learning via observation, as well as verbal threatening information (Goubert et al. 2011; Helsen et al. 2011; den Hollander et al. 2010). Olsson and Phelps (2004) directly compared three different fear learning formats, whereby the conditioned stimuli were paired with a painful shock (direct experience), with observed fear expression in another person (observational learning) or with verbal instructions (learning by verbal threat information) (Olsson and Phelps 2004). Fear responses to the conditioned stimuli were of comparable magnitude across the three learning formats (Olsson and Phelps 2004). Recently, Karos et al (2015) demonstrated that pain-related fear acquisition can be facilitated when learning occurs in a threatening social context (Karos, Meulders, and Vlaeyen 2015).

In Western society, there is a pervasive view that the lower back is easy to damage and hard to heal (Darlow et al. 2015). It has been suggested that disability in people with persistent LBP partly relates to negative and threatening information received during healthcare encounters (Darlow et al. 2013; Lin et al. 2013). Threatening information gathered from healthcare practitioners and social environments may facilitate verbal learning (Darlow 2016; Meier et al. 2016). When the information provided has an unhelpful connotation (i.e. "you have poor back stability") it can lead to a negative interpretation (i.e. "my back can be easily damaged"), resulting in hypervigilance (i.e. searching for bodily signs of danger), catastrophising (i.e. "I will never be able to lift my child again") and consequent fear and avoidance of activities that are perceived as dangerous (i.e. "it is dangerous to move my back"). Studies have shown that a large proportion of people with LBP believe that a wrong movement could lead to serious negative consequences to their back (Hodges and Smeets 2015). The belief that there is something seriously wrong increases the expectancy of pain, the perception of pain and pain-related fear, shaping people's behaviour (Karos et al. 2017; Biggs et al. 2017; Bunzli, Smith, Schutze, et al. 2015; Roussel et al. 2013; Boersma and Linton 2006). This behaviour is associated with avoidance, excessive muscle guarding and altered movement (Karos et al. 2017; Laird et al. 2014; Karayannis et al. 2013; Geisser et al. 2004), and often considered mal-adaptive (unhelpful) (Dankaerts et al. 2009; O'Sullivan 2005). It has been postulated that unhelpful protective motor control responses to perceived threat can abnormally load sensitised spinal tissues leading to increased pain and persistence (van Dieen et al. 2018; van Dieen, Flor, and Hodges 2017; Dankaerts et al. 2009;O'Sullivan 2005). This might be modulated by central pain processes (George and Bishop 2018; Karos et al. 2017; Gay et al. 2015). Importantly, these unhelpful behaviours are modifiable and may offer an opportunity for targeted management (O'Sullivan et al. 2018; Kent, Laird, and Haines 2015; Caneiro et al. 2013; van Hooff et al. 2011).

2.2.2.2 Fear generalization

When people in pain exhibit fear not only of an identifiable stimulus or threat, but also of activities that are seen to be closely linked to the original stimulus, it is considered that fear generalization has occurred to other situations, which are now recognised as being potential threats (Meulders et al. 2017; Vancleef et al. 2007; Lissek et al. 2010). The inability to distinguish what is safe from what is dangerous has been proposed as a core mechanism in the spreading of protective responses that lead to disability (Meulders et al. 2018). The extent of generalization is inversely related to the precision by which the brain encodes the original painful events (Moseley and Vlaeyen 2015). Therefore, the less precise the encoding, the more generalization occurs, meaning that pain is triggered by more functionally dissimilar stimuli. An example of imprecise encoding of the original painful trigger is where bending and lifting was associated with a LBP episode, that now results in generalization of pain-related fear and LBP to similar (e.g. vacuuming, putting on shoes) and dissimilar (e.g. walking, washing dishes) movements and activities (Moseley and Vlaeyen 2015). This generalization and subsequent avoidance response reduces the opportunities to challenge and disconfirm a person's feared expectations, reinforcing the behaviour and perpetuating disability (Vlaeyen, Crombez, and Linton 2016; Vlaeyen 2016; Bunzli, Smith, Schutze, et al. 2015). This sustained perceived lack of safety may play a role in the maintenance of pain-related fear (Meulders et al. 2018; Vlaeyen, Morley, and Crombez 2016; Elsenbruch and Wolf 2015).

2.2.2.3 Challenges to the fear-avoidance model

While the fear-avoidance model has broad support in the LBP literature, some aspects of the model have been questioned. Originally, the fear-avoidance model was conceptually based on psychopathology (e.g. phobia) models, which describes the person's fear response as an abnormal reaction (e.g. irrational) to a normal situation. Recent research however, suggests that pain-related fear beliefs are normative and culturally endorsed (Darlow et al. 2015; Darlow 2016; Crombez et al. 2012). Therefore, chronic pain is an abnormal situation to which patients are responding normally, in a culturally endorsed manner (Bunzli et al. 2017; Bunzli, Smith, Schutze, et al. 2015; Crombez et al. 2012).

The original fear-avoidance model was grounded on the notion that patients with persistent pain endorse beliefs that pain equals harm, underpinning the threat value of pain. However, recent qualitative work has challenged that notion, demonstrating that people with persistent LBP and pain-related fear present varied beliefs, indicating motivational heterogeneity for avoidance (Bunzli, Smith, Schutze, et al. 2015; Bunzli, Smith, Watkins, et al.

2015). Crombez et al (2012) proposed that fear avoidance behaviour may persist because of repetitive goal failure (Crombez et al. 2012). Indeed, repeated attempts to control pain and the impact of pain on daily goals was reported by people 'stuck' in a cycle of pain and fear (Bunzli et al. 2017; Bunzli, Smith, Schutze, et al. 2015;). Therefore, it was suggested that the fear-avoidance model included a motivational perspective in which the patient's values and goals are considered (Bunzli et al. 2017; Crombez et al. 2012; Vlaeyen, Crombez, and Linton 2009). This may have implications for exposure-based interventions, which by targeting the belief that pain is a sign of damage (Vlaeyen et al. 2012) have been successful at reducing pain-related fear in some, but have failed to help others (Crombez et al. 2012; Leeuw et al. 2008; Woods and Asmundson 2008; Linton et al. 2008). Considering that avoidance may be learned through association between movement and pain and used as a strategy to reduce pain (Gay et al. 2015), it is plausible that for these patients who use avoidance to minimize suffering, strategies that provide pain control before and/or during exposure may be helpful (O'Sullivan et al. 2018; Bunzli et al. 2017), however this warrants testing.

Another challenge was proposed by Wideman et al (2013), who suggested that the cyclical nature of the fear-avoidance model fails to capture the complex interplay of multidimensional factors and their variability over time (Wideman et al. 2013; Wideman, Adams, and Sullivan 2009). It is argued that a broader range of processes (e.g. social, cultural and environmental) influence disability in a dynamic and context-specific manner, leading to individual responses to pain; of which avoidance of movement is only one of them (Wideman et al. 2013). In line with that, Bunzli et al (2017) suggested that the process of 'making sense of pain' is dynamic and informed by the interaction of cognitive, emotional, somatic, behavioural and contextual factors that influence a person's behaviour (Bunzli et al. 2017). Collectively, the above-mentioned remarks challenge the role of fear (i.e. characterised as a phobia) and its relationship with pain in the fear-avoidance model, and might have implications for promoting change and evaluating the process of change in people with pain-related fear.

2.2.3 The common-sense model

The common-sense model of self-regulation (CSM) was described by Leventhal (1980) as a framework to explore the perceptual, behavioural, cognitive and emotional processes involved in a person's understanding and management of their health (Leventhal, Meyer, and Nerenz 1980). The common-sense model accommodates the complexity of persistent pain as it describes a dynamic multilevel process that constitutes a person's representation of their problem, their actions and responses (Leventhal, Phillips, and Burns 2016).

Broadly, a person's representation is comprised by five dimensions: identity (What is this pain?), cause (What caused this pain?), consequences (What are the consequences of having this pain?), time-line (For how long will this pain last?) and cure/controllability (Can this pain be cured or controlled?) (Leventhal, Meyer, and Nerenz 1980). How a person represents their pain problem will influence how they respond to it from a behavioural and emotional perspective (Leventhal, Meyer, and Nerenz 1980; Bunzli et al. 2017). The action taken will be directed by the person's goal. For instance, if a person's goal is to prevent back pain when lifting, and they believe that flexing their spine will cause pain, the person will avoid flexion while lifting. If the outcome is coherent with their representation (i.e. avoiding flexion prevents pain), then their behaviour will be maintained. In contrast, if the outcome is incoherent with their representation (i.e. avoiding flexion does not prevent pain), then their representation will be updated and the response (behavioural and emotional) likely adjusted (Bunzli et al. 2017; Leventhal, Meyer, and Nerenz 1980) - **Figure 2.2**.

Although the application of the common-sense model is well-established in the study of chronic diseases (Broadbent et al. 2006; Moss-Morris et al. 2002), and non-musculoskeletal chronic pain (Donovan et al. 2007), it still in its infancy in the field of LBP (Chen et al. 2017; van Wilgen, van Ittersum, and Kaptein 2013; Siemonsma et al. 2013; O'Hagan, Coutu, and Baril 2013). Bunzli et al (2016) conducted a prospective qualitative study in individuals with persistent LBP and high pain-related fear and identified that a common narrative in this group was of an attempt to make sense of a threatening pain experience that individuals perceived as uncontrollable (Bunzli 2016). Thus, Bunzli et al (2017) proposed the utility of the common-sense model as a framework to assist physiotherapists in the understanding and management of patients with pain-related fear (Bunzli et al. 2017). Within this framework, pain-related fear may be understood as a 'common-sense' response based on a threatening LBP representation, and the lack of a coherent representation may lead to perpetuation of a fearful experience (Bunzli et al. 2017). Participants from the prospective study who reported reduction in fear described that developing control over their pain experience helped them to aquire a new conceptualization of their pain, leading to positive emotional and behavioural reposes (Bunzli et al. 2016).

It was proposed that exposure-based behavioural interventions might be optimised by including strategies that facilitate patients to make sense of their persistent LBP based on a contemporary biopsychosocial perspective, and that enhance pain control while engaging in valued activities (Bunzli et al. 2017).

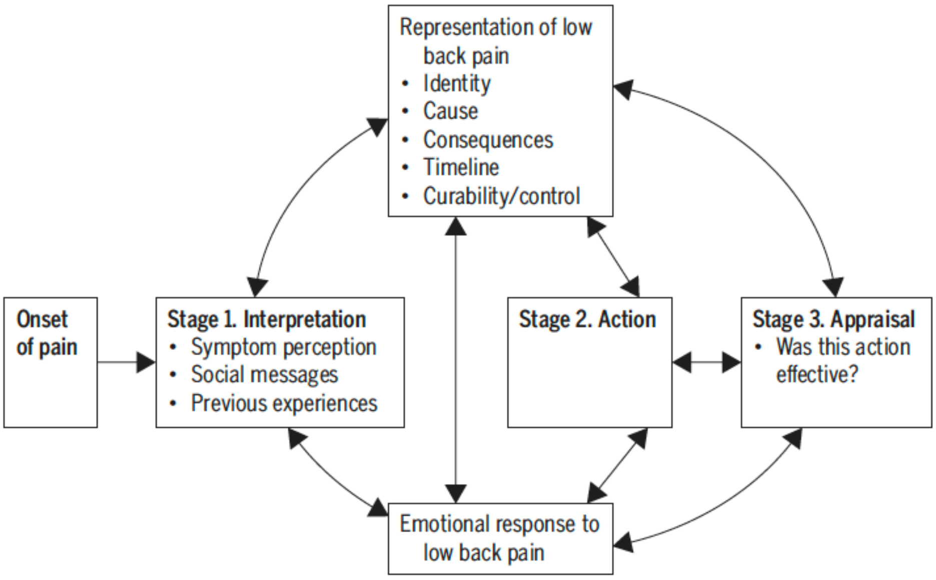

Figure 2.2 The common-sense model (Leventhal, Meyer, and Nerenz 1980) adapted to LBP (Bunzli et al. 2017).

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2.2.4 Fear related to bending and lifting with a round-back

Bending and lifting are the most commonly identified triggers for the onset of LBP (Steffens et al. 2016; Stevens et al. 2016; Coenen et al. 2013; Verbeek et al. 2012). These activities are commonly reported as pain provoking and are feared by people with and without LBP, holding a high threat-value in western society (Munigangaiah et al. 2016; Stevens et al. 2016; Darlow, Perry, Mathieson, et al. 2014; Pagare et al. 2015; Briggs et al. 2010; Gross et al. 2006).

Bending and lifting, especially with a round-back posture (i.e. lumbar spine flexion) is commonly believed to cause undue load to spinal structures, having been described as “pathogenic for the lower back” (Plouvier et al. 2008). This belief partly stems from interpreting the results of *in vivo* (Nachemson 1965, 1975) and *in vitro* studies, which have used direct measures to investigate the effect of load on the spine (Koblauch 2015; Gallagher and Marras 2012; Callaghan and McGill 2001; Adams and Hutton 1982). Broadly, these studies suggest that repetitive spinal flexion can lead to structural damage (e.g. disc injury), and based on these findings extrapolations have been made that adopting straight-back postures such as the squat lifting technique protects the spine from undue loads, minimizing the risk of injury (Gallagher and Marras 2012; Callaghan and McGill 2001; Nachemson 1965, 1975).

These studies have formed the basis for current ergonomic training, which commonly teaches cautious lifting techniques, whereby individuals are advised to keep the back straight and bend their knees (Nolan et al. 2018; Verbeek et al. 2012). Nonetheless, ergonomic interventions teaching people how to bend and lift, with the aim to reduce the risk of LBP, have lacked empirical support (Van Hoof et al. 2018; Driessen et al. 2010). Treatments directed at postural modification and motor control training for attainment of a “neutral spine” have been tested several times yielding disappointing results (Saragiotto et al. 2016). Specifically, core stability exercises designed to protect the spine are not more effective than any other form of exercise in the treatment or prevention of LBP (Smith, Littlewood, and May 2014). The lack of effectiveness of various interventions to target bending and lifting as a risk factor, questions the interventions themselves as well as the exact role of physical loading of the spine with regard to LBP risk during lifting (Coenen et al. 2014; Gallagher et al. 2005).

Results from recent *in vivo* studies further question the assumption that the back is in danger when lifting with a round posture (Dreischarf, Rohlmann, et al. 2016; Kingma, Faber, and van Dieen 2010). Specifically, beliefs related to the increased risk of LBP associated with lifting with a round-back (vs. straight-back) have not been supported by biomechanical *in vivo* measurements (Dreischarf, Rohlmann, et al. 2016; Kingma, Faber, and van Dieen 2010; Marras et al. 2001; Marras et al. 2004; Lariviere, Gagnon, and Loisel 2000) and several systematic reviews (Ribeiro et al. 2012; Kwon et al. 2011; Roffey et al. 2010; Wai et al. 2010a, 2010b). Furthermore, no difference in spinal loads between round-back and straight-back lifting techniques has been identified in pain-free people (Straker and Duncan 2000; Straker 2002; Straker 2003; Hagen and Harms-Ringdahl 1994). Interestingly, adopting a round-back posture while bending and lifting has been shown to be more efficient than adopting a straight-back posture (Holder 2013; Hagen and Harms-Ringdahl 1994). Considering the lack of *in vivo* evidence that bending and lifting with a round-back posture is dangerous or that straight-back is safe, it makes sense that teaching people how to lift cautiously has not been effective in preventing LBP (Martimo et al. 2008; Hignett 2003; Maher 2000; Bos et al. 2006). Nolan et al

(2017) suggested that educating patients with LBP to protect their backs by keeping a straight-back when lifting may be unhelpful, and it might reinforce the belief that the spine is vulnerable (Nolan et al. 2018).

As discussed earlier in this chapter, beliefs about the vulnerability of the spine appear to be in part informed by healthcare practitioners (Lin et al. 2013; Darlow et al. 2013; Darlow et al. 2012). Healthcare practitioners self-report a common belief that the cause of LBP is attributed to structural or biomechanical factors, such as 'improper' posture while bending and lifting (Stevens et al. 2016; Nijs et al. 2013; Darlow et al. 2012). Importantly, fear-avoidant beliefs of healthcare practitioners can strongly influence the beliefs of their patients (Lakke et al. 2015; Darlow et al. 2013). Threatening advice to patients suggesting vulnerability of the spinal structures (e.g. 'you have a slipped disc because of your lifting posture'), or providing an explanation that does not make sense to the patient can create fear and uncertainty, which can lead to, or reinforce avoidance and/or protective behaviours (Lakke et al. 2015; Darlow et al. 2013; Darlow et al. 2012; Bishop et al. 2008; Vlaeyen and Linton 2006). There is compelling evidence that people with persistent LBP present excessive muscle guarding, lack flexion-relaxation during bending, have reduced range of movement and move slowly (van Dieen, Flor, and Hodges 2017; Laird et al. 2014; Geisser et al. 2004; McGorry and Lin 2012). These altered behavioural responses to bending and lifting are likely to be influenced by levels of pain-related fear (Hodges and Smeets 2015; McGorry and Lin 2012; Sullivan et al. 2009; Geisser et al. 2004).

Regrettably, the message that bending and lifting is dangerous and straight-back posture is important to protect the back has been widely-disseminated in society (Munigangaiah et al. 2016; Stevens et al. 2016; Darlow, Perry, Mathieson, et al. 2014; Pagare et al. 2015; Briggs et al. 2010; Gross et al. 2006). Not surprisingly, people with LBP commonly avoid bending and lifting and report high expectation of pain and harm prior to performing these tasks (Trost, France, and Thomas 2008; Crombez et al. 2002). Nonetheless, the underlying motive for avoiding these tasks vary between people (Bunzli, Smith, Schutze, et al. 2015).

Together this body of work supports that fear related to bending and lifting with a round-back may be a common sense response to a task widely perceived in society as threatening to the back (Bunzli et al. 2017). This is likely to be an important consideration for the treatment of people with persistent LBP and high pain-related fear as understanding beliefs underlying fear may play a role in promoting behavioural change.

2.2.5 What is known about people with persistent LBP and high pain-related fear?

Over half of those presenting with persistent LBP in primary care show high levels of pain-related fear (Sieben et al. 2002). High levels of pain-related fear have been associated with avoidance of physical activities (Kroska 2016; Linton and Shaw 2011). Avoidance behaviour leads to an inability or unwillingness to pursue valued activities, a reduction of positive experiences, affective distress and eventually, social isolation (van Vliet et al. 2018; Crombez et al. 2012; Vlaeyen and Linton 2012; Vlaeyen, Crombez, and Linton 2016). People with persistent LBP and higher levels of pain-related fear commonly report greater pain intensity (Kroska 2016; Sullivan et al. 2009), greater pain duration (Jensen et al. 2009), greater disability (Zale et al. 2013; Crombez et al. 1999), less physical (Sullivan et al. 2009) and social participation (Thibault et al. 2008), prolonged work disability (Martel, Thibault, and Sullivan 2010), and more work absenteeism and unemployment (Martel, Thibault, and Sullivan 2010; Braden et al. 2008) than people with persistent LBP and lower levels of pain-related fear. This highlights the social and health economic burden attributed to this challenging group of patients.

Although avoidance behaviour is common amongst people with high pain-related fear, not all avoidance behaviour is driven by the same motive. A recent qualitative study revealed that not all participants with persistent LBP and high pain-related fear believe that movement is harmful. Some avoid physical activity because they believe it may cause more pain, suffering and/or functional loss, using avoidance as a strategy to control the intensity and functional impact of pain (Bunzli, Smith, Schutze, et al. 2015). Negative LBP beliefs and pain-related fear are more predictive of disability than pain intensity levels (Briggs et al. 2010). Negative beliefs influence a person's perception about certain physical activities. This is demonstrated in experimental studies which reported that people with persistent LBP and high pain-related fear attributed higher threat value to pictures of common daily activities (e.g. bending, lifting) than healthy controls (Leeuw, Peters, et al. 2007; Kronshage, Kroener-Herwig, and Pfingsten 2001). In preparation to performing a reaching task, people with persistent LBP and high pain-related fear reported higher levels of pain and harm expectancies, than people with persistent LBP and low pain-related fear (Trost, France, and Thomas 2009). Furthermore, in anticipation to the performance of a task deemed harmful, and which they were led to believe they had to perform, participants with persistent LBP and high pain-related fear presented increased sympathetic response (indexed by increased skin conductance levels and heart rate) (Glombiewski et al. 2015).

It is suggested that complex interactions exist between pain-related fear and pain sensitivity profiles that may explain individual differences in behaviour (Gay et al. 2015). Pain-related fear beliefs are thought to influence sensory input, with negative beliefs being associated with the development of an exaggerated pain perception (Vlaeyen and Linton 2000). An experimental movement model showed that pain-related fear mediated differences in perceived pain intensity in anticipation to and during hand movement (Meulders and Vlaeyen 2012). There is however, little research in sensory changes in people with persistent LBP, specifically when comparing people with high and low pain-related fear (Hubscher et al. 2013). Prolonged stress and fear have been associated with impaired endogenous pain modulation system (Elsenbruch and Wolf 2015; Neugebauer et al. 2009), which might be potentially related to changes to the hypothalamic-pituitary-adrenal axis function (Campbell and Edwards 2009). This may facilitate sensitization and pain response during the performance of threatening tasks. For instance, Sullivan et al (2009) demonstrated that people with persistent LBP and high levels of fear of movement had greater summation of pain in a repeated lifting task (Sullivan et al. 2009). Rabey et al (2016) showed that people with high psychological distress had lower pain pressure threshold and greater summation of pain with repeated movement, than people with lower psychological distress (Rabey et al. 2016). People who are sensitized may also learn associations between movement and pain (Meulders and Vlaeyen 2012; Moseley and Vlaeyen 2015; Zusman 2008), which could influence their behavioural response towards avoidance as a form of pain control. The results of these studies suggest possible neurophysiological mechanisms (peripheral and central), which can influence individual behavioural responses in people with persistent LBP (Nijs et al. 2017; Sullivan et al. 2009; Wand et al. 2011).

It has been recently demonstrated that fear of pain changes motor behaviour (Karos et al. 2017). People with persistent LBP exhibit different movement patterns (van Dieen et al. 2018; O'Sullivan 2005) and demonstrate increased trunk muscle co-activation and an inability to relax the back muscles (Dankaerts et al. 2009; Geisser et al. 2004). Higher levels of back muscle electromyography correlate with a range of psychosocial factors, such as pain-related anxiety, catastrophizing and pain self-efficacy (Lewis et al. 2012). Specifically, people with persistent LBP reporting high pain-related fear exhibit higher levels of trunk stiffness (Karayannis et al. 2013), reduced lumbar flexion range of motion, greater back muscle activity and reduced flexion-relaxation response (Geisser et al. 2004). In an arm lifting paradigm, back pain patients with catastrophic interpretations of pain and injury, did not restore normal back muscle activity even after the experimental pain stimulus was withdrawn (Moseley and Hodges 2006).

Together these studies provide insight to the complexity (Main et al. 2012) and heterogeneity of the drivers of pain-related fear response in this group of people (Bunzli, Smith, Schutze, et al. 2015), highlighting the importance of developing assessments and interventions that are tailored to the individual's needs.

2.2.6 Pain-related fear assessment

Given the role of cognitions and appraisals in persistence of LBP, the assessment of people's beliefs and emotional attitudes towards activities perceived as threatening or dangerous to the body (e.g. bending and lifting) is relevant. Beliefs and attitudes can be assessed via explicit and implicit measures.

2.2.6.1 Explicit measures

Studies assessing beliefs of people with and without pain typically employed explicit measures (e.g. self-reported questionnaires) (Bunzli, Smith, Schutze, et al. 2015; Leeuw, Goossens, et al. 2007). Several questionnaires have been used to assess slightly different constructs of the fear-avoidance model in people with persistent LBP, including: fear of movement/re-injury, pain-related fear beliefs, pain-related anxiety and pain catastrophizing (George et al. 2009).

The **Tampa Scale of Kinesiophobia-TSK** (Kori, Miller, and Todd 1990) is widely-used to assess *fear of movement/re-injury* (Bunzli, Smith, Watkins, et al. 2015). Scores range from 17 to 68, with higher scores indicating higher levels of fear of movement, and a cut-off of 40 typically used to define a high degree of pain-related fear (Vlaeyen et al. 2012). A change of 8 points is suggested as a minimal clinically important change (MCIC) (Lundberg et al. 2011). Despite its wide use, there have been questions as to what construct(s) the TSK actually measures (Lundberg et al. 2011). Therefore, Bunzli et al (2015) performed a mixed methods study aimed to identify the beliefs that underlie high scores on the TSK to better understand what construct(s) the TSK measures (Bunzli, Smith, Watkins, et al. 2015). The study described how individuals scoring highly on the TSK (≥ 40/68) interpret the persistent LBP experience and its consequences in qualitative one-on-one interviews. Results from that study identified 2 distinct beliefs: (1) The belief that painful activity will result in damage to their spine ('damage beliefs'); and (2) The belief that painful activity will increase suffering and/or functional loss ('suffering and/or functional loss'); with some people presenting mixed beliefs. Bunzli et al (2015) proposes that rather than a measure of "fear of movement/(re)injury," the TSK is better described as a measure of *pain-related fear beliefs*. Specifically, a measure of the "*beliefs that painful activity will result in damage and/or increased suffering and/or functional loss*" (Bunzli, Smith, Watkins, et al. 2015). It was argued that this possibly relates to the differential discriminatory ability of the subscales (Bunzli, Smith, Watkins, et al. 2015). While the somatic focus subscale was able to discriminate the two belief groups, participants of both belief groups would endorse similar items because of ambiguous wording of the activity avoidance subscale. Meaning that items containing the word 'injure', could be interpreted as synonymous of 'damage' by the damage beliefs group, whereas the suffering/functional loss belief group could interpret the word 'injure' as synonymous of 'pain increase' (Bunzli, Smith, Watkins, et al. 2015).

Pain-related anxiety can be assessed with the **Pain Anxiety Symptoms Scale-PASS-20** (McCracken and Dhingra 2002). The PASS-20 is used to assess cognitive anxiety symptoms, escape and avoidance responses, fearful appraisals of pain and physiological anxiety symptoms associated with pain. The participant makes a frequency rating for each item (where 0 = never and 5 = always). The PASS-20 has acceptable psychometric properties (McCracken and Dhingra 2002). Scores range from zero to 100, with higher scores indicating higher levels of pain-anxiety

The **Pain Catastrophizing Scale – PCS** (Sullivan, Bishop, and Pivik 1995) is used to assess *catastrophic thinking*. The PCS consists of 13 statements that are rated on 0 to 4 Likert scales to indicate the degree of a person's thoughts or feelings about a painful experience. This scale has a three-factor structure providing scores on subscales of rumination, magnification and helplessness. The PCS has good psychometric properties, with scores ranging from zero to 52, and scores over 20 are typically used as a cut-off to define a high degree of catastrophizing (Sullivan, Bishop, and Pivik 1995). A change of 9 points considered as the minimal detectable change (MDC) (George, Valencia, and Beneciuk 2010).

A limitation of these questionnaires is that they do not provide information about which specific movements and activities the patient fears or avoids. For that purpose, sets of photographs were designed, each showing a person performing a specific movement or activity of daily living (Leeuw, Goossens, et al. 2007). The **Photographs of Daily Activities** tool (PHODA) is a valid and reliable measure of the *perceived harmfulness of activities* in people with persistent LBP (Leeuw, Goossens, et al. 2007). Interestingly, the PHODA does not ask directly about fear. Rather, it assesses perceived harmfulness as an indication of the belief that an activity may cause harm or damage. However, based on the recent findings of Bunzli et al (2015) some people with high pain-related fear may believe that physical activity may not cause damage, but rather an increase in pain and incapacity to do the things they love (Bunzli, Smith, Watkins, et al. 2015). This may be a limiting factor of this measure.

An adapted version of the PHODA is the **Fear of Daily Activities Questionnaire** (FDAQ) (George et al. 2009). The FDAQ outlines 10 activities commonly reported as feared by people with LBP (e.g. reaching to the floor, lifting 20 pounds or more). It also asks the participant to nominate two additional activities that they fear that are not listed. The person rates each item using an 11-item NRS scale (where 0 = no fear and 10 = maximal fear). This questionnaire is practical for clinicians as it less time consuming than the PHODA. The FDAQ has adequate internal consistency (Cronbach alpha=.91), adequate 48-hour test-retest properties (intraclass correlation coefficient= .90). A change of 12.9 points is considered the MDC (George et al. 2009).

2.2.6.2 Implicit measures

Current assessment of perceived danger to the body relies solely on explicit, or self-report, measures (Leeuw, Goossens, et al. 2007; McCracken and Dhingra 2002; Kori, Miller, and Todd 1990). Self-reported measures, however maybe susceptible to self-presentational strategies. That is, people may be motivated to control their response to enhance social desirability (Gawronski and Bodenhausen 2006; Greenwald and Banaji 1995). Research in the field of social psychology has shown that people might either be reluctant to report their evaluations, or the evaluations may reside outside conscious awareness or control (Buhlmann, Teachman, and Kathmann 2011; Greenwald and Banaji 1995). Therefore, self-reported measures may assess beliefs that are deliberately formed upon reflection and that require a certain amount of conscious reflection and introspection (Fazio and Olson 2003; Vlaeyen et al. 2001).

In order to overcome such limitations, implicit measures have been suggested as an additional tool (Goubert et al. 2003). Implicit measures assess beliefs based on ‘automatic’ associations in memory (e.g. bending posture and danger). These associations can be assessed via computer-based reaction-time tasks, which are designed to reduce the person’s ability to control their response, minimizing effects of social desirability (Gawronski and Bodenhausen 2006; Greenwald, McGhee, and Schwartz 1998). The implicit association test (IAT) (Greenwald, McGhee, and Schwartz 1998) and the affective priming task (Fazio & Olson 2003) are frequently used paradigms to measure implicit associations (Grumm et al. 2008; Goubert et al. 2003). The Implicit

Association Test (IAT) measures differential associations of two target categories by comparing reaction times of two different combined classification tasks [Greenwald, McGhee, and Schwartz 1998]. The Implicit Association Test (IAT), is a well-validated and extensively used measure, which requires the person to associate words or images as quickly and as accurately as possible [Harvard 2011; Greenwald, Nosek, and Banaji 2003;]. The speed with which the person performs the task reflects the strength of the associations, and can indicate the degree of implicit bias [Nosek, Hawkins, and Frazier 2011]. In an Affective Priming Task (APT) a series of positive or negative target stimuli (words) is presented, which have to be evaluated by the participant as quickly as possible as either "positive" or "negative". Each target is preceded by a prime stimulus (picture), which can be positive or negative, and which has to be ignored by the participant. The time to evaluate the target stimuli is moderated by the valence of the primes [Fazio et al. 1986].

Previous explorations that investigated people with and without persistent LBP and high fear of movement have not found evidence of implicit association between a wide range of back-related movements and danger for the back [Leeuw, Peters, et al. 2007; Goubert et al. 2003]. Goubert et al (2003) investigated people with persistent LBP and high fear of movement in comparison to pain-free people [Goubert et al. 2003]. The authors found that only the pain-free group displayed an implicit bias towards a range of back-stressing movement pictures (e.g. driving, hanging a coat, carrying, digging, jumping, running) and negative words (e.g. war, AIDS). Leeuw et al (2007) also assessed people with and without persistent LBP, and did not find an implicit association between words representing back-stressing movements (e.g. falling, bending, pushing, lifting, running) and threat-related words (e.g. fatal, warning, terrible, dangerous, horrible) in either group [Leeuw, Peters, et al. 2007]. A key element of pain-related fear assessment is to identify the specific activity the person is fearful of. Thus, an aspect which may have played a role in the results of these studies was the use of a wide range of stimuli. In other words, the use of several words and images that are not representative of a specific and personal threat may have been a limiting factor in these studies.

Most studies investigating both explicit and implicit measures report no, or only moderate relationships between these measures [Fazio and Olson 2003; Greenwald, McGhee, and Schwartz 1998]. This is not surprising when considered in light of the limitations described above. A meta-analysis of correlations between explicit measures and the IAT across 126 studies in the field of social psychology suggested that the association between these measures is influenced by the conceptual correspondence of the constructs being assessed [Hofmann et al.

2005). Therefore, implicit measures are suggested to be conceived as valuable additional tools and not as a replacement to explicit measures (Leeuw, Peters, et al. 2007; De Houwer and Beckers 2002).

2.2.6.3 Physiological threat-response

Fear is an aversive emotional state elicited by threatening cues that activate a person's defence system. In people with specific phobias (e.g. spider phobia) this defence system seems to be over reactive, as it is easily activated even by symbolic representations of their feared objects (e.g. picture of a spider) (Wendt et al. 2008). This phobic defensive response can be detected by physiological measures such as the eye-blink startle reflex and skin conductance, which are used to assess physiological responses to threatening stimuli in a picture-viewing paradigm (Bradley and Lang 2007).

The eye blink startle reflex is an involuntary protective response originating in the brainstem following presentation of a sudden and intense stimulus (Carleton et al. 2006). It consists of the activation of the orbicularis oculi muscle surrounding the eye in response to a startling stimulus (e.g. sudden noise burst via headphones) (Ceunen et al. 2014; Lang, Bradley, and Cuthbert 1990). This response is modulated by the affective valence the person attributes to the picture stimulus, that is, the response is potentiated by a negative emotional state or inhibited by a positive emotional state relative to a neutral state (Lang, Davis, and Ohman 2000; Lang, Bradley, and Cuthbert 1999). Affective modulation of the eye-blink startle reflex is a well-established physiological measure of emotion (Bradley and Lang 2007; Lang, Davis, and Ohman 2000; Lang, Bradley, and Cuthbert 1999). While the eye-blink startle indicates whether a stimulus is pleasant or unpleasant, skin conductance levels reflect emotional arousal independent of stimulus valence (Lang, Bradley, and Cuthbert 1990). Autonomic arousal, can be measured by skin conductance levels and heart rate changes in the presence of threatening stimulus (Glombiewski et al. 2015). When presented with highly fearful stimuli, individuals prepare for action by arousal of the autonomic nervous system, displaying enhanced skin conductance responses (SCR) and heart rate acceleration (Vos, De Cock, et al. 2012; Bradley and Lang 2007). Only two studies have used these methodologies to investigate physiological threat-responses in people with persistent LBP (Glombiewski et al. 2015; Kronshage, Kroener-Herwig, and Pfingsten 2001). These studies reported conflicting results.

Kronshage et al (2001) questioned the conceptualization of fear of movement as a phobia. They hypothesised that if participants with persistent LBP are in fact phobic of certain movements, they would show an enhancement of the startle response when confronted with pictures of back-stressing movements (e.g. bending, rotation) in comparison to pleasant movement pictures (e.g. lying in supine) (Kronshage, Kroener-Herwig, and Pfingsten 2001). Furthermore, this effect would be larger in participants scoring high on a fear-avoidance beliefs questionnaire. However, participants with persistent LBP and high or low fear beliefs did not show the predicted startle potentiation while viewing pictures of back-stressing movements. The fear beliefs questionnaire used to classify participants as high or low fear was not specific to a task relevant to the person. The questionnaire includes statements such as "Physical activity makes my pain worse" and "Physical activity might harm my back", but it does not specify what type of physical activity. Possibly, selecting the sample a priori based on a specific task to which people have different fear perceptions, with some being fearful and others reporting no fear of the task might yield different results.

In contrast, Glombiewski et al (2015) investigated whether participants with persistent LBP and high and low pain-related fear showed distinct physiological reaction patterns when led to believe they actually had to perform a back-stressing movement (Glombiewski et al. 2015). Two response patterns were identified: 1) attention reaction (non-phobic response) characterized by moderate increase in skin conductance and muscle reactivity, and decrease in heart rate; and 2) a fear reaction (phobic response) characterized by high increase in skin conductance, heart rate and muscle activity. Self-reported measures of pain-related fear did not discriminate between the 'non-phobic' and 'phobic' participants. These results suggest that pain-related fear may be conceptualized as a phobia for some, but not for all individuals with persistent LBP and high pain-related fear, and that explicit measures may not differentiate between these two groups.

Overall, studies investigating implicit evaluations or physiological threat-responses to pictures of back-threatening movements in people with persistent LBP and pain-related fear have found mixed results. A key element of pain-related fear assessment is to identify the specific activity the person is fearful of. Therefore, threat-specificity is critical for evaluating perceived danger to the body and/or to a person's valued goals. These studies may have been limited by a non-specific sample, selected based on a generic pain-related fear beliefs questionnaire, and by not using task-specific or personally-threatening stimuli. These limitations add to the challenges posed about the role of 'fear' and its relationship with pain in the fear-avoidance model.

2.2.6.4 Key Points

What is known and not known about pain-related fear?

- Pain and protective behaviour are dependent on implicit evaluations of danger to the body. Thus far, studies investigating implicit evaluation have been limited by: (i) selecting a non-specific sample based on a generic fear beliefs questionnaire; (ii) not using task-specific or personally-threatening stimuli; and (iii) using only one of either implicit or physiological measures, providing a narrow perspective on the assessment of pain-related fear in people with persistent LBP.

- Although, (i) threat-specificity is critical for evaluating perceived danger to the body, and (ii) bending and lifting with a round-back are one of the most feared tasks for people with and without LBP; it is not known how people with persistent LBP and fear of bending with a round-back evaluate danger at an implicit and physiological level. A study investigating both implicit and physiological evaluations of danger in people with persistent LBP selected based on fear of bending with a round-back would provide a broader understanding of the role of 'fear' and its relationship with pain in the fear-avoidance model.

- Pain-related fear affects multiple interacting factors that shape a person's pain experience. Nonetheless, how the multiple factors that influence a person's experience change over time has not been quantitatively evaluated.

- Pain-related fear is one of the strongest modifiable predictors of disability in people with LBP, however the pathway to recovery is not well-understood.

2.3 SECTION 3: Interventions and process of change

2.3.1 Current interventions for people with persistent LBP and (high) pain-related fear

Results from clinical trials of physical, psychological, social or combined interventions for people with persistent LBP have indicated at best moderate improvements in outcomes when compared with minimal or no treatment, and with effects that are often not maintained at long-term follow up (Buchbinder et al. 2018; Foster et al. 2018; O'Keeffe et al. 2016; Kamper et al. 2015; Artus et al. 2010). Specifically, a recent systematic review reported no differences in the reduction of disability and pain between these interventions (O'Keeffe et al. 2016). Failure to target appropriate risk profiles that may be more likely to benefit from a particular intervention, and the lack of tailoring the treatment to the individual's needs have been proposed as potential limiting factors for current interventions (O'Keeffe et al. 2016; Williams, Eccleston, and Morley 2012; Main and George 2011).

Pain-related fear has been identified as a key mediator to disability (Wertli, Rasmussen-Barr, Weiser, et al. 2014). For people with (*high*) pain-related fear, behavioural interventions are considered optimal (den Hollander et al. 2010; Bailey et al. 2010). Behavioural interventions have a well-established history since the original work of Fordyce (1976) (Butler 2017; Main et al. 2014), who was a pioneer in the use of behavioural theory for the treatment of chronic pain. Fordyce described a program for the extinction of unhelpful pain behaviours (Butler 2017; Vlaeyen 2015). One of Fordyce's famous sayings was that patients with persistent pain often display "superstitious over-guarding" (Butler 2017), meaning that people would protect themselves from a potential catastrophic consequence. Fordyce proposed that "a person cannot manifest two incompatible behaviours at the same time" (Butler 2017), so his program would focus on 'normalizing' these behaviours with the goal to increase functional healthy behaviours.

Behavioural interventions for pain do not aim to treat pain directly (Henschke et al. 2010; Vlaeyen et al. 1995). Instead, their aim is to modify unhelpful behaviours and their underlying cognitive processes, and thereby reduce disability (Main et al. 2014; Vlaeyen et al. 2012; Henschke et al. 2010). Behavioural interventions often include a cognitive component aimed at educating the patient about the biopsychosocial nature of pain (Williams, Eccleston, and Morley 2012; Keefe 1982), and the interventions can be generally distinguished as *operant* and *respondent* treatment (Henschke et al. 2010).

2.3.1.1 Operant treatment

The most prominent and applied operant treatment is Graded Activity (Sanders 2002). Graded activity aims to build a person's activity tolerance, and does not focus on pain reduction. Instead, time-contingent quotas are used to encourage activity engagement despite pain. Although this may include activities the person is fearful of and/or avoidant, Graded activity does not explicitly target the person's feared activity (Macedo et al. 2010). Instead, GA's progression is based on meeting the activity quotas (George et al. 2010). Pacing and positive reinforcement by the achievement of each quota are key features of Graded activity (Macedo et al. 2010). For people with persistent LBP, systematic reviews reported that graded activity is more effective at reducing disability than minimal or no treatment in the short-term (Lopez-de-Uralde-Villanueva et al. 2016; Macedo et al. 2010), intermediate term (Macedo et al 2010) and long term (Lopez-de-Uralde-Villanueva et al. 2016). However, when compared with other forms of exercise, graded activity was not more effective at any timepoints (Lopez-de-Uralde-Villanueva et al. 2016; Macedo et al. 2010).

2.3.1.2 Respondent treatment

Graded Exposure *in vivo* is a treatment approach that was developed by Vlaeyen et al (2001) as an evolution of Fordyce's behavioural program (Butler 2017) to a specific group of patients with pain-related fear (Vlaeyen et al. 2001). Graded exposure is grounded on the fear-avoidance model of chronic pain described by Vlaeyen & Linton (2000), which postulates that fear and avoidance of movement contributes to the maintenance of pain via mechanisms of classical conditioning (Vlaeyen and Linton 2000). Different to graded activity, Graded exposure specifically targets pain-related fear by repeatedly exposing the person to their feared/avoided activity, while challenging unhelpful cognitions, disconfirming threat expectations (performance of task without the occurrence of the feared outcome). The use of behavioural experiments during exposure provide an experience in which learned associations between threatening tasks and increased pain or harm may be corrected (Vlaeyen, Morley, and Crombez 2016). This process follows a hierarchical order based on the person's perceived harmfulness for each task, starting from the least and progressing to the most feared task, and each task is performed until fear reduces (Vlaeyen et al. 2012; George et al. 2010).

Because fear reduction is at the heart of this intervention, there is a widely held notion that graded exposure is the treatment of choice for people with persistent pain and pain-related fear (Vlaeyen et al. 2012; den Hollander et al. 2010; Lohnberg 2007). Early single-case experimental design studies (SCEDs) reported promising results. SCEDs demonstrated that graded exposure was effective in reducing pain-related fear (measured as fear of movement, perceived harmfulness of activity, or pain catastrophizing), and disability in individuals with persistent LBP and high pain-related fear (de Jong et al. 2005; Boersma et al. 2004; Vlaeyen, De Jong, Onghena, et al. 2002; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001). Some of these SCEDs also claimed that graded exposure was more effective than graded activity (Vlaeyen, de Jong, Geilen, et al. 2002; de Jong et al. 2005; Vlaeyen et al. 2001). SCEDs however, are limited in determining treatment effectiveness, and their results have restricted generalizability (Borckardt et al. 2008). Therefore, larger randomized controlled trials (RCTs) were conducted to investigate the comparative effectiveness of graded exposure to a wait list control group (Woods and Asmundson 2008), to graded activity (Leeuw et al. 2008) and to treatment as usual (Linton et al. 2008). These studies reported that although graded exposure was more effective than any of the control conditions at reducing pain-related fear (Leeuw et al. 2008; Woods and Asmundson 2008; Linton et al. 2008), only one study reported reduction in disability (Linton et al. 2008). Therefore, results from RCTs have not been as positive as those from earlier single-case studies. Furthermore, while all RCTs (Leeuw et al. 2008; Woods and Asmundson 2008; Linton et al. 2008) included participants with pain-related fear, only two RCTs intentionally targeted people with *high* pain-related fear selected by higher cut-offs of measures of fear (Woods and Asmundson 2008; Linton et al. 2008). Leeuw et al (2008) performed a subgroup analysis of participants with higher pain-related fear, reporting that the effects of graded exposure were not superior in this group (Leeuw et al. 2008).

The mixed results presented here suggest that graded exposure does not work for every patient, and that the overall treatment effect is only moderate, indicating the need for improvement of this treatment for people with persistent LBP (Vlaeyen, Morley, and Crombez 2016; Vlaeyen and Linton 2012; Vlaeyen et al. 2012). Furthermore, considering the nature of graded exposure as an intervention to reduce fear and disability, the mixed results between trials and earlier single-case studies raise the question as to how effective graded exposure is for people with persistent LBP and *high* pain-related fear.

2.3.1.3 Hybrid treatments

In light of the mixed results reported for graded exposure, and its foundation on the strong theoretical framework of the fear-avoidance model, *hybrid treatments* have been proposed to augment existing behavioural interventions for people with higher levels of pain-related fear.

2.3.1.3.1 Contextual Cognitive Behavioural Therapy

Contextual Cognitive Behavioural Therapy (Contextual-CBT) was proposed as a hybrid treatment for people with high pain-related fear, including principles of graded exposure and Acceptance and Commitment Therapy (Pincus et al. 2013). Acceptance and Commitment Therapy is based on concepts of mindfulness, acceptance and values-based action and is thought to have the potential to reduce pain-related fear through a process called psychological flexibility (Vowles, Sowden, and Ashworth 2014; McCracken, Vowles, and Eccleston 2005). This process involves moving attention away from pain and its consequences towards valued life goals (Vowles, Sowden, and Ashworth 2014; Vowles, McCracken, and Eccleston 2007). Contextual-CBT thus aim to increase psychological flexibility and pain acceptance to improve function. Similar to other behavioural interventions contextual-CBT is not focused on pain reduction (Pincus et al. 2013).

Contextual-CBT for people with persistent LBP and high pain-related fear was tested in a feasibility trial against physiotherapy treatment (Pincus et al. 2015). Physiotherapy involved 'back to fitness' group sessions with at least 60 % of exercise-based content, and up to 3 individual sessions (if required) (Pincus et al. 2013). Participants included in this study were considered as 'fear-avoidant', reporting scores ≥ 38/68 on the TSK (acceptable cut-off for high pain-related fear) (Wertli, Rasmussen-Barr, Weiser, et al. 2014), and completing at least a single-item on the psychological subset of the STartBack Tool as entry requirements (Pincus et al. 2013). Results of the trial suggest that there was greater improvement in acceptance in the contextual-CBT group from baseline to 6-months post treatment, than in the physiotherapy group. However, there was no difference in reduction of disability, comparing mean scores at baseline, three and six months post the interventions (Pincus et al. 2015). When comparing mean differences between baseline to 6-months, there were greater changes for disability and pain in the contextual-CBT group than in the physiotherapy group. Considering this was a feasibility trial, inferential testing was not possible.

Therefore, the authors suggest the results are promising, but they should be cautiously interpreted [Pincus et al. 2015].

2.3.1.3.2 Emotion-focused exposure

It has been proposed that movement may not be the only stimulus that is feared by people with persistent pain [Linton and Fruzzetti 2014]. Other factors such as emotional states [Lumley et al. 2008] and pain itself [De Peuter et al. 2011] have been proposed as possible triggers for avoidance behaviour [Linton and Fruzzetti 2014]. Certain emotions may generate unhelpful responses and patients may learn to avoid personally-relevant emotional stimuli [Schutze et al. 2017; Flink, Boersma, and Linton 2013]. Developing skills to regulate emotional responses may empower patients to engage in their valued goals, potentially enhancing generalisation of treatment effects [Linton and Fruzzetti 2014]. Dialectical Behaviour Therapy is an approach that aims to develop emotion regulation skills to achieve personal goals [Linton 2010]. Therefore, a hybrid treatment combining an emotion-regulation approach informed by Dialectical Behaviour Therapy with a traditional exposure in vivo program was proposed and tested in a SCED [Linton and Fruzzetti 2014]. Six people with persistent LBP and high levels of catastrophizing (PCS > 24/52) were included in the study. The results suggest that the hybrid emotion-focused exposure treatment improved disability and pain catastrophizing for all participants, and pain-related fear and pain intensity for most, with effects sustained up to 5-months post treatment [Linton and Fruzzetti 2014]. While the results are promising, the authors indicate the limitations of a single-case design, and the need for further testing of this hybrid intervention [Linton and Fruzzetti 2014].

2.3.1.3.3 Psychologically-informed physiotherapy practice

In order to improve the ability to manage patients with persistent LBP and higher levels of distress and pain-related fear, physiotherapists were trained on how to integrate cognitive behavioural skills to their traditional physiotherapy knowledge [George 2017a; Main et al. 2012; Main and George 2011]. The approach, called psychologically-informed physiotherapy practice, was tested on a large RCT [Hill et al. 2011]. Using a prognostic screening tool (STarT Back), Hill et al (2011) compared this targeted approach to non-stratified best care, showing overall greater reductions in disability for patients with persistent LBP receiving care targeted to risk strata, as assessed by the screening tool [Hill et al. 2011]. However, for patients classified as high-risk, who were characterised by increased levels of psychological distress (including those with high pain-related fear), the effects were not sustained at longer term of 12 months (Hill et al. 2011). The authors suggest that CBT-trained physiotherapists do not target psychological factors as effectively as the traditional CBT treatment delivered by psychologists (Mansell, Hill, Main, Vowles, et al. 2016). In contrast, a recent systematic review indicates that psychological interventions delivered by physiotherapists improve pain and disability in people with musculoskeletal pain conditions (Guerrero Silva et al. 2018). The integration of psychological skills to physiotherapy practice bears merit, and presents a challenging and promising pathway (Keefe, Main, and George 2018; Guerrero Silva et al. 2018; O'Sullivan et al. 2018; George 2017a, 2017b; Main and George 2011).

2.3.2 Proposed limitations of current treatment approaches for persistent LBP and high pain-related fear

There is compelling evidence that pain is influenced by multiple interacting factors across the biopsychosocial spectrum, making it an individual experience (Rabey et al. 2017a; Gatchel et al. 2007). A possible limiting factor and potential reason for the modest effects of current interventions relates to the uni-dimensional nature of current approaches (Rabey et al. 2017a; O'Sullivan et al. 2014; Gatchel et al. 2007). Many approaches fail to consider the numerous interacting factors known to be associated with persistent LBP such as: person's motivation and goals, pain sensitivity profiles, safety-seeking behaviours during feared movements and activities (i.e. how a person performs a task) and unhelpful lifestyle behaviours. Another potential limitation relates to the lack of individualised management (Saragiotto, Maher, Hancock, et al. 2017; Foster et al. 2013), thus failing to address the complex interplay of factors at an individual level. Finally, not targeting pain as a modifiable experience may also be a limiting factor.

Advancements of the fear-avoidance model suggest that the extent to which avoidance behaviour impacts on disability is related to the individual's underlying motives for such behaviour (Crombez et al. 2012) and the motives vary according to the individual's beliefs, emotions and the values attributed to their goals (Wideman et al. 2013; Vlaeyen and Linton 2012; Crombez et al. 2012). While some individuals may avoid lifting because they believe it may cause damage to their spine, others may avoid lifting because it does hurt and the more they do it, the more it hurts. (Bunzli, Smith, Schutze, et al. 2015). These findings highlight the *motivational heterogeneity* of patients with high pain-related fear. This has implications for fear reduction interventions in terms of the need for different strategies used for exposure training (Bunzli, Smith, Schutze, et al. 2015; Wideman et al. 2013; Crombez et al. 2012). For instance, for patients who avoid lifting because they fear damage, exposure may be effective to disconfirm their catastrophic expectations; whereas those who avoid lifting because they fear and/or experience an increase in pain may need to modify their movement behaviour to gain control over pain before and/or during exposure (Bunzli, Smith, Schutze, et al. 2015) otherwise, their expectations may not be disconfirmed.

A possible reason for the limitation of exposure-based interventions in this group may relate to the fact that people with persistent LBP demonstrate variable *pain responses to repeated movement* (Rabey et al. 2017b). That is, while for some a pain response may be momentarily provoked and relieved by specific spinal movements, for others pain may be amplified or escalated with repeated movement (Rabey et al. 2017b; Rabey, Beales, et al. 2015; O'Sullivan et al. 2014). Rabey et al (2017) assessed 300 people with persistent LBP and demonstrated that people's pain response to movement is varied, with many (50%) reporting pain exacerbation with repeated spinal movement, and few (10%) reporting pain relief (Rabey et al. 2017b). In a study involving people with high fear of movement, repeated lifting was associated with an escalation of pain intensity during the task (temporal summation) (Sullivan et al. 2009). Thus, repetitive exposure to a threatening task that may lead to escalation of pain could potentially lead to increased perception of threat related to the movement and an unsuccessful outcome, of non-response or even dropping out of treatment. Similarly, interventions that use a time quota to promote activity engagement despite pain may also lead to pain escalation potentially hindering their effectiveness.

How a person performs a task is also an important consideration. During performance of daily tasks such as sitting, bending and lifting, people with persistent LBP often present with protective behaviours such as excessive muscle guarding and altered movement patterns (Dankaerts et al. 2009). Specifically, those with high pain-related fear present greater trunk stiffness, reducing their ability to bend forward in a relaxed manner (Karayannis et al. 2013; Geisser et al. 2004). For instance, when faced with a lifting task a person may breathe-hold and brace their trunk muscles to avoid lumbar spine flexion while performing the task because they are frightened that flexing the spine may cause pain or damage. It has been suggested that these 'overprotective' *safety-seeking behaviours* may lead to increased tissue loading and pain persistence, being often unhelpful and provocative (O'Sullivan 2005). Therefore, normalization of these behaviours could lead to reduction of pain during task performance (O'Sullivan 2005).

Pain intensity is positively associated with pain-related fear and avoidance behaviour (Kroska 2016). Consideration of a person's pain response to movement, and how they move while performing a threatening task could provide opportunities for behavioural modification and *pain control* (O'Sullivan et al. 2018). Although symptom attenuation is an important construct of recovery for people with persistent LBP (Hush et al. 2009), pain is not a common target in the behavioural management of persistent LBP (Saragiotto, Maher, Traeger, et al. 2017). Behavioural interventions in particular, do not target pain directly (Henschke et al. 2010). This suggests that there is an underlying assumption that pain is not controllable or modifiable. However, a review of 17 Cochrane systematic reviews, comparing the effect of LBP treatments on pain and disability indicated that trials typically reported larger effects on pain reduction than on disability (Saragiotto, Maher, Traeger, et al. 2017). This supports that pain is modifiable (Saragiotto, Maher, Traeger, et al. 2017), and developing pain control is associated with less future episodes of LBP (Main, Foster, and Buchbinder 2010). This was recently supported by a qualitative study, which reported that gaining control over pain was an important step in the process of fear reduction for people with persistent LBP and high pain-related fear (Bunzli, Smith, Schutze, et al. 2015; Bunzli et al. 2016).

Lifestyle factors such as chronic stress, inactivity and excessive activity levels, sedentary behaviour, sleep impairment, poor diet, excessive alcohol and smoking can modulate pain by acting both peripherally and centrally to sensitize spinal structures (Gatchel et al. 2007). Identifying an individual's perceived barriers to engaging in a healthy lifestyle with pain control may facilitate achievement of personally-relevant goals. This may play a role in generalization of effects to daily life, a common limitation with exposure therapy (Goubert, Crombez, and Lysens 2005).

The above-mentioned limitations highlight how many current interventions may fail to adequately target the complex and individual inter-relationships of factors in people with persistent LBP and high pain-related fear. Considering the complexity (Pincus et al. 2015; Main et al. 2012) and heterogeneity (Bunzli, Smith, Schutze, et al. 2015) of this group of patients, and the inter-related multidimensional nature of factors affecting a person's LBP experience, individualised interventions that target multiple dimensions associated with the disorder have been advocated (Keefe, Main, and George 2018; Rabey et al. 2017a; O'Sullivan et al. 2016; Foster et al. 2013; O'Sullivan 2012; Gatchel et al. 2007; Main and George 2011).

2.3.3 Cognitive Functional Therapy for people with persistent LBP and high pain-related fear

In response to the limitations of current approaches for managing persistent LBP an individualised multidimensional approach called *Cognitive Functional Therapy* (CFT) was developed. Cognitive functional therapy is an integrated physiotherapy-led exposure-based behavioural approach for individualising the management of people with persistent LBP once serious (e.g. malignancy, infection, inflammatory disorder, and fracture) and specific pathology (e.g. nerve root compression with progressive neurological deficit) has been excluded (O'Sullivan et al. 2018).

Cognitive functional therapy was specifically developed as an approach for targeting modifiable cognitive, emotional, physical and lifestyle behaviours considered unhelpful and/or provocative of a person's LBP experience. While evolving from an integration of physiotherapy rehabilitation with foundational behavioural interventions (Vlaeyen et al. 2001; Keefe 1982; Fordyce 1976), CFT differs from the other interventions, as it uses a multidimensional clinical-reasoning framework to identify and target modifiable contributors to pain and disability in a person-centred manner (O'Sullivan et al. 2018). This approach enables the physiotherapist to take the person on an individual journey to effectively self-manage their persistent LBP with a program that is tailored to their unique clinical presentation and context. Cognitive functional therapy can be integrated with medical management where pain levels dominate, and/or with psychological management where co-morbid mental health disorders are a significant barrier to behavioural change (O'Sullivan et al. 2018; O'Sullivan et al. 2015).

The CFT intervention involves 3 key aspects, which can be briefly described as: (i) *Making sense of pain* - a personally relevant multidimensional understanding of pain, which occurs via experience, self-reflection and disconfirmation of previously held unhelpful beliefs; (ii) *Exposure with 'control'* - exposure training directed to pain-provocative, feared, and/or avoided personally relevant goals, during which pain control is explicitly targeted by challenging negative cognitions and modifying how the person physically performs the task (via body relaxation, body control, and discouraging safety-seeking behaviours); and (iii) *Lifestyle change* - individually designed plan addressing unhelpful lifestyle factors such as sleep and activity levels (O'Sullivan et al. 2018). In cases of people for whom pain is not controllable, reconceptualization of pain and its impact in life is discussed within an acceptance framework, where the focus changes from controlling pain towards the engagement in meaningful activities despite pain. CFT is described in more detail in **Appendix 1**) (O'Sullivan et al. 2018). The 3 aspects described are targeted in an integrated manner by the physiotherapist, rather than in separate stages by different disciplines, as is common in multidisciplinary pain settings (Schutze et al. 2014). The intervention is underpinned by a strong therapeutic alliance and motivational interviewing style (open, nonjudgmental, reflective) (O'Keeffe et al. 2015; Hall, Gibbie, and Lubman 2012), providing validation (Linton 2015; Edmond and Keefe 2015). This is based on an increasing body of evidence which demonstrates that harnessing a positive patient-therapist interaction that empowers self-management has a positive effect on outcomes such as pain, disability and patient satisfaction across many different health conditions, including persistent LBP (Taccolini Manzoni et al. 2018; Testa and Rossettini 2016; Fuentes et al. 2014; Ferreira, Ferreira, et al. 2013; Hall et al. 2010).

The efficacy of CFT has been tested in a recent RCT (Vibe Fersum et al. 2013), which reported that compared with a combined program of manual therapy and exercise CFT demonstrated larger effect sizes for reductions in pain-related fear, pain intensity and disability in people with persistent LBP and moderate disability (Vibe Fersum et al. 2013). In a recent case-series (O'Sullivan et al. 2015), CFT has also shown to be effective and long lasting (one year), in a group of highly disabled people with persistent LBP waitlisted on a pain clinic. CFT demonstrated large reductions in pain, disability, and fear of physical activity, as well as development of positive back beliefs and self-efficacy enhancement (O'Sullivan et al. 2015). To date however, this approach has not been specifically tested in people with persistent LBP and high pain-related fear. Furthermore, the mediating factors underpinning improvements observed in the CFT intervention are yet to be investigated.

2.3.3.1 Key Points

What is known and not known about interventions for persistent LBP and high pain-related fear?

- It is not clear what intervention works best for people with persistent LBP and high pain-related fear. Considering that there are not many studies specifically investigating interventions for people with persistent LBP and high pain-related fear, a systematic review study aimed to determine the current state of evidence concerning the effectiveness of behavioural interventions in reducing disability, pain and fear for this challenging group of patients would be valuable.

- There is compelling evidence that pain is influenced by multiple interacting factors, however, there are few interventions that are multidimensional in nature.

- It has been suggested that unhelpful behaviours are modifiable, and that gaining control over pain may offer an opportunity for targeted management in people with persistent LBP. However, this has not been evaluated in people with high pain-related fear.

- The individual complexity and heterogeneity of people with high pain-related fear highlights the importance of developing individualized interventions that are tailored to the person's needs (e.g. CFT).

- Although the perspectives of people with persistent LBP undergoing CFT has been studied qualitatively, the effectiveness of CFT has not been quantified in people with persistent LBP and high pain-related fear. Considering the novelty of CFT and the heterogeneity of the high-fear group, it would be valuable to investigate the effectiveness of CFT in this group of patients.

2.3.4 Evaluating temporal changes in people with persistent LBP and high pain-related fear

2.3.4.1 The experience of LBP fluctuates over time

Low back pain has been historically viewed as one or few discrete acute episodes of pain that occur independently at different time points; and that either resolved rapidly or that became chronically painful (Dunn, Hestbaek, and Cassidy 2013). This dualistic view of acute and chronic stages was potentially due do the belief that LBP is caused by an injury that causes damage to spinal structures. Over the last decade, research groups conducting longitudinal observational studies using frequent measures (daily, weekly or monthly) identified that for many, LBP is a condition of persistent or fluctuating symptoms over time (Chen et al. 2017; Kongsted et al. 2016; Axén and Leboeuf-Yde 2013; Dunn and Croft 2004). This fluctuating behaviour identified in many people living with LBP resembles the behaviour of long-term conditions such as asthma, in that patients experience fluctuations of symptoms and disability (O'Sullivan et al. 2016; Axén and Leboeuf-Yde 2013). Considering this variability in a person's trajectory, intervention studies that collect data at single timepoints may capture LBP experience at different 'phases' of the condition's trajectory, which can potentially portray a misguided representation of a person's experience, and how this experience is affected by the intervention (Dunn, Hestbaek, and Cassidy 2013; Axén and Leboeuf-Yde 2013; Borckardt et al. 2008). For example, if a person is going reasonably well at the time of pre-treatment data collection, but goes through a period of temporary exacerbation of symptoms (flare up) at the time of post-treatment data collection, the intervention may appear ineffective (Kongsted et al. 2016). Therefore, the use of repeated and frequent measures may provide a representation that better reflects the person's LBP experience over a period of time.

