Illness Perceptions; Mediators and/or Moderators in Disabling Persistent Low Back Pain? A Multiple Baseline Single-Case Experimental Design

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Research Article

Keywords: Low back pain, Illness Perceptions, Mediation, Moderation, SCED-study, Physiotherapy

DOI: https://doi.org/10.21203/rs.3.rs-145891/v1

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Abstract

Introduction

Illness Perceptions (IPs) may be important in the management of persistent low back pain. The mediation and/or moderation effect of IPs on primary outcomes in physiotherapy treatment is unknown.

Methods

A multiple single-case experimental design, using a matched care physiotherapy intervention, with 3 phases (phases A-B-A') was used including a 3-month follow up (phase A'). Primary outcomes: pain intensity, physical functioning and pain interference in daily life. Analyzes: linear mixed models, adjusted for fear of movement, catastrophizing, avoidance, sombreness and sleep.

Results

Nine patients were included by six different primary care physiotherapists. Repeated measures on 196 data points showed that IPs Consequences, Personal control, Identity, Concern and Emotional response had a mediation effect on all three primary outcomes. The IP Personal control acted as a moderator for all primary outcomes, with clinically relevant improvements at 3-month follow up.

Conclusion

This is the first study to shed some light in the mediating effects of IPs on the outcome of a matched care physiotherapy treatment. At baseline, assessing Personal control is relevant to determine the outcome prognosis of successful physiotherapy management of persistent low back pain.

1. Introduction

For decades now, low back pain (LBP) has been recognized as the main cause of Years Lived with Disabilities. Managing the global impact of LBP on patients, the increase of economic costs and the impact on society are challenging issues and therefore The Lancet Series on Low Back Pain 2018 included a call for action. Management of persistent LBP has been proposed to shift from a unidimensional (focused on a patho-anatomical disorder) to a more holistic approach, making the transition from the biomedical model to a more biopsychosocial model. Following this proposal, a physiotherapy treatment of LBP that incorporates biopsychosocial factors that play an important role in the patients' LBP has the potential to increase the positive effect of physiotherapy. Examples of such treatment strategies are described in a Cochrane review on behavioral therapy for LBP; operant, cognitive- and respondent strategies.

Most of the extensive body of knowledge on the management of LBP derives from systematic reviews and randomized controlled trials (RCTs). These designs represent the highest level of evidence in Evidence Based Medicine. In addition, the randomized n-of-1 trials are also recognized as level 1 evidence in the Oxford Center for Evidence-Based Medicine 2011 levels of evidence. The use of evidence from systematic reviews and RCTs is a form of “reference class forecasting” and can be challenging for clinicians when making clinical relevant decisions for individual patients. Does this patient fit within the “reference class” that has been
reported to progress well with the intervention? Recently, the call for a more personalized approach for LBP was made\(^{13}\). Such an approach could be a ‘matched-care’ intervention, in which patients’ individual prognostic factors for recovery are assessed, and a response guided treatment package can be designed. A response guided treatment means that the treatment is matched to the ‘risk-profile’ of the patient and that the specific content of the treatment is established before each intervention by assessing this ‘risk-profile’. Known factors in such risk-profiles are psychological factors like fear of movement\(^{14}\), catastrophizing\(^{15}\), avoidance\(^{16}\), somberness\(^{17}\) and sleep\(^{18}\). It is hypothesized that such ‘matched-care’ intervention may result in better treatment outcomes\(^{19}\). In this study we investigate the impact of taking into account another psychological factor in the risk-profile, namely Illness Perceptions’ (IPs), which is the core element of Leventhal’s Common Sense Model of health and Illness Representations (CSM)\(^{20}\)\(^{21}\).

The CSM is a parallel processing model that describes both cognitive and emotional representations of perceived health threats, leading to patients’ IPs resulting from these health threats. Higher IPs scores reflect a more threatening perception of illness and can be called ‘dysfunctional IPs’. These dysfunctional IPs may mediate or moderate persistent pain and disability\(^{22}\). To personalize management of LBP, IPs might be addressed. Dysfunctional IPs have shown to attribute to higher pain intensity and lower physical functioning and quality of life in a variety of conditions\(^{23}\). It is not known how this attribution unfolds during treatment. For instance, whether IPs act as a mediator or moderator for LBP outcomes. This has not yet been researched in primary care physiotherapy, whilst physiotherapists are important primary care practitioners in our healthcare system.

It is hypothesized IPs can mediate and/or moderate the association between intervention and outcome. To research the possible mediation and/or moderation effect of IPs on pain and disability, a multiple baseline Single Case Experimental Design (SCED) can be used to screen and measure patients’ individual prognostic factors for recovery before, during and after an intervention. In this study we use ‘matched-care’ physiotherapy as the intervention for patients with persistent LBP and dysfunctional levels of IPs. In order to analyze the results from our experiment in this study, we pose the following three research questions:

1. Do pain intensity, physical function and pain interference change significantly during and after matched-care physiotherapy treatment?
2. Do Illness Perceptions mediate the effect of matched-care physiotherapy on pain intensity, physical function and pain interference?
3. Do baseline Illness Perceptions moderate the effect of matched-care physiotherapy on pain intensity, physical function and pain interference?

2. Method

This study is designed according to The Single-Case Reporting Guideline In Behavioural Interventions (SCRIBE) checklist\(^{24}\) and six primary care physiotherapy practices in The Netherlands participated. After a recruitment call on social media and within the professional network of the lead author (EdR), a group of physiotherapists signed up for a 2-day’s course, 6 hours/day. Within the course, the aim of the study, the design and lay-out of the ‘matched-care’ intervention (treatment package see paragraph 2.3) were addressed. After this course, 6 eligible physiotherapists, each from different primary care physiotherapy practice, were included in the study
after signing an informed consent. They had access to videos that summarized the discussed topics. The lead author was available at any time during the research period for support on the implementation of the project.

