Effect of perceived injustice-targeted pain neuroscience education compared with biomedically focused education in breast cancer survivors

Roose, Eva; Huysmans, Eva; Leysen, Laurence; Mostaqim, Kenza; Van Wilgen, Paul; Beckwée, David; De Couck, Marijke; Timmermans, Annick; Bults, Rinske; Nijs, Jo; Lahousse, Astrid

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Effect of perceived injustice-targeted pain neuroscience education compared with biomedically focused education in breast cancer survivors: a study protocol for a multicentre randomised controlled trial (BCS-PI trial)

Eva Roose,1,2,3,4 Eva Huysmans,1,5,6 Laurence Leysen,1 Kenza Mostaqim,1,6 Paul Van Wilgen,1,7 David Beckwée1,4,8 Marijke De Couck,1 Annick Timmermans,2 Rinske Buls,1 Jo Nijs,1,3,9 Astrid Lahousse1,3

ABSTRACT

Introduction Current treatments for pain in breast cancer survivors (BCSs) are mostly biomedically focused rather than biopsychosocially driven. However, 22% of BCSs with pain are experiencing perceived injustice, which is a known predictor for adverse pain outcomes and opioid prescription due to increased maladaptive pain behaviour. Educational interventions such as pain neuroscience education (PNE) are suggested to target perceived injustice. In addition, motivational interviewing can be an effective behavioural change technique. This trial aims to examine whether perceived injustice-targeted PNE with the integration of motivational interviewing is superior to biomedically focused pain education in reducing pain after 12 months in BCS with perceived injustice and pain. In addition, improvements in quality of life, perceived injustice and opioid use are evaluated, and a cost-effectiveness analysis will finally result in a recommendation concerning the use of perceived injustice-targeted PNE in BCSs with perceived injustice and pain.

Methods and analysis This two-arm multicentre randomised controlled trial will recruit female BCS (n=156) with pain and perceived injustice. Participants will be randomly assigned to perceived injustice-targeted PNE or biomedically focused pain education in each centre. Both interventions include an online session, an information leaflet and three one-to-one sessions. The primary outcome (pain), secondary outcomes (quality of life, perceived injustice and outcomes for cost-effectiveness analysis) and explanatory outcomes (pain phenotyping, sleep, fatigue and cognitive-emotional factors) will be assessed at baseline and at 0, 6, 12 and 24 months postintervention using self-reported questionnaires online. Treatment effects over time will be evaluated using linear mixed model analyses. Additionally, a cost-utilty analysis will be done from a healthcare payer and societal perspective.

Ethics and dissemination The ethical agreement was obtained from the Main Ethics Committee

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This trial is the first to examine the (cost-)effectiveness of an innovative perceived injustice-targeted intervention in the cancer population.
⇒ A multicentre study including both university and peripheral hospitals.
⇒ Comparison of balanced treatment arms.
⇒ A blended intervention with patient-centred disease management.
⇒ Due to the innovative nature of this study, results will not be easily compared with other study trials.

INTRODUCTION

Worldwide, the most frequently diagnosed malignancy in women is breast cancer.1 The Global Burden of Disease Cancer Collaboration demonstrated that 2.3 million people were diagnosed with breast cancer in 2020, accounting for 11.7% of all cancer cases.2–5 Due to improved screening and treatment methods, survival rates have increased to 90.0% 5 years after diagnosis in high-income countries.1,5 Since the number of survivors is increasing, new long-term symptoms are emerging after treatment.6 After fatigue, pain is the most frequent treatment-related debilitating morbidity.7 The prevalence of persistent pain is 29.8% post surgery, 27.3% postradiotherapy and 21.8% after receiving various combinations of breast...
cancer treatment. This high prevalence is of considerable concern since pain not only impacts the quality of life but also prevents the reuptake of activities, leading to a huge socioeconomic burden. In 22% of breast cancer survivors (BCSs) with pain, feelings of injustice are reported.

Perceived injustice has been conceptualised as a multidimensional appraisal process characterised by a tendency to interpret one’s losses as severe and irreparable, to attribute blame to others for one’s suffering and to experience a sense of unfairness (eg, someone who survived breast cancer but has to deal with pain afterwards). Perceived injustice inherently presumes a discrepancy between expected and actual outcomes, which may lead to feelings of anger, frustration or other forms of emotional distress. Perceived injustice is also associated with increased opioid prescription and predicts opioid use at 1 year, urging the need for targeted interventions diminishing perceived injustice. Individuals who view their pain as unjust may display more pain behaviour by an intense communication of their suffering and losses increasing the likelihood of being prescribed opioids.

Perceived injustice is related to lower quality of life, and perceived injustice rather than pain catastrophising mediates the relationship between pain and quality of life in BCSs. Moreover, perceived injustice is an important mediator in the relationship of pain on fatigue and sleep. The mediating effect of perceived injustice with quality of life, sleep and fatigue among BCSs shows that perceived injustice is not only understudied but also underappreciated and undertreated. Therefore, it might be important to incorporate perceived injustice as a treatment target in the rehabilitation of BCSs. Literature suggests the use of cognitive-behaviour interventions, pain acceptance and educational interventions comprising elements of reassurance and encouragement towards activity re-engagement. One such intervention is pain neuroscience education (PNE).

PNE is an intervention primarily aiming at changing illness perceptions of patients with pain. During this education, easy-to-understand pain neurophysiology examples (central sensitisation) and metaphors are used and adapted to the patient. PNE covers topics such as acute versus chronic pain, the purpose of acute pain, the origins of acute pain, the transition to chronic pain and potential factors that sustain chronic pain, explained from a biopsychosocial view rather than a pure patho-anatomical output, and as a consequence, patients’ illness perceptions also change to the biopsychosocial perspective. Previous single-arm studies using PNE in BCSs showed positive results on central sensitisation symptoms and pain-related function and quality of life, whereas results in a large randomised controlled trial comparing PNE combined with physical activity with biomedically focused education did not find any significant differences in different pain-related outcomes. However, the latter trial was conducted in BCSs who were not preselected for having significant pain, which might explain the absence of an added value of the respective PNE-based intervention. Moreover, all these previously conducted studies providing PNE to BCSs did not yet account for perceived injustice, which seems an important construct to target in people having feelings of injustice.

In addition to targeting perceived injustice during PNE, motivational interviewing can be used as a communication strategy throughout PNE to obtain behavioural change. Motivational interviewing is a directive, collaborative, patient-centred communication approach for eliciting and enhancing motivation for behavioural change by helping patients resolve ambivalence and uncertainty. Especially in people with perceived injustice, motivational interviewing techniques can be useful to shift the focus from that feeling of injustice to working on valuable life goals, changing their pain-related coping.

Therefore, an innovative treatment, including PNE, focused on perceived injustice with the integration of motivational interviewing in BCSs with pain and perceived injustice. The primary objective of this study is to examine whether perceived injustice-targeted PNE is superior to biomedically focused pain education in reducing pain after 12 months in BCSs with perceived injustice and pain. The secondary objectives are to examine whether perceived injustice-targeted PNE results in improved quality of life and reduced perceived injustice and opioid use and can be found to be cost-effective as compared with biomedically focused pain education at 12 months of follow-up. The aforementioned objectives will lead to recommendations concerning the use of perceived injustice-targeted PNE combined with motivational interviewing in clinical practice. This is a protocol for a multicentre randomised controlled clinical trial with balanced treatment arms, 4 weeks of intervention and 0, 12 and 24 months of follow-up conducted in BCSs with perceived injustice and pain.

**METHODS AND ANALYSIS**

This protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials recommendations and was registered prior to recruitment on ClinicalTrials.gov: NCT04730134. All items from the WHO Trial Registration Data Set can be found in online supplemental appendix I and all protocol versions in online supplemental appendix 2.

**Study design and study setting**

This is a multicentre randomised controlled trial with two balanced treatment arms and with blinding of assessors and investigators. The trial is spread over five different hospitals in Flanders, Belgium (online supplemental appendix 3).

**Eligibility criteria**

To be eligible, participants must fulfil the definition of survivorship introduced by the European Organisation for Research and Treatment of Cancer (EORTC).
Survivorship Task Force, in which a cancer survivor is as follows: any person who has been diagnosed with cancer, has completed his or her primary treatment (with the exception of maintenance therapy) and has no evidence of active disease.33 Additionally, participants need to:
1. be women aged ≥18 years;
2. be in complete remission and should have finished their primary breast cancer treatment with curative intent ≥3 months (adjuvant hormonal therapy and immunotherapy are tolerated);
3. report a pain severity of ≥3/10 on the Brief Pain Inventory (BPI);
4. be able to speak and read Dutch;
5. show a level of perceived injustice of ≥17/48 on the Injustice Experience Questionnaire (IEQ).
Participants will be excluded if they:
1. are diagnosed with new neoplasms or metastases;
2. have a chronic disease which is not well controlled and/or is causing pain (eg, fibromyalgia and rheumatoid arthritis);
3. are suffering from a severe psychological/psychiatric disease;
4. are suffering from dementia or cognitive impairment (unable to understand instructions and/or ≤11/28 on the Six-item Cognitive Impairment Test (6-item CIT));34,35
5. recently started a new treatment/training which is not yet at a stable level.
To facilitate participant recruitment and optimise the external validity of the study findings, assessments will take place at five different hospitals in Belgium (online supplemental appendix 3). Additionally, pharmacies, patient support groups, occupational health services, social media and advertisements in local newspapers will be used as recruitment strategies. The initial screening of interested participants will be executed by independent investigators at the hospitals or by phone. After this short screening, an online questionnaire (±5 min) will be sent to the participant to define the BPI pain severity score and the total IEQ score. Eligible patients will be asked to provide written informed consent (online supplemental appendix 4). With this consent, participants agree to keep appointments for treatment sessions, not to initiate any new treatment/medication from the moment they are contacted by phone for study inclusion until 3 months after the intervention or to participate in any other medical-scientific study during participation.

