National Institute for Health and Care Excellence

Final

Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain

[F] Evidence review for psychological therapy for chronic primary pain

NICE guideline NG193

Intervention evidence review underpinning recommendations 1.2.3 and 1.2.4 and the research recommendations in the NICE guideline

April 2021

This evidence review was developed by the National Guideline Centre based at the Royal College of Physicians

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1.1 Review question: What is the clinical and cost effectiveness of psychological therapy for the management of chronic primary pain?

1.2 Introduction

Psychological factors are recognised to play a role in the experience of chronic pain. Chronic pain has an impact on how we think, feel and behave. In turn various psychological factors are thought to exacerbate or ameliorate wellbeing and improve or decrease functioning. There are many pain-specific psychological factors that have attracted interest in the literature, for example fear avoidance, pain catastrophizing, self-efficacy, psychological flexibility and acceptance. As the limitations of a purely biomedical approach to chronic pain were recognised, psychological interventions have been developed to improve functioning, mood and quality of life. These approaches are widely used for chronic primary pain although access to these interventions is still variable and there is uncertainty about their effectiveness. Current practice tends to focus on Cognitive Behavioural Therapy (CBT) and the "Third Wave" therapies including Acceptance and Commitment Therapy and Mindfulness.

There are a range of psychological interventions included in this review. Psychodynamic psychotherapy focuses on enabling the person to become conscious of their early experiences and how they may impact on our reactions to the present. Behavioural therapy focuses on the modification of learned behaviours which may be unhelpful. CBT incorporates a focus on changing unhelpful or distorted beliefs and automatic thoughts which affect the person's emotional and behavioural response to events. There are CBT protocols which focus on different aspects, for example managing chronic pain or focusing on sleep. More recently there has been interest in "Third Wave" cognitive therapies which aim to help people live a richer life in the presence of pain. These include a focus on developing psychological flexibility enabling the person to move towards living in accordance with their values.

This evidence review sets out to determine the effectiveness of these interventions specifically in people with chronic primary pain.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People, aged 16 years and over, with chronic primary pain (whose pain management is not addressed by existing NICE guidance) (chronic widespread pain, complex regional pain syndrome, chronic visceral pain, chronic orofacial pain, chronic primary musculoskeletal pain other than orofacial)
Intervention(s)	• Cognitive behavioural therapy (CBT) • Cognitive analytic therapy (CAT) • Behaviour therapy • Solution-focused therapy • Problem-solving therapy • Acceptance and commitment therapy (ACT)

	• Pain education • Relaxation techniques • Mindfulness • Hypnosis • EMDR (eye movement desensitisation reprocessing) • Psychotherapy (psychodynamic and psychoanalytic) • Sleep management/hygiene • Biofeedback.
Comparison(s)	• Each other • Usual care • Attention control.
Outcomes	CRITICAL: • Health related quality of life (including meaningful activity) • Physical function (5 minute walk, sit to stand, Roland Morris Disability Questionnaire, Oswestry Disability Index, Canadian Occupational Performance Measure) • Psychological distress (depression/anxiety) (preferably Hospital Anxiety and Depression Scale) • Pain interference (brief pain inventory interference subscale) • Pain self-efficacy (pain self-efficacy questionnaire). IMPORTANT: • Use of healthcare services • Sleep • Discontinuation • Pain reduction (any validated scale). Outcomes will be extracted at the longest time point up to 3 months and at the longest time point after 3 months.
Study design	Randomised controlled trials (RCTs) and systematic reviews of RCTs Cross-over RCTs will be considered if no non-cross-over RCT evidence is identified.

1.4 Clinical evidence

1.4.1 Included studies

Forty-seven studies were included in the review;[6, 7, 11, 12, 14, 15, 18, 29, 30, 38, 41, 44, 56, 92, 94, 96, 146, 165, 166, 170, 187, 201, 215, 216, 233, 245, 247, 260, 265, 289-291, 294, 299, 300, 304, 310, 314, 315, 319, 445, 452, 453, 455, 477, 480, 494, 500, 520, 522, 538, 549, 551, 556, 564, 570, 577] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary tables below (Table 3, Table 4, Table 5, Table 6, Table 7, Table 8, Table 9, Table 10, Table 11, Table 12, Table 13, Table 14, Table 15, Table 16, Table 17, Table 18, Table 19, Table 20, Table 21).

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix F.

1.4.2 Excluded studies

Nine potentially relevant Cochrane reviews[142-144, 163, 192, 254, 324, 519, 567] were identified and assessed for eligibility, but none were included. This was mainly due to the included populations being too broad (i.e. all types of chronic pain or chronic, subacute and acute pain), differences in the analysis methods (for example combining all types of psychological

interventions for analysis) and incorrect comparators (for example non-psychological interventions). All included studies were cross-checked for inclusion in this review as relevant.

See the excluded studies list in appendix I.

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Details	Population	Outcomes	Comments
Alda 2011[6] (Garcia-campayo 2009[170], Luciano 2014[289])	Cognitive behavioural therapy (CBT) Vs. Usual care	**CBT (n=57)** 10 x 90 minute group (max. 8 patients) sessions delivered by trained therapists and consisting of 2 major components: cognitive restructuring, which focuses on reducing pain-specific dysfunctional cognitions and coping, which focuses on teaching cognitive and behavioural coping strategies. Sessions included e.g. evaluation of automated thoughts, expressive writing, coping with ruminations, obsessions and worrying. Duration 10-12 weeks. Vs. **Standard care (n=56)** Offered by general practitioners at their health centres. To improve this groups' treatment, the doctors received the 'Guide for the Treatment of Fibromyalgia in Primary Care', which is edited and distributed by the Aragonese Health Service. Treatment as usual implies that doctors selected a pharmacological treatment as well as the frequency of patient visits that they considered adequate. However, the treatment recommended in the guide matched that of the recommended pharmacological intervention arm of the trial.	Fibromyalgia N=169 (113 in groups relevant to this protocol) Age - Mean (SD): CBT 46.35 (6.71) years, usual care 47.04 (6.53) years Duration of pain not reported/ All female	At post intervention (9 weeks) and 6 month follow up: • Quality of life • Psychological distress • Discontinuation • Pain reduction	Serious indirectness of the usual care arm: GPs received a treatment guide 3 armed trial, third arm: pharmacological treatment not extracted
Alonso-fernandez 2016[7]	Acceptance and commitment therapy (ACT) Vs. Usual care	**ACT (n=53)** 9 x 120-min weekly group sessions, max. 8 participants led by a psychologist. Intervention based on Acceptance and Commitment Therapy and Selective Optimization with Compensation model. Program sets out to promote the use of	Chronic MSK pain N=101	At post intervention (9 weeks): • Psychological distress	Serious indirectness of usual care: 2 hour education session not considered sufficient for an education

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		SOC strategies and reduce efforts to struggle with pain. The general session structure was: a) review of the task carried out during the week, b) therapeutic training, and c) explanation of a new between-session assignment. Duration 9 weeks approx. Vs. **Usual care (n=48)** Minimal support group: 2 h educational group session about factors that can influence pain conditions and pain perception and information about selective optimisation and compensation strategies. The MS group did not receive any type of psychological training.	Age - Mean (SD): 83.04 (6.82) years Duration of pain, at least 6 months, mean ACT 21.30 (20.91), usual care 25.34 (20.36) years	• Pain interference • Discontinuation	intervention but may be more than usual care.
Amer-Cuenca 2019 [11]	Pain education Vs. Attention control	**Pain education (n=84)** Pain neuroscience education by physiotherapists, provided in accordance with published guidelines in groups of 4-6 patients. PowerPoint addressed the following topics: physiology of the nervous system, characteristics of acute vs. chronic pain, the purpose of acute pain, how acute pain originates in the nervous system, how pain becomes chronic and potential sustaining factors of central sensitization such as illness, emotions, stress, perceptions, pain cognitions, and pain behaviour. Information presented in an understandable way, using pictures, examples and metaphors. Also explained how various treatment components are likely to contribute to decreasing the hypersensitivity of the central nervous system. All participants asked to read the Spanish translation of the book 'Explain Pain'. After each session, therapists answered questions from patients, patients asked if they had applied	Fibromyalgia N=103 Age – Mean (SD): high dose 54.75 (10.14), low concentrated 55.2 (8.19), diluted low dose 51.67 (7.38), control 51.27 (10.57) years Duration of pain 12.64 – 23.53 years Gender (M:F): 6/71	At post intervention (unclear duration) and 3 month follow up: • Quality of life • Psychological distress • Discontinuation • Pain reduction	Three trial arms: 1) high dose (6 x 45 minute sessions), 2) low concentrated dose (2 x 45 minute sessions), 3) diluted low dose (6 x 15 minute sessions). Content identical but adapted to the different doses/durations. Arms combined for analysis.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		learning in daily life and what their experiences were and coached to apply insights to daily life. Vs. **Attention control (n=19)** Biomedical education 2 x 45 minute sessions by physiotherapists in groups of 4-6 patients.			
Amirova 2017[12]	Relaxation Vs. Usual care	**Relaxation (n=67)** Written instructions of the Mitchell Method Relaxation Technique and a short audio recording of the guided technique to use every day for 1 month. Participants sat at a desk/in a chair/laid on the floor and were given verbal orders to engage in a series of muscle relaxation exercises, followed by deep breathing and finally an imagery task, recalling a pleasant occasion or concentrating on a pleasant repetitive sequence for 1 minute. Duration 4 weeks. Vs. **Usual care (n=58)** Waiting list.	Fibromyalgia N=191 (125 relevant to this protocol) Age - Mean (SD): MMRT 48.1 (11.08) years, waiting list 48.95 (10.13) years Duration of pain, at least 3 months, mean for relaxation 11.61 (6.99) and usual care 10.97 (6.77) years. Gender (M:F): 12/179	At post intervention (4 weeks): • Quality of life • Psychological distress • Sleep • Discontinuation • Pain reduction	3 arm trial. Third arm – attention control of recording of white noise. Excluded from this analysis (inappropriate attention control). Follow up for 8 weeks but full results only reported at 4 weeks. HRQOL – only one SF36 sub scale reported, FIQ extraction instead. Study reports selected subscales of the MOS and the Sleep Problems Index, which summarizes responses using an abbreviated six-item index, containing questions from the sleep disturbance, sleep inadequacy, respiratory

Study	Intervention and comparison	Details	Population	Outcomes	Comments
					impairment, and somnolence domains, but not sleep quantity. SPI extracted.
Amutio 2015[14] Amutio 2018 [15]	Mindfulness Vs. Usual care	**Mindfulness (n=20)** 7 x weekly 2 hour sessions. Participants' reflections about their mindfulness meditation exercise practice during the week, practice of body scan for 10 minutes, presentation of metaphors through different animations and stories and also some exercises for each of the sessions (observing physical sensations of different body parts, breathing, observing thoughts, accepting uncomfortable private events), practice of mindfulness, attending to the breath for 30 minutes. Requested to practice body scan for 10 minutes and mindfulness breathing for 30 minutes and record the practice using a register sheet. Duration 7 weeks. Vs. **Usual care (n=19)** Waiting list.	Fibromyalgia N=39 Age - Mean (SD): 51.82 (10.18) years Duration of pain not stated All female	At post intervention (7 weeks) and 3 month follow up: • Psychological distress • Discontinuation • Sleep	
Ang 2010[18]	Telephone CBT Vs. Usual care	**Telephone CBT (n=17)** 6 x weekly 30-40 minute sessions of CBT over the telephone by a single trained therapist (psychology graduate student under supervision of a clinical psychologist) and a companion workbook to encourage active participation. Components of CBT included time-contingent activity pacing, pleasant activity scheduling, relaxation, automatic thoughts and pain, cognitive restructuring and stress management. Duration 6 weeks.	Fibromyalgia N=32 Age - Mean (SD): 49 (11) years Duration of pain CBT: 11.8 (4.6), usual care 12.3 (7.9) years	At post intervention (6 weeks) and 12 weeks: • Physical function • Psychological distress • Discontinuation • Pain reduction	FIQ total reported as responder analysis according to author-determined cut off so not extracted – physical impairment and pain sub scales extracted instead. Serious indirectness of the intervention:

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		Vs. **Usual care (n=15)** Customary care received from treating physicians.	All female		included relaxation elements.
Babu 2007 [29]	Biofeedback Vs. Attention control	**Biofeedback (n=15)** A continuous 6-day treatment schedule of EMG biofeedback, with each session lasting 45 min. Treatment was given to the forearm extensors, upper trapezius and frontalis. Patients were taught to relax through techniques like positioning, breathing and hold-relax with the help of visual and auditory feedback. Patients were gradually taught how to include relaxation into their activities of daily life. Vs. **Sham biofeedback (n=15)** A continuous 6-day treatment schedule, with each session lasting 45 min. This provided a constant visual feedback to the patient, irrespective of the muscle activity. Treatment was given to the forearm extensors, upper trapezius and frontalis. Patients were taught to relax through techniques like positioning, breathing and hold-relax with the help of visual and auditory feedback. Patients were gradually taught how to include relaxation into their activities of daily life.	Fibromyalgia N=30 Age – Mean (SD): biofeedback 43.2 (10.5) years; sham 35.3 (9.7) years Duration of pain not stated	At post intervention (6 days): • Quality of life • Physical function • Discontinuation • Pain reduction	Serious indirectness of the intervention and comparator: included relaxation elements
Bahremand 2015[30]	Relaxation Vs. Attention control	**Relaxation training (n=13)** 4 x weekly 2 hour group sessions led by clinical psychologists. Session 1: introduced to procedures used in Ost's treatment and placed in progressive relaxation therapy after diaphragmatic	Non-cardiac chest pain	At post intervention (5 weeks): • Discontinuation • Pain reduction	3 armed trial, third arm (metaphor therapy) not extracted

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		breathing training. Session 2: release-only technique was taught. Session 3: cue-control relaxation method and a different relaxation method. Session 4: rapid relaxation method and application to real life. At the end of each session homework to practice the techniques and record relaxation conditions was set. Vs. **Attention control (n=14)** Only discussions about the physical conditions of the patients and their assessments of future problems were conducted, without any training or medical therapy trends.	N=41 (27 in groups included in this protocol) Age – Mean (SD): relaxation 52.69 (10.8) years; control group 51.8 (10.68) years Duration of pain, at least 3 months		
Baumueller 2017[38]	Biofeedback Vs. Usual care	**Biofeedback (n=20)** 14 sessions over 8 weeks, led by a medical student in 4th and 5th year and a nurse in a chronic pain unit, training delivered individually. Electrodes placed on upper and lower trapezius muscle, apparatus displayed 1 EMG curve for each side, instructor taught patients that an ascending curve corresponds to increasing and a descending curve to decreasing muscle tension. Patients instructed to strain the muscles for 3 minutes then relax for 10 minutes, while receiving visual feedback of the muscle tension. Feeling of muscle tension in relation to EMG curves was discussed at the end of the session. Encouraged to do a home exercise programme of muscle relaxation for 15 minutes per day and in stressful situations. Duration 8 weeks. Vs. **Usual care (n=20)** Same as before starting the study.	Fibromyalgia N=40 Age - Mean (SD): biofeedback: 55.4 (6.1) years, usual care 56 (6.1) years Duration of pain not stated All female	At post intervention (8 weeks) and 3 months follow up: • Quality of life • Psychological distress • Discontinuation	SCL-90-R measure of psychological distress reported, but only reported at longer time point and not commonly reported by other studies; Beck Depression Inventory extracted instead Pain reduction: tender point score (patients rated pain from 0-5 on 24 common tender points) and patients' global impression of change scores

Study	Intervention and comparison	Details	Population	Outcomes	Comments
					reported – not relevant, not extracted
Bergeron 2001[44]	Biofeedback Vs. Group CBT	**Biofeedback (n=29)** 8 x 45 minute sessions over 12 weeks led by 1 of 2 PhD level clinical psychologists. Self-insertion of a single-user sEMG sensor in to the vagina. Automated protocol - 60 second pre-baseline rest period; 6 max. intensity rapid contractions or flicks, each contraction preceded by a 12 second rest period; 1 max. intensity 60 second contraction preceded by 30 seconds rest; 1 60 second post-baseline rest period. Training in the use of a portable sEMG home trainer for daily practice. Duration 12 weeks. Vs. **Group CBT (n=29)** Led by 1 of 2 PhD level clinical psychologists in 8 x 2 hour sessions over 12 weeks, 7-8 participants per group. Treatment package included education and information about vulvar vestibulitis, how dyspareunia impacts desire and arousal, a multifactorial view of pain and sexual anatomy; progressive muscle relaxation; abdominal breathing; Kegel exercises; vaginal dilation; distractive techniques; rehearsal of coping self-statements; communication skills training and cognitive restructuring. Duration 12 weeks.	Vulvar vestibulitis (dyspareunia) N=87 (58 relevant to this protocol) Age - Mean (SD): 26.8 (5.4) years Duration of pain, at least 6 months, mean Biofeedback 63.4 (65.2), CBT 52.3 (41.0) months	At post intervention (12 weeks): • Discontinuation • Pain reduction	3 arm trial. Third arm (vestibulectomy) excluded from this analysis. Serious indirectness of CBT intervention: included education and relaxation elements
Castel 2009[94]	CBT Vs. Usual care	**CBT (n=18)** 12 x 90-minute sessions including: information about fibromyalgia and theory of pain perception, relaxation training, cognitive restructuring, assertiveness training, behavioural goal setting, problems solving, and training in outcome	Fibromyalgia N=47 (30 relevant to this protocol)	At unclear follow-up (assumed >3 months): • Quality of life • Discontinuation • Pain reduction	3 arm trial. Third arm (CBT and hypnosis) excluded from this analysis.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		generalization and maintenance of gains. In the last 20 minutes of the group CBT sessions, participants received a group session of relaxation training, which consisted of 5 minutes of relaxing different parts of the body by means of sensation awareness. Then, for 10 minutes, participants focused on diaphragmatic breathing and finally, feelings of well-being and general relaxation were suggested for the last 5 minutes. Following the first relaxation training session, the participant was given an audio CD of a relaxation exercise to listen to at home. Vs. **Usual care (n=12)** Standard medication management conventional pharmacological treatments including analgesics, antidepressants, sedatives and myorelaxants, as appropriate.	Age - Mean (SD): 44.2 (10.2) years Duration of pain, at least 6 months, mean 11 (10.2) years Gender (M:F): 2/37		Serious indirectness of CBT intervention: included education and relaxation elements
Castel 2012[92]	CBT Vs. Usual care	**CBT (n=34)** 14 x weekly 120 minute group sessions including education about FM and pain perception theory, Schultz Autogenic training, cognitive restructuring techniques, CBT for insomnia, assertiveness training, activity pacing and pleasant activity scheduling training, goal setting and life values and relapse prevention. Participants were given a manual describing the contents of the programme, a CD to practice Schultz Autogenic training at home and record sheets to register practices of CBT contents. Duration 14 weeks. Vs. **Usual care (n=30)**	Fibromyalgia N=93 (64 relevant to this protocol) Age - Mean (SD): 49.6 (6.8) years Duration of pain CBT 13.6 (9.2) control 11.6 (6.9) years 96.8% female	At 6 months follow up: • Quality of life • Sleep • Discontinuation • Pain reduction	3 arm trial. Third arm (CBT and hypnosis) excluded from this analysis. Serious indirectness of CBT intervention: included relaxation and education elements. Hospital Anxiety and Depression scale reported as total score – not validated

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		Conventional pharmacological treatments including analgesics, antidepressants, anticonvulsants and myorelaxants as appropriate.			for use in this way so not extracted. Unclear outcome: MOS sleep problems index scale info not reported. CBT group results higher than usual care indicating worse problems (from other studies) but discussion suggests improvement after CBT.
Castro 2012[96]	CBT Vs. Usual care	**CBT (n=48)** 2-hour sessions of CBT per week, for ten weeks (no further details provided). Vs. **Usual care (n=47)** Standard care (no further details provided).	Chronic MSK pain N=95 Age - Mean (SD): CBT 45.9 (8.1) years, standard care 48.7 (14.3) years Duration of pain at least 3 months	At post intervention (10 weeks): • Quality of life • Discontinuation • Pain reduction	No further info on location or cause of pain
Edinger 2005[146]	CBT Vs. Sleep hygiene Vs. Usual care	**CBT (n=18)** 6 x weekly individual sessions (1st session 45-60 minutes, subsequent sessions 15-30 minutes) led by 2 licensed clinical psychologists. During the initial session, recipients listened to an audiocassette cognitive therapy module designed to correct misconceptions about sleep needs and	Fibromyalgia and insomnia N=47	At post intervention (6 weeks) and 6 month follow up: • Quality of life • Sleep	Insomnia symptom questionnaire extracted as it provides an overall measure of sleep problems, but scale not reported. Also

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		the effects of aging, circadian rhythms, and sleep loss on sleep/wake functioning. The therapist then provided verbal and written (pamphlet) stimulus control instructions encouraging the following: (a) a standard rising time, (b) exiting bed during extended awakenings, (c) using the bedroom only for sleep and s2ex, and (d) avoiding daytime naps. An initial time in bed prescription set at the average baseline log sleep time plus 30 minutes was also provided to each patient. Remaining sessions entailed reviewing instructions and adjusting TIB. Duration 6 weeks. Vs. **Sleep hygiene (n=18)** 6 x weekly individual sessions (1st session 45-60 minutes, subsequent sessions 15-30 minutes) led by 2 licensed clinical psychologists. During the initial session, recipients listened to an audiocassette that provided them generic sleep education (i.e., descriptions of sleep stages and sleep architecture).The therapist then provided verbal and written (pamphlet) instructions to (a) limit caffeine and alcohol, (b) engage in regular moderate exercise, (c) have a light bedtime snack (e.g., cheese or yogurt), and (d) keep the bedroom dark, quiet, and cool. During subsequent sessions, the therapist reviewed and individually tailored SH therapy recommendations to address adherence issues. Duration 6 weeks. Vs. **Usual care (n=11)** No behavioural therapy but met weekly with a study coordinator to provide sleep log/actigraphy data and to complete questionnaires while	Age - Mean (SD): 48.6 (8.2) years Duration of pain not reported. Gender (M:F): 2/45	• Discontinuation • Pain reduction	reported: sleep efficiency, total wake time, total sleep time, sleep latency, and wake after onset, all measured by both sleep logs and actigraphy. Brief Pain Inventory reported but unclear which subscale (intensity or interference), so McGill Pain Questionnaire extracted instead.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		continuing their ongoing FM medical care. After follow-up assessment, offered CBT.			
Friesen 2017[165]	CBT Vs. Usual care	**CBT (n=30)** The Pain Course - 5 online lessons (images and text in slide show format), lesson summaries (similar to a self-help book), homework assignments, additional resources and standardised automated weekly emails to reinforce course completion, encourage use of skills etc. Access to patient stories demonstrating skills. Weekly 5-10 minute telephone contact with a doctorate-level clinical psychology graduate student (supervised by a registered psychologist) to summarise content, answer questions, reinforce progress, encourage skills, but no therapeutic advice. Duration 8 weeks. Vs. **Usual care (n=30)** Waiting list. Offered access to the pain course once the 8 week waiting period had elapsed.	Fibromyalgia N=60 Age - Mean (SD): 48 (11) years Duration of pain at least 3 months Gender (M:F): 3/57	At post intervention (8 weeks): • Quality of life • Psychological distress • Pain interference • Pain self-efficacy • Discontinuation • Pain reduction	4 week follow up outcomes only reported for intervention group, not extracted as not analysable.
Funch, 1984[166]	Biofeedback vs. Relaxation	**Biofeedback (n=27)** Grass Model 7 polygraph with 4 7P3 amplifiers and either a Dana Model 4600 Digital Multimeter with multiple range shift or a Wavetech Model 180 sweep/function generator was used. Output from integrated amplifiers with a 0.5-s time constant was fed directly into one of the 2 instruments. Silver-silver chloride electrodes were taped bilaterally over the masseteric area. At the initial session the patient was asked to bite down and observe the numbers on the meter increase or the frequency of the audio tone increase. Patients then received 10 1 minute trials with a minimum of 15-s inter-trial interval. Also given general	Temporomandibular joint pain N=57 Duration of pain, at least 2 years Age - Mean (SD): relaxation 35.6 (12.7) years, biofeedback 43 (15) years	At post intervention (12 weeks): • Pain reduction	Serious indirectness of the biofeedback intervention: included relaxation elements.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		instructions to practice relaxation for 20 minutes each day. Duration: average 12 weeks. Vs. **Relaxation (n=30)** 3 x 20 minute recorded relaxation tapes and daily muscle relaxation practice. Duration: average 12 weeks.			
Goldway 2019 [187]	Biofeedback Vs. Attention control	**Biofeedback (n=31)** Neurofeedback - 10 biweekly sessions, each composed of training to down-regulate Amygdala Electrical fingerprint using an auditory interface (in which the neural signal correlated with the volume of a soft piano tune; sessions 1, 3 & 5), an animated scenario interface (a 3D audio-visual animated scenario in which the neural signal is correlated with the level of unrest in a scenario where virtual characters in a waiting room become impatient, leave their seats and gesture loudly at the front desk receptionist; sessions 2, 4 & 6), or both (sessions 7, 8, 9 & 10). Within each session, NF trials contained two conditions: rest and regulate. Participants were instructed to modulate the interface only during the regulate condition. The real-NF group received feedback reflecting their Amyg-EFP signal level modulation. Vs. **Attention control (n=12)** Sham neurofeedback. 10 biweekly sessions, each composed of training to down-regulate Amygdala Electrical fingerprint using an auditory interface (in which the neural signal correlated with the volume of a soft piano tune; sessions 1, 3 & 5), an animated scenario interface (a 3D audio-visual	Fibromyalgia N=43 Age – mean (SD): intervention 35.5 (12.6) years, sham 35.9 (10.6) years Duration of pain Biofeedback, 4.3 (4.1), Attention control 41. (4.4) years	At post intervention (5 weeks) and mean 16.2 (8.72) months: • Psychological distress • Sleep • Discontinuation • Pain reduction	

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		animated scenario in which the neural signal is correlated with the level of unrest in a scenario where virtual characters in a waiting room become impatient, leave their seats and gesture loudly at the front desk receptionist; sessions 2, 4 & 6), or both (sessions 7, 8, 9 & 10). Within each session, NF trials contained two conditions: rest and regulate. Participants were instructed to modulate the interface only during the regulate condition. The control group received feedback reflecting a pre-recorded Amyg-EFP signal obtained from another successful participant in the real-NF group, indicating approximately 85 percent success in each session.			
Hallman 2011[201]	Biofeedback Vs. Usual care	**Biofeedback (n=12)** First training session to assess resonance frequency. Session 2–9, respiratory pacer was set at the particular frequency found in the previous session. Each session included four five-minute periods of resonant breathing with two minutes of rest after each period. Subjects received visual HRV feedback during resonance frequency breathing. They were instructed to try to maximize their peak-to-peak HRV as well as to attain the phase between respiration and HRV changes as closely as possible. Between sessions, subjects were instructed to practice paced breathing for at least 15 min a day, five days a week using a regular watch as a pacer and also given pacer software to use on their home computer. Duration: 10 weeks. Vs. **Usual care (n=12)**	Stress-related chronic neck pain N=24 Age - Mean (range): 40.5 (25-50) years Duration of pain at least 6 months, mean biofeedback 5.7 (5.5), usual care 6.0 (3.4) years	At post intervention (10 weeks): • Quality of life • Physical function • Psychological distress • Discontinuation	Control group took part in the breathing protocol in Session 1 and 10 in order to measure changes in heart rate variability.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		Instructed to perform their usual activities and were not refrained from any pharmacological or behavioural treatment, besides those stated as exclusion criteria			
Hedman-lagerlof 2018[215] Hedman-lagerlof 2019 [216]	CBT Vs. Usual care	**CBT (n=70)** Internet-delivered exposure therapy - 8 modules on the role of avoidance behaviours; psychoeducation about exposure; identification of personal avoidance behaviours; design of individually tailored exposure exercises based on refraining from avoidance behaviours and approaching situations or behaviours normally avoided. Progress monitored by a therapist (licensed psychologists/graduate psychology students), regular contact 1-3 times/week through text messages to guide, assist with problem-solving and remind participants to logon if they had been inactive. Relapse prevention program including an intervention on life values and scheduled mindfulness practices as a way to facilitate exposure. Duration 10 weeks. Vs. **Usual care (n=70)** Waiting list.	Fibromyalgia N=140 Age - Mean (SD): 50.3 (10.9) years Duration of pain, mean 10.1 (7.5) years Gender (M:F): 3/137	At post intervention (10 weeks) • Quality of life • Physical function • Psychological distress • Sleep • Discontinuation • Pain reduction	Outcomes also reported at 6 and 12 months but no comparative data because waiting list group started intervention at 10 weeks. Serious indirectness of CBT intervention: included education and mindfulness elements.
Jensen 2012[233] (Wicksell 2013[564])	ACT Vs. Usual care	**ACT (n=25)** 12 x weekly 90 minute sessions in groups of 6 participants conducted by 2 CBT-trained psychologists (10 sessions) and 1 CBT-trained physician (2 sessions) organised in to 4 phases - phase 1 (preparing for behaviour change) dysfunctional character of long-standing pain syndromes were discussed; phase 2 (shifting perspective) clarification of individual life values combined with an exercise in evaluating previous	Fibromyalgia N=43 Age - Mean (SD): 45.1 (6.6) years Duration of pain CBT 10.5 (1.2),	At post intervention (12 weeks) and 3 month follow up: • Quality of life • Psychological distress • Pain interference	

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		strategies to reduce pain; phase 3 (values oriented behaviour activation) short and long term behaviour goals based on identified life values; phase 4 (acceptance and cognitive diffusion) emphasis on utility of a more flexible behavioural repertoire in relation to pain and distress, strategies practiced in sessions and in homework assignments . Duration 12 weeks. Vs. **Usual care (n=18)** Waiting list.	control 11.8 (2.0) years All female	• Pain reduction	
Karlsson 2015[245]	CBT Vs. Usual care	**CBT (n=24)** 20 x 3 hour group CBT sessions (5-7 per group) over 6 months plus 3 x 3 hour booster sessions over the following 6 months by 2 psychologists trained in CBT. Components included knowledge, self-monitoring, behavioural skills training, cognitive restructuring, and life value issues. Therapeutic material included case illustrations, audio-visual material, readings, hand-outs, exercises, and thematic discussions. Homework assignments were applied between each session and included self-monitoring by simple diaries as well as a booklet with behavioural and cognitive exercises. A short relaxation technique (Jacobsen's progressive relaxation technique) was taught. Duration 12 months. Vs. **Usual care (n=24)** Patients' local physicians were responsible for the every-day care of the patients. No restrictions in changing medication or other treatment modalities.	Fibromyalgia N=48 Age - Mean (SD): CBT: 48.3 (11.5) years, usual care: 48.8 (6.5) years Duration of pain, at least 3 months, mean CBT 5.3 (4.67) Usual care 5.0 (4.01) All female	At 6 months: • Psychological distress • Pain interference • Discontinuation • Pain reduction	Serious indirectness of CBT intervention: included a relaxation element.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
Kemani 2015[247]	ACT Vs. Relaxation	**ACT (n=30)** 90 minute weekly sessions delivered by 5 therapists. A psychologist conducted10 sessions, and a pain physician with a formal therapist training in CBT and ACT conducted 2 sessions. Intervention had 4 phases: (1) dysfunctional character of pain symptoms and pain-related behaviours discussed to reduce influence of pain (2) workability of previous strategies to address pain were evaluated and the utility of a more flexible behavioural repertoire in relation to pain and distress were emphasised. (3) disengagement from verbal process, to decrease the negative impact of thoughts and experience on behaviour (4) participants defined short and long term behavioural goals and practiced the application of ACT strategies. Duration 12 weeks. Vs. **Relaxation (n=30)** 90 minute weekly sessions delivered by 5 therapists. Phases included (1) rational of using relaxation in the context of longstanding pain and a therapist guided in session practice of the long version of progressive relaxation (2) conditioned and differential relaxation was implemented, by prompting participants to think about their breathing and how this related to relaxation (3) the final phase consisted of rapid relaxation and the application of this in daily life. Duration 12 weeks.	Longstanding pain for more than 6 months (88.3% idiopathic pain) N=60 Age - Mean (SD): 40.3(11.4) years Duration of pain, at least 6 months, mean 9.9 (7.5) years	At post intervention (12 weeks) and 6 month follow up: • Quality of life • Physical function • Psychological distress • Discontinuation • Pain reduction	
Lami 2018[260]	CBT Vs. Usual care	**CBT pain (n=42)** 9 x 90 minute weekly group sessions led by therapists with a high level of professional training and experience in chronic pain and sleep disorders. Based on fear-avoidance model of chronic pain, aimed at modifying the	Fibromyalgia and insomnia N=126	At post intervention (9 weeks) and 3 months follow up: • Quality of life	3 armed trial - CBT pain vs. CBT insomnia and pain vs. usual care; CBT arms compared individually with

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		reinforcement contingencies that maintain pain behaviours and dysfunctional attitudes and emotional reactions. Participants given a therapy manual containing information and tasks involved in each session. Duration 9 weeks. Vs. **CBT insomnia and pain (n=42)** 9 x 90 minute weekly group sessions led by therapists with a high level of professional training and experience in chronic pain and sleep disorders. Covered the same objectives as CBT-pain and extended them to a sleep approach through training in cognitive, affective and behavioural skills for better management of sleep problems. Based on recommendations of the American Academy of Sleep and therapeutic guidelines for insomnia. Participants given a therapy manual containing information and tasks involved in each session. Duration 9 weeks. Vs. **Usual care (n=42)** No further details provided, but of the majority of participants used antidepressants, anxiolytics, anti-inflammatory drugs and/or analgesics.	Age - Mean (SD): 50.19 (8.24) years Duration of pain at least 6 months All female	• Psychological distress • Sleep • Discontinuation • Pain reduction	usual care but not with each other for analysis. Study reports 'Chronic pain self-efficacy scale' – sum of scores for 3 sub scales as a total score not extracted as not a validated measure. Serious indirectness of both interventions: included psycho education and relaxation elements.
Lazaridou 2017[265]	CBT Vs. Pain education	**CBT (n=8)** 4 x 60–70 minute visits conducted by a licensed clinical psychologist - sessions used active, structured techniques to alter distorted thoughts, with a focus on acquiring and practicing cognitive and emotion-regulation skills. Techniques such as relaxation, visual imagery, thought challenging, and distraction were used. CBT prominently emphasized in-vivo practice during each session, and featured home practice using written	Fibromyalgia N=16 Age - Mean (SD): 45.7 (12.2) years Duration of pain at least 1 year,	At post intervention (4 weeks): • Psychological distress • Pain interference • Discontinuation • Pain reduction	Serious indirectness of CBT intervention: included relaxation elements.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		exercises. Cognitive restructuring was used to help patients recognize the relationships between thoughts, feelings and behaviours. Patients learned to identify, evaluate, and challenge negative thoughts and to diminish the degree of catastrophizing about pain. Duration 4 weeks. Vs. **Pain education (n=8)** Information about fibromyalgia and about chronic pain. The sessions provided a variety of information about the nature and presumed causes of fibromyalgia, but they involved no active skills training or homework assignments. Duration 4 weeks.	mean 12.5 (12.2) years Gender (M:F): 3/13		
EFFIGACT study trial: Luciano 2014[291] (Luciano 2017[290])	ACT Vs. Usual care	**ACT (n=51)** 8 x 2.5 hour weekly group sessions; 10-15 patients; covering exercises and topics within the context of ACT practice and training; including various types of formal mindfulness practice; daily homework assignments of 15-30 minutes; led by a clinical psychologist . Duration 8 weeks. Vs. **Usual care (n=53)** Waiting list - no active treatment and offered preferred intervention at study conclusion.	Fibromyalgia N=156 (104 relevant to this protocol) Age - Mean (SD): ACT group: 48.88 (5.94) years, waiting list:48.28 (5.71) years Duration of pain approximately 13 years Gender (M:F): not reported	At post intervention (8 weeks) and 6 months follow up: • Quality of life • Psychological distress • Use of healthcare services • Discontinuation • Pain reduction	3 arm trial. Third arm (recommended pharmacological treatment) excluded from this analysis. Serious indirectness of ACT intervention: included mindfulness elements.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
Lumley, 2017[294] Pain and Stress Treatment for Fibromyalgia (PAST-FM) trial	CBT Vs. Education	**CBT (n=75)** 8 x 90 minute weekly sessions with a therapist (with doctoral degrees and experience in CBT pain management) focussing on coping and skills training for pain and symptom management. Each session included a topic driven brief lecture, teaching and practice of a skill and homework applying skills to everyday life e.g. self-monitoring, time-based pacing, guided imagery, cognitive reframing and goal setting. Duration: 8 weeks. Vs. **Education (n=76)** 8 x 90 minute weekly sessions with a therapist (nurse educator) covering the history and diagnosis of fibromyalgia, assessment of pain, fibromyalgia mechanisms, comorbid disorders, medications, evaluating fibromyalgia research and using the internet for information on health care. Duration: 8 weeks.	Fibromyalgia N=230 (151 relevant to this protocol) Age – Mean (SD): 49.13 (12.22) years Duration of pain, mean 13.61 (10.52) years 94% female	At post treatment (10 weeks) and 6 month follow up: • Quality of life • Physical function • Psychological distress • Sleep • Use of health care services • Discontinuation • Pain reduction	3 armed trial – 3rd arm not reported here (emotional awareness and expression therapy including prolonged exposure, expressive writing etc.). Serious indirectness of CBT intervention: included relaxation elements.
Martinez 2014[299]	CBT Vs. Sleep hygiene	**CBT (n=32)** 6 x 1.5 hour group sessions (5–6 participants) once a week led by 3 female therapists with experience in the management of chronic pain and sleep disorders. Session 1: focused on information about the relationship between sleep and FM, basic notions about sleep, and sleep hygiene education. Session 2: instructions for applying sleep restriction and stimulus control. Session 3: training physiological deactivation procedures (slow breathing, passive relaxation and imagery training). Sessions 4 and 5: cognitive therapy to change negative thoughts about insomnia through verbal discussion and behavioural experiments. Session 6: maintaining	Fibromyalgia and insomnia N=64 Age - Mean (SD): 47.58 (6.82) years Duration of pain at least 6 months, mean 14.33 (9.17) years All female	At post intervention (6 weeks): • Quality of life • Psychological distress • Pain self-efficacy • Sleep • Discontinuation • Pain reduction	Serious indirectness of CBT intervention: included relaxation elements 3 and 6 month follow up also reported but sleep hygiene group had CBT directly following intervention phase, so comparisons no longer appropriate

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		achievements and preventing relapses. Duration 6 weeks. Vs. **Sleep hygiene (n=32)** 6 x 1.5 hour group sessions (5–6 participants) once a week led by 3 female therapists with experience in the management of chronic pain and sleep disorders. Aim of the intervention only to provide training about sleep hygiene rules. Session 1: participants given the same information about sleep as those in the CBT-I program. Session 2: sleep hygiene rules related to environmental factors (e.g. noise, temperature, light). Session 3: learning about lifestyle factors that influence sleep (use of stimulants and other substances). Sessions 4 and 5: information about diet and physical exercise, respectively. Session 6: maintaining achievements and preventing relapses, as in the CBT-I program. Duration 6 weeks.			
Masheb 2009[300]	CBT Vs. Psychotherapy	**CBT (n=25)** 10 x weekly individual 60-minute sessions by doctoral level research therapists to assist participants in taking control of pain by creating understanding of the relationship of thoughts, feelings and behaviours. Participants taught self-management skills that alter thoughts, feelings and behaviours. 3 overlapping phases: orientation to a self-management approach, skills acquisition, and skills practice. Motivational enhancement, role-playing, problem-solving, and contingent reinforcement to increase patient adherence. Final component of each session involved session review and collaboration in the development of goals and homework for the coming week. Self-	Vulvodynia N=50 Age - Mean (SD): 43 (12.1) years Duration of pain at least 6 months, mean 8.4 (7.8) years	At post intervention (10 weeks) and 1 year follow up: • Psychological distress • Discontinuation • Pain reduction	Study reported Multidimensional pain inventory pain intensity sub scale and McGill pain questionnaire, McGill extracted as MPI scale unclear (says 3 items 0-6, but total scores are e.g. 1.8, seems like an average). Serious indirectness of CBT intervention:

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		management skills included behavioural, sex therapy, cognitive, and relaxation skills that were practiced in session and at home. Behavioural skills included gate control, activity pacing, and goal setting. Sex therapy skills included sensate focus and assertive communication regarding sexual relations. Cognitive component involved a series of cognitive skills: identifying triggers for negative mood states, identifying automatic negative thoughts, identifying cognitive distortion associated with the automatic negative thought, challenging negative thoughts, and restructuring the negative thought. Relaxation skills: diaphragmatic breathing, progressive muscle relaxation, and relaxation that was specific to the pelvic floor musculature. Duration 10 weeks. Vs. **Supportive psychotherapy (n=25)** 10 x weekly individual 60-minute sessions by doctoral level research therapists. Non-directive talk therapy that lacks specific behavioural interventions. Therapists assisted participants in expressing feelings while not making specific suggestions for how the person might wish to change. The therapist's role was to have unconditional positive regard, to engage in empathic understanding, and to mirror. Sessions began with, "How has your week been generally and with regard to your vulvar pain?" The remainder of each session was directed by the participant, unstructured, and generally focused on complaints of vulvar pain and associated problems. Therapists did not make interpretations, problem-solve, challenge or restructure			included relaxation elements.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		cognitions, or initiate goal-setting. Duration 10 weeks.			
Mcbeth 2012[304] Beasley 2015[41]	Telephone CBT Vs. Usual care	**Telephone CBT (n=112)** Delivered by 4 therapists: initial 45-60 minute assessment, 7 x 30-45 minute weekly sessions, 1 session 3 months and 6 months after randomisation. 2-3 patient-defined goals. Patients received a self-management CBT manual including stories of fictitious patients using specific CBT techniques (behavioural activation, cognitive restructuring and lifestyle changes) to enable an informed choice on which form they preferred. Sessions 2 to 9 involved implementing CBT techniques, working toward goals, and problem solving barriers to improvement. Later sessions focused on relapse prevention. Duration 6 months. Vs. **Usual care (n=109)** No drugs approved for use in fibromyalgia, and access to CBT or exercise programs is limited, if available at all. Received the usual care from their family physician, although the precise care delivered, was not reported.	Fibromyalgia N=442 (221 relevant to this protocol) Age - Mean (SD): 56 (13) years Duration of pain not reported. 70.5% female	At 9 months (3 months follow up): • Quality of life • Sleep • Discontinuation	3 arm trial, third arm (combined exercise and CBT) excluded from this analysis.
McCrae 2018[310] SPIN (Sleep and Pain Interventions in Fibromyalgia) trial	CBT for pain Vs CBT for insomnia Vs Usual care	**CBT for pain (n=37)** 8 individually delivered 50 minute sessions by pre-doctoral students in clinical psychology. Treatment developed by psychologists who provided training, weekly supervision, and on-going monitoring. Participants were given a workbook detailing treatment instructions and rationale. They were questioned during sessions about home practice of techniques and procedural modifications were	Fibromyalgia and insomnia N=113 Age – mean (SD): CBTp 51.54 (10.62) years, CBTi 54.13 (11.03) years,	At post intervention (8 weeks) and 6 months: • Psychological distress • Pain interference • Sleep • Pain	Serious indirectness of CBT interventions: included sleep hygiene and relaxation elements.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		adopted as needed (e.g. pacing activities differently and adjusting bed/wake times). Interventionists encouraged adherence and emphasized the importance of regular home practice, which was monitored by daily practice logs. Session topics: pain education and diaphragmatic breathing, progressive muscle relaxation, activity-rest cycle and autogenic relaxation, visual imagery, cognitive therapy (3 sessions), review of skills and long-term maintenance. Vs. **CBT for insomnia (n=39)** 8 individually delivered 50 minute sessions by pre-doctoral students in clinical psychology. Treatment developed by psychologists who provided training, weekly supervision, and on-going monitoring. Participants were given a workbook detailing treatment instructions and rationale. They were questioned during sessions about home practice of techniques and procedural modifications were adopted as needed (e.g. pacing activities differently and adjusting bed/wake times). Interventionists encouraged adherence and emphasized the importance of regular home practice, which was monitored by daily practice logs. Session topics: sleep education, sleep hygiene and stimulus control, relaxation, sleep restriction, cognitive therapy (3 sessions), review of skills and long-term maintenance. Vs. **Usual care (n=37)** Waiting list	waiting list 52.27 (11.19) years Duration of pain at least 6 months, mean CBTp 94.64 (76.16) months, CBTi 114.52 (91.10) months, waiting list 109.46 (88.62) months		

Study	Intervention and comparison	Details	Population	Outcomes	Comments
Menzies 2006[315]	Relaxation Vs. Usual care	**Relaxation (n=24)** 3 x 20 minute guided imagery audiotapes. First tape: training to develop familiarity with relaxation and imagery, muscle relaxation and release of tension, signal breath practiced daily for 2 weeks. Second tape: shortened version of the signal breath relaxation script, followed by imagery of a pleasant scene, practiced daily for 2 weeks. Third tape: reinforced the signal breath conditioning for relaxation, instructed to imagine themselves walking onto a theatre stage where they were to perform actions and behaviours that represented how they would most like to be when they are free of all symptoms of FM (end state imagery), practiced daily for 2 weeks. During a 4-week follow-up, participants could choose to use any of the three tapes in any order and were requested to use at least one of the tapes once daily. Duration 10 weeks. Vs. **Usual care (n=24)** No further details provided.	Fibromyalgia N=48 Age - Mean (SD): 49.6 (10.53) years Duration of pain not reported. Gender (M:F): 1/47	At post intervention (10 weeks): • Quality of life • Pain self-efficacy • Pain reduction	Pain reported by McGill pain questionnaire short form (total score 0-45 plus sub scale reported); extracted pain VAS sub scale only, as this is the most commonly reported.
Menzies 2014[314]	Relaxation Vs. Usual care	**Relaxation (n=36)** 3 x 20 minute guided imagery audiotapes. First tape: training to develop familiarity with relaxation and imagery, muscle relaxation and release of tension, signal breath practiced daily for 2 weeks. Second tape: shortened version of the signal breath relaxation script, followed by imagery of a pleasant scene, practiced daily for 2 weeks. Third tape: guided the participant on an imaginary journey through their immune system, practiced daily for 2 weeks. During a 4-week follow-up, participants could choose to use any of the three tapes in any order and were requested to use at	Fibromyalgia N=72 Age – Mean (SD): 46.9 (12.8) years Duration of pain not reported All female	At post intervention (10 weeks): • Psychological distress • Pain interference • Pain self-efficacy • Discontinuation • Pain reduction	

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		least one of the tapes once daily. Duration 10 weeks. Vs. **Usual care (n=36)** Asked to maintain their current care practices in managing FMS symptoms. All participants were asked not to initiate any new treatments, if possible, for the duration of their 10-week participation.			
Miro 2011[319]	CBT Vs. Sleep hygiene	**CBT (n=22)** 6 x weekly 90 minute group sessions (5-6 participants) led by 3 female CBT experts with experience in FM. Information about relationship between FM and sleep and sleep hygiene education; sleep restriction and stimulus control instructions; relaxation training; cognitive therapy for dysfunctional beliefs related to insomnia; maintaining achievements and preventing relapses. Duration 6 weeks. Vs. **Sleep hygiene (n=22)** 6 x weekly 90 minute group sessions (5-6 participants) led by 3 female CBT experts with experience in FM. Information about relationship between FM and sleep and sleep hygiene education; sleep hygiene rules related to environmental factors; lifestyle factors that influence sleep; information about diet and physical exercise; maintaining achievements and preventing relapse. Duration 6 weeks.	Fibromyalgia and insomnia N=44 Age - Mean (SD): 46.45 (7.03) years Duration of pain mean 4.47 (3.83) years All female	At post intervention (7 weeks): • Quality of life • Psychological distress • Sleep • Discontinuation • Pain reduction	Serious indirectness of CBT intervention: included education and relaxation elements.
Parra-delgado 2013[445]	Mindfulness Vs. Usual care	**Mindfulness (n=17)** Mindfulness based cognitive therapy. 8 x structured 2.5 hr group sessions led by a therapist with certified training in MBCT. Practical	Fibromyalgia N=33	At post intervention (3 months) and 3 month follow up:	

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		mindfulness exercises with a focus on pain-related stimuli and aiming to teach patients to relate pain experiences to thoughts and feelings in a different way psycho-educational activities on causes and development of depression and anxiety; identification of methods of self-care; formal practice at home (body scanning, sitting/walking medication, mindful breathing) 6 days a week. Duration 3 months. Vs. **Usual care (n=16)** Usual medication, medical visits, rehabilitation sessions and activities proposed by the Fibromyalgia Association.	Age - Mean (SD): MBCT 53.13 (10.5) years, usual care 52.69 (10.58) years Duration of pain, mean 21.27 (15.22) All female	• Quality of life • Psychological distress • Discontinuation	
Peski-oosterbaan 1999[452] (Van peski-oosterbaan 1999[549])	CBT Vs. Usual care	**CBT (n=36)** 4 to 12 weekly sessions of 45-60 minutes, depending on severity of problem, final 1 or 2 sessions were monthly, maximum duration of therapy was 6 months, delivered by physicians with basic training in CBT and a senior psychologist. Written information about therapy, procedures, alternative explanations, related factors and possible consequences of the complaints. First session: physical symptoms, results of medical investigations, coping strategies. Sessions 2-4: breathing and relaxation. Subsequent sessions: identifying and challenging irrational beliefs using diaries. Session 8 and on: behavioural experiments to challenge negative thoughts. Duration up to 6 months. Vs. **Usual care (n=36)** Free to use health resources as they saw fit.	Non cardiac chest pain N=72 Age - Mean (SD): 48.9 (10.6) years Duration of pain not reported	At 12 months: • Psychological distress • Use of healthcare services • Discontinuation • Pain reduction	Serious indirectness of CBT intervention: included relaxation elements.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
Peters, 2017[453]	Internet CBT Vs. Usual care	**Internet CBT (n=116)** Each module provided online written information about the topic of that week and practical assignments. Assignments could either be completed online or in a workbook that was provided to participants at the start of the intervention. To promote adherence, telephone and e-mail support was provided by 5 graduate or recently graduated students in Psychology. Every participant had a single assistant assigned to them. Main purpose of the program was to teach participants more active ways of coping with their pain and to improve their level of functioning. The original Swedish texts were translated in Dutch and slightly adapted to Dutch culture. The program consisted of 7 modules teaching applied relaxation, stretching exercises, cognitive restructuring, and coping techniques. In module 2, 3, and 4 body scan exercises were provided, in text and in mp3 format, and could be downloaded. In the eighth module participants made a 6 relapse prevention plan, that is, how to continue with the strategies they had learned. Vs. **Usual care (n=51)** In the waiting list control group participants were initially only given access to the online pre-treatment questionnaires. After an 8-week waiting period, participants were contacted and 1 asked to complete the post measurements. After completion, they could start with the treatment program of their choice.	Chronic MSK (2/3 fibromyalgia; unclear other % made up of back neck shoulder pain) N=284 (167 relevant to this protocol) Age - Mean (SD): 49.4(11.5) years Duration of pain at least 3 months (mean 11.95 (9.5) years)	At post intervention (8 weeks): • Physical function • Psychological distress • Discontinuation • Pain reduction	3 armed trial – 3rd arm (internet based positive psychology) excluded. Serious indirectness; of the CBT intervention: included relaxation elements.
Picard 2013[455]	Hypnosis Vs.	**Hypnosis (n=31)** 5 x 1 hour sessions (8, 15, 21 and 28 day intervals) conducted by a psychologist qualified in	Fibromyalgia	At post intervention (3	

Study	Intervention and comparison	Details	Population	Outcomes	Comments
	Usual care	hypnotherapy. Interventions were patient-tailored and directed toward enhancing patient competence and mastery in managing pain and stress related to disease. Sessions involved hypnotic induction, analgesic and non-analgesic suggestions, including reinterpreting pain sensation as numbness through the use of imagery, improving individual coping, improving stress-management skills and changing relationship with disease. Patients instructed to practice self-hypnosis daily. Duration 3 months. Vs. **Usual care (n=31)** Waiting list. Allowed to continue pain medications and antidepressants if necessary.	N=62 Age - Mean (SD): hypnosis 48.1 (9.3) years, waiting list 49.3 (8.5) years Duration of pain at least 6 months All female	months) and 3 month follow up: • Quality of life • Psychological distress • Sleep • Discontinuation • Pain reduction	
Sánchez 2012[477]	CBT Vs. Sleep hygiene	**CBT (n=13)** 2 sessions of individual interviews focusing on the origin and evolution of the problem and domiciliary polysomnography. 3 female CBT experts with experience in FM provided the therapy guided by a treatment manual designed for the study. Treatment delivered in 6 x 90 minute weekly group sessions including 5-6 participants. Duration 6 weeks. Vs. **Sleep hygiene (n=13)** Identical format to CBT but sessions focused on sleep hygiene only. This included sleep hygiene education, rules related to environmental and lifestyle factors, and information about diet and physical exercise, as well as goal making and maintaining achievements. Duration 6 weeks.	Fibromyalgia and insomnia N=26 Age - Mean (SD): 46.79 (5.15) years Duration of pain, mean 5.02 (4.28) years All female	At post intervention (6 weeks): • Sleep	

Study	Intervention and comparison	Details	Population	Outcomes	Comments
Scheidt 2013[480]	Psychotherapy vs. Usual care	**Psychotherapy (n=24)** 25 weekly sessions of psychodynamic psychotherapy specifically adapted to the needs of patients with pain symptoms. Sessions lasted between 50min to 1 hour. Treatment approach based on a dysregulation model of psychosomatic illness and on research on attachment styles and affect regulation in somatoform disorders, with integrated components of interpersonal therapy. Duration 25 weeks. Vs. **Usual care (n=23)** Treatment as usual, with 4 contacts during a 6 month period, each lasting about 10-15 minutes in which patients were advised with regard to medication and health behaviour and were encouraged to increase physical activity and gentle stretching exercises Duration 25 weeks.	Fibromyalgia N=47 Age - Mean (SD): 48.76 (7.92) years Duration of pain 8.12 (7.88) years All female	At 12 month follow up (18 months): • Quality of life • Physical function • Psychological distress • Pain interference • Discontinuation	Pain disability index – extracted under pain interference: “assesses the degree to which chronic pain interferes with daily activities”.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
Simister 2018[494]	ACT Vs. Usual care	**ACT (n=33)** Online ACT programme under the guidance of a registered psychologist - 7 modules, each containing a written unit including metaphors, experiential exercises and recurring vignettes describing the experiences of 4 people with FM, enhanced with audio recordings, videos and experiential homework exercises. Completed at own pace but encouraged to spend 1 week per module, sent weekly email reminders. Duration 2 months. Vs. **Usual care (n=34)** Treatment as usual - continued current treatment regime such as guidance from GP. Prescribed and over the counter analgesics were the most commonly reported treatments (others included mood stabilisers, anticonvulsants and supplements). Participants additionally reported spinal nerve blocks, massage, physiotherapy, exercise programmes, acupuncture, heat/cold therapy and dietary changes before the study.	Fibromyalgia N=67 Age - Mean (SD): 39.7 (9.36) years Duration of pain, mean 10.16 (7.83) years 95% female	At post intervention (2 months) and 3 month follow up: • Quality of life • Physical function • Psychological distress • Sleep Discontinuation • Pain reduction	Serious indirectness: some participants used treatments which would not be considered usual care, but unclear how many.
Soares, 2002[500]	Education Vs. CBT Vs. Usual care	**Education (n=20)** 2 individual sessions (2h each) and 15 groups sessions (2 hours each, 3-5 patients in each group) over a 10 week period (totalling 102 hours). Conducted by a licensed physiotherapist and occupational therapist. The focus of the intervention was on information about various health-related topics, about: the body, FMS, pain, sleep hygiene, stress, education, managing crises, ergonomic education, and self-management. An element of body awareness training was also included.	Fibromyalgia N=60 Age- Mean(SD) 45(9) years Duration of pain at least 2 years, mean 42.77(39.01) months	At 10 weeks and 6 months: • Quality of life • Pain self-efficacy • Sleep • Pain reduction • Discontinuation	Serious indirectness of the CBT intervention: included relaxation and biofeedback elements.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		Vs. **CBT (n=20)** 5 individual sessions (1h each) and 15 group sessions (2h each/3-5 patients in each group) over a 10 week period (totalling 120h of therapy). Sessions were conducted by a licensed psychologist/CB therapist. The intervention focused mainly on the acquisition and development of diverse skills to manage pain. Practical management covered the types of pain, and the 3 component model of pain, stress and its reactions, behavioural patterns that increase the risk for stress and ill health, how to create calm in the week days, thought traps, attitudes and patterns of thinking, problem solving, pain management, environmental issues, self-management, estimation of risk, plans and goals for the future, maintenance and relapse. Vs, **Usual care (n=20)** Waiting list control. No further details.	All female		
Thieme 2006[520]Thieme 2007	CBT Vs. Behaviour therapy	**CBT (n=42)** 15 x weekly 2 hour sessions co led by a psychologist and a rheumatologist, conducted in groups of 5 patients; spouses attended 4 sessions. Focus on patients' thinking and involved problem-solving, stress and pain coping strategies and relaxation. Patients taught the meaning of the stress tension pain circle as a cognitive pain model and learned coping strategies and the reduction of catastrophising thoughts. Weekly homework tasks, encouragement to engage in physical activities, asked to reduce analgesic medication at a gradual rate. Relaxation exercises were also encouraged between the sessions.	Fibromyalgia N=125 (85 relevant to this protocol) Age - Mean (SD): 47.46(9.75) years Duration of pain at least 6 months, mean 8 (9.5) years	At 12 months: • Physical function • Use of health care services • Pain reduction	3 armed trial – 3rd arm (general discussions among patients in groups guided by therapists) excluded from analysis here. Serious indirectness of the CBT intervention: included relaxation elements.

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		Therapists identified instances of maladaptive thinking and encouraged the group to challenge these instances and to provide more appropriate interpretations and alternatives. Although the importance of behaviour change was noted, the focus of this treatment was on the change of maladaptive thoughts and attitudes. Duration 15 weeks. Vs. **Behaviour therapy (n=43)** 15 x weekly 2 hour sessions co-led by a psychologist and a rheumatologist, conducted in groups of 5 patients; spouses attended 4 of the sessions. Operant behaviour therapy based on changing observable pain behaviours and included video feedback of expressions of pain as well as contingent positive reinforcement of pain incompatible behaviours and punishment of pain behaviours. Structured time-contingent exercises were provided according to operant principles in the sessions and as homework exercises. Treatment also included time contingent intake and reduction of medication, increase of bodily activity, reduction of interference of pain with activities, reduction of pain behaviours, and training in assertive pain-incompatible behaviours. Patients also engaged in role playing to reduce pain behaviours and increase healthy behaviours. Patients, spouses and group members used a reinforced plan consisting of the presentation of a red card when pain behaviours were displayed and a green card when healthy behaviours were displayed. Patients encouraged to increase activity levels and reduce medication. Duration 15 weeks.	All female		

Study	Intervention and comparison	Details	Population	Outcomes	Comments
Turner, 2006[538]	CBT Vs. Education	**Cognitive behavioural therapy (n=79)** 12 week intervention. 4 biweekly sessions over 8 weeks. Participants were given a manual with materials to read between sessions and discuss in sessions. Participants saw one of 3 licensed clinical psychologists, and treatment was based on standard CB pain therapies. The manual included articles concerning psychological aspects of pain, challenging negative thoughts about pain, relaxation, and other behavioural techniques for pain management, coping with pain flare-ups, and relapse prevention. Also included relaxation and breathing techniques. Vs. **Education (n=79)** Same protocol but sessions didn't include specific CBT techniques and conducted by patient educations trained and supervised by a clinical psychologist. No advice or recommendations were given beyond the protocol and participants were given information about TMD, general health care information and reviewing each point in the manual, as well as answering patient questions.	TMD pain N=158 Age – Mean(SD) 36(10.9) years Duration of pain at least 3 months, median 13.5 months (4-78 months)	At 12 weeks and 12 months: • Physical function • Pain self-efficacy • Discontinuation • Pain reduction	
Van Santen, 2002[551]	Biofeedback Vs. Usual care	**Biofeedback (n=56)** Individual 30 minute sessions twice weekly for 8 weeks, in a hospital. In the first session patients were given general suggestions to accomplish muscle relaxation and were given feedback using a tonometer. In the subsequent 15 sessions patients were taught the progressive relaxation technique consisting of alternately tightening and relaxation different groups of muscles, led by a regular supervisor (psychologist or physiotherapist). Also included progressive relaxation technique twice daily at	Fibromyalgia N=143 (85 relevant to this protocol) Age-Mean(range): 43.9 (26-60) years	At 24 weeks: • Quality of life (Arthritis impact measurement scale)? • Psychological distress • Pain reduction • Discontinuation	3 arm trial. Third arm (fitness training) excluded from this analysis Patients in the intervention group also randomised to receive an educational component aimed at improving adherence

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		home using an audiotape. Half of individuals were also randomised to receive an educational program aimed to improve compliance, which consisted of 6 health promotion sessions of 90 minutes each, spread over the 24 weeks. Vs. **Usual care (n=29)** Control patients received the usual care at the outpatient department and by their GP: this included analgesics, NSAIDS, tricyclic antidepressant agents if appropriate, and physiotherapy and counselling was allowed	Duration of pain 10.1 (range 1-38) years in biofeedback group, 15.4, range 3-40 in control		Serious indirectness of biofeedback intervention: included relaxation elements
Viljanen 2003[556]	Relaxation Vs. Usual care	**Relaxation (n=128)** Instructed by a physiotherapist 3 times a week, for 30 minutes for 12 weeks. Relaxation training comprised various techniques training, functional relaxation, and systematic desensitisation. 15 different techniques were incorporated into the training during the 12 weeks. Exercises aimed to teach participants to activate only those muscles needed for different daily activities and to relax the other muscles. Participants were taught to perform the techniques independently from the fifth week and to avoid unnecessary tension in the neck muscles. Duration 12 weeks. Vs. **Usual care (n=130)** Instructed not to change their physical activity or means of relaxation during the 12 months of follow up.	Chronic non-specific neck pain N=393 Age - Mean (SD): 44(6.9) years Duration of pain at least 3 months, mean 10.7(6.3) years All female	At post intervention (12 weeks) and 12 months (9 month follow up): • Physical function • Discontinuation • Pain reduction	3 armed trial – 3rd arm (dynamic muscle training) excluded
Williams 2010[570]	Internet CBT Vs. Usual care	**Internet CBT (n=59)** Web-enhanced behavioural self-management - translated content from traditional face-to-face cognitive-behavioural therapy for FM. 13 modules	Fibromyalgia N=118	At post intervention (6 months):	Serious indirectness of CBT intervention: included education elements

Study	Intervention and comparison	Details	Population	Outcomes	Comments
		segregated into three broad segments: (a) educational lectures providing background knowledge about FM as a disease state, (b) education, behavioural, and cognitive skills designed to help with symptom management, and (c) behavioural and cognitive skills designed to facilitate adaptive life style changes for managing FM. Video lecture on the topic by a clinician experienced in applying the selected topic with respect to FM, written summaries of the video lecture for reading or downloading, homework and self-monitoring forms for applying the behavioural strategies described in the video lecture, and supplemental educational materials unique to each topic. Duration 6 months. Vs. **Usual care (n=59)** Usual and customary care from primary care physician.	Age - Mean (SD): 50.46 (11.45) years Duration of pain at least 3 months, mean 9.4 (6.5) years Gender (M:F): 6/112	• Physical function • Psychological distress • Sleep • Discontinuation • Pain reduction	
Woolfolk 2012[577]	CBT Vs. Usual care	**CBT (n=38)** Affective cognitive behavioural therapy: 10-session, individually-administered, manualized intervention including relaxation training, activity regulation, facilitation of emotional awareness, cognitive restructuring, and interpersonal communication training. Duration 10 weeks. Vs. **Usual care (n=38)** Treatment as usual - no further details.	Fibromyalgia N=76 Age - Mean (SD): CBT 47.79 (9.28) years, usual care 50.21 (10.14) years Gender (M:F): 9/67	At 3 months and 9 months: • Pain reduction • Discontinuation	Serious indirectness of CBT intervention: included relaxation training.

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: CBT versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Quality of life (EQ-5D) final values ≤3 months Scale from: 0-1.	140 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean quality of life (EQ-5D) final values ≤3 months in the control groups was 0.44	The mean quality of life (EQ-5D) final values ≤3 months in the intervention groups was 0.16 higher (0.06 to 0.26 higher)
Quality of life (EQ-5D) final values >3 months Scale from: 0-1.	256 (2 studies) 6-9 months	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean quality of life (EQ-5D) final values >3 months in the control groups was 0.59	The mean quality of life (EQ-5D) final values >3 months in the intervention groups was 0.1 higher (0.03 to 0.16 higher)
Quality of life (EuroQoL VAS) final values ≤3 months Scale from: 0 to 100.	113 (1 study) 9 weeks	⨁⊖⊖⊖ VERY LOW1,3,4 due to risk of bias, indirectness, imprecision		The mean quality of life (euroqol VAS) final values ≤3 months in the control groups was 53.49	The mean quality of life (euroqol VAS) final values ≤3 months in the intervention groups was 6.96 higher (1.23 to 12.69 higher)
Quality of life (FIQ) final values ≤3 months - CBT for pain Scale from: 0 to 100.	99 (2 studies) 9-10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean quality of life (FIQ) final values ≤3 months - CBT for pain in the control groups was 40.98	The mean quality of life (FIQ) final values ≤3 months - CBT for pain in the intervention groups was 2.43 lower (6.17 lower to 1.31 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Quality of life (FIQ) final values ≤3 months - CBT for pain + insomnia Scale from: 0 to 100.	63 (1 study) 9 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness		The mean quality of life (FIQ) final values ≤3 months - CBT for pain + insomnia in the control groups was 55.45	The mean quality of life (FIQ) final values ≤3 months - CBT for pain + insomnia in the intervention groups was 0.37 higher (7.38 lower to 8.12 higher)
Quality of life (FIQ) final values >3 months - CBT for pain Scale from: 0 to 100.	73 (2 studies) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness		The mean quality of life (FIQ) final values >3 months - CBT for pain in the control groups was 59.68	The mean quality of life (FIQ) final values >3 months - CBT for pain in the intervention groups was 0.91 lower (8.74 lower to 6.92 higher)
Quality of life (FIQ) final values >3 months - CBT for pain + insomnia Scale from: 0 to 100.	112 (2 studies) 5-9 months	⨁⊖⊖⊖ VERY LOW1,2,3,6 due to risk of bias, inconsistency, indirectness, imprecision		The mean quality of life (FIQ) final values >3 months - CBT for pain + insomnia in the control groups was 60.86	The mean quality of life (FIQ) final values >3 months - CBT for pain + insomnia in the intervention groups was 7.78 lower (28.65 lower to 13.08 higher)
Quality of life (SF36 mental composite) final values ≤3 months - CBT for pain + insomnia Scale from: 0 to 100.	13 (1 study) 6 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36 mental composite) final values ≤3 months in the control groups was 45.5	The mean quality of life (SF36 mental composite) final values ≤3 months in the intervention groups was 5.2 higher (1.82 to 8.58 higher)
Quality of life (SF36 mental composite) final values >3 months - CBT for pain + insomnia Scale from: 0 to 100.	24 (1 study) 8 months	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean quality of life (SF36 mental composite) final values >3 months - CBT for pain + insomnia in the	The mean quality of life (SF36 mental composite) final values >3 months - CBT for pain + insomnia in the intervention groups was 11.3 higher (9.05 to 13.55 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
				control groups was 40	
Quality of life (SF36) final values ≤3 months - Functional capacity Scale from: 0 to 100.	93 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - functional capacity in the control groups was 32.9	The mean quality of life (SF36) final values ≤3 months - functional capacity in the intervention groups was 3.8 higher (4.15 lower to 11.75 higher)
Quality of life (SF36) final values ≤3 months - Physical limitations Scale from: 0 to 100.	93 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - physical limitations in the control groups was 13.5	The mean quality of life (SF36) final values ≤3 months - physical limitations in the intervention groups was 8.9 higher (0.95 to 16.85 higher)
Quality of life (SF36) final values ≤3 months - General health Scale from: 0 to 100.	93 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - general health in the control groups was 33.1	The mean quality of life (SF36) final values ≤3 months - general health in the intervention groups was 9.1 higher (0.96 to 17.24 higher)
Quality of life (SF36) final values ≤3 months - Pain Scale from: 0 to 100.	93 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - pain in the control groups was 33.1	The mean quality of life (SF36) final values ≤3 months - pain in the intervention groups was 0.7 higher (6.26 lower to 7.66 higher)
Quality of life (SF36) final values ≤3 months - Vitality Scale from: 0 to 100.	93 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - vitality in the control groups was 28.2	The mean quality of life (SF36) final values ≤3 months - vitality in the intervention groups was 6.8 higher (1 lower to 14.6 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Quality of life (SF36) final values ≤3 months - Social aspects Scale from: 0 to 100.	93 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - social aspects in the control groups was 44.7	The mean quality of life (SF36) final values ≤3 months - social aspects in the intervention groups was 5.3 higher (3.04 lower to 13.64 higher)
Quality of life (SF36) final values ≤3 months - Emotional limitations Scale from: 0 to 100.	93 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - emotional limitations in the control groups was 20.7	The mean quality of life (SF36) final values ≤3 months - emotional limitations in the intervention groups was 11.1 higher (0.97 lower to 23.17 higher)
Quality of life (SF36) final values ≤3 months - Mental health Scale from: 0 to 100.	93 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - mental health in the control groups was 44.2	The mean quality of life (SF36) final values ≤3 months - mental health in the intervention groups was 5 higher (3.29 lower to 13.29 higher)
Quality of life (SF12 physical component) final values ≤3 months Scale from: 0 to 100.	60 (1 study) 8 weeks	⨁⨁⊖⊖ LOW1,3 due to risk of bias, imprecision		The mean quality of life (sf12 physical component) final values ≤3 months in the control groups was 32.82	The mean quality of life (sf12 physical component) final values ≤3 months in the intervention groups was 1.88 higher (2.2 lower to 5.96 higher)
Quality of life (SF12 mental component) final values ≤3 months Scale from: 0 to 100.	60 (1 study) 8 weeks	⨁⨁⊖⊖ LOW1,3 due to risk of bias, imprecision		The mean quality of life (sf12 mental component) final values ≤3 months in the control groups was 38.95	The mean quality of life (sf12 mental component) final values ≤3 months in the intervention groups was 0.67 higher (4.51 lower to 5.85 higher)
Physical function (WHO Disability Assessment Schedule) final values ≤3	140 (1 study) 10 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of		The mean physical function (who disability assessment schedule) final values ≤3 months	The mean physical function (who disability assessment schedule) final values ≤3 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
months Scale from: 0 to 100.		bias, indirectness		in the control groups was 40.83	16.19 lower (22.1 to 10.28 lower)
Physical function (FIQ physical impairment sub scale) final values ≤3 months Scale from: 0 to 27.	162 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean physical function (FIQ physical impairment sub scale) final values ≤3 months in the control groups was 20.63	The mean physical function (FIQ physical impairment sub scale) final values ≤3 months in the intervention groups was 2.69 lower (4.6 to 0.78 lower)
Physical function (FIQ physical function sub scale) change scores ≤3 months Scale from: 0 to 10.	28 (1 study) 6 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean physical function (FIQ physical function sub scale) change scores ≤3 months in the control groups was 0.2	The mean physical function (FIQ physical function sub scale) change scores ≤3 months in the intervention groups was 0.5 lower (1.95 lower to 0.95 higher)
Physical function (SF36 physical function sub scale) final values >3 months Scale from: 0 to 100.	118 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean physical function (SF36 physical function sub scale) final values >3 months in the control groups was 38.9	The mean physical function (SF36 physical function sub scale) final values >3 months in the intervention groups was 2.2 higher (0.92 lower to 5.32 higher)
Physical function (FIQ physical function sub scale) change scores >3 months Scale from: 0 to 10.	28 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean physical function (FIQ physical function sub scale) change scores >3 months in the control groups was 0.5	The mean physical function (FIQ physical function sub scale) change scores >3 months in the intervention groups was 1.1 lower (2.43 lower to 0.23 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Psychological distress (Hamilton Rating Scale for Depression; HADS depression; Patient Health Questionnaire-9; Symptoms Checklist 90-R depression; BDI) final values ≤3 months - CBT for pain	597 (6 studies) 8-10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3,6 due to risk of bias, inconsistency, indirectness, imprecision			The mean psychological distress (Hamilton rating scale for depression; HADs depression; patient health questionnaire-9; symptoms checklist 90-r depression; BDI) final values ≤3 months - CBT for pain in the intervention groups was 0.35 standard deviations lower (0.74 lower to 0.05 higher)
Psychological distress (Symptoms Checklist 90-R depression; BDI) final values ≤3 months - CBT for pain + insomnia	118 (2 studies) 8-9 weeks	⨁⊖⊖⊖ VERY LOW1,2,3,6 due to risk of bias, inconsistency, indirectness, imprecision			The mean psychological distress (symptoms checklist 90-r depression; BDI) final values ≤3 months - CBT for pain + insomnia in the intervention groups was 0.19 standard deviations higher (1.28 lower to 0.89 higher)
Psychological distress (Hamilton Rating Scale for Depression; Symptoms Checklist 90-R depression; HADS depression; Center for Epidemiological Studies Depression Scale; BDI) final values >3 months - CBT for pain	394 (5 studies) 5-12 months	⨁⊖⊖⊖ VERY LOW1,2,6 due to risk of bias, inconsistency, indirectness			The mean psychological distress (Hamilton rating scale for depression; symptoms checklist 90-r depression; hospital anxiety and depression scale depression; center for epidemiological studies depression scale; BDI) final values >3 months - CBT for pain in the intervention groups was 0.05 standard deviations lower (0.39 lower to 0.29 higher)
Psychological distress (Symptoms Checklist 90-R depression; BDI) final values >3 months - CBT for pain + insomnia	95 (2 studies) 5-6 months	⨁⊖⊖⊖ VERY LOW1,2,3,6 due to risk of bias,			The mean psychological distress (symptoms checklist 90-r depression; BDI) final values >3 months - CBT for pain + insomnia in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
		inconsistency, indirectness, imprecision			0.02 standard deviations higher (1.13 lower to 1.17 higher)
Psychological distress (Patient Health Questionnaire 8-item depression) change scores >3 months Scale from: 0 to 24.	28 (1 study) 3 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (patient health questionnaire 8-item depression) change scores >3 months in the control groups was 0	The mean psychological distress (patient health questionnaire 8-item depression) change scores >3 months in the intervention groups was 0.9 lower (4.35 lower to 2.55 higher)
Psychological distress (Hamilton Anxiety Rating Scale; HADS anxiety; Symptoms checklist 90-R anxiety; State-Trait Anxiety Inventory) final values ≤3 months - CBT for pain	457 (5 studies) 8-9 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness			The mean psychological distress (Hamilton anxiety rating scale; HADs anxiety; symptoms checklist 90-r anxiety; state-trait anxiety inventory) final values ≤3 months - CBT for pain in the intervention groups was 0.10 standard deviations lower (0.29 lower to 0.09 higher)
Psychological distress (Symptoms checklist 90-R anxiety; State-Trait Anxiety Inventory) final values ≤3 months - CBT for pain + insomnia	118 (2 studies) 8-9 weeks	⊕⊖⊖⊖ VERY LOW1,2,3,6 due to risk of bias, inconsistency, indirectness, imprecision			The mean psychological distress (symptoms checklist 90-r anxiety; state-trait anxiety inventory) final values ≤3 months - CBT for pain + insomnia in the intervention groups was 0.17 standard deviations lower (1.15 lower to 0.8 higher)
Psychological distress (Hamilton Anxiety Rating Scale; Symptoms Checklist 90-R anxiety; HADS anxiety; State-Trait Personality Inventory	394 (5 studies) 5-12 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness			The mean psychological distress (Hamilton anxiety rating scale; symptoms checklist 90-r anxiety; HADs anxiety; state-trait personality inventory anxiety) final values >3 months - CBT

