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## Research

## Patients with worse disability respond best to cognitive functional therapy for chronic low back pain: a pre-planned secondary analysis of a randomised trial

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## KEY WORDS

Low back pain  
Moderation  
Cognitive functional therapy  
Randomised controlled trial  
Physical therapy



## ABSTRACT

**Question:** Do five baseline moderators identify patients with chronic low back pain who respond best to cognitive functional therapy (CFT) when compared with usual care? **Design:** Secondary analysis of the RESTORE randomised controlled trial. **Participants:** A total of 492 adults with low back pain for > 3 months with at least moderate pain-related activity limitation. **Intervention:** Participants were allocated to CFT alone or CFT plus biofeedback; these two groups were combined for this secondary analysis. The control group was usual care. **Outcome measures:** The outcome was activity limitation measured using the Roland Morris Disability Questionnaire (RMDQ) at 3, 6, 13, 26, 40 and 52 weeks. Investigated effect modifiers were baseline measures of activity limitation, cognitive flexibility, pain intensity, self-efficacy and catastrophising. **Results:** Baseline levels of activity limitation and, potentially, cognitive flexibility were associated with different effects of CFT treatment, while pain intensity, self-efficacy and catastrophising were not. Patients who had higher baseline activity limitation had greater treatment effects at 13 and 52 weeks. A person with a baseline RMDQ score of 18 (90th percentile) would on average be 6.1 (95% CI 4.8 to 7.4) points better at 13 weeks if they received CFT compared with usual care. However, a person with a baseline score of 7 (10th percentile) would on average be 3.6 (95% CI 2.6 to 4.6) points better at 13 weeks. **Conclusion:** The finding that CFT is most effective among patients who are most disabled and incur the greatest burden strongly suggests that CFT should be considered as a treatment for this group of patients. **Registration:** ACTRN12618001396213. [Hancock M, Smith A, O'Sullivan P, Schütze R, Caneiro JP, Hartvigsen J, O'Sullivan K, McGregor A, Haines T, Vickery A, Campbell A, Kent P (2024) Patients with worse disability respond best to cognitive functional therapy for chronic low back pain: a pre-planned secondary analysis of a randomised trial. *Journal of Physiotherapy* 70:294–301]

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## Introduction

The cause and symptoms of chronic low back pain are heterogeneous, with a wide range of factors contributing in different combinations to each individual's pain and disability.<sup>1</sup> As such, it is unsurprising that interventions such as medicines or manual therapy, which are usually passive in nature and do not address this complexity, typically produce small and short-lasting effects in people with chronic low back pain.<sup>2,3</sup> One approach to potentially optimise effects is to develop treatment approaches that are more personalised and target the range of factors believed to be driving each individual patient's pain and disability.<sup>4</sup> Another complimentary approach is to identify patient characteristics (subgroups) associated with improved responses to specific interventions, also known as treatment effect moderators.<sup>5</sup>

Cognitive functional therapy (CFT) is a patient-centred, individualised biopsychosocial approach for the management of people with chronic disabling low back pain.<sup>4</sup> It aims to identify and target individual factors contributing to low back pain, including unhelpful cognitions, emotions and behaviours. The approach focuses on empowering patients to self-manage their condition and includes three main components: 'making sense of pain' – reconceptualising pain towards a biopsychosocial perspective; 'exposure with control' – developing pain control strategies and confidence to re-engage in valued activities; and 'lifestyle coaching' – adopting healthy lifestyle habits.

The recent RESTORE clinical trial found large and sustained benefits of CFT compared with usual care in people with chronic low back pain.<sup>6</sup> While these effects were larger than typically reported in the literature, there was variability in the outcomes reported by patients

who received CFT. For example, approximately two-thirds of patients receiving CFT improved by  $\geq 5$  points on the Roland Morris Disability Questionnaire (RMDQ), while the remaining one-third had smaller improvements or were not improved. Identifying patient characteristics that are related to an increased response to CFT can help to select patients for whom CFT is most likely to be effective and those for whom other or additional interventions may be more appropriate. No previous studies have investigated moderators of response to CFT. There are relatively few high-quality moderation studies for any low back pain interventions, despite identification of treatment subgroups being a research priority.<sup>7-9</sup> Greater baseline disability and psychological constructs, such as catastrophising and low self-efficacy, have some preliminary evidence as moderators for behavioural or psychological interventions.<sup>7,10,11</sup>

Investigations of treatment effect moderators are prone to spurious findings if not conducted rigorously. It is important to prespecify a small number of plausible moderators and investigate these using interaction terms in randomised controlled trials.<sup>12,13</sup> Given that CFT targets behaviour change and unhelpful cognitions, it seems theoretically plausible that patients who are more open to new ways of thinking (greater cognitive flexibility) and who have less helpful pain-related cognitions (low self-efficacy and higher levels of pain catastrophising) may respond best to CFT.<sup>14</sup> Equally, CFT may be most helpful in people with more impactful low back pain (high activity limitation) or with higher pain intensity where other interventions tend to be less effective.

Therefore, the research question for this secondary analysis of the RESTORE randomised controlled trial was:

Do five prospectively selected, theoretically derived, baseline moderators (activity limitation, cognitive flexibility, pain intensity, self-efficacy and catastrophising) identify patients who respond best to CFT compared with usual care?

