Home-based CBM-I and Expectancy in Chronic Pain Patients

CONFIDENTIAL

STATEMENT OF COMPLIANCE

This document is a protocol for a clinical research study. The study will be conducted in compliance with all stipulations of this protocol, the conditions of ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95)

Protocol synopsis

Title	Home-based cognitive bias modification (CBM-I) and Expectancy in Chronic Pain Patients
Objectives	To assess whether home-based CBM-I for pain can reduce pain-related interpretive biases and, by doing so, reduce pain related outcomes in chronic pain patients when compared to a placebo. To manipulate participant expectancy to examine whether perceived credibility of CBM-I impacts the efficacy of the intervention.
Study Design	2x2 randomised, double blind, placebo controlled trial. Predictor variables: intervention type (CBM-I vs placebo) and expectancy manipulation Dependent measures: pain outcomes (pain severity, pain interference, fear of movement, pain catastrophizing, depression, anxiety), credibility and expectancy
Planned Sample Size	220 patients with chronic pain (55 per group)
Recruitment	Participants will be recruited via advertisements in patient advocacy group newsletters (e.g. Arthritis and Osteoporosis NSW). Participants will be made aware that their advocacy group will receive $5 in the form of a finder's fee for each participant who completes the study.
Selection Criteria	Patients with chronic pain who are able to use the computer and have access to the internet over the 3 week day study period. All participants must be over the age of 18 years, speak English, and be able to provide informed consent.
Study Procedures	All components of the study will be completed online. After providing informed consent, participants who meet the inclusion criteria will complete a series of questionnaires, and will then be randomised to one of 4 groups (CBM-I vs placebo; expectancy high vs low). Participants in the high expectancy group will then receive psychoeducation and a rationale for the training. Next, all participants will complete either CBM-I or placebo. Participants will be asked to complete another 3 training sessions over the course of the following week (one every 2 days). On day 8, participants will complete the follow-up questionnaires. Participants will also be asked to complete another set of follow-up questionnaires two weeks after.
Expected duration of the study	12 months

1. STUDY MANAGEMENT

1.1 Principal Investigator

Professor Louise Sharpe, Professor of Clinical Psychology, University of Sydney

1.2 Associate Investigators

Emma Jones, PhD candidate, University of Sydney
Ben Colaguiri, Associate Professor, University of Sydney

1.3 Funding and resources

Emma Jones has been awarded an Australian Government Research Training Program (RTP) Scholarship to complete her PhD. She has also received funding from the University of Sydney to assist with recruitment costs under the Postgraduate Research Support Scheme (PRSS).

The University of Sydney's SONA pool, consisting of first year psychology students, may also be used to identify and recruit any eligible participants.

2. INTRODUCTION AND BACKGROUND

2.1 Background information

Chronic pain is a major global health concern due to its pervasiveness and immense health and social consequences. It places a great financial burden both directly and indirectly on individuals and the health service alike (IASP, 2011). Moreover, approximately 9.9 million workdays were lost over one year in Australia alone due to chronic pain (van Leeuwen, Blyth, March, Nicholas & Cousins, 2006). In light of the enormous burden of chronic pain, introduction of novel and innovative treatment options is timely. Research indicates the enormous importance of psychosocial factors in chronic pain (Casey, Greenberg, Nicassio, Harpin & Hubbard, 2004). Despite early theories having a predominant biomedical orientation, it is now commonly accepted that chronic pain cannot be explained purely in medical terms. Indeed, more recent models of the development and maintenance of chronic pain e.g. (Asmundsen, Vlaeyen & Crombez, 2004; Turk & Okifuji, 2002) highlight the important role of psychological factors in the transition from acute to chronic pain and in the maintenance of chronicity once developed.

Most well-known models of chronic pain e.g. (Eccleston & Crombez, 1999; Vlaeyen & Linton, 2000) propose that maladaptive interpretations of pain as threatening are important in the development of the condition. In general, the models propose that when an individual experiences an onset of pain and they interpret this pain as harmful, they start to scan their body and environment for any potential signs of pain. This tends to lead to anxiety about future pain occurring, which then leads to avoidance of potentially pain provoking activities or situations (e.g. exercise, social outings, daily chores). An overall reduction in activity levels due to fear of pain then causes muscle deconditioning, which ultimately results in an increase in pain, as well as disability.