2.1. Design

A multiple baseline SCED was applied. Participants completed repeated measurements during pre-treatment (phase A), during the treatment period (phase B) and a post-treatment period (phase A'). During all three phases of the study, the patients were asked to complete an online questionnaire (appendix B), twice a week in phase A and weekly in phases B and A'.

Phase A acts as a control phase (no treatment given) for comparison with phases B and A'. The duration of phase A was 3 weeks with 5-6 measures. During phase B the patients received a ‘matched-care’ treatment package (paragraph 2.3) by their physiotherapist. The number of sessions was left to the discretion of the physiotherapist, and therefore the duration of this phase varies across patients. The content of the ‘matched-care’ was response guided, meaning the intervention was based on the outcomes of the online questionnaires, which were administered by the patient the day before each consecutive intervention. The post-intervention period phase A' took 12 weeks, independent of the duration of phase B. The study followed the guidelines of the declaration of Helsinki and the code of conduct for scientific research of our institute and was approved by the Medical Ethical Committee of the University of Applied Sciences, Utrecht (ref. no. 950002019).

2.2. Patients

| Box 1 |
|-------|
| **IP-dimension** | **Threshold** |
| IP1 | Consequences | 8 |
| IP2 | Timeline | 8 |
| IP3 | Personal control | 7 |
| IP4 | Treatment control | 4 |
| IP5 | Identity | 8 |
| IP6 | Concern | 8 |
| IP7 | Comprehensibility | 5 |
| IP8 | Emotional | 8 |

Eligible patients for this study were enrolled from 6 different primary care physiotherapy practices in The Netherlands. Inclusion criteria were age 18 years or older, LBP for at least 3-months, experiencing a movement problem in daily life due to LBP and having dysfunctional levels of at least one out of eight IP dimensions. Dysfunctional levels of IPs were based on a secondary analysis of an earlier study on the associations of IPs with patient burden with musculoskeletal pain\textsuperscript{22}. We choose the fourth quartile as threshold (box 1), expecting these high-level scores to represent dysfunctional IPs.
Exclusion criteria were specific LBP and existing (and diagnosed) psychiatric illness. When matching the inclusion criteria, patients were invited to participate by their physiotherapist after reading the patient information letter. Their decision on participating in the study did not have consequences for their treatment. After signing the informed consent, patients were included in the study.

2.3. ‘Matched-care’ treatment package

We used the Dutch guideline for LBP, and added a treatment package which was based on three frequently applied strategies for persistent LBP (Appendix A). The specific aim of this response guided treatment package was to alter the dysfunctional levels of IPs by using cognitive, exposure and/or respondent strategies. For instance, a cognitive strategy showed successful improvements in patient-relevant physical activities in patients with more than 1-year LBP.

The treatment package offered the patient and physiotherapist the possibility to create a ‘matched-care’ intervention as advised in the Dutch Guideline for Low Back Pain. This means that patients’ ‘risk-profile’ scores were assessed before each intervention and consequently these scores were used to design the response guided treatment, thereby providing ‘matched-care’ (see paragraph 2.4).

2.4. Measures

An online questionnaire was developed for assessing primary outcomes (pain intensity, physical function, and pain interference), secondary outcome (Illness Perceptions) and the co-variates (fear for damage/pain, pain anxiety, depressive mood, avoidance beliefs and sleep). Frequent administration allowed for monitoring the effect of the treatment package on all outcomes. These items are described below.

2.4.1. Primary outcome

Three outcome measures were chosen as primary outcome based on consensus recommendations from the literature; 1) pain intensity last 24-hours. 2) limitation in patients’ own selected physical function and 3) pain interference in daily activities. All three primary outcome were assessed with a 11-point numeric rating scale (0-10). High scores for these three primary outcome measures mean respectively 1) higher levels of pain intensity, 2) stronger limitations in physical function and 3) greater interference of pain in daily activities. The physical function measure was adjusted to patients’ specific limitation in physical function (i.e. bending forward).

2.4.2. Illness Perceptions secondary outcome

The Brief Illness Perception Questionnaire was used to assess patients’ Illness Perceptions representation on LBP. This questionnaire contains 9 questions, of which the questions IP1 – IP8 were used in this study. Each item represents a different dimension of IPs. In order to ensure that all higher scores signify stronger dysfunctional IPs, data of the IP3-4 and 7 were reversed before entering into the analyses.

2.4.3. Co-variates

The selection of co-variates was based on research showing these factors being associated with treatment outcome of LBP. They have also previously been used in a SCED study on persistent LBP. The co-variates are:
fear of movement\textsuperscript{14}, catastrophizing\textsuperscript{15}, avoidance\textsuperscript{16}, somberness\textsuperscript{17} and sleep\textsuperscript{18}. For all these co-variates we hypothesized that the higher their scores, the more negative impact they will have on the primary outcome.

2.4.4. Statistical analysis

To investigate whether primary outcomes change during and after matched-care physiotherapy treatment, linear mixed model analyses were performed, including all repeated measurements as outcome, and ‘phase’ as independent variables. First a crude analysis was performed. In a next analysis we controlled for the co-variates.

To investigate whether IPs mediate the effect of matched-care physiotherapy on primary outcomes, these adjusted analyses were performed including the IPs. Based on the change in the coefficient for treatment-phase (two dummies, with phase A as reference category) the mediating role of each IP was evaluated independently. The magnitude of the mediation effect, the Indirect Effect, was calculated by subtracting the Direct Effect from the Total Effect.