## Method

### Design

This study was a secondary analysis of data from the RESTORE trial,<sup>6</sup> which investigated CFT with or without biofeedback compared with usual care for the treatment of chronic back pain. The trial methods incorporated concealed allocation, blinded assessment of some outcomes and intention-to-treat analysis. The trial was conducted in 20 primary care clinics in Australia and included 492 patients between October 2018 and August 2023. The RESTORE trial protocol has previously been published,<sup>15</sup> including the prospective plans for investigation of treatment effect moderators. A more detailed update of the analysis plan for the current moderation analysis on open science framework (<https://osf.io/drwe5/>) was also published prior to commencing analyses. The primary effectiveness and cost-effectiveness results of the RESTORE study have been published elsewhere.<sup>6</sup>

Participants were randomly allocated with a 1:1:1 allocation ratio to one of three groups: usual care, CFT only or CFT plus biofeedback. However, for the purposes of this analysis, the CFT and CFT plus biofeedback groups were combined, as described in the analysis plan, because no clinically meaningful difference was found between the two CFT groups in treatment effectiveness. The randomisation schedule used minimisation factors of site (Perth or Sydney), sex (female or male) and baseline activity limitation (RMDQ). Participants were not blinded to the group allocation.

### Participants, therapists and centres

All patients from the RESTORE trial were included in this analysis. Eligible participants were adults (aged  $\geq 18$  years) who had chronic low back pain for  $> 3$  months, had sought care from a primary care clinician for their back pain  $\geq 6$  weeks previously, had an average

back pain intensity  $\geq 4$  on a 0 to 10 numerical pain rating scale, and had at least moderate pain-related interference with normal work or daily activities measured by item 8 of the 36-item Short Form Health Survey. Exclusion criteria were: serious spinal pathology (eg, fracture, infection or cancer); any medical condition that prevented being physically active; being pregnant or having given birth within the previous 3 months; inadequate English literacy for the study's questionnaires and instructions; a skin allergy to hypoallergenic tape adhesives; surgery scheduled within 3 months; and an unwillingness to travel to trial sites. Participants were recruited from general medical practitioners, physiotherapists and surgeons, as well as by social media and community posters.

### Intervention

A detailed description of the interventions was published previously.<sup>15</sup> In the usual care group, patients received treatment that the participant's health providers recommended or the participant chose. Participants were informed that:

*If you are allocated to the usual care group, your treatment options can be any of those offered by the healthcare professionals you would normally choose to see in the community. In other words, you will choose your treatment, but it is not determined by the study or funded by it.*

Only usual care participants were paid a small reimbursement (AU\$30 to 110) for their time completing key follow-up questionnaires.

In the two CFT groups, participants received up to seven treatment sessions over 12 weeks plus a booster session at 26 weeks. The physiotherapists used a flexible clinical-reasoning approach to identify movements, postures, pain-related cognitions, emotions and lifestyle factors contributing to each participant's ongoing pain and disability. This approach informed an individualised treatment plan oriented to the patient's goals, with three broad components. The first component was 'making sense of pain'; this involved a reflective process drawing from the patient's own story and examination findings to help them reconceptualise their low back pain from a biopsychosocial perspective. The second component was 'exposure with control', a process of functional behavioural change and pain control through graded exposure to movements and activities nominated as painful, feared or avoided. The third component was 'lifestyle change'. When relevant, this included coaching to develop healthy lifestyle behaviours such as paced physical activity based on preference, adopting healthy sleep and dietary habits, stress management and social engagement. A more detailed description of the CFT intervention can be found in previous publications.<sup>4,6</sup>

### Baseline measures/moderators

Five potential effect modifiers were prospectively selected based on their theoretical rationale for being associated with different responses to CFT (Table 1). All variables were collected as part of the baseline questionnaire completed prior to randomisation. The five investigated variables were: baseline activity limitation (RMDQ),<sup>16</sup> cognitive flexibility (Cognitive Flexibility Scale),<sup>17</sup> baseline pain intensity (numeric pain rating scale), pain self-efficacy (Pain Self-efficacy Questionnaire)<sup>18</sup> and pain catastrophising (Pain Catastrophising Scale).<sup>19</sup> The selected moderators included specific targets of CFT (pain self-efficacy and pain catastrophising), characteristics of patients who were felt would be most open to the intervention and behavioural change (high cognitive flexibility) and characteristics of those who were believed to most need a complex intervention such as CFT (high pain intensity and disability). Table 1 lists each potential moderator, how it was collected (and analysed), the rationale for selection and the hypothesised direction of effect.