**Interventions**

To balance non-specific treatment effects, the duration, format, number of sessions and didactical approach will be identical in both treatment groups (see structured description of treatments in [table 1](#)). All participants will receive an online session (±1 hour) followed by three individual one-to-one sessions (±45 min), allowing them to individually tailor the sessions. After each session, all participants will be asked to report the content of the session in a personal logbook and to report co-interventions, medical consumption (eg, the type, dose, method of administration and frequency of medication) and any other healthcare visits and interventions. The one-to-one sessions are provided by trained physiotherapists at the study site of the participant’s preference and will be spread over a 4-week period.

**Treatment development and training**

The treatment manuals, including the pre-recorded sessions, were developed before study initiation. The perceived injustice-targeted PNE and motivational interviewing manual were developed by combining research and the input of clinical experts in the field of PNE, perceived injustice and motivational interviewing. The biomedically focused pain education was developed by research experts in the field of breast cancer.

The training of the physiotherapist will be done by one of the developers of the manuals. Both trainings consist of a minimum of two contact moments of ±2 hours spread over ±3 weeks. The physiotherapists will be selected based on their experience and/or interest in working with cancer survivors. Moreover, experience with one of the two types of education provided in the trial was screened in advance in order to control for contamination (eg, a therapist with experience providing PNE cannot provide biomedically focused pain education).

**Experimental treatment: perceived injustice-targeted PNE + motivational interviewing**

The first online pre-recorded PNE session focuses on a better understanding of post-cancer pain prior to the first one-to-one session. The primary focus of the treatment plan is to shift maladaptive pain behaviour to beneficial pain behaviour. Therefore, the mechanisms underlying pain will be explained to clarify the rationale for changing. Perceived injustice will be introduced as a contributing factor for pain and central nervous system sensitisation. This can serve as a first step in accepting their condition and the associated suffering and should ease talking about perceived injustice during the next session. The content will be based on the books ‘Explain Pain’ and ‘Pijneducatie, een praktische handleiding voor para-mediici’ as previously used in other chronic pain populations36,37 but adapted to BCSs.38 The information will be presented in different ways by using pictures, examples and metaphors.22 At the end of the first session, participants will have to read the perceived injustice-targeted PNE information leaflet summarising the information of the online session. Since an important portion of BCSs reports impairments in attention due to the so-called ‘chemo brain’,39 40 it will be valuable to have additional written information as well as the recorded session at the participant’s disposal to minimise the impact of loss of concentration.

Therapists will start the first one-to-one PNE session by discussing the participant’s responses to the online questionnaires, as well as their experience and questions regarding the online PNE session and the information
## Table 1  Overview of the content of the sessions in both intervention groups

<table>
<thead>
<tr>
<th>Perceived injustice-targeted PNE + MI</th>
<th>Session (duration)</th>
<th>Biomedically-focused pain education</th>
</tr>
</thead>
<tbody>
<tr>
<td>► PNE adapted to BCSs discussing:</td>
<td>Online session</td>
<td>► Differences between the characteristics of nociceptive pain, neuropathic pain and central sensitisation</td>
</tr>
<tr>
<td>- Pain as a fire alarm</td>
<td>(1 hour)</td>
<td>- Pain as a fire alarm</td>
</tr>
<tr>
<td>- Characteristics of acute versus chronic pain</td>
<td></td>
<td>- Characteristics of acute versus chronic pain</td>
</tr>
<tr>
<td>- How does acute pain arise in the nervous system?</td>
<td></td>
<td>- Oncological causes of pain after breast cancer: (1) cancer itself/metastases from it resulting in nerve pain, bone pain or oncological ulcer or (2) the cancer treatment (radiotherapy, surgery/operation, chemotherapy, hormone therapy and general consequences of cancer treatment)</td>
</tr>
<tr>
<td>- How does pain become chronic?</td>
<td></td>
<td>► Introduction to the logbook + questions to prepare at home:</td>
</tr>
<tr>
<td>- Explaining the importance of long-term instead of short-term treatment options</td>
<td></td>
<td>- ‘Which symptoms do you recognise in yourself per treatment that we have discussed?’</td>
</tr>
<tr>
<td>► Introduction of perceived injustice as a possible sustaining factor for pain and central nervous system sensitisation</td>
<td></td>
<td>- ‘Do you have any other symptoms that cause you pain?’</td>
</tr>
<tr>
<td>► Introduction to the logbook + change talk questions to prepare at home:</td>
<td></td>
<td>- ‘How did you feel about pain before the online session?’</td>
</tr>
<tr>
<td>- ‘What would you like to see different in your current situation?’</td>
<td></td>
<td>- ‘What has changed about the way you look at your pain after watching the online session?’</td>
</tr>
<tr>
<td>- ‘Why do you think you need to change?’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ‘What will happen if you don’t change?’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ‘What will have changed when you complete this treatment programme?’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ‘What would be the benefits of changing the way you deal with the pain?’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ‘What would your life be like in 3 years if you changed your way of dealing with the pain?’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ‘Why do you think others are concerned about your pain experience?’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>► Summary of the online PNE session</td>
<td>Information leaflet</td>
<td>► Summary of the online biomedically-focused pain education session</td>
</tr>
<tr>
<td>► Completing the anamnesis in addition to the biopsychosocial baseline assessments</td>
<td>1st one-to-one session (45 min)</td>
<td>► Completing the anamnesis in addition to the biomedical baseline assessments</td>
</tr>
<tr>
<td>► Discussing the online PNE (short recapitulation) and information leaflet to define the behavioural stage of change of the participant</td>
<td></td>
<td>► Discussing responses to the online education and information leaflet</td>
</tr>
<tr>
<td>► Using MI based on the phase of behavioural change</td>
<td></td>
<td>► Discussing the relationship between the treatment, symptoms and limitations in daily life</td>
</tr>
<tr>
<td>► Defining and discussing sustaining factors for pain such as perceived injustice, anger, (pain) acceptance and frustrations</td>
<td></td>
<td>► Types of pain medication based on the WHO classification and side effects</td>
</tr>
<tr>
<td>► Reviewing the logbook</td>
<td></td>
<td>► Reviewing the logbook</td>
</tr>
<tr>
<td>► Continuing motivational interviewing based on the phase of behavioural change</td>
<td>2nd one-to-one session (45 min)</td>
<td>► Discussing other treatment possibilities instead of pain medication</td>
</tr>
<tr>
<td>► Defining life goals and restarting valued occupations by improving the predefined sustaining factors for pain and central sensitisation</td>
<td></td>
<td>► Defining goals to overcome the tissue damage to improve symptoms and limitations in daily life</td>
</tr>
<tr>
<td>► Reviewing the logbook</td>
<td></td>
<td>► Reviewing the logbook</td>
</tr>
</tbody>
</table>

Continued
leaflet. This information will be used to situate the participant within the phases of behavioural change, as well as to define perpetuating factors (e.g., acceptance and opioid use) to start an individually tailored treatment. The practical guideline accounting for perceived injustice in cancer survivors will be used.31 Both valued life goals and treatment goals will be set within a shared decision-making process.

The second and third one-to-one PNE sessions will consist of individually tailored PNE based on the participant’s stage of change. The (perceived injustice-targeted PNE and motivational interviewing will aim at encouraging participants in pursuing life goals again and restart valued occupations while experiencing pain by eliminating the feeling of wanting to control or avoid pain.45–47 In addition, pain acceptance will be addressed by broadening their understanding of their pain problem, including discussing the possible pain-aggravating role of anger and frustration. During the communication, following motivational interviewing principles, the therapist is supportive, empathetic, positive and hopeful and relies on the therapeutic alliance to assist in changing certain health behaviours based on the person’s internal thoughts such as perceived injustice, decisions and motivation. Motivational interviewing also aims to strengthen personal commitment by respecting the individual’s autonomy and assists in reaching a specific goal by exploring personal intentions or reasons for change.29–30

### Active comparator: biomedically focused pain education

The first online pre-recorded biomedically focused pain education session will contain information about the different types of pain (nociceptive pain, neuropathic pain and nociplastic pain) and how oncological treatment methods, such as surgery, chemotherapy, radiotherapy and hormone therapy, are able to provoke pain with a primary focus on structural tissue damage. The role of different structures and injured versus healthy tissue in acute and persistent pain will be discussed. Pain will be explained from a biomedical perspective (e.g., injured tissues causing pain) and a biomechanical point of view (e.g., pain is explained as deviation from, e.g., normal expected movement patterns and postures). At the end of the first session, participants will have to read the information leaflet from Stand Up to Cancer regarding ‘Pain in and after treatment’ summarising the information provided during the online session. The use of the leaflet within the study has been approved by Stand Up to Cancer.