A large body of research supports this theory that interpretations of pain as harmful or dangerous are a fundamental component in the development of chronic pain. Numerous studies (e.g. McKellar, Clark & Shriner, 2003; Griffith, McLean & Pearce, 1996; Pincus, Pearce & Perrott, 1996; Edwards & Pearce, 1994; Pincus, Pearce, McClelland, Farley and Vogel, 1994) show that people with chronic pain have an interpretation bias towards pain. Notably, interpretation bias was invariant across the range of tasks the studies used to measure it, indicating the robustness of the finding. These findings demonstrate that chronic pain patients have a tendency to interpret ambiguous situations as painful rather than non-painful when compared with the general population

Cognitive Bias Modification for interpretation (CBM-I) refers to procedures that aim to directly change these automatic interpretive biases (MacLeod & Mathews, 2012). CBM-I requires participants to solve a task that disambiguates a sentence, paragraph, or picture to be either positively or negatively valenced. Doing so leads participants to interpret new ambiguous stimuli in the same manner that matches their training (positive or negative). CBM-I has been utilized to target interpretive biases in a variety of contexts, including depression, anxiety. The span of CBM-I is evidenced by its evaluation in four separate meta-analyses (Cristea et al., 2015a; Cristea et al., 2015b, Hallion & Ruscio, 2011, Menne-Lothmann et al., 2014). A recent systematic review (Jones & Sharpe, 2017) synthesized these meta-analyses, and found that CBM-I consistently changed targeted biases with associated improvements on outcome measures of anxiety.

Despite the body of literature that supports CBM-I, and evidence that people with chronic pain exhibit interpretive biases towards pain, very little research has been done investigating whether CBM-I might have clinical applications in the management of pain. There is only one published study (Jones & Sharpe, 2014) that has utilized CBM-I specific in relation to pain outcomes. Jones & Sharpe (2014) adapted the ambiguous scenarios task from the anxiety literature (Mathews & Mackintosh, 2000) and found that

healthy participants who were trained to interpret situations as pain-related avoided a painful task for longer than those trained to interpret them as neutral, or non-pain related. Further, interpretive bias mediated the relationship between bias condition and avoidance, supporting the integral role of interpretive biases in avoidance behaviors in current chronic pain models.

A finding that was striking from the Jones & Sharpe (2017) systematic review of the broader CBM literature, was that CBM-I is only effective when delivered in a laboratory setting and not when delivered remotely. One reason why CBM-I may be ineffective when administered remotely is that its simplicity may compromise its face validity and mean that participants do not engage in the task as well when administered remotely. That is, participants might believe the training is a sham, and may be more likely to disengage from the task. In support of this notion, when researchers have asked participants at the end of a CBM-I task to guess which condition they were in, only 46% correctly guessed that they received CBM-I training rather than a placebo (Beard & Amir, 2008). Notably, when Beard, Weisberg & Amir (2011) provided psychoeducation about CBM-I prior to training, 75% of participants correctly identified that they had received active training rather than placebo. Further, the authors revealed that participants' credibility and expectancy ratings correlated positively with the targeted social anxiety outcomes, indicating the potential influence of face validity on the efficacy of CBM-I. However, whether psychoeducation that promotes the rationale for CBM-I improves engagement and subsequently outcomes has not been systematically investigated.

Research Questions

Primary (RQ1): Can home-based CBM-I modify interpretive biases towards pain and have ensuing effects on pain outcomes in people with chronic pain?

Secondary (RQ2): Does expectancy of CBM-I influence the efficacy of the intervention in a chronic pain sample?

2.2 Rationale for Current Study

Interpretive biases towards pain play a key role in the development and maintenance of chronic pain. There is robust evidence to support the presence of interpretive biases in chronic pain patients. There is also substantial evidence that CBM-I is effective at modifying interpretive biases and impacting clinical outcomes in a range of samples. Further, CBM-I for pain has shown promise in altering avoidance of a

painful task with healthy participants. However, it appears no published study has utilized CBM-I in a chronic pain population. Therefore, the current study aims to assess whether CBM-I for pain can be effective in reducing negative interpretive biases towards pain and reducing pain outcomes in a chronic pain sample when delivered in a home setting (online).

While CBM-I has been found to consistently change targeted biases and have ensuing effects on outcome measures in the anxiety literature, these effects are limited to the training being delivered in a laboratory. Due to the simple nature of CBM-I it appears that remote delivery may compromise the face validity of the task. However, when participants receive psychoeducation regarding the rationale for CBM-I, it appears the training is more credible. Further, previous research indicates that participant expectancy and credibility ratings correlate with targeted clinical outcomes. Therefore, the current study aims to manipulate participant expectancy to assess whether it is possible to increase the credibility of CBM-I for pain in a chronic pain sample. The study also aims to assess whether the perceived utility of CBM-I impacts on the efficacy of the intervention.

3. STUDY OBJECTIVES

3.1 To compare the efficacy of home-based CBM-I with a placebo in improving pain outcomes in people with chronic pain

3.2 To examine whether expectancy of CBM-I increases following psychoeducation about the intervention

3.3 To assess whether perceived credibility of CBM-I increases the efficacy of the intervention

4. STUDY DESIGN

4.1 Type of Study

This is an online, randomized, double-blind, placebo controlled trial assessing the efficacy of home-based CBM-I in people with chronic pain.

4.2 Study Design

A two factor (two level) design will be employed. CBM-I will be compared with placebo on pain outcome measures and a measure of interpretation bias, and the expectancy manipulation (psychoeducation vs no psychoeducation) will be compared on a credibility and expectancy measure. Interaction effects will be analysed to examine whether psychoeducation impacts on the efficacy of CBM-I. Participants' pain outcomes will be compared using pre and post intervention measures, with the primary outcome being changes in pain interference (Brief Pain Inventory).

4.3 Number of Participants

We aim to recruit 200 people with chronic pain via advertisements in patient advocacy group newsletters such as Arthritis & Osteoporosis NSW, Arthritis QLD, Pain Australia and Chronic Pain Australia.

4.4 Study Site

This study will be conducted entirely online.

4.5 Expected Duration of Study

We expect the duration of the study to be 12 months. It is estimated that the recruitment period will take 6 months and that analyses and write-up will take a further 3-6 months.

4.6 Intervention

4.6.1 Cognitive Bias Modification for Interpretation (CBM-I)

Participants will be randomly presented with 30 scenarios, repeated once each. Each scenario will remain ambiguous, such that it could be interpreted to be pain or illness related, or neutral in its meaning until resolution of the final word fragment. Participants will be instructed to imagine they are the person being described, and must use their understanding of the paragraph to guide solution of the word fragment. There is only one solution that fits the possible interpretation of the preceding paragraph, and given the nature of the intervention, the scenarios will be solved to reveal a neutral (non-pain related) meaning. Once the word fragment is solved, a comprehension question will follow, which can only be correctly answered by having the appropriate interpretation of the previous paragraph.

4.6.2 Placebo

The placebo condition will be structured identically to CBM-I. However, the scenarios in this case will not include emotional content or ambiguity. Resolution of the final word fragment and answering the comprehension question will not require any interpretation of the paragraph.

4.6.3 Expectancy Manipulation

If participants are randomized to the psychoeducation condition, they will learn about the rationale for CBM-I. Participants will firstly see the following information:

> *The intervention you will receive over the course of this study is called Cognitive Bias Modification (CBM).*
>
> *Cognitive Bias Modification (CBM) has had promising results in previous research, reducing symptoms of depression and anxiety in both healthy and clinical populations. It has also been helpful in reducing fears about dying from cancer, therefore reducing anxiety in people with cancer.*
>
> *In a study from our laboratory, CBM significantly reduced the amount of time university students spent avoiding a painful task. However, CBM has not been trialed with people experiencing chronic pain. Due to the success of CBM in other populations, we believe CBM will be helpful for you. It is a novel, promising intervention, and you are the first ones to have the opportunity to try it.*

Then, they will view a short animated video with a voice over, explaining the basic mechanisms and theory behind the development of chronic pain, and the central role of interpretation biases.

Participants allocated to proceed with the intervention as usual will not view any of the psychoeducation, and will be presented with instructions for completing the training immediately after they complete the questionnaires.

4.7 Outcome Measures

4.7.1. Participant characteristics

- Demographics (age, gender, education, marital status, employment, SES)
- Pain specific information (region, duration, any specific diagnoses)

Primary outcome measure

4.7.2 Brief Pain Inventory (intensity and interference subscales)

This measure will be used to evaluate the severity of participants' pain (intensity subscale) and the impact of this pain on their daily functioning (interference subscale) It will be administered pre-training, after each subsequent training session (x3), at follow-up point 1 and at follow-up point 2.

Manipulation checks

4.7.3 The Recognition Task

This task is a measure of interpretation bias, and will therefore assess whether the intervention has modified the targeted mechanism of change. Participants will be presented with ten ambiguous pain/health-related paragraphs, each uniquely identified by a title, that require completion of the final word fragment. A filler task will then be administered. Then, in a randomized order, the identifying title of each scenario followed by four alternative versions of the final sentence will be presented to participants. Participants will be asked to rate each sentence, independently of all others, for its similarity in meaning to the original. The recognition task will be administered at follow-up point 1.

4.7.3 Credibility and Expectancy Questionnaire

This questionnaire will be administered to measure participants' treatment expectancy and rationale credibility. It will assist us to gauge whether the expectancy manipulation (psychoeducation) has been effective (Therapy Evaluation Form). It will be administered pre-training, after the expectancy manipulation.

Secondary outcome measures

4.7.4 The TAMPA Scale of Kinesiophobia

Participants' fear of movement will be assessed using the 17-item TAMPA scale. It will be administered at pre-training, at follow-up point 1, and follow-up point 2.

4.7.5 Pain Catastrophising Scale

This 13-item scale will help quantify participants' attitudes towards and emotional distress related to pain (PCS). It will be administered at pre-training, at follow-up point 1, and follow-up point 2.

4.7.6 Depression and anxiety

Participants' depression and anxiety will be measured using the 21-item Depression, Anxiety, and Stress Scale (DASS-21). It will be administered at pre-training, at follow-up point 1, and follow-up point 2.

5. PARTICIPANT ENROLLMENT

5.1 Recruitment

Patient advocacy groups (Arthritis & Osteoporosis NSW, Arthritis QLD, Pain Australia and Chronic Pain Australia) will be contacted and asked to advertise the online study through their newsletters. The advocacy groups will be offered a 'finder's fee' of $5 for each participant that completes the study. If the participants are interested, they will respond to the advertisement and 'self-select' by emailing the research team. An email account will be created for the sole purpose of the study. Once the research team receives an email from an interested participant, the participant will be sent a link to the online study. From there, they will have access to the participant information statement and consent form and can decide whether to commence the study or not. Participant emails will be used to distribute links to each online training session and the follow-up questionnaires. Participants will be advised that their email address will only be used for the purposes of the study and that their details will remain confidential. Participants will also be asked for their phone number before commencing the study so the research team has their number in the event of requiring a risk assessment.

5.2 Eligibility Criteria

5.2.1 Inclusion Criteria

To be included in the study, patients must:

- Have chronic pain
- Be over 18 years
- Be able to read English fluently
- Have access to the internet and be able to use the computer confidently

5.2.2 Exclusion Criteria

Patients will be excluded from participation if any of the following criteria are met:

- Under the age of 18 years
- Not experiencing chronic pain
- Unable to access the internet and be able to use the computer

5.3 Informed Consent Process

In keeping with the National Statement for Ethical Conduct in Human Research, all patients who express an interest in participating in the research project will be provided with study information in sufficient detail that they are able to make an informed decision on the risks and benefits of their participation. The study information form (attached with this application) contains all details of the study as required by section 2.2.6 of the National Guidelines. The information form will allow patients to determine their eligibility to participate. Patients who are eligible to participate will provide consent by making this selection on the initial online survey.

5.4 Participant Withdrawal

5.2.1 Reasons for withdrawal

Circumstances for early termination may include:

- Fatigue
- Boredom
- Not able to commit to 8 day study period
- Actively suicidal as determined by the risk assessment

Given the nature of this study being online, participants are able to decide whether they choose to proceed with each component of the study. In the Participant Information Statement, it is made explicit that the study is entirely voluntary and that withdrawing from the study will not affect the participant's relationship with the University. If participants have selected in the initial survey that they wish to receive a summary of results via email, they will receive this regardless of their decision to withdraw.

6. STUDY PROCEDURES

The study will be conducted over a period of 3 weeks and will comprise of a pre-training stage, a training stage, and two follow-up points; one a week after pre-training and one 3 weeks after pre-training.

Pre-training stage:

Participants will self-select by responding to an advertisement and emailing the research team via an account created for the sole purpose of this study. The link to the initial survey (containing participant information, consent form, pre-training questionnaires, psychoeducation and the first training session) will be sent to their email address. After reading the participant information and providing consent, participants will be asked to complete a series of questionnaires including the Depression, Anxiety Stress Scale (DASS-21); Pain Catastrophising Scale (PCS), The TAMPA Scale of Kinesiophobia, and The Brief Pain Inventory (BPI). These measures are theoretically related to interpretation biases and chronic pain and are hypothesised to change as a result of training. After this, participants will be presented with either of the expectancy manipulations (psychoeducation or no psychoeducation), and will complete the Credibility and Expectancy questionnaire. This initial stage is estimated to take up to 1 hour.

Training stage:

Immediately after participants have completed the pre-training stage, they will be asked to commence the first training (CBM-I or placebo) session. This is estimated to take up to 20 minutes. Two days after completion of the first training session (day 3), participants will be sent a link via email to the next training session, which will contain the expectancy manipulation, the training condition (CBM-I or placebo), and the BPI. Participants will have 2 days to complete the training before the link expires. On day 5, participants will be emailed a link to the next training session, containing the same components and allowing the same time for completion. On day 7, participants will be emailed the final training session, with the same stipulations as the prior 2 sessions. Participants will therefore complete 4 training sessions in total over the course of 8 days.

Follow-up 1:

On day 8, participants will be contacted via email and asked to complete follow-up questionnaires including the DASS-21, PCS, TAMPA, and BPI. They will also be asked to complete the Recognition Test (measure of interpretation bias). This is estimated to take up to 45 minutes.

Follow-up 2:

Exactly two weeks after follow-up stage 1, participants will be emailed the final link for the study, containing the same follow-up questionnaires, minus the Recognition Test. This is estimated to take 30

minutes. As outlined in the debrief statement, if the CBM-I intervention appears to be beneficial at the conclusion of the study, we will provide access to the training for all placebo group participants.

7. ADVERSE EVENTS

The researchers do not anticipate any risks as a result of participating in this study. However, if a participant reports a score in the severe range for anxiety or depression on the DASS-21 at any point throughout the study, they will be contacted via telephone and a risk assessment will be conducted by researcher Emma Jones, who is a provisionally registered psychologist. Additionally, participants' scores on all questionnaires will be closely monitored throughout the study, such that if there are any significant increases in measures of depression, anxiety or pain, the research team will contact the participant and conduct a risk assessment. Participants are also urged in the participant information statement to contact the research team if they become distressed at any point during the study *(please see PIS)*. Further, all participants will be debriefed at the conclusion of their participation in the study and will be given the opportunity to address any concerns with the research team via email *(please see debriefs)*. If participants express any distress to the research team at this point or at any other time point during study participation, a risk assessment will be conducted.

7.1 Risk Assessment

Please see the suicide risk assessment document for information regarding the decision tree. The risk action plan follows:

Action Plan

- If any part of this assessment was completed then it must be clearly documented that you have a) conducted a suicide risk assessment b) the level of risk that was determined including the reasons that led to this level of risk being decided AND c) clearly record any verbal contracts and/or actions carried out.

For Low Risk

- Ensure to document your assessment, level of risk and verbal agreement made with the client. Also follow up with any actions required to ensure the client receives the therapy session or GP session that they have agreed to in their verbal contract.

For Moderate/High Risk

- "I can understand considering everything that is going on for you that you are feeling very distressed. Given your answers today, I am quite concerned for your safety. What I would like to

do is to phone a senior clinician so that we can make the best decision to ensure your safety. Could you please stay on the line while I phone her on the other line now?"

- Phone Professor Louise Sharpe (clinical psychologist) on 0422 317 724
- The supervisor may decide that the CRISIS team needs to be contacted. The CRISIS team will ask you some questions and determine whether they are required to come on site to evaluate for hospitalisation, whether they will call the person themselves or whether an ambulance should be arranged to transport the person to hospital.
- Any occasion of suicidal risk must be carefully documented in the notes. The actions taken must be clearly documented in the individual's file.

8. STATISTICAL METHODS

8.1 Sample Size Estimation

Based on our previous CBM-I study (Jones & Sharpe, 2014) that found the training significantly affected participant's avoidance of an ensuing pain task, an effect size of 0.35 is expected. It is estimated that with an alpha of 0.05 and 80% power that a sample size of 110 per training group (CBM-I vs placebo) will be sufficient to detect an effect. Therefore, we will aim to recruit 220 people in total (55 per condition).

8.2 Statistical Analysis Plan

Preliminary analyses will include a series of 2 (training) x 2 (expectancy) ANOVAs performed on all baseline questionnaires and demographic variables to assess for covariates.

Primary analyses will be a series of 2 (time) x 2 (training) x 2 (expectancy) ANOVAs conducted on the primary outcomes of the BPI: pain interference and pain intensity.

The secondary analyses will be a series of 2 (time) x 2 (training) x 2 (expectancy) mixed model ANOVAs conducted on the other pain outcome measures to determine pre and post change scores.

It is also of interest to determine whether changes in interpretation bias are associated with pain outcomes. Hence, an interpretive bias score will be calculated with responses from the Recognition Test, using the technique employed in our previous (Jones & Sharpe, 2014) study:

Bias score = (average pain target) – (average benign target).

Then, in order to determine whether interpretive biases are the mechanisms of change for the observed changes in pain outcomes, a multiple regression will be conducted.

Any missing questionnaire item responses will be mean-imputed, provided at least half of the other items in the questionnaire are non-missing. Any questionnaire that is missing completely, or missing more than half of its items, will be treated as missing in the analysis.

9. DATA MANAGEMENT

9.1 Data Collection

All data (questionnaire and training responses) will be collected online using the external survey host, Qualtrics.

9.2 Data Storage

During the data collection phase, the data will initially be stored via the survey host, Qualtrics, in a password protected account. Upon completion of data collection, responses will be collated, organized, and analysed using a secure University of Sydney server. Only the Principal Investigator and Associate Investigator will have access to this data.

We may submit the information from this project to a public database for research information, so that other researchers can access it and use it in their projects. Before we do so, we will take out all the identifying information so that the people we give it to won't know whose information it is. They won't know who participated in the project and they won't be able to link any of the individuals to the information provided.

9.3 Data Confidentiality

Although participant email addresses are the method of survey and training distribution, participants who provide informed consent to participate will be assigned a participant number to ensure their anonymity in all analyses. Participants will be made explicitly aware in the participant information and initial survey that their email address will be used for the sole purpose of training, questionnaire distribution and assessing adherence. It will be made clear that after participants have completed the study, they will not

receive any contact from the research team, unless they have elected to receive a summary of the findings via email after the project is complete or if they have indicated interest in future research.

As previously stated, participant confidentiality will be ensured by allocating participant ID numbers to each person rather than using names or email addresses, by using a password protected online survey host account, and by using an encrypted University of Sydney data server. Participant data will not be identifiable in publications, as we will present only patterns of association and group-level outcomes

9.4 Study Record Retention

As per legal requirements of a Clinical Trial, electronic data will be retained for a minimum of 20 years. In the interest of transparency, fully anonymised data may be stored indefinitely for the purposes of open-access practice on the same password protected University of Sydney server.

10. ADMINISTRATIVE ASPECTS

10.1 Participant Reimbursement

There will be no direct patient reimbursement for participation. However, participants will be aware that a payment of $5 will be made to their referring advocacy group, contingent on their completion of the study.

10.2 Financial Disclosure and Conflicts of Interest

Emma Jones has been awarded an Australian Government Research Training Program (RTP) Scholarship to complete her PhD. She has also received funding from the University of Sydney to assist with recruitment costs under the Postgraduate Research Support Scheme (PRSS).

11. USE OF DATA AND PUBLICATIONS POLICY

We anticipate that the results of our study will be published in a peer-reviewed journal, and presented at conferences. Emma Jones will take the lead author in the publication of research articles, and Prof. Louise Sharpe and Dr. Ben Colagiuri will be the co-authors of all publications.

RERERENCES

Asmundsen GJ, Vlaeyen JW, Crombez G: Understanding and treating fear of pain. Oxford: Oxford University Press; 2004.

Beard, C., & Amir, N. (2008). A multi-session interpretation modification program: Changes in interpretation and social anxiety symptoms. Behaviour research and therapy, 46(10), 1135-1141.

Beard, C., Weisberg, R. B., & Amir, N. (2011). Combined cognitive bias modification treatment for social anxiety disorder: a pilot trial. Depression and anxiety, 28(11), 981-988.

Casey CY, Greenberg MA, Nicassio PM, Harpin RE, Hubbard D: Transition from acute to chronic pain and disability: A model including cognitive, affective, and trauma factors. PAIN 2008, 134(1-2):69-79.

Cristea, I. A., Kok, R. N., & Cuijpers, P. (2015). Efficacy of cognitive bias modification interventions in anxiety and depression: meta-analysis. The British Journal of Psychiatry, 206(1), 7-16.

Cristea, I. A., Mogoașe, C., David, D., & Cuijpers, P. (2015). Practitioner review: cognitive bias modification for mental health problems in children and adolescents: a meta-analysis. Journal of Child Psychology and Psychiatry,56(7), 723-734.

Eccleston, C., & Crombez, G. (1999). Pain demands attention: A cognitive–affective model of the interruptive function of pain. Psychological bulletin,125(3), 356.

Edwards, L., & Pearce, S. (1994). Word completion in chronic pain: Evidence for schematic representation of pain. Journal of Abnormal Psychology, 103, 379-382.

Griffith, J., McLean, M., & Pearce, S. (1996). Information processing across three chronic pain groups. Abstracts of 8th World Congress on Pain. Seattle, WA: International Association for the Study of Pain.

(IASP) IAftSoP: Fact sheet: Unrelieved Pain is a Major Global Healthcare Problem. In.; 2011.

Hallion, L. S., & Ruscio, A. M. (2011). A meta-analysis of the effect of cognitive bias modification on anxiety and depression. Psychological bulletin, 137(6), 940.

Jones, E. B., & Sharpe, L. (2017). Cognitive bias modification: A review of meta-analyses. Journal of affective disorders, 223, 175-183.

Jones, E. B., & Sharpe, L. (2014). The effect of cognitive bias modification for interpretation on avoidance of pain during an acute experimental pain task. *PAIN®*, *155*(8), 1569-1576.

MacLeod, C., & Mathews, A. (2012). Cognitive bias modification approaches to anxiety. Annual Review of Clinical Psychology, 8, 189-217.

McKellar, J. D., Clark, M. E., & Shriner, J. (2003). The cognitive specificity of associative responses in patients with chronic pain. British Journal of Clinical Psychology, 42, 27-39.

Menne-Lothmann, C., Viechtbauer, W., Höhn, P., Kasanova, Z., Haller, S. P., Drukker, M., ... & Lau, J. Y. (2014). How to boost positive interpretations? A meta-analysis of the effectiveness of cognitive bias modification for interpretation. PloS one, 9(6), e100925.

Pincus, T., Pearce, S., & Perrott, A. (1996). Pain patients' bias in the interpretation of ambiguous homophones. British Journal of Medical Psychology, 69, 259-266.

Pincus, T., Pearce, S., McClelland, A., Farley, S., & Vogel, S. (1994). Interpretative bias of ambiguous stimuli in chronic pain patients. Journal of Psychosomatic Research, 38, 347-353.

Turk DC, Okifuji A: Psychological Factors in Chronic Pain: Evolution and Revolution. Journal of Consulting and Clinical Psychology 2002, 70(3):678-690.

van Leeuwen MT, Blyth FM, March LM, Nicholas MK, Cousins M: Chronic pain and reduced work effectiveness: The hidden cost to Australian employers. European Journal of Pain 2006, 10(2):161.

Vlaeyen, J. W., & Linton, S. J. (2000). Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain, 85(3), 317-332.