**Table 1**  
Potential moderators, rationale and direction of effect.

Moderator	Hypothesised direction of effect	Rationale	Data structure/level as collected
Baseline activity limitation	Greater effect in those with more limitation	Greater need for this complex intervention. Unlikely to improve with usual care.	Continuous RMDQ <sup>16</sup> (0 to 24); high scores = greater disability
Cognitive flexibility	Greater effect in those with higher cognitive flexibility	A key element of CFT is changing unhelpful beliefs and behaviours. Those individuals that are more open to this are therefore expected to gain more benefit.	Continuous Cognitive Flexibility Scale <sup>17</sup> (12 questions scored from 1 to 6) 12 to 72 sumscore, higher scores = more flexible
Baseline pain intensity	Greater effect in those with more pain	Greater need for this complex intervention. Unlikely to improve with usual care.	Continuous Average pain intensity over last 14 days (0 to 10 numerical rating scale); high scores = greater pain
Self-efficacy	Greater effect in those with low self-efficacy	Improving self-efficacy is a target for CFT. Therefore, it is proposed that those with low self-efficacy will respond more to CFT.	Continuous Pain Self-efficacy Questionnaire <sup>18</sup> (10 questions with 0 to 6 response options), sumscore 0 to 60, higher scores = more self-efficacy
Catastrophising	Greater effect in those with higher catastrophising	Reducing catastrophising is a target for CFT. Therefore, it is proposed that those with high catastrophising will respond more to CFT.	Continuous Pain Catastrophising Scale <sup>19</sup> (13 questions with 0 to 4 response options), sumscore 0 to 52, higher scores = more catastrophising

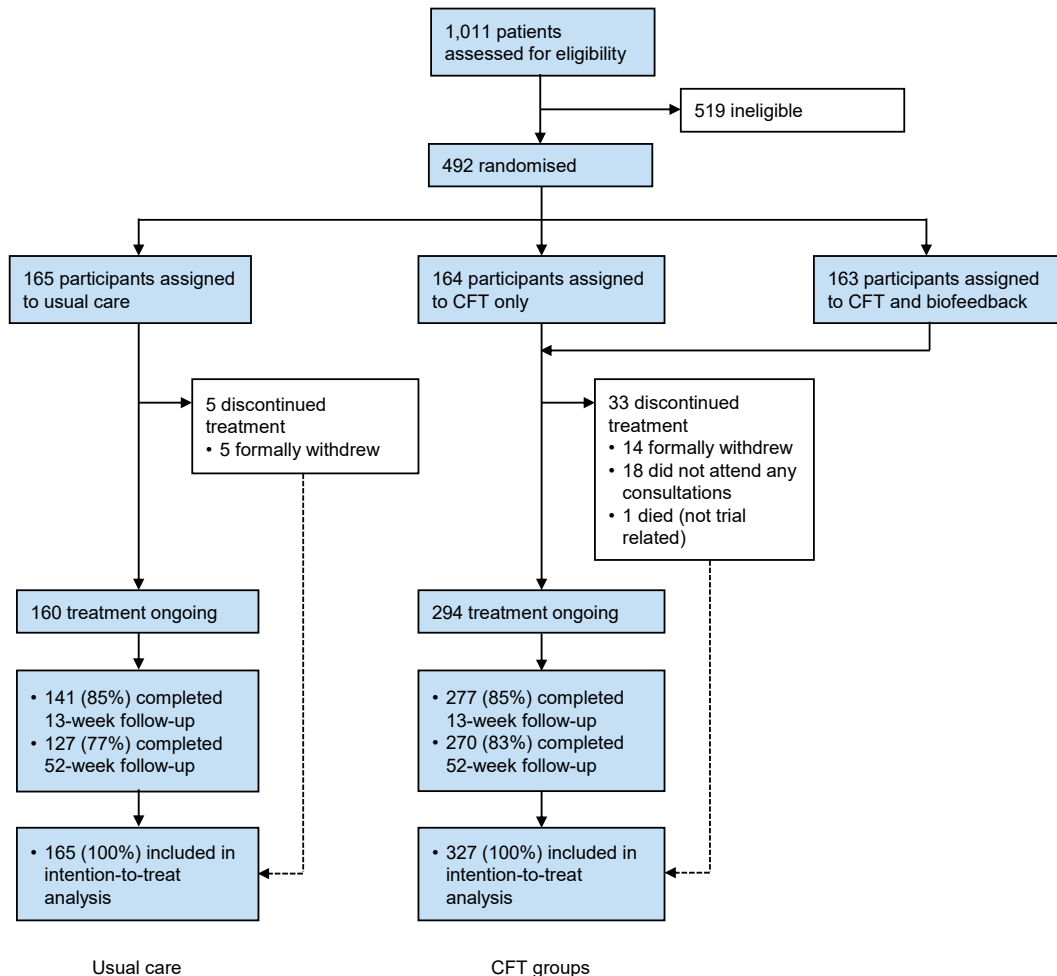
CFT = cognitive functional therapy, RMDQ = Roland Morris Disability Questionnaire.

**Outcome measures**

The outcome reported in this analysis and in the primary analysis of the main trial was pain-related physical activity limitation (activity limitation) using the RMDQ (0 to 24 scale).<sup>16</sup> This was collected at 3, 6, 13, 26, 40 and 52 weeks using online data capture. The primary time point for comparison in this moderation study was 13 weeks, as per the primary analysis, and the key secondary time point was 52 weeks.