During the first one-to-one session, participants’ responses to the online questionnaires and the participant’s experience will be discussed and questions regarding the online education module and the information leaflet will be discussed at the beginning of this session. After this, participants will receive accurate information about pain medication (e.g., indication of use and adverse effects), if relevant, based on the cancer pain management proposed by WHO (World Health Organization).32

During the second one-to-one session, additional questions that arose after reading the information leaflet will be addressed. Second, additional pain treatment methods are explained, such as specialised techniques for nerve pain (e.g., transcutaneous electrical nerve stimulation) and others (e.g., physical activity). Therefore, participants will receive advice, including concluding treatment options, on how to deal with their pain. Goals will be set from a biomedical point of view.

The third one-to-one session will be used to support self-management. The latter will adhere to current evidence practice guidelines43–45 including advice on activity self-management (e.g., to stretch muscles, increase their physical activity level gradually and tips regarding nutrition).

### Outcome measures

The primary outcome is pain severity. The secondary outcomes are health-related quality of life, perceived injustice and outcomes for a cost-utility analysis. Sleep, fatigue, pain cognitions, depression, anger, acceptance, treatment adherence and compliance, and co-interventions will be added as explanatory outcomes. The outcomes are all self-reported questionnaires and based on the Dutch Oncoline recommendations and on previous studies performed in cancer46–54 and non-cancer pain populations.55–61 An overview of the assessments is presented in Table 2. Assessments will be performed online at the following timepoints:

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Overview of the content of the sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perceived injustice-targeted PNE + MI</td>
<td>Session (duration)</td>
</tr>
<tr>
<td>● Further defining life goals and restarting valued occupations</td>
<td>3rd one-to-one session (45 min)</td>
</tr>
<tr>
<td>● Supporting self-management based on motivational interviewing techniques in the planning phase</td>
<td></td>
</tr>
<tr>
<td>● Reviewing the logbook</td>
<td></td>
</tr>
</tbody>
</table>

BCSs, breast cancer survivors; MI, motivational interviewing; min, minutes; PNE, pain neuroscience education; WHO, World Health Organization.

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Table 2  Study outcome measures by assessment time point

<table>
<thead>
<tr>
<th></th>
<th>Assessment tools</th>
<th>T₀ baseline assessments</th>
<th>T₁ 0 months of follow-up</th>
<th>T₂ 6 months of follow-up</th>
<th>T₃ 12 months of follow-up</th>
<th>T₄ 24 months of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>BPI</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR-QoL</td>
<td>EORTC-QLQ-C30</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Perceived injustice</td>
<td>IEQ</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Outcomes for cost-effectiveness analysis</td>
<td>MCQ</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>PCQ</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>EQ-5D-5L</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td><strong>Explanatory outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain phenotyping</td>
<td>CSI</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>7-item DN-4</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Sleep</td>
<td>PSQI</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>ISI</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Fatigue</td>
<td>FSS</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Pain cognitions</td>
<td>PCS</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>Brief IPQ-DLV</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>PVAQ</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Depression, anxiety and stress</td>
<td>DASS-21</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Anger</td>
<td>STAXI-II</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Acceptance</td>
<td>AAQ-II</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Treatment adherence and compliance</td>
<td>Logbook</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Co-interventions</td>
<td>Logbook</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

AAQ-II, Acceptance and Action Questionnaire-II; BPI, Brief Pain Inventory; Brief IPQ-DLV, Brief Illness Perception Questionnaire Dutch Language Version; CSI, Central Sensitisation Inventory; DASS-21, Depression Anxiety Stress Scale 21 items; 7-item DN-4, 7-item Douleur Neuropathique-4; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire; EQ-5D, EuroQol 5D instrument; FSS, Fatigue Severity Scale; IEQ, Injustice Experience Questionnaire; ISI, Insomnia Severity Index; MCQ, Medical Consumption Questionnaire; PCQ, Productivity Cost Questionnaire; PCS, Pain Catastrophizing Scale; PSQI, Pittsburgh Sleep Quality Index; PVAQ, Pain Vigilance and Awareness questionnaire; STAXI-II, State-Trait Anger Expression Inventory—II.
► $T_0$: within the week before the randomisation and the intervention (baseline)
► $T_1$: immediately after intervention
► $T_2$: 6 months after intervention
► $T_3$: 12 months after intervention (primary endpoint)
► $T_4$: 24 months after interventions (extended endpoint)

Personal characteristics
Personal characteristics including date of birth, nationality, race/ethnicity, level of education, professional situation, family income, relationship status, physical activity, smoking status, alcohol consumption, body mass index, comorbidities, lymphoedema, type of breast cancer treatments received, time since onset of complaints, time since complement of breast cancer treatment and treatment expectations will be collected at baseline.

Primary outcome: pain
BPI is developed by the Pain Research Group of the WHO Collaborating Centre for Symptom Evaluation in Cancer Care. It is a 14-item self-reported questionnaire assessing worst pain, pain severity and pain interference in patients over the past week on a scale of 0 to 10. Pain interference is measured as the average of the seven interference items. BPI is the most common, reliable and valid outcome measure to assess pain in cancer survivors (Cronbach’s alpha and test-retest reliability score >0.80).

Secondary outcome measure: quality of life
Health-related quality of life is an established prognostic indicator of breast cancer. The EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30) is a 30-item cancer-specific questionnaire developed for the assessment of the quality of life in patients with cancer. The EORTC QLQ-C30 is widely used in cancer studies, has been translated and validated in Dutch and shows acceptable psychometric properties. The internal consistency measured by Cronbach’s alpha resulted in 0.94.

Secondary outcome measure: perceived injustice
The 12-item IEQ will be used to assess perceived injustice. Participants must rate the frequency of 12 different pain-related statements on a 5-point Likert scale ranging from 0 (not at all) to 4 (all the time). The sum of all items gives the total score which ranges from 0 to 48. The higher the score on the IEQ, the higher the level of perceived injustice. A cut-off value of 17 was calculated by taking the 75th percentile, which suggests a clinically relevant degree of perceived injustice in BCS. The IEQ has good (test-retest) reliability (ICC=0.86–0.87) in its Dutch version. The scores derived from the IEQ are found to be valid with an excellent internal consistency in advanced cancer.

Secondary outcome measures for cost-effectiveness analysis
A cost-effectiveness analysis will be conducted following the manual by Hakkart-Van Roijen et al. Healthcare use (including co-interventions) will be assessed using the Medical Consumption Questionnaire (MCQ). This is a well-established, generic, instrument-to-measure total (in-)direct medical consumption. Indirect costs will include costs related to productivity loss. These will be assessed using the Productivity Cost Questionnaire (PCQ). Both questionnaires are easy to use and able to generate valid data. In accordance with their user manuals, the questionnaires will be modified to match the respective setting.

Health-state utilities will be obtained from the EuroQol 5D-5L and will be used to calculate quality-adjusted life years (QALY). The EQ-5D-5L items are scored on a 5-point Likert scale for five different dimensions. The EQ-5D-5L is a reliable and valid measurement tool for the evaluation of overall health in breast cancer. Moreover, Belgian population norms are available for the EQ-5D-5L. The use of the latter three tools is recommended by the Institute for Medical Technology Assessment, Erasmus University Rotterdam.

Explanatory outcomes
A detailed overview of several explanatory outcomes which all have been proven to be related to the development of chronic pain can be found in table 3.

Treatment fidelity
Fidelity criteria will be developed before the start of the interventions. Independent investigators, experienced with the treatment, will evaluate a random selection of the tapes of each therapist using the fidelity criteria to score the audiotapes of the treatment sessions provided.

Patient and public involvement
One of the biggest Belgian Cancer charities, Kom tegen Kanker, reviewed all parts of the trial, including the design, management and conduct of the trial. We received input from their experience with patients who survived breast cancer. We carefully assessed the burden of the trial interventions on patients. We intend to disseminate the main results to trial participants and will seek patient and public involvement in the development of an appropriate method of dissemination.