2.3.4.2 The process of change

The process of change is here defined as the journey by which patients go through while receiving treatment to modify their disabling LBP experience. Intervention studies are often interested in answering questions of improvement such as, '*Do people report improvement after treatment*?' Other important questions, which are not so frequently asked are: '*How does change unfold during treatment*?' '*What underpins this change*?' '*Is the process the same for each person*?' These questions provide insight to the process of change, which informs on *what* changes *when*, for *whom* and *why*. Studies that consider these questions may provide a detailed description of the "anatomy of therapeutic change" (Borckardt et al. 2008; Laurenceau, Hayes, and Feldman 2007).

Considering the complex multifactorial and individual nature of persistent LBP and high pain-related fear this process is unlikely to be linear. Rather, the interplay of multiple factors is likely to vary for each person, and fluctuate temporally (Kongsted et al. 2016; O'Sullivan et al. 2016) making this process an individual experience. This inherent non-linearity is a central feature of a complex system, in which the relationships between components are key to understanding change and adaptation over time (Brown 2009, 2006). Therefore, understanding how changes in factors across multiple domains relate to changes in the selected outcome (disability and/or pain) may provide important insight about how change unfolds during treatment for individuals with persistent LBP and high levels of pain-related fear.

2.3.4.3 Factors that potentially mediate treatment response/change in outcomes

2.3.4.3.1 What are mediators?

When a person is exposed to a treatment, changes in the desired outcome may occur directly, meaning that the treatment caused a changed in the outcome; or indirectly, meaning the treatment caused changes in factors, which then caused changes in the selected outcome. These factors are termed mediators. Mediators are defined statistically as factors that 'lie on the causal path between the exposure and the outcome' (Lee et al. 2017; Mansell, Kamper, and Kent 2013b; Kazdin 2007), meaning that mediators change because of an intervention and correlate with changes in the selected outcome. Conceptually, this provides information regarding factors that contributed the most to the treatment effect (Lee et al. 2017). Understanding the factors that underlie changes in treatment response provide clinicians with an ability to identify which aspects of the management need to be strengthened in order to target desired outcomes (Hill and Fritz 2011). It also provides knowledge as to how treatment effects maybe occurring.

Specifically, in persistent LBP research, few studies have reported analysis of potential mediators for treatment response (Mansell, Kamper, and Kent 2013), and those have been criticized for their quality (Lee et al. 2015). The main criticism relates to the number of timepoints assessed during the intervention period, with many studies often assessing a single factor at a single timepoint during the intervention (Lee et al. 2017; Mansell, Hill, Main, Vowles, et al. 2016). Studies that do not include repeated measurement of both the proposed mediator and the selected outcome, make it challenging to know the timing and the order in which the change occurred (Mansell et al. 2017; Laurenceau, Hayes, and Feldman 2007).

2.3.4.4 What are the potential mediators of treatment response/change in persistent LBP?

The fear-avoidance model (Vlaeyen, Crombez, and Linton 2016; Vlaeyen and Linton 2012; Vlaeyen and Linton 2000) proposes that pain-related cognitive and emotional responses to pain can fuel an unhelpful cycle that leads to disability. Many studies (15) have investigated mediators of treatment response in people with musculoskeletal pain conditions (Fordham et al. 2017; Whittle et al. 2017; Mansell, Hill, Main, Von Korff, et al. 2017; Mansell, Hill, Main, Vowles, et al. 2016; Tetsunaga et al. 2016; Hall et al. 2016; Robinson et al. 2013; Wicksell, Olsson, and Hayes 2010; Seymour et al. 2009; Leeuw et al. 2008; Turner, Holtzman, and Mancl 2007; Smeets et al. 2006; Focht et al. 2005; Spinhoven et al. 2004; Nicassio et al. 1997), with only eight specifically investigating mediators of treatment response in people with persistent LBP (Fordham et al. 2017; Mansell, Hill, Main, Von Korff, et al. 2017; Mansell, Hill, Main, Vowles, et al. 2016; Tetsunaga et al. 2016; Leeuw et al. 2008; Smeets et al. 2006; Focht et al. 2005; Spinhoven et al. 2004). Only two of these studies conducted a mediation analysis in interventions targeting specific groups of people with persistent LBP (Mansell, Hill, Main, Vowles, et al. 2016; Leeuw et al. 2008). Mansell et al (2016) conducted a mediation analysis on data from a randomized controlled trial (RCT) that compared stratified care (according to risk of poor outcome) with non-stratified best care for people with persistent LBP in primary care (Mansell, Hill, Main, Vowles, et al. 2016). In the original trial, those reporting increased levels of psychological distress (including those with pain-related fear) were classified to the high-risk group, and received psychologically-informed physiotherapy (delivered by physiotherapists trained in CBT skills) (Hill et al. 2011). The analysis by Mansell et al (2016) focussed on the high-risk group, and found that improvements in pain-related distress and pain intensity mediated the relationship between treatment allocation and reductions in disability, explaining a considerable proportion of improvement seen in those receiving psychologically-informed physiotherapy treatment (Mansell, Hill, Main, Vowles, et al. 2016). Leeuw et al (2008) conducted a multicentre RCT to compare the effectiveness of two behavioural interventions, graded exposure *in vivo* and graded activity in people with persistent LBP and moderate pain-related fear (TSK>33/68) (Leeuw et al. 2008). The results demonstrated that graded exposure was more effective than graded activity in reducing disability, and these results were mediated by reductions in pain catastrophizing and perceived harmfulness of daily activities (Leeuw et al. 2008).

Collectively, these studies indicate that improvement in pain self-efficacy, and reductions in pain-related fear, avoidance behaviour, pain catastrophizing, perceived harmfulness and pain-related distress mediate treatment response for people with persistent LBP (Lee et al. 2017; Mansell, Kamper, and Kent 2013). Specifically, for people with high psychological distress and pain-related fear, it appears that reductions in pain intensity may also be an important treatment target (Mansell, Hill, Main, Vowles, et al. 2016). This is supported by qualitative data from individuals with persistent LBP and high pain-related fear (TSK≥40/68) that indicated that failure to control pain played a role in the maintenance of pain-related fear and disability (Bunzli, Smith, Schutze, et al. 2015). Furthermore, in a cohort receiving a variety of interventions gaining control over pain and the effects of pain on daily life activities were important factors in the reduction of pain-related fear and disability (Bunzli et al. 2016). However, there is a paucity of studies that have used quantitative measures to evaluate potential mediators of treatment response in interventions specifically designed for people with persistent LBP and *high* pain-related fear.

2.3.4.5 Assessment of factors that potentially mediate treatment response/change

Mediation analysis provides a useful method to investigate how multiple factors relate over time. This method is used to explore the direct and indirect relationships between treatment exposure and changes in the desired outcome (Mansell, Kamper, and Kent 2013; MacKinnon 2008). *Randomized controlled trials* present the most accepted framework to conduct mediation analysis (VanderWeele and Vansteelandt 2014; Hill and Fritz 2011; Imai et al. 2011; Kazdin 2007), whereby large samples and inferential statistics are used to identify mediating variables that partially or wholly account for the treatment effect in the outcome. This provides information about mediation that are averaged over samples (Dunn et al. 2015; MacKinnon 2008; Kazdin 2007).

However, there are some challenges for mediation analysis conducted in RCTs of complex behavioural interventions. *First*, considering that mediation models assume a causal order to the variables, meaning that changes in the mediator must precede downstream changes in the outcome, several timepoints might need to be assessed to capture the exact points in which change has occurred. However, RCTs are limited in the number of variables and timepoints that can be captured, rendering them insensitive to the timing of mediator and outcome change, an important consideration in establishing mediation [(Mansell, Hill, Main, Vowles, et al. 2016; Riley and Gaynor 2014; Mansell, Kamper, and Kent 2013; Laurenceau, Hayes, and Feldman 2007)]. To overcome this limitation some studies have added a long-term follow-up timepoint, which provides information on the sustainability of outcomes over a longer period, but does not inform on factors underlying the effect of the intervention on the outcome whilst the treatment is being received [(Mansell, Hill, Main, Von Korff, et al. 2017; Mansell, Hill, Main, Vowles, et al. 2016; Dunn et al. 2015)]. *Second*, in a complex system, the process of change may not be steady over the course of an intervention for either the mediator or the outcome, and between individuals. Unlikely the simple linear form of a pre-post treatment change, change over multiple timepoints may be curvilinear and different for each person [(Morley, Vlaeyen, and Linton 2015; Emsley, Dunn, and White 2010; Laurenceau, Hayes, and Feldman 2007)]. *Third*, complex systems involve feedback loops which means that changes in the mediator can change the outcome, which in turn can change the mediator [(VanderWeele and Vansteelandt 2014; Vanderweele 2012)]. Although there are methodological advancements that accommodate non-linear models [(Lee et al. 2017; Daniel et al. 2015; Valeri and Vanderweele 2013)], these may not provide information at an individual level. *Fourth*, in individualised interventions different factors are targeted for each individual, which means that a summary mediation analysis conducted in a RCT will inform on an overall trajectory of change, only capturing common pathways of change at a group level (unless pre-planned subgroup analysis is conducted). How well a group trajectory adequately represents the individual trajectories of change in a complex intervention has been raised as a limitation [(Laurenceau, Hayes, and Feldman 2007)]. *Fifth*, RCT's require large samples and thus large expenditure.

Collectively these challenges highlight the limitations of conducting mediation analysis in RCTs to inform the process of change at an individual level using complex interventions. It has been proposed that smaller scale studies may provide a robust framework to evaluate the process of therapeutic change at an individual level [(Borckardt et al. 2008)]. Furthermore, the information gathered from these studies can be informative to the design of larger scale RCTs [(Morley 2018; Morley, Vlaeyen, and Linton 2015)].

2.3.4.5.1 Single-case experimental research design

Single-case experimental designs are an intensive, prospective and controlled study of the individual, using each person as their own control (Morley 2018; Tate et al. 2017; Morley, Vlaeyen, and Linton 2015). SCEDs are characterized by the following key features: a baseline period demonstrating the outcome has a relatively stable behaviour over a period preceding the treatment phase; the intervention is under experimental control across a series of discrete phases; the targeted behaviour is assessed repetitively and frequently across all phases; the behavioural outcome is robust, specific to the outcome and sensitive to change (Tate et al. 2017; Vlaeyen, Morley, and Crombez 2016; Kratochwill et al. 2013; Onghena and Edgington 2005). These features enable SCEDs to answer questions of treatment effectiveness by strengthening the inference that the intervention itself is responsible for changes from baseline (Kratochwill et al. 2010).

Studies evaluating change over time are vulnerable to plausible rival hypotheses that may explain the outcomes, thus threatening the design's internal validity. Some of the hypotheses are: (i) maturation (change could be caused by natural history or processes that are coincidental, yet unrelated to the treatment); (ii) regression to the mean (when a variable that is extreme on its first measurement, it will tend to be closer to the average on its second measurement which could be interpreted as treatment response); (iii) external factors (occurrence of an extra-treatment event that could plausibly cause a change), and (iv) measures (repeated administration of the same measures may result in participants recalling and recalibrating their responses, which can affect the reliability of the measure) (Morley, Vlaeyen, and Linton 2015). RCTs control several of these plausible rival hypotheses by having a control group, randomly allocating subjects to treatment and control groups, and using statistical analysis to account for any imbalance in confounding factors that may have occurred despite randomisation (Morley, Vlaeyen, and Linton 2015; Kratochwill et al. 2013, 2010). In a single-case experimental design, confounding in the form of rival hypotheses can be systematically controlled for within subject by using the person as their own control, and by assessing the outcome of interest repetitively and frequently (Morley 2018). Other strategies such as, replication over patients and clinicians, conducting interviews with the participant and significant others (to identify potential external factors that could affect treatment response) can increase internal validity of the design. Although RCTs are the gold standard to determine treatment efficacy, SCEDs are used frequently in the behavioural sciences, where systematic observation of one or a few patients can be scientifically sound and informative, providing a strong level of evidence (Tate et al. 2017;

Morley, Vlaeyen, and Linton 2015; Morley and Williams 2015; Borckardt et al. 2008). Therefore, SCEDs are not a replacement but a complementary design in the process of building evidence for behavioural change (Tate et al. 2017; Kratochwill et al. 2010; Borckardt et al. 2008). Indeed, SCEDs have been recommended in the developmental stages of novel complex interventions for chronic pain before progressing to a RCT design (Norell-Clarke, Nyander, and Jansson-Frojmark 2011).

In relation to describing the process of change, SCEDs have characteristics that provide a flexible framework, which may assist to overcome some of the above-mentioned challenges presented by mediation analyses conducted in RCTs. A key advantage of SCEDs over RCTs, lies in the richness of data captured via repeated measures. The assessment of *multiple timepoints* allows identification of a systematic change in the outcome and other factors (e.g. potential mediators) during the treatment phase in comparison to a stable baseline, enabling an evaluation of treatment effectiveness. Furthermore, it provides detailed information about the process of change in the outcome and potential mediators of treatment response (Morley 2018; Morley, Vlaeyen, and Linton 2015; Kratochwill et al. 2010; Borckardt et al. 2008).

As well as facilitating more detailed assessment at more frequent time points than larger RCTs, single-case experimental designs involve the possibility to c*apture multiple potential mediators* which may be related to each person's presentation and response to a given intervention (Vlaeyen et al. 2012; MacKinnon 2008). As outlined earlier in this chapter, in a complex problem such as persistent LBP different patterns of mediator-outcome relationships may interplay temporally and vary at each timepoint (**Figure 4**). The interplay of these factors may potentially shape a person's response to treatment, leading to different individual trajectories of change, which may be influenced by different underlying factors (Morley 2018; Morley, Vlaeyen, and Linton 2015; Vlaeyen et al. 2012; MacKinnon 2008). SCEDs accommodate this interaction of multiple factors and the within-person temporal variations, therefore reflecting individuality in the evaluation of the therapeutic change process (Borckardt et al. 2008).

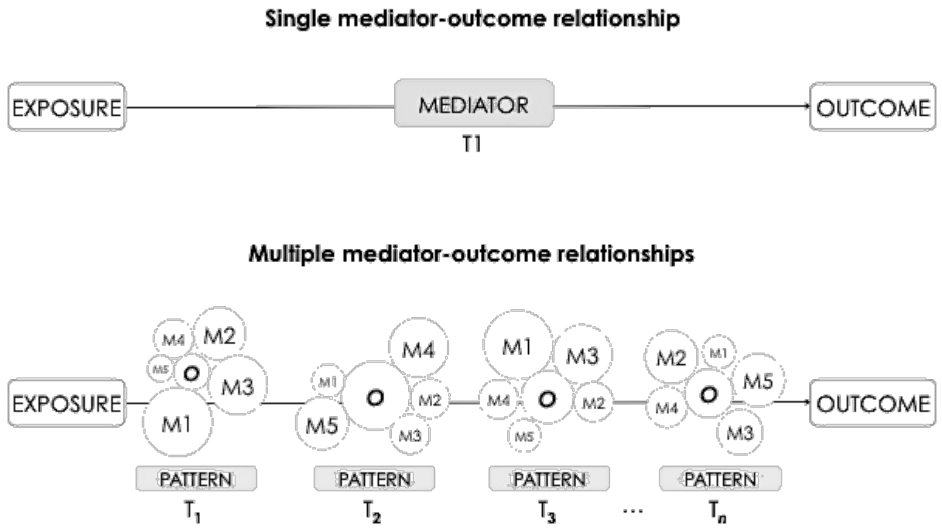

Figure 2.3 Schematic representation comparing single and multiple mediator-outcome relationships.

Note: Schematic representation comparing a mediator-outcome relationship at a single timepoint outlining causal mechanism (linear model, group analysis; common methodological framework: RCT) *versus*, multiple patterns of different mediator-outcome relationships at multiple timepoints outlining the process of change (non-linear, individual, complex model; potential methodological framework: SCED). ***Exposure*****:** treatment intervention; ***outcome*****:** selected outcome assessed post-intervention; ***T*****:** timepoint of assessment during intervention (from 1 to the n^{th} possibility); ***O:*** selected outcome assessed during the intervention; ***M*****:** mediators assessed during the intervention (number indicates different potential mediators); ***Pattern*****:** describes different patterns of relationships between the potential mediators and the selected outcome that can occur at each timepoint. ***Arrow*****:** causal pathway.

Overall, the features of SCEDs accommodate within-person temporal variability, between-person heterogeneity, the complexity of the problem and the complexity of individualized interventions (Morley 2018; Morley, Vlaeyen, and Linton 2015; Tate et al. 2017; Norell-Clarke, Nyander, and Jansson-Frojmark 2011; Borckardt et al. 2008). This is particularly relevant for the study of people living with persistent LBP and high pain-related fear, who present heterogeneous experiences influenced by different beliefs, lifestyle, social context, sensitivity profiles, emotional and behavioural responses (Bunzli et al. 2017). Larger group-level analysis frequently conducted in RCTs may lose these person-specific effects, informing on a summary or a common pathway to change, rather than a person's individual journey (Maric, Wiers, and Prins 2012). Thus, information gathered from SCEDs might be valuable to inform development, refinement, targeting and ultimately the testing of mediators in future RCTs.

2.3.4.6 Key Points

What is known and not known about temporal changes in persistent LBP and high pain-related fear?

- Although pain-related fear is one of the strongest modifiable predictors of disability in people with LBP the process by which pain-related fear is modified to reduce disability is unclear.

- Mediation analysis conducted in RCTs of complex interventions may be limited in terms of the ability to adequately inform on the process of change at an individual level.

- Single-case experimental design studies are inherently tailored to the individual, accommodating the between-person heterogeneity and within-person temporal variability commonly described in persistent LBP populations. These features indicate that SCEDs might provide an adequate framework to evaluate the change process, unravelling "the anatomy of therapeutic change" (Borckardt et al 2008).

- Thus far, no studies have used a SCED to specifically evaluate the process of change and factors that underlie treatment response in people with persistent LBP and high pain-related fear. This would allow to better understand "what changes when, for whom and why". Understanding this process and the factors that underlie treatment response in this group would be informative and valuable.

2.4 Summary

Low back pain is the leading cause of disability worldwide, placing a significant burden on society and impacting on people at various levels (i.e. cognitive, emotional, behavioural, social and lifestyle). Persistent LBP that is associated with high pain-related fear is disabling. The prevailing model that explains the pathway to disability is the fear avoidance model, which proposes that pain that is interpreted as a sign of threat leads to distress, avoidance, disengagement from valued activities and disability. However, several challenges have been posed to this model including, but not limited to the definition and role of fear and its relationship with pain. Modern understanding of the relationship between pain and fear poses that both can be considered emergent protective responses. This protective response is modulated by an array of influences across biopsychosocial domains, and is dependent on implicit evaluations of danger to the body and/or to a person's valued goals. Previous explorations to understand the role of 'fear' in the fear-avoidance model might have been limited in that they failed to provide a broader understanding of how people with persistent LBP and pain-related fear implicitly evaluate and physiologically respond to threats that are personally meaningful.

Pain-related fear is thought to be a key mediator of the relationship between pain and disability, supporting the notion that it is an important target for behavioural interventions. However, it is not clear what behavioural intervention works best for people with persistent LBP and high pain-related fear. Exposure-based interventions are grounded on the fear-avoidance model, and provide an adequate framework to manage pain-related fear. However, explorations of these approaches for people with persistent LBP and pain-related fear have yielded moderate treatment effects, raising some potential limitations to this approach. These include, the uni-dimensional nature of current approaches, the lack of a motivational perspective, not considering pain responses to movement and not targeting pain as a modifiable experience. Despite these limitations, there is a widely held notion that exposure-based interventions are the treatment of choice for people with high levels of pain-related fear. Nonetheless, the evidence for behavioural interventions in general or, specifically for exposure-based interventions for the management of people with persistent LBP and high pain-related fear has not been evaluated.

There is compelling evidence that persistent LBP is an individual experience influenced by multiple factors across the biopsychosocial spectrum. Recent studies have proposed that an individualized approach that is multidimensional in nature, goal-oriented and that promotes control over pain or its impact on daily life might promote change in the challenging group of people with persistent LBP and high pain-related fear. However, this has not been explored specifically in people with high pain-related fear.

Considering persistent LBP is an individual experience, 'how change unfolds' and 'what factors underlie change' at an individual level emerge as important questions. However, these questions have not been evaluated at an individual level. This review of the scientific literature suggests that a multiple SCED study is an adequate framework for such an evaluation as it accommodates the between-person heterogeneity, within-person variability over time, and enables assessment of multiple factors at multiple timepoints. Information from this evaluation may give insight to the anatomy of the therapeutic change at an individual level, and inform design, refinement and mediation testing in future RCTs.

2.5 Aims of Thesis

1. To investigate implicit evaluations of danger and physiological responses to images of people bending and lifting with a flexed lumbar spine (round-back), in people with persistent LBP reporting different levels of self-reported fear of bending with a round-back. It was hypothesized that people who differ in self-reported fear of bending with a round-back would also differ in implicit evaluations and physiological responses.

2. To determine the current state of evidence concerning the effectiveness (in terms of disability, pain and fear reduction) of behavioural interventions intentionally designed for people with persistent LBP and high pain-related fear.

3. To evaluate temporal changes in pain-related fear (generic fear beliefs and specific fear of bending), and pain (pain expectancy and pain experience related to bending with a round-back), in a person with persistent LBP and high pain-related fear undergoing Cognitive Functional Therapy intervention. The use of clinical interviews at 6, 12 and 18 month follow-ups will allow to explore qualitative factors underlying this process of change.

4.

a. To evaluate temporal changes in outcome (disability) and factors that underlie treatment response (potential mediators from cognitive and emotional dimensions) before, during and after (three months) a three-month Cognitive Functional Therapy intervention in four people with persistent LBP and high pain-related fear.

b. To evaluate how changes in potential mediators related to changes in disability at different timepoints during a Cognitive Functional Therapy intervention in four people with persistent LBP and high pain-related fear.

2.6 Significance of Thesis

This body of research is responding to challenges posed to the current understanding and management of people with persistent LBP and high pain-related fear. The results of this work will provide insight into the understanding of the relationship between 'fear' and pain, and inform current practice about the current state of evidence concerning the effectiveness of behavioural interventions for the management of people with persistent LBP and high pain-related fear. This research will utilize an individualized physiotherapy-led multidimensional approach called CFT, which is grounded on foundational behavioural sciences and the common-sense model to promote change in people that are disabled by LBP and high pain-related fear.

Thus far, no studies have evaluated the process of change in people with persistent LBP and high pain-related fear at an individual level. The evaluation of temporal changes in disability and factors that underlie treatment response will provide insight to individual pathways and patterns of therapeutic change.

Overall, the results of this body of research will inform clinical practice by providing an understanding of the key factors that need targeting to promote change in this challenging group of patients. Furthermore, this study will inform the design, refinement of interventions and mediator testing in future RCTs.

Chapter 3 Experimental study - Implicit evaluations and physiological threat responses in people with persistent low back pain and fear of bending

Modern understanding of the relationship between pain and fear poses that both can be considered emergent protective responses. This protective response is modulated by an array of influences across biopsychosocial domains, and is dependent on implicit evaluations of danger to the body and/or to a person's valued goals. The fear-avoidance model describes how pain that is interpreted as threatening leads to an unhelpful cycle of fear, avoidance, and disability. Previous explorations to understand the role of fear in the fear-avoidance model might have been limited in that they failed to provide a broader understanding of how people with persistent LBP and pain-related fear implicitly evaluate and physiologically respond to threats that are personally meaningful.

The aim of this study was to investigate implicit evaluations of danger and physiological responses to images of people bending and lifting with a flexed lumbar spine (round-back), in people with persistent LBP reporting different levels of self-reported fear of bending with a round-back. It was hypothesized that people who differ in self-reported fear of bending with a round-back would also differ in implicit evaluations and physiological responses.

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3.1 Abstract

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Clinical pain research

Implicit evaluations and physiological threat responses in people with persistent low back pain and fear of bending

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HIGHLIGHTS

- Self-report does not always reflect implicit associations of movement and threat.
- People with back pain showed implicit associations between bending and danger.
- Viewing a threat was not sufficient to elicit physiological defensive responses.
- Exposure to unavoidable movement may be needed to elicit physiological responses.
- Results are consistent with contemporary views on 'fear' in the fear-avoidance model.

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ABSTRACT

Background and aims: Pain and protective behaviour are dependent on implicit evaluations of danger to the body. However, current assessment of perceived danger relies on self-report, on information of which the person is aware and willing to disclose. To overcome this limitation, attempts have been made to investigate implicit evaluation of movement-related threatening images in people with persistent low back pain (PLBP) and pain-related fear. Lack of specificity of the sample and stimuli limited those explorations. This study investigated implicit evaluations and physiological responses to images of tasks commonly reported as threatening by people with PLBP: bending and lifting. We hypothesized that people who differ in self-reported fear of bending with a flexed lumbar spine (*fear of bending*) would also differ in implicit evaluations and physiological responses.

Methods: This study used a convenience sample of 44 people (54% female) with PLBP, who differed in self-reported *fear of bending*. Participants completed a picture-viewing paradigm with pleasant, neutral and unpleasant images, and images of people bending and lifting with a flexed lumbar spine ('round-back') to assess physiological responses (eye-blink startle modulation, skin conductance). They also completed an implicit association test (IAT) and an affective priming task (APT). Both assessed implicit associations between (i) images of people bending/lifting with a flexed lumbar spine posture ('round-back' posture) or bending/lifting with a straight lumbar spine posture ('straight-back' posture), and (ii) perceived threat (safe vs. dangerous).

Results: An implicit association between 'danger' and 'round-back' bending/lifting was evident in all participants (IAT (0.5, CI [0.3; 0.6]; $p < 0.001$) and APT (24.2, CI [4.2; 44.3]; $p = 0.019$)), and unrelated to self-reported fear of bending (IAT ($r = -0.24$, 95% CI [−0.5, 0.04], $p = 0.117$) and APT ($r = -0.00$, 95% CI [−0.3, 0.3], $p = 0.985$)). Levels of self-reported fear of bending were not associated with eye-blink startle ($F(3, 114) = 0.7$, $p = 0.548$) or skin conductance responses ($F(3, 126) = 0.4$, $p = 0.780$) to pictures of bending/lifting.

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3.2 Introduction

Conclusions: Contrary to our expectation, self-reported fear of bending was not related to physiological startle response or implicit measures. People with PLBP as a group (irrespective of fear levels) showed an implicit association between images of a round-back bending/lifting posture and danger, but did not display elevated physiological responses to these images. These results provide insight to the understanding of the relationship between pain and fear of movement.
Implications: The potential clinical implications of our findings are twofold. First, these results indicate that self-report measures do not always reflect implicit associations between particular movements and threat. Implicit association tasks may help overcome this limitation. Second, a lack of the predicted physiological and behavioural responses may reflect that the visualization of a threatening task by people in pain does not elicit the same physiological defensive responses measured in people with fear of specific objects. It may be necessary to expose the person to the actual movement to elicit threat-responses. Together, these results are consistent with current views of the role of 'fear' in the fear-avoidance model, in which a fear response may only be elicited when the threat is unavoidable.

1. Introduction

Modern understanding of the relationship between pain and fear poses that both can be considered emergent protective feelings [1,2], broadly captured by the idea that pain emerges when the organism concludes that a body part needs protecting and fear emerges when the organism concludes that the entire body needs protecting [3–5]. Within this conceptualization, pain and fear are dependent on implicit evaluations of danger to the body [3–5]. However, current assessment of perceived danger to the body relies solely on explicit, or self-report, measures [6–8], which require conscious reflection, only accessing information of which a person is aware and which they are willing to disclose [1,9–11]. To overcome this limitation, attempts have been made to investigate implicit evaluation of movement-related threatening images in people with persistent low back pain (PLBP) and pain-related fear [1,2,12].

Explorations of implicit attitudes of people with PLBP found no implicit association between 'danger words' and movement-related threatening images, despite participants explicitly evaluating the stimuli as aversive [1,2]. A common limitation of these studies [1,2,12] was the use of a wide range of threatening images (e.g. driving, hanging a coat, digging, running) [1,2] and words (e.g. warning, AIDS, fatal) [1,2]. Those stimuli lack threat-specificity, which is an important aspect of fear/danger assessment [13,14].

Investigations of physiological threat-responses in people with PLBP and pain-related fear [12–14] report mixed results [14]. One study found that people with high fear display enhanced autonomic arousal (indexed by skin conductance) in anticipation of performing a task they perceived as harmful [15]. Different from autonomic arousal measures, eye-blink startle modulation enables assessment of the emotional valence of stimuli [16–18]. Thus far, only one study recorded eye-blink startle as a measure of threat-responses in people with PLBP [12], and found no difference between those reporting high and low fear beliefs [12] when presented with pictures of back pain-related movements (e.g. bending and rotation). Although a pilot sample determined the images were sufficiently aversive, participants did not report feeling 'fearful' of performing the depicted tasks [12]. That study may have been limited by a non-specific sample, based on a generic fear-avoidance beliefs questionnaire [12], and by not using task-specific or personally-threatening stimuli.

Considering that threat-specificity is critical for evaluating perceived danger to the body, the current study selected a group of people with PLBP reporting different levels of explicit fear of bending with a flexed lumbar spine (*fear of bending*). This movement was chosen because bending and lifting are one of the most feared tasks for people with and without LBP, holding a high threat-value in western society [19–23]. To investigate implicit evaluations of danger, we employed implicit measures of attitude (affective priming task – APT [28], and implicit association test – IAT [19]), and physiological responses (eye-blink startle modulation [16–18], and skin conductance [15,18]) to images of people bending and lifting with a flexed lumbar spine ('round-back' posture). We hypothesized that: (1) Higher levels of explicit *fear of bending* would be positively associated with higher levels of implicit association between round-back bending/lifting and danger. (2) Physiological threat-responses to pictures of round-back bending/lifting would be enhanced in people with higher self-reported *fear of bending*.

2. Materials and methods

This section and Table 1 report only key aspects of the methodology. Full detailed methods are provided in Appendix.

2.1. Study design

Exploratory cross-sectional experimental study.

2.2. Participants and recruitment

Participants were sequentially recruited from a cohort who had indicated willingness to participate in future studies [24], and via physiotherapists and general practitioners. Adults aged 18 years and older with dominant axial low back pain (LBP), greater than 6 months duration, and average pain in the past week ≥3/10 on the Numerical Rating Scale (NRS: 0–10 – Appendix), were included in the study. Participants who reported red flags, dominant leg pain, radicular pain with nerve compression, uncorrected hearing impairment (restriction for the acoustic stimulus during the eye-blink startle), pregnancy, taking opioids, or were unable to read English were excluded. Long-term analgesics or medications for other co-morbidities were allowed, however participants were asked not to take non-prescribed analgesics on experiment day.

To ensure balanced sequential recruitment of equal numbers of participants with and without fear of bending, potential participants were screened over the phone with the question: "*Are you fearful of reaching to the floor without bending your knees? Yes or No*". Recruitment continued until a minimum of 20 participants in both groups was reached.

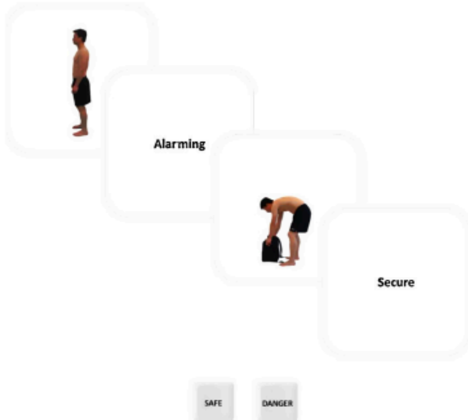
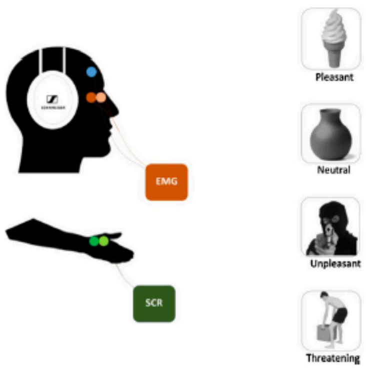
The study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences-Curtin University (HR157/2015). All participants provided informed consent.

3.3 Material and Methods

Table 1
Summary description of the implicit and physiology measures.

Measure	Stimulus		Procedure	Schematic representation
IAT	Target: back posture (*round-back* and *straight-back*) Pictures of a person bending and lifting objects with a flexed lumbar spine ("Round-back"), and with a straight spine ("Straight-back").	Attribute: perceived risk to the spine (*Safe* and *Danger*) Words[a] [32,33]: "Danger": *damaging, vulnerable, threatening, alarming, risky, unpredictable.* "Safe": *harmless, confident, secure, protecting, certainty, reliable.*	*The IAT consisted of 7 phases:* Phase1 (target-discrimination): 20 trials. Phase 2 (*attribute*-discrimination): 20 trials. Phases 3–4 (*combined*-discrimination): 30 and 40 trials/each. Phase 5 (*target*-discrimination): 20 trials Phases 6–7 (*combined*-discrimination): 40 trials/each. Each trial started with the display of a fixation cross for 1000 ms followed by a word or image for 1000 ms and an intertrial interval of 1000 ms. To sort the stimuli, participants pressed the left "Shift" key for categories displayed in the left upper corner of the screen, and the right "Shift" key for categories displayed in the right upper corner of the screen. On each trial the participant was given feedback ("correct" or "wrong"). Categories remained on screen throughout an entire phase.	

Table 1 (*Continued*)

Measure	Stimulus		Procedure	Schematic representation
APT	Target: Words[a] [32,33] related to safe and danger. "Danger": *damaging, vulnerable, threatening, alarming, risky, unpredictable.* "Safe": *harmless, confident, secure, protecting, certainty, reliable.*	Prime: images of a person standing adopting a flexed lumbar spine posture while bending or lifting.	The APT consisted of 8 blocks of 12 trials involving the presentation of a negative or positive word that was preceded by one of the prime pictures. Each block consisted of 6 affectively congruent (straight–safe, bending–dangerous) and 6 affectively incongruent image-word pairs (straight– dangerous, bending–safe). Each trial began with the presentation of two white fixation crosses in the centre of a black screen for 200 ms, a picture for 200 ms, a black screen for 100 ms, and a word for 1 s or until the participant responded by pressing either button. The intertrial interval was 1 s. A series of positive and negative *target* words was presented. Participants were instructed to decide whether the word represented the category "Safe" or "Danger", by pressing left "Shift" key for "Safe", and the right "Shift" key for "Danger". Each target was preceded by a *prime* picture.	
	Four categories of pictures (*neutral, pleasant, unpleasant* and *bending/lifting*) were represented by six images each.			
Picture viewing	*Pictures in the first three categories were selected from the IAPS*[b] [35]: *neutral:* rolling pin (7000), towel (7002), mug (7009), wooden stool (70,025), lamp (7175), clock (7211); *pleasant:* wedding (4626), children (2347), ice cream (7330), fireworks (5480), beach (5833), man and woman kissing (4660); *unpleasant:* snake (1050), spider (1201), shark (1930), baby with eye lesion (3170), aimed gun (6230), attack (3530).	*The bending and lifting-related pictures were selected from* PHODA-SeV[c] [6] and round-back lifting from IAT (as per example depicted here). *Bending/lifting:* shovelling (2), lifting a pot plant (4), 20 (lifting a heavy crate out of car), 27 (unloading dishwasher), 29 (vacuuming), 33 (mopping the floor), 83 (picking up a toddler).	Participants looked at the blank computer screen for 3 minutes, while baseline data were collected. After baseline, the picture-viewing task was initiated. Three startle probes were administered to reduce the novelty of the startle probe and the 24 pictures were presented pseudo randomly such that no more than two pictures from the same category were presented in a row. Four picture sequences were predetermined and counterbalanced across participants. Probes were presented at 3.5 s or 4.5 s after picture onset during four of the six pictures per category as well as during one third of the inter-picture intervals. Participants were asked to relate to the bending and lifting pictures by imagining they were performing the action displayed.	

[a] Words selected from interviews with people with PLBP and high pain-related fear [32,33].
[b] IAPS – International Affective Pictorial System [35].
[c] PHODA-SeV – Photographs of Daily Living Activities-Short Electronic Version [6].

3.4 Experimental procedure

2.3. Outcome measures

This study involved three computer-based tasks measuring implicit attitudes (IAT, APT) and psychophysiology (eye-blink startle modulation and skin conductance response) related to bending and lifting back posture and perceived threat to the spine.

2.3.1. Beliefs

2.3.1.1. Explicit measures. To minimize potential influence of self-report assessments on results, the following questionnaires were completed online a week prior data collection: fear of bending (FearBend), pain-related fear (TSK) [8], pain-anxiety (PASS-20) [7], disability (RMDQ) [25], and pain in the past week.

2.3.1.1.1. Fear of bending. To assess fear of bending with a flexed lumbar spine (herewith called *fear of bending*), participants were presented with a side view picture of a person bending forward with a flexed lumbar spine, straight knees and fingers touching the floor, followed by the question: *"How fearful are you of reaching to the floor without bending your knees?"* (NRS anchored on "0: No fear of bending", and "10: Maximum fear of bending"). This measure (FearBend) ensured specificity of the fear-provoking task [6].

The FearBend question was adapted from the item "reaching to the floor" from the Fear of Daily Activities Questionnaire [26], which has sound psychometric properties and adequate reliability in determining fear of specific activities [26].

2.3.1.1.2. Pain-related fear, anxiety and disability. These measures were taken for sample descriptive purposes. Pain-related fear beliefs were assessed with the *Tampa Scale of Kinesiophobia-TSK* [8,27]. Pain-related anxiety symptoms were assessed with the *Pain Anxiety Symptoms Scale-PASS-20* [7]. Pain-related disability was assessed with the *Roland Morris Disability Questionnaire-RMDQ* [25,28]. Psychometric properties and descriptions of scoring ranges for these well-established questionnaires are detailed in Appendix.

2.3.1.1.3. Demographic data. A questionnaire including age, LBP duration and pain intensity (NRS: 0 = 'no pain' and 10 = 'worst pain' – Appendix) was completed on experiment day.

2.3.1.2. Implicit measures. The IAT [11] and the APT [29] are well-established measures, which were adapted for this study to assess associations between bending/lifting posture and risk (Table 1). In the IAT, five stimuli representing each target ("Round-back" and "Straight-back") and attribute category ("Safe" and "Danger") were presented. Participants had to assign a single stimulus displayed in the centre of the screen to its proper category (displayed at the upper corners of the screen), by pressing the left or right "Shift" key as fast as possible while avoiding mistakes. A bias score ($IAT_{D\text{-}score}$) was calculated using the improved scoring algorithm recommended by Greenwald et al. [63] with an error penalty of 2 standard deviations (see Appendix for details). The IAT exhibits adequate reliability and, internal, construct and predictive validity [11,30].

In the APT, a series of positive and negative target words was presented (for 10 s or until a response was made), which had to be evaluated as either "safe" or "dangerous" by pressing the right or left "Shift" key, respectively. Each target word was preceded by a prime picture of person standing or bending/lifting with a round-back (for 200 ms) – see Appendix for APT priming score calculation. The APT presents adequate predictive validity [10] and sensitivity [31].

The category "Danger" was represented by six words (selected from interviews with people with PLBP and high-fear [32,33]) frequently used to describe danger associated with movement. Words matching in length, frequency, and emotionality represented the category "Safe" [34]. Twelve side view images of males and females standing, bending and lifting with a straight ("Straight-back") and flexed lumbar spine ("Round-back"), were developed for this experiment after piloting with people with PLBP to confirm their suitability (Table 1).

2.3.1.3. Physiological measures. Using a picture-viewing paradigm, participants' eye-blink startle reflex and skin conductance were assessed in response to four categories of foreground stimulus: *neutral*; *pleasant*; *unpleasant*; and *bending/lifting*, represented by six images each. Pictures in the first three categories were selected from the International Affective Picture System (IAPS [35]). Bending/lifting images (persons bending/lifting with a flexed lumbar spine) were selected from PHODA-SeV (Photographs of Daily Activities-Short electronic version – a valid and reliable measure of perceived harmfulness of activities) [6] (Table 1). During the presentation of bending/lifting images, participants were instructed to imagine themselves performing the action displayed.

The primary outcomes for startle blink reflex were eye-blink EMG magnitude and response latency (Appendix). The startle probe used to elicit a response was a 105dBA burst of white noise with instantaneous rise time, generated with a custom-built noise generator and presented to both ears for 50 ms through Sennheiser headphones (HD 25-1; 70 Ω). Orbicularis oculi electromyographic activity (EMG) was measured using two 4 mm Ag/AgCl electrodes placed underneath the participant's left eye (1 cm apart), and a ground electrode placed on the centre of the forehead. All electrodes were connected to a BIOPAC EMG amplifier (amplification: 5000; filters: low pass of 500 Hz and high pass of 10 Hz). Skin conductance response (SCR) was recorded with two pre-gelled Ag/AgCl electrodes attached to the thenar and hypothenar eminences of the participant's non-dominant hand. Electrodes were connected to BIOPAC SCR amplifier with a gain of 2 µS/V. The primary outcome for SCR was the magnitude of the increase in skin conductance (Appendix).

Picture rating: At the end of this task, each picture was rated on dimensions of pleasantness and arousal, using a 9-point scale ('1': unpleasant/low arousal; '9': pleasant/high arousal). The keyboard keys 1–9 were used to record the values for each image (Full protocol in Appendix).

2.4. Experimental procedure

All data collection was undertaken in the Emotion, Learning and Psychophysiology Laboratory, School of Psychology & Speech Pathology, Curtin University, Western Australia, and lasted approximately 80 min. Participants were told the experiment related to measuring their body's reaction and automatic thinking processes while looking at words and images representing daily activities. To minimize potential for task interference, assessment of physiological response was performed first. The order in which the implicit tasks were performed was counterbalanced using a Latin-square design.

Data processing, scoring and response definition followed standard procedure for each task (details in Appendix).

2.5. Statistical analysis

Descriptive statistics were used to describe participants' characteristics and scores on the self-reported questionnaires. Pearson's correlations between self-reported measures (TSK, PASS-20), and fear of bending (FearBend) were calculated.

One-sample *t*-tests were used to evaluate the size (and 95% confidence intervals) and significance of the sample mean deviation from zero, which indicates the direction of the implicit bias. A positive score indicates an implicit bias to associate "round-back" and "danger". Pearson's correlation was used to evaluate

3.5 Results

associations between the magnitude of implicit bias (i.e. IAT_{D_score} and APT_{Diff_score}) and fear of bending (FearBend).

To test differences in eye-blink latency, eye-blink magnitude, SCR magnitude and ratings across each picture conditions (pleasant, unpleasant, neutral and bending/lifting) a mixed model ANOVA (RM ANOVA) with FearBend as a covariate was used. A picture condition*fear of bending interaction was evaluated to test whether the pattern of responses differed according to the degree of FearBend. The effect size measure η_p^2 is reported for significant effects. For interpretative purposes only, graphical results are provided for the interaction test of picture condition*fear of bending by splitting the sample into groups based on fear of bending level. A score of >5 indicates high *fear of bending* (23 participants; 52.3%), while ≤5 indicates low *fear of bending* (21 participants; 47.7%).

Greenhouse–Geisser corrections were applied when the assumption of sphericity was violated. Corrected degrees of freedom and corrected *p*-values are reported together with ε. All statistical analyses were run using IBM SPSS Statistics 24.

2.5.1. Power analysis

An a priori power calculation indicated a sample of 40 participants would provide 80% power to detect small to moderate effect size of $\eta_p^2 = 0.05$ to 0.08 for condition*fear interactions, at $\alpha = 0.05$ and assuming a conservative intra-subject correlation of 0.3 between conditions (GPower Version 3.1.9).

3. Results

3.1. Demographics

Forty-four people with PLBP (54% female) participated in the study. The mean (SD) age was 50 years (14; range 24–72), pain duration was 16 years (13; range 1–50), pain intensity in the week prior to the experiment was 4.8 (2.3), and pain on the day was 3.7 (1.9). The mean disability index on RMDQ was 8.2 (34%) (SD = 5).

3.2. Beliefs

3.2.1. Explicit measures

The mean level of self-reported specific fear of bending (FearBend) was 4.4 (SD = 3.3; range 0–10). The mean level of pain-related fear (TSK) was 41.0 (SD = 9.0; range 22–59), and pain-anxiety (PASS-20) 37.5 (SD = 21.8; range 2–89).

There were high correlations between self-reported FearBend and TSK ($r = 0.68$, 95% CI [0.51, 0.81], $p < 0.001$), between FearBend and PASS-20 ($r = 0.62$, 95% CI [0.40, 0.81], $p < 0.001$); and between TSK and PASS-20 ($r = 0.66$, 95% CI [0.45, 0.82], $p < 0.001$).

3.2.2. Implicit measures

The mean IAT_{D_score} (Mean = 0.46, 95% CI [0.30, 0.61]) was significantly larger than zero ($t(43) = 5.8$, $p < 0.001$), which indicates an implicit bias towards the association between pictures of bending/lifting with a 'round-back' and 'danger' words. There was no correlation between FearBend and the IAT_{D_score} ($r = -0.24$, 95% CI [−0.50, 0.044], $p = 0.117$).

APT data from six participants were invalid due to response times larger than 1000 ms, which suggests a lack of automatic target evaluation. The mean APT_{Diff_score} ($N = 38$, Mean = 24.2, 95% CI [4.2, 44.3]) was also significantly larger than zero ($t(37) = 2.4$, $p = 0.019$), which indicates an association between pictures of bending/lifting and 'round-back' and 'danger' words. There was no correlation between FearBend and the APT_{Diff_score} ($r = -0.00$, 95% CI [−0.30, 0.30], $p = 0.985$).

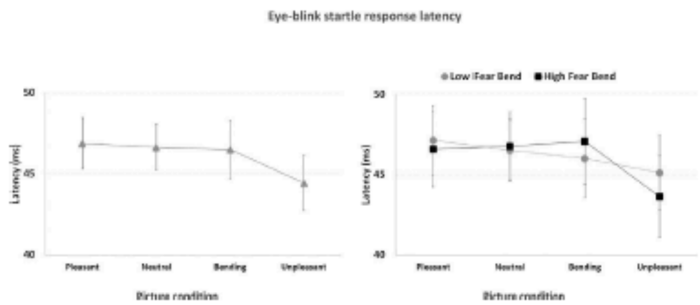


Fig. 1. Estimated means of eye-blink response latency across picture conditions. Bars indicate Standard Error (SE). Participants grouped by high (>5) and low (≤5) levels of *fear of bending*.

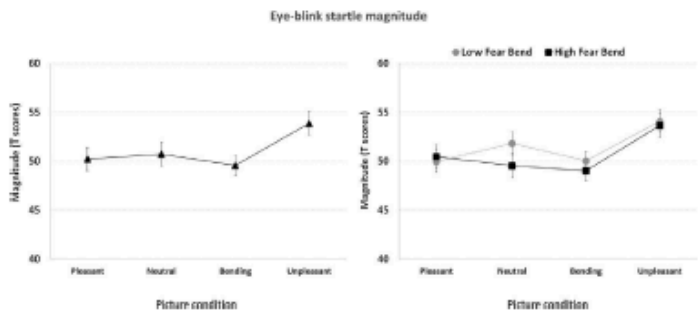


Fig. 2. Estimated means of eye-blink magnitude across picture conditions. Bars indicate Standard Error (SE). Participants grouped by high (>5) and low (≤5) levels of *fear of bending*.

3.6 Discussion

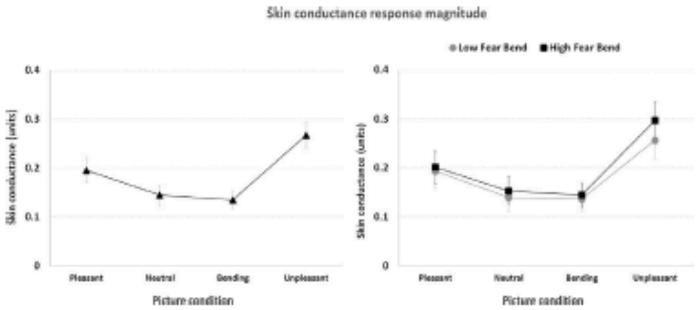


Fig. 3. Estimate means of skin conductance magnitude across picture conditions. Bars indicate Standard Error (SE). Participants grouped by high (>5) and low (≤5) levels of *fear of bending*.

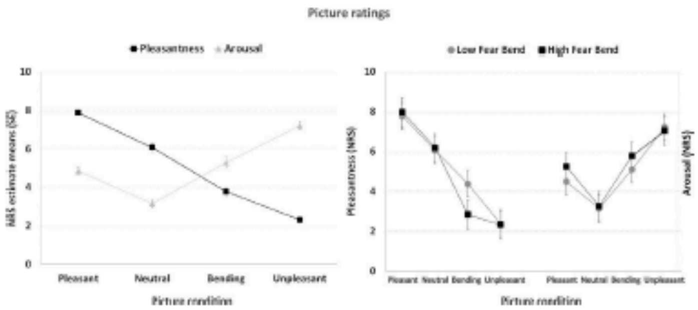


Fig. 4. Estimated means of picture ratings across picture conditions. Bars indicate Standard Error (SE). Participants grouped by high (>5) and low (≤5) levels of *fear of bending*.

3.3. Physiological measures

3.3.1. Eye-blink response latency

Eye-blink response latency did not differ across picture conditions ($F(2.5, 81.8) = 0.2$, $p = 0.878$). Similarly, eye-blink latency across picture conditions did not differ according to self-reported level of fear of bending (FearBend) (picture condition*fear of bending interaction $F(2.5, 81.8) = 0.6$, $p = 0.614$) (Fig. 1).

3.3.2. Eye-blink magnitude

As shown in Fig. 2, the eye-blink magnitude differed across picture conditions ($F(3, 114) = 4.7$, $p = 0.04$, $\varepsilon = 0.938$, $\eta_p^2 = 0.109$). Contrasts indicated larger eye-blink magnitude to probes during unpleasant pictures than during pleasant ($F(1, 38) = 8.2$, $p = 0.007$, $\eta_p^2 = 0.177$), neutral ($F(1, 38) = 5.7$, $p = 0.022$, $\eta_p^2 = 0.131$) and bending/lifting pictures ($F(1, 38) = 12.3$, $p = 0.001$, $\eta_p^2 = 0.245$). The eye-blink magnitude across picture conditions did not differ according to level of fear of bending (FearBend) (picture condition*fear of bending interaction $F(3, 114) = 0.7$, $p = 0.548$).

3.4. Skin conductance response

Participant's SCR differed according to the type of picture viewed ($F(3, 126) = 3.2$, $p = 0.026$, $\varepsilon = 0.903$, $\eta_p^2 = 0.070$). As displayed in Fig. 3, the SCRs to unpleasant pictures were significantly larger than to bending/lifting pictures ($F(1, 42) = 7.4$, $p = 0.009$, $\varepsilon = 0.903$, $\eta_p^2 = 0.150$). However, there was no difference in emotional arousal across picture conditions according to level of fear of bending (FearBend) (picture condition*fear of bending interaction $F(3, 126) = 0.4$, $p = 0.780$).

3.4.1. Subjective evaluation of picture conditions

Pleasantness ($F(2.5, 99.8) = 56.2$, $p < 0.001$, $\varepsilon = 0.831$, $\eta_p^2 = 0.584$) and arousal ratings ($F(2.3, 96.0) = 21.0$, $p < 0.001$, $\varepsilon = 0.781$, $\eta_p^2 = 0.339$) differed across picture conditions (Fig. 4). Contrasts indicated that bending/lifting pictures were rated as less pleasant than neutral ($F(1, 40) = 45.5$, $p < 0.001$, $\eta_p^2 = 0.532$) and pleasant ($F(1, 40) = 205.0$, $p < 0.001$, $\eta_p^2 = 0.837$) pictures, but more pleasant than unpleasant pictures ($F(1, 40) = 30.5$, $p < 0.001$, $\eta_p^2 = 0.433$). Bending/lifting pictures were rated as more arousing than pleasant ($F(1, 41) = 26.75$, $p < 0.001$, $\eta_p^2 = 0.395$) and neutral pictures ($F(1, 41) = 62.945$, $p < 0.001$, $\eta_p^2 = 0.606$), but less arousing than unpleasant pictures ($F(1, 41) = 28.3$, $p < 0.001$, $\eta_p^2 = 0.408$).

There was an interaction between FearBend and picture condition for pleasantness ratings ($F(2.5, 99.7) = 6.7$, $p = 0.001$, $\eta_p^2 = 0.144$). As shown in Fig. 4, participants with higher FearBend rated the bending/lifting pictures as less pleasant ($F(1, 40) = 12.4$, $p = 0.01$, $\eta_p^2 = 0.236$). In contrast, there was no interaction for arousal ratings ($F(2.3, 96.1) = 1.2$, $p = 0.319$).

4. Discussion

This study investigated implicit evaluations and physiological responses to images of bending and lifting in people with PLBP, who differed in self-reported fear of bending with a flexed lumbar spine (*fear of bending*). Contrary to our hypotheses, *fear of bending* was not associated with implicit evaluations or physiological responses to viewing images of people bending and lifting with a flexed lumbar spine ('round-back' posture). Participants were faster to associate images of bending/lifting with a 'round-back' with words representing 'danger' rather than with words representing 'safety'. This indicates that people with PLBP display an implicit 'danger bias' towards bending and lifting with a flexed lumbar spine. Critically, that bias is unrelated to their self-reported fear of bending.

3.7 Conclusion

Previous explorations that investigated people with and without PLBP and high fear of movement have not found evidence of implicit association between a wide range of back-related movements and danger in PLBP [1,2]. In contrast, the current study used images of bending and lifting for the implicit tasks, because these have been reported to be the two most commonly feared and pain-provoking movements for people with and without LBP [36–39]. Specifically, we used images of bending/lifting in two distinct postures that are often advocated as ergonomically safe ('straight-back') and dangerous ('round-back') [40,41]. In addition, the words representing 'danger' in our study are highly relevant for this population, as they were selected from interviews with people with PLBP and high pain-related fear [32,33]. Interestingly, despite this enhanced level of stimulus specificity, there was no association between higher self-reported fear and an implicit 'danger bias' to bending/lifting with a 'round-back'. These findings suggest that people with PLBP have discordant explicit beliefs but share concordant implicit beliefs about bending and lifting back posture, and danger.

In terms of physiology, participants' responses across the picture conditions was not associated with self-reported fear level. Blink startle potentiation and skin conductance responses were higher during unpleasant pictures than during other picture categories, confirming the sensitivity of the picture-viewing paradigm [42]. However, despite the personally-relevant nature of the stimuli and irrespective of self-reported fear, participants did not present a typical physiological threat response pattern to images of threatening bending/lifting tasks. Such response would be typically represented by enhanced eye-blink magnitude and skin conductance responses, similar to or higher than those during unpleasant images [16,18].

These findings are at odds with previous work in specific fears/phobias in which a defensive response is activated even by the symbolic representation of the feared object (e.g. spiders) [43,44]. Nevertheless, this result is in line with other studies that investigated threat responses to images of threatening tasks in people with PLBP using eye-blink startle [12], heart rate and back muscle activity [13] and fMRI [14]. Only one study has found physiological response differences between people with high and low fear, and notably, this was when participants with PLBP were led to believe they had to actually perform the lifting task that they reported to be harmful [15]. While recent fMRI studies have demonstrated that viewing movement-related threatening images [45] and imagining performing these movements [46] was sufficient to activate brain regions associated with threat-processing, the findings in this study confirm previous results using eye-blink startle modulation [12]. That is, simply viewing and imagining performing a threatening task seems insufficient to activate a defensive response in persons with PLBP, even when confronted with personally-relevant stimuli. It appears that visual images of spiders still hold immediate protection value, but visual images of other people performing a task do not. In order to induce a physiological response a person may need to be confronted with the task [15,47].

Contemporary understanding of threat-processing proposes fear as an intertwined cognitive-emotional process, in which the amygdala plays an important role [48,49]. In the presence of a stimulus, a fundamental function of the amygdala, is related to determining "what is it?", and also "what needs to be done?", thus guiding decision-making [48]. In this study, it is plausible to speculate that while the stimuli were implicitly detected, and likely identified as threatening, there was no imminent threat to the person and no protective action required. That is, in this context the conclusion may have been that "nothing needed to be done", resulting in no physiological response. While the results of the current study contradict our initial predictions, they lend support to more recent views of the role of 'fear' in the fear-avoidance model, in which defensive responses (physiology and behaviour) vary according to context and motivation [50,51], and are most prominent when the threat is unavoidable [15,50,52].

According to the common sense model of self-regulation [53], when a person experiences pain, their behavioural response is influenced by their pre-existing *schema*, which is informed by media, healthcare providers, family, friends, their own experience and that of others [33]. Considering the general belief that the back is vulnerable [22,23,54,55], it is plausible to infer that a person's schema includes information that is congruent with the idea that bending and lifting with a round-back represents danger to their back or to their goals. Experimental studies, investigating how movements of the back are perceived by asymptomatic subjects [2,45,56], suggest that '*the back is vulnerable to bending and lifting*' may in fact be a *common schema*.

Modern conceptualization of pain would support that an implicit association between danger and forward bending with a flexed spine could potentially influence both pain and behavioural responses to the 'dangerous' task [3–5]. In the context of our results, we speculate that once pain is felt during bending or lifting, it provides a salient learning experience [33,50,57] in which a '*protect the back*' *schema* may be activated. In line with this thinking, experimental studies have reported pain reduction during forward bending following interventions that aim to de-threaten bending via pain education [58], the use of visual observation of the spine during the movement [59], or providing cognitive and functional control during behavioural exposure [60]. Together, our results provide support for the argument that self-reported pain-related fear may be more cognitively-driven, in which an unhelpful schema may influence avoidance behaviour, and a physiological threat-response may only occur when the person is exposed to the task itself [15,61].

A potential weakness of this study is the use of visual stimuli only, rather than inducing participants to believe they would be required to actually perform the tasks. Although the eye-blink startle has been successfully used previously to assess physiological responses in threat-specific picture-viewing paradigms [43,44], people with PLBP may need to be exposed to the task itself to elicit these responses. Future studies may benefit from investigating physiological startle response in anticipation of and during performance of back-related threatening tasks. Another limitation is the lack of a pain-free group, which could have informed whether these findings are unique to people with PLBP, although we were interested in how people with similar pain but different self-reported fear of bending compare, not in how people with and without pain compare. A unique aspect of this study was the use of combined implicit and physiology measures to compare people with PLBP with high or low fear of tasks relevant to PLBP (bending and lifting), using stimuli specific to these tasks and that holds a societal threat-value.

5. Conclusion

Contrary to our expectation, self-reported fear of bending was not related to physiological startle responses or implicit measures. People with PLBP as a group showed an implicit association between images of a round-back bending/lifting posture and danger, but did not display elevated physiological responses to these images. These results provide insight to the understanding of the relationship between pain and fear of movement.

6. Implications

The findings of this study suggest that independent of explicitly reported fear levels, people with PLBP implicitly associate bending and lifting with a flexed spine with danger, but this is not

3.8 Appendix

accompanied by enhanced physiological threat-related responses. The potential clinical implications of our findings are twofold. First, these results indicate that self-report measures do not always reflect implicit associations between particular movements and threat. Implicit association tasks may help overcome this limitation. Second, a lack of the predicted physiological and behavioural responses may reflect that the visualization of a threatening task by people in pain does not elicit the same physiological defensive responses measured in people with fear of specific objects. It may be necessary to expose the person to the actual movement to elicit threat-responses. Together, these results are consistent with current views of the role of 'fear' in the fear-avoidance model, in which a fear response may only be elicited when the threat is unavoidable.

Ethical issues

The study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences-Curtin University (HR157/2015). All participants provided informed consent.

Conflicts of interest

Peter O'Sullivan receives speaker fees for workshops on pain management. G. Lorimer Moseley has received support from Pfizer, Kaiser Permanente, USA; Workers' Compensation Boards in Australia, North America, and Europe; Agile Physiotherapy, USA; Results Physiotherapy, USA; the International Olympic Committee and the Port Adelaide Football Club, Australia. He receives royalties for books on pain and rehabilitation, including two books that are cited in this article. He receives speaker fees for lectures on pain and rehabilitation.

All the other authors declare no conflict of interest.

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Appendix A. Methods – complementary details

A.1. Explicit measures

A.1.1. Pain in the past week

The question "*How would you rate the pain you have had on average during the past week?*" on a Numerical Rating Scale anchored on: 0= "no pain", 10= "worst pain".

A.1.2. Pain today

The question "*How would you rate the pain you have today?*" on a Numerical Rating Scale anchored on: 0= "no pain", 10= "worst pain".

A.1.3. Tampa Scale of Kinesiophobia – TSK

The TSK is a widely-used measure of pain-related fear beliefs [8,28]. Scores range from 17 to 68, with higher scores indicating higher levels of fear of movement and a cut-off of 40 is typically used to define a high degree of pain-related fear [37,38].

A.1.4. Pain Anxiety Symptoms Scale – PASS-20

The PASS-20 [7] was used to assess cognitive anxiety symptoms, escape and avoidance responses, fearful appraisals of pain and physiological anxiety symptoms associated with pain. The participant makes a frequency rating for each item (where 0 = never and 5 = always). The PASS-20 has acceptable psychometric properties [7]. Scores range from zero to 100, with higher score indicating higher levels of pain-anxiety.

A.1.5. Roland Morris Disability Questionnaire – RMDQ

The RMDQ measures effects of LBP on physical activities and activities of daily living. It is valid, reliable, and responsive to change [26,29]. Scores range from zero to 24, with higher scores indicating higher levels of disability.

A.2. Implicit measures

Apparatus and stimulus material: The stimuli used in all tasks followed a theme: forward bending and lifting, representing a highly socially and clinically significant activity for people with PLBP [41–43].

The category "Danger" was represented by the following six words: *damaging, vulnerable, threatening, alarming, risky, unpredictable*. The category "Safe" was represented by the following six words: *harmless, confident, secure, protecting, certainty, reliable*. All words were used in the affective priming task (APT), whereas only the first five of each category were used in the implicit association test (IAT).