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
anxiety) final values >3 months - CBT for pain					for pain in the intervention groups was 0.01 standard deviations lower (0.2 lower to 0.19 higher)
Psychological distress (Symptoms Checklist 90-R anxiety; State-Trait Personality Inventory anxiety) final values >3 months - CBT for pain + insomnia	95 (2 studies) 5-6 months	⊕⊖⊖⊖ VERY LOW1,2,3,6 due to risk of bias, inconsistency, indirectness, imprecision			The mean psychological distress (symptoms checklist 90-r anxiety; state-trait personality inventory anxiety) final values >3 months - CBT for pain + insomnia in the intervention groups was 0.05 standard deviations higher (0.86 lower to 0.97 higher)
Psychological distress (Multiple Pain Inventory-affective distress) final values >3 months Scale from: 0 to 6.	47 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (multiple pain inventory-affective distress) final values >3 months in the control groups was 2.92	The mean psychological distress (multiple pain inventory-affective distress) final values >3 months in the intervention groups was 0.02 higher (0.34 lower to 0.38 higher)
Pain interference (BPI - pain interference) final values ≤3 months Scale from: 0 to 10.	60 (1 study) 8 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean pain interference (bpi - pain interference) final values ≤3 months in the control groups was 7.32	The mean pain interference (bpi - pain interference) final values ≤3 months in the intervention groups was 1.86 lower (2.8 to 0.92 lower)
Pain interference (Pain Disability Index) final values ≤3 months – CBT for pain Scale from: 0 to 70.	58 (1 study) 8 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain interference (pain disability index) final values ≤3 months – CBT for pain in the control groups was 35.68	The mean pain interference (pain disability index) final values ≤3 months – CBT for pain in the intervention groups was 2.35 higher (6.09 lower to 10.79 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Pain interference (Pain Disability Index) final values ≤3 months – CBT for insomnia Scale from: 0 to 70.	55 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain interference (pain disability index) final values ≤3 months – CBT for insomnia in the control groups was 35.68	The mean pain interference (pain disability index) final values ≤3 months – CBT for insomnia in the intervention groups was 7.38 lower (16.72 lower to 1.06 higher)
Pain interference (Pain Disability Index) final values >3 months – CBT for pain Scale from: 0 to 70.	50 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain interference (pain disability index) final values >3 months – CBT for pain in the control groups was 34.87	The mean pain interference (pain disability index) final values >3 months – CBT for pain in the intervention groups was 1.5 higher (8.33 lower to 11.33 higher)
Pain interference (Pain Disability Index) final values >3 months – CBT for insomnia Scale from: 0 to 70.	47 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain interference (pain disability index) final values >3 months – CBT for insomnia in the control groups was 34.87	The mean pain interference (pain disability index) final values >3 months – CBT for insomnia in intervention groups was 7.11 lower (17.42 lower to 3.2 higher)
Pain interference (Multiple Pain Inventory - pain interference) final values >3 months Scale from: 0 to 6.	47 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain interference (multiple pain inventory - pain interference) final values >3 months in the control groups was 3.43	The mean pain interference (multiple pain inventory - pain interference) final values >3 months in the intervention groups was 0.62 higher (0.14 to 1.1 higher)
Pain self-efficacy (Pain Self-efficacy Questionnaire; Chronic Pain Self-efficacy Scale; Coping Skills	160 (3 studies) 8-10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3			The mean pain self-efficacy (pain self-efficacy questionnaire; chronic pain self-efficacy scale) final values ≤3

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Questionnaire self-efficacy sub scale) final values ≤3 months - CBT for pain		due to risk of bias, indirectness, imprecision			months - CBT for pain in the intervention groups was 0.48 standard deviations higher (0.16 to 0.80 higher)
Pain self-efficacy (Pain Self-efficacy Questionnaire; Chronic Pain Self-efficacy Scale) final values ≤3 months - CBT for pain + insomnia	63 (1 study) 9 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision			The mean pain self-efficacy (pain self-efficacy questionnaire; chronic pain self-efficacy scale) final values ≤3 months - CBT for pain + insomnia in the intervention groups was 0.19 standard deviations higher (0.31 lower to 0.69 higher)
Pain self-efficacy (Chronic Pain Self-efficacy scale) final values >3 months - CBT for pain	50 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain self-efficacy (chronic pain self-efficacy scale) final values >3 months - CBT for pain in the control groups was 81.79	The mean pain self-efficacy (chronic pain self-efficacy scale) final values >3 months - CBT for pain in the intervention groups was 3.43 lower (25.7 lower to 18.84 higher)
Pain self-efficacy (Chronic Pain Self-efficacy scale) final values >3 months - CBT for pain + insomnia	48 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain self-efficacy (chronic pain self-efficacy scale) final values >3 months - CBT for pain + insomnia in the control groups was 81.79	The mean pain self-efficacy (chronic pain self-efficacy scale) final values >3 months - CBT for pain + insomnia in the intervention groups was 8.62 higher (13.06 lower to 30.3 higher)
Sleep (Pittsburgh Sleep Quality Index; Karolinska Sleep Questionnaire sleep quality sub scale; self-reported sleep quality rating) final values ≤3 months - CBT for pain	157 (3 studies) 9-10 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness			The mean sleep (Pittsburgh sleep quality index; self-reported sleep quality rating) final values ≤3 months - CBT for pain in the intervention groups was 0.03 standard deviations higher (0.29 lower to 0.34 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Sleep (Insomnia Severity Index) final values ≤3 months - CBT for pain	140 (1 study) 10 weeks	⨁⨁⨀⨀ LOW1,2 due to risk of bias, indirectness			The mean sleep (insomnia severity index) final values ≤3 months - CBT for pain in the intervention groups was 0.44 standard deviations lower (0.77 to 0.10 lower)
Sleep (Pittsburgh Sleep Quality Index; self-reported sleep quality rating) final values ≤3 months - CBT for pain + insomnia	118 (2 studies) 8-9 weeks	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, indirectness			The mean sleep (Pittsburgh sleep quality index; self-reported sleep quality rating) final values ≤3 months - CBT for pain + insomnia in the intervention groups was 0.08 standard deviations lower (0.44 lower to 0.28 higher)
Sleep (Insomnia Symptoms Questionnaire) final values ≤3 months - CBT for pain + insomnia	24 (1 study) 6 weeks	⨁⨁⨀⨀ LOW1 due to risk of bias			The mean sleep (insomnia severity index) final values ≤3 months - CBT for pain + insomnia in the intervention groups was 3.8 standard deviations lower (5.24 to 2.36 lower)
Sleep (Pittsburgh Sleep Quality Index; Sleep Scale; self-reported sleep quality rating) final values >3 months - CBT for pain	289 (3 studies) 5-9 months	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, indirectness			The mean sleep (Pittsburgh sleep quality index; sleep scale; self-reported sleep quality rating) final values >3 months - CBT for pain in the intervention groups was 0.04 standard deviations higher (0.27 lower to 0.2 higher)
Sleep (MOS Sleep Problems Index (scale inverted for analysis)) final values >3 months - CBT for pain	118 (1 study) 6 months	⨁⨀⨀⨀ VERY LOW1,2,3 due to risk of bias,			The mean sleep (MOS sleep problems index (scale inverted for analysis)) final values >3 months - CBT for pain in the intervention groups was 0.26 standard deviations higher (0.11 lower to 0.62 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
		indirectness, imprecision			
Sleep (Pittsburgh Sleep Quality Index; self-reported sleep quality rating) final values >3 months - CBT for pain + insomnia	195 (2 studies) 5-6 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision			The mean sleep (pittsburgh sleep quality index; self-reported sleep quality rating) final values >3 months - CBT for pain + insomnia in the intervention groups was 0.11 standard deviations higher (0.3 lower to 0.51 higher)
Sleep (MOS Sleep Problems Index (scale inverted for analysis; Insomnia Symptom Questionnaire) final values >3 months - CBT for pain + insomnia	77 (2 studies)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness			The mean sleep (mos sleep problems index (scale inverted for analysis); insomnia symptom questionnaire) final values >3 months - CBT for pain + insomnia in the intervention groups was 6.37 standard deviations lower (7.56 to 5.18 lower)
Use of healthcare services (GP visits for non-cardiac chest pain) >3 months	63 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	RR 0.52 (0.1 to 2.62)	Moderate	
				125 per 1000	60 fewer per 1000 (from 112 fewer to 202 more)
Use of healthcare services (referral to a specialist for non-cardiac chest pain) >3 months	63 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	RR 1.03 (0.07 to 15.79)	Moderate	
				31 per 1000	1 more per 1000 (from 29 fewer to 458 more)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Use of healthcare services (use of additional psychological services) >3 months	63 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness	OR 0.12 (0.02 to 0.62)	188 per 1000	161 fewer per 1000 (from 62 fewer to 183 fewer)
Discontinuation - CBT for pain	1258 (13 studies) 2-6 months	⊕⊖⊖⊖ VERY LOW1,2,6,7 due to risk of bias, inconsistency, indirectness	OR 1.99 (1.36 to 2.89)	Moderate	
				54 per 1000	48 more per 1000 (from 18 more to 88 more)
Discontinuation - CBT for pain + insomnia	177 (3 studies) 6-14 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	OR 2.06 (0.68 to 6.21)	Moderate	
				33 per 1000	33 more per 1000 (from 10 fewer to 142 more)
Pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain Scale from: 0 to 10.	683 (8 studies) 6-10 weeks	⊕⊖⊖⊖ VERY LOW1,2,6 due to risk of bias, inconsistency, indirectness		The mean pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain in the control groups was 6.11	The mean pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain in the intervention groups was 0.57 lower (1.14 lower to 0 higher)
Pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain + insomnia Scale from: 0 to 10.	63 (1 study) 9 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain + insomnia in the control groups was 7.4	The mean pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain + insomnia in the intervention groups was 0.11 lower (0.8 lower to 0.58 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Pain (VAS/NRS) final values and change scores >3 months - CBT for pain Scale from: 0 to 10.	309 (4 studies) 3-6 months	⨁⊖⊖⊖ VERY LOW1,4 due to risk of bias, indirectness		The mean pain (VAS/NRS) final values and change scores >3 months - CBT for pain in the control groups was 5.51	The mean pain (VAS/NRS) final values and change scores >3 months - CBT for pain in the intervention groups was 0.39 lower (0.67 to 0.11 lower)
Pain (VAS/NRS) final values and change scores >3 months - CBT for pain + insomnia Scale from: 0 to 10.	112 (2 studies) 5-6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (VAS/NRS) final values and change scores >3 months - CBT for pain + insomnia in the control groups was 7	The mean pain (VAS/NRS) final values and change scores >3 months - CBT for pain + insomnia in the intervention groups was 1.07 lower (1.27 to 0.88 lower)
Pain (30% reduction in pain from baseline) ≤3 months	76 (1 study) 3 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness	RR 12.5 (3.18 to 49.11)	Moderate	
				53 per 1000	610 more per 1000 (from 116 more to 1000 more)
Pain (30% reduction in pain from baseline) >3 months	76 (1 study) 9 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness	RR 24 (3.42 to 168.55)	Moderate	
				26 per 1000	598 more per 1000 (from 63 more to 1000 more)
Pain (McGill Pain Questionnaire) final values ≤3 months – CBT for pain Scale from: 0 to 78.	93 (2 studies) 8-10 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness		The mean pain (McGill pain questionnaire) final values ≤3 months in the control groups was 37.54	The mean pain McGill pain questionnaire) final values ≤3 months in the intervention groups was 1.81 lower (8.82 lower to 5.21 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
Pain (McGill Pain Questionnaire) final values ≤3 months – CBT for insomnia Scale from: 0 to 78.	79 (2 studies) 6-8 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean pain (McGill pain questionnaire) final values ≤3 months in the control groups was 32.12	The mean pain (McGill pain questionnaire) final values ≤3 months in the intervention groups was 6.31 lower (9.35 to 3.28 lower)
Pain (Multiple Pain Inventory - pain severity) final values >3 months - CBT for pain Scale from: 0 to 6.	47 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (multiple pain inventory - pain severity) final values >3 months - CBT for pain in the control groups was 3.67	The mean pain (multiple pain inventory - pain severity) final values >3 months - CBT for pain in the intervention groups was 0.21 higher (0.31 lower to 0.73 higher)
Pain (McGill Pain Questionnaire) final values >3 months - CBT for pain Scale from: 0 to 78.	50 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (McGill pain questionnaire) final values >3 months in the control groups was 23.3	The mean pain (McGill pain questionnaire) final values >3 months in the intervention groups was 5.69 higher (2.97 lower to 14.35 higher)
Pain (McGill Pain Questionnaire) final values >3 months - CBT for pain +/ insomnia Scale from: 0 to 78.	61 (2 studies) 6 months	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean pain (McGill pain questionnaire) final values >3 months - CBT for pain +/ insomnia in the control groups was 28.7	The mean pain (McGill pain questionnaire) final values >3 months - CBT for pain + insomnia in the intervention groups was 4.22 lower (8.26 to 0.17 lower)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
4 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect comparisons

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Usual care (95% CI)
5 Downgraded by 1 or 2 increments because the point estimate varies widely across studies, unexplained by subgroup analysis 6 Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis 7 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes					

Table 4: Clinical evidence summary: ACT versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Usual care (95% CI)
Quality of life (SF36 physical component) final values ≤3 months Scale from: 0 to 100.	36 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36 physical component) final values ≤3 months in the control groups was 30.1	The mean quality of life (SF36 physical component) final values ≤3 months in the intervention groups was 1.7 lower (7.69 lower to 4.29 higher)
Quality of life (SF36 physical component) final values >3 months Scale from: 0 to 100.	33 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36 physical component) final values >3 months in the control groups was 31.1	The mean quality of life (SF36 physical component) final values >3 months in the intervention groups was 2.7 lower (9.5 lower to 4.1 higher)
Quality of life (SF36 mental component) final values ≤3 months Scale from: 0 to 100.	36 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36 mental component) final values ≤3 months in the control groups was 36.8	The mean quality of life (SF36 mental component) final values ≤3 months in the intervention groups was 8.8 higher (1.42 to 16.18 higher)
Quality of life (SF36 mental component) final values >3 months Scale from: 0 to 100.	33 (1 study) 6 months	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean quality of life (SF36 mental component) final values >3 months in the control groups was 34.7	The mean quality of life (SF36 mental component) final values >3 months in the intervention groups was 11.3 higher (3.64 to 18.96 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Usual care (95% CI)
Quality of life (EQ-5D VAS) final values ≤3 months Scale from: 0 to 100.	104 (1 study) 8 weeks	⨁⨁⨀⨀ LOW1,3 due to risk of bias, indirectness		The mean quality of life (EQ-5D VAS) final values ≤3 months in the control groups was 51	The mean quality of life (EQ-5D VAS) final values ≤3 months in the intervention groups was 15.2 higher (11.47 to 18.93 higher)
Quality of life (EQ-5D) final values >3 months Scale from: 0 to 1.	104 (1 study) 6 months	⨁⨁⨀⨀ LOW1,3 due to risk of bias, indirectness		The mean quality of life (EQ-5D VAS) final values >3 months in the control groups was 0.57	The mean quality of life (EQ-5D VAS) final values >3 months in the intervention groups was 0.23 higher (0.18 to 0.28 higher)
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 100.	61 (1 study) 2 months	⨁⨀⨀⨀ VERY LOW1,3,4 due to risk of bias, indirectness		The mean quality of life (FIQ) final values ≤3 months in the control groups was 55.3	The mean quality of life (FIQ) final values ≤3 months in the intervention groups was 16.23 lower (22.69 to 9.77 lower)
Quality of life (FIQ) final values >3 months Scale from: 0 to 100.	61 (1 study) 5 months	⨁⨀⨀⨀ VERY LOW1,3,4 due to risk of bias, indirectness		The mean quality of life (FIQ) final values >3 months in the control groups was 53.82	The mean quality of life (FIQ) final values >3 months in the intervention groups was 21.87 lower (28.83 to 14.91 lower)
Physical function (6 minute walk test) final values ≤3 months	61 (1 study) 2 months	⨁⨀⨀⨀ VERY LOW1,2,3,4 due to risk of bias, indirectness, imprecision		The mean physical function (6 minute walk test) final values ≤3 months in the control groups was 364.69 meters	The mean physical function (6 minute walk test) final values ≤3 months in the intervention groups was 6.39 lower (62.01 lower to 49.23 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Usual care (95% CI)
Physical function (6 minute walk test) final values >3 months	61 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2,3,4 due to risk of bias, indirectness, imprecision		The mean physical function (6 minute walk test) final values >3 months in the control groups was 349.33 meters	The mean physical function (6 minute walk test) final values >3 months in the intervention groups was 34.51 higher (26.32 lower to 95.34 higher)
Psychological distress (Geriatric Depression Scale; BDI; HADS depression; Center for Epidemiologic Studies depression scale) final values ≤3 months	254 (4 studies) 9-12 weeks	⨁⊖⊖⊖ VERY LOW1,2,3,5 due to risk of bias, inconsistency, indirectness, imprecision			The mean psychological distress (geriatric depression scale; BDI; HADs depression; center for epidemiologic studies depression scale) final values ≤3 months in the intervention groups was 0.92 standard deviations lower (1.62 to 0.23 lower)
Psychological distress (BDI; HADS depression; Center for Epidemiologic Studies depression scale) final values >3 months	198 (3 studies) 5-6 months	⨁⊖⊖⊖ VERY LOW1,2,3,5 due to risk of bias, inconsistency, indirectness, imprecision			The mean psychological distress (BDI; HADs depression; center for epidemiologic studies depression scale) final values >3 months in the intervention groups was 0.88 standard deviations lower (1.5 to 0.26 lower)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - State Scale from: 20 to 80.	36 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (Spielberger trait-state anxiety inventory) final values ≤3 months - state in the control groups was 47.6	The mean psychological distress (Spielberger trait-state anxiety inventory) final values ≤3 months - state in the intervention groups was 6.8 lower (15.68 lower to 2.08 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Usual care (95% CI)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - Trait Scale from: 20 to 80.	36 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (Spielberger trait-state anxiety inventory) final values ≤3 months - trait in the control groups was 49.3	The mean psychological distress (Spielberger trait-state anxiety inventory) final values ≤3 months - trait in the intervention groups was 8.7 lower (16.73 to 0.67 lower)
Psychological distress (Pain Anxiety Symptoms Scale; HADS anxiety) final values ≤3 months	157 (2 studies) 8-9 weeks	⨁⊖⊖⊖ VERY LOW1,2,3,5 due to risk of bias, inconsistency, indirectness, imprecision			The mean psychological distress (pain anxiety symptoms scale; HADs anxiety) final values ≤3 months in the intervention groups was 0.73 standard deviations lower (1.24 to 0.21 lower)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - State Scale from: 20 to 80.	33 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (Spielberger trait-state anxiety inventory) final values >3 months - state in the control groups was 45.4	The mean psychological distress (Spielberger trait-state anxiety inventory) final values >3 months - state in the intervention groups was 5.6 lower (13.11 lower to 1.91 higher)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - Trait Scale from: 20 to 80.	33 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (sSpielberger trait-state anxiety inventory) final values >3 months - trait in the control groups was 47.9	The mean psychological distress (Spielberger trait-state anxiety inventory) final values >3 months - trait in the intervention groups was 8 lower (15.59 to 0.41 lower)
Psychological distress (HADS - anxiety) final values >3 months Scale from: 0 to 21.	104 (1 study) 6 months	⨁⨁⊖⊖ LOW1,3 due to risk of		The mean psychological distress (HADs - anxiety) final values >3 months in	The mean psychological distress (HADs - anxiety) final values >3 months in the intervention groups

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Usual care (95% CI)
		bias, indirectness		the control groups was 12.15	was 3.42 lower (4.68 to 2.16 lower)
Pain interference (BPI - pain interference) final values ≤3 months - General activity Scale from: 0 to 10.	53 (1 study) 9 weeks	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision		The mean pain interference (BPI - pain interference) final values ≤3 months - general activity in the control groups was 4.96	The mean pain interference (BPI - pain interference) final values ≤3 months - general activity in the intervention groups was 0.19 lower (2.19 lower to 1.81 higher)
Pain interference (BPI - pain interference) final values ≤3 months - Mood Scale from: 0 to 10.	53 (1 study) 9 weeks	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision		The mean pain interference (BPI - pain interference) final values ≤3 months - mood in the control groups was 5.03	The mean pain interference (BPI - pain interference) final values ≤3 months - mood in the intervention groups was 1.03 lower (3.06 lower to 1 higher)
Pain interference (BPI - pain interference) final values ≤3 months - Walking ability Scale from: 0 to 10.	53 (1 study) 9 weeks	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision		The mean pain interference (BPI - pain interference) final values ≤3 months - walking ability in the control groups was 6.53	The mean pain interference (BPI - pain interference) final values ≤3 months - walking ability in the intervention groups was 1.38 lower (3.21 lower to 0.45 higher)
Pain interference (BPI - pain interference) final values ≤3 months - Relations with other people Scale from: 0 to 10.	53 (1 study) 9 weeks	⨁⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision		The mean pain interference (BPI - pain interference) final values ≤3 months - relations with other people in the control groups was 3.8	The mean pain interference (BPI - pain interference) final values ≤3 months - relations with other people in the intervention groups was 1.47 lower (3.31 lower to 0.37 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Usual care (95% CI)
Pain interference (BPI - pain interference) final values ≤3 months - Sleep Scale from: 0 to 10.	53 (1 study) 9 weeks	⊕⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision		The mean pain interference (BPI - pain interference) final values ≤3 months - sleep in the control groups was 5.04	The mean pain interference (BPI - pain interference) final values ≤3 months - sleep in the intervention groups was 2.64 lower (4.7 to 0.58 lower)
Pain interference (Pain disability index) final values ≤3 months Scale from: 0 to 70.	36 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain interference (pain disability index) final values ≤3 months in the control groups was 37.8	The mean pain interference (pain disability index) final values ≤3 months in the intervention groups was 10.6 lower (20.19 to 1.01 lower)
Pain interference (Pain disability index) final values >3 months Scale from: 0 to 70.	33 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain interference (pain disability index) final values >3 months in the control groups was 38.1	The mean pain interference (pain disability index) final values >3 months in the intervention groups was 10 lower (19.83 to 0.17 lower)
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months Scale from: 0 to 21.	61 (1 study) 8 weeks	⊕⊖⊖⊖ VERY LOW1,2,3,4 due to risk of bias, indirectness, imprecision		The mean sleep (Pittsburgh sleep quality index) final values ≤3 months in the control groups was 13	The mean sleep (Pittsburgh sleep quality index) final values ≤3 months in the intervention groups was 2.76 lower (4.54 to 0.98 lower)
Sleep (Pittsburgh Sleep Quality Index) final values >3 months Scale from: 0 to 21.	61 (1 study) 5 months	⊕⊖⊖⊖ VERY LOW1,2,3,4 due to risk of bias,		The mean sleep (Pittsburgh sleep quality index) final values >3 months in the control groups was 13.21	The mean sleep (Pittsburgh sleep quality index) final values >3 months in the intervention groups was 2.51 lower (4.89 to 0.13 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Usual care (95% CI)
		indirectness, imprecision			
Discontinuation	312 (4 studies) 8-12 weeks	⊕⊖⊖⊖ VERY LOW1,2,4 due to risk of bias, indirectness, imprecision	RR 1.64 (1.03 to 2.6)	74 per 1000	47 more per 1000 (from 2 more to 118 more)
Pain (VAS/NRS; McGill pain questionnaire) final values ≤3 months	201 (3 studies) 8-12 weeks	⊕⊖⊖⊖ VERY LOW1,2,3,5 due to risk of bias, inconsistency, indirectness, imprecision			The mean pain (VAS/NRS; McGill pain questionnaire) final values ≤3 months in the intervention groups was 0.84 standard deviations lower (1.31 to 0.37 lower)
Pain (VAS/NRS; McGill pain questionnaire) final values >3 months	198 (3 studies) 5-6 months	⊕⊖⊖⊖ VERY LOW1,2,3,5 due to risk of bias, inconsistency, indirectness, imprecision			The mean pain (VAS/NRS; McGill pain questionnaire) final values >3 months in the intervention groups was 0.67 standard deviations lower (1.32 to 0.02 lower)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
3 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
4 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect comparisons
5 Downgraded by 1 or 2 increments because heterogeneity, I^2=50%, p=0.04, unexplained by subgroup analysis

Table 5: Clinical evidence summary: Relaxation versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Relaxation versus Usual care (95% CI)
Quality of life (FIQ) final values ≤3 months	173 (2 studies) 4-10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision			The mean quality of life (FIQ) final values ≤3 months in the intervention groups was 1.46 standard deviations lower (4.69 lower to 1.77 higher)
Physical function (Neck disability index) final values ≤3 months Scale from: 0 to 80.	258 (1 study) 12 weeks	⨁⨁⨁⊖ MODERATE1 due to risk of bias		The mean physical function (neck disability index) final values ≤3 months in the control groups was 14	The mean physical function (neck disability index) final values ≤3 months in the intervention groups was 0 higher (3.21 lower to 3.21 higher)
Physical function (Neck disability index) final values >3 months Scale from: 0 to 80.	258 (1 study) 12 months	⨁⨁⨁⊖ MODERATE1 due to risk of bias		The mean physical function (neck disability index) final values >3 months in the control groups was 17	The mean physical function (neck disability index) final values >3 months in the intervention groups was 2 higher (1.47 lower to 5.47 higher)
Psychological distress (HADS depression; Center for Epidemiologic Studies depression scale) final values ≤3 months	189 (2 studies) 4-10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision			The mean psychological distress (HADs depression; center for epidemiologic studies depression scale) final values ≤3 months in the intervention groups was 0.26 standard deviations lower (0.54 lower to 0.03 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Relaxation versus Usual care (95% CI)
Psychological distress (HADS anxiety) final values ≤3 months Scale from: 0 to 21.	125 (1 study) 4 weeks	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean psychological distress (HADs anxiety) final values ≤3 months in the control groups was 9.73	The mean psychological distress (HADs anxiety) final values ≤3 months in the intervention groups was 0.27 higher (1.03 lower to 1.57 higher)
Pain interference (BPI - interference) final values ≤3 months Scale from: 0 to 10.	64 (1 study) 10 weeks	⨁⨀⨀⨀ VERY LOW1,3 due to risk of bias, imprecision		The mean pain interference (bpi - interference) final values ≤3 months in the control groups was 4.9	The mean pain interference (bpi - interference) final values ≤3 months in the intervention groups was 0.7 lower (2.05 lower to 0.65 higher)
Pain self-efficacy (Arthritis Self-efficacy Scale - pain sub scale) final values ≤3 months Scale from: 10 to 100.	48 (1 study) 10 weeks	⨁⨁⨁⨀ MODERATE1 due to risk of bias		The mean pain self-efficacy (arthritis self-efficacy scale - pain sub scale) final values ≤3 months in the control groups was 49.83	The mean pain self-efficacy (arthritis self-efficacy scale - pain sub scale) final values ≤3 months in the intervention groups was 14.9 higher (12.3 to 17.5 higher)
Pain self-efficacy (Arthritis Self-efficacy Scale - self-efficacy for managing other symptoms sub scale) final values ≤3 months Scale from: 10 to 100.	64 (1 study) 10 weeks	⨁⨀⨀⨀ VERY LOW1,3 due to risk of bias, imprecision		The mean pain self-efficacy (arthritis self-efficacy scale - self-efficacy for managing other symptoms sub scale) final values ≤3 months in the control groups was 52.5	The mean pain self-efficacy (arthritis self-efficacy scale - self-efficacy for managing other symptoms sub scale) final values ≤3 months in the intervention groups was 10.6 higher (0.12 to 21.08 higher)
Sleep (MOS sleep problems index) final values ≤3 months	125 (1 study) 4 weeks	⨁⨀⨀⨀ VERY LOW1,3 due to risk of		The mean sleep (MOS sleep problems index) final values ≤3 months in the control groups was 5.73	The mean sleep (MOS sleep problems index) final values ≤3 months in the intervention groups was 9.27 lower (14.35 to 4.19 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Relaxation versus Usual care (95% CI)
		bias, imprecision			
Discontinuation	455 (3 studies) 4-12 weeks	⨁⨀⨀⨀ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision	RR 0.66 (0.19 to 2.29)	Moderate	
				85 per 1000	29 fewer per 1000 (from 69 fewer to 110 more)
Pain (VAS/NRS) final values ≤3 months Scale from: 0 to 10.	485 (4 studies) 4-12 weeks	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean pain (VAS/NRS) final values ≤3 months in the control groups was 5.12	The mean pain (VAS/NRS) final values ≤3 months in the intervention groups was 0.49 lower (0.71 to 0.28 lower)
Pain (VAS/NRS) final values >3 months Scale from: 0 to 10.	258 (1 study) 12 months	⨁⨁⨁⨀ MODERATE1 due to risk of bias		The mean pain (VAS/NRS) final values >3 months in the control groups was 3.2	The mean pain (VAS/NRS) final values >3 months in the intervention groups was 0.1 higher (0.52 lower to 0.72 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the point estimate varies widely across studies, unexplained by subgroup analysis
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
4 Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis

Table 6: Clinical evidence summary: Relaxation versus Attention control

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Relaxation versus Attention control (95% CI)
Pain reduction Brief pain inventory pain severity sub scale (VAS). Scale from: 0 to 10.	23 (1 study) 5 days	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain reduction in the control groups was 4.2	The mean pain reduction in the intervention groups was 1.35 lower (2.88 lower to 0.18 higher)
Discontinuation	27 (1 study) 4 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision	OR 0.11 (0.01 to 0.91)	Moderate	
				286 per 1000	244 fewer per 1000 (from 19 fewer to 282 fewer)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 7: Clinical evidence summary: Biofeedback versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Usual care (95% CI)
Quality of life (SF36) final values ≤3 months – EMG biofeedback Physical functioning Scale from: 0 to 100.	38 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - physical functioning in the control groups was 54.2	The mean quality of life (SF36) final values ≤3 months - physical functioning in the intervention groups was 4.9 lower (18.88 lower to 9.08 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Usual care (95% CI)
Quality of life (SF36) final values ≤3 months - EMG biofeedback Role physical Scale from: 0 to 100.	38 (1 study) 8 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - role physical in the control groups was 33.3	The mean quality of life (SF36) final values ≤3 months - role physical in the intervention groups was 19.2 lower (40.39 lower to 1.99 higher)
Quality of life (SF36) final values ≤3 months - EMG biofeedback Bodily pain Scale from: 0 to 100.	38 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - bodily pain in the control groups was 30.4	The mean quality of life (SF36) final values ≤3 months - bodily pain in the intervention groups was 6.3 higher (4.16 lower to 16.76 higher)
Quality of life (SF36) final values ≤3 months - EMG biofeedback General health Scale from: 0 to 100.	38 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - general health in the control groups was 44.7	The mean quality of life (SF36) final values ≤3 months - general health in the intervention groups was 8.2 lower (20.19 lower to 3.79 higher)
Quality of life (SF36) final values ≤3 months - EMG biofeedback Vitality Scale from: 0 to 100.	38 (1 study) 8 weeks	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean quality of life (SF36) final values ≤3 months - vitality in the control groups was 41.7	The mean quality of life (SF36) final values ≤3 months - vitality in the intervention groups was 13.5 lower (23.81 to 3.19 lower)
Quality of life (SF36) final values ≤3 months - EMG biofeedback Social functioning Scale from: 0 to 100.	38 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - social functioning in the control groups was 60.4	The mean quality of life (SF36) final values ≤3 months - social functioning in the intervention groups was 10.4 lower (26.16 lower to 5.36 higher)
Quality of life (SF36) final values ≤3 months - EMG biofeedback Role	38 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2		The mean quality of life (SF36) final values ≤3 months - role emotional	The mean quality of life (SF36) final values ≤3 months - role emotional in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Usual care (95% CI)
emotional Scale from: 0 to 100.		due to risk of bias, imprecision		in the control groups was 57.4	9.5 lower (38.48 lower to 19.48 higher)
Quality of life (SF36) final values ≤3 months - EMG biofeedback Mental health Scale from: 0 to 100.	38 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - mental health in the control groups was 60.7	The mean quality of life (SF36) final values ≤3 months - mental health in the intervention groups was 9.3 lower (22.53 lower to 3.93 higher)
Quality of life (SF36) final values ≤3 months – HRV biofeedback Physical functioning Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - physical functioning in the control groups was 84.5	The mean quality of life (SF36) final values ≤3 months - physical functioning in the intervention groups was 8 higher (2.34 lower to 18.34 higher)
Quality of life (SF36) final values ≤3 months - HRV biofeedback Role physical Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - role physical in the control groups was 67.5	The mean quality of life (SF36) final values ≤3 months - role physical in the intervention groups was 9.6 higher (24.3 lower to 43.5 higher)
Quality of life (SF36) final values ≤3 months - HRV biofeedback Bodily pain Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - bodily pain in the control groups was 58.4	The mean quality of life (SF36) final values ≤3 months - bodily pain in the intervention groups was 13.4 higher (12.83 lower to 39.63 higher)
Quality of life (SF36) final values ≤3 months - HRV biofeedback General health Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of		The mean quality of life (SF36) final values ≤3 months - general health in the control groups was 60.5	The mean quality of life (SF36) final values ≤3 months - general health in the intervention groups was 2.9 higher (17.7 lower to 23.5 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Usual care (95% CI)
		bias, imprecision			
Quality of life (SF36) final values ≤3 months - HRV biofeedback Vitality Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - vitality in the control groups was 48	The mean quality of life (SF36) final values ≤3 months - vitality in the intervention groups was 9.5 higher (12.88 lower to 31.88 higher)
Quality of life (SF36) final values ≤3 months - HRV biofeedback Social functioning Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - social functioning in the control groups was 82.5	The mean quality of life (SF36) final values ≤3 months - social functioning in the intervention groups was 8.1 higher (8.25 lower to 24.45 higher)
Quality of life (SF36) final values ≤3 months - HRV biofeedback Role emotional Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - role emotional in the control groups was 83.3	The mean quality of life (SF36) final values ≤3 months - role emotional in the intervention groups was 0 higher (25.49 lower to 25.49 higher)
Quality of life (SF36) final values ≤3 months - HRV biofeedback Mental health Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values ≤3 months - mental health in the control groups was 72.8	The mean quality of life (SF36) final values ≤3 months - mental health in the intervention groups was 0.7 lower (17.72 lower to 16.32 higher)
Quality of life (SF36) final values >3 months - Physical functioning Scale from: 0 to 100.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values >3 months - physical functioning in the control groups was 50.9	The mean quality of life (SF36) final values >3 months - physical functioning in the intervention groups was 0.7 higher (10.91 lower to 12.31 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Usual care (95% CI)
Quality of life (SF36) final values >3 months - Role physical Scale from: 0 to 100.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values >3 months - role physical in the control groups was 20.8	The mean quality of life (SF36) final values >3 months - role physical in the intervention groups was 5.2 lower (24.28 lower to 13.88 higher)
Quality of life (SF36) final values >3 months - Bodily pain Scale from: 0 to 100.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values >3 months - bodily pain in the control groups was 36.2	The mean quality of life (SF36) final values >3 months - bodily pain in the intervention groups was 0.7 higher (8.14 lower to 9.54 higher)
Quality of life (SF36) final values >3 months - General health Scale from: 0 to 100.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values >3 months - general health in the control groups was 44.4	The mean quality of life (SF36) final values >3 months - general health in the intervention groups was 0.9 lower (12.28 lower to 10.48 higher)
Quality of life (SF36) final values >3 months - Vitality Scale from: 0 to 100.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values >3 months - vitality in the control groups was 38.8	The mean quality of life (SF36) final values >3 months - vitality in the intervention groups was 10.2 lower (20.62 lower to 0.22 higher)
Quality of life (SF36) final values >3 months - Social functioning Scale from: 0 to 100.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values >3 months - social functioning in the control groups was 61.1	The mean quality of life (SF36) final values >3 months - social functioning in the intervention groups was 7.4 lower (24.19 lower to 9.39 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Usual care (95% CI)
Quality of life (SF36) final values >3 months - Role emotional Scale from: 0 to 100.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values >3 months - role emotional in the control groups was 59.3	The mean quality of life (SF36) final values >3 months - role emotional in the intervention groups was 23.9 lower (53.64 lower to 5.84 higher)
Quality of life (SF36) final values >3 months - Mental health Scale from: 0 to 100.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36) final values >3 months - mental health in the control groups was 57.5	The mean quality of life (SF36) final values >3 months - mental health in the intervention groups was 6.4 lower (18.26 lower to 5.46 higher)
Quality of life (Arthritis Impact Measurement Scale) change scores >3 months Scale from: 0 to 10.	65 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean quality of life (arthritis impact measurement scale) change scores >3 months in the control groups was 0.8	The mean quality of life (arthritis impact measurement scale) change scores >3 months in the intervention groups was 0.4 lower (1.34 lower to 0.54 higher)
Physical function (Neck disability index) final values ≤3 months Scale from: 0 to 100.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean physical function (neck disability index) final values ≤3 months in the control groups was 20.6	The mean physical function (neck disability index) final values ≤3 months in the intervention groups was 6.6 lower (17.17 lower to 3.97 higher)
Physical function (Maximal Watt bicycle ergometer) change scores >3 months	65 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean physical function (maximal watt bicycle ergometer) change scores >3 months in the control groups was -27.1	The mean physical function (maximal watt bicycle ergometer) change scores >3 months in the intervention groups was 14.1 higher (4.46 to 23.74 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Usual care (95% CI)
Psychological distress (BDI) – EMG biofeedback final values ≤3 months Scale from: 0 to 63.	38 (1 study) 8 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (BDI) final values ≤3 months in the control groups was 12.9	The mean psychological distress (BDI) final values ≤3 months in the intervention groups was 3.2 higher (1.94 lower to 8.34 higher)
Psychological distress (HADS - depression) – HRV biofeedback final values ≤3 months Scale from: 0 to 21.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs - depression) final values ≤3 months in the control groups was 4.91	The mean psychological distress (HADs - depression) final values ≤3 months in the intervention groups was 2.49 lower (5.65 lower to 0.67 higher)
Psychological distress (BDI) – EMG biofeedback final values >3 months Scale from: 0 to 63.	36 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (BDI) final values >3 months in the control groups was 12.3	The mean psychological distress (BDI) final values >3 months in the intervention groups was 4.6 higher (0.21 lower to 9.41 higher)
Psychological distress (Symptoms Checklist-90-revised) change scores >3 months	65 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (symptoms checklist-90-revised) change scores >3 months in the control groups was -8.1	The mean psychological distress (symptoms checklist-90-revised) change scores >3 months in the intervention groups was 1.3 lower (19.16 lower to 16.56 higher)
Psychological distress (HADS anxiety) – HRV biofeedback final values ≤3 months Scale from: 0 to 21.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs anxiety) final values ≤3 months in the control groups was 6.45	The mean psychological distress (HADs anxiety) final values ≤3 months in the intervention groups was 0.95 lower (3.77 lower to 1.87 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Usual care (95% CI)
Discontinuation	147 (3 studies) 2-6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	OR 2.65 (1.01 to 6.97)	Moderate	
				74 per 1000	101 more per 1000 (from 1 more to 284 more)
Pain (VAS/NRS) final values ≤3 months Scale from: 0 to 10.	22 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain (VAS/NRS) final values ≤3 months in the control groups was 2	The mean pain (VAS/NRS) final values ≤3 months in the intervention groups was 0.3 lower (1.62 lower to 1.02 higher)
Pain (VAS) change scores >3 months Scale from: 0 to 10.	65 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (VAS) change scores >3 months in the control groups was 1.3	The mean pain (VAS) change scores >3 months in the intervention groups was 1.9 lower (10.18 lower to 6.38 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
3 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions

Table 8: Clinical evidence summary: Biofeedback versus Sham biofeedback

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with	Risk difference with Biofeedback versus Sham (95% CI)
Quality of life (FIQ) changes scores<3 months	30 (1 study) 6 days	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean quality of life (FIQ) changes scores<3 months in the control groups was -12.3	The mean quality of life (FIQ) changes scores<3 months in the intervention groups was 9.6 lower (20.14 lower to 0.94 higher)
Physical function (6 minute walk test) change scores <3 months	30 (1 study) 6 days	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean physical function (6 minute walk test) change scores <3 months in the control groups was 16	The mean physical function (6 minute walk test) change scores <3 months in the intervention groups was 53 higher (4.18 lower to 110.18 higher)
Psychological distress (BDI) change scores ≤3 months Scale from: 0 to 63.	34 (1 study) 5 weeks	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (BDI) change scores ≤3 months in the control groups was 3.8	The mean psychological distress (BDI) change scores ≤3 months in the intervention groups was 0.7 lower (7.71 lower to 6.31 higher)
Psychological distress (BDI) change scores >3 months Scale from: 0 to 63.	32 (1 study) 16.2 months	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean psychological distress (BDI) change scores >3 months in the control groups was 2.6	The mean psychological distress (BDI) change scores >3 months in the intervention groups was 3.9 higher (3.99 lower to 11.79 higher)
Psychological distress (State trait anxiety inventory - trait) change scores ≤3 months Scale from: 20 to 80.	34 (1 study) 5 weeks	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (state trait anxiety inventory - trait) change scores ≤3 months in the control groups was 4.2	The mean psychological distress (state trait anxiety inventory - trait) change scores ≤3 months in the intervention groups was 0.3 lower (9.18 lower to 8.58 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with	Risk difference with Biofeedback versus Sham (95% CI)
Psychological distress (State trait anxiety inventory - trait) change scores >3 months Scale from: 20 to 80.	32 (1 study) 16.2 months	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean psychological distress (state trait anxiety inventory - trait) change scores >3 months in the control groups was 2	The mean psychological distress (state trait anxiety inventory - trait) change scores >3 months in the intervention groups was 3.5 higher (4 lower to 11 higher)
Sleep (Pittsburgh sleep quality index) change scores ≤3 months Scale from: 0 to 21.	34 (1 study) 5 weeks	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean sleep (Pittsburgh sleep quality index) change scores ≤3 months in the control groups was 1.2	The mean sleep (Pittsburgh sleep quality index) change scores ≤3 months in the intervention groups was 0.8 lower (4.15 lower to 2.55 higher)
Sleep (Pittsburgh sleep quality index) change scores >3 months Scale from: 0 to 21.	32 (1 study) 16.2 months	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean sleep (pittsburgh sleep quality index) change scores >3 months in the control groups was -0.5	The mean sleep (pittsburgh sleep quality index) change scores >3 months in the intervention groups was 2 higher (1.56 lower to 5.56 higher)
Discontinuation	73 (2 studies)	⨁⨁⨁⨀ MODERATE 2 due to imprecision	RD -0.03 (-0.19 to 0.13)	Moderate	
					-
Pain (VAS) change scores ≤3 months - neurofeedback Scale from: 0 to 10.	34 (1 study) 5 weeks	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean pain (VAS) change scores ≤3 months - neurofeedback in the control groups was 1.1	The mean pain (VAS) change scores ≤3 months - neurofeedback in the intervention groups was 0.9 lower (2.06 lower to 0.26 higher)
Pain (VAS) change scores ≤3 months Scale from: 0 to 10.	30 (1 study) 6 days	⨁⨁⨀⨀ LOW1,2 due to risk of		The mean pain (VAS) change scores ≤3 months in the control	The mean pain (VAS) change scores ≤3 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with	Risk difference with Biofeedback versus Sham (95% CI)
		bias, imprecision		groups was 2.6	1.7 higher (0.27 lower to 3.67 higher)
Pain (VAS) change scores >3 months - neurofeedback Scale from: 0 to 10.	32 (1 study) 16.2 months	⨁⨁⨀⨀ LOW1,2 due to risk of bias, imprecision		The mean pain (VAS) change scores >3 months - neurofeedback in the control groups was 0	The mean pain (VAS) change scores >3 months - neurofeedback in the intervention groups was 1.10 higher (0.2 lower to 2.4 higher)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

Table 9: Clinical evidence summary: Mindfulness versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Mindfulness versus Usual care (95% CI)
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 100.	31 (1 study) 12 weeks	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (FIQ) final values ≤3 months in the control groups was 66.2	The mean quality of life (FIQ) final values ≤3 months in the intervention groups was 4.43 lower (15.33 lower to 6.47 higher)
Quality of life (FIQ) final values >3 months Scale from: 0 to 100.	31 (1 study) 6 months	⨁⨀⨀⨀ VERY LOW1,2 due to risk of		The mean quality of life (FIQ) final values >3 months in the control groups was 70.77	The mean quality of life (FIQ) final values >3 months in the intervention groups was 7.52 lower (17.04 lower to 2 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Mindfulness versus Usual care (95% CI)
		bias, imprecision			
Psychological distress (BDI) final values ≤3 months Scale from: 0 to 63.	63 (2 studies) 7-12 weeks	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean psychological distress (BDI) final values ≤3 months in the control groups was 28.66	The mean psychological distress (BDI) final values ≤3 months in the intervention groups was 3.67 lower (7.39 lower to 0.05 higher)
Psychological distress (BDI) final values >3 months Scale from: 0 to 63.	63 (2 studies) 5-6 months	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (BDI) final values >3 months in the control groups was 30.22	The mean psychological distress (BDI) final values >3 months in the intervention groups was 5.46 lower (8.79 to 2.12 lower)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - State Scale from: 20 to 80.	32 (1 study) 7 weeks	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean psychological distress (spielberger trait-state anxiety inventory) final values ≤3 months - state in the control groups was 41.12	The mean psychological distress (spielberger trait-state anxiety inventory) final values ≤3 months - state in the intervention groups was 11.83 lower (18.47 to 5.19 lower)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - Trait Scale from: 20 to 80.	32 (1 study) 7 weeks	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (spielberger trait-state anxiety inventory) final values ≤3 months - trait in the control groups was 36.24	The mean psychological distress (spielberger trait-state anxiety inventory) final values ≤3 months - trait in the intervention groups was 3.95 lower (10.05 lower to 2.15 higher)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - State Scale from: 20 to 80.	32 (1 study) 5 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean psychological distress (spielberger trait-state anxiety inventory) final values >3 months - state in the	The mean psychological distress (spielberger trait-state anxiety inventory) final values >3 months - state in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Mindfulness versus Usual care (95% CI)
				control groups was 40.29	12.44 lower (18.05 to 6.83 lower)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - Trait Scale from: 20 to 80.	32 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (spielberger trait-state anxiety inventory) final values >3 months - trait in the control groups was 34.97	The mean psychological distress (spielberger trait-state anxiety inventory) final values >3 months - trait in the intervention groups was 3.26 lower (9.26 lower to 2.74 higher)
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months Scale from: 0 to 21.	39 (1 study) 7 weeks	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean sleep (Pittsburgh sleep quality index) final values ≤3 months in the control groups was 13.1	The mean sleep (Pittsburgh sleep quality index) final values ≤3 months in the intervention groups was 4 lower (6.07 to 1.93 lower)
Sleep (Pittsburgh Sleep Quality Index) final values >3 months Scale from: 0 to 21.	39 (1 study) 5 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean sleep (Pittsburgh sleep quality index) final values >3 months in the control groups was 12.8	The mean sleep (Pittsburgh sleep quality index) final values >3 months in the intervention groups was 2.43 lower (4.54 to 0.32 lower)
Discontinuation	72 (2 studies) 7-12 weeks	⨁⨁⊖⊖ LOW1,3 due to risk of bias, indirectness	OR 5.63 (1.39 to 22.84)	Moderate	
				26 per 1000	105 more per 1000 (from 10 more to 353 more)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
3 Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes

Table 10: Clinical evidence summary: Pain education versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Pain education versus Usual care (95% CI)
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 10	35 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (FIQ) final values ≤3 months in the control groups was 2.65	The mean quality of life (FIQ) final values ≤3 months in the intervention groups was 0.01 higher (0.42 lower to 0.44 higher)
Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months	35 (1 study) 10 weeks	⨁⨁⊖⊖ LOW1,3 due to risk of bias, imprecision		The mean pain self-efficacy (coping skills questionnaire self-efficacy sub scale) final values ≤3 months in the control groups was 5.59	The mean pain self-efficacy (coping skills questionnaire self-efficacy sub scale) final values ≤3 months in the intervention groups was 0.47 higher (0.83 lower to 1.77 higher)
Sleep (Karolinska sleep questionnaire - sleep quality sub scale) final values ≤3 months	35 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean sleep (Karolinska sleep questionnaire - sleep quality sub scale) final values ≤3 months in the control groups was 3.74	The mean sleep (Karolinska sleep questionnaire - sleep quality sub scale) final values ≤3 months in the intervention groups was 0.13 higher (0.41 lower to 0.67 higher)
Pain (McGill Pain Questionnaire) final values ≤3 months Scale from: 0 to 78.	35 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean pain (McGill pain questionnaire) final values ≤3 months in the control groups was 45.24	The mean pain (McGilll pain questionnaire) final values ≤3 months in the intervention groups was 3.9 higher (20.73 lower to 28.53 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 11: clinical evidence summary: Pain education versus Attention control

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Attention control	Risk difference with Pain education (95% CI)
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 100.	77 (1 study) unclear	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (FIQ) final values ≤3 months in the control groups was 53.38	The mean quality of life (FIQ) final values ≤3 months in the intervention groups was 2.92 higher (6.34 lower to 12.18 higher)
Quality of life (FIQ) final values >3 months Scale from: 0 to 100.	77 (1 study) unclear	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (FIQ) final values >3 months in the control groups was 57.04	The mean quality of life (FIQ) final values >3 months in the intervention groups was 5.6 lower (15.93 lower to 4.73 higher)
Psychological distress (Pain Anxiety Symptom Scale) final values ≤3 months - PASS1	77 (1 study) unclear	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (pain anxiety symptom scale) final values ≤3 months - pass1 in the control groups was 32.2	The mean psychological distress (pain anxiety symptom scale) final values ≤3 months - pass1 in the intervention groups was 3.66 higher (3.06 lower to 10.38 higher)
Psychological distress (Pain Anxiety Symptom Scale) final values ≤3 months - PASS2	77 (1 study) unclear	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (pain anxiety symptom scale) final values ≤3 months - pass2 in the control groups was 12.26	The mean psychological distress (pain anxiety symptom scale) final values ≤3 months - pass2 in the intervention groups was 1.81 higher (1.79 lower to 5.41 higher)
Psychological distress (Pain Anxiety Symptom Scale) final values >3 months - PASS1	77 (1 study) unclear	⨁⊖⊖⊖ VERY LOW1,2 due to risk		The mean psychological distress (pain anxiety symptom scale) final values >3 months - pass1 in the	The mean psychological distress (pain anxiety symptom scale) final values >3 months - pass1 in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Attention control	Risk difference with Pain education (95% CI)
		of bias, imprecision		control groups was 28.53	6.41 higher (1.77 lower to 14.59 higher)
Psychological distress (Pain Anxiety Symptom Scale) final values >3 months - PASS2	77 (1 study) unclear	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (pain anxiety symptom scale) final values >3 months - pass2 in the control groups was 11.53	The mean psychological distress (pain anxiety symptom scale) final values >3 months - pass2 in the intervention groups was 2.6 higher (1.59 lower to 6.79 higher)
Pain (NRS) final values ≤3 months Scale from: 0 to 10.	77 (1 study) unclear	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean pain (NRS) final values ≤3 months in the control groups was 8.16	The mean pain (NRS) final values ≤3 months in the intervention groups was 2.23 lower (3.04 to 1.43 lower)
Pain (NRS) final values >3 months Scale from: 0 to 10.	77 (1 study) unclear	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain (NRS) final values >3 months in the control groups was 7.75	The mean pain (NRS) final values >3 months in the intervention groups was 1.47 lower (2.41 to 0.53 lower)
Discontinuation	103 (1 study) unclear	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	Peto OR 3.78 (0.65 to 21.87)	Moderate	
				0 per 1000	110 more per 1000 (from 10 to 200 more)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 12: Clinical evidence summary: Sleep hygiene versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sleep hygiene versus Usual care (95% CI)
Quality of life (SF36 mental composite) final values ≤3 months Scale from: 0 to 100.	26 (1 study) 6 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36 mental composite) final values ≤3 months in the control groups was 45.5	The mean quality of life (SF36 mental composite) final values ≤3 months in the intervention groups was 4.8 higher (2.07 to 7.53 higher)
Quality of life (SF36 mental composite) final values >3 months Scale from: 0 to 100.	14 (1 study) 6 months	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean quality of life (SF36 mental composite) final values >3 months in the control groups was 40	The mean quality of life (SF36 mental composite) final values >3 months in the intervention groups was 9.4 higher (6.52 to 12.28 higher)
Sleep (Insomnia Symptom Questionnaire) final values ≤3 months	26 (1 study) 6 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean sleep (insomnia symptom questionnaire) final values ≤3 months in the control groups was 53.2	The mean sleep (insomnia symptom questionnaire) final values ≤3 months in the intervention groups was 22.7 lower (26.26 to 19.14 lower)
Sleep (Insomnia Symptom Questionnaire) final values >3 months	14 (1 study) 6 months	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean sleep (insomnia symptom questionnaire) final values >3 months in the control groups was 52.9	The mean sleep (insomnia symptom questionnaire) final values >3 months in the intervention groups was 21.6 lower (26.21 to 16.99 lower)
Discontinuation	29 (1 study) 6 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.31 (0.03 to 2.99)	Moderate 182 per 1000	126 fewer per 1000 (from 177 fewer to 362 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Sleep hygiene versus Usual care (95% CI)
Pain (McGill pain questionnaire) final values ≤3 months Scale from: 0 to 78.	26 (1 study) 6 weeks	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean pain (McGill pain questionnaire) final values ≤3 months in the control groups was 34.4	The mean pain (McGill pain questionnaire) final values ≤3 months in the intervention groups was 10.7 lower (14.1 to 7.3 lower)
Pain (McGill pain questionnaire) final values >3 months Scale from: 0 to 78.	14 (1 study) 6 months	⨁⨁⊖⊖ LOW1 due to risk of bias		The mean pain (McGill pain questionnaire) final values >3 months in the control groups was 34.1	The mean pain (McGill pain questionnaire) final values >3 months in the intervention groups was 11.7 lower (16.34 to 7.06 lower)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 13: Clinical evidence summary: Hypnosis versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Hypnosis versus Usual care (95% CI)
Quality of life (FIQ) change scores ≤3 months Scale from: 0 to 100.	59 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (FIQ) change scores ≤3 months in the control groups was 0.19	The mean quality of life (FIQ) change scores ≤3 months in the intervention groups was 1.09 lower (5.83 lower to 3.65 higher)
Quality of life (FIQ) change scores >3 months Scale from: 0 to 100.	59 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2		The mean quality of life (FIQ) change scores >3 months in	The mean quality of life (FIQ) change scores >3 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Hypnosis versus Usual care (95% CI)
		due to risk of bias, imprecision		the control groups was -0.7	3.9 lower (11.21 lower to 3.41 higher)
Psychological distress (HADS - depression) change scores ≤3 months Scale from: 0 to 21.	59 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs - depression) change scores ≤3 months in the control groups was -0.39	The mean psychological distress (HADs - depression) change scores ≤3 months in the intervention groups was 0.73 lower (2.25 lower to 0.79 higher)
Psychological distress (HADS - depression) change scores >3 months Scale from: 0 to 21.	59 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs - depression) change scores >3 months in the control groups was -0.1	The mean psychological distress (HADs - depression) change scores >3 months in the intervention groups was 1.3 lower (2.63 lower to 0.03 higher)
Psychological distress (HADS - anxiety) change scores ≤3 months Scale from: 0 to 21.	59 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs - anxiety) change scores ≤3 months in the control groups was -0.74	The mean psychological distress (HADs - anxiety) change scores ≤3 months in the intervention groups was 0.12 lower (1.07 lower to 0.83 higher)
Psychological distress (HADS - anxiety) change scores >3 months Scale from: 0 to 21.	59 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs - anxiety) change scores >3 months in the control groups was -0.5	The mean psychological distress (HADs - anxiety) change scores >3 months in the intervention groups was 0.7 lower (9.05 lower to 7.65 higher)
Sleep (MOS Sleep Scale) change scores ≤3 months	59 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk		The mean sleep (MOS sleep scale) change scores ≤3 months in the control groups was -2.3	The mean sleep (MOS sleep scale) change scores ≤3 months in the intervention groups was 3.5 lower (9.45 lower to 2.45 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Hypnosis versus Usual care (95% CI)
		of bias, imprecision			
Sleep (MOS Sleep Scale) change scores >3 months	59 (1 study) 6 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean sleep (MOS sleep scale) change scores >3 months in the control groups was 1.7	The mean sleep (MOS sleep scale) change scores >3 months in the intervention groups was 10.3 lower (12.28 to 8.32 lower)
Discontinuation	62 (1 study) 6 months	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision	RR 0.5 (0.05 to 5.23)	Moderate	
				65 per 1000	32 fewer per 1000 (from 62 fewer to 275 more)
Pain (NRS) final values >3 months Scale from: 0 to 10.	59 (1 study) 6 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean pain (NRS) final values >3 months in the control groups was 6.64	The mean pain (NRS) final values >3 months in the intervention groups was 0.6 lower (1.19 to 0.01 lower)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 14: Clinical evidence summary: Psychotherapy versus Usual care

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Psychotherapy versus Usual care (95% CI)
Quality of life (SF36 physical component) final values >3 months Scale from: 0 to 100.	46 (1 study) 18 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36 physical component) final values >3 months in the control groups was 32.9	The mean quality of life (SF36 physical component) final values >3 months in the intervention groups was 1.1 lower (2.2 lower to 0 higher)
Quality of life (SF36 mental component) final values >3 months Scale from: 0 to 100.	46 (1 study) 18 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36 mental component) final values >3 months in the control groups was 39.4	The mean quality of life (SF36 mental component) final values >3 months in the intervention groups was 4.1 higher (2.77 to 5.43 higher)
Physical function (Somatoform disorders-7) final values >3 months Scale from: 0 to 100.	46 (1 study) 18 months	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean physical function (somatoform disorders-7) final values >3 months in the control groups was 22	The mean physical function (somatoform disorders-7) final values >3 months in the intervention groups was 4.5 lower (5.77 to 3.23 lower)
Psychological distress (HADS - depression) final values >3 months Scale from: 0 to 21.	46 (1 study) 18 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs - depression) final values >3 months in the control groups was 9.7	The mean psychological distress (HADs - depression) final values >3 months in the intervention groups was 0.7 lower (1.28 to 0.12 lower)
Psychological distress (HADS - anxiety) final values >3 months Scale from: 0 to 21.	46 (1 study) 18 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk		The mean psychological distress (HADs - anxiety) final values >3 months in	The mean psychological distress (HADs - anxiety) final values >3 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Psychotherapy versus Usual care (95% CI)
		of bias, imprecision		the control groups was 8.1	0.5 lower (0.96 to 0.04 lower)
Pain interference (Pain disability index) final values >3 months	46 (1 study) 18 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain interference (pain disability index) final values >3 months in the control groups was 36.5	The mean pain interference (pain disability index) final values >3 months in the intervention groups was 2 lower (4.02 lower to 0.02 higher)
Discontinuation	47 (1 study) 18 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.64 (0.12 to 3.48)	Moderate	
				130 per 1000	47 fewer per 1000 (from 114 fewer to 322 more)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 15: Clinical evidence summary: CBT (for insomnia) versus Sleep hygiene

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Sleep hygiene (95% CI)
Quality of life (SF36 mental composite) final values ≤3 months Scale from: 0 to 100.	32 (1 study) 6 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean quality of life (SF36 mental composite) final values ≤3 months in the control groups was 50.3	The mean quality of life (SF36 mental composite) final values ≤3 months in the intervention groups was 0.4 higher (1.51 lower to 2.31 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Sleep hygiene (95% CI)
Quality of life (SF36 mental composite) final values >3 months Scale from: 0 to 100.	13 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (SF36 mental composite) final values >3 months in the control groups was 49.4	The mean quality of life (SF36 mental composite) final values >3 months in the intervention groups was 1.9 higher (0.99 lower to 4.79 higher)
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 100.	97 (2 studies) 6-7 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean quality of life (FIQ) final values ≤3 months in the control groups was 64.07	The mean quality of life (FIQ) final values ≤3 months in the intervention groups was 14.14 lower (21.15 to 7.13 lower)
Psychological distress (Symptom Checklist-90-Revised - depression sub scale; HADS - depression) final values ≤3 months	97 (2 studies) 6-7 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision			The mean psychological distress (symptom checklist-90-revised - depression sub scale; HADs - depression) final values ≤3 months in the intervention groups was 0.61 standard deviations lower (1.02 to 0.2 lower)
Psychological distress (Symptom Checklist-90-Revised - anxiety sub scale; HADS - anxiety) final values ≤3 months	97 (2 studies) 6-7 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision			The mean psychological distress (symptom checklist-90-revised - anxiety sub scale; HADs - anxiety) final values ≤3 months in the intervention groups was 0.32 standard deviations lower (0.72 lower to 0.08 higher)
Pain self-efficacy (Chronic Pain Self-efficacy Scale) final values ≤3 months	57 (1 study) 6 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias,		The mean pain self-efficacy (chronic pain self-efficacy scale) final values ≤3 months in the control groups	The mean pain self-efficacy (chronic pain self-efficacy scale) final values ≤3 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Sleep hygiene (95% CI)
		indirectness, imprecision		was 70.48	23.48 higher (4.83 to 42.13 higher)
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months	97 (2 studies) 6-7 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean sleep (Pittsburgh sleep quality index) final values ≤3 months in the control groups was 13.34	The mean sleep (pittsburgh sleep quality index) final values ≤3 months in the intervention groups was 1.96 lower (3.39 to 0.54 lower)
Sleep (Insomnia Symptom Questionnaire) final values ≤3 months	32 (1 study) 6 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean sleep (insomnia symptom questionnaire) final values ≤3 months in the control groups was 30.5	The mean sleep (insomnia symptom questionnaire) final values ≤3 months in the intervention groups was 5.8 higher (3.28 to 8.32 higher)
Sleep (total sleep time, hours) final values ≤3 months	26 (1 study) 6 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean sleep (total sleep time, hours) final values ≤3 months in the control groups was 6.57 hours	The mean sleep (total sleep time, hours) final values ≤3 months in the intervention groups was 0.04 lower (1.27 lower to 1.19 higher)
Sleep (Insomnia Symptom Questionnaire) final values >3 months	13 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean sleep (insomnia symptom questionnaire) final values >3 months in the control groups was 31.3	The mean sleep (insomnia symptom questionnaire) final values >3 months in the intervention groups was 3.4 higher (0.19 to 6.61 higher)
Discontinuation	144 (3 studies) 6 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias,	OR 1.53 (0.43 to 5.53)	Moderate	
				56 per 1000	27 more per 1000 (from 31 fewer to 191 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Sleep hygiene (95% CI)
		indirectness, imprecision			
Pain (McGill VAS) final values ≤3 months Scale from: 0 to 10.	97 (2 studies) 6-7 weeks	⨁⨁⨀⨀ LOW1,3 due to risk of bias, indirectness		The mean pain (McGill VAS) final values ≤3 months in the control groups was 8.25	The mean pain (McGill VAS) final values ≤3 months in the intervention groups was 1.59 lower (2.33 to 0.86 lower)
Pain (McGill Pain Questionnaire) final values ≤3 months Scale from: 0 to 78.	32 (1 study) 6 weeks	⨁⨀⨀⨀ VERY LOW1,2 due to risk of bias, imprecision		The mean pain (McGill pain questionnaire) final values ≤3 months in the control groups was 23.7	The mean pain (McGill pain questionnaire) final values ≤3 months in the intervention groups was 3.9 higher (1.06 to 6.74 higher)
Pain (McGill Pain Questionnaire) final values >3 months Scale from: 0 to 78.	13 (1 study) 6 months	⨁⨁⨀⨀ LOW1 due to risk of bias		The mean pain (McGill pain questionnaire) final values >3 months in the control groups was 22.4	The mean pain (McGill pain questionnaire) final values >3 months in the intervention groups was 6.4 higher (2.32 to 10.48 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
3 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
4 Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis

Table 16: Clinical evidence summary: CBT versus Pain education

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Pain education (95% CI)
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 10	36 (1 study) 10 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean quality of life (FIQ) final values ≤3 months in the control groups was 2.66	The mean quality of life (FIQ) final values ≤3 months in the intervention groups was 0.41 lower (0.89 lower to 0.07 higher)
Quality of life (FIQ) final values >3 months Scale from: 0 to 10	36 (1 study) 6 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean quality of life (FIQ) final values >3 months in the control groups was 2.36	The mean quality of life (FIQ) final values ≤3 months in the intervention groups was 0.03 lower (0.52 lower to 0.46 higher)
Quality of life (Satisfaction with life scale) final values ≤3 months	151 (1 study) 10 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, indirectness		The mean quality of life (satisfaction with life scale) final values ≤3 months in the control groups was 19.15	The mean quality of life (satisfaction with life scale) final values ≤3 months in the intervention groups was 0.08 higher (2.43 lower to 2.59 higher)
Quality of life (Satisfaction with life scale) final values >3 months	151 (1 study) 6 months	⊕⊕⊖⊖ LOW1,2 due to risk of bias, indirectness		The mean quality of life (satisfaction with life scale) final values >3 months in the control groups was 18.58	The mean quality of life (satisfaction with life scale) final values >3 months in the intervention groups was 1.06 higher (1.42 lower to 3.54 higher)
Physical function (SF12 physical function sub scale) final values ≤3 months Scale from: 0 to 100.	151 (1 study) 10 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, indirectness		The mean physical function (sf12 physical function sub scale) final values ≤3 months in the control groups was 36.63	The mean physical function (sf12 physical function sub scale) final values ≤3 months in the intervention groups was 0.87 higher (2.12 lower to 3.86 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Pain education (95% CI)
Physical function (SF12 physical function sub scale) final values >3 months Scale from: 0 to 100.	151 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean physical function (sf12 physical function sub scale) final values >3 months in the control groups was 35.91	The mean physical function (sf12 physical function sub scale) final values >3 months in the intervention groups was 0.87 higher (2.12 lower to 3.86 higher)
Psychological distress (BDI) change scores ≤3 months Scale from: 0 to 63.	16 (1 study) 4 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (BDI) change scores ≤3 months in the control groups was -2	The mean psychological distress (BDI) change scores ≤3 months in the intervention groups was 1.5 lower (7.77 lower to 4.77 higher)
Psychological distress (Center for Epidemiologic Studies - depression) final values ≤3 months Scale from: 0 to 60.	151 (1 study) 10 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness		The mean psychological distress (center for epidemiologic studies - depression) final values ≤3 months in the control groups was 18.22	The mean psychological distress (center for epidemiologic studies - depression) final values ≤3 months in the intervention groups was 1.87 lower (5.48 lower to 1.74 higher)
Psychological distress (Center for Epidemiologic Studies - depression) final values >3 months Scale from: 0 to 60.	151 (1 study) 6 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness		The mean psychological distress (center for epidemiologic studies - depression) final values >3 months in the control groups was 18.46	The mean psychological distress (center for epidemiologic studies - depression) final values >3 months in the intervention groups was 1.13 lower (4.95 lower to 2.69 higher)
Psychological distress (Generalised anxiety disorder-7) final values ≤3 months Scale from: 0 to 21.	151 (1 study) 10 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness		The mean psychological distress (generalised anxiety disorder-7) final values	The mean psychological distress (generalised anxiety disorder-7) final values ≤3 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Pain education (95% CI)
				≤3 months in the control groups was 6.53	0.3 lower (1.95 lower to 1.35 higher)
Psychological distress (Generalised anxiety disorder-7) final values >3 months Scale from: 0 to 21.	151 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (generalised anxiety disorder-7) final values >3 months in the control groups was 7.12	The mean psychological distress (generalised anxiety disorder-7) final values >3 months in the intervention groups was 1.3 lower (2.93 lower to 0.33 higher)
Pain interference (BPI - interference) change scores ≤3 months Scale from: 0 to 10.	16 (1 study) 4 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain interference (bpi - interference) change scores ≤3 months in the control groups was -0.39	The mean pain interference (bpi - interference) change scores ≤3 months in the intervention groups was 1.11 lower (3.41 lower to 1.19 higher)
Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months	36 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain self-efficacy (coping skills questionnaire self-efficacy sub scale) final values ≤3 months in the control groups was 6.06	The mean pain self-efficacy (coping skills questionnaire self-efficacy sub scale) final values ≤3 months in the intervention groups was 0.38 higher (0.83 lower to 1.59 higher)
Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values >3 months	36 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain self-efficacy (coping skills questionnaire self-efficacy sub scale) final values >3 months in the control groups was 5.27	The mean pain self-efficacy (coping skills questionnaire self-efficacy sub scale) final values >3 months in the intervention groups was 0.20 lower (0.91 lower to 1.51 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Pain education (95% CI)
Sleep (Karolinska Sleep Questionnaire sleep quality) final values ≤3 months	36 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision			The mean sleep (karolinska sleep questionnaire sleep quality) final values ≤3 months in the intervention groups was 0.26 standard deviations higher (0.4 lower to 0.91 higher)
Sleep (Pittsburgh Sleep Quality Index - sleep problems) final values ≤3 months	151 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision			The mean sleep (pittsburgh sleep quality index - sleep problems) final values ≤3 months in the intervention groups was 0.55 standard deviations lower (0.88 to 0.23 lower)
Sleep (Karolinska Sleep Questionnaire sleep quality) final values >3 months	36 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision			The mean sleep (karolinska sleep questionnaire sleep quality) final values >3 months in the intervention groups was 0.76 standard deviations higher (0.08 to 1.44 higher)
Sleep (Pittsburgh Sleep Quality Index - sleep problems) final values >3 months	151 (1 study) 6 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness			The mean sleep (pittsburgh sleep quality index - sleep problems) final values >3 months in the intervention groups was 0.14 standard deviations lower (0.46 lower to 0.18 higher)
Use of healthcare services (physician/other health professional visits in past 3 months) final values ≤3 months	151 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness		The mean use of healthcare services (physician/other health professional visits in past 3 months) final values ≤3 months in	The mean use of healthcare services (physician/other health professional visits in past 3 months) final values ≤3 months in the intervention groups was 0.81 lower (2.48 lower to 0.86 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Pain education (95% CI)
				the control groups was 4.54 visits	
Use of healthcare services (physician/other health professional visits in past 3 months) final values >3 months	151 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness		The mean use of healthcare services (physician/other health professional visits in past 3 months) final values >3 months in the control groups was 4.8 visits	The mean use of healthcare services (physician/other health professional visits in past 3 months) final values >3 months in the intervention groups was 1.41 lower (3.08 lower to 0.26 higher)
Discontinuation	167 (2 studies) 4-10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	See comment	Moderate	
				20 per 1000	34 more per 1000 (from 11 fewer to 78 more)
Pain (VAS/NRS) final values/change scores ≤3 months Scale from: 0 to 10.	167 (2 studies) 4-10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (VAS/NRS) final values/change scores ≤3 months in the control groups was 5.2	The mean pain (VAS/NRS) final values/change scores ≤3 months in the intervention groups was 0.48 lower (0.99 lower to 0.03 higher)
Pain (VAS/NRS) final values >3 months Scale from: 0 to 10.	151 (1 study) 6 months	⨁⨁⊖⊖ LOW1,2 due to risk of bias, indirectness		The mean pain (VAS/NRS) final values >3 months in the control groups was 4.94	The mean pain (VAS/NRS) final values >3 months in the intervention groups was 0.12 lower (0.7 lower to 0.46 higher)
Pain (McGill Pain Questionnaire) final values ≤3 months Scale from: 0 to 78	36 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (mcgill pain questionnaire) final values ≤3 months in the control groups was 49.14	The mean pain (mcgill pain questionnaire) final values ≤3 months in the intervention groups was 5.5 lower

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Pain education (95% CI)
					(30.73 lower to 19.73 higher)
Pain (McGill Pain Questionnaire) final values >3 months Scale from: 0 to 78	36 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (mcgill pain questionnaire) final values >3 months in the control groups was 47.29	The mean pain (mcgill pain questionnaire) final values >3 months in the intervention groups was 3.08 lower (24.44 lower to 18.28 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 17: Clinical evidence summary: CBT versus Biofeedback

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Biofeedback (95% CI)
Discontinuation	58 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	RR 0.33 (0.04 to 3.02)	Moderate	
				35 per 1000	23 fewer per 1000 (from 34 fewer to 71 more)
Pain (NRS) final values ≤3 months Scale from: 0 to 10.	56 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (NRS) final values ≤3 months in the control groups was 5.43	The mean pain (NRS) final values ≤3 months in the intervention groups was 0.57 higher (0.61 lower to 1.75 higher)
Pain (NRS) final values >3 months Scale from: 0 to 10.	56 (1 study) 6 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias,		The mean pain (NRS) final values >3 months in the control	The mean pain (NRS) final values >3 months in the intervention groups

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Biofeedback (95% CI)
		indirectness, imprecision		groups was 4.5	was 0.04 lower (1.38 lower to 1.30 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 18: Clinical evidence summary: CBT versus Psychotherapy

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Psychotherapy (95% CI)
Psychological distress (BDI) final values ≤3 months Scale from: 0 to 63.	48 (1 study) 10 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (BDI) final values ≤3 months in the control groups was 9.9	The mean psychological distress (BDI) final values ≤3 months in the intervention groups was 0.8 higher (4.19 lower to 5.79 higher)
Psychological distress (BDI) final values >3 months Scale from: 0 to 63.	47 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (BDI) final values >3 months in the control groups was 11.5	The mean psychological distress (BDI) final values >3 months in the intervention groups was 4.2 lower (9.61 lower to 1.21 higher)
Psychological distress (Pain Anxiety Symptoms Scale) final values ≤3 months Scale from: 0 to 200.	48 (1 study) 10 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (pain anxiety symptoms scale) final values ≤3 months in the control groups was 62.8	The mean psychological distress (pain anxiety symptoms scale) final values ≤3 months in the intervention groups was 4.9 higher (13.81 lower to 23.61 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Psychotherapy (95% CI)
Psychological distress (Pain Anxiety Symptoms Scale) final values >3 months Scale from: 0 to 200.	47 (1 study) 12 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean psychological distress (pain anxiety symptoms scale) final values >3 months in the control groups was 65.2	The mean psychological distress (pain anxiety symptoms scale) final values >3 months in the intervention groups was 9.9 lower (29.45 lower to 9.65 higher)
Discontinuation	50 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	RR 0.6 (0.16 to 2.25)	Moderate	
				200 per 1000	80 fewer per 1000 (from 168 fewer to 250 more)
Pain (McGill Pain Questionnaire) final values ≤3 months Scale from: 0 to 78.	48 (1 study) 10 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (McGill pain questionnaire) final values ≤3 months in the control groups was 14	The mean pain (McGill pain questionnaire) final values ≤3 months in the intervention groups was 4.5 higher (2.85 lower to 11.85 higher)
Pain (McGill Pain Questionnaire) final values >3 months Scale from: 0 to 78.	47 (1 study) 12 months	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (McGill pain questionnaire) final values >3 months in the control groups was 13.3	The mean pain (McGill pain questionnaire) final values >3 months in the intervention groups was 0.2 higher (7.84 lower to 8.24 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 19: Clinical evidence summary: CBT versus Behaviour therapy

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with CBT versus Behaviour therapy (95% CI)
Physical function (FIQ physical function sub scale) final values >3 months	85 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean physical function (FIQ physical function sub scale) final values >3 months in the control groups was 2.63	The mean physical function (FIQ physical function sub scale) final values >3 months in the intervention groups was 0.79 higher (0.05 lower to 1.63 higher)
Use of healthcare services (Physician visits) >3 months	85 (1 study) 12 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean use of healthcare services (physician visits) >3 months in the control groups was 16.35	The mean use of healthcare services (physician visits) >3 months in the intervention groups was 8.92 higher (1.11 to 16.73 higher)
Discontinuation	85 (1 study) 15 weeks	⊕⊖⊖⊖ VERY LOW2,3 due to indirectness, imprecision	RR 0.68 (0.12 to 3.88)	Moderate	
				70 per 1000	22 fewer per 1000 (from 62 fewer to 202 more)
Pain (West Haven-Yale Multidimension Pain Inventory) final values >3 months	85 (1 stud) 12 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (west haven-yale multidimension pain inventory) final values >3 months in the control groups was 3.05	The mean pain (west haven-yale multidimension pain inventory) final values >3 months in the intervention groups was 0.13 higher (0.47 lower to 0.73 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 20: Clinical evidence summary: Biofeedback versus Relaxation

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Biofeedback versus Relaxation (95% CI)
Pain (% reduction in pain from baseline) ≤3 months Scale from: 0 to 100.	57 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain (% reduction in pain from baseline) ≤3 months in the control groups was 56% reduction	The mean pain (% reduction in pain from baseline) ≤3 months in the intervention groups was 20 lower (41.55 lower to 1.55 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 21: Clinical evidence summary: ACT versus Relaxation

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Relaxation (95% CI)
Quality of life (SF12 mental component) final values ≤3 months Scale from: 0 to 100.	43 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf12 mental component) final values ≤3 months in the control groups was 34.9	The mean quality of life (sf12 mental component) final values ≤3 months in the intervention groups was 6 higher (0.36 lower to 12.36 higher)
Quality of life (SF12 mental component) >3 months Scale from: 0 to 100.	37 (1 study) 9 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf12 mental component) >3 months in the control groups was 38.8	The mean quality of life (sf12 mental component) >3 months in the intervention groups was 0.5 higher (7.51 lower to 8.51 higher)
Quality of life (SF12 physical component) final values ≤3 months Scale from: 0 to 100.	43 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2		The mean quality of life (sf12 physical component) final	The mean quality of life (sf12 physical component) final values ≤3 months in the intervention groups

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Relaxation (95% CI)
		due to risk of bias, imprecision		values ≤3 months in the control groups was 32.1	was 2.8 higher (2.38 lower to 7.98 higher)
Quality of life (SF12 physical component) final values >3 months Scale from: 0 to 100.	37 (1 study) 9 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf12 physical component) final values >3 months in the control groups was 32.3	The mean quality of life (sf12 physical component) final values >3 months in the intervention groups was 7 higher (0.56 to 13.44 higher)
Pain interference (Pain disability index) final values ≤3 months Scale from: 0 to 70.	43 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain interference (pain disability index) final values ≤3 months in the control groups was 40.3	The mean pain interference (pain disability index) final values ≤3 months in the intervention groups was 11.5 lower (20.38 to 2.62 lower)
Pain interference (Pain disability index) final values >3 months Scale from: 0 to 70.	37 (1 study) 9 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain interference (pain disability index) final values >3 months in the control groups was 34	The mean pain interference (pain disability index) final values >3 months in the intervention groups was 2.8 lower (14.16 lower to 8.56 higher)
Psychological distress (HADS depression) final values ≤3 months Scale from: 0 to 21.	43 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs depression) final values ≤3 months in the control groups was 9.1	The mean psychological distress (HADs depression) final values ≤3 months in the intervention groups was 2 lower (5.06 lower to 1.06 higher)
Psychological distress (HADS depression) final values >3 months Scale from: 0 to 21.	37 (1 study) 9 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs depression) final values >3 months	The mean psychological distress (HADs depression) final values >3 months in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ACT versus Relaxation (95% CI)
				in the control groups was 8.4	0 higher (3.58 lower to 3.58 higher)
Psychological distress (HADS anxiety) final values ≤3 months Scale from: 0 to 21.	43 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs anxiety) final values ≤3 months in the control groups was 9	The mean psychological distress (HADs anxiety) final values ≤3 months in the intervention groups was 1.7 lower (4.27 lower to 0.87 higher)
Psychological distress (HADS anxiety) final values >3 months Scale from: 0 to 21.	37 (1 study) 9 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean psychological distress (HADs anxiety) final values >3 months in the control groups was 9.1	The mean psychological distress (HADs anxiety) final values >3 months in the intervention groups was 0 higher (3.32 lower to 3.32 higher)
Discontinuation	49 (1 study) 12 weeks	⨁⨁⨁⊖ MODERATE1 due to risk of bias	OR 0.11 (0.02 to 0.67)	Moderate	
				208 per 1000	180 fewer per 1000 (from 58 fewer to 203 fewer)
Pain (NRS 0-6) final values ≤3 months Scale from: 0 to 6.	43 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain (NRS 0-6) final values ≤3 months in the control groups was 4	The mean pain (NRS 0-6) final values ≤3 months in the intervention groups was 0.3 lower (1.18 lower to 0.58 higher)
Pain (NRS 0-6) final values >3 months Scale from: 0 to 6.	37 (1 study) 9 months	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain (NRS 0-6) final values >3 months in the control groups was 4.1	The mean pain (NRS 0-6) final values >3 months in the intervention groups was 0.3 higher (0.61 lower to 1.21 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

Three health economic studies were identified with the relevant comparison and have been included in this review.[41, 289, 290] These are summarised in the health economic evidence profiles below (**Note that Table 22** includes only the relevant comparisons for this review, although the evidence table in Appendix H: includes all comparators in the study.