Sample size calculation
Sample size calculations were performed with G*Power 3.1.3 for between-group differences (t test) at 12 months of follow-up. The sample size calculation was based on an earlier trial regarding a conservative intervention for treating pain in BCS that had the same primary outcome (eg, BPI) and identical 12-month follow-up. Based on that earlier trial and calculation methods described by Lakens, the effect size was set to 0.44, based on an observed difference of 1.8 on BPI and a CI between 0.9 and 2.6 for 85 participants. The type I error was set to 0.05 and the type II error to 0.2. The resulting sample size for a one-sided test was 65 per treatment arm. Accounting for a risk of loss to follow-up of 20%, a total sample size of 156 participants is needed.
### Table 3 The explanatory outcomes with their measurement tool(s)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Measurement tool(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain phenotyping</strong></td>
<td>Central sensitisation inventory (CSI): is a questionnaire evaluating symptoms of central sensitisation. The CSI score ranges from 0 to 100, with higher scores indicating increased symptom frequency/severity. The cut-off score of 40 or higher on the CSI indicates the presence of a clinically relevant level of symptoms of central sensitisation. The Dutch CSI has excellent test-retest reliability and showed good clinical properties in chronic pain populations. The 7-item Douleur Neuropatique-4 (7-item DN-4): is a questionnaire to discriminate neuropathic pain from nociceptive pain. The 7-item DN-4 questionnaire is on the first 7 items of the 10-item DN-4 questionnaire. The items are related to the quality of pain (burning, painful cold and electric shocks) and their association with abnormal sensations (tingling, pins and needles, numbness and itching). Each item is scored as 0 (no) or 1 (yes). A total score of ≥4/7 is indicative of the presence of dominant neuropathic pain. The Dutch version of the DN-4 is valid and reliable.</td>
</tr>
<tr>
<td><strong>Sleep</strong></td>
<td>Pittsburgh Sleep Quality Index (PSQI): is a self-rated questionnaire to measure sleep quality and disturbance over 1 month. It is based on 19 items which generate a global score, ranging between 0 and 21, and 7 component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. Scores above 5 signify a poor sleeper. It is a reliable and valid measurement tool, and internal consistency is acceptable in patients with breast cancer (Cronbach’s alpha=0.80). Insomnia Severity Index (ISI): is a questionnaire to detect cases of insomnia and assess the insomnia severity of both nighttime and daytime components of insomnia. It is based on 7 items measured on a 5-point Likert scale (0–4) which generates a total score ranging from 0 (no insomnia) to 28 (great insomnia severity). The cut-off score of 10 is optimal for detecting insomnia cases, and a change score of -8.4 points is associated with moderate improvement. ISI is a valid and reliable instrument in patients with cancer. The Fatigue Severity Scale (FSS): is used to evaluate global fatigue severity in a number of chronic medical conditions such as palliative cancer. It is a short questionnaire with 9 items and the total score ranges between 9 (no fatigue) and 63 (maximum fatigue). The FSS is a reliable and valid measurement in patients with cancer. The Dutch score has an adequate concurrent validity of r=0.65. The Internal consistency of the FSS is excellent (Cronbach’s alpha=0.96).</td>
</tr>
<tr>
<td><strong>Fatigue</strong></td>
<td>Fatigue Severity Scale (FSS): is used to evaluate global fatigue severity in a number of chronic medical conditions such as palliative cancer. It is a short questionnaire with 9 items and the total score ranges between 9 (no fatigue) and 63 (maximum fatigue). The FSS is a reliable and valid measurement in patients with cancer. The Dutch score has an adequate concurrent validity of r=0.65. The Internal consistency of the FSS is excellent (Cronbach’s alpha=0.96).</td>
</tr>
<tr>
<td><strong>Pain cognitions</strong></td>
<td>Pain Catastrophising Scale (PCS): is a self-reported questionnaire to assess catastrophic thoughts or feelings accompanying experienced pain. It is a 13-item measure that evaluates 3 subscales of catastrophising: ruminative, magnification and helplessness on a 5-point Likert scale. This scale ranges from 0 (not at all) to 4 (all the time) with a total score between 0 and 52. The PCS factor scales are valid and reliable. Brief Illness Perception Questionnaire-Dutch Language Version (Brief IPQ-DLV): measures five illness perceptions and consists of 9 items. 5 items assess cognitive illness (consequences, personal control, treatment control and identity), 2 items assess emotional perceptions (concern and emotions), 1 item assesses illness comprehensibility and 1 item assesses causal perception. The first 8 items are rated on a 10-point Likert scale and the 9th item is rated on an open-ended question which asks to list the 3 most important causal factors of the illness. The Brief IPQ-DLV has acceptable psychometric properties. Pain Vigilance and Awareness Questionnaire (PVAQ): consists of 16 items that assess attention to (changes in) pain. The frequency of experience of each item is rated on a 6-point Likert scale ranging from 0 (never) to 5 (always) with a total score between 0 and 90. The higher the score, the more suggestive of a higher degree of vigilance and awareness to pain. The PVAQ is a reliable and valid measurement in chronic patients.</td>
</tr>
<tr>
<td><strong>Depression, anxiety and stress</strong></td>
<td>Depression, Anxiety, Stress Scale 21 items (DASS-21): is an instrument that is used to assess anxiety and depression. 21 items are subdivided into 3 categories: depression (7 items), anxiety (7 items) and stress (7 items). Each item is scored on a 4-point Likert scale ranging from 0 (not at all) to 3 (most of the time). The higher the item score, the more severe the symptom of psychological distress. The total score, used for the interpretation, is the sum of all items multiplied by 2. The DASS-21 is a valid and reliable assessment tool for patients with cancer.</td>
</tr>
<tr>
<td><strong>Anger</strong></td>
<td>State-Trait Anger Expression Inventory-II (STAXI-II): is a self-reported 57-item questionnaire that assesses the level and frequency of anger experience, expression and control. It consists of three parts: (a) how angry the examinee currently feels, (b) how angry the examinee generally feels and (c) how the examinee reacts when angry. Every item in each subscale is assessed on a 4-point Likert scale. The validity and reliability of the STAXI-II questionnaire are acceptable.</td>
</tr>
</tbody>
</table>

Continued
Table 3 Continued

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Measurement tool(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptance</td>
<td>Acceptance and Action Questionnaire-II (AAQ-II):111 is a self-reported 7-item questionnaire that assesses the amount of acceptance and experiential avoidance, or its opposite, psychological flexibility.112 Every item is a statement that is scored on a 7-point Likert scale in which one can indicate to what extent these are applicable.111 The higher the total score, the lower the acceptance and the higher the experiential avoidance.111 The psychometric qualities of the Dutch translation of the AAQ-II are good with an internal reliability of 0.87 and a construct validity of −0.67 to −0.79 for oppression and psychological symptoms.113</td>
</tr>
</tbody>
</table>

Treatment adherence and compliance

Patients’ attendance at treatment sessions will be recorded. Patient adherence for the treatment sessions will be calculated as the ratio of the number of treatment sessions that were carried out versus the number of prescribed sessions. For the home sessions (incl. working with the information leaflet), patients will be asked to record the session’s content in a personal logbook. Treatment adherence will be calculated as a ratio of the number of sessions that were carried out at home versus the total number of prescribed home sessions. Patient drop-out and the reason for withdrawal will be registered.

Co-interventions

Co-interventions will be closely monitored. Medical consumption, including the type, dose, method of administration and frequency of medication, as well as any other interventions, will be recorded.

AAQ-II, Acceptance and Action Questionnaire-II; BPI, Brief Pain Inventory; CSI, Central Sensitisation Inventory; DASS-21, Depression Anxiety Stress Scale 21 items; 7-item DN-4, 7-item Douleur Neuropathique-4; FSS, Fatigue Severity Scale; Brief IPO-DLV, Brief Illness Perception Questionnaire-Dutch Language Version; ISI, Insomnia Severity Index; PCS, Pain Catastrophising Scale; PSQI, Pittsburgh Sleep Quality Index; PVAQ, Pain Vigilance and Awareness Questionnaire; STAXI-II, State-Trait Anger Expression Inventory-II.

Treatment allocation

Randomisation (figure 1) will be done separately for each treatment centre by an independent researcher. Randomisation occurs using a computer-generated random number sequence (developed by Gerard E Dallal, PhD—http://www.randomization.com). A list with participant numbers and the group allocation that results from this randomisation procedure will be stored on a private SharePoint which is only accessible by the independent researcher. Participants will be scheduled by the therapists to receive their first assessment within 1 week of randomisation.

Blinding

Due to the nature of the intervention, blinding participants to the content of the intervention is impossible. However, participants will not be informed about whether they received the experimental or control intervention. The statistician will be blinded to group allocation. All outcome measures are self-reported and eventual queries...
concerning the questionnaires will be addressed by a blinded independent assessor. The interventions will take place at different times during the day so that participants of different intervention groups do not meet and between-group contamination is avoided.

**Data collection, data management and confidentiality**

All questionnaires will be processed in an online software program REDCap.83 REDCap is General Data Protection Regulation compliant. Data, both numeric and textual, filled in by the participants online will be saved automatically. Encrypted identifiers (ie, *a unique pseudonymised participant ID*) will be used to separate the personally identifiable information from the clinical data. This link will be stored securely in REDCap. Clinical data will be saved under the pseudonymised participant ID. REDCap will be used for data storage, management and processing. Additionally, data will be stored on an encryption and password-secured Institutional SharePoint with sufficient storage space and limited access to the research team trained in human subject protection. Confidential individually identifiable data, including the pseudonymisation key, will be stored in a separate folder. Long-term data preservation will be done in the Vrije Universiteit Brussel University Archive.

To avoid loss to follow-up, REDCap automatically sends follow-up assessments and a reminder in case of no response for each endpoint. In addition, participants will be contacted by telephone and/or get reminders by email to complete all assessments.

**Statistical analysis**

A linear mixed model for repeated measures will be used to evaluate treatment effects over time in terms of pain, health-related quality of life, perceived injustice and opioid use. Such analysis allows more precise parameter estimates and can handle missing data. The baseline value of the outcome, explanatory outcomes (table 3), medication use and demographics will be considered covariates. Statistical and clinically significant differences will be defined, and the effect size will be determined. In addition, the numbers needed to treat will be calculated.

QALY’s (health effect) for the cost-effectiveness analysis will be calculated from utility scores derived from the EQ-5D-5L using Belgian population norms.78 Both direct healthcare costs (calculated based on the information gained from the MCQ) and indirect costs (productivity loss costs calculated based on the information gained from the PCQ)84 will be determined. Healthcare use will be valued using unit reference prices published by RIZIV-INAMI85 86 and BCFI-CBIP.87 All costs will be expressed in euros; indexed using the Health Index for Belgium, if necessary84; and reported in detail in a non-aggregated form. The incremental cost-effectiveness ratio will be calculated, and probabilistic sensitivity analysis will be performed. The impact of methodological choices will be evaluated by scenario analyses. Dissemination of the cost-utility analyses will follow the Consolidated Health Economic Evaluation Reporting Standards.88

**ETHICS AND DISSEMINATION**

**Ethics**

The agreement was obtained by all Ethics Committees, with the University Hospital Brussels as the Main Ethics Committee (B.U.N.143202000068). Every modification will be sent to the Main Ethics Committee for approval. Participants included in the trial will be informed of any important modifications. All participants will provide informed written consent for their voluntary participation. They will always be able to withdraw from the study. No adverse effects are expected since this study includes no risk-involving measurements and treatments. Withdrawing from the study is possible at any time without the necessity to provide a reason for the withdrawal. If one intervention proves to be more effective than the other intervention (after total trial completion), participants will receive access to the most effective intervention. If participants do not properly follow the procedures, they may be withdrawn from the study prematurely.