Presentation of the tasks and reaction time recording was controlled by DMDX [62]. The words were presented in bold, 20-point Arial font in white lower case on a black background. The images were presented embedded in a white square image of 800 × 800 pixels on a black background.

A.3. Implicit association test

Procedure: Following well-established guidelines [11], the bending-IAT comprised seven phases separated by a pause for instructions. In the first phase (20 trials), participants sorted each of the 10 images twice, into the categories "Round-back" and "Straight-back". In the second phase (20 trials), participants sorted the 10 words twice into the categories "Safe" and "Danger". In phases, three and four (30 and 40 trials each) participants sorted words and images into the combined categories (e.g. *Danger/Round-back* and *Safe/Straight-back* or *Danger/Straight-back* and *Safe/Round-back*). In phase five (20 trials) participants sorted images with the location of the categories switched. Phases six and seven (40 trials each) reversed category combinations of phases three and four (e.g. *Danger/Straight-back* and *Safe/Round-back* or *Danger/Round-back* and *Safe/Straight-back*). The sequence of congruent and incongruent matches during phases three and four and six and seven were counterbalanced across participants.

On each trial the participant was given feedback ("correct" or "wrong"). Categories remained on screen throughout an entire phase. Each trial started with the display of a fixation cross for 1000 ms followed by a word or image for 1000 ms and an intertrial interval of 1000 ms.

A.4. Affective priming task

Procedure: Participants were informed that the task was to categorize words. The APT consisted of 8 blocks of 12 trials involving the presentation of a negative or positive word that was preceded by one of the prime pictures. Each block consisted of 6 affectively congruent (straight–safe, bending–dangerous) and 6 affectively incongruent image-word pairs (straight–dangerous, bending–safe).

Each trial began with the presentation of two white fixation crosses in the center of a black screen for 200 ms, a picture for 200 ms, a black screen for 100 ms, and a word for 10 s or until the participant responded by pressing either button. The intertrial interval was 1 s.

In order to validate the APT in this sample, each participant also performed a standard animal-APT using pleasant and unpleasant animal pictures as primes (snakes, spiders, fish and birds) selected from the International Affective Picture System (IAPS [36]). Both APT and animal-APT were performed consecutively; the order however was counterbalanced.

A.5. Physiological measures

Apparatus and stimulus material: Four categories of pictures (neutral, pleasant, unpleasant and bending/lifting) were represented by six images each. Pictures in the first three categories were selected from the (IAPS [36]) (*neutral:* rolling pin – 7000, towel – 7002, mug – 7009, wooden stool – 70,025, lamp – 7175, clock – 7211; *pleasant:* wedding – 4626, children – 2347, ice cream – 7330, fireworks – 5480, beach – 5833, man and woman kissing – 4660; *unpleasant:* snake – 1050, spider – 1201, shark – 1930, baby with eye lesion – 3170, aimed gun – 6230, attack – 3530). The bending and lifting-related images selected from PHODA-SeV (Photographs of Daily Activities-Short electronic version [6]) were images number: 2, 4, 20, 27, 29, 33, 83. The presentation of these stimuli was also controlled by DMDX [62].

Orbicularis occuli electromyographic activity (EMG): The first electrode was placed on the skin directly underneath the participant's left eye. The second electrode was placed approximately 1 cm to the left below the corner of the participant's left eye. A ground electrode was placed on the centre of the forehead. All electrodes were connected to a BIOPAC EMG 100C amplifier (amplification: 5000; filters: low pass of 500 Hz and high pass of 10 Hz).

Skin conductance (SCR): The electrodes were attached to the thenar and hypothenar eminences of the participant's non-dominant hand and connected to a BIOPAC SCR 100C amplifier with a gain of 2 µS/V.

Procedure: Participants washed their face and hands with non-allergic soap and water prior to the task to remove skin residue, minimizing skin impedance in the areas where the electrodes would be attached [44]. Electrode gel was applied under the participant's left eye and on the centre of the forehead to facilitate conductivity. The gel was allowed time to absorb into the skin and any excess was wiped off. A respiration belt was fitted over the participant's thorax. The participant was then asked to sit comfortably on an adjustable chair and the electrodes were attached.

Once the set up was ready, the participant was left alone in the room, while the researcher (JPC) controlled the experiment and monitored the participants through a CCTV system from the adjacent room. Participants looked at the blank computer screen for 3 min, while baseline data were collected. After baseline, the picture-viewing task was initiated. Three startle probes were administered to reduce the novelty of the startle probe and the 24 pictures were presented pseudo randomly such that no more than two pictures from the same category were presented in a row. Four picture sequences were predetermined and counterbalanced across participants. Probes were presented at 3.5 s or 4.5 s after picture onset during four of the six pictures per category as well as during one third of the inter-picture intervals.

A.6. Data processing, scoring and response definition

A.6.1. Implicit assessment data

For each participant, two measures of implicit attitude were obtained, one for the IAT ($IAT_{D\text{-score}}$) and one for the APT ($APT_{Diff\text{-score}}$). For both measures, response time was defined as the time elapsed from the presentation of the stimulus (word or picture) to when the shift key was pressed. This time was recorded and incorrect responses, responses shorter than 100 ms or longer than 1000 ms, and trials on which the participant had pressed the incorrect button were considered as errors.

A.6.2. IAT

An IAT bias score ($IAT_{D\text{-score}}$) was calculated using the improved scoring algorithm recommended by Greenwald et al. [63] with an error penalty of 2 standard deviations. This algorithm has been thoroughly tested and shown to outperform conventional scoring algorithms, providing valid measures of implicit associations [63]. A positive score indicates an implicit bias to associate "round-back" and "danger".

A.6.3. APT

Preparation of the affective priming data began with the removal of errors (as above) and outliers, which were defined as response times deviating by more than three standard deviations from the mean of the individual. Response times were sorted into 4 variables based on prime (standing and bending) and target (safe or danger word). A priming score ($APT_{Diff\text{-score}}$) was calculated as the difference in response time between incongruent (Round-back/Safe + Straight/Danger) and congruent (Round-back/Danger + Straight/Safe) trials. ($APT_{Diff\text{-score}} = RT_{incongruent} - RT_{congruent}$). A positive score indicates a bias to associate "round-back" and "danger".

A.7. Physiological measures

A.7.1. Eye-blink startle reflex

EMG data were recorded using a hardware bandpass 10–500 Hz filter, and processed with a software 50 Hz notch filter, followed by 30–500 Hz bandpass filter. Baseline eye-blink activity was the average magnitude of EMG recorded during the period of 50 ms prior to the startle stimulus. Response latency was determined as the interval between the beginning of the startle stimulus and the onset of EMG activity, visually-detected within 20–70 ms after startle stimulus onset. Blink magnitude was defined as the peak of the rectified and smoothed (moving average across three consecutive values) orbicularis oculi EMG activity occurring within 20–120 ms after startle stimulus onset.

A trial was scored as missing if the EMG signal was unstable due to noise, movement artifacts or if a spontaneous or voluntary blink occurred within the latency response window (20–70 ms after startle onset), or if the response lasted longer than 100 ms. Baseline EMG (within 50 ms prior to startle stimulus onset) was inspected to determine whether it was stable [34]. If visual inspection of the waveform failed to identify a response onset, then the trial was classified as a nonresponse trial and a magnitude of zero was recorded [44].

Given the interest in intra-individual rather than inter-individual differences in response amplitude, startle responses were standardized within each individual to T-scores with a mean of 50 and SD of 10 [44].

A.7.2. Skin conductance

Using visual inspection, the SCR data were scored with consideration of the respiration trace, where SCRs associated with atypical respiration were removed. A SCR was considered stimulus-elicited

3.9 References

if it began within 1–4 s of picture onset. Zero responses were scored if no response was observed within that window.

Data processing followed standard procedure, which involved square root transformation and range correction of SCRs to approximate to a normal distribution [18]. The average response of all pictures (six) per condition was calculated and analysed.

A.7.3. Picture ratings

Measures of pleasantness and arousal for each of the four conditions (neutral, pleasant, bending/lifting and unpleasant) were analysed for all participants.

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Chapter 4 Systematic review - Behavioural interventions for people with chronic low back pain and high pain-related fear: a systematic review of their effectiveness in reducing disability, pain and fear

Pain-related fear is thought to be a key mediator of the relationship between pain and disability, supporting the notion that it is an important target for behavioural interventions. Behavioural interventions can be broadly grouped as exposure-based and activity-based interventions. Exposure-based interventions are grounded on the fear-avoidance model, and provide an adequate framework to manage pain-related fear. Consequently, there is a widely held notion that exposure-based interventions are the treatment of choice for people with high pain-related fear. Nonetheless, the evidence for behavioural interventions in general or, specifically for exposure-based interventions in the management of people with persistent LBP and high pain-related fear has not been evaluated.

The aim of this systematic review study was to determine the current state of evidence concerning the effectiveness of behavioural interventions (broadly grouped as exposure-based and activity-based) that were intentionally designed to target people with CLBP and high pain-related fear, on reducing disability, pain and fear.

Note: for search strategy purposes, the term Chronic LBP (instead of Persistent LBP) has been used in this chapter

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"Behavioural interventions for people with chronic low back pain and high pain-related fear: a systematic review of their effectiveness in reducing disability, pain and fear" (*under review*)

4.1 Abstract

Objective: To determine the current state of evidence concerning the effectiveness (disability, pain and fear reduction) of behavioural interventions (broadly grouped as exposure-based and activity-based) intentionally designed for people with CLBP and high pain-related fear.

Methods: Prospectively registered review (PROSPERO CRD42016037175). Two reviewers conducted an electronic search in five databases, including randomized controlled trials (RCTs) and single-case experimental designs (SCEDs). Methodological quality was assessed using the Cochrane Risk of Bias Tool and PEDro scale (RCTs); and the Risk of Bias In N-of-1 Trials scale (SCEDs). For RCTs, meta-analysis compared change in disability, pain and fear between groups. For SCEDs, narrative synthesis of outcomes was used.

Results: RCTs provide moderate quality evidence that exposure-based interventions are more effective than wait-list control for disability (MD= -8.8; CI [-17.47, -0.13]; p=0.05) and fear (MD= -8.48; CI [-13.16, -3.8]; p=0.0004), but the effect size is small (less than the minimal clinical important change). There was no evidence of the superiority of exposure-based over activity-based interventions for disability, pain or fear. SCEDs provide low to moderate quality evidence that exposure-based interventions are effective in reducing disability and fear, and low quality evidence that they are superior to activity-based interventions. Pain reduction was only reported in SCEDs.

Discussion: Behavioural interventions for people with CLBP and high pain-related fear are effective in reducing disability and fear, but only modestly effective in reducing pain. Surprisingly, the widely held assumption that exposure-based interventions are the treatment of choice for this group is only poorly supported by existing literature.

Key-words: Chronic back pain; pain-related fear; behavioural interventions; exposure; activity

4.2 Introduction

Chronic low back pain (CLBP) exerts significant personal and societal burden worldwide (Abajobir et al. 2017; Vos, Flaxman, et al. 2012); often being associated with high disability and psychosocial co-morbidity (Abajobir et al. 2017; Dunn and Croft 2004). High levels of pain-related fear have been identified as a predictor of increased disability and poorer outcomes in people with CLBP (Wertli, Rasmussen-Barr, Held, et al. 2014; Zale et al. 2013). People with CLBP and higher levels of pain-related fear[5] commonly report greater pain intensity (Kroska 2016; Sullivan et al. 2009), greater disability (Zale et al. 2013; Crombez et al. 1999), less physical (Sullivan et al. 2009) and social (Thibault et al. 2008) participation, more work absenteeism and unemployment (Martel, Thibault, and Sullivan 2010; Braden et al. 2008), than people with CLBP who have lower levels of pain-related fear. Pain-related fear is thought to be a key mediator of the relationship between pain and disability (Lee et al. 2015), supporting the notion that it is an important target for behavioural interventions (Bunzli et al. 2017).

Behavioural interventions are widely used for the treatment of people with CLBP (Morley 2011), and have a well-established history since the original work of Fordyce (1976) (Main et al. 2014). Behavioural interventions for pain aim to modify unhelpful behaviours and their underlying cognitive processes, and thereby reduce disability (Main et al. 2014; Vlaeyen et al. 2012; Henschke et al. 2010). For people with high pain-related fear, behavioural interventions are considered optimal (den Hollander et al. 2010; Bailey et al. 2010). In general, behavioural interventions include a cognitive component (e.g. education, cognitive restructuring), and can be broadly distinguished as respondent or *exposure-based* (e.g. graded exposure in vivo – GEXP; contextual cognitive behavioural therapy (CCBT) (Pincus et al. 2015), and operant or *activity-based* (e.g. graded activity – GA; exercise-based physical therapy – PT (Pincus et al. 2015). Both these approaches are commonly advocated and recommended for people with CLBP. The key difference between them, is that exposure-based interventions specifically target pain-related fear by repeatedly exposing the person to their feared/avoided activity to disconfirm threat expectations (performance of task without the occurrence of feared outcome). In contrast, activity-based interventions encourage physical re-activation to build activity tolerance, but do not directly target the person's feared activity (Macedo et al. 2010). In light of this difference, there is a widely held notion that exposure-based behavioural interventions are recommended over activity-based behavioural interventions as the treatment of choice for people with high levels of pain-related fear (van der Giessen, Speksnijder, and Helders 2012; Vlaeyen et al. 2012; den Hollander et al. 2010). However, there has been no

5 **Pain-related fear** is here used as an umbrella term that describes key constructs of the fear-avoidance model (Vlaeyen & Linton 2000), including: fear of movement/(re)injury, pain anxiety and catastrophizing.

attempt to evaluate the evidence of either of these interventions specifically for people with CLBP and high pain-related fear.

We aimed to determine the current state of evidence concerning the effectiveness of behavioural interventions (broadly grouped as exposure-based and activity-based) that were intentionally designed to target people with CLBP and high pain-related fear, on reducing disability, pain and fear. To ensure comprehensive coverage of pertinent literature, we considered single-case experimental designs (SCEDs) in addition to randomized controlled trials (RCTs), as SCEDs form an important part of the historical development of behavioural interventions for pain-related fear in CLBP [(Vlaeyen et al. 2012; Vlaeyen et al. 2001)].

4.3 Methods

This systematic review followed the recommendations of the PRISMA statement [(Moher et al. 2009)], and it was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; http://www.crd.york.ac.uk/prospero/, reference CRD42016037175).

4.3.1 Search strategy

An electronic search was conducted by two independent reviewers (JPC and LN) on titles and abstracts from inception to May 2016, and updated in February 2018, in the following databases: PubMed, MEDLINE, CINAHL, EMBASE, PsycINFO; limited to trials that involved humans and published in English. **Table 4.1** displays the key terms used in this search strategy. The database searches were accompanied by hand searches of the reference list of included articles. All references were downloaded to referencing software Endnote, and duplicates removed manually.

4.3.2 Study selection

Two authors (JPC and LN) independently examined the titles and abstract that matched the inclusion and exclusion criteria using Covidence (www.covidence.org), an online platform supported by Cochrane. Where there were disagreements between the authors, a final decision was determined through consensus by three authors (JPC, LN and SB). Two authors (JPC and LN) then independently examined full-text articles; discrepancies were resolved through discussions with a third author (SB) until a consensus decision was reached. Where applicable, authors of original studies were contacted to provide further details on their results.

4.3.3 Inclusion criteria

4.3.3.1 Study design

Randomized controlled trials (RCTs) and single case experimental designs (SCEDs) [(Tate et al. 2017; Tate et al. 2014)] reporting interventions that had been completed were included. SCEDs form an important part of the behavioural sciences literature [(Tate et al. 2017)]. The strength of SCEDs lie in the richness of data captured via repeated measures over time [(Borckardt et al. 2008)]. Furthermore, SCEDs accommodate the heterogeneity and intra-subject variability commonly described in CLBP populations by using each person as their own control [(Morley 2018; Vlaeyen, Morley, and Crombez 2016; Morley, Vlaeyen, and Linton 2015; Morley and Adams 1989)] . Typical group design analysis that conveys information about aggregate benefit are inappropriate for analysis of data from SCEDs [(Maggin and Odom 2014; Borckardt et al. 2008)].

4.3.3.2 Population

Studies involving adults (≥18 years) with CLBP (i.e. article reported participants' pain as chronic or stated that they had LBP for ≥3 months duration) [(Chou et al. 2007)] and **high pain-related fear** (herewith referred to as ***Fear***)**.** For the latter, we included studies that recruited participants based on high scores on measures of pain-related fear (TSK≥38/68) [(Wertli, Rasmussen-Barr, Weiser, et al. 2014)], anxiety (PASS-20 ≥68/100) [(Brede et al. 2011)], or catastrophizing (PCS≥24/52) [(Sullivan, Bishop, and Pivik 1995)], either in isolation or combined with a more specific measure of fear of movement (e.g. PHODA >50/100) [(Vlaeyen et al. 2012; Leeuw, Goossens, et al. 2007)].

4.3.3.3 Interventions

Studies that reported on interventions that were cognitive, behavioural, physical or of combined nature, which aimed to reduce disability and/or pain in individuals with CLBP and high pain-related fear.

4.3.3.4 Clinical outcomes

Studies reporting on disability, function, and/or pain intensity (primary), and pain-related fear outcomes (secondary).

Table 4.1 Search strategy.

	SEARCH TERMS
#1. PARTICIPANTS	“Low back pain” **OR** “back pain” **OR** backpain **OR** “LBP” **OR** “NSLBP” **OR** “CLBP” **OR** “NSCLBP” **OR** “back ache*” **OR** backache **OR** “low back syndrome” **OR** “lumbar pain” **OR** “spine pain” **OR** “spinal pain” **OR** “lumbago” **(title and abstract)** **AND** Fear **OR** fearful **OR** "fear of movement" **OR** "fear of movement/re-injury" **OR** "fear of re-injury" **OR** kinesiophobia **OR** “pain-related fear" **OR** "pain-related anxiety" **OR** "negative back beliefs" **OR** "negative back pain beliefs" **OR** avoidant **OR** avoidance **OR** “fear-avoidant” **OR** “fear-avoidance” **OR** anxiety **OR** anxious **OR** catastrophi* **OR** distress **OR** “pain-related distress” **OR** “psychological distress” OR “psychological risk" **(title and abstract)**
#2. INTERVENTIONS	therapy **OR** therapeutic **OR** training **OR** treat* **OR** approach **OR** program **OR** intervention **OR** management **OR** psychological **OR** psychosocial **OR** psycho social **OR** psychotherapy **OR** “psychologically informed” **OR** “physiotherapy-led” **OR** “acceptance-based” **OR** behaviour **OR** behaviour **OR** behavioural **OR** behavioural **OR** care **OR** CBT **OR** CCBT **OR** cognitive **OR** operant **OR** “classical conditioning” **OR** counsel* **OR** exposure **OR** “exposure in vivo” **OR** “exposure treatment” **OR** graded **OR** “graded activity” **OR** “graded in vivo exposure” **OR** advi* **OR** education* **OR** instruction **OR** learning **OR** school **OR** teaching **OR** mindfulness **OR** mindbody **OR** “mind-body” **OR** yoga **OR** physical **OR** physiotherapy **OR** “Physical therapy” **OR** exercise **OR** functional **OR** rehabilitation **OR** “classification based” **OR** “cognitive functional” **OR** interdisciplinary **OR** stratified **OR** multidisc* **OR** “person-centred” **OR** “person-centered” **OR** “client-centred” **OR** “client-centered” **OR** personalized **OR** personalised **OR** individualized **OR** individualized **(title and abstract)**
#3. OUTCOMES	Disability **OR** Pain **OR** Function (**abstract)**
COMBINED TERMS	**#1 AND# 2 AND #3**
LIMITATIONS	Humans English [la]

4.3.4 Data extraction

Two authors (JPC and LN) independently extracted and crosschecked the data using a standardized form. This form was piloted in two studies prior to use. The following data were extracted: 1) Characteristics of participants: sample size, gender, age, inclusion criteria; 2) Characteristics of interventions: type, content and duration; 3) Outcomes assessed: primary (disability, function, and/or pain), secondary (pain-related fear: kinesiophobia, fear-avoidance, anxiety and catastrophizing) at a *post-treatment* timepoint (less than 3months after end of the treatment), and follow-up period at two timepoints that were established for this review: *Short-term follow up* (from 3 to < 6 months), and *Medium-term follow up* (from 6 to 12 months); when multiple timepoints fell within the same category, the timepoint that was closer to 3 months after the end of treatment for the short-term, and closer to 6 months for the medium-term was used (Higgins et al. 2011). 4) Results summary of each study. For the RCTs, mean score and standard deviations were extracted, or calculated (when the information was not provided) by using methods recommended by the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2011). Scores for *disability*, *pain* and *fear* were converted to a 0 to 100 scale. Where more than one outcome measure was used to assess disability, pain and fear, the outcome measure described as the primary outcome for the trial was included in this review. For SCEDs, descriptive data for the main outcomes were extracted. Heterogeneity regarding the timeframe of follow up assessments for both study designs, was managed by providing descriptive synthesis of outcomes at short and medium-term follow ups.

4.3.5 Risk of Bias and Quality assessment

Assessment was completed by two independent reviewers (JPC and LN), using tools appropriate to each study design. The criteria used to rate the risk of bias was based on recommendations from the Cochrane collaboration (Higgins et al. 2011) and Tate et al (Tate et al. 2014; Tate et al. 2013), in which: RCTs were assessed using the Cochrane Risk of Bias Tool (RoB) (Higgins et al. 2011), and SCEDs, were assessed using the Risk Of Bias In N-of-1 Trials scale (RoBiNT) (Tate et al. 2014; Tate et al. 2013).

The methodological quality assessment of the included RCTs was performed using the PEDro scale, which is reliable (Maher et al. 2003) and valid (de Morton 2009). Following the PEDro criteria (11 items, of which 10 are scored), each item was scored as 'yes' if it fulfilled the criteria, and 'no' if there was a risk of bias or a lack of clarity. According to PEDro scores, quality of evidence was classified as 'high' (≥6/10), 'fair' (≥4–6/10) or 'poor' (<4/10). Quality of SCEDs (internal and external validity) was assessed with the RoBiNT scale (Tate et al. 2013). For assessment of both risk of bias and methodological quality, results were compared and discrepancies resolved through discussions with a third author (SB) until a consensus decision was reached.

4.3.6 Data analysis

Two design-specific analyses were planned and conducted. *First*, for RCT studies only, meta-analysis compared changes in disability, pain and fear between groups. Heterogeneity between treatment studies was assessed using I^2 (i squared) statistics. Substantial heterogeneity was determined using the cut-off point $I^2 \geq 50\%$ (Higgins et al. 2011). For trials that were statistically homogenous (I^2<50%), pooled effects (weighted mean differences) were calculated using a fixed-effects model. For trials that were statically heterogeneous (I^2≥50%), estimates of pooled effects (weighted mean differences) were calculated using a random-effects model [(Higgins et al. 2011)]. Two contrasts were conducted: exposure-based vs control (Figure 2), and exposure-based vs activity-based (Figure 3). In one study where multiple contrasts were examined (e.g. exposure-based vs activity-based intervention vs waitlist control) [(Woods and Asmundson 2008)], the sample size in the shared comparison was halved in order to avoid double counting of participants in the analyses. The timepoints considered for meta-analyses were post-treatment, short-term and medium-term follow ups. Analyses of the RCTs were conducted in Review Manager 5.3 (version 5.3; The Nordic Cochrane Centre, Copenhagen, Denmark) [(RevMan 2014)].

Second, we analysed changes in disability, pain and fear in SCED studies. As there is not yet consensus with regard to methods for meta-analysis of SCEDs [(Kratochwill et al. 2013)], and given the considerable heterogeneity of studies with regard to design and analysis, only a descriptive and narrative synthesis of these studies was performed [(Maggin and Odom 2014)]. Single-subject studies are designed to evaluate intra-person changes over time, using each participant as their own control [(Morley 2018; Morley, Vlaeyen, and Linton 2015; Onghena and Van Damme 1994; Morley and Adams 1989; Kazdin 1982)]. To evaluate treatment effectiveness, multiple timepoints are necessary to allow identification of systematic change in the outcome during the treatment phase in comparison to a baseline [(Borckardt et al. 2008)]. In this review, level of evidence gathered from SCEDs was considered according to the frequency of timepoints in which the variable was measured. SCEDs reporting on data from multiple timepoints were considered to provide a higher level of evidence than SCEDs reporting on data from single timepoints [(Tate et al. 2017)].

4.4 Results

4.4.1 Literature search

The PRISMA flowchart is presented in **Figure 4.1**.

4.4.2 Description of studies

Three RCTs and seven SCEDs satisfied our *a priori* criteria and were included. Authors of one study[(Linton et al. 2008)] were contacted to provide data from participants with CLBP only. The details and data extracted from each study are summarized in **Table 4.2**. Although one of the RCTs [(Pincus et al. 2015)] was a feasibility trial, it satisfied our a priori criteria.

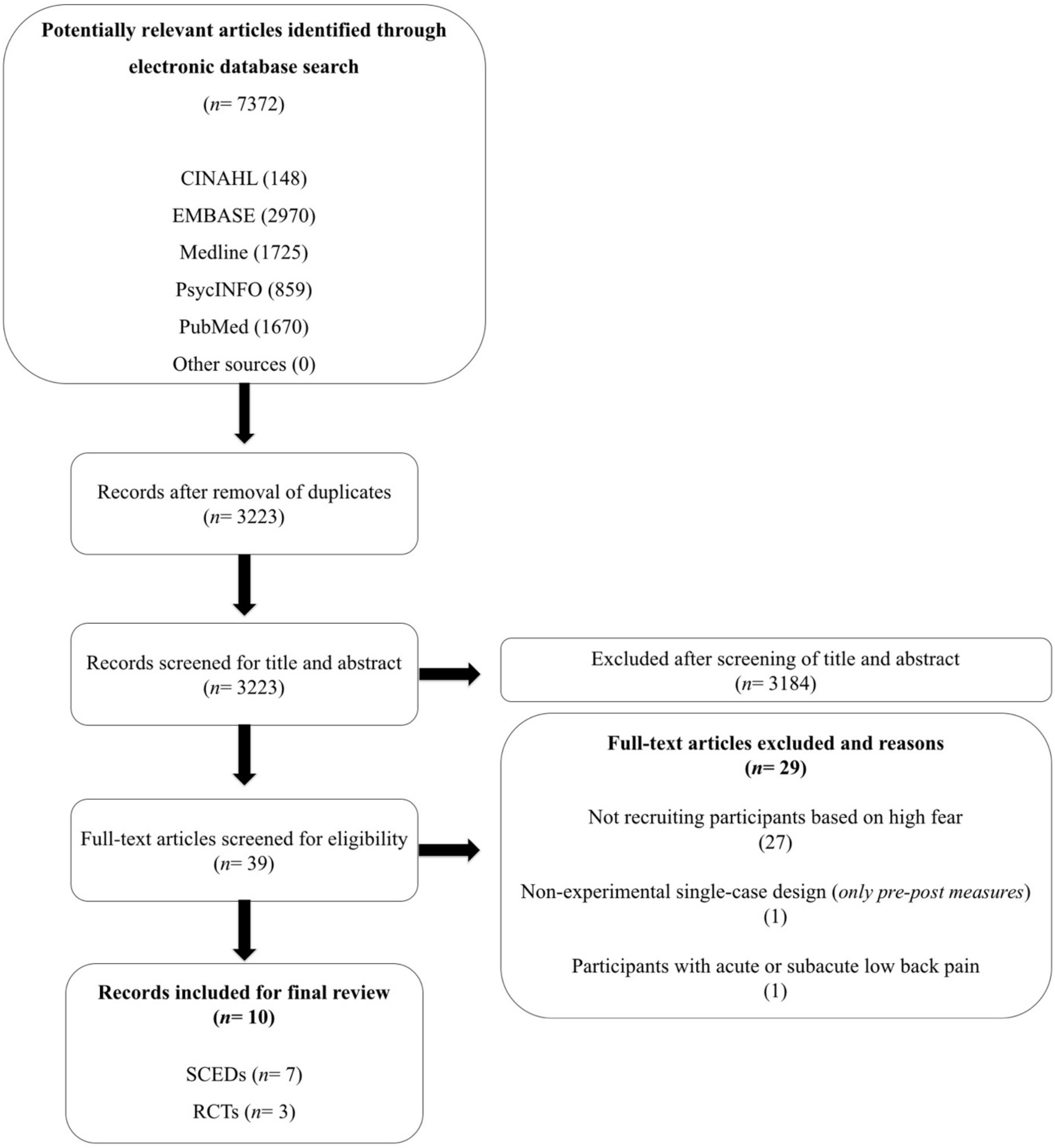


Figure 4.1 PRISMA flow chart describing selection, screening and inclusion processes.

Table 4.2 Characteristics of included studies (participants, interventions and measures)

STUDY	DESIGN	INTERVENTION			SAMPLE	INCLUSION CRITERIA	OUTCOME MEASURES **MT**= multiple timepoints (*daily, weekly*); **ST**= single timepoints (*end of phases*)		
		Content	Period	Follow up	(N, gender, age)	(Fear level^{+}, LBP duration)	**Disability**	**Pain**	**Fear**
Vlaeyen 2001 (Vlaeyen et al. 2001)	SCED (AB) *crossover*: Baseline-A-B Baseline-B-A	GEXP $^{(A)}$ vs GA $^{(B)}$ (in comprehensive rehabilitation program)	3 weeks per intervention (21 days of baseline)	n/a	N=4 M: 1, F: 3 Age: 31-40 yrs.	TSK≥40/68 (High-fear) CLBP>6mo	RMDQ$_D$ ST PCL-disability ST	n/a for pain intensity Measured pain control ST	Fear appraisals ^{MT} (Fear of movement, Fear of pain, Catastrophizing) TSK$_D$ ST, PHODA ST, PCL-catastrophizing ST
Vlaeyen 2002-A (Vlaeyen, de Jong, Geilen, et al. 2002)	SCED (AB) *crossover*: Baseline-A-B Baseline-B-A	GEXP $^{(A)}$ vs GA $^{(B)}$ (in comprehensive rehabilitation program)	4 weeks per intervention (28 days of baseline)	12 months	N=6 M: 2, F: 4 Age: 26-51 yrs.	TSK≥40/68 (High-fear) CLBP>6mo	RMDQ ST Physical activity ST	VAS ^{MT} PVAQ ST	Fear appraisals ^{MT} TSK ST, PHODA ST
Vlaeyen 2002-B (Vlaeyen, De Jong, Onghena, et al. 2002)	SCED (AB)	GEXP (stand-alone)	5 weeks (15 sessions–90min/each) (1 week of baseline)	n/a	N=2 F: 2 Age: 45 & 47 yrs.	TSK≥40/68 (High-fear) CLBP>6mo	RMDQ ST	VAS ^{MT} PVAQ ST	Fear appraisals ^{MT} TSK$_D$ ST, PHODA ST
Boersma 2004 (Boersma et al. 2004)	SCED (MBD)	GEXP (stand-alone)	~ 3 weeks (6-10 sessions–60-90min/each) (varied baseline length)	3 months (participant P4 had follow up at week 9)	N=6 Gender not stated Age: 34-61 yrs.	TSK≥35/68 (Moderate-fear All included had >40/68) Fear-Avoidance^=60/90 PHODA=30/98 cards >50 (with 15 of the 30 >80) CLBP>6mo	Function ^{MT} (Avoidance items 20-25 OMPQ$_S$)	VAS ^{MT}	Fear-avoidance ^{MT} (OMPQ, PAIRS, FABQ) TSK$_S$ ST, PHODA ST
De Jong 2005 (de Jong et al. 2005)	SCED (ABC/D) *crossover*: Baseline-A-B-C Baseline- A-B-D	Bas$^{(A)}$-EDU $^{(B)}$-GEXP $^{(C)}$ vs Bas$^{(A)}$- EDU $^{(B)}$-GA $^{(D)}$	6 weeks EXP (24 hours) 8 weeks GA (32 hours) (3weeks no treatment 2x)	6 months	N=6 Gender not stated Age not stated	TSK≥39/68 (High-fear) CLBP>6mo	Personally-relevant activities ^{MT} RMDQ ST Physical activity monitor ST	VAS ^{MT}	Fear appraisals ^{MT} TSK$_D$ ST, PHODA ST
Linton 2014 (Linton and Fruzzetti 2014)	SCED (AB)	Hybrid emotional exposure (GEXP + DBT)	6-9 weeks (9-10 sessions–11-15h) (9-15 days baseline)	5 months	N=6 M: 1, F: 5 Age: 33-71 yrs.	PSC>24 (High-fear) CLBP>3mo	QBPS ST	VAS ^{MT}	PCS ^{MT} TSK$_S$ ST, HADS ST
Guck 2015 (Guck et al. 2015)	SCED (MBD+CCD)	Primary care walking exposure - visual feedback (GEXP-based)	2-3 days (2-6 days baseline)	2 weeks	N=4 M: 2, F: 2 Age: 42-64 yrs.	TSK$_{11}$≥26/44 (represents 40/68 in full TSK) (High-fear) CLBP>6mo	Speed walking time ^{MT}	VAS ST PAIRS ST MPI-IS ST	TSK-11 ST CSQ-CAT ST BDI ST

Linton 2008 (Linton et al. 2008)	RCT	GEXP-TAU vs WLC-TAU	13-15 sessions (8-10 of GEXP)	Post-treatment (between-group comparison)	N=34 M: 16, F: 18 Age: 46-49 yrs. (SD: 9.9-7.3)	TSK>35/68 (Moderate-fear) PHODA= substantial fear (PHODA >50/100) CLBP>3mo	Activities Daily Living ST (5items OMPQ - work, sleep, walk, house chores, shopping) QBPDS ST Sick Leave ST	OMPQ ST (intensity, location, duration)	TSK ST, PCS ST, PHODA ST
Woods 2008 (Woods and Asmundson 2008)	RCT	GEXP vs GA vs WLC	4 weeks (2 sessions/week – 45min/each 8 sessions per intervention	1 month	N=44 M: 15, F: 29 GEXP:15, GA:13, WLC:16 Age: 43.78 yrs. (SD: 9.88)	TSK≥38/68 (High-fear) CLBP>3mo	PDI ST	SF-MPQ ST PSEQ ST	TSK ST, PCS ST, PASS-20 ST
Pincus 2015 (Pincus et al. 2015)	Feasibility RCT#	CCBT vs Physiotherapy (PT) (back to fitness group with at least 60 % of exercise-based content; and up to 3 individual sessions if required)	8 sessions per intervention (60min/each)	3 and 6 months	N=89 M: 35, F: 54 CCBT: 45, PT: 44 Age: 44.6 yrs. (SD: 16.01)	TSK>38/68 (High-fear) Avoidance (single-item STarTBack) CLBP>3mo	RMDQ ST CPAQ ST	BPI ST	HADS ST

SCED: Single Case Experimental Design (includes repetitive measures)**; A, B, C, D:** phases of design**; MBD:** Multiple Baseline Design**; CCD:** Changing Criterion Design**; RCT:** Randomized Controlled Trial**; GEXP:** Graded Exposure in vivo**; GA:** Graded Activity**; M:** Male**; F:** Female**; Ag:** Age in years (yrs.)**; n/a:** Not Assessed**; TSK:** Tampa Scale of Kinesiophobia**; PCS:** Pain Catastrophizing Scale**; CLBP:** Chronic Low Back Pain**; Fear Level**[†]**:** TSK cut off based on *Wertli et al 2014* (TSK: High≥38/68)(Wertli, Rasmussen-Barr, Weiser, et al. 2014)**,** PCS cut off based on *Sullivan et al 1995* (PCS: High≥24/52)(Sullivan, Bishop, and Pivik 1995)**; MT:** measures taken at Multiple Timepoints (daily, weekly)**; ST:** measures taken at Single Timepoints (end of phases)**; RMDQ:** Roland Morris Disability Questionnaire**; PCL:** Patient Cognitions List (*dis*: disability; *cat*: catastrophizing; *con*: pain control)**; Fear appraisals:** short instrument containing items from TSK, PASS (Pain Anxiety Symptom Scale), PCS (Pain Catastrophizing Scale) – measured daily**; PHODA:** Photograph Series of Daily Activities (*SeV:* Short electronic Version)**; VAS:** Pain intensity**; PVAQ:** Pain vigilance and Awareness Questionnaire**; OMPQ:** Orebro Musculoskeletal Questionnaire**; MPQ:** McGill Pain Questionnaire**; QBPDS:** Quebec Back Pain Disability Scale**; PSC:** Patient Specific Complaints**; TAU:** Treatment As Usual**; WLC:** Waitlist Control**; SF-MPQ:** Short Form McGill Pain Questionnaire**; PSEQ:** Pain Self-Efficacy**; PDI:** Pain Disability Index**; DBT:** Dialectical behaviour therapy**; CPAQ:** Chronic Pain Acceptance Questionnaire**; HADS:** Hospital Anxiety and Depression Scale**; TSK-11:** TSK short form (11 items)**; PAIRS:** Pain and Impairment Relationship Scale**; MPI:** Multidimensional Pain Inventory (IS: interference scale)**; CSQ:** Coping Strategies Questionnaire (CAT: Catastrophizing subscale)**; BDI:** Beck Depression Inventory**; CCBT:** Contextual Cognitive Behavioural Therapy**; BPI:** Brief Pain Inventory**; ^Fear-Avoidance scale:** consisted of selected items from PAIRS, OMPSQ, FABQ and back pain worry questions – all scored from 0-10. **Subscript *D* or *S*:** language of questionnaire used – *Dutch*, *Swedish***. #:** Feasibility trials are not often powered to inform on the efficacy of either of the interventions. Nonetheless, the study had a larger sample size than the other RCTs included in this review, and it reported the outcomes adequately.

4.4.3 Quality assessment

Quality assessments of included studies are presented at the bottom of **Figures 4.2** and **4.3** (RoB) (Higgins et al. 2011), and in **Appendix 4.1** (**Tables 4.4** (RoBiNT) (Tate et al. 2014; Tate et al. 2013) and **4.5** (PEDro) (de Morton 2009; Maher et al. 2003)). Initial agreement of quality ratings was 91% (RoB), 86% (PEDro) and 89% (RoBiNT) between reviewers (JPC and LN). Following discussion with a third reviewer (SB), consensus was reached on all items. All three RCTs scored 'moderate to high' risk of bias with most common methodological limitations being selection bias (lack of allocation concealment), performance bias (blinding of both therapists and patients, which are practically unavoidable in trials using behavioural interventions), detection bias, and attrition bias (loss to follow up). According to the PEDro scale, two studies were rated as 'fair quality' (scores of 5/10 (Woods and Asmundson 2008) and 4/10 (Linton et al. 2008)) and one was rated as 'high quality' (score of 7/10 (Pincus et al. 2015)). According to the RoBiNT, all SCEDs had moderate risk of bias, and were rated as low to moderate quality (mean scores: 4.7/14 for internal validity, and 11.4/14 for external validity).

4.4.4 Population

All studies included participants with CLBP and high fear. The total number of participants over 3 RCTs was 167 (n= 34 (Linton et al. 2008), 44 (Woods and Asmundson 2008) and 89 (Pincus et al. 2015) participants), and the total number of participants over 7 SCEDs was 34, with these studies ranging from 2 to 6 participants. Two studies (one RCT (Linton et al. 2008) and one SCED (Boersma et al. 2004)) used a moderate cut-off score on a standard measure of fear (TSK>35/68) in combination with a fear profile on a more specific measure (PHODA – details in **Table 4.2**). The RCT (Linton et al. 2008) had two stages, the first was a between-group comparison between active treatment and usual care groups. The second was a within-group comparison of participants that were offered to crossover from the usual care group to the active treatment group. However, a proportion of participants in the second stage of the RCT (Linton et al. 2008) (within-group comparison) were excluded because they did not have substantial fear as determined by the PHODA. Therefore, we only included participants from the first stage of that RCT (between-group comparison). Despite the lower inclusion criteria of TSK>35/68, all 6 participants recruited in the SCED (Boersma et al. 2004) had high fear (TSK≥38/68) (Wertli, Rasmussen-Barr, Weiser, et al. 2014). The mean (range) age across all studies was 48 (26 to 71) years.

4.4.5 Intervention characteristics

All studies reported on *exposure-based* behavioural interventions, including graded exposure in vivo (GEXP) (Woods and Asmundson 2008; Linton et al. 2008; de Jong et al. 2005; Boersma et al. 2004; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen, De Jong, Onghena, et al. 2002; Vlaeyen et al. 2001), hybrid emotional exposure (combining GEXP with dialectical behaviour therapy - DBT) (Linton and Fruzzetti 2014), primary care-based walking exposure (Guck et al. 2015) and contextual cognitive behavioural therapy (CCBT) (Pincus et al. 2015). Three RCTS (Woods and Asmundson 2008; Linton et al. 2008; Pincus et al. 2015) and three SCEDs (de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001) also reported on *activity-based* behavioural interventions, including graded activity (GA) (Pincus et al. 2015; Linton et al. 2008; Woods and Asmundson 2008; de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001) and physiotherapy (PT) (Pincus et al. 2015) (back to fitness group exercises with at least 60 % of content being exercise-based). Two RCT studies (Pincus et al. 2015; Woods and Asmundson 2008) compared exposure-based and activity-based interventions directly, and two RCTs compared an exposure-based intervention to a waitlist control (Linton et al. 2008; Woods and Asmundson 2008). Only one SCED (de Jong et al. 2005) reported on the education component of behavioural interventions. The characteristics of the interventions are described in **Table 4.2**.

4.4.6 Clinical outcome measures

All RCTs reported assessments of disability, pain and fear post-treatment (Pincus et al. 2015; Woods and Asmundson 2008; Linton et al. 2008), with only one (Pincus et al. 2015) presenting data from short and medium-term follow up. Therefore, meta-analysis was only conducted on post-treatment data from the three RCTs. Follow up outcomes for Pincus et al (2015) (Pincus et al. 2015) were reported descriptively.

All SCEDs reported on disability, but only three reported assessments at multiple timepoints (Guck et al. 2015; de Jong et al. 2005; Boersma et al. 2004). Six SCEDs reported on pain (Guck et al. 2015; Linton and Fruzzetti 2014; de Jong et al. 2005; Boersma et al. 2004; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen, De Jong, Onghena, et al. 2002), with five reporting assessments at multiple timepoints (Linton and Fruzzetti 2014; de Jong et al. 2005; Boersma et al. 2004; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen, De Jong, Onghena, et al. 2002). All SCEDs reported measures of fear, with six reporting it at multiple timepoints (Linton and Fruzzetti 2014; de Jong et al. 2005; Boersma et al. 2004; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001a; Vlaeyen, De Jong, Onghena, et al. 2002). There was considerable variability in design, outcome measures used, the frequency in which outcomes were collected, and the type of analysis utilised to evaluate outcomes across SCEDs (details in **Table 4.2** and **Appendix 4.2**). This heterogeneity precluded meta-analysis of these data (Maggin and Odom 2014; Bailey et al. 2010), so we undertook a narrative assessment, synthesis and descriptive frequency quantification of the available evidence from SCEDs.

4.4.7 Intervention effects for Randomized controlled trials (RCTs)

4.4.7.1 Post-treatment outcomes

Three RCTs reported on comparisons between: exposure-based behavioural interventions and wait list control (Woods and Asmundson 2008; Linton et al. 2008); and between two types of behavioural interventions: exposure-based (Woods and Asmundson 2008) and activity-based (Pincus et al. 2015) (**Appendix 4.3 -Table 4.9**).

4.4.7.1.1 Exposure-based Behavioural intervention versus Wait list control

Two trials with a total of 56 participants (31 (Woods and Asmundson 2008); 25 (Linton et al. 2008)) compared an exposure-based behavioural intervention (GEXP) with a wait list control (Woods and Asmundson 2008; Linton et al. 2008). According to the PEDro scale, the methodological quality of these trials was fair (scores of 5/10 (Woods and Asmundson 2008) and 4/10 (Linton et al. 2008)). Data for pooling were available for disability, pain and fear post-treatment. Data were pooled using fixed-effects model for all outcomes (I^2 <50%).

The meta-analysis revealed a statistically significant difference for disability between exposure-based interventions and wait list control, favouring the intervention (MD = -8.8; 95% CI, -17.47, -0.13; p=0.05) (Figure 2). However, the effect was small; -8.8 points difference on a scale from 0 to 100, which is less than the minimal clinically important change (MCIC) for the QBPDS (15 points change on 0-100 scale) (Fritz and Irrgang 2001) and RMDQ (10.4 points change on 0-100 scale) (Roland and Morris 1983). The outcome measure used by Woods & Asmundson (2008) (Woods and Asmundson 2008) (Pain Disability Index) does not have an established MCIC. No statistically significant difference was found between exposure-based interventions and wait list control for pain (MD = -4.61; 95% CI, -13.75, 4.53; p=0.32). Results for fear favoured the exposure-based intervention (MD = -8.48; 95% CI, -13.16, -3.8; p=0.0004), but the effect was small; only -8.5 on a 100 points scale, which is less than the MCIC for the TSK (17.6 points change on 0-100 scale) (Lundberg et al. 2011). To put these effects in perspective, recent studies have determined that people with LBP need to experience a minimum change of 20 points on pain and disability (on a 100 points scale) to consider the intervention effect worthwhile (Christiansen et al. 2018; Ferreira, Herbert, et al. 2013). The relatively small number of participants in both trials (Woods and Asmundson 2008; Linton et al. 2008) may have limited their statistical power and generalization of results.

4.4.7.1.2 Exposure-based versus Activity-based behavioural interventions

Two trials with a total of 77 participants (49 [Pincus et al. 2015]; 28 [Woods and Asmundson 2008]) compared exposure-based (GEXP and CCBT) with activity-based behavioural interventions (GA and PT) [Woods and Asmundson 2008; Pincus et al. 2015]. The methodological quality of these trials was high (7/10 [Pincus et al. 2015]) for one and fair (5/10 [Woods and Asmundson 2008]) for the other according to the PEDro scale. Data for pooling were available for disability, pain and fear post-treatment. Data were pooled using fixed-effects models for disability and pain (I^2 <50%), and a random-effects model for the fear outcome (I^2 >50%).

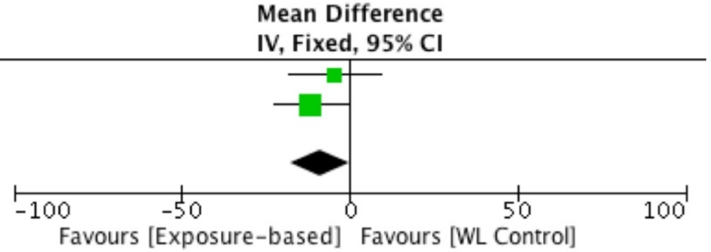
The meta-analyses revealed no statistically significant differences between treatment groups for disability (MD = -5.5; 95% CI, -16.07, 5.08; p=0.31), pain (MD = -3.31; 95% CI, -9.84, 3.21; p=0.32) or fear (MD = -5.62; 95% CI, -16.32, 5.07; p=0.30) (**Figure 4.3**).

4.4.7.2 Short and medium-term follow up outcomes

Only one RCT [20] assessed outcomes at both *short* and *medium-term* follow ups, therefore its follow up data were synthesized, but not analysed. That study compared exposure-based (CCBT) and activity-based (PT) interventions [20]. Although it reported improvements for disability, pain and fear for both interventions, there was no difference between them (CCBT and PT).

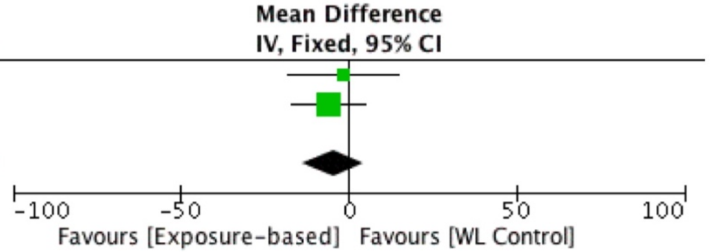
Disability

Study or Subgroup	Exposure-based Mean	SD	Total	Wait list Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Linton et al 2008	42.4	15.5	9	47	19	16	39.7%	-4.60 [-18.36, 9.16]
Woods & Asmundson 2008 (EXP)	16	14.71	15	27.57	17	16	60.3%	-11.57 [-22.74, -0.40]
Total (95% CI)			**24**			**32**	**100.0%**	**-8.80 [-17.47, -0.13]**



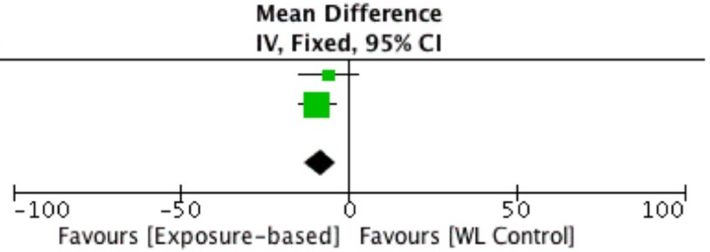
Pain

Study or Subgroup	Exposure-based Mean	SD	Total	Wait list Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Linton et al 2008	51.55	21	9	52.98	19	16	30.4%	-1.43 [-18.01, 15.15]
Woods & Asmundson 2008 (EXP)	23.78	14.44	15	29.78	16.67	16	69.6%	-6.00 [-16.96, 4.96]
Total (95% CI)			**24**			**32**	**100.0%**	**-4.61 [-13.75, 4.53]**



Fear

Study or Subgroup	Exposure-based Mean	SD	Total	Wait list Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Linton et al 2008	49.26	11.18	9	55.29	10.44	16	27.5%	-6.03 [-14.95, 2.89]
Woods & Asmundson 2008 (EXP)	48.09	7.06	15	57.5	8.53	16	72.5%	-9.41 [-14.91, -3.91]
Total (95% CI)			**24**			**32**	**100.0%**	**-8.48 [-13.16, -3.80]**



Risk of Bias

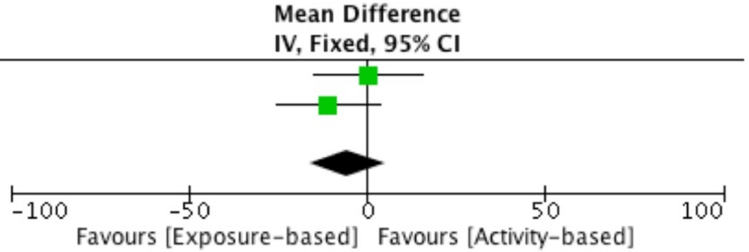
	A	B	C	D	E	F	G
Linton et al 2008	+	-	-	?	-	+	+
Woods & Asmundson 2008	+	-	-	?	-	?	?

A: Random sequence generation (*selection bias*)
B: Allocation concealment (*selection bias*)
C: Blinding of participants and personnel (*performance bias*)
D: Blinding of outcome assessment (*detection bias*)
E: Incomplete outcome data (*attrition bias*)
F: Selective reporting (*reporting bias*)
G: Other bias

Figure 4.2 Exposure-based Behavioural interventions versus wait list control on disability, pain and fear (post-treatment outcomes: < 3 months).

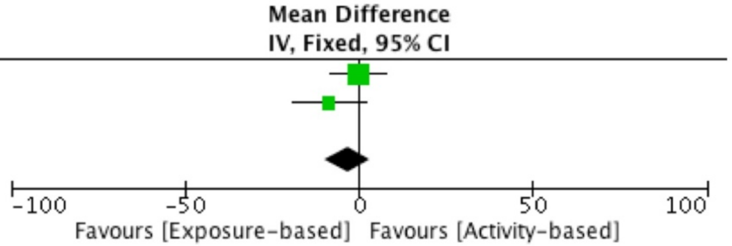
Disability

Study or Subgroup	Exposure-based Mean	Exposure-based SD	Exposure-based Total	Activity-based Mean	Activity-based SD	Activity-based Total	Weight	Mean Difference IV, Fixed, 95% CI
Pincus et al 2015	37.5	26.29	23	37.08	28.08	26	48.2%	0.42 [-14.81, 15.65]
Woods & Asmundson 2008	16	14.7	15	27	23.3	13	51.8%	-11.00 [-25.69, 3.69]
Total (95% CI)			**38**			**39**	**100.0%**	**-5.50 [-16.07, 5.08]**



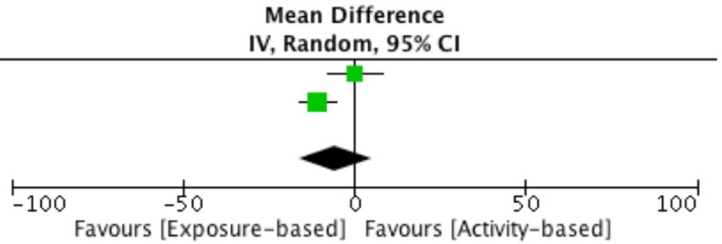
Pain

Study or Subgroup	Exposure-based Mean	Exposure-based SD	Exposure-based Total	Activity-based Mean	Activity-based SD	Activity-based Total	Weight	Mean Difference IV, Fixed, 95% CI
Pincus et al 2015	37.25	14.5688	23	37.5	14.6073	26	63.6%	-0.25 [-8.43, 7.93]
Woods & Asmundson 2008	23.78	14.44	15	32.44	14.67	13	36.4%	-8.66 [-19.48, 2.16]
Total (95% CI)			**38**			**39**	**100.0%**	**-3.31 [-9.84, 3.21]**



Fear

Study or Subgroup	Exposure-based Mean	Exposure-based SD	Exposure-based Total	Activity-based Mean	Activity-based SD	Activity-based Total	Weight	Mean Difference IV, Random, 95% CI
Pincus et al 2015	36.67	14.1063	23	36.43	14.4595	27	46.4%	0.24 [-7.70, 8.18]
Woods & Asmundson 2008	48.1	7.1	15	58.8	7.6	13	53.6%	-10.70 [-16.18, -5.22]
Total (95% CI)			**38**			**40**	**100.0%**	**-5.62 [-16.32, 5.07]**



Risk of Bias

	A	B	C	D	E	F	G
Pincus et al 2015	+	?	−	−	?	+	+
Woods & Asmundson 2008	+	−	−	?	−	?	?

A: Random sequence generation (*selection bias*)
B: Allocation concealment (*selection bias*)
C: Blinding of participants and personnel (*performance bias*)
D: Blinding of outcome assessment (*detection bias*)
E: Incomplete outcome data (*attrition bias*)
F: Selective reporting (*reporting bias*)
G: Other bias

Figure 4.3 Exposure-based versus Activity-based Behavioural interventions on disability, pain and fear (post-treatment outcomes: < 3 months).

4.4.8 Intervention effects for Single-case experimental designs (SCEDs)

The outcomes of seven SCEDs (Linton and Fruzzetti 2014; de Jong et al. 2005; Boersma et al. 2004; Vlaeyen, De Jong, Onghena, et al. 2002; Vlaeyen et al. 2001) with a total combined sample size of 34 participants with CLBP and high pain-related fear are displayed in **Table 4.3**. There was considerable design heterogeneity among the SCEDs. Specifically, there were four SCEDs that reported *within-person* effects of exposure-based (GEXP) interventions on disability, pain and fear (Guck et al. 2015; Linton and Fruzzetti 2014; Boersma et al. 2004; Vlaeyen, De Jong, Onghena, et al. 2002), and three SCEDs that reported *between- person* effects of exposure-based (GEXP) and activity-based (GA) behavioural interventions (de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001).

4.4.8.1 Narrative synthesis of outcomes for SCEDs

Post-treatment outcomes

4.4.8.1.1 Within-person design: Exposure-based behavioural interventions alone

Four SCEDs with a total of 18 participants reported the within-person effects of exposure-based (GEXP) interventions on disability, pain and fear (Guck et al. 2015; Linton and Fruzzetti 2014; Boersma et al. 2004; Vlaeyen, De Jong, Onghena, et al. 2002). These studies had moderate risk of bias, and low to moderate methodological quality (**Appendix 4.1**, **Table 4.4**).

Two studies presented data captured at multiple timepoints (Guck et al. 2015; Boersma et al. 2004), reporting reductions in disability for most participants. These results were supported by results of three of the studies (Linton and Fruzzetti 2014; Boersma et al. 2004; Vlaeyen, De Jong, Onghena, et al. 2002), which used standard measures of disability (RMDQ, OMPQ, QBPDS) captured at single timepoints (pre-post).

Three SCEDs presented data captured at multiple timepoints (Guck et al. 2015; Linton and Fruzzetti 2014; Boersma et al. 2004; Vlaeyen, De Jong, Onghena, et al. 2002), reporting mixed results for reductions in pain after GEXP was introduced. Vlaeyen et al (2002-B) (Vlaeyen, De Jong, Onghena, et al. 2002) reported significant reduction for both participants. Boersma et al (2004) (Boersma et al. 2004) reported that pain reductions were large for two of the six participants, minimal for three, and negligible for one. Linton & Fruzzetti (2014) (Linton and Fruzzetti 2014), reported that four of the six participants had reductions that reached criteria after treatment. At single timepoints (pre-post), four SCEDs (Guck et al. 2015; Linton and Fruzzetti 2014; Vlaeyen, De Jong, Onghena, et al. 2002) reported reduction in pain intensity for most participants.

Three studies presented data captured at multiple timepoints (Linton and Fruzzetti 2014; Boersma et al. 2004; Vlaeyen, De Jong, Onghena, et al. 2002), reporting substantial fear reduction for most participants. These results were supported by standard measures of fear (TSK and PHODA) captured at single timepoints (pre-post) in four studies [Guck et al. 2015; Linton and Fruzzetti 2014; Boersma et al. 2004; Vlaeyen, De Jong, Onghena, et al. 2002] (**Table 4.3**).

Considering only SCEDs that measured outcomes at multiple timepoints, these studies suggest that an exposure-based behavioural intervention (GEXP) promoted improvements in most participants for disability (22/25) and fear (26/27), and in about half of the participants for pain (14/23) (*post-treatment*, *short-term* and *medium-term*).

4.4.8.1.2 Between-person design: Exposure-based versus Activity-based behavioural interventions

Three SCEDs with a total of 16 participants compared exposure-based (GEXP) with activity-based (GA) behavioural interventions [de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001]. These studies had moderate risk of bias, and low to moderate methodological quality (**Appendix 4.1**, **Table 4.4**). In view of the methodological restrictions of these studies (see discussion), their results should be considered with caution.

Overall, these three SCEDs [de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001] reported improvement in disability favouring GEXP. Only one of the three studies [de Jong et al. 2005] assessed disability at multiple timepoints, reporting improvement for GEXP compared to GA. This was supported by results reported on standard measures of disability (RMDQ) captured at single timepoints (pre-post) [de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001]. Two studies [Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001] reported improvement in disability after GEXP (reduction greater than pre-set criteria for RMDQ). This was supported by results reported on standard measures of disability (RMDQ) captured at single timepoints (pre-post) that reported improvement after GEXP (reduction greater than pre-set criteria for RMDQ) [Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001], and similar improvements in disability after both interventions (GEXP and GA) [de Jong et al. 2005]. However, data from the activity monitor and self-reported difficulties in performing daily tasks indicated that changes only occurred after the introduction of GEXP [de Jong et al. 2005].

Two SCEDs presented data captured at multiple timepoints [de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002], reporting statistically significant reductions in pain after GEXP was introduced. All three studies measured fear at multiple timepoints [de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001], reporting visual and statistical evidence that fear improved substantially after the introduction of GEXP. This was not the case when GA was introduced as the treatment [de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001]. De Jong et al (2005) [de Jong et al. 2005] reported substantial reductions in fear for all participants after an education component (introduced before the start of each intervention), followed by further reduction in participants that received GEXP, but not in those that received GA (de Jong et al. 2005). The results from VAS scales at multiple timepoints were supported by standard measures of pain-related fear (TSK and PHODA) captured at single timepoints (pre-post) in all three SCEDs (de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001) (**Table 4.3**).

4.4.8.2 Short and medium-term follow up outcomes

4.4.8.2.1 Short-term (from 3 to < 6 months)

Two SCEDs investigating exposure-based interventions (GEXP and GEXP + Dialectical Behaviour Therapy) (Linton and Fruzzetti 2014; Boersma et al. 2004) reported that exposure-based interventions improved disability and fear in the short-term, with one also reporting improvement in pain (Linton and Fruzzetti 2014). The other study (Boersma et al. 2004) did not report pain outcomes at this timeframe.

4.4.8.2.2 Medium-term (from 6 to 12 months)

Two SCEDs comparing exposure-based (GEXP) and activity-based (GA) interventions (de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002) reported improvement in disability and fear only after the introduction of GEXP, with one also reporting improvement in pain (Vlaeyen, de Jong, Geilen, et al. 2002) in the medium-term. The other study (de Jong et al. 2005) did not assess pain at this timeframe.