Table 22, **Table 23**,

Table 24) and the health economic evidence tables in appendix H.

1.5.2 Excluded studies

Three economic studies relating to this review question were identified but were excluded due to a combination of limited applicability and methodological limitations and the availability of more applicable evidence.[216, 247, 304] These are listed in appendix I, with reasons for exclusion given.

See also the health economic study selection flow chart in appendix G.

1.5.3 Summary of studies included in the economic evidence review

Note that **Table 22** includes only the relevant comparisons for this review, although the evidence table in Appendix H: includes all comparators in the study.

Table 22: Health economic evidence profile: Telephone-delivered cognitive behaviour therapy (TCBT) vs usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental QALYs (c)	Cost effectiveness	Uncertainty
Beasley 2015.[41] [UK]	Directly applicable [(a)]	Potentially serious limitations [(b)]	• Within-trial analysis (same paper) • Cost-utility analysis (QALYs) • Population: Aged over 25 with chronic widespread pain according to the definition of fibromyalgia, and had consulted their GP in the previous year. • 6 month interventions • Follow-up: 30 months (24 months post treatment) Comparators: 1. Telephone-delivered cognitive behaviour therapy (TCBT): initial assessment (45-60mins) followed by 7 weekly sessions (30-45mins each). 2. Treatment as usual	**Complete case analysis:** £574 **Multiple imputation analysis:** £554	**Complete case analysis:** 0.097 **Multiple imputation analysis:** 0.140	**Complete case analysis:** £5,917 per QALY gained **Multiple imputation analysis:** £3,957 per QALY gained	Used non-parametric bootstrapping.

(a) UK NHS study, used EQ-5D. Participation in study based on self-reported symptoms and recruited through primary care, may not necessarily be representative of general population with chronic widespread pain caused by fibromyalgia.

(b) Treatment as usual not defined, usual care provided by GP was not restricted and may not be the same across all participants in that group. Within-study analysis which may not reflect full body of evidence.

(c) Note that looking at the unadjusted EQ-5D values and their pattern over the outcome measurement periods of baseline, 6,9 and 24 months, then at 24 months the CBT group had an EQ-5D the same as baseline but the control group got worse than baseline at 24 months. So there is a benefit from treatment because people in the intervention group didn't get worse, rather than got better.

Table 23: Health economic evidence profile: Group based cognitive behaviour therapy (CBT) vs usual care

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental QALYs	Cost effectiveness	Uncertainty
Luciano 2014 [289] [Spain]	Partially applicable [(a)]	Potentially serious limitations [(b)]	• Within-trial analysis (based on Alda 2011 trial)[6] • Cost-utility analysis (QALYs) • Population: people with Fibromyalgia • 6 month intervention Comparators: 1. Group based CBT: 9 sessions 2. Treatment as usual	**Complete case:** -£1,560	**Complete case:** 0.01	**Complete case:** CBT dominant	Used non-parametric bootstrapping. Sensitivity analyses: • Intention to treat analysis where missing data was imputed. • Per protocol analysis where excluded 14 patients who did not attend the 9 sessions. Both analyses still showed CBT remained dominant.

(a) Non-UK study, used Spanish EQ-5D.
(b) Drug costs include VAT, UK costs wouldn't. Based on one trial. Self-reported resource use. Only minor medication was allowed to be continued in the CBT arm so it is not in addition to usual care and therefore costs of CBT arm might be underestimated without medication.

Table 24: Health economic evidence profile: Group based acceptance and commitment therapy (GACT) versus waiting list

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental QALYs	Cost effectiveness	Uncertainty
Luciano 2017.[290] [Spain]	Partially applicable [(a)]	Potentially serious limitations [(b)]	• Within-trial analysis (Based on the EFFIGACT trial)[291] • Cost-utility analysis (QALYs) • Population: People aged 18-65 years with fibromyalgia with no pharmacological or psychological treatment during the previous year. • 6 month interventions Comparators: 1. GACT, 8 x 2.5 hour weekly group sessions; 10-15 patients; covering exercises and topics within the context of ACT practice and training; including various types of formal mindfulness practice; daily homework assignments of 15-30 minutes; led by a clinical psychologist. 2. Treatment as usual	**Complete case:** -£1,897	**Complete case:** 0.05	**Complete case:** GACT dominant	Used non-parametric bootstrapping. Sensitivity analyses: • Intention to treat analysis where missing data was imputed. • Per protocol analysis where excluded 14 patients who did not attend the sessions. Both analyses still showed GACT remained dominant.

(a) Non-UK study, used Spanish EQ-5D.
(b) Drug costs include VAT, UK costs wouldn't. Based on one trial. Self-reported resource use. Co-medication not allowed in ACT arm so it is not in addition to usual care and therefore costs of ACT arm might be underestimated without medication.

1.5.4 Unit costs

Staff costs:

Table 25: UK costs of clinical psychologists (community based)

Staff member	Band	Cost per hour of patient contact	Detail/source
Clinical psychology assistant practitioner (higher level)	5	£51	PSSRU 2018.[118] Includes direct and indirect patient time at a ratio of 1:0.37, and qualification costs.
Clinical psychology trainee	6	£64	
Clinical psychologist	7	£78	

The training costs for psychologists are not included in the PSSRU, so it is assumed the costs would be similar to that of another role (dietician in this case, to use a more conservative estimate. The ratio of direct to indirect time is assumed to be the same as that of a physiotherapist, as the ratio for a clinical psychologist is not reported in this version of the PSSRU.

Psychological programs costs:

Clinical practice is highly variable in terms of how psychological programmes would be funded. For example some programmes may use NHS reference costs demonstrated below, some may absorb the costs into outpatient attendance codes, and some may locally negotiate tariffs for group therapy. Programmes that are provided in the community can also vary with contracts being based on volume and cost or block contracts providing a certain amount of reimbursement per course of treatment.

Some illustrations of the costs that could be involved in running psychological therapies are demonstrated below.

Table 26: UK costs of CBT as part of a pain management programme - NHS reference costs

Therapy	Detail	Cost	Detail/source
Cognitive Behavioural Therapy as part of a Pain Management Programme (Day case)	HRG code: AB11Z	£118	NHS reference costs 2017-18.[133]
Cognitive Behavioural Therapy as part of a Pain Management Programme (Outpatient)	HRG code: AB11Z	£123	

The NHS reference costs apply per person per session/attendance, regardless of whether the intervention is delivered in a group.

Table 27: UK costs of clinical Cognitive therapy based programs – PSSRU 2017

Therapy	Detail	Cost per hour	Detail/source
Cognitive behaviour therapy – **individual** (a)	Telephone based	£89	Hammond et al 2012. Quoted in PSSRU 2017.[117]
	Face to face	£134	
Mindfulness based cognitive therapy – **group based** (a)	Based on a band 7 staff member.	£52 per hour £88 per hour of direct contact 2 hour sessions for a group of 12:	Cost for direct contact based on a ratio of face-to-face time to non-face-to-face time of 1:0.67 based on opinion of 3 therapists from the PSSRU.[117]

Therapy	Detail	Cost per hour	Detail/source
		£175/12 = £15 per person per session.	

(a) These have been removed from PSSRU 2018 so costs are taken from PSSRU 2017.

1.5.5 Threshold calculations:

The clinical review was looked through to identify studies comparing ACT or CBT with usual care that reported utilities (preferably on the EQ-5D scale) or quality of life data that could be transformed to utilities, and multiplied by a timeframe to derive QALYs. These have then been added to QALYs already reported in the included economic evaluations.

Table 28: Summary of QALYs from clinical review and included economic evaluations

Intervention	Study	Intervention length/Follow up	Incremental EQ-5D	Incremental QALY	N
ACT (a)	Luciano 2017[290]	8 weeks, 8 sessions, **group based**. 6 month follow up.		0.05	
CBT	Luciano 2014[289]	10-12 weeks, 10 sessions, **group based**. 6 month follow up.		0.01	112
	Castro 2012[96] (c)	10 weeks, 10 sessions, **unclear if group based**	0.064	0.064*10 weeks = 0.012	93
	Friesen 2017[165] (d)	8 weeks, 8 sessions, **online CBT**.	0.093	0.093*8 weeks = 0.014	60
	Beasley 2015[41] (e)	6 month intervention, **phone CBT**. 30 months follow up		0.097	218
	Pooled incremental QALY gain from CBT			***0.05***	

*(a) Adjusted incremental QALY from **Table 24**.*
*(b) Adjusted incremental QALY from **Table 23**.*
(c) SF-36 mapped onto EQ-5D, using Ara & Brazier 2008 algorithm.[24] Taking into account the difference from follow up and baseline EQ-5D for the intervention and control groups, and then taking the difference between the intervention and control group EQ-5D values.
(d) SF-12 mapped onto EQ-5D, using Franks 2004 algorithm.[164] Taking into account the difference from follow up and baseline EQ-5D for the intervention and control groups, and then taking the difference between the intervention and control group EQ-5D values.

Adjusted incremental QALY from Note that **Table 22** includes only the relevant comparisons for this review, although the evidence table in Appendix H: includes all comparators in the study.
*(e) **Table 22**.*

The QALYs from each study for CBT have been pooled by weighting the QALY by the number of people in each study. A rearrangement of the ICER equation can identify the incremental costs needed to make ACT and CBT borderline cost effective at a threshold of £20,000 per QALY gained. As both interventions resulted in the same QALY gain:

ACT/CBT: £20,000*0.05 = **£1,000 per person**

This is the maximum amount that could be spent on the interventions, per person, that would make them cost effective.

Alternatively, because the QALY gain for the Beasley study seems quite high compared to the other studies for CBT, excluding this to see the impact results in a QALY gain of 0.01, which would lead to a maximum cost per person that would make CBT borderline cost effective of:

ACT/CBT: £20,000*0.01 = **£236 per person**

If an intervention is group based, then this would lower the cost per person, and it is possible that the cost per person could be below the costs suggested above. However, these calculations are based on limited trial data, and the likelihood of ACT/CBT being cost effective are highly dependent on both the benefits and costs of the treatment.

1.6 Evidence statements

1.6.1 Clinical evidence statements

CBT versus usual care

Quality of life

Very low quality evidence from 2 studies with a total of 233 participants showed a clinically important benefit of CBT at time points up to 3 months, but low to very low quality evidence from 5 studies with a total of 365 participants showed no clinically important difference between CBT and usual care. Low quality evidence from two studies with a total of 256 participants showed a clinically important benefit of CBT at time points after 3 months, but very low quality evidence from 2 studies with a total of 73 participants showed no clinically important difference between CBT and usual care. Very low quality evidence from one study with a total of 13 participants showed a clinically important benefit of CBT-I at time points up to 3 months, but very low quality evidence from one study with a total of 63 participants showed no clinically important difference between CBT-I and usual care. Low to very low quality evidence from three studies with a total of 136 participants showed a clinically important benefit of CBT-I at time points up to and after 3 months.

Physical function

Low quality evidence from one study with a total of 140 participants showed a clinically important benefit of CBT at time points up to 3 months, but very low quality evidence from two studies with a total of 190 participants showed no clinically important difference between CBT and usual care. Very low quality evidence from one study with a total of 28 participants showed a clinically important benefit of CBT at time points after 3 months, but very low quality evidence from one study with a total of 118 participants showed no clinically important difference between CBT and usual care.

Psychological distress

Very low quality evidence from 6 studies with a total of 597 participants and very low quality evidence from 5 studies with a total of 457 participants showed no clinically important difference between CBT and usual care at time points up to 3 months. Very low quality evidence from 7 studies with a total of 75 participants and very low quality evidence from 5 studies with a total of 394 participants showed no clinically important difference between CBT and usual care at time points after 3 months. Very low quality evidence from 2 studies with a total of 118 participants showed no clinically important difference between CBT-I and usual care at time points up to 3 months. Very low quality evidence from 2 studies with a total of 95 participants showed no clinically important difference between CBT-I and usual care at time points after 3 months.

Pain interference

Moderate quality evidence from one study with a total of 60 participants showed a clinically important benefit of CBT at time points up to 3 months, but very low quality evidence from one study with a total of 58 participants showed no clinically important difference between CBT and usual care. Very low quality evidence from one study with a total of 50 participants showed no clinically important difference between CBT and usual care at time points after 3 months, but very low quality evidence from one study with a total of 47 participants showed the opposite. Very low quality evidence from one study with a total of 47-55 participants showed no clinically important difference between CBT-I and usual care at time points before or after 3 months.

Pain self-efficacy

Very low quality evidence from 3 studies with a total of 160 participants showed no clinically important difference between CBT and usual care at time points up to 3 months. Very low quality evidence from one study with a total of 50 participants showed no clinically important difference between CBT and usual care at time points after 3 months. Very low quality evidence from one study with a total of 63 participants showed no clinically important difference between CBT-I and usual care at time points up to 3 months. Very low quality evidence from one study with a total of 48 participants showed no clinically important difference between CBT-I and usual care at time points after 3 months.

Sleep

Low quality evidence from 4 studies with a total of 297 participants showed no clinically important difference between CBT and usual care at time points up to 3 months. Very low quality evidence from 4 studies with a total of 407 participants showed no clinically important difference between CBT and usual care at time points after 3 months. Low quality evidence from one study with a total of 24 participants showed a clinically important benefit of CBT-I at time points up to 3 months, but very low quality evidence from 2 studies with a total of 118 participants showed no clinically important difference. Very low quality evidence from 2 studies with a total of 77 participants showed a clinically important benefit of CBT-I at time points after 3 months, but very low quality evidence from 2 studies with a total of 195 participants showed no clinically important difference.

Use of healthcare services

Very low quality evidence from one study with a total of 63 participants showed a clinically important benefit of CBT (GP visits and additional psychological services) at time points after 3 months, but very low quality evidence from the same study showed no clinically important difference (referral to a specialist).

Pain

Low to very low quality evidence from 10 studies with a total of 776 participants showed no clinically important difference between CBT and usual care at time points up to 3 months. Very low quality evidence from one study with a total of 76 participants showed a clinically important benefit of CBT at time points up to and after 3 months.Very low quality evidence from 6 studies with a total of 406 participants showed no clinically important difference between CBT and usual care at time points after 3 months. Very low quality evidence from 1 study with a total of 63 participants showed no clinically important difference between CBT-I and usual care at time points up to 3 months, but evidence from 2 studies with a total of 79 participants showed a clinically important benefit of CBT-I compared to usual care. Very low quality evidence from 2 studies with a total of 112 participants showed a clinically important benefit of CBT-I at time points after 3 months, but very low quality evidence from 2 studies with a total of 61 participants showed no clinically important difference between CBT-I and usual care.

Discontinuation

Very low quality evidence from 13 studies with a total of 1258 participants showed more trial discontinuations from the CBT arms than from usual care. Very low quality evidence from 3 studies with a total of 177 participants showed more trial discontinuations from the CBT-I arms than from usual care.

Acceptance and commitment therapy (ACT) versus usual care

Quality of life

Low to very low quality evidence from 3 studies with a total of 201 participants showed a clinically important benefit of ACT at time points up to 3 months, but very low quality evidence from 1 study with a total of 63 participants showed no clinically important difference between ACT and usual care. Low to very low quality evidence from 3 studies with a total of 198 participants showed a clinically important benefit of ACT at time points after 3 months, but very low quality evidence from one study with a total 33 participants showed usual care to lead to a clinically important improvement compared ACT.

Physical function

Very low quality evidence from one study with a total of 61 participants showed no clinically important difference between ACT and usual care at time points up to or after 3 months.

Psychological distress

Very low quality evidence from 4 studies with a total of 254 participants showed a clinically important benefit of ACT at time points up to 3 months, but very low quality evidence from one study with a total of 36 participants showed no clinically important difference between ACT and usual care. Very low quality evidence from 1 study with a total of 36 participants and 2 studies with a total of 157 participants showed a clinically important benefit of ACT at time points up to 3 months. Very low quality evidence from 3 studies with a total of 198 participants and from 1 study of 33 participants showed a clinically important benefit of ACT at time points after 3 months, but very low quality evidence from one study with a total of 33 participants showed no clinically important difference between ACT and usual care. Low quality evidence from 1 study of 104 participants showed a clinically important benefit of ACT at time points after 3 months.

Pain interference

Very low quality evidence from 2 studies with a total of 89 participants showed a clinically important benefit of ACT at time points up to 3 months, but very low quality evidence from one study with a total of 53 participants showed no clinically important difference between ACT and usual care. Very low quality evidence from one study with a total of 33 participants showed a clinically important benefit of ACT at time points after 3 months.

Sleep

Very low quality evidence from one study with a total of 61 participants showed a clinically important benefit of ACT at time points up to and after 3 months.

Pain

Very low quality evidence from 3 studies with a total of 201 participants showed a clinically important benefit of ACT at time points up to and after 3 months.

Discontinuation

Very low quality evidence from 4 studies with a total of 312 participants showed more trial discontinuations from the ACT arms than from usual care.

Relaxation versus usual care/attention control

Quality of life

Very low quality evidence from 2 studies with a total of 173 participants showed a clinically important benefit of relaxation at time points up to 3 months.

Physical function

Moderate quality evidence from one study with a total of 258 participants showed no clinically important difference between relaxation and usual care at time points up to or after 3 months.

Psychological distress

Low to very low quality evidence from 2 studies with a total of 189 participants showed no clinically important difference between relaxation and usual care at time points up to 3 months.

Pain interference

Very low quality evidence from one study with a total of 64 participants showed no clinically important difference between relaxation and usual care at time points up to 3 months.

Pain self-efficacy

Moderate quality evidence from one study with a total of 48 participants showed a clinically important benefit of relaxation at time points up to 3 months, but very low quality evidence from one study with a total of 64 participants showed no clinically important difference between relaxation and usual care.

Sleep

Very low quality evidence from one study with a total of 125 participants showed a clinically important benefit of relaxation at time points up to 3 months.

Pain

Low quality evidence from 4 studies with a total of 485 participants showed no clinically important difference between relaxation and usual care at time points up to 3 months. Moderate quality evidence from 1 study with a total of 258 participants showed no clinically important difference between relaxation and usual care at time points after 3 months. Very low quality evidence from one study with a total of 23 participants showed a clinically important benefit of relaxation over attention control at time points up to 3 months.

Discontinuation

Very low quality evidence from 3 studies with a total of 455 participants showed fewer trial discontinuations from the relaxation arms than from usual care. Low quality evidence from one study with a total of 27 participants showed fewer trial discontinuations from the relaxation arm than from attention control.

Biofeedback versus usual care/attention control (sham biofeedback)

Quality of life

Very low quality evidence from one study with a total of 22 participants showed a clinically important benefit of HRV biofeedback over usual care at time points up to 3 months, but low to very low quality evidence from one study with a total of 38 participants showed the opposite for EMG biofeedback. Very low quality evidence from one study with a total of 65 participants showed no clinically important difference between biofeedback and usual care at time points after 3 months. Very low quality evidence from one study with a total of 36

participants showed no clinically important difference between biofeedback and usual care on some SF36 sub scales, but a negative effect from biofeedback that was clinically important on others. Low quality evidence from one study with a total of 30 participants showed a clinically important benefit of biofeedback over sham biofeedback at time points up to 3 months.

Physical function

Very low quality evidence from one study with a total of 22 participants showed no clinically important difference between biofeedback and usual care at time points up to 3 months. Very low quality evidence from one study with a total of 65 participants showed a clinically important benefit of biofeedback at time points after 3 months. Low quality evidence from one study with a total of 30 participants showed a clinically important benefit of biofeedback over sham biofeedback at time points up to 3 months.

Psychological distress

Very low quality evidence from one study with a total of 38 participants showed no clinically important difference between EMG biofeedback and usual care at time points up to 3 months. Very low quality evidence from one study with a total of 22 participants showed a clinically important benefit of HRV biofeedback over usual care for depression at time points up to 3 months, but no clinically important difference for anxiety. Very low quality evidence from one study with a total of 65 participants showed no clinically important difference between biofeedback and usual care at time points after 3 months, but very low quality evidence from one study with a total of 36 participants showed a clinically important negative effect of EMG biofeedback compared to usual care. Very low quality evidence from one study with a total of 34 participants showed no clinically important difference between biofeedback and sham biofeedback at time points up to 3 months. Low quality evidence from one study with a total of 32 participants showed no clinically important difference between biofeedback and sham biofeedback at time points after 3 months.

Sleep

Very low quality evidence from one study with a total of 34 participants showed no clinically important difference between biofeedback and sham biofeedback at time points up to 3 months. Low quality evidence from one study with a total of 32 participants showed no clinically important difference between biofeedback and sham biofeedback at time points after 3 months.

Pain

Very low quality evidence from one study with a total of 22 participants showed no clinically important difference between biofeedback and usual care at time points up to 3 months. Very low quality evidence from one study with a total of 65 participants showed no clinically important difference between biofeedback and usual care at time points after 3 months. Low quality evidence from one study with a total of 30 participants showed a clinically important benefit of biofeedback over sham biofeedback at time points up to 3 months, but low quality evidence from one study with a total of 34 participants showed the opposite for neurofeedback. Low quality evidence from one study with a total of 32 participants showed a clinically important benefit of neurofeedback over sham biofeedback at time points after 3 months.

Discontinuation

Very low quality evidence from 3 studies with a total of 147 participants showed more trial discontinuations from the biofeedback arms than usual care. Moderate quality evidence from 2 studies with a total of 73 participants showed no difference between biofeedback and sham biofeedback in discontinuations.

Mindfulness versus usual care

Quality of life

Very low quality evidence from one study with a total of 31 participants showed no clinically important difference between mindfulness and usual care at time points up to 3 months, but a clinically important benefit of mindfulness at time points after 3 months.

Psychological distress

Low quality evidence from one study with a total of 32 participants showed a clinically important benefit of mindfulness at time points up to 3 months, but low to very low quality evidence from 2 studies with a total of 63 participants and from 1 study with a total of 32 participants showed no clinically important difference between mindfulness and usual care. Low to very low quality evidence from 2 studies with a total of 63 participants and from 1 study with a total of 32 participants showed a clinically important benefit of mindfulness at time points after 3 months, but very low quality evidence from one study with 32 participants showed no clinically important difference between mindfulness and usual care.

Sleep

Low quality evidence from one study with a total of 39 participants showed a clinically important benefit of mindfulness at time points up to 3 months and very low quality evidence from the same study also showed a clinically important benefit of mindfulness at time points after 3 months.

Discontinuation

Low quality evidence from 2 studies with a total of 72 participants showed more trial discontinuations from the mindfulness arms than from usual care.

Pain education versus usual care/attention control

Quality of life

Very low quality evidence from one study with a total of 35 participants showed no clinically important difference between pain education and usual care at time points up to 3 months. Very low quality evidence from one study with a total of 77 participants showed no clinically important difference between pain education and attention control at time points up to or after 3 months.

Psychological distress

Very low quality evidence from one study with a total of 77 participants showed no clinically important difference between pain education and attention control at time points up to or after 3 months.

Pain self-efficacy

Low quality evidence from one study with a total of 35 participants showed no clinically important difference between pain education and usual care at time points up to 3 months.

Sleep

Very low quality evidence from one study with a total of 35 participants showed no clinically important difference between pain education and usual care at time points up to 3 months.

Pain

Very low quality evidence from one study with a total of 35 participants showed no clinically important difference between pain education and usual care at time points up to 3 months.

Low quality evidence from one study with a total of 77 participants showed a clinically important benefit of pain education at time points up to 3 months and very low quality evidence from the same study also showed a clinically important benefit at time points after 3 months.

Discontinuation

Very low quality evidence from one study with a total of 103 participants showed more discontinuations from the pain education arm than attention control.

Sleep hygiene versus usual care

Quality of life

Very low quality evidence from one study with a total of 26 participants showed a clinically important benefit of sleep hygiene at time points up to 3 months. Low quality evidence from one study with a total of 14 participants showed a clinically important benefit of sleep hygiene at time points after 3 months.

Sleep

Low quality evidence from one study with a total of 26 participants showed a clinically important benefit of sleep hygiene at time points up to 3 months. Low quality evidence from one study with a total of 14 participants showed a clinically important benefit of sleep hygiene at time points after 3 months.

Pain

Low quality evidence from one study with a total of 26 participants showed a clinically important benefit of sleep hygiene at time points up to 3 months. Low quality evidence from one study with a total of 14 participants showed a clinically important benefit of sleep hygiene at time points after 3 months.

Discontinuation

Very low quality evidence from one study with a total of 29 participants showed fewer trial discontinuations from the sleep hygiene arm than from usual care.

Hypnosis versus usual care

Quality of life

Very low quality evidence from one study with a total of 59 participants showed no clinically important difference between hypnosis and usual care at time points up to or after 3 months.

Psychological distress

Very low quality evidence from one study with a total of 59 participants showed no clinically important difference between hypnosis and usual care at time points up to 3 months. Very low quality evidence from one study with a total of 59 participants showed a clinically important benefit of hypnosis for depression, but no clinically important difference for anxiety at time points after 3 months.

Sleep

Very low quality evidence from one study with a total of 59 participants showed no clinically important difference between hypnosis and usual care at time points up to 3 months. Low quality evidence from one study with a total of 59 participants showed a clinically important benefit of hypnosis at time points after 3 months.

Pain

Low quality evidence from one study with a total of 59 participants showed a clinically important benefit of hypnosis at time points after 3 months.

Discontinuation

Very low quality evidence from one study with a total of 62 participants showed no clinically important difference between hypnosis and usual care.

Psychotherapy versus usual care

Quality of life

Very low quality evidence from one study with a total of 46 participants showed a clinically important benefit of psychotherapy on the SF36 mental component, but no clinically important difference on the physical component at time points after 3 months.

Physical function

Low quality evidence from one study with a total of 46 participants showed a clinically important benefit of psychotherapy at time points after 3 months.

Psychological distress

Very low quality evidence from one study with a total of 46 participants showed a clinically important benefit of psychotherapy at time points after 3 months.

Pain interference

Very low quality evidence from one study with a total of 46 participants showed a clinically important benefit of psychotherapy at time points after 3 months.

Discontinuation

Very low quality evidence from one study with a total of 46 participants showed fewer trial discontinuations from the psychotherapy arm than usual care.

CBT-I versus Sleep hygiene

Quality of life

Very low quality evidence from 2 studies with a total of 97 participants showed a clinically important benefit of CBT-I at time points up to 3 months, but one study with a total of 32 participants showed no clinically important difference between CBT-I and sleep hygiene. Very low quality evidence from one study with a total of 13 participants showed no clinically important difference between CBT-I and sleep hygiene at time points after 3 months.

Psychological distress

Very low quality evidence from 2 studies with a total of 97 participants showed a clinically important benefit of CBT-I at time points up to 3 months for depression, but very low quality evidence from the same studies showed no clinically important difference between CBT-I and sleep hygiene for anxiety.

Pain self-efficacy

Very low quality evidence from one study with a total of 57 participants showed a clinically important benefit of CBT-I at time points up to 3 months.

Sleep

Low quality evidence from 2 studies with a total of 97 participants showed a clinically important benefit of CBT-I at time points up to 3 months, but very low quality evidence from

one study with a total of 26 participants showed no clinically important difference between CBT-I and sleep hygiene and low quality evidence from one study with a total of 32 participants showed a clinically important benefit of sleep hygiene. Very low quality evidence from one study with a total of 13 participants showed a clinically important benefit of sleep hygiene at time points after 3 months.

Pain

Low quality evidence from 2 studies with a total of 97 participants showed a clinically important benefit of CBT-I at time points up to 3 months, but very low quality evidence from one study with a total of 32 participants showed a clinically important benefit of sleep hygiene. Low quality evidence from one study with a total of 13 participants showed a clinically important benefit of sleep hygiene at time points after 3 months.

Discontinuation

Very low quality evidence from 3 studies with a total of 144 participants showed more discontinuations from the CBT-I arms than sleep hygiene.

CBT versus other interventions

Quality of life

Very low quality evidence from one study with a total of 36 participants showed a clinically important benefit of CBT over pain education at time points up to 3 months, but low quality evidence from one study with a total of 151 participants showed no clinically important difference between CBT and pain education. Low to very low quality evidence from 2 studies showed no clinically important difference between CBT and pain education at time points after 3 months.

Physical function

Low quality evidence from one study with a total of 151 participants showed no clinically important difference between CBT and pain education at time points up to 3 months. Very low quality evidence from one study with a total of 151 participants showed no clinically important difference between CBT and pain education at time points after 3 months. Very low quality evidence from one study with a total of 85 participants showed a clinically important benefit of behaviour therapy over CBT at time points after 3 months.

Psychological distress

Low to very low quality evidence from 2 studies with a total of 167 participants showed no clinically important difference between CBT and pain education at time points up to 3 months. Low to very low quality evidence from one study with a total of 151 participants showed no clinically important difference between CBT and pain education at time points after 3 months. Very low quality evidence from one study with a total of 48 participants showed no clinically important difference between CBT and psychotherapy at time points up to or after 3 months.

Pain interference

Very low quality evidence from one study with a total of 16 participants showed a clinically important benefit of CBT over pain education at time points up to 3 months.

Pain self-efficacy

Very low quality evidence from one study with a total of 36 participants showed no clinically important difference between CBT and pain education at time points up to or after 3 months.

Sleep

Very low quality evidence from one study with a total of 151 participants showed a clinically important benefit of CBT over pain education at time points up to 3 months, but very low quality evidence from one study with a total of 36 participants showed no clinically important difference between CBT and pain education. Very low quality evidence from one study with a total of 36 participants showed a clinically important benefit of pain education over CBT at time points up to 3 months, but low quality evidence from one study with a total of 151 participants showed no clinically important difference between CBT and pain education.

Use of healthcare services

Very low quality evidence from one study with a total of 151 participants showed no clinically important difference between CBT and pain education at time points up to or after 3 months. Very low quality evidence from one study with a total of 85 participants showed no clinically important difference between CBT and behaviour therapy at time points after 3 months.

Pain

Very low quality evidence from 2 studies with a total of 167 participants showed no clinically important difference between CBT and pain education at time points up to 3 months. Low quality evidence from one study with a total of 151 participants showed no clinically important difference between CBT and pain education at time points after 3 months. Very low quality evidence from one study with a total of 56 participants showed no clinically important difference between CBT and biofeedback at time points up to or after 3 months. Very low quality evidence from one study with a total of 48 participants showed no clinically important difference between CBT and psychotherapy at time points up to or after 3 months. Very low quality evidence from one study with a total of 85 participants showed no clinically important difference between CBT and behaviour therapy at time points after 3 months.

Discontinuation

Very low quality evidence from 2 studies with a total of 167 participants showed more discontinuations from the CBT arms than from pain education. Very low quality evidence from one study with a total of 58 participants showed more discontinuations from the biofeedback arm than from CBT. Very low quality evidence from one study with a total of 50 participants showed more discontinuations from the psychotherapy arm than from CBT. Very low quality evidence from one study with a total of 85 participants showed no clinically important difference between CBT and behaviour therapy.

Other interventions compared with each other

Quality of life

Very low quality evidence from one study with a total of 43 participants showed a clinically important benefit of ACT over relaxation on SF12 mental component at time points up to 3 months, but no clinically important difference between ACT and relaxation on the physical component. Very low quality evidence from one study with a total of 37 participants showed a clinically important benefit of ACT over relaxation on SF12 physical component at time points after 3 months, but no clinically important difference between ACT and relaxation on the mental component.

Psychological distress

Very low quality evidence from one study with a total of 43 participants showed no clinically important difference between ACT and relaxation at time points up to or after 3 months.

Pain interference

Very low quality evidence from one study with a total of 43 participants showed a clinically important benefit of ACT at time points up to 3 months, but no clinically important difference between ACT and relaxation at time points after 3 months.

Pain

Very low quality evidence from one study with a total of 57 participants showed a clinically important benefit of relaxation over biofeedback at time points up to 3 months. Very low quality evidence from one study with a total of 43 participants showed no clinically important difference between ACT and relaxation at time points up to or after 3 months.

Discontinuation

Moderate quality evidence from one study with a total of 49 participants showed more discontinuations from the relaxation arm than from ACT.

1.6.2 Health economic evidence statements

- One cost–utility analysis found that telephone-delivered cognitive behaviour therapy:
    - was cost effective compared to usual care for treating chronic widespread pain when using complete case analysis (ICER: £5,917 per QALY gained in complete case analysis).
    - was cost effective compared to usual care for treating chronic widespread pain when using multiple imputation analysis (ICER: £3,957 per QALY gained in complete case analysis).

  This analysis was assessed as partially applicable with potentially serious limitations.
- One cost–utility analysis found that group based cognitive behaviour therapy was dominant compared to usual care for treating fibromyalgia. This analysis was assessed as partially applicable with potentially serious limitations.
- One cost–utility analysis found that group based acceptance and commitment therapy was dominant compared to a wait list control for treating fibromyalgia. This analysis was assessed as partially applicable with potentially serious limitations.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The outcomes that matter most

The committee considered health-related quality of life, physical function, psychological distress, pain interference and pain self-efficacy to be critical outcomes for decision-making. Use of healthcare services, sleep, discontinuation and pain reduction were also considered to be important outcomes. The critical and important outcomes agreed by the committee were adapted by consensus from relevant core outcome sets registered under the Core Outcome Measures in Effectiveness Trials (COMET) Initiative. This included the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommendations.

Pain reduction was considered to be a critical outcome for some other reviews included in this guideline; however the committee considered that the aim of psychological-based interventions is not to reduce pain severity but the extent to which pain impacts on daily living and therefore it was only included as an important outcome in this protocol.

Evidence was identified for all critical and important outcomes.

1.7.1.2 The quality of the evidence

Evidence from 47 randomised controlled trials was identified for 18 different comparisons. The majority of the evidence identified compared psychological therapies with usual care and the comparison with the most evidence was CBT versus usual care. No evidence was identified for cognitive analytic therapy, solution-focussed therapy, problem-solving therapy or eye movement desensitisation reprocessing.

The majority of the evidence was of low to very low quality. The main reasons for downgrading were risk of bias, intervention indirectness and imprecision. There was a lack of blinding in the studies due to the nature of the interventions; this combined with the mostly subjective outcomes resulted in a high risk of performance bias. The majority of the studies had small sample sizes, which increased the uncertainty around the point estimates, and very few could be combined in a meta-analysis due to substantial differences in the interventions and outcome measures. Several of the studies used interventions which were considered to be indirect as they included elements of other types of psychological therapy. This was more common for CBT and biofeedback interventions, which often included elements of relaxation and pain education. The committee agreed that this is common in clinical practice and that the distinction between the different types of therapy is not always clear. However, for the purposes of this review, the intention was to identify the evidence for independent psychological therapies to inform which are effective. The inclusion of elements of other types of therapy limited the ability to determine that the effects were due to the intervention of interest.

The committee took into account the low to very low quality in their interpretation of the evidence, particularly when considering the small amount of evidence for comparisons of mindfulness, pain education, sleep hygiene, hypnosis and psychotherapy versus usual care and several of the head-to-head comparisons.

1.7.1.3 Benefits and harms

ACT

The majority of the evidence showed a benefit of ACT over usual care for quality of life and psychological distress at both the short and longer-term time points, although there was some uncertainty around the evidence for psychological distress. Evidence for pain interference was conflicting between a benefit of ACT and no difference at time points up to 3 months, but evidence from one small study showed a benefit of ACT after 3 months. Despite some uncertainty around the evidence, this was consistent with the committee's understanding of time taken to master new techniques through therapy. Evidence for sleep and pain reduction showed a benefit of ACT at both follow-up time points with uncertainty. There was no clinically important difference between ACT and usual care for physical function at either time point, but an increased discontinuation rate in those receiving ACT. The committee decided that there was enough evidence of benefit to make a recommendation to consider ACT, but that the evidence was too uncertain and not of high enough quality to justify a stronger recommendation to offer ACT. There was some suggestion from the evidence that ACT may confer additional benefits, particularly in improving psychological distress, compared with CBT. However, no evidence comparing ACT with CBT was identified to support a preference for either intervention.

CBT

CBT for pain was considered separately from both CBT for insomnia (CBT-I) and hybrid CBT for insomnia and pain (CBT-I/P) as these were considered to be distinct versions ofCBT. Where the report states 'CBT' this is CBT for pain.

Evidence for CBT versus usual care for quality of life, physical function and pain reduction was conflicting; with some outcomes showing a benefit of CBT and some showing no

difference at both the shorter and longer term follow up. Evidence showed no difference in psychological distress, pain self-efficacy or sleep outcomes. Evidence for pain interference at time points up to 3 months was conflicting between benefit of CBT and no difference, however the evidence of benefit for this outcome was of moderate quality, which the committee placed more weight on than the very low quality evidence of no difference. At time points after 3 months, 1 pain interference outcome measure (pain disability index) showed CBT to be less beneficial than usual care and 1 (multidimensional pain inventory – pain interference sub scale) showed no difference. The committee noted that the evidence of usual care producing better results than CBT was of very low quality and based on one small study. There was also some evidence of benefit for reducing use of some healthcare services (GP visits and psychological services), but no difference for others (cardiac specialists). The committee noted that this evidence was based on one study in a specific non-cardiac chest pain population and may not be generalisable to the wider chronic primary pain population due to the recurrent nature and the specific anxieties associated with chest pain.

Evidence for CBT-I and CBT-I/P for quality of life at time points up to 3 months was conflicting, with some outcomes showing benefit of the two types of CBT and others showing no difference, whereas at the longer-term follow up, evidence showed a benefit of CBT. There was no clinically important difference between CBT and usual care for psychological distress, pain interference or pain self-efficacy at either time point, or pain reduction at time points up to 3 months. Evidence for pain reduction after 3 months was conflicting, with some outcomes showing benefit and some showing no difference. Evidence showed a benefit of CBT for improving sleep problems/insomnia at both time points, but no difference in scales measuring sleep quality.

More people in both CBT and CBT-I discontinued from the intervention than in the usual care groups and this was also true of several of the other interventions in this review. The committee suggested that this may be because psychological therapy requires more active participation and is more demanding than usual care, however the small event numbers and imprecision were also noted giving lower confidence in this evidence.

The committee agreed that overall, there was evidence for benefit of CBT for improving quality of life, although there was some uncertainty around the evidence. The committee considered that the effectiveness of CBT may be dependent on the level of training of the person delivering it. Some studies did not report who delivered the CBT, and some CBT interventions were internet-based, therefore the evidence identified may underestimate a potential beneficial effect. With this in mind, as well as having no strong evidence of harm, the committee decided to make a recommendation to consider offering CBT.

The committee considered that although there was also a signal for benefit of CBT-I and CBT-I/P, particularly in terms of improving quality of life and sleep, the evidence base was smaller and health economic evidence was lacking. The committee considered that there was not enough evidence to make a recommendation for CBT-I or CBT-I/P given that it was not routinely provided for people with chronic primary pain, and that further research was needed. The committee also drew on their knowledge of epidemiological research which suggests a role of sleep in the aetiology of conditions such as fibromyalgia. Therefore the committee decided to make a research recommendation for CBT-I and CBT-I/P.

Sleep hygiene

The evidence showed a benefit of sleep hygiene compared with usual care at both short and longer term follow-up for quality of life, sleep, pain reduction and discontinuation. The committee discussed the general pattern across the body of evidence of psychological therapies that interventions addressing sleep appeared to be beneficial. However, it was considered that evidence for sleep hygiene was of low to very low quality and based on one small study. In addition, the comparison between CBT-I and sleep hygiene showed sleep hygiene to be no more effective than CBT-I overall. The committee also considered that

sleep hygiene is a component of CBT-I. Taking these factors in to account, the committee decided not to make a practice or research recommendation for sleep hygiene.

Relaxation

The evidence showed a benefit of relaxation techniques for quality of life, sleep and discontinuation at time points up to 3 months with some uncertainty, but no difference in physical function, psychological distress, pain interference or pain reduction. For pain self-efficacy, evidence was conflicting, with one outcome measure showing a benefit of relaxation and one showing no difference. When compared against attention control, evidence showed a benefit of relaxation for pain reduction and discontinuation, although there was some uncertainty around the evidence. It was noted that most of the outcomes were only reported at earlier time points (less than or equal to 3 months). The committee considered that there was insufficient evidence of benefit, as well as the lack of evidence at longer follow up points and decided not to make a recommendation for relaxation techniques as a stand-alone therapy for chronic primary pain. The committee agreed that studies with longer-term follow up are required in order to inform future recommendations and therefore decided to make a research recommendation. It was also noted that relaxation is a common component of other types of psychological therapies and may still be useful as such.

Biofeedback

The evidence for biofeedback compared with usual care for quality of life was conflicting, with some SF-36 subscales showing a benefit of biofeedback, some showing no difference and some showing biofeedback to be less effective than usual care in terms of improving quality of life. Evidence for physical function showed no difference at short term follow up and a benefit after 3 months. The majority of the evidence showed no difference in psychological distress at the early time point and evidence was conflicting at the later follow up, with no difference on the Symptoms Checklist-90-revised and worse results from biofeedback on the Beck Depression Inventory. Evidence showed no difference in pain reduction and an increased incidence of discontinuation for biofeedback compared with usual care. When biofeedback was compared with sham biofeedback, evidence showed a benefit of biofeedback for quality of life and physical function at time points up to 3 months, but no difference for psychological distress or sleep at either time point. Evidence for pain reduction at the earlier follow up showed a benefit of electromyogram (EMG) biofeedback and an increase of pain for neurofeedback. There was a benefit from neurofeedback at the later follow up. The committee noted that the benefits shown were based on low quality evidence from single small studies and there was very serious uncertainty around several of the outcomes. There was also variation in the type of biofeedback interventions used in the studies. Some interventions such as neurofeedback (based on the amygdala electrical fingerprint) were not considered to be specific for symptoms associated with chronic pain and not commonly used in practice. The committee considered the overall lack of evidence of benefit, as well as the evidence of harm. Although evidence of negative effects was based on single small studies and there was very serious uncertainty, the committee noted that it was shown across two of the critical outcomes as well as two of the important outcomes. The committee also noted that in clinical practice, biofeedback is often used in physiotherapy as a method of monitoring progress rather than as a treatment in itself. Therefore stopping the use of the intervention as a management strategy would not be likely to cause harm for people currently receiving it. Therefore, they decided to make a recommendation that biofeedback should not be offered as a stand-alone therapy.

Mindfulness

The evidence showed no difference in quality of life between mindfulness and usual care at time points up to 3 months and a benefit of mindfulness after 3 months, although with uncertainty. The majority of the evidence showed no difference in psychological distress at the earlier time point and a benefit after 3 months. There was a benefit of mindfulness for sleep at both time points, although there was some uncertainty around the evidence at the

later time point. No evidence was identified for any other outcomes other than discontinuation, which showed more discontinuations among the mindfulness group. The committee agreed that the delayed benefit observed in the evidence for quality of life and psychological distress was in line with their clinical experience and suggested that a possible reason is that it can take some time to understand this type of therapy and master the techniques. The committee considered that there was insufficient evidence to make a recommendation for mindfulness but that there was an indication of a benefit, particularly after 3 months, that warranted further investigation. The committee were aware that mindfulness is often used in clinical settings to help with symptoms associated with chronic pain, and that people are actively enquiring about it. Therefore the committee decided to make a research recommendation for mindfulness to inform future updates of the guideline.

Pain education

The evidence showed no clinically important difference between pain education and usual care in outcomes of quality of life, pain self-efficacy, sleep or pain before three months and no difference for quality of life at time points after 3 months. The evidence was low to very low quality and based on one small study. Evidence comparing pain education with attention control showed a benefit of pain education for reducing pain, but no clinically important difference in quality of life or psychological distress at time points before and after three months. There were more discontinuations in the pain education group. Evidence for this comparison was also based on a single study and was of low to very low quality. The committee considered the evidence to be insufficient to support a recommendation for or against pain education. Therefore no recommendation was made. The committee discussed that education should be part of good clinical practice and is not specific to chronic primary pain, which is addressed by the NICE patient experience guideline (CG138). It was agreed that education about the science of pain addresses a different element, and may be a useful enabler to people with chronic primary pain being able to effectively cope with and manage their pain, but may not be expected to improve patient reported outcomes as a standalone intervention. The committee therefore agreed not to include a research recommendation.

Hypnosis

The evidence, which was based on one small study, showed no clinically important difference in quality of life between hypnosis and usual care. Evidence showed no difference in psychological distress at the earlier time point and a mixture of no difference and a benefit of hypnosis with some uncertainty at the later time point. There was no difference in sleep at the earlier time point and a benefit of hypnosis to sleep and pain reduction after 3 months. There were fewer study discontinuations in the hypnosis group. The committee noted that the evidence was based on a study in which the intervention included an element of self-hypnosis, which they considered may explain the apparent delayed benefit, as this is a technique that requires practice. The committee considered that there was insufficient evidence of benefit, the lack of evidence for several critical outcomes, the low to very low quality of the evidence and decided not to make a recommendation for or against hypnosis. The committee decided not to make a research recommendation because the results of the evidence available were not promising enough to warrant further research as a priority and in their opinion hypnosis is not widely used to manage chronic primary pain in current clinical practice.

Psychotherapy

The evidence for psychotherapy was based on a single study of psychodynamic psychotherapy. Evidence for quality of life was conflicting, with one outcome measure showing a benefit with uncertainty and one showing no difference after three months. Evidence showed a benefit for physical function, psychological distress, pain interference and discontinuation at the time points after 3 months, although there was some uncertainty around the evidence for psychological distress, pain interference and discontinuation. The committee considered that although there was an overall benefit of psychodynamic

psychotherapy, the evidence was of low to very low quality with a lot of uncertainty. Therefore, it was decided that a recommendation for psychotherapy could not be made without further research. A research recommendation to develop the evidence for psychodynamic psychotherapy was therefore made.

Comparisons between psychological therapies

Evidence comparing CBT-I with sleep hygiene showed conflicting results for outcomes of quality of life and psychological distress. There was both a benefit of CBT-I and no difference between CBT-I and sleep hygiene. There was a benefit of CBT-I over sleep hygiene for pain self-efficacy, no difference in sleep at earlier time points and a benefit of sleep hygiene over CBT-I after three months. Evidence for pain reduction was also conflicting, showing both a benefit of CBT-I and a benefit of sleep hygiene. There was a benefit of sleep hygiene for discontinuation. Overall, the committee considered that the benefits of CBT-I to the critical outcomes outweighed the benefits of sleep hygiene to the important outcomes and this supported the decision to make a research recommendation for CBT for insomnia.

The evidence showed no difference between CBT and pain education for quality of life, physical function, psychological distress, use of healthcare services or pain reduction at either time point. Evidence showed a benefit of CBT for pain interference at the earlier time point only and a benefit of pain education for discontinuation. Evidence for sleep was conflicting. The committee considered that the small benefits of CBT over pain education were in line with the evidence comparing both interventions with usual care and in support of the recommendation to consider CBT. However, the committee also noted that the majority of outcomes were based on individual studies and the low to very low quality of the evidence.

None of the other head-to-head comparisons were considered to provide sufficient evidence to inform recommendations. The majority of the outcomes were of low to very low quality and based on single studies.

1.7.2 Cost effectiveness and resource use

Three economic evaluations were included for this question on psychological therapies. Three additional studies were also identified but excluded; one was based on the same trial as one of the included papers but with a shorter time horizon, and the other two had methodological limitations and more applicable evidence was included.

One UK study compared 6 months of telephone delivered CBT (TCBT) delivered over 10 sessions versus exercise therapy, treatment as usual, and a combination of the two active treatments, in people with fibromyalgia. The study was a within-trial analysis with follow up of 30 months (24 months post treatment), and used the EQ-5D questionnaire as a measure of quality of life. The study found that TCBT was cost-effective compared to treatment as usual (£5,917 per QALY gained in the complete case data analysis), and remained cost-effective when missing data was imputed. The study was rated as directly applicable because it was from the UK NHS perspective, and used the EQ-5D. It had potentially serious limitations because participation in the study was based on self-reported symptoms, and it is also a within-trial analysis only reflecting the outcomes of one study. There were large differences in the unadjusted baseline EQ-5D between the groups, with an interesting point being when comparing the unadjusted EQ-5D data at baseline and at 30 months, the treatment as usual group had a lower EQ-5D value at 30 months than at baseline whereas the TCBT group had the same EQ-5D value as at baseline. This highlights that an improvement in the intervention group can be for a variety of reasons when compared to a control group, such as that it stops symptoms getting worse, rather than improves them. The committee commented that the cost of the intervention reported in the paper was low. This is because fewer sessions than that described in the intervention detail were actually delivered, as supplementary data from the economic evaluation (McBeth 2012) based on the same trial but with a shorter time horizon, reported an average of 6.8 sessions, whereas the intervention is described as

having 10 sessions in total. A higher intervention cost is likely to make TCBT less cost effective, but this is unlikely to be to an extent that the ICER would exceed the £20,000 per additional QALY threshold.

Two Spanish economic evaluations were also included. Both were within trial analyses, in people with fibromyalgia, with one comparing group based CBT (9 sessions) to usual care, and the other comparing group based ACT to usual care (8 sessions). Both were by the same author and therefore had similar methodology and limitations. Follow up was 6 months, which was the length of the interventions. Both found that the interventions were dominant (less costly and more effective), and remained dominant in sensitivity analyses where missing data was imputed. They were found to be partially applicable because they were non-UK studies, and used the EQ-5D using the Spanish tariff. The studies were rated as having potentially serious limitations because the costs of medicines included VAT which would not be included in the UK. Also, the authors state the trial designs were not intended to look at the interventions on top of usual care, and the intervention groups were only allowed to continue taking minor medicines (occasionally minor analgesics but no pregabalin, gabapentin, opioids, or antidepressants were permitted), therefore costs may be underestimated in the intervention arms. Given that the interventions are dominant, additional costs may not impact the overall conclusion. Additionally, the studies are only reflecting the outcomes of single trials.

Unit costs were presented to the committee to illustrate the costs of psychological therapies. CBT is usually the most common type of psychological intervention, and NHS reference costs provide some unit costs associated with CBT as part of pain management programmes such as £123 for CBT as an outpatient (per session), or £118 as a day case. Examples of costs of CBT based on staff time are also provided in the PSSRU 2017, such as £88 per hour of direct contact for mindfulness-based cognitive therapy. Using the staff bands that a clinical psychologist could fall into, the cost per hour can range from £50 to £77 per hour depending on the band (bands 5 and 7 respectively). A group intervention is likely to be cheaper as the costs would be spread over more people (even if more staff are required). The committee agreed that who is providing the intervention is important and can have an impact on the treatment effect.

Some threshold calculations were undertaken to assess the likely cost effectiveness of the main types of interventions identified of CBT and ACT. Quality of life data was identified in the clinical review, and where it was possible to map outcomes onto the EQ-5D this was undertaken to be able to pool EQ-5D to generate an average QALY. ACT had only one study, and CBT had 4 studies that reported outcomes as utilities, or outcomes that could be transformed to utilities. Using these EQ-5D values (weighted average pooling for CBT) and assuming a timeframe based on the length of the interventions, the incremental QALY gain from the intervention versus control could be calculated. Rearranging the ICER equation to find the incremental cost needed to make the intervention cost effective at the £20,000 threshold showed that for both CBT and ACT, an incremental cost would have to be £1,000 or below per person to make ACT cost effective. Excluding the study with the highest QALY gain from the CBT calculations showed the maximum cost per person for CBT would be lower at £236. Whether these calculations mean that psychological interventions are cost effective are dependent on a number of factors that have not been taken into account in the threshold analysis, such as whether the effect from the intervention is maintained after the end of the intervention, whether group-based or individual treatment are similarly effective, and whether the intervention impacts other resource use like reducing use of healthcare services. Some outcomes in the clinical review for CBT did show a benefit from CBT in reducing use of healthcare services.

Overall, the committee agreed that the interventions that had shown evidence of benefit warranting a recommendation were ACT and CBT. These also had evidence of cost effectiveness.

The committee made a ‘do not use biofeedback’ recommendation as the evidence suggested a mixed picture with a general lack of benefit and sometimes negative effects of the intervention. There were also other interventions for which there was some signal of benefit but the limited evidence meant that these areas would benefit from further research.

Overall as the recommendations made are ‘consider’ recommendations, then any resource impact is dependent on uptake, and also how the intervention is delivered (group or individual for example). ACT and CBT are currently used in practice, however practice can vary across the country.

1.7.3 Other factors the committee took into account

The committee discussed the generalisability of the evidence to all people with chronic primary pain as the majority of the evidence identified was for women with fibromyalgia. Where heterogeneity was present in the effect estimates, this was not explained with subgroup analysis by type of chronic primary pain. The committee agreed that there was therefore no evidence that response differed according to type of pain and no reason not to consider this applicable to all chronic primary pain. The committee also discussed that distress, loss of quality of life and psychological comorbidity are common in people living with all types of chronic primary pain. The committee agreed that the main aim of psychological therapies is to improve quality of life and wellbeing rather than to treat the underlying condition and improve pain and response to treatment would be sufficiently similar to allow recommendations to be made across all chronic primary pain conditions.

Evidence was not available for people aged 16-17. The committee agreed that although young adults may require different considerations in the type of CBT or ACT, these would equally be tailored to the individual for adults as well and therefore separate recommednations were not required.

The committee discussed the common comorbidities in people with chronic primary pain such as depression, anxiety and post-traumatic stress disorder. It was highlighted that psychological therapies for these conditions should still be offered in accordance with existing NICE guidelines.

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Appendices

Appendix A: Review protocols

Review protocol for psychological therapy

ID	Field	Content
0.	PROSPERO registration number	Not registered.
1.	Review title	What is the clinical and cost effectiveness of psychological therapy for the management of chronic primary pain?
2.	Review question	What is the clinical and cost effectiveness of psychological therapy for the management of chronic primary pain?
3.	Objective	To determine the clinical and cost effectiveness of psychological therapy for the management of chronic primary pain.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • CINAHL, Current Nursing and Allied Health Literature. Searches will be restricted by: • English language • Human studies • Letters and comments are excluded.

		Other searches: • Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.
5.	Condition or domain being studied	Chronic pain in one or more anatomical regions that is characterized by significant emotional distress (anxiety, anger/frustration or depressed mood) and functional disability (interference in daily life activities and reduced participation in social roles). The diagnosis is appropriate independently of identified biological or psychological contributors unless another diagnosis would better account for the presenting symptoms.
6.	Population	Inclusion: People, aged 16 years and over, with chronic primary pain (whose pain management is not addressed by existing NICE guidance) (chronic widespread pain, complex regional pain syndrome, chronic visceral pain, chronic orofacial pain, chronic primary musculoskeletal pain other than orofacial) Exclusion: Those whose pain management is addressed by existing NICE guidance.
7.	Intervention/Exposure/Test	Interventions: • cognitive behavioural therapy (CBT) • cognitive analytic therapy (CAT) • behaviour therapy • solution-focused therapy • problem-solving therapy • acceptance and commitment therapy (ACT) • pain education • relaxation techniques • mindfulness • hypnosis • EMDR (eye movement desensitisation reprocessing) • psychotherapy (psychodynamic and psychoanalytic)

		• sleep management/hygiene • biofeedback
8.	Comparator/Reference standard/Confounding factors	Comparators: • each other • usual care • attention control
9.	Types of study to be included	Randomised controlled trials (RCTs) and systematic reviews of RCTs Cross-over RCTs will be considered if no non-cross-over RCT evidence is identified.
10.	Other exclusion criteria	Non-English language studies.
11.	Context	A clear understanding of the evidence for the effectiveness of chronic primary pain treatments: • improves the confidence of healthcare professionals in their conversations about pain, and • helps healthcare professionals and patients to have realistic expectations about outcomes of treatment.
12.	Primary outcomes (critical outcomes)	• Health related quality of life (including meaningful activity) • physical function (5 minute walk, sit to stand, Roland Morris Disability Questionnaire, Oswestry Disability Index, Canadian Occupational Performance Measure) • psychological distress (depression/anxiety) (preferably Hospital Anxiety and Depression Scale) • pain interference (brief pain inventory interference subscale) and pain self-efficacy (pain self-efficacy questionnaire). Outcomes will be extracted at the longest time point up to 3 months and at the longest time point after 3 months.
13.	Secondary outcomes (important outcomes)	• Use of healthcare services • sleep • discontinuation • pain reduction (any validated scale).

		Outcomes will be extracted at the longest time point up to 3 months and at the longest time point after 3 months.
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. EviBASE will be used for data extraction. Study investigators may be contacted for missing data where time and resources allow.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the Cochrane Risk of Bias (2.0) tool. Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
16.	Strategy for data synthesis	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome.
17.	Analysis of sub-groups	Proposed sensitivity / subgroup analysis to be explored where there is heterogeneity: • chronic widespread pain • complex regional pain syndrome • chronic visceral pain • chronic orofacial pain • chronic primary musculoskeletal pain • cognitive impairment • learning difficulties • first language not English

		• sensory impairment • homelessness • people aged16-25 years.	
18.	Type and method of review	☒	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	
20.	Country	England	
21.	Anticipated or actual start date	NA – not registered on PROSPERO	
22.	Anticipated completion date	19/08/2020	
23.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail Chronicpain@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre	

24.	Review team members	From the National Guideline Centre: Serena Carville, Guideline Lead Maria Smyth, Senior Systematic Reviewer Rebecca Boffa, Senior Systematic Reviewer Margaret Constanti, Senior Health Economist Joseph Runicles, Information Specialist Katie Broomfield, Project Manager
25.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10069
28.	Other registration details	NA
29.	Reference/URL for published protocol	NA
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:

		notifying registered stakeholders of publication publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
31.	Keywords	-
32.	Details of existing review of same topic by same authors	NA
33.	Additional information	-
34.	Details of final publication	www.nice.org.uk

Table 29: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002. Abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[334] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable).

	• OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2002 or later but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'. • Studies published before 2002 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[334]

For more information, please see the Methods Report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 20 May 2020	Exclusions Randomised controlled trials Systematic review studies
Embase (OVID)	1974 – 20 May 2020	Exclusions Randomised controlled trials Systematic review studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 5 of 12	None

Database	Dates searched	Search filter used
	CENTRAL to 2020 Issue 5 of 12	
PsycINFO (ProQuest)	Inception – 20 May 2020	Exclusions

Medline (Ovid) search terms

1.	Chronic pain/
2.	((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain).ti,ab.
3.	exp Complex Regional Pain Syndromes/
4.	(complex regional pain syndrome* or CRPS or causalgia).ti,ab.
5.	((reflex or sympathetic) adj2 dystroph*).ti,ab.
6.	fibromyalgia/
7.	(fibromyalgia* or fibrositis or myofascial pain syndrome).ti,ab.
8.	vulvodynia/
9.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis).ti,ab.
10.	interstitial cystitis/
11.	(interstitial adj2 cystitis).ti,ab.
12.	algodystrophy/
13.	(algodystroph* or sudek or sudeck*).ti,ab.
14.	exp myofascial pain syndromes/
15.	cystitis, interstitial/
16.	(loin pain adj (haematuria or hematuria) adj syndrome*).ti,ab.
17.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS).ti,ab.
18.	((pelvic or pelvis) adj pain syndrome*).ti,ab.
19.	((non-cardiac or noncardiac) adj3 chest adj3 pain).ti,ab.
20.	(temporomandibular adj3 joint adj3 pain).ti,ab.
21.	((prostate or vulv* or bladder or perineal) adj3 pain).ti,ab.
22.	(functional pain syndrome* or non-cancer pain or noncancer pain).ti,ab.
23.	((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)).ti,ab.
24.	or/1-23
25.	letter/
26.	editorial/
27.	news/
28.	exp historical article/
29.	Anecdotes as Topic/
30.	comment/
31.	case report/
32.	(letter or comment*).ti.
33.	or/25-32
34.	randomized controlled trial/ or random*.ti,ab.
35.	33 not 34
36.	animals/ not humans/
37.	exp Animals, Laboratory/
38.	exp Animal Experimentation/
39.	exp Models, Animal/

40.	exp Rodentia/
41.	(rat or rats or mouse or mice).ti.
42.	or/35-41
43.	24 not 42
44.	limit 43 to English language
45.	psychotherapy/ or behavior therapy/ or biofeedback, psychology/ or exp relaxation therapy/ or mind-body therapies/ or conditioning, operant/ or exp cognitive therapy/ or relaxation/ or reality therapy/ or hypnosis/
46.	(meditat* or psychotherap* or psycho dynamic or psycho analytic or group therapy or self-regulation training or coping skill or pain-related thought or "mind and body relaxation technique*" or mind-body relaxation technique* or operant conditioning or pain education or hypnosis).ti,ab.
47.	(biofeedback or mindfulness or "eye movement disensitisation and reprocessing").ti,ab.
48.	(CBASP or CBT or SFT or BSFT or ACT or EMDR).ti,ab.
49.	(acceptance based or commitment therapy or exposure therapy or implosive therapy or "acceptance and commitment" or psycho-education or psychoeducation or occupational therapy).ti,ab.
50.	((behavio#r* or cognitive or relax* or psycho* or respondent or compassion or solution) adj3 (technique* or therap* or treatment* or training or rehabilitat* or strateg*)).ti,ab.
51.	Patient Education as Topic/ or health education/ or information services/ or teaching/ or pamphlets/ or exp teaching materials/
52.	((professional or physician or doctor) adj2 patient adj2 (communication or interact* or relation*)).ti,ab.
53.	((educat* or information or advice) adj3 (patient* or consumer* or health*)).ti,ab.
54.	exp Sleep Wake Disorders/ or sleep hygiene/
55.	insomnia.ti,ab.
56.	(sleep adj3 (manag* or program* or regulat* or therap* or disorder* or deprivation or hygiene)).ti,ab.
57.	or/45-56
58.	randomized controlled trial.pt.
59.	controlled clinical trial.pt.
60.	randomi#ed.ti,ab.
61.	placebo.ab.
62.	randomly.ti,ab.
63.	Clinical Trials as topic.sh.
64.	trial.ti.
65.	or/58-64
66.	Meta-Analysis/
67.	exp Meta-Analysis as Topic/
68.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
69.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
70.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
71.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
72.	(search* adj4 literature).ab.
73.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
74.	cochrane.jw.
75.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.

76.	or/66-75
77.	44 and 57 and (65 or 76)

Embase (Ovid) search terms

1.	Chronic pain/
2.	((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain).ti,ab.
3.	exp Complex regional pain syndrome/
4.	(complex regional pain syndrome* or CRPS or causalgia).ti,ab.
5.	((reflex or sympathetic) adj2 dystroph*).ti,ab.
6.	fibromyalgia/
7.	(fibromyalgia* or fibrositis or myofascial pain syndrome).ti,ab.
8.	vulvodynia/
9.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis).ti,ab.
10.	interstitial cystitis/
11.	(interstitial adj2 cystitis).ti,ab.
12.	algodystrophy/
13.	(algodystroph* or sudek or sudeck*).ti,ab.
14.	myofascial pain/
15.	noncardiac chest pain/
16.	cystalgia/
17.	Pelvis pain syndrome/
18.	(loin pain adj (haematuria or hematuria) adj syndrome*).ti,ab.
19.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS).ti,ab.
20.	((pelvic or pelvis) adj pain syndrome*).ti,ab.
21.	((non-cardiac or noncardiac) adj3 chest adj3 pain).ti,ab.
22.	(temporomandibular adj3 joint adj3 pain).ti,ab.
23.	((prostate or vulv* or bladder or perineal) adj3 pain).ti,ab.
24.	(functional pain syndrome* or non-cancer pain or noncancer pain).ti,ab.
25.	((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)).ti,ab.
26.	or/1-25
27.	letter.pt. or letter/
28.	note.pt.
29.	editorial.pt.
30.	case report/ or case study/
31.	(letter or comment*).ti.
32.	or/27-31
33.	randomized controlled trial/ or random*.ti,ab.
34.	32 not 33
35.	animal/ not human/
36.	nonhuman/
37.	exp Animal Experiment/
38.	exp Experimental Animal/
39.	animal model/
40.	exp Rodent/
41.	(rat or rats or mouse or mice).ti.

42.	or/34-41
43.	26 not 42
44.	limit 43 to English language
45.	exp psychotherapy/
46.	alternative medicine/
47.	instrumental conditioning/
48.	(meditat* or psychotherap* or psycho dynamic or psycho analytic or group therapy or self-regulation training or coping skill or pain-related thought or "mind and body relaxation technique*" or mind-body relaxation technique* or operant conditioning or pain education or hypnosis).ti,ab.
49.	(biofeedback or mindfulness or "eye movement disensitisation and reprocessing").ti,ab.
50.	(CBASP or CBT or SFT or BSFT or ACT or EMDR).ti,ab.
51.	(acceptance based or commitment therapy or exposure therapy or implosive therapy or "acceptance and commitment" or psycho-education or psychoeducation or occupational therapy).ti,ab.
52.	((behavio#r* or cognitive or relax* or psycho* or respondent or compassion or solution) adj3 (technique* or therap* or treatment* or training or rehabilitat* or strateg*)).ti,ab.
53.	patient education/
54.	health education/
55.	information service/
56.	teaching/
57.	publication/
58.	((professional or physician or doctor) adj2 patient adj2 (communication or interact* or relation*)).ti,ab.
59.	((educat* or information or advice) adj3 (patient* or consumer* or health*)).ti,ab.
60.	sleep disorder/ or insomnia/
61.	sleep hygiene/
62.	insomnia.ti,ab.
63.	(sleep adj3 (manag* or program* or regulat* or therap* or deprivation or disorder* or hygiene)).ti,ab.
64.	or/45-63
65.	random*.ti,ab.
66.	factorial*.ti,ab.
67.	(crossover* or cross over*).ti,ab.
68.	((doubl* or singl*) adj blind*).ti,ab.
69.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
70.	crossover procedure/
71.	single blind procedure/
72.	randomized controlled trial/
73.	double blind procedure/
74.	or/65-73
75.	systematic review/
76.	meta-analysis/
77.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
78.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
79.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
80.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.

81.	(search* adj4 literature).ab.
82.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
83.	cochrane.jw.
84.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
85.	or/75-84
86.	44 and 64 and (74 or 85)

PsycINFO (ProQuest) search terms

1.	((su.exact("Chronic Pain") OR ti,ab((chronic OR persist* OR idiopathic OR atypical OR a-typical) NEAR/3 pain) OR SU.EXACT.EXPLODE("Complex Regional Pain Syndrome (Type I)") OR ti,ab(complex regional pain syndrome* OR CRPS OR causalgia) OR ti,ab((reflex OR sympathetic) NEAR/2 dystroph*) OR su.exact("fibromyalgia") OR ti,ab(fibromyalgia OR fibrositis OR myofascial pain syndrome) OR su.exact("vulvodynia") OR ti,ab(vulvodynia OR vestibulodynia OR dyspareunia OR vulvar vestibulitis OR vulvitis) OR su.exact("interstitial cystitis") OR ti,ab(interstitial NEAR/2 cystitis) OR ti,ab(algodystop* OR sudek OR sudeck) OR SU.EXACT.EXPLODE("Myofascial Pain") OR ti,ab(loin pain NEAR/2 (haematuria OR hematuria) NEAR/2 syndrome*) OR ti,ab(lphs OR prostatodynia OR cpps OR atypic* odontalgia OR a-tupic* odontalgia OR burning mouth syndrom* OR phantom tooth pain OR neuropathic orofacial pain OR myofascial pain OR mps) OR ti,ab((pelvic OR pelvis) NEAR/2 pain syndrome*) OR ti,ab((non-cardiac OR noncardiac) NEAR/2 chest pain) OR ti,ab(temporomandibular NEAR/2 joint NEAR/2 pain) OR ti,ab((prostate OR vulv* OR bladder OR perineal) NEAR/2 pain) OR ti,ab(functional pain syndrome* OR non-cancer pain OR noncancer pain) OR ti,ab((pelvic OR pelvis OR abdominal) NEAR/2 pain NEAR/2 (unknown OR un-known OR idiopathic OR atypic* OR a-typic*))) NOT (su.exact.explode("rodents") OR su.exact.explode("mice") OR (su.exact("animals") NOT (su.exact("human males") OR su.exact("human females"))) OR ti(rat OR rats OR mouse OR mice))) AND (su.exact.explode("psychotherapy") OR su.exact.explode("behavior therapy") OR su.exact("cognitive therapy") OR su.exact("relaxation therapy") OR su.exact("operant conditioning") OR su.exact("hypnosis") OR su.exact("reality therapy") OR su.exact("biofeedback") OR su.exact(" psycholy, biofeedback") OR su.exact("biofeedback, psychology") OR ti,ab(meditat* OR psychotherap* OR psycho dynamic OR psycho analytic OR group therapy OR self-regulation training OR coping skill OR pain-related thought OR "mind and body relaxation technique*" OR mind-body relaxation technique* OR operant conditioning OR pain education OR hypnosis) OR ti,ab(biofeedback OR mindfulness OR "eye movement disensitisation and reprocessing") OR ti,ab(CBASP OR CBT OR SFT OR BSFT OR ACT OR EMDR) OR ti,ab(acceptance based OR commitment therapy OR exposure therapy OR implosive therapy OR "acceptance and commitment" OR psycho-education OR psychoeducation OR occupational therapy) OR ti,ab((behavior* OR beahviour* OR cognitive OR relax* OR psycho* OR respondent OR compassion OR solution) NEAR/2 (technique* OR therap* OR treatment* OR training OR rehabilitat* OR strateg*)) OR su.exact("patient education as topic") OR su.exact("health education") OR su.exact("information services") OR su.exact("teaching materials") OR su.exact("pamphlets") OR su.exact("sleep wake disorders") OR su.exact("sleep hygiene") OR su.exact("sleep deprivation") OR su.exact("sleep disorders") OR ti,ab((professional OR physician OR doctor) NEAR/2 patient NEAR/2 (communication OR interact* OR relation*)) OR ti,ab((educat* OR information OR advice) NEAR/2 (patient* OR consumer* OR health*)) OR ti,ab(insomnia) OR ti,ab(sleep NEAR/2 (manag* OR program* OR regulat* OR therap* OR disorder* OR deprivation OR hygiene)))

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Chronic Pain] explode all trees
#2.	((chronic or persist* or idiopathic or atypical or a-typical) near/4 pain):ti,ab
#3.	MeSH descriptor: [Complex Regional Pain Syndromes] explode all trees
#4.	(complex regional pain syndrome* or CRPS or causalgia):ti,ab

#5.	((reflex or sympathetic) near/2 dystroph*):ti,ab
#6.	MeSH descriptor: [Fibromyalgia] explode all trees
#7.	(fibromyalgia* or fibrositis or myofascial pain syndrome):ti,ab
#8.	MeSH descriptor: [Vulvodynia] explode all trees
#9.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis):ti,ab
#10.	MeSH descriptor: [Cystitis, Interstitial] explode all trees
#11.	(interstitial near/2 cystitis):ti,ab
#12.	MeSH descriptor: [Reflex Sympathetic Dystrophy] explode all trees
#13.	(algodystroph* or sudek or sudeck*):ti,ab
#14.	MeSH descriptor: [Myofascial Pain Syndromes] explode all trees
#15.	(loin pain near (haematuria or hematuria) near syndrome*):ti,ab
#16.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS):ti,ab
#17.	((pelvic or pelvis) near pain syndrome*):ti,ab
#18.	((non-cardiac or noncardiac) near/3 chest near/3 pain):ti,ab
#19.	(temporomandibular near/3 joint near/3 pain):ti,ab
#20.	((prostate or vulv* or bladder or perineal) near/3 pain):ti,ab
#21.	(functional pain syndrome* or non-cancer pain or noncancer pain):ti,ab
#22.	((pelvic or pelvis or abdominal) near/3 pain near/3 (unknown or un-known or idiopathic or atypic* or a-typic*)):ti,ab
#23.	(or #1-#22)
#24.	MeSH descriptor: [Psychotherapy] explode all trees
#25.	MeSH descriptor: [Behavior Therapy] explode all trees
#26.	MeSH descriptor: [Cognitive Therapy] explode all trees
#27.	MeSH descriptor: [Biofeedback, Psychology] explode all trees
#28.	MeSH descriptor: [Relaxation Therapy] explode all trees
#29.	MeSH descriptor: [Reality Therapy] explode all trees
#30.	MeSH descriptor: [Hypnosis] explode all trees
#31.	MeSH descriptor: [Conditioning, Operant] explode all trees
#32.	MeSH descriptor: [Mind-Body Therapies] explode all trees
#33.	(meditat* or psychotherap* or psycho dynamic or psycho analytic or group therapy or self-regulation training or coping skill or pain-related thought or "mind and body relaxation technique*" or mind-body relaxation technique* or operant conditioning or pain education or hypnosis):ti,ab
#34.	(biofeedback or mindfulness or "eye movement disensitisation and reprocessing"):ti,ab
#35.	(CBASP or CBT or SFT or BSFT or ACT or EMDR):ti,ab
#36.	(acceptance based or commitment therapy or exposure therapy or implosive therapy or "acceptance and commitment" or psycho-education or psychoeducation or occupational therapy):ti,ab
#37.	((behavio?r* or cognitive or relax* or psycho* or respondent or compassion or solution) near/3 (technique* or therap* or treatment* or training or rehabilitat* or strateg*)):ti,ab
#38.	MeSH descriptor: [Patient Education as Topic] explode all trees
#39.	MeSH descriptor: [Health Education] explode all trees
#40.	MeSH descriptor: [Information Services] explode all trees
#41.	MeSH descriptor: [Teaching] explode all trees
#42.	MeSH descriptor: [Teaching Materials] explode all trees
#43.	MeSH descriptor: [Pamphlets] explode all trees

#44.	((professional or physician or doctor) near/2 patient near/2 (communication or interact* or relation*)):ti,ab
#45.	((educat* or information or advice) near/3 (patient* or consumer* or health*)):ti,ab
#46.	MeSH descriptor: [Sleep Wake Disorders] explode all trees
#47.	MeSH descriptor: [Sleep Hygiene] explode all trees
#48.	insomnia:ti,ab
#49.	(sleep near/3 (manag* or program* or regulat* or therap* or disorder* or deprivation or hygiene)):ti,ab
#50.	(or #24-#49)
#51.	#23 and #50

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a Chronic Pain population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics and economic modelling.

Table 30: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 20 May 2020	Exclusions Health economics studies Health economics modelling studies
Embase	2014 – 20 May 2020	Exclusions Health economics studies Health economics modelling studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 20 May 2020 NHSEED - Inception to March 2015	None

Medline search terms

1.	chronic pain/ or pain, intractable/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain).ti,ab.
4.	exp Complex Regional Pain Syndromes/
5.	(complex regional pain syndrome* or CRPS or causalgia).ti,ab.
6.	fibromyalgia/
7.	((reflex or sympathetic) adj2 dystroph*).ti,ab.
8.	vulvodynia/
9.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis).ti,ab.