**Dissemination**

The Consolidated Standards of Reporting Trials guideline89 will be used to report the findings. We will try to improve the knowledge of this topic area among researchers, patients (support groups), professional organisations and healthcare providers through presentations, conferences, social media campaigns, press and publications in journals. The funder will not be involved in or have any influence on the analysis and interpretation of the study results and will not impose any restrictions in terms of the dissemination of the study findings.

**Author affiliations**

1Pain in Motion Research Group (PAIN), Department of Physiotherapy, Human Physiology and Anatomy, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussels, Brussels, Belgium
2REVAL Research Group, Universiteit Hasselt, Diepenbeek, Belgium
3Department of Physical Medicine and Physiotherapy, Universitair Ziekenhuis Brussel, Brussels, Belgium
4Rehabilitation Research Group, Vrije Universiteit Brussel, Brussels, Belgium
5Department of Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium
6Research Foundation-Flanders (FWO), Brussels, Belgium
7Transcare Pain Transdisciplinary Pain Treatment Center, Groningen, Netherlands
8Department of Rehabilitation Sciences and Physiotherapy, University of Antwerp, Antwerpen, Belgium
9Department of Health and Rehabilitation, Unit of Physiotherapy, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

**Contributors** JN was involved in all aspects of protocol design. PW, RB, LL, DB, AT, MDC, AL, EH, ER and KM assisted with the design of the protocol respective to their expertise. EH and DB led the statistical aspects of the protocol. For the design of and training in the interventions, the following authors shared their expertise for specific components: JN, PW, EH and LL. PNE, JN and PW, motivational interviewing; RB, perceived injustice; and LL, biomedically focused pain education. ER was the lead author of the manuscript. All authors critically reviewed the manuscript and approved the final version for submission.

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from the Vrije Universiteit Brussel Chair of the Berekely Academy for Oncological Rehabilitation (JN). These funding sources had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data or decision to disseminate the results.

Competing interests JN and the Vrije Universiteit Brussel received lecturing/teaching fees from various professional associations and educational organisations. JN, PW, LL and EH authored a book on PNE, but the royalties are collected by the Vrije Universiteit Brussel and not them personally.

Patient and public involvement Patients and/or the public were involved in the design, conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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ORCID iDs

Eva Roose http://orcid.org/0000-0001-8720-6543
David Beckwée http://orcid.org/0000-0001-9951-9993
Astrid Lhoussae http://orcid.org/0000-0003-3967-8348

REFERENCES


Roose E, et al. BMJ Open 2024;14:e075779. doi:10.1136/bmjopen-2023-075779

11


50 Lee CF, Ng R, Luo N, et al. The English and Chinese versions of the five-level Euroqol group’s five-dimension questionnaire (EQ-5D) were valid and reliable and provided comparable scores in Asian breast cancer patients. Support Care Cancer 2013;21:201–9.


77 IMTA. The IMTA is a university-based scientific Institute that is distinguished by independent and excellent research in medical technology assessment, including health economics and health outcomes research. n.d. Available: https://www.imta.nl


80 Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for T-tests and Anovas. Front Psychol 2013;4:863.


Prices for reimbursed and non-reimbursed drugs in Belgium, Available: http://www.cbip.be


McCracken LM. What does the acceptance and action questionnaire (AAQ-II) really measure. Behav Ther 2014;45:831-9.

## Appendix 1. Items from the World Health Organization Trial Registration Data Set for the BCS-PI-trial

<table>
<thead>
<tr>
<th>Data category</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary registry and trial identifying number</td>
<td>ClinicalTrial.gov, NCT04730154</td>
</tr>
<tr>
<td>Date of registration in primary registry</td>
<td>28 January, 2021</td>
</tr>
<tr>
<td>Source(s) of monetary or material support</td>
<td>Stand up to Cancer (Kom op Tegen Kanker, project code ANI251)</td>
</tr>
<tr>
<td>Primary sponsor</td>
<td>Vrije Universiteit Brussel</td>
</tr>
<tr>
<td>Secondary sponsor(s)</td>
<td>Universiteit Hasselt</td>
</tr>
<tr>
<td>Contact for public queries</td>
<td>Jo Nijs, Prof. Dr., PT, <a href="mailto:jo.nijs@vub.be">jo.nijs@vub.be</a></td>
</tr>
<tr>
<td>Contact for scientific queries</td>
<td>Jo Nijs, Prof. Dr., PT, <a href="mailto:jo.nijs@vub.be">jo.nijs@vub.be</a></td>
</tr>
<tr>
<td>Public title</td>
<td>The effect of perceived injustice-targeted pain neuroscience education with motivational interviewing compared to biomedically focused education among breast cancer survivors: a study protocol for a multicentred randomized controlled trial (BCS-Pi-trial)</td>
</tr>
<tr>
<td>Overview of study design</td>
<td>A randomized controlled clinical trial with balanced treatment arms, 4 weeks of intervention, and 24 months follow-up</td>
</tr>
<tr>
<td>Countries of recruitment</td>
<td>Belgium</td>
</tr>
<tr>
<td>Study population</td>
<td>Breast cancer survivors experiencing perceived injustice and pain</td>
</tr>
<tr>
<td>Interventions</td>
<td>Perceived injustice-targeted pain neuroscience education + motivational interviewing + Biomedical-focused pain education</td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>1) Women aged 18 years or older.</td>
</tr>
<tr>
<td></td>
<td>2) In complete remission, they should have finished their primary treatment with curative intent at least 3 months before study participation. Adjuvant hormonal therapy and immunotherapy are tolerated.</td>
</tr>
<tr>
<td></td>
<td>3) Report a pain severity of at least 3 to 10 on the Brief Pain Inventory.</td>
</tr>
<tr>
<td></td>
<td>4) Be able to speak and read Dutch to give informed consent and complete the assessment tools.</td>
</tr>
<tr>
<td></td>
<td>5) Show evidence of perceived injustice, defined as ≥17 or higher on the Injustice Experience Questionnaire (IEQ).</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>1) Diagnosed with new neoplasms or metastases.</td>
</tr>
<tr>
<td></td>
<td>2) Not reached the stable level of chronic disease and/or which is causing pain complaints (e.g., fibromyalgia, rheumatoid arthritis).</td>
</tr>
<tr>
<td></td>
<td>3) Suffering from severe psychological or psychiatric diseases.</td>
</tr>
<tr>
<td></td>
<td>4) Suffering from dementia or cognitive impairment (unable to understand the test instructions and/or a result of ≤11, corresponding with MMSE ≤23, on the Six-item Cognitive Impairment Test (6-item CIT), which is a short questionnaire containing 6 items.</td>
</tr>
<tr>
<td></td>
<td>5) Recently started a new therapy which has not yet resulted in a stable level and might interfere with one of the treatments (mentioned below).</td>
</tr>
<tr>
<td>Study type</td>
<td>Interventional</td>
</tr>
<tr>
<td>Allocation</td>
<td>1:1 randomised</td>
</tr>
<tr>
<td>Intervention model</td>
<td>parallel assignment</td>
</tr>
<tr>
<td>Masking</td>
<td>double-blind (outcome assessor, statistician)</td>
</tr>
<tr>
<td>Primary purpose</td>
<td>pain management</td>
</tr>
<tr>
<td>Date of first enrolment</td>
<td>May 2021</td>
</tr>
<tr>
<td>Target sample size</td>
<td>156</td>
</tr>
<tr>
<td>Recruitment status</td>
<td>Recruiting</td>
</tr>
<tr>
<td>Primary outcome(s)</td>
<td>Pain: Brief Pain Inventory</td>
</tr>
<tr>
<td>Key secondary outcomes</td>
<td>Health-related Quality of Life: European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30)</td>
</tr>
<tr>
<td></td>
<td>Perceived injustice: Injustice Experience Questionnaire</td>
</tr>
<tr>
<td>Outcomes for cost-effectiveness analysis</td>
<td>Medical Consumption Questionnaire, Productivity Cost Questionnaire, EuroQol EQ-5D</td>
</tr>
<tr>
<td>Endpoints</td>
<td>T1: immediately after intervention</td>
</tr>
<tr>
<td></td>
<td>T2: 6 months after intervention</td>
</tr>
<tr>
<td></td>
<td>T3: 12 months after intervention (primary endpoint)</td>
</tr>
<tr>
<td></td>
<td>T4: 24 months after interventions (extended endpoint)</td>
</tr>
</tbody>
</table>
Appendix 2. Protocol version history of the BCS-PI-trial