Table 4.3 Summary of outcomes for SCEDs (ordered based on ROB)

STUDIES		OUTCOMES			ORIGINAL AUTHORS' CONCLUSIONS
SCEDs		Disability	Pain	Fear	
Vlaeyen 2001 (Vlaeyen et al. 2001a)	MT	Not measured	Not measured	***Fear appraisals***: visual inspection revealed reduction only occurs after GEXP. A time-series analysis (AR1 procedure) supported these findings. Significant reduction in 3/4 participants for all three measures (Fear of movement, Fear of pain, Catastrophizing) - for one patient, only catastrophizing did not reduce significantly).	**"***Using time series analysis on the daily measures of pain-related cognitions and fears, we found that improvements only occurred during the graded exposure in vivo, and not during the graded activity, irrespective of the treatment order. Analysis of the pre–post treatment differences also revealed that decreases in pain-related fear concurred with decreases in pain catastrophising and pain disability, and in half of the cases an increase in pain control.***"** (Vlaeyen et al 2001; Page 151)
	ST	**RMDQ:** reduced in 3/4 based on preset criteria (>=5-point reduction)	Not measured	This was supported by reductions in standard measures for 4/4 participants only after GEXP (**TSK:** from 80th to 10th percentile; **PHODA:** reduced 70%; **PCL-Cat:** reduced in 3/4 participants (z-score of 0.5))	
Vlaeyen 2002-A (Vlaeyen, de Jong, Geilen, et al. 2002)	MT	Not measured	Statistical analysis reveals significant reduction in pain intensity after GEXP for all participants	***Fear appraisals***: visual and statistical analysis confirm reduction only occurred after GEXP for all participants.	**"***Compared with a nontreatment baseline period and a GA program, the individually tailored EXP treatment was superior in decreasing levels of fear of movement/(re)-injury, fear of pain, and pain catastrophizing. There was an overall improvement in self-reported disability after EXP, suggesting that reductions of pain-related fear generalized to an improvement of functional ability in daily life. Last but not least, the treatment gains were intact at the 1-year follow-up, supporting the robustness of the intervention.***"** (Vlaeyen et al 2002-A; Page 258)
	ST	**RMDQ:** reduced greater than preset criteria for 5/6 participants in both groups after GEXP. ***Physical activity***: considerable increase after GEXP (z-score about 7SDs, compared to 1.5SDs for GA).	Not measured	This was supported by reductions in standard measures (**TSK:** to <10th percentile and **PHODA**)	
Vlaeyen 2002-B (Vlaeyen, De Jong, Onghena, et al. 2002)	MT	Not measured	***Pain intensity:*** Visual and statistical analysis revealed significant, but slow reduction in both participants	Visual and statistical analysis revealed substantial clinical improvements in **fear appraisals** in both participants**.**	**"***When applying a more systematic exposure in vivo treatment with behavioural experiments in patients with chronic low back pain reporting substantial fear of movement/(re)injury, a dramatic decrease in pain-related fear occurs. Finally, the effects of the fear reduction appear to generalize toward a significant improvement of daily functional status as measured with the RMDQ.***"** (Vlaeyen et al 2002-B; Page 150)
	ST	Descriptive analysis revealed substantial clinical improvements in **disability** for 2/2 participants (**RMDQ** scores < Vlaeyen 2001).	Not measured	Descriptive analysis revealed **TSK (**<10th percentile)	
Boersma 2004 (Boersma et al. 2004)	MT	**Function** increased for 5/6 post treatment. 1/6 only improved at 3-month follow up. 1/6 did not have follow up data.	Reductions in pain (VAS) were **large for 2/6** (>65% change: 4.1/10), minimal for 3/6 (14-22%: 1-1.2/10) and negligible for 1/6 (5%: 0.4/10).	***Fear appraisals:*** Visual inspection demonstrates 4/6 had considerable reduction and 2/6 less so (one was small and gradual, and the other negligible) – overall, **5/6** improved.	**"***The results of this study demonstrated clear decreases in rated fear and avoidance beliefs accompanied by significant increases in function. These improvements were seen even though rated pain intensity actually decreased.***"** (Boersma et al 2004; Page 14)
	ST	Not measured	Not measured	This was supported by reductions in standard measures (**TSK:** 5/6 had reductions beyond the criteria (25% reduction), 1/6 didn't have all data; **PHODA:** 6/6 reached criteria of clinically significant reduction)	

De Jong 2005 (de Jong et al. 2005)	MT	***Personally-relevant activities:*** decreased for 3/3 after GEXP and 1/3 after GA.	Statistical significant reduction of pain from baseline to follow up (6mo) in the GEXP group	***Fear appraisals:*** Visual and statistical analysis revealed substantial reductions in 6/6 participants after EDU. Further reduction was seen in 3/3 only after EXP.	**"***Randomization tests of the daily measures showed that improvements in pain-related fear and catastrophizing occurred after the education was introduced. The results also showed a further improvement when exposure in vivo followed the no treatment period after the education and not during the operant graded activity program***."** (De Jong et al 2005; Page 9)
	ST	**RMDQ:** disability was reduced for 6/6 participants in both groups beyond the pre-set criterion ***Activity monitor and self-reported difficulties in performance of personal relevant daily activities at home*****:** changes only occurred after the introduction of GEXP	Not measured	This was supported by considerable reductions in standard measures (TSK and PHODA) after GEXP and EDU)	
Linton 2014 (Linton and Fruzzetti 2014)	MT	Not measured	4/6 reached clinical significance at *follow up* (criteria: pain <baseline, and reduction >2 points from baseline to follow up) – (*descriptive*)	***Catastrophizing*****:** substantial improvement for 6/6 participants - sustained at follow up, for 5/6 (< cut-off of 20) and 1/6 (at cut off level)	**"***In summary, this study has demonstrated that a hybrid treatment combining an emotion regulation-focused DBT inspired treatment with standard exposure for patients with chronic low back pain resulted in considerable improvements. It is striking that patients achieved clinically relevant improvements, often to "normal" ranges, on key outcome variables.***"** (Linton & Fruzzeti 2014; Page 158)
	ST	**QBPDS:** 6/6 improved **function** at *post* and 5/6 at *follow up* (criteria: change of >=15pts, or score of <=30). However, 3/6 had lower disability scores at baseline and presented the smallest relative change.	Not measured	***TSK*****:** 5/6 had substantial reduction in **fear** (<39) at post, 1/6 had a small reduction at post (baseline score already <39); 3/6 continue to improve to follow up (<28). ***HADS-A*****:** all had reduction post	
Guck 2015 (Guck et al. 2015)	MT	Visual and non-overlap analysis revealed increased **speed walking times** (4/4 participants were faster at follow up).	Not measured	Not measured	**"***A multiple baseline across subjects with a changing criterion design indicated that speed walking times improved from baseline only after the PCB intervention was delivered. Six fear avoidance model outcome measures improved from baseline to end of study and five of six outcome measures improved from end of study to follow-up.***"** (Guck et al 2015; Page 113)
	ST	Not measured	Comparison of means and inferential statistics (inappropriate for SCEDs) revealed reduction in **pain intensity** in 4/4 participants at follow up.	Comparison of means revealed improvement **in fear, catastrophizing** (CSQ-CAT) in 3/4 participants, post-treatment and at follow up.	

Combined (n=34)	**Disability**	**Pain**	**Fear**	**Summary**
Exposure-based (GEXP)	**22/25** (88%)	**14/23** (60%)	**26/27** (96%)	Number of participants (relative to sample size) that were reported to have improved after the respective interventions. This summary indicates that GEXP promoted changes in a greater number of participants for disability, pain and fear than GA. Combined, behavioural interventions promoted improvement in disability and fear for a large proportion of participants, while only about half reported improvement in pain.
Activity-based (GA)	**1/13** (8%)	**0/13** (0%)	**0/13** (0%)	
COMBINED	**23/28** (82%)	**14/26** (53%)	**26/30** (86%)	

MT: measures captured at multiple timepoints; **ST:** measures captured at single timepoints **SCED:** Single Case Experimental Design (includes repetitive measures); **A,B,C,D:** phases of design; **SCNED:** Single Case Non-Experimental Design (pre-post measure); **MBD:** Multiple Baseline Design; **CCD:** Changing Criterion Design; **GEXP:** Graded Exposure in vivo; **GA:** Graded Activity; **TSK:** Tampa Scale of Kinesiophobia; **CLBP:** Chronic Low Back Pain; **RMDQ:** Roland Morris Disability Questionnaire; **Fear appraisals:** short instrument containing items from TSK, PASS (Pain Anxiety Symptom Scale), PCS (Pain Catastrophizing Scale) – measured daily; **PHODA:** Photograph Series of Daily Activities (*Sev:* Short electronic Version); **PCL**: Patient Cognitions List (***cat*****:** catastrophizing**;** ***con*****:** pain control); **OMPQ:** Orebro Musculoskeletal Questionnaire; **MPQ:** McGill Pain Questionnaire; **QBPDS:** Quebec Back Pain Disability Scale; **SF-MPQ:** Short Form McGill Pain Questionnaire; **PDI:** Pain Disability Index; **DBT:** Dialectical behaviour therapy; **HADS:** Hospital Anxiety and Depression Scale; **TSK-11:** TSK short form (11 items); **BPI:** Brief Pain Inventory; **N:** sample size

4.5 Discussion

We aimed to determine the current state of evidence concerning the effectiveness of behavioural interventions (broadly grouped as exposure-based and activity-based) that were intentionally designed to target people with CLBP and high pain-related fear, on reducing disability, pain and fear. To capture the breadth of knowledge in this area, this review included RCTs as well as SCEDs.

4.5.1 Summary of main findings

The results of this review suggest that behavioural interventions are effective in reducing disability and fear (*post-treatment, and at short and medium-term follow ups*) in people with CLBP and high pain-related fear, but the magnitude of this interaction varies across study designs (small in RCTs and moderate-large in SCEDs).

Specifically, there is evidence from SCEDs that exposure-based behavioural interventions are effective in reducing disability and fear (*post-treatment* and at *short-term*). This is weakly supported by RCTs, in which exposure was compared to usual care and wait list control. SCEDs also reported that exposure-based interventions are effective in reducing pain *post-treatment* in half of the cases, and most cases at *short-term*. This however, is not supported by RCT outcomes.

There is no evidence from the RCTs of the superiority of one behavioural intervention over another in reducing disability, fear and pain at any timepoints. In view of the methodological restrictions of the SCEDs comparing the two interventions, there is only very weak evidence of the superiority of exposure-based interventions over activity-based interventions for people with CLBP and high pain-related fear (*post-treatment, short-term or medium-term*). The SCEDs presenting between-person comparisons [(de Jong et al. 2005; Vlaeyen, de Jong, Geilen, et al. 2002; Vlaeyen et al. 2001)] used a cross-over design, which was strengthened by the use of sequence randomization, and randomization of treatment commencement [(Morley, Vlaeyen, and Linton 2015; Onghena and Edgington 2005)]. However, the lack of a no-treatment period after the first intervention was introduced makes it difficult to determine if the first intervention did (or did not) influence the second intervention [(Kratochwill et al. 2013)]. As no evaluation of carryover effects was possible with this design due to the small sample (2-3 participants in each group) caution should be taken in interpreting the results of those studies [(Kratochwill et al. 2013; Macedo et al. 2010)]. Furthermore, in De Jong et al (2005) [(de Jong et al. 2005)] participants were randomized to two groups to receive two different interventions (GEXP or GA). This was a limiting factor, as SCEDs are not an adequate design to perform between-group comparisons, especially in such small samples (two groups of 3 participants) [(Kratochwill et al. 2013)].

Collectively, the results of this review suggest that exposure-based behavioural interventions are an effective treatment in reducing disability and fear (*post-treatment, short-term or medium-term*), and modestly effective in reducing pain (*post-treatment* and *short-term*) in people with CLBP and high pain-related fear. However, there is no evidence to support that exposure-based behavioural interventions are superior to activity-based behavioural interventions on reducing disability, pain and fear in people with CLBP and high pain-related fear.

4.5.2 Why are the results of the RCTs different to the results of the SCEDs?

RCTs sit higher than SCEDs on the hierarchy of evidence because of their capacity to control for biases that cannot be controlled for in SCEDs. RCTs are undeniably the framework to test treatment effectiveness, providing results at a population level that are more robust and generalizable than SCEDs (Borckardt et al. 2008). Other potential reasons for the discrepancy between results of RCTs and SCEDs have been previously outlined (Vlaeyen et al. 2012), and include the items listed here: **1)** trials lacking statistical power (Woods and Asmundson 2008; Linton et al. 2008), which may reflect some of the complexities of designing RCTs in this population group; **2)** the issue of high dropout rates in exposure-based RCTs (30-50%) (Bailey et al. 2010; Linton et al. 2008; Woods and Asmundson 2008), affecting sample size; **3)** use of standardised outcome measures in RCTs versus more precise and individualised items used in SCEDs (Vlaeyen et al. 2012), which potentially allow tailored treatment targeting; **4)** frequency of assessment in SCEDs potentially acting as a mechanism for behavioural change (Vlaeyen et al. 2012); **5)** smaller studies with repeated measures may be influenced by 'non-specific' elements such as 'care factor' due to their personalised nature, which may minimize attrition in SCEDs relative to RCTs; **6)** clinician experience with the intervention and delivery setting (multidisciplinary versus stand-alone) (Linton et al. 2008; Vlaeyen et al. 2001); and **7)** differences between RCTs and SCEDs in terms of the criteria used for participant recruitment (fear 'cut-offs'). Previous studies have argued that exposure-based interventions in particular, may not have been as effective due to participants not having 'enough' fear (Leeuw et al. 2008). This systematic review addressed this point by only including studies that had strategies to recruit people with CLBP and high pain-related fear, using standardised measures in isolation (e.g. TSK) (Woods and Asmundson 2008) or combined with more specific measures such as the PHODA (Linton et al. 2008; Boersma et al. 2004).

These aspects highlight some of the inherent methodological differences between the two study designs. Although SCEDs are informative, in particular when testing new interventions or specific populations, RCTs are the framework to test treatment effectiveness at a population level (Borckardt et al. 2008) thus, providing more robust results than SCEDs. Considering the existing number of SCEDs, it appears that there is a need for more RCTs that are high-quality, using strict criteria to target people with CLBP and high pain-related fear. Such trials may be informed by SCEDs to better understand the process of change for an individual undergoing an intervention, potentially optimizing behavioural interventions and their effectiveness (Vlaeyen, Morley, and Crombez 2016).

4.5.3 Why are behavioural interventions not as effective in reducing pain as they are in reducing disability and fear in people with CLBP and high pain-related fear?

That the results suggest that behavioural interventions are not as effective in reducing pain as they are at reducing disability and fear is not surprising. Since the emergence of psychological pain management strategies, they have targeted unhelpful beliefs, emotions and behaviours, and pain coping strategies (Broderick et al. 2016; Henschke et al. 2010), rather than pain (Saragiotto, Maher, Traeger, et al. 2017) (see Moseley and Butler 2015 for a critique of this position)(Moseley and Butler 2015). Activity-based interventions such as graded activity, use time-contingent quotas to increase activity engagement despite pain and do not target the person's feared activity (Vlaeyen et al. 2001). Exposure-based interventions directly target avoidance of feared tasks as the key to promote disconfirmation of erroneous beliefs, and behaviour change (Kroska 2016). This is achieved by repeatedly confronting the feared tasks without the expected catastrophic outcome occurring (Leeuw et al. 2008). Pain however, is not directly targeted.

Pain responses to movement likely reflect complex sensorimotor interactions influenced by physical, psychological, contextual and neurophysiological factors that account for the individual's sensitivity profile (Wallwork, Bellan, and Moseley 2017; Rabey et al. 2017b; Hodges and Smeets 2015) . Thus, one possible reason for the lack of efficacy for exposure-based interventions in this group may relate to the fact that people with CLBP demonstrate variable pain responses to repeated movement (O'Sullivan et al. 2014; Rabey et al. 2017b). For example, in a cohort of 300 people with chronic low back pain, approximately 50% reported pain exacerbation with repeated spinal movement, whereas only a small group (approximately 10%) reported pain reductions with the same movements (Rabey et al. 2017b). In a study involving people with high fear of movement, repeated forward bending was associated with an escalation of pain intensity during the task (Sullivan et al. 2009). We speculate that escalation of pain with repeated movement, during an exposure-based or activity engagement intervention could potentially lead to increased perception of threat and distress related to the movement resulting in an unsuccessful outcome or dropout. Therefore, considering the individual's movement-related pain responses could potentially enhance the efficacy of behavioural interventions in reducing pain.

Another aspect for consideration is that during exposure specifically, people who are fearful or anxious may often use **safety-seeking behaviours** in an attempt to prevent or minimise the feared outcome (Meulders et al. 2016). These behaviours in many cases are considered to be unhelpful, because they occur in response to an erroneous interpretation of cues that signal danger (feared outcome) during a situation that is in fact safe (Meulders et al. 2016; Tabor et al. 2016; Moseley and Butler 2016) - see Tabor et al 2017 (Tabor et al. 2017) for a statistical account of this idea. A recent meta-analysis investigated whether engaging in safety-seeking behaviours during exposure-based interventions was beneficial or detrimental in reducing fear (Meulders et al. 2016). The study was inconclusive and could not support the use or removal of safety-seeking behaviours during exposure treatment (Meulders et al. 2016). That review however, did not include studies of people with pain-related fear. Clinical studies in people with CLBP and pain-related fear have reported that such 'overprotective' behaviours are common (Karayannis et al. 2013; Geisser et al. 2004) and associated with tissue sensitivity profile, altered body perception (Rabey et al. 2017b) and motivation for avoidance (Bunzli, Smith, Schutze, et al. 2015; Bunzli, Smith, Watkins, et al. 2015). For instance, people with back pain may move slowly, breath-hold and co-contract their trunk muscles (Karayannis et al. 2013) to avoid lumbar spine flexion while bending and lifting because they are frightened that flexing the spine may cause pain or damage (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017; Caneiro, Smith, et al. 2017; Bunzli, Smith, Schutze, et al. 2015). This strategy may be considered protective in the presence of acute tissue pathology and/or traumatic injury. Nonetheless, when it persists beyond tissue healing time, or is disproportionate to the pathology or level of trauma, engaging in safety-seeking behaviours is unhelpful, and can be provocative (sustained nociceptive input / tissue sensitivity) (O'Sullivan et al. 2018; Rabey et al. 2017b; Nijs et al. 2017; Dankaerts et al. 2009; O'Sullivan 2005), potentially limiting treatment response.

4.5.4 The 'opportunity' of targeting pain reduction

Taking in consideration that fear and pain intensity are positively associated (Kroska 2016), that pain is modifiable (Saragiotto, Maher, Traeger, et al. 2017), and that experiencing pain control reduces disability in future episodes of back pain (Main, Foster, and Buchbinder 2010), behavioural interventions for people with CLBP and high pain-related fear could be optimized by enhancing their capacity to target and effect change in pain. Consideration of the person's pain responses to movement may promote individualized strategies such as relaxation strategies prior to, and abolishing safety-seeking behaviours during exposure (O'Sullivan et al. 2018). Furthermore, systematic reviews of a pain education approach concluded that targeted pain biology education is probably effective for reducing pain and disability in people with CLBP (Tegner et al. 2018; Louw et al. 2016; Moseley and Butler 2015; Louw et al. 2011; Clarke, Ryan, and Martin 2011). Therefore, integrating pain education that aims at reconceptualizing pain as a marker of perceived danger rather than damage to change pain itself (Moseley and Butler 2015) with exposure may reduce the threat associated with experiencing pain during exposure (O'Sullivan et al. 2018; Lotze and Moseley 2015).

An exposure-based behavioural intervention that considers these aspects and explicitly targets pain control during exposure to feared and/or provocative movements has showed reductions in pain and disability in people with CLBP and moderate (Vibe Fersum et al. 2013) and high (O'Sullivan et al. 2015) disability. However, this intervention is yet to be specifically evaluated in the high-fear group. Qualitative data from patients with CLBP and pain-related fear who received this intervention indicated that enhanced pain control was a key to engage in valued activities and achieving independence (generalization) (Bunzli et al. 2016). Targeting pain control may be an opportunity to optimize exposure-based interventions for people with CLBP and high pain-related fear.

Despite a common and intuitive view, our findings suggest that there is very limited, low quality evidence to support the view that exposure-based interventions are the treatment of choice for people with CLBP and high pain-related fear. Therefore, optimization of these interventions for the treatment of this challenging group of patients is very much needed.

4.6 Strengths and limitations

A key strength of this study is that it comprehensively extends the previous reviews on behavioural interventions for CLBP (Kamper et al. 2015; Macedo et al. 2010; Henschke et al. 2010) and for pain-related fear in chronic musculoskeletal pain (Bailey et al. 2010) by specifically evaluating their effectiveness for people with CLBP and high pain-related fear. This review was prospectively registered, and it was conducted by two independent reviewers following the PRISMA guidelines.

Limitations also exist. *First*, this review included only studies published in English, therefore potentially relevant studies in other languages may have been excluded. *Second*, only a small number of studies were included, which may reflect the strict inclusion criteria (necessary to reach the target population), and/or the small number of studies specifically targeting people with CLBP and high pain-related fear (especially RCTs). *Third*, one of the included studies was a feasibility trial (Pincus et al. 2015), and not powered to inform on the efficacy of the interventions. Nonetheless, the study satisfied our a priori criteria, and it reported the outcomes adequately. *Fourth*, we did not retrieve data specifically from people with high fear from studies that included patients with a range of levels of fear. Pain-related fear is a key mediator to disability (Wertli, Rasmussen-Barr, Held, et al. 2014), and several studies target it to reduce disability in people with CLBP (Monticone et al. 2016; Marchand et al. 2015;

O'Sullivan et al. 2015; Monticone et al. 2014; Linden, Scherbe, and Cicholas 2014; Gremeaux et al. 2013; Monticone et al. 2013; Froholdt et al. 2012; Hill et al. 2011; Leeuw et al. 2008; Walti, Kool, and Luomajoki 2015; Kernan and Rainville 2007; Smeets et al. 2006; Woby et al. 2004).

However, these interventions (cognitive, behavioural, physical or of combined nature) were not specifically designed to target people with high pain-related fear, thus excluding those papers from this review. *Fifth*, interventions were classified as exposure-based versus activity-based behavioural interventions based on consensus in the authorship team. There remains some ambiguity in the field about what exactly determines this classification and our own perspectives may have influenced the comparative results.

4.7 Conclusions

Behavioural interventions for people with CLBP and high pain-related fear are effective in reducing disability and fear, but only modestly effective on pain. Surprisingly, current rationale for advocating exposure-based interventions for the treatment of people with CLBP and high pain-related fear is poorly supported by existing literature. This is likely due to the average quality, limited statistical power and small number of RCTs, and methodological limitations of SCEDs. High-quality, adequately powered RCTs are needed to determine if one behavioural intervention is superior to another on reducing disability, pain and fear in people with CLBP and high pain-related fear. Behavioural interventions may be optimized by enhancing their capacity to target and affect change in pain.

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Ethical issues: Ethic Board approval was not required for this systematic review, as only secondary data was examined. This review was prospectively registered with PROSPERO (CRD42016037175).

Conflicts of interest: *Peter O'Sullivan* receives speaker fees for lectures and workshops on pain management. *G. Lorimer Moseley* has received support from Pfizer, Kaiser Permanente, USA; Workers' Compensation Boards in Australia, North America, and Europe; AIA Australia, the International Olympic Committee, Arsenal Football Club and the Port Adelaide Football Club. He receives royalties for books on pain and rehabilitation, including two books that are cited in this article. He receives speaker fees for lectures on pain and rehabilitation. *All the other authors* declare no conflict of interest.

4.8 Appendix 4.1

Appendix 4.1 Table 4.4 Risk of Bias in N-of-1 Trials (RoBiNT) Scale

RoBiNT Scoring Key (Tate et al. 2014; Tate et al. 2013)	***Vlaeyen 2001*** (Vlaeyen et al. 2001)	***Vlaeyen 2002-A*** (Vlaeyen, de Jong, Geilen, et al. 2002)	***Vlaeyen 2002-B*** (Vlaeyen, De Jong, Onghena, et al. 2002)	***Boersma 2004*** (Boersma et al. 2004)	***De Jong 2005*** (de Jong et al. 2005)	***Linton 2014*** (Linton and Fruzzetti 2014)	***Guck 2015*** (*Guck et al. 2015*)
1. Design: Does the design of the study meet requirements to demonstrate experimental control?	1	1	0	2	1	2	2
2. Randomisation: Was the phase sequence and/ or phase commencement randomised?	2	2	0	0	1	0	0
3. Sampling: Were there a sufficient number of data points (as defined) in each of baseline and intervention phases?	2	2	2	2	2	2	1
4. Blind participants/therapists: Were the participants and therapists blinded to the treatment condition (phase of study)?	0	0	0	0	0	0	0
5. Blind assessors: Were assessors blinded to treatment condition (phase of study)?	1	0	1	0	0	0	0
6. Inter-rater reliability (IRR): Was IRR adequately conducted for the required proportion of data, and did it reach a sufficiently high level (as defined)?	0	0	0	0	0	0	2
7. Treatment adherence: Was the intervention delivered in the way it was planned?	0	0	0	0	0	0	2
Internal validity subscale – score (max 14 points)	**6**	**5**	**3**	**4**	**4**	**4**	**7**
8. Baseline characteristics: Were the participant's relevant demographic and clinical characteristics, as well as characteristics maintaining the condition adequately described?	2	2	2	1	0	1	1
9. Therapeutic setting: Were both the specific environment and general location of the investigation adequately described?	1	0	1	1	0	0	2
10. Dependent variable (target behaviour): Was the target behaviour defined, operationalised, and the method of its measurement adequately described?	2	2	2	2	2	2	2
11. Independent variable (intervention): Was the intervention described in sufficient detail, including the number, duration and periodicity of sessions?	2	2	2	2	1	2	1
12. Raw data record: Were the data from the target behaviour provided for each session?	2	1	2	2	2	2	2
13. Data analysis: Was a method of data analysis applied and rationale provided for its use?	2	2	2	2	2	1	2
14. Replication: Was systematic and/or inter-subject replication incorporated into the design?	2	2	1	0	2	2	0
15. Generalisation: Were generalisation measures taken prior to, during, and at the conclusion of treatment	0	1	0	0	2	0	0
External validity and interpretation subscale – score (max 16 points)	**13**	**12**	**12**	**10**	**11**	**10**	**10**
TOTAL SCORE (max 30 points)	19	17	15	14	15	14	17
	Mod	**Mod**	**Mod**	**Mod**	**Mod**	**Mod**	**Mod**

Bias Scoring system: 0 = criteria not met (or item not stated); **1 =** criteria met with restrictions; **2 =** criteria met; **High risk** (0-10/30); **Moderate risk** (10-20/30); **Low risk** (20-30/30)

Appendix 4.1 Table 4.5 PEDro quality assessment scores for included studies

Study	*Random Allocation*	*Allocation concealment*	*Baseline Comparability*	*Blinding of subjects*	*Blinding of therapists*	*Blinding of assessors*	*Adequate follow-up*	*Intention to treat analysis*	*Between group statistical comparison*	*Point Measures and Variability Data*	*PEDro Score*	*Overall quality of RCT*
Woods & Asmundson 2008 (Woods and Asmundson 2008)	yes	no	yes	no	no	no	no	yes	yes	yes	5/10	Fair
Linton et al 2008 (Linton et al. 2008)	yes	no	no	no	no	no	no	yes	yes	yes	4/10	Fair
Pincus et al 2015 (Pincus et al. 2015)	yes	yes	yes	no	no	no	yes	yes	yes	yes	7/10	High

4.9 Appendix 4.2

Appendix 4.2 Table 4.6 Primary outcome – *Disability*

MULTIPLE TIMEPOINTS								
Study	**Design**	**Disability Measures**	**Visual** analysis	**Descriptive** Pre-Post (criteria)	**Statistical:** Randomiz. tests	**Statistical:** Time-series ARIMA	**Statistical:** PND	**Statistical:** HLM
Vlaeyen 2001 (Vlaeyen et al. 2001)	SCED (AB)	x						
Vlaeyen 2002-A (Vlaeyen, de Jong, Geilen, et al. 2002)	SCED (AB)	x						
Vlaeyen 2002-B (Vlaeyen, De Jong, Onghena, et al. 2002)	SCED (AB)	x						
Boersma 2004 (Boersma et al. 2004)	SCED (MBD)	Function (proxy of avoidance: items 20-25 OMPQ)	√	√				
De Jong 2005 (de Jong et al. 2005)	SCED (ABC/D)	Personally-relevant activities (daily ratings of difficulty)	√		√			
Linton 2014 (Linton and Fruzzetti 2014)	SCED (AB)	x						
Guck 2015 (Guck et al. 2015)	SCED (MBD+CCD)	Speed walking times (seconds)	√				√	√
SINGLE TIMEPOINTS								
Study	**Design**	**Disability Measures**	**Visual** analysis	**Descriptive** Pre-Post (criteria)	**Statistical:** Randomiz. tests	**Statistical:** Time-series ARIMA	**Statistical:** PND	**Statistical:** HLM
Vlaeyen 2001 (Vlaeyen et al. 2001)	SCED (AB)	RMDQ PCL-*dis* (disability items)		√				
Vlaeyen 2002-A (Vlaeyen, de Jong, Geilen, et al. 2002)	SCED (AB)	RMDQ Physical activity (monitor 1 week) *		√				
Vlaeyen 2002-B (Vlaeyen, De Jong, Onghena, et al. 2002)	SCED (AB)	RMDQ		√				
Boersma 2004 (Boersma et al. 2004)	SCED (MBD)	Function (proxy of avoidance: items 20-25 OMPQ)		√				
De Jong 2005 (de Jong et al. 2005)	SCED (ABC/D)	RMDQ Physical activity (monitor)	√		√			
Linton 2014 (Linton and Fruzzetti 2014)	SCED (AB)	Function (QBPDS)		√				
Guck 2015 (Guck et al. 2015)	SCED (MBD+CCD)	x						

SCED: Single Case Experimental Design; **A,B,C,D:** phases of design; **MBD:** Multiple Baseline Design; **CCD:** Changing Criterion Design; **Criteria:** pre-set criteria based on existing cut offs from well-established questionnaires; **ARIMA:** Autoregressive Integrated Moving Average; **PND:** Percentage Nonoverlapping Data; **HLM:** Hierarchical Linear Model; **GEXP:** Graded Exposure in vivo; **GA:** Graded Activity; **TSK:** Tampa Scale of Kinesiophobia; **TSK-11:** TSK short form (11 items); **CLBP:** Chronic Low Back Pain; **RMDQ:** Roland Morris Disability Questionnaire; **QBPDS:** Quebec Back Pain Disability Scale **PCL:** Patient Cognitions List (dis: disability); **OMPQ:** Orebro Musculoskeletal Questionnaire; *: Physical activity was monitored for 1 weeks at three time points, however it was analyzed as a pre-post measured; **PVAQ:** Pain vigilance and Awareness Questionnaire; **PAIRS:** Pain and Impairment Relationship Scale; **MPI:** Multidimensional Pain Inventory (**IS:** interference scale); **PHODA:** Photograph Series of Daily Activities; **HADS:** Hospital Anxiety and Depression Scale (**A** – anxiety subscale); **CSQ:** Coping Strategies Questionnaire (CAT: Catastrophizing subscale). **Subscript *D* or *S*:** language of questionnaire used – *Dutch*, *Swedish*.

Appendix 4.2 Table 4.7 Primary outcome – *Pain*

MULTIPLE TIMEPOINTS								
Study	**Design**	**Pain** Measures	**Visual** analysis	**Descriptive** Pre-Post (criteria)	**Statistical:** Randomiz. tests	**Statistical:** Time-series ARIMA	**Statistical:** PND	**Statistical:** HLM
Vlaeyen 2001 (Vlaeyen et al. 2001)	SCED (AB)	x						
Vlaeyen 2002-A (Vlaeyen, de Jong, Geilen, et al. 2002)	SCED (AB)	Pain intensity (VAS) (daily ratings)				√		
Vlaeyen 2002-B (Vlaeyen, De Jong, Onghena, et al. 2002)	SCED (AB)	Pain intensity (VAS) (daily ratings)			√	√		
Boersma 2004 (Boersma et al. 2004)	SCED (MBD)	Pain intensity (VAS) (daily ratings)	√	√				
De Jong 2005 (de Jong et al. 2005)	SCED (ABC/D)	Pain intensity (VAS) (daily ratings)			√			
Linton 2014 (Linton and Fruzzetti 2014)	SCED (AB)	Pain intensity (VAS) (daily ratings)	√					
Guck 2015 (Guck et al. 2015)	SCED (MBD+CCD)	x						
SINGLE TIMEPOINTS								
Study	**Design**	**Pain Measures**	**Visual** analysis	**Descriptive** Pre-Post (criteria)	**Statistical:** Randomiz. tests	**Statistical:** Time-series ARIMA	**Statistical:** PND	**Statistical:** HLM
Vlaeyen 2001 (Vlaeyen et al. 2001)	SCED (AB)	x						
Vlaeyen 2002-A (Vlaeyen, de Jong, Geilen, et al. 2002)	SCED (AB)	Pain vigilance (PVAQ)		√				
Vlaeyen 2002-B (Vlaeyen, De Jong, Onghena, et al. 2002)	SCED (AB)	Pain vigilance (PVAQ)		√				
Boersma 2004 (Boersma et al. 2004)	SCED (MBD)	x						
De Jong 2005 (de Jong et al. 2005)	SCED (ABC/D)	x						
Linton 2014 (Linton and Fruzzetti 2014)	SCED (AB)	x						
Guck 2015 (Guck et al. 2015)	SCED (MBD+CCD)	Pain intensity Pain beliefs (PAIRS) Pain interference (MPI-IS)		√ (paired t-test)			√	

SCED: Single Case Experimental Design; **A,B,C,D:** phases of design; **MBD:** Multiple Baseline Design; **CCD:** Changing Criterion Design; **Criteria:** pre-set criteria based on existing cut offs from well-established questionnaires; **ARIMA:** Autoregressive Integrated Moving Average; **PND:** Percentage Nonoverlapping Data; **HLM:** Hierarchical Linear Model; **GEXP:** Graded Exposure in vivo; **GA:** Graded Activity; **TSK:** Tampa Scale of Kinesiophobia; **TSK-11:** TSK short form (11 items); **CLBP:** Chronic Low Back Pain; **RMDQ:** Roland Morris Disability Questionnaire; **QBPDS:** Quebec Back Pain Disability Scale **PCL:** Patient Cognitions List (dis: disability); **OMPQ:** Orebro Musculoskeletal Questionnaire; *: Physical activity was monitored for 1 weeks at three time points, however it was analyzed as a pre-post measured; **PVAQ:** Pain vigilance and Awareness Questionnaire; **PAIRS:** Pain and Impairment Relationship Scale; **MPI:** Multidimensional Pain Inventory (**IS:** interference scale); **PHODA:** Photograph Series of Daily Activities; **HADS:** Hospital Anxiety and Depression Scale (**A –** anxiety subscale); **CSQ:** Coping Strategies Questionnaire (CAT: Catastrophizing subscale). **Subscript *D* or *S*:** language of questionnaire used – *Dutch*, *Swedish*.

Appendix 4.2 Table 4.8 Secondary outcome – *Fear*

Study	Design	ROB	Disability Measures	Visual analysis	Descriptive Pre-Post (criteria)	**Statistical:** Randomiz. tests	**Statistical:** Time-series ARIMA	**Statistical:** PND	**Statistical:** HLM
MULTIPLE TIMEPOINTS									
Vlaeyen 2001 (Vlaeyen et al. 2001)	SCED (AB)	Low (20/30)	Fear appraisals (Fear of movement, Fear of pain, Catastrophizing)	√			√		
Vlaeyen 2002-A (Vlaeyen, de Jong, Geilen, et al. 2002)	SCED (AB)	Mod (18/30)	Fear appraisals (Fear of movement, Fear of pain, Catastrophizing)	√			√		
Vlaeyen 2002-B (Vlaeyen, De Jong, Onghena, et al. 2002)	SCED (AB)	Mod (15/30)	Fear appraisals (Fear of movement, Fear of pain, Catastrophizing)	√		√	√		
Boersma 2004 (Boersma et al. 2004)	SCED (MBD)	Mod (14/30)	Fear-avoidance (OMPQ, PAIRS, FABQ)	√					
De Jong 2005 (de Jong et al. 2005)	SCED (ABC/D)	Mod (17/30)	Fear appraisals (Fear of movement, Fear of pain, Catastrophizing)	√		√			
Linton 2014 (Linton and Fruzzetti 2014)	SCED (AB)	Mod (14/30)	Catastrophizing (PCS – daily ratings)	√					
Guck 2015 (Guck et al. 2015)	SCED (MBD+CCD)	Mod (17/30)	x						
SINGLE TIMEPOINTS									
Study	**Design**	**ROB**	**Disability Measures**	**Visual** analysis	**Descriptive** Pre-Post (criteria)	**Statistical:** Randomiz. tests	**Statistical:** Time-series ARIMA	**Statistical:** PND	**Statistical:** HLM
Vlaeyen 2001 (Vlaeyen et al. 2001)	SCED (AB)	Low (20/30)	TSK$_D$ PHODA PCL-catastrophizing	√	√				
Vlaeyen 2002-A (Vlaeyen, de Jong, Geilen, et al. 2002)	SCED (AB)	Mod (18/30)	TSK PHODA	√	√				
Vlaeyen 2002-B (Vlaeyen, De Jong, Onghena, et al. 2002)	SCED (AB)	Mod (15/30)	TSK$_D$ PHODA	√	√				
Boersma 2004 (Boersma et al. 2004)	SCED (MBD)	Mod (14/30)	TSK$_S$ PHODA	√	√				
De Jong 2005 (de Jong et al. 2005)	SCED (ABC/D)	Mod (17/30)	TSK$_D$ PHODA	√	√				
Linton 2014 (Linton and Fruzzetti 2014)	SCED (AB)	Mod (14/30)	TSK$_S$ HADS-A	√	√				
Guck 2015 (Guck et al. 2015)	SCED (MBD+CCD)	Mod (17/30)	TSK-11 Catastrophizing (CSQ-CAT)	√	√ (paired t-test)				

SCED: Single Case Experimental Design; **A,B,C,D:** phases of design; **MBD:** Multiple Baseline Design; **CCD:** Changing Criterion Design; **Criteria:** pre-set criteria based on existing cut offs from well-established questionnaires; **ARIMA:** Autoregressive Integrated Moving Average; **PND:** Percentage Nonoverlapping Data; **HLM:** Hierarchical Linear Model; **GEXP:** Graded Exposure in vivo; **GA:** Graded Activity; **TSK:** Tampa Scale of Kinesiophobia; **TSK-11:** TSK short form (11 items); **CLBP:** Chronic Low Back Pain; **RMDQ:** Roland Morris Disability Questionnaire; **QBPDS:** Quebec Back Pain Disability Scale **PCL:** Patient Cognitions List (dis: disability); **OMPQ:** Orebro Musculoskeletal Questionnaire; *: Physical activity was monitored for 1 weeks at three time points, however it was analyzed as a pre-post measured; **PVAQ:** Pain vigilance and Awareness Questionnaire; **PAIRS:** Pain and Impairment Relationship Scale; **MPI:** Multidimensional Pain Inventory (**IS:** interference scale); **PHODA:** Photograph Series of Daily Activities; **HADS:** Hospital Anxiety and Depression Scale (**A –** anxiety subscale); **CSQ:** Coping Strategies Questionnaire (CAT: Catastrophizing subscale). **Subscript *D* or *S*:** language of questionnaire used – *Dutch*, *Swedish*.

4.10 Appendix 4.3

Appendix 4.3 Table 4.9 Summary of outcomes for RCTs (ordered based on ROB, from high to low)

STUDIES	**OUTCOMES**			**ORIGINAL AUTHORS' CONCLUSIONS**
RCTs	**Disability**	**Pain**	**Fear-Avoidance**	
Woods & Asmundson 2008 (Woods and Asmundson 2008)	GEXP vs WLC: NO difference **PDI** GEXP vs GA: NO difference **PDI** GA vs WLC: NO difference **PDI**	GEXP vs WLC: significant improvement in *pain* and *self-efficacy* GEXP vs GA: significant improvement in *self-efficacy* GA vs WLC: NO difference	GEXP vs WLC: significant improvement in *fear, pain anxiety, catastrophizing* GEXP vs GA: sig. improvement in *fear, pain anxiety* GA vs WLC: NO difference	**"***The findings provide substantial (though not unequivocal) support for the efficacy of GivE over no treatment or graded activity. Specifically, it was observed that individuals receiving GivE showed statistically significantly greater improvement on six out of the eight measures (TSK, FABQ, PASS-20, PCS, HADS, SF-MPQ) compared to wait-list controls, and four out of eight of the measures (TSK, FABQ, PASS-20, and PSEQ) compared to graded activity participants. It is notable that participants in the GivE condition did not demonstrate statistically significant improvements on the primary outcome measure, the PDI, compared to the other treatment conditions***."** (Woods & Asmundson 2008; Page 277-278)
Linton et al 2008 (Linton et al. 2008)	GEXP vs WLC: Significant improvement in disability (**ADL**) for GEXP NO significant difference in **QBPDS** **Effect size:** medium for **QBPDS, ADL**	NO sig. difference in **pain**. **Effect size:** small for pain	NO significant difference in **TSK** and **PCS** **Effect size:** medium for **TSK**; small for **PCS**	**"***Compared to a group receiving usual treatment and waiting for exposure, the exposure in vivo group demonstrated a significantly larger improvement on function. Overall exposure had moderate effects on function, fear and pain intensity. We conclude that exposure may be important in treatment, but is not recommended as a ''stand alone'' adjunct to usual treatment***."** (Linton et al 2008; Page 722)
Pincus et al 2015 (Pincus et al. 2015)	CCBT vs PT: NO difference in reduction of ***disability*** (RMDQ), comparing mean scores at baseline, three and six months post the interventions. Greater improvement in *acceptance* for CCBT	NO difference in reduction of ***pain severity* (BPI)**	NO difference in reduction of ***anxiety*** (HADS-A) and *depression*.	**"***In addition, despite the fact that small numbers did not enable inferential testing, changes in both acceptance and disability were greater in the group receiving CCBT than the control physiotherapy, suggesting that the intervention is promising. This was a feasibility trial, and as such, was not powered to inform on the superiority of either of the interventions."* (Pincus et al 2015; Page 9)

RCT: Randomized Controlled Trial; **GEXP:** Graded Exposure in vivo; **GA:** Graded Activity; **TSK:** Tampa Scale of Kinesiophobia; **CLBP:** Chrinic Low Back Pain; **RMDQ:** Roland Morris Disability Questionnaire; **PCL:** Patient Cognitions List (*dis*: disability; *cat*: catastrophizing; *con*: pain control)**; Fear appraisals:** short instrument containing items from TSK, PASS (Pain Anxiety Symptom Scale), **PCS** (Pain Catastrophizing Scale)**; PHODA:** Photograph Series of Daily Activities (*Sev:* Short electronic Version); **PVAQ:** Pain vigilance and Awareness Questionnaire; **OMPQ:** Orebro Musculoskeletal Questionnaire; **MPQ:** McGill Pain Questionnaire; **QBPDS:** Quebec Back Pain Disability Scale; **PSC:** Patient Specific Complaints; **TAU:** Treatment As Usual; **WLC:** Waitlist Control; **SF-MPQ:** Short Form McGill Pain Questionnaire; **PSEQ:** Pain Self-Efficacy; **PDI:** Pain Disability Index; **DBT:** Dialectical behaviour therapy; **CPAQ:** Chronic Pain Acceptance Questionnaire; **HADS:** Hospital Anxiety and Depression Scale; **TSK-11:** TSK short form (11 items); **PAIRS:** Pain and Impairment Relationship Scale; **MPI:** Multidimensional Pain Inventory (IS: interference scale); **CSQ:** Coping Strategies Questionnaire (CAT: Catastrophizing subscale); **BDI:** Beck Depression Inventory; **CCBT:** Contextual Cognitive Behavioural Therapy; **PT:** Physiotherapy; **BPI:** Brief Pain Inventory**; N:** sample size.

Chapter 5 Clinical study one - Process of Change in Pain-Related Fear: Clinical Insights from a Single Case Report of Persistent Back Pain Managed with Cognitive Functional Therapy.

There is compelling evidence that persistent LBP is an individual experience influenced by multiple factors across the biopsychosocial spectrum. Recent studies have proposed that an individualized approach (Cognitive Functional Therapy - CFT) that is multidimensional in nature, goal-oriented and that promotes control over pain and its impact on daily life might promote change in the challenging group of people with persistent LBP and high pain-related fear. However, this has not been explored specifically in people with high pain-related fear. A repeated measures single-case study was used to explore this individualized approach in a person with persistent LBP and high pain-related fear of bending, providing insight to some of the potential mediators linked to reduction in pain-related fear.

The aims of this study were to evaluate temporal changes in *pain-related fear* (generic fear beliefs and specific fear of bending), and *pain* (pain expectancy and pain experience related to bending with a round-back) in a person with persistent LBP and high pain-related fear undergoing CFT. The use of clinical interviews at 6, 12 and 18 month follow-ups have allowed to explore qualitative factors underlying this process of change.

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Caneiro JP, *Smith A, Rabey M, Moseley GL, O'Sullivan P.*

"Process of Change in Pain-Related Fear: Clinical Insights from a Single Case Report of Persistent Back Pain Managed with Cognitive Functional Therapy" JOSPT. *2017 Sep;47(9):637-651*. doi: 10.2519/jospt.2017.7371.

5.1 Abstract

Study Design: Single-case report with repeated measures over 18 months.

Background: Management of persistent low back pain (PLBP) associated with high pain-related fear is complex. This single-case report aims to provide clinicians with an insight to the process of change in a person with PLBP and high bending-related fear, managed with an individualized behavioural approach - Cognitive Functional Therapy (CFT).

Case Description: a retired manual worker with PLBP believed that his spine was degenerating, that bending would hurt him and avoidance was the only form of pain control. At baseline, he presented high levels of pain-related fear on the Tampa Scale of Kinesiophobia (TSK: 47/68) and a high-risk profile on the Orebro Musculoskeletal Pain Questionnaire (OMPQ score: 61/100). Unhelpful beliefs and behaviours led to a vicious cycle of fear and disengagement of life-valued activities. Guided behavioural experiments were used to challenge his thoughts and protective responses, indicating his behaviour was modifiable and the pain controllable. Using a multidimensional clinical reasoning framework (MDCRF), CFT management was tailored to target key drivers of PLBP, and delivered over six sessions in a three-month period.

Outcomes: Over an 18-month clinical journey he demonstrated improvements in bending-related fear, pain expectancy and pain experience; and substantial changes in pain-related fear (TSK: -14 points to 33/68) and risk profile (OMPQ: -25 points to 36/100). Clinical interviews at 6 and 18 months revealed positive changes in mindset, understanding of pain, perceived pain control, and behavioural responses to pain.

Discussion: This report provides clinicians with an insight to using a MDCRF to identify and target the key drivers of the disorder, and using CFT to address unhelpful psychological and behavioural responses to pain in a person with PLBP and high pain-related fear.

Key Words: kinesiophobia, low back pain, behavioural interventions, clinical journey, case-report.

5.2 Introduction

[CASE REPORT]

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Process of Change in Pain-Related Fear: Clinical Insights From a Single Case Report of Persistent Back Pain Managed With Cognitive Functional Therapy

Pain-related fear in people with persistent low back pain (PLBP) is associated with greater levels of pain and disability,[14,21,101] linked to reduced participation in work[75] and physical and social activities.[80] Disengagement from valued life activities can lead to distress and isolation.[47,89,98] This high-fear group poses a challenge to clinicians managing these disorders.[69]

STUDY DESIGN: Single case report with repeated measures over 18 months.

BACKGROUND: Management of persistent low back pain (PLBP) associated with high pain-related fear is complex. This case report aims to provide clinicians with insight into the process of change in a person with PLBP and high bending-related fear, who was managed with an individualized behavioral approach of cognitive functional therapy.

CASE DESCRIPTION: A retired manual worker with PLBP believed that his spine was degenerating, that bending would hurt him, and that avoidance was the only form of pain control. At baseline, he presented high levels of pain-related fear on the Tampa Scale of Kinesiophobia (score, 47/68) and a high-risk profile on the Örebro Musculoskeletal Pain Questionnaire (score, 61/100). Unhelpful beliefs and behaviors led to a vicious cycle of fear and disengagement from valued life activities. Guided behavioral experiments were used to challenge his thoughts and protective responses, indicating that his behavior was modifiable and the pain controllable. Using a multidimensional clinical-reasoning framework, cognitive functional therapy management was tailored to target key drivers of PLBP and delivered over 6 sessions in a 3-month period.

OUTCOMES: Over an 18-month clinical journey, he demonstrated improvements in bending-related fear, pain expectancy, and pain experience, and substantial changes in pain-related fear (Tampa Scale of Kinesiophobia: 33/68; change, –14 points) and risk profile (Örebro Musculoskeletal Pain Questionnaire: 36/100; change, –25 points). Clinical interviews at 6 and 18 months revealed positive changes in mindset, understanding of pain, perceived pain control, and behavioral responses to pain.

DISCUSSION: This case report provides clinicians with an insight to using a multidimensional clinical-reasoning framework to identify and target the key drivers of the disorder, and to using cognitive functional therapy to address unhelpful psychological and behavioral responses to pain in a person with PLBP and high pain-related fear.

LEVEL OF EVIDENCE: Therapy, level 5. *J Orthop Sports Phys Ther 2017;47(9):637-651. Epub 13 Jul 2017. doi:10.2519/jospt.2017.7371*

KEY WORDS: *behavioral interventions, case report, kinesiophobia, low back pain, pain management*

One challenge relates to the complexity of this group, as people within it often present changes across multiple dimensions, including cognitive,[7,8,84,85] emotional,[23,43] and behavioral responses,[13,22,29,30,33,80,82] lifestyle,[3,7,71,83] social,[69] and pain processing.[65,70,78]

Management of people with PLBP and high pain-related fear may therefore require an approach that considers multiple dimensions and tailors treatment to the individual's presentation and goals.[20,62] However, recent systematic reviews identified that physical therapists feel unprepared to deal with the multidimensional nature of PLBP[2,76,79] and unsure of how to integrate adequate interventions to their practice.[1]

Many studies have investigated approaches to reduce pain-related fear in people with PLBP to more effectively manage the disorder.[16,27,28,38,44,45,67,100] Although no intervention is recommended over another,[67,72] graded exposure in vivo[38,94] and, to a lesser extent, graded activity[53,89] and cognitive behavioral therapy–based approaches[27,28,67] are considered the treatment of choice for people with pain and high fear.[27,94]

Cognitive functional therapy (CFT) is another approach that can be employed

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5.3 Methods

5.3.1 Case description

[CASE REPORT]

in the management of people with high pain-related fear. While evolving from an integration of physical therapy rehabilitation with foundational cognitive and behavioral interventions,[19,34,89] CFT differs from the other interventions, as it is physical therapist led and uses a multidimensional clinical-reasoning framework (MDCRF) to identify and target modifiable contributors to pain and disability in a person-centered manner.[60,62,63] Its components include a personally relevant multidimensional understanding of pain; exposure training directed to pain-provocative, feared, and/or avoided personally relevant goals, during which pain control is explicitly targeted by challenging negative cognitions and modifying how the person physically performs the task (via body relaxation, control, and extinction of protective and safety behaviors); and addressing unhelpful lifestyle factors.[60,62,63] Cognitive functional therapy has shown promising results in the reduction of fear, pain, and disability.[7,60,88] **TABLE 1** outlines key elements of CFT compared to key cognitive behavioral interventions.

To date, however, the process of change in people with high pain-related fear managed with CFT has not been specifically outlined. This case report provides insight into the process of change, using CFT, in a person with PLBP and specific fear related to forward bending.

CASE DESCRIPTION

A 57-YEAR-OLD RETIRED MANUAL worker, Barry (fictitious name), presented with a 25-year history of PLBP. The pain, localized over the lumbar and upper gluteal regions, started insidiously and gradually became worse, affecting work and daily life. The explanation Barry received for his pain was based on computed tomography (CT) scanning, which revealed lumbar spine disc degen-

TABLE 1 — OUTLINE OF THE KEY ELEMENTS OF CFT IN COMPARISON WITH OTHER MAIN COGNITIVE AND BEHAVIORAL INTERVENTIONS FOR PEOPLE WITH PERSISTENT LOW BACK PAIN

Cognitive Behavioral Interventions	Assessment	Management
Shared principles		
CBT/PCST, ACT, GA, GEXP, CFT	Person-centered interview • Collaborative, goal-oriented, and motivational approach using validating communication, facilitating self-disclosure[34,53,63,80,96,98] • Explore a person's beliefs, interpretation, and evaluation about his or her health and symptoms, making the person more aware of his or her reasoning and automatic responses • Explore aspects such as pain (eg, story, behavior, impact on life), coping strategies (eg, avoidance, endurance), biopsychosocial factors and their relationship with pain experience Clinical examination • A physical examination is performed to determine the relevance of physical and radiological findings • Some approaches have the examination performed by a member of the multidisciplinary team (CBT, ACT, GEXP) as part of the referral process, while others have it performed by the treating clinician (GA, CFT)	Collaborative and reflective exploration leads to identification of alternative ways of thinking, reasoning, and behaving, which are encouraged to be gradually tested in daily life[34,53,63,80,96,98] Education • Reduce the negative impact of unhelpful or misconceived beliefs and modify associated behaviors, providing the person with a personalized understanding of his or her pain and disability from a biopsychosocial perspective, as well as identify barriers to achievement of personal goals and set targets for the intervention • Most approaches (CBT, GEXP, GA, ACT) provide education as an individual component of management, using a stand-alone session at the start of the program Physical activation • Encourages physical activation linked to a person's goals Lifestyle • Encourages healthy lifestyle behaviors
Unique principles		
CBT/PCST	Focuses on mental processes such as attention, beliefs, emotions, and associated behavior considered to contribute to the persistence of pain, distress, and disability[34,98]	Psychoeducation • Although the content varies, CBT interventions can comprise techniques to enhance coping skills such as relaxation, attention diversion, reduction of negative thinking and emotions, communication training, and activity pacing[5,34,98] • Provides instruction and guided practice of new coping skill, followed by home assignments and generalization of skill to other areas[5]
ACT	Focuses on functional and contextual psychological experiences[95,96] Uses the hexaflex dimensional approach to diagnostics,[55] a framework that describes the interaction of the processes underlying psychological flexibility	Exposure- and experience-based methods targeting psychological flexibility (including acceptance, present-focused attention, cognitive defusion, committed action) to reduce suffering and allow behavior to be directed to the achievement of value-based goals[95,96] Explicitly does not seek to control pain
GA	Determines activity baseline by requesting the person to engage in goal-related physical activities until pain prevents him or her from continuing[38,53]	Education session explaining the effects of physical inactivity/activity Uses time-contingent quotas to increase activity engagement despite pain. Pacing and positive reinforcement are key features of GA[53]

Table continues on page 639

eration, or "thinning of the discs," as it was explained to him. Barry related that the "damage" to his spine was caused by repetitive lifting and heavy manual work. On the basis of the scan, the physician advised Barry to be careful of his back and suggested physical therapy. Barry reported experiencing pain with physical therapy exercises involving bending, which he believed to have caused more pain and possibly harm to his spine: "I'm not doing that [bending] again!"

Barry reported high levels of contextual stress around the onset of pain from a difficult relationship with his father, with whom he worked, and the loss of his brother. The pain worsened over the last 5 years, and was affecting daily life. Barry reported that in response to his pain, he had become fearful and avoidant of specific movements involving forward bending of the trunk and flexion of his spine (eg, lifting, gardening, manual work in the shed and the car) and of physical activities (eg, bush walking, racing his car). Barry described feeling stiff, fatigued, and sensitive to cold most days and having poor sleep, low energy levels, and low mood. Most of his social interactions were with a group of friends, which he described as an "old men's club," as they often shared their "aches and pains." Barry reported comorbid neck pain and headaches. When asked about the future, Barry believed he was getting old and fragile, and there was little he could do to reverse it. He also reported a history of anxiety and panic attacks throughout his life, and feelings of anger, frustration, and depression, for which he had previously sought psychological treatment. A high-risk profile for pain persistence was identified with the Örebro Musculoskeletal Pain Questionnaire (ÖMPQ; score, 61/100).[46] Based on the screening tool and clinical interview, the key multidimensional factors assessed to be relevant to Barry's presentation are outlined in **FIGURE 1**.

TABLE 1 OUTLINE OF THE KEY ELEMENTS OF CFT IN COMPARISON WITH OTHER MAIN COGNITIVE AND BEHAVIORAL INTERVENTIONS FOR PEOPLE WITH PERSISTENT LOW BACK PAIN (CONTINUED)

Cognitive Behavioral Interventions	Assessment	Management
GEXP	Determines hierarchical perceived harmfulness using the Photograph Series of Daily Activities[38,89]	Education session(s) explaining rationale for treatment based on a person's individual presentation using the fear-avoidance model[38,89] Uses behavioral experiments to expose a person to his or her feared/avoided tasks while challenging unhelpful cognitions and safety behaviors, disconfirming pain expectations[94]
CFT	Interview • Specific questioning regarding beliefs about body posture, activation of core muscles, and "protective" behaviors[60,63,88] • Identification of discrepancies in a person's story between body control (eg, "I must sit tall and brace my core") and his or her pain experience (eg, "It hurts to sit tall and I get relief when I relax") • Examination using guided behavioral experiments • Explore a person's beliefs, emotions, expectations, and body perceptions about feared, avoided, or pain-related tasks linked to personally relevant goals • Observe pain responses and "protective"/safety behaviors during feared, avoided, or pain-related tasks (**FIGURE 3**) • Assess whether protective functional behaviors during feared, avoided, or pain-related tasks are modifiable (**FIGURE 4**) • Assess whether the pain responses during feared, avoided, or pain-related tasks are controllable when protective functional tasks are modified (**FIGURES 4** and **7**) • Assess levels of lower-limb and trunk conditioning linked to provocative tasks and goals • Identify a new strategy that enhances pain and movement control* and reflect this back to the patient to disconfirm his or her beliefs that the task is dangerous or threatening	Making sense of pain • Occurs at the end of the first session and is guided by findings from the interview and examination, considering the experiential learning from guided behavioral experiments[60,63,88] • Use a person's own story/words/metaphors and experience during the behavioral experiments to provide a (new) understanding of his or her pain, disability, and distress: develop a new schema (beliefs and strategies to control pain response) Exposure with "control" • Exposure to feared, avoided, or pain-related tasks as directed by the behavioral experiments and guided by level of pain sensitivity (**FIGURE 1**) • Exposure is preceded by body relaxation, visualization, and reducing protective functional behaviors in order to explicitly enhance emotional, pain, and body control during the task • New strategy is immediately incorporated into rehearsing valued functional activities linked to goals Targeted lifestyle modification • Uses new strategy incorporated in the performance of activities of preference (linked to goals) and based on a person's clinical profile (**FIGURE 1**)

Abbreviations: ACT, acceptance and commitment therapy; CBT, cognitive behavioral therapy; CFT, cognitive functional therapy; GA, graded activity; GEXP, graded exposure; PCST, pain coping skills training.

**In cases where the tissue sensitivity is high and normalizing movement strategies does not promote pain reduction (eg, pain summation occurs during testing) and/or the person is highly distressed, strategies such as diaphragmatic breathing, body relaxation, positive affective labeling, and exposure by visualization of the threatening task are initially used to promote reduction of anxiety response and sympathetic arousal. In these instances, the person will be gradually taken through a process to develop nonthreatening body awareness and relaxation to control his or her response to pain. This often leads to pain control and distress reduction, allowing progress of exposure with functional control. In the few cases for whom pain is not controllable, the person is then encouraged to engage in meaningful activities with a focus away from pain, while encouraging relaxed normalized functional movement to replace "protective"/safety behaviors.*

5.3.2 Multidimensional clinical reasoning framework

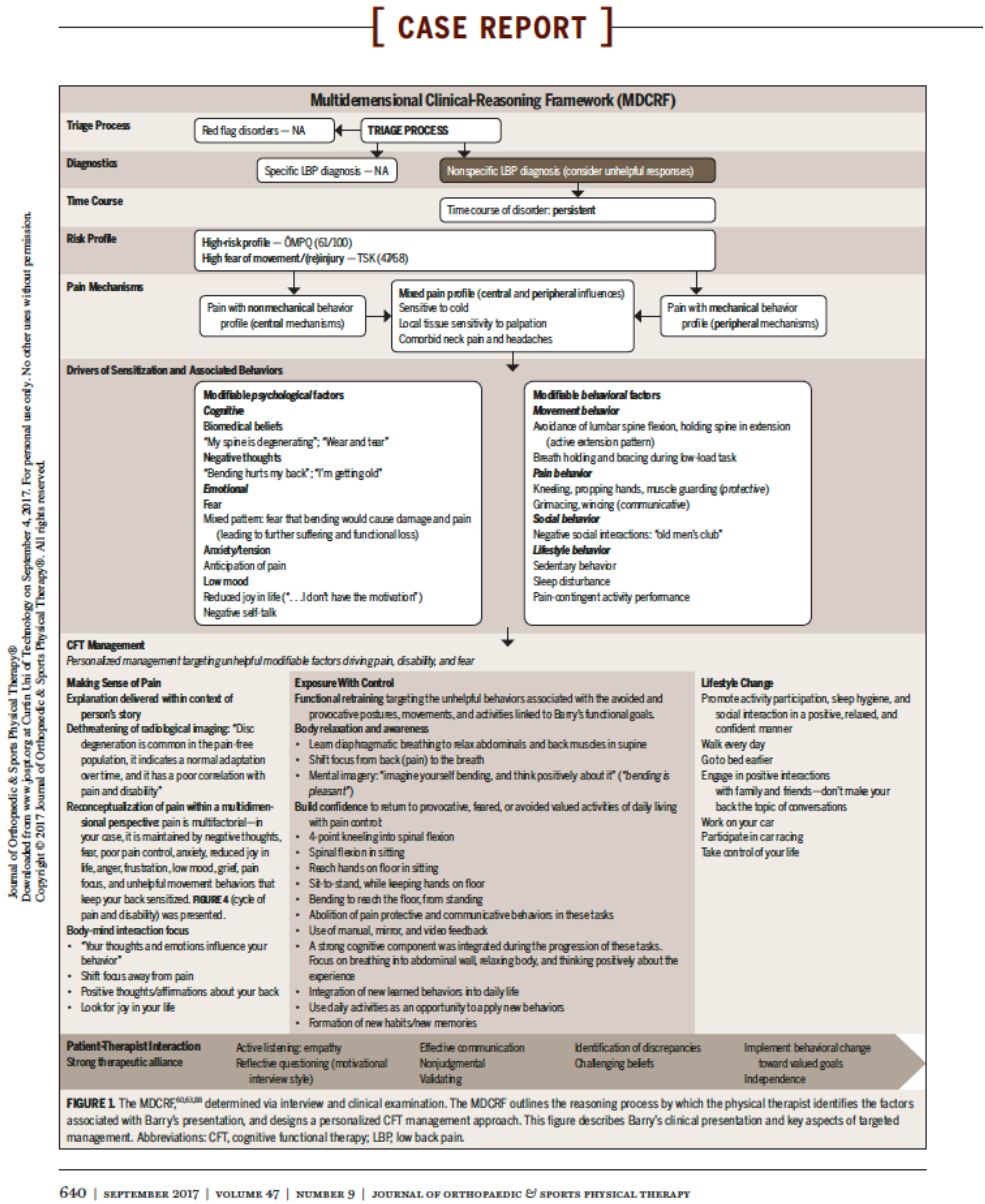

Figure 5.1 Multidimensional clinical reasoning framework

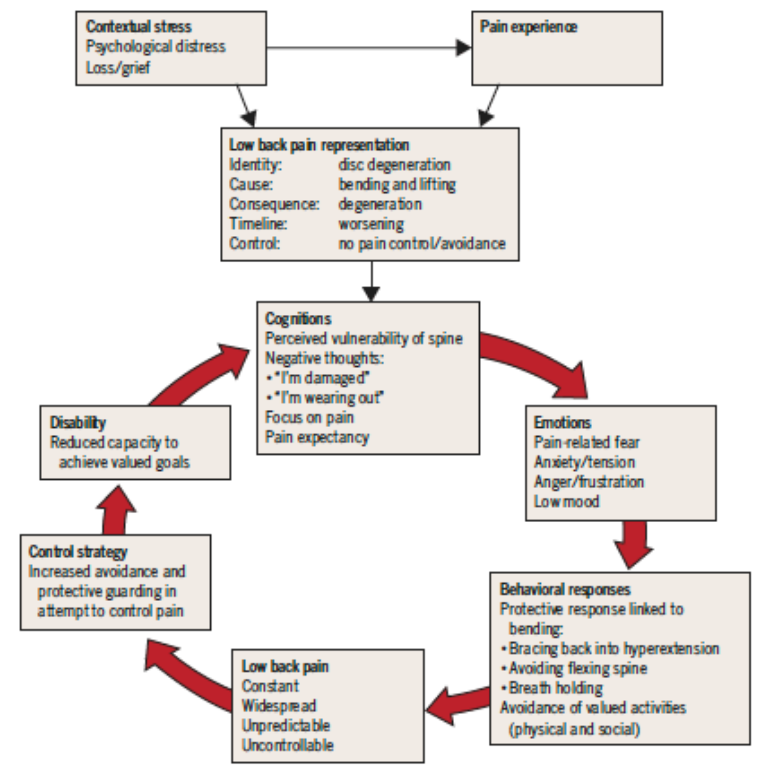

FIGURE 2. Schematic diagram that illustrates Barry's vicious cycle of pain and disability as it was explained to him. The arrows indicate the dynamic interplay across the different dimensions relevant to Barry's presentation. This diagram is an adaptation of the fear-avoidance model[92] based on the common-sense model.[40,41]

Barry reported that his goals were to understand his pain and learn to manage it, so that he could resume the activities that gave him meaning in life (values), such as gardening, manual work, renovating his house, working on his car (all involving bending forward), bush walking, and car racing.