10.	interstitial cystitis/
11.	(interstitial adj2 cystitis).ti,ab.
12.	algodystrophy/
13.	(algodystroph* or sudek or sudeck*).ti,ab.
14.	exp myofascial pain syndromes/
15.	cystitis, interstitial/
16.	(loin pain adj (haematuria or hematuria) adj syndrome*).ti,ab.
17.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS).ti,ab.
18.	((pelvic or pelvis) adj pain syndrome*).ti,ab.
19.	((non-cardiac or noncardiac) adj3 chest adj3 pain).ti,ab.
20.	(temporomandibular adj3 joint adj3 pain).ti,ab.
21.	((prostate or vulv* or bladder or perineal) adj3 pain).ti,ab.
22.	(functional pain syndrome* or non-cancer pain or noncancer pain).ti,ab.
23.	((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)).ti,ab.
24.	(fibromyalgia* or fibrositis or myofascial pain syndrome).ti,ab.
25.	or/1-24
26.	letter/
27.	editorial/
28.	news/
29.	exp historical article/
30.	Anecdotes as Topic/
31.	comment/
32.	case report/
33.	(letter or comment*).ti.
34.	or/26-33
35.	randomized controlled trial/ or random*.ti,ab.
36.	34 not 35
37.	animals/ not humans/
38.	exp Animals, Laboratory/
39.	exp Animal Experimentation/
40.	exp Models, Animal/
41.	exp Rodentia/
42.	(rat or rats or mouse or mice).ti.
43.	or/36-42
44.	25 not 43
45.	Economics/
46.	Value of life/
47.	exp "Costs and Cost Analysis"/
48.	exp Economics, Hospital/
49.	exp Economics, Medical/
50.	Economics, Nursing/
51.	Economics, Pharmaceutical/
52.	exp "Fees and Charges"/
53.	exp Budgets/
54.	budget*.ti,ab.

55.	cost*.ti.
56.	(economic* or pharmaco?economic*).ti.
57.	(price* or pricing*).ti,ab.
58.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
59.	(financ* or fee or fees).ti,ab.
60.	(value adj2 (money or monetary)).ti,ab.
61.	or/45-60
62.	exp models, economic/
63.	*Models, Theoretical/
64.	*Models, Organizational/
65.	markov chains/
66.	monte carlo method/
67.	exp Decision Theory/
68.	(markov* or monte carlo).ti,ab.
69.	econom* model*.ti,ab.
70.	(decision* adj2 (tree* or analy* or model*)).ti,ab.
71.	or/62-70
72.	44 and (61 or 71)

Embase (Ovid) search terms

1.	chronic pain/ or pain, intractable/
2.	((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*).ti,ab.
3.	((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain).ti,ab.
4.	exp Complex regional pain syndrome/
5.	(complex regional pain syndrome* or CRPS or causalgia).ti,ab.
6.	((reflex or sympathetic) adj2 dystroph*).ti,ab.
7.	fibromyalgia/
8.	(fibromyalgia* or fibrositis or myofascial pain syndrome).ti,ab.
9.	vulvodynia/
10.	(vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis).ti,ab.
11.	interstitial cystitis/
12.	(interstitial adj2 cystitis).ti,ab.
13.	algodystrophy/
14.	(algodystroph* or sudek or sudeck*).ti,ab.
15.	myofascial pain/
16.	noncardiac chest pain/
17.	cystalgia/
18.	Pelvis pain syndrome/
19.	(loin pain adj (haematuria or hematuria) adj syndrome*).ti,ab.
20.	(LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS).ti,ab.
21.	((pelvic or pelvis) adj pain syndrome*).ti,ab.
22.	((non-cardiac or noncardiac) adj3 chest adj3 pain).ti,ab.
23.	(temporomandibular adj3 joint adj3 pain).ti,ab.
24.	((prostate or vulv* or bladder or perineal) adj3 pain).ti,ab.

25.	(functional pain syndrome* or non-cancer pain or noncancer pain).ti,ab.
26.	((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)).ti,ab.
27.	or/1-26
28.	letter.pt. or letter/
29.	note.pt.
30.	editorial.pt.
31.	case report/ or case study/
32.	(letter or comment*).ti.
33.	or/28-32
34.	randomized controlled trial/ or random*.ti,ab.
35.	33 not 34
36.	animal/ not human/
37.	nonhuman/
38.	exp Animal Experiment/
39.	exp Experimental Animal/
40.	animal model/
41.	exp Rodent/
42.	(rat or rats or mouse or mice).ti.
43.	or/35-42
44.	27 not 43
45.	health economics/
46.	exp economic evaluation/
47.	exp health care cost/
48.	exp fee/
49.	budget/
50.	funding/
51.	budget*.ti,ab.
52.	cost*.ti.
53.	(economic* or pharmaco?economic*).ti.
54.	(price* or pricing*).ti,ab.
55.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
56.	(financ* or fee or fees).ti,ab.
57.	(value adj2 (money or monetary)).ti,ab.
58.	or/45-57
59.	statistical model/
60.	exp economic aspect/
61.	59 and 60
62.	*theoretical model/
63.	*nonbiological model/
64.	stochastic model/
65.	decision theory/
66.	decision tree/
67.	monte carlo method/
68.	(markov* or monte carlo).ti,ab.
69.	econom* model*.ti,ab.
70.	(decision* adj2 (tree* or analy* or model*)).ti,ab.

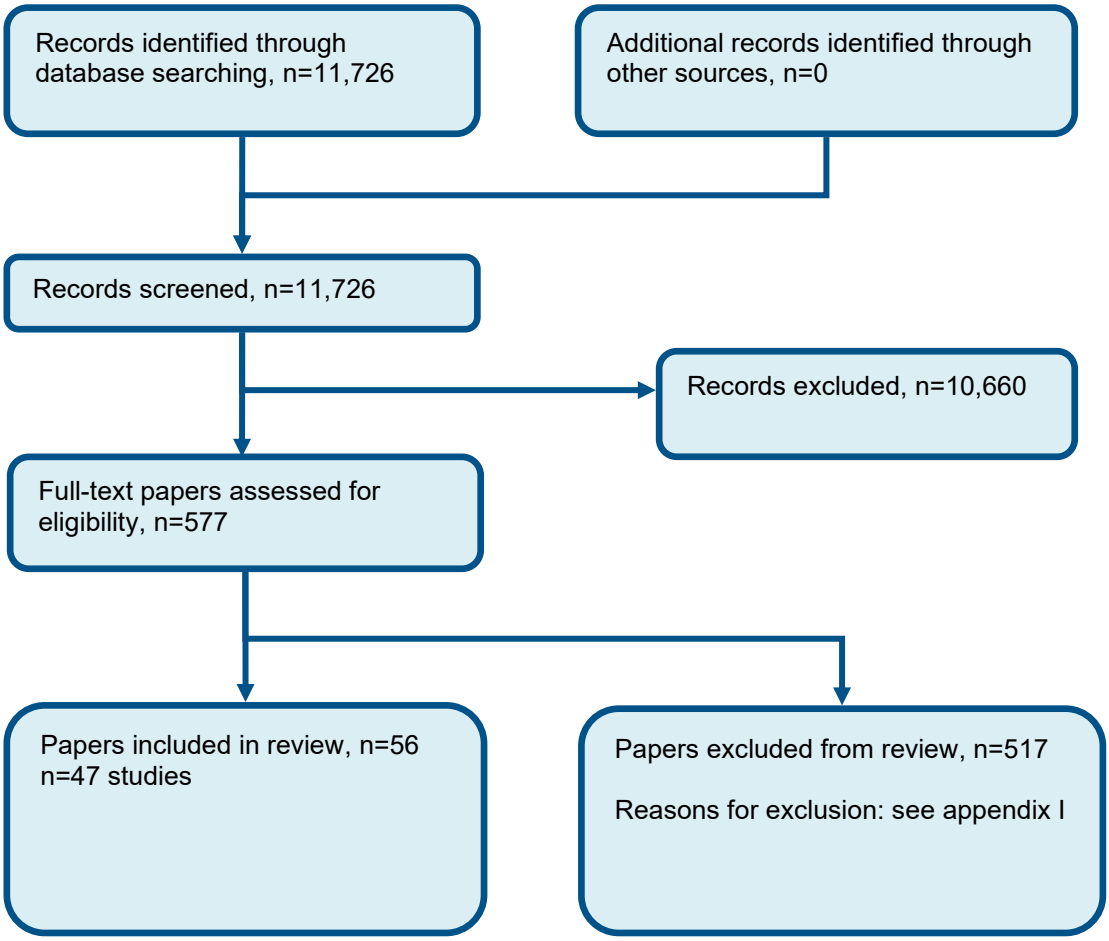
71.	or/61-70
72.	44 and (58 or 71)

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Chronic Pain EXPLODE ALL TREES
#2.	(((persist* or intract* or chronic or longstanding or long standing or longterm or long term or refractory or prolong* or long last* or sustain* or linger* or syndrome*) adj3 pain*))
#3.	(((chronic or persist* or idiopathic or atypical or a-typical) adj4 pain))
#4.	MeSH DESCRIPTOR Complex Regional Pain Syndromes EXPLODE ALL TREES
#5.	((complex regional pain syndrome* or CRPS or causalgia))
#6.	MeSH DESCRIPTOR Fibromyalgia EXPLODE ALL TREES
#7.	(((reflex or sympathetic) adj2 dystroph*))
#8.	MeSH DESCRIPTOR Vulvodynia EXPLODE ALL TREES
#9.	((vulvodynia or vestibulodynia or dyspareunia or vulvar vestibulitis or vulvitis))
#10.	MeSH DESCRIPTOR Cystitis, Interstitial EXPLODE ALL TREES
#11.	((interstitial adj2 cystitis))
#12.	MeSH DESCRIPTOR Reflex Sympathetic Dystrophy EXPLODE ALL TREES
#13.	((algodystroph* or sudek or sudeck*))
#14.	MeSH DESCRIPTOR Myofascial Pain Syndromes EXPLODE ALL TREES
#15.	((loin pain adj (haematuria or hematuria) adj syndrome*))
#16.	((LPHS or prostatodynia or CPPS or atypic* odontalgia or a-typic* odontalgia or burning mouth syndrome* or phantom tooth pain or neuropathic orofacial pain or "myofascial pain" or MPS))
#17.	(((pelvic or pelvis) adj pain syndrome*))
#18.	(((non-cardiac or noncardiac) adj3 chest adj3 pain))
#19.	((temporomandibular adj3 joint adj3 pain))
#20.	(((prostate or vulv* or bladder or perineal) adj3 pain))
#21.	((functional pain syndrome* or non-cancer pain or noncancer pain))
#22.	(((pelvic or pelvis or abdominal) adj3 pain adj3 (unknown or un-known or idiopathic or atypic* or a-typic*)))
#23.	((fibromyalgia* or fibrositis or myofascial pain syndrome))
#24.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of Psychological therapy for chronic primary pain



Appendix D: Clinical evidence tables

Study (subsidiary papers)	Alda 2011[6] (Garcia-campayo 2009[170], Luciano 2014[289])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=169)
Countries and setting	Conducted in Spain; Setting: health centre
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 weeks + 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: fulfilled the criteria for FM according to the American College of Rheumatology
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18 to 65 years of age, able to understand and read Spanish, fulfilled the criteria for FM according to the American College of Rheumatology, had undergone no psychological treatment during the preceding two years, were receiving no pharmacological treatment at that time or were willing to discontinue it for two weeks before the start of the study, and had signed an informed consent statement
Exclusion criteria	severe axis I psychiatric disorders (dementia, schizophrenia, paranoid disorder and alcohol and/or drug abuse); patients with severe axis II psychiatric disorders or other medical disorders that, from the clinician's point of view prevented the patient from following the treatment protocol; women who were pregnant or nursing; and those who declined to participate
Recruitment/selection of patients	patients recruited by doctors working in 41 primary care centres
Age, gender and ethnicity	Age - Mean (SD): CBT 46.35 (6.71), usual care 47.04 (6.53). Gender (M:F): /159. Ethnicity: 100% European
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Extra comments	NA
Indirectness of population	No indirectness: NA

Study (subsidiary papers)	Alda 2011[6] (Garcia-campayo 2009[170], Luciano 2014[289])
Interventions	(n=57) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 10 x 90 minute group (max. 8 patients) sessions delivered by trained therapists and consisting of 2 major components: cognitive restructuring, which focuses on reducing pain-specific dysfunctional cognitions and coping, which focuses on teaching cognitive and behavioural coping strategies. Sessions included e.g. evaluation of automated thoughts, expressive writing, coping with ruminations, obsessions and worrying. Duration 10-12 weeks . Concurrent medication/care: occasionally allowed to use minor analgesics during the study, but not pregabalin, gabapentin, opioids or antidepressants. Indirectness: No indirectness; Indirectness comment: NA (n=56) Intervention 2: Usual care. Standard care offered by general practitioners at their health centres. To improve this groups' treatment, the doctors received the 'Guide for the Treatment of Fibromyalgia in Primary Care', which is edited and distributed by the Aragonese Health Service. Treatment as usual' implies that doctors selected a pharmacological treatment as well as the frequency of patient visits that they considered adequate. However, the treatment recommended in the guide matched that of the recommended pharmacological intervention arm of the trial. Duration study duration. Concurrent medication/care: NA. Indirectness: Serious indirectness; Indirectness comment: doctors received guide
Funding	Academic or government funding (Carlos III Health Institute of the Spanish Ministry of Health and Consumption)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: EuroQoL VAS at Post treatment (9 weeks); Group 1: mean 60.45 (SD 16.63); n=57, Group 2: mean 53.49 (SD 14.4); n=56; EQ-5D VAS 0-100 Top=High is good outcome; Comments: Baseline values: CBT 44.55 (16.47), usual care 43.87 (14.5)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 1, Reason: lack of efficacy; Group 2 Number missing: 3, Reason: adverse events (2), moved away (1)
- Actual outcome: EuroQoL VAS at 6 months follow up; Group 1: mean 58.39 (SD 16.27); n=57, Group 2: mean 52.26 (SD 14.03); n=56; EQ-5D VAS 0-100 Top=High is good outcome; Comments: Baseline values: CBT 44.55 (16.47), usual care 43.87 (14.5)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: lack of efficacy (1), patient decision (4), lost to follow up (3); Group 2 Number missing: 10, Reason: adverse events (2), moved away (1), lack of efficacy (3), patient decision (2), loss to follow up (2)
- Actual outcome: EQ-5D utility score at 6 months follow up; Group 1: mean 0.61 (SD 0.25); n=53, Group 2: mean 0.54 (SD 0.28); n=49; EQ-5D utility score 0-1 Top=High is good outcome; Comments: Baseline values: CBT 0.4 (0.26), usual care 0.38 (0.27)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Study (subsidiary papers)	Alda 2011[6] (Garcia-campayo 2009[170], Luciano 2014[289])

Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 4, Reason: unclear; Group 2 Number missing: 7, Reason: unclear

Protocol outcome 2: Psychological distress
- Actual outcome: Hamilton Rating Scale for Depression at Post treatment (9 weeks); Group 1: mean 7.78 (SD 2.46); n=57, Group 2: mean 8.17 (SD 2.25); n=56; Hamilton Rating Scale for Depression 0-50 Top=High is poor outcome; Comments: Baseline values: CBT 14.47, usual care 14.09 (4.64)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 1, Reason: lack of efficacy; Group 2 Number missing: 3, Reason: adverse events (2), moved away (1)
- Actual outcome: Hamilton Rating Scale for Depression at 6 months follow up; Group 1: mean 7.91 (SD 2.5); n=57, Group 2: mean 8.57 (SD 2.47); n=56; Hamilton Rating Scale for Depression 0-50 Top=High is poor outcome; Comments: Baseline values: CBT 14.47, usual care 14.09 (4.64)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: lack of efficacy (1), patient decision (4), lost to follow up (3); Group 2 Number missing: 10, Reason: adverse events (2), moved away (1), lack of efficacy (3), patient decision (2), loss to follow up (2)
- Actual outcome: Hamilton Anxiety Rating Scale at Post treatment (9 weeks); Group 1: mean 7.09 (SD 2.96); n=57, Group 2: mean 7.4 (SD 2.18); n=56; Hamilton Anxiety Rating Scale 0-56 Top=High is poor outcome; Comments: Baseline values: CBT 10.84 (4.27), 9.5 (2.98)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 1, Reason: lack of efficacy; Group 2 Number missing: 3, Reason: adverse events (2), moved away (1)
- Actual outcome: Hamilton Anxiety Rating Scale at 6 months follow up ; Group 1: mean 7.25 (SD 3.02); n=57, Group 2: mean 7.58 (SD 2.07); n=56; Hamilton Anxiety Rating Scale 0-56 Top=High is poor outcome; Comments: Baseline values: CBT 10.84 (4.27), 9.5 (2.98)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: lack of efficacy (1), patient decision (4), lost to follow up (3); Group 2 Number missing: 10, Reason: adverse events (2), moved away (1), lack of efficacy (3), patient decision (2), loss to follow up (2)

Protocol outcome 3: Discontinuation
- Actual outcome: Study withdrawal at Post treatment (9 weeks); Group 1: 1/57, Group 2: 3/56; Comments: CBT: withdrawal due to lack of efficacy (n=1), usual care: withdrawal due to adverse events (n=2), moved away (n=1)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain reduction
- Actual outcome: Visual analogue scale at Post treatment (9 weeks); Group 1: mean 36.88 (SD 8.29); n=57, Group 2: mean 38.68 (SD 7.48); n=56; Pain VAS 0-100 Top=High is poor outcome; Comments: Baseline values: CBT 64.2 (10.78), usual care 64.72 (10.44)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Study (subsidiary papers)	Alda 2011[6] (Garcia-campayo 2009[170], Luciano 2014[289])
Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 1, Reason: lack of efficacy; Group 2 Number missing: 3, Reason: adverse events (2), moved away (1) - Actual outcome: Visual analogue scale at 6 months follow up ; Group 1: mean 40.68 (SD 10.93); n=57, Group 2: mean 44.34 (SD 8.56); n=56; Pain VAS 0-100 Top=High is poor outcome; Comments: Baseline values: CBT 64.2 (10.78), usual care 64.72 (10.44) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: lack of efficacy (1), patient decision (4), lost to follow up (3); Group 2 Number missing: 10, Reason: adverse events (2), moved away (1), lack of efficacy (3), patient decision (2), loss to follow up (2)	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Alonso-Fernandez 2016[7]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=101)
Countries and setting	Conducted in Spain; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 9 weeks
Method of assessment of guideline condition	Method of assessment /diagnosis not stated: NA
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	age 65 years old or older, diagnosis of chronic musculoskeletal pain for at least 6 months, non-malignant pain (e.g., no cancer pain, ALS, etc.) and ability to read and write at an adequate level of proficiency
Exclusion criteria	dementia or severe cognitive impairment, sensory disability or serious psychiatric or psychological disorder that could compromise study participation
Recruitment/selection of patients	recruited through 5 nursing homes
Age, gender and ethnicity	Age - Mean (SD): 83.04 (6.82) years. Gender (M:F): 78.1% female. Ethnicity: not reported
Further population details	1. Chronic orofacial pain: No 2. Chronic primary musculoskeletal pain: Yes 3. Chronic visceral pain: No 4. Chronic widespread pain: No 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: No

Study	Alonso-Fernandez 2016[7]
Indirectness of population	No indirectness: NA
Interventions	(n=53) Intervention 1: Psychological therapy - Acceptance and commitment therapy. 9 x 120-min weekly group sessions, max. 8 participants led by a psychologist. Intervention based on Acceptance and Commitment Therapy and Selective Optimization with Compensation model. Program sets out to promote the use of SOC strategies and reduce efforts to struggle with pain. The general session structure was: a) review of the task carried out during the week, b) therapeutic training, and c) explanation of a new between-session assignment. Duration 9 weeks approx. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA (n=48) Intervention 2: Usual care. Minimal support: a 2 h educational group session about factors that can influence pain conditions and pain perception and information about selective optimisation and compensation strategies. The MS group did not receive any type of psychological training. Duration 9 weeks approx. Concurrent medication/care: not reported. Indirectness: Serious indirectness; Indirectness comment: 2 hour education session not considered sufficient for an education intervention but may be more than usual care
Funding	Academic or government funding (MAPFRE Foundation, Spanish Ministry of Economy and Competitiveness, Spanish Ministry of Science and Innovation, Community of Madrid and the Rey Juan Carlos University)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ACCEPTANCE AND COMMITMENT THERAPY versus USUAL CARE

Protocol outcome 1: Psychological distress
- Actual outcome: Geriatric Depression Scale at 9 weeks ; Group 1: mean 8.88 (SD 5.62); n=27, Group 2: mean 11.92 (SD 7.24); n=26; Geriatric Depression Scale 0-30 Top=High is poor outcome; Comments: Baseline values: ACT 10.81 (6.39), usual care 12 (6.87)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: usual care group had better cognitive status; Group 1 Number missing: 26, Reason: discontinued intervention (23), refused post-treatment assessment (3); Group 2 Number missing: 22, Reason: discontinued (14), refused post-treatment assessment (8)
- Actual outcome: Pain Anxiety Symptoms Scale-Short Form at 9 weeks ; Group 1: mean 28.92 (SD 16.9); n=27, Group 2: mean 38 (SD 24.15); n=26; Pain Anxiety Symptoms Scale short form not reported Top=High is poor outcome; Comments: Baseline values: ACT 38.37 (21.91), usual care 37.26 (23.86)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: usual care group had better cognitive status; Group 1 Number missing: 26, Reason: discontinued intervention (23), refused post-treatment assessment (3); Group 2 Number missing: 22, Reason: discontinued (14), refused post-treatment assessment (8)

Study	Alonso-Fernandez 2016[7]
Protocol outcome 2: Pain interference - Actual outcome: BPI interference general activity sub scale at 9 weeks ; Group 1: mean 4.77 (SD 3.85); n=27, Group 2: mean 4.96 (SD 3.59); n=26; Brief Pain Inventory interference general activity sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: ACT 4.7 (3.24), usual care 5.36 (3.59) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: usual care group had better cognitive status; Group 1 Number missing: 26, Reason: discontinued intervention (23), refused post-treatment assessment (3); Group 2 Number missing: 22, Reason: discontinued (14), refused post-treatment assessment (8) - Actual outcome: BPI interference mood sub scale at 9 weeks ; Group 1: mean 4 (SD 3.48); n=27, Group 2: mean 5.03 (SD 4.04); n=26; Brief pain inventory interference mood sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: ACT 5.48 (3.29), usual care 5.19 (3.17) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: usual care group had better cognitive status; Group 1 Number missing: 26, Reason: discontinued intervention (23), refused post-treatment assessment (3); Group 2 Number missing: 22, Reason: discontinued (14), refused post-treatment assessment (8) - Actual outcome: BPI interference walking ability sub scale at 9 weeks ; Group 1: mean 5.15 (SD 3.6); n=27, Group 2: mean 6.53 (SD 3.21); n=26; Brief pain inventory interference walking ability sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: ACT 6.5 (3.25), usual care 6.07 (3.23) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: usual care group had better cognitive status; Group 1 Number missing: 26, Reason: discontinued intervention (23), refused post-treatment assessment (3); Group 2 Number missing: 22, Reason: discontinued (14), refused post-treatment assessment (8) - Actual outcome: BPI interference relations with other people sub scale at 9 weeks ; Group 1: mean 2.33 (SD 2.9); n=27, Group 2: mean 3.8 (SD 3.84); n=26; Brief pain inventory interference relations with other people sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: ACT 2.96 (3.03), usual care 2.61 (2.94) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: usual care group had better cognitive status; Group 1 Number missing: 26, Reason: discontinued intervention (23), refused post-treatment assessment (3); Group 2 Number missing: 22, Reason: discontinued (14), refused post-treatment assessment (8) - Actual outcome: BPI interference sleep sub scale at 9 weeks ; Group 1: mean 2.4 (SD 3.53); n=27, Group 2: mean 5.04 (SD 4.08); n=26; Brief pain inventory interference sleep sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: ACT 3.03 (3.83), usual care 4.28 (3.94) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: usual care group had better cognitive status; Group 1 Number missing: 26, Reason: discontinued intervention (23), refused post-treatment assessment (3); Group 2 Number missing: 22, Reason: discontinued (14), refused post-treatment assessment (8) Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation at 9 weeks ; Group 1: 23/53, Group 2: 14/48; Comments: ACT: lost interest in study (n=8), medical illness (n=4),

Study	Alonso-Fernandez 2016[7]
difficulty with homework (n=5), problems with other residents (n=3), family caregivers (n=3) Usual care: lost interest in study (n=4), medical illness (n=5), moved out of nursing home (n=5) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: usual care group had better cognitive status; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Pain reduction

Study	Amer-Cuenca 2019[11]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=103)
Countries and setting	Conducted in Spain; Setting: 3 fibromyalgia centres, Spain
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	fulfilled 1990 ACR classification criteria for fibromyalgia; reported an average pain intensity ≥4 on a 0-10 VAS during the week before study commencement; stable dose of medication for FM for 4 or more weeks; aged 18-65 years
Exclusion criteria	inflammatory rheumatic condition; planned surgery during the study period; symptoms of bipolar disorder, major depressive disorder, panic disorder or psychosis; did not speak Spanish fluently
Recruitment/selection of patients	referred from 3 Spanish fibromyalgia associations
Age, gender and ethnicity	Age - Mean (SD): high dose 54.75 (10.14), low concentrated 55.2 (8.19), diluted low dose 51.67 (7.38), control 51.27 (10.57). Gender (M:F): 6/71. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning

Study	Amer-Cuenca 2019[11]
	difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=84) Intervention 1: Psychological therapy - Pain education. Pain neuroscience education by physiotherapists, provided in accordance with published guidelines in groups of 4-6 patients. PowerPoint addressed the following topics: physiology of the nervous system, characteristics of acute vs. chronic pain, the purpose of acute pain, how acute pain originates in the nervous system (nociception, ion gates, neurons, action potential, peripheral sensitisation, synapses, synaptic gap, inhibitory/excitatory chemicals, spinal cord, descending/ascending pain pathways, the role of the brain, pain memory, pain perception), how pain becomes chronic (plasticity of the nervous system, modulation, modulation, modification, central sensitisation, the pain neuromatrix theory) and potential sustaining factors of central sensitization such as illness, emotions, stress, perceptions, pain cognitions, and pain behaviour. Information presented in an understandable way, using pictures, examples and metaphors. Also explained how various treatment components are likely to contribute to decreasing the hypersensitivity of the central nervous system. All participants asked to read the Spanish translation of the book 'Explain Pain'. After each session, therapists answered questions from patients. Patients asked if they had applied learning in daily life and what their experiences were. Patients motivated and coached to apply insights to daily life. Three trial arms: 1) high dose (6 x 45 minute sessions), 2) low concentrated dose (2 x 45 minute sessions), 3) diluted low dose (6 x 15 minute sessions). Content identical but adapted to the different doses/durations. Duration unclear. Concurrent medication/care: All participants instructed to continue current medication but not to initiate new medication or any other new treatment. Indirectness: No indirectness; Indirectness comment: NA (n=19) Intervention 2: Attention control . Biomedical education: 2 x 45 minute sessions by physiotherapists in groups of 4-6 patients. Duration unclear. Concurrent medication/care: All participants instructed to continue current medication but not to initiate new medication or any other new treatment. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PAIN EDUCATION versus ATTENTION CONTROL

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact Questionnaire at post-intervention ; Group 1: mean 56.3 (SD 18.97); n=60, Group 2: mean 53.38 (SD 16.67); n=17; Fibromyalgia Impact Questionnaire 0-100 Top=High is poor outcome; Comments: Baseline values: pain education 60.17 (19.65), control 61.35 (15.48)

Three pain neuroscience education arms combined for analysis.

Study	Amer-Cuenca 2019[11]
	Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 24, Reason: loss to follow up n=15, discontinued intervention n=9; Group 2 Number missing: 2, Reason: loss to follow up n=2 - Actual outcome: Fibromyalgia Impact Questionnaire at 3 month follow up post-intervention ; Group 1: mean 51.44 (SD 23.54); n=60, Group 2: mean 57.04 (SD 17.76); n=17; Fibromyalgia Impact Questionnaire 0-100 Top=High is poor outcome; Comments: Baseline values: pain education 60.17 (19.65), control 61.35 (15.48) Three pain neuroscience education arms combined for analysis. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 24, Reason: loss to follow up n=15, discontinued intervention n=9; Group 2 Number missing: 2, Reason: loss to follow up n=2 Protocol outcome 2: Psychological distress - Actual outcome: Pain Anxiety Symptoms Scale (PASS-1) at post-intervention ; Group 1: mean 35.86 (SD 12.99); n=60, Group 2: mean 32.2 (SD 12.32); n=17; Pain anxiety symptoms scale unclear Top=High is poor outcome; Comments: Baseline values: pain neuroscience education 38.37 (12.94), control 35.73 (15.13) 3 pain neuroscience education trial arms combined for analysis. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 24, Reason: loss to follow up n=15, discontinued intervention n=9; Group 2 Number missing: 2, Reason: loss to follow up n=2 - Actual outcome: Pain Anxiety Symptoms Scale (PASS-1) at 3 month follow up post-intervention ; Group 1: mean 34.94 (SD 14.96); n=60, Group 2: mean 28.53 (SD 15.26); n=17; pain anxiety symptom scale unclear Top=High is poor outcome; Comments: Baseline values: pain neuroscience education 38.37 (12.94), control 35.73 (15.13) 3 pain neuroscience education trial arms combined for analysis. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 24, Reason: loss to follow up n=15, discontinued intervention n=9; Group 2 Number missing: 2, Reason: loss to follow up n=2 - Actual outcome: Pain Anxiety Symptoms Scale (PASS-2) at post-intervention ; Group 1: mean 14.07 (SD 6.837); n=60, Group 2: mean 12.26 (SD 6.64); n=17; pain anxiety symptom scale unclear Top=High is poor outcome; Comments: Baseline values: pain neuroscience education 15.29 (5.795), control 13.86 (7.52) 3 pain neuroscience education trial arms combined for analysis. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 24, Reason: loss to follow up n=15, discontinued intervention n=9; Group 2 Number missing: 2, Reason: loss to follow up n=2 - Actual outcome: Pain Anxiety Symptoms Scale (PASS-2) at 3 month follow up post-intervention ; Group 1: mean 14.13 (SD 6.46); n=60, Group 2: mean 11.53 (SD 8.12); n=17; pain anxiety symptom scale unclear Top=High is poor outcome; Comments: Baseline values: pain neuroscience education 15.29 (5.795), control 13.86 (7.52) 3 pain neuroscience education trial arms combined for analysis.

Study	Amer-Cuenca 2019[11]
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 24, Reason: loss to follow up n=15, discontinued intervention n=9; Group 2 Number missing: 2, Reason: loss to follow up n=2 Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation at Intervention time ; Group 1: 9/84, Group 2: 0/19; Comments: reasons for discontinuation not reported Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA Protocol outcome 4: Pain reduction - Actual outcome: Numeric rating scale at post-intervention ; Group 1: mean 5.927 (SD 2.481); n=60, Group 2: mean 8.16 (SD 1.06); n=17; Comments: Baseline values: pain neuroscience education 7.2 (1.891), control 8.42 (1.39) 3 pain neuroscience education trial arms combined for analysis. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: pain higher in the control group at baseline ; Group 1 Number missing: 24, Reason: loss to follow up n=15, discontinued intervention n=9; Group 2 Number missing: 2, Reason: loss to follow up n=2 - Actual outcome: Numeric rating scale at 3 month follow up post-intervention ; Group 1: mean 6.28 (SD 2.51); n=60, Group 2: mean 7.75 (SD 1.45); n=17; numeric rating scale 0-10 Top=High is poor outcome; Comments: Baseline values: pain neuroscience education 7.2 (1.891), control 8.42 (1.39) 3 pain neuroscience education trial arms combined for analysis. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: pain higher in the control group at baseline ; Group 1 Number missing: 24, Reason: loss to follow up n=15, discontinued intervention n=9; Group 2 Number missing: 2, Reason: loss to follow up n=2	
Protocol outcomes not reported by the study	Physical function ; Pain interference; Pain self-efficacy; Use of healthcare services; Sleep

Study	Amirova 2017[12]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=191)
Countries and setting	Conducted in United Kingdom; Setting: home-based
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 4 weeks + 4 weeks

Study	Amirova 2017[12]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosed with Fibromyalgia syndrome as outlined by American College of Rheumatology classification criteria of widespread pain persistent for at least 3 months and tenderness at a minimum of 11 of the 18 tender points
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	aged between 18 to 80 years, have internet access and to be diagnosed with fibromyalgia syndrome as outlined by American College of Rheumatology classification criteria of widespread pain persistent for at least 3 months and tenderness at a minimum of 11 of the 18 tender points; additionally participants had to satisfy the new preliminary diagnostic criteria for fibromyalgia
Exclusion criteria	participants reporting severe psychiatric comorbidities, life-threatening conditions, substance abuse and pregnancy as well as recipients of any non-pharmaceutical treatment
Recruitment/selection of patients	participants approached online via regional support groups
Age, gender and ethnicity	Age - Mean (SD): MMRT 48.1 (11.08), waiting list 48.95 (10.13). Gender (M:F): 12/179. Ethnicity: predominantly Caucasian (90%)
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: No 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Extra comments	NA. NA
Indirectness of population	No indirectness: NA
Interventions	(n=67) Intervention 1: Psychological therapy - Relaxation techniques. Written instructions of the Mitchell Method Relaxation Technique and a short audio recording of the guided technique to use every day for 1 month. Participants sat at a desk/in a chair/laid on the floor and were given verbal orders to engage in a series of muscle relaxation exercises, followed by deep breathing and finally an imagery task, recalling a pleasant occasion or concentrating on a pleasant repetitive sequence for 1 minute. Duration 4 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA (n=58) Intervention 2: Usual care. Waiting list - no active treatment and proceeded with usual care. Duration 4 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

Study	Amirova 2017[12]

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RELAXATION TECHNIQUES versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: Revised Fibromyalgia Impact Questionnaire at 4 weeks ; Group 1: mean 68.79 (SD 16.9); n=67, Group 2: mean 66.1 (SD 15.34); n=58; Comments: Baseline values: MMRT 68.09 (20.03), waiting list 65.5 (16.1)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in baseline VAS - MMRT group higher than waiting list group; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 12, Reason: not reported

Protocol outcome 2: Psychological distress
- Actual outcome: Hospital Anxiety and Depression Scale depression sub scale at 4 weeks ; Group 1: mean 10.4 (SD 0.46); n=67, Group 2: mean 10.5 (SD 0.4); n=58; HADS depression sub scale 0-21 Top=High is poor outcome; Comments: Baseline values: MMRT 10.4 (0.27), waiting list 10.06 (0.31)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in baseline VAS - MMRT group higher than waiting list group; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 12, Reason: not reported
- Actual outcome: Hospital Anxiety and Depression Scale anxiety sub scale at 4 weeks ; Group 1: mean 10 (SD 4.09); n=67, Group 2: mean 9.73 (SD 3.33); n=58; HADS anxiety sub scale 0-21 Top=High is poor outcome; Comments: Baseline values: MMRT 9.72 (3.56), waiting list 10.28 (2.97)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in baseline VAS - MMRT group higher than waiting list group; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 12, Reason: not reported

Protocol outcome 3: Sleep
- Actual outcome: Medical Outcome Sleep Scale at 4 weeks ; Group 1: mean 46.46 (SD 14.16); n=67, Group 2: mean 55.73 (SD 14.71); n=58; Comments: Baseline values: MMRT 49.5 (16.88), waiting list 54.86 (15.1)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in baseline VAS - MMRT group higher than waiting list group; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 12, Reason: not reported

Protocol outcome 4: Discontinuation
- Actual outcome: Dropout rate at 4 weeks ; Group 1: 3/67, Group 2: 12/58; Comments: Dropouts resulted from the disregarding of emails, difficultly in contacting the participants and withdrawals for personal reasons (i.e. holidays).
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: unclear whether participants completed the intervention or not; Baseline details: difference in baseline VAS - MMRT group higher than waiting list group; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 5: Pain reduction

Study	Amirova 2017[12]
- Actual outcome: Visual Analogue Scale at 4 weeks ; Group 1: mean 7.03 (SD 1.81); n=67, Group 2: mean 6.87 (SD 1.69); n=58; Comments: Baseline values: MMRT 7.44 (1.69), waiting list 6.7 (1.42) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference in baseline VAS - MMRT group higher than waiting list group; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 12, Reason: not reported	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services

Study	Amutio 2015[14 15]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=39)
Countries and setting	Conducted in Spain; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 7 weeks + 3 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated: NA
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	Able to prove a current diagnosis of FMS (e.g., via a letter from a doctor or pain consultant); female; aged 18–70 years
Exclusion criteria	Currently undergoing mindfulness training and/or formal psychotherapy (stable prescription medication was permitted for both the intervention and control group)
Recruitment/selection of patients	recruited through the Fibromyalgia Association of Alemria
Age, gender and ethnicity	Age - Mean (SD): 51.82 (10.18). Gender (M:F): Define. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Extra comments	NA. NA

Study	Amutio 2015[14 15]
Indirectness of population	No indirectness: NA
Interventions	(n=20) Intervention 1: Psychological therapy - Mindfulness. Weekly 2 hour sessions for 7 consecutive weeks. Participants' reflections about their mindfulness meditation exercise practice during the week, practice of body scan for 10 minutes, presentation of metaphors through different animations and stories and also some exercises for each of the sessions (observing physical sensations of different body parts, breathing, observing thoughts, accepting uncomfortable private events), practice of mindfulness, attending to the breath for 30 minutes. Requested to practice body scan for 10 minutes and mindfulness breathing for 30 minutes and record the practice using a register sheet. Duration 7 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA (n=19) Intervention 2: Usual care. Waiting list - informed that due to space constraints they would receive the course at a later time. Duration 7 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MINDFULNESS versus USUAL CARE

Protocol outcome 1: Psychological distress
- Actual outcome: Beck Depression Inventory at 7 weeks ; Group 1: mean 36.02 (SD 7.49); n=14, Group 2: mean 41.87 (SD 10.36); n=18; Beck Depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: mindfulness 41.79 (8.96), waiting list 40.15 (9.19)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 1, Reason: not reported
- Actual outcome: State-Trait Anxiety Questionnaire (state anxiety) at 7 weeks ; Group 1: mean 29.29 (SD 9.69); n=14, Group 2: mean 41.12 (SD 9.25); n=18; STAI state anxiety 20-80 Top=High is poor outcome; Comments: Baseline values: mindfulness 38.63 (8.75), waiting list 39.93 (8.34)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 1, Reason: not reported
- Actual outcome: State-Trait Anxiety Questionnaire (trait anxiety) at 7 weeks ; Group 1: mean 32.29 (SD 8.53); n=14, Group 2: mean 36.24 (SD 8.98); n=18; STAI trait anxiety 20-80 Top=High is poor outcome; Comments: Baseline values: mindfulness 35.81 (9.61), waiting list 34.03 (7.58)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 1, Reason: not reported
- Actual outcome: Beck Depression Inventory at 3 months follow up ; Group 1: mean 35.12 (SD 8.26); n=14, Group 2: mean 42.68 (SD 9.79); n=18; Beck depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: mindfulness 41.79 (8.96), waiting list 40.15 (9.19)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Study	Amutio 2015[14 15]
	Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 1, Reason: not reported - Actual outcome: State-Trait Anxiety Questionnaire (state anxiety) at 3 months follow up; Group 1: mean 27.85 (SD 8.14); n=14, Group 2: mean 40.29 (SD 7.89); n=18; STAI state anxiety 20-80 Top=High is poor outcome; Comments: Baseline values: mindfulness 38.63 (8.75), waiting list 39.93 (8.34) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 1, Reason: not reported - Actual outcome: State-Trait Anxiety Questionnaire (trait anxiety) at 3 months follow up; Group 1: mean 31.71 (SD 7.93); n=14, Group 2: mean 34.97 (SD 9.37); n=18; STAI trait anxiety 20-80 Top=High is poor outcome; Comments: Baseline values: mindfulness 35.81 (9.61), waiting list 34.03 (7.58) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 1, Reason: not reported Protocol outcome 2: Sleep - Actual outcome: Pittsburgh Sleep Quality Index at 7 weeks ; Group 1: mean 9.1 (SD 3.3); n=20, Group 2: mean 13.1 (SD 3.3); n=19; Pittsburgh Sleep Quality Index 0-21 Top=High is poor outcome; Comments: Baseline values: mindfulness 13 (3.9), usual care 12.4 (3.1) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA - Actual outcome: Pittsburgh Sleep Quality Index at 3 months follow up ; Group 1: mean 10.37 (SD 3.1); n=20, Group 2: mean 12.8 (SD 3.6); n=19; Comments: Baseline values: mindfulness 13 93.9), usual care 12.4 (3.1) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA Protocol outcome 3: Discontinuation - Actual outcome: Excluded due to non-completion of the course or questionnaires at 7 weeks ; Group 1: 6/20, Group 2: 1/19 Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: unclear how many didn't complete the course; Baseline details: no statistically significant differences between groups in the mean scores of the target variables ; Group 1 Number missing: 0; Group 2 Number missing: 0
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Pain reduction

Study	Ang 2010[18]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=32)
Countries and setting	Conducted in USA; Setting: telephone-based intervention
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 weeks + 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology classification criteria for fibromyalgia
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	moderately symptomatic with respect to pain intensity (FIQ pain score >3 and FIQ physical impairment score ≥2), taking stable doses of pain- related medications (antidepressants, anticonvulsants, NSAIDs and opiates) for at least 4 weeks
Exclusion criteria	peripheral neuropathy, diabetes, demyelinating disorders and inflammatory rheumatic diseases
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 49 (11). Gender (M:F): 0/32. Ethnicity: 78% white
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Extra comments	NA. NA
Indirectness of population	No indirectness: NA
Interventions	(n=17) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 6 weekly 30-40 minute sessions of CBT over the telephone by a single trained therapist (psychology graduate student under supervision of a clinical psychologist) and a companion workbook to encourage active participation. Components of CBT included time-contingent activity pacing, pleasant activity scheduling, relaxation, automatic thoughts and pain, cognitive restructuring and stress management. Duration 6 weeks. Concurrent medication/care: allowed to continue pain related medications and asked to stay on the same regimen and complete a drug diary throughout the study period. Indirectness: Serious indirectness; Indirectness comment: included relaxation elements (n=15) Intervention 2: Usual care. Customary care received from treating physicians. Duration 6 weeks.

Study	Ang 2010[18]
	Concurrent medication/care: allowed to continue pain related medications and asked to stay on the same regimen and complete a drug diary throughout the study period. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated (Ang has received consulting fees from Eli Lilly)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Physical function
- Actual outcome: Fibromyalgia Impact Questionnaire physical impairment sub scale at 6 weeks ; Group 1: mean -0.3 (SD 2.2); n=15, Group 2: mean 0.2 (SD 1.7); n=13; FIQ physical impairment sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 5.6 (1.8), usual care 5.4 (1.7)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more participants in the CBT group took NSAIDs ; Group 1 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful; Group 2 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful
- Actual outcome: Fibromyalgia Impact Questionnaire physical impairment sub scale at 12 weeks ; Group 1: mean -0.6 (SD 2.3); n=15, Group 2: mean 0.5 (SD 1.2); n=13; FIQ physical impairment sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 5.6 (1.8), usual care 5.4 (1.7)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more participants in the CBT group took NSAIDs ; Group 1 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful; Group 2 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful

Protocol outcome 2: Psychological distress
- Actual outcome: Patient Health Questionnaire 8-item depression scale at 12 weeks ; Group 1: mean -0.9 (SD 5.2); n=15, Group 2: mean 0 (SD 4.1); n=13; Patient Health Questionnaire 8-item depression scale 0-24 Top=High is poor outcome; Comments: Baseline values: CBT 10 (5.4), usual care 13 (4.5)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more participants in the CBT group took NSAIDs ; Group 1 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful; Group 2 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful

Protocol outcome 3: Discontinuation
- Actual outcome: Discontinuation at 6 weeks ; Group 1: 2/17, Group 2: 2/17; Comments: 1 from each group refused further follow up, 1 from each group stated that NFR assessment was too painful
Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: unclear whether participants discontinued intervention; Baseline details: more participants in the CBT group took NSAIDs ; Group 1 Number missing: 0; Group 2 Number missing: 0

Study	Ang 2010[18]
Protocol outcome 4: Pain reduction - Actual outcome: Fibromyalgia Impact Questionnaire pain sub scale at 6 weeks ; Group 1: mean -0.2 (SD 1.8); n=15, Group 2: mean -0.3 (SD 1.6); n=13; FIQ pain sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 7.6 (1.8), usual care 7.8 (1.4) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more participants in the CBT group took NSAIDs ; Group 1 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful; Group 2 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful - Actual outcome: Fibromyalgia Impact Questionnaire pain sub scale at 12 weeks ; Group 1: mean -0.6 (SD 1.6); n=15, Group 2: mean -0.3 (SD 1.7); n=13; FIQ pain sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 7.6 (1.8), usual care 7.8 (1.4) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more participants in the CBT group took NSAIDs ; Group 1 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful; Group 2 Number missing: 2, Reason: 1 refused follow up, 1 stated NFR measurement too painful	
Protocol outcomes not reported by the study	Health related quality of life ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Babu 2007[29]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=30)
Countries and setting	Conducted in India; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention time: 6 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: fulfilled the ACR criteria
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	ACR criteria for fibromyalgia
Exclusion criteria	major psychiatric disorders, malignancies, osteomalacia, New York Heart Association (NYHA) class 3 and 4, recent stroke or myocardial infarction, renal failure and neuropathic pain
Recruitment/selection of patients	patients attending a single outpatient department
Age, gender and ethnicity	Age - Mean (SD): biofeedback 43.2 (10.5) years; sham 35.3 (9.7) years. Gender (M:F): 8/22. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=15) Intervention 1: Psychological therapy - Biofeedback. A continuous 6-day treatment schedule of EMG biofeedback, with each session lasting 45 min. Treatment was given to the forearm extensors, upper trapezius and frontalis. Patients were taught to relax through techniques like positioning, breathing and hold-relax with the help of visual and auditory feedback. Patients were gradually taught how to include relaxation into their activities of daily life. Duration 6 days. Concurrent medication/care: Not reported. Indirectness: Serious indirectness; Indirectness comment: included elements of relaxation (n=15) Intervention 2: Attention control . Sham biofeedback - A continuous 6-day treatment schedule, with each session lasting 45 min. This provided a constant visual feedback to the patient, irrespective of the muscle activity. Treatment was given to the forearm extensors, upper trapezius and frontalis. Patients were taught to relax through techniques like positioning, breathing and hold-relax with the help of visual and

	auditory feedback. Patients were gradually taught how to include relaxation into their activities of daily life. Duration 6 days. Concurrent medication/care: Not reported. Indirectness: Serious indirectness; Indirectness comment: included elements of relaxation
Funding	Academic or government funding (Fluid Research Grant)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BIOFEEDBACK versus ATTENTION CONTROL

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia impact questionnaire at 6 days ; Group 1: mean -21.9 (SD 12.8441); n=15, Group 2: mean -12.3 (SD 16.4009); n=15; Fibromyalgia impact questionnaire not reported Top=High is poor outcome; Comments: standard deviations calculated from confidence intervals
Baseline values: biofeedback 61 (13.3), sham 65 (15.6)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Mean age higher in treatment group ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Physical function
- Actual outcome: 6 minute walk test at 6 days ; Group 1: mean 69 meters (SD 79.9); n=15, Group 2: mean 16 meters (SD 79.9); n=15; 6 minute walk test NA Top=High is good outcome; Comments: estimated standard deviations calculated from p value
Baseline values: biofeedback 314.5 (63.4), sham 309.1 (81.3)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Mean age higher in treatment group ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: Discontinuation
- Actual outcome: Discontinuation at 6 days ; Group 1: 0/15, Group 2: 0/15
Risk of bias: All domain - Low, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Mean age higher in treatment group ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: Pain reduction
- Actual outcome: VAS at 6 days ; Group 1: mean -4.3 (SD 1.976); n=15, Group 2: mean -2.6 (SD 3.359); n=15; VAS 0-10 Top=High is poor outcome; Comments: standard deviations calculated from confidence intervals
Baseline values: biofeedback 7.1 (1.8), sham 8.1 (1.8)
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Mean age higher in treatment group ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Psychological distress; Pain interference; Pain self-efficacy; Use of healthcare services; Sleep

Study	Bahremand 2015[30]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=41)
Countries and setting	Conducted in Iran; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	Ages between 35 and 75 years old; minimum background of 3 months of prior chest pain; natural and healthy angiography; existence of extreme pain, at a level higher than 2 out of 10 degrees on the pain scale; continued persistent pain for at least one month after the angiography; lack of physical origin for the pain
Exclusion criteria	Receiving a simultaneous diagnosis of psychological intervention at any stage of the treatment plan; unwillingness to continue treatment
Recruitment/selection of patients	patients who had visited the heart emergency section of the hospital during one summer on account of chest pain
Age, gender and ethnicity	Age - Mean (SD): relaxation 52.69 (10.8) years; control group 51.8 (10.68) years . Gender (M:F): 14/27. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: Yes 4. Chronic widespread pain: No 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=13) Intervention 1: Psychological therapy - Relaxation techniques. Relaxation training - 4 x weekly 2 hour group sessions led by clinical psychologists. Session 1: introduced to procedures used in Ost's treatment and placed in progressive relaxation therapy after diaphragmatic breathing training. Session 2: release-only technique was taught. Session 3: cue-control relaxation method and a different relaxation method. Session 4: rapid relaxation method and application to real life. At the end of each session homework to practice the techniques and record relaxation conditions was set. Duration 4 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness; Indirectness comment: NA

	(n=14) Intervention 2: Attention control . In the control sessions, only discussions about the physical conditions of the patients and their assessments of future problems were conducted, without any training or medical therapy trends. Duration 4 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RELAXATION TECHNIQUES versus ATTENTION CONTROL Protocol outcome 1: Discontinuation - Actual outcome: Discontinuation at 4 weeks ; Group 1: 0/13, Group 2: 4/14; Comments: reason not reported Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Pain reduction - Actual outcome: Brief pain inventory - pain severity sub scale (VAS) at 5 weeks ; Group 1: mean 2.85 (SD 1.67); n=13, Group 2: mean 4.2 (SD 1.99); n=10; Brief pain inventory-pain severity 0-10 Top=High is poor outcome; Comments: Baseline values: relaxation 6.15 (1.77), attention control 5.1 (1.73) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 4, Reason: not reported	
Protocol outcomes not reported by the study	Health related quality of life; Physical function ; Psychological distress; Pain interference; Pain self-efficacy; Use of healthcare services; Sleep

Study	**Baumueller 2017[38]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Germany; Setting: single centre
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 8 weeks + 3 months

Study	Baumueller 2017[38]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosis of fibromyalgia according to American College of Rheumatology criteria
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	diagnosis of FM, female gender, age between 18 and 65 years, cognitive ability, sufficient German language skills
Exclusion criteria	major medical disorders, i.e. cancer, chronic heart failure, or asthma requiring cortisone, suffering from psychosis or major affective disorders, substance abuse, co medication with opiates or benzodiazepines, transmeridian flight in the last weeks, shift work or gravidity
Recruitment/selection of patients	consecutive patients from a waiting list for a fibromyalgia day hospital programme meeting the inclusion criteria
Age, gender and ethnicity	Age - Mean (SD): biofeedback: 55.4 (6.1), usual care 56 (6.1). Gender (M:F): 0/40. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Extra comments	NA.
Indirectness of population	No indirectness: NA
Interventions	(n=20) Intervention 1: Psychological therapy - Biofeedback. 14 sessions over 8 weeks, led by a medical student in 4th and 5th year and a nurse in a chronic pain unit, training delivered individually. Electrodes placed on upper and lower trapezius muscle, apparatus displayed 1 EMG curve for each side, instructor taught patients that an ascending curve corresponds to increasing and a descending curve to decreasing muscle tension. Patients instructed to strain the muscles for 3 minutes then relax for 10 minutes, while receiving visual feedback of the muscle tension. Feeling of muscle tension in relation to EMG curves was discussed at the end of the session. Encouraged to do a home exercise programme of muscle relaxation for 15 minutes per day and in stressful situations. Duration 8 weeks. Concurrent medication/care: usual care and scheduled for multidisciplinary treatment programmes after the study. Indirectness: No indirectness; Indirectness comment: NA (n=20) Intervention 2: Usual care. Usual care - same as before starting the study. Duration 8 weeks. Concurrent medication/care: scheduled for multidisciplinary treatment programme after the study. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

Study	Baumueller 2017[38]

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BIOFEEDBACK versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: SF36 physical functioning at 8 weeks ; Group 1: mean 49.3 (SD 19.4); n=19, Group 2: mean 54.2 (SD 24.3); n=19; SF36 physical functioning 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 47.6 (13.4), usual care 54.2 (19.2)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason
- Actual outcome: SF36 physical functioning at 3 months follow up; Group 1: mean 51.6 (SD 21); n=18, Group 2: mean 50.9 (SD 13.8); n=18; SF36 physical functioning 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 47.6 (13.4), usual care 54.2 (19.2)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason, reason unknown (1)
- Actual outcome: SF36 role physical at 8 weeks ; Group 1: mean 14.1 (SD 27.3); n=19, Group 2: mean 33.3 (SD 38.4); n=19; SF36 role physical 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 26.6 (34.7), usual care 38.9 (39.5)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason
- Actual outcome: SF36 role physical at 3 months follow up; Group 1: mean 15.6 (SD 25.6); n=18, Group 2: mean 20.8 (SD 32.4); n=18; SF36 role physical 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 26.6 (34.7), usual care 38.9 (39.5)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason, reason unknown (1)
- Actual outcome: SF36 bodily pain at 8 weeks ; Group 1: mean 36.7 (SD 16); n=19, Group 2: mean 30.4 (SD 16.9); n=19; SF36 bodily pain 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 38.6 (10.7), usual care 37 (12.5)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason
- Actual outcome: SF36 bodily pain at 3 months follow up; Group 1: mean 36.9 (SD 11.5); n=18, Group 2: mean 36.2 (SD 15.3); n=18; SF36 bodily pain 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 38.6 (10.7), usual care 37 (12.5)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason, reason unknown (1)

Study	Baumueller 2017[38]
	- Actual outcome: SF36 general health at 8 weeks ; Group 1: mean 36.5 (SD 19.2); n=19, Group 2: mean 44.7 (SD 18.5); n=19; SF36 general health 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 37.9 (18.9), usual care 41.8 (14.4) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason - Actual outcome: SF36 general health at 3 months follow up; Group 1: mean 43.5 (SD 16.5); n=18, Group 2: mean 44.4 (SD 18.3); n=18; SF36 general health 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 37.9 (18.9), usual care 41.8 (14.4) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason (1), reason unknown (1) - Actual outcome: SF36 vitality at 8 weeks ; Group 1: mean 28.2 (SD 17.5); n=19, Group 2: mean 41.7 (SD 14.8); n=19; SF36 vitality 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 26.8 (17.3), 37.2 (12.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason - Actual outcome: SF36 vitality at 3 months follow up; Group 1: mean 28.6 (SD 16.4); n=18, Group 2: mean 38.8 (SD 15.5); n=18; SF36 vitality 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 26.8 (17.3), usual care 37.2 (12.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason, reason unknown (1) - Actual outcome: SF36 social functioning at 8 weeks ; Group 1: mean 50 (SD 22.1); n=19, Group 2: mean 60.4 (SD 27.2); n=19; SF36 social functioning 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 53.7 (24.9), usual care 60.4 (23.6) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason - Actual outcome: SF36 social functioning at 3 months follow up; Group 1: mean 53.7 (SD 25.7); n=18, Group 2: mean 61.1 (SD 25.7); n=18; SF36 social functioning 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 53.7 (24.9), usual care 60.4 (23.6) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason, reason unknown (1) - Actual outcome: SF36 role emotional at 3 months follow up; Group 1: mean 35.4 (SD 43); n=18, Group 2: mean 59.3 (SD 47.9); n=18; SF36 role emotional 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 25 (35.5), usual care 57.4 (44) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional

Study	Baumueller 2017[38]
	and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason, reason unknown (1) - Actual outcome: SF36 mental health at 8 weeks ; Group 1: mean 51.4 (SD 20.1); n=19, Group 2: mean 60.7 (SD 21.5); n=19; SF36 mental health 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 50.8 (15.5), usual care 57.3 (16.8) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason - Actual outcome: SF36 mental health at 3 months follow up; Group 1: mean 51.1 (SD 17.9); n=18, Group 2: mean 57.5 (SD 18.4); n=18; SF36 mental health 0-100 Top=High is good outcome; Comments: Baseline values: 50.8 (15.5), 57.3 (16.8) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason, reason unknown (1) - Actual outcome: SF36 role emotional at 8 weeks ; Group 1: mean 47.9 (SD 47.1); n=19, Group 2: mean 57.4 (SD 44); n=19; SF36 role emotional 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 25 (35.5), usual care 57.4 (44) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason Protocol outcome 2: Psychological distress - Actual outcome: Beck Depression Inventory at 8 weeks ; Group 1: mean 16.1 (SD 8.8); n=19, Group 2: mean 12.9 (SD 7.3); n=19; Beck Depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: biofeedback 17.6 (8.2), usual care 12.8 (6.4) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 1, Reason: personal reason; Group 2 Number missing: 1, Reason: personal reason - Actual outcome: Beck Depression Inventory at 3 months follow up; Group 1: mean 16.9 (SD 8.3); n=18, Group 2: mean 12.3 (SD 6.3); n=18; Beck Depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: biofeedback 17.6 (8.2), usual care 12.8 (6.4) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 2, Reason: personal reason (1), reason unknown (1); Group 2 Number missing: 2, Reason: personal reason, reason unknown (1) Protocol outcome 3: Discontinuation - Actual outcome: Discontinued intervention at 8 weeks ; Group 1: 1/20, Group 2: 1/20; Comments: discontinued interventions due to personal reasons Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: difference between groups in SF36 vitality, role emotional and BDI at baseline ; Group 1 Number missing: 0; Group 2 Number missing: 0

Study	Baumueller 2017[38]
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Pain reduction

Study	Bergeron 2001[44]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=87)
Countries and setting	Conducted in Canada; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 weeks + 12 weeks + 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: 2 independent gynaecological evaluations
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	pain during intercourse which is subjectively distressing, occurs on most intercourse attempts and has lasted for at least 6 months; women who stopped attempting intercourse were include if the pain could be confirmed by gynaecological exam; pain limited to intercourse and other activities involving vestibular pressure; moderate to severe pain in one or more locations of the vestibule during the cotton swab test (minimum average pain rating of 4 on a scale of 0-10)
Exclusion criteria	pelvic or vulvar pain not clearly linked to intercourse; presence of major medical and/or psychiatric illness, active infection or vaginismus; ongoing treatment for dyspareunia; pregnancy; age below 18 or above 50
Recruitment/selection of patients	local media announcements and professional referral
Age, gender and ethnicity	Age - Mean (SD): 26.8 (5.4) years. Gender (M:F): 0/87. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: Yes 4. Chronic widespread pain: No 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=29) Intervention 1: Psychological therapy - Biofeedback. 8 x 45 minute sessions over 12 weeks led by 1 of 2 PhD level clinical psychologists. Self-insertion of a single-user sEMG sensor in to the vagina. Automated protocol - 60 second pre-baseline rest period; 6 max. intensity rapid contractions or flicks, each

Study	Bergeron 2001[44]
	contraction preceded by a 12 second rest period; 1 max. intensity 60 second contraction preceded by 30 seconds rest; 1 60 second post-baseline rest period. Training in the use of a portable sEMG home trainer for daily practice. Duration 12 weeks. Concurrent medication/care: all participants required to forgo receiving other interventions for the entire duration of the study. Indirectness: No indirectness; Indirectness comment: NA (n=29) Intervention 2: Psychological therapy - Cognitive behavioural therapy. Group CBT led by 1 of 2 PhD level clinical psychologists in 8 x 2 hour sessions over 12 weeks, 7-8 participants per group. Treatment package included education and information about vulvar vestibulitis, how dyspareunia impacts desire and arousal, a multifactorial view of pain and sexual anatomy; progressive muscle relaxation; abdominal breathing; Kegel exercises; vaginal dilation; distractive techniques; rehearsal of coping self-statements; communication skills training and cognitive restructuring. . Duration 12 weeks. Concurrent medication/care: all participants required to forgo receiving other interventions for the entire duration of the study. Indirectness: Serious indirectness; Indirectness comment: CBT included relaxation and education
Funding	Academic or government funding (Social Sciences and Humanities Research Council of Canada and Health Canada)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BIOFEEDBACK versus COGNITIVE BEHAVIOURAL THERAPY

Protocol outcome 1: Discontinuation
- Actual outcome: Discontinuation at 12 weeks; Group 1: 3/29, Group 2: 1/29; Comments: Biofeedback: drop out before receiving treatment (n=1), drop out at post-treatment assessment (n=2)
CBT: drop out before receiving treatment (n=1)
Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Pain reduction
- Actual outcome: Pain intensity during intercourse numeric rating scale at 12 weeks; Group 1: mean 5.43 (SD 2.36); n=28, Group 2: mean 6 (SD 2.13); n=28; numeric rating scale 0-10 Top=High is poor outcome; Comments: Baseline values: biofeedback 6.93 (1.8), CBT 7.14 (1.53)
Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 3, Reason: drop out; Group 2 Number missing: 1, Reason: drop out
- Actual outcome: Pain intensity during intercourse numeric rating scale at 6 months follow up ; Group 1: mean 4.5 (SD 2.63); n=28, Group 2: mean 4.46 (SD 2.47); n=28; numeric rating scale 0-10 Top=High is poor outcome; Comments: Baseline values: biofeedback 6.93 (1.8), CBT 7.14 (1.53)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Study	Bergeron 2001[44]
Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 11, Reason: drop out; Group 2 Number missing: 1, Reason: drop out	
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Castel 2009[94]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=47)
Countries and setting	Conducted in Spain; Setting: pain unit, single centre
Line of therapy	Not applicable
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR diagnostic criteria
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	Having a fibromyalgia diagnosis using the ACR diagnostic criteria; being between 18 years old and less than 60 years old; having a minimum of 6 months history of chronic pain; and having at least 6 years of education.
Exclusion criteria	One or more additional severe chronic medical pain conditions; significant suicidal ideation; severe psychopathology (e.g. psychosis); moderate to severe cognitive impairment; or the presence of pending litigation.
Recruitment/selection of patients	study described to all eligible participants, and those who elected to participate were asked to sign the study consent form
Age, gender and ethnicity	Age - Mean (SD): 44.2 (10.2) years. Gender (M:F): 2/37. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=18) Intervention 1: Psychological therapy - Cognitive behavioural therapy. CBT sessions included: didactic presentation of information about fibromyalgia and theory of pain perception, relaxation training,

Study	Castel 2009[94]
	cognitive restructuring, assertiveness training, behavioural goal setting, problems solving, and training in outcome generalization and maintenance of gains. In the last 20 minutes of the group CBT sessions, participants received a group session of relaxation training, which consisted of 5 minutes of relaxing different parts of the body by means of sensation awareness. Then, for 10 minutes, participants focused on diaphragmatic breathing and finally, feelings of well-being and general relaxation were suggested for the last 5 minutes. Following the first relaxation training session, the participant was given an audio CD of a relaxation exercise to listen to at home. Duration 12 x 90-minute sessions. Concurrent medication/care: standard medication management conventional pharmacological treatments including analgesics, antidepressants, sedatives and myorelaxants, as appropriate. Indirectness: Serious indirectness; Indirectness comment: intervention included relaxation component (n=12) Intervention 2: Usual care. Conventional pharmacological treatments including analgesics, antidepressants, sedatives and myorelaxants, as appropriate. Duration unclear. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact Questionnaire at unclear; Group 1: mean 60.96 (SD 22.69); n=16, Group 2: mean 66.14 (SD 18.81); n=7; Fibromyalgia Impact Questionnaire 0-100 Top=High is poor outcome; Comments: Baseline values: CBT 67.44 (16.08), usual care 72.14 (8.95)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: No statistically significant differences ; Group 1 Number missing: 2, Reason: did not complete treatment; Group 2 Number missing: 5, Reason: did not attend second visit

Protocol outcome 2: Discontinuation
- Actual outcome: Discontinuation at unclear; Group 1: 2/18, Group 2: 5/12; Comments: 2 CBT participants did not complete treatment and 5 control group participants did not come to a second visit.
Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: No statistically significant differences ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Pain reduction
- Actual outcome: Numeric rating scale at unclear; Group 1: mean 6.1 (SD 2.52); n=16, Group 2: mean 7 (SD 1.01); n=7; Numeric rating scale 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 6.16 (1.69), usual care 6.6 (1.18)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Study	Castel 2009[94]
Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: No statistically significant differences ; Group 1 Number missing: 2, Reason: did not complete treatment; Group 2 Number missing: 5, Reason: did not attend second visit	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Castel 2012[92]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=93)
Countries and setting	Conducted in Spain; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 14 weeks + 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR diagnostic criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	FM diagnosis according to ACR criteria; age between 18 and 65 years
Exclusion criteria	1 or more additional severe chronic medical pain conditions; significant suicidal ideation; severe psychopathology; moderate to severe cognitive impairment
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 49.6 (6.8) years. Gender (M:F): 96.8% female. Ethnicity: 100% white
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=34) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 14 weekly 120 minute group sessions including education about FM and pain perception theory, Schultz Autogenic training, cognitive restructuring techniques, CBT for insomnia, assertiveness training, activity pacing and pleasant activity scheduling training, goal setting and life values and relapse prevention. Participants given a manual describing contents of the programme, a CD to practice Schultz Autogenic training at home and record sheets to register practices of CBT contents. Duration 14 weeks. Concurrent medication/care: standard care:

Study	Castel 2012[92]
	conventional pharmacological treatments including analgesics, antidepressants, anticonvulsants and myorelaxants as appropriate. Indirectness: Serious indirectness; Indirectness comment: CBT intervention included pain education element (n=30) Intervention 2: Usual care. Standard care: conventional pharmacological treatments including analgesics, antidepressants, anticonvulsants and myorelaxants as appropriate. Duration study duration. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact Questionnaire at 6 months follow up (14 weeks + 6 months); Group 1: mean 50.5 (SD 3.5); n=34, Group 2: mean 68.5 (SD 3.7); n=30; Fibromyalgia Impact Questionnaire 0-100 Top=High is poor outcome; Comments: Baseline values: CBT 62.7 (2.8), usual care 66.1 (3)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: not reported ; Group 2 Number missing: 8, Reason: not reported

Protocol outcome 2: Sleep
- Actual outcome: Medical Outcomes Study Sleep Problems Index at 6 months follow up (14 weeks + 6 months); Group 1: mean 39.9 (SD 1.5); n=34, Group 2: mean 28 (SD 1.6); n=30; MOS sleep problems index 0-100 Top=High is poor outcome; Comments: Baseline values: CBT 30.4 (1.5), usual care 27.9 (1.6)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: not reported ; Group 2 Number missing: 8, Reason: not reported

Protocol outcome 3: Discontinuation
- Actual outcome: Number not completing treatment at 14 weeks ; Group 1: 3/34, Group 2: 1/30; Comments: reasons for non-completion not reported
Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: not reported ; Group 2 Number missing: 8, Reason: not reported

Protocol outcome 4: Pain reduction
- Actual outcome: Numeric rating scale at 6 months follow up (14 weeks + 6 months); Group 1: mean 5.7 (SD 0.4); n=34, Group 2: mean 6.8 (SD 0.4); n=30; Numeric rating scale 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 6.1 (0.3), usual care 6.9 (0.3)

Study	Castel 2012[92]
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: not reported ; Group 2 Number missing: 8, Reason: not reported	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services

Study	Castro 2012[96]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=95)
Countries and setting	Conducted in Brazil; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention time: 10 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnoses were made by two pain specialists according to the International Association for the Study of Pain (IASP) criteria
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	musculoskeletal pain diagnostic for at least three months, and those under medication treatment (anti-inflammatory and muscle relaxant in their usual doses), according to protocols
Exclusion criteria	chronic pain of oncological or neuropathic origin, or mixed (nociceptive and neuropathic pain including fibromyalgia); use of antidepressant or other drugs that act at the central nervous system; and being disabled to write
Recruitment/selection of patients	from a group of 400 patients, who were cared for in a single pain clinic
Age, gender and ethnicity	Age - Mean (SD): CBT 45.9 (8.1), standard care 48.7 (14.3). Gender (M:F): 10/83. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: Yes 3. Chronic visceral pain: No 4. Chronic widespread pain: No 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain

Study	Castro 2012[96]
	syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=48) Intervention 1: Psychological therapy - Cognitive behavioural therapy. Two-hour sessions of CBT per week, for ten weeks (no further details provided). Duration 10 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA (n=47) Intervention 2: Usual care. Standard care (no further details provided). Duration 10 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: SF36 functional capacity at 10 weeks ; Group 1: mean 36.7 (SD 20.4); n=48, Group 2: mean 32.9 (SD 18.7); n=45; SF36 functional capacity 0-100 Top=High is good outcome; Comments: Baseline values: CBT 28.6 (15), usual care 28.8 (22.1)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal
- Actual outcome: SF36 physical limitations at 10 weeks ; Group 1: mean 22.4 (SD 20.1); n=48, Group 2: mean 13.5 (SD 19); n=45; SF36 physical limitations 0-100 Top=High is good outcome; Comments: Baseline values: CBT 14.6 (24.9), usual care 11.9 (21.2)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal
- Actual outcome: SF36 pain at 10 weeks ; Group 1: mean 33.8 (SD 16); n=48, Group 2: mean 33.1 (SD 18.1); n=45; SF36 pain 0-100 Top=High is good outcome; Comments: Baseline values: CBT 25.1 (16), usual care 32.3 (16.5)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal
- Actual outcome: SF36 general state of health at 10 weeks ; Group 1: mean 42.2 (SD 21.8); n=48, Group 2: mean 33.1 (SD 18.2); n=45; SF36 general state of health 0-100 Top=High is good outcome; Comments: Baseline values: CBT 36 (19.6), usual care 30 (16.1)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal
- Actual outcome: SF36 vitality at 10 weeks ; Group 1: mean 35 (SD 19.9); n=48, Group 2: mean 28.2 (SD 18.5); n=45; SF36 vitality 0-100 Top=High is

Study	Castro 2012[96]
	good outcome; Comments: Baseline values: CBT 29.9 (19.8), usual care 28.1 (17.3) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: SF36 social aspects at 10 weeks ; Group 1: mean 50 (SD 22.8); n=48, Group 2: mean 44.7 (SD 18.1); n=45; SF36 social aspects 0-100 Top=High is good outcome; Comments: Baseline values: CBT 39.5 (21), usual care 36.7 (21.4) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: SF36 emotional limitations at 10 weeks ; Group 1: mean 31.8 (SD 30.1); n=48, Group 2: mean 20.7 (SD 29.3); n=45; SF36 emotional limitations 0-100 Top=High is good outcome; Comments: Baseline values: CBT 22 (28.9), usual care 12.2 (23.6) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: SF36 mental health at 10 weeks ; Group 1: mean 49.2 (SD 19.5); n=48, Group 2: mean 44.2 (SD 21.2); n=45; SF36 mental health 0-100 Top=High is good outcome; Comments: Baseline values: CBT 43 (20), usual care 40.3 (19.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal Protocol outcome 2: Discontinuation - Actual outcome: number not completing the study at 10 weeks ; Group 1: 0/48, Group 2: 2/47; Comments: reason for withdrawal not reported Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: Pain reduction - Actual outcome: Visual Analogue Scale at 10 weeks ; Group 1: mean 5.7 (SD 1.7); n=48, Group 2: mean 5.3 (SD 1.1); n=45; VAS 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 6.92 (2.11), usual care 6.38 (1.75) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: CBT group were all female, usual care group 78% female. Difference in SF36 pain domain - CBT group lower; Group 1 Number missing: 0; Group 2 Number missing: 2, Reason: withdrawal
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Edinger 2005[146]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=47)
Countries and setting	Conducted in USA; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 weeks + 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	aged 21 to 65 years, meet the American College of Rheumatology criteria for FM, insomnia, meet structured interview criteria for and have 60 minutes or more of total nocturnal wake time on average over 1week of sleep log monitoring
Exclusion criteria	pregnant, breastfeeding, or not practicing contraception; having a comorbid sleep-disruptive medical condition; meeting structured interview criteria for Axis 1 depressive disorder, anxiety or substance abuse disorder; having a severe hypnotic dependence; symptoms of sleep apnea, restless leg syndrome or circadian rhythm disorder; apnea-hypnopnea index or periodic limb movement-related arousal index of 15 or more per hour on a screening polysomnogram
Recruitment/selection of patients	primarily through newspaper advertisements
Age, gender and ethnicity	Age - Mean (SD): 48.6 (8.2). Gender (M:F): 2/45. Ethnicity: 44 white, 2 African American, 1 Asian
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: Not stated / Unclear 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Extra comments	NA
Indirectness of population	No indirectness: NA
Interventions	(n=18) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 6 weekly individual sessions (1st session 45-60 minutes, subsequent sessions 15-30 minutes) led by 2 licensed clinical psychologists. During the initial session, recipients listened to an audiocassette cognitive therapy module designed to

Study	Edinger 2005[146]
	correct misconceptions about sleep needs and the effects of aging, circadian rhythms, and sleep loss on sleep/wake functioning. The therapist then provided verbal and written (pamphlet) stimulus control instructions encouraging the following: (a) a standard rising time, (b) exiting bed during extended awakenings, (c) using the bedroom only for sleep and sex, and (d) avoiding daytime naps. An initial time in bed prescription set at the average baseline log sleep time plus 30 minutes was also provided to each patient. Remaining sessions entailed reviewing instructions and adjusting TIB. Duration 6 weeks. Concurrent medication/care: continued ongoing medical care for FM. Indirectness: No indirectness; Indirectness comment: NA (n=18) Intervention 2: Psychological therapy - Sleep management/hygiene . 6 weekly individual sessions (1st session 45-60 minutes, subsequent sessions 15-30 minutes) led by 2 licensed clinical psychologists. During the initial session, recipients listened to an audiocassette that provided them generic sleep education (i.e., descriptions of sleep stages and sleep architecture).The therapist then provided verbal and written (pamphlet) instructions to (a) limit caffeine and alcohol, (b) engage in regular moderate exercise, (c) have a light bedtime snack (e.g., cheese or yogurt), and (d) keep the bedroom dark, quiet, and cool. During subsequent sessions, the therapist reviewed and individually tailored SH therapy recommendations to address adherence issues. Duration 6 weeks. Concurrent medication/care: continued ongoing medical care for FM. Indirectness: No indirectness; Indirectness comment: NA (n=11) Intervention 3: Usual care. No behavioural therapy but met weekly with a study coordinator to provide sleep log/actigraphy data and to complete questionnaires while continuing their ongoing FM medical care. After follow-up assessment, offered CBT. Duration 6 weeks. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (National Institute of Arthritis and Musculoskeletal and Skin Diseases)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus SLEEP MANAGEMENT/HYGEINE

Protocol outcome 1: Health related quality of life
- Actual outcome: SF36 mental composite score at 6 months follow up ; Group 1: mean 51.3 (SD 2.6); n=6, Group 2: mean 49.4 (SD 2.7); n=7; SF36 mental composite score 0-100 Top=High is good outcome; Comments: Baseline values: CBT 47.9 (3.6), 46.1 (3.3)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: not reported ; Group 2 Number missing: 11, Reason: not reported
- Actual outcome: SF36 mental composite score at 6 weeks; Group 1: mean 50.7 (SD 2.6); n=15, Group 2: mean 50.3 (SD 2.9); n=17; SF36 mental

Study	Edinger 2005[146]
composite score 0-100 Top=High is good outcome; Comments: Baseline values: CBT 47.9 (3.6), 46.1 (3.3) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: withdrew; Group 2 Number missing: 1, Reason: withdrew Protocol outcome 2: Sleep - Actual outcome: Insomnia Symptom Questionnaire at 6 weeks ; Group 1: mean 36.3 (SD 3.9); n=15, Group 2: mean 30.5 (SD 3.3); n=17; Insomnia Symptom Questionnaire not reported Top=High is poor outcome; Comments: Baseline values: CBT 49.3 (4.6), SH 54.9 (4) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: withdrew; Group 2 Number missing: 1, Reason: withdrew - Actual outcome: Insomnia Symptom Questionnaire at 6 months follow up ; Group 1: mean 34.7 (SD 2.8); n=6, Group 2: mean 31.3 (SD 3.1); n=7; Insomnia Symptom Questionnaire not reported Top=High is poor outcome; Comments: Baseline values: CBT 49.3 (4.6), SH 54.9 (4) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: not reported ; Group 2 Number missing: 11, Reason: not reported Protocol outcome 3: Discontinuation - Actual outcome: Number not completing post-treatment assessment at 6 weeks ; Group 1: 3/18, Group 2: 1/18; Comments: CBT: 2 patients completed baseline then withdrew, 1 patient withdrew after 1 CBT session; SH 1 patient completed baseline then withdrew Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA Protocol outcome 4: Pain reduction - Actual outcome: McGill Pain Questionnaire at 6 weeks ; Group 1: mean 27.6 (SD 3.8); n=15, Group 2: mean 23.7 (SD 4.4); n=17; McGill Pain Questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBT 30.6 (3.2), SH 27.6 (4.1) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 1, Reason: not reported - Actual outcome: McGill Pain Questionnaire at 6 months follow up ; Group 1: mean 28.8 (SD 3.6); n=6, Group 2: mean 22.4 (SD 3.9); n=7; McGill Pain Questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBT 30.6 (3.2), SH 27.6 (4.1) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: not reported ; Group 2 Number missing: 11, Reason: not reported RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE	