<table>
<thead>
<tr>
<th>Version No.</th>
<th>Approval Date</th>
<th>Lead EC</th>
<th>Adaptations made in the protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>Temporary advice</td>
<td>Original</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>16/12/2020</td>
<td>Original with adaptations of temporarily advice</td>
<td></td>
</tr>
<tr>
<td>Amendment 1 – 2.1</td>
<td>21/01/2021</td>
<td>Addition of ethical committee centre Universiteit Hasselt (Diepenbeek, Belgium)</td>
<td></td>
</tr>
<tr>
<td>Amendment 2 – 2.2</td>
<td>11/02/2021</td>
<td>Addition of ethical committee centre AZ Rivierenland (Bornem, Belgium)</td>
<td></td>
</tr>
<tr>
<td>Amendment 3 – 2.3</td>
<td>11/03/2021</td>
<td>Addition of ethical committee centre Imeldaziekenhuis (Bonheiden, Belgium)</td>
<td></td>
</tr>
<tr>
<td>Amendment 4 – 2.4</td>
<td>29/04/2021</td>
<td>Grammatical corrections New phone number for the BCS-PI-trial Addition of statistics with data at 24 months follow-up Addition of CSI and DN-4 questionnaires to improve patient-tailored pain education</td>
<td></td>
</tr>
<tr>
<td>Amendment 5 – 2.5</td>
<td>27/05/2021</td>
<td>Additional therapist hired</td>
<td></td>
</tr>
<tr>
<td>Amendment 6 – 2.6</td>
<td>24/12/2021</td>
<td>Addition of three new researchers working on the data of the BCS-PI-trial</td>
<td></td>
</tr>
<tr>
<td>Amendment 7 – 2.7</td>
<td>09/11/2022</td>
<td>Update recruitment poster Update sponsor logo Addition of ethical committee centre Ziekenhuis Oost-Limburg (Genk, Belgium) Addition of a therapist hired in the BCS-PI-trial Addition of two new researchers working on the data of the BCS-PI-trial</td>
<td></td>
</tr>
</tbody>
</table>
## Appendix 3. List of study sites of the BCS-PI-trial

<table>
<thead>
<tr>
<th>Ethical committee (EC)</th>
<th>Date of request</th>
<th>Date of approval</th>
<th>Contact details EC</th>
<th>Reference code(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead EC – Commissie medische ethiek UZ Brussel (O.G.016)</td>
<td>06/12/2022</td>
<td>16/12/2020</td>
<td>Laarbeeklaan 101 1090 Jette <a href="mailto:commissie.ethiek@uzbrussel.be">commissie.ethiek@uzbrussel.be</a> +32 24 77 55 84</td>
<td>B.U.N. 1432020000269 2020/399</td>
</tr>
<tr>
<td>Local EC – Comité voor Medische Ethiek UHasselt</td>
<td>06/01/2021</td>
<td>12/01/2021</td>
<td>Agoralaan 3590 Diepenbeek <a href="mailto:CME@uhasselt.be">CME@uhasselt.be</a> +32 11 26 92 45</td>
<td>B.U.N. 1432020000269 2020/399</td>
</tr>
<tr>
<td>Local EC – Ethische commissie AZ Rivierenland (O.G.104)</td>
<td>12/01/2021</td>
<td>03/02/2021</td>
<td><a href="mailto:olivier.opdenakker@azr.be">olivier.opdenakker@azr.be</a> 03 880 90 11</td>
<td>2102CP003</td>
</tr>
<tr>
<td>Local EC – Ethische commissie AZ Imeldaziekehuis</td>
<td>23/02/2021</td>
<td>09/03/2021</td>
<td>Dr. Stijn Gysenbergs / Margit Van Camp + 32 15 50 52 57 / +32 15 50 55 29</td>
<td>Erk. Nr. 689</td>
</tr>
<tr>
<td>Local EC – Comité Medische Ethiek Ziekenhuis Oost-Limburg (ZOL)</td>
<td>21/06/2022</td>
<td>13/01/2023</td>
<td>Ziekenhuis Oost-Limburg Secretariaat Comité Medische Ethiek Synaps Park 1 3600 Genk <a href="mailto:ec.submission@zol.be">ec.submission@zol.be</a> 089 32 15 09 / 089 32 79 00</td>
<td>Z-2022066</td>
</tr>
</tbody>
</table>
Appendix 4. Informed Consent of the BCS-PI-trial

Informatiebrochure voor deelnemers aan het onderzoek

Via deze brochure informeren we u over het wetenschappelijk onderzoek dat het effect van pijneducatie (+ een doorgedreven uitleg over wat pijn is, hoe het komt dat pijn ontstaat, en hoe het komt dat pijn langerdurig aanwezig kan zijn) op emoties zoals boosheid, verdriet en onrechtvaardigheid die gepaard gaan met pijn na borstkanker onderzocht. Het betreft een studie georganiseerd door de Vrije Universiteit Brussel in samenwerking met het UZ Brussel.

Onderstaande informatie heeft tot doel u te informeren en u te helpen beslissen over uw deelname aan dit onderzoek. Indien u vragen heeft betreffende deze informatie, kan u zich wenden tot de personen vermeld onderaan deze brief. Als u beslist om deel te nemen aan dit onderzoek, zal u gevraagd worden een “Toestemmingsoverbrenging” (bijgevoegd bij deze informatiebrochure) te ondertekenen. U mag deze brochure bijhouden zodat u deze in de toekomst nog kan raadplegen.

Welke informatie vindt u in deze informatiebrochure?

1. Waarom willen we dit onderzoek uitvoeren?
2. Wat houdt het onderzoek in en hoe zou het verlopen?
3. Wat betekent het voor u als u meedoet aan het onderzoek?
4. Wat verwachten wij van u als u meedoet?
5. Zijn er risico’s of bijwerkingen?
6. Wanneer stopt het onderzoek?
7. Hoe gaan we om met uw gegevens?
8. Vertrouwelijkheid van uw gegevens?
9. Wat gebeurt er na de meting in mijn gegevens?
10. Toegang tot uw gegevens voor controle?
11. Bent u verzekerd voor letseels ongelopen ten gevolge van dit onderzoek?
12. Wat zijn de kosten of de vergoedingen?
13. Contactpersonen.

Titel van de studie:

Het effect van pijneducatie na kanker

1. Waarom willen we dit onderzoek uitvoeren?

Een groot aantal borstkankeroverlevers (tussen de 21% en 76%) kampen met pijn, wat niet alleen de levenskwaliteit maar ook de heropstart van dagelijkse activiteiten vermindert. Momenteel wordt de inname van pijnmedicatie als de grondstand op gezien door de WHO (Wereldgezondheidsorganisatie) om pijn te verminderen die ontstaat ten gevolge van kankertherapie of door kanker zelf. Dit blijkt echter niet voor iedereen de beste oplossing te zijn aangezien velen hierbij neo-effecten ervaren en pijnklachten vaak hand in hand gaan met emoties zoals boosheid, verdriet en onrechtvaardigheid waarop medicatie niet inspect. Desondanks het feit dat ze vaak worden gezien als onderhoudende factoren. Daarom verkennen we momenteel andere behandelaanvullers.
2. Wat houdt het onderzoek in en hoe zou het verlopen?

Dit onderzoek is een interventieonderzoek, wat een experimentele studie inhoudt, waarbij het effect van een interventie (in dit geval één van beide vormen van pijneducatie) wordt onderzocht. Voor het onderzoek zijn we op zoek naar 156 vrijwillige deelnemers die een verleden hebben van borstkanker en die momenteel kampen met pijn en negatieve emoties ten aanzien van deze pijn. Bij deelnemers wordt uitleg (door loting) toegewezen aan één van de 2 volgende groepen:

- **Biomedische pijneducatie**: een behandelprogramma bestaande uit pijneducatie met een biomedische focus.
- **Neurowetenschappelijke pijneducatie**: een behandelprogramma bestaande uit pijneducatie met een neurowetenschappelijke focus gecombineerd met motiverende gespreksvoering.

U heeft dus 50% kans om in de traditionele of vernieuwde groep terecht te komen. De behandeling in beide groepen start met een online sessie die wordt gevolgd door 3 één-op-één sessies. Na de online sessie wordt u een informatiebrochure opgestuurd met extra toelichting die duidelijk en wetenschappelijk onderbouwd is.

Beide behandelingen worden door een ervaren therapeut gegeven in het UZ Brussel (Jette), AZ Rivierenland (Borinage), Integraalzorgcentrum Borinage of Universiteit Hasselt (campus Siepenbeek). Om de werkingseffecten van de interventies te achterhalen, zowel op korte als op lange termijn, zullen er voor en na de behandelperiode verschillende evaluatiemomenten plaatsvinden. Alle evaluaties bestaan uit online vragenlijsten en gebeuren van thuis uit.

Voor de aanvang van het behandelprogramma zal er nagegaan worden of u geschikt bent voor dit onderzoek. Een lid van het onderzoeksteam zal op basis van een telefonisch gesprek een vaste online vragenlijst van circa 5 minuten nagaan of u voldoet aan al de specifieke in- en exclusievoorwaarden om deel te nemen aan het onderzoek.

Indien u voldoet aan de criteria voor deelneming, zal er een eerste evaluatiemoment plaatsvinden via de online vragenlijsten die u thuis kan invullen. Dit testmoment omvat het invullen van enkele vragenlijsten. Deze gaan over uw emoties en pijn, de impact van die emoties en pijn op uw dagelijks functioneren en levenskwaliteit, uw gezondheidsverzorging en ideeën/ervaringen/overtuigingen die u heeft rond uw pijn. Het invullen van de vragenlijsten zal ongeveer 1 uur en 25 à 10 minuten in beslag nemen en gebeurt van thuis uit. Indien er onduidelijkheden zijn bij het invullen van de vragenlijsten, is er steeds iemand van het onderzoeksteam bereikbaar die u kan contacteren om uw vragen te beantwoorden of u te helpen met het invullen van de vragenlijsten. De contactgegevens van deze persoon zullen u ten gepeste tijden meegedeeld worden.

U zal na de online therapiessessie gedurende 4 weken een behandelprogramma bestaande uit 3 sessies volgen. In de eerste sessie wordt het overlegd of u vragen heeft m.b.t. de vragenlijsten en de online sessie die u reeds gevolgd
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heeft. Er zal dieper worden ingegaan in uw aangewezen manier van pijneducatie. Tijdens de volgende 2 sessies zal hierop verder gewerkt worden. De vragenlijsten worden direct, 6 maanden, 12 maanden en 24 maanden na het behandel programma afgenomen.

3. Wat betekent het voor u als u meedoet aan het onderzoek?
U krijgt een gratis behandel programma voor uw pijn. Het deel van het onderzoek is om na te gaan of er een onderscheid bestaat tussen de effecten van beide behandelprogramma’s die vergeleken worden. Indien één van de behandel programma’s betere resultaten behaalt, zal na afronding van de studie een mail verzonden worden naar alle deelnemers (indien u dit wenst) met daarin de bevindingen van de studie en therapietoebeleidingen naar de toekomst toe. Er wordt een gratis groepsassistance worden voor deelnemers die in de groep belanden met minder goede resultaten. Aan deze deelnemers wordt er via email een datum doorgestuurd voor de groepsassistance en eveneens een lijst met de contactgegevens van ervaren therapeuten.

4. Wat verwachten wij van u als u meedoet?
Voor het welzijn van de studie is het uitermate belangrijk dat u volledig meewerkt met de onderzoeker/behandelend therapeut en dat u de instructies van de onderzoeker/behandelend therapeut nauwkeurig volgt.

Bovendien moet u onderstaande items respecteren:

- Dat u uw afspraken voor bezoeken neemt.
- Dat u geen nieuwe behandeling/medicatie opstart voor uw pijn vanaf het moment dat wij u telefonisch hebben gecoördineerd voor mogelijke studie-inclusie tot 3 maanden na de interventie.
- Dat u niet aan een ander medische-wetenschappelijke onderzoek deelneemt.
- Dat u traint geen extra pijnmedicatie (niet-opioïden: Paracetamol (vb. Daffa, Gan) en NSAID (vb. Nurofen, Ibuprofen) en opladen (vb. buprenorfine, fentanyl, hydromorphan, methadon, morfine, oxycodeon, pirrametamid, tapentadol)) in te nemen vanaf het moment dat wij telefonisch contact met u opnemen (voor deelname) tot aan het toestemming 3 maanden na afronding van het behandelprogramma. Indien dit onmogelijk is, zal u uw pijnmedicatiegebruik gedetailleerder moeten rapporteren in de vragenlijsten.

Uw behandelende arts wordt op de hoogte gebracht van uw deelname aan deze studie, tenzij u dit weigert.

5. Zijn er risico’s of bijwerkingen?
Er worden geen risico’s of bijwerkingen verwacht door deelname aan deze studie. U hebt het recht op elk ogenblik vragen te stellen over de mogelijke risico’s en/of nadelen van dit onderzoek. Indien er gedurende het verloop van het onderzoek een nieuw risico aan het licht komt dat een invloed zou kunnen hebben op de bereidheid om te blijven deelnemen aan dit onderzoek, zult u daarvan op de hoogte worden gebracht.

Deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Éthiek verbonden aan het UZ Brussel en wordt uitgevoerd volgens de richtlijnen voor de goede klinische praktijk en de verklaring van Helsinki opgesteld ter bescherming van mensen deelnemend aan klinische studies. In geen geval dient u de goedkeuring door de Commissie voor Medische Éthiek te beschouwen als een aanzet tot deelname aan deze studie.

6. Wanneer stopt het onderzoek?
De deelname aan dit onderzoek vindt plaats op vrijwillige basis. U kan weigeren om deel te nemen aan het onderzoek en u kan zich op elk ogenblik terugtrekken uit de studie zonder dat u hiervoor een reden moet opgeven en zonder dat dit op enige wijze een invloed zal hebben op uw verdere relatie en/of behandeling met de onderzoeker.

Uw deelname aan deze studie zal worden beëindigd als de onderzoeker/behandelend therapeut meent dat dit in uw belang is. U kan voorzichtig uit de studie worden teruggetrokken als u de in deze informatiebrief beschreven
7. Hoe gaan we om met uw gegevens?

Volgens de nieuwe bijkomende versies van de Europese Algemene Verordening omtrent Gegevensbescherming (AVG), die sinds 25 mei 2018 van kracht zijn, zullen uw persoonsgegevens gebruikt worden. Een van die versten is dat we (het onderzoeksteam) u onderstaande informatie bezorgen voor de verwerking van uw gegevens.

Er worden in het kader van het onderzoek naar waar u deelneemt, persoonsgegevens van u verzameld. Wij, het onderzoeksteam, zijn verantwoordelijk voor de correcte verwerking en de informatie die daarmee gepaard gaat. Daarom vragen wij graag nogmaals uw aandacht voor het feit dat naast gewone persoonsgegevens, zoals gegevens over uw leeftijd en geslacht, ook "bijkomende categoriën” van persoonsgegevens verzameld worden.

Voorbeelden hiervan zijn:
- Uw culturele/ethische achtergrond;
- Uw gezondheidsstoornis en medische aandoeningen, inclusief uw medische voorgeschiedenis;
- Uw behandelingen en uw respons op de behandelingen.

Uiteraard mogen wij uw persoonsgegevens enkel gebruiken voor de wetenschappelijke onderzoekdoeleinden die beschreven staan in het formulier voor geïnformeerde toestemming, zoals door u ondertekend bij het begin van uw deelname aan het onderzoek.

Het kan dat uw gegevens worden ingezien door personen die zich in landen bevinden die op het vlak van wetelijke bescherming van gegevens niet dezelfde normen gebruiken als de EU. In dat geval verbinden wij er ons toe om de voorwaarden van de Europese en de Belgische wetgeving rond de bescherming van persoonsgegevens te respecteren.

Vervolgens geven wij u graag nog mee dat, conform de relevante wetgeving, de gegevens die als deel van het onderzoek verzameld worden gedurende minstens 20 jaar worden bewaard.

Volgens de AVG hebt u een aantal rechten rond de verwerking van uw gegevens. Indien u hierover verdere vragen hebt, kan u Hervormingssteekheven bij het onderzoeksteam (zie contactgegevens hieronder). Ook de functionaris voor gegevensbescherming van het onderzoekscenrum, staat te u beschikking. Hierbij vindt u (zijn) contactgegevens:

Gegevensbeschermingsautoriteit (GBA)
Gravensteen 35
1000 Brussel
Tel. +32 2 274 48 00
E-mail: contact@ord-gbe.be
Website: www.gegevensbeschermingsautoriteit.be

8. Vertrouwelijkheid van uw gegevens.

Om uw privacy te beschermen, krijgen uw gegevens een code. Uw naam en andere gegevens die u direct kunnen identificeren worden daarbij weggelegd. Alleen met de sleutel van de code zijn de gegevens tot u toegankelijk. De sleutel van de code blijft veilig opgeslagen in de lokale onderzoeksinstelling. Als we uw gegevens verwerken, dan gebruiken we alleen de code, maar niet uw naam of andere gegevens waarmee u kunt worden geïdentificeerd. Ook in rapporten en publicaties over het onderzoek zijn de gegevens niet tot u te herleiden.

9. Wat gebeurt er na de metingen met mijn gegevens?

Na afsluiting van deze studie zullen de studieafschriften en de resultaten van de studie gepubliceerd worden in gespecialiseerde medische tijdschriften. Een kopie van de wetenschappelijke publicaties en een begrijpelijke
10. Toegang tot uw gegevens voor controle.

Sommige personen (vertegenwoordigers van de opdrachtgever, auditoren, de commissie voor Medische Ethiek en de bevoegde overheden) hebben rechtstreeks toegang tot uw verzamelde gegevens (ook tot de gegevens zonder code). Dit is nodig om te kunnen controleren of het onderzoek goed en betrouwbaar is uitgevoerd. Zij houden uw gegevens geheim. Door het toestemmingsovertuig, na voorafgaande uitleg, te ondertekenen stemt u in met deze toegang.

11. Bent u verzekerd voor letsel, opgelopen ten gevolge van dit onderzoek?

Indien u schade heeft geleden bij deelname aan deze studie, voorziet de onderzoeker een vergoeding en/of medische behandeling. Voor dit doelinaar is een verzekering afgesloten met foutloze aansprakelijkheid conform de wet inzake experimenten op de menselijke persoon van 7 mei 2004. Op dat ogenblik kunnen uw gegevens doorgegeven worden aan de verzekeraar.

Ethiek
Print-Bisschopssingel 73, 3500 Hasselt
Tel. 011 85 11 11 Fax 011 85 53 10
E-mail: info@ethius.be

12. Wat zijn de kosten of de vergoedingen?

Er zijn voor uw gedeelte geen kosten verbonden aan de deelname aan de studie. U wordt niet betaald voor deelname aan dit onderzoek. Alle deelnemers krijgen een gratis behandelprogramma onder begeleiding van ervaren therapeuten en een gratis informatiefolder over de therapie, hetzij biomedische, hetzij neurowetenschappelijke pijnpredicatie, aangereikt.

13. Contactpersonen:

Als u aanvullende informatie wens over de studie of over uw rechten en plichten, kunt u in de loop van de studie op elk ogenblik contact opnemen met:

Onderzoekssteam:
info@ethius.be
Tel. 011 85 11 11

Onderzoekers:
Drs. Eva Roose
Instituut voor Orthopedie en Traumatologie, KULeuven
Drs. Kenza Mostajir
Instituut voor Orthopedie en Traumatologie, KULeuven

Prof. Dr. Laurence Lefevre
Instituut voor Orthopedie en Traumatologie, KULeuven
Prof. Dr. Anikki Timmermans
Instituut voor Orthopedie en Traumatologie, KULeuven

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Supplemental material

Prof. Dr. Jo Nijs
Jo.Nijs@vub.be

Dr. Eve Huymans
Eve.Huymans@vub.be

Prof. Dr. Paul van Wegen
p.vanWegen@transcare.nl

Drs. Wouter Van Bogaert
Wouter.Timmermans@vub.be

Prof. Dr. Eric De Jonge
eric.dejonge@vub.be

Vrije Universiteit Brussel
Vakgroep KIMA, Rehabilitation Research & Pain in Motion
Medische Campus Jette
Laarbeeklaan 103, 1090 Brussels
Toestemmingsformulier (Informed Consent)

Ik, [naam], heb het document "Informatiebrochure voor deelnemers aan het onderzoek" (Informed consent number 31) geleden van pagina 1 tot en met 6 en er een kopie van gekregen. Ik bevestig met het ondertekenen en dateren van het toestemmingsformulier dat ik instem met de inhoud van de informatiebrochure en dat ik vrijwillig deelneem aan het onderzoek.

☐ Ik bevestig dat ik voldoende werd geïnformeerd over de aard, het doel, de duur en de te voorziene effecten van de studie en wat er precies van me verwacht wordt. Ik heb uitleg gekregen over de mogelijke risico's en voordelen van het onderzoek. Bij onduidelijkheden heb ik de gelegenheid gekregen om aanvullende vragen te stellen en deze werden voldoende beantwoord, ook op medisch vlak.

☐ Ik stem ermee in om volledig samen te werken met het onderzoeksteam. Ik breng hen onmiddellijk op de hoogte als ik mij mogelijks onverwachte of ongebruikelijke symptomen ervarr.

☐ Ik bevestig dat ik op de hoogte ben gebracht van het bestaan van een verzekeringsspolis in het geval er latere(s) zou/den ontstaan door de gegeven therapie.

☐ Ik heb voldoende tijd gekregen om te beslissen of ik bereid was om deel te nemen aan het onderzoek. Ik weet tevreden dat dit volledig vrijwillig is en dat ik mij op ieder moment kan terugtrekken van het onderzoek zonder enige toelichting te geven voor deze beslissing en zonder dat dit op enigerlei wijze een invloed zal hebben op mijn verdere relatie met de onderzoekers.

☐ Ik ben me ervan bewust dat het onderzoek goedgekeurd werd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan het UZ Brussel en dat het onderzoek zal uitgevoerd worden volgens de richtlijnen voor de goede klinische praktijk en de verklaring van Helsinki, opgesteld ter bescherming van mensen deelnemend aan experimenten. Deze goedkeuring was in geen geval om te beslissen om deel te nemen aan het onderzoek.

☐ Ik werd ingelicht dat zowel mijn persoonlijke gegevens als gegevens aangaande mijn gezondheid worden verwerkt en bewaard gedurende minstens 20 jaar. Aangezien deze gegevens verwerkt worden in het kader van medische-wetenschappelijke doeleinden begrijp ik dat de toegang tot mijn gegevens kan uitgesteld worden tot na beëindiging van het onderzoek. Indien ik toegang wenst tot mijn gegevens zal ik mij richten tot de toezichtende ondernemer die verantwoordelijk is voor de verwerking.

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Indien één van de behandelprogramma's betere resultaten behaalt, kan je na afloop van de studie een mail toegestuurd krijgen met de bevindingen van de studie en therapiereacties van de toekomst toe. Er wordt een gratis groepsbegeleiding voor de deelnemers die in de groep met minder goede resultaten werden ingedeeld. Aan deze deelnemers wordt er via e-mail een datum doorgestuurd voor de groepsbegeleiding en eventueel een lijst met de contactgegevens van ervaren therapeuten.

☐ Ik wens de bevindingen van de studie na afloop te ontvangen.
☐ Ik wens de bevindingen van de studie na afloop niet te ontvangen.

Uw behandelende arts wordt op de hoogte gebracht van uw deelname aan deze studie.

☐ Ik wens dat mijn huisarts op de hoogte wordt gebracht van mijn deelname.

Naam + voornaam huisarts: ...................................................................................................................
Adres huisarts: .....................................................................................................................................
Telefoonnummer huisarts: ....................................................................................................................
E-mail huisarts: ....................................................................................................................................

☐ Ik wens dat mijn huisarts niet op de hoogte wordt gebracht van mijn deelname.

Om een kwaliteitscontrole van de behandelsessies te kunnen uitvoeren, zullen alle sessies via audio opgenomen worden mits uw toestemming:

☐ Ik ga akkoord dat alle behandelsessies worden opgenomen via audio.
☐ Ik ga niet akkoord dat alle behandelsessies worden opgenomen via audio.

☐ Ik stem in met de inhoud van het toestemmingsformulier en ben bereid op vrijwillige basis deel te nemen aan deze studie.

Naam van de deelnemer: ......................................................................................................................
Datum (dag/maand/jaar): ....../....../......,
Handtekening:

Ik verklaar hierbij dat ik de deelnemer voldoende heb geïnformeerd over de aard en de te voortrekkende effecten van het onderzoek aan de bovenvermelde deelnemer. De deelnemer stemde toe om deel te nemen door zijn/hun persoonlijk gedateerde handtekening te plaatsen.

Naam van de persoon die voorafgaande uitleg heeft gegeven: ............................................................
Datum (dag/maand/jaar): ....../....../......,
Handtekening:

2
### Appendix 5. Roles and responsibilities in the BCS-PI-trial

<table>
<thead>
<tr>
<th>Roles</th>
<th>Responsible(s)</th>
</tr>
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<tbody>
<tr>
<td>Lead Ethical Comité</td>
<td>Commissie medische ethiek UZ Brussel (O.G.016)</td>
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| Local Ethical Comité             | Comité voor Medische Ethiek Uhasselt  
Ethische commissie AZ Rivierenland (O.G.104) 
Ethische commissie AZ Imeldaziekenhuis 
Comité Medische Ethiek Ziekenhuis Oost-Limburg (ZOL) |
| Principal investigator           | Prof. Dr. Jo Nijs (Pain in Motion Research Group)                            |
| Researcher(s)                    | Drs. Eva Roose (Pain in Motion Research Group & Rehabilitation Research Department & REVAL)  
Drs. Astrid Lahousse (Pain in Motion Research Group & Rehabilitation Research Department)  
Drs. Kenza Mostaqim (Pain in Motion Research Group)  
Prof. dr. Laurent Leysen (Pain in Motion Research Group)  
Prof. dr. David Beckwee (Rehabilitation Research Department)  
Dr. Eva Huysmans (Pain in Motion Research Group)  
Prof. dr. Paul van Wilgen (Transcare Pain Transdisciplinary pain treatment centre)  
Drs. Rinske Buls (Transcare Pain Transdisciplinary pain treatment centre)  
Prof. dr. Marijke De Coo (Odisee University College and Department of Public Health)  
Prof. dr. Annick Timmermans (UHasselt, Fa&uuml;ulteit Revalidatiewetenschappen, REVAL Research) |
| Therapist(s)                     | Drs. Eva Roose (Pain in Motion Research Group & Rehabilitation Research Department)  
Drs. Kenza Mostaqim (Pain in Motion Research Group)  
Thomas Corten (physiotherapist)  
Jitte Van Bavel (physiotherapist)  
Karen Leper (physiotherapist) |
| Randomisator(s)                  | Prof. dr. Laurent Leysen (Pain in Motion Research Group)  
Dr. Eva Huysmans (Pain in Motion Research Group) |
| Assessor(s)                      | Drs. Wouter Van Bogaert (Pain in Motion Research Group)                       |
| Medical staff contributing to recruitment | Dr. Christel Fontaine (Universitair Ziekenhuis Brussel)  
Dr. Marian Vanhoeij (Universitair Ziekenhuis Brussel)  
Tina Vandendaelen (Universitair Ziekenhuis Brussel)  
Dr. Carine De Rop (Imeldaziektenhuis, Bornheiden)  
Dr. Eric De Jonge (Ziekenhuis Oost-Limburg, Genk)  
Dr. Martine Puylaert (Ziekenhuis Oost-Limburg, Genk)  
Dr. Brenda de Petter (AZ Rivierenland, Bornem)  
Greet Vergauwen (AZ Rivierenland, Bornem)  
Karin Oby (AZ Rivierenland, Bornem)  
Dr. Stevens Marianne (AZ Rivierenland, Bornem)  
Dr. Janssens Greet (AZ Rivierenland, Bornem)  
Dr. Najim Omar (AZ Rivierenland, Bornem)  
Dr. Spaepen Annemie (AZ Rivierenland, Bornem)  
Dr. Vermeersch Frank (AZ Rivierenland, Bornem)  
Dr. Papadimitriou Konstantinos (AZ Rivierenland, Bornem) |