Barry's story illustrates the complexity of a person's journey related to his pain disorder and the factors that can coexist to maintain a vicious cycle of pain and disability.[43,63,93] Using a validating[17] and motivational communication style,[25] Barry's story was summarized verbally and in a diagram (**FIGURE 2**) and reflected back to him, highlighting how his fear of pain and damage beliefs had led to him avoiding valued activities,[92] in turn leading to a negative cycle of declining functional capacity, leaving him feeling depressed and disabled.[47] Barry concurred with this explanation. This diagram was used as the basis for his management plan. Barry took a copy with him so he could revisit the aspects discussed in the first session.

Clinical Examination and Findings

Sensory Characteristics Palpation of the lumbar and gluteal regions revealed tenderness to touch over the muscles, and not the spine (L1-L5). This was used to demonstrate to Barry that the location of symptoms did not correlate well with the findings of the CT scan, challenging Barry's beliefs (that his pain was linked to his "damaged" spine).

Observation of Feared and Avoided Activities The examination focused on forward bending and lifting, because these were Barry's most feared/avoided and provocative activities and were directly related to his functional goals (ie, bending over while working under the hood of his car and gardening and lifting tools in the shed).

When asked to bend forward to touch the floor, Barry reported feeling anxious, as he thought it would hurt him (**TABLE 2**, day 1). Barry was asked to pick up his shoe off the floor; his strategy involved kneeling with one leg and propping a hand on his knee, while keeping his trunk erect and maintaining lumbar lordosis (**FIGURE 3A**). Barry was asked to repeat the task without kneeling, and his strategy was to bend forward by flexing the hips and knees, maintaining his lumbar lordosis (**FIGURE 3B**). During this movement, Barry held his breath, braced one hand on his knee, and presented overt communicative pain behavior (grimacing, wincing). Questioning about his thoughts while performing the task revealed that he was worried about the "thin discs" and focusing on the feeling of his back ("warning signs"). Palpation of the abdominal muscles during these tasks revealed high levels of muscle contraction. Active flexion of the hips in supine lying (a less threatening position, as described by Barry) reproduced a similar pain response to previous bending tasks, involving breath holding, abdominal bracing, and thoughts that bending his back would hurt him.

Guided Behavioral Experiments In order to assess whether the strategies/behaviors used by Barry were modifiable and the pain response controllable, the clinician performed guided behavioral experiments that challenged Barry's thoughts and protective responses related to bending.

Because his pain and protective functional behaviors during bending in standing were not modifiable, he was placed into supine. In supine, Barry was guided on how to perform diaphragmatic breathing and focus his attention on his breath and relaxation of the back and abdominal muscles (with palpation feedback from the physical therapist). Barry was then asked to repeat the active hip flexion task. He reported feeling apprehensive about flexing the hip, which would cause his lower back to bend. The physical therapist advised Barry to flex the hip while focusing on the breath, relaxing and thinking positively about the movement: "bending is pleasant." Barry reported no pain during the task and that he was surprised at this. This was repeated, and the same result achieved, in more provocative positions such as flexing both hips simultaneously, into 4-point kneeling, sitting (touching hands on floor), and moving from sitting to standing (keeping hands on the floor) (**FIGURE 4**).

Clinical Reasoning

Central to Barry's story was the belief that his spine was degenerating, bending would hurt him, and avoidance was his only way of controlling pain. Although the CT scan demonstrated lower lumbar disc degeneration, the changes reported in the scan were consistent with pain-free populations of his age,[4] correlating poorly with pain and disability.[4,31,35] This was discussed with the patient (**FIGURE 1**).

The results from the guided behavioral experiments highlighted the unhelpful beliefs (linked to perceived vulnerability of his spine during bending) and behavioral response related to bending and lifting (bracing his back into extension to avoid spinal flexion). These behavioral responses were pain provocative and functionally limiting (**TABLE 2**). Barry's attempts to make sense of his pain led to increased fear avoidance toward valued activities, promoting disability (**TABLE 2**).

It was clear from the guided behavioral experiments that these protective behaviors were modifiable and, when modified, reduced his pain. These interacting factors were used to disconfirm Barry's belief that flexing his back was dangerous. The cycle, displayed in **FIGURE 2**, highlights aspects of Barry's presentation related to his pain experience and behavioral response. As suggested by recent calls,[12,93] this cycle expands on the original fear-

TABLE 2 Barry's Representation of His Back Pain Related to Understanding, Perceived Pain Controllability, Future Consequences, and Behavioral and Emotional Response to Pain*

	Pre-CFT	End of CFT	Post-CFT		
	Day 1	**3 mo**	**6 mo**	**12 mo**	**18 mo**
Understanding	Biomedical, fixed mindset: • "Pain equals harm" • "Thinning of the discs" • "Pain means I shouldn't do it . . . I could be causing more damage"	Biopsychosocial, mindset change: • "I put my scans in the bin—they have no meaning to my back" • "Experiencing less pain helped to understand the body-mind link . . . That was important to me"	Enhanced biopsychosocial understanding, perception of other factors that influence LBP: • "When I feel pain is mostly due to feeling anxious or tense"	Biopsychosocial: • "Occasionally, I have some background pain, but I generally ignore it and get on with doing things. The level of pain varies and can increase mainly due to overdoing things, or when feeling anxious/tense about things"	Biopsychosocial: • "I can get a bit sorer during the cold weather . . . am also less consistent with my walking when it is cold and wet"
Perceived control	Lack of pain control: • "Pain guides my every day" • "Not bending used to work; now I have pain with most activities" • "The only way of alleviating pain is not doing stuff"	Gained pain control: • "Pain is ok . . . it's under control" • "I have a strategy to manage it now" • "I'm more confident in my body. I know if I continue to be active and move normally, nothing bad will happen . . . because I've done it many times and nothing bad happened so far" • "I stopped taking painkillers"	Sustained pain control: • "[in case of a flare-up] I'd continue with the regime [strategies] . . . If that didn't work, I would seek help"	Sustained pain control under flare-up: • "Two weeks ago, I was lifting some 20-kg bags of cement onto my car and hurt my lower back [stabbing pain]. I have continued walking and doing my usual activities, apart from the more strenuous things I have been doing, and some exercises with dumbbells, but I am still suffering" • "I didn't seek help because I managed it myself"	Sustained pain control: • "I can still suffer from a certain amount of pain and have minor flare-ups occasionally but am able to manage it much better than before"
Consequences	Worse with time/age: • "I'm getting old . . . not much I can do about it" • "My spine is degenerating"	Manageable: • "I don't see myself as an old man"	Under control	Hopes it will continue under control: • "Hopefully in 12 months I will be the same, ie, still with some background pain but able to manage it so I can continue what I am doing, which is far more than I could before this management program"	Under control
Response	Unhelpful	Helpful			

Table continues on page 643

5.3.5 Outcome measures

avoidance model[92] by considering the dynamic interaction of the somatic pain experience, motive for avoidance, and behavioral strategy linked to performance of valued activities (eg, avoidance of spinal flexion).[7,89] It also includes Barry's representation of his problem as a driver of sense-making processes to the maintenance of pain-related fear.[6,39,41] The MDCRF based on Barry's presentation outlines multiple factors driving his disorder (**FIGURE 1**). The MDCRF was used by the physical therapist and Barry to elaborate and guide management. Informed consent was received directly from the participant and his rights protected.

Outcome Measures

Repeated measures allow for temporal evaluation of change in factors of interest over the course of an intervention.[35] All

TABLE 2 Barry's Representation of His Back Pain Related to Understanding, Perceived Pain Controllability, Future Consequences, and Behavioral and Emotional Response to Pain* (continued)

	Pre-CFT	End of CFT	Post-CFT		
	Day 1	**3 mo**	**6 mo**	**12 mo**	**18 mo**
Behavioral	Passive coping, protection/avoidance movement, pain communicative behavior, reduced social interaction, sedentary lifestyle: • "I can't do what I normally do anymore . . . like gardening, walking, working on my car . . . normal stuff" • "I don't go out as much either . . . I fear that the pain will get worse" • "Anything that involves bending hurts me . . . so I don't do it"	New behavior, enhanced pain self-efficacy, active coping: • "I'm more active and not as painful as I anticipated" • "Bending was good because I was not paying attention to my back . . . when I paid attention to my breath and used my legs, it hurt less" • "I raced my car last week and I had no pain . . . first time in years" • "I'm sleeping better"	New behavior, more automatic: • "I'm doing more normal stuff now . . . working in the shed, moving a roller door, ride-on mowing, etc. It gets sore sometimes, but I do the exercises and I recover quicker" • "I'm walking 5 days per week, harder than initially, and it feels better"	Continued active, avoided specific provoking tasks for first few days (adaptive), reverts to old behavior if tired or doing too much (need to refocus): • "No problems with the actual action of bending, and the pain level doesn't increase" • "I was doing a lot of things with my tractor (I have done 50 hours with it in 12 months), including cleaning up overgrown bushes and trees (even chainsawing), moving large rocks and bricks" • "I was chopping wood about every second day and walking when I could. I have built a trailer for a firefighting unit, installed a 5000-L water tank, built some retaining walls (digging trenches and holes), and backfilled them with earth and rocks using the tractor. Just before Christmas, I started a project to renovate and paint our house. This is going to be a big job, as it is a 100-year-old weatherboard house. [I'm] Walking a 5-km route with 2 km of uphill sections every weekday, except when it is cold and wet"	Continued active, attempting new tasks: • "I am in pretty good condition" • "[I'm] very active, walking 5 km at least 4 times a week. I have removed a lot more vegetation around the house to decrease the fire risk. Renovations have slowed a bit due to the weather, but there is still much to do" • "I have used a chainsaw this week to cut a small amount of firewood" • "I haven't cut firewood for about 6 years due to worrying about my back pain. I never thought I would be able to do it again, but this program has given me the confidence to do this and many other things"
Emotional	High fear of movement (bending-related fear/anxiety), low mood: • "I fear that bending will make it worse . . . more painful" • "It makes me nervous just watching someone bending on TV" • "My mood is low most of the time . . ." • "[Pain] is a weight on my shoulders"	Reported to be more hopeful, less fearful, and more engaged in his daily activities: • "Bending is not as scary now" • "My mood has been better . . . I have more energy, too"	No bending-related fear, nonspecific anxiety: • "I'm living my normal life again" • "I can get a bit anxious about other things in life"	Low bending-related fear, frustrated with pain flare, emotional control: • "I think I became overconfident in what I was able to do, as I had been ok for 6 months . . . not ideal, but no need to panic"	Low bending-related fear, increased confidence

Abbreviations: CFT, cognitive functional therapy; LBP, low back pain.
**Excerpts from the clinical interviews (before and after CFT) illustrate changes in Barry's representation over the period of 18 months.*

FIGURE 3. Forward bending strategy adopted by Barry. (A) Illustrates his habitual strategy of bending, whereby he avoids flexing the lumbar spine to pick up his shoe from the floor. Note his kneeling with the right knee on the ground and a hand propped on the left knee. (B) Illustrates a similar trunk movement pattern when he was requested to bend forward to pick up his shoe without kneeling. Note the propping of weight on the knee.

outcome measures, described below, were collected during at least 4 time points.

Self-reported bending-related appraisals of fear and pain were measured at the start of every physical therapy session and immediately prior to and after performing a bending task: "What is your fear of bending?" (fear of bending), "How much pain do you expect to have if you were to bend?" (pain expectancy), and "How much pain did you experience when you bent?" (pain experience). These appraisals were used as part of the guided behavioral experiments to identify discrepancies in pain expectancy versus pain experience when an alternative movement strategy was introduced. Each question was scored on a numeric rating scale (0-10, where 0 is "none" and 10 is "maximum"). The numeric rating scale has established validity and sensitivity,[32] with a 2-point change recommended as the minimal clinically important change.[50,59]

A clinician who was not involved in the treatment conducted clinical interviews after each physical therapy session to capture the patient's perspective as changes occurred. Follow-up clinical interviews at 6, 12, and 18 months were conducted to identify the patient's perception of the intervention, beliefs and attitudes about his back, perceived control and responses to pain, expectations of the future, and the factors that potentially facilitated change.

The Tampa Scale of Kinesiophobia (TSK)[37] was used to assess pain-related fear before and at 6, 12, and 18 months following the intervention. The TSK has acceptable psychometric properties,[51,73] with a suggested minimal clinically important change of 8 points.[50] Barry rated the extent to which he agreed with 17 items on a 4-point Likert scale, from "strongly disagree" to "strongly agree." Considering recent publications[52,94,97] and an earlier validation study,[91] a cutoff value of 40/68 was selected to represent high fear levels.

The short-form ÖMPQ[46] was used as a multidimensional screening tool before and after (6, 12, and 18 months) the intervention. The ÖMPQ has predictive ability for use in clinical and research situations.[46] A cutoff value of 50/100 indicates moderate to high risk for pain persistence.[46]

Intervention

Based on the MDCRF[60,61,63] (**FIGURE 1**), CFT was tailored to target cognitions, pain-related fear, and movement and lifestyle behaviors identified by the physical therapist to be unhelpful and/or provocative to the patient's disorder.[62,88] The intervention (more detail in **TABLES 1** and **3**) involved 3 key aspects:

1. Making sense of pain: focused on reconceptualization of pain within a biopsychosocial context relevant to Barry's story. This occurred as part of the examination, and it was formally presented to Barry at the end of the first session. To facilitate this process, Barry was directed to online resources, including similar patient stories.[66]
2. Exposure with "control": guided exposure to pain-provocative, feared, and/or avoided activities with explicit focus on controlling his responses to pain (cognitive, emotional, and movement). This functional retraining targeted unhelpful cognitions, body relaxation, and reduction of protective behaviors in order to disconfirm that flexion is dangerous and build confidence to return Barry to personally relevant activities of daily living, with pain control.
3. Targeted lifestyle modification: aimed at increasing activity participation (eg, bush walking), sleep hygiene (eg, going to bed earlier), and social interaction (eg, working on a car with friends), integrating the new learned understanding and strategy. The activities (physical and social) were directed by Barry's preference and linked to personally relevant goals.

These 3 aspects were targeted in an integrated manner by the physical therapist, rather than in separate stages by different disciplines, as is common in multidisciplinary pain settings[74] (**FIGURE 5**). The intervention was underpinned by a strong therapeutic alliance and motivational interviewing style (open, nonjudgmental, reflective),[25,58] providing validation.[17,42] The initial session was 1 hour, and the 6 follow-ups were 30 to 45 minutes.

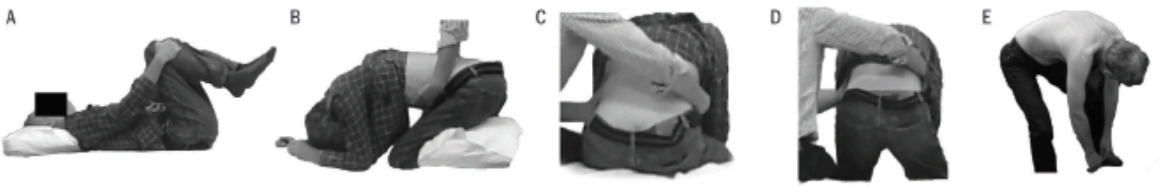

FIGURE 4. Sequence of behavioral tests performed to challenge Barry's thoughts and protective responses related to bending: (A) double hip flexion; (B) 4-point kneeling, sitting on heels; (C) trunk forward bending from seated position; (D) trunk forward bending from standing with guidance; and (E) trunk forward bending from standing independently.

OUTCOMES

Repeated measures tracked Barry's trajectory over 18 months, providing valuable insight to his process of change (**FIGURE 6**).

Bending-Related Appraisals

Barry demonstrated improvements in bending-related fear, pain expectancy, and pain experience at follow-ups of 3, 6, 12, and 18 months (**FIGURE 6**). Although not quantified, Barry's forward bending behavior presented observable changes during the intervention (**FIGURE 7A**), and was maintained at 18 months (**FIGURE 7B**).

Clinical Interview Findings

At 6 months, the clinical interview revealed that Barry had positively changed his mindset, understanding of his pain, perceived control over pain, and responses to pain. At the 12-month clinical interview, Barry described having had a pain flare, which he managed on his own, resuming his valued activities. At 18 months, Barry reported doing well despite a slight increase in pain levels. Barry attributed the increase in pain to his inconsistency in exercising due to cold and wet weather. **TABLE 2** displays the contrast between excerpts from the clinical interviews before (week 1) and after CFT (6, 12, and 18 months).

These findings were observational assessments and interpreted from the clinical interviews. Paraphrasing and reframing Barry's responses to scientific language, the clinical interviews revealed

TABLE 3 Description of the CFT Intervention Used in This Case Report*

Week	CFT Intervention: Key Elements
1 (initial consult, 60 min)	Considering that Barry's findings from the initial consult were described in the body of the article and in **FIGURE 1**, weeks 2-12 are here described
2 (45 min)	Reported feeling more hopeful, less fearful, and more engaged in his daily activities: more active and not as painful as he anticipated Reviewed mismatch of radiology findings and pain levels Reinforced body-mind interaction: anxiety, fear, and muscle tension sensitizing back rather than damaged structures. Explained in a way that helped make sense of the interaction of multiple factors (ie, simple language, examples and metaphors relevant to Barry's story) Reinforced cessation of protective behaviors (breath holding, bracing, and propping hand on knee) Body awareness of breathing to relax trunk muscle tension, followed by repetitive practice of bending with new, nonprovocative movement strategy for forward bending (breathing into abdominal wall, flexing the lumbar spine, and using legs to return to upright) until legs fatigued Encouraged daily walks
4 (45 min)	Discussed flare-up, identifying that pain increase was related to worry and tension associated with working on his car with a friend, who in Barry's view was adopting "dangerous" postures for his back Reported that breathing while bending and lifting was becoming more natural: he identified that relaxing and bending, even when in pain, helped him to recover quicker from the flare-up Practiced "reverse squats," keeping his hands on the floor and lifting his hips (**FIGURE 7B**) until reduced worry and pain anticipation, continued until point of leg fatigue Practiced sustained bending (mimics working under the hood of car) while breathing into abdominal wall, which led to relaxation of the back muscles Practiced lunge pick-up of 5-kg weight, alternating sides: focus on breathing and using the legs until fatigue (mimics manual work, picking up tools) Reinforced sleep hygiene (go to bed earlier) and daily walk
6 (30 min)	Reported feeling encouraged to be more active after last session: walked hills every couple of days; improved mood Reported negative social interactions with friends, which made him think negatively about his back and age Encouraged to participate in positive social interactions: limit discussing health problems or pain; asked family not to ask about back; could ask about achievements (exercise, house and car work) Encouraged to work in shed, car, and garden: activity engagement Practiced picking up 5-kg weight off the floor while on 1 leg without pain; repeated until worry reduced; practiced at faster speed
8 (30 min)	Reported feeling more confident: walking 5-km track with hills, more active around the house and garden (riding on mower, chainsawing, working under the hood of car); some discomfort afterward, but recovers well after doing relaxed movement routine Practiced bending and lifting 10-kg and 15-kg weights off the floor repetitively (15 repetitions to fatigue); moved weights from side to side (mimics lifting and moving heavy objects during manual work); increased speed during practice Encouraged to increase speed of walk and "charge" up the hills for cardio and conditioning
12 (30 min)	Reported no fear of bending, no pain expectation or experience with bending and lifting Reported that new movement strategy became a habit: feeling confident in managing symptom fluctuation and possible flare-up Still working on conditioning: walking hills most days Discussed a "flare-up routine," including strategies to relax body and restore awareness to breathe, positive thoughts during visualization of provocative movements, non–weight-bearing and weight-bearing movements that encouraged relaxed spinal flexion (**FIGURES 2, 5,** and **7C**), sleep hygiene, and physical activation. Should the symptoms persist or worry increase, Barry was instructed to contact the clinic; this did not occur

Abbreviations: CFT, cognitive functional therapy.
A breakdown of the key elements of each session is provided. Considering that Barry's findings from the initial consult were described in the body of the article and in* **FIGURE 1, *a standard CFT initial assessment is not described here for week 1.*

5.5 Discussion

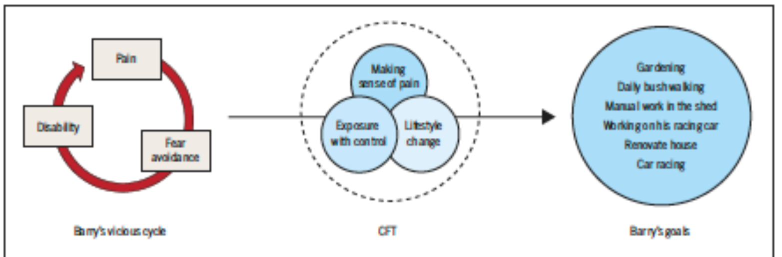

FIGURE 5. Schematic representation of the CFT intervention (center of figure) and the interaction (indicated by arrow) with Barry's disorder and his ability to achieve his valued goals. The diagram illustrates how CFT targets the barrier created by the vicious cycle of pain, fear avoidance, and disability in which Barry is stuck (left of figure), enabling him to achieve his goals (activities that are meaningful to him: right of figure). The dotted line forming the components of the intervention represents the dynamic interaction between the CFT components. Abbreviation: CFT, cognitive functional therapy.

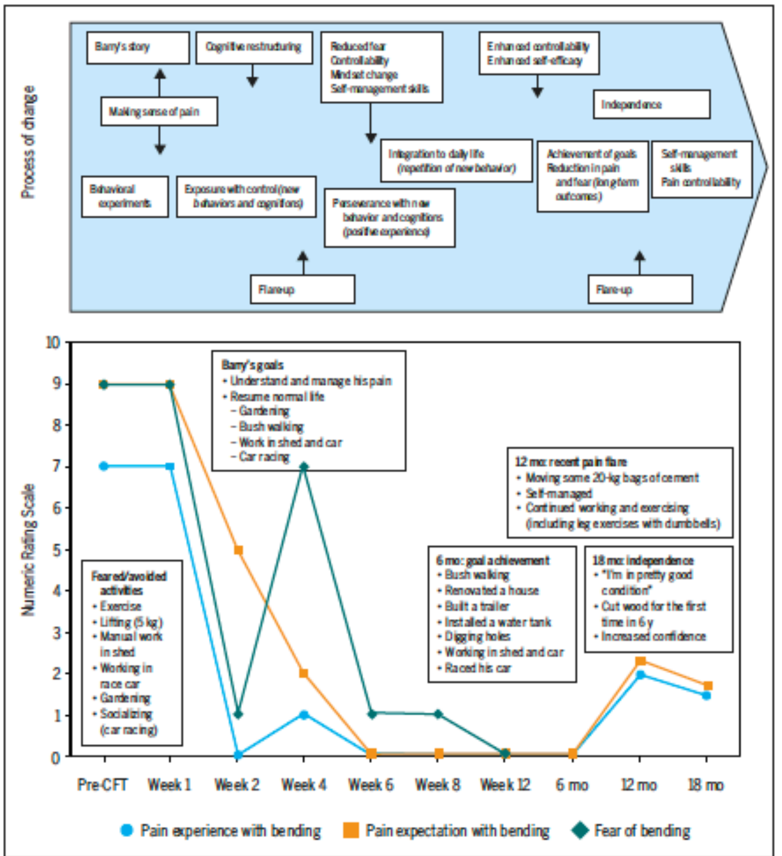

FIGURE 6. The graph on the bottom of the figure outlines changes to bending-related appraisals of fear, pain expectancy, and pain experience before, during, and after CFT management. Three boxes display activities that were feared/avoided by the participant pre-CFT, physical achievement at 6 months, and comments related to a flare-up close to the 12- and 18-month follow-ups. The diagram at the top of the figure is a schematic representation of the proposed process of change for Barry. It outlines the key factors that changed during and after CFT management. The process follows the timeline of the study. Abbreviation: CFT, cognitive functional therapy.

that Barry's perceived facilitators for change were the therapeutic alliance, new movement behaviors, and mindset change (linked to person-relevant explanation, dethreatening of radiology, and watching videos of other patients' stories of change).

The TSK

There was a reduction of 16 points in pain-related fear between the first week (47/68) and 6-month follow-up (31/68) (**FIGURE 8**). This change is double the recommended minimal clinically important difference[50]; the 6-month score was below the cutoff for high fear (40/68),[89,91,94,97] and later scores reached moderate fear levels[38,44,52] (12 months, 33/68; 18 months, 33/68).

The ÖMPQ

There was a substantial change, from high risk (61/100) at the first week to moderate to low risk (37/100) at 12-month follow-up, which was sustained at 18 months (36/100) (**FIGURE 8**).

DISCUSSION

This single case report provides clinicians with insight to using a clinical-reasoning framework to identify key drivers of pain and disability and address these drivers using CFT for a person with PLBP and high pain-related fear (**FIGURE 1**).

Barry was unable to make sense of his pain, and his high level of pain-related fear was associated with an escalation of functional avoidance and distress. Barry's presentation reflects growing evidence that high pain-related fear impacts a person's cognitive (pain and damage beliefs related to fear,[8] higher expectancy of pain and perceived harm related to bending[77,84]), emotional (anxiety related to bending,[23] poor emotional regulation[43]), and behavioral responses (protective movement behaviors while bending,[13,22,33] activity avoidance,[30] reduced social participation[80]). The dynamic interaction of these dimensions highlights that pain-related cognitions and behaviors cannot be separated when managing high-fear patients. Pain-related fear may be dynamic and responsive to changes in the pain experience.[12] Bunzli[6] and Bunzli et al[7] suggest that new iterations of the fear-avoidance model should consider the person's somatic pain experience to better understand the basis for fear avoidance in the management of people with PLBP and high fear.

This report used repeated measures to capture temporal changes in bending-related appraisals of fear, pain expectancy, and pain experience in the longer term, in line with recent trajectory research in low back pain.[96] Use of a qualitative element via clinical interviews provided insight into Barry's perspective on this process. In the 6-month follow-up clinical interview, Barry reported the key aspects of the intervention that helped him attain independence: new behaviors and mindset change, underpinned by a strong therapeutic alliance. Drawing from these findings and current knowledge, the following builds an understanding of the potential processes of change for this patient.

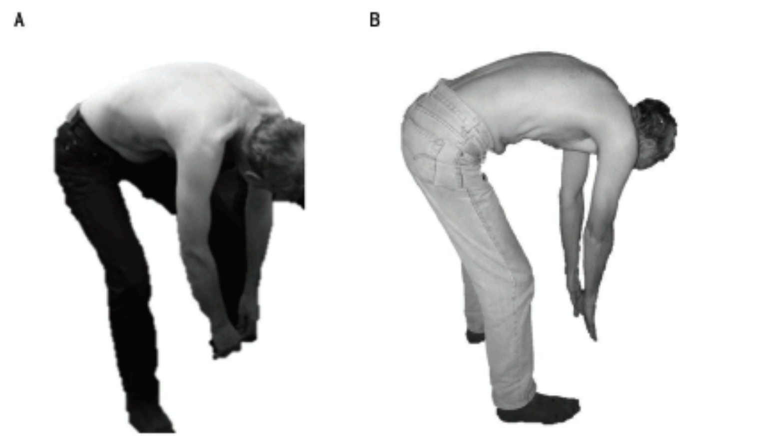

FIGURE 7. Illustrates a change in forward bending behavior. (A) Barry's new movement behavior, demonstrating spinal flexion at week 6 and (B) at 18-month follow-up (photo provided by Barry). Compare with **FIGURE 3B**.

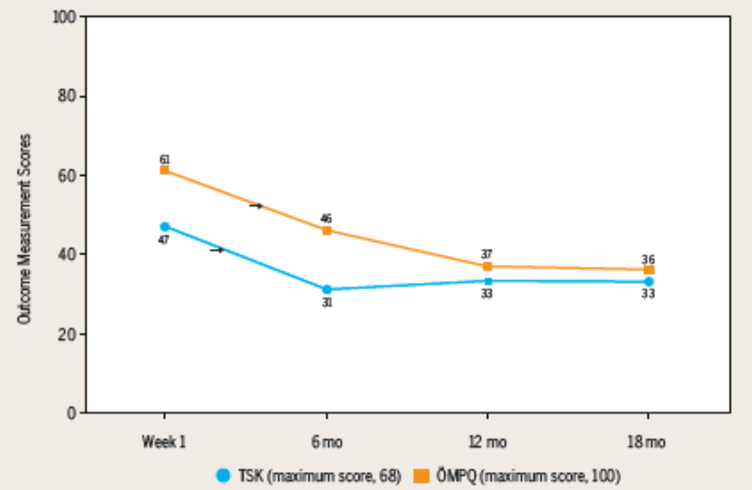

FIGURE 8. Barry's outcomes of pain-related fear (TSK: blue circles) and multidimensional risk profile (ÖMPQ: orange squares) before (week 1) and after (6, 12, and 18 months) CFT intervention. The arrows indicate the cutoff points for the respective outcome measures: ÖMPQ scores above 50 indicate moderate to high risk,[46] and TSK scores above 40 indicate high fear.[52,94,97] Abbreviations: CFT, cognitive functional therapy; ÖMPQ, Örebro Musculoskeletal Pain Questionnaire; TSK, Tampa Scale of Kinesiophobia.

New Behaviors

The use of guided behavioral experiments to challenge Barry's pain-related beliefs was central to his management. The aim was to gradually expose him, with pain "control," to threatening movements and activities related to lumbar spine flexion and forward bending, which he believed would be "damaging and pain provocative." Challenging his behavioral responses associated with these tasks using relaxed diaphragm breathing, relaxation of his back into flexion, and reassurance that the movement was safe resulted in pain reduction during bending. This confronted his beliefs that bending was dangerous, while developing body awareness. Relaxed, mindful breathing directed to the person's awareness of the experience has been linked to a reduction in pain perception and autonomic arousal.[9] This could have reduced protective responses to the thought of bending.

The experience of bending without pain challenged Barry's expectations, illustrated by substantial change in pain appraisals between the first and second sessions (**FIGURE 6**). Inhibitory learning theories suggest that a new strategy that violates expected negative outcomes and allows repetitive exposure to a positive experience, without the use of pain-protective responses (cognitive and behavioral), can lead to formation of new (safe) memories.[11,48,87,89] This supports that Barry's experience in the first session provided him with a safe opportunity for learning a new behavior[11] (**FIGURE 7**).

This new behavioral learning was challenged when Barry experienced a

5.6 Proposed Considerations

pain flare in the fourth week of the intervention. Despite an increase in perceived threat, Barry continued the new behavior, which he reported resulted in a quicker recovery. This experience provided further support that the new strategy was effective in controlling his pain. This was further challenged when Barry experienced a second pain flare just before the 12-month follow-up. Barry self-managed this episode, resuming normal activities soon after the flare (**FIGURE 6, TABLE 2**) (12-month follow-up). Barry's response (behavioral and emotional) to both these situations suggests that he has reached independence and is living effectively (**FIGURE 6, TABLE 2**) (12- and 18-month follow-ups).

The experience of control over pain is a predictor of reduced pain-related anxiety[7,99] and disability in future pain episodes.[54] It is therefore possible that perceived pain controllability reduced the intensity and unpredictable nature of pain, enhancing confidence and allowing perseverance of the new behaviors. Flare-ups offer an opportunity for learning, as the person's response to an aversive situation is tested.[11] In this case, Barry responded differently to flare-ups, and this positive self-management experience enhanced self-efficacy and facilitated fear reduction, as observed in a group of PLBP patients who improved with CFT.[7] It appears that experiencing pain control through behavioral learning was central to Barry's reduction in fear and pain (**FIGURE 6**, weeks 6-12 and **TABLE 2**).

Mindset Change

Paraphrasing Barry's responses, behavioral learning provided positive experiences, helping him develop a new understanding of the body-mind interaction (mindset change) (**TABLE 2**). This change evolved slowly throughout the intervention period and was influenced by cognitive and behavioral components (**FIGURE 6**). The provision of personalized, multidimensional education to make sense of his pain (a key element of CFT) was valued by Barry, and likely played a role in his adherence to the intervention.[58] Barry reported that the dethreatening explanation of his radiology was important for his understanding of its relevance to his problem,[36,86,89] and that watching videos of people with PLBP who had experienced positive change[66] assisted him in feeling more hopeful. Although education may promote moderate reduction in pain-related fear in PLBP patients,[10,49,56] it does not promote change in behavioral response to fear when delivered alone.[15] In Barry's case, behavioral learning was essential for self-efficacy enhancement and mindset change, important steps toward achieving independence.[7] This is supported by Barry's response to the pain flares (**TABLE 2, FIGURE 6**) and results of the outcome measures, which were sustained at lower "risk" levels[38,94] at long-term follow-ups (**FIGURE 8**). Despite the fact that he still describes having "low-grade pain," Barry continues to perform activities that he values (eg, "walking 5 km, gardening, cutting firewood for the first time in 6 years . . ."), suggesting that he is living effectively.

Therapeutic Alliance

The collaboration formed by a trusting relationship between physical therapist and patient[18] is considered central to CFT.[63] A systematic review investigating factors influencing this relationship demonstrated that physical therapist communication and interpersonal (eg, active listening, empathy, understanding) and practical skills (eg, personalized education, individualized care) were key elements in enhancing treatment interaction, adherence, and outcomes.[58] Strong therapeutic alliance predicted positive outcomes in musculoskeletal,[18,24] psychological,[87] and medical interventions.[26,81]

Therapeutic alliance has a role in challenging a person's beliefs through effective communication.[7] The use of a validating[17] and motivational interview style[25] provided insight into discrepancies in Barry's beliefs, coping strategies, and understanding about (his) pain, which assisted the physical therapist in identifying modifiable barriers for targeting behavioral change.[42,63] Clear and directive communication was used at times to implement behavioral change, especially in relation to abolition of unhelpful biomedical beliefs (eg, avoidance of spinal flexion) and pain behaviors. Barry reported that the physical therapist's confidence and "toughness" were important to his adherence to CFT. This directive communication style has been reported to be important for treatment outcomes, and is linked with higher enablement and patient satisfaction,[68] providing patients with more confidence in taking an active role in their journey to recovery.[64]

Proposed Considerations

It is proposed that the new behaviors and mindset provided a platform for confronting avoidance behaviors and returning to valued functional activities with reduced pain. Although speculative, this is likely to have modulated changes in cognitive, emotional, behavioral, and sensory processes.

The proposed process of change for this patient (**FIGURE 6**) is in line with hypothesized mechanisms of change attributed to CFT, which are likely to be multifactorial given the personalized body-mind behavioral approach, influencing factors known to affect pain sensitivity and disability.[7,63,88] This is supported by previous work showing reduction in fear and improved mood in a randomized controlled trial with moderately disabled PLBP patients.[88] A recent case series with disabled PLBP patients demonstrated large reductions in pain, disability, and fear of physical activity, as well as development of positive back beliefs and self-efficacy enhancement.[60] The authors value the importance of these measures and acknowledge their absence as a limitation of this case report. Cognitive functional therapy may also have affected physical-behavioral aspects, such as relaxation of trunk muscles, normalization of provocative movement, and pain behaviors[60,88] (**FIGURE 7**). Although evidence for these changes is lacking, further studies are under way to test such mechanisms.

Summary

The MDCRF enabled the clinician to identify and target unhelpful cognitions, emotions, and behavioral responses that drive PLBP and disability,[60,61,88] tailoring the CFT intervention to the person's needs and goals. Although the outcomes must be considered within the limitations of a single case, this approach appeared to assist Barry to reduce his fear via enhanced pain controllability, providing alternative understanding and behavioral response to his pain. This single case report enabled frequent and in-depth repeated assessment to elucidate elements of change over time. ◉

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Chapter 6 Clinical study two - An evaluation of the process of change in four people with persistent low back pain and high pain-related fear managed with Cognitive Functional Therapy: a replicated single-case experimental design study

Considering persistent LBP is an individual experience, 'how change unfolds' and 'what factors underlie change' at an individual level emerge as important questions. However, these questions have not been evaluated at an individual level. Chapter 2 features single-case experimental design as an adequate framework for an evaluation of the process of change at an individual level because of its flexibility that accommodates the between-person heterogeneity, within-person variability over time, and because it enables assessment of multiple factors at multiple timepoints. Thus far, no studies had used single-case experimental designs to evaluate temporal changes in multiple potential mediators of treatment response in interventions specifically designed for people with persistent LBP and high pain-related fear.

The aims of this study were (i) to evaluate temporal changes in disability and potential mediators from cognitive and emotional dimensions before, during and after a Cognitive Functional Therapy intervention; (ii) to evaluate how changes in potential mediators related to changes in disability at different timepoints during this intervention in four people with persistent LBP and high pain-related fear.

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"*How does change unfold*? An evaluation of the process of change in four people with persistent low back pain and high pain-related fear managed with Cognitive Functional Therapy: a replicated single-case experimental design study" (*under review*)

6.1 Abstract

Purpose: To understand the process of change at an individual level, this study used a single-case experimental design to evaluate how changes in potential mediators related to changes in disability at different timepoints during an exposure-based behavioural intervention in four people with persistent low back pain and high pain-related fear.

Results: For all participants, visual and statistical analysis indicated that changes in disability and proposed mediators were clearly related to the commencement of Cognitive Functional Therapy. This was supported by standard outcome assessments at single timepoints (pre-post). Cross-lag correlation analysis determined that, for all participants, changes in most of the proposed mediators (pain, pain controllability, and fear) were most strongly associated with changes in disability at *lag zero*, indicating that changes occurred concomitantly and not before changes in disability. Importantly, these changes occurred at different rates and patterns, highlighting the individual variability of the temporal process of change.

Conclusion: This study demonstrated the interplay of factors associated with treatment response, highlighting "*how change unfolded*" uniquely for each individual. The findings of an early temporal relationship between factors underpinning treatment response and outcome, and the individual variability in the process of change challenge the linear understanding of therapeutic change. Replication of these results is needed.

Key words: Process of change; mediators; low back pain; pain-related fear; behavioural change.

6.2 Introduction

Persistent low back pain (PLBP) that is associated with high pain-related fear is disabling (Vlaeyen, Crombez, and Linton 2016), impacting on work (Coggon et al. 2013), physical (Martel, Thibault, and Sullivan 2010) and social (Hoogendoorn et al. 2000) participation. This high-fear group often presents with changes across multiple interacting factors, including cognitive (Bunzli, Smith, Schutze, et al. 2015), emotional Glombiewski (Glombiewski et al. 2015), behavioural (Karayannis et al. 2013; Thomas and France 2007; Geisser et al. 2004), lifestyle and social (Bunzli, Watkins, et al. 2013), and pain processing (Rabey, Slater, et al. 2015; O'Sullivan et al. 2014). The interplay of these factors is likely to vary for each person, and fluctuate over time (O'Sullivan et al. 2016; Kongsted et al. 2016).

This inherent non-linearity is a central feature of a complex system, in which the relationships between components is key to understanding behavioural adaptation over time (Brown 2009). Therefore, understanding how changes in these factors relate to fear and disability reduction over the course of an intervention may provide important insight in change processes involved in behavioural change in people with high levels of pain-related fear. Mediation analysis provides a useful method to investigate how multiple factors relate over time. Mediators are defined statistically as factors that 'lie on the causal path between the exposure and the outcome' (Lee et al. 2017), meaning that mediators change because of an intervention and correlate with changes in the selected outcome. This can provide information regarding factors that contributed the most to the treatment effect. Randomized controlled trials (RCTs) are the most common framework for analysis of mediators (Mansell, Kamper, and Kent 2013). However, they require large samples and expenditure and critically, they are limited in the number of variables and timepoints that can be captured, with many studies often assessing a single mediator at a single timepoint during the intervention (Mansell, Hill, Main, Vowles, et al. 2016). This is an obvious limitation when investigating complex systems because the time course of the mediator-outcome relationship is likely to vary between individuals. RCTs may therefore be insensitive to the timing of mediator and outcome change in relation to the intervention (Riley and Gaynor 2014), an important limitation in establishing mediation (Kazdin 2007).

In contrast to mediation analysis conducted in RCTs, single-case experimental design studies (SCEDs) facilitate detailed assessment at frequent time points, capturing multiple potential factors related to an individual's response to treatment (Morley 2018; Morley, Vlaeyen, and Linton 2015; Borckardt et al. 2008; Gaynor and Harris 2008). SCEDs are an intensive, prospective and controlled study of the individual, using each person as their own control to enhance reliability (Morley 2018; Morley, Vlaeyen, and Linton 2015). SCEDs enable the adoption of a complex system perspective, which accommodates interaction of multiple factors and within-person temporal variations, therefore reflecting individuality in the evaluation of the therapeutic change process. Well-designed SCEDs, that include repeated measures and a stable baseline, can answer questions of improvement and change process, to unravel the anatomy of therapeutic change (Borckardt et al. 2008).

Considering the need to understand how change unfolds at an individual level, we employed a SCED. The aim was to evaluate how changes in potential mediators are related to changes in outcome (disability) at different timepoints during a behavioural intervention for people with PLBP and high fear. A pre-requisite was that the intervention changed both the outcome and proposed mediators. The intervention was an individualized exposure-based behavioural approach for the management of people with PLBP called Cognitive Functional Therapy (CFT). Although CFT has shown promising results in the reduction of fear, pain and disability (Caneiro, Smith, et al. 2017; Bunzli et al. 2016; Vibe Fersum et al. 2013; O'Sullivan et al. 2015), the process by which reduction in disability is mediated is yet to be quantitatively investigated (Bunzli et al. 2016). The fear-avoidance model (Vlaeyen and Linton 2000) proposes that pain-related cognitive and emotional responses to pain can fuel an unhelpful cycle that leads to disability. We hypothesized (Mansell et al. 2017; Caneiro, Smith, et al. 2017; Bunzli et al. 2016; O'Sullivan et al. 2015; Vibe Fersum et al. 2013; Leeuw et al. 2008; Lee et al. 2015) that pain, pain controllability, fear, distress and sleep would mediate reduction in disability.

6.3 Methods

This study complies with The Single-Case Reporting guideline In BEhavioural interventions (SCRIBE) 2016 (Tate et al 2016).

6.3.1 Design

A single-case experimental design (SCED) with replication across 4 participants was employed. There were three-phases (A-B-A'/B') with a criterion-based phase changing (A'/B') sequence. **Phase A** consisted of an eight-week baseline period with no intervention. **Phase B** was a twelve-week period of CFT. Behavioural interventions are non-withdrawable, meaning their effect is expected to carry over after the intervention is terminated. Therefore, a subsequent **Phase A'** was used as a follow up period of twelve weeks, with an embedded criterion-based phase changing (A'/B') sequence. A **criterion** was set *a priori* to trigger **Phase B'**, a second treatment phase with up to 5 'booster' sessions. The criterion was defined as: *disability scores during follow up (phase A') that were equal or greater than the average disability scores during baseline (phase A) + 1 point for two consecutive weeks*. Phase B' would allow a second manipulation of the outcome targeted by the intervention (Tate et al. 2017).

6.3.2 Participants

Participants were recruited from the cohort of a recently completed laboratory study involving persons with PLBP and pain-related fear (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017). **Inclusion criteria were:** Adults aged 18 years and older with dominant axial LBP (between T12 and gluteal fold), greater than 6 months duration; pain intensity ≥4/10 on the numerical rating scale (NRS 0-10) for average pain in the past week; and high pain-related fear (scoring ≥40 on Tampa Scale of Kinesiophobia - TSK) (Kori, Miller, and Todd 1990) and have specific fear of bending and lifting with a flexed lumbar spine (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017). This was operationalised as a score of ≥7/10 on a pictorial NRS displaying a side view picture of a person bending and lifting a box with a flexed lumbar spine followed by the question: "How fearful are you of performing this task?" - anchored on "0: No fear", and "10: Maximum fear") - adapted from Caneiro et al (2017). **Exclusion criteria were:** report of dominant leg pain, diagnosis of serious pathology (infection, cancer, inflammatory disorders, fracture), radicular pain with neurological deficit, grade 3 or 4 spondylolisthesis, pregnancy or inability to speak English. Fifteen people responded and completed the criteria questionnaires. Nine met the criteria. Four agreed to participate (**Figure 6.1**). Characteristics of the participants at baseline (week 1) are detailed in **Table 6.1**.

This study was approved by the health research ethics committee at Curtin University – approval number HRE157/2015. Written informed consent was obtained from each participant prior to start of the study.

Figure 6.1 Flowchart of recruitment procedure and study design.

Table 6.1 Detailed characteristics of the participants at baseline (weeks 1 and 8)

	P1	P2	P3	P4
Age (*years*)	66	40	52	67
LBP duration (*years*)	6	22	13	45
Person-specific disability (*PSFS*)	Lifting and carrying heavy	Bending and lifting heavy	Bending and lifting/gardening	Vacuuming/Mopping and gardening
Action (*Past management – B-IPQ*)	Manual therapy, core work, Pilates, injections	Chiro, Physio, massage, Pilates, injections, Opioids++	Rest, manual therapy, inversion table, TENS, injections	Massage, exercise, medication, injections+
Appraisal (*Was the action effective?*)	ineffective	ineffective	ineffective	ineffective
Standardised outcome measures	**BAS-W1**	**BAS-W1**	**BAS-W1**	**BAS-W1**
Disability (RMDQ)	11	10	16	10
Pain-related fear beliefs (TSK)	48	45	55	50
Pain catastrophizing (PCS)	40	25	42	21
Pain-related anxiety (PASS-20)	51	42	67	32
Back beliefs (BackPAQ)	-11	-7	-11	-10
Illness perceptions (B-IPQ)	61	58	63	55
Back awareness (FreBAQ)	18	13	15	3

PSFS (Patient Specific Functional Scale – most disabling activity for each participant is presented here); **B-IPQ** (score range 0-80): higher scores indicate more negative illness perceptions; **Disability** (score range 0-24. High scores indicate higher disability); **TSK** (score range 17-68. High scores indicate higher fear of damage/pain); **PCS** (score range 0-52. High scores indicate higher pain-related catastrophic thoughts); **PASS-20** (score range 0-100. High scores indicate higher pain anxiety); **BackPAQ$_{10}$** (score range -20-20. Negative scores indicate negative beliefs); **FreBAQ** (2 items; score range 0-20. High scores indicate poor back awareness); **BAS-W1:** assessment at first week of baseline (week 1).

6.3.3 Assessment timepoints

Following SCED guidelines (Tate et al. 2017; Kratochwill et al. 2010), weekly assessments of the outcome and proposed mediators were taken for each participant during the baseline (8 data points, allowing for assessment of stability of data during this period) (Morley, Vlaeyen, and Linton 2015), treatment phase (12 data points) and follow up phase (12 data points); a total of 32 data points were collected. Establishment of stability over the baseline phase enhances the internal validity of the design by controlling for time and thus maturation and regression to the mean, therefore serving a similar function as a no-treatment control group (Auld et al. 2017; Polli et al. 2017; Morley, Vlaeyen, and Linton 2015; Kratochwill et al. 2013; Moseley, Zalucki, and Wiech 2008) (**Figure 6.1**). The follow up period provides information about the short-term maintenance of the intervention effect. Direct inter-subject (original + 3 cases) and inter-clinician (2 physiotherapists) replication enhances the strength and generalizability of the findings (Morley, Vlaeyen, and Linton 2015).

6.3.3.1 Assessment at multiple timepoints

A 23-item online questionnaire (**Appendix 6.1**) was developed to assess the primary outcome (disability) and proposed mediators of change on a *weekly* basis. Each of the items was rated on an 11-point NRS (0-10 anchored accordingly) (Dworkin et al. 2005). The items are described below.

6.3.3.1.1 Primary outcome

Disability was assessed with the *Patient Specific Functional Scale – PSFS* (Beurskens et al. 1999). At the initial assessment, participants listed 3 activities of daily living, each item was rated on a 11-point NRS in response to the question "*How difficult is it for you to perform this activity because of your back pain?*", anchored with '0 = able' and '10 = unable'. The activity with the highest rating was selected and used as the personalised disability item for the remaining weekly measures. The PSFS has a smallest detectable change (SDC) of 2.5 points, and has been shown to be reliable (Beurskens, de Vet, and Koke 1996).

6.3.3.1.2 Proposed mediators

Potential mediators were hypothesised from theory (Mansell et al. 2017; Caneiro, Smith, et al. 2017; Bunzli et al. 2016; Lee et al. 2015; O'Sullivan et al. 2015; Vibe Fersum et al. 2013; Leeuw et al. 2008). A total of ten potential mediators (allocated into five 'mediator groupings') were assessed: **(1) Pain:** Pain intensity, Pain interference; **(2) Pain controllability:** Pain control, Pain self-efficacy; **(3) Fear:** Fear of damage/pain, Pain anxiety, Pain catastrophizing, Avoidance beliefs; **(4) Distress:** Depression, Anxiety and Pain bothersomeness, and **(5) Sleep:** Sleep difficulty. This short instrument can be seen in **Appendix-A**.

6.3.3.2 Assessment at single timepoints

The use of **standardised outcome measures** with established psychometric properties provides information as to whether participants have made a reliable change (Morley 2018; Onghena and Van Damme 1994; Morley and Adams 1989; Kazdin 1982). The following were assessed online at *four timepoints*: twice during baseline (weeks 1 and 8), at the end of the intervention (week 12 of phase A) and at the end of follow up (week 12 of phase A').

Disability was assessed with the *Roland Morris Disability Questionnaire-RMDQ* (Roland and Morris 1983). The RMDQ measures effects of LBP on physical activities and activities of daily living. It is valid, reliable, and responsive to change. Scores range from zero to 24, with higher scores indicating higher levels of disability, and a change of 2.5 points considered to be a minimal clinically important change (MCIC) (Roland and Morris 1983).

Pain-related fear beliefs (fear of damage and/or pain) were assessed with the *Tampa Scale of Kinesiophobia-TSK* (Kori, Miller, and Todd 1990). The TSK is a widely-used to assess fear of damage and/or pain (Bunzli, Smith, Watkins, et al. 2015). Scores range from 17 to 68, with higher scores indicating higher levels of fear of movement and a cut-off of 40 is typically used to define a high degree of pain-related fear (Vlaeyen et al. 2012). A change of 8 points is suggested as a MCIC (Lundberg et al. 2011).

Pain-related anxiety symptoms were assessed with the *Pain Anxiety Symptoms Scale-PASS-20* (McCracken and Dhingra 2002). The PASS-20 was used to assess cognitive anxiety symptoms, escape and avoidance responses, fearful appraisals of pain and physiological anxiety symptoms associated with pain. The participant makes a frequency rating for each item (where 0 = never and 5 = always). The PASS-20 has acceptable psychometric properties (McCracken and Dhingra 2002). Scores range from zero to 100, with higher score indicating higher levels of pain-anxiety.

Pain catastrophizing was assessed with the Pain Catastrophizing Scale – PCS (Sullivan, Bishop, and Pivik 1995). The PCS has good psychometric properties, assessing catastrophic thinking with 13 statements that are rated on 0–4 Likert scales. Scores range from zero to 52, with scores over 20 typically used as a cut-off to define a high degree of catastrophizing (Sullivan, Bishop, and Pivik 1995); and a change of 9 points considered as the MDC (George, Valencia, and Beneciuk 2010).

Back beliefs were assessed with the Back Pain Attitudes Questionnaire (BackPAQ) (Darlow, Perry, Mathieson, et al. 2014). The BackPAQ10 consists of 10 items using a five-point Likert scale rating that ranges from 'false' to 'true', assessing five key components: relationship between back pain and injury, vulnerability of the back, activity participation during back pain, psychological influences on pain and recovery, and prognosis of back pain. The responses are scored from -2 ('true') to +2 ('false'), with scores ranging from -20 to +20. Negative scores reflect beliefs that are unhelpful for recovery from back pain. Eleven (11) items are inverted from the normal survey direction. BackPAQ has been shown to have acceptable internal consistency, with a Cronbach's alpha of 0.70 (Darlow, Perry, Mathieson, et al. 2014).

Illness perceptions were assessed with the Brief Illness Perception Questionnaire (B-IPQ) (Broadbent et al. 2006). The B-IPQ covers the five dimensions and has nine items, of which eight are rated on a 11-point NRS. Five items assess cognitive illness perceptions: consequences (Item 1), timeline (Item 2), Control (Item 3), Curability (Item 4), and Identity or diagnostic label (Item 5). Two items assess emotional perceptions: concern (Item 6) and emotional response (Item 8) and one item assesses understanding of the condition or coherence (Item 7). Scores range from zero to 80, with higher scores indicating more negative illness perceptions. Item nine assesses causal beliefs; participants are requested to list the three most important causal factors in their illness; this is treated as an open-ended response (Item 9). B-IPQ has good test-retest reliability (Broadbent et al. 2006), with a MDC of 3 points for items 1-8 for individual evaluation purpose (de Raaij et al. 2014).

Back Awareness was assessed with Fremantle Back Awareness Questionnaire (FreBAQ) (Wand et al. 2014). The FreBAQ contains 9 items on 5-point Likert scale (0= never feels like that, 4= always, or most of the time feels like that). Based on a Rasch analysis of the FreBAQ (Wand et al. 2016) two of the best-performing items with the highest item-test correlations were selected: “When I am performing everyday tasks, I am not sure exactly what position my back is in” and “I can’t perceive the exact outline of my back”. The scores were transformed to an 11-point NRS scale and summed (max= 20), with higher scores indicating poorer back awareness.

6.3.4 Intervention

6.3.4.1 Cognitive Functional Therapy (CFT)

CFT is an integrated behavioural approach for individualising the management of people with PLBP once serious and specific pathology has been excluded. CFT has evolved from foundational cognitive and behavioural interventions (Vlaeyen et al. 2001; Keefe 1982; Fordyce 1976), and has shown promising results in the reduction of fear, pain and disability (Mansell et al. 2017; Bunzli et al. 2016; Caneiro, Smith, et al. 2017; Lee et al. 2015; O'Sullivan et al. 2015; Vibe Fersum et al. 2013; Leeuw et al. 2008). Based on an interview and examination, the clinician identifies and targets modifiable contributors to pain, distress and disability in a person-centred manner (O'Sullivan et al. 2018). There are three broad components to the intervention:

Making sense of pain: a reflective process that combined the person’s own narrative (interview) and experience (during guided behavioural experiments) to disconfirm unhelpful beliefs and responses to pain, developing a personally-relevant multidimensional understanding of pain.

Exposure with ‘control’: a process of behavioural change through experiential learning. Designed to violate expectations of pain and damage consequences via guided behavioural experiments, in which sympathetic responses and safety-seeking behaviours that manifested during exposure to painful, feared or avoided functional tasks are explicitly targeted and controlled. The new strategies are immediately integrated to daily activities to build self-efficacy (O'Sullivan et al. 2018).

Lifestyle change: behavioural modification addressing unhelpful lifestyle factors aimed at increasing activity and social participation, and regulation of tension and sleep.

CFT is underpinned by strong therapeutic alliance and motivational interviewing style (open, non-judgmental, reflective) (O'Sullivan et al. 2018) providing validation and facilitating disclosure

(Linton 2015; Edmond and Keefe 2015). The initial session was 1hour and the follow-ups were 30–45 minutes. **Treatment compliance** was measured weekly during the treatment phase, with the question: "*Over the past week, how many days have you practised your management routine?*

6.3.5 Treating clinicians and setting

Two experienced physiotherapists who were trained in CFT delivered the intervention. The clinicians were trained by two specialist physiotherapists (POS and JPC) during a program purposefully developed for this study. The training consisted of: theoretical and clinical sessions, including observation and practice with real patients with disabling back pain and high-fear. The treatment was delivered in a primary care musculoskeletal physiotherapy practice in Perth, Western Australia.

6.3.6 Treatment fidelity

To ensure treatment fidelity, the developer of CFT (POS) was present as an observer in the first session, as well as two follow-ups (week 6 and week 12), using a form previously used in another CFT study (Vibe Fersum et al. 2013). *Therapeutic alliance* was also assessed as a measure of treatment fidelity. The Working Alliance Theory of Change Inventory (WATOCI) has well-accepted clinometric properties, and holds its one-dimensional characteristic when used with LBP. Scores vary from 16-112, with higher scores indicating higher therapeutic alliance (Ferreira, Ferreira, et al. 2013).

6.3.7 Internal validity

Internal validity for attribution of any systematic change to the intervention was assessed by: **a)** short interview with the participant (at the last week of the baseline), **b)** short interview with participant's spouse (at the end of the treatment phase), and **c)** therapist log to identify explanations for change other than the intervention.

6.3.8 Data analysis

Although there is no consensus regarding methods for analysis of SCEDs (Maggin and Odom 2014; Kratochwill et al. 2013), this study followed the recommendation that a combination of visual and statistical analyses that consider design requirements and data assumptions be conducted (Manolov et al. 2014).

6.3.8.1 Assessment of treatment effect

This study used three analysis methods to determine if changes had occurred once the intervention was introduced: visual analysis, conservative dual-control (CDC) (Swoboda, Kratochwill, and Levin 2010; Fisher, Kelley, and Lomas 2003), and non-overlap analysis (Tau-U) (Parker et al. 2011). All three methods were used for analysis of the primary outcome and all proposed mediators.

6.3.8.1.1 Visual analysis

This process involved a systematic analysis of the visual display of the data. Following well-established guidelines in the field (Kratochwill et al. 2010) data were visually examined for *level* (stability of data within a phase); *trend* (slope of the best fitting straight line for the data), and *immediacy of the effects* (comparison of last three data points from the baseline, phase A with the first three data points from the treatment phase, phase B).

6.3.8.1.2 Statistical analysis

Conservative Dual-Control (CDC)

CDC uses *a priori* criteria to determine the occurrence of systematic change (treatment effect) between baseline and treatment phases (Swoboda, Kratochwill, and Levin 2010; Fisher, Kelley, and Lomas 2003). This method was developed to refine visual inspection and interpretation of graphed data, and it was used in this study for analysis of the primary outcome and all potential mediators. This was done by: **1)** plotting two lines (linear trend and mean of the baseline data points); **2)** subtracting 0.25 of the standard deviation of the baseline mean from both lines, and superimposing them on the treatment phase (these lines determined the predicted direction the data would take should no intervention took place, or the treatment had no effect); **3)** comparing the number of data points (observations) in the treatment phase that were below the criteria lines, to the minimum number of points required by guidelines (Fisher, Kelley, and Lomas 2003) to determine that change occurred (effect). The CDC method allows multiple assessors to review a graph and achieve the same conclusion about the pattern of the data, increasing interrater reliability of the visual decision-making process (Swoboda, Kratochwill, and Levin 2010).

Non-overlap - Tau-U

Tau-U is the most robust non-overlap method for analysis of single-case research data (Parker et al. 2011). Tau-U uses pairwise comparison of individual data points across phases A and B to determine a dominance index of the score of one data set over the other. This index provided the percentage of non-overlap after controlling for baseline trend (Parker et al. 2011).

6.3.8.2 Determining potential mediators of treatment response

Cross-lag correlation analysis

To assess the temporal association between changes in proposed mediators and disability, a series of cross-lag correlation analyses adjusted for autocorrelation was performed using Simulation Modelling Analysis (program freely downloaded from http://clinicalresearcher.org) (Borckardt et al. 2008). This analysis estimates temporality (*lag*) of changes in two variables over the course of a SCED (i.e. change in one factor preceded or lagged change in the outcome) after adjusting for autocorrelation. Correlations between mediators and disability were estimated and compared at *lags* -2 to +2, with negative lags indicating that change in a proposed mediator occurred prior to a change in the outcome. *Positive lags* indicating that change occurred after, and a *lag* 0 (zero) indicating contemporaneous change. As recommended (Borckardt et al. 2008), this analysis used the last data point of the baseline phase (before introduction of the intervention) and all points of the treatment phase.

6.4 Results

6.4.1 Participant's characteristics

Four people (1 male) with PLBP and high pain-related fear participated– see **Table 6.1** for detailed characteristics of the participants at baseline 1 (week 1), and **Appendix 6.2 – Table 6.1** for details at baseline 2 (week 8).