**Data analysis**

Repeated measures linear mixed models were used to investigate each of the five potential effect modifiers. Each model included activity limitation as the outcome (RMDQ score) using data collected at all time points (3, 6, 13, 26, 40 and 52 weeks). Separate models were conducted for each of the five potential baseline moderators. In each model we entered the moderator, group allocation (CFT or usual care),



**Figure 1.** Study flow chart. CFT = cognitive functional therapy.

time and the interaction (created by multiplying the moderator variable by group allocation) between the moderator and group allocation. The interaction term was used to assess the size and statistical significance of the potential moderation effect.

This study investigated all moderators in their continuous form and assessed the linearity of moderated effects by comparing model fit with and without a quadratic interaction term. To enhance interpretation of the results, the moderator effect (ie, difference in effects of CFT versus control) was assessed at different levels of the moderator variable (10%, 25%, median, 75% and 90%) for each moderator. We conducted sensitivity analyses adjusted for baseline treatment expectation as this was unbalanced between the groups.

Given that this study was a secondary analysis and moderation studies require larger samples to detect an interaction the same size as the main effect, we focused on the point estimate of the interaction and its precision to determine whether a moderating effect was likely. We then assessed whether the moderating effect suggested a meaningful difference in the treatment effect (likely to change clinical recommendations) for individuals by calculating and plotting treatment effect for different baseline scores on the moderator, at 3 and 12 months.<sup>20</sup> Data analysis was performed using commercial software<sup>a</sup>.

## Results

### Flow of participants, therapists and centres through the study

The flow of patients through the trial is described in [Figure 1](#), showing that 165 patients were randomly assigned to the usual care group and 327 were assigned to either of the two CFT groups (164 CFT only and 163 CFT plus biofeedback). The percentage of patients completing the follow-up RMDQ was 85% at 13 weeks and 80% at 52 weeks.

The patients included in the trial had high levels of activity limitation (mean 13.5, SD 5.2), were more commonly female (59%) and typically middle aged (mean 47 years, SD 15), as shown in [Table 2](#). At baseline, the participants were well matched for almost all key variables, including the four moderators. The exception was baseline treatment expectation, with higher levels of expectation in those allocated to CFT.

### Compliance with trial method

This paper reports the moderation analysis of the first registered outcome measure: pain-related activity limitation. In the patients allocated to CFT, the median number of consultations was 7 (IQR 4 to 8). Twenty-six (8%) patients included in the CFT groups did not attend any consultations, some because of the COVID-19 pandemic. In the usual care control group, 38% of participants reported seeking care from a healthcare practitioner during the first 3 months of the trial, and 56% reported taking low back pain-related medications at baseline. These patients had a median of 3 (IQR 2 to 7) consultations during this period.

### Moderation effects

This study found that baseline level of activity limitation was associated with different effects of CFT treatment both in the short and long term ([Table 3](#) and [Table 4](#)). Patients who had higher baseline activity limitation had greater effects from CFT at both 13 and 52 weeks compared with those with lower levels of baseline activity limitation. For each additional RMDQ point at baseline, the treatment effect increased by 0.18 points (95% CI 0.01 to 0.34) at 13 weeks and by 0.23 points (95% CI 0.04 to 0.42) at 52 weeks. For example, a person with a baseline RMDQ score of 18 (90th percentile) would on average be 6.1 points (95% CI 4.8 to 7.4) better at 13 weeks if they received CFT compared with usual care ([Table 4](#)). However, a person with a baseline score of 7 (10th percentile) would on average only be 3.6 points (95% CI 2.6 to 4.6) better at 13 weeks if they received CFT compared with usual care ([Table 4](#) and [Figure 2](#)).

**Table 2**  
Baseline characteristics including potential moderators.

Characteristic	Usual care (n = 165)	CFT (CFT and CFT plus biofeedback) (n = 327)
Sex, n (%) female	98 (59)	194 (59)
Age (y), mean (SD)	48 (16)	47 (15)
Duration of care seeking (y), median (IQR)	4.0 (1.3 to 10.0)	4.0 (1.0 to 11.0)
Length of current episode (y), median (IQR)	5.0 (1.8 to 10.0)	5.0 (1.4 to 11.1)
University education, n (%) <sup>a</sup>	89 (54)	154 (48)
Confidence in treatment assigned, n (%) <sup>b</sup>		
very unconfident	14 (10)	1 (< 1)
unconfident	27 (19)	4 (1)
uncertain	64 (46)	82 (28)
somewhat confident	9 (6)	80 (27)
confident	18 (13)	88 (30)
very confident	8 (6)	37 (13)
Activity limitation (0 to 24), mean (SD)	13.5 (5.4)	13.6 (5.1)
Cognitive flexibility (12 to 72), mean (SD)	59.9 (7.4)	58.3 (7.6)
Pain intensity (0 to 10), mean (SD) <sup>c</sup>	5.8 (1.6)	5.8 (1.7)
Pain self-efficacy (0 to 60), mean (SD)	36.4 (13.5)	34.0 (13.9)
Pain catastrophising (0 to 52), mean (SD)	24.3 (12.4)	24.7 (12.6)

CFT = cognitive functional therapy.

<sup>a</sup> n = 164 for usual care, n = 324 for CFT.

<sup>b</sup> n = 140 for usual care, n = 292 for CFT.

<sup>c</sup> Average pain intensity in the last 14 days.

Patients who had high baseline cognitive flexibility may have greater effects of CFT at 13 weeks compared with those with low levels of baseline cognitive flexibility. The moderating effect may be clinically informative, as shown in [Table 3](#) and [Figure 2](#); however, the CIs included no moderating effect. For each additional point on the Cognitive Flexibility Scale at baseline, the treatment effect increased by 0.10 points (95% CI -0.04 to 0.25) at 13 weeks. For example, a person with a baseline score of 69 (90th percentile) would on average be 6.1 points (95% CI 4.5 to 7.7) better at 13 weeks if they received CFT compared with usual care ([Table 4](#) and [Figure 2](#)). However, a person with a baseline score of 49 (10th percentile) would on average only be 4.1 points (95% CI 2.2 to 5.8) better at 13 weeks if they received CFT compared with usual care. Cognitive flexibility did not appear to have a moderating effect at 52 weeks ([Table 4](#)). Pain intensity, pain self-efficacy and catastrophising did not appear to have a moderating influence in the short or long term ([Table 3](#) and [Table 4](#)).

Results for the sensitivity analyses adjusted for baseline treatment expectation were similar to the primary analyses (see [Table 5](#) on the eAddenda).

## Discussion

This study found that baseline activity limitation and, potentially, cognitive flexibility appear to be clinically important moderators for

**Table 3**  
Moderator effects (from bootstrapped model) on RMDQ at 13 and 52 weeks.

Moderator	RMDQ	
	Week 13	Week 52
Activity limitation	-0.18 (-0.34 to -0.01)	-0.23 (-0.42 to -0.04)
Cognitive flexibility	-0.10 (-0.25 to 0.04)	-0.04 (-0.20 to 0.11)
Pain intensity	-0.10 (-0.64 to 0.44)	-0.01 (-0.61 to 0.59)
Self-efficacy	-0.03 (-0.08 to 0.03)	0.04 (-0.03 to 0.11)
Catastrophising	-0.02 (-0.09 to 0.06)	-0.04 (-0.13 to 0.05)

RMDQ = Roland Morris Disability Questionnaire.

The coefficients are the interaction terms and represent the difference in effect (CFT versus usual care) for a single point change on the baseline moderator score. Negative coefficients represent greater effect of CFT versus usual care for each unit of higher score on the moderator at baseline.

**Table 4**  
Estimated within-group outcomes and between-group effects for different baseline scores of moderators.

Moderator	Week 13 RMDQ, mean (95% CI)			Week 52 RMDQ, mean (95% CI)		
	Usual care		Treatment effect	Usual care	CFT	Treatment effect
<b>Activity limitation</b>						
90 <sup>th</sup>	18.1 (17.2 to 18.9)	12.0 (10.9 to 13.0)	6.1 (4.8 to 7.4)	17.6 (16.4 to 18.8)	10.6 (9.5 to 11.8)	7.0 (5.3 to 8.6)
75 <sup>th</sup>	16.3 (15.5 to 16.9)	10.5 (9.7 to 11.4)	5.7 (4.6 to 6.2)	15.8 (14.8 to 16.8)	9.3 (8.4 to 10.2)	6.5 (5.1 to 7.8)
50 <sup>th</sup>	12.7 (11.2 to 13.1)	7.7 (7.2 to 8.3)	5.0 (4.2 to 5.7)	12.1 (11.4 to 12.9)	6.7 (6.1 to 7.3)	5.4 (4.5 to 6.4)
25 <sup>th</sup>	8.3 (7.6 to 8.6)	4.3 (3.8 to 4.8)	4.0 (3.2 to 4.8)	7.6 (6.8 to 8.5)	3.4 (2.9 to 4.0)	4.2 (3.2 to 5.2)
10 <sup>th</sup>	6.5 (5.7 to 7.3)	2.9 (2.3 to 3.6)	3.6 (2.6 to 4.6)	5.8 (4.8 to 6.8)	2.1 (1.4 to 2.8)	3.7 (2.5 to 4.9)
<b>Cognitive flexibility</b>						
90 <sup>th</sup>	10.5 (9.2 to 11.9)	4.4 (3.5 to 5.3)	6.1 (4.5 to 7.7)	9.6 (8.1 to 11.1)	3.6 (2.7 to 4.5)	6.0 (4.3 to 7.7)
75 <sup>th</sup>	11.5 (10.6 to 12.4)	5.9 (5.2 to 6.5)	5.6 (4.5 to 6.7)	10.7 (9.7 to 11.8)	4.9 (4.3 to 5.6)	5.8 (4.6 to 7.0)
50 <sup>th</sup>	12.2 (11.4 to 12.9)	7.0 (6.4 to 7.6)	5.2 (4.1 to 6.0)	11.6 (10.7 to 12.5)	6.0 (5.4 to 6.6)	5.6 (6.7 to 4.5)
25 <sup>th</sup>	13.3 (12.3 to 14.3)	8.7 (8.0 to 9.5)	4.6 (3.3 to 5.8)	12.9 (11.8 to 14.0)	7.6 (6.8 to 8.3)	5.3 (3.9 to 6.8)
10 <sup>th</sup>	14.2 (12.7 to 15.6)	10.1 (9.1 to 11.2)	4.1 (2.2 to 5.8)	14.0 (12.4 to 15.6)	8.9 (7.8 to 10.0)	5.1 (3.2 to 7.2)
<b>Pain intensity</b>						
90 <sup>th</sup>	15.1 (13.9 to 16.2)	10.1 (9.0 to 11.2)	5.0 (3.4 to 5.8)	14.7 (13.3 to 16.1)	9.5 (8.4 to 10.6)	5.2 (3.4 to 7.0)
75 <sup>th</sup>	13.8 (12.9 to 14.6)	8.9 (8.1 to 9.7)	4.9 (3.7 to 6.0)	13.3 (12.2 to 14.4)	8.1 (7.3 to 8.9)	5.2 (3.9 to 6.5)
50 <sup>th</sup>	12.4 (11.7 to 13.2)	7.7 (7.1 to 8.3)	4.7 (3.9 to 5.6)	11.9 (11.0 to 12.8)	6.7 (6.1 to 7.3)	5.2 (4.2 to 6.2)
25 <sup>th</sup>	11.1 (10.3 to 12.0)	6.5 (5.9 to 7.1)	4.6 (3.7 to 5.6)	10.5 (9.5 to 11.4)	5.3 (4.7 to 5.9)	5.2 (4.1 to 6.2)
10 <sup>th</sup>	9.8 (8.7 to 10.9)	5.3 (4.5 to 6.1)	4.5 (3.3 to 5.8)	9.1 (7.8 to 10.3)	3.9 (3.2 to 4.7)	5.2 (3.8 to 6.5)
<b>Self-efficacy</b>						
90 <sup>th</sup>	8.8 (7.9 to 9.8)	3.2 (2.5 to 3.9)	5.6 (4.5 to 6.9)	7.7 (6.6 to 8.8)	2.5 (1.8 to 3.3)	5.2 (3.8 to 6.5)
75 <sup>th</sup>	10.0 (9.2 to 10.8)	4.4 (3.9 to 5.0)	5.6 (4.5 to 6.5)	9.1 (8.1 to 10.0)	3.7 (3.1 to 4.3)	5.4 (4.2 to 6.5)
50 <sup>th</sup>	12.1 (11.4 to 12.7)	6.8 (6.2 to 7.3)	5.3 (4.5 to 6.1)	11.5 (10.7 to 12.3)	5.8 (5.2 to 6.3)	5.7 (4.7 to 6.7)
25 <sup>th</sup>	14.6 (13.8 to 15.4)	9.6 (8.9 to 10.3)	5.0 (4.0 to 6.1)	14.4 (13.5 to 15.4)	8.2 (7.5 to 9.1)	6.2 (4.8 to 7.5)
10 <sup>th</sup>	17.4 (16.2 to 18.5)	12.7 (11.5 to 13.8)	4.7 (3.1 to 6.3)	17.7 (16.2 to 19.1)	11.1 (9.8 to 12.3)	6.6 (4.6 to 8.6)
<b>Catastrophising</b>						
90 <sup>th</sup>	16.3 (14.9 to 17.7)	11.1 (9.8 to 12.4)	5.2 (3.3 to 7.0)	15.8 (14.3 to 17.4)	9.7 (8.4 to 11.1)	6.1 (4.0 to 8.2)
75 <sup>th</sup>	14.3 (13.4 to 15.3)	9.3 (8.4 to 10.2)	5.0 (3.7 to 6.3)	13.8 (12.7 to 15.0)	8.1 (7.2 to 9.0)	5.7 (4.3 to 7.2)
50 <sup>th</sup>	12.0 (11.3 to 12.7)	7.1 (6.6 to 7.7)	4.9 (4.0 to 5.8)	11.4 (10.5 to 12.3)	6.1 (5.5 to 6.7)	5.3 (4.2 to 6.4)
25 <sup>th</sup>	10.2 (9.4 to 11.1)	5.5 (4.9 to 6.1)	4.7 (3.7 to 5.8)	9.6 (8.6 to 10.6)	4.6 (4.0 to 5.3)	5.0 (3.8 to 6.2)
10 <sup>th</sup>	9.0 (7.8 to 10.1)	4.3 (3.5 to 5.1)	4.7 (3.3 to 6.0)	8.3 (7.0 to 9.6)	3.5 (2.7 to 4.4)	4.8 (3.2 to 6.3)

RMDQ = Roland Morris Disability Questionnaire.

CFT in patients with chronic low back pain. Patients with greater baseline activity limitation typically received large clinically important benefits from CFT compared with usual care, while patients with low baseline activity limitation received smaller but still clinically meaningful benefits (assuming a smallest worthwhile effect of 20%).<sup>21</sup> The moderating effects of cognitive flexibility were smaller and not statistically significant but may be important for short-term effects. Pain intensity, pain self-efficacy and pain catastrophising were not found to be important moderators.

Patients with higher levels of baseline activity limitation are often considered the most difficult to help, and at the same time incur much of the burden due to low back pain.<sup>1,22,23</sup> This study's finding that CFT is most effective in this group of patients (eg, 6.1 RMDQ points after 13 weeks) is important and provides a highly effective treatment option for those most in need. CFT has also been found to be more effective and much cheaper than multidisciplinary care, which is sometimes considered the optimal intervention for this highly disabled group of patients.<sup>24,25</sup>

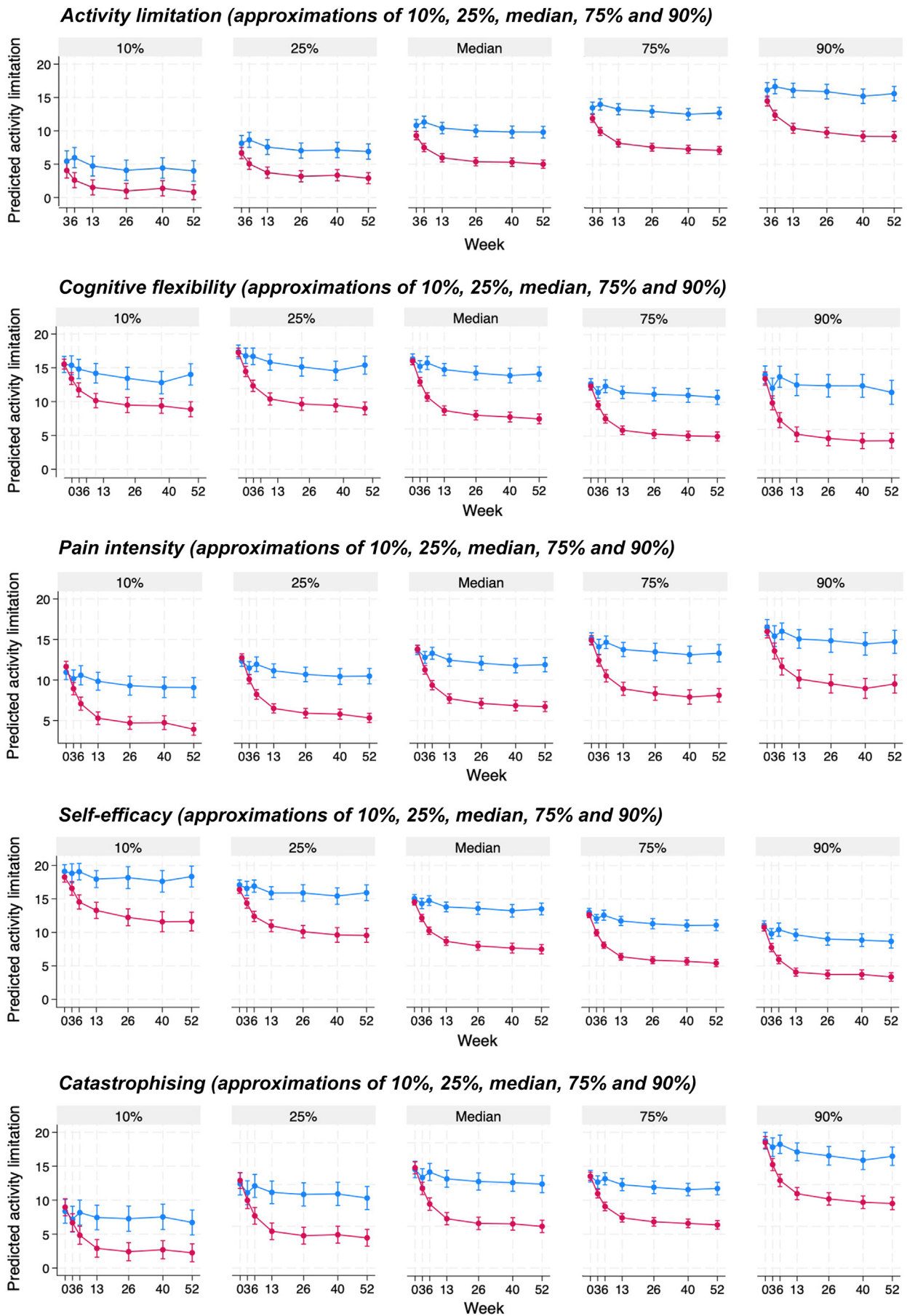
Importantly, CFT is still effective in patients with lower levels of activity limitation, but the effects are smaller. This is consistent with a previous trial of CFT that included patients with relatively low baseline activity limitation (Oswestry Disability Index of 21.3 in patients receiving CFT) and found that it was more effective than manual therapy and exercise. Therefore, CFT remains an evidence-based intervention for patients with chronic low back pain and low levels of activity limitation. We did not identify a group of patients for whom we would recommend against the use of CFT. Importantly, the effect was greatest in those with higher baseline disability. This suggests that if availability to CFT is limited, it should be targeted at patients who are most disabled.

Identifying treatment effect moderators, also known as subgroups, has been a priority in the field of low back pain for over two decades;<sup>9</sup> however, few high-quality studies have been conducted and few promising moderators have been identified.<sup>8,26</sup> Most previous studies investigating moderators of treatment effect have failed to identify worthwhile moderators.<sup>27-29</sup> An individual patient data meta-analysis that included 27 studies of exercise interventions did not

find that baseline activity limitation moderated the effect of the interventions. This suggests that the finding of greater effects in those with higher activity limitations is specific to CFT.<sup>30</sup>

There are a few reasons that might explain why worthwhile moderators were identified. First, the mean effects in the main trial were relatively large.<sup>6</sup> When there is no main effect or it is very small, the plausibility of finding important moderators of effect is reduced.<sup>13</sup> In these situations, for there to be a subgroup who respond well to the intervention, there would need to be a group who respond substantially better to the control intervention, which is unlikely in most studies. Second, the intervention tested in this study was developed with a strong theoretical and clinical basis and clear intervention targets, while many low back pain interventions lack a strong rationale or theoretical mechanism<sup>3</sup> and therefore identifying plausible moderators is difficult. Cognitive flexibility was prespecified as a hypothesised moderator, given that CFT aims to change unhelpful beliefs about low back pain and dispel common myths, so flexible thinking should facilitate this, as suggested elsewhere.<sup>31</sup> Our results suggest that people with higher cognitive flexibility may respond more quickly to CFT but experience similar longer term physical functioning benefits as people with low cognitive flexibility. These inconclusive findings require further investigation but could suggest that psychological inflexibility is not a barrier to improving activity limitation through CFT. Third, our analysis kept the moderators as continuous variables; this is rare in the field. While dichotomising the moderator makes it easier to interpret the results, it also reduces the data and results are dependent on the threshold used. To overcome the difficulties in interpreting the interaction terms for a continuous predictor, we have provided the treatment effect for a range of baseline values on the moderators (Table 4); these demonstrate how the effect increased with greater baseline activity limitation and cognitive flexibility.

Contrary to our hypotheses, baseline catastrophising and self-efficacy were not predictors of CFT response. We expected that CFT's explicit focus on targeting these established mediator variables to differentially benefit those with baseline deficits in catastrophising and self-efficacy. Their lack of moderation effect for catastrophising and self-efficacy in this trial contrasts with some other studies showing



**Figure 2.** Estimated within-group outcomes and between-group effects for different baseline scores of moderators. Error bars represent 95% confidence intervals. Blue = usual care, red = CFT groups.

poor response to physical therapy,<sup>32</sup> graded exposure<sup>10</sup> and multidisciplinary rehabilitation<sup>11,33</sup> when baseline catastrophising and self-efficacy are worse. This contrast may suggest that CFT is able to improve activity limitation in people with varying degrees of contribution from these psychological variables. Baseline pain intensity was also not a moderator of response to CFT. Patients with high pain intensity had similar effects to those with low pain intensity, despite pain intensity typically being reported as a poor prognostic factor.<sup>34</sup>

We followed guidance on conducting subgroup analyses,<sup>12,20,35–37</sup> including publishing a prospective analysis protocol, specifying a limited number of plausible moderators and the hypothesised direction of effect. To enhance interpretation of the clinical importance of the interaction effects, we avoided dichotomising continuous moderators and presented the interaction terms to provide evidence of moderation and the treatment effects for different scores of the moderators.<sup>20</sup>

This study was a secondary analysis and not powered specifically for this type of analysis; however, combining the two CFT groups provided some additional power. It is possible that we missed a moderation effect for pain intensity, catastrophising and self-efficacy; however, the confidence intervals were relatively narrow, making worthwhile interactions unlikely. The confidence intervals for cognitive flexibility included both worthwhile effects and no effect, so there is uncertainty about whether cognitive flexibility is an important moderator for CFT. We are confident in our results that baseline disability is a moderator, but larger samples would provide more precision on the moderation effect. Moderation analysis, like main effect analyses, are always relative to the control group.<sup>20</sup> Therefore, our moderator results may have been different if CFT was compared with a different control condition. For example, we cannot confidently conclude that baseline activity limitation identifies patients who respond best to CFT compared with manual therapy or pain education.

In conclusion, this study found that higher baseline levels of activity limitation and, potentially, cognitive flexibility were associated with greater effects of CFT as per our hypotheses, but pain intensity, self-efficacy and catastrophising were not. The finding that CFT is most effective in the patients who are most disabled, who experience the greatest health burden, and are often the most challenging for clinicians strongly suggests CFT should be considered as a treatment for these patients, especially before progressing to more expensive and risky interventions.

**What was already known on this topic:** Current evidence including the recent RESTORE trial indicates that cognitive functional therapy is effective for chronic low back pain with large and sustained average effects compared with usual care. Identifying patients with low back pain who respond best to specific interventions is a research priority, but little progress has been made. No previous studies have investigated moderators for cognitive functional therapy.

**What this study adds:** Higher baseline levels of activity limitation and, potentially, cognitive flexibility were associated with greater effects of cognitive functional therapy. Levels of pain intensity, catastrophising and self-efficacy did not influence the treatment effects.

**Footnotes:** <sup>a</sup> Stata/BE 18.0, StataCorp LLC, College Station, TX, USA.

**eAddenda:** Table 5 can be found online at <https://doi.org/10.1016/j.jphys.2014.07.001>.

**Ethics approval:** The Curtin University Ethics Committee approved this study. All participants gave written informed consent before data collection began.

**Competing interests:** PO, JPC, MH and KO have received speaker fees for lectures or workshops on the biopsychosocial management of pain, including on CFT, from special interest physiotherapy groups and multidisciplinary audiences of clinicians and researchers.

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