Study	Edinger 2005[146]
Protocol outcome 1: Health related quality of life - Actual outcome: SF36 mental composite score at 6 months follow up ; Group 1: mean 51.3 (SD 2.6); n=15, Group 2: mean 40 (SD 2.8); n=9; SF36 mental composite score 0-100 Top=High is good outcome; Comments: Baseline values: CBT 47.9 (3.6), usual care 51.3 (3.5) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: not reported ; Group 2 Number missing: 4, Reason: not reported - Actual outcome: SF36 mental composite score at 6 weeks; Group 1: mean 50.7 (SD 2.6); n=6, Group 2: mean 45.5 (SD 3.6); n=7; SF36 mental composite score 0-100 Top=High is good outcome; Comments: Baseline values: CBT 47.9 (3.6), usual care 51.3 (3.5) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: withdrew; Group 2 Number missing: 2, Reason: withdrew Protocol outcome 2: Sleep - Actual outcome: Insomnia Symptom Questionnaire at 6 weeks ; Group 1: mean 36.3 (SD 3.9); n=15, Group 2: mean 53.2 (SD 4.9); n=9; Insomnia Symptom Questionnaire not reported Top=High is poor outcome; Comments: Baseline values: 49.3 (4.6), usual care 53.6 (4.2) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: withdrew; Group 2 Number missing: 2, Reason: withdrew - Actual outcome: Insomnia Symptom Questionnaire at 6 months follow up ; Group 1: mean 34.7 (SD 2.8); n=6, Group 2: mean 52.9 (SD 5.4); n=7; Insomnia Symptom Questionnaire not reported Top=High is poor outcome; Comments: Baseline values: 49.3 (4.6), usual care 53.6 (4.2) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: not reported ; Group 2 Number missing: 4, Reason: not reported Protocol outcome 3: Discontinuation - Actual outcome: Number not completing post-treatment assessment at 6 weeks ; Group 1: 3/18, Group 2: 2/11; Comments: CBT: 2 patients completed baseline then withdrew, 1 patients withdrew after 1 session; usual care 2 patients completed baseline then withdrew Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA Protocol outcome 4: Pain reduction - Actual outcome: McGill Pain Questionnaire at 6 weeks ; Group 1: mean 27.6 (SD 3.8); n=15, Group 2: mean 34.4 (SD 4.1); n=9; McGill Pain Questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBT 30.6 (3.2), usual care 27.5 (5.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: withdrew; Group 2 Number missing: 2, Reason: withdrew - Actual outcome: McGill Pain Questionnaire at 6 months follow up ; Group 1: mean 28.8 (SD 3.6); n=7, Group 2: mean 34.1 (SD 4.9); n=7; McGill Pain

Study	Edinger 2005[146]
Questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBT 30.6 (3.2), usual care 27.5 (5.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: not reported ; Group 2 Number missing: 4, Reason: not reported RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SLEEP MANAGEMENT/HYGEINE versus USUAL CARE Protocol outcome 1: Health related quality of life - Actual outcome: SF36 mental composite score at 6 weeks; Group 1: mean 50.3 (SD 2.9); n=17, Group 2: mean 45.5 (SD 3.6); n=9; SF36 mental composite score 0-100 Top=High is good outcome; Comments: Baseline values: SH 46.1 (3.3), usual care 51.3 (3.5) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: withdrew; Group 2 Number missing: 2, Reason: withdrew - Actual outcome: SF36 mental composite score at 6 months follow up ; Group 1: mean 49.4 (SD 2.7); n=7, Group 2: mean 40 (SD 2.8); n=7; Comments: Baseline values: SH 46.1 (3.3), usual care 51.3 (3.5) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: not reported ; Group 2 Number missing: 4, Reason: not reported Protocol outcome 2: Sleep - Actual outcome: Insomnia Symptom Questionnaire at 6 weeks ; Group 1: mean 30.5 (SD 3.3); n=17, Group 2: mean 53.2 (SD 4.9); n=9; Insomnia Symptom Questionnaire not reported Top=High is poor outcome; Comments: Baseline values: SH 54.9 (4), usual care 53.6 (4.2) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: withdrew; Group 2 Number missing: 2, Reason: withdrew - Actual outcome: Insomnia Symptom Questionnaire at 6 months follow up ; Group 1: mean 31.3 (SD 3.1); n=7, Group 2: mean 52.9 (SD 5.4); n=7; Comments: Baseline values: SH 54.9 (4), usual care 53.6 (4.2) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: not reported ; Group 2 Number missing: 4, Reason: not reported Protocol outcome 3: Discontinuation - Actual outcome: Number not completing post-treatment assessment at 6 weeks ; Group 1: 1/18, Group 2: 2/11; Comments: completed baseline then withdrew Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA	

Study	Edinger 2005[146]
Protocol outcome 4: Pain reduction - Actual outcome: McGill Pain Questionnaire at 6 weeks ; Group 1: mean 23.7 (SD 4.4); n=17, Group 2: mean 34.4 (SD 4.1); n=9; McGill Pain Questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: SH 27.6 (4.1), usual care 27.5 (5.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: withdrew; Group 2 Number missing: 2, Reason: withdrew - Actual outcome: McGill Pain Questionnaire at 6 months follow up ; Group 1: mean 22.4 (SD 3.9); n=7, Group 2: mean 34.1 (SD 4.9); n=7; McGill Pain Questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: SH27.6 (4.1), usual care 27.5 (5.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: not reported ; Group 2 Number missing: 4, Reason: not reported	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services

Study (subsidiary papers)	EFFIGACT study trial: Luciano 2014[291] (Luciano 2017[290])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=156)
Countries and setting	Conducted in Spain; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR 1990 criteria for fibromyalgia
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18-65 years; could speak and read Spanish fluently; fulfilled ACR criteria for FM; no pharmacological treatment or agreement to discontinue use; no previous psychological treatment during the previous year
Exclusion criteria	severe axis I psychiatric disorders; severe somatic disorders that prevented them from carrying out psychological assessment; participation in other clinical trials
Recruitment/selection of patients	patients recruited from primary health care centers by GPs
Age, gender and ethnicity	Age - Mean (SD): ACT group: 48.88 (5.94), waiting list: 48.28 (5.71). Gender (M:F): Define. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Extra comments	stratified by presence of major depression
Indirectness of population	No indirectness: NA
Interventions	(n=51) Intervention 1: Psychological therapy - Acceptance and commitment therapy. 8 x 2.5 hour weekly group sessions; 10-15 patients; covering exercises and topics within the context of ACT practice and training; including various types of formal mindfulness practice; daily homework assignments of 15-30 minutes; led by a clinical psychologist . Duration 8 weeks. Concurrent medication/care: not reported. Indirectness: Serious indirectness; Indirectness comment: included mindfulness (n=53) Intervention 2: Usual care. Waiting list - no active treatment and offered preferred intervention at study conclusion. Duration 6 months. Concurrent medication/care: not reported. Indirectness: No

	indirectness; Indirectness comment: NA
Funding	Academic or government funding (Instituto de Salud Carlos III; European Union European Regional Development Funds)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ACCEPTANCE AND COMMITMENT THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: EQ-5D VAS at 8 weeks; Group 1: mean 66.2 (SD 8.64); n=51, Group 2: mean 51 (SD 10.69); n=53; EQ-5D VAS 0-100 Top=High is good outcome; Comments: Baseline values: ACT 50.88 (15.48), usual care 48.78 (12.76)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5, Reason: lack of efficacy (3), patient decision (2); Group 2 Number missing: 3, Reason: patient decision (3)
- Actual outcome: EQ-5D VAS at 6 months; Group 1: mean 63.33 (SD 10.23); n=51, Group 2: mean 51.17 (SD 11.76); n=53; EQ-5D VAS 0-100 Top=High is good outcome; Comments: Baseline values: ACT 50.88 (15.48), usual care 48.78 (12.76)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: lack of efficacy (3), patient decision (2), loss to follow up (1); Group 2 Number missing: 6, Reason: patient decision (6)
- Actual outcome: EQ-5D utility at 6 months; Group 1: mean 0.8 (SD 0.11); n=51, Group 2: mean 0.57 (SD 0.16); n=53; EQ-5D utility 0-1 Top=High is good outcome; Comments: Baseline values: ACT 0.58 (0.17), usual care 0.54 (0.15)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: lack of efficacy (3), patient decision (2), loss to follow up (1); Group 2 Number missing: 6, Reason: patient decision (6)

Protocol outcome 2: Psychological distress
- Actual outcome: Hospital Anxiety and Depression Scale anxiety at 8 weeks; Group 1: mean 8.28 (SD 2.38); n=51, Group 2: mean 11.36 (SD 3.8); n=53; HADS-anxiety 0-21 Top=High is poor outcome; Comments: Baseline values: ACT 12.67 (4.36), usual care 12.4 (4.31)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5, Reason: lack of efficacy (3), patient decision (2); Group 2 Number missing: 3, Reason: patient decision (3)
- Actual outcome: Hospital Anxiety and Depression Scale anxiety at 6 months; Group 1: mean 8.73 (SD 2.04); n=51, Group 2: mean 12.15 (SD 4.2); n=53; HADS-anxiety 0-21 Top=High is poor outcome; Comments: Baseline values: ACT 12.67 (4.36), usual care 12.4 (4.31)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: lack of efficacy (3), patient decision (2), loss to follow up (1); Group 2 Number missing: 6, Reason: patient decision (6)
- Actual outcome: Hospital Anxiety and Depression Scale depression at 8 weeks ; Group 1: mean 5.41 (SD 1.36); n=51, Group 2: mean 9.34 (SD 2.63); n=53; HADS-depression 0-21 Top=High is poor outcome; Comments: Baseline values: ACT 8 (2.88), usual care 9.23 (3.56)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

	Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5, Reason: lack of efficacy (3), patient decision (2); Group 2 Number missing: 3, Reason: patient decision (3) - Actual outcome: Hospital Anxiety and Depression Scale depression at 6 months ; Group 1: mean 5.84 (SD 1.6); n=51, Group 2: mean 9.32 (SD 3.04); n=53; HADS-depression 0-21 Top=High is poor outcome; Comments: Baseline values: ACT 8 (2.88), usual care 9.23 (3.56) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: lack of efficacy (3), patient decision (2), loss to follow up (1); Group 2 Number missing: 6, Reason: patient decision (6) Protocol outcome 3: Discontinuation - Actual outcome: Drop out before post-treatment assessment at 8 weeks; Group 1: 5/51, Group 2: 3/53; Comments: ACT: lack of efficacy (3), patient decision (2) usual care: patient decision (3) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: Pain reduction - Actual outcome: Visual Analogue Scale at 8 weeks ; Group 1: mean 48.07 (SD 10.5); n=51, Group 2: mean 64.28 (SD 15.76); n=53; VAS 0-100 Top=High is poor outcome; Comments: Baseline: ACT 65.43 (18.34), usual care 64.04 (18.72) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5, Reason: lack of efficacy (3), patient decision (2); Group 2 Number missing: 3, Reason: patient decision (3) - Actual outcome: Visual Analogue Scale at 6 months; Group 1: mean 49.58 (SD 10.98); n=51, Group 2: mean 64.36 (SD 15.34); n=53; VAS 0-100 Top=High is poor outcome; Comments: Baseline: ACT 65.43 (18.34), usual care 64.04 (18.72) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: lack of efficacy (3), patient decision (2), loss to follow up (1); Group 2 Number missing: 6, Reason: patient decision (6)
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Sleep

Study	Friesen 2017[165]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Canada; Setting: internet-based
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 8 weeks + 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosis by a physician
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	residents of Canada; 18 years or older; diagnosis of FM by a physician; pain >3 months; pain assessed by GP/specialist; clinically significant symptoms of FM (Fibromyalgia Impact Questionnaire score ≥42); at least mild symptoms of depression (Patient Health Questionnaire ≥5) or anxiety (Generalised Anxiety Disorder score ≥5)
Exclusion criteria	not reported
Recruitment/selection of patients	advertisements in newsletters, newspapers and social media and referrals from GPs, pharmacists, community medical clinicians and FM support groups across 10 provinces in Canada
Age, gender and ethnicity	Age - Mean (SD): 48 (11) years. Gender (M:F): 3/57. Ethnicity: white/caucasian 95%, Spanish/Hispanic/Latino 2%, mixed ethnicity 3%
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=30) Intervention 1: Psychological therapy - Cognitive behavioural therapy. The Pain Course - 5 online lessons (images and text in slide show format), lesson summaries (similar to a self-help book), homework assignments, additional resources and standardised automated weekly emails to reinforce course completion, encourage use of skills etc. Access to patient stories demonstrating skills. Weekly 5-10 minute telephone contact with a doctorate-level clinical psychology graduate student (supervised by a registered psychologist) to summarise content, answer questions, reinforce progress, encourage skills, but no therapeutic advice. Duration 8 weeks. Concurrent medication/care: not reported. Indirectness: No

Study	Friesen 2017[165]
	indirectness; Indirectness comment: NA (n=30) Intervention 2: Usual care. Waiting list - offered access to the pain course once the 8 week waiting period had elapsed. Duration 8 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	Academic or government funding (Canadian Institutes of Health Research, University of Regina, Saskatchewan Health Research Foundation, Rx & D Health Research Foundation.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: SF12 physical component at 8 weeks ; Group 1: mean 34.7 (SD 7.94); n=30, Group 2: mean 32.82 (SD 8.2); n=30; SF12 physical component 0-100 Top=High is good outcome; Comments: Baseline values: CBT 30.81 (7.82), usual care 32.17 (7.35)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 1 withdrawal, 4 could not be contacted; Group 2 Number missing: 3, Reason: could not be contacted
- Actual outcome: SF12 mental component at 8 weeks ; Group 1: mean 39.62 (SD 11.22); n=30, Group 2: mean 38.95 (SD 9.16); n=30; SF12 mental component 0-100 Top=High is good outcome; Comments: Baseline values: CBT 34.42 (8.52), usual care 36.12 (7.6)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 1 withdrawal, 4 could not be contacted; Group 2 Number missing: 3, Reason: could not be contacted

Protocol outcome 2: Psychological distress
- Actual outcome: Hospital Anxiety and Depression Scale - depression at 8 weeks ; Group 1: mean 7.97 (SD 3.55); n=30, Group 2: mean 10.17 (SD 3.42); n=30; HADS depression 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 9.9 (3.77), usual care 9.97 (3.82)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 1 withdrawal, 4 could not be contacted; Group 2 Number missing: 3, Reason: could not be contacted
- Actual outcome: Hospital Anxiety and Depression Scale - anxiety at 8 weeks ; Group 1: mean 9.22 (SD 4.33); n=30, Group 2: mean 10.43 (SD 4.69); n=30; HADS anxiety 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 11.6 (4), usual care 10.17 (3.98)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 1 withdrawal, 4 could not be contacted; Group 2 Number missing: 3, Reason: could not be contacted

Protocol outcome 3: Pain interference
- Actual outcome: Brief Pain Inventory - interference at 8 weeks ; Group 1: mean 5.46 (SD 2.11); n=30, Group 2: mean 7.32 (SD 1.58); n=30; BPI

Study	Friesen 2017[165]
interference 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 6.56 (1.9), usual care 7.48 (1.71) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 1 withdrawal, 4 could not be contacted; Group 2 Number missing: 3, Reason: could not be contacted Protocol outcome 4: Pain self-efficacy - Actual outcome: Pain Self-Efficacy Questionnaire at 8 weeks ; Group 1: mean 29.99 (SD 11.1); n=30, Group 2: mean 22 (SD 10.18); n=30; Pain self-efficacy questionnaire 0-60 Top=High is good outcome; Comments: Baseline values: CBT 22.93 (9.78), usual care 19.83 (10.25) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 1 withdrawal, 4 could not be contacted; Group 2 Number missing: 3, Reason: could not be contacted Protocol outcome 5: Discontinuation - Actual outcome: Withdrawal at 8 weeks ; Group 1: 1/30, Group 2: 0/30; Comments: Reason for withdrawal : not a good time Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 6: Pain reduction - Actual outcome: Brief Pain Inventory - intensity at 8 weeks ; Group 1: mean 4.99 (SD 1.66); n=30, Group 2: mean 6.28 (SD 1.28); n=30; Brief pain inventory - pain severity 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 5.45 (1.1), usual care 6.02 (1.39) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: 1 withdrawal, 4 could not be contacted; Group 2 Number missing: 3, Reason: could not be contacted	
Protocol outcomes not reported by the study	Physical function ; Use of healthcare services ; Sleep

Study	Funch 1984[166]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=57)
Countries and setting	Conducted in USA; Setting: relaxation therapy delivered in therapist's office; biofeedback not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 weeks + 2 years

Study	Funch 1984[166]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosis based on physical exam, history and report from referring dentist of physician
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	TMJ pain of at least 2 year's duration
Exclusion criteria	when there was doubt of possible internal joint derangements, referral was made to experts; consulting dentist ruled out poor fitting dentures, small fractures in restorations and impacted wisdom teeth
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): relaxation 35.6 (12.7) years, biofeedback 43 (15) years. Gender (M:F): not reported . Ethnicity: not reported
Further population details	1. Chronic orofascial pain: Yes 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: No 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=27) Intervention 1: Psychological therapy - Relaxation techniques. 20 minute recorded relaxation tape once a week teaching general relaxation techniques. 3 different tapes and encouraged to practice daily muscle relaxation Duration average 12 weeks. Concurrent medication/care: discussions about possible causes of TMJ pain; emphasis placed on oral habits as etiological factors; discussion of progress and theories and facts associated with the disorder and therapy. Indirectness: No indirectness; Indirectness comment: NA (n=30) Intervention 2: Psychological therapy - Biofeedback. Grass Model 7 polygraph with 4 7P3 amplifiers and either a Dana Model 4600 Digital Multimeter with multiple range shift or a Wavetech Model 180 sweep/function generator was used. Output from integrated amplifiers with a 0.5-s time constant was fed directly into one of the 2 instruments. Silver-silver chloride electrodes were taped bilaterally over the masseteric area. At the initial session the patient was asked to bite down and observe the numbers on the meter increase or the frequency of the audio tone increase. Patients then received 10 1 minute trials with a minimum of 15-s inter-trial interval. Also given general instructions to practice relaxation for 20 minutes each day. Duration average 12 weeks. Concurrent medication/care: discussions about possible causes of TMJ pain; emphasis placed on oral habits as etiological factors; discussion of progress and theories and facts associated with the disorder and therapy. Indirectness: Serious indirectness; Indirectness comment: included relaxation elements

Study	Funch 1984[166]
Funding	Academic or government funding (National Institute of Dental Research)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RELAXATION TECHNIQUES versus BIOFEEDBACK Protocol outcome 1: Pain reduction - Actual outcome: Percentage pain reduction at Post treatment (12 weeks); Group 1: mean 56 (SD 40); n=27, Group 2: mean 36 (SD 43); n=30; Comments: Baseline pain severity (0-25): relaxation 15.1 (5.6), biofeedback 16.7 (5.3) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Discontinuation

Study	Goldway 2019[187]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=43)
Countries and setting	Conducted in Israel; Setting: single centre - brain institute, medical center
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 weeks (5 weeks + 1 week)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: diagnosis of Fibromyalgia according to the American College of Rheumatology criteria
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	diagnosis of Fibromyalgia according to the American College of Rheumatology 2010 criteria which was confirmed by a clinical interview and physical examination by an expert rheumatologist or pain specialist
Exclusion criteria	other chronic pain syndromes, major neuropsychiatric illness and recently changed/initiated pharmacotherapy
Recruitment/selection of patients	recruited from a Fibromyalgia clinic and from an Institute of Pain Medicine Medical Center
Age, gender and ethnicity	Age - Mean (SD): intervention 35.5 (12.6) years, sham 35.9 (10.6) years. Gender (M:F): 3/31. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain

Study	Goldway 2019[187]
	syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=31) Intervention 1: Psychological therapy - Biofeedback. Neurofeedback - 10 biweekly sessions, each composed of training to down-regulate Amygdala Electrical fingerprint using an auditory interface (in which the neural signal correlated with the volume of a soft piano tune; sessions 1, 3 & 5), an animated scenario interface (a 3D audio-visual animated scenario in which the neural signal is correlated with the level of unrest in a scenario where virtual characters in a waiting room become impatient, leave their seats and gesture loudly at the front desk receptionist; sessions 2, 4 & 6), or both (sessions 7, 8, 9 & 10). Within each session, NF trials contained two conditions: rest and regulate. Participants were instructed to modulate the interface only during the regulate condition. The real-NF group received feedback reflecting their Amyg-EFP signal level modulation. Duration 5 weeks. Concurrent medication/care: Not reported. SSRI/SNRI 16%, Gabapentinoids 24%, Cannabis 20%, Analgesics 8%, Miscellaneous 12%. Indirectness: No indirectness; Indirectness comment: NA (n=12) Intervention 2: Attention control . Sham neurofeedback. 10 biweekly sessions, each composed of training to down-regulate Amygdala Electrical fingerprint using an auditory interface (in which the neural signal correlated with the volume of a soft piano tune; sessions 1, 3 & 5), an animated scenario interface (a 3D audio-visual animated scenario in which the neural signal is correlated with the level of unrest in a scenario where virtual characters in a waiting room become impatient, leave their seats and gesture loudly at the front desk receptionist; sessions 2, 4 & 6), or both (sessions 7, 8, 9 & 10). Within each session, NF trials contained two conditions: rest and regulate. Participants were instructed to modulate the interface only during the regulate condition. The control group received feedback reflecting a pre-recorded Amyg-EFP signal obtained from another successful participant in the real-NF group, indicating approximately 85 percent success in each session. Duration 5 weeks. Concurrent medication/care: Not reported. SSRI/SNRI 33.33%, Gabapentinoids 33.33%, Cannabis 22.22%, Analgesics 0%, Miscellaneous 11%. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (Israeli Ministry of Science, Technology and Space; Israeli Pain Association; European Union's Seventh Framework Programme for research, technological development and demonstration)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BIOFEEDBACK versus ATTENTION CONTROL

Protocol outcome 1: Psychological distress
- Actual outcome: Beck depression inventory at 5 weeks (immediately post intervention); Group 1: mean 3.1 (SD 6); n=25, Group 2: mean 3.8 (SD 10.1);

Study	Goldway 2019[187]
	n=9; Beck depression inventory 0-63 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 3, Reason: not reported - Actual outcome: Beck depression inventory at mean 16.2 (8.72) months ; Group 1: mean 6.5 (SD 5.4); n=23, Group 2: mean 2.6 (SD 11.6); n=9; Beck depression inventory 0-63 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: not reported ; Group 2 Number missing: 3, Reason: not reported - Actual outcome: Trait anxiety (STAI-T) at 5 weeks (immediately post intervention) ; Group 1: mean 3.9 (SD 8.5); n=25, Group 2: mean 4.2 (SD 12.6); n=9; State trait anxiety inventory - trait 20-80 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 3, Reason: not reported - Actual outcome: Trait anxiety (STAI-T) at mean 16.2 (8.72) months ; Group 1: mean 5.5 (SD 8.1); n=23, Group 2: mean 2 (SD 10.3); n=9; State trait anxiety inventory - trait 20-80 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: not reported ; Group 2 Number missing: 3, Reason: not reported Protocol outcome 2: Sleep - Actual outcome: Pittsburgh sleep quality index at 5 weeks (immediately post intervention) ; Group 1: mean 0.4 (SD 4.4); n=25, Group 2: mean 1.2 (SD 4.4); n=9; Pittsburgh sleep quality index 0-21 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 3, Reason: not reported - Actual outcome: Pittsburgh sleep quality index at mean 16.2 (8.72) months ; Group 1: mean 1.5 (SD 4.1); n=23, Group 2: mean -0.5 (SD 4.8); n=9; Pittsburgh sleep quality index 0-21 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: not reported ; Group 2 Number missing: 3, Reason: not reported Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation at 5 weeks ; Group 1: 6/31, Group 2: 3/12; Comments: reasons for discontinuation not reported Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA

Study	Goldway 2019[187]
Protocol outcome 4: Pain reduction - Actual outcome: VAS at 5 weeks ; Group 1: mean 0.2 (SD 1.6); n=25, Group 2: mean 1.1 (SD 1.5); n=9; VAS 0-10 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: not reported ; Group 2 Number missing: 3, Reason: not reported - Actual outcome: VAS at mean 16.2 (8.72) months ; Group 1: mean 1.1 (SD 2.1); n=23, Group 2: mean 0 (SD 1.5); n=9; VAS 0-10 Top=High is poor outcome; Comments: Baseline values not reported Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 8, Reason: not reported ; Group 2 Number missing: 3, Reason: not reported	
Protocol outcomes not reported by the study	Health related quality of life; Physical function ; Pain interference; Pain self-efficacy; Use of healthcare services

Study	Hallman 2011[201]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=24)
Countries and setting	Conducted in Sweden; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention time: 10 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of neck-shoulder pain and stress related symptoms were evaluated by a specialized psychologist
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	age between 20 and 50 years and perceived pain and/or other symptoms of muscle discomfort primarily located to the neck-shoulder area, observed for at least 6 months and persistently over the last six consecutive weeks
Exclusion criteria	regular use of medications known to affect ANS function or pain perception two weeks prior to participation including antidepressants, benzodiazepines, anti-inflammatory medications and beta-blockers. Subjects

Study	Hallman 2011[201]
	reporting diagnoses of rheumatism, diabetes, traumatic musculoskeletal system damage, chronic neurological and endocrinology syndromes as well as hypertension, coronary artery diseases, substance abuse and overweight (BMI >30)
Recruitment/selection of patients	recruited through the stress clinic (PBMSweden), advertisements on the website, recommendations from associated physiotherapists and invitations to public service employees in two cities north of Stockholm, Sweden
Age, gender and ethnicity	Age - Mean (range): 40.5 (25-50) years. Gender (M:F): 2/22. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: Yes 3. Chronic visceral pain: No 4. Chronic widespread pain: No 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=12) Intervention 1: Psychological therapy - Biofeedback. Resonance heart rate variability biofeedback led by a licensed psychologist: first training session to assess resonance frequency. Session 2–9, respiratory pacer was set at the particular frequency found in the previous session. Each session included four five-minute periods of resonant breathing with two minutes of rest after each period. Subjects received visual HRV feedback during resonance frequency breathing. They were instructed to try to maximize their peak-to-peak HRV as well as to attain the phase between respiration and HRV changes as closely as possible. Between sessions, subjects were instructed to practice paced breathing for at least 15 min a day, five days a week using a regular watch as a pacer and also given pacer software to use on their home computer. Duration 10 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA (n=12) Intervention 2: Usual care. Instructed to perform their usual activities and were not refrained from any pharmacological or behavioural treatment, besides those stated as exclusion criteria. Duration 10 weeks. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA Comments: Control group took part in the breathing protocol in Session 1 and 10 in order to measure changes in heart rate variability
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BIOFEEDBACK versus USUAL CARE Protocol outcome 1: Health related quality of life	

Study	Hallman 2011[201]
	- Actual outcome: SF36 physical function at 10 weeks ; Group 1: mean 92.5 (SD 8); n=12, Group 2: mean 84.5 (SD 15); n=10; SF36 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 89.6 (7), usual care 77.5 (17) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment - Actual outcome: SF36 role physical at 10 weeks ; Group 1: mean 77.1 (SD 42); n=12, Group 2: mean 67.5 (SD 39); n=10; SF36 0-100 Top=High is good outcome; Comments: Baseline values: 60.4 (43), usual care 57.5 (38) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment - Actual outcome: SF36 bodily pain at 10 weeks ; Group 1: mean 71.8 (SD 18); n=12, Group 2: mean 58.4 (SD 39); n=10; SF36 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 46.5 (21), usual care 49.9 (18) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment - Actual outcome: SF36 general health at 10 weeks ; Group 1: mean 63.4 (SD 24); n=12, Group 2: mean 60.5 (SD 25); n=10; SF36 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 60.8 (22), usual care 61.4 (23) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment - Actual outcome: SF36 vitality at 10 weeks ; Group 1: mean 57.5 (SD 22); n=12, Group 2: mean 48 (SD 30); n=10; SF36 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 37.1 (22), usual care 49 (27) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment - Actual outcome: SF36 social function at 10 weeks ; Group 1: mean 90.6 (SD 12); n=12, Group 2: mean 82.5 (SD 24); n=10; SF36 0-100 Top=High is good outcome; Comments: Baseline values: 76 (23), 85 (24) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment - Actual outcome: SF36 role emotional at 10 weeks ; Group 1: mean 83.3 (SD 33); n=12, Group 2: mean 83.3 (SD 28); n=10; SF36 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 72.2 (40), usual care 86.7 (28) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment - Actual outcome: SF36 mental health at 10 weeks ; Group 1: mean 72.1 (SD 18); n=12, Group 2: mean 72.8 (SD 22); n=10; SF36 0-100 Top=High is good outcome; Comments: Baseline values: biofeedback 66.3 (20), usual care 69.9 (18)

Study	Hallman 2011[201]
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment Protocol outcome 2: Physical function - Actual outcome: Neck disability index at 10 weeks ; Group 1: mean 14 (SD 10); n=12, Group 2: mean 20.6 (SD 14.4); n=10; Neck disability index 0-100 Top=High is poor outcome; Comments: Baseline values: biofeedback 21.3 (7.5), usual care 25.6 (15.2) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment Protocol outcome 3: Psychological distress - Actual outcome: Hospital anxiety and depression scale - anxiety at 10 weeks ; Group 1: mean 5.5 (SD 3.06); n=12, Group 2: mean 6.45 (SD 3.59); n=10; HADS anxiety 0-20 Top=High is poor outcome; Comments: Baseline values: biofeedback 6.83 (2.52), usual care 7.64 (4.15) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment - Actual outcome: Hospital anxiety and depression scale - depression at 10 weeks ; Group 1: mean 2.42 (SD 2.71); n=12, Group 2: mean 4.91 (SD 4.46); n=10; HADS depression 0-20 Top=High is poor outcome; Comments: Baseline values: biofeedback 3.5 (3.37), usual care 6.27 (5.18) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment Protocol outcome 4: Discontinuation - Actual outcome: Drop out at 10 weeks ; Group 1: 0/12, Group 2: 1/12; Comments: Reason for drop out not reported Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA Protocol outcome 5: Pain reduction - Actual outcome: Borg CR10 scale at 10 weeks ; Group 1: mean 1.7 (SD 1.4); n=12, Group 2: mean 2 (SD 1.7); n=10; Borg CR10 0-10 Top=High is poor outcome; Comments: Baseline values: biofeedback 2.6 (1.3), usual care 2.5 (1.1) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 2, Reason: 1 drop out, 1 did not complete post treatment assessment	
Protocol outcomes not reported by the study	Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Hedman-lagerlof 2018[215 216]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=140)
Countries and setting	Conducted in Sweden; Setting: internet based
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 10 weeks + 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: physician diagnosis
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	≥18 years; confirmed FM diagnosis; internet access; agreement to refrain from other psychological treatment for study duration; psychotropic medication allowed if dose had been stable for at least 6 weeks
Exclusion criteria	>29 weeks gestation; psychosis; severe physical illness; severe depression; suicidal ideation; alcohol/substance abuse/dependency; insufficient computer/language skills
Recruitment/selection of patients	self-referred by study web page; study advertised in a national newspaper, social media and FM patient organisations
Age, gender and ethnicity	Age - Mean (SD): 50.3 (10.9). Gender (M:F): 3/137. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=70) Intervention 1: Psychological therapy - Cognitive behavioural therapy. Internet-delivered exposure therapy - 8 modules on the role of avoidance behaviours; psychoeducation about exposure; identification of personal avoidance behaviours; design of individually tailored exposure exercises based on refraining from avoidance behaviours and approaching situations or behaviours normally avoided. Progress monitored by a therapist (licensed psychologists/graduate psychology students), regular contact 1-3 times/week through text messages to guide, assist with problem-solving and remind participants to logon if they had been inactive. Relapse prevention program including an intervention on life values and scheduled mindfulness practices as a way to facilitate exposure. Duration 10 weeks. Concurrent medication/care: not reported. Indirectness: Serious indirectness; Indirectness comment: included education and mindfulness

Study	Hedman-lagerlof 2018[215 216]
	(n=70) Intervention 2: Usual care. Waiting list. Duration 10 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA
Funding	Other (Fredrick and Ingrid Thuring Foundation, Soderstrom-Konig Foundation, Stockholm County Council and Karolinska Institutet)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: EQ-5D at 10 weeks ; Group 1: mean 0.6 (SD 0.3); n=70, Group 2: mean 0.44 (SD 0.32); n=70; EQ-5D 0-1 Top=High is good outcome; Comments: Baseline vales: CBT 0.48 (0.3), waiting list 0.41 (0.32)

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: not reported ; Group 2 Number missing: 0, Reason: NA

Protocol outcome 2: Physical function
- Actual outcome: WHO Disability Assessment Schedule at 10 weeks ; Group 1: mean 24.64 (SD 17.71); n=70, Group 2: mean 40.83 (SD 17.96); n=70; WHO Disability Assessment Schedule 0-100 Top=High is poor outcome; Comments: Baseline values: CBT 32.23 (15.33), waiting list 38.63 (16.25)

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: not reported ; Group 2 Number missing: 0, Reason: NA

Protocol outcome 3: Psychological distress
- Actual outcome: Patient Health Questionnaire-9 at 10 weeks ; Group 1: mean 7.12 (SD 5.57); n=70, Group 2: mean 10.57 (SD 4.81); n=70; Patient Health Questionnaire-9 0-27 Top=High is poor outcome; Comments: Baseline values: CBT 10.46 (5.48), waiting list 10.8 (5.27)

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: not reported ; Group 2 Number missing: 0, Reason: NA
- Actual outcome: GAD-7 at 10 weeks ; Group 1: mean 4.29 (SD 4.98); n=70,

Risk of bias: All domain - ; Indirectness of outcome: No indirectness, Comments: NA

Protocol outcome 4: Sleep
- Actual outcome: Insomnia Severity Index at 10 weeks ; Group 1: mean 13.1 (SD 6.93); n=70, Group 2: mean 16.06 (SD 6.49); n=70; Insomnia severity index 0-28 Top=High is poor outcome; Comments: Baseline values: CBT 16.11 (5.38), waiting list 15.44 (5.54)

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: not reported ; Group 2 Number missing:

Study	Hedman-lagerlof 2018[215 216]
0, Reason: NA Protocol outcome 5: Discontinuation - Actual outcome: Discontinuation at 10 weeks ; Group 1: 9/70, Group 2: 0/70; Comments: Reasons for non-participation not reported Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: Pain reduction - Actual outcome: Fibromyalgia Impact Questionnaire pain sub scale at 10 weeks ; Group 1: mean 4.19 (SD 3.25); n=70, Group 2: mean 6.7 (SD 2.57); n=70; FIQ pain sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 5.95 (2.21), waiting list 6.29 (2.03) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Pain interference ; Pain self-efficacy ; Use of healthcare services

Study (subsidiary papers)	Jensen 2012[233] (Wicksell 2013[564])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=43)
Countries and setting	Conducted in Sweden; Setting: pain clinic
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 weeks + 3-4 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR classification criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18-55 years old; fulfilling ACR criteria for FM; weekly self-reported average pain intensity >40 (VAS 0-100)
Exclusion criteria	left handed; pregnant; breastfeeding; metal implants; claustrophobia; treatments that could influence pain perception (antidepressants, mood stabilizers, analgesics, strong opioids, anticonvulsants, centrally acting relaxants, injections, biofeedback, TENS) had to be discontinued before the study; severe psychiatric comorbidity; ongoing or planned (within 6 months) CBT
Recruitment/selection of patients	referral from primary care physicians

Study (subsidiary papers)	Jensen 2012[233] (Wicksell 2013[564])
Age, gender and ethnicity	Age - Mean (SD): 45.1 (6.6) years. Gender (M:F): 0/43. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=25) Intervention 1: Psychological therapy - Acceptance and commitment therapy. weekly 90 minute sessions in groups of 6 participants conducted by 2 CBT-trained psychologists (10 sessions) and 1 CBT-trained physician (2 sessions) organised in to 4 phases - phase 1 (preparing for behaviour change) dysfunctional character of long-standing pain syndromes were discussed; phase 2 (shifting perspective) clarification of individual life values combined with an exercise in evaluating previous strategies to reduce pain; phase 3 (values oriented behaviour activation) short and long term behaviour goals based on identified life values; phase 4 (acceptance and cognitive defusion) emphasis on utility of a more flexible behavioural repertoire in relation to pain and distress, strategies practiced in sessions and in homework assignments . Duration 12 weeks. Concurrent medication/care: small doses of NSAIDs allowed as rescue medication if discontinued 48 hours prior to study assessments. Indirectness: No indirectness; Indirectness comment: NA (n=18) Intervention 2: Usual care. Waiting list. Duration study duration. Concurrent medication/care: small doses of NSAIDs allowed as rescue medication if discontinued 48 hours prior to study assessments. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (Swedish Society for Medical Research; Swedish research Council; Swedish Council for Working Life and Social Research; Stockholm County Council; Swedish Rheumatism Association)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ACCEPTANCE AND COMMITMENT THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: SF36 physical component at 12 weeks ; Group 1: mean 28.4 (SD 8); n=20, Group 2: mean 30.1 (SD 9.9); n=16; SF36 physical component 0-100 Top=High is good outcome; Comments: Baseline values: ACT 25.2 (6.6), usual care 29.1 (9.9)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 5, Reason: withdrawal; Group 2 Number missing: 2, Reason: withdrawal
- Actual outcome: SF36 mental component at 12 weeks ; Group 1: mean 45.6 (SD 8.7); n=20, Group 2: mean 36.8 (SD 12.9); n=16; SF36 mental component 0-100 Top=High is good outcome; Comments: Baseline values: ACT 40.1 (9.1), usual care 38.6 (12.4)

Study (subsidiary papers)	Jensen 2012[233] (Wicksell 2013[564])
	Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 5, Reason: withdrawal; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: SF36 physical component at 6 months (3 months follow up); Group 1: mean 28.4 (SD 8.4); n=19, Group 2: mean 31.1 (SD 10.8); n=14; SF36 physical component 0-100 Top=High is good outcome; Comments: Baseline values: ACT 25.2 (6.6), usual care 29.1 (9.9) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrawal; Group 2 Number missing: 4, Reason: withdrawal - Actual outcome: SF36 mental component at 6 months (3 months follow up); Group 1: mean 46 (SD 9.4); n=19, Group 2: mean 34.7 (SD 12.2); n=14; SF36 mental component 0-100 Top=High is good outcome; Comments: Baseline values: ACT 40.1 (9.1), usual care 38.6 (12.4) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrawal; Group 2 Number missing: 4, Reason: withdrawal Protocol outcome 2: Psychological distress - Actual outcome: Beck Depression Inventory at 12 weeks ; Group 1: mean 11.7 (SD 6); n=20, Group 2: mean 14.8 (SD 7.8); n=16; Beck Depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: ACT 15.9 (6.3), usual care 19.3 (13) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 5, Reason: withdrawal; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: Beck Depression Inventory at 6 months (3 months follow up) ; Group 1: mean 10.7 (SD 4.8); n=19, Group 2: mean 16.4 (SD 12.5); n=14; Beck depression inventory 0-63 Top=High is poor outcome; Comments: Baseline values: ACT 15.9 (6.3), usual care 19.3 (13) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrawal; Group 2 Number missing: 4, Reason: withdrawal - Actual outcome: Spielberger Trait-State Anxiety Inventory - state at 12 weeks ; Group 1: mean 40.8 (SD 12.3); n=20, Group 2: mean 47.6 (SD 14.4); n=16; state anxiety 20-80 Top=High is poor outcome; Comments: Baseline values: ACT 45.7 (12), usual care 48 (15.1) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 5, Reason: withdrawal; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: Spielberger Trait-State Anxiety Inventory - state at 6 months (3 months follow up); Group 1: mean 39.8 (SD 7.5); n=19, Group 2: mean 45.4 (SD 12.8); n=14; state anxiety 20-80 Top=High is poor outcome; Comments: Baseline values: ACT 45.7 (12), usual care 48 (15.1) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrawal; Group 2 Number missing: 4, Reason: withdrawal - Actual outcome: Spielberger Trait-State Anxiety Inventory - trait at 12 weeks ; Group 1: mean 40.6 (SD 10.4); n=20, Group 2: mean 49.3 (SD 13.5); n=16; trait anxiety 20-80 Top=High is poor outcome; Comments: Baseline values: ACT 45.6 (9.4), usual care 50.9 (14.5)

Study (subsidiary papers)	Jensen 2012[233] (Wicksell 2013[564])
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 5, Reason: withdrawal; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: Spielberger Trait-State Anxiety Inventory - trait at 6 months (3 months follow up); Group 1: mean 39.9 (SD 9.8); n=19, Group 2: mean 47.9 (SD 11.8); n=14; trait anxiety 20-80 Top=High is poor outcome; Comments: Baseline values: ACT 45.6 (9.4), usual care 50.9 (14.5) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrawal; Group 2 Number missing: 4, Reason: withdrawal Protocol outcome 3: Pain interference - Actual outcome: Pain Disability Index at 12 weeks ; Group 1: mean 27.2 (SD 13.2); n=20, Group 2: mean 37.8 (SD 15.6); n=16; Pain disability index 0-70 Top=High is poor outcome; Comments: Baseline values: ACT 40 (10.9), usual care 39 (10.2) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 5, Reason: withdrawal; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: Pain Disability Index at 6 months (3 months follow up); Group 1: mean 28.1 (SD 12.5); n=19, Group 2: mean 38.1 (SD 15.4); n=14; Pain disability index 0-70 Top=High is poor outcome; Comments: Baseline values: ACT 40 (10.9), usual care 39 (10.2) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrawal; Group 2 Number missing: 4, Reason: withdrawal Protocol outcome 4: Discontinuation - Actual outcome: Withdrawal during treatment phase at 12 weeks ; Group 1: 3/23, Group 2: 1/17; Comments: Reasons for withdrawal not reported Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Pain reduction - Actual outcome: Numeric rating scale at 12 weeks ; Group 1: mean 4 (SD 1.1); n=20, Group 2: mean 4.4 (SD 1.2); n=16; numeric rating scale 0-10 Top=High is poor outcome; Comments: Baseline values: ACT 4.2 (1), usual care 4.3 (1.1) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 5, Reason: withdrawal; Group 2 Number missing: 2, Reason: withdrawal - Actual outcome: Numeric rating scale at 6 months (3 months follow up) ; Group 1: mean 3.9 (SD 1.1); n=19, Group 2: mean 4.8 (SD 1.1); n=14; numeric rating scale 0-10 Top=High is poor outcome; Comments: Baseline values: ACT 4.2 (1), usual care 4.3 (1.1) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Study (subsidiary papers)	Jensen 2012[233] (Wicksell 2013[564])
Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: comparable for baseline outcome measures but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrawal; Group 2 Number missing: 4, Reason: withdrawal	
Protocol outcomes not reported by the study	Physical function ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Karlsson 2015[245]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=48)
Countries and setting	Conducted in Sweden; Setting: municipality in central Sweden
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 18 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FM diagnosis
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18–64 years, being Swedish-speaking, and fulfilment of the 1990 ACR criteria (generalized pain for more than three months, distributed in all four body quadrants, and at least 11 tender points in typical locations)
Exclusion criteria	major psychiatric or somatic disease, and substance abuse
Recruitment/selection of patients	advertising in the local daily newspaper and an information meeting with the local branch of the Fibromyalgia Patient Association
Age, gender and ethnicity	Age - Mean (SD): CBT: 48.3 (11.5) years, usual care: 48.8 (6.5) years. Gender (M:F): 0/48. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged 16-25 years 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=24) Intervention 1: Psychological therapy - Cognitive behavioural therapy. CBT stress management programme - 20 x 3 hour group CBT sessions (5-7 per group) over 6 months plus 3 x 3 hour booster sessions over the following 6 months by 2 psychologists trained in CBT. Components included knowledge,

Study	Karlsson 2015[245]
	self-monitoring, behavioural skills training, cognitive restructuring, and life value issues. Therapeutic material included case illustrations, audio- visual material, readings, hand-outs, exercises, and thematic discussions. Homework assignments were applied between each session and included self-monitoring by simple diaries as well as a booklet with behavioural and cognitive exercises. A short relaxation technique (Jacobsen's progressive relaxation technique) was taught. Duration 12 months. Concurrent medication/care: Patients' local physicians were responsible for the every-day care of the patients. No restrictions in changing medication or other treatment modalities. Indirectness: Serious indirectness; Indirectness comment: included a relaxation element (n=24) Intervention 2: Usual care. Patients' local physicians were responsible for the every-day care of the patients. No restrictions in changing medication or other treatment modalities. Duration 6 months. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Psychological distress
- Actual outcome: Multiple Pain Inventory - affective distress at 6 months; Group 1: mean 2.94 (SD 0.69); n=23, Group 2: mean 2.92 (SD 0.57); n=24; Multiple Pain Inventory affective distress 0-6 Top=High is poor outcome; Comments: Baseline values: CBT 3.12 (0.62), usual care 2.83 (0.79)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: severe depression; Group 2 Number missing: 0, Reason: NA

Protocol outcome 2: Pain interference
- Actual outcome: Multiple Pain Inventory - pain interference at 6 months; Group 1: mean 4.05 (SD 0.85); n=23, Group 2: mean 3.43 (SD 0.82); n=24; Multiple pain inventory - pain interference 0-6 Top=High is poor outcome; Comments: Baseline values: CBT 4.04 (0.57), usual care 3.37 (1.09)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: severe depression; Group 2 Number missing: 0, Reason: NA

Protocol outcome 3: Discontinuation
- Actual outcome: Non-participation at 6 months; Group 1: 1/24, Group 2: 0/24; Comments: Reason: severe depression
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA

Protocol outcome 4: Pain reduction

Study	Karlsson 2015[245]
- Actual outcome: Multiple Pain Inventory - pain severity at 6 months; Group 1: mean 3.88 (SD 1.05); n=23, Group 2: mean 3.67 (SD 0.75); n=24; Multiple pain inventory - pain severity 0-6 Top=High is poor outcome; Comments: Baseline values: CBT 3.85 (0.8), usual care 3.38 (0.92) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1, Reason: severe depression; Group 2 Number missing: 0, Reason: NA	
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Kemani 2015[247]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=60)
Countries and setting	Conducted in Sweden; Setting: Behavioural medicine pain treatment services at the Karolinska University hospital
Line of therapy	Unclear
Duration of study	Intervention + follow up: 12 week intervention plus 6 month follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Formal diagnosis made by physicians
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	18-65 years, longstanding pain for more than 6 months, no further medical assessments needed, pain medication stable during the past 2 months and no changes in medication were planned
Exclusion criteria	Participation in CBT based treatment. If other treatment changes were planned, participation in ongoing nonmedical non-CBT based treatment would be allowed. Psychiatric comorbidity that may have significantly interfered with treatment, and which needed to be addressed primarily and separately, resulted in exclusion (the MINI interview was used to screen for psychiatric comorbidity).
Recruitment/selection of patients	From primary and tertiary care units in Stockholm County, Sweden
Age, gender and ethnicity	Age - Mean (SD): 40.3(11.4) years. Gender (M:F): 16:44. Ethnicity: Not specified
Further population details	1. Chronic orofascial pain: Not applicable (Mixed population). 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: No 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: No 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: Not applicable 11. Sensory impairment: No

Study	Kemani 2015[247]
Extra comments	Duration of pain 9.9(7.5) years, pain types: 88.3% idiopathic pain 8.3% neuropathic pain 3.3% nociceptive pain 18.3% fibromyalgia
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Psychological therapy - Acceptance and commitment therapy. 90 minute weekly sessions delivered by 5 therapists. A psychologist conducted10 sessions, and a pain physician with a formal therapist training in CBT and ACT conducted 2 sessions. Intervention had 4 phases: (1) dysfunctional character of onstanding pain symptoms and pain-related behaviours discussed to reduce influence of pain (2) workability of previous strategies to address pain were evaluated and the utility of a more flexible behavioural repertoire in relation to pain and distress were emphasised. (3) disengagement from verbal process, to decrease the negative impact of thoughts and experience on behaviour (4) participants defined short and long term behavioural goals and practiced the application of ACT strategies. Duration 12 weeks. Concurrent medication/care: Other ongoing interventions allowed other than CBT, if no treatment changes due. Indirectness: No indirectness (n=30) Intervention 2: Psychological therapy - Relaxation techniques. 90 minute weekly sessions delivered by 5 therapists. Phases included (1) rational of using relaxation in the context of longstanding pain and a therapist guided in session practice of the long version of progressive relaxation (2) conditioned and differential relaxation was implemented, by prompting participants to think about their breathing and how this related to relaxation (3) the final phase consisted of rapid relaxation and the application of this in daily life. Duration 12 weeks. Concurrent medication/care: Other ongoing interventions allowed other than CBT, if no treatment changes due. Indirectness: No indirectness
Funding	Academic or government funding (Karolinska university hospital grant)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ACCEPTANCE AND COMMITMENT THERAPY versus RELAXATION TECHNIQUES

Protocol outcome 1: Health related quality of life
- Actual outcome: SF-12 mental component at 12 weeks; Group 1: mean 40.9 (SD 10.4); n=24, Group 2: mean 34.9 (SD 10.7); n=19; SF-12 mental component 0-100 Top=High is good outcome; Comments: Baseline: 38.8(8.9);37.7(10)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: Lost interest, adverse events, moved abroad, lost to follow up; Group 2 Number missing: 6, Reason: Lost interest, lost to follow up, increased pain symptoms, time demands of work
- Actual outcome: SF-12 mental component at 6 months; Group 1: mean 39.3 (SD 10.8); n=19, Group 2: mean 38.8 (SD 13.8); n=18; SF-12 mental

Study	Kemani 2015[247]
component 0-100 Top=High is good outcome; Comments: Baseline: 38.8(8.9);37.7(10) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: NR; Group 2 Number missing: 12, Reason: NR - Actual outcome: SF-12 physical component at 12 weeks; Group 1: mean 34.9 (SD 9.1); n=24, Group 2: mean 32.1 (SD 8.2); n=19; SF-12 physical component 0-100 Top=High is good outcome; Comments: Baseline: 29.4(8.5); 29.4(7.6) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: Lost interest, adverse events, moved abroad, lost to follow up; Group 2 Number missing: 6, Reason: Lost interest, lost to follow up, increased pain symptoms, time demands of work - Actual outcome: SF-12 physical component at 6 months; Group 1: mean 39.3 (SD 10.2); n=19, Group 2: mean 32.3 (SD 9.8); n=18; SF-12 0-100 Top=High is good outcome; Comments: Baseline: 29.4(8.5); 29.4(7.6) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: NR; Group 2 Number missing: 12, Reason: NR Protocol outcome 2: Pain interference - Actual outcome: Pain disability index at 12 weeks; Group 1: mean 28.8 (SD 16.1); n=24, Group 2: mean 40.3 (SD 13.6); n=19; PDI 0-100 Top=High is poor outcome; Comments: BASELINE: 39.1(14);40.7(14.1) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: NR; Group 2 Number missing: 12, Reason: NR - Actual outcome: Pain disability index at 6 months; Group 1: mean 31.2 (SD 19); n=19, Group 2: mean 34 (SD 16.2); n=18; PDI 0-100 Top=High is poor outcome; Comments: BASELINE: 39.1(14);40.7(14.1) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: Lost interest, adverse events, moved abroad, lost to follow up; Group 2 Number missing: 6, Reason: Lost interest, lost to follow up, increased pain symptoms, time demands of work Protocol outcome 3: Psychological distress - Actual outcome: Hospital anxiety and depression scale (depression subscale) at 12 weeks; Group 1: mean 7.1 (SD 4.8); n=24, Group 2: mean 9.1 (SD 5.3); n=19; HADS:D 0-21 Top=High is poor outcome; Comments: Baseline: 10(4.1); 9.6(4.3) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: Lost interest, adverse events, moved abroad, lost to follow up; Group 2 Number missing: 6, Reason: Lost interest, lost to follow up, increased pain symptoms, time demands of work - Actual outcome: Hospital anxiety and depression scale (depression subscale) at 6 months; Group 1: mean 8.4 (SD 5.6); n=19, Group 2: mean 8.4 (SD 5.5); n=18; HADS:D 0-21 Top=High is poor outcome; Comments: Baseline: 10(4.1); 9.6(4.3) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: NR; Group 2 Number missing: 12, Reason: NR - Actual outcome: Hospital anxiety and depression scale (anxiety subscale) at 6 months; Group 1: mean 9.1 (SD 5.1); n=19, Group 2: mean 9.1 (SD 5.2); n=18; HADS:A 0-21 Top=High is poor outcome; Comments: Baseline: 9(3.9)10.3(4.9) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low,

Study	Kemani 2015[247]
Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: NR; Group 2 Number missing: 12, Reason: NR - Actual outcome: Hospital anxiety and depression scale (anxiety subscale) at 12 weeks; Group 1: mean 7.3 (SD 3.8); n=24, Group 2: mean 9 (SD 4.6); n=19; HADS:A 0-21 Top=High is poor outcome; Comments: Baseline: 9(3.9); 10.3(4.9) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: Lost interest, adverse events, moved abroad, lost to follow up; Group 2 Number missing: 6, Reason: Lost interest, lost to follow up, increased pain symptoms, time demands of work Protocol outcome 4: Discontinuation - Actual outcome: Discontinuation at 12 weeks ; Group 1: 0/25, Group 2: 5/24; Comments: reasons for discontinuation (relaxation): lost interest in study (n=2), unknown (n=2), increased pain related symptoms (n=1) All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 5: Pain reduction - Actual outcome: Pain intensity at 12 weeks; Group 1: mean 3.7 (SD 1.4); n=24, Group 2: mean 4 (SD 1.5); n=19; Pain scale (referenced core outcome measures from IMMPACT) 0-6 Top=High is poor outcome; Comments: Baseline: 4.3(0.79);4.4(1) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 5, Reason: Lost interest, adverse events, moved abroad, lost to follow up; Group 2 Number missing: 6, Reason: Lost interest, lost to follow up, increased pain symptoms, time demands of work - Actual outcome: Pain intensity at 6 months; Group 1: mean 4.4 (SD 1.3); n=19, Group 2: mean 4.1 (SD 1.5); n=18; Pain scale 0-6 Top=High is poor outcome; Comments: Baseline: 4.3(0.79);4.4(1) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Very high, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: NR; Group 2 Number missing: 12, Reason: NR	
Protocol outcomes not reported by the study	Physical function; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Lami 2018[260]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=126)
Countries and setting	Conducted in Spain; Setting: Psychology clinic of a University
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 9 weeks + 3 months

Study	Lami 2018[260]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	women aged between 25 and 65; meeting the diagnostic criteria for FM (ACR) for >6 months; stable drug intake; at least 1 month before the study and no treatment with other psychological therapy; meeting diagnostic criteria for insomnia
Exclusion criteria	major concomitant medical conditions; pregnancy; mental disorders with severe symptoms or other organic sleep disorder; severe dependence of hypnotic drugs; irregularities in circadian rhythms at the time of the study
Recruitment/selection of patients	patients recruited from the Rheumatology service and the Pain unit of a single hospital and from a FM association from the same area
Age, gender and ethnicity	Age - Mean (SD): 50.19 (8.24) years. Gender (M:F): 0/126. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=42) Intervention 1: Psychological therapy - Cognitive behavioural therapy. CBT - pain. 9 x 90 minute weekly group sessions led by therapists with a high level of professional training and experience in chronic pain and sleep disorders. Based on fear-avoidance model of chronic pain, aimed at modifying the reinforcement contingencies that maintain pain behaviours and dysfunctional attitudes and emotional reactions. Participants given a therapy manual containing information and tasks involved in each session. Duration 9 weeks. Concurrent medication/care: Participants required to follow usual medical care. Indirectness: Serious indirectness; Indirectness comment: included psycho education and relaxation elements (n=42) Intervention 2: Psychological therapy - Cognitive behavioural therapy. CBT - insomnia and pain. 9 x 90 minute weekly group sessions led by therapists with a high level of professional training and experience in chronic pain and sleep disorders. Covered the same objectives as CBT-pain and extended them to a sleep approach through training in cognitive, affective and behavioural skills for better management of sleep problems. Based on recommendations of the American Academy of Sleep and therapeutic guidelines for insomnia. Participants given a therapy manual containing information and tasks involved in each session.

Study	Lami 2018[260]
	Duration 9 weeks. Concurrent medication/care: Participants required to follow usual medical care. Indirectness: Serious indirectness; Indirectness comment: included psycho education, relaxation and sleep hygiene elements (n=42) Intervention 3: Usual care. Usual medical care - no further details provided, but of the majority of participants used antidepressants, anxiolytics, anti-inflammatory drugs and/or analgesics. Duration study duration. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (Spanish Ministry of Science and Innovation and Spanish Ministry of Economy and Competitiveness)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact Questionnaire (CBTpain vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 57.93 (SD 14.16); n=28, Group 2: mean 55.45 (SD 16.79); n=36; Fibromyalgia Impact Questionnaire not reported Top=High is poor outcome; Comments: Baseline values: CBTpain 65.53 (11.08), usual care 55.57 (18.14)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 14, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment
- Actual outcome: Fibromyalgia Impact Questionnaire (CBTpain+insomnia vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 55.82 (SD 14.52); n=27, Group 2: mean 55.45 (SD 16.79); n=36; Fibromyalgia Impact Questionnaire not reported Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 61.98 (11.14), usual care 55.57 (18.14)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment
- Actual outcome: Fibromyalgia Impact Questionnaire (CBTpain vs. UC) at 5 months (3 months follow up); Group 1: mean 53.33 (SD 14.85); n=24, Group 2: mean 53.22 (SD 16.59); n=26; FIQ not reported Top=High is poor outcome; Comments: Baseline values: CBTpain 65.53 (11.08), usual care 55.57 (18.14)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 18, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment, 4 did not complete follow up assessment; Group 2 Number missing: 16, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment, 10 did not complete follow up assessment
- Actual outcome: Fibromyalgia Impact Questionnaire (CBTpain+insomnia vs. UC) at 5 months (3 months follow up); Group 1: mean 56.53 (SD 13.97); n=22, Group 2: mean 53.22 (SD 16.59); n=26; FIQ not reported Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 61.98

Study	Lami 2018[260]
(11.14), usual care 55.57 (18.14) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 20, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment, 5 did not attend follow up assessment ; Group 2 Number missing: 16, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment, 10 did not attend follow up assessment Protocol outcome 2: Psychological distress - Actual outcome: Symptoms Checklist 90-Revised - Depression (CBTpain vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 2.15 (SD 0.78); n=28, Group 2: mean 1.68 (SD 0.98); n=36; SCL-90-R Depression 0-4 Top=High is poor outcome; Comments: Baseline values: CBTpain 2.15 (0.88), usual care 1.77 (0.95) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 14, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment - Actual outcome: Symptoms Checklist 90-Revised - Anxiety (CBTpain vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 1.71 (SD 0.94); n=28, Group 2: mean 1.37 (SD 0.91); n=36; SCL-90-R anxiety 0-4 Top=High is poor outcome; Comments: Baseline values: CBTpain 1.63 (0.81), usual care 1.5 (0.93) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 14, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment - Actual outcome: Symptoms Checklist 90-Revised - Depression (CBTpain+insomnia vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 2.03 (SD 0.96); n=27, Group 2: mean 1.68 (SD 0.98); n=36; SCL-90-R depression 0-4 Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 2.2 (0.79), usual care 1.77 (0.95) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment - Actual outcome: Symptoms Checklist 90-Revised - Anxiety (CBTpain+insomnia vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 1.68 (SD 1.05); n=27, Group 2: mean 1.37 (SD 0.91); n=36; SCL-90-R anxiety 0-4 Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 1.78 (0.93), usual care 1.5 (0.93) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment - Actual outcome: Symptoms Checklist 90-Revised - Depression (CBTpain vs. UC) at 5 months (3 months follow up); Group 1: mean 2.11 (SD 0.9); n=24, Group 2: mean 1.47 (SD 0.78); n=26; SCL-90-R depression 0-4 Top=High is poor outcome; Comments: Baseline values: CBTpain 2.15 (0.88), usual	

Study	Lami 2018[260]
care 1.77 (0.95) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 18, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment, 4 did not complete follow up assessment; Group 2 Number missing: 16, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment, 10 did not complete follow up assessment - Actual outcome: Symptoms Checklist 90-Revised - Anxiety (CBTpain vs. UC) at 5 months (3 months follow up); Group 1: mean 1.6 (SD 1.05); n=24, Group 2: mean 1.18 (SD 0.69); n=26; SCL-90-R anxiety 0-4 Top=High is poor outcome; Comments: Baseline values: CBTpain 1.63 (0.81), usual care 1.5 (0.93) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 18, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment, 4 did not complete follow up assessment; Group 2 Number missing: 16, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment, 10 did not complete follow up assessment - Actual outcome: Symptoms Checklist 90-Revised - Depression (CBTpain+insomnia vs. UC) at 5 months (3 months follow up); Group 1: mean 2.02 (SD 1.01); n=22, Group 2: mean 1.47 (SD 0.78); n=26; SCL-90-R 0-4 Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 2.2 (0.79), usual care 1.77 (0.95) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 20, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment, 5 did not attend follow up assessment ; Group 2 Number missing: 16, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment, 10 did not attend follow up assessment - Actual outcome: Symptoms Checklist 90-Revised - Anxiety (CBTpain+insomnia vs. UC) at 5 months (3 months follow up); Group 1: mean 1.62 (SD 0.98); n=22, Group 2: mean 1.18 (SD 0.69); n=26; SCL-90-R anxiety 0-4 Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 1.78 (0.93), usual care 1.5 (0.93) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 20, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment, 5 did not attend follow up assessment ; Group 2 Number missing: 16, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment, 10 did not attend follow up assessment Protocol outcome 3: Pain self-efficacy - Actual outcome: Chronic Pain Self-efficacy Scale (CBTpain vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 87.14 (SD 30.21); n=28, Group 2: mean 79.53 (SD 25.66); n=36; Chronic Pain Self-efficacy Scale unclear Top=High is good outcome; Comments: Baseline values: CBT 72.85 (36.54), usual care 76.56 (30.16) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 14, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment - Actual outcome: Chronic Pain Self-efficacy Scale (CBTpain+insomnia vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 85.52 (SD 38.22); n=27, Group 2: mean 79.53 (SD 25.66); n=36; Chronic Pain Self-efficacy Scale unclear Top=High is good outcome; Comments: Baseline

Study	Lami 2018[260]
values: CBT 76.38 (31.29), usual care 76.56 (30.16) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment - Actual outcome: Chronic Pain Self-efficacy Scale (CBTpain vs. UC) at 5 months (3 months follow up); Group 1: mean 78.36 (SD 41.32); n=24, Group 2: mean 81.79 (SD 38.82); n=26; Chronic Pain Self-efficacy Scale unclear Top=High is good outcome; Comments: Baseline values: CBT 72.85 (36.54), usual care 76.56 (30.16) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 18, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment, 4 did not complete follow up assessment; Group 2 Number missing: 16, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment, 10 did not complete follow up assessment - Actual outcome: Chronic Pain Self-efficacy Scale (CBTpain+insomnia vs. UC) at 5 months (3 months follow up); Group 1: mean 90.41 (SD 37.64); n=22, Group 2: mean 81.79 (SD 38.82); n=26; Chronic Pain Self-efficacy Scale unclear Top=High is good outcome; Comments: Baseline values: CBT 76.38 (31.29), usual care 76.56 (30.16) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 20, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment, 5 did not attend follow up assessment ; Group 2 Number missing: 16, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment, 10 did not attend follow up assessment Protocol outcome 4: Sleep - Actual outcome: Pittsburgh Sleep Quality Index - total score (CBTpain vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 13.68 (SD 4.61); n=28, Group 2: mean 13.08 (SD 5.33); n=36; Pittsburgh Sleep Quality Index 0-21 Top=High is poor outcome; Comments: Baseline values: CBTpain 13.47 (4.45), usual care 12.88 (5.01) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 14, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment - Actual outcome: Pittsburgh Sleep Quality Index - total score (CBTpain+insomnia vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 13.19 (SD 4.31); n=27, Group 2: mean 13.08 (SD 5.33); n=36; Pittsburgh Sleep Quality Index 0-21 Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 14.68 (3.7), usual care 12.88 (5.01) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment - Actual outcome: Pittsburgh Sleep Quality Index - total score (CBTpain vs. UC) at 5 months (3 months follow up); Group 1: mean 13.79 (SD 4.22); n=24, Group 2: mean 11.88 (SD 4.68); n=26; Pittsburgh sleep quality index total score 0-21 Top=High is poor outcome; Comments: Baseline values: CBTpain

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13.47 (4.45), usual care 12.88 (5.01) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 18, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment, 4 did not complete follow up assessment; Group 2 Number missing: 16, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment, 10 did not complete follow up assessment - Actual outcome: Pittsburgh Sleep Quality Index - total score (CBTpain+insomnia vs. UC) at 5 months (3 months follow up); Group 1: mean 13.57 (SD 3.64); n=22, Group 2: mean 11.88 (SD 4.68); n=26; Pittsburgh sleep quality index 0-21 Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 14.68 (3.7), usual care 12.88 (5.01) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 20, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment, 5 did not attend follow up assessment ; Group 2 Number missing: 16, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment, 10 did not attend follow up assessment Protocol outcome 5: Discontinuation - Actual outcome: Discontinuation (CBTpain vs. UC) at 9 weeks (immediately post-intervention); Group 1: 8/42, Group 2: 1/42; Comments: Reasons for discontinuation: CBTpain changes in personal life, usual care changes in personal life Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: Discontinuation (CBTpain+insomnia vs. UC) at 9 weeks (immediately post-intervention); Group 1: 4/42, Group 2: 1/42; Comments: Reasons for discontinuation: CBTpain+insomnia changes in personal life, usual care changes in personal life Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 6: Pain reduction - Actual outcome: Pain intensity VAS (McGill Pain Questionnaire) (CBTpain vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 7.35 (SD 2.08); n=28, Group 2: mean 7.4 (SD 1.29); n=36; McGill Pain Questionnaire VAS pain 0-10 Top=High is poor outcome; Comments: Baseline values: CBTpain 7.58 (1.75), usual care 7.16 (1.27) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 14, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment - Actual outcome: Pain intensity VAS (McGill Pain Questionnaire) (CBTpain+insomnia vs. UC) at 9 weeks (immediately post-intervention); Group 1: mean 7.29 (SD 1.46); n=27, Group 2: mean 7.4 (SD 1.29); n=36; McGill Pain Questionnaire VAS pain 0-10 Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 7.44 (1.33), usual care 7.16 (1.27) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment; Group 2 Number missing: 6, Reason: 1 did not receive usual medical care, 5 did not complete post treatment

Study	Lami 2018[260]
assessment - Actual outcome: Pain intensity VAS (McGill Pain Questionnaire) (CBTpain vs. UC) at 5 months (3 months follow up); Group 1: mean 7.21 (SD 1.79); n=24, Group 2: mean 7.2 (SD 1.58); n=26; VAS 0-10 Top=High is poor outcome; Comments: Baseline values: CBTpain 7.58 (1.75), usual care 7.16 (1.27) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 18, Reason: 8 did not receive intervention, 6 did not complete post treatment assessment, 4 did not complete follow up assessment; Group 2 Number missing: 16, Reason: 1 did not receive usual care, 5 did not complete post treatment assessment, 10 did not complete follow up assessment - Actual outcome: Pain intensity VAS (McGill Pain Questionnaire) (CBTpain+insomnia vs. UC) at 5 months (3 months follow up); Group 1: mean 6.62 (SD 1.47); n=22, Group 2: mean 7.2 (SD 1.58); n=26; VAS 0-10 Top=High is poor outcome; Comments: Baseline values: CBTpain+insomnia 7.44 (1.33), usual care 7.16 (1.27) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 20, Reason: 4 did not receive intervention, 11 did not complete post treatment assessment, 5 did not attend follow up assessment ; Group 2 Number missing: 16, Reason: 1 did not receive usual medical care, 5 did not complete post treatment assessment, 10 did not attend follow up assessment	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Use of healthcare services

Study	Lazaridou 2017[265]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=16)
Countries and setting	Conducted in USA; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 1 month + 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	At least 18 years old; documented presence of rheumatologist-diagnosed FM for at least 1 year; meet the revised Wolfe et al. ACR criteria for FM; score on the Pain Catastrophizing Scale (PCS) of at least 21
Exclusion criteria	History of clinically significant anxiety symptoms interfering with fMRI procedures (e.g., claustrophobia, panic disorder); recent history of

Study	Lazaridou 2017[265]
	cardiac events such as myocardial infarction; history of significant head injury; peripheral neuropathy; use of certain centrally-acting analgesic medications such as opioids; history of substance abuse; concurrent autoimmune or inflammatory disease; implanted metallic objects; pregnancy; diseases affecting the central nervous system (e.g., multiple sclerosis, Parkinson's disease); serious psychiatric conditions precluding participation (e.g., psychotic disorders)
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 45.7 (12.2). Gender (M:F): 3/13. Ethnicity: 81.4% white
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=8) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 4 x 60–70 minute visits conducted by a licensed clinical psychologist - sessions used active, structured techniques to alter distorted thoughts, with a focus on acquiring and practicing cognitive and emotion-regulation skills. Techniques such as relaxation, visual imagery, thought challenging, and distraction were used. CBT prominently emphasized in-vivo practice during each session, and featured home practice using written exercises. Cognitive restructuring was used to help patients recognize the relationships between thoughts, feelings and behaviours. Patients learned to identify, evaluate, and challenge negative thoughts and to diminish the degree of catastrophizing about pain. Duration 4 weeks. Concurrent medication/care: Not reported. Indirectness: Serious indirectness; Indirectness comment: included relaxation elements (n=8) Intervention 2: Psychological therapy - Pain education. Information about fibromyalgia and about chronic pain. The sessions provided a variety of information about the nature and presumed causes of fibromyalgia, but they involved no active skills training or homework assignments. Duration 4 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (National Institutes of Health; Arthritis Foundation; American College of Rheumatology; National Center for complementary and Integrative Health)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus PAIN EDUCATION

Protocol outcome 1: Psychological distress
- Actual outcome: Beck Depression Inventory at 4 weeks ; Group 1: mean -3.5 (SD 7.9); n=8, Group 2: mean -2 (SD 4.4); n=8; Beck depression

Study	Lazaridou 2017[265]
inventory 0-63 Top=High is poor outcome; Comments: Baseline values reported overall Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Pain interference - Actual outcome: Brief Pain Inventory interference sub scale at 4 weeks ; Group 1: mean -1.5 (SD 2.9); n=8, Group 2: mean -0.39 (SD 1.6); n=8; BPI interference 0-10 Top=High is poor outcome; Comments: Baseline values reported overall Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation at 4 weeks ; Group 1: 0/8, Group 2: 0/8 Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Pain reduction - Actual outcome: Brief Pain Inventory severity sub scale at 4 weeks ; Group 1: mean -0.35 (SD 2); n=8, Group 2: mean -0.28 (SD 1.8); n=8; BPI severity 0-10 Top=High is poor outcome; Comments: Baseline values reported overall Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Martinez 2014[299]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=64)
Countries and setting	Conducted in Spain; Setting: Clinical Psychology Unit of University hospital
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 weeks + 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR diagnostic criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA

Study	Martinez 2014[299]
Inclusion criteria	women aged between 25 and 60; meeting the ACR diagnostic criteria for FM; having had this disorder for more than 6 months so that adaptation to the impact of the diagnosis had already occurred; being stable as regards the intake of analgesics, antidepressants or other drugs at least 1 month before the study; meeting the diagnostic criteria for insomnia (DSM-IV-TR, American Psychiatric Association, APA, 2000).
Exclusion criteria	being pregnant; having a medical history of significant head injury or neurological disorder; having major concomitant medical conditions; having major depressive disorder with suicide ideation or other major Axis I diagnoses (APA, 2000); having symptoms of sleep-disruptive comorbidities with insomnia; having an apnea-hypopnea index or periodic limb movement-related arousal index of 15 or more per hour of sleep; having a severe hypnotic dependence; and being treated with another psychological or physical therapy at the time of the study.
Recruitment/selection of patients	recruited from the Rheumatology Service and Pain Unit of a Hospital
Age, gender and ethnicity	Age - Mean (SD): 47.58 (6.82) years. Gender (M:F): 0/64. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=32) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 6 x 1.5 hour group sessions (5–6 participants) once a week led by 3 female therapists with experience in the management of chronic pain and sleep disorders. Session 1: focused on information about the relationship between sleep and FM, basic notions about sleep, and sleep hygiene education. Session 2: instructions for applying sleep restriction and stimulus control. Session 3: training physiological deactivation procedures (slow breathing, passive relaxation and imagery training). Sessions 4 and 5: cognitive therapy to change negative thoughts about insomnia through verbal discussion and behavioural experiments. Session 6 was devoted to maintaining achievements and preventing relapses. Duration 6 weeks. Concurrent medication/care: continued with their usual medical care for FM (on stable doses of medication) during the study. Patients also agreed not to participate in other interventions until the trial ended. Indirectness: Serious indirectness; Indirectness comment: included relaxation and imagery (n=32) Intervention 2: Psychological therapy - Sleep management/hygiene. 6 x 1.5 hour group sessions (5–6 participants) once a week led by 3 female therapists with experience in the management of chronic pain and sleep disorders. Aim of the intervention only to provide training about sleep hygiene rules. Session 1:

Study	Martinez 2014[299]
	participants given the same information about sleep as those in the CBT-I program. Session 2: sleep hygiene rules related to environmental factors (e.g. noise, temperature, light). Session 3: learning about lifestyle factors that influence sleep (use of stimulants and other substances). Sessions 4 and 5: information about diet and physical exercise, respectively. Session 6: maintaining achievements and preventing relapses, as in the CBT-I program. Duration 6 weeks. Concurrent medication/care: continued with their usual medical care for FM (on stable doses of medication) during the study. Patients also agreed not to participate in other interventions until the trial ended. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (Spanish Ministry of Science and Innovation; Spanish Ministry of Education)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus SLEEP MANAGEMENT/HYGEINE

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact Questionnaire at 6 weeks ; Group 1: mean 50.47 (SD 18.43); n=30, Group 2: mean 64.46 (SD 15.23); n=27; Fibromyalgia impact questionnaire not reported Top=High is poor outcome; Comments: Baseline values: CBT 60.71 (11.83), sleep hygiene 64.09 (13.61)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2; Group 2 Number missing: 5

Protocol outcome 2: Psychological distress
- Actual outcome: Symptom Checklist-90-Revised - depression sub scale at 6 weeks ; Group 1: mean 1.63 (SD 0.84); n=30, Group 2: mean 2.29 (SD 0.77); n=27; Symptom Checklist-90-Revised - depression 0-4 Top=High is poor outcome; Comments: Baseline values: CBT 2.09 (0.84), sleep hygiene 2.37 (0.74)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2; Group 2 Number missing: 5
- Actual outcome: Symptom Checklist-90-Revised - anxiety sub scale at 6 weeks ; Group 1: mean 1.23 (SD 0.79); n=30, Group 2: mean 1.62 (SD 0.92); n=27; Symptom checklist 90 revised anxiety 0-4 Top=High is poor outcome; Comments: Baseline values: CBT 1.49 (0.96), sleep hygiene 1.75 (0.86)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2; Group 2 Number missing: 5

Protocol outcome 3: Pain self-efficacy
- Actual outcome: Chronic Pain Self-efficacy Scale at 6 weeks ; Group 1: mean 93.96 (SD 33.6); n=30, Group 2: mean 70.48 (SD 37.81); n=27; Chronic pain self-efficacy scale not reported Top=High is good outcome; Comments: Baseline values: CBT 86.5 (36.63), sleep hygiene 71.59 (35.39)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2; Group 2 Number missing: 5

Study	Martinez 2014[299]
Protocol outcome 4: Sleep - Actual outcome: Pittsburgh Sleep Quality Index total score at 6 weeks ; Group 1: mean 11.33 (SD 4.03); n=30, Group 2: mean 13.48 (SD 2.88); n=27; Pittsburgh Sleep Quality Index 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 15.3 (3.03), sleep hygiene 14.93 (3.35) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2; Group 2 Number missing: 5 Protocol outcome 5: Discontinuation - Actual outcome: Not receiving intervention at 6 weeks ; Group 1: 2/32, Group 2: 3/32; Comments: reason: changes in personal life Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 6: Pain reduction - Actual outcome: McGill Pain Questionnaire at 6 weeks ; Group 1: mean 6.72 (SD 2.08); n=30, Group 2: mean 8.23 (SD 1.34); n=27; McGill pain questionnaire 1-10 Top=High is poor outcome; Comments: Baseline values: CBT 7.32 (1.94), sleep hygiene 8.46 (1.1) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - ; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2; Group 2 Number missing: 5	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Use of healthcare services

Study	Masheb 2009[300]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in USA
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 10 weeks + 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: independent evaluation by 2 gynaecologists including standardized medical history, pelvic examination and bimanual palpation, and laboratory findings
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	Women with known or suspected vulvodynia, or with vulvar or vaginal itching, stinging or burning, and/or painful intercourse and/or painful intercourse for at least a six-month duration, were 21-years or older, and were not pregnant

Study	Masheb 2009[300]
Exclusion criteria	psychotic, suicidal, or substance dependent, individuals with a life-threatening illness, or potential participants who had initiated psychotherapy, psychopharmacologic treatment or pain medication within one month prior to the assessment, other diagnoses known to cause vulvar pain
Recruitment/selection of patients	advertisements in local newspapers or referrals from healthcare providers
Age, gender and ethnicity	Age - Mean (SD): 43 (12.1) years. Gender (M:F): 0/50. Ethnicity: Caucasian 82%, non-Caucasian 18%
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: Yes 4. Chronic widespread pain: No 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=25) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 10 weekly individual 60-minute sessions by doctoral level research therapists -goal to assist participants in taking control of pain by creating understanding of the relationship of thoughts, feelings and behaviours, on pain, and sexual and emotional function. Participants taught self-management skills that alter thoughts, feelings and behaviours. 3 overlapping phases: orientation to a self-management approach, skills acquisition, and skills practice. Motivational enhancement, role-playing, problem-solving, and contingent reinforcement to increase patient adherence. Final component of each session involved session review and collaboration in the development of goals and homework for the coming week. Self-management skills included behavioural, sex therapy, cognitive, and relaxation skills that were practiced in session and at home. Behavioural skills included gate control, activity pacing, and goal setting. Sex therapy skills included sensate focus and assertive communication regarding sexual relations. Cognitive component involved a series of cognitive skills: identifying triggers for negative mood states, identifying automatic negative thoughts, identifying cognitive distortion associated with the automatic negative thought, challenging negative thoughts, and restructuring the negative thought. Relaxation skills: diaphragmatic breathing, progressive muscle relaxation, and relaxation that was specific to the pelvic floor musculature. Duration 10 weeks. Concurrent medication/care: Participants were asked not to initiate psychotherapy, psychopharmacologic treatment or pain medication, or other medical or alternative treatments for vulvodynia during the 10-week treatment. Indirectness: Serious indirectness; Indirectness comment: included relaxation (n=25) Intervention 2: Psychological therapy - Psychotherapy (psychodynamic and psychoanalytic). Supportive psychotherapy - 10 weekly individual 60-minute sessions by doctoral level research therapists. Non-directive talk therapy that lacks specific behavioural interventions. Therapists assisted participants in expressing feelings while not making specific suggestions for how the person might wish to change. The therapist's role was to have unconditional positive regard, to engage in empathic understanding, and to

Study	Masheb 2009[300]
	mirror. Sessions began with, “How has your week been generally and with regard to your vulvar pain?” The remainder of each session was directed by the participant, unstructured, and generally focused on complaints of vulvar pain and associated problems. Therapists did not make interpretations, problem-solve, challenge or restructure cognitions, or initiate goal-setting. Duration 10 weeks. Concurrent medication/care: Participants were asked not to initiate psychotherapy, psychopharmacologic treatment or pain medication, or other medical or alternative treatments for vulvodynia during the 10-week treatment. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (National Institutes of Health/National Institute of Child Health and Human Development)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus PSYCHOTHERAPY (PSYCHODYNAMIC AND PSYCHOANALYTIC)

Protocol outcome 1: Psychological distress
- Actual outcome: Beck Depression Inventory at 10 weeks (post treatment); Group 1: mean 10.7 (SD 8.63); n=23, Group 2: mean 9.9 (SD 9); n=25; Beck Depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: CBT 12.1 (9), SP 12.5 (9)
Estimated marginal means. Standard deviations calculated from standard errors.
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: not reported ; Group 2 Number missing: 0, Reason: NA
- Actual outcome: Pain Anxiety Symptoms Scale at 10 weeks (post treatment); Group 1: mean 67.7 (SD 32.61); n=23, Group 2: mean 62.8 (SD 33.5); n=25; Pain Anxiety Symptoms Scale 0-200 Top=High is poor outcome; Comments: Baseline values: CBT 72.6 (32.13), SP 73 (33.5)
Estimated marginal means. Standard deviations calculated from standard errors.
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: not reported ; Group 2 Number missing: 0, Reason: NA
- Actual outcome: Beck Depression Inventory at 1 year follow up; Group 1: mean 7.3 (SD 9.38); n=22, Group 2: mean 11.5 (SD 9.5); n=25; Beck Depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: CBT 12.1 (9), SP 12.5 (9)
Estimated marginal means. Standard deviations calculated from standard errors.
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 0, Reason: NA
- Actual outcome: Pain Anxiety Symptoms Scale at 1 year follow up; Group 1: mean 55.3 (SD 33.77); n=22, Group 2: mean 65.2 (SD 34.5); n=25; Pain Anxiety Symptom Scale 0-200 Top=High is poor outcome; Comments: Baseline values: CBT 72.6 (32.13), SP 73 (33.5)
Estimated marginal means. Standard deviations calculated from standard errors.
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Study	Masheb 2009[300]
Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 0, Reason: NA Protocol outcome 2: Discontinuation - Actual outcome: Discontinuation at 10 weeks ; Group 1: 3/25, Group 2: 5/25; Comments: Reasons not reported. Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: , Reason: NA; Group 2 Number missing: , Reason: NA Protocol outcome 3: Pain reduction - Actual outcome: McGill Pain Questionnaire at 10 weeks (post treatment); Group 1: mean 18.5 (SD 12.95); n=23, Group 2: mean 14 (SD 13); n=25; McGill Pain Questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBT 29.1(13), SP 22.2(13) Estimated marginal means. Standard deviations calculated from standard errors. Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: not reported ; Group 2 Number missing: 0, Reason: NA - Actual outcome: McGill Pain Questionnaire at 1 year follow up; Group 1: mean 13.5 (SD 14.07); n=22, Group 2: mean 13.3 (SD 14); n=25; McGill Pain Questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBT 29.1(13), SP 22.2(13) Estimated marginal means. Standard deviations calculated from standard errors. Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 3, Reason: not reported ; Group 2 Number missing: 0, Reason: NA	
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Mcbeth 2012[304] Beasley 2015[41]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=442)
Countries and setting	Conducted in United Kingdom; Setting: Research nurse-led clinic
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 9 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology criteria for fibromyalgia

Study	Mcbeth 2012[304] Beasley 2015[41]
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	>25 years old with chronic widespread pain (ACR definition) for which physician was contacted in last year
Exclusion criteria	Severe psychiatric disorder, health condition which would prevent exercise or which was not suitable for intervention
Recruitment/selection of patients	Screening questionnaire sent to people registered with 8 practices in Aberdeen and Macclesfield
Age, gender and ethnicity	Age - Mean (SD): 56 (13) years. Gender (M:F): 70.5% female. Ethnicity: Not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Extra comments	NA
Indirectness of population	No indirectness: NA
Interventions	(n=112) Intervention 1: Psychological therapy - Cognitive behavioural therapy. Telephone CBT delivered by 4 therapists: initial 45-60 minute assessment, 7 x 30-45 minute weekly sessions, 1 session 3 months and 6 months after randomisation. 2-3 patient-defined goals. Patients received a self-management CBT manual including stories of fictitious patients using specific CBT techniques (behavioural activation, cognitive restructuring and lifestyle changes) to enable an informed choice on which form they preferred. Sessions 2 to 9 involved implementing CBT techniques, working toward goals, and problem solving barriers to improvement. Later sessions focused on relapse prevention. Duration 6 months. Concurrent medication/care: Treatment as usual: No drugs are approved for use in fibromyalgia, and access to CBT or exercise programs is limited, if available at all. The TAU group received the usual care from their family physician, although the precise care delivered, if any, was not recorded. Indirectness: No indirectness; Indirectness comment: NA (n=109) Intervention 2: Usual care. No drugs are approved for use in fibromyalgia, and access to CBT or exercise programs is limited, if available at all. The TAU group received the usual care from their family physician, although the precise care delivered, if any, was not recorded. Duration 6 months. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (Arthritis Research UK)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE	

Study	Mcbeth 2012[304] Beasley 2015[41]
Protocol outcome 1: Health related quality of life - Actual outcome: EQ-5D at 9 months (3 months follow up); Group 1: mean 0.754 (SD 0.214); n=71, Group 2: mean 0.645 (SD 0.262); n=83; EQ-5D 0-1 Top=High is good outcome; Comments: Baseline values: CBT 0.73 (0.151), TAU 0.649 (0.216) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 41, Reason: NR; Group 2 Number missing: 26, Reason: NR Protocol outcome 2: Sleep - Actual outcome: Sleep scale at 9 months (3 months follow up); Group 1: mean 12.4 (SD 5.7); n=91, Group 2: mean 13.1 (SD 5.4); n=98; Sleep Scale 0-20 Top=High is poor outcome; Comments: Baseline values: CBT 13.3 (5.5), TAU 13.8 (5.5) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 21, Reason: NR; Group 2 Number missing: 11, Reason: NR Protocol outcome 3: Discontinuation - Actual outcome: Withdrawal from treatment at 6 months ; Group 1: 24/112, Group 2: 2/109; Comments: reasons for withdrawal not reported Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Pain reduction

Study	Menzies 2006[315]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=48)
Countries and setting	Conducted in USA; Setting: unclear
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 10 weeks
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA

Study	Menzies 2006[315]
Inclusion criteria	Age ≥ 18, diagnosis of FM, Mini-Mental Status Examination (MMSE) score >25, and a Fibromyalgia Impact Questionnaire (FIQ) score >20.
Exclusion criteria	Presence of other systemic rheumatologic conditions or, a major communicative disorder.
Recruitment/selection of patients	recruited from physicians' offices and clinics in the University of Virginia Health System
Age, gender and ethnicity	Age - Mean (SD): 49.6 (10.53) years. Gender (M:F): 1/47. Ethnicity: 43 white; 4 black; 1 other
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=24) Intervention 1: Psychological therapy - Relaxation techniques. 3 x 20 minute guided imagery audiotapes. First tape: training to develop familiarity with relaxation and imagery, muscle relaxation and release of tension, signal breath practiced daily for 2 weeks. Second tape: shortened version of the signal breath relaxation script, followed by imagery of a pleasant scene, practiced daily for 2 weeks. Third tape: reinforced the signal breath conditioning for relaxation, instructed to imagine themselves walking onto a theater stage where they were to perform actions and behaviours that represented how they would most like to be were they free of all symptoms of FM (end state imagery), practiced daily for 2 weeks. During a 4-week follow-up, participants could choose to use any of the three tapes in any order and were requested to use at least one of the tapes once daily. Duration 10 weeks. Concurrent medication/care: usual care. Indirectness: No indirectness; Indirectness comment: NA (n=24) Intervention 2: Usual care. Usual care - no further details provided. Duration 10 weeks. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (National Center for Complementary and Alternative Medicine; National Institute of Nursing Research)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RELAXATION TECHNIQUES versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact questionnaire at 10 weeks; Group 1: mean 39.73 (SD 3.03); n=24, Group 2: mean 49.17 (SD 2.9); n=24; Fibromyalgia impact questionnaire 0-80 Top=High is poor outcome; Comments: Baseline values: relaxation 53.69 (2.28), usual care 52.99 (2.18) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Demographic data not reported but statement that no

Study	Menzies 2006[315]
significant differences; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Pain self-efficacy - Actual outcome: Arthritis Self-efficacy Scale - pain sub scale at 10 weeks; Group 1: mean 64.73 (SD 4.69); n=24, Group 2: mean 49.83 (SD 4.49); n=24; Arthritis Self-efficacy scale - pain sub scale 10-100 Top=High is good outcome; Comments: Baseline values: relaxation 51.91 (4.72), usual care 50.75 (4.52) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Demographic data not reported but statement that no significant differences; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Pain reduction - Actual outcome: McGill Pain Questionnaire pain VAS at 10 weeks; Group 1: mean 5.06 (SD 0.46); n=24, Group 2: mean 5.79 (SD 0.44); n=24; VAS 0-10 Top=High is poor outcome; Comments: Baseline values: relaxation 5.79 (0.45), usual care 6.36 (0.44) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Demographic data not reported but statement that no significant differences; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Use of healthcare services ; Sleep ; Discontinuation

Study	Menzies 2014[314]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=72)
Countries and setting	Conducted in USA
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 10 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age ≥18, female, diagnosis of FMS, no known major psychiatric or neurological conditions that would interfere with study participation, and ability to understand and sign the consent form and complete the study questionnaires

Study	Menzies 2014[314]
Exclusion criteria	Presence of other systemic rheumatologic conditions, history of epilepsy, presence of any psychiatric disorder involving a history of psychosis, being immune-compromised (e.g., HIV/AIDS), receiving corticosteroid treatments, or being pregnant
Age, gender and ethnicity	Age - Mean (SD): 46.9 (12.8) years. Gender (M:F): all female. Ethnicity: Hispanic or Latino 6%, Not Hispanic or Latino 94%
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=36) Intervention 1: Psychological therapy - Relaxation techniques. 3 x 20 minute guided imagery audiotapes. First tape: training to develop familiarity with relaxation and imagery, muscle relaxation and release of tension, signal breath practiced daily for 2 weeks. Second tape: shortened version of the signal breath relaxation script, followed by imagery of a pleasant scene, practiced daily for 2 weeks. Third tape: guided the participant on an imaginary journey through their immune system, practiced daily for 2 weeks. During a 4-week follow-up, participants could choose to use any of the three tapes in any order and were requested to use at least one of the tapes once daily. Duration 10 weeks. Concurrent medication/care: Asked to maintain their current care practices in managing FMS symptoms. All participants were asked not to initiate any new treatments, if possible, for the duration of their 10-week participation . Indirectness: No indirectness; Indirectness comment: NA (n=36) Intervention 2: Usual care. Asked to maintain their current care practices in managing FMS symptoms. All participants were asked not to initiate any new treatments, if possible, for the duration of their 10-week participation. Duration 10 weeks. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (National Institute of Nursing Research; National Center for Research Resources and NIH Roadmap for Medical Research, National Institutes of Health)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RELAXATION TECHNIQUES versus USUAL CARE

Protocol outcome 1: Psychological distress
- Actual outcome: Center for Epidemiological Studies – Depression at 10 weeks; Group 1: mean 18.7 (SD 13.69); n=30, Group 2: mean 23 (SD 13.59); n=34; Center for Epidemiological Studies- Depression scale 0-60 Top=High is poor outcome; Comments: Baseline values: relaxation 23.1 (13.58), usual care 22.4 (13.53) Standard deviations calculated from standard errors.

Study	Menzies 2014[314]
	Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: lost to follow up (n=4), discontinued intervention (n=2); Group 2 Number missing: 2, Reason: unclear Protocol outcome 2: Pain interference - Actual outcome: Brief Pain Inventory – interference at 10 weeks; Group 1: mean 4.2 (SD 2.74); n=30, Group 2: mean 4.9 (SD 2.74); n=34; Brief Pain Inventory (BPI) Short form - pain interference sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: relaxation 5.5 (2.74), usual care 5.3 (2.74). Standard deviations calculated from standard errors. Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: lost to follow up (n=4), discontinued intervention (n=2); Group 2 Number missing: 2, Reason: unclear Protocol outcome 3: Pain self-efficacy - Actual outcome: Arthritis Self-Efficacy Scale - self-efficacy for managing other symptoms sub scale at 10 weeks; Group 1: mean 63.1 (SD 21.36); n=30, Group 2: mean 52.5 (SD 21.34); n=34; Arthritis Self-Efficacy Scale self-efficacy for managing other symptoms sub scale 10-100 Top=High is good outcome; Comments: Baseline values: relaxation 47.9 (21.2), usual care 49 (21.1) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: lost to follow up (n=4), discontinued intervention (n=2); Group 2 Number missing: 2, Reason: unclear Protocol outcome 4: Discontinuation - Actual outcome: Discontinuation at 10 weeks; Group 1: 2/36, Group 2: 2/36; Comments: Reasons: relaxation - too sick to continue (n=1), hospitalised (n=1), usual care - heart surgery (n=1), family crisis/illness (n=1) Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Pain reduction - Actual outcome: Brief Pain Inventory – severity at 10 weeks; Group 1: mean 4.6 (SD 2.14); n=30, Group 2: mean 5.1 (SD 2.16); n=24; Brief Pain Inventory short form - pain severity sub scale 0-10 Top=High is poor outcome; Comments: Baseline values: relaxation 5.3 (2.14), usual care 4.7 (2.16). Standard deviations calculated from standard errors. Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: lost to follow up (n=4), discontinued intervention (n=2); Group 2 Number missing: 2, Reason: unclear
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Use of healthcare services ; Sleep

Study	Miro 2011[319]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=44)
Countries and setting	Conducted in Spain; Setting: Clinical Psychology Unit
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 7 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	ACR diagnostic criteria for FM and APA criteria for insomnia
Exclusion criteria	being pregnant; history of head injury or neurological disorder; major concomitant medical conditions; major depressive disorder and suicidal ideation or other Axis I diagnoses; sleep-disruptive comorbidities; apnea-hypopnea index or periodic limb movement-related arousal index of 15 or more per hour of sleep; severe hypnotic dependence; treatment with another psychological or physical therapy
Recruitment/selection of patients	selected from the Rheumatology Service and Pain Unit of a single hospital
Age, gender and ethnicity	Age - Mean (SD): 46.45 (7.03) years. Gender (M:F): 0/44. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=22) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 6 x weekly 90 minute group sessions (5-6 participants) led by 3 female CBT experts with experience in FM. Information about relationship between FM and sleep and sleep hygiene education; sleep restriction and stimulus control instructions; relaxation training; cognitive therapy for dysfunctional beliefs related to insomnia; maintaining achievements and preventing relapses. Duration 6 weeks . Concurrent medication/care: usual medical treatment - stable doses of medication. Indirectness: Serious indirectness; Indirectness comment: included relaxation and education components

Study	Miro 2011[319]
	(n=22) Intervention 2: Psychological therapy - Sleep management/hygiene. 6 x weekly 90 minute group sessions (5-6 participants) led by 3 female CBT experts with experience in FM. Information about relationship between FM and sleep and sleep hygiene education; sleep hygiene rules related to environmental factors; lifestyle factors that influence sleep; information about diet and physical exercise; maintaining achievements and preventing relapse. Duration 6 weeks. Concurrent medication/care: usual medical treatment - stable doses of medication. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (Spanish Ministry of Science and Innovation)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus SLEEP MANAGEMENT/HYGEINE

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact Questionnaire at 7 weeks (1 week post treatment); Group 1: mean 49.25 (SD 21.38); n=20, Group 2: mean 63.67 (SD 16.08); n=20; Fibromyalgia Impact Questionnaire not reported Top=High is poor outcome; Comments: Baseline values: CBT 59.66 (12.83), SH 62.19 (13.97)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: did not receive CBT (n=1), did not attend post treatment assessment (n=1); Group 2 Number missing: 2, Reason: did not attend post treatment assessment (n=2)

Protocol outcome 2: Psychological distress
- Actual outcome: Hospital Anxiety and Depression scale - anxiety at 7 weeks (1 week post treatment); Group 1: mean 10.95 (SD 4.26); n=20, Group 2: mean 11.55 (SD 3.84); n=20; HADS- anxiety 0-42 Top=High is poor outcome; Comments: Baseline values: CBT 10.6 (4.13), SH 11.6 (4.12)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: did not receive CBT (n=1), did not attend post treatment assessment (n=1); Group 2 Number missing: 2, Reason: did not attend post treatment assessment (n=2)
- Actual outcome: Hospital Anxiety and Depression scale - depression at 7 weeks (1 week post treatment); Group 1: mean 9.65 (SD 4.39); n=20, Group 2: mean 11.3 (SD 4.61); n=20; HADS-depression 0-42 Top=High is poor outcome; Comments: Baseline values: CBT 10.5 (3.69), SH 12.2 (3.73)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: did not receive CBT (n=1), did not attend post treatment assessment (n=1); Group 2 Number missing: 2, Reason: did not attend post treatment assessment (n=2)

Protocol outcome 3: Sleep
- Actual outcome: Pittsburgh Sleep Quality Index total at 7 weeks (1 week post treatment); Group 1: mean 11.55 (SD 4.29); n=20, Group 2: mean 13.2 (SD 3.12); n=20; Pittsburgh Sleep Quality Index 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 15.05 (3.39), SH 14.15 (3.11)

Study	Miro 2011[319]
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: did not receive CBT (n=1), did not attend post treatment assessment (n=1); Group 2 Number missing: 2, Reason: did not attend post treatment assessment (n=2) Protocol outcome 4: Discontinuation - Actual outcome: Discontinuation at 6 weeks; Group 1: 1/22, Group 2: 0/22; Comments: reason: changes in work time Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Pain reduction - Actual outcome: McGill Pain Questionnaire at 7 weeks (1 week post treatment); Group 1: mean 6.5 (SD 2.46); n=20, Group 2: mean 8.26 (SD 1.48); n=20; McGill Pain Questionnaire VAS pain intensity 0-100 Top=High is poor outcome; Comments: Baseline values: CBT 7.02 (1.92), SH 8.26 (1.7) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: did not receive CBT (n=1), did not attend post treatment assessment (n=1); Group 2 Number missing: 2, Reason: did not attend post treatment assessment (n=2)	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services

Study	Pain and Stress Treatment for Fibromyalgia (PAST-FM) trial: Lumley 2017[294]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=230)
Countries and setting	Conducted in USA; Setting: not reported
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 8 weeks + 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	FM defined by ACR criteria
Exclusion criteria	comorbid autoimmune disorders; serious medical illness, cognitive impairment, psychosis, suicidality, or recent alcohol/drug dependence; pending FM related litigation or disability; non-English speaking; inappropriate for group participation (borderline personality features)

Study	Pain and Stress Treatment for Fibromyalgia (PAST-FM) trial: Lumley 2017[294]
Recruitment/selection of patients	flyers sent to rheumatologists; advertisements in the community; announcements to FM associations; informational workshops
Age, gender and ethnicity	Age - Mean (SD): 49.13 (12.22) years. Gender (M:F): 14/216. Ethnicity: 77.8% white, 17.8% black, 4.3% other
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=75) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 8 x 90 minute weekly sessions with a therapist (with doctorial degrees and experience in CBT pain management) focussing on coping and skills training for pain and symptom management. Each session included a topic driven brief lecture, teaching and practice of a skill and homework applying skills to everyday life e.g. self-monitoring, time-based pacing, guided imagery, cognitive reframing and goal setting. Duration 8 weeks. Concurrent medication/care: continued usual care (no further details reported). Indirectness: Serious indirectness; Indirectness comment: included relaxation elements (n=76) Intervention 2: Psychological therapy - Pain education. 8 x 90 minute weekly sessions with a therapist (nurse educator) covering the history and diagnosis of fibromyalgia, assessment of pain, fibromyalgia mechanisms, comorbid disorders, medications, evaluating fibromyalgia research and using the internet for information on health care. Duration 8 weeks. Concurrent medication/care: continued usual care (no further details reported). Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (National Institute of Arthritis, Musculoskeletal and Skin Diseases)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus PAIN EDUCATION

Protocol outcome 1: Health related quality of life
- Actual outcome: Satisfaction with life scale at 10 weeks ; Group 1: mean 19.23 (SD 8.07); n=75, Group 2: mean 19.15 (SD 7.64); n=76; Satisfaction with life scale not reported Top=High is good outcome; Comments: Baseline values: CBT 18.28 (7.83), education 18.21 (7.39)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: withdrew from trial ; Group 2 Number missing: 3, Reason: unavailable (1), withdrew from trial (2)
- Actual outcome: Satisfaction with life scale at 6 months ; Group 1: mean 19.64 (SD 7.81); n=75, Group 2: mean 18.58 (SD 7.72); n=76; Satisfaction with life scale not reported Top=High is good outcome; Comments: Baseline values: CBT 18.28 (7.83), education 18.21 (7.39)

Study	Pain and Stress Treatment for Fibromyalgia (PAST-FM) trial: Lumley 2017[294]
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: withdrew from trial (7), unavailable (2); Group 2 Number missing: 4, Reason: unavailable (1), withdrew from trial (3) Protocol outcome 2: Physical function - Actual outcome: SF12 physical function at 10 weeks ; Group 1: mean 37.5 (SD 10.14); n=75, Group 2: mean 36.63 (SD 8.52); n=76; SF12 0-100 Top=High is good outcome; Comments: Baseline values: CBT 35.51 (9.24), education 34.86 (8.84) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: withdrew from trial ; Group 2 Number missing: 3, Reason: unavailable (1), withdrew from trial (2) - Actual outcome: SF12 physical function at 6 months ; Group 1: mean 39.08 (SD 9.88); n=75, Group 2: mean 36.91 (SD 9.48); n=76; SF12 0-100 Top=High is good outcome; Comments: Baseline values: CBT 35.51 (9.24), education 34.86 (8.84) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: withdrew from trial (7), unavailable (2); Group 2 Number missing: 4, Reason: unavailable (1), withdrew from trial (3) Protocol outcome 3: Psychological distress - Actual outcome: Center for Epidemiological Studies - depression at 10 weeks ; Group 1: mean 16.35 (SD 11.44); n=75, Group 2: mean 18.22 (SD 11.21); n=76; CES-D 0-60 Top=High is poor outcome; Comments: Baseline values: CBT 20.2 (11.88), education 18.3 (11.69) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: withdrew from trial ; Group 2 Number missing: 3, Reason: unavailable (1), withdrew from trial (2) - Actual outcome: Center for Epidemiological Studies - depression at 6 months ; Group 1: mean 17.33 (SD 11.9); n=75, Group 2: mean 18.46 (SD 12.07); n=76; CES-D 0-60 Top=High is poor outcome; Comments: Baseline values: CBT 20.2 (11.88), education 18.3 (11.69) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: withdrew from trial (7), unavailable (2); Group 2 Number missing: 4, Reason: unavailable (1), withdrew from trial (3) - Actual outcome: Generalised anxiety disorder-7 at 10 weeks ; Group 1: mean 6.23 (SD 5.19); n=75, Group 2: mean 6.53 (SD 5.14); n=76; GAD-7 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 7.57 (5.56), education 6.51 (5.21) Risk of bias: All domain - ; Indirectness of outcome: No indirectness - Actual outcome: Generalised anxiety disorder-7 at 6 months ; Group 1: mean 5.82 (SD 5.03); n=75, Group 2: mean 7.12 (SD 5.2); n=76; GAD-7 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 7.57 (5.56), education 6.51 (5.21) Risk of bias: All domain - ; Indirectness of outcome: No indirectness Protocol outcome 4: Use of healthcare services - Actual outcome: Health care use (number of times a person had seen a physician or other health professional in past 3 months) at 10 weeks ; Group 1: mean 3.73 visits (SD 4.68); n=75, Group 2: mean 4.54 visits (SD 5.73); n=76; Comments: Baseline values: CBT 4.32 (5.82), education 4.12 (4.89)	

Study	Pain and Stress Treatment for Fibromyalgia (PAST-FM) trial: Lumley 2017[294]
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: withdrew from trial ; Group 2 Number missing: 3, Reason: unavailable (1), withdrew from trial (2) - Actual outcome: Health care use (number of times a person had seen a physician or other health professional in past 3 months) at 6 months ; Group 1: mean 3.39 visits (SD 4.13); n=75, Group 2: mean 4.8 visits (SD 6.13); n=76; Comments: Baseline values: CBT 4.32 (5.82), education 4.12 (4.89) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: withdrew from trial (7), unavailable (2); Group 2 Number missing: 4, Reason: unavailable (1), withdrew from trial (3) Protocol outcome 5: Sleep - Actual outcome: Pittsburgh sleep quality index - sleep problems at 10 weeks ; Group 1: mean 10.09 (SD 4.27); n=75, Group 2: mean 12.5 (SD 4.4); n=76; Pittsburgh sleep quality index not reported Top=High is poor outcome; Comments: Baseline values: CBT 12.36 (4.06), education 12.53 (4.35) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: withdrew from trial ; Group 2 Number missing: 3, Reason: unavailable (1), withdrew from trial (2) - Actual outcome: Pittsburgh sleep quality index - sleep problems at 6 months ; Group 1: mean 10.13 (SD 4.18); n=75, Group 2: mean 10.74 (SD 4.29); n=76; Pittsburgh sleep quality index not reported Top=High is poor outcome; Comments: Baseline values: CBT 12.36 (4.06), education 12.53 (4.35) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: withdrew from trial (7), unavailable (2); Group 2 Number missing: 4, Reason: unavailable (1), withdrew from trial (3) Protocol outcome 6: Discontinuation - Actual outcome: Attending less than 3 sessions at 10 weeks ; Group 1: 8/75, Group 2: 3/76; Comments: reasons for non-attendance unclear Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: Pain reduction - Actual outcome: Brief pain inventory (severity) at 10 weeks ; Group 1: mean 4.69 (SD 1.65); n=75, Group 2: mean 5.2 (SD 1.68); n=76; BPI severity 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 5.35 (1/62), education 5.47 (1.74) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: withdrew from trial ; Group 2 Number missing: 3, Reason: unavailable (1), withdrew from trial (2) - Actual outcome: Brief pain inventory (severity) at 6 months ; Group 1: mean 4.82 (SD 1.7); n=75, Group 2: mean 4.94 (SD 1.96); n=76; BPI severity 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 5.35 (1/62), education 5.47 (1.74) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9, Reason: withdrew from trial (7), unavailable (2); Group 2 Number missing: 4, Reason: unavailable (1), withdrew from trial (3)	

Study	Pain and Stress Treatment for Fibromyalgia (PAST-FM) trial: Lumley 2017[294]
Protocol outcomes not reported by the study	Pain interference ; Pain self-efficacy

Study	Parra-delgado 2013[445]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=33)
Countries and setting	Conducted in Spain; Setting: unclear
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 3 months + 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	ACR diagnosis of FM and commitment to daily practice of mindfulness
Exclusion criteria	alcohol/substance dependence/abuse; receiving psychological therapy from the Castilla-La Mancha Health Service fibromyalgia team
Recruitment/selection of patients	recruited from the Fibromyalgia Association of Almansa
Age, gender and ethnicity	Age - Mean (SD): MBCT 53.13 (10.5) years, usual care 52.69 (10.58) years. Gender (M:F): 0/33. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=17) Intervention 1: Psychological therapy - Mindfulness. Mindfulness based cognitive therapy. 8 x structured 2.5 hr group sessions led by a therapist with certified training in MBCT. Practical mindfulness

Study	Parra-delgado 2013[445]
	exercises with a focus on pain-related stimuli and aiming to teach patients to relate pain experiences to thoughts and feelings in a different way psycho-educational activities on causes and development of depression and anxiety; identification of methods of self-care; formal practice at home (body scanning, sitting/walking medication, mindful breathing) 6 days a week. Duration 3 months. Concurrent medication/care: usual medication, medical visits, rehabilitation sessions and activities proposed by the Fibromyalgia Association. Indirectness: No indirectness; Indirectness comment: NA (n=16) Intervention 2: Usual care. Usual medication, medical visits, rehabilitation sessions and activities proposed by the Fibromyalgia Association. Duration study duration. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MINDFULNESS versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact Questionnaire at 3 months; Group 1: mean 61.77 (SD 13.65); n=15, Group 2: mean 66.2 (SD 17.22); n=16; Fibromyalgia Impact Questionnaire 0-100 Top=High is poor outcome; Comments: Baseline values: MBCT 77.09 (13.45), usual care 64.74 (14.06)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: discontinued intervention ; Group 2 Number missing: 0, Reason: NA
- Actual outcome: Fibromyalgia Impact Questionnaire at 6 months (3 months follow up); Group 1: mean 63.25 (SD 15.8); n=15, Group 2: mean 70.77 (SD 10.54); n=16; Fibromyalgia Impact Questionnaire 0-100 Top=High is poor outcome; Comments: Baseline values: MBCT 77.09 (13.45), usual care 64.74 (14.06)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: discontinued intervention ; Group 2 Number missing: 0, Reason: NA

Protocol outcome 2: Psychological distress
- Actual outcome: Beck Depression Inventory at 3 months; Group 1: mean 13 (SD 6.35); n=15, Group 2: mean 15.44 (SD 6.88); n=16; Beck Depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: MBCT 18.6 (7.2), usual care 16.88 (5.85)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: discontinued intervention ; Group 2 Number missing: 0, Reason: NA
- Actual outcome: Beck Depression Inventory at 6 months (3 months follow up); Group 1: mean 13.13 (SD 5.34); n=15, Group 2: mean 17.75 (SD 5.86); n=16; Beck Depression Inventory 0-63 Top=High is poor outcome; Comments: Baseline values: MBCT 18.6 (7.2), usual care 16.88 (5.85)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Study	Parra-delgado 2013[445]
Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 2, Reason: discontinued intervention ; Group 2 Number missing: 0, Reason: NA Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation at 3 months; Group 1: 2/17, Group 2: 0/16; Comments: reason for discontinuation not reported Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep ; Pain reduction

Study (subsidiary papers)	Peski-oosterbaan 1999[452] (Van peski-oosterbaan 1999[549])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=72)
Countries and setting	Conducted in Netherlands; Setting: single cardiology clinic
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: cardiologist diagnosis (several clinical and laboratory assessments)
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18-75 years old; chest pain as the main complaint; minimum of 1 episode weekly; normal cardiovascular system according to a cardiologist
Exclusion criteria	proven coronary artery disease or myocardial ischemia as demonstrated by coronary angiography, exercise testing, laboratory examination, electrocardiogram or chest x-ray; a history of typical angina pectoris; insufficient fluency in Dutch; current psychiatric treatment for noncardiac chest pain; current diagnosis of an organic mental syndrome, psychotic disorder, major depression, bipolar disorder or use of psychoactive substances within 3 months before study entry
Recruitment/selection of patients	referral by GP
Age, gender and ethnicity	Age - Mean (SD): 48.9 (10.6) years. Gender (M:F): 29/36. Ethnicity: not reported

Study (subsidiary papers)	Peski-oosterbaan 1999[452] (Van peski-oosterbaan 1999[549])
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: Yes 4. Chronic widespread pain: No 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=36) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 4 to 12 weekly sessions of 45-60 minutes, depending on severity of problem, final 1 or 2 sessions were monthly, maximum duration of therapy was 6 months, delivered by physicians with basic training in CBT and a senior psychologist. Written information about therapy, procedures, alternative explanations, related factors and possible consequences of the complaints. First session: physical symptoms, results of medical investigations, coping strategies. Sessions 2-4: breathing and relaxation. Subsequent sessions: identifying and challenging irrational beliefs using diaries. Session 8 and on: behavioural experiments to challenge negative thoughts. Duration up to 6 months. Concurrent medication/care: not reported. Indirectness: Serious indirectness; Indirectness comment: CBT included relaxation (n=36) Intervention 2: Usual care. Free to use health resources as they saw fit. Duration 12 months (6 month intervention + 6 months follow up). Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Psychological distress
- Actual outcome: Hospital Anxiety and Depression Scale anxiety at 12 months; Group 1: mean 6.9 (SD 3.1); n=31, Group 2: mean 7.2 (SD 4); n=32; HADS anxiety 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 10.3 (4.4), usual care 7.9 (3.9)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5; Group 2 Number missing: 4
- Actual outcome: Hospital Anxiety and Depression Scale depression at 12 months; Group 1: mean 3.9 (SD 3.3); n=31, Group 2: mean 5.6 (SD 4.2); n=32; HADS depression 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 5.3 (4.8), usual care 5.1 (3.9)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5; Group 2 Number missing: 4

Protocol outcome 2: Use of healthcare services
- Actual outcome: visits to GP for non-cardiac chest pain at 12 months; Group 1: 2/31, Group 2: 4/32; Comments: measured by GP report. observed

Study (subsidiary papers)	Peski-oosterbaan 1999[452] (Van peski-oosterbaan 1999[549])
agreement between GPs and patients was 86% Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5; Group 2 Number missing: 4 - Actual outcome: referral to a specialist for non-cardiac chest pain at 12 months; Group 1: 1/31, Group 2: 1/32; Comments: measured by GP report. observed agreement between GPs and patients was 86% Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5; Group 2 Number missing: 4 - Actual outcome: use of additional psychological services at 12 months; Group 1: 0/31, Group 2: 6/32; Comments: measured by GP report. observed agreement between GPs and patients was 86% Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5; Group 2 Number missing: 4 Protocol outcome 3: Discontinuation - Actual outcome: discontinuation at 6 months; Group 1: 4/36, Group 2: 3/36; Comments: CBT: 3 dropped out at the beginning of the study because they believed treatment and assignments would be too time consuming, 1 developed a major depressive episode during treatment and had to be excluded usual care: 3 dropped out at the beginning of the study because they did not want to enter the control group Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: Pain reduction - Actual outcome: number free of non-cardiac chest pain at 12 months; Group 1: 15/31, Group 2: 4/31 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 5; Group 2 Number missing: 5
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Pain interference ; Pain self-efficacy ; Sleep

Study	Peters 2017[453]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=284)
Countries and setting	Conducted in Multiple countries; Setting: N/A (through internet)
Line of therapy	Unclear
Duration of study	Intervention + follow up: 8 week intervention and 6 month follow up

Study	Peters 2017[453]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Formal diagnosis of musculoskeletal pain for longer than 3 months, either generalized pain (i.e., fibromyalgia) or localized in back, neck or shoulders
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	Above 18 years, having musculoskeletal pain for longer than 3 months, either generalized pain (i.e., fibromyalgia) or localized in back, neck or shoulders, good command of Dutch, and having access to the internet
Exclusion criteria	not being able to perform simple physical exercises, having a degenerative muscle diseases or a condition that could aggravate due to physical activity (e.g., spinal stenosis), heart or vascular diseases, being diagnosed with psychiatric disorders in the past 3 months, pregnancy and having had psychological or multidisciplinary pain treatment in the past 3 months
Recruitment/selection of patients	Recruitment: took place in 2012 newspapers and magazines and through an announcement on the websites of the Dutch and Belgian Societies for Fibromyalgia patients. Individuals with fibromyalgia could apply by e-mail or through a link on a dedicated website.
Age, gender and ethnicity	Age - Mean (SD): 49.4(11.5) years. Gender (M:F): 44:232. Ethnicity: Not stated
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: Yes 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: Yes 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: Not applicable 11. Sensory impairment: No
Extra comments	Duration of pain 11.95 (9.5) years, 70% had fibromyalgia
Indirectness of population	No indirectness: NA
Interventions	(n=116) Intervention 1: Psychological therapy - Cognitive behavioural therapy. Delivered through the internet. Participants could access the site where the program was hosted through a username and password and a 6-digit security code that was provided to their mobile phone at every login. 8 modules. In the first week, only the first module could be accessed. Exactly 1 week later, module 2 became available, again 1 week later module 3, etc. Seven weeks after participants had started with the first module, the complete treatment program was available to them. Mean duration of the intervention for intervention completers was 9.3 weeks (range, 7 to 16 wk). Each module provided online written information about the topic of that week and practical assignments. Assignments could either be completed online or in a workbook that was provided to participants at the start of the intervention. To promote adherence, telephone (weeks 1, 3, 5, and 7) and e-mail (weeks 2, 4, 6, and 8) support was provided by 5 graduate or recently graduated students in Psychology. Every participant had a single assistant assigned to them. The telephone calls were semi structured and covered participants' efforts on the assignments of the previous weeks, possible problems, or questions regarding the modules. The average duration of the telephone calls was 15

Study	Peters 2017[453]
	to 20 minutes. Semi standardized e-mails were sent to participants in the weeks between the telephone contacts encouraging them to continue with the program and to share any problems they might have encountered. The main purpose of the program was to teach participants more active ways of coping with their pain and to improve their level of functioning. The original Swedish texts were translated in Dutch and slightly adapted to Dutch culture. The program consisted of 7 modules teaching applied relaxation, stretching exercises, cognitive restructuring, and coping techniques. In module 2, 3, and 4 body scan exercises were provided, in text and in mp3 format, and could be downloaded. In the eighth module participants made a 6 relapse prevention plan, that is, how to continue with the strategies they had learned. Duration 8 weeks. Concurrent medication/care: Not specified. Indirectness: Serious indirectness; Indirectness comment: included relaxation elements (n=51) Intervention 2: Usual care. In the waiting list control group participants were initially only given access to the online pretreatment questionnaires. After an 8-week waiting period, participants were contacted and 1 asked to complete the post measurements. After completion, they could start with the treatment program of their choice (iCBT or PPI). No further data were obtained from these patients after completion of the program and no support was provided during the intervention period, except for assistance in case of technical problems. Duration 8 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Academic or government funding (VICI innovative research grant from the Netherlands Organization of Scientific Research)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus WAITING LIST CONTROL

Protocol outcome 1: Physical function
- Actual outcome: Fibromyalgia impact questionnaire - physical impairment sub scale at Post intervention (8 weeks); Group 1: mean 17.94 (SD 5.44); n=112, Group 2: mean 20.63 (SD 5.86); n=50; Fibromyalgia Impact Questionnaire physical impairment sub scale 0-27 Top=High is poor outcome; Comments: Baseline values: CBT 19.46 (5.4), usual care 21.22 (5.71). Two items inquiring about the ability to drive a car and to work in the garden were excluded from the total score because these items were not relevant for all participants.
Risk of bias: All domain – Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 36, Reason: did not start n=4, drop out with notification n=18, drop out without notification n=14; Group 2 Number missing: 10, Reason: did not start n=1, drop out with notification n=1, drop out without notification n=8

Protocol outcome 2: Psychological distress
- Actual outcome: Hospital Anxiety and Depression Scale - anxiety at Post intervention (8 weeks); Group 1: mean 6.63 (SD 3.41); n=112, Group 2: mean

Study	Peters 2017[453]
7.27 (SD 3.58); n=50; HADS anxiety 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 9.05 (4.06), usual care 7.31 (3.75) Risk of bias: All domain - ; Indirectness of outcome: No indirectness, Comments: NA - Actual outcome: Hospital Anxiety and Depression Scale - depression at Post intervention (8 weeks); Group 1: mean 4.99 (SD 2.86); n=112, Group 2: mean 7.73 (SD 3.27); n=50; HADS depression 0-21 Top=High is poor outcome; Comments: Baseline values: CBT 7.33 (3.42), usual care 7.2 (3.32) Risk of bias: All domain – Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 36, Reason: did not start n=4, drop out with notification n=18, drop out without notification n=14; Group 2 Number missing: 10, Reason: did not start n=1, drop out with notification n=1, drop out without notification n=8 Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation at Post intervention (8 weeks); Group 1: 36/116, Group 2: 10/51; Comments: CBT: did not start (n=4), dropped out with notification (n=18), dropped out without notification (n=14). Usual care: did not start (n=1), dropped out with notification (n=1), dropped out without notification (n=9) Risk of bias: All domain – High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: Pain reduction - Actual outcome: Pain intensity numeric rating scale at Post intervention (8 weeks); Group 1: mean 5.71 (SD 2.25); n=112, Group 2: mean 6.2 (SD 1.99); n=50; Comments: Baseline values: CBT 6.11 (2.05), usual care 6.44 (1.46) Risk of bias: All domain – Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 36, Reason: did not start n=4, drop out with notification n=18, drop out without notification n=14; Group 2 Number missing: 10, Reason: did not start n=1, drop out with notification n=1, drop out without notification n=8	
Protocol outcomes not reported by the study	Health related quality of life ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Picard 2013[455]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=62)
Countries and setting	Conducted in France; Setting: single pain clinic
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FM
Stratum	Overall: NA

Study	Picard 2013[455]
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	women with FM syndrome for at least 6 months diagnosed by a rheumatologist using ACR criteria
Exclusion criteria	Chronic inflammatory arthritis. peripheral or central neuropathic pain; treated with opioids; severe psychiatric illness including major depression or major personality disorders; history of substance abuse
Recruitment/selection of patients	consecutive patients referred to the pain clinic meeting the inclusion criteria
Age, gender and ethnicity	Age - Mean (SD): hypnosis 48.1 (9.3) years, waiting list 49.3 (8.5) years. Gender (M:F): 0/62. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=31) Intervention 1: Psychological therapy - Hypnosis. 5 x 1 hour sessions (8, 15, 21 and 28 day intervals) conducted by a psychologist qualified in hypnotherapy. Interventions were patient-tailored and directed toward enhancing patient competence and mastery in managing pain and stress related to disease. Sessions involved hypnotic induction, analgesic and non-analgesic suggestions, including reinterpreting pain sensation as numbness through the use of imagery, improving individual coping, improving stress-management skills and changing relationship with disease. Patients instructed to practice self-hypnosis daily. Duration 3 months. Concurrent medication/care: allowed to continue pain medications and antidepressants if necessary. All patients received an educational session on fibromyalgia delivered by a nurse prior to the intervention. Indirectness: No indirectness (n=31) Intervention 2: Usual care. Waiting list control. Duration 3 months. Concurrent medication/care: allowed to continue pain medications and antidepressants if necessary. All patients received an educational session on fibromyalgia delivered by a nurse prior to the intervention. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HYPNOSIS versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: FIQ at 12 weeks; Group 1: mean -0.9 (SD 9.28); n=29, Group 2: mean 0.19 (SD 9.28); n=30; FIQ 0-100 Top=High is poor outcome;
Comments: Standard deviation calculated from p-value: 0.77
Baseline: 50.1(13.6); 49.5(11.6)

Study	Picard 2013[455]
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention - Actual outcome: FIQ at 6 months; Group 1: mean -4.6 (SD 14.32); n=29, Group 2: mean -0.7 (SD 14.32); n=30; FIQ 0-100 Top=High is poor outcome; Comments: Standard deviation calculated from p value: 0.3 baseline: 50.1(13.6); 49.5(11.6) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention Protocol outcome 2: Psychological distress - Actual outcome: HADS anxiety subscale at 12 weeks; Group 1: mean -0.86 (SD 1.87); n=30, Group 2: mean -0.74 (SD 1.87); n=29; Hospital anxiety and depression anxiety subscale Not specified Top=High is poor outcome; Comments: Standard deviation calculated from p-value: 0.87 Baseline: 9.9(4.1); 10.8(3.7) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention - Actual outcome: HADS anxiety subscale at 6 months; Group 1: mean -1.2 (SD 16.35); n=30, Group 2: mean -0.5 (SD 16.35); n=29; Hospital anxiety and depression scale, anxiety subscale Not specified Top=High is poor outcome; Comments: Standard deviation calculated from p-value: 0.87 Baseline: 9.9(4.1); 10.8(3.7) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention - Actual outcome: HADS depression subscale at 12 weeks; Group 1: mean -1.12 (SD 2.97); n=30, Group 2: mean -0.39 (SD 2.97); n=29; Hospital anxiety and depression scale, depression subscale Not specified Top=High is poor outcome; Comments: Standard deviation calculated from p-value: 0.35 Baseline: 12.1(4); 12(4.6) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention - Actual outcome: HADS depression subscale at 6 months; Group 1: mean -1.4 (SD 2.6); n=30, Group 2: mean -0.1 (SD 2.6); n=29; Hospital anxiety and depression scale, depression subscale Not specified Top=High is poor outcome; Comments: Standard deviation calculated from p-value: 0.06 Baseline: 12.1(4); 12(4.6) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention Protocol outcome 3: Sleep

Study	Picard 2013[455]
	- Actual outcome: Medical outcome study sleep scale, index I at 12 weeks; Group 1: mean -5.8 (SD 11.65); n=29, Group 2: mean -2.3 (SD 11.65); n=30; MOS Sleep Not specified Top=High is poor outcome; Comments: Standard deviation calculated from p-value: 0.36 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention - Actual outcome: Medical outcome study sleep scale, index I at 6 months; Group 1: mean -8.6 (SD 3.87); n=29, Group 2: mean 1.7 (SD 3.87); n=30; MOS Sleep Not specified Top=High is poor outcome; Comments: Standard deviation calculated from p-value: 0.01 Baseline scores not specified Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention Protocol outcome 4: Discontinuation - Actual outcome: Discontinuation at 24 weeks; Group 1: 1/31, Group 2: 2/31; Comments: UC: due to committing to physical rehabilitation programme Hypnosis: discontinued intervention before starting Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention Protocol outcome 5: Pain reduction - Actual outcome: Numeric rating scale at 24 weeks; Group 1: mean 6.04 (SD 1.15); n=30, Group 2: mean 6.64 (SD 1.15); n=29; NRS 0-10 Top=High is poor outcome; Comments: Standard deviation calculated from p-value: 0.05 Baseline: 7.16(0.5);6.8(1.5) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Initiation of physical rehabilitation program; Group 2 Number missing: 1, Reason: Discontinued intervention
Protocol outcomes not reported by the study	Physical function ; Pain interference ; Pain self-efficacy ; Use of healthcare services

Study	Sánchez 2012[477]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=26)
Countries and setting	Conducted in Spain; Setting: Clinical Psychology Unit at the University of Grenada
Line of therapy	Unclear

Study	Sánchez 2012[477]
Duration of study	Intervention time: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged between 25-60 years; met the diagnostic criteria for FM as defined by the American College of Rheumatology; have chronic insomnia according to DSM-IV
Exclusion criteria	Pregnancy, significant head or neurological disorders, any other major concomitant medical condition, other sleep-disruptive comorbidities or receiving any other psychological of physical therapy.
Recruitment/selection of patients	referred from the Clinical Psychology Unit at the University of Grenada
Age, gender and ethnicity	Age - Mean (SD): 46.79 (5.15) years. Gender (M:F): All women. Ethnicity: Not specified
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: No 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: No
Extra comments	Duration of fibromyalgia 5.02 (4.28) years
Indirectness of population	No indirectness
Interventions	(n=13) Intervention 1: Psychological therapy - Cognitive behavioural therapy. The whole evaluation consisted of two sessions of individual interviews focusing on the origin and evolution of the problem and domiciliary PSG. Three female CBT experts with experience in FM provided the therapy guided by a treatment manual designed for the study. Each therapist applied both treatments (CBT-I and SH). Therapists delivered CBT-I and SH treatment in 6 weekly groups sessions. Each session included 5-6 participants and lasted around 90 minutes. The CBT-I program was designed according the works of Edinger et al. (2005), and met the recommendations of the American Academy of Sleep Medicine (Morgenthaler et al., 2006). Subjects who participated in SH therapy just received sleep hygiene instructions and were offered CBT-I after their post-treatment assessment. Duration 6 weeks. Concurrent medication/care: All participants on stable medication during the trial. Indirectness: No indirectness (n=13) Intervention 2: Psychological therapy - Sleep management/hygiene. Identical format to CBT but sessions focused on sleep hygiene only. This included sleep hygiene education, rules related to environmental and lifestyle factors, and information about diet and physical exercise, as well as goal making and maintaining achievements. Duration 6 weeks. Concurrent medication/care: All participants on stable medication throughout trial. Indirectness: No indirectness

Study	Sánchez 2012[477]
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus SLEEP MANAGEMENT/HYGEINE Protocol outcome 1: Sleep - Actual outcome: Sleep (total sleep time, hours) at 6 weeks; Group 1: mean 6.53 (SD 2.19); n=13, Group 2: mean 6.57 (SD 0.55); n=13; Comments: 7.03(1.04); 7.31(0.54) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Discontinuation ; Pain reduction

Study	Scheidt 2013[480]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=47)
Countries and setting	Conducted in Germany; Setting: University of Freiburg medical center
Line of therapy	Unclear
Duration of study	Intervention time: 25 weeks plus 12 months follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 18-70 years, women, met the fibromyalgia criteria (ACR), current depression or anxiety disorder as per ICD-10
Exclusion criteria	Any severe or life-threatening diseases, psychiatric or neuropsychiatric conditions associated with cognitive impairments and/or suicidal ideation, current psychotherapy or participation in other clinical trials
Recruitment/selection of patients	Via patient self-help groups, news media and referrals from the department of rheumatology at the University of Freiburg Medical Center
Age, gender and ethnicity	Age - Mean (SD): 48.76 (7.92) years. Gender (M:F): All women. Ethnicity: Not specified

Study	Scheidt 2013[480]
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: 6. Complex regional pain syndrome: No 7. First language not English: No 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: Not applicable 11. Sensory impairment: No
Extra comments	Duration of pain 8.12 (7.88) years
Indirectness of population	No indirectness
Interventions	(n=24) Intervention 1: Psychological therapy - Psychotherapy (psychodynamic and psychoanalytic). 25 weekly sessions of psychodynamic psychotherapy specifically adapted to the needs of patients with pain symptoms. Sessions lasted between 50min to 1 hour. Treatment approach based on a dysregulation model of psychosomatic illness and on research on attachment styles and affect regulation in somatoform disorders, with integrated components of interpersonal therapy. Duration 25 weeks. Concurrent medication/care: 52% on anti-depressant medication at baseline, 76% taking analgesic medication and 90% aerobic exercise. Indirectness: No indirectness (n=23) Intervention 2: Usual care. Treatment as usual, with contacts during a 6 month period, each lasting about 10-15 minutes in which patients were advised with regard to medication and health behaviour and were encouraged to increase physical activity and gentle stretching exercises. Duration 25 weeks. Concurrent medication/care: 61% on anti-depressant medication at baseline, 91% taking analgesic medication and 70% aerobic exercise. Indirectness: No indirectness
Funding	Academic or government funding (Freiburg institute of advanced studies)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PSYCHOTHERAPY (PSYCHODYNAMIC AND PSYCHOANALYTIC) versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: SF-36 physical summary component score at 18 months; Group 1: mean 31.8 (SD 1.9); n=23, Group 2: mean 32.9 (SD 1.9); n=23; SF-36 summary score 0-100 Top=High is good outcome; Comments: Baseline 28.9(1.5); 30.7(1.5)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of participants on other treatments at baseline (91% versus 76% taking analgesic medication; 70% versus 90% taking part in exercise); Blinding details: Downgraded for difference at baseline for different care being received under 'selection bias' domain; Group 1 Number missing: 6, Reason: Stopped intervention, death, moving house, lost to follow up; Group 2 Number missing: 7, Reason: Discontinued intervention, lost to follow-up
- Actual outcome: SF-36 mental summary component score at 18 months; Group 1: mean 43.5 (SD 2.3); n=23, Group 2: mean 39.4 (SD 2.3); n=23; SF-36 summary scale 0-100 Top=High is good outcome; Comments: Baseline: 39.3(2.2);37.6(2.2)
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Study	Scheidt 2013[480]
Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of participants on other treatments at baseline (91% versus 76% taking analgesic medication; 70% versus 90% taking part in exercise); Blinding details: Downgraded for difference at baseline for different care being received under 'selection bias' domain; Group 1 Number missing: 6, Reason: Stopped intervention, death, moving house, lost to follow up; Group 2 Number missing: 7, Reason: Discontinued intervention, lost to follow-up Protocol outcome 2: Physical function - Actual outcome: Somatoform disorders-7 at 18 months; Group 1: mean 17.5 (SD 2.2); n=23, Group 2: mean 22 (SD 2.2); n=23; SOMS complaints Not specified Top=High is poor outcome; Comments: Baseline: 22.7(2.1); 23.9(2.1) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of participants on other treatments at baseline (91% versus 76% taking analgesic medication; 70% versus 90% taking part in exercise); Blinding details: Downgraded for difference at baseline for different care being received under 'selection bias' domain; Group 1 Number missing: 6, Reason: Stopped intervention, death, moving house, lost to follow up; Group 2 Number missing: 7, Reason: Discontinued intervention, lost to follow-up Protocol outcome 3: Psychological distress - Actual outcome: HADS anxiety at 18 months; Group 1: mean 7.6 (SD 0.8); n=23, Group 2: mean 8.1 (SD 0.8); n=23; Hospital anxiety and depression scale, anxiety subscale Not specified Top=High is poor outcome; Comments: Baseline: 9.3(0.9);8.4(0.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of participants on other treatments at baseline (91% versus 76% taking analgesic medication; 70% versus 90% taking part in exercise); Blinding details: Downgraded for difference at baseline for different care being received under 'selection bias' domain; Group 1 Number missing: 6, Reason: Stopped intervention, death, moving house, lost to follow up; Group 2 Number missing: 7, Reason: Discontinued intervention, lost to follow-up - Actual outcome: HADS depression at 12 months; Group 1: mean 9 (SD 1); n=23, Group 2: mean 9.7 (SD 1); n=23; hospital anxiety and depression scale, depression subscale Not specified Top=High is poor outcome; Comments: Baseline: 9.6(0.9); 9.3(0.9) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of participants on other treatments at baseline (91% versus 76% taking analgesic medication; 70% versus 90% taking part in exercise); Blinding details: Downgraded for difference at baseline for different care being received under 'selection bias' domain; Group 1 Number missing: 6, Reason: Stopped intervention, death, moving house, lost to follow up; Group 2 Number missing: 7, Reason: Discontinued intervention, lost to follow-up Protocol outcome 4: Pain interference - Actual outcome: Pain disability index at 18 months; Group 1: mean 34.5 (SD 3.5); n=23, Group 2: mean 36.5 (SD 3.5); n=23; Pain disability index 0-70 Top=High is poor outcome; Comments: Baseline: 41.6(2.6); 40.3(2.6) Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of participants on other treatments at baseline (91% versus 76% taking analgesic medication; 70% versus 90% taking part in exercise); Blinding details: Downgraded for difference at baseline for different care being received under 'selection bias' domain; Group 1 Number missing: 6, Reason: Stopped intervention, death, moving house, lost to follow up;	

Study	Scheidt 2013[480]
Group 2 Number missing: 7, Reason: Discontinued intervention, lost to follow-up Protocol outcome 5: Discontinuation - Actual outcome: Discontinuation at 18 months; Group 1: 2/24, Group 2: 3/23 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in number of participants on other treatments at baseline (91% versus 76% taking analgesic medication; 70% versus 90% taking part in exercise); Blinding details: Downgraded for difference at baseline for different care being received under 'selection bias' domain; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Pain self-efficacy ; Use of healthcare services ; Sleep ; Pain reduction

Study	Simister 2018[494]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=67)
Countries and setting	Conducted in Canada; Setting: internet based
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 2 months + 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: formal diagnosis
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18 years and older; formal diagnosis of FM; self-reported pain intensity of at least 4 out of 10; also screened using the FM diagnostic criteria according to Wolfe et al.
Exclusion criteria	presence of comorbidities such as rheumatologic conditions, conditions affecting the immune system, brain injury, cognitive impairment, active psychosis, substance abuse, untreated severe major depression/bipolar disorder, active suicidality, current active injury claim
Recruitment/selection of patients	referrals by physicians, advertisements in a local newspaper, waiting rooms at local clinics, various self-help groups for FM
Age, gender and ethnicity	Age - Mean (SD): 39.7 (9.36). Gender (M:F): 95% female. Ethnicity: not reported
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=33) Intervention 1: Psychological therapy - Acceptance and commitment therapy. Online ACT programme under the guidance of a registered psychologist - 7 modules, each containing a written unit including metaphors, experiential exercises and recurring vignettes describing the experiences of 4 people with FM, enhanced with audio recordings, videos and experiential homework exercises. Completed at own pace but encouraged to spend 1 week per module, sent weekly email reminders. Duration 2 months. Concurrent medication/care: Treatment as usual - continued current treatment regime such as guidance from GP. Prescribed and over the counter analgesics were the most commonly reported treatments (others included mood stabilisers, anticonvulsants and supplements). Participants additionally reported spinal nerve blocks, massage, physiotherapy, exercise programmes, acupuncture, heat/cold therapy and dietary changes before

	the study. Indirectness: No indirectness; Indirectness comment: NA (n=34) Intervention 2: Usual care. Treatment as usual - continued current treatment regime such as guidance from GP. Prescribed and over the counter analgesics were the most commonly reported treatments (others included mood stabilisers, anticonvulsants and supplements). Participants additionally reported spinal nerve blocks, massage, physiotherapy, exercise programmes, acupuncture, heat/cold therapy and dietary changes before the study. Duration 5 months (2 month intervention + 3 month follow up). Concurrent medication/care: NA. Indirectness: Serious indirectness; Indirectness comment: some participants used treatments which would not be considered usual care, but unclear how many
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ACCEPTANCE AND COMMITMENT THERAPY versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: Fibromyalgia Impact Questionnaire at 2 months; Group 1: mean 39.07 (SD 13.07); n=30, Group 2: mean 55.3 (SD 12.65); n=31; Fibromyalgia impact questionnaire 0-100 Top=High is poor outcome; Comments: Baseline values: ACT 55.83 (12.56), usual care 55.28 (16.39)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrew prior to treatment (3), withdrew during treatment (3); Group 2 Number missing: 3, Reason: withdrew prior to treatment (3)
- Actual outcome: Fibromyalgia Impact Questionnaire at 5 months (3 month follow up); Group 1: mean 31.95 (SD 13.8); n=30, Group 2: mean 53.82 (SD 13.92); n=31; Fibromyalgia impact questionnaire 0-100 Top=High is poor outcome; Comments: Baseline values: ACT 55.83 (12.56), usual care 55.28 (16.39)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 8, Reason: withdrew prior to treatment (3), withdrew during treatment (3), lost to follow up (2); Group 2 Number missing: 9, Reason: withdrew prior to treatment (3), lost to follow up (6)

Protocol outcome 2: Physical function
- Actual outcome: 6 minute walk test at 2 months; Group 1: mean 358.3 meters (SD 113); n=30, Group 2: mean 364.69 meters (SD 108.51); n=31; 6 minute walk test NA Top=High is good outcome; Comments: Baseline values: ACT 371.53 (100.98), usual care 345.61 (100.98)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrew prior to treatment (3), withdrew during treatment (3); Group 2 Number missing: 3, Reason: withdrew prior to treatment (3)
- Actual outcome: 6 minute walk test at 5 months (3 month follow up); Group 1: mean 383.84 meters (SD 122.05); n=30, Group 2: mean 349.33 meters (SD 120.29); n=31; 6 minute walk test NA Top=High is good outcome; Comments: Baseline values: ACT 371.53 (100.98), usual care 345.61 (100.98)

Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 8, Reason: withdrew prior to treatment (3), withdrew during treatment (3), lost to follow up (2); Group 2 Number missing: 9, Reason: withdrew prior to treatment (3), lost to follow up (6)

Protocol outcome 3: Psychological distress
- Actual outcome: Center for Epidemiological Studies Depression Scale at 2 months; Group 1: mean 17.76 (SD 10.83); n=30, Group 2: mean 26.97 (SD 10.46); n=31; Center for epidemiological studies depression scale 0-60 Top=High is poor outcome; Comments: Baseline vales: ACT 26.6 (12.38), usual care 27.81 (12.38)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrew prior to treatment (3), withdrew during treatment (3); Group 2 Number missing: 3, Reason: withdrew prior to treatment (3)
- Actual outcome: Center for Epidemiological Studies Depression Scale at 5 months (3 month follow up); Group 1: mean 18.36 (SD 12.12); n=30, Group 2: mean 25.13 (SD 12.29); n=31; Center for epidemiological studies depression scale 0-60 Top=High is poor outcome; Comments: Baseline vales: ACT 26.6 (12.38), usual care 27.81 (12.38)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 8, Reason: withdrew prior to treatment (3), withdrew during treatment (3), lost to follow up (2); Group 2 Number missing: 9, Reason: withdrew prior to treatment (3), lost to follow up (6)

Protocol outcome 4: Sleep
- Actual outcome: Pittsburgh Sleep Quality Index at 2 months; Group 1: mean 10.24 (SD 3.6); n=30, Group 2: mean 13 (SD 3.47); n=31; Pittsburgh sleep quality index 0-21 Top=High is poor outcome; Comments: Baseline values: ACT 12.67 (3.8), usual care 13.26 (3.8)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrew prior to treatment (3), withdrew during treatment (3); Group 2 Number missing: 3, Reason: withdrew prior to treatment (3)
- Actual outcome: Pittsburgh Sleep Quality Index at 5 months (3 month follow up); Group 1: mean 10.7 (SD 4.71); n=30, Group 2: mean 13.21 (SD 4.76); n=31; Pittsburgh sleep quality index 0-21 Top=High is poor outcome; Comments: Baseline values: ACT 12.67 (3.8), usual care 13.26 (3.8)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 8, Reason: withdrew prior to treatment (3), withdrew during treatment (3), lost to follow up (2); Group 2 Number missing: 9, Reason: withdrew prior to treatment (3), lost to follow up (6)

Protocol outcome 5: Discontinuation
- Actual outcome: withdrawal before or during treatment phase at 2 months; Group 1: 6/33, Group 2: 3/34; Comments: ACT: withdrew prior to treatment due to preferring alternative treatment (n=1), unable to contact (n=2); withdrew during treatment n=3, reason not reported

Usual care: withdrew prior to treatment due to unable to contact (n=3) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: Pain reduction - Actual outcome: McGill Pain Questionnaire at 2 months; Group 1: mean 13.8 (SD 8.81); n=30, Group 2: mean 21 (SD 8.41); n=31; McGill pain questionnaire short form 0-45 Top=High is poor outcome; Comments: Baseline values: ACT 26.07 (8.41), usual care 25.84 (8.41) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 6, Reason: withdrew prior to treatment (3), withdrew during treatment (3); Group 2 Number missing: 3, Reason: withdrew prior to treatment (3) - Actual outcome: McGill Pain Questionnaire at 5 months (3 month follow up); Group 1: mean 21.46 (SD 9.1); n=30, Group 2: mean 22.49 (SD 9.21); n=31; McGill pain questionnaire 0-45 Top=High is poor outcome; Comments: Baseline values: ACT 26.07 (8.41), usual care 25.84 (8.41) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Comparable to outcome measures at baseline but group demographics not reported ; Group 1 Number missing: 8, Reason: withdrew prior to treatment (3), withdrew during treatment (3), lost to follow up (2); Group 2 Number missing: 9, Reason: withdrew prior to treatment (3), lost to follow up (6)	
Protocol outcomes not reported by the study	Pain interference ; Pain self-efficacy ; Use of healthcare services

Study	**Soares 2002[500]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=60)
Countries and setting	Conducted in Sweden; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention + follow up: 10 weeks and 6 month follow up

Study	Soares 2002[500]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Fibromyalgia diagnosis during the past 2 years, female, aged 18-64 years, no other serious illnesses, no ongoing substance abuse, not receiving other therapies
Exclusion criteria	No more specified
Recruitment/selection of patients	From GPs in Stockholm southwest healthcare region
Age, gender and ethnicity	Age - Mean (SD): 45(9) years. Gender (M:F): All female. Ethnicity: Not specified
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: No 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: Not applicable 11. Sensory impairment: No
Extra comments	42.77(39.01) months duration of pain
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Psychological therapy – Cognitive behavioural therapy. 5 individual sessions (1h each) and 15 group sessions (2h each/3-5 patients in each group) over a 10 week period (totalling 120h of therapy). Sessions were conducted by a licensed psychologist/CB therapist. 2 individual sessions focused on preparation of a personal guide for maintenance. In the remaining 3, the patients received applied relaxation evaluated through biofeedback in a psychophysiological laboratory. The intervention focused mainly on the acquisition and development of diverse skills to manage pain. Group sessions on practical management covered the types of pain, and the 3 component model of pain, stress and its reactions, behavioural patterns that increase the risk for stress and ill health, how to create calm in the week days, thought traps, attitudes and patterns of thinking, problem solving, pain management, environmental issues, self-management, estimation of risk, plans and goals for the future, maintenance and relapse. Duration 10 weeks. Concurrent medication/care: Not specified. Indirectness: Serious indirectness; Indirectness comment: included relaxation and biofeedback elements (n=20) Intervention 2: Psychological therapy - Pain education. 2 individual sessions (2h each) and 15 group sessions (2 hours each, 3-5 patients in each group) over a 10 week period (totalling 102 hours). Conducted by a licensed physiotherapist and occupational therapist. The focus of the intervention was on information about various health-related topics, about: the body, FMS, pain, sleep hygiene, stress, education, managing crises, ergonomic education, and self-management. An element of body awareness training was also included. Duration 10 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness

Study	Soares 2002[500]
	(n=20) Intervention 3: Usual care. Waiting list control. No further details. Duration 10 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus PAIN EDUCATION

Protocol outcome 1: Health related quality of life
- Actual outcome: FIQ at 6 months; Group 1: mean 2.33 (SD 0.78); n=18, Group 2: mean 2.36 (SD 0.73); n=18; FIQ 0-10 Top=High is poor outcome; Comments: Baseline: 2.11(0.8); 2.33(0.78)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR
- Actual outcome: FIQ at 10 week; Group 1: mean 2.25 (SD 0.73); n=18, Group 2: mean 2.66 (SD 0.73); n=18; FIQ 0-10 Top=High is poor outcome; Comments: Baseline: 2.11(0.8); 2.33(0.78)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR

Protocol outcome 2: Pain self-efficacy
- Actual outcome: Coping Skills Questionnaire; self-efficacy subscale at 10 weeks; Group 1: mean 6.44 (SD 1.79); n=18, Group 2: mean 6.06 (SD 1.92); n=18; CSQ self-efficacy ? Top=High is good outcome; Comments: Baseline: 4.98(1.33); 5.86(1.64)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR
- Actual outcome: Coping Skills Questionnaire; self-efficacy subscale at 6 months; Group 1: mean 5.07 (SD 2.43); n=18, Group 2: mean 5.27 (SD 2.79); n=18; CSQ self-efficacy ? Top=High is good outcome; Comments: Baseline: 4.98(1.33); 5.86(1.64)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR

Protocol outcome 3: Sleep
- Actual outcome: Karolinska sleep questionnaire sleep quality at 10 weeks; Group 1: mean 3.64 (SD 0.91); n=18, Group 2: mean 3.87 (SD 0.83); n=18; KSQ sleep quality ? Top=High is good outcome; Comments: Baseline: 3.69(0.83); 3.94(0.8)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR
- Actual outcome: Karolinska sleep questionnaire sleep quality at 6 months; Group 1: mean 3.21 (SD 1.19); n=18, Group 2: mean 4.08 (SD 1.04); n=18; KSQ sleep quality ? Top=High is good outcome; Comments: Baseline: 3.69(0.83); 3.94(0.8)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR

Study	Soares 2002[500]
	Protocol outcome 4: Pain reduction - Actual outcome: McGill Pain questionnaire (total) at 10 weeks; Group 1: mean 43.64 (SD 35.06); n=18, Group 2: mean 49.14 (SD 41.87); n=18; MPQ 0-78 Top=High is poor outcome; Comments: Baseline: 44.29(31.36);54.36(30.53) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR - Actual outcome: McGill Pain questionnaire (total) at 6 months; Group 1: mean 44.21 (SD 29.12); n=18, Group 2: mean 47.29 (SD 35.92); n=18; MPQ 0-78 Top=High is poor outcome; Comments: Baseline: 44.29(31.36);54.36(30.53) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE Protocol outcome 1: Health related quality of life - Actual outcome: FIQ at 10 week; Group 1: mean 2.25 (SD 0.73); n=18, Group 2: mean 2.65 (SD 0.56); n=17; FIQ 0-10 Top=High is poor outcome; Comments: Baseline: 2.11(0.8); 2.7(0.74) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR Protocol outcome 2: Pain self-efficacy - Actual outcome: Coping Skills Questionnaire; self-efficacy subscale at 10 weeks; Group 1: mean 6.44 (SD 1.79); n=18, Group 2: mean 5.59 (SD 2.01); n=18; ? CSQ self-efficacy scale Top=High is good outcome; Comments: Baseline: 4.98(1.33); 5.76(2.01) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR Protocol outcome 3: Sleep - Actual outcome: Karolinska sleep questionnaire sleep quality at 10 weeks; Group 1: mean 3.64 (SD 0.8); n=18, Group 2: mean 3.74 (SD 0.8); n=17; KSQ sleep quality ? Top=High is good outcome; Comments: Baseline: 3.69(0.83); 3.62(0.81) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR Protocol outcome 4: Pain reduction - Actual outcome: McGill Pain questionnaire (total) at 10 weeks; Group 1: mean 43.64 (SD 35.06); n=18, Group 2: mean 45.24 (SD 32.09); n=17; MPQ 0-78 Top=High is poor outcome; Comments: Baseline: 44.29(31.36);18.88(15.05): difference at baseline Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in PSQ at baseline; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR

Study	Soares 2002[500]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PAIN EDUCATION versus USUAL CARE Protocol outcome 1: Health related quality of life - Actual outcome: FIQ at 10 weeks; Group 1: mean 2.66 (SD 0.73); n=18, Group 2: mean 2.65 (SD 0.56); n=17; FIQ 0-10 Top=High is poor outcome; Comments: Baseline: 2.63(0.58); 2.7(0.74) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR Protocol outcome 2: Pain self-efficacy - Actual outcome: Coping Skills Questionnaire; self-efficacy subscale at 10 weeks; Group 1: mean 6.06 (SD 1.92); n=18, Group 2: mean 5.59 (SD 2.01); n=17; CSQ self-efficacy scale ? Top=High is good outcome; Comments: Baseline: 5.86(1.64); 5.76(2.01) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR Protocol outcome 3: Sleep - Actual outcome: Karolinska sleep questionnaire sleep quality at 10 weeks; Group 1: mean 3.87 (SD 0.83); n=18, Group 2: mean 3.74 (SD 0.8); n=17; KSQ sleep quality ? Top=High is good outcome; Comments: Baseline: 3.94(0.8); 3.62(0.81) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR Protocol outcome 4: Pain reduction - Actual outcome: McGill Pain questionnaire (total) at 10 weeks; Group 1: mean 49.14 (SD 41.87); n=18, Group 2: mean 45.24 (SD 32.09); n=17; MPQ 0-78 Top=High is poor outcome; Comments: Baseline: 54.36(30.53); 18.88(15.05) Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Difference in PSQ at baseline; Group 1 Number missing: 2, Reason: NR; Group 2 Number missing: 3, Reason: NR	
Protocol outcomes not reported by the study	Physical function ; Psychological distress ; Pain interference ; Use of healthcare services ; Discontinuation

Study	SPIN (Sleep and Pain Interventions in Fibromyalgia) trial: McCrae 2018[310]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=113)
Countries and setting	Conducted in USA; Setting: not reported

Study	SPIN (Sleep and Pain Interventions in Fibromyalgia) trial: McCrae 2018[310]
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 8 weeks + 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: American College of Rheumatology guidelines
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	aged 18 or older; willing to undergo randomization; able to read and understand English; FM criteria were pain for at least 6 months and confirmation of FM by tender point testing, using guidelines established by the American College of Rheumatology (with application of 4 kg force, participants reported pain in at least 11 of 18 points, including points in all four body quadrants); chronic insomnia criteria were insomnia complaints (sleep onset or awake time during night >30 min) at least three nights per week for more than 6 months; sleep diary confirmation of insomnia (sleep onset or awake time during night >30 min) at least six nights during the 2 week baseline period; daytime dysfunction due to insomnia (mood, cognitive, social, or occupational impairment); and no prescribed or over-the-counter sleep medications for at least 1 month or stabilized on sleep medication for at least 6 months; participants taking pain medications as well as those with common psychological comorbidities (e.g. depression and anxiety) were included to increase generalizability
Exclusion criteria	sleep disorders other than insomnia; bipolar or seizure disorders; significant medical (e.g. cancer) or neurological disorder (e.g. dementia); severe untreated psychiatric comorbidity (e.g. schizophrenia and substance abuse); cognitive impairment based on Mini-Mental State Examination (MMSE) score below 26; concurrent participation in CBT or other nonpharmacological treatment outside of the study
Recruitment/selection of patients	recruited from rheumatology and sleep clinics at a single university and from the surrounding area through community advertisements
Age, gender and ethnicity	Age - Mean (SD): CBTi 54.13 (11.03) years, CBTp 51.54 (10.62) years, waiting list 52.27 (11.19) years. Gender (M:F): 3/110. Ethnicity: CBTi white 82%, black 15%, native Indian/Alaskan native 3%, biracial 0% CBTp white 92%, black 8%, native Indian/Alaskan native 0%, biracial 3% Waiting list white 65%, black 30%, native Indian/Alaskan native 3%, biracial 3%
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA

Study	SPIN (Sleep and Pain Interventions in Fibromyalgia) trial: McCrae 2018[310]
Interventions	(n=39) Intervention 1: Psychological therapy - Cognitive behavioural therapy. CBT-I - 8 individually delivered 50 minute sessions by pre-doctoral students in clinical psychology. Treatment developed by psychologists who provided training, weekly supervision, and on-going monitoring. Participants were given a workbook detailing treatment instructions and rationale. They were questioned during sessions about home practice of techniques and procedural modifications were adopted as needed (e.g. pacing activities differently and adjusting bed/wake times). Interventionists encouraged adherence and emphasized the importance of regular home practice, which was monitored by daily practice logs. Session topics: sleep education, sleep hygiene and stimulus control, relaxation, sleep restriction, cognitive therapy (3 sessions), review of skills and long-term maintenance. Duration 8 weeks. Concurrent medication/care: Not reported. Sleep medication 33.33%, Benzodiazepines 7.69%, Benzodiazepine-like Hypnotics 5.12%, Antidepressants 12.82%, Antihistamines 12.82%. Indirectness: Serious indirectness; Indirectness comment: included elements of sleep hygiene and relaxation (n=37) Intervention 2: Psychological therapy - Cognitive behavioural therapy. CBT-P - 8 individually delivered 50 minute sessions by pre-doctoral students in clinical psychology. Treatment developed by psychologists who provided training, weekly supervision, and on-going monitoring. Participants were given a workbook detailing treatment instructions and rationale. They were questioned during sessions about home practice of techniques and procedural modifications were adopted as needed (e.g. pacing activities differently and adjusting bed/wake times). Interventionists encouraged adherence and emphasized the importance of regular home practice, which was monitored by daily practice logs. Session topics: pain education and diaphragmatic breathing, progressive muscle relaxation, activity-rest cycle and autogenic relaxation, visual imagery, cognitive therapy (3 sessions), review of skills and long-term maintenance. Duration 8 weeks. Concurrent medication/care: Not reported. Sleep Medication 45.95%, Benzodiazepines 10.81%, Benzodiazepine-like Hypnotics 10.81%, Antidepressants 21.62%, Antihistamines 13.51%. Indirectness: Serious indirectness; Indirectness comment: included pain education and relaxation elements (n=37) Intervention 3: Usual care. Waiting list. Duration 8 weeks. Concurrent medication/care: Not reported. Sleep Medication 29.73%, Benzodiazepines 16.22%, Benzodiazepine-like Hypnotics 0.00%, Antidepressants 13.51%, Antihistamines 8.11%. Indirectness: Serious indirectness; Indirectness comment: NA
Funding	Academic or government funding (National Institute of Arthritis and Musculoskeletal and Skin Diseases)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Psychological distress
- Actual outcome: Beck depression inventory (CBTi vs. usual care) at 8 weeks (immediately post intervention); Group 1: mean 8.52 (SD 11.12); n=27,

Study	SPIN (Sleep and Pain Interventions in Fibromyalgia) trial: McCrae 2018[310]
Group 2: mean 16.94 (SD 10.94); n=28; Beck depression inventory 0-63 Top=High is poor outcome; Comments: Baseline values: CBTi 14.08 (10.37), waiting list 19.12 (10.53) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 12, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: Beck depression inventory (CBTp vs. usual care) at 8 weeks (immediately post intervention); Group 1: mean 15.58 (SD 10.68); n=30, Group 2: mean 16.94 (SD 10.94); n=28; Beck depression inventory 0-63 Top=High is poor outcome; Comments: Baseline values: CBTp 16.87 (10.26), waiting list 19.12 (10.53) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 7, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: Beck depression inventory (CBTi vs. usual care) at 6 months ; Group 1: mean 8.22 (SD 11.93); n=24, Group 2: mean 15.01 (SD 11.68); n=23; Beck depression inventory 0-63 Top=High is poor outcome; Comments: Baseline values: CBTi 14.08 (10.37), waiting list 19.12 (10.53) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear - Actual outcome: Beck depression inventory (CBTp vs. usual care) at 6 months ; Group 1: mean 14.38 (SD 11.22); n=27, Group 2: mean 15.01 (SD 11.68); n=23; Beck depression inventory 0-63 Top=High is poor outcome; Comments: Baseline values: CBTp 16.87 (10.26), waiting list 19.12 (10.53) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 10, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear - Actual outcome: State-trait anxiety inventory (CBTi vs. usual care) at 8 weeks (immediately post intervention) ; Group 1: mean 38.95 (SD 12.72); n=27, Group 2: mean 47.72 (SD 12.87); n=28; State-trait anxiety inventory 20-80 Top=High is poor outcome; Comments: Baseline values: CBTi 43.35 (11.64), waiting list 48.29 (12.63) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 12, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: State-trait anxiety inventory (CBTp vs. usual care) at 8 weeks (immediately post intervention) ; Group 1: mean 45.22 (SD 12.12); n=30, Group 2: mean 47.72 (SD 12.87); n=28; State-trait anxiety inventory 20-80 Top=High is poor outcome; Comments: Baseline values: CBTp 45.55 (11.76), waiting list 48.29 (12.63) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 7, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: State-trait anxiety inventory (CBTi vs. usual care) at 6 months ; Group 1: mean 38.07 (SD 13.73); n=24, Group 2: mean 43.87 (SD 13.7); n=23; State-trait anxiety inventory 20-80 Top=High is poor outcome; Comments: Baseline values: CBTi 43.35 (11.64), waiting list 48.29 (12.63) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: unclear ; Group 2 Number missing:

Study	SPIN (Sleep and Pain Interventions in Fibromyalgia) trial: McCrae 2018[310]
	14, Reason: unclear - Actual outcome: State-trait anxiety inventory (CBTp vs. usual care) at 6 months ; Group 1: mean 43.86 (SD 12.78); n=27, Group 2: mean 43.87 (SD 13.7); n=23; State-trait anxiety inventory 20-80 Top=High is poor outcome; Comments: Baseline values: CBTp 45.55 (11.76), waiting list 48.29 (12.63) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 10, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear Protocol outcome 2: Pain interference - Actual outcome: Pain disability index (CBTi vs. usual care) at 8 weeks (immediately post intervention) ; Group 1: mean 27.85 (SD 16.86); n=27, Group 2: mean 35.68 (SD 16.79); n=28; Pain disability index 0-70 Top=High is poor outcome; Comments: Baseline values: CBTi 34.14 (15.6), waiting list 37.59 (15.92) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 12, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: Pain disability index (CBTp vs. usual care) at 8 weeks (immediately post intervention) ; Group 1: mean 38.03 (SD 15.95); n=30, Group 2: mean 35.68 (SD 16.79); n=28; Pain disability index 0-70 Top=High is poor outcome; Comments: Baseline values: CBTp 37.27 (15.25), waiting list 37.59 (15.92) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 7, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: Pain disability index (CBTi vs. usual care) at 6 months ; Group 1: mean 27.76 (SD 17.97); n=24, Group 2: mean 34.87 (SD 18.07); n=23; Pain disability index 0-70 Top=High is poor outcome; Comments: Baseline values: CBTi 34.14 (15.6), waiting list 37.59 (15.92) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear - Actual outcome: Pain disability index (CBTp vs. usual care) at 6 months ; Group 1: mean 36.37 (SD 17.2); n=27, Group 2: mean 34.87 (SD 18.07); n=23; Pain disability index 0-70 Top=High is poor outcome; Comments: Baseline values: CBTp 37.27 (15.25), waiting list 37.59 (15.92) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 10, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear Protocol outcome 3: Sleep - Actual outcome: Self-reported sleep quality rating (CBTi vs. usual care) at 8 weeks (immediately post intervention); Group 1: mean 3.32 (SD 3.44); n=27, Group 2: mean 2.66 (SD 3.35); n=28; sleep quality rating 1-5 Top=High is good outcome; Comments: Baseline values: CBTi 2.62 (3.43), waiting list 2.47 (3.34) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 12, Reason: unclear ; Group 2 Number missing: 9,

Study	SPIN (Sleep and Pain Interventions in Fibromyalgia) trial: McCrae 2018[310]
	Reason: unclear - Actual outcome: Self-reported sleep quality rating (CBTp vs. usual care) at 8 weeks (immediately post intervention); Group 1: mean 3.1 (SD 3.35); n=30, Group 2: mean 2.66 (SD 3.35); n=28; sleep quality rating 1-5 Top=High is good outcome; Comments: Baseline values: CBTp 2.61 (3.34), waiting list 2.47 (3.34) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 7, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: Self-reported sleep quality rating (CBTi vs. usual care) at 6 months ; Group 1: mean 3.27 (SD 3.45); n=24, Group 2: mean 2.65 (SD 3.36); n=23; sleep quality rating 1-5 Top=High is good outcome; Comments: Baseline values: CBTi 2.62 (3.43), waiting list 2.47 (3.34) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear - Actual outcome: Self-reported sleep quality rating (CBTp vs. usual care) at 6 months ; Group 1: mean 3.14 (SD 3.35); n=27, Group 2: mean 2.65 (SD 3.36); n=23; sleep quality rating 1-5 Top=High is good outcome; Comments: Baseline values: CBTp 2.61 (3.34), waiting list 2.47 (3.34) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 10, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear Protocol outcome 4: Pain reduction - Actual outcome: McGill pain questionnaire (CBTi vs. usual care) at 8 weeks (immediately post intervention); Group 1: mean 26.26 (SD 15.01); n=27, Group 2: mean 29.84 (SD 14.53); n=28; McGill pain questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBTi 25.85 (13.15), waiting list 28.53 (13.4) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 12, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: McGill pain questionnaire (CBTp vs. usual care) at 8 weeks (immediately post intervention); Group 1: mean 28.01 (SD 14.15); n=30, Group 2: mean 29.84 (SD 14.53); n=28; McGill pain questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBTp 29.95 (13.27), waiting list 28.53 (13.4) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 7, Reason: unclear ; Group 2 Number missing: 9, Reason: unclear - Actual outcome: McGill pain questionnaire (CBTi vs. usual care) at 6 months; Group 1: mean 23.62 (SD 16.22); n=24, Group 2: mean 23.3 (SD 16.02); n=23; McGill pain questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBTi 25.85 (13.15), waiting list 28.53 (13.4) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 15, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear - Actual outcome: McGill pain questionnaire (CBTp vs. usual care) at 6 months; Group 1: mean 28.99 (SD 15.01); n=27, Group 2: mean 23.3 (SD 16.02);

Study	SPIN (Sleep and Pain Interventions in Fibromyalgia) trial: McCrae 2018[310]
n=23; McGill pain questionnaire 0-78 Top=High is poor outcome; Comments: Baseline values: CBTp 29.95 (13.27), waiting list 28.53 (13.4) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 10, Reason: unclear ; Group 2 Number missing: 14, Reason: unclear	
Protocol outcomes not reported by the study	Health related quality of life; Physical function ; Pain self-efficacy; Use of healthcare services; Discontinuation

Study	Thieme 2006[520]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=125)
Countries and setting	Conducted in Multiple countries
Line of therapy	Unclear
Duration of study	Intervention + follow up: 15 week intervention plus 12 month follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for fibromyalgia
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	(1) meeting ACR criteria for fibromyalgia (2) pain for a period of at least 6 months (3) married (4) willing for spouse to participate
Exclusion criteria	Any inflammatory rheumatologic diseases and any concurrent major disease such as cancer, diabetes or kidney failure.
Recruitment/selection of patients	From 10 outpatient rheumatological clinics
Age, gender and ethnicity	Age - Mean (SD): 47.46(9.75) years. Gender (M:F): All female. Ethnicity: Not specified
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: 6. Complex regional pain syndrome: No 7. First language not English: No 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years : People aged >25 years 11. Sensory impairment: No
Extra comments	Duration of pain 8 (9.5) years
Indirectness of population	No indirectness
Interventions	(n=42) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 15 weekly 2 hour sessions co led by a psychologist and a rheumatologist, conducted in groups of 5 patients. Spouses attended 4 of the sessions. CBT based on a structured manual. Focused on patients' thinking and involved problem-solving, stress and pain coping strategies and relaxation. Patients were taught the meaning of the stress tension pain circle as a cognitive pain model and learned coping strategies and the reduction of catastrophising thoughts. There were weekly homework tasks, encouragement to engage in physical activities, asked to reduce analgesic medication at a gradual rate. Relaxation exercises were also encouraged between the sessions. Therapists identified instances of maladaptive thinking and encouraged the group to challenge these instances and to provide more appropriate interpretations and alternatives. Although the importance of behaviour change was noted, the focus of this treatment was on the change of maladaptive thoughts and attitudes. Duration 15 weeks. Concurrent medication/care: Reduction of analgesic usage. Indirectness:

	Serious indirectness; Indirectness comment: included relaxation elements (n=43) Intervention 2: Psychological therapy - Behaviour therapy. 15 weekly 2 hour sessions co-led by a psychologist and a rheumatologist, conducted in groups of 5 patients. Spouses attended 4 of the sessions. Operant behaviour therapy. Based on changing observable pain behaviours and included video feedback of expressions of pain as well as contingent positive reinforcement of pain incompatible behaviours and punishment of pain behaviours in a group setting. Structured time-contingent exercises were provided according to operant principles in the sessions and as homework exercise. The treatment also included time contingent intake and reduction of medication, increase of bodily activity, reduction of interference of pain with activities, reduction of pain behaviours, and training in assertive pain-incompatible behaviours. Patients also engaged in role playing to reduce pain behaviours and increase healthy behaviours. Patients, spouses and group members used a reinforcer plan that consisted of the presentation of a red card when pain behaviours were displayed and a green card when healthy behaviours were displayed. Patients were encouraged to increase activity levels and reduce medication. Duration 15 weeks. Concurrent medication/care: Analgesic usage reduced. Indirectness: No indirectness (n=40) Intervention 3: Usual care. Attention placebo; general discussions among patients in groups guided by therapists. Discussions were centred around medical and psychosocial problems of fibromyalgia. Patients were given the opportunities to speak about problems with coping, fatigue, pain stress and medication. The therapist did not initiate these topics. No homework was given. Duration 15 weeks. Concurrent medication/care: Not reported. Indirectness: No indirectness
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus BEHAVIOUR THERAPY

Protocol outcome 1: Physical function
- Actual outcome: FIQ physical function subscale at 12 months; Group 1: mean 3.42 (SD 2.29); n=42,
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Depression; Group 2 Number missing: 3, Reason: Major depression, lack of motivation

Protocol outcome 2: Use of healthcare services
- Actual outcome: Number of physician visits at 12 months; Group 1: mean 25.27 (SD 18.47); n=42, Group 2: mean 16.35 (SD 18.26); n=43; Comments: Baseline: 30.55(16.2); 36.87(15.15)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Depression; Group 2 Number missing: 3, Reason: Major depression, lack of motivation

Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation at 15 weeks; Group 1: 2/42, Group 2: 3/43; Comments: CBT: due to depression BT: due to major depression, lack of motivation Risk of bias: All domain - Low, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: Pain reduction - Actual outcome: Pain intensity (West Haven-Yale multidimensional pain inventory (MPI)) at 12 months; Group 1: mean 3.18 (SD 1.42); n=42, Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Depression; Group 2 Number missing: 3, Reason: Major depression, lack of motivation	
Protocol outcomes not reported by the study	Health related quality of life ; Psychological distress ; Pain interference ; Pain self-efficacy ; Sleep

Study	Turner 2006[538]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=158)
Countries and setting	Conducted in USA; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention time: 12 weeks plus 9 months follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Formal diagnosis of temporomandibular disorder
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 18 years and older, a diagnosis of temporomandibular disorder (research diagnostic criteria/TMD RDC/TMD axis 1 TMD diagnosis, facial pain for at least 3 months with pain related disability defined by a chronic pain grade (von Korgg) of II, III or IV
Exclusion criteria	Need for further diagnostic evaluation, pending litigation or disability compensation for pain, current or previous CBT for pain, and major medical or psychiatric conditions that would interfere with ability to participate
Recruitment/selection of patients	Patients seeking care at the UW orofacial pain clinic between 2001 and 2004
Age, gender and ethnicity	Age - Mean (SD): 36(10.9) years. Gender (M:F): Define. Ethnicity: Not specified
Further population details	1. Chronic orofascial pain: Yes 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: No 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: No 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: Not applicable 11. Sensory impairment: No
Extra comments	Duration of pain episode median 13.5 months (4-78 months)
Indirectness of population	No indirectness
Interventions	(n=79) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 12 week intervention. 4 biweekly sessions over 8 weeks. Participants were given a manual with materials to read between sessions and discuss in sessions. Participants saw one of 3 licensed clinical psychologists, and treatment was based on standard CB pain therapies (turner and Romano) and a previously studied CB intervention for chronic TMD pain (Dworkin). The manual included articles concerning psychological aspects of pain, challenging negative thoughts about pain, relaxation, and other behavioural techniques for pain management, coping with pain flare-ups, and relapse prevention.

Study	Turner 2006[538]
	At each session patients completed a healthcare plan for activities to complete between sessions. Activities were recommended to all participants such as checking the correct jaw posture and progressive relaxation practice, and breathing exercises. Others were individualised to the patients, via the psychologist helping patients to identify potential obstacles and solutions. The session also included practice in progressive relaxation and breathing techniques, participants were given a relaxation audiotape and asked to practice it daily. Duration 12 weeks. Concurrent medication/care: Not specified (n=79) Intervention 2: Psychological therapy - Pain education. Same protocol but sessions didn't include specific CBT techniques and conducted by patient educations trained and supervised by a clinical psychologist. No advice or recommendations were given beyond the protocol and participants were given information about TMD, general health care information and reviewing each point in the manual, as well as answering patient questions. Duration 8 weeks. Concurrent medication/care: Not specified
Funding	Academic or government funding (National institute of dental and craniofascial research)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus PAIN EDUCATION

Protocol outcome 1: Physical function
- Actual outcome: MFIQ mandibular function impairment questionnaire at 12 weeks; Group 1: mean 0.48 (SD 0.26); n=79, Group 2: mean 0.54 (SD 0.23); n=79; MFIQ masticatory ? Top=High is poor outcome; Comments: Baseline: 0.6(0.26); 0.56(0.25)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9
- Actual outcome: MFIQ mandibular function impairment questionnaire at 12 months; Group 1: mean 0.4 (SD 0.27); n=7979, Group 2: mean 0.5 (SD 0.25); n=79; MFIQ masticatory scale ? Top=High is poor outcome; Comments: Baseline: 0.6(0.26); 0.56(0.25)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9

Protocol outcome 2: Pain self-efficacy
- Actual outcome: TMD self-efficacy scale at 12 months; Group 1: mean 7.1 (SD 2.3); n=79, Group 2: mean 5.8 (SD 2); n=79; TMD self-efficacy scale ? Top=High is good outcome; Comments: Baseline: 4.8(2.1); 5(2.1)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9
- Actual outcome: TMD self-efficacy scale at 12 weeks; Group 1: mean 6.4 (SD 1.9); n=79, Group 2: mean 5.3 (SD 1.9); n=79; TMD self-efficacy scale ? Top=High is good outcome; Comments: Baseline: 4.8(2.1); 5(2.1)
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9

Study	Turner 2006[538]
Protocol outcome 3: Discontinuation - Actual outcome: Discontinuation at 12 weeks; Group 1: 9/79, Group 2: 7/79 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9 Protocol outcome 4: Pain reduction - Actual outcome: Pain intensity VAS at 12 weeks; Group 1: mean 5.2 (SD 1.9); n=79, Group 2: mean 5.2 (SD 2.1); n=79; VAS 0-10 Top=High is poor outcome; Comments: Baseline:6.8(1.7);6.8(1.7) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9 - Actual outcome: Pain intensity VAS at 12 months; Group 1: mean 3.9 (SD 2.6); n=79, Group 2: mean 4.7 (SD 2.3); n=79; VAS 0-10 Top=High is poor outcome; Comments: Baseline:6.8(1.7);6.8(1.7) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9 - Actual outcome: Beck depression inventory at 12 months; Group 1: mean 8.3 (SD 9.1); n=79, Group 2: mean 11.4 (SD 10.1); n=79; BDI 0-61 Top=High is poor outcome; Comments: Baseline: 13.4(8.6); 13.4(8.8) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9 - Actual outcome: Beck depression inventory at 12 weeks; Group 1: mean 0.48 (SD 0.26); n=79, Group 2: mean 0.54 (SD 0.23); n=79; BDI 0-61 Top=High is poor outcome; Comments: Baseline: 13.4(8.6); 13.4(8.8) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 9	
Protocol outcomes not reported by the study	Health related quality of life ; Psychological distress ; Pain interference ; Use of healthcare services ; Sleep

Study	Van Santen 2002[551]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=143)
Countries and setting	Conducted in Netherlands; Setting: Not specified
Line of therapy	Unclear
Duration of study	Intervention + follow up: 8 week intervention and 16 weeks follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	18 to 60 years, women, living within 30km of either centre.
Exclusion criteria	Known comorbidities and those with more localised myalgia, heart disease, asthma, unsettled disability compensation disputes or incapacitating psychological distress
Recruitment/selection of patients	From the central registry for the diagnosis of rheumatic diseases
Age, gender and ethnicity	Age - Mean (range): 43.9(26-60) years. Gender (M:F): All women. Ethnicity: Not specified
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: No 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: Not applicable 11. Sensory impairment: No
Extra comments	Duration of pain 10.1 (range 1-38) years in biofeedback group, 15.4, range 3-40 in control
Indirectness of population	No indirectness
Interventions	(n=56) Intervention 1: Psychological therapy - Biofeedback. Individual 30 minute sessions twice weekly for 8 weeks, in a hospital. In the first session patients were given general suggestions to accomplish muscle relaxation and were given feedback using a tonometer. In the subsequent 15 sessions patients were taught the progressive relaxation technique consisting of alternately tightening and relaxation different groups of muscles, led by a regular supervisor (psychologist or physiotherapist). They additionally encouraged each subject to practice the progressive relaxation technique twice daily at home using an audiotape, and to continue this for 16 weeks after the biofeedback sessions had ended. Duration 8 weeks. Concurrent medication/care: Half of individuals were also randomised to receive an educational program aimed to improve compliance, which consisted of 6 health promotion sessions of 90 minutes each, spread over the 24 weeks. Included information on FM, general health education, self-management, and relapse prevention principles. Indirectness: Serious indirectness; Indirectness comment: included relaxation elements

	(n=29) Intervention 2: Usual care. Control patients received the usual care at the outpatient department and by their GP: this included analgesics, NSAIDS, tricyclic antidepressant agents if appropriate, and physiotherapy and counselling was allowed. Duration 8 weeks. Concurrent medication/care: Half of individuals were also randomised to receive an educational program aimed to improve compliance, which consisted of 6 health promotion sessions of 90 minutes each, spread over the 24 weeks. Included information on FM, general health education, self-management, and relapse prevention principles. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BIOFEEDBACK versus USUAL CARE

Protocol outcome 1: Health related quality of life
- Actual outcome: Arthritis Impact Measurement Scale at 24 weeks; Group 1: mean 0.4 (SD 1.57); n=38, Group 2: mean 0.8 (SD 2.12); n=27; Arthritis Impact Measurement Scale 0-10 Top=High is poor outcome; Comments: Baseline values: biofeedback 3.1 (2.1); usual care 5.4 (2)
SDs calculated from CIs: biofeedback -0.1-0.9; usual care -1.8--0.2 Weighted mean of 11 sub scales.
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 18, Reason: Other commitments, stress, death in family, no benefit; Group 2 Number missing: 2, Reason: Not specified

Protocol outcome 2: Physical function
- Actual outcome: Maximal Watt bicycle ergometer at 24 weeks; Group 1: mean -13 (SD 18.24); n=38, Group 2: mean -27.1 (SD 20.41); n=27; Comments: Baseline values: biofeedback 131.2 (37.9); usual care 136.3 (30.5)
SDs calculated from CIs: biofeedback -7.2--18.8; usual care -34.8--19.4
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 18, Reason: Other commitments, stress, death in family, no benefit; Group 2 Number missing: 2, Reason: Not specified

Protocol outcome 3: Psychological distress
- Actual outcome: Symptom Checklist-90-Revised at 24 weeks; Group 1: mean -9.4 (SD 42.46); n=38, Group 2: mean -8.1 (SD 31.02); n=27; SCL-90-R not reported Top=High is poor outcome; Comments: Baseline values: biofeedback 176.5 (40.5); usual care 183.9 (51.3)
SDs calculated from CIs: biofeedback -22.9-4.1; usual care -19.8-3.6
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 18, Reason: Other commitments, stress, death in family, no benefit; Group 2 Number missing: 2, Reason: Not specified

Protocol outcome 4: Discontinuation
- Actual outcome: Discontinuation at 24 weeks; Group 1: 18/56, Group 2: 2/27

Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA Protocol outcome 5: Pain reduction - Actual outcome: VAS pain reduction at 24 weeks; Group 1: mean -0.6 (SD 18.56); n=38, Group 2: mean 1.3 (SD 15.38); n=27; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 59.1(18.5); 62.4(20.5) SDs calculated from CIs: -6.5-5.3; -4.5-7.1 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 18, Reason: Other commitments, stress, death in family, no benefit; Group 2 Number missing: 2, Reason: Not specified	
Protocol outcomes not reported by the study	Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Viljanen 2003[556]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=393 (258 relevant to this review; from 2 arms of the study))
Countries and setting	Conducted in Finland; Setting: Not specified
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 12 weeks and 12 months follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Non-specific neck pain for at least 12 weeks
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 30-60 years, non-specific neck pain for at least 12 weeks
Exclusion criteria	Any other major condition such as cancer, major trauma, rheumatic disease, neural entrapment, or major rehabilitation within the previous 3 months
Recruitment/selection of patients	From the catchment population of female office workers whose employers had a contract with one of the large occupational healthcare centres in Tampere, Finland.
Age, gender and ethnicity	Age - Mean (SD): 44(6.9) years. Gender (M:F): Women. Ethnicity: Not specified
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: Yes 3. Chronic visceral pain: No 4. Chronic widespread pain: No 5. Cognitive impairment: No 6. Complex regional pain syndrome: No 7. First language not English: No 8. Homeless: No 9. Learning difficulties: No 10. People aged 16-25 years: People aged >25 years 11. Sensory impairment: No
Extra comments	Duration of pain at least 12 weeks. Mean duration of pain 10.7(6.3) years
Indirectness of population	No indirectness
Interventions	(n=128) Intervention 1: Psychological therapy - Relaxation techniques. Instructed by a physiotherapist 3 times a week, for 30 minutes for 12 weeks. Relaxation training comprised various techniques training, functional relaxation, and systematic desensitisation. 15 Different techniques were incorporated into the training during the 12 weeks. The exercises aimed to teach the participants to activate only those muscles needed for different daily activities and to relax the other muscles. Participants were taught to perform the techniques independently from the fifth week and to avoid unnecessary tension in the neck muscles. Duration 12 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness (n=130) Intervention 2: Usual care. MV instructed the women in the control group not to change their

Study	Viljanen 2003[556]
	physical activity or means of relaxation during the 12 months of follow up. Duration 12 weeks. Concurrent medication/care: Not specified. Indirectness: No indirectness
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RELAXATION TECHNIQUES versus USUAL CARE Protocol outcome 1: Physical function - Actual outcome: Neck disability index at 12 weeks; Group 1: mean 14 (SD 12.5); n=128, Group 2: mean 14 (SD 13.8); n=130; NDI 0-80 Top=High is poor outcome; Comments: Baseline: 29(14.3); 26(13.8) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 18, Reason: Lost to follow up; Group 2 Number missing: 11, Reason: Lost to follow up - Actual outcome: Neck disability index at 12 months; Group 1: mean 19 (SD 14.7); n=128, Group 2: mean 17 (SD 13.7); n=130; NDI 0-80 Top=High is poor outcome; Comments: Baseline: 29(14.3); 26(13.8) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 18, Reason: Lost to follow up; Group 2 Number missing: 11, Reason: Lost to follow up Protocol outcome 2: Discontinuation - Actual outcome: Discontinuation at 12 weeks; Group 1: 14/128, Group 2: 11/130; Comments: Lost to follow up Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: Pain reduction - Actual outcome: Pain VAS at 12 months; Group 1: mean 3.3 (SD 2.6); n=128, Group 2: mean 3.2 (SD 2.5); n=130; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 4.8 (2.3); 4.1(2.2) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 18, Reason: Lost to follow up; Group 2 Number missing: 11, Reason: Lost to follow up - Actual outcome: Pain VAS at 12 weeks; Group 1: mean 2.9 (SD 2.4); n=128, Group 2: mean 2.7 (SD 2.5); n=130; VAS 0-10 Top=High is poor outcome; Comments: Baseline: 4.8 (2.3); 4.1(2.2) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 18, Reason: Lost to follow up; Group 2 Number missing: 11, Reason: Lost to follow up	
Protocol outcomes not reported by the study	Health related quality of life ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Study	Williams 2010[570]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=118)
Countries and setting	Conducted in USA; Setting: Internet-based
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	fulfilment of the American College of Rheumatology (ACR) research classification criteria for FM; 18 years of age; be under the standard medical care of a physician for at least 3 months prior to enrolment so as to minimize the initiation of new pharmacological agents across subjects; possess basic computer literacy and computer access.
Exclusion criteria	severe physical impairment that precluded receiving/using the website or using the self-management skills contained on the website; co-morbid medical illnesses capable of causing a worsening of physical functional status independent of FM; any present psychiatric disorder involving a history of psychosis, current suicide risk or attempt within 2 years of the study, or substance abuse within 2 years; prior CBT for pain management; pending status associated with disability compensation or the receipt of disability compensation for less than two years
Recruitment/selection of patients	referred to the study by primary or specialist care physician, who received recruitment materials through their local provider network
Age, gender and ethnicity	Age - Mean (SD): 50.46 (11.45) years. Gender (M:F): 6/112. Ethnicity: 97% white, 3% other
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not stated / Unclear 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA

Study	Williams 2010[570]
Interventions	(n=59) Intervention 1: Psychological therapy - Cognitive behavioural therapy. Web-enhanced behavioural self-management - translated content from traditional face-to-face cognitive-behavioural therapy for FM. 13 modules segregated into three broad segments: (a) educational lectures providing background knowledge about FM as a disease state, (b) education, behavioural, and cognitive skills designed to help with symptom management, and (c) behavioural and cognitive skills designed to facilitate adaptive life style changes for managing FM. Video lecture on the topic by a clinician experienced in applying the selected topic with respect to FM, written summaries of the video lecture for reading or downloading, homework and self-monitoring forms for applying the behavioural strategies described in the video lecture, and supplemental educational materials unique to each topic. Duration 6 months. Concurrent medication/care: no additional coaching or professional contact with participants regarding the use of the WEB-SM program. Usual and customary care from their primary care physician. Indirectness: Serious indirectness; Indirectness comment: included education (n=59) Intervention 2: Usual care. Usual and customary care from their primary care physician. The only "care" that excluded participants from the study was prior CBT for pain management. Duration 6 months. Concurrent medication/care: NA. Indirectness: No indirectness; Indirectness comment: NA
Funding	Academic or government funding (Department of Defence)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE

Protocol outcome 1: Physical function
- Actual outcome: SF36 physical function at 6 months; Group 1: mean 41.1 (SD 8.7); n=59, Group 2: mean 38.9 (SD 8.6); n=59; SF36 physical function sub scale 0-100 Top=High is good outcome; Comments: Baseline values: CBT 38.9 (8.6), usual care 38.9 (9.5)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 4, Reason: medical complications (1), personal choice (3); Group 2 Number missing: 8, Reason: relocation (1), medical complications (1), personal choice (6)

Protocol outcome 2: Psychological distress
- Actual outcome: Center for Epidemiological Studies Depression Scale at 6 months; Group 1: mean 16.4 (SD 11.9); n=59, Group 2: mean 17.5 (SD 11.5); n=59; Center for Epidemiological Studies Depression Scale 0-60 Top=High is poor outcome; Comments: Baseline values: CBT 15.1 (10.1), usual care 17.1 (11.5)
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 4, Reason: medical complications (1), personal choice (3); Group 2 Number missing: 8, Reason: relocation (1), medical complications (1), personal choice (6)
- Actual outcome: State-Trait Personality Inventory for anxiety at 6 months; Group 1: mean 18.1 (SD 7.1); n=59, Group 2: mean 18.4 (SD 5.9); n=59; State-Trait Personality Inventory anxiety unclear Top=Unclear; Comments: Baseline values: 17.1 (6), usual care 16.9 (6.3)

Study	Williams 2010[570]
	Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 4, Reason: medical complications (1), personal choice (3); Group 2 Number missing: 8, Reason: relocation (1), medical complications (1), personal choice (6) Protocol outcome 3: Sleep - Actual outcome: composite of sleep problems from the MOS Sleep Scale at 6 months; Group 1: mean 51.1 (SD 16.5); n=59, Group 2: mean 46.8 (SD 16.7); n=59; MOS Sleep Scale sleep problems composite not reported Top=Unclear; Comments: Baseline values: CBT 51.3 (16.1), usual care 47.9 (16.6) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 4, Reason: medical complications (1), personal choice (3); Group 2 Number missing: 8, Reason: relocation (1), medical complications (1), personal choice (6) Protocol outcome 4: Discontinuation - Actual outcome: Loss to follow up at 6 months; Group 1: 4/59, Group 2: 8/59; Comments: CBT: medical complications (1), personal choice (3) usual care: relocation 91), medical complications (1), personal choice (6) Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: unclear whether participants continued the intervention or not ; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA Protocol outcome 5: Pain reduction - Actual outcome: Brief Pain Inventory at 6 months; Group 1: mean 4.3 (SD 1.6); n=59, Group 2: mean 4.9 (SD 1.5); n=59; Brief Pain Inventory pain intensity 0-10 Top=High is poor outcome; Comments: Baseline values: CBT 5.1 (1.4), usual care 4.9 (1.4) Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 4, Reason: medical complications (1), personal choice (3); Group 2 Number missing: 8, Reason: relocation (1), medical complications (1), personal choice (6)
Protocol outcomes not reported by the study	Health related quality of life ; Pain interference ; Pain self-efficacy ; Use of healthcare services

Study	Woolfolk 2012[577]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=76)
Countries and setting	Conducted in USA; Setting: academic medical clinic
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 9 months

Study	Woolfolk 2012[577]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ACR criteria for FM
Stratum	Overall: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18 to 70 years; met ACR criteria for FM, as diagnosed by their rheumatologists and confirmed by a medical history review
Exclusion criteria	Pain from traumatic injury or structural or regional rheumatic disease; rheumatoid arthritis; inflammatory arthritis; autoimmune disease; unstable medical or psychiatric illness; active suicidal ideation; history of psychosis; current psychoactive substance dependence, or a medication regimen that had not been stable for at least 2 months prior to baseline; pregnant or attempting to conceive; participation in psychotherapy concurrent with the period between the baseline and post treatment appointment
Recruitment/selection of patients	referred to the study by treating rheumatologists
Age, gender and ethnicity	Age - Mean (SD): CBT 47.79 (9.28), usual care 50.21 (10.14). Gender (M:F): 9/67. Ethnicity: White 58, African American 2, Hispanic 9, Other 7
Further population details	1. Chronic orofascial pain: No 2. Chronic primary musculoskeletal pain: No 3. Chronic visceral pain: No 4. Chronic widespread pain: Yes 5. Cognitive impairment: Not stated / Unclear 6. Complex regional pain syndrome: No 7. First language not English: Not applicable 8. Homeless: Not stated / Unclear 9. Learning difficulties: Not stated / Unclear 10. People aged 16-25 years: Not stated / Unclear 11. Sensory impairment: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=38) Intervention 1: Psychological therapy - Cognitive behavioural therapy. 10-session, individually-administered, manualized intervention including relaxation training, activity regulation, facilitation of emotional awareness, cognitive restructuring, and interpersonal communication training. Duration 10 weeks. Concurrent medication/care: treatment as usual - details not reported. Indirectness: Serious indirectness; Indirectness comment: included relaxation training (n=38) Intervention 2: Usual care. Treatment as usual - no further details. Duration study duration. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COGNITIVE BEHAVIOURAL THERAPY versus USUAL CARE Protocol outcome 1: Discontinuation	

Study	Woolfolk 2012[577]
- Actual outcome: Number withdrawing from study at 3 months; Group 1: 4/38, Group 2: 3/38; Comments: Reasons for withdrawal not reported Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 0, Reason: NA; Group 2 Number missing: 0, Reason: NA Protocol outcome 2: Pain reduction - Actual outcome: 30% reduction in pain from baseline at 3 months; Group 1: 25/38, Group 2: 2/38; Comments: Measured by visual analogue scale 0-10. Baseline values not reported. Intention to treat analysis. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 4, Reason: withdrew; Group 2 Number missing: 3, Reason: withdrew - Actual outcome: 30% reduction in pain from baseline at 9 months; Group 1: 24/38, Group 2: 1/38; Comments: Measured by VAS scale 0-10. Baseline values not reported. Intention to treat analysis. Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Group 1 Number missing: 6, Reason: withdrew; Group 2 Number missing: 6, Reason: withdrew	
Protocol outcomes not reported by the study	Health related quality of life ; Physical function ; Psychological distress ; Pain interference ; Pain self-efficacy ; Use of healthcare services ; Sleep

Appendix E: Forest plots

E.1 CBT versus Usual care

Figure 2: Quality of life (EQ-5D) final values ≤3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Hedman-lagerlof 2018	0.6	0.3	70	0.44	0.32	70	100.0%	0.16 [0.06, 0.26]
Total (95% CI)			**70**			**70**	**100.0%**	**0.16 [0.06, 0.26]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.05 (P = 0.002)

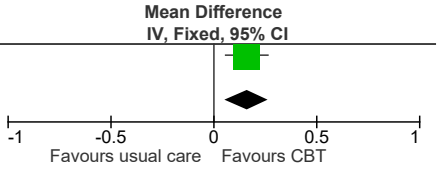


Figure 3: Quality of life (EQ-5D) final values >3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Alda 2011	0.61	0.25	53	0.54	0.28	49	34.6%	0.07 [-0.03, 0.17]
McBeth 2012	0.754	0.214	71	0.645	0.262	83	65.4%	0.11 [0.03, 0.18]
Total (95% CI)			**124**			**132**	**100.0%**	**0.10 [0.03, 0.16]**

Heterogeneity: Chi² = 0.36, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 3.08 (P = 0.002)

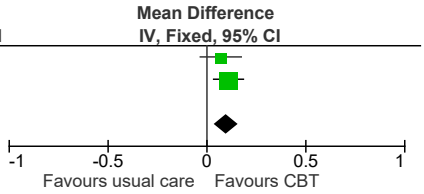


Figure 4: Quality of life (EuroQoL VAS) final values ≤3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
Alda 2011	60.45	16.63	57	53.49	14.4	56	100.0%	6.96 [1.23, 12.69]
Total (95% CI)			**57**			**56**	**100.0%**	**6.96 [1.23, 12.69]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.38 (P = 0.02)

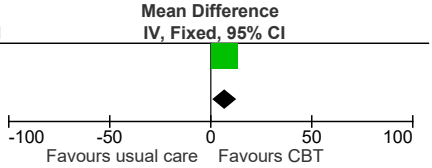
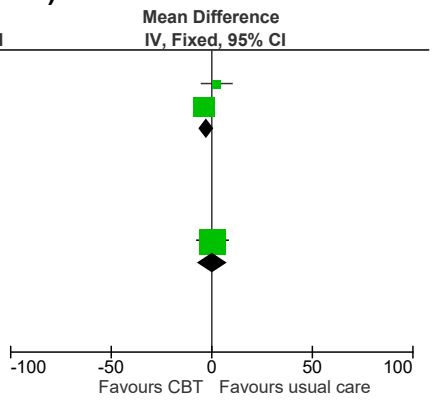


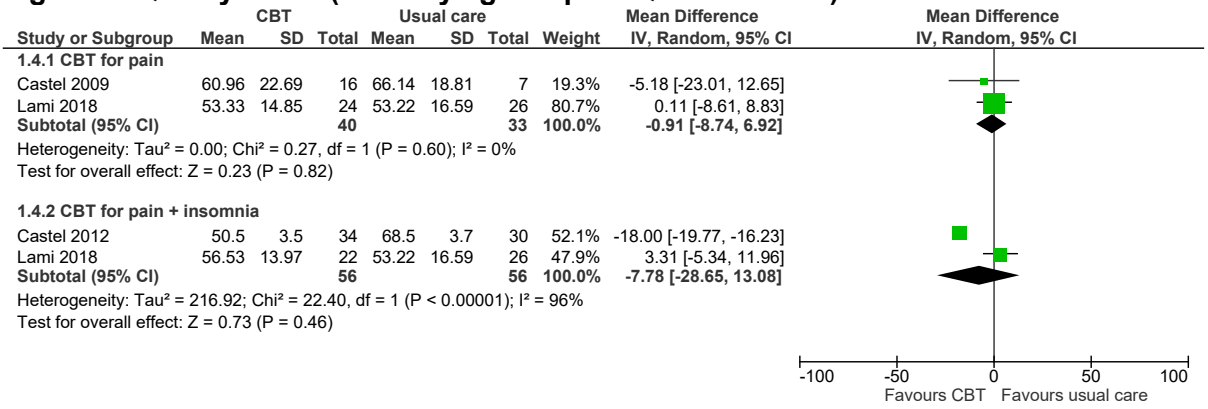
Figure 5: Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
1.4.1 CBT for pain								
Lami 2018	57.93	14.16	28	55.45	16.79	36	24.3%	2.48 [-5.11, 10.07]
Soares 2002	22.5	7.3	18	26.5	5.6	17	75.7%	-4.00 [-8.30, 0.30]
Subtotal (95% CI)			**46**			**53**	**100.0%**	**-2.43 [-6.17, 1.31]**
Heterogeneity: Chi² = 2.12, df = 1 (P = 0.15); I² = 53%								
Test for overall effect: Z = 1.27 (P = 0.20)								
1.4.2 CBT for pain + insomnia								
Lami 2018	55.82	14.52	27	55.45	16.79	36	100.0%	0.37 [-7.38, 8.12]
Subtotal (95% CI)			**27**			**36**	**100.0%**	**0.37 [-7.38, 8.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.09 (P = 0.93)								



Source/Note: Where statistical heterogeneity was present, but all point estimates were consistent with the same clinical interpretation (benefit/no difference/harm), a fixed effects model was applied

Figure 6: Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months



Source/Note: *Random effects has been applied where there was unexplained heterogeneity*

Figure 7: Quality of life (SF36 mental composite) final values ≤3 months

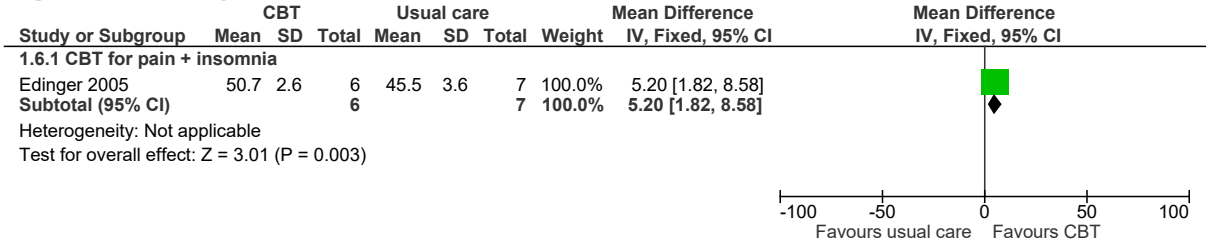


Figure 8: Quality of life (SF36 mental composite) final values >3 months

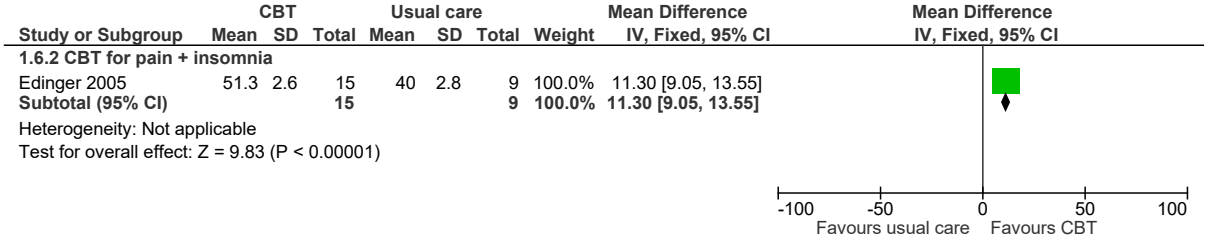


Figure 9: Quality of life (SF36) final values ≤3 months

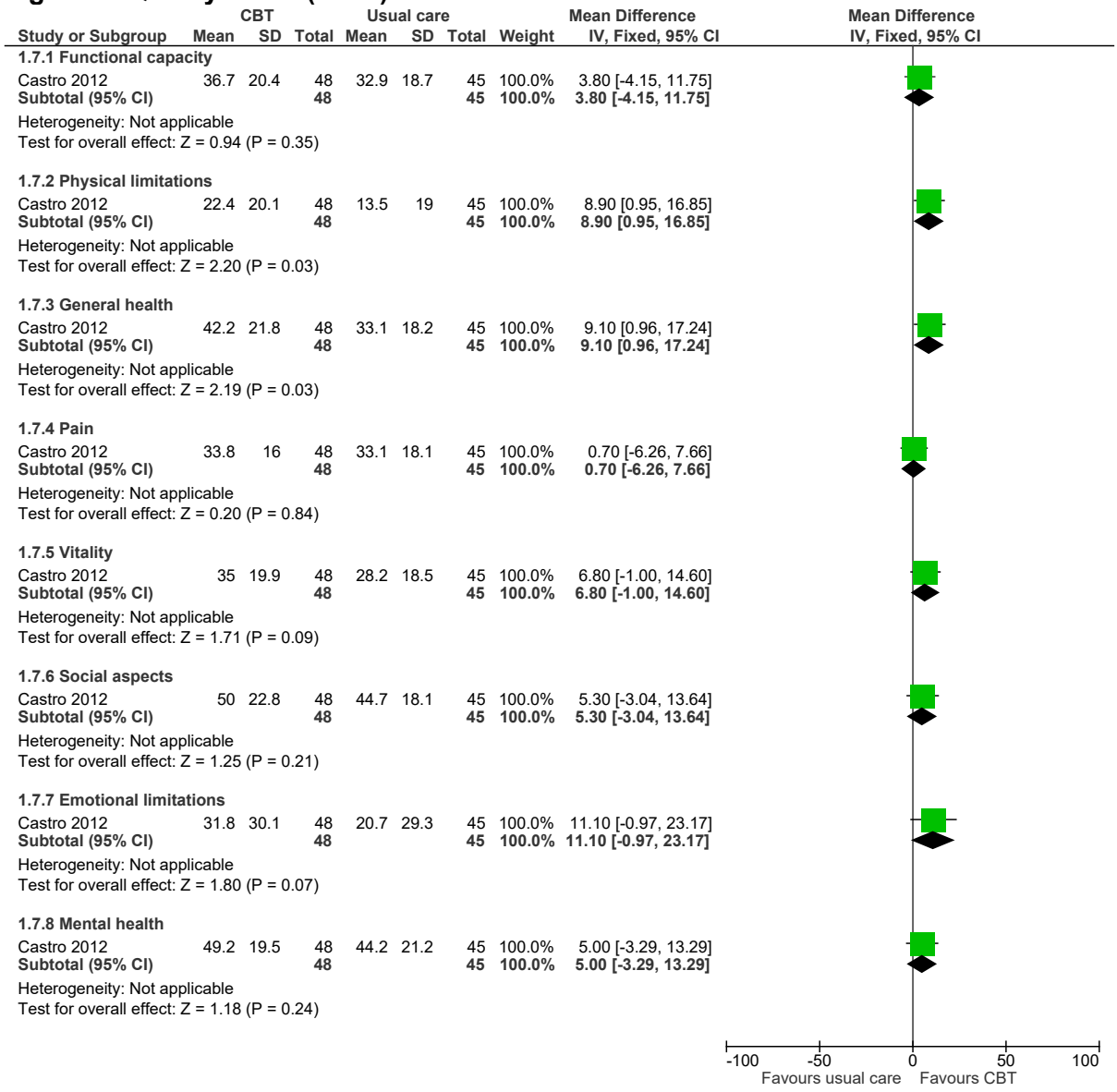


Figure 10: Quality of life (SF12 physical component) final values ≤3 months

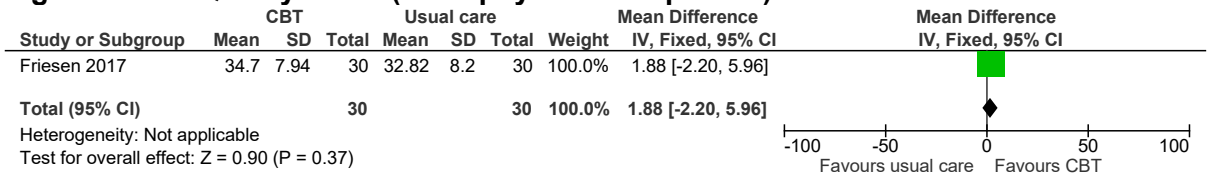


Figure 11: Quality of life (SF12 mental component) final values ≤3 months

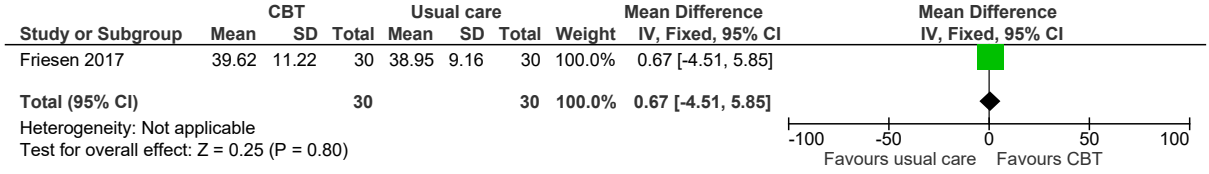


Figure 12: Physical function (WHO Disability Assessment Schedule) final values ≤3 months

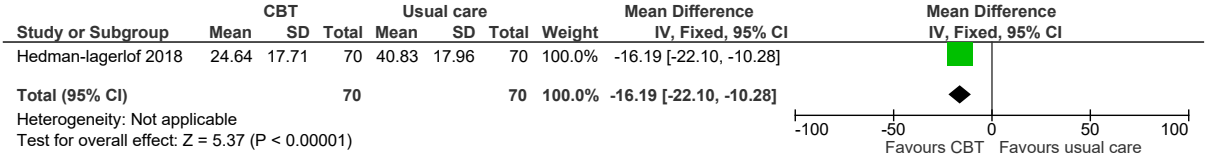


Figure 13: Physical function (Fibromyalgia Impact Questionnaire physical impairment sub scale) final values ≤3 months

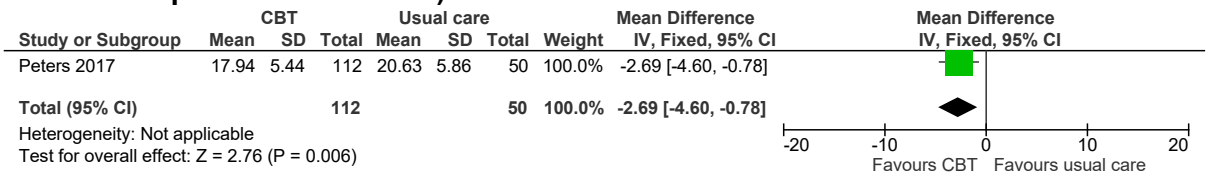


Figure 14: Physical function (FIQ physical function sub scale) change scores ≤3 months

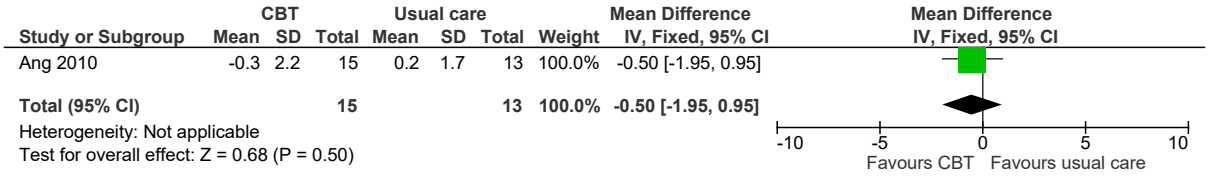


Figure 15: Physical function (SF36 physical function sub scale) final values >3 months

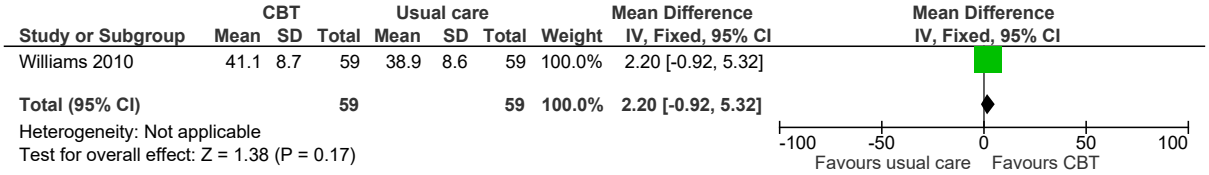


Figure 16: Physical function (FIQ physical function sub scale) change scores >3 months

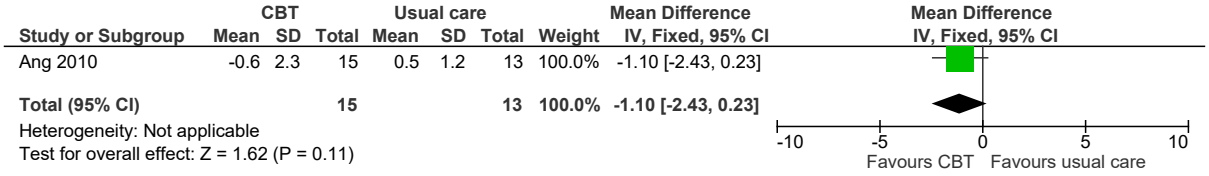
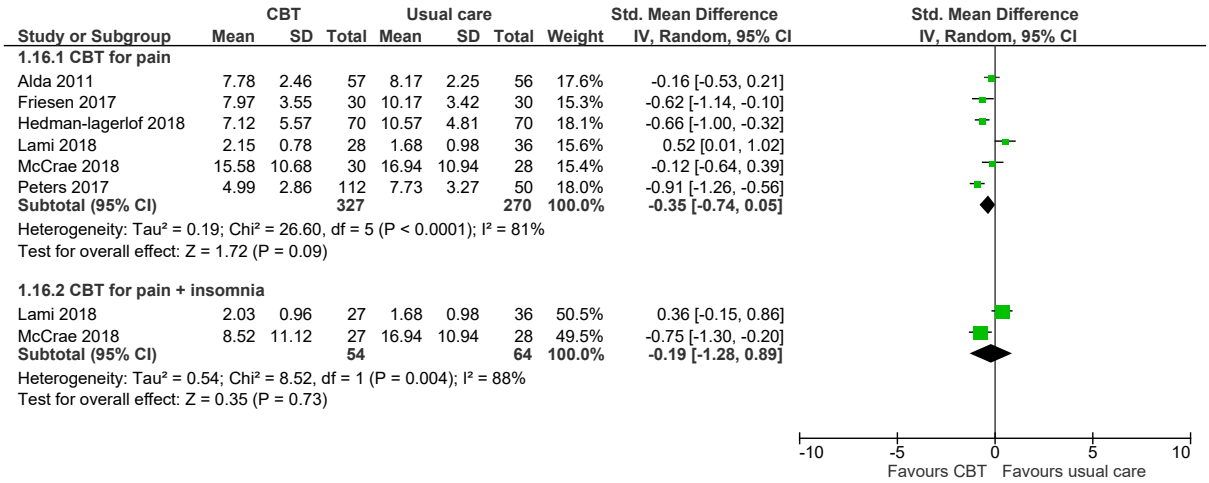
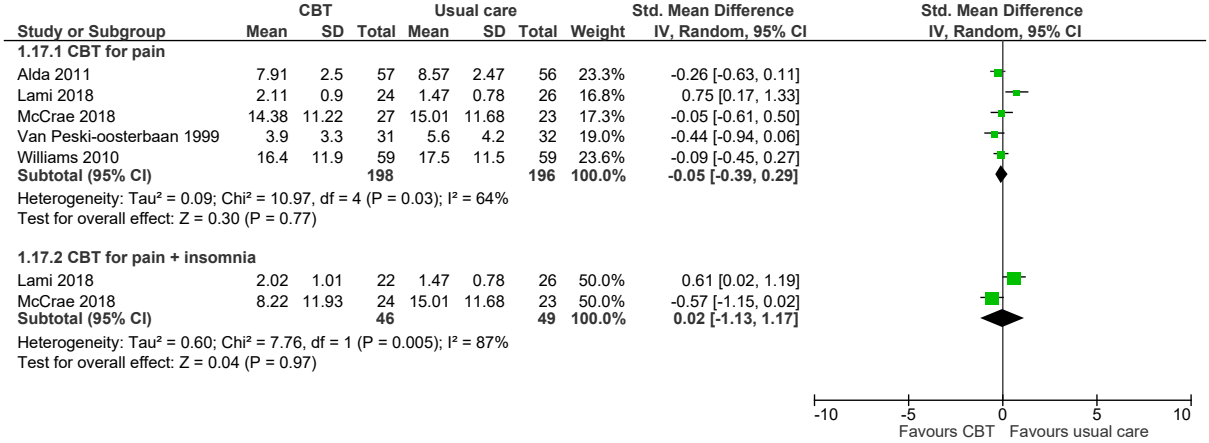


Figure 17: Psychological distress (Hamilton Rating Scale for Depression; Hospital Anxiety and Depression Scale depression; Patient Health Questionnaire-9; Symptoms Checklist 90-R depression; Beck Depression Inventory) final values ≤3 months



Source/Note: Random effects has been applied where there was unexplained heterogeneity

Figure 18: Psychological distress (Hamilton Rating Scale for Depression; Symptoms Checklist 90-R depression; Beck Depression Inventory; Hospital Anxiety and Depression Scale depression; Center for Epidemiological Studies Depression Scale) final values >3 months



Source/Note: Random effects has been applied where there was unexplained heterogeneity

Figure 19: Psychological distress (Patient Health Questionnaire 8-item depression) change scores >3 months

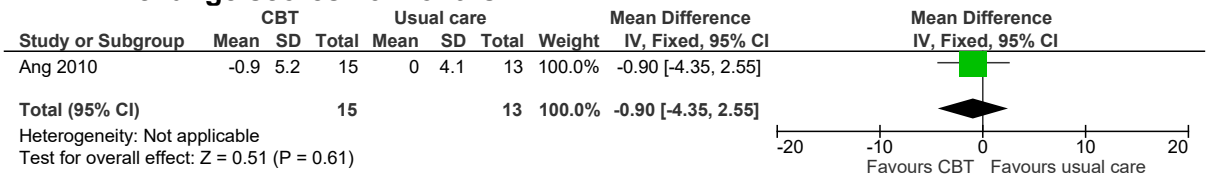


Figure 20: Psychological distress (Hamilton Anxiety Rating Scale; Hospital Anxiety and Depression Scale anxiety; Symptoms checklist 90-R anxiety; State-Trait Anxiety Inventory) final values ≤3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.19.1 CBT for pain								
Alda 2011	7.09	2.96	57	7.4	2.18	56	26.3%	-0.12 [-0.49, 0.25]
Friesen 2017	9.22	4.33	30	10.43	4.69	30	13.8%	-0.26 [-0.77, 0.24]
Lami 2018	1.71	0.94	28	1.37	0.91	36	14.4%	0.36 [-0.13, 0.86]
McCrae 2018	45.22	12.12	30	47.72	12.87	28	13.4%	-0.20 [-0.71, 0.32]
Peters 2017	6.63	3.41	112	7.27	3.58	50	32.1%	-0.18 [-0.52, 0.15]
Subtotal (95% CI)			**257**			**200**	**100.0%**	**-0.10 [-0.29, 0.09]**

Heterogeneity: Chi² = 4.12, df = 4 (P = 0.39); I² = 3%
Test for overall effect: Z = 1.04 (P = 0.30)

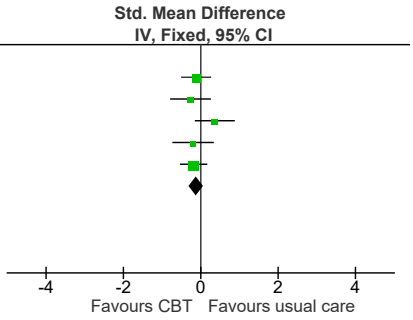
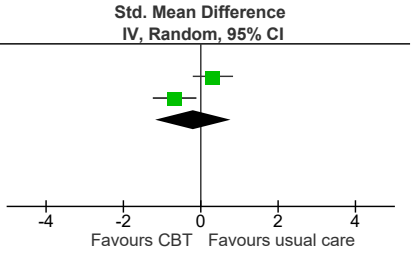


Figure 21: Psychological distress (Symptoms checklist 90-R anxiety; State-Trait Anxiety Inventory) final values ≤3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.20.2 CBT for pain +/ insomnia								
Lami 2018	1.68	1.05	27	1.37	0.91	36	50.6%	0.31 [-0.19, 0.82]
McCrae 2018	38.95	12.72	27	47.72	12.87	28	49.4%	-0.68 [-1.22, -0.13]
Subtotal (95% CI)			**54**			**64**	**100.0%**	**-0.17 [-1.15, 0.80]**

Heterogeneity: Tau² = 0.42; Chi² = 6.87, df = 1 (P = 0.009); I² = 85%
Test for overall effect: Z = 0.35 (P = 0.72)



Source/Note: Random effects has been applied where there was unexplained heterogeneity

Figure 22: Psychological distress (Hamilton Anxiety Rating Scale; Symptoms Checklist 90-R anxiety; Hospital Anxiety and Depression Scale anxiety; State-Trait Personality Inventory anxiety) final values >3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
1.21.1 CBT for pain								
Alda 2011	7.25	3.02	57	7.58	2.07	56	28.8%	-0.13 [-0.50, 0.24]
Lami 2018	1.6	1.05	24	1.18	0.69	26	12.4%	0.47 [-0.09, 1.03]
McCrae 2018	43.86	12.78	27	43.87	13.7	23	12.7%	-0.00 [-0.56, 0.56]
Van Peski-oosterbaan 1999	6.9	3.1	31	7.2	4	32	16.1%	-0.08 [-0.58, 0.41]
Williams 2010	18.1	7.1	59	18.4	5.9	59	30.1%	-0.05 [-0.41, 0.32]
Subtotal (95% CI)			**198**			**196**	**100.0%**	**-0.01 [-0.20, 0.19]**

Heterogeneity: Chi² = 3.28, df = 4 (P = 0.51); I² = 0%
Test for overall effect: Z = 0.05 (P = 0.96)

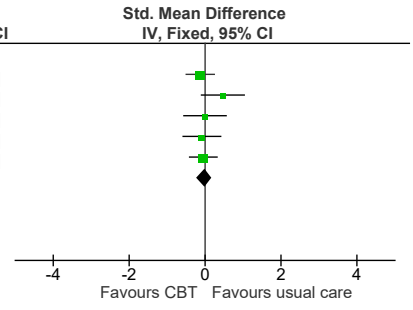
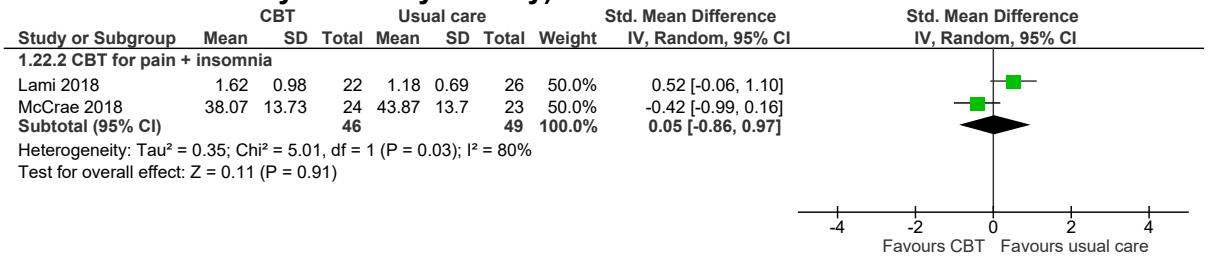


Figure 23: Psychological distress (Symptoms Checklist 90-R anxiety; State-Trait Personality Inventory anxiety) final values >3 months



Source/Note: *Random effects has been applied where there was unexplained heterogeneity*

Figure 24: Psychological distress (Multiple Pain Inventory-affective distress) final values >3 months

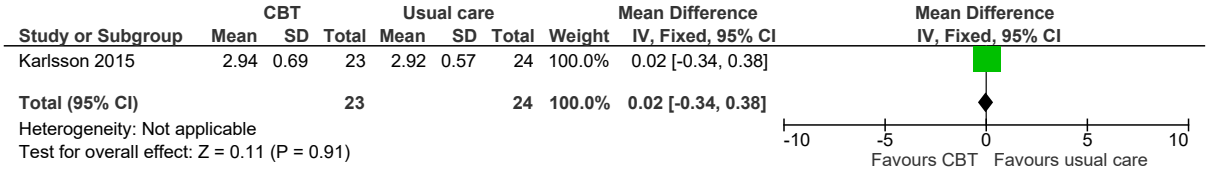


Figure 25: Pain interference (Brief Pain inventory - pain interference) final values ≤3 months

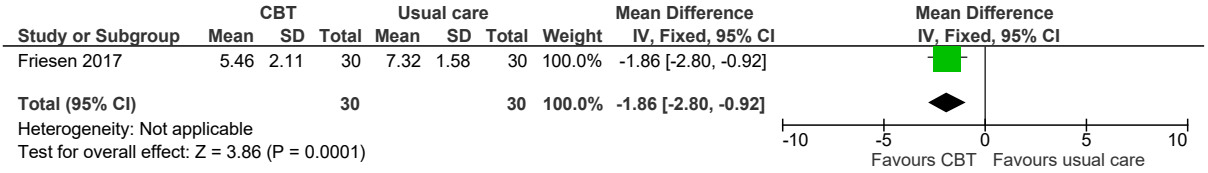


Figure 26: Pain interference (Pain disability index) final values ≤3 months

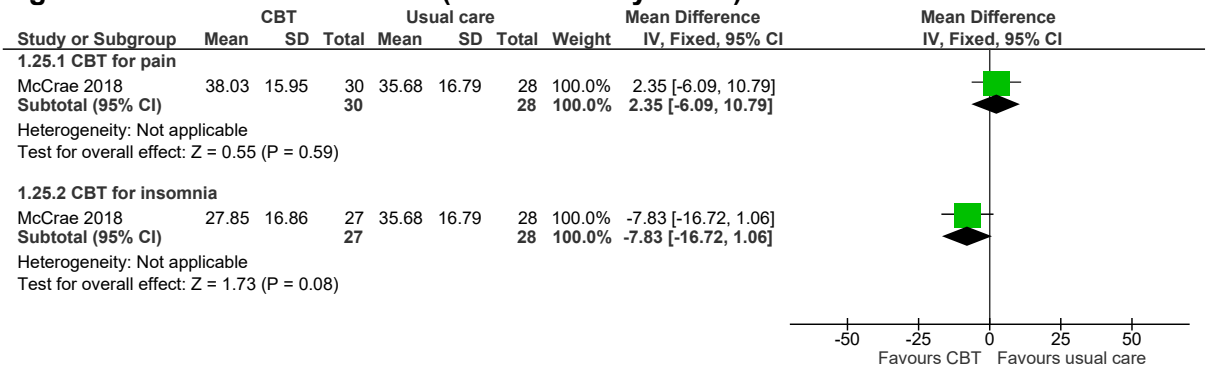


Figure 27: Pain interference (Pain disability index) final values >3 months

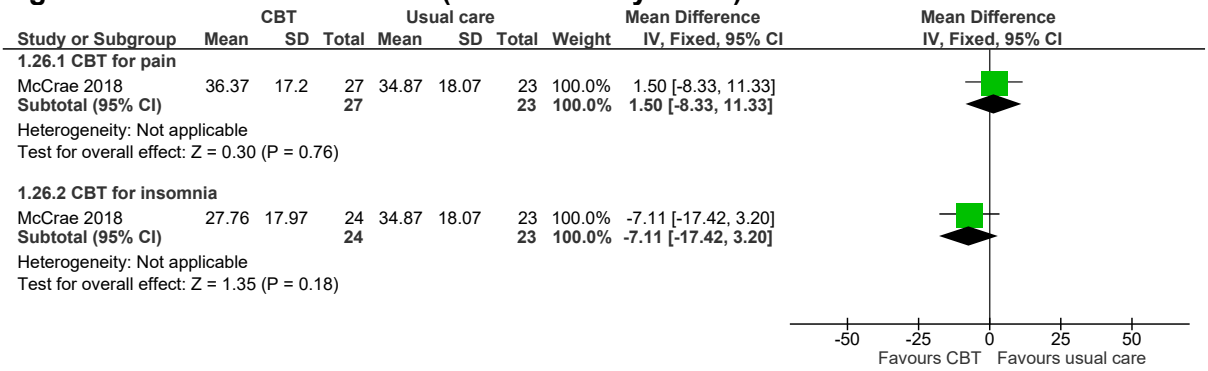


Figure 28: Pain interference (Multiple Pain Inventory - pain interference) final values >3 months

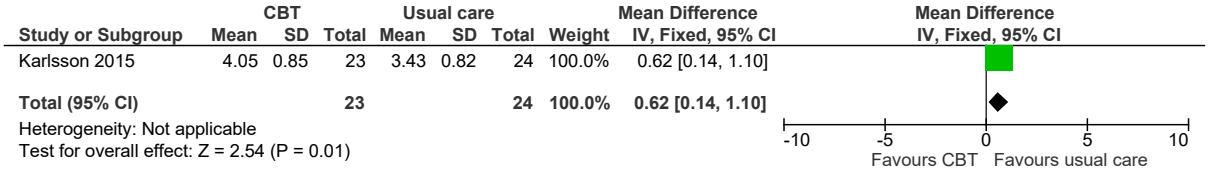


Figure 29: Pain self-efficacy (Pain Self-efficacy Questionnaire; Chronic Pain Self-efficacy Scale) final values ≤3 months

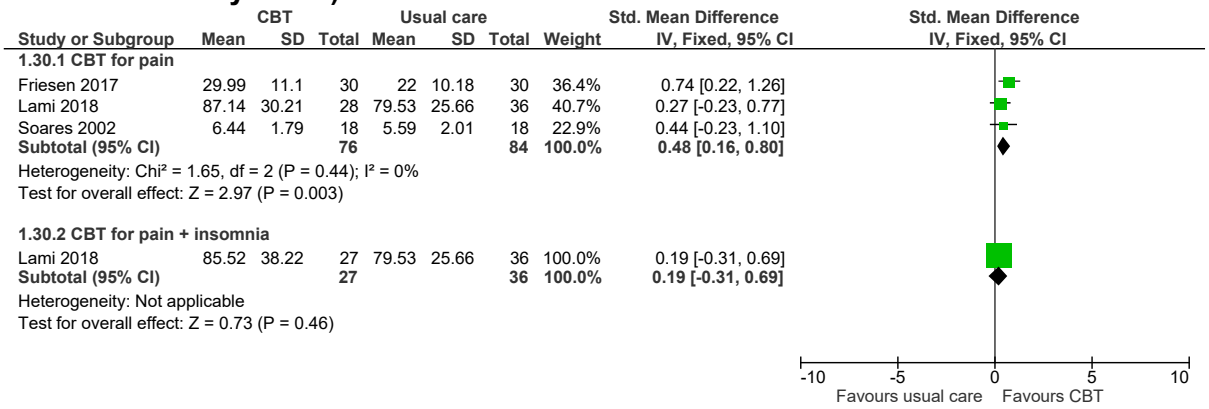


Figure 30: Pain self-efficacy (Chronic Pain Self-efficacy scale) final values >3 months

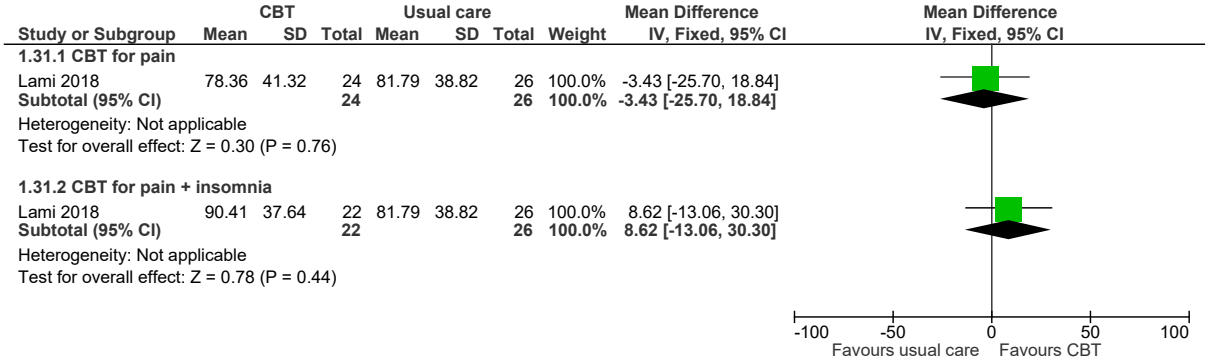
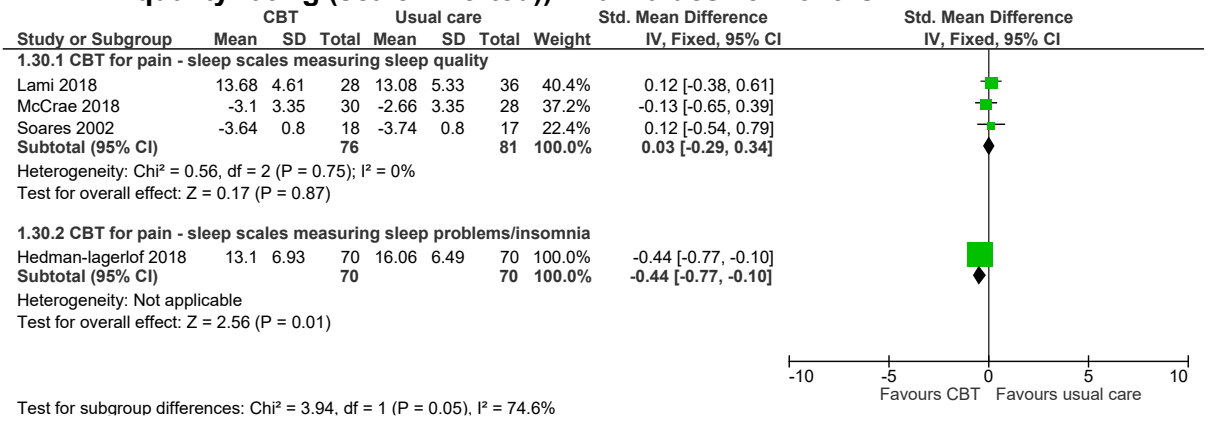
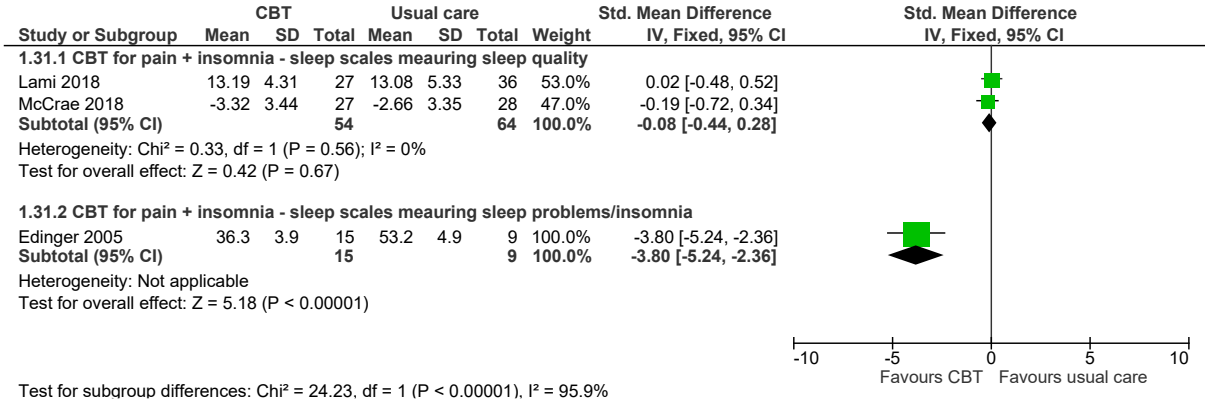


Figure 31: Sleep (Insomnia Severity Index; Pittsburgh Sleep Quality Index; Karolinska Sleep Questionnaire sleep quality subscale; self-reported sleep quality rating (scale inverted)) final values ≤3 months



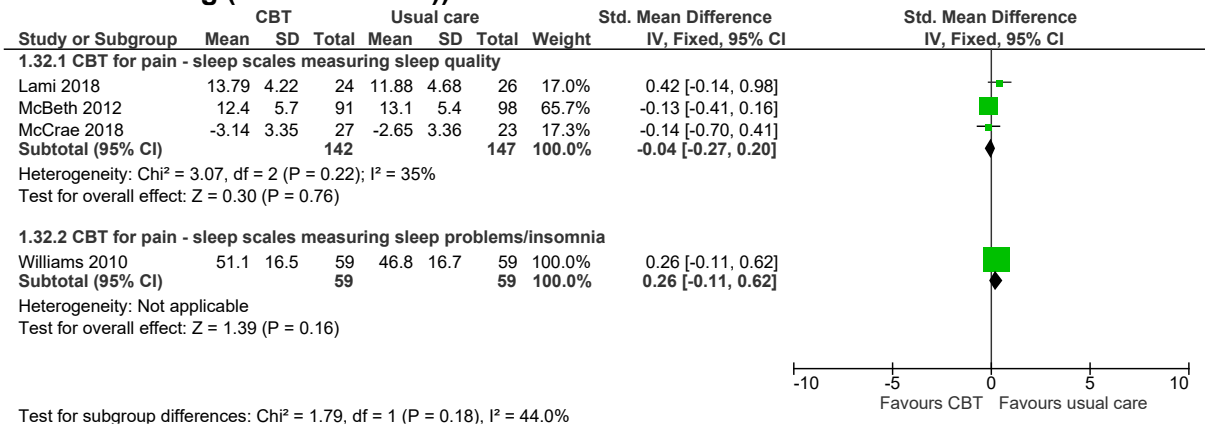
Source/Note: *Sensitivity analysis splitting sleep scales measuring sleep quality and sleep scales measuring sleep problems/insomnia explained the heterogeneity and is presented here.*

Figure 32: Sleep (Insomnia Symptoms Questionnaire; Pittsburgh Sleep Quality Index; self-reported sleep quality rating (scale inverted)) final values ≤3 months



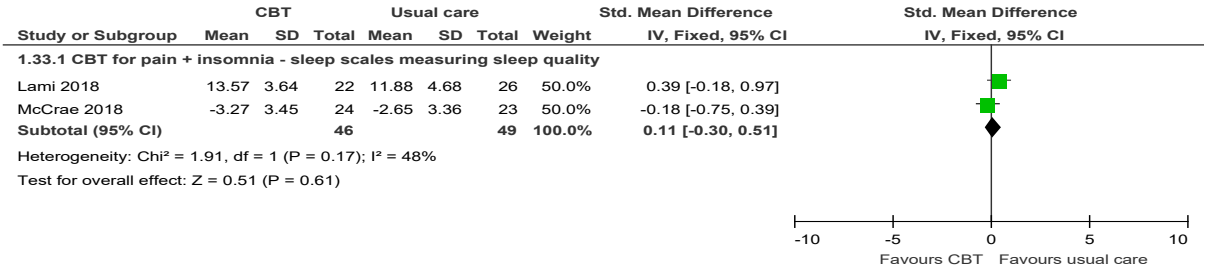
Source/Note: *Sensitivity analysis splitting sleep scales measuring sleep quality and sleep scales measuring sleep problems/insomnia explained the heterogeneity and is presented here.*

Figure 33: Sleep (Medical Outcomes Study Sleep Problems Index (scale inverted); Pittsburgh Sleep Quality Index; Sleep Scale; self-reported sleep quality rating (scale inverted)) final values >3 months



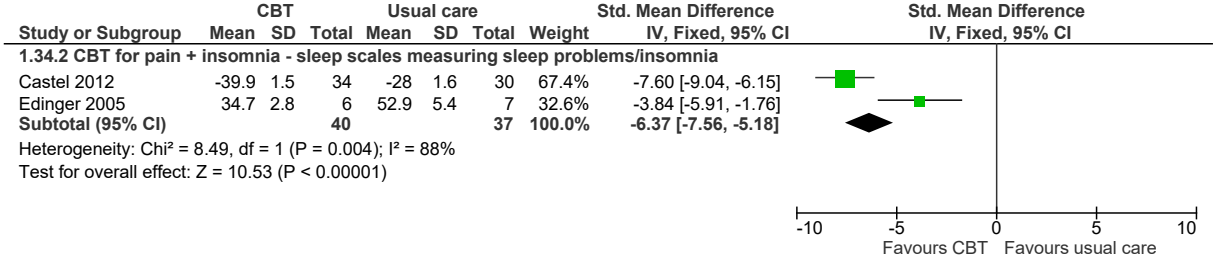
Source/Note: Sensitivity analysis splitting sleep scales measuring sleep quality and sleep scales measuring sleep problems/insomnia explained the heterogeneity and is presented here.

Figure 34: Sleep (Pittsburgh Sleep Quality Index; self-reported sleep quality rating (scale inverted) final values >3 months



Source/Note: Sensitivity analysis splitting sleep scales measuring sleep quality and sleep scales measuring sleep problems/insomnia explained the heterogeneity and is presented here.

Figure 35: Sleep (Medical Outcomes Study Sleep Problems Index (scale inverted for analysis); Insomnia Symptom Questionnaire) final values >3 months



Source/Note: Sensitivity analysis splitting sleep scales measuring sleep quality and sleep scales measuring sleep problems/insomnia explained the heterogeneity and is presented here.

Source/Note: Where statistical heterogeneity was present, but all point estimates were consistent with the same clinical interpretation (benefit/no difference/harm), a fixed effects model was applied

Figure 36: Use of healthcare services (GP visits for non-cardiac chest pain) >3 months

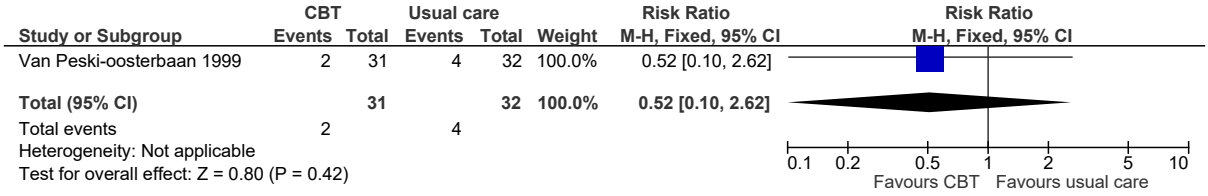


Figure 37: Use of healthcare services (referral to a specialist for non-cardiac chest pain) >3 months

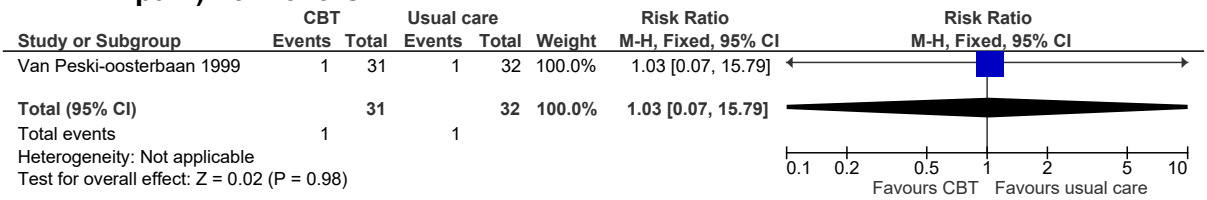


Figure 38: Use of healthcare services (use of additional psychological services) >3 months

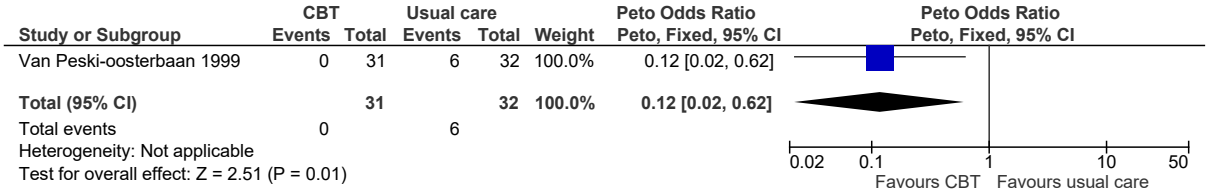


Figure 39: CBT for pain - Discontinuation

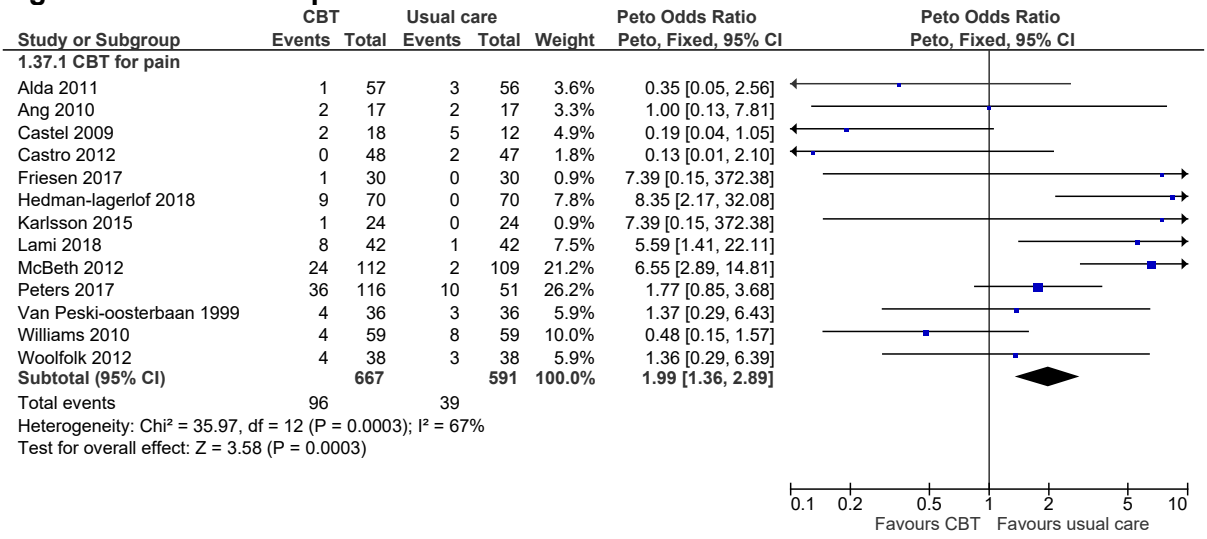


Figure 40: CBT for pain + insomnia - Discontinuation

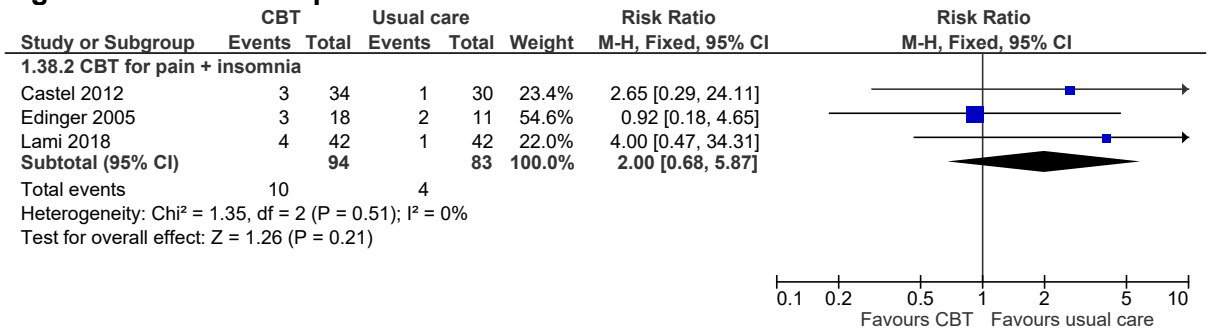
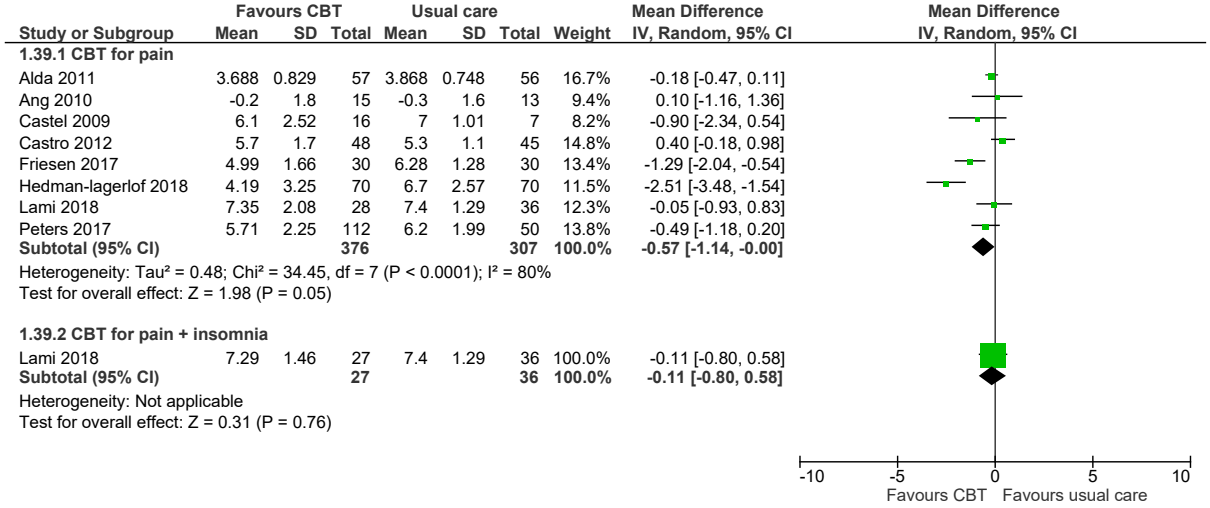


Figure 41: Pain (VAS/NRS) final values and change scores ≤3 months



Source/Note: *Random effects has been applied where there was unexplained heterogeneity*

Figure 42: Pain (VAS/NRS) final values and change scores >3 months

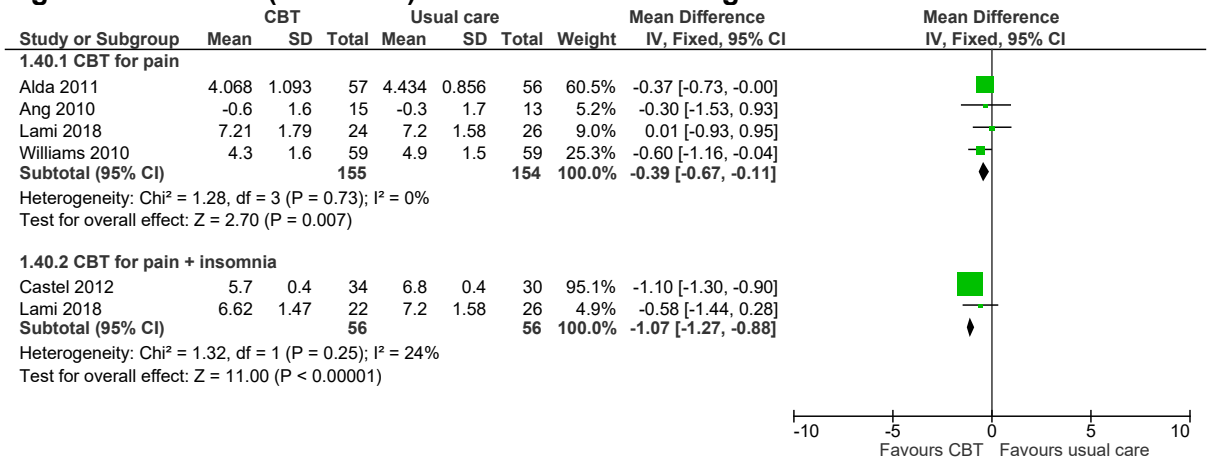


Figure 43: Pain (30% reduction in pain from baseline) ≤3 months

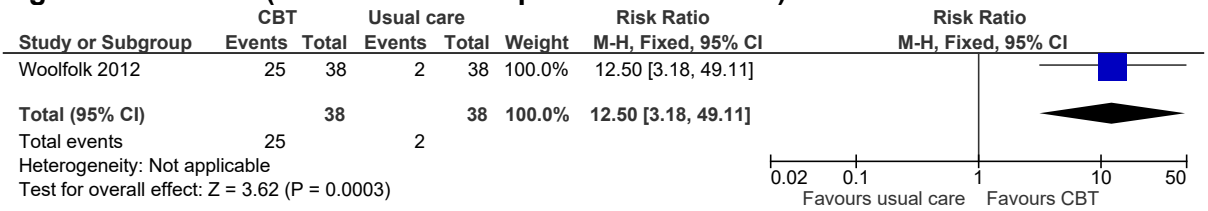


Figure 44: Pain (30% reduction in pain from baseline) >3 months

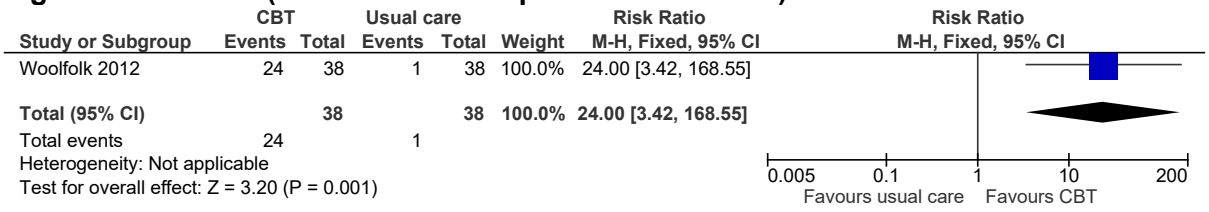


Figure 45: Pain (McGill Pain Questionnaire) final values ≤3 months

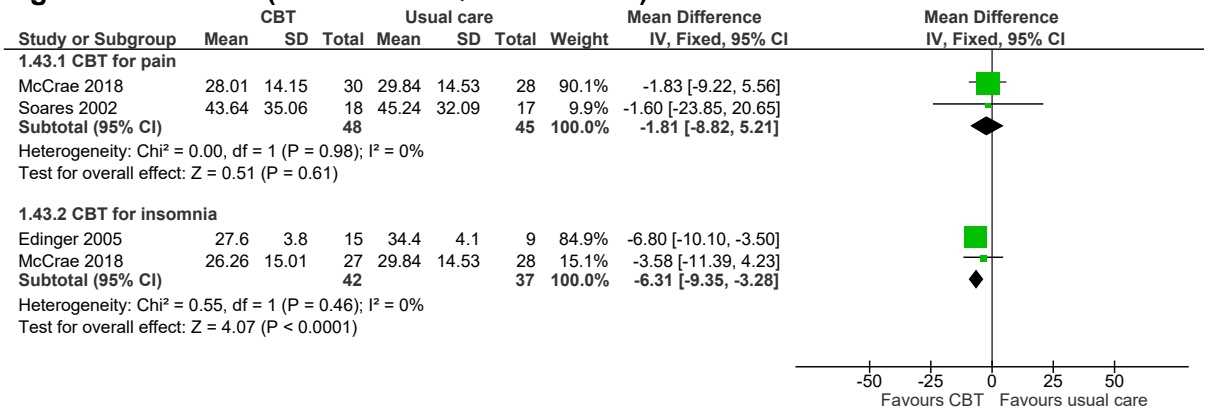


Figure 46: CBT for pain - Pain (Multiple Pain Inventory - pain severity) final values >3 months

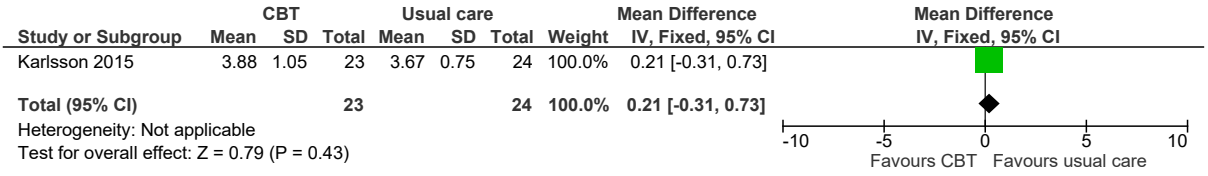
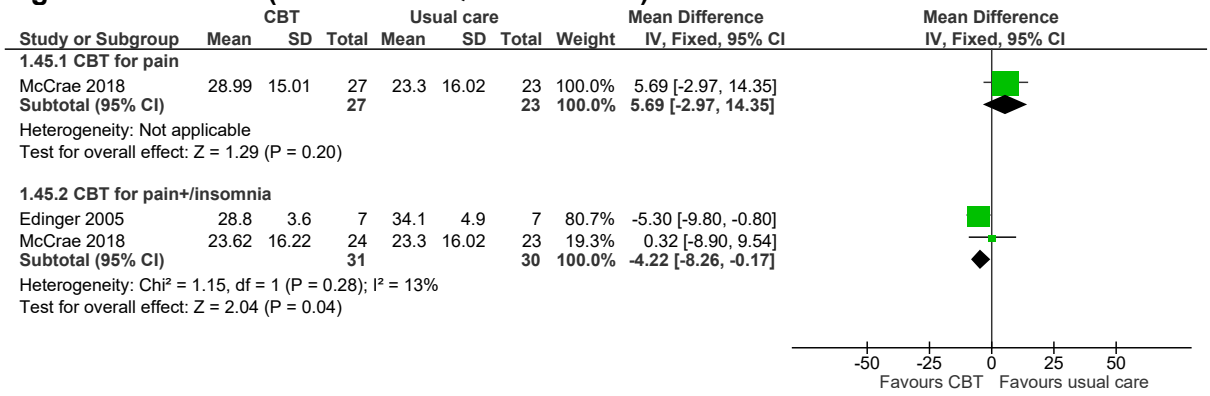


Figure 47: Pain (McGill Pain Questionnaire) final values >3 months



E.2 ACT versus Usual care

Figure 48: Quality of life (SF36 physical component) final values ≤3 months

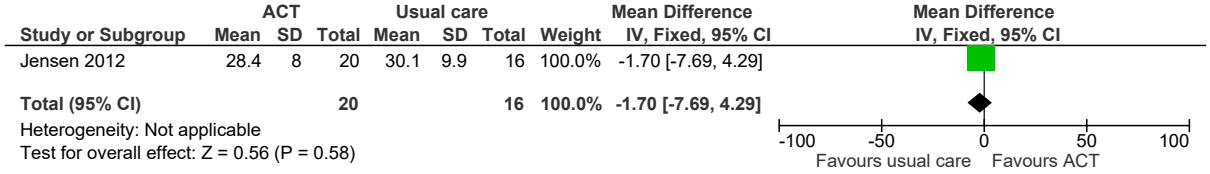


Figure 49: Quality of life (SF36 physical component) final values >3 months

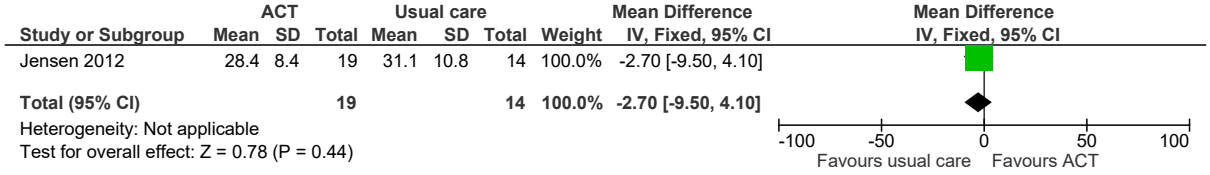


Figure 50: Quality of life (SF36 mental component) final values ≤3 months

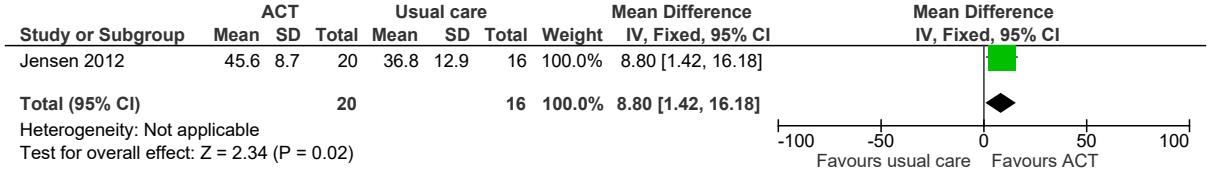


Figure 51: Quality of life (SF36 mental component) final values >3 months

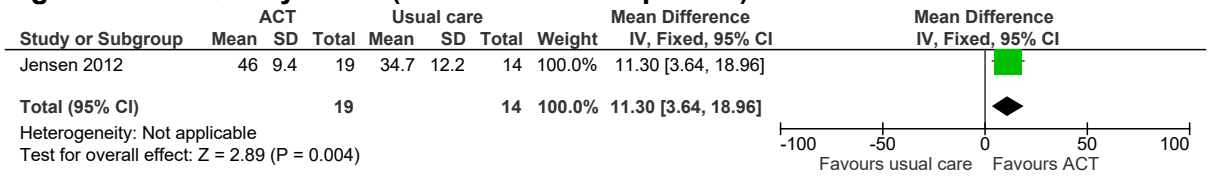


Figure 52: Quality of life (EQ-5D VAS) final values ≤3 months

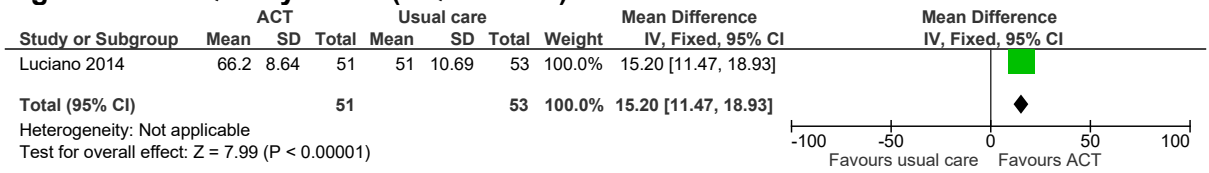


Figure 53: Quality of life (EQ-5D) final values >3 months

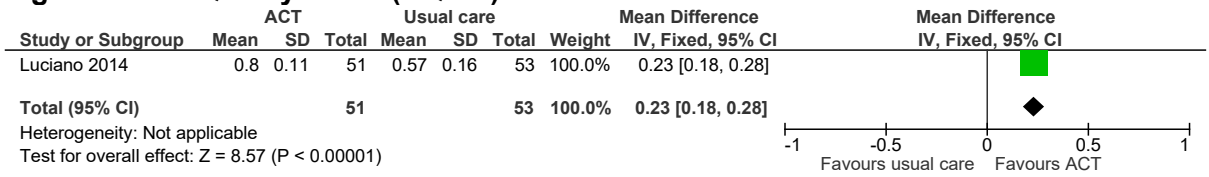


Figure 54: Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months

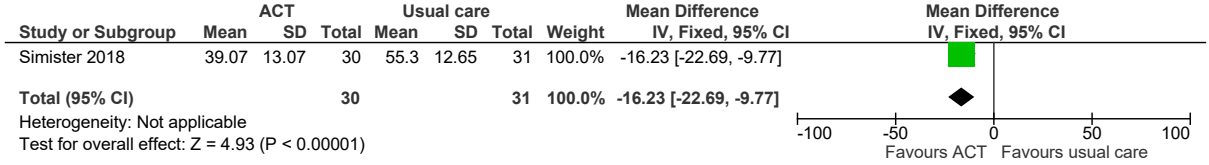


Figure 55: Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months

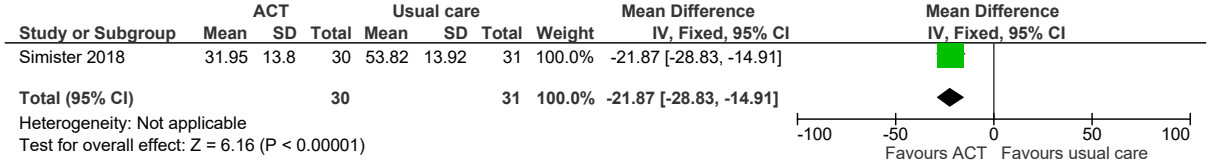


Figure 56: Physical function (6 minute walk test) final values ≤3 months

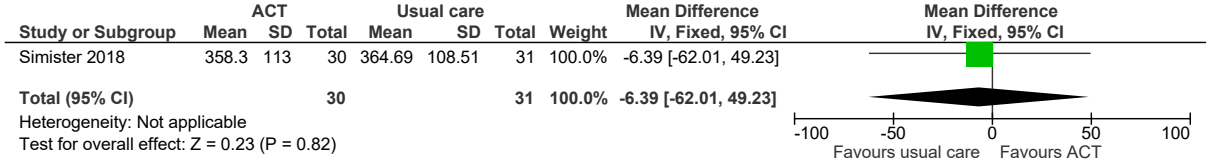


Figure 57: Physical function (6 minute walk test) final values >3 months

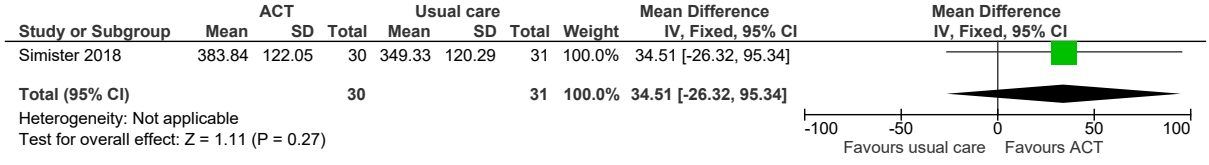
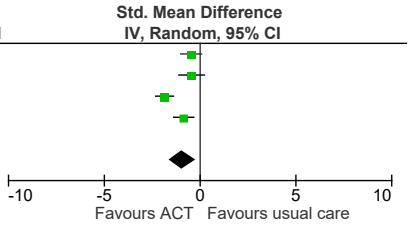


Figure 58: Psychological distress (Geriatric Depression Scale; Beck Depression Inventory; HADS depression; Center for Epidemiologic Studies depression scale) final values ≤3 months

Study or Subgroup	ACT Mean	ACT SD	ACT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Random, 95% CI
Alonso-Fernandez 2016	8.88	5.62	27	11.92	7.24	26	25.1%	-0.46 [-1.01, 0.08]
Jensen 2012	11.7	6	20	14.8	7.8	16	23.3%	-0.44 [-1.11, 0.22]
Luciano 2014	5.41	1.36	51	9.34	2.63	53	26.2%	-1.85 [-2.32, -1.39]
Simister 2018	17.76	10.83	30	26.97	10.46	31	25.4%	-0.85 [-1.38, -0.33]
Total (95% CI)			**128**			**126**	**100.0%**	**-0.92 [-1.62, -0.23]**

Heterogeneity: Tau² = 0.43; Chi² = 19.72, df = 3 (P = 0.0002); I² = 85%
Test for overall effect: Z = 2.59 (P = 0.010)

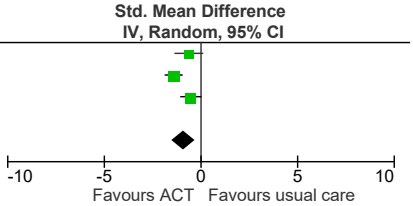


Source/Note: Random effects has been applied where there was unexplained heterogeneity

Figure 59: Psychological distress (Beck Depression Inventory; HADS depression; Center for Epidemiologic Studies depression scale) final values >3 months

Study or Subgroup	ACT Mean	ACT SD	ACT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Random, 95% CI
Jensen 2012	10.7	4.8	19	16.4	12.5	14	28.4%	-0.63 [-1.33, 0.08]
Luciano 2014	5.84	1.6	51	9.32	3.04	53	37.1%	-1.41 [-1.85, -0.98]
Simister 2018	18.63	12.12	30	25.13	12.29	31	34.6%	-0.53 [-1.04, -0.01]
Total (95% CI)			**100**			**98**	**100.0%**	**-0.88 [-1.50, -0.26]**

Heterogeneity: Tau² = 0.22; Chi² = 7.88, df = 2 (P = 0.02); I² = 75%
Test for overall effect: Z = 2.80 (P = 0.005)



Source/Note: Random effects has been applied where there was unexplained heterogeneity

Figure 60: Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months

Study or Subgroup	ACT Mean	ACT SD	ACT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Mean Difference IV, Fixed, 95% CI
2.13.1 State								
Jensen 2012	40.8	12.3	20	47.6	14.4	16	100.0%	-6.80 [-15.68, 2.08]
Subtotal (95% CI)			**20**			**16**	**100.0%**	**-6.80 [-15.68, 2.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.50 (P = 0.13)								
2.13.2 Trait								
Jensen 2012	40.6	10.4	20	49.3	13.5	16	100.0%	-8.70 [-16.73, -0.67]
Subtotal (95% CI)			**20**			**16**	**100.0%**	**-8.70 [-16.73, -0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.12 (P = 0.03)								

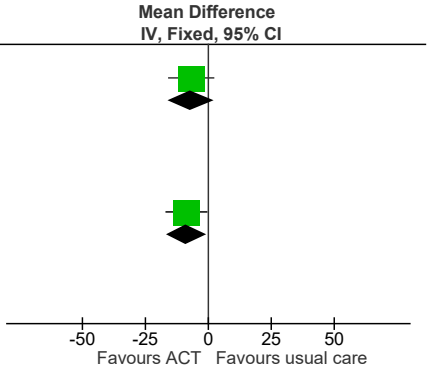
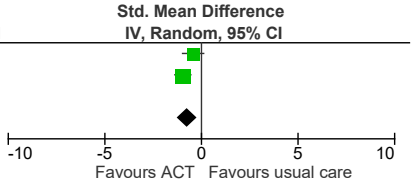


Figure 61: Psychological distress (Pain Anxiety Symptoms Scale; HADS anxiety) final values ≤3 months

Study or Subgroup	ACT Mean	ACT SD	ACT Total	Usual care Mean	Usual care SD	Usual care Total	Weight	Std. Mean Difference IV, Random, 95% CI
Alonso-Fernandez 2016	28.92	16.9	27	38	24.15	26	43.9%	-0.43 [-0.98, 0.11]
Luciano 2014	8.28	2.38	51	11.36	3.8	53	56.1%	-0.96 [-1.37, -0.55]
Total (95% CI)			**78**			**79**	**100.0%**	**-0.73 [-1.24, -0.21]**

Heterogeneity: Tau² = 0.08; Chi² = 2.33, df = 1 (P = 0.13); I² = 57%
Test for overall effect: Z = 2.77 (P = 0.006)



Source/Note: Random effects has been applied where there was unexplained heterogeneity

Figure 62: Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months

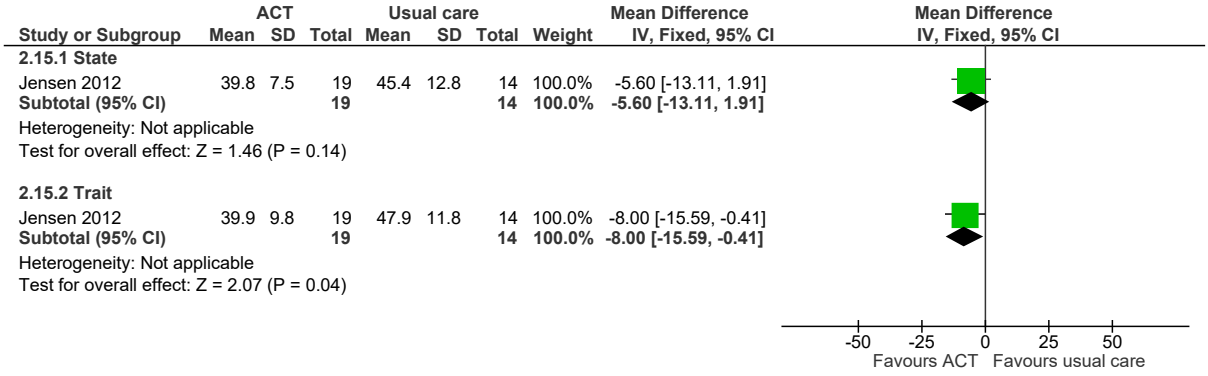


Figure 63: Psychological distress (Hospital anxiety and depression scale - anxiety) final values >3 months

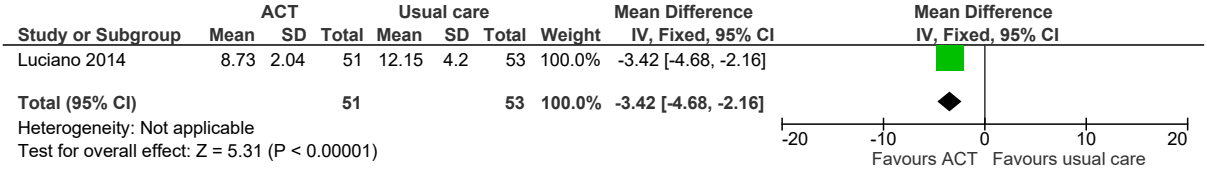


Figure 64: Pain interference (Brief Pain inventory - pain interference) final values ≤3 months

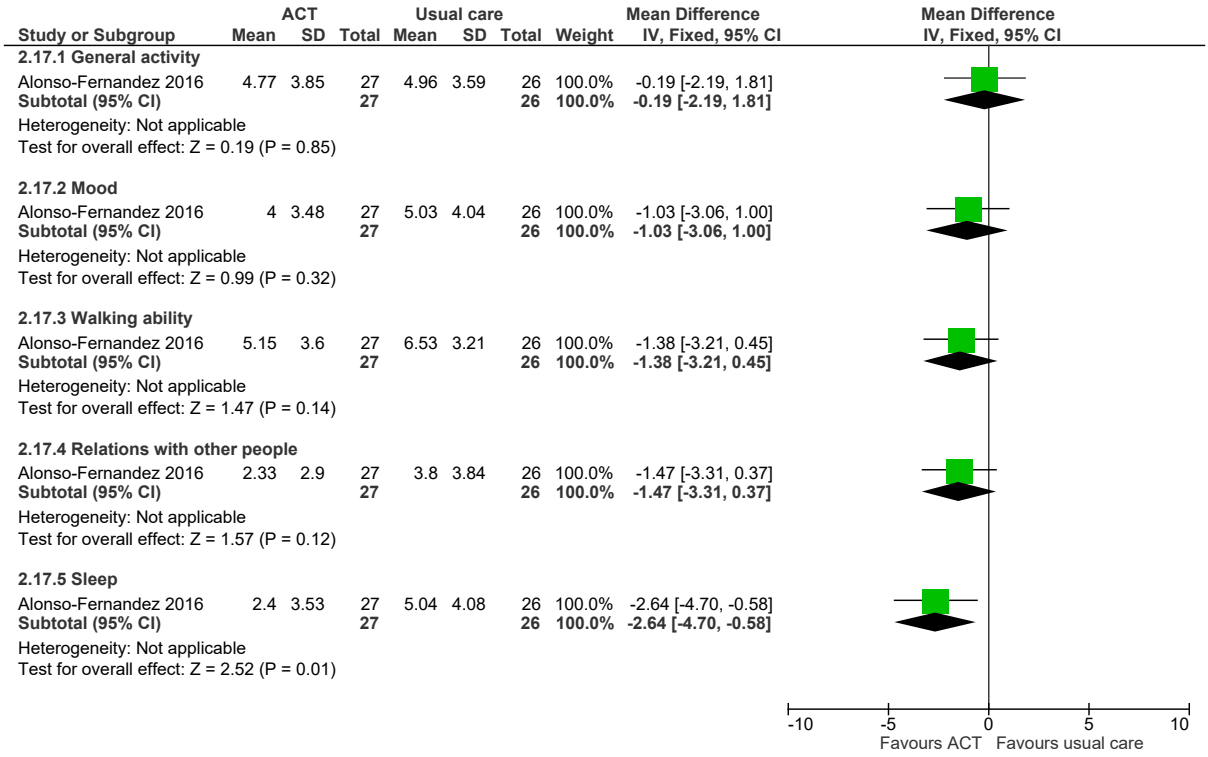


Figure 65: Pain interference (Pain disability index) final values ≤3 months

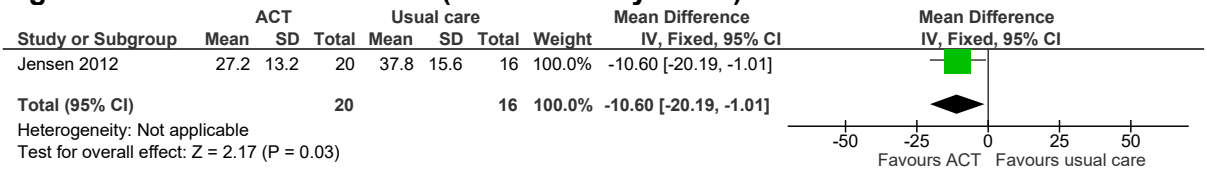


Figure 66: Pain interference (Pain disability index) final values >3 months

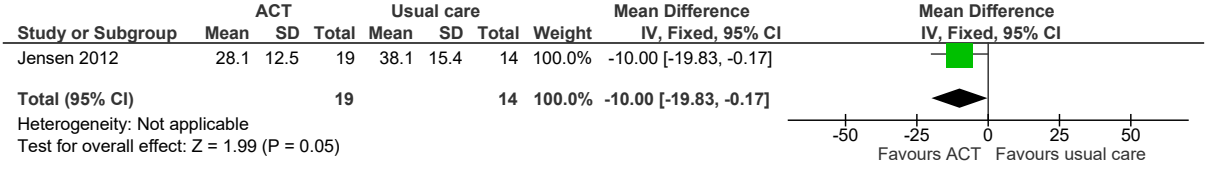


Figure 67: Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months

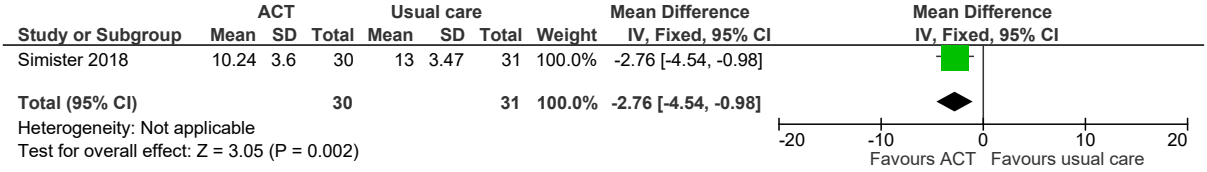


Figure 68: Sleep (Pittsburgh Sleep Quality Index) final values >3 months

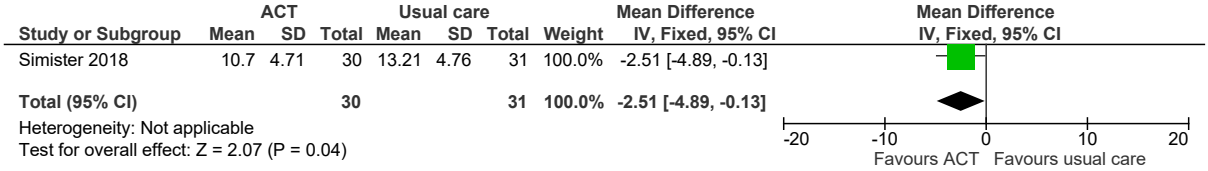


Figure 69: Discontinuation

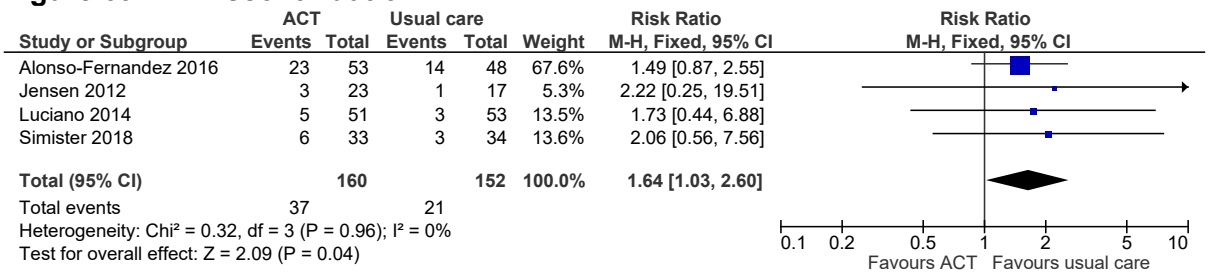
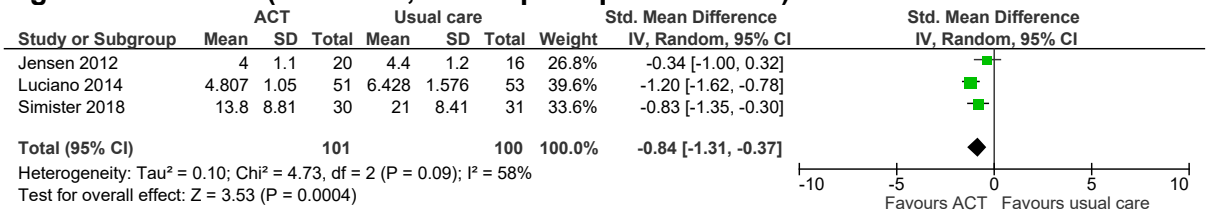
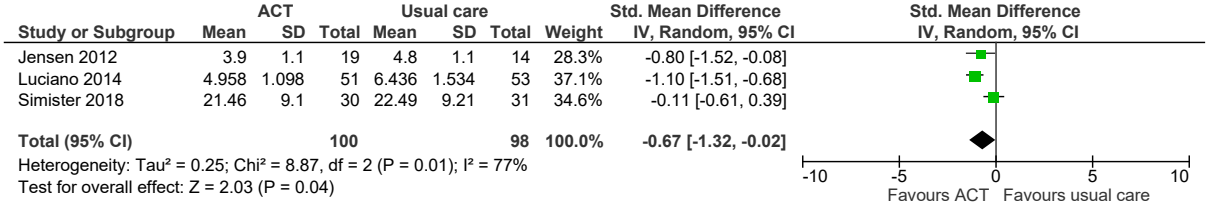


Figure 70: Pain (VAS/NRS; McGill pain questionnaire) final values ≤3 months



Source/Note: Random effects has been applied where there was unexplained heterogeneity

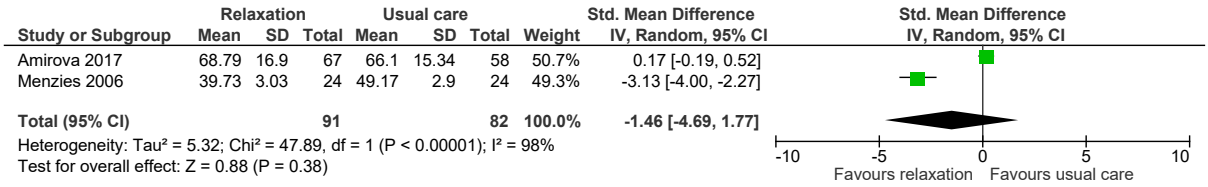
Figure 71: Pain (VAS/NRS; McGill pain questionnaire) final values >3 months



Source/Note: Random effects has been applied where there was unexplained heterogeneity

E.3 Relaxation versus Usual care

Figure 72: Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months



Source/Note: Random effects has been applied where there was unexplained heterogeneity

Figure 73: Physical function (Neck disability index) final values ≤3 months

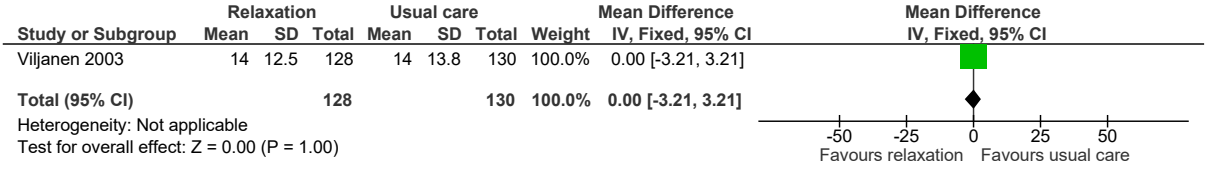


Figure 74: Physical function (Neck disability index) final values >3 months

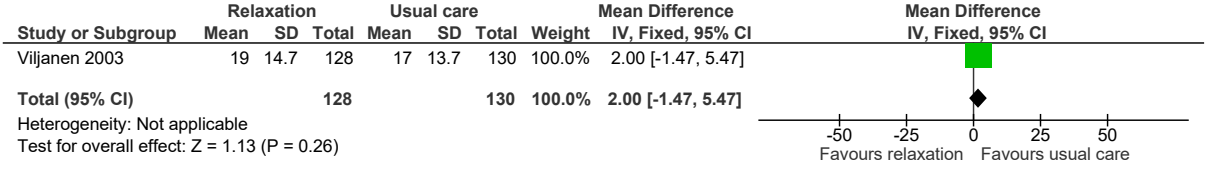


Figure 75: Psychological distress (Hospital Anxiety and Depression Scale depression; Center for Epidemiologic Studies depression scale) final values ≤3 months

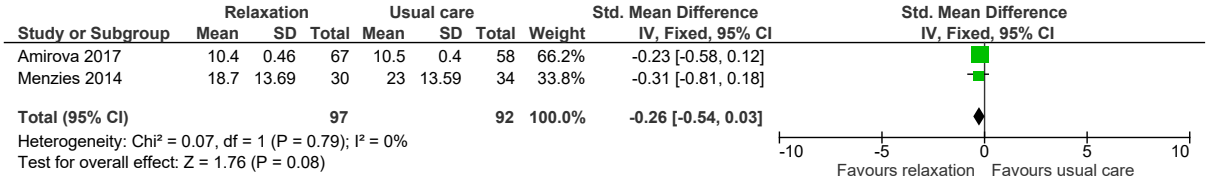


Figure 76: Psychological distress (Hospital Anxiety and Depression Scale anxiety) final values ≤3 months

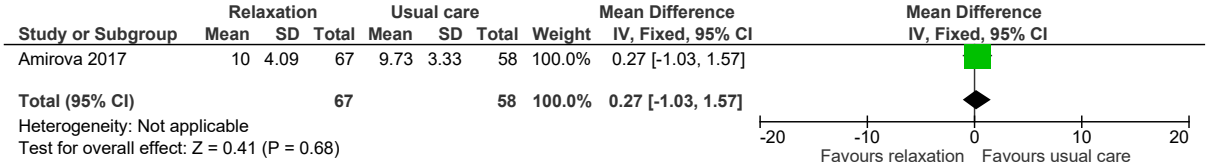


Figure 77: Pain interference (Brief Pain Inventory - interference) final values ≤3 months

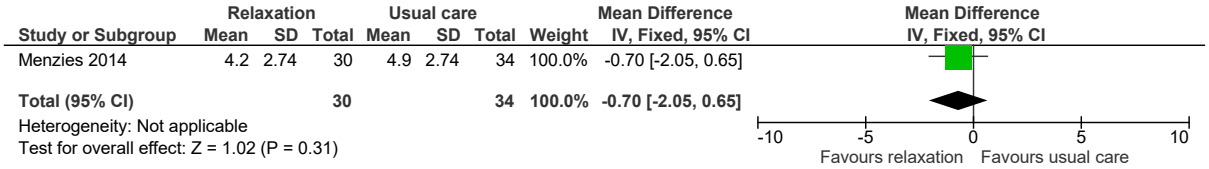


Figure 78: Pain self-efficacy (Arthritis Self-efficacy Scale - pain sub scale) final values ≤3 months

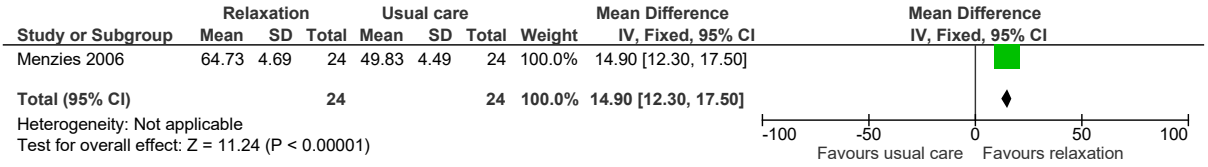


Figure 79: Pain self-efficacy (Arthritis Self-efficacy Scale - self-efficacy for managing other symptoms sub scale) final values ≤3 months

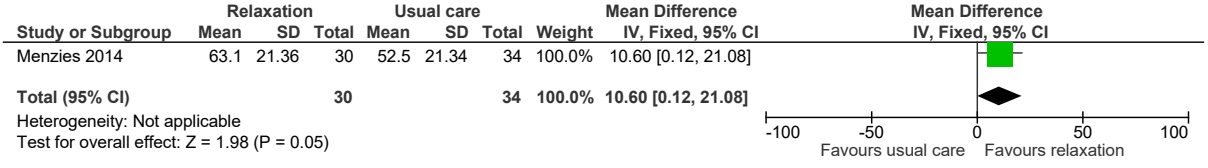


Figure 80: Sleep (Medical Outcome Sleep Scale sleep problems index) final values ≤3 months

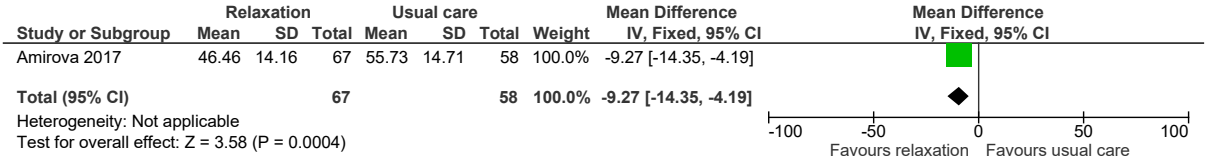
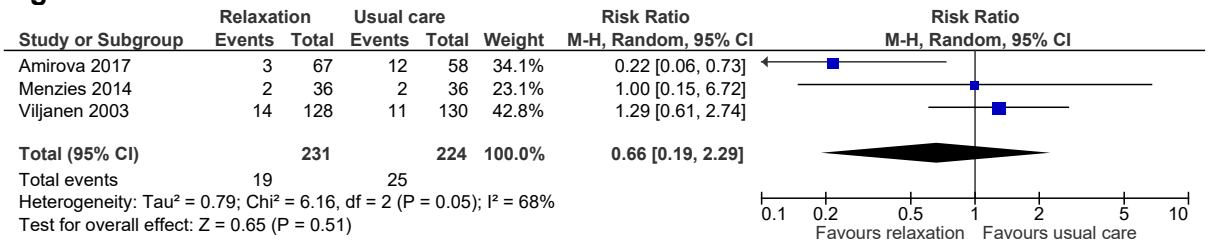
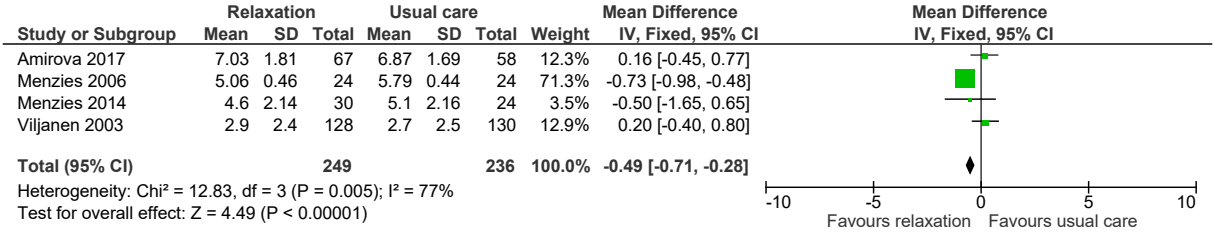


Figure 81: Discontinuation



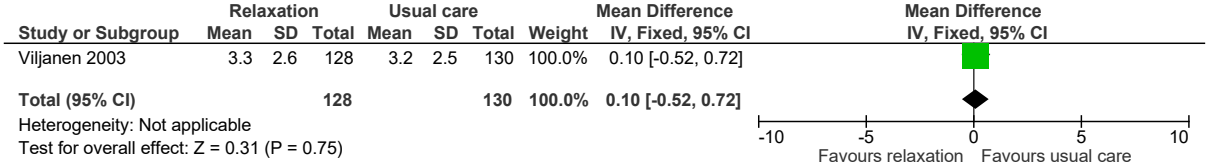
Source/Note: Random effects has been applied where there was unexplained heterogeneity

Figure 82: Pain (VAS/NRS) final values ≤3 months



Source/Note: Where statistical heterogeneity was present, but visual inspection indicated estimates were consistent with the same clinical interpretation (benefit/no difference/harm), a fixed effects model was applied

Figure 83: Pain (VAS/NRS) final values >3 months



E.4 Relaxation versus Attention control

Figure 84: Pain (VAS) final values ≤3 months

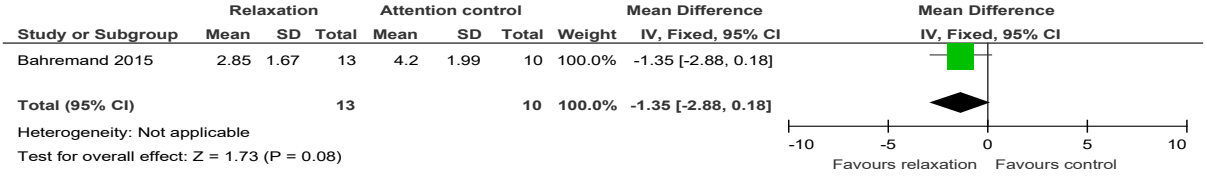
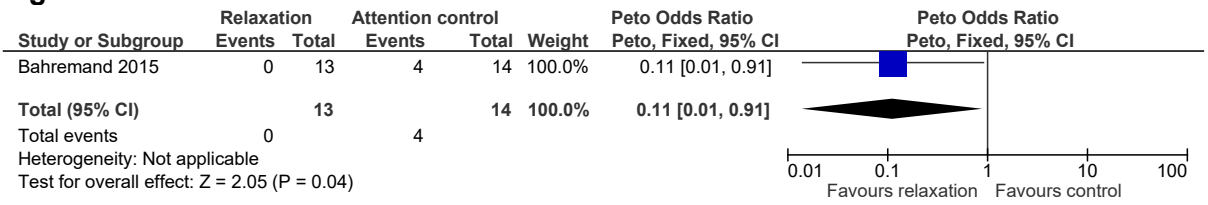


Figure 85: Discontinuation



E.5 Biofeedback versus Usual care

Figure 86: Quality of life (SF36) final values ≤3 months (EMG biofeedback)

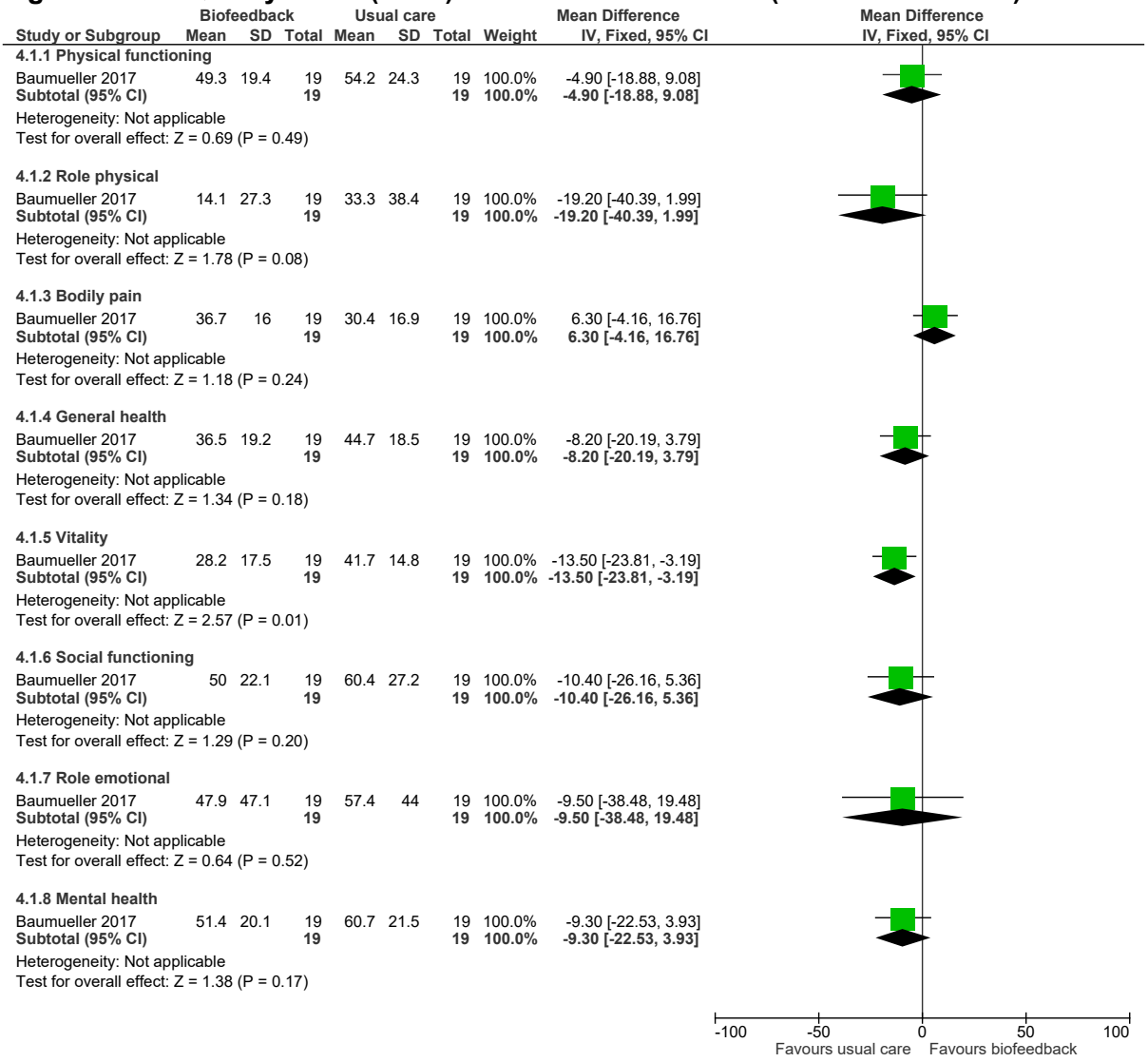


Figure 87: Quality of life (SF36) final values ≤3 months (HRV biofeedback)

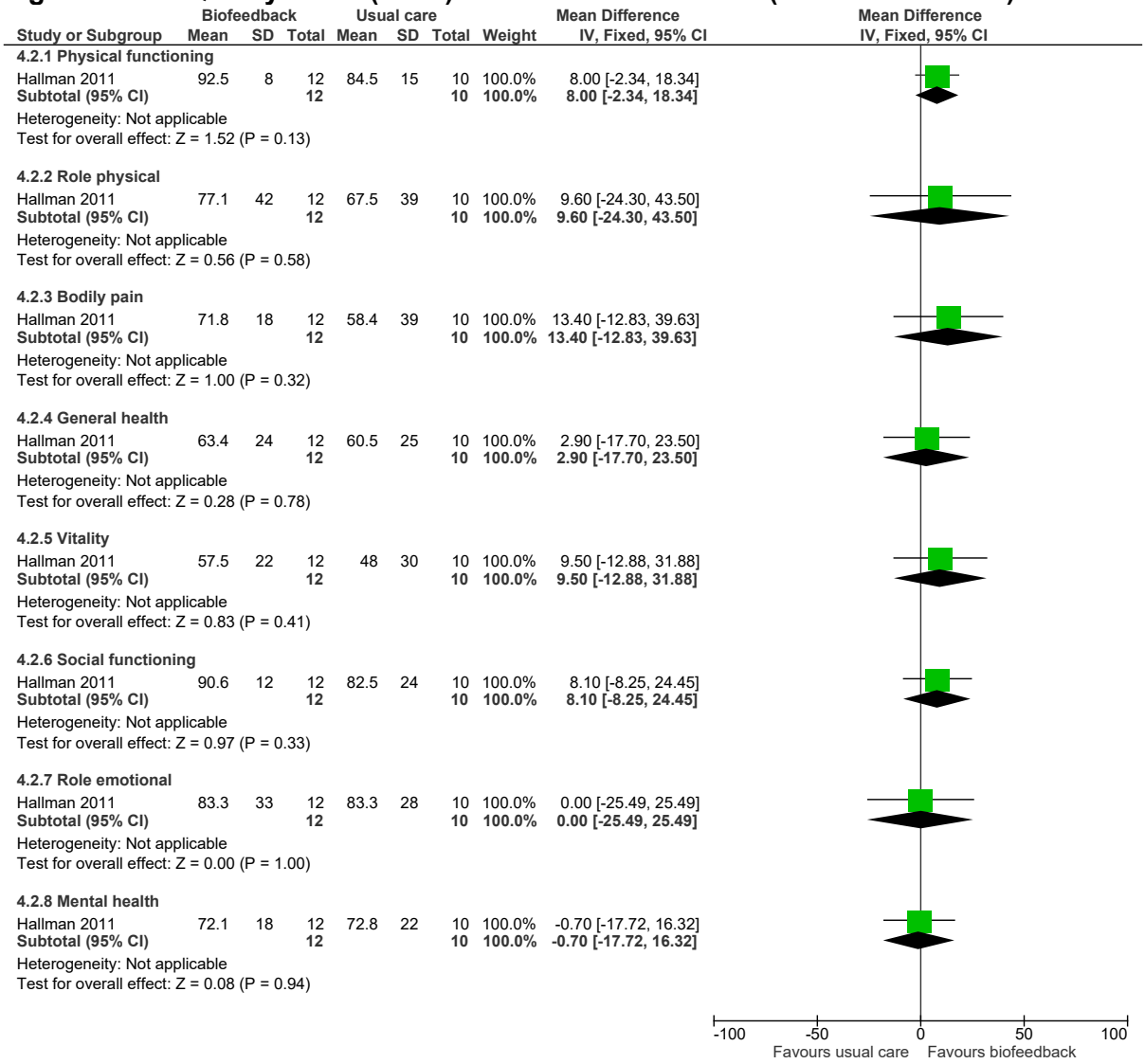


Figure 88: Quality of life (SF36) final values >3 months

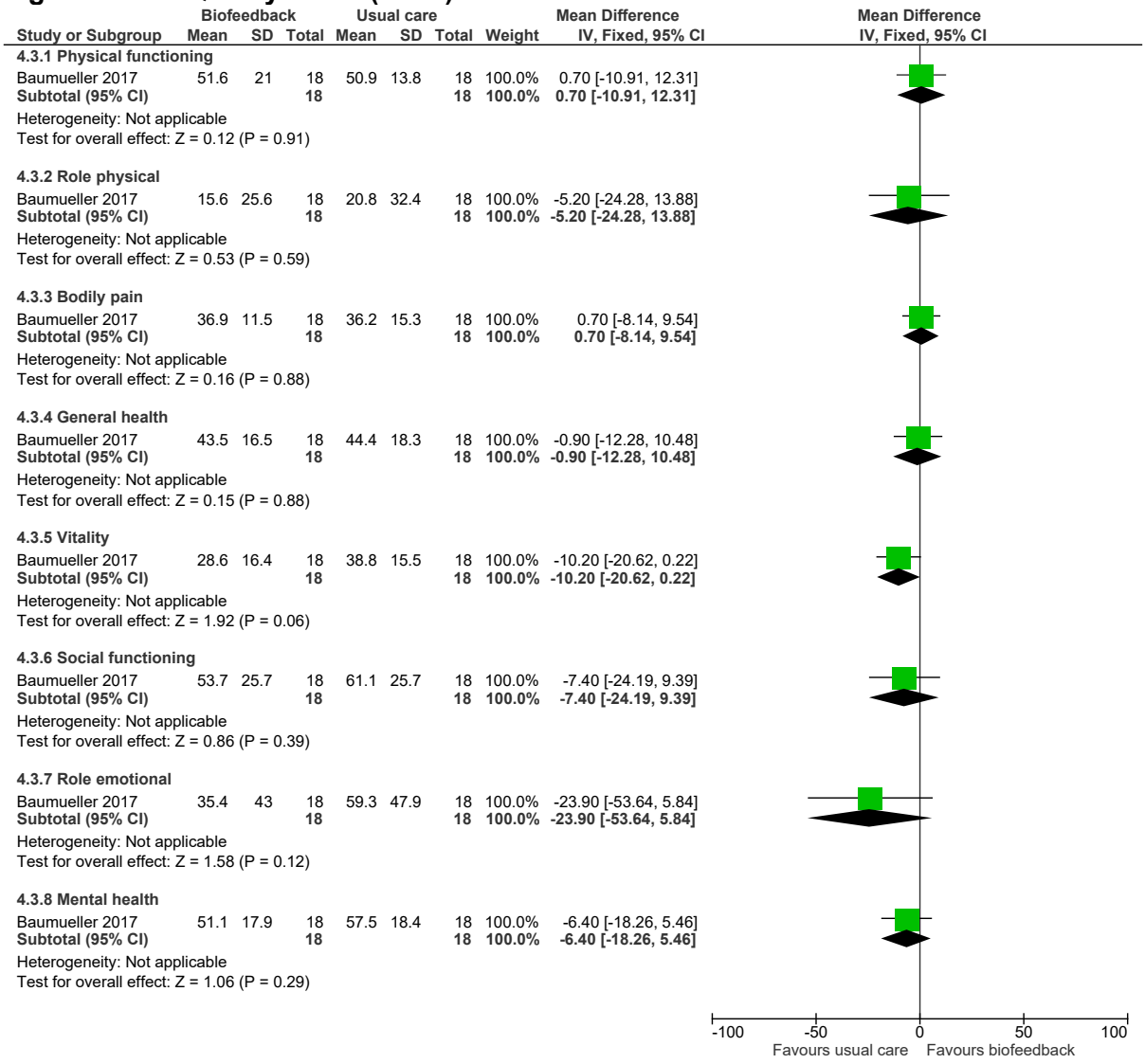


Figure 89: Quality of life (Arthritis Impact Measurement Scale) change scores >3 months

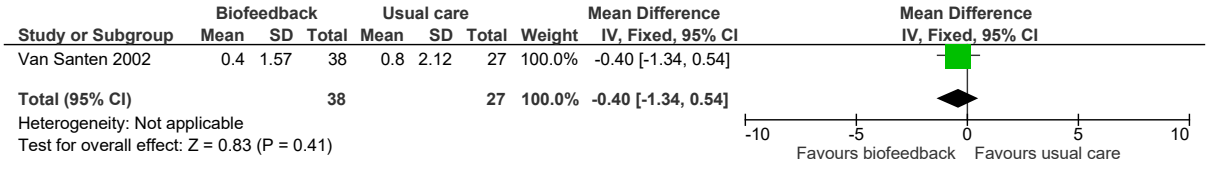


Figure 90: Physical function (Neck disability index) final values ≤3 months

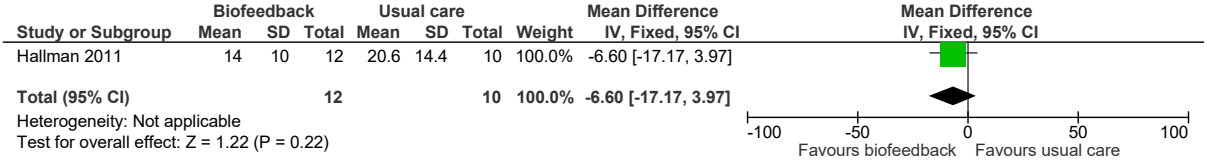


Figure 91: Physical function (Maximal Watt bicycle ergometer) change scores >3 months

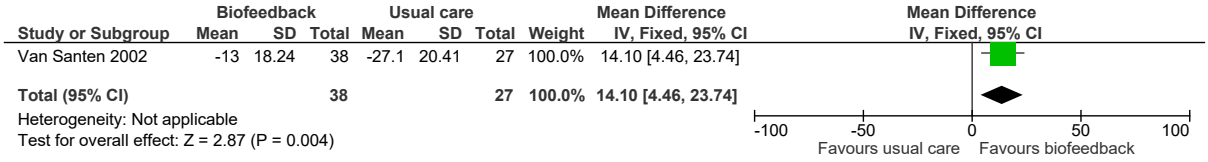


Figure 92: Psychological distress (Beck Depression Inventory) final values ≤3 months

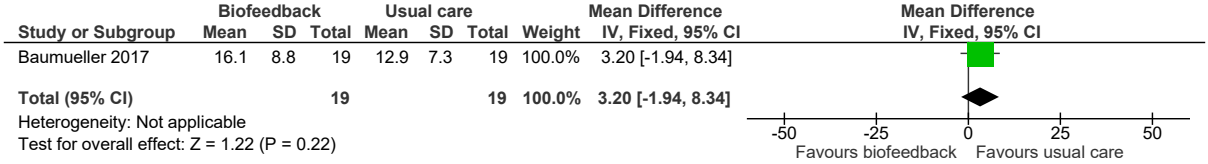


Figure 93: Psychological distress (Hospital Anxiety and Depression Scale - depression) final values ≤3 months

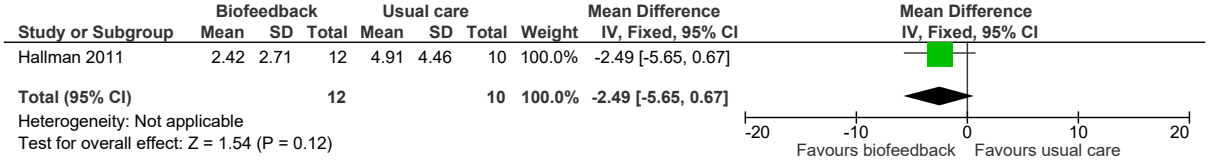


Figure 94: Psychological distress (Beck Depression Inventory) final values >3 months

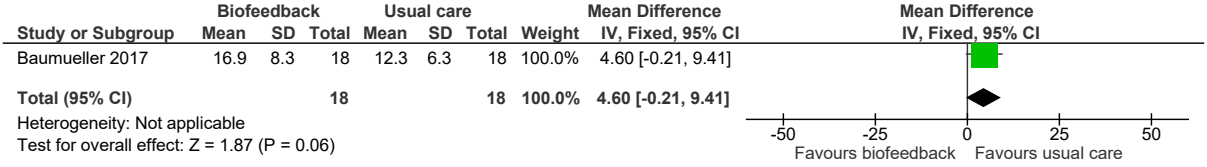


Figure 95: Psychological distress (Symptoms Checklist-90-revised) change scores >3 months

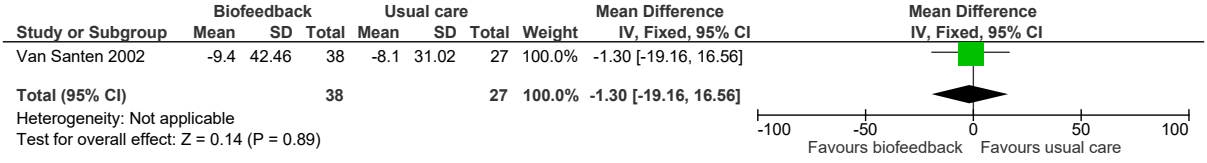


Figure 96: Psychological distress (Hospital Anxiety and Depression Scale anxiety) final values ≤3 months

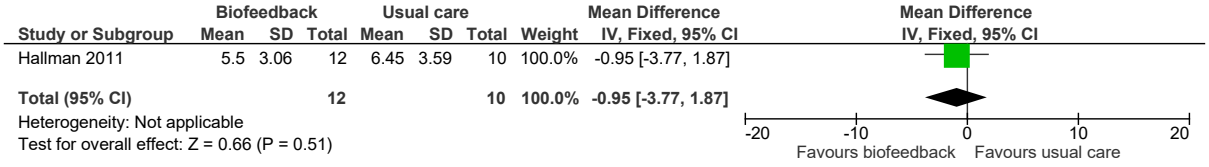


Figure 97: Discontinuation

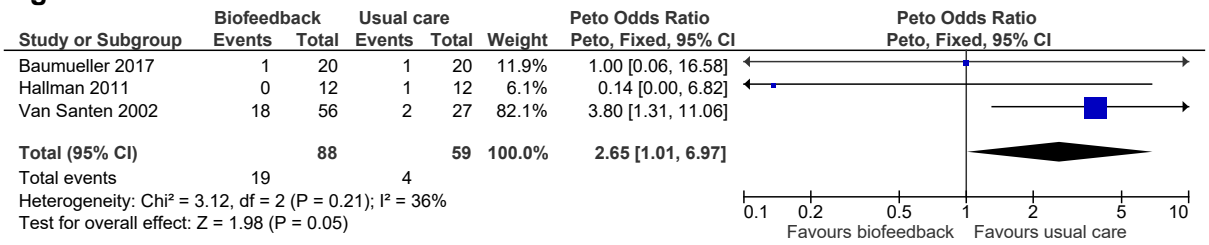


Figure 98: Pain (VAS/NRS) final values ≤3 months

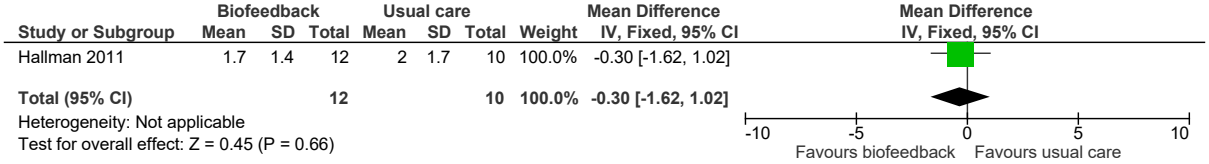
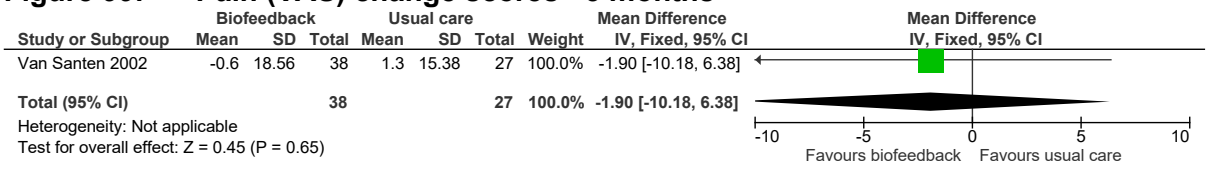


Figure 99: Pain (VAS) change scores >3 months



E.6 Biofeedback versus Sham biofeedback

Figure 100: Quality of life (Fibromyalgia impact questionnaire) change scores<3 months

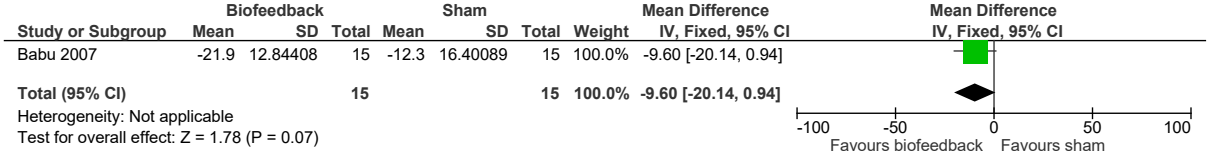


Figure 101: Physical function (6 minute walk test) change scores <3 months

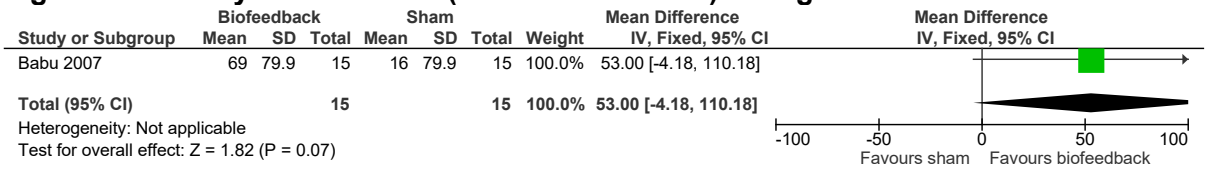


Figure 102: Psychological distress (Beck depression inventory) change scores ≤3 months

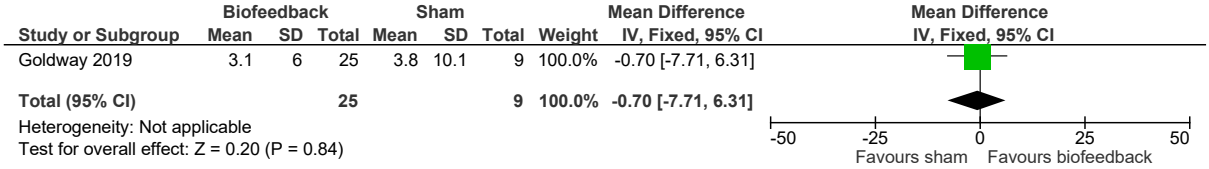


Figure 103: Psychological distress (Beck