All participants completed the treatment and assessments across the three phases of the study, and there were no adverse events. None of the participants reached the criterion for booster sessions. Therefore, **Phase A'** served as a three-month follow up period, and only descriptive analysis was performed for this phase. The mean number of sessions was 10.2 (range 7-12). One participant (P1) had a break from treatment for two weeks because of illness. Nonetheless, the weekly online assessments continued and this participant had 2 extra data points during phase B (i.e. 14 weeks). The clinicians reported in the therapist log that for all participants, behaviour was modifiable and pain was controllable via guided behavioural experiments used in the first appointment. Therapeutic alliance, measured after the first session, was high across participants (P1: 80; P2: 100; P3: 97; P4: 102 - score range 16-112) [(Ferreira, Ferreira, et al. 2013)]. Treatment compliance was also high across participants (see **Appendix 6.2 – Table 6.1** for details).

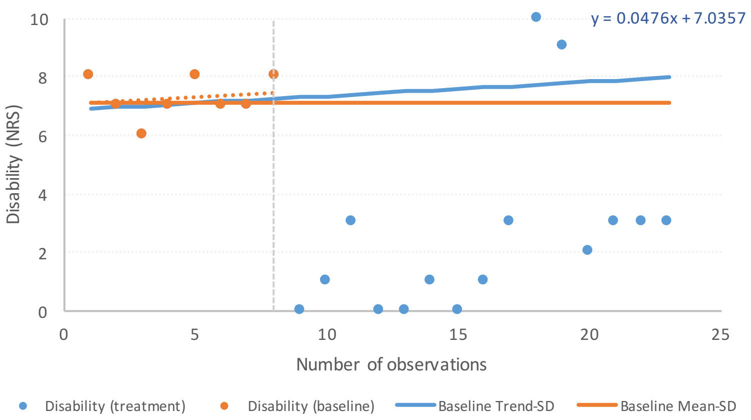
6.4.2 Treatment effect

6.4.2.1 Effect of CFT on Disability

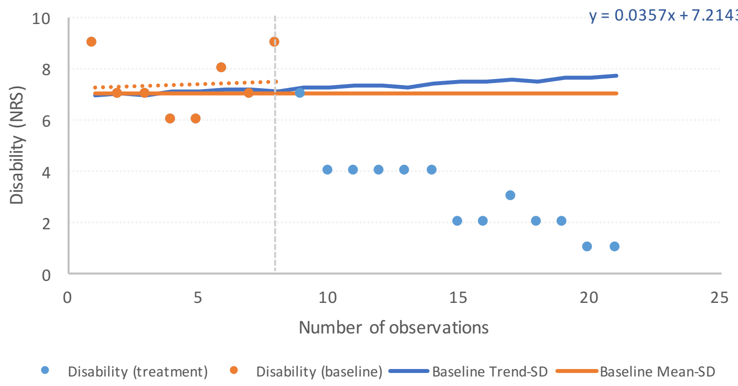
For all participants, visual and CDC analysis indicated reduction in **disability** after the start of the intervention (**Figure 6.2** - see footnotes for detailed explanation). The Tau-U index indicated that after controlling for baseline trend, a large proportion of the data from baseline and treatment phases was non-overlapping and phase-dependent (**Table 6.2)**, meaning that disability improved significantly for all participants in the treatment phase. Together, these results suggest the presence of treatment effect (i.e. reduction in disability) for all participants. Attribution of change to the intervention was further supported by therapist log and interview content (participant and significant other), which did not identify other explanations for change other than the intervention.

6.4.2.2 Effect of CFT on Potential mediators of treatment response

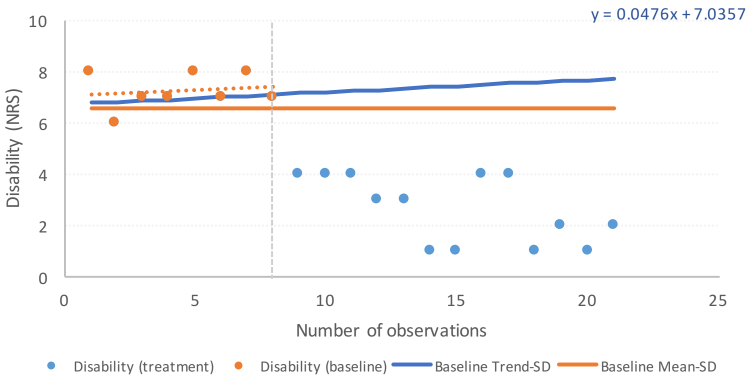
Visual and statistical analysis (CDC and Tau-U) indicated a treatment effect for proposed mediators in the *pain* and *fear* groupings for all participants (**Table 6.2** for details). In *pain controllability,* pain control was enhanced in all participants, and pain self-efficacy improved in three participants (P1, P3, P4). *Distress* was reduced in three participants (P2, P3, 4), and *Sleep* was improved in two participants (P3 and P4). **Appendix 6.3, Figure 6.1** illustrates the CDC analysis process in one of the proposed mediators, indicating treatment was effective in reducing **pain intensity** in all cases.



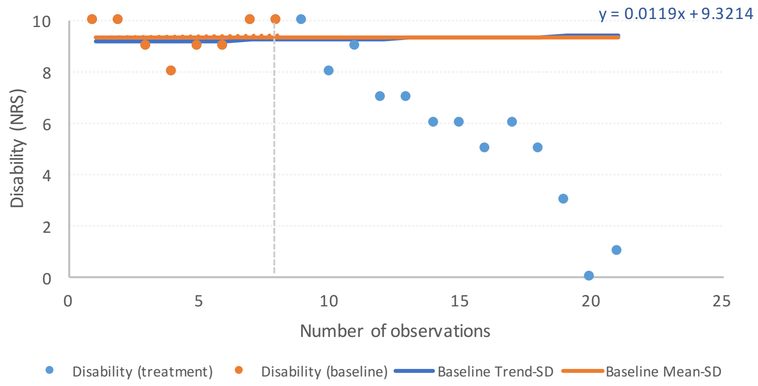
(P1) Disability: Lifting and carrying



(P2) Disability: Bending and lifting heavy



(P3) Disability: Bending and lifting/gardening



(P4) Disability: Vacuuming/Mopping and gardening

Disability (*baseline*): baseline datapoints (8 weeks); **Dotted line (*baseline linear trend*):** least squares regression line of the baseline datapoints; **Baseline Trend-SD:** linear trend minus 0.25 SD of the baseline mean plotted across the treatment phase using linear equation; **Baseline Mean-SD:** mean of the baseline datapoints minus 0.25 SD of its mean plotted across the treatment phase – both Trend-SD and Mean-SD determine the predicted direction which the data would follow should no intervention took place, or if the treatment had no effect. **Disability (*treatment*):** treatment phase datapoints (15 weeks for P1; 13 weeks for P2-P4).

Figure 6.2 Graphical display of disability data across baseline and treatment phases, for visual and CDC analysis of treatment effect.

Table 6.2 Statistical analysis of treatment effect on disability and proposed mediators employing CDC and Tau-U methods.

	P-1				P-2				P-3				P-4			
	CDC		TAU-U		CDC		TAU-U		CDC		TAU-U		CDC		TAU-U	
	n criterion (criterion=12)	Effect (Y/N)	Non-overlap (%)	*p* -value	n criterion (criterion=10)	Effect (Y/N)	Non-overlap (%)	*p* -value	n criterion (criterion=10)	Effect (Y/N)	Non-overlap (%)	*p* -value	n criterion (criterion=10)	Effect (Y/N)	Non-overlap (%)	*p* -value
Disability	13	Y	76	0.0045	12	Y	94	0.0004	13	Y	100	0.0002	12	Y	84	0.0018
Pain intensity	12	Y	63	0.0136	13	Y	99	0.0004	13	Y	100	0.0001	12	Y	92	0.0010
Pain Interference	13	Y	93	0.0002	12	Y	87	0.0012	13	Y	93	0.0002	13	Y	100	0.0003
Pain Control	13	Y	88	0.0018	13	Y	97	0.0002	13	Y	94	0.0002	13	Y	100	0.0002
Pain Self-Efficacy	12	Y	73	0.0097	7	N	49	0.0277	11	Y	76	0.0036	13	Y	100	0.0003
Fear of damage/pain	15	Y	100	0.0001	13	Y	100	0.0002	13	Y	100	0.0002	13	Y	100	0.0002
Pain Anxiety	13	Y	92	0.0004	13	Y	100	0.0002	13	Y	99	0.0002	13	Y	100	0.0002
Catastrophizing	14	Y	89	0.0007	13	Y	100	0.0002	12	Y	94	0.0002	13	Y	100	0.0002
Avoidance beliefs	12	Y	83	0.0023	13	Y	100	0.0002	13	Y	100	0.0002	13	Y	99	0.0002
Distress	10	N	55	0.0442	12	Y	99	0.0003	11	Y	91	0.0002	12	Y	95	0.0002
Sleep	8	N	37	0.3393	7	N	40	0.1733	13	Y	99	0.0002	12	Y	70	0.0160

P-1-4: participants 1 to 4; **criterion:** minimum number of data points required to reach a systematic change**; n criterion:** identified number of data points below the criterion lines; **Effect:** presence (Y) or absence (N) of a systematic change; **Non-overlap (%):** Tau-U index

6.4.3 Temporal association between changes in proposed mediators and changes in disability

Cross-lag correlation analysis indicated that most of the proposed mediators **changed concomitantly** with disability, with the strongest correlations observed at *lag zero*. **Appendix 6.4, Table 6.1** reports correlations between each of the proposed mediators and disability at lag zero, and respective p-values; and **Figure 6.1** displays all lag zero correlations between proposed mediators and disability for each participant.

The three mediators with the highest correlation at lag zero for each participant were from *pain*, *pain controllability*, and *fear* groupings. For summary visualization of the change process across the three phases of the study and for discussion purposes, these results are graphically displayed by mediator groupings in **Figure 6.3**. It illustrates that for all participants, changes in *pain*, *pain controllability*, and *fear* were most strongly associated with concomitant changes in disability after the first treatment session. In addition, **Figure 6.3** illustrates that large changes occurred immediately for P1 and P2, whereas changes occurred more gradually for P3 and P4.

6.4.4 Standardised outcome measures

Changes in standardised outcome measures assessed at single timepoints supported results of assessments at multiple timepoints. Reductions in standardised measures of disability (RMDQ), pain-related fear (TSK), pain anxiety (PASS-20), pain catastrophizing (PCS), illness perceptions (B-IPQ), and improvements in back beliefs (BackPAQ), and back awareness (FreBAQ) were observed over the treatment phase for all participants. Specifically, scores at end of follow up are considered representative of minimal (P1, P2, P4) to low disability levels (P3) with changes beyond the minimal clinically important change (MCIC of 2.5 points) in the RMDQ for all four participants. Three participants (P1, P2, P4) had changes that were more than double the MCIC for pain-related fear (TSK) and pain catastrophising (PCS). All participants had substantial changes in standardized measures of illness perceptions, back beliefs, back awareness and pain anxiety. At follow up, all but one participant (P3) had scores below cut-off levels of fear, catastrophising and pain anxiety (see **Appendix 6.2** for details).

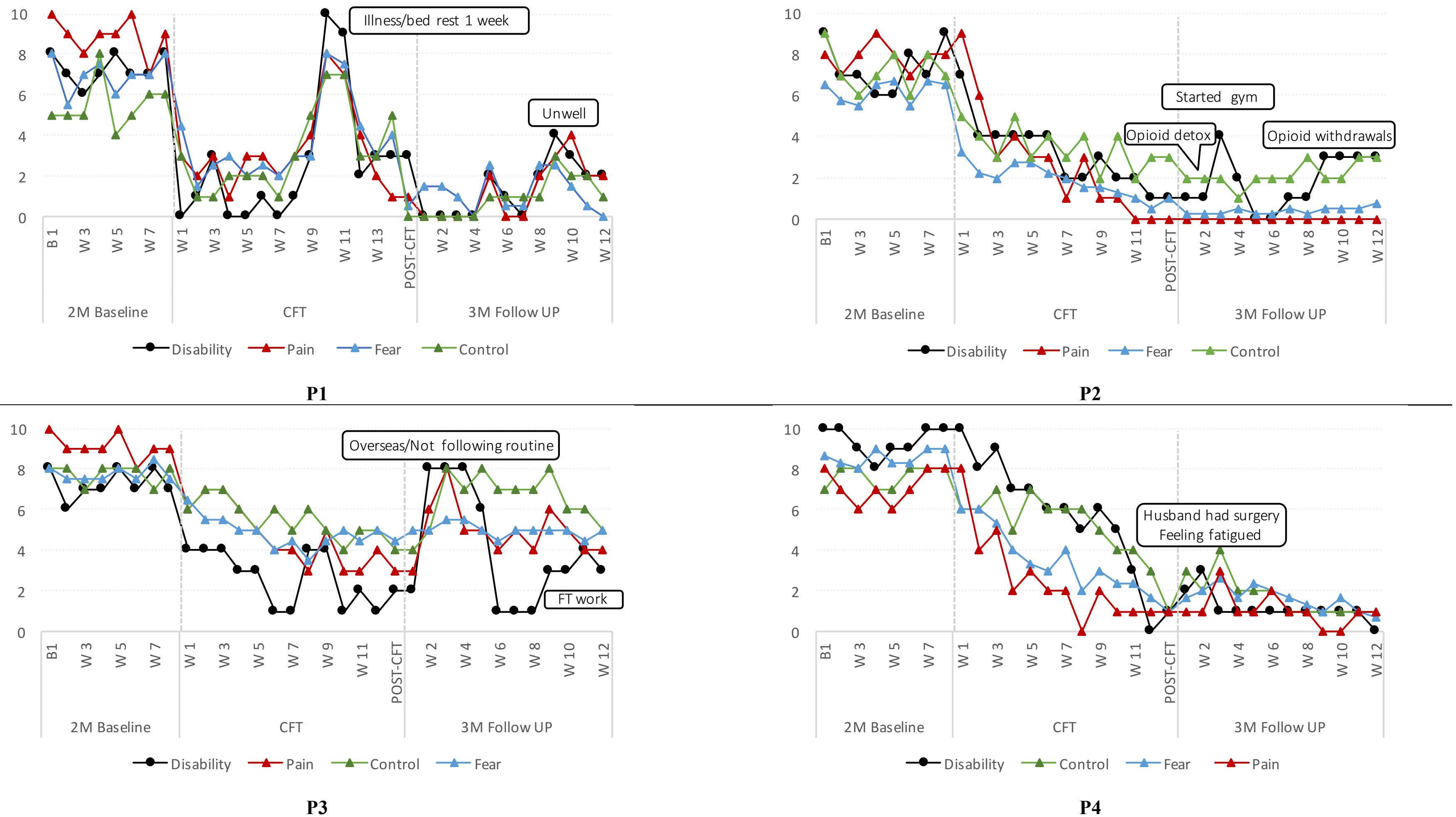


Figure 6.3 Illustration of the change process; '*How change unfolds*' for each person across the phases of the study.

Note: This figure displays the top three 'mediator groupings' of factors associated with treatment response with the highest association at *lag zero*. **Pain control and self-efficacy:** for visualization purposes, original scores were reversed, so that reduction in scores indicate improvement. **FT:** full time work.

6.5 Discussion

The aim of this study was to evaluate how change in potential mediators related to change in disability at different timepoints during the intervention period, in four people with PLBP and high pain-related fear of bending and lifting undergoing a CFT intervention.

First, it was verified that reductions in disability and proposed mediators (*pain*, pain *controllability* and *fear* in all participants, *distress* in three participants and *sleep* in two participants) were clearly related to the commencement of the CFT intervention. This was identified via visual and statistical analyses, and supported by standard outcome assessments at single timepoints (pre-post), which demonstrated changes beyond the minimal clinically important change for disability (for all), and fear (for most). Therapists log and interview content (participant and significant other), did not reveal any other explanations for change during the study period other than the intervention.

Second, statistical analyses determined that, for all participants, changes in most of the proposed mediators (*pain*, pain *controllability*, and *fear*) were most strongly associated with changes in disability at *lag zero*, indicating that the changes occurred concomitantly and not before changes in disability. Furthermore, visual analysis indicated how these changes occurred at different rates and patterns, highlighting the individual variability of the temporal process of change. Specifically, two participants (P1, P2) had a fast response, presenting large changes immediately after the first treatment session, whereas the other two participants had a more gradual response, presenting moderate changes soon after the start of treatment. While all participants presented changes in *pain*, pain *controllability* and *fear*, the specific factors within these groupings that were associated with the treatment response varied between individuals. For *pain,* three participants (P1, P2, P3) had improvement in pain interference, and one (P4) in pain intensity. For *pain controllability,* two participants (P1, P4) improved in self-efficacy, and two (P2, P3) in pain control. For *fear,* two participants (P1, P3) presented a reduction in avoidance beliefs, one (P2) in fear of damage/pain, and one (P4) in catastrophizing. In terms of **factors underpinning treatment response**, our findings are somewhat in line with results from RCTs using psychological interventions for people with PLBP that identified fear (Mansell, Hill, Main, Vowles, et al. 2016; Leeuw et al. 2008), self-efficacy (Lee et al. 2015), pain and distress (Mansell, Hill, Main, Vowles, et al. 2016) as factors that underpin reduction in disability. This study nonetheless, furthers this knowledge by providing evidence that several of these factors improved at the same time as disability, with changes occurring immediately or soon after the first treatment session. The findings of an **early temporal relationship** between potential 'mediators' and the outcome, and the **individual variability in the process of change** challenge the linear understanding of therapeutic change.

In the analysis of mediator-outcome relationships, there is an assumption of temporal precedence, in which the mediator must change before the outcome so causal inference of therapeutic change is established (Kazdin 2007). This assumption of linearity within the process of change appears too limited to understand changes in a non-linear complex system. From a complex systems perspective, different mediator-outcome relationships may interplay in the process of change while varying for each person and over time. Albeit from a small sample, our findings suggest that when the **person's system (*pain schema*) was disrupted**, the pattern of change was different for each person, but all the **changes occurred rapidly, and contemporaneously within the one week assessment period**. These findings challenge current assessment of clinical change, which posits that changes in the mediator and the outcome follow a linear temporal sequence, and lends support to a complex systems model of understanding the therapeutic change process in PLBP.

A **complex system is here defined** as the multiple and interrelated influences of all factors that can modulate a person's experience (Brown 2009). Modulation occurs via feedback loops, eliciting negative experiences (unhelpful cycle) or positive experiences (helpful cycle). Complex systems are governed by simple rules and schemas (Brown 2009), which are constantly updated by new information, experiences and perception of bodily sensations, influencing ongoing behaviour (Bunzli et al. 2017). In people with PLBP, rules such as 'bending is dangerous' and 'pain is an indication of harm' may govern actions that drive overprotection against perceived threats to the person's goals. When the experience is in fact threatening, and often painful, preventing goal achievement, the system is updated confirming the expected threat. Lacking positive/safe experiences, this confirmatory loop continuously updates the system, reinforcing a *pain schema* that perpetuates an unhelpful cycle of fear, pain and disability (Bunzli et al. 2017; Wiech 2016; Vlaeyen, Crombez, and Linton 2016). In contrast, inhibitory learning theories suggest that a *new experience* that violates expectations and allows repetitive exposure to a positive experience can lead to formation of new memories that may form a *safety schema* (Craske et al. 2014; Craske et al. 2012). A new experience that involves behavioural strategies that enhances the perception of control over pain, reduces the threat associated with pain, and enables people to make sense of their pain has been proposed as a 'way out' of this unhelpful cycle (Bunzli et al. 2017; Vlaeyen et al. 2001; Leventhal, Diefenbach, and Leventhal 1992; Leventhal, Meyer, and Nerenz 1980; Fordyce 1976).

The process described in this study provides insight as to how four people 'stuck' in a chronic state of pain, fear and disability could change considerably over the course of a twelve-week intervention, and subsequently be led on a pathway of self-management and independence. Whether this relates to the specific intervention used in this study is unknown, and this study design is unable to answer it. Different biopsychosocial treatment approaches are likely to be effective through shared underlying mechanisms (Burns 2016), but from the perspective of an exposure-based behavioural intervention such as CFT, the rapid disruption in pain schema may be related to a *new experience* that violated the system's rules and expectations and promoted learning. This is supported by qualitative data on people with PLBP and high pain-related fear that underwent a CFT intervention (Bunzli et al. 2016). The new experience may have been facilitated by CFT's behavioural experimentation with a focus on violating pain expectations during exposure to feared and avoided movements. Pain control may have been enhanced by the use of body relaxation and explicit targeting of safety-seeking behaviours linked with a strong therapeutic alliance during exposure (Bunzli et al. 2016; Bunzli, Smith, Schutze, et al. 2015). This *experiential learning* that disrupted the person's pain schema may be a plausible mechanism for change soon after the first treatment session. Vlaeyen et al (2001) proposed that changes that occurred quickly after exposure could only be related to insight learning, which occurs when people make novel associations and recognize relationships that can help them solve new problems (Vlaeyen et al. 2001). People who develop the capacity to learn through experimentation may become able to adapt and self-regulate/manage (Vlaeyen 2015; Brown 2009; Vlaeyen, de Jong, Geilen, et al. 2002), an important aspect of generalization of treatment response and independence. **Follow up** data from this study supports this. At three-months post-intervention, all participants experienced reduction in pain and development of more positive perceptions and back beliefs, which are important predictors of long-term trajectory of people with LBP (Chen et al. 2017). During the follow up phase, it appears the four participants were able to self-manage, indicating generalization of learning, increase in confidence and capacity for independent management of relapses. In this process, all participants experienced transitory increase in symptoms ('flare-ups') at variable intensities and duration. Interestingly, these were triggered by non-physical factors (**P1:** viral illness and fatigue, **P2:** opioids withdrawal, **P4:** feeling of fatigue) and changes in geographical context (**P3**). This may reflect the close link between immune, endocrine and nervous systems in the context of learning and adaptation in response to a threat (Lenaert et al. 2018; Rubinow and Rubinow 2017; Davies 2016).

Data from this study raise some interesting questions in relation to promoting clinical change in chronic disorders such as PLBP: *What is necessary for change to occur*? *Is it important to target specific 'mediators'*? *Do several factors need targeting at once*? The individualized experience illustrated by the four participants in this study supports the idea of a 'pain schema disruption' promoting change in several factors at the same time. Furthermore, it suggests that how the system is disrupted, and which factors change vary between and within individuals over time. Although speculative, we propose that experiential learning that enhances pain control via adoption of a new behaviour may be a potential underpinning mechanism of change in disability in people with PLBP and high pain-related fear. This however, warrants further testing.

6.6 Limitations

This is the first study to use a SCED to analyse temporal associations of change in outcome and proposed mediators in people with PLBP and high pain-related fear. Although, this provided novel information of the relationship of change in outcome and factors associated with treatment response, some limitations should be noted.

First, SCEDs are vulnerable to plausible rival hypotheses that may explain the outcomes such as, maturation, regression to the mean and external factors. To enhance internal validity and minimize the influence of such hypotheses this study used a stable baseline with eight data points (above the recommended five) (Tate et al. 2017; Kratochwill et al. 2010), a therapist log and interview content (with the participant and their spouse). *Second,* as most studies investigating behavioural interventions, data were collected via self-report which can be vulnerable to self-preservation bias. *Third,* most SCEDs in this field used daily measures of the outcome, whereas this study used weekly measures. It has been suggested that the use of repetitive (daily) measures in previous SCEDs, could be a mechanism for behavioural change in itself (Vlaeyen et al. 2012). Furthermore, repeated administration of the same measures may have resulted in participants recalling and recalibrating their responses, which would affect the reliability of the measure. Therefore, the current study used weekly measures, which provided the necessary frequency to measure change (Kratochwill et al. 2013), while minimizing its potential effect as a behaviour change mechanism and the participant's ability to recall previous answers. However, this cannot be confirmed in this study. *Fourth,* the use of weekly measures means that any sequential changes that occurred within the week were not be captured. Future studies evaluating mediator-outcome relationship may include more frequent measures to enhance temporal resolution. *Fifth,* the fact that all of the measures were rated at the same time may have increased their correlation. Although this was mitigated by the use of SMA which accounts for the autocorrelation in each measure before estimating the cross correlations [(Borckardt et al. 2008)]. In addition, some of the measured constructs may overlap conceptually, also potentially increasing their correlation.

6.7 Future directions

Future RCTs aiming to evaluate mediators of treatment effect may need to include frequent and early measures (after each treatment session for instance) of the outcome and proposed mediators to allow adequate temporal evaluation of change in the mediators-outcome relationships. New technologies including online registries, smartphone apps, wearable sensors may provide an avenue to enhance frequency of measurement in larger trials. To minimize participant burden, the decision of which factors to measure can be informed by well-designed SCEDs.

6.8 Conclusion

This single-case experimental design study demonstrated the interplay of factors associated with treatment response, highlighting "*how change unfolded*" uniquely for each individual. Changes in *pain*, *pain controllability*, and *fear* occurred concomitantly to changes in disability, suggesting a disruption in the person's entire pain schema. Experiential learning that enhances control over the pain experience via adoption of a new behavior, and that facilitates people to make sense of their pain, may be an underlying mechanism for behavioural change in people with PLBP and high pain-related fear. However, replication of these results is needed.

6.8.1 Author's statements

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6.9 Appendix 6.1

Online questionnaire – employed to assess outcome and potential mediators weekly.

NRS consisting of 11 numerical points (0 – 10) will follow the items derived from these questionnaires. Anchored by words appropriately related to each question. Items were reversed accordingly, so lower score indicate improvement.

Disability *(adapted from Beurskens et al., 1999)*

(1) In the last week, I had most difficulty with/or I was unable to perform *(nominated activity**) *because of my back pain*.

Pain *(from Dionne et al 2008)*

(2) How bad has your low back pain been this week? (*Pain intensity past week*)

(3) How much has the pain limited your usual activities or changed your daily routine for more than one day? (*Pain interference*)

Pain controllability

Pain control *(developed from Bunzli et al 2015)*

(4) How much control do you have over your pain?

Pain self-efficacy (PSEQ-2 - *Nicholas et al 2015*)

(5) I can do some form of work, despite the pain (‘‘work’’ includes housework, paid or unpaid work)

(6) I can live a normal lifestyle, despite the pain

Fear

Fear of damage/pain *(adapted and modified from TSK):*

(7) If I exercise I might be in danger of reinjuring myself. (*Harm*)

(8) My body is telling me I have something dangerously wrong. (*Fear*)

(9) My pain complaints will decrease if I were to exercise. (*Exercise*)

(10) I can't do everything because it's too easy for me to get injured. (*Avoidance*)

Pain anxiety *(adapted from PASS-20 – McCracken et al 2002):*

(11) Pain seems to cause my heart to pound or race. (*Physiological anxiety*)

(12) During painful episodes, it is difficult for me to think of anything besides pain. (*Cognitive anxiety*)

(13) When I feel pain, I am afraid that something terrible will happen". (*Fear*)

(14) I avoid important activities when I hurt. (*Escape/avoidance*)

Pain catastrophizing *(adapted from PCS):*

(15) When I am in pain I keep thinking about how badly I want the pain to stop. (*Rumination*)

(16) When I am in pain I wonder whether something serious may happen. (*Magnification*)

(17) When I am in pain I feel, I can't go on with my daily activities. (*Helplessness*)

Avoidance beliefs *(OMPQ – Linton et al 2010)*

(18) An increase in pain is an indication that I should stop what I'm doing until the pain decreases.

(19) I can do ordinary household chores that involve bending and lifting. (*adapted*)

Distress *(Depression and Anxiety from OMPQ – Linton et al 2010; Pain bothersomeness from STarT Back Hill et al 2008)*

(20) How tense or anxious have you felt in the past week?

(21) How much have you been bothered by feeling depressed in the past week?

(22) Overall, how bothersome has your back pain been in the last week?

Sleep *(OMPQ – Linton et al 2010)*

(23) I can sleep at night?

*This activity was identified at the first week of baseline using a PSFS, which asked the person to nominate 3 activities they had most difficulty with/or that they were unable to perform. The activity with the highest rating was selected and used as the personalized disability item, allowing personalization of the questionnaire for the remaining weekly measures.

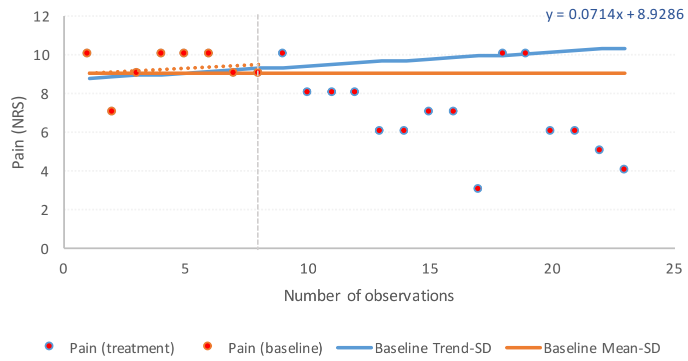
6.10 Appendix 6.2

Appendix 6.2 Table 6.1 Single timepoints measures: Standardized outcome measures across the three phases of the study.

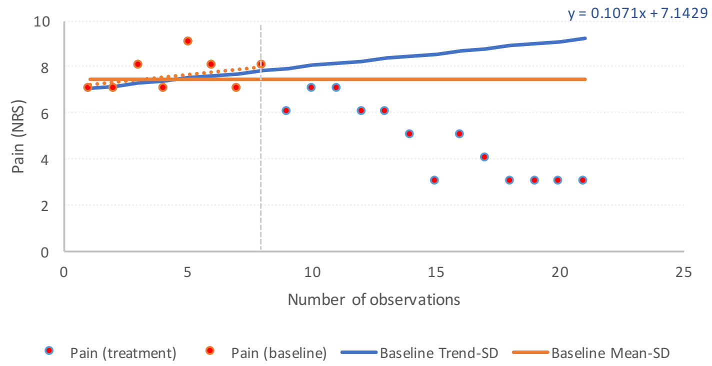
MEASURES	TIMELINE	P1	P2	P3	P4
Disability (RMDQ)	Baseline 1 (BAS-W1)	11	10	16	10
	Baseline 2 (BAS-W8)	11	10	17	11
	End-CFT	1	2	6	0
	Follow up (3mo)	2	3	8	0
Pain-related fear (TSK)	**Baseline 1** (BAS-W1)	48	45	55	50
	Baseline 2 (BAS-W8)	49	47	56	51
	End-CFT	19	26	34	18
	Follow up (3mo)	19	25	35	18
Pain catastrophizing (PCS)	Baseline 1 (BAS-W1)	40	25	42	21
	Baseline 2 (BAS-W8)	40	26	44	22
	End-CFT	7	8	28	0
	Follow up (3mo)	3	9	26	3
Pain-related anxiety (PASS-20)	**Baseline 1** (BAS-W1)	51	42	67	32
	Baseline 2 (BAS-W8)	53	46	66	35
	End-CFT	14	14	49	6
	Follow up (3mo)	3	15	44	4
Back beliefs (BackPAQ)	Baseline 1 (BAS-W1)	-11	-7	-11	-10
	Baseline 2 (BAS-W8)	-11	-6	-12	-9
	End-CFT	4	6	1	5
	Follow up (3mo)	8	4	0	4
Illness perceptions (B-IPQ)	**Baseline 1** (BAS-W1)	61	58	63	55
	Baseline 2 (BAS-W8)	63	56	62	59
	End-CFT	29	15	41	5
	Follow up (3mo)	15	19	42	3
Back awareness (FreBAQ)	Baseline 1 (BAS-W1)	18	13	15	3
	Baseline 2 (BAS-W8)	15	12	15	3
	End-CFT	2	2	10	0
	Follow up (3mo)	0	3	9	0
Treatment compliance		84%	92%	90%	92%

TSK (score range 17-68. High scores indicate higher fear of damage/pain); **PASS-20** (score range 0-100. High scores indicate higher pain anxiety); **PCS** (score range 0-52. High scores indicate higher pain-related catastrophic thoughts); **Disability** (score range 0-24. High scores indicate higher disability); **BackPAQ$_{10}$** (score range -20-20. Negative scores indicate negative beliefs); **B-IPQ** (score range 0-80): higher scores indicate more negative illness perceptions; **FreBAQ** (2 items; score range 0-20. High scores indicate poor back awareness); **Treatment compliance** (proportion of days which the management routine was practiced in a week, measured over the treatment and follow up periods); **BAS-W1:** assessment at first week of baseline (week 1); **BAS-W2:** assessment at last week of baseline (week 8).

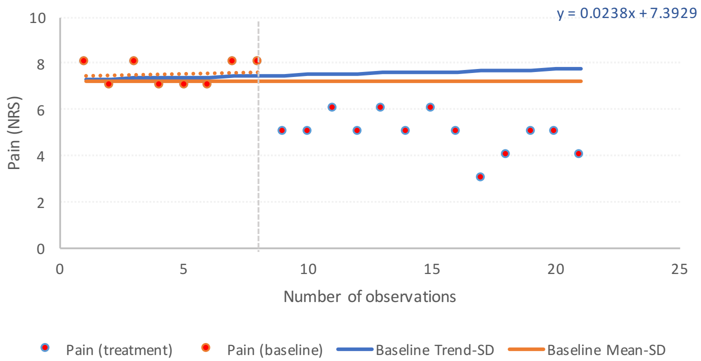
6.11 Appendix 6.3



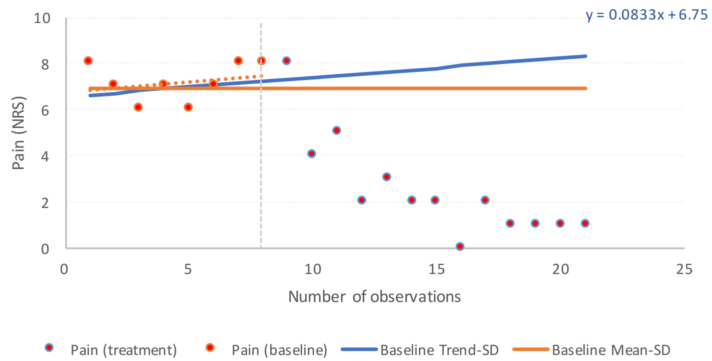
(P1)



(P2)



(P3)



(P4)

Pain (*baseline*): baseline datapoints (8 weeks); **Dotted line (*baseline linear trend*):** least squares regression line of the baseline datapoints; **Baseline Trend-SD:** linear trend minus 0.25 SD of the baseline mean plotted across the treatment phase using linear equation; **Baseline Mean-SD:** mean of the baseline datapoints minus 0.25 SD of its mean plotted across the treatment phase – both Trend-SD and Mean-SD determine the predicted direction which the data would follow should no intervention took place, or if the treatment had no effect. **Pain (*treatment*):** treatment phase datapoints (15 weeks for P1; 13 weeks for P2-P4).

Appendix 6.3 Figure 1.1 Graphical display of pain data across baseline and treatment phases, for visual and CDC analysis of treatment effect.

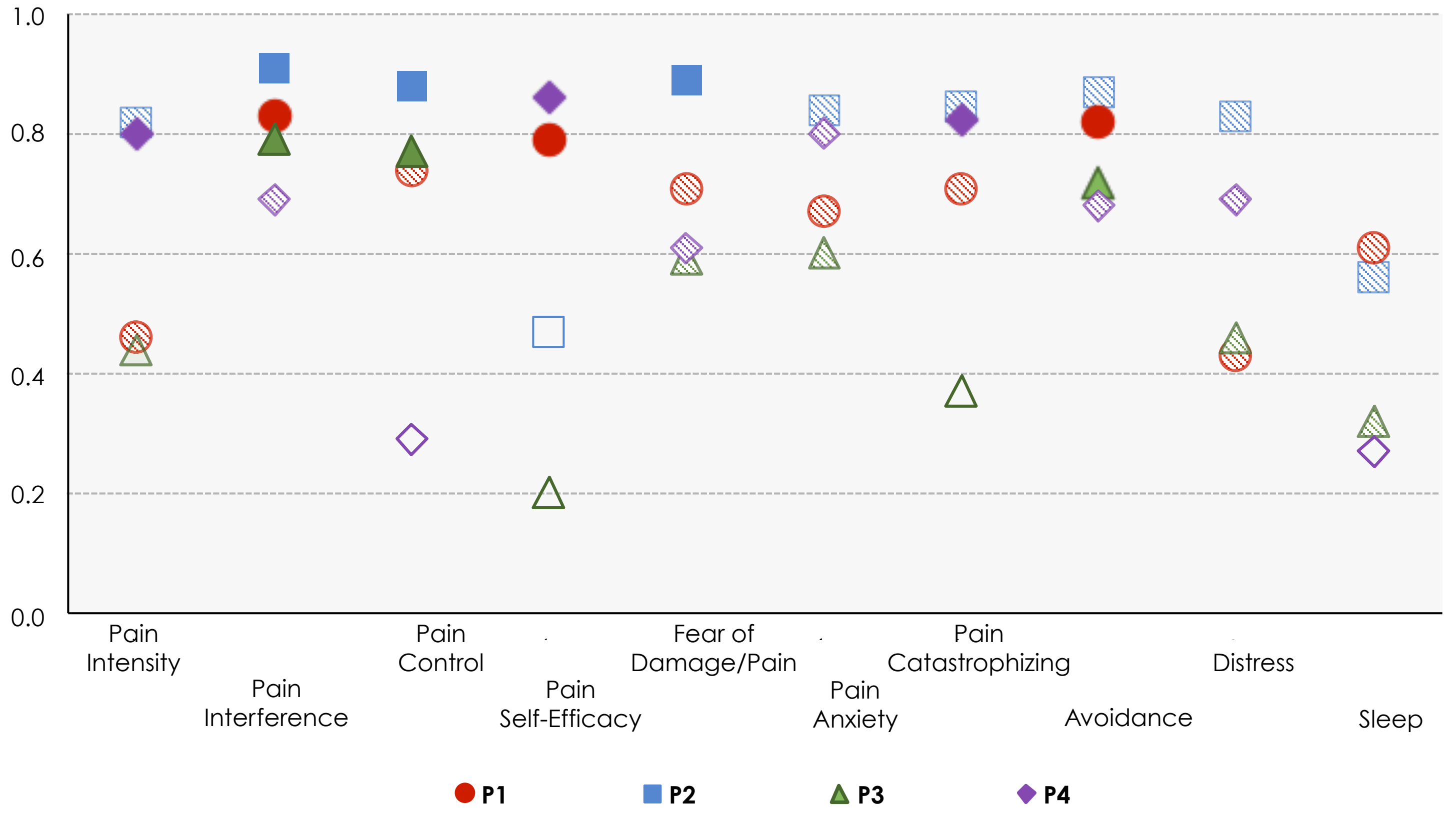
Note: Pain intensity is used as an example to illustrate this process. This analysis was repeated for every proposed mediator.

6.12 Appendix 6.4

Appendix 6.4 Table 1.2 Cross-correlations at *lag zero* indicating the level of association between each proposed mediator and disability, and respective p-values.

		P1		**P2**		**P3**		**P4**	
		r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Pain	Pain intensity	0.46	*0.053*	0.82	*0.001*	0.44	*0.051*	**0.80***	*0.002*
	Pain Interference	**0.83***	*0.001*	**0.91***	*0.000*	**0.79***	*0.001*	0.69	*0.003*
Pain controllability	Pain control	0.75	*0.000*	**0.88***	*0.000*	**0.76***	*0.000*	0.29	*0.111*
	Pain Self-Efficacy	**0.79***	*0.000*	0.47	*0.089*	0.2	*0.433*	**0.86***	*0.001*
Fear	Fear damage/pain	0.71	*0.003*	**0.89***	*0.000*	0.59	*0.016*	0.61	*0.024*
	Pain Anxiety	0.67	*0.004*	0.84	*0.001*	0.60	*0.007*	0.80	*0.002*
	Pain Catastrophizing	0.71	*0.002*	0.84	*0.001*	0.37	*0.087*	**0.83***	*0.003*
	Avoidance beliefs	**0.82***	*0.000*	0.87	*0.000*	**0.71***	*0.007*	0.69	*0.008*
Distress	Depression/Anxiety/ Pain bothersomeness	0.44	*0.032*	0.83	*0.000*	0.45	*0.041*	0.69	*0.016*
Sleep	Capacity	0.61	*0.012*	0.56	*0.066*	0.32	*0.117*	0.27	*0.147*

*****Indicates the three correlation coefficients (r) with the highest association at lag zero for each participant.*



Appendix 6.4 Figure 1.2 Cross-correlations of all proposed mediators and disability at *lag zero*, illustrating factors associated with change in each participant.

Note: Colour gradient of each data point indicates strength of correlation at lag zero. **Colour-filled markers:** indicate highest correlations (top 3) that reached statistical significance; **Pattern-filled markers:** indicate other correlations that reached statistical significance; **Unfilled markers:** indicate correlations that did not reach statistical significance.

Chapter 7 Discussion of Thesis

The main aims of this thesis were (i) to understand how people with persistent LBP and pain-related fear evaluate danger at an implicit level, (ii) to determine the current state of evidence concerning the effectiveness of behavioural interventions in reducing disability, pain and fear in people with persistent LBP and high pain-related fear, and (iii) to understand the process of change and the factors underlying treatment response in people with persistent LBP and high pain-related fear undergoing CFT.

This chapter discusses the main findings of this thesis, conceptualizing the findings through the notion of a pain schema in people with persistent LBP and high pain-related fear and its process of change over the course of an individualized exposure-based behavioural intervention. A safety learning model is proposed to understand the process of pain schema disruption. The chapter concludes by describing the strengths and limitations of this body of work, future research directions and the concluding remarks of this thesis.

7.1 Making sense of change in low back pain-related fear

Modern pain science proposes that pain and protective behaviour are dependent upon an implicit evaluation of danger to a person's goals. This evaluation is influenced by a complex interaction of multiple factors across the biopsychosocial spectrum, varying between and within people over time. This complex interplay makes pain an individual experience. The fear-avoidance model describes how pain that is interpreted as threatening leads to an unhelpful cycle of fear, avoidance, and disability. Whilst pain is an individual experience, the fear-avoidance model proposes a common linear pathway to change, whereby confrontation of the threatening activity would lead to recovery. Despite several investigations of the fear-avoidance model, the process by which recovery occurs has not been clearly outlined. Recently, a qualitative investigation suggested that beliefs underlying pain-related fear vary between people, and the process of recovery may be unique for the individual and influenced by attempts to make sense of the pain experience. However, this process and the factors underlying change were not quantitatively evaluated. The main aims of this thesis were (i) to understand how people with persistent LBP and pain-related fear evaluate danger at an implicit level, (ii) to determine the current state of evidence concerning the effectiveness of behavioural interventions for people with persistent LBP and high pain-related fear, and (iii) to understand the process of change and the factors underlying treatment response in people with persistent LBP and high pain-related fear undergoing CFT.

The first study, presented in Chapter 3, investigated implicit evaluations of danger and physiological responses to images of people bending and lifting with a flexed lumbar spine (round-back), in people with persistent LBP reporting different levels of self-reported fear of bending with a round-back. This study found that irrespective of self-reported fear levels, people with persistent LBP implicitly evaluated round-back bending and lifting as dangerous. However, viewing threatening images was not sufficient to elicit physiological fear responses. This work suggests that self-reported pain-related fear may be cognitively driven. That is, an unhelpful pain schema may influence avoidance and protective behaviours, and a physiological fear response may only occur when the person is exposed to the threat itself. The results of this study raised the possibility that a 'round-back/danger' schema may be pervasive in society, and that people with persistent LBP may hold a 'protect the back' *pain schema*.

The second study, presented in Chapter 4, reports a systematic review of the literature to determine the current state of evidence concerning the effectiveness (in terms of reductions in disability, pain and pain-related fear) of behavioural interventions (broadly grouped as exposure-based and activity-based) intentionally designed for people with persistent LBP and high pain-related fear. It was determined that while behavioural interventions are moderately effective in reducing disability and fear, they are only modestly effective in reducing pain. Surprisingly, the widely held notion that exposure-based interventions are the treatment of choice for this group is poorly supported by existing literature. This is due to the average quality and small number of RCTs comparing exposure-based interventions to usual care and to activity-based interventions, and methodological limitations of the SCEDs comparing exposure-based interventions to activity-based interventions. Importantly, this systematic review highlighted that there may be opportunities to optimize behavioural interventions because it found that behavioural interventions are not effective in reducing pain. It is proposed that considering the individuals understanding of pain (i.e. how they make sense of their pain experience), their pain responses to movement (i.e. pain exacerbation during movement exposures) and explicitly targeting pain control strategies during exposure (e.g. changing pain cognitions emotional responses, enhancing body awareness and relaxation, and discouraging safety-seeking behaviours) may optimize behavioural interventions by enhancing their capacity to target and affect change in pain.

The third study of this thesis, presented in Chapter 5, evaluated temporal changes in pain-related fear and pain related to bending with a round-back, in a person with persistent LBP and high pain-related fear undergoing CFT. The person experienced reductions in pain-related fear and pain expectancy and pain experience related to bending and lifting. The use of repeated measures and clinical interviews enabled tracking of this person's process of change at nine timepoints over 18 months, providing insight to some of the potential mediators of reduction in pain-related fear. The clinical interviews revealed that learning new behaviours that promoted pain control, and having a biopsychosocial understanding of pain that 'made sense' allowed this person to achieve independence. However, several other cognitive (e.g. back beliefs, self-efficacy) and emotional (e.g. pain anxiety, distress) factors that could have mediated reductions in fear were not evaluated.

Chapter 6 describes the fourth and final study of this thesis. In this study, a SCED was used (i) to evaluate temporal changes in disability and factors from cognitive and emotional dimensions considered to be potential mediators of reductions in disability before, during and after a CFT intervention; (ii) to evaluate how changes in potential mediators related to changes in disability at different timepoints during this intervention in four people with persistent LBP and high pain-related fear. Firstly, this study demonstrated that systematic changes in disability and proposed mediators were identified after the introduction of CFT, indicating the intervention was effective. Secondly, this study demonstrated that for all participants the reductions in pain and fear, and improvement in perceived pain controllability occurred concomitantly and not before reductions in disability; although, the pattern of this change differed between participants. This study demonstrated "how change unfolded" uniquely for each individual, highlighting the process of change is as individual as the experience of pain.

The results of this thesis add knowledge to the current understanding of the relationship between pain, pain-related fear and disability by:

i. Providing a broader view of the 'protect the back' *pain schema* held by people with persistent LBP and pain-related fear.

ii. Identifying *opportunities* to optimize behavioural interventions that aim to modify this pain schema.

iii. Demonstrating that the *process of clinical change* is complex, individual and that *disruption* of a person's pain schema may occur rapidly and concomitantly with change in several factors in this process.

Overall, this body of work lends support to a complex systems model of understanding the therapeutic change process in persistent LBP. This highlights the need for an intervention that is flexible, multidimensional and person-centred in nature. The following section will discuss the three key aspects outlined above.

7.1.1 The pain schema

A person's *schema* can be defined as pre-existing knowledge formed by a set pattern of beliefs, memories, emotions, and cognitions that were learned over time to represent a construct (e.g. the back), and that guide a person's behaviour (Banaji and Greenwald 2013). This likely occurs through feedback loops that modulate the interaction of neuro-immune-endocrine systems (Brodal 2017). A person's schema can be updated by information that is heard (e.g. media, family, health care encounters), observed (e.g. vicarious experience from friends or family) and felt (e.g. bodily sensations, a perceived painful sensation), thus influencing behaviour in a new context. Societal views are thought to influence a person's schema formation (Banaji and Greenwald 2013).

The belief that that the back is vulnerable and easily harmed is pervasive in Western society (Munigangaiah et al. 2016; Stevens et al. 2016; Darlow et al. 2015; Bunzli, Smith, Schutze, et al. 2015; Bunzli, Smith, Watkins, et al. 2015; Pagare et al. 2015; Briggs et al. 2010; Gross et al. 2006). Particularly, the adoption of a round-back posture during bending and lifting is perceived as dangerous (Nolan et al. 2018; Darlow, Perry, Mathieson, et al. 2014), and this perception may influence how a person performs these tasks regardless of the presence of LBP (de Jong et al. 2005). It has been proposed that decisions about behaviours adopted in daily life may occur as part of a dual-process, in which explicit (conscious, intentional) and implicit (non-conscious, automatic) processes are involved in the appraisal of risk versus benefit associated with the task (LeDoux and Brown 2017; LeDoux 2012;Leeuw, Peters, et al. 2007; de Jong et al. 2005). The influence of each of these processes on a person's behaviour may vary depending on the person's context, time and motivation or goals (Van Ryckeghem et al. 2013; Hofmann et al. 2005; de Jong et al. 2005; Goubert et al. 2003). This is very pertinent for people with persistent LBP for whom avoiding pain and/or damage is only one of many concomitant competing goals (Van Damme and Kindermans 2015; Van Damme et al. 2012; Van Damme, Crombez, and Eccleston 2008). This dynamic context was well illustrated in recent qualitative studies:

"*It's always a weigh-up: how many groceries am I getting, therefore can I walk back with the shopping? Versus sitting in the car to drive. (016, line 635)*" [(Bunzli, Smith, Schutze, et al. 2015); pg7]

"*If I bend I know I will irritate my back, so I choose not to irritate it. If it is going to irritate me for half an hour when I could achieve half an hour pain free why would I do* *that? I can achieve a lot in half an hour if I am pain free (032).*" [(Bunzli, Smith, Watkins, et al. 2015); pg625].

Thus, similarly to pain, (Tabor et al. 2016; Wallwork et al. 2016) pain-related fear and consequent behaviour (e.g. avoidance) is influenced by a fine balance between explicit and implicit processes, which may vary depending on context and motivation (Vlaeyen, Crombez, and Linton 2016; Crombez et al. 2012; Vlaeyen and Linton 2012). Our experimental study presented in Chapter 3 is in line with this understanding. This study demonstrated that in a reaction-time task, people with persistent LBP displayed an implicit 'danger bias' towards bending and lifting with a round-back. Critically, that bias was unrelated to the participant's self-reported fear of bending, suggesting that self-reported pain-related fear may be more cognitively driven rather than characterized as a phobia. This lends support to more recent views of the role of 'fear' in the fear-avoidance model, in which defensive responses (physiology and behaviour) vary according to the person's goals and imminent context, and are most prominent when the person is directly exposed to the threat (Vlaeyen, Crombez, and Linton 2016; Glombiewski et al. 2015; Wideman et al. 2013; Vlaeyen and Linton 2012; Meulders, Vansteenwegen, and Vlaeyen 2011).

The results of the study (Chapter 3) raised two hypotheses: (i) that this implicit association between bending and lifting with a round-back and danger could be common in people without pain, indicating this could be a pre-existing *schema*; (ii) that this implicit association could potentially influence both pain and behavioural responses to the task. That is, an experience of pain associated with bending and lifting could activate the pre-existing schema and update it to a 'protect the back' *pain schema*.

The first hypothesis was recently tested, employing the same implicit association test in a group of people without LBP **(Appendix A)**. The results of that study indicate that people without LBP also displayed similar implicit associations between round-back bending and lifting and danger. These results support the notion that an implicit bias towards bending and lifting with a 'round-back' as dangerous is common among people without LBP, and may in fact be a pre-existing schema. Additionally, a study investigating the implicit beliefs of physiotherapists who worked with musculoskeletal conditions, found they also displayed an implicit bias towards round-back bending and lifting as dangerous for the back; and while speculative, this implicit bias may influence their advice to people with LBP on bending and lifting posture **(Appendix B)**.

In relation to the second hypothesis, that this implicit bias could influence both pain and behavioural responses to bending and lifting, the common-sense model of self-regulation (Leventhal, Phillips, and Burns 2016; Leventhal, Diefenbach, and Leventhal 1992; Leventhal, Meyer, and Nerenz 1980) suggests that a person's pre-existing schema, which is informed by media, healthcare providers, family, friends, their own experience and that of others influences their behavioural response when they experience a heath complaint, such as LBP (Bunzli et al. 2017). Qualitative data highlighted that family members and friends are common sources of information often sought by people with persistent LBP however, they often endorse damage beliefs themselves, reinforcing the notion that the back is vulnerable and needs protection (Bunzli, Smith, Schutze, et al. 2015). Healthcare practitioners are also an influential source of information for people who seek a diagnosis for their LBP, reassurance and pain relief. However, when met with diagnostic uncertainty and/or threatening medical information, or when treatment fails to provide control over their pain, people are commonly left with a pain experience that is threatening and uncontrollable, fuelling a cycle of pain-related fear and disability (Bunzli, Smith, Schutze, et al. 2015). It is then possible that a person's schema (e.g. the back is vulnerable) is updated by new information (e.g. painful sensation associated with bending or lifting, combined with advice from a family member or a healthcare practitioner that endorses negative back beliefs about bending and lifting), reinforcing the 'protect the back' *pain schema*, and further influencing behavioural and emotional responses to their LBP. Protective behaviours (e.g. bracing while bending and lifting) and/or avoidance (e.g. not performing bending and lifting) commonly demonstrated by people in pain would therefore not be irrational, but rather a common-sense response to their underlying implicit danger bias. Although this hypothesis has not been formally tested, it conforms with the modern conceptualization that both pain and fear act as protective mechanisms that occur in response to an implicit evaluation of danger to a person's body and valued goals (Tabor et al. 2016; Wallwork et al. 2016; O'Sullivan et al. 2016; Lotze and Moseley 2015).

In summary, it appears that perceiving the back as vulnerable and in danger when rounded is common among those with and without low back pain as well as healthcare practitioners. This may be an issue of societal conditioning, highlighting the need for public health initiatives for dissemination of positive messages that debunk widely held unfounded and unhelpful beliefs about the back and LBP. Healthcare practitioners have a core role in this process due to their capacity to access evidence-based information and their direct contact with people seeking care for LBP. Clinical encounters provide a valuable learning opportunity in which a person's pain schema may be challenged and adapted with information that is conducive to developing body confidence and that empowers self-management. This is in line with a recent international call for action in shifting the understanding and management of LBP (Buchbinder et al. 2018; Hartvigsen et al. 2018; Foster et al. 2018). Importantly, although the problem of LBP is global and driven by common public health issues and unhelpful beliefs, a person's pain schema and how it influences their experience is individual.

7.1.2 Opportunities to change the pain schema

In this section, three key potential areas to enhance the treatment for people with persistent LBP and high pain-related fear are proposed: (i) targeting pain control, (ii) controlling safety-seeking behaviours, and (iii) adopting a sense-making framework that facilitates understanding of pain. These are presented below.

Many studies have investigated approaches to reduce pain-related fear in people with persistent LBP (Pincus et al. 2015; Linton and Fruzzetti 2014; Hill et al. 2011; Henschke et al. 2010; Eccleston, Williams, and Morley 2009; Leeuw et al. 2008; Linton et al. 2008; Woods and Asmundson 2008). Although no intervention is recommended over another (Pincus et al. 2015; Reese and Mittag 2013), there is a common belief that exposure-based approaches (Pincus et al. 2015; Hill et al. 2011; Henschke et al. 2010) are optimal for the treatment of people with high pain-related fear (den Hollander et al. 2010; Bailey et al. 2010). This view likely stem from the fact that the origin of exposure-based interventions is grounded on the fear-avoidance model, which posits that pain-related fear is a phobic experience, and the fact that exposure treatments are effective in managing phobias (Craske et al. 2017; Kindt 2014; Wendt et al. 2008). Thus, targeting fear reduction is at the heart of exposure treatments for people with pain-related fear (Vlaeyen et al. 2001). Exposure-based interventions in this context specifically and repeatedly expose the person with pain to their threatening activity. The success of early single-case experimental studies for people with persistent LBP and high pain-related fear provided preliminary support for this approach and possibly led to a common view that considers exposure as the treatment of choice for high pain-related fear. Nonetheless, there had been no attempts to evaluate the evidence of behavioural interventions specifically for people with persistent LBP and high pain-related fear.

The systematic review presented in Chapter 4 provided the first evaluation to determine the current state of evidence regarding the effectiveness of behavioural interventions for people with persistent LBP and high pain-related fear. Broadly, the results of that review suggest that while exposure-based behavioural interventions for people with persistent LBP and high pain-related fear are moderately effective in reducing disability and fear compared to waitlist control and usual care, they are only modestly effective in reducing pain intensity. This is not surprising considering that behavioural interventions do not aim to treat pain directly [(Henschke et al. 2010; Vlaeyen et al. 1995)]. Specifically, the results of Chapter 4 challenge the common and intuitive view that exposure-based interventions are the treatment of choice for this group of people. The findings suggest that there is limited and only weak evidence that exposure-based interventions are superior to activity-based behavioural interventions on reducing disability, pain and fear in people with persistent LBP and high pain-related fear. This is due to: (i) the small number of RCTs (n=3) comparing exposure-based interventions to usual care and to activity-based interventions, with average quality (two studies were rated as 'fair quality' and one was rated as 'high quality') and 'moderate to high' risk of bias; and (ii) due to methodological limitations of the SCEDs comparing exposure-based interventions to activity-based interventions. It appears that high-quality RCTs are needed to determine if one behavioural intervention is superior to another (exposure-based vs. activity-based) on reducing disability, pain and fear in this challenging group. What also emerged from these findings is that optimization of behavioural interventions, specifically exposure-based interventions for the treatment of people with persistent LBP and high pain-related fear is very much needed. Targeting pain control may represent a potential opportunity for optimization of behavioural interventions.

7.1.2.1 Targeting pain control

Pain control is not an explicit target of behavioural interventions. Instead, their aim is to modify unhelpful behaviours and their underlying cognitive processes, and thereby reduce disability [(Main et al. 2014; Vlaeyen et al. 2012; Henschke et al. 2010)]. In fact, traditional behavioural interventions hold an underlying assumption that pain cannot be modified (Saragiotto, Maher, Traeger, et al. 2017; Moseley and Butler 2015; Nicholas et al. 2002). However, pain is modifiable (Saragiotto, Maher, Traeger, et al. 2017), and gaining control over pain is associated with less future episodes of LBP (Main, Foster, and Buchbinder 2010). Specifically, for people with high psychological distress and pain-related fear, enhancing pain control may be an important treatment target (Mansell, Hill, Main, Vowles, et al. 2016).

Pain intensity (severity) has been associated with pain related fear (Kroska 2016; Sullivan et al. 2009), disability (Zale and Ditre 2015; Zale et al. 2013; Lee et al. 2015; Crombez et al. 1999) and a worse long-term trajectory in people with LBP (Chen et al. 2017). Recently, a series of qualitative studies investigating beliefs underlying pain-related fear and factors associated with improvement in pain-related fear indicated that aspects related to the somatic pain experience such as the 'severity' of pain, how 'predictable' pain is and how much 'control' a person has over pain might be important both for maintaining and reducing pain-related fear (Bunzli et al. 2016; Bunzli, Smith, Schutze, et al. 2015). Moreover, sense-making processes (i.e. gaining a biopsychosocial understanding of their LBP that made sense and that guided helpful behaviours towards goal achievement) were proposed to play a role in reducing pain related fear in people with persistent LBP and high pain-related fear undergoing treatment (Bunzli et al. 2017).

Pain intensity and pain-related fear have an intricate and variable relationship (Vlaeyen 2016). This relationship has been explored (i) qualitatively, indicating that pain that is perceived as a threat to the person's body and/or to their goals reinforces pain-related fear (Bunzli, Smith, Schutze, et al. 2015); (ii) objectively, in a meta-analysis of 118 studies, which demonstrated that pain intensity and pain-related fear have a positive association (Kroska 2016); and (iii) experimentally, demonstrating that pain-related fear mediated the effects of pain intensity on activities of daily living (Gay et al. 2015). The level of this association might vary between people as fear varies according to the meaning the person attributes to the pain experience (Vlaeyen 2016). Furthermore, it may vary within a person over time depending on context (Karos, Meulders, and Vlaeyen 2015), individual understanding of the experience (Moseley and Butler 2016; Bunzli et al. 2017) and coherence between the actions taken and how effective they were in helping the person achieve their goals (Bunzli et al. 2017). This supports the notion that the relationship between pain and fear is amenable to change.

Behavioural interventions based on the fear-avoidance model suggest that exposing a person to their threat without the occurrence of the expected catastrophic outcome changes a person's interpretation of pain, reducing fear and disability, and for some it may have an impact on pain (Vlaeyen et al. 2012). This implies that the relationship between pain and fear would only be disrupted by a reduction in fear. However, considering factors related to the person's somatic experience might suggest that the relationship between pain and fear may also be amenable to change by a reduction in pain (Bunzli et al. 2017; Moseley and Butler 2015; Lotze and Moseley 2015). This was recently supported by a qualitative study, which reported that gaining control over pain was an important step in the reduction of fear for people with persistent LBP and high pain-related fear (Bunzli et al. 2016; Bunzli, Smith, Schutze, et al. 2015).

Interventions that aim to explicitly target pain may need to consider that each person presents an individual sensitivity profile, which is determined by a complex interaction of multiple systems (neuro, immune and endocrine) that influence nociceptive processing, tissue sensitivity, and pain perception through peripheral and central mechanisms. This complex interplay may lead to changes in body awareness (perceived body distortions), behavioural (safety-seeking behaviours) and emotional (fear, distress) responses to pain that shape a person's individual pain experience (Fillingim 2017; Rabey et al. 2017b; Butera, Fox, and George 2016; Moseley and Butler 2016; Tabor et al. 2016; Rabey, Slater, et al. 2015; Gatchel et al. 2007). Specific interactions between pain-related fear and pain sensitivity profiles may explain individual differences in motor behaviour (Karos et al. 2017; Gay et al. 2015), which is likely reflected in a person's **pain response to movement** (Butera, Fox, and George 2016; Hodges and Smeets 2015; Rabey, Beales, et al. 2015; Dankaerts et al. 2009; O'Sullivan 2005). This is well illustrated by a recent investigation of 300 people with persistent LBP, which indicated that people display variable pain responses to repeated forward and backward bending tasks, with half presenting an increase in pain and only 10% reporting pain relief (Rabey et al. 2017b). Furthermore, variable pain responses have also been reported during a repetitive lifting task (Sullivan 2009). This variability in pain responses to movement likely reflects complex sensorimotor interactions that account for the individual's sensitivity and movement profile (Fillingim 2017; Rabey et al. 2017b; Butera, Fox, and George 2016; Wallwork et al. 2016; Moseley and Butler 2016; Hodges and Smeets 2015).