Finally, to investigate whether baseline IPs moderate the effect of matched-care physiotherapy on primary outcomes. For the effect size on the three primary outcome during the treatment-phase and post-treatment phase (two dummies, with phase A as reference category) the baseline IPs were added to the adjusted linear mixed models. The importance of the moderation was evaluated on significance (p<0.05) of the interaction terms.

in addition to statistical significant effects, we evaluated the outcomes on their clinical meaningful effect using a threshold of 30\% change in phase A on primary outcome from baseline scores phase A\textsuperscript{31}. All analyses were performed with STATA\textsuperscript{®} (version 15).

3. Results

Table 1 presents the characteristics of participating physiotherapists. Six physiotherapists participated in the study, all working in different primary care physiotherapy practices across the Netherlands.
Table 1 Participating physiotherapists

| Pht | Work setting | Years’ experience | Specialist | Particularities                        |
|-----|--------------|------------------|------------|----------------------------------------|
| I   | Primary care | 11               | PSF        | - ACT-trainer                          |
| II  | Primary care | 6                | PSF*       | - none                                 |
| III | Primary care | 4,5              | MT*        | - member pain network                  |
| IV  | Primary care | 4,5              | PSF        | - none                                 |
| V   | Primary care | 35               | MT         | - Lecturer                             |
| VI  | Primary care | 34               | MT         | - Lecturer                             |
|     |              |                  |            | - EFIC pain physiotherapist            |

Pht = participating physiotherapist, MSc = Master of Science, BSc = Bachelor of Science, PSF = Psycho-Social Physiotherapy, MT = Manual Therapy, MMT = Master Manual Therapy, ACT = Acceptance and Commitment Therapy, * = student

Table 2 presents the characteristics of the nine participating patients. Age ranged from 25 – 74 years. Reported baseline primary outcomes, mean (SD) were for Pain Intensity 5.6 (2.5), Physical Functioning 5.8 (2.7) and Pain Interference in Daily Life 5.9 (2.7).

Table 2 Baseline scores participating patients

| Patient | Gender | Age | Duration LBP (in weeks) | Oswestry (0-100) | Co-morbidity                  | PI  | PF  | PIDL |
|---------|--------|-----|-------------------------|------------------|------------------------------|-----|-----|------|
| 1       | Male   | 74  | > 500                   | 70               | Heart condition              | 8   | 6   | 8    |
| 2       | Male   | 40  | 15                      | 52               | -                            | 7   | 8   | 8    |
| 3       | Female | 43  | 12                      | 38               | -                            | 3   | 2   | 2    |
| 4       | Male   | 49  | > 250                   | 70               | Rheumatoid arthritis         | 7   | 8   | 9    |
| 5       | Male   | 49  | > 150                   | 42               | -                            | 7   | 9   | 8    |
| 6       | Female | 25  | 32                      | 80               | Rheumatoid arthritis         | 9   | 8   | 8    |
| 7       | Female | 40  | > 200                   | 32               | -                            | 7   | 9   | 7    |
| 8       | Male   | 66  | 12                      | 24               | Osteoarthritis               | 2   | 5   | 1    |
| 9       | Female | 30  | 52                      | 38               | PCOS. Hashimoto              | 3   | 6   | 6    |

PI = Pain Intensity, PF = Physical Functioning, PIDL = Pain Interference in Daily Life

Table 3 shows which baseline IPs dimensions reached the threshold score, as one of the inclusion criteria, per patient.
Table 3 IPs dimension inclusion criteria per patients’ exceeded threshold

| Patient | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---------|---|---|---|---|---|---|---|---|---|
| IP-dimension | | | | | | | | | |
| Consequences | | | | | | | | | |
| Timeline | | | | | | | | | |
| Personal control | | | | | | | | | |
| Treatment control | | | | | | | | | |
| Identity | | | | | | | | | |
| Concern | | | | | | | | | |
| Comprehensibility | | | | | | | | | |
| Emotional | | | | | | | | | |

Table 4 shows the results of the linear mixed model analyses to investigate whether primary outcomes changed during and after matched-care physiotherapy. During treatment, all three outcomes show a significant and clinical meaningful improvement of 30% effect. The adjust effects shows clinical meaningful improvement of 30% for pain for physical functioning. Post treatment, the effect did not wash-out. Remaining in significant and clinical meaningful improvement of 30% for all three outcomes.

Table 4 Final linear mixed model Regression effects, study phase A as reference class

| During treatment | Post treatment |
|------------------|----------------|
|                  | Effect crude  | Effect adjusted* | Effect crude  | Effect adjusted* |
|                  | 95% CI        | 95% CI           | 95% CI        | 95% CI           |
| Pain Intensity   | -2.23*        | -2.91 / -1.54    | -1.3          | -1.9 / -0.7      |
|                  | -3.52*        | -4.21 / -2.84    | -1.8          | -2.4 / -1.2      |
| Physical Functioning | -2.41*        | -3.07 / -1.76    | -1.3          | -2.2 / -1.1      |
|                  | -4.10*        | -4.50 / -3.44    | -2.6          | -3.2 / -1.1      |
| Pain Interference Daily Life | -2.39*        | -3.05 / -1.73    | -1.3          | -1.9 / 0.7       |
|                  | -4.21*        | -4.87 / -3.55    | -2.4          | -3.0 / -1.8      |

SD = Standard deviation, All outcome = $P < .05$, * = Clinical meaningful improvement 30% baseline score. *adjusted for: fear of movement, catastrophizing, avoidance, somberness and sleep