A person's response to pain that is perceived as threatening is unique. Although movement is a common threat for people with persistent LBP, thoughts, emotional states, and bodily feelings (e.g. feeling of instability, vulnerability, and variations of the pain sensation itself) may also be threat-provoking and elicit pain responses that may need to be controlled [(Linton and Fruzzetti 2014)]. In that context, exposure to threat is not restricted to movement, and it may also occur through imagery (e.g. visualization of a threatening context or activity), body perception (e.g. using bodily feelings as interoceptive cues to elicit a threat response), and adoption of provocative postures; to which the person may display cognitive, emotional and/or behavioural responses. Developing control over these responses, such as emotional regulation prior to and/or during exposure, may be an avenue to enhance the effectiveness of the intervention and provide control over the pain experience [(O'Sullivan et al. 2018; Linton and Fruzzetti 2014;)].

7.1.2.2 Controlling safety-seeking behaviours

Consideration of **how a person moves** when exposed to a threat also appears important. People with pain-related fear may often use *safety-seeking behaviours* in an attempt to prevent or minimise the feared outcome [(Meulders et al. 2016)]. For instance, people with persistent LBP commonly move slowly, breath-hold and co-contract their trunk muscles [(Laird et al. 2014; Karayannis et al. 2013)] to avoid lumbar spine flexion while bending and lifting. This is in fact a common instruction ('rule') for people with LBP, who are often told, "Keep your back straight when lifting!" [(Darlow, Perry, Stanley, et al. 2014)]. Adopting such behaviours during exposure to threatening and/or provocative tasks have been proposed to increase local tissue sensitivity and perpetuate threat perception related to movement, thus being unhelpful and provocative [(Rabey et al. 2017b; Nijs et al. 2017; Dankaerts et al. 2009; O'Sullivan 2005)].

In the context of a healthcare practitioner consultation, people may also display subtle safety-seeking behaviours that work as cognitive and emotional avoidance [(Volders et al. 2015; Volders et al. 2012; Linton 2005)], such as changing subjects, making jokes, distractive conversation or shifting attention. Identifying and responding to these cues may allow the clinician to act upon these behaviours to enhance the effect of exposure [(Volders et al. 2012)].

Controlling safety-seeking behaviours during exposure appears to be a sensible strategy to facilitate and/or enhance exposure-based interventions. However, this topic is strongly debated in behavioural psychology (Vlaeyen et al. 2012). A recent meta-analysis investigating whether engaging in safety-seeking behaviours during exposure-based interventions was beneficial or detrimental to fear reduction was inconclusive, and could not support the use or removal of safety-seeking behaviours during exposure treatment (Meulders et al. 2016). That review however, did not include studies of people with pain-related fear. More recently, an experimental study determined that engaging in avoidance behaviour (i.e. avoiding a painful stimulus) increased pain-related fear. The authors suggest that allowing the use of safety-seeking behaviours to avoid pain during treatment may hamper fear reduction (van Vliet et al. 2018).

7.1.2.3 Adopting sense-making processes

An attempt to make sense of a threatening pain experience perceived as uncontrollable was the overarching theme of a qualitative exploration of the lived experience of people with persistent LBP and high pain-related fear (Bunzli, Smith, Schutze, et al. 2015). People's negative perceptions about their illness (i.e. LBP condition) have been associated with worse long-term outcomes for people with LBP (Chen et al. 2017). Therefore, another aspect that may be considered is targeting a person's **understanding of pain**. Changing how an individual makes sense of their pain by developing an understanding that pain is a marker of perceived danger that is influenced by several modifiable factors, rather than an accurate reflection of tissue damage, may change the experience of pain itself (Louw et al. 2016; Lotze and Moseley 2015; Moseley and Butler 2015). Indeed, gaining an understanding of pain that makes sense and that guides helpful behaviours towards goal achievement has been proposed as an important aspect of reducing pain-related fear (Bunzli et al. 2017; Bunzli et al. 2016). Within the 'common sense model', this process consists of addressing the five dimensions that encompass beliefs by which a person 'represents' (understands) their pain problem: *Identity or diagnostic label* (labels that define the condition), *causes* (what triggers this pain?), *timeline* (is this pain the same, better or getting worse?), *consequences* (what will happen in the future? Will I suffer further damage, pain and/or functional loss?), and *control* (can this pain be controlled?) (Bunzli et al. 2017; Leventhal, Meyer, and Nerenz 1980).

Although pain education may promote moderate reduction in pain-related fear in people with persistent LBP (Louw et al. 2016; Moseley and Butler 2015; Clarke, Ryan, and Martin 2011) it does not promote change in behavioural response to fear when delivered alone (de Jong et al. 2005). In contrast, exposure strategies integrated with a personalised education approach may reduce the threat associated with pain during exposure, and provide a safe experience linked to a sensible explanation to a person's pain. Therefore, consideration of a person's understanding of pain, their pain response to the targeted activity for exposure, while discouraging safety-seeking behaviours, may enhance the capacity of exposure-based interventions to more effectively control pain. Some of the proposed strategies align closely with strategies employed in the treatment of non-pain related fear and anxiety disorders such as spider phobia and social anxiety (Craske et al. 2014).

7.1.3 What can we learn from the research into non-pain related fear and anxiety disorders?

Traditionally, exposure-based interventions for people with non-pain related fear and anxiety disorders (e.g. spider phobia, social anxiety, fear of heights, general anxiety disorder) have focused on fear reduction however, a substantial number of people fail to improve (Craske et al. 2012). Recently, a body of work has emerged proposing a shift from models that use cognitive restructuring and fear habituation as an index of corrective learning, towards developing non-threatening (safe) associations. In other words, a change from models that focuses on fear reduction as an outcome towards approaches that incorporate strategies to enhance learning of a new experience of safety (Craske et al. 2017; Craske et al. 2014; Craske et al. 2008; Craske et al. 2012). This idea is grounded on the inhibitory learning theory, which proposes that the original fear memory (threat association between stimulus and response) is not erased during exposure, but rather is left intact and a secondary inhibitory association between stimulus and response develops (non-threat association in which the stimulus does not predict the expected aversive response) (Bouton and King 1983). Recently, inhibitory learning strategies have been proposed to maximize learning of new safe memories, including: (i) developing new safe associations, (ii) enhancing accessibility and retrieval of newly learned associations (Craske et al. 2014; Craske et al. 2012). These strategies have been derived from research in anxiety disorders, and have not been specifically evaluated in people with pain. Nonetheless, it appears that some of these strategies could be integrated in interventions for people with persistent LBP and high pain-related fear – **Table 7.1**.

The results of the systematic review in Chapter 4 indicate that there are opportunities for better targeting the pain schema of people with persistent LBP and high pain-related fear. These might include consideration of their cognitive, emotional and behavioural responses to exposure, their movement-related pain responses, how a person performs a threatening and/or provocative movement, and how they make sense of their pain experience (pain schema). Furthermore, integrating strategies nested in the inhibitory learning theory may maximize the effects of exposure-based interventions. Targeting these aspects in light of the person's goals may provide an opportunity to challenge their pain schema and promote pain control.

Table 7.1 Inhibitory learning strategies and their clinical application for people with persistent LBP and high pain-related fear

Strategies to develop new non-threatening (safe) associations:		Clinical application for people with persistent LBP
Maximize violation of expectancy	Procedures that challenge and disconfirm existing beliefs and expected (threatening) outcomes modify threat associations with the task, promoting learning of a safe association in memory [(Craske et al. 2017; Craske et al. 2014; Liao and Craske 2013)]. Pain control strategies suggested above may play a role in promoting violation of expectation in people with persistent LBP by providing people with a different way of performing a threatening task that results in a positive outcome.	For example, for people with pain related to bending with a round-back asking the person to rate on a NRS scale how fearful they are, how much pain they expect to feel and what is the likelihood of that occurring when performing such task would give an objective measure of the person's expected threatening outcome. When the person bends with a round-back without safety-seeking behaviours and experiences reduced pain, the person's threatening outcome does not occur causing a significant violation of their expectation.
Educate after exposure	It is well established that cognitive approaches that target a person's beliefs and/or reflect on discrepancies can create non-threat associations [(Weisman and Rodebaugh 2018; Craske et al. 2014)].	Therefore, attempts to reconceptualise pain prior to exposing the person to the threatening and/or provocative task may minimize the violation of expectancy during exposure.
Promote deepened extinction	This relates to building on behavioural exposure. It is proposed that exposing the person to two threatening cues after having violated expectations to one of them can enhance the effect of exposure [(Weisman and Rodebaugh 2018; Craske et al. 2014; Craske et al. 2012)].	In the context of LBP, this may involve exposing the person to bending then progressing to lifting a heavy object and then adding twisting. The speed with which this would be progressed would depend on the person's pain and emotional responses to the tasks. However, fast progressions within the session may promote greater learning salience.
Target safety-seeking behaviours	Although there is still debate on the use or abolishment of safety-seeking behaviours during exposure [(Meulders et al. 2016)], several mechanisms have been proposed to explain their likely hindrance on anxiety symptoms [(Weisman and Rodebaugh 2018)]. These include limiting disconfirmation because attentional resources are being used towards the implementation of safety behaviours, reinforcing threat mechanisms by sending sensorimotor signals to the amygdala, and they can reinforce erroneous perception of safety [(Weisman and Rodebaugh 2018; Sloan and Telch 2002)].	Common safety-behaviours for people with persistent LBP include: breath-holding, propping with hands, avoidance of spinal flexion and rotation, and co-contraction of the abdominal and paraspinal muscles (bracing). Therefore, discouraging these behaviours during exposure may enhance learning.
Consider flare-ups as a learning opportunity	Occasionally exposing anxious people to a task in association with a threat (CS-US pairing)[*] to elicit an aversive response is thought to promote reinforced extinction [(Craske et al. 2014)]. [*] Conditioned stimulus: CS; Unconditioned stimulus: US.	In people with persistent LBP this could relate to a person experiencing pain during to a task that he had already experienced control over. This could be used as an opportunity to reinforce previous messages and to re-gain control over the experience and the person's response to it in order to reinforce safety learning.
Label emotional experience during exposure	Asking the person to verbally label their emotional experience during behavioural experiments can potentiate learning of safe associations and regulate their emotional response to the task or bodily sensation [(Craske et al. 2012)]. This strategy represents a behavioural method of enhancing inhibitory regulation via the	This is illustrated in Chapter 5, when the participant was questioned about his thoughts and emotions during exposure, and then asked to modify this by thinking positively about the experience.

	prefrontal cortex [Craske et al. 2008]. Engaging cortical areas related to executive function dampens the limbic system activity. Specifically, this process has been shown to activate the right ventrolateral prefrontal cortex, reducing activity in the amygdala during extinction training, and consequently attenuating fear response [Lieberman, Eisenberger, and Crockett 2007]. The redirection of attention away from pain and towards emotion may also increase connectivity with brain anti-nociceptive system [Kucyi and Davis 2015].	
Strategies to enhance accessibility and retrieval of newly learned associations:		
Promote variability during exposure	Variability of stimulus and contexts are though to enhance the storage capacity and retention of newly formed information [Craske et al. 2008]. This means that the greater the number of associations at the time of learning a new memory, the more options there are for later retrieval of this information. If a person learned a safe association in various contexts and stimuli, it is easier for them to retrieve that safe memory. It leads to variations of emotional state, similar to what will happen in real life situations post-exposure where retrieval is necessary. It also increases salience of feared stimulus, enhancing learning of inhibitory associations. Furthermore, it is thought this process may expedite learning and may also enhance generalization [Weisman and Rodebaugh 2018; Craske et al. 2014].	Variability of stimulus (low and high loads), context (daily activities, work, physical activities) and exposure (timing between sessions; environment – room vs gym). Conducting interoceptive (e.g. body scan), imaginary (e.g. visualisation) and in vivo exposure (e.g. activities related to the person's goals) in varied contexts (alone, in unfamiliar places, in places related to goals). Progress of exposure into real life scenarios. The more exposure to varied contexts and emotional states, the less likely the person is to not face the feared stimulus after the intervention. This can reduce spontaneous recovery (return of fear) and fear re-acquisition.
Create space between exposure sessions	This relates to varying the intervals between sessions. This may facilitate accessibility of newly-formed safe associations [Craske et al. 2008]. A possible mechanism is that people that have space between sessions often have opportunities to practice homework and to experiment in their own environments, promoting learning between sessions [Weisman and Rodebaugh 2018].	To stimulate experimentation, people are encouraged to reflect on what was learned; practice strategies used in the session; read materials; watch educational videos, or videos of people with similar stories (e.g. the participant in Chapter 5 described stories of hope were helpful); and focus on changing habits in goal-linked contexts.
Offset reinstatement and context renewal effects	Progressing exposure into real life scenarios is important because the more exposure to a variety of contexts and emotional states, the less likely the person is to not face the feared stimulus after the intervention. This can reduce spontaneous recovery and fear reinstatement, which are common problems in exposure [Craske et al. 2014]. Mental reinstatement of what was learned during exposure (instructional retrieval cue) has been show to achieve strong effects in reducing context renewal [Craske et al. 2014].	For people with LBP, providing them with key healthy messages or positive affirmations about the health of their spine and capability of their body that they can remember and use it in situations of daily life may be helpful. These could be statements the person used during exposure in the clinic (e.g. lifting a box with no pain – 'what does that make you think?'...."makes me think my back is strong enough to do it" – 'On your day to day I want you to think that "my back is strong" when you are lifting objects'). Replication of provocative activities with the new behaviour when experiencing pain in that task (e.g. the participant described in Chapter 5 - bending again, but focussing on the breath and not on protecting the spine).

7.1.4 Cognitive Functional Therapy for people with high pain-related fear

The notion that pain would be a target for behavioural interventions in people with high pain-related fear demands interventions that are in line with contemporary understanding of pain. That is, that pain is an individual experience that is influenced by a complex interplay of multiple factors that vary over time, shaping a person's pain experience (Rabey et al. 2017a; Moseley and Butler 2016; Tabor et al. 2016; Gatchel et al. 2007). Furthermore, interventions for people with high pain-related fear may benefit from incorporating inhibitory learning strategies (Craske et al. 2017; Craske et al. 2014; Liao and Craske 2013; Craske et al. 2008). *Cognitive Functional Therapy* emerges as a behavioural intervention that is likely to conform to these requirements. Cognitive Functional Therapy evolved from an integration of physiotherapy rehabilitation with foundational behavioural interventions (Vlaeyen et al. 2001; Keefe 1982; Fordyce 1976), as an exposure-based behavioural approach for individualising the management of people with persistent LBP. Cognitive Functional Therapy differs from other behavioural interventions, as it uses a multidimensional clinical-reasoning framework to identify and target modifiable contributors to pain and disability in a person-centred manner. This enables the physiotherapist to design a management plan that is tailored to the person's unique clinical presentation and context. Moreover, traditional exposure behavioural experiments focus on testing catastrophic predictions about the performance of tasks (e.g. "If I bend, I will damage my disc"), while specifically avoiding testing predictions of pain. This is because pain often occurs, minimizing the mismatch between prediction and experience, an important aspect of learning (Vlaeyen et al. 2012). A critical point of difference to these approaches is that CFT explicitly targets pain control during exposure to feared and/or provocative movements. This is done by challenging negative cognitions and modifying how the person physically performs the task (via body relaxation, body control, and extinction of safety-seeking behaviours). Therefore, CFT inherently uses strategies that maximise inhibitory learning. Personalised reconceptualization of pain is achieved via experience, self-reflection and education, disconfirming previously held unhelpful beliefs and allowing the person to make sense of their pain experience (O'Sullivan et al. 2018).

Although CFT has showed reductions in pain and disability in people with persistent LBP with moderate (Vibe Fersum et al. 2013) and high (O'Sullivan et al. 2015) disability, this intervention had not been specifically evaluated for people with high pain-related fear. The studies presented in Chapter 5 and 6 provide the first evaluation of CFT to specifically target people with persistent LBP and high pain-related fear. Although the design of those studies was not to test the effectiveness of CFT, they provide valuable insight to the individual process of change over the course of the CFT intervention.

7.1.5 The process of changing the pain schema is individual and may occur rapidly

The single-case report presented in Chapter 5 provides an illustration of the temporal changes in pain-related fear, and aspects of the somatic pain experience (pain expectancy and pain experience) in a person undergoing CFT. A person, who self-reported high pain-related fear associated with bending and lifting that had led to an escalation of functional avoidance and disability. This study provided detailed description of the use of the clinical reasoning framework to identify modifiable factors related to this person's disorder; and how this was used to tailor an individualized management plan to help him achieve independence. Explicitly controlling safety-seeking behaviours during exposure was key to achieve pain reduction early in his journey. Based on clinical interviews (at 6, 12 and 18 months follow up), it appears that gaining pain control provided this person with a safe opportunity for learning a new behaviour linked to pain that was less intense and more predictable. Whilst constrained by the limitations of a single-case report this study provided valuable insight to factors that are potentially important in the process of change in pain-related fear.

Informed by the knowledge gathered from the single-case report, the study reported in Chapter 6 used a single-case experimental design to evaluate temporal changes in disability and potential mediators of treatment response to CFT. This design accommodates the within-person temporal variability, the large between-person heterogeneity, the complexity of persistent LBP, and that of individualized interventions (Morley 2018; Morley, Vlaeyen, and Linton 2015; Tate et al. 2017; Norell-Clarke, Nyander, and Jansson-Frojmark 2011; Borckardt et al. 2008). It was hypothesized that pain, pain controllability, fear, distress and sleep would mediate a reduction in disability in four people with persistent LBP undergoing CFT, who had high pain-related fear of bending and lifting with a round-back. Results of the study presented in Chapter 6 indicate that reductions in disability and proposed mediators were clearly related to the commencement of the CFT intervention. Although causal inference cannot be determined from this study design, attribution of change to the intervention was further supported by physiotherapist log and interview content (participant and significant other), which did not identify explanations for change other than the intervention. Analysis of temporal associations between proposed mediators and disability indicated that changes in pain intensity levels, pain controllability, and fear occurred concomitantly and not before changes in disability. This *early temporal relationship between potential 'mediators' and the outcome*, with changes occurring immediately or soon after the first treatment session was an important and novel finding of this study.

These rapid changes are unlikely to be solely explained by a biomedical account, which would suggest the need for changes in tissue healing, muscle strength, flexibility or physical conditioning for improvement to occur (George 2017b; Vlaeyen et al. 2001). Rather, these changes are more likely to be understood from a neurobiological account, in which learning and perceptual changes play a significant role (Brodal 2017). Research in cognitive neuroscience indicates that changes in expectation and meaning of a stimulus can rapidly modulate a person's pain experience (Hedderson et al. 2018; Moseley and Butler 2016; Tracey and Mantyh 2007). This has been demonstrated in experimental manipulations of context (Buchel et al. 2014), motivation (Wiech and Tracey 2013; Seymour et al. 2005), learning (Colloca et al. 2010) and perception (Moseley and Arntz 2007). Furthermore, research into the neural mechanisms underlying 'extinction' in people with fear demonstrates the amygdala (highly active during fear conditioning) appears to be downregulated by pre-frontal cortical influences as a result of inhibitory learning during exposure (Shin and Liberzon 2010; Milad et al. 2007; Milad et al. 2005). Specifically, the dorsolateral prefrontal cortex is thought to play a key role in control of pain, not only in a top-down direction (Eippert et al. 2009), but also in a bottom-up direction (Buchel et al. 2014); and the ventromedial prefrontal cortex plays a role in emotional regulation (Wiech and Tracey 2013). Combined, these studies indicate the effects of cognitions and emotions in pain and fear modulation (Wiech 2016; Buchel et al. 2014; Wiech and Tracey 2013; Bushnell, Ceko, and Low 2013; Tracey and Mantyh 2007).

While all participants presented changes in pain (pain intensity, pain interference), pain controllability (pain control, pain self-efficacy) and fear (pain-related fear of damage and/or pain, pain catastrophizing or pain anxiety), the specific factors or 'ingredients' within these mediator groupings varied between individuals (details in Chapter 6). Critically, the rate of change, the pattern of change and the factors that changed were different for each person, featuring the *individual variability in the process of change*. This indicates that there are probably many individual pathways to reducing disability related to persistent LBP in people with high pain-related fear. This is supported by previous qualitative reports of different pathways to reduction of pain-related fear in people with persistent LBP [(Bunzli et al. 2016)]. These reports have highlighted that a key factor in all pathways to improvement was a new experience that involved gaining control over pain and/or responses to pain, developing a new understanding of their pain and achieving independence [(Bunzli et al. 2016)].

The individualized experience illustrated by the four participants in this study (Chapter 6) supports the idea of a '*pain schema disruption*' promoting change in several factors at the same time. Furthermore, it suggests that how the schema is disrupted, and which factors change vary between and within individuals over time.

7.1.5.1 Pain schema disruption – a safety learning model

Under a modern conceptualization of pain, persistent disabling LBP is more accurately understood as an emergent protective mechanism produced by the complex interaction of neuro-immune-endocrine systems in response to the individual's perceived level of threat to their health homeostasis [(Brodal 2017; Moseley and Butler 2016; O'Sullivan et al. 2016)].

The multiple and interrelated influences of all factors that can modulate a person's pain experience is here defined as a complex system [(Brown 2009)]. Complex systems are governed by simple rules and schemas [(Brown 2009)], which are constantly updated by new information, experiences and perception of bodily sensations, influencing ongoing behaviour [(Bunzli et al. 2017)]. A person's schema is considered to be highly plastic enabling the person to quickly learn new associations and adapt to new salient contexts [(Brodal 2017; Davies 2016; Vlaeyen 2015)]. Predictive learning models propose that when discrepancy occurs between what is expected and what is experienced, a 'prediction error message' is generated in the brain that serves as a signal to update the schema [(Wiech 2016; Wiech and Tracey 2013)]. In this context, new rules are created and the schema is altered, which may influence the person's response. For instance, a salient learning experience such as pain, may shift a person's system beyond its homeostatic threshold. Over time, as the threat and pain associations become stronger the pain schema is reinforced, which may maintain the system beyond its homeostatic threshold and lead to an unhelpful cycle of pain, fear and disability. There is evidence that learning and adaptation in people with persistent pain may be less plastic and the pain schema may become more resistant to change [(Wiech 2016; Vlaeyen 2015)]. This could be related to the unpredictability of pain that can lead to sustained prediction signalling of an aversive outcome (Vlaeyen 2015), likely reinforcing the existing pain schema and restricting its ability to be updated. In the absence of safe experiences, a confirmatory feedback loop continuously reinforces a pain schema that perpetuates the unhelpful cycle (Bunzli et al. 2017; Vlaeyen, Crombez, and Linton 2016; Wiech 2016).

In contrast, a positive experience that is linked to the formation of non-threat associations during the performance of a threatening task may lead to a perception of safety (rather than threat), which may potentially update the schema, returning the system to its homeostatic balance. Expectancy violation is at the heart of inhibitory learning (or safety learning), meaning that new safe memories are developed and compete with the original fear memory (Pittig et al. 2018; Craske et al. 2012). For example, an experience that is linked to pain control during exposure to a pain provocative task could promote a salient learning experience of safety. This safe experience may generate a new rule that disrupts the existing pain schema, reducing unpredictability and potentially updating the person's habitual overprotective response. Considering fear and avoidance as rational emotional and behavioural responses to a pain experience that is perceived as threatening and uncontrollable (Bunzli et al. 2017), safety learning processes such as developing behavioural strategies that give control over pain and reduce avoidance may have a positive impact on both fear and pain (Bunzli et al. 2017; Linton 2013). This process of a pain schema disruption that updates the person's system and its response is supported by inhibitory safety learning, which suggests that repetitive exposure to a positive experience can lead to formation of a *safety schema* (Craske et al. 2017; Craske et al. 2012; Craske et al. 2014). This could be a pathway out of the unhelpful cycle towards a helpful response, bridging the gap between the person and their valued goals in life.

Although speculative, these findings may support a *safety learning model* to understand a person's pain schema disruption. This model outlines that experiential safety learning ('learning by doing') that enhances control via adoption of new behavioural strategies may be a potential mechanism of change in disability in people with persistent LBP and high pain-related fear. This model is grounded on the understanding of persistent LBP as an individual and complex experience; it is based on the Fear Avoidance Model (Vlaeyen and Linton 2000) and the Common-Sense Model (Leventhal, Meyer, and Nerenz 1980), and it includes principles of predictive (Wiech 2016) and inhibitory learning (Craske et al. 2014) that account for modulation of the pain experience. The proposed model is schematically illustrated in

Figure 7.1, displaying a comparison between two common sense responses to LBP: one which is an *unhelpful* response, illustrated by a vicious cycle leading to disability (adapted from the fear-avoidance model) (Vlaeyen and Linton 2000); and the other which is a *helpful* response, illustrated by a cycle towards engagement in valued goals and ultimately, independence. The factors underlying change, and their order in each cycle may vary according to the person's individual experience. Notably, the findings of the study in Chapter 6 demonstrated that several factors changed concomitantly with disability; thus, many of the changes illustrated in Figure 7.1 may occur soon after the start of treatment, and not necessarily in a sequential manner. Therefore, the cyclical nature of this schematic representation is to illustrate an ongoing process beyond what happens soon after treatment, and that reinforces a feedback loop of safety.

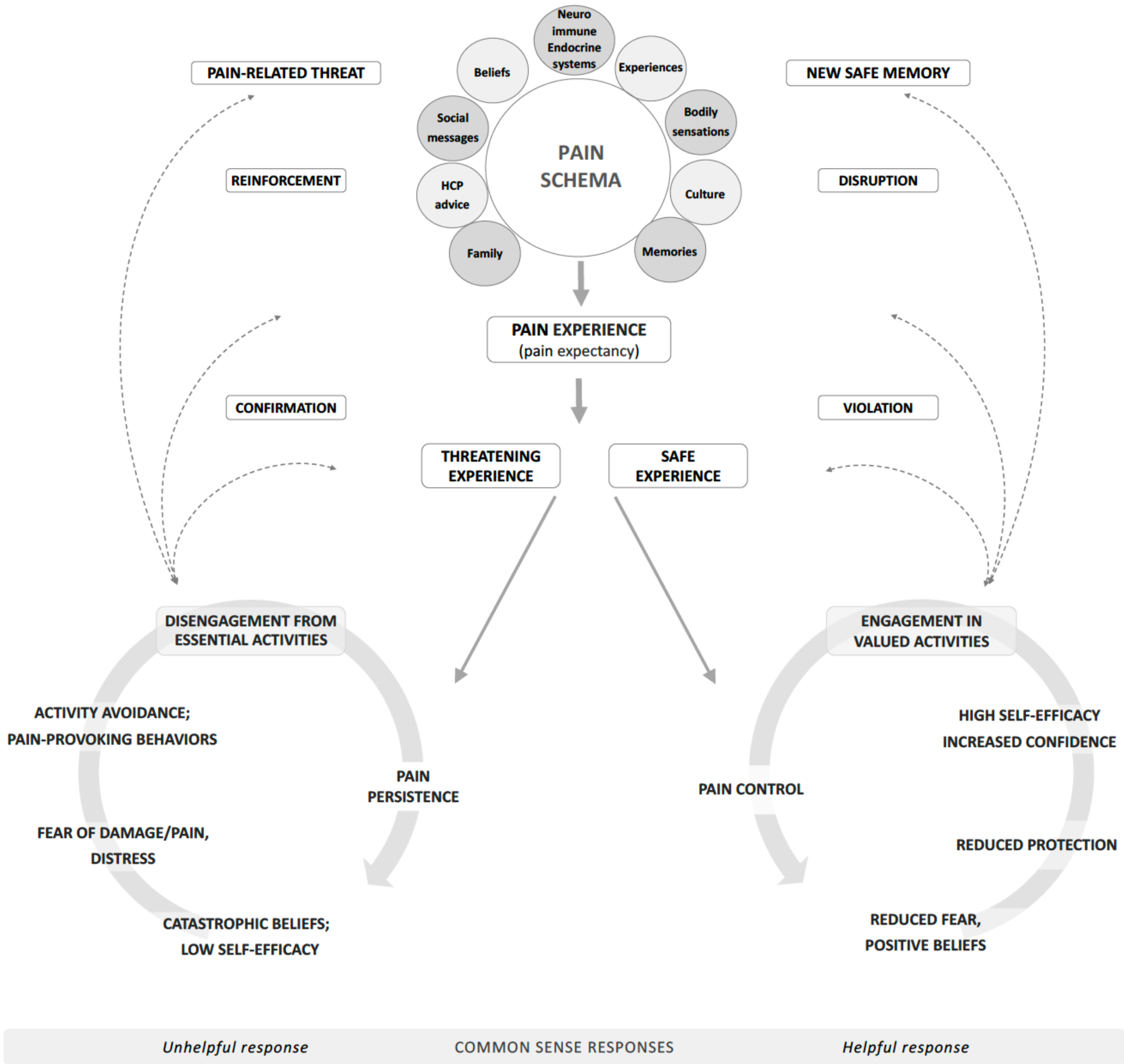


Figure 7.1 Schematic illustration of the proposed mechanism for pain schema disruption.

Different to the Fear Avoidance Model (Vlaeyen and Linton 2000), which proposes confrontation as a single pathway for recovery, this model outlines a process by which the person's pain schema is targeted, facilitating learning of a new experience of safety that violates the person's expectancy of an adverse outcome related to pain.

Considering a person's pain response during exposure to a feared activity, and their underlying motive for avoidance, control during exposure may be achieved by (*i*) promoting body awareness and relaxation prior to the performance of the task (e.g. diaphragmatic breathing, focal body relaxation), (*ii*) modifying a person's posture and/or how a person moves (e.g. allowing spinal flexion during sitting, lifting), (*iii*) controlling safety-seeking behaviours (e.g. not bracing during bending), and (*iv*) controlling thoughts and emotional response (e.g. focus on new strategies, positive thinking) during the performance of a threatening and/or provocative task. This process of experiential learning complemented by a sensible explanation may enable the person to make sense of their pain experience in a helpful adaptive manner. As described in Chapter 5, this new mindset and behaviour may allow the person to experiment the 'new way' (vs. 'old way') and how they respond in different contexts, reflecting the development of self-efficacy and body confidence. This process is thought to empower the individual towards self-management and re-engagement in valued activities, and it may facilitate generalization of treatment effects to valued activities.

The multidimensional and person-centred nature of this model allows for individual pathways of change, thus accommodating the variability of the individual's unique LBP experience. Despite the logical structure and sound underlying scientific rationale, this proposed model of understanding pain schema disruption warrants further testing, as outlined in a section below.

7.2 Strengths and limitations of thesis

This doctoral thesis has some noteworthy strengths. A unique aspect of the experimental study in Chapter 3 was the use of combined implicit and physiology measures to evaluate people with persistent LBP varying from low to high fear of bending and lifting, using stimuli that holds a societal threat-value and that are specific to these tasks. The systematic review in Chapter 4 was prospectively registered, and was conducted by two independent reviewers following the PRISMA guidelines. This systematic review comprehensively extended previous reviews on behavioural interventions for persistent LBP (Kamper et al. 2015; Macedo et al. 2010; Henschke et al. 2010) and for pain-related fear in chronic musculoskeletal pain (Bailey et al. 2010) by specifically evaluating their effectiveness for people with persistent LBP and high pain-related fear. The first clinical study in Chapter 5 reported temporal changes over a period of 18 months using repeated measures, including clinical interviews at three timepoints. The second clinical study in Chapter 6 is the first study to use a SCED to analyse temporal associations between change in disability and factors proposed as mediators of disability reduction in people with persistent LBP and high pain-related fear. This study used both visual and statistical analyses of data as recommended by current guidelines. Furthermore, both clinical studies conform with The Single-Case Reporting guideline In BEhavioural interventions (SCRIBE) 2016 (Tate et al. 2017).

This thesis also has some limitations. A potential weakness of the experimental study in Chapter 3 was the use of visual stimuli only, and not inducing participants to believe they would be required to perform the threatening tasks. Future studies may benefit from investigating physiological startle response in anticipation of, and during performance of personally-relevant threatening tasks. The systematic review in Chapter 4 included only studies published in English, potentially missing relevant studies in other languages. Furthermore, only a small number of studies were included possibly reflecting the strict inclusion criteria, which is necessary to include the target population, and the small number of studies (especially RCTs) specifically targeting people with persistent LBP and high pain-related fear. Interventions were classified as exposure-based or activity-based upon consensus in the authorship team. There remains some ambiguity in the field about what exactly determines this classification and our own perspectives may have influenced the comparative results. The conclusions which can be drawn from the clinical study in Chapter 5 are limited due to the inability of a single-case report to rule out bias in terms of attribution of a treatment effect; nonetheless, the aim of this study was to provide insight to factors that are potentially important in the process of change in pain-related fear, rather than the effect of the intervention. A limitation of the clinical study in Chapter 6 is the small sample (n=4) however, SCEDs are specifically used to study the individual, using replication over participants as a way of strengthening the validity of the results. Although, there was a pre-requisite that the intervention changed both the outcome and proposed mediators to enable mediation analysis, the core aim of this study was to evaluate the process of change (rates, patterns and factors), and not to estimate the effectiveness of the intervention. Another limitation was the fact that all of the measures were rated at the same time, which may have increased their correlation. In addition, some of the measured constructs may overlap conceptually, also potentially increasing their correlation. The issue of correlation was mitigated using Simulation Modelling Analysis, which accounts for the autocorrelation in each measure before estimating the cross correlations (Borckardt et al. 2008).

Finally, although safety-seeking behaviours (e.g. breath-holding, trunk muscle tension, avoidance of spinal flexion) were directly targeted during the intervention, these physical aspects were not measured objectively during exposure. This precludes drawing inferences about the relationship of changes in these factors with changes in disability. Notwithstanding, psychological and physical interventions for persistent LBP appear to effect improvements in pain and disability via cognitive and emotional factors (Lee et al. 2017; Mansell, Kamper, and Kent 2013; Leeuw et al. 2008; Smeets et al. 2006), and it is possible these interventions share similar mechanisms that influence nervous system sensitivity (Moseley and Butler 2016; Wand and O'Connell 2008; O'Sullivan et al. 2015). In line with this, previous RCT (Vibe Fersum et al. 2013) and case-series (O'Sullivan et al. 2015) found that physical factors (posture, range and daily physical activity) were not significantly different after CFT intervention.

7.3 Future research directions

Three key objectives emerge as opportunities for future research: (i) to better understand a person's fear response during actual exposure to a threatening task; (ii) to test the effectiveness of CFT in reducing disability, pain and fear for people with persistent LBP and high pain-related fear, and to test its superiority over another exposure-based behavioural intervention; (iii) to better understand how CFT works for persistent LBP. The rationale and recommendations to achieve these objectives are described below.

Current understanding of the science of fear posits that the feeling of fear is conscious, whereas threat detection processes and response are implicit or non-conscious (LeDoux and Brown 2017; Boeke et al. 2017; Pessoa 2017; Pessoa 2015; LeDoux 2014; LeDoux 2012; Pessoa 2010). Although the results of the experimental study in Chapter 3 are in line with this understanding, not exposing participants to the threatening task limited the ability to distinguish between explicit (self-reported fear) and implicit (fear as an automatic defensive response during exposure) fear responses to a threat. To better inform the distinction between explicit and implicit fear responses to an unavoidable threat, an experimental study exploring physiological response (eye-blink startle reflex and skin conductance response) during actual exposure would be valuable. In this situation exposure would occur when the person performs a personally relevant threatening task (e.g. lifting with a round-back), rather than being exposed to threatening images (e.g. picture of a person lifting with a round-back). The use of objective evaluation of movement behaviour (e.g. spinal kinematics and trunk muscle activity) and pain expectancy and experience during task performance, would provide insight to behavioural responses to a threat (e.g. controlling safety-seeking behaviours) and how it relates to changes in perceived pain control (e.g. reduction in pain experience). Furthermore, it is not known if the implicit bias identified in the experiments of this thesis (Chapter 3 and Appendices A and B), influences bending and lifting behaviour. This relationship is worth investigating because if implicit bias does influence behaviour, then investigating if this bias is amenable to change in people with persistent LBP, would also be of value.

Based on the findings of the systematic review in this thesis, it was clear that high-quality, adequately powered RCTs are needed to determine if one behavioural intervention is superior to another on reducing disability, pain and fear in people with persistent LBP and high pain-related fear. Limited benefits for pain reduction of current behavioural interventions may provide an opportunity for optimization of these interventions in the treatment of people with persistent LBP and high pain-related fear. CFT emerges as a behavioural intervention well suited to address this limitation as it explicitly targets pain control during exposure to feared and/or provocative movements.

The CFT approach was tested in a small-scale, efficacy RCT in people with persistent LBP with moderate disability (Vibe Fersum et al. 2013), and in a case-series in people with high disability (O'Sullivan et al. 2015), the findings of which showed reductions in pain, disability, and fear beliefs. Although the SCED study presented in Chapter 6 provides the first quantitative evaluation of CFT specifically targeting people with persistent LBP and high pain-related fear, the design precludes a robust assessment of the effectiveness of this approach. In addition, qualitative data from patients with persistent LBP and pain-related fear who received this intervention indicated that enhanced pain control was a key component to their recovery (Bunzli et al. 2016). Considering the promising results of CFT in reducing disability, pain intensity and pain-related fear, there is sufficient evidence to warrant formally assessing the efficacy of CFT in people with persistent LBP and high levels of pain-related fear. A well-designed, adequately powered, three-arm RCT would be the ideal framework to test the effectiveness of CFT by comparing it to both usual care and another exposure-based behavioural intervention (e.g. exposure *in vivo*).

Although well conducted RCTs can provide robust estimates of the average causal effect of an intervention, traditional statistical analysis cannot inform on how an intervention works (Lee and Lamb 2017; Imai et al. 2011). In contrast, mediation analysis is a research method that provides information regarding factors that contributed the most to the treatment effect, allowing identification of the mechanisms through which treatments work (Lee et al. 2017; Mansell, Kamper, and Kent 2013). Thus, another opportunity for future research relates to better understanding how behavioural interventions work by embedding causal mediation analysis into RCTs. Understanding the factors that underlie changes in treatment response provide clinicians with an ability to identify which aspects of the intervention need to be adapted and optimized in order to target desired outcomes (Lee and Lamb 2017; Hill and Fritz 2011). Specifically, in relation to CFT, the results of the SCED study presented in Chapter 6 provided important insight to factors related to disability reduction in people with persistent LBP and high pain-related fear. In addition, it provided knowledge regarding the early temporal relationship between changes in these factors and changes in disability over the course of the intervention. Although, SCEDs are not the gold standard framework to evaluate mediators of treatment response the results of Chapter 6 are informative to future trials evaluating mediators of treatment effect. The results inform about the need to assess both outcome and proposed mediators at frequent (e.g. weekly) and early (e.g. before and after the first session) timepoints to allow adequate temporal evaluation of change in the mediators-outcome relationships. New technologies including online registries, smartphone apps, wearable sensors may provide an avenue to enhance frequency of measurement in larger trials.

In light of the variability of the individual's unique LBP experience the use of a complex systems model to understand clinical change is recommended in future research. This model would need to accommodate for testing of several interacting mediators and their interaction with the outcome over time. This would allow testing of the *safety learning model* proposed in this thesis, which posits that experiential learning disrupts a person's pain schema at several levels. A multilevel structural equation model framework can be used to investigate whether improvement in disability was mediated by changes in pain-related cognitions, emotions, behaviours, or by a combination and/or interaction of these factors. The model may need to incorporate estimation of covariance between changes in cognitions, emotions and movement factors and the proportion of mediation that is due to shared versus independent mediation by these factors. The counterfactual framework may be another option as it accommodates non-linear models, and it handles multiple intertwined mediators, such as when mediator-outcome relationships are influenced by the effect of one mediator on another [(Lee et al. 2017; VanderWeele and Vansteelandt 2014; Vanderweele 2012)].

Moreover, to improve the quality of future trials testing mediators of treatment effect, recent expert recommendations [(Lee et al. 2017)] should be followed by: planning RCTs with a priori mechanism evaluation (e.g. testing safety learning as a putative mechanism), identifying and adjusting for possible confounders, and conducting a sensitivity analyses to assess the impact of unknown post-randomisation confounding [(Lee et al. 2017)].

Understanding treatment mechanisms will help refine interventions such as CFT by identifying how factors from different dimensions might be jointly and optimally targeted to achieve better outcomes. This research can provide important information for clinical practice, research and implementation.

7.4 Conclusions of Thesis

The body of work presented in this doctoral thesis has provided information that is valuable for the understanding of the relationship between LBP, fear and disability. The *experimental study* in Chapter 3 supported the notion that self-reported pain-related fear is not a phobia; rather it is a cognitively driven construct, an unhelpful pain schema developed in response to a threatening experience. This pain schema is influenced by negative beliefs such as that the back is in danger when rounded and that it needs protecting. This pain schema may influence behaviour, and may be accompanied by a physiological fear response when the person is exposed to the threatening task itself. The clinician may need to expose the person to threatening and/or provocative tasks that are linked to the person's valued goals to elicit fear responses (physiological and behavioural). These responses may be used as targets to promote control over the pain experience and promote new learning. Clinical encounters should be seen as an important learning opportunity in which a person's pain schema may be challenged and updated with information that empowers self-management. In this context, healthcare practitioners have an important role to disseminate positive, evidence-based messages that challenge pervasive, unfounded and unhelpful beliefs about the back and pain. Public health initiatives may be needed to address this societal belief that the back is vulnerable.

The *systematic review* in Chapter 4, determined that the evidence for effectiveness of current exposure-based behavioural interventions is limited. While exposure-based interventions are moderately effective in reducing disability and pain-related fear when compared to a control group, there is no evidence that exposure-based interventions are superior to activity-based interventions in the treatment of people with persistent LBP and high pain-related fear. Furthermore, current behavioural interventions have limited benefit on pain reduction. Targeting pain control may be an opportunity to optimize behavioural interventions for people with persistent LBP and high pain-related fear. These findings suggest that further high-quality RCTs are needed to determine if one behavioural intervention is superior to another on reducing disability, pain and fear in people with persistent LBP and high pain-related fear. The first *clinical study* in Chapter 5, demonstrated that an individualised multidimensional exposure-based behavioural intervention (Cognitive Functional Therapy) that explicitly targets pain control promoted change in pain and pain-related fear, which were sustained to 18 months; and gave valuable insight to an individual's process of change towards recovery. The second *clinical study* in Chapter 6, investigated how changes in pain-related cognitions and emotions unfolded over the course of CFT, and how changes to these factors related to reductions in disability, providing understanding of the process of change at an individual level. This study demonstrated that the process of change in people with persistent disabling LBP and high pain-related fear is complex, multifactorial, variable, and individual, as is the experience of LBP.

The notion that clinical change occurs incrementally over the course of treatment, and that it follows a linear temporal sequence, with one factor preceding the change of another was not supported. In fact, changes across several factors related to the person's pain experience occurred concomitantly to changes in disability suggesting a disruption of the person's pain schema. These results support a complex systems framework for the understanding of clinical change, and may have clinical implications. Although speculative, interventions may be more effective when targeting all aspects of the pain schema (cognitions, emotions and behaviour) in an integrated manner, rather than its individual components. Based on the body of work of this doctoral thesis, a *safety learning model* is proposed as a theoretical framework to make sense of a person's pain schema disruption. This model outlines that experiential learning that disrupts the pain schema at several levels may be a potential underlying mechanism for behavioural change and formation of a new safety schema in people with persistent LBP and high pain-related fear. The multidimensional and person-centred nature of this model allows for individual pathways of change, thus accommodating the variability of the individual's unique LBP experience. This model however, warrants further testing.

Cognitive Functional Therapy is grounded on a sense-making framework, and uses strategies that maximise inhibitory safety learning. The results of the clinical studies in this thesis provide support to further pursue CFT as an optimized exposure-based behavioural intervention for this clinically challenging group. However, a high-quality RCT is necessary to firmly evaluate the effectiveness of this intervention in this specific group of people with persistent LBP and high pain-related fear. To better understand the mechanisms through which an intervention works evaluation of mediators of treatment effect is required. Informed by the results of this thesis, this trial would assess outcome and proposed mediators at frequent and early timepoints to allow adequate temporal evaluation of change in the mediators-outcome relationships. The use of a complex systems model is recommended in future research to accommodate the intricacies of the individual, the temporal variability of the LBP experience and the multifactorial nature of clinical change.

Chapter 8 APPENDIX A - Evaluation of implicit associations between back posture and safety of bending and lifting in people without pain

There is a pervasive view in western society that the lower back is easy to injure and hard to heal. This belief likely stem from earlier in vivo and in vitro studies, which suggest that lumbar spine flexion (i.e. round-back posture) is dangerous and should be avoided. Despite a lack of support from recent in vivo studies, bending and lifting (especially with a round-back posture) are perceived as dangerous. It has been proposed that pain-free people may hold a common implicit belief that is congruent with the idea that bending and lifting with a round-back represents danger to a person's back, but this has not been evaluated. This chapter reports an experimental study that evaluated implicit associations between back posture and safety of bending and lifting in people without LBP. Furthermore, this study also analysed the participant's qualitative descriptions of the safest lifting posture.

The aims of this study were (i) to evaluate implicit associations (IAT) between back posture (straight-back vs round-back) and safety (safe vs danger) related to bending and lifting in pain-free people; (ii) to explore correlations between implicit (IAT) and explicit measures of beliefs towards vulnerability of the back (bending safety beliefs, back beliefs, and fear of movement); (iii) to investigate participants' qualitative appraisal of safe lifting. Based on our previous work, we hypothesised that (i) pain-free people would display an implicit bias towards evaluating bending and lifting with a round-back as dangerous, (ii) this bias would correlate only moderately with their explicit beliefs, and (iii) pain-free people would qualitatively appraise straight-back lifting as safest.

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8.1 Abstract

Background and aims: There is a pervasive view in western society that the lower back is easy to injure and hard to heal. This belief likely stem from earlier in vitro studies, which suggest that lumbar spine flexion (i.e. round-back posture) is dangerous and should be avoided Despite lack of support from recent in vivo studies, bending and lifting (especially with a round-back posture) are perceived as dangerous. This may influence the way a person performs these tasks. Pain-free people may hold a common implicit belief that is congruent with the idea that bending and lifting with a round-back represents danger to a person's back, but this has not been evaluated. The **aims** of this study were: **1)** to evaluate implicit associations between back posture and safety related to bending and lifting in pain-free people; **2)** to explore correlations between the implicit measure and explicit measures of back beliefs, fear of movement and safety of bending; **3)** to investigate self-reported qualitative appraisal of safe lifting.

Methods: Exploratory cross-sectional study including 67 pain-free participants (52% male), who completed an online survey containing demographic data and self-reported measures of: fear of movement (Tampa Scale for Kinesiophobia for General population - TSK-G), back beliefs (Back Pain Attitudes Questionnaire BackPAQ), and bending beliefs (Bending Safety Belief – BSB - a pictorial scale with images of a person bending/lifting with round and straight back postures). Implicit associations between back posture and safety related to bending and lifting were evaluated with the Implicit Association Test (IAT). A qualitative assessment of descriptions of safe lifting was performed.

Results: An implicit association between 'danger' and 'round-back' bending/lifting was evident in all participants ($IAT_{D\text{-}score}$=0.65 (SD=0.45; 95% CI [0.54, 0.76]). Participants' profile indicated high fear of movement, unhelpful back beliefs, and perceived danger to round-back bending and lifting ($BSB_{Thermometer}$: 5.2 (SD=3.8; 95% CI [4.26, 6.13] range -10-10; $t_{(67)}$ = 11.09, p<0.001). There was a moderate correlation between IAT and $BSB_{Thermometer}$ (r=0.38, 95% CI [0.16, 0.62], p=0.001). There were weaker and non-statistically significant correlations between IAT and TSK-G (r=0.28, 95% CI [-0.02, 0.47], p=0.065), and between IAT and $BackPAQ_{Danger}$ (r=0.21, 95% CI [-0.03, 0.45], p=0.089). Qualitative assessment of safe lifting descriptions indicated that keeping a "straight back" and "squatting" when lifting were the most common themes.

Conclusion: Pain-free people displayed an implicit bias towards bending and lifting with a 'round-back' as dangerous. Our findings support the idea that pain-free people may have a pre-existing belief about lifting, that the back is in danger when rounded. Research to evaluate the relationship between this implicit bias and lifting behaviour is indicated.

Implication: The findings of this study highlight the need for better dissemination of recent evidence related to bending and lifting to the public, and may have implications for ergonomic guidelines related to bending and lifting back postures. Additionally, clinicians may need to be aware of this common belief, as this may be reflected in how a person responds when they experience pain.

Key words: implicit beliefs, explicit beliefs, pain-free people, back posture, bending, lifting.

8.2 Introduction

Low back pain (LBP) is a leading cause of disability worldwide (Vos, Flaxman, et al. 2012; Balague et al. 2012). There is a pervasive belief in western society that the lower back is easy to injure and hard to heal (Darlow et al. 2015; Bunzli, Smith, Schutze, et al. 2015; Bunzli, Smith, Watkins, et al. 2015; Darlow, Perry, Stanley, et al. 2014), and that bending and lifting (especially with a round-back posture) are dangerous (Nolan et al. 2018; Darlow, Perry, Stanley, et al. 2014). Perceiving the back as vulnerable during bending and lifting (Bunzli, Smith, Schutze, et al. 2015) may influence a person's behaviour while performing these tasks (Darlow 2016; Darlow et al. 2015; Darlow, Perry, Stanley, et al. 2014). It has been proposed that decisions about task behaviours adopted in daily life may occur as part of a dual-process, in which explicit (deliberate, analytical) and implicit (automatic) processes are involved in the appraisal of risk versus benefit associated with the task (Leeuw, Peters, et al. 2007; de Jong et al. 2005). The influence of each process on task behaviour may vary depending on context, time and motivation (Hofmann et al. 2005; de Jong et al. 2005; Goubert et al. 2003). Therefore, assessment of beliefs related to the bending and lifting back posture is important. Specifically, evaluating these processes in people who are not experiencing pain provides a framework un-confounded by recent experience of LBP to understand the relationship between explicit and implicit beliefs.

Self-reported questionnaires are widely used to assess back beliefs (explicit measures) (Darlow, Perry, Mathieson, et al. 2014; George, Valencia, and Beneciuk 2010). However, these are vulnerable to self-presentational bias and might only capture what the individual is aware of, or willing to disclose (Nosek, Hawkins, and Frazier 2011; Fazio and Olson 2003). In addition, these do not assess beliefs about specific postures, being more generic evaluations of back beliefs (Bunzli, Smith, Watkins, et al. 2015; George et al. 2009; Leeuw, Goossens, et al. 2007). Implicit attitudes however, are better evaluated in a spontaneous context in which time for introspection and motivation is reduced (Greenwald, McGhee, and Schwartz 1998). The Implicit Association Test (IAT) is commonly used to measure implicit associations in social (Greenwald, McGhee, and Schwartz 1998; Greenwald and Banaji 1995), health psychology (Chapman, Kaatz, and Carnes 2013; Sabin and Greenwald 2012; Grumm et al. 2008), and pain (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017; Van Ryckeghem et al. 2013; Goubert et al. 2003) research, but to date the IAT has not been used to investigate perceptions of safety in relation to specific back postures during bending and lifting in pain-free people.

A recent study valuating implicit associations between back posture (straight-back vs round-back) and safety related to bending and lifting in people experiencing back pain found that irrespective of self-reported fear of bending/lifting with a round-back, people were faster to associate images of round-back bending and lifting with words representing danger, rather than safety [Caneiro, O'Sullivan, Smith, Moseley, et al. 2017]. Inferring from previous studies involving asymptomatic individuals [Barke et al. 2016; Taylor et al. 2015; Leeuw, Peters, et al. 2007; Goubert et al. 2003], the authors proposed this may reflect a pre-existing pervasive societal schema or belief [Caneiro, O'Sullivan, Smith, Moseley, et al. 2017], that is informed by media, healthcare providers, family, friends, and past experiences [Darlow 2016; Bunzli, Smith, Schutze, et al. 2015]. Nevertheless, that study did not evaluate a pain-free group. Based on our previous work [Caneiro, O'Sullivan, Smith, Moseley, et al. 2017], we hypothesised that **i)** pain-free people would display an implicit bias towards evaluating bending and lifting with a round-back as dangerous, **ii)** this bias would correlate only moderately with their explicit beliefs, and **iii)** pain-free people would qualitatively appraise straight-back lifting as safest.

Therefore, **the aims of this study were:**

1) to evaluate implicit associations (IAT) between back posture (straight-back vs round-back) and safety (safe vs danger) related to bending and lifting in pain-free people;

2) to explore correlations between implicit (IAT) and explicit measures of beliefs towards vulnerability of the back (bending safety beliefs, back beliefs, and fear of movement);

3) to investigate participants' qualitative appraisal of safe lifting.

8.3 Methods

8.3.1 Study design

An exploratory cross-sectional study.

8.3.2 Participants and recruitment

Participant recruitment and data collection commenced in August 2017 and was completed by September 2017. Participants were recruited through social media, flyers and posters on Curtin University campus as well as approached in person.

Adults over 18 years of age, who had no low back pain (LBP) within the past 12 months were included (indicated by no pain, or pain ≤ 3/10 on average for less than a week, on a Numerical Rating Scale – NRS – anchored on 0= 'no pain', 10= 'worst pain'(Dionne et al. 2008)). Participants were excluded if they had difficulty to read and understand English, or if they were trained physiotherapists or currently studying physiotherapy (as this population has already been studied [(Caneiro, O'Sullivan, Smith, Ovrebekk, et al. 2017)].

Participants were screened over the phone or in person to check if they fulfilled the inclusion criteria. An information sheet clearly explaining the study was sent via email. This study was approved by Curtin University's Human Research Ethics Committee prior to study commencement (HRE2017-0500). All participants provided informed consent, and were informed that they could withdraw from the study at any time.

8.3.3 Procedure

Data collection occurred in two stages: **1) Online:** completion of a survey online (using Curtin University's Qualtrics online platform); **2) Experiment**: completion of a computer-based task (IAT) measuring implicit attitudes related to bending and lifting back posture and perceived safety to the spine. This was followed by completion of the BSB questionnaire (measuring explicit attitudes related to bending and lifting back posture and perceived safety to the spine). Participants were required to meet with investigators at the research laboratory in the School of

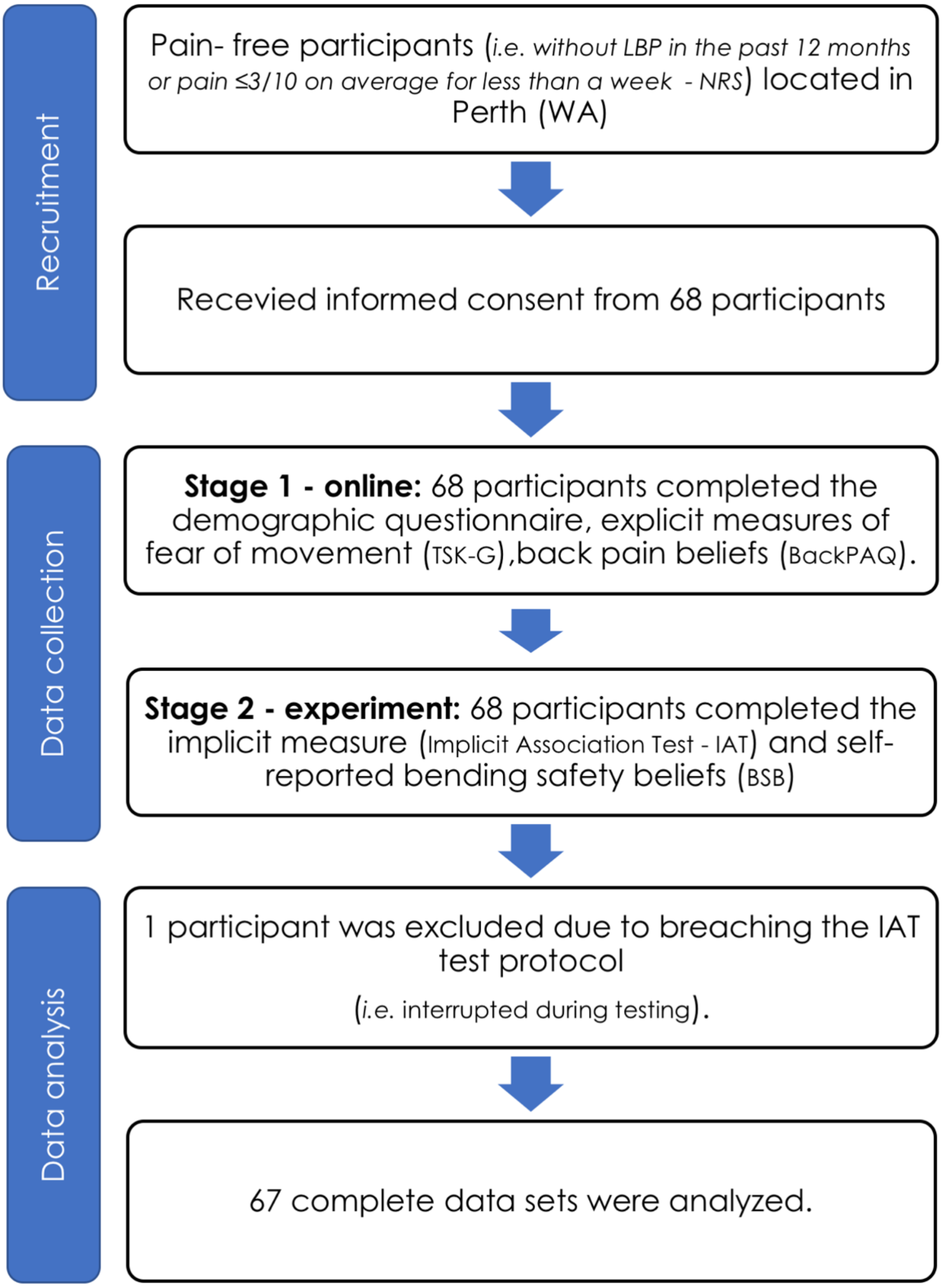
Physiotherapy & Exercise Science (Curtin University), or at an agreed upon external location to complete this stage. A flow chart of the study recruitment and procedure is displayed in **Figure 8.1**.

8.3.4 Demographic data

Participants completed an online demographic questionnaire including age, gender, occupation, previous and current history of back pain, and information related to previous manual handling instructions received about lifting and bending. Participants also provided a subjective description of their understanding of 'safe lifting' – this is described later in this section.

8.3.5 Outcome measures

The outcome measures assessed in this study were measures of fear of movement beliefs, back beliefs, explicit and implicit beliefs about bending/lifting posture and safety of the spine.



Appendix A Figure 8.1 flow chart of the study recruitment and procedure.

8.3.5.1 Implicit Association Test (IAT)

The IAT (Greenwald, McGhee, and Schwartz 1998) is a well-established measure, which was adapted to assess associations between bending/lifting posture and safety in a group of people with back pain (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017). The IAT is a computer based test comprising seven phases, separated by pauses for the instructions in between phases (Greenwald, McGhee, and Schwartz 1998). This IAT is the same used in our previous work (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017), which had five stimuli representing each target ("Round-back" and "Straight-back") and attribute category ("Safe" and "Danger"). Twelve side view images of males and females standing, bending and lifting with an extended ("Straight-back") and flexed lumbar spine ("Round-back"), were developed for this experiment after piloting with people with persistent LBP to confirm their suitability. The category "Danger" was represented by five words frequently used to describe danger associated with movement (selected from interviews with people with persistent LBP and high-fear (Bunzli, Smith, Schutze, et al. 2015; Bunzli, Smith, Watkins, et al. 2015). Words matching in length, frequency, and emotionality represented the category "Safe" (Mallan and Lipp 2007). The category "Danger" consisted of words such as damaging, vulnerable, threatening, alarming and risky. The category "Safe" consisted of works such as harmless, confident, secure, protecting and certainty.

Procedure: Participants were instructed to assign each stimulus displayed in the centre of the screen to its suitable category (displayed at the upper corners of the screen), by pressing the left or right "Shift" keys, as fast as possible while avoiding mistakes. On each trial the participant was given feedback (''correct'' or ''wrong''). The words were presented in bold, 20-point Arial font in white lower case on a black background. The images were presented embedded in a white square image of 800 x 800 pixels on a black background. In the first phase (20 trials), participants sorted each of the 10 images twice, into the categories "Round-back" and "Straight-back". In the second phase (20 trials), participants sorted the 10 words twice into the categories "Safe" and "Danger". In phases, three and four (20 and 40 trials each) participants sorted words and images into the combined categories (e.g., Danger / Round-back and Safe / Straight-back or Danger / Straight-back and Safe / Round-back). In phase five (20 trials) participants sorted images with the location of the categories switched. Phases six and seven (30 and 40 trials) reversed category combinations of phases three and four (e.g., Danger / Straight-back and Safe / Round-back or Danger / Round-back and Safe / Straight-back). As per recommendations[22], the sequence of congruent and incongruent matches during phases three and four, and six and seven were counterbalanced across participants.

Data processing: Each trial started with the display of a fixation cross for 1000ms followed by a word or image for 1000msand an inter-trial interval of 1000ms. Response time was defined as the time elapsed from the presentation of the stimulus to when the shift key was pressed. This time was recorded and incorrect responses, responses shorter than 100 ms or longer than 1000ms were considered as errors. Presentation of the tasks and reaction time recording was controlled by DMDX(Forster and Forster 2003). The performance is faster when highly associated categories share a response [(Greenwald, McGhee, and Schwartz 1998)]. The phases of the IAT being used in this study have been included in **Appendix 8.1.**

A bias score ($IAT_{D\text{-}score}$) was calculated using the improved scoring algorithm recommended by Greenwald et al (2003) [(Greenwald, Nosek, and Banaji 2003)] with an error penalty of 2 standard deviations. This was calculated as the difference between each individual's mean response speeds on the two tasks where danger is paired with round back versus the two tasks where danger is paired with a straight back. The **$IAT_{D\text{-}score}$** could therefore be either positive or negative, with zero indicating no implicit bias in either direction, a positive score indicating implicit bias towards a round-back posture as dangerous and a negative score indicating implicit bias towards a straight-back posture as dangerous. The IAT exhibits adequate reliability and internal, construct and predictive validity [(Nosek, Hawkins, and Frazier 2011; Greenwald et al. 2009; Nosek, Greenwald, and Banaji 2005)].