Table 5 shows the results of the mediation analyses performed on the adjusted models.
Five of the 8 IP dimensions substantially mediated the total effect on all three primary outcomes (table 5). For instance, the IP dimension Consequences mediated for 42.8% the effect of the treatment on pain intensity during the treatment (Phase B) and this increased to 56.3% for the post-treatment (Phase A'). The IP
Consequences was a strong mediator in all three primary outcomes. The other dimensions that mediated the effect of the treatment on the outcome were Identity, Concern, Emotional and Personal control. Three IPs showed lesser mediation effects, with Timeline being the smallest mediator by 1.7% for Physical functioning post treatment.

| Table 5 Results of the analyses to evaluate the mediating influence of IPs on treatment adjusted effect on primary outcomes |
|-------------------------------------------------|
| **Total adjusted effect of treatment on primary outcomes** |
| **Pain Intensity** | **Physical functioning** | **Pain interference daily life** |
| **During Treatment** | **Post Treatment** | **During Treatment** | **Post Treatment** | **During Treatment** | **Post Treatment** |
| Pain Intensity | -1.3 (CI -1.9 / -0.7) | Post Treatment | -1.8 (CI -2.4 / -0.7) |
| Physical functioning | -1.6 (CI -2.2 / -0.1) | Post Treatment | -2.6 (CI -3.2 / -1.1) |
| Pain interference daily life | -1.3 (CI -1.9 / -0.7) | Post Treatment | -2.4 (CI -3.0 / -1.8) |
| IE % | IE % | IE % | IE % | IE % | IE % |
| Consequences | -0.5  42.8 | -0.7  56.3 | -0.5  32.4 | -1.2  45.2 | -0.6  44.8 | -1.3  54.5 |
| Timeline | 0.0  0.0 | 0.0  0.0 | 0.0  0.0 | 1.7  0.0 | 0.0  0.0 | -0.1  2.6 |
| Personal Control | -0.2  19.0 | -0.2  15.7 | -0.2  14.9 | -0.3  12.4 | -0.1  11.1 | -0.2  8.1 |
| Treatment Control | -0.1  8.8 | -0.1  5.6 | -0.1  9.9 | 0.0  0.7 | -0.1  8.9 | 0.0  0.0 |
| Identity | -0.5  41.3 | -0.7  52.9 | -0.5  32.4 | -1.2  46.7 | -0.7  49.2 | -1.5  60.1 |
| Concern | -0.4  27.7 | -0.2  15.6 | -0.5  33.5 | -0.8  30.9 | -0.4  30.4 | -0.8  34.3 |
| Comprehensibility | -0.1  7.8 | -0.1  5.6 | -0.1  6.3 | -0.1  3.6 | -0.1  6.9 | -0.1  4.7 |
| Emotional | -0.2  14.2 | -0.7  38.9 | -0.1  12.5 | -0.6  24.3 | -0.2  17.0 | -0.8  31.3 |

CI = 95% Confidence Interval, * = Clinical meaningful improvement 30% baseline score 31, IE = Indirect Effect (Mediation Effect), % = Percentage mediation
Table 6 Final linear mixed model effects for IPs as moderator for Primary Outcomes with Study phase A as reference class, adjusted for co-variates

|                           | Pain Intensity | Physical functioning | Pain interference daily life |
|---------------------------|----------------|----------------------|------------------------------|
|                           | During Treatment | Post Treatment | During Treatment | Post Treatment | During Treatment | Post Treatment |
| Illness Perception        | TE  CI          | TE  CI              | TE  CI                      | TE  CI          | TE  CI          | TE  CI          |
| Personal control          |                |                     |                             |                 |                 |                 |
| Low baseline score (0-7)  | -2.1<sup>¶</sup> / -2.9 | -2.7<sup>¶</sup> / -3.5 | -2.1<sup>¶</sup> / -2.9 | -3.3<sup>¶</sup> / -4.2 | -2.1<sup>¶</sup> / -3.0 | -3.7<sup>¶</sup> / -4.5 |
| n=140                     | -2.1<sup>¶</sup> / -1.2 | -2.9<sup>¶</sup> / -1.8 | -2.1<sup>¶</sup> / -1.2 | -3.3<sup>¶</sup> / -2.6 | -2.1<sup>¶</sup> / -1.3 | -3.7<sup>¶</sup> / -2.8 |
| High baseline score (8-10)| -0.8 / -1.5    | -1.3 / -2.0          | -1.3 / -2.0                 | -2.1<sup>¶</sup> / -2.8 | -0.8 / -1.5    | -1.6 / -2.3     |
| n=56                      | -0.1 / -0.5    | -2.0 / -0.7          | -1.4 / -0.1                 | -1.4 / -0.1     | -1.0 / -0.1    | -0.9 / -0.9     |
| Treatment control         |                |                     |                             |                 |                 |                 |
| Low baseline score (0-4)  | -2.1<sup>¶</sup> / -2.8 | -2.9<sup>¶</sup> / -3.6 | -2.1<sup>¶</sup> / -2.5 | -2.9<sup>¶</sup> / -3.2 | -2.1<sup>¶</sup> / -2.5 | -3.2<sup>¶</sup> / -2.9 |
| n=127                     | -2.1<sup>¶</sup> / -1.4 | -2.9<sup>¶</sup> / -2.2 | -2.1<sup>¶</sup> / -1.0 | -2.9<sup>¶</sup> / -1.9 | -2.1<sup>¶</sup> / -1.0 | -2.9<sup>¶</sup> / -1.9 |
| High baseline score (5-10)| -1.0 / -1.8    | -2.3<sup>¶</sup> / -3.1 | -1.0 / -1.8                 | -2.3<sup>¶</sup> / -3.1 | -1.0 / -1.8    | -2.3<sup>¶</sup> / -3.1 |
| n=69                      | -0.2 / -0.2    | -1.5 / -1.5          | -0.2 / -0.2                 | -1.5 / -1.5     | -0.2 / -0.2    | -1.5 / -1.5     |
| Identity                  |                |                     |                             |                 |                 |                 |
| Low baseline score (0-8)  | -2.0<sup>¶</sup> / -2.8 | 2.8<sup>¶</sup> / -3.6 | -2.0<sup>¶</sup> / -2.5 | 2.8<sup>¶</sup> / -3.2 | -2.0<sup>¶</sup> / -2.5 | 2.8<sup>¶</sup> / -3.2 |
| n=144                     | -2.0<sup>¶</sup> / -1.2 | 2.8<sup>¶</sup> / -2.0 | -2.0<sup>¶</sup> / -1.0 | 2.8<sup>¶</sup> / -1.9 | -2.0<sup>¶</sup> / -1.0 | 2.8<sup>¶</sup> / -1.9 |
| High baseline score (9-10)| -0.7 / -1.5    | 2.1<sup>¶</sup> / -3.0 | -0.7 / -1.5                 | 2.1<sup>¶</sup> / -3.0 | -0.7 / -1.5    | 2.1<sup>¶</sup> / -3.0 |
| n=52                      | -0.7 / -0.1    | 2.1<sup>¶</sup> / -1.3 | -0.7 / -0.1                 | 2.1<sup>¶</sup> / -1.3 | -0.7 / -0.1    | 2.1<sup>¶</sup> / -1.3 |
| Concern                   |                |                     |                             |                 |                 |                 |
| Low baseline score (0-8)  | -1.8<sup>¶</sup> / -2.5 | 2.6<sup>¶</sup> / -3.2 | -1.8<sup>¶</sup> / -2.5 | 2.6<sup>¶</sup> / -3.2 | -1.8<sup>¶</sup> / -2.5 | 2.6<sup>¶</sup> / -3.2 |
| n=153                     | -1.8<sup>¶</sup> / -1.0 | 2.6<sup>¶</sup> / -1.9 | -1.8<sup>¶</sup> / -1.0 | 2.6<sup>¶</sup> / -1.9 | -1.8<sup>¶</sup> / -1.0 | 2.6<sup>¶</sup> / -1.9 |
| High baseline score (9-10)| -0.8 / -1.6    | 2.3<sup>¶</sup> / -3.2 | -0.8 / -1.6                 | 2.3<sup>¶</sup> / -3.2 | -0.8 / -1.6    | 2.3<sup>¶</sup> / -3.2 |
| n=43                      | -0.8 / 0.1     | 2.3<sup>¶</sup> / -1.4 | -0.8 / 0.1                  | 2.3<sup>¶</sup> / -1.4 | -0.8 / 0.1     | 2.3<sup>¶</sup> / -1.4 |
| Emotional response        |                |                     |                             |                 |                 |                 |
| Low baseline score (0-8)  | -2.0<sup>¶</sup> / -2.8 | 2.8<sup>¶</sup> / -3.6 | -2.0<sup>¶</sup> / -2.5 | 2.8<sup>¶</sup> / -3.2 | -2.0<sup>¶</sup> / -2.5 | 2.8<sup>¶</sup> / -3.2 |
| n=145                     | -2.0<sup>¶</sup> / -1.2 | 2.8<sup>¶</sup> / 2.0 | -2.0<sup>¶</sup> / -1.2 | 2.8<sup>¶</sup> / 2.0 | -2.0<sup>¶</sup> / -1.2 | 2.8<sup>¶</sup> / 2.0 |
| High baseline             | -0.7 / -1.5    | -3.0 / -3.0          | -0.7 / -1.5                 | -3.0 / -3.0     | -0.7 / -1.5    | -3.0 / -3.0     |
Table 6 shows the statistically significant results of the moderation analyses performed on the adjusted models. The IPs dimension Personal control moderated the treatment effects for all three primary outcomes. There is a stronger treatment effect for patients with a low baseline score (0-7) on Personal control versus patients with high baseline scores (8-10) on Personal control. This means that when patients experienced higher control (0-7) over their condition at baseline, the stronger the positive effect on the primary outcome was in both the treatment and the post-treatment phases.

The IPs dimension Treatment control showed a moderating effect for Physical functioning. This indicates a stronger treatment effect for patients with a low baseline score (0-4) on Treatment control versus patients with high baseline scores (5-10) on Treatment control. This means that the more patients expected treatment to control their condition at baseline, the stronger the effect on the primary outcome was in both the treatment phase B and the post-treatment phase A'.

For Pain Interference in Daily Life, baseline low scores in the IPs dimensions Identity (0-8), Concern (0-8) and Emotional response (0-8) showed stronger effects for both treatment and post-treatment phase versus patients with high baseline scores.

The moderating effect of the IPs dimensions Personal Control, Identity, Concern and Emotional response did not wash out during the post treatment phase.

4. Discussion

In this matched-care physiotherapy treatment for patients with persistent LBP SCED-study, we showed a statistically significant and clinical meaningful improvement in decreasing pain intensity, increased physical function and lesser pain interference in daily life during and 3-months post-treatment. We did not observe a wash-out phenomenon during the post treatment phase. Furthermore, we found five IP dimensions to substantially mediate the effect on all three primary outcomes; namely, Consequences (45.2-56.3) Personal control (8.1-15.7), Identity (46.7-52.9), Concern (15.6-34.3) and Emotional response (24.3-38.9). At baseline, the IP Personal control acted as a moderator for all primary outcomes. In the post treatment phase the IPs Personal Control, Identity, Concern and Emotional response also acted as moderator.

4.1 Illness Perceptions as mediator

The search for causal mechanisms for non-specific LBP has been a quest for decades now. Identifying such mechanisms is useful, for instance, when designing a ‘Magic Bullet’ cure, for a condition that is primarily caused by a pathoanatomical impairment. In the case of persistent musculoskeletal pain like LBP, such pathoanatomical impairment most likely cannot be identified. LBP is considered to be more a symptom of a complex condition with multiple contributors to both pain and associated limitations in physical function, including psychological factors, social factors, biophysical factors, comorbidities, and pain-processing mechanisms. Models for management of complex conditions should incorporate these multiple contributors,
including patients’ beliefs about their condition\textsuperscript{35,36}. IPs are thought of as one aspect of these beliefs\textsuperscript{35}. Through mediation analyses we identified 5 IP dimensions that mediated the total effect of our matched-care physiotherapy treatment package\textsuperscript{17}. Intervention studies on how to alter IPs in LBP are scarce. We know of one RCT that looked at altering baseline IPs with cognitive treatment to improve patient relevant physical activities\textsuperscript{25}. In this study IP dimensions Timeline cyclical, Consequences, Personal control and Coherence attributed 14.4\% of the explained variance to physical activities. This partly overlaps with our results. We found IP dimensions Consequences and Personal control also significantly mediating the total effect on all three primary outcomes.

The effects in our study are found within a non-controlled design and should be further tested in a larger population and with a different design such as a randomized controlled trial.

4.2 Illness Perceptions as moderator

The course and prognosis of developing persistent LBP have been extensively researched\textsuperscript{36}. The overall findings are reported as; “Low to moderate levels of pain and disability were still present at one year, especially in the cohorts with persistent pain.” In a Cochrane review on individual recovery expectations it is concluded: “Our findings suggest that recovery expectations should be considered in future studies, to improve prognosis and management of low back pain”\textsuperscript{37}. We found the IP dimension Personal control to be moderating the effect on all three primary outcomes. This IP dimension can be seen as reflecting patients’ expectations about the effect of the treatment. We therefore would like to advise to include the IP Personal control in future research concerning treatment and prognosis of LBP.

4.3 Limitations & strengths

Several limitations need to be considered. First, there was no randomization. The effects in our study are found within a non-controlled design. We explicitly focused on a ‘matched care intervention’. Meaning that the intervention was tailored on the patients’ clinical presentation, and therefor randomization was not included in our design. Secondly, selection bias of patients. The patients were selected by the participating physiotherapists, therefore the generalizability of our results is somewhat limited. Thirdly, patients were required to complete a questionnaire, monitoring their progress on a weekly basis for several months. This may have given rise to the awareness of being studied. This possibly impacted behavior\textsuperscript{38}, resulting in a Hawthorne effect.

Fourthly, there is a potential sampling bias of treating / participating physiotherapists due to the use of convenience sampling of physiotherapists via social media and within the network of the first author. They were invited to our 2-day course to be informed on the design of the study. These physiotherapists might not be representative of the physiotherapy community in the Netherlands. Fifthly, we do not have data to analyze the treatment fidelity of participating physiotherapists on delivering the matched-care treatment package. The weight this has on the effects is not clear. We tried to minimize this limitation by including several implementation interventions addressing fidelity of the physiotherapists to participate in the study: a 2-days course, videos were assesible demonstrating how to apply treatment strategies and the use of repeated measures during the treatment phase.

Finally, due to the design of this study conclusions about causal relations between IPs and the primary
outcome cannot be drawn. Further studies on the temporal order of the associations between matched-care physiotherapy, IPs and treatment outcomes are recommended.

There are several strengths of this study to be considered. First, the use of repeated measures and a matched-care intervention instead of a strict treatment protocol allowed the physiotherapists to adjust their interventions to the clinical status of the patient with each new appointment. This dynamic and cyclical process is commonly used by physiotherapists and is a reflection of their clinical reasoning process, making this design representative for daily practice. For example, if the patient shows a sufficient decrease of safety behaviors, than withdrawal of safety behavior strategy is justified. Secondly, within the model of Illness Representations by Leventhal it is hypothesized that dysfunctional perceptions affect pain and limitations in physical functioning. The use of an IP threshold as an inclusion criterium implies good diagnostics for creating a window of opportunity to improve pain and physical functioning by altering IPs. Thirdly, this study is a good example of how to include physiotherapists’ clinical relevant decisions for avoiding problems concerning “reference class forecasting”. Such forecasting relies on prediction from past reference classes, a model which may not be the most suitable because of the large variability in clinical signs and symptoms in patients with low back pain. In our study we explicitly incorporated psycho-social elements which were relevant for that patient as was shown in their ‘risk-profile’.

4.4 Practical implications

The use of a matched-care physiotherapy treatment is accompanied by a decrease of pain and physical function related health problems in patients with persistent low back pain. This type of research, looking at treatments that incorporate a dynamic and cyclical process is a reproduction of daily physiotherapy practice. We would like to encourage this way of working and researching the effectiveness of physiotherapy. In earlier research, we concluded based on a longitudinal study with 2 timepoints that baseline IPs did not predict poor recovery on pain and/or physical function after 3-months (de Raaij et al., 2020). The results of this study are not in line with these findings. For instance, dysfunctional baseline IP Personal control scores (8-10) moderate the effect significantly, meaning that physiotherapists can be encouraged to use item 3 of the Brief IPQ-DLV for the baseline assessment of patients’ perceptions on controllability of their condition. A specific intervention targeting this dysfunctional perception can be advised. Further, it can be advised to evaluate the change in the IPs dimension Consequences, Personal control, Identity, Concern and Emotional response because our results show a mediating effect of change in these perceptions on the effect of the treatment. If one of these perceptions does not change during treatment there could still be room for improvement by specifically targeting these perceptions with interventions. Thereby, applying the principles of ‘matched-care’ treatment.

5. Conclusion

This is the first study shedding some light on how IPs may affect pain intensity, physical function and pain interference during primary care physiotherapy treatment. Our findings indicate that the IP dimensions Consequences, Personal control, Identity, Concern and Emotional response, might be important to include in a matched-care treatment of LBP, because they enhance the positive mediation effect of all three primary
outcomes. In addition, at baseline, assessing Personal control may be relevant to determine the outcome prognosis of successful physiotherapy management of persistent LBP.

Declarations

Ethics approval and consent to participate:

- Medical Ethical Committee of the University of Applied Sciences Utrecht (ref. no. 430002016) for ethical approval
- Written informed consent was obtained from participating patients as well as from participating physiotherapists

Consent for publication

All attributing authors read the final version and agreed with the submission.

Availability of data and materials

the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. The datasets are stored in a repository of the University of applied sciences Utrecht, which can be accessed from a University account.

Competing interest:

Not applicable

Funding:

This study is supported by a grant of the Dutch government; NWO- 023.005.029

Authors' contributions

All authors contributed to the paper and discussed the results and commented on the manuscript. EJ de Raaij participated in the design of the study, data collection, discussion of core ideas and writing of the paper. HW Wittink participated in the design of the study, discussion of core ideas and writing of the paper. RWJG Ostelo and JF Maissan participated in discussion of core ideas and writing of the paper. J. Twisk participated in designing the statistic strategies and calculation of the results.

Acknowledgements

We would like to thank the attributing patients for participating in this research. Further, the contribution to this study by primay care physiotherapists Alisha van den Waarsenburg, Esther Beker, Jef Huibers, Daron Buenting and Ben van Koppen are much appreciated.

This study is supported by a grant of the Dutch government; NWO- 023.005.029

References
1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *lancet*. 2013;380(9859):2163-2196. doi:10.1016/S0140-6736(12)61729-2.

2. Buchbinder R, van Tulder M, Öberg B, et al. Low back pain: a call for action. *lancet*. March 2018. doi:10.1016/S0140-6736(18)30488-4.

3. Clark S, Horton R. Low back pain: a major global challenge. *lancet*. March 2018. doi:10.1016/S0140-6736(18)30725-6.

4. Hartvigsen J, Hancock MJ, Kongsted A, Lancet QLT, 2018. What low back pain is and why we need to pay attention. *Elsevier*. 2018;391(10137):2356-2367. doi:10.1016/S0140-6736(18)30480-X.

5. Foster NE, Anema JR, Cherkin D, et al. Prevention and treatment of low back pain: evidence, challenges, and promising directions. *lancet*. March 2018. doi:10.1016/S0140-6736(18)30489-6.

6. OSullivan P. It’s time for change with the management of non-specific chronic low back pain. *British Journal of Sports Medicine*. 2012;46(4):224-227. doi:10.1136/bjsm.2010.081638.

7. Caneiro JP, Roos EM, Barton CJ, et al. It is time to move beyond “body region silos” to manage musculoskeletal pain: five actions to change clinical practice. *British Journal of Sports Medicine*. October 2019:bjsports–2018–100488–2. doi:10.1136/bjsports-2018-100488.

8. OSullivan P, Caneiro JP, O’Keeffe M, O’Sullivan K. Unraveling the Complexity of Low Back Pain. *J Orthop Sports Phys Ther*. 2016;46(11):932-937. doi:10.2519/jospt.2016.0609.

9. Henschke N, Ostelo RW, van Tulder MW, et al. Behavioural treatment for chronic low-back pain. *Cochrane Database Syst Rev*. 2010;(7):CD002014. doi:10.1002/14651858.CD002014.pub3.

10. Medicine OCFE-B. *OCEBM Levels of Evidence Working Group. the Oxford 2011 Levels of Evidence*. 2011.

11. Shamseer L, Bukutu C, Schmid CH, et al. CONSORT extension for reporting N-of-1 trials (CENT) 2015: explanation and elaboration. *Journal of Clinical Epidemiology*. 2016;76:18-46. doi:10.1016/j.jclinepi.2015.05.018.

12. Kent DM, Steyerberg E, van Klaveren D. Personalized evidence based medicine: predictive approaches to heterogeneous treatment effects. *BMJ*. 2018;45:k4245–18. doi:10.1136/bmj.k4245.

13. Linton SJ, Nicholas M, Shaw W. Why wait to address high-risk cases of acute low back pain? A comparison of stepped, stratified, and matched care. *Pain*. 2018;159(12):2437-2441. doi:10.1097/j.pain.0000000000001308.

14. Vlaeyen JW, Kole-Snijders AM, Boeren RG, van Eek H. Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. *Pain*. 1995;62(3):363-372.

15. Picavet HSJ. Pain Catastrophizing and Kinesiophobia: Predictors of Chronic Low Back Pain. *American Journal of Epidemiology*. 2002;156(11):1028-1034. doi:10.1093/aje/kwf136.

16. Vlaeyen JW, de Jong J, Geilen M, Heuts PH, van Breukelen G. Graded exposure in vivo in the treatment of pain-related fear: a replicated single-case experimental design in four patients with chronic low back pain. *Behav Res Ther*. 2001;39(2):151-166. doi:10.1016/s0005-7967(99)00174-6.

17. LEE H, Mansell G, McAuley JH, et al. Causal mechanisms in the clinical course and treatment of back pain. *Best Practice & Research Clinical Rheumatology*. 2016;30(6):1074-1083. doi:10.1016/j.berh.2017.04.001.
18. Sivertsen B, Lallukka T, Petrie KJ, Steingrímsson ÓA, Stubhaug A, Nielsen CS. Sleep and pain sensitivity in adults. *Pain*. 2015;156(8):1433-1439. doi:10.1097/j.pain.0000000000000131.

19. Nicholas MK, Linton SJ, Watson PJ, Physical CM, 2011. Early identification and management of psychological risk factors (“yellow flags”) in patients with low back pain: a reappraisal. *academicoupcom*.

20. Leventhal H, Meyer D, nerenz D. The Common Sense Representation of Illness Danger. In: Rachman S, ed. *Medical Psychology*. Vol II. Pergamon Press; 1980:7-29.

21. de Raaij EJ, Ostelo RW, Maissan F, Mollema J, Wittink H. The Association of Illness Perception and Prognosis for Pain and Physical Function in Patients With Noncancer Musculoskeletal Pain: A Systematic Literature Review. *J Orthop Sports Phys Ther*. 2018;48(10):789-800. doi:10.2519/jospt.2018.8072.

22. de Raaij EJ, Ostelo RWJG, Maissan JF, Pool J, Westers P, Wittink H. Illness perceptions associated with patient burden with musculoskeletal pain in outpatient physical therapy practice, a cross-sectional study. *Musculoskeletal Science and Practice*. 2020;45:102072. doi:10.1016/j.msksp.2019.102072.

23. Hagger M, Orbell S. A Meta-Analytic Review of the Common-Sense Model of Illness Representations. *Psychology & Health*. 2003;18(2):141-184.

24. Tate RL, Perdices M, Rosenkoetter U, et al. The Single-Case Reporting Guideline In BEhavioural Interventions (SCRIBE) 2016: Explanation and elaboration. *Archives of Scientific Psychology*. 2016;4(1):10-31. doi:10.1037/arc0000027.

25. Siemonsma PC, Stuive I, Roorda LD, et al. Cognitive treatment of illness perceptions in patients with chronic low back pain: a randomized controlled trial. *physical therapy*. 2013;93(4):435-448. doi:10.2522/ptj.20110150.

26. Beurskens AJ, de Vet HC, Köke AJ, et al. A patient-specific approach for measuring functional status in low back pain. *Journal of Manipulative and Physiological Therapeutics*. 1999;22(3):144-148.

27. Dionne CE, Dunn KM, Croft PR, et al. A consensus approach toward the standardization of back pain definitions for use in prevalence studies. *spine*. 2008;33(1):95-103. doi:10.1097/BRS.0b013e31815e7f94.

28. de Raaij EJ, Schröder C, Maissan FJ, Pool JJ, Wittink H. Cross-cultural adaptation and measurement properties of the Brief Illness Perception Questionnaire-Dutch Language Version. *manual therapy*. 2012;17(4):330-335. doi:10.1016/j.math.2012.03.001.

29. Hallegraeff JM, Van Der Schans CP, Krijnen WP, de Greef MH. Measurement of acute nonspecific low back pain perception in primary care physical therapy: reliability and validity of the brief illness perception questionnaire. *BMC Musculoskelet Disord*. 2013;14(1):1-1. doi:10.1186/1471-2474-14-53.

30. Caneiro JP, Smith A, Linton SJ, Moseley GL, OSullivan P. “How does change unfold?” an evaluation of the process of change in four people with chronic low back pain and high pain-related fear managed with Cognitive Functional Therapy_ A replicated single-case experimental design study. *Behav Res Ther*. March 2019:1-12. doi:10.1016/j.brat.2019.02.007.

31. Ostelo RWJG, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. In: Vol 33. 2008:90-94. doi:10.1097/BRS.0b013e31815e3a10.

32. Maher C, Underwood M, Buchbinder R. Non-specific low back pain. *lancet*. 2017;389(10070):736-747. doi:10.1016/S0140-6736(16)30970-9.
33. Hoy D, Brooks P, BLYTH F, Buchbinder R. The Epidemiology of low back pain. *Best Practice & Research Clinical Rheumatology*. 2010;24(6):769-781. doi:10.1016/j.berh.2010.10.002.

34. Delitto A. Research in low back pain: time to stop seeking the elusive "magic bullet". *Physical Therapy*. 2005;85(3):206-208.

35. Caneiro JP, Bunzli S, OSullivan P. Beliefs about the body and pain: the critical role in musculoskeletal pain management. *Brazilian Journal of Physical Therapy*. June 2020:1-13. doi:10.1016/j.bjpt.2020.06.003.

36. Costa L, Maher CG, Hancock MJ, J JMCMA, 2012. *Prognosis in People with Back Pain*. Vol 184. 2012:1229-1230. doi:10.1503/cmaj.120627.

37. Hayden JA, Tougas ME, Riley R, Iles R. Individual recovery expectations and prognosis of outcomes in non-specific low back pain: prognostic factor exemplar review. 2014. doi:10.1002/14651858.CD011284.

38. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: New concepts are needed to study research participation effects. *Journal of Clinical Epidemiology*. 2014;67(3):267-277. doi:10.1016/j.jclinepi.2013.08.015.

39. Doody C, McAteer M. Clinical Reasoning of Expert and Novice Physiotherapists in an Outpatient Orthopaedic Setting. *Physiotherapy*. 2002;88(5):258-268. doi:10.1016/S0031-9406(05)61417-4.

40. Hoffman LJ, Chu BC. When Is Seeking Safety Functional? Taking a Pragmatic Approach to Distinguishing Coping From Safety. *Cognitive and Behavioral Practice*. 2019;26(1):176-185. doi:10.1016/j.cbpra.2018.11.002.

41. Turk DC, Flor H. Etiological theories and treatments for chronic back pain. II. Psychological models and interventions. *Pain*. 1984;19(3):209-233.

42. O’Sullivan PB, Caneiro JP, O’Keeffe M, et al. Cognitive Functional Therapy: An Integrated Behavioral Approach for the Targeted Management of Disabling Low Back Pain. *Physical Therapy*. 2018;98(5):408-423. doi:10.1093/ptj/pzy022.

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