8.3.5.2 Bending Safety Belief (BSB)

In order to assess specific beliefs related to back posture and safety of the spine during bending and lifting, the BSB was developed and used in a previous study [(Caneiro, O'Sullivan, Smith, Ovrebekk, et al. 2017)] **(Figure 8.2)**. The BSB consists of a pictorial scale containing two images of a person bending forward and lifting a light object – one with a round-back and one with a straight-back. The participants were asked "how would you rate the level of risk to this person's back?" for each image using a Likert scale (anchored on "0" meaning safe, and "10" meaning danger). These questions are clinically relevant when assessing people's beliefs around bending, the way they bend and whether there is a perception of danger in relation to the way they bend (i.e. safe or dangerous). A thermometer score ($BSB_{Thermometer}$) was derived to determine the participant's belief about safety of bending forward and lifting a light object. The danger rating of the picture illustrating bending with a 'straight-back' was subtracted from the danger rating of the picture illustrating bending with a 'round-back'. In line with the implicit $IAT_{D\text{-score}}$, a **positive value** therefore indicated a **higher danger rating for round-back** than a straight-back and a negative score indicated higher danger rating for straight-back than a round-back.

a. b.

Appendix A Figure 8.2 Images used for the bending and lifting safety beliefs thermometer score. a. Round-back posture. b. Straight-back posture.

8.3.5.3 Tampa Scale of Kinesiophobia General (TSK-G)

The TSK was specifically designed to measure pain related fear/or fear of movement in people with pain. It has been adapted (TSK-G), to measure fear of movement beliefs in the general population and who do not have back pain [Houben, Leeuw, et al. 2005]. The TSK-G consists of 17 items that the participants rate on a four-point Likert scale, which ranges from 'totally agree' to 'totally disagree'. Scores range from 17-68 and as the original TSK scale, higher scores on the TSK-G indicate higher levels of fear of movement, even without the presence of pain [Houben, Leeuw, et al. 2005]. Cronbach's alpha for TSK-G was found to be 0.78 for people without low back pain, which is acceptable internal consistency [Houben, Leeuw, et al. 2005].

8.3.5.4 Back Pain Attitudes Questionnaire (BackPAQ)

The BackPAQ was designed to assess attitudes and underlying beliefs about the back pain among the general population, people with back pain and health professionals [Darlow, Perry, Mathieson, et al. 2014]. The questionnaire consists of 34 items representing five belief themes; the participant's own back, looking after their back, back pain in general, what should be done if back pain develops, and recovery of back pain. The participants answered the items on a 5-point Likert scale from "false" to "true" (intermediate labels: 'Possibly False', 'Unsure', 'Possibly True) and 11 items are reversed scored. The 'True' response option normally represents beliefs that are unhelpful for recovery from back pain. Scores range from 34-170, with higher scores indicating more unhelpful beliefs about the back. For the purpose of this study, a subscale called 'danger scale' ($BackPAQ_{Danger}$) was formed by using 14 items from the questionnaire. These items are questions 1-12, 14 and 21 as they are representative of 'vulnerability and 'protection' themes. These themes emerged from the qualitative study which the BackPAQ originated from (Darlow, Perry, Mathieson, et al. 2014). Scores range from 14-70, with higher scores indicating greater perception that the back is danger, for example, that the back needs protection as it is easily injured. The total score of the 'danger scale' was used to find its correlation with other explicit and implicit scores. The 34-item long form of the questionnaire has been shown to have acceptable internal consistency (α=0.70; 95% CI 0.66 to 0.73), construct validity and test-retest reliability (Moran, Rushworth, and Mason 2017; Darlow, Perry, Mathieson, et al. 2014).

8.3.6 Statistical analysis

Descriptive statistics were used to describe the sample. A one-sample t-test was used to assess the degree and direction of deviation of the $IAT_{D\text{-}score}$ and $BSB_{Thermometer}$ score from zero. Additionally, Cohen's *d* was calculated to provide a standardised effect size to assist in the interpretation of the size of the estimated bias. Pearson's correlation coefficients, with associated 95% confidence interval estimates, were used to assess the correlation between implicit and explicit beliefs. Linearity of associations and absence of influential outliers were confirmed by visual assessment of scatterplots. SPSS version 24 statistical software was used for statistical analysis (IBM SPSS Statistics for Windows, version 24, IBM Corp., Armonk, N.Y., USA). An *a priori* power calculation estimated a sample of 60 participants would have 80% power to detect a standardised $IAT_{D\text{-}score}$ difference from 0 of at least ±0.35 and correlations between implicit and explicit measures of ±0.35 or greater (two-sided tests, α=.05).

8.3.7 Qualitative Appraisal of 'Safe Lifting'

A qualitative appraisal of participants' views regarding 'safe lifting' was evaluated by subjective descriptions of how safe lifting should be performed. Participant's qualitative description of their understanding of a "safe" lifting technique (n=52/67) were analysed by two independent investigators and grouped into common themes, and the frequency of these themes were compared.

8.4 Results

8.4.1 Demographics

Sixty-eight pain-free participants were included in the study. One participant was excluded due to a computer error during the experiment, becoming unable to complete the IAT as required, therefore 67 participants were included in final analysis (52% male). The mean (SD) age was 29 years (9.44; range 18-60). The participants reported their occupation as office workers (54%), students (19%), manual workers (11%), or other (16%). Eleven participants (16%) stated a previous episode of lower back pain, with the remaining 56 participants (84%) having no history of back pain. Sixty participants (90%) stated receiving previous manual handling instruction and 52 participants (78%) provided subjective information of their understanding of "safe" lifting technique.

8.4.2 Beliefs

8.4.2.1 Implicit Measure

The mean $IAT_{D\text{-}score}$ was 0.65 (SD=0.45; 95% CI [0.54, 0.76] range -0.88-1.50), which was significantly greater than zero ($t_{(67)} = 11.76$, $p<0.001$). The magnitude of this estimated effect size as measured by Cohen's d was 1.44. This indicates a strong implicit bias of the sample towards the association between images of "round-back" bending/lifting, rather than "straight-back", with words representing "danger", rather than "safety".

8.4.2.2 Explicit Measures

The mean level of fear of movement (TSK-G) was 36.5 (SD=5.6; range 21-49). The mean level of back pain beliefs (BackPAQ) was 105.5 (SD=13.8; range 63-139) and the mean of the subscale $\text{BackPAQ}_{\text{Danger}}$ was 48.5 (SD=6.5; range 22-61). The mean of beliefs related to back posture and safety ($\text{BSB}_{\text{Thermometer}}$) was 5.2 (SD=3.8; 95% CI [4.26, 6.13] range -10-10). The $\text{BSB}_{\text{Thermometer}}$ was significantly greater than zero ($t_{(67)} = 11.09$, $p<0.001$), with the positive value indicating a higher danger ratings for round-back bending and lifting, rather than straight-back.

8.4.2.3 Associations Between Implicit and Explicit Measures

There was a moderate correlation between $\text{IAT}_{\text{D-score}}$ and $\text{BSB}_{\text{Thermometer}}$ (r=0.38, 95% CI [0.16, 0.62], p=0.001). There were weaker and non-statistically significant correlations between $\text{IAT}_{\text{D-score}}$ and TSK-G (r=0.28, 95% CI [-0.02, 0.47], p=0.065), between $\text{IAT}_{\text{D-score}}$ and BackPAQ (r=0.21, 95% CI [-0.03, 0.45], p=0.089), and between $\text{IAT}_{\text{D-score}}$ and $\text{BackPAQ}_{\text{Danger}}$ (r=0.22, 95% CI [-0.02, 0.46], p=0.072).

8.4.3 Subjective Description of "Safe" Lifting

Fifty-two participants (n=52/67, 77.6%) described their understanding of a "safe" lifting technique. The most common theme with respect to back posture was keeping a *straight back*, which included phrases such as "*keep back straight*", "*keep a flat back*", "*don't bend back*" or "*chest up*" (n=27/52, 52%). Two participants were classified to the *neutral back* theme as they mentioned "neutral spine" (n=2/52, 4%), whilst one participant mentioned "bending over naturally" (n=1/52, 2%) potentially indicating using a flexed spine and therefore were classified as *round back*. If there was uncertainty regarding what back posture participants were describing, such as "good back position", then they were not classified into the aforementioned themes but were included in the table **(Appendix A2)**.

Another common theme was related to *squatting*, which included "bend knees"/"squat" (n=35/52, 67%) and "use legs" (n=22/52, 42%). In combination 88.5% (n=46/52) of the participants mentioned either or both phrases. Twenty-two participants only described the legs, without a mention of spinal postures (22/52, 42%).

It was common for descriptions to include both keeping a straight back and squatting, for example: "*Lifting from the legs rather than the back. Keep the back as straight as possible, bend your knees and lift through the legs*" (P09, male, 22yo, office worker), "*Keep your back straight and bend at the knees*" (P55, male, 27yo, manual worker), and "*Back straight, chest up, weight close to body and wide base of support*" (P59, male 22yo, exercise physiologist).

The one participant who mentioned "*bending over naturally*" had the following response: "*Many years ago (at least 30) I was instructed to bend at the knees and keep back straight, using the strength of my legs to do the lifting. In recent years I have been instructed to bend over naturally and pick up the objec*t" (P31, female, 53yo, office worker). See Appendix 6 for detailed table outlining all subjective descriptions of "*safe*" lifting technique grouped into themes.

8.5 Discussion

The primary aim of this study was to test a hypothesis generated in our previous work (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017) by evaluating implicit associations between images of bending and lifting with a round-back posture (vs straight-back) and words meaning safety (vs danger) in pain-free people. Results from the implicit task (IAT), indicate that participants were faster to associate images of bending and lifting with a 'round-back' with words representing 'danger', rather than with words representing 'safety'. This means the sample displayed an implicit bias towards bending and lifting with a 'round-back' as dangerous. These results support our previous hypothesis, which proposed that pain-free people have a pervasive pre-existing belief (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017). Critically, our results indicate this belief appears to be specifically related to 'how' a person performs bending and lifting (i.e. back posture adopted during task).

Our results are consistent with a previous study. Goubert et al (2003) investigated implicit attitudes of pain-free people and found that they have a negative implicit attitude towards back-stressing activities (Goubert et al. 2003). The authors used a variety of tasks (e.g. driving a car, hanging up a coat and, digging in the garden) and negative words (eg. war, AIDS), making their research question more generic, and not specific to back posture during bending and lifting tasks. Notwithstanding, their results support the notion that pain-free people perceive the back as vulnerable both explicitly and implicitly [(Goubert et al. 2003)]. They also assessed people with persistent LBP, and found no implicit bias. The authors therefore suggested, the experience of pain was not the driver of this bias [(Goubert et al. 2003)]. Leeuw et al (2007) also assessed implicit attitudes in people with and without persistent LBP [(Leeuw, Peters, et al. 2007)]. Whilst the groups differed in self-reported fear of movement, the study did not find an implicit association between words representing back-stressing movements (e.g. falling, bending, pushing, lifting, running) and threat-related words (e.g. fatal, warning, terrible, dangerous, horrible) in either group [(Leeuw, Peters, et al. 2007)]. In addition, people with and without pain did not differ in their level of implicit fear of movement [(Leeuw, Peters, et al. 2007)].

Recently, our group investigated implicit attitudes of people with back pain, specifically evaluating beliefs about back posture during bending and lifting [(Caneiro, O'Sullivan, Smith, Moseley, et al. 2017)]. This study found that irrespective of their self-reported fear of bending/lifting with a round-back, all participants had a similar implicit bias towards bending and lifting with a 'round-back' as dangerous [(Caneiro, O'Sullivan, Smith, Moseley, et al. 2017)]. Additionally, a study investigating the implicit and explicit beliefs of physiotherapists (pain-free in the year of the experiment), also found an implicit danger bias towards bending and lifting with a round-back [(Caneiro, O'Sullivan, Smith, Ovrebekk, et al. 2017)]. The results of these studies support the hypothesis that this implicit 'danger bias' to round-back bending and lifting may be pervasive in people with LBP and in health care workers, however this implicit bias had not been specifically investigated in a pain-free population. Collectively, these results support the idea that pain-free people may have a pre-existing schema. The results of the current study expand on this knowledge, providing evidence that this schema may be specifically biased to bending and lifting with round-back postures, supporting the idea of a '*round-back danger' schema*.

A secondary aim was to explore if implicit measures (IAT) correlated with explicit measures of back beliefs ($BackPAQ_{Danger}$), fear of movement (TSK-G) and safety of bending (BSB). Sample profiling indicated that participants generally displayed negative beliefs about the back, high levels of pain-related fear, and perceived danger related to bending and lifting with a round-back posture. There was a moderate statistically significant correlation between the implicit measure and the explicit measure specifically assessing beliefs related to back posture and safety of the spine during bending and lifting (BSB). There were only weak, non-statistically significant correlations with more explicit beliefs related to fear of movement

(TSK-G) and beliefs about back (BackPAQ$_{Danger}$), which are less specific to back posture. This is in line with research of implicit measures, which reports that correlations are likely to be higher when the specific constructs assessed by both measures (implicit and explicit) have conceptual correspondence (Hofmann et al. 2005). This was the case in the current study, with both the IAT and the BSB assessing back posture and safety.

Finally, a qualitative appraisal of subjective descriptions of 'safe' lifting was performed. This revealed that descriptions related to a "*straight back*" and "*squatting*" were the most common, with considerably fewer participants describing a "neutral" or a "round-back" posture. This supports our findings that pain-free people perceived round-back lifting as dangerous in both the implicit (IAT) and the more specific explicit measure (BSB). Furthermore, a recent study by Nolan et al (2017) investigated the beliefs of manual handling advisors and physiotherapists regarding 'safe' lifting technique (Nolan et al. 2018). In this study, the participants were presented with images of 4 different lifting techniques, and asked to choose the one perceived as the safest and justify their choice. The results align with the current study, with the majority of the participants preferring a straight-back lifting posture (Nolan et al. 2018). These straight-back postures were preferred on the basis that they avoided rounding the back, indicating a perception that 'round-back' is dangerous. Additionally, the participants who preferred a straight-back posture, tended to have more negative back beliefs (Nolan et al. 2018). This provides further support for the idea that beliefs about the danger of 'round-back' postures are common in western society.

This pervasive belief about back posture and danger makes sense when considered in context of the information available in the public domain. As illustrated by the subjective descriptions in this study **(Appendix A.2)**, people are commonly presented with 'safety' regulations about the back and which posture to adopt when bending and lifting. A 'straight-back' during bending and lifting is often advocated as ergonomically safe, whilst a 'round-back' is often viewed as dangerous (Wai et al. 2010a, 2010b; Straker 2003; Straker 2002; van Dieen, Hoozemans, and Toussaint 1999). This belief likely stem from earlier *in vitro* studies, which suggest that flexion of the lumbar spine (i.e. round-back posture) is dangerous and should be avoided (Callaghan and McGill 2001). However, there is a lack of *in vivo* evidence (Dreischarf, Rohlmann, et al. 2016; Dreischarf, Shirazi-Adl, et al. 2016; Kingma, Faber, and van Dieen 2010; Wai et al. 2010a, 2010b) that support the notion of using a 'straight-back' in preference to a 'round-back' to reduce risk of LBP. Biomechanical studies have found no significant differences in spinal loads and compression forces between the two postures (Dreischarf, Rohlmann, et al. 2016; Dreischarf, Shirazi-Adl, et al. 2016; Kwon et al. 2011; Kingma, Faber, and van Dieen 2010). Studies have been unable to establish a link between lifting and causation of low back pain (Kwon et al. 2011; Wai et al. 2010a, 2010b; van Dieen, Hoozemans, and Toussaint 1999). Additionally, it has been shown that squat lifting (straight-back with deeper knee bend) is a less efficient lifting technique, when compared to adopting a more round-back posture during lifting heavier loads (Holder 2013). Further, a recent systematic review reported no clear evidence supporting manual handling training in the prevention and treatment of LBP in nurses (Van Hoof et al. 2018).

Together, the results of this study and others suggest that pain-free people may have a common belief that the back is vulnerable and that bending and lifting with a 'round-back' is dangerous (Darlow 2016; Darlow et al. 2015; Bunzli, Smith, Schutze, et al. 2015; Bunzli, Smith, Watkins, et al. 2015; Darlow, Perry, Stanley, et al. 2014). The common-sense model of self-regulation (Leventhal, Phillips, and Burns 2016; Leventhal, Meyer, and Nerenz 1980), suggests that a person's pre-existing schema influences their behavioural response when they experience pain. While speculative, our previous study investigating implicit beliefs in people experiencing back pain proposed that if pain-free people did in fact hold a similar implicit danger bias, as it was reported in the current study ('round-back danger'), then an experience of pain during bending/lifting may activate a '*protect the back' schema* (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017). Protective behaviour demonstrated by people in pain would therefore not be irrational, but rather a common-sense response given their underlying implicit danger bias. However, it is not known if this implicit bias influence bending and lifting behaviour. This relationship is worth investigating because if implicit bias does influence behaviour, then investigating if it is amenable to change in both pain-free and pain populations, will also be of value.

This study was unique in that it investigated a group of people without current pain or pain in the last year, with the majority of participants reporting having never experienced back pain. The results therefore provide an insight into 'general population' beliefs. However, a limitation of this study is that only a small sample of participants from an Australian city was investigated. Investigating a larger and more diverse population across different geographical areas and cultures (western vs eastern), may provide a more complete understanding of general population beliefs and the influence of culture on beliefs and behaviour (Kroska 2016; Vlaeyen 2016).

8.6 Conclusion

The results of this study provide insight in beliefs of people without low back pain. Pain-free participants displayed an implicit association between images of 'round-back' bending and lifting postures and words representing 'danger'. Importantly, our findings support the idea that pain-free people may have a pre-existing belief that the back is in danger when rounded during bending and lifting. To understand the behavioural implications of these findings, further research evaluating the influence of implicit bias on behaviour in both pain-free and people in pain, may be worth pursuing.

8.7 Implications

The findings of this study highlight the need for better dissemination of evidence related to bending and lifting to the public, to address this misperception of vulnerability of the back to round postures. This may have implications for ergonomic guidelines and public health information related to bending and lifting back postures. Additionally, clinicians may need to be aware of this common belief in society, as this pre-existing schema may be reflected in how a person responds when they experience pain and present for treatment. Future research is warranted to evaluate the relationship between implicit attitudes and task behaviour in people both with and without pain.

8.8 Authors' statements

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Conflict of interest: *Peter O'Sullivan* receives speaker fees for workshops on pain management. *All the other authors* declare no conflicts of interest.

Ethics approval: This study was approved by Curtin University's Human Research Ethics Committee prior to study commencement (HRE2017-0500). All participants provided informed consent, and were informed that they could withdraw from the study at any time.

8.9 Appendix A.1

Appendix A.1 Table 8.1 Phases of the implicit association test (IAT).

PHASE	TASK	SEQUENCE 1	
1	*Target-discrimination*	**Images**	
		Round-back	Straight-back
2	*Attribute-discrimination*	**Words**	
		Danger	Safe
3	*Combined-discrimination_1*	**Words / Images**	
		Danger/Round-back	Safe/Straight-back
4	*Combined-discrimination_2*	**Words /Pictures**	
		Danger/Round-back	Safe/Straight-back
5	*Target-discrimination reversed*	**Images**	
		Straight-back	Round-back
6	*Combined-discrimination_3*	**Words / Images**	
		Danger/Straight-back	Safe/Round-back
7	*Combined-discrimination_4*	**Words / Images**	
		Danger/Straight-back	Safe/Round-back

Note: **Targets:** Round-back and Straight-back | **Attributes:** Safe and Danger

8.10 Appendix A.2

Appendix A.2 Table 8.2 Subjective description of "safe" lifting*.

Common themes	Participant Number	Subjective lifting description (for 52 participants that responded)	TSK-G	$BSB_{Thermometer}$	BackPAQ	$BackPA_{Danger}$
Straight back - eg. "straight back", "flat back", "don't bend back", and "chest up) - many also included comment about bending knees or using legs	P02	Use the legs for any vertical lifting by squatting with legs shoulder width apart, keeping the back straight and drive upwards using the leg muscles.	35	4	102	52
	P04	Do not bend back, use 2 to lift.	49	2	139	61
	P08	Brace abs. Push hips back. Keep chest up	36	3	97	41
	P09	Lifting from the legs rather than the back. Keep the back as straight as possible, bend your knees and lift through the legs.	36	5	118	53
	P10	Keep your back straight and bend your knees	44	8	110	45
	P14	Lift with your legs not your back, straight back when ever lifting heavy objects.	38	10	118	51
	P16	Stop and assess the load, check pathways where the lifted object will be carried, ensure enough space available to lift safely, bend at the knees, keep your back straight, avoid over-reaching and use a team lift if the item is too heavy.	38	5	99	50
	P18	Bend your knees not your back to lift. Don't lift too heavy.	42	0	97	49
	P24	Completed manual handling mandatory computer education through the health department. Lift through legs, not through back. Don't bend over when lifting.	35	6	97	48

P26	Bend at the knees and keep back straight, not bent.	40	1	110	57
P30	Bend from the knees not the hips. Keep your back straight. Seek assistance if needed with something heavy	33	0	88	52
P33	Bend knees and keep soft when bending down/and moving up while lifting. Do not round spine while lifting, keep spine stacked above lower body while lifting.	31	6	83	44
P34	Squat low, keep back straight.	38	5	117	55
P39	Lifting with knees bent, back straight, and contracting abdominal core whilst lifting. Only lifting a certain amount on own, always seeking help lifting heavier items	38	6	86	40
P40	Bend your knees/squat and keep a straight back while lifting heavy objects. I use your legs and not your back to lift.	39	10	101	40
P41	Always keep your back straight and bend your knees.	34	9	104	50
P42	Adapt a stable position & keep the load close to the waist, ensure a good hold on the load, bend your knees and do not bend your back or twist when lifting.	37	7	102	47
P44	It was a small part of a course - Health and Safety at Work - by bending your knees and not your back	38	10	98	37
P45	Keep core activated. Bend at knees, using leg muscles, keeping spine straight. Lift smaller loads. Do not twist spine while lifting. Keep head upright without looking down.	25	10	98	50
P47	Bend your knees and keep your back straight, use your core.	41	6	104	50
P49	Keep back straight, lift with legs.	42	5	122	53

	P50	Bend your knees, keep your back straight and lift the object close to your body	33	10	107	47
	P54	Bending at the hips lifting with the legs, keeping load close to body and keeping spine strait	31	10	93	45
	P55	Keep your back straight and bend at the knees	34	9	113	50
	P59	Back straight, chest up, weight kept close to body, wise base of support	32	8	96	45
	P07	Set your back in a flat 45 degree activated position with knees bent and lift using your legs, maintaining the natural flat position of your back	29	2	98	42
	P48	Lift with a flat back. Use your knees and hips to drive upwards, not your back muscles.	34	0	100	47
Neutral back	P20	Don't have the time to list them all or go into detail but I will summarise the important points: -Lift with neutral spine -Lift will legs -Hold load close to body -2 hands always -No twisting -Both feet firmly on ground -No lifting above shoulder height (possible shoulder injury) -Grip load firmly from underside	40	6	130	60
	P03	Adopt a stable position. The feet should be apart with one leg slightly forward to maintain balance (alongside the load, if it is on the ground). Be prepared to move your feet during the lift to maintain your stability. Avoid tight clothing or unsuitable footwear, which may make this difficult. Get a good hold. Where possible, the load should be hugged	36	-5	109	51

		as close as possible to the body. This may be better than gripping it tightly with hands only. Start in a good posture. At the start of the lift, slight bending of the back, hips and knees is preferable to fully flexing the back (stooping) or fully flexing the hips and knees (squatting). Don't flex the back any further while lifting. This can happen if the legs begin to straighten before starting to raise the load. Keep the load close to the waist. Keep the load close to the body for as long as possible while lifting. Keep the heaviest side of the load next to the body. If a close approach to the load is not possible, try to slide it towards the body before attempting to lift it. Avoid twisting the back or leaning sideways, especially while the back is bent. Shoulders should be kept level and facing in the same direction as the hips. Turning by moving the feet is better than twisting and lifting at the same time. Keep the head up when handling. Look ahead, not down at the load, once it has been held securely. Move smoothly. The load should not be jerked or snatched as this can make it harder to keep control and can increase the risk of injury.				
Round back	P31	Many years ago (at least thirty) I was instructed to bend at the knees and keep back straight, using the strength of my legs to do the lifting. In recent years I have been instructed to bend over naturally and pick up object.	21	-10	63	22
Squatting - Bend knees or use legs without mention of back posture	P13	Bend at knees to lift. Carry items at chest height. Avoid twisting while carrying items	34	6	120	57
	P22	Bend with your knees and keep both feet firmly planted on the ground.	38	7	96	42

P36	Bend at the knees, hold close to your body and use leg strength to raise yourself up	37	7	120	52
P38	Bend at the knees and hold the item to the body	37	6	106	43
P46	Bend at the knees and don't just use your back	36	10	117	52
P51	Bend through the knees and lift from legs rather than from back.	31	10	94	50
P53	Bend you knees, strong spine, don't reach, don't carry heavy things far away from your body, don't turn at the waist - turn with your feet, get assistance for awkward objects and/or items over 20kg, take your time, check surroundings	32	1	111	54
P56	Keep the object you are lifting close to your body. Bend your knees (squat down to the object). Don't twist or make sharp movements whilst holding an object. Don't lift it if its too heavy - better to get help than slip a disc	30	7	107	53
P57	To bend knees and hips	37	10	99	46
P58	Bend and the knees not waist.	38	1	107	48
P61	Bend your hips and knees to squat down to your load, keep it close to your body, and straighten your legs to lift.	45	5	102	46
P62	Bend knees to lift heavy items	45	0	101	48
P63	Bend your knees	44	5	118	51
P01	Bend at the knees	37	5	107	51
P11	In nursing training we were instructed to lift mainly using our leg muscles and not to solely rely on our backs.	24	1	89	44

P13	Lift with your legs	40	7	117	51
P17	When lifting heavy objects to make sure and lift from the legs instead of your back	40	3	124	54
P19	Use your legs not your back to lift. If possible lift heavy items with more than one person.	36	5	110	46
P21	Bend at the knees. Make sure your centre of gravity is not over the object. Lift with arms and legs.	38	4	118	51
P32	Get close to the item, balanced, lift using your legs, don't twist	27	9	104	43
P27	Squat with a good back position to pick up and put down heavy items. Don't lift heavy items from a certain height.	36	5	102	47
P52	Stand close to load, knees slightly wider then shoulder width apart, bend knees and don't hinge back forward, grab load and use legs to lift with load close to body.	37	7	98	52

*15 participants did not provide descriptions of safe lifting technique – 8 of them said only where they learnt to lift, 7 of them had no response.

Chapter 9 APPENDIX B - Physiotherapists have an implicit danger bias to bending and lifting with a round-back posture

Beliefs that the back is vulnerable, and requires protection are common among people with and without LBP. Encounters with healthcare practitioners such as physiotherapists, who provide advice about LBP, are thought to play a role in the development of such societal beliefs. Healthcare practitioners share the view that 'improper' posture (e.g. round-back) while bending and lifting is dangerous for the back, and possibly one of the causes of LBP. This chapter reports an experimental study that evaluated implicit associations between images of bending and lifting with a round-back and words representing danger, in physiotherapists that provide treatment for people with musculoskeletal pain conditions.

The aims of this study were (i) to evaluate implicit associations (IAT) between bending and lifting back posture (straight-back vs round-back) and safety (safe vs danger) in physiotherapists; (ii) to explore correlations between implicit (IAT) and explicit measures of beliefs towards vulnerability of the back (bending safety beliefs, back beliefs, and fear of movement). We hypothesised that (i) physiotherapists would display an implicit bias towards evaluating bending and lifting with a round-back as dangerous, and (ii) this bias would correlate only moderately with their explicit beliefs.

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"Physiotherapists have an implicit danger bias to bending and lifting with a round-back posture" (*under review*)

9.1 Abstract

Background: Beliefs can be assessed using explicit measures (e.g. questionnaires) that rely on information of which the person is 'aware' and willing to disclose. Conversely, implicit measures evaluate beliefs using computer-based tasks that allow reduced time for introspection thus reflecting 'automatic' associations. Thus far, physiotherapists' beliefs about back posture and safety have not been evaluated with implicit measures.

Objectives: **(1)** Evaluate implicit associations between bending lifting *back posture* (straight-back *vs* round-back) and *safety* (safe *vs* danger); **(2)** Explore correlations between implicit and explicit measures of beliefs towards vulnerability of the back.

Design: Exploratory cross-sectional quantitative study.

Methods: 47 musculoskeletal physiotherapists completed explicit measures of fear of movement (TSK-HC), back beliefs ($\text{BackPAQ}_{\text{Danger}}$) and beliefs related to bending and lifting back posture and safety (BSB). An Implicit Association Task (IAT) was used to assess implicit associations between (*i*)images of people bending/lifting with a 'round-back' or with a 'straight-back' posture, and (*ii*)words representing 'safety' and 'danger'. A one-sample t-test assessed the degree and direction of the sample's IAT score. Cohen's *d* provided an effect size of the estimated bias. Correlation between IAT and each explicit measure was assessed using Pearson's coefficient.

Results: The sample displayed an implicit association between 'round-back' and 'danger' (μ = 0.213, p=.003, CI: .075-.350), with an effect size magnitude of 0.45. There were moderate correlations between IAT and BSB (r = .320, CI [.036-.556], p=.029) and, IAT and $\text{BackPAQ}_{\text{Danger}}$ (r=.413, 95%CI [.143-.626], p=.004).

Conclusions: Physiotherapists displayed an implicit bias towards bending and lifting with a round-back as dangerous.

Key-Words: Implicit bias; Musculoskeletal physiotherapists; Bending and lifting beliefs

9.2 Introduction

Beliefs that the back is vulnerable, and requires protection are common among people with (Darlow et al. 2015; Bunzli, Smith, Schutze, et al. 2015) and without (Munigangaiah et al. 2016; Darlow, Perry, Stanley, et al. 2014; Briggs et al. 2010; Gross et al. 2006) LBP. **Encounters with health care clinicians such as physiotherapists**, who provide advice about LBP, are thought to play a role in the development of such societal beliefs (Darlow et al. 2013). Several studies have investigated beliefs of clinicians towards LBP (Darlow 2016; Synnott et al. 2015; Bishop, Thomas, and Foster 2007; Coudeyre et al. 2006). Despite limited evidence (Dreischarf, Rohlmann, et al. 2016; Roffey et al. 2010; Bazrgari, Shirazi-Adl, and Arjmand 2007), clinicians share the view that 'improper' posture (e.g. round-back) while bending and lifting is dangerous for the back (Stevens et al. 2016; Synnott et al. 2015; Darlow et al. 2012; Nijs et al. 2013), and possibly one of the causes of LBP (Stevens et al. 2016; Synnott et al. 2015; Darlow et al. 2012; Nijs et al. 2013). Specifically, physiotherapists have self-reported a perception of the back as vulnerable and a belief that adopting **straight-back** postures is **safest** (Nolan et al. 2018). Physiotherapist' beliefs can strongly influence their advice to patients, potentially fuelling unhelpful protective and/or avoidance behaviours (O'Sullivan et al. 2016; Darlow et al. 2013; Darlow et al. 2012; Bishop et al. 2008; Vlaeyen and Linton 2006). For example, Lakke et al (2015) found that healthy adults' lifting capacity was significantly reduced when examined by physiotherapy students with high fear-avoidant beliefs (Lakke et al. 2015). Clinicians who hold such beliefs are also less likely to adopt evidence-based treatments (Darlow et al. 2012; Coudeyre et al. 2006). Not surprisingly, it has been proposed that disability associated with LBP may be in part iatrogenic (Lin et al. 2013; Darlow et al. 2013).

Beliefs can be assessed via explicit and implicit measures. Studies assessing beliefs of clinicians typically employed **explicit** measures (e.g. self-reported questionnaires (Darlow, Perry, Mathieson, et al. 2014; George et al. 2009; Houben et al. 2004), which evaluate beliefs that are deliberately formed upon reflection. However, explicit measures are sensitive only to what people are aware of and are willing to disclose (Nosek, Hawkins, and Frazier 2011; Fazio and Olson 2003; Greenwald, McGhee, and Schwartz 1998). **Implicit** measures on the other hand, assess beliefs based on 'automatic' associations in memory (e.g. bending posture and danger). These associations can be assessed via computer-based reaction-time tasks, which reduce the person's ability to control their response, minimizing effects of social desirability (Gawronski and Bodenhausen 2006; Greenwald, McGhee, and Schwartz 1998). The Implicit Association Test (IAT), is a well-validated and extensively used measure (Harvard 2011; Greenwald, Nosek, and Banaji 2003), which requires the person to associate words or images as quickly and as accurately as possible (Van Ryckeghem et al. 2013;

Greenwald, McGhee, and Schwartz 1998). The speed with which the person performs the task reflects the strength of the associations, and can indicate the degree of **implicit bias** (Nosek, Hawkins, and Frazier 2011). Depending on factors such as time and context (Nosek, Hawkins, and Frazier 2011; Fazio and Olson 2003; Greenwald, McGhee, and Schwartz 1998), implicit biases can influence behaviour (Sabin and Greenwald 2012; Nosek, Hawkins, and Frazier 2011; Greenwald et al. 2009) in a manner that a person may not be aware of (Gawronski, Hofmann, and Wilbur 2006; Greenwald, McGhee, and Schwartz 1998).

Considering physiotherapists often make clinical decisions under contexts of pressure (e.g. time, patient's expectations and distress), an implicit bias may influence their advice to patients with LBP on bending and lifting posture (Houben, Gijsen, et al. 2005). **Thus far, physiotherapists' implicit associations between back posture and safety have not been investigated.** Based on studies assessing explicit beliefs about bending/lifting (Nolan et al. 2018; Darlow et al. 2015; Darlow, Perry, Stanley, et al. 2014), we **hypothesised** that **i)** physiotherapists would display an implicit bias towards evaluating bending and lifting with a round-back as dangerous, and **ii)** this bias would correlate only moderately with their explicit beliefs. Therefore, the **aims** were:

1) To evaluate implicit associations (IAT) between bending and lifting back posture (straight-back vs round-back) and safety (safe vs danger) in physiotherapists;

2) To explore correlations between implicit (IAT) and explicit measures of beliefs towards vulnerability of the back (bending safety beliefs, back beliefs, and fear of movement).

9.3 Materials & Methods

9.3.1 Design

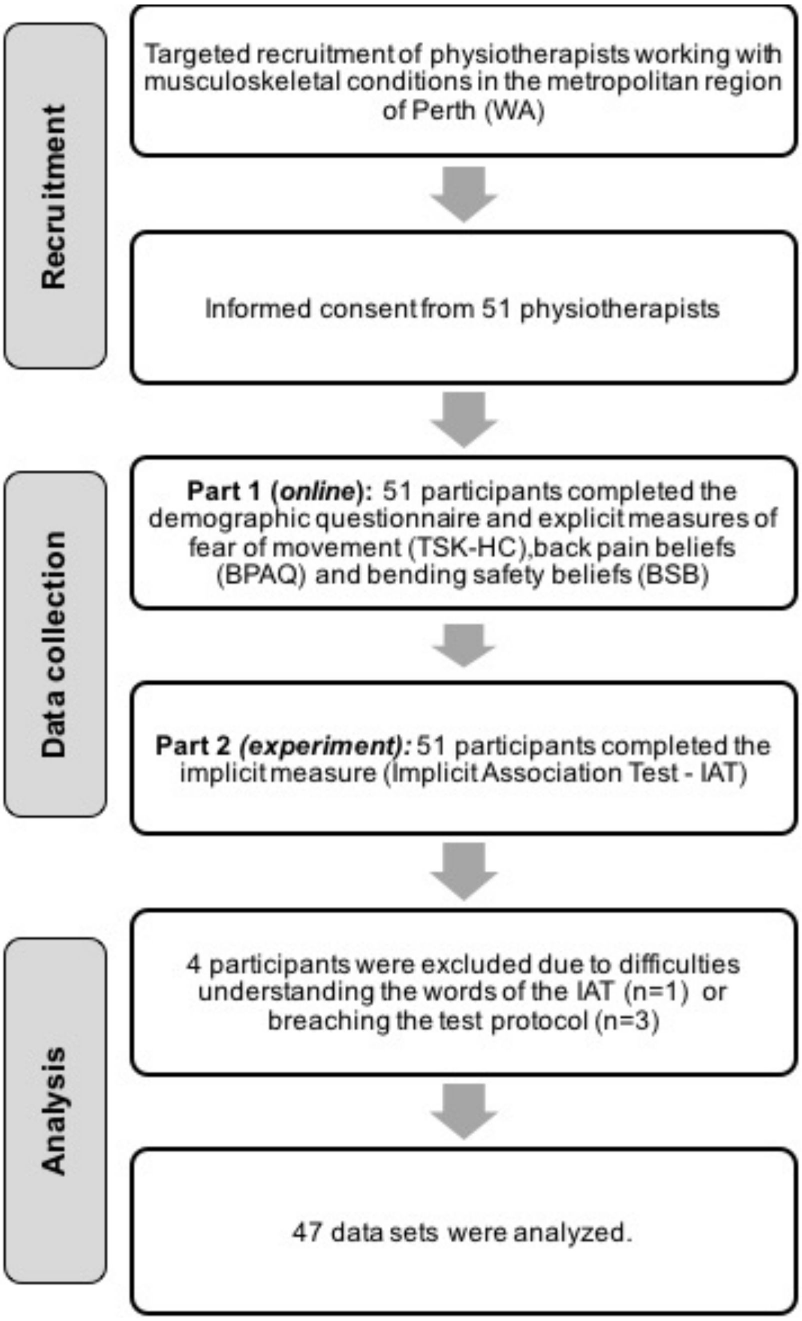
This was an exploratory cross-sectional quantitative study.

9.3.2 Participants and recruitment

Physiotherapists from the metropolitan area of Perth (WA) were recruited in the period of April to June 2016 via email, phone call (to place of work) or approached in person by one of the investigators for participation in this study. Fifty-one (51) Physiotherapists currently registered with Australian Health Practitioners Registration Authority (AHPRA) and treating patients with musculoskeletal conditions were included in the study. Informed consent was obtained upon agreement to participate. Ethics approval (HREC number: HRE2016-0192) was obtained from Curtin University's Health Science Human Research Ethics Committee.

9.3.3 Procedure

Participants were first invited to complete three questionnaires *online*. Thereafter, time was arranged with each participant to complete the *experiment* (IAT) at an agreed upon location, either at Curtin University or the participant's workplace. The study procedure is summarized in **Figure 9.1**.



Appendix B Figure 9.1 Flow diagram outlining study procedure

9.3.4 Demographic questionnaire

Participants' age, gender, years of practice, educational level, previous and current history, and management of LBP were recorded.

9.3.5 Outcome measures

This study employed an *implicit* measure of bending/lifting back posture and safety of the spine, and *explicit* measures of beliefs towards vulnerability of the back (bending safety beliefs, back beliefs, and fear of movement).

9.3.5.1 Implicit measure

9.3.5.1.1 Implicit Association Task (IAT)

The IAT is a computer-based task that assesses strength of association between categories, indicating implicit biases (Harvard 2011; Greenwald, McGhee, and Schwartz 1998). The IAT is a well-established measure, which was adapted to assess associations between bending/lifting posture and safety in a group of people with back pain (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017). The same IAT was used in this study, and included two categories of stimuli (either word or image). The *target categories* (images) were **'Round-back'** and **'Straight-back'** while the *attribute categories* (words) were '**Safe'** and '**Danger'**.

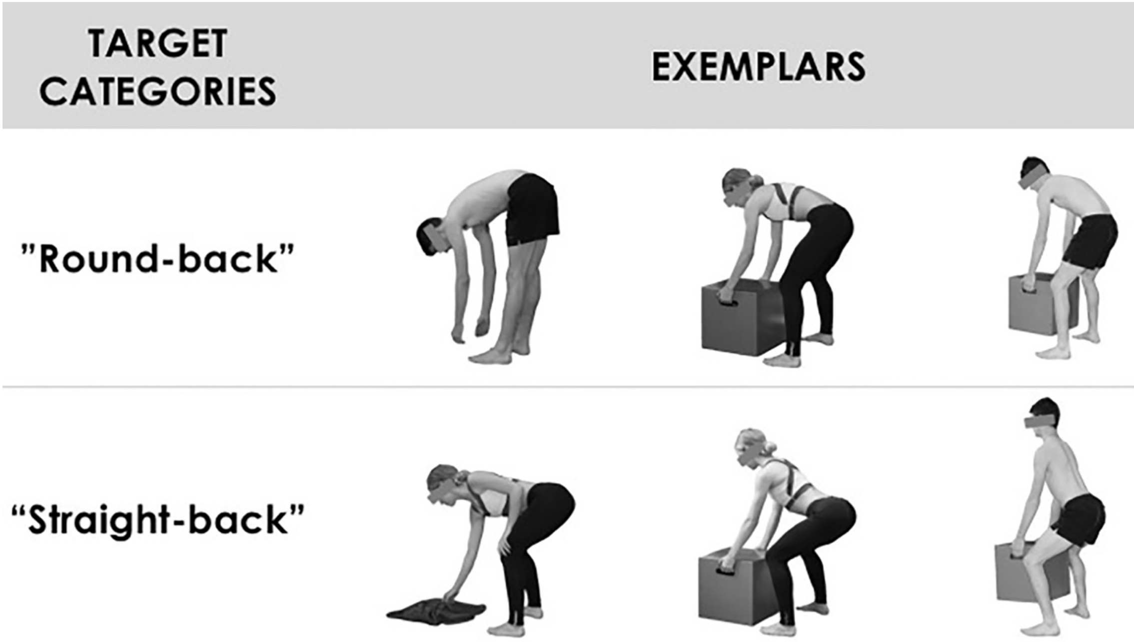
The words selected to represent the attribute category **'Safe'** *were: harmless, certainty, protecting, confident, secure*; and **'Danger'** *were: alarming, vulnerable, risky, damaging, threatening*. To represent the target categories**,** twelve (10) side view images of males and females bending and lifting an object with a round back (target category **'Round-back'**) or with a straight back (target category **'Straight-back'**), were created for this task **(Figure 9.2)**.

The IAT was set up on the researchers' laptops, allowing data collection at the physiotherapists' workplace. The words were presented in bold, 20-point Arial font in white lower case on a black background. The images were presented embedded in a white square frame of 450x440 pixels on a black background. Categories remained on screen throughout an entire phase.

<u>*Procedure*</u>: Instructions were provided on the screen prior to commencement of the experiment. The IAT consisted of 7 stages, **(Table 9.1)**. For each stage, the participant was instructed to assign a stimulus (image/word displayed in the centre of the screen) to its suitable category (displayed in the left and right upper hand corner of the screen) by pressing the left or right "Shift" keys, as quickly as possible, while avoiding mistakes.

Feedback (‘‘correct’’ or ‘‘wrong’’) was provided to participants on each trial. In stage 1 (20 trials), participants sorted each of the 10 images twice, into the categories “Round-back” and “Straight-back”. In stage 2 (20 trials), participants sorted the 10 words twice into the categories “Safe” and “Danger”. In stages 3 and 4 (20 and 40 trials each) participants sorted words and images into the combined categories (e.g. Danger / Round-back and Safe / Straight-back). In stage 5 (20 trials) participants sorted images with the location of the categories switched. In stages 6 and 7 (30 and 40 trials each) the category combinations of phases three and four were reversed (e.g. Danger / Straight-back and Safe / Round-back). Half the participants were tested with the category combination (Danger / Round-back and Safe / Straight-back) first whereas the remaining saw the combinations (Danger / Straight-back and Safe / Round-back) first.

Data processing: Each trial started with the display of a fixation cross for 1000ms followed by a word or image for 1000ms and an inter-trial interval of 1000ms. Presentation of the tasks and reaction time recording was controlled by DMDX (Forster and Forster 2003). Response time was defined as the time elapsed from the presentation of the word or image to when the left or right shift key was pressed. This time was recorded and incorrect responses, times shorter than 100 ms or longer than 1000ms were considered as errors. A bias score ($IAT_{D\text{-}score}$) was calculated using the improved scoring algorithm recommended by Greenwald et al (2003) with an error penalty of 2 standard deviations (Greenwald, Nosek, and Banaji 2003). The $IAT_{D\text{-}score}$ is a standardised difference between response times during the two stages when danger is paired with round back versus the two stages when danger is paired with a straight back. The **$IAT_{D\text{-}score}$** can therefore be either positive or negative, with **zero indicating no implicit bias**, a **positive score indicating implicit bias towards a round-back posture as dangerous** and a negative score indicating implicit bias towards a straight-back posture as dangerous. The IAT exhibits adequate reliability and, internal, construct and predictive validity (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017; Gawronski and Bodenhausen 2006; Houben, Ostelo, et al. 2005).



Appendix B Figure 9.2 Exemplars of the images developed to represent target categories in the IAT.

9.3.5.2 Explicit measures

9.3.5.2.1 Bending Safety Belief (BSB)

To assess specific beliefs related to bending and lifting back posture and safety of the spine, the BSB was adapted from the item "reaching to the floor" on the Fear of Daily Activities Questionnaire (George et al. 2009), which has been shown to have sound psychometric properties and adequate reliability in determining fear of specific activities (George et al. 2009). The BSB consists of a pictorial scale containing two images of a person bending forward and lifting a light object – one with a round-back and one with a straight-back. The participants were asked "how would you rate the level of risk to this person's back?" for each image using a Likert scale (anchored on "0" meaning safe, and "10" meaning danger). A **thermometer score ($BSB_{Thermometer}$)** was derived to determine the participant's belief about safety of bending. The danger rating of the picture illustrating bending with a 'straight-back' was subtracted from the danger rating of the picture illustrating bending with a 'round-back'. In line with the implicit $IAT_{D\text{-}score}$, a **positive value** therefore indicated a **higher danger rating for round-back** than a straight-back and a negative score indicated higher danger rating for straight-back than a round-back.

9.3.5.2.2 Back Pain Attitudes Questionnaire (Back-PAQ)

The Back-PAQ was designed to assess back pain attitudes of the public, healthcare professionals, or those with back pain (Darlow, Perry, Mathieson, et al. 2014). The Back-PAQ consists of 34 items that assesses five key components including, but not limited to 'vulnerability and 'protection' of the back (Darlow, Perry, Mathieson, et al. 2014). Participants answered the items on a 5-point Likert scale from "false" to "true" (intermediate labels: 'Possibly False', 'Unsure', 'Possibly True). Scoring boundaries range from 34-170, with higher scores indicating more unhelpful beliefs about the back. The 34-item long form of the questionnaire has been shown to have acceptable internal consistency (α=0.70; 95% CI 0.66 to 0.73), construct validity and test-retest reliability (Moran, Rushworth, and Mason 2017; Darlow, Perry, Mathieson, et al. 2014). For the purpose of this study, a subscale called 'danger scale' **($BackPAQ_{Danger}$)** was formed by 14 items from the questionnaire (questions 1-12, 14 and 21), which are representative of 'vulnerability and 'protection' themes. These themes emerged from the qualitative study that the BackPAQ originated from[26]. The 'danger scale' score was assessed for correlation with other explicit and implicit scores.

9.3.5.2.3 Tampa Scale of Kinesiophobia – Health Care clinicians (TSK-HC)

The TSK was designed to measure fear of movement in patients and has been adapted to measure concerns for movement clinicians may have for their patients (Houben, Gijsen, et al. 2005; Houben, Ostelo, et al. 2005). The adapted TSK (TSK-HC) consists of 17 items using a six-point Likert scale that ranges from 'totally agree' to 'totally disagree'. Scores range from 17 to 68, with a high score reflecting a strong concern for the possibility of physical movement being harmful (Houben, Gijsen, et al. 2005). Cronbach's alpha in the study by Houben et al (2004) was 0.81, which showed high internal consistency (Houben et al. 2004).

9.3.6 Statistical analysis

Summary descriptive statistics were calculated for demographic data. For the measure of implicit bias ($IAT_{D\text{-}score}$), a one-sample t-test was used to assess the degree and direction of the deviation of the score from zero, with 95% confidence intervals used to interpret the size and precision of the estimate. Additionally, Cohen's *d* was calculated to provide a standardised effect size to assist in the interpretation of the size of the estimated bias (Sabin, Rivara, and Greenwald 2008).

As for the $IAT_{D\text{-score}}$, a one-sample t-test was used to assess the degree and direction of the deviation of the $BSB_{Thermometer}$ score from zero. The correlation between the $IAT_{D\text{-score}}$ and each of the explicit measures ($BSB_{Thermometer}$, $BackPAQ_{Danger}$ and TSK-HC) was assessed using Pearson's correlation coefficient with associated 95% confidence intervals. An *a priori* power calculation estimated a sample of 50 participants would have 80% power to detect a standardised $IAT_{D\text{-score}}$ difference from 0 of ±0.4 and correlations between implicit and explicit measures of ±0.4 or greater (two-sided tests, α=.05). SPSS version 24 statistical software was used for statistical analysis (IBM SPSS Statistics for Windows, version 24, IBM Corp., Armonk, N.Y., USA).

Appendix B Table 9.1 Schematic representation of Implicit Association Test (IAT)

PHASE	TASK	SEQUENCE 1	
1	Target-discrimination	**Pictures** Round-back	Straight-back
2	Attribute-discrimination	**Words** Danger	Safe
3	Combined-discrimination_1	**Words /Pictures** Danger/Round-back	Safe/Straight-back
4	Combined-discrimination_2	**Words /Pictures** Danger/Round-back	Safe/Straight-back
5	Target-discrimination reversed	**Pictures** Straight-back	Round-back
6	Combined-discrimination_3	**Words /Pictures** Danger/Straight-back	Safe/Round-back
7	Combined-discrimination_4	**Words /Pictures** Danger/Straight-back	Safe/Round-back

9.4 Results

9.4.1 Participants

Data was collected for 51 participants; four participants were excluded due to difficulties understanding the words of the IAT (1), or breaching the test protocol (3) – e.g. asking for instructions during the test, being disrupted during the test. Forty-seven data sets were included in the analysis, and there was no missing data for any of the participants. Participants' demographic characteristics are summarized in **Table 9.2**.

Appendix B Table 9.2 Participant's characteristics

Characteristics	n (percentage)	Mean (SD (range))
Age	-	31.9 (6.6 (21-56))
Female	22 (46.8)	-
Male	25 (53.2)	-
Years as physiotherapist	-	7.9 (7.1 (1-35)
Undergraduate	31 (66)	-
Postgraduate	16 (34)	-
Present back pain	11 (23)	-
Previous history of back pain	20 (42)	-
Family history of back pain	26 (55)	-
Use of medication for back pain	15 (31)	-
Physical impairment from back pain	18 (38)	-
Use of management for back pain	26 (55)	-

9.4.2 Implicit measure

The mean $IAT_{D\text{-score}}$ was 0.213 (SD=0.470) and significantly larger than zero (p=.003, 95%CI [.075-.350], t(46)=3.103), indicating a **bias** towards **round-back being associated with danger** in this group of physiotherapists currently treating musculoskeletal conditions. The magnitude of this estimated effect size as measured by Cohen's d was 0.45.

9.4.3 Explicit measures

The mean $BSB_{Thermometer}$ score was -0.7 (SD=3.6), which was **not significantly different from zero** (p=.193, 95%CI [-1.8 – 0.4], t(46)=-1.32). Analysis of the distribution of **BSB** $_{\textbf{Thermometer}}$ score across the sample revealed that **30%** of the sample had a **positive** score indicating a **higher danger rating for round-back** than a straight-back as dangerous, **23%** had score of **zero**, and **47%** had a **negative** score indicating a **higher danger rating for straight-back** than a round-back as dangerous. The mean TSK-HC score was 30.3 (SD= 6.2) for fear of movement, and the mean BackPAQ score was 29.4 (SD= 15.7) for back beliefs with the subscale $BackPAQ_{Danger}$ having a mean of 31.4 (SD=10.0).

9.4.4 Associations between implicit and explicit measures

There were moderate positive correlations between the $IAT_{D\text{-}score}$ and the $BSB_{Thermometer}$ score (r = .320, CI [.036-.556], p=.029) and between the $IAT_{D\text{-}score}$ and the $BackPAQ_{Danger}$ score (r=.413, 95%CI [.143-.626], p=.004). The correlation between the $IAT_{D\text{-}score}$ and TSK-HC was weaker and non-significant (.231, CI [-.060-.486], p=.119).

9.5 Discussion

This study aimed to evaluate physiotherapists' implicit associations between bending and lifting *back posture* (straight-back vs. round-back) and *safety* (safe vs. danger); and whether the implicit measure correlated with explicit measures of beliefs towards vulnerability of the back (bending safety beliefs, back beliefs, and fear of movement).

Our first hypothesis was supported. Results from the ***implicit*** measure (IAT), indicate that physiotherapists were faster to associate images of bending and lifting with a 'round-back' with words representing 'danger', rather than with words representing 'safety', meaning that this sample of physiotherapists displayed an **implicit bias** towards 'round-back' bending and lifting as dangerous for the back.

Our second hypothesis was only partially supported because only two of three explicit measures correlated moderately and significantly with the implicit measure. These correlations were between bending safety belief ($BSB_{Thermometer}$) and the $IAT_{D\text{-}score}$, and between LBP beliefs ($BackPAQ_{Danger}$) and the $IAT_{D\text{-}score}$, indicating some alignment of the constructs assessed by these measures. The magnitude of these correlations nonetheless indicates a level of mismatch between the reports in the different measures, and suggests that these measures may assess a common core construct, but distinct aspects of that construct. The three explicit measures have varying degrees of alignment to the specific construct that was assessed by the IAT. While the TSK-HC assesses fear of movement, none of its items relate to how a person moves or specifically, about the person's back posture during bending and lifting. In contrast, the $BackPAQ_{Danger}$ scale has specific questions about back posture, bending and lifting, and the BSB uses an image to ensure specificity of the construct assessed (bending posture and safety) [(Leeuw, Goossens, et al. 2007; Hofmann et al. 2005)]. In support of our results, a meta-analysis of correlations between explicit measures and the IAT across 126 studies in the field of social psychology suggested that the association between these measures is influenced by the conceptual correspondence of the constructs being assessed (Hoffman et al. 2007).

Our results are intriguing as they provide some indication that under a time-constraint *context*, physiotherapists may display associations in memory that are not entirely reflective of their self-reported beliefs. Considering the proposed role of implicit attitudes on a person's behaviour (Dovidio and Fiske 2012; Nosek, Hawkins, and Frazier 2011; Greenwald et al. 2009) such as the clinical choices physiotherapists make, our results require further consideration. The following section will make sense of these results and reflect on the potential impact of this *implicit 'round-back/danger' bias* in **physiotherapy practice**.

Physiotherapy training in musculoskeletal pain has historically been largely based on a patho-anatomical and biomechanical paradigm (Synnott et al. 2015; Pincus et al. 2006). This includes amongst other factors, the ability to recognize patterns of posture and movement and its relationship with clinical presentations (e.g. lifting posture and LBP). With training and experience, these clinical profiles may be accessed with reduced deliberate thought for efficient decision-making (Chapman, Kaatz, and Carnes 2013; Harman et al. 2009). In physiotherapy practice however, managing patient's beliefs, expectations and pain-related distress, while providing treatment under the time constraints of an appointment poses a significant challenge. In that *context*, reliance on automatic associations of clinical profiles (e.g. lifting posture and LBP) and treatment advice (e.g. protect the back) may influence the clinician's treatment behaviour unintendedly (Chapman, Kaatz, and Carnes 2013; Gawronski and Bodenhausen 2006; Gawronski, Hofmann, and Wilbur 2006). For instance, Houben et al (2005) investigated explicit and implicit attitudes (biomedical vs. biopsychosocial) of physiotherapy students on treatment recommendation for LBP (Houben, Gijsen, et al. 2005). The authors used three videos of different clinical contexts (1: examination of patient with back pain; 2: advice on activity or rest after a flare up of back pain; 3: advice on time-contingent vs pain-contingent approach after a flare up of back and leg pain) to which the students had one minute to provide treatment advice, creating time-pressure resembling clinical practice. The study reported that explicit biomedical attitudes were predictive of treatment advice by physiotherapy students in two videos, while implicit biomedical attitudes were predictive of biomedical treatment advice in one video. Their results suggest that both explicit and implicit attitudes can predict behaviour depending on the clinical context (Houben, Gijsen, et al. 2005).

It has been proposed that a person's behaviour may be the result of the interaction of implicit associations and deliberate reasoning on the situation at hand (Nosek, Hawkins, and Frazier 2011; Gawronski and Bodenhausen 2006; Fazio and Olson 2003). The level to which this interaction influences a person's behaviour relates to several factors that form a *context*, including *motivation*, *opportunity*, *ability*, and *awareness* (Nosek, Hawkins, and Frazier 2011; Fazio and Olson 2003). In the context of physiotherapy practice for example, the clinician may have the knowledge and motivation to adopt an evidence-based biopsychosocial approach, however factors such as restricted consultation time (opportunity), experience and clinical reasoning level (ability), and beliefs (awareness of how one feels about a construct - e.g. round-back lifting is safe) may affect the clinician's advice in the consult. Although speculative, it is plausible that in certain *contexts*, the implicit 'round-back/danger bias' displayed by the physiotherapists in our study may have the potential to influence their recommendations in practice. For example, this may involve reinforcing prevailing beliefs in society that bending and lifting are dangerous and 'good' posture (e.g. straight-back posture) protects the back (Stevens et al. 2016; Darlow 2016; Darlow et al. 2015). However, the extent to which physiotherapists' implicit bias influences clinical processes is not known (Houben, Gijsen, et al. 2005). Future research examining potential influences of this implicit 'round-back/danger bias' on clinical decision-making and physiotherapy advice for people with LBP, would be valuable.

9.5.1 Limitations

To the authors' knowledge, this is the first study to assess implicit attitudes of experienced physiotherapists, specifically related to bending and lifting safety. **However, this study has some limitations.** *First,* the use of a cohort from a single city could potentially reflect similar training backgrounds. However, demographics of this group indicate that physiotherapists with varied education level, years of experience and training background were included. *Second,* the question used in the BSB is clinically relevant when assessing beliefs about bending, as it provides information whether there is a perception of danger in relation to the way a person bends. However, although this question was adapted from a validated questionnaire (George et al. 2009), and used in a previous study involving people with LBP (Caneiro, O'Sullivan, Smith, Moseley, et al. 2017), its psychometric properties have not been tested. *Third,* the reliability of implicit measures has been questioned in the past (Leeuw, Peters, et al. 2007). Although the IAT has adequate psychometric properties (Greenwald, Nosek, and

Banaji 2003), the task used in this study was purposefully adapted to address a question of interest. Therefore, before firmer conclusions can be derived from this study replication of these findings is warranted.

9.6 Conclusion

The current study demonstrated that physiotherapists displayed an implicit bias to associate bending and lifting with a round-back (vs. straight-back) with danger, while generally reporting mixed explicit beliefs about bending safety. There was some concordance between explicit bending/lifting safety beliefs and the implicit measure. Considering implicit attitudes may influence behaviour, future studies investigating whether this implicit 'round-back/danger bias' is associated with physiotherapist's clinical advice on bending and lifting posture for people with LBP are indicated.

9.7 Authors' statement

Authors contribution: JP Caneiro, Peter O'Sullivan, Anne Smith and Ottmar Lipp provided concept/idea/research design. Ingrid Ovrebekk, Luke Tozer, Michael Williams and Magdalene Teng performed data collection. JP Caneiro, Peter O'Sullivan, Ottmar Lipp, Anne Smith, Ingrid Ovrebekk, and Magdalene Teng provided data analysis. All authors contributed to discussion of results and writing of the manuscript (including review of manuscript before submission).

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Conflicts of interest: None declared

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Appendix C Evidence of ethical approval

MEMORANDUM

Curtin University

To:	Prof Peter O'Sullivan School of Physiotherapy and Exercise Science
CC:	Joao Paulo Torres Caneiro
From	Professor Peter O'Leary, Chair HREC
Subject	Ethics approval Approval number: HR157/2015
Date	10-Aug-15

Office of Research and Development
Human Research Ethics Office

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAIL hrec@curtin.edu.au

Thank you for your application submitted to the Human Research Ethics Office for the project: 5794

An investigation of people with persistent nonspecific low back pain and high pain-related fear

Your application was reviewed by Human Research Ethics Committee at Curtin University at their meeting on the 04/08/2015

Thankyou for providing the additional information requested by the Human Research Ethics Committee. The information you provided was satisfactory and your proposal is now approved.

Please note the following conditions of approval:

1. Approval is granted for a period of four years fror **11-Aug-15** to **11-Aug-19**
2. Research must be conducted as stated in the approved protocol.
3. Any amendments to the approved protocol must be approved by the Ethics Office.
4. An annual progress report must be submitted to the Ethics Office annually, on the anniversary of approval.
5. All adverse events must be reported to the Ethics Office.
6. A completion report must be submitted to the Ethics Office on completion of the project.
7. Data must be stored in accordance with WAUSDA and Curtin University policy.
8. The Ethics Office may conduct a randomly identified audit of a proportion of research projects approved by the HREC.

Should you have any queries about the consideration of your project please contact the Ethics Support Officer for your faculty, or the Ethics Office at hrec@curtin.edu.au or on 9266 2784. All human research ethics forms and guidelines are available on the ethics website.

Yours sincerely

Professor Peter O'Leary
Chair, Human Research Ethics Committee

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Title: Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art

Author: Johan Vlaeyen and Steven Linton

Publication: Pain

Publisher: Wolters Kluwer Health, Inc.

Date: Apr 1, 2001

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Figure 1.1 The fear-avoidance model

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I look forward to your response.

Kind regards,

JP Caneiro

Implicit evaluations and physiological threat responses in people with persistent low back pain and fear of bending.
Caneiro JP, O'Sullivan P, Smith A, Moseley GL, Lipp OV.
Scand J Pain. 2017 Oct;17:355-366. doi: 10.1016/j.sjpain.2017.09.012. Epub 2017 Oct 12.

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Hi JP,

Thanks for writing to us about this. It is fine if you want to use the article as part of your thesis, provided you include the full citation (as you have done below, with the DOI). If you have other requests in the future, you can e-mail me directly.

Thanks,
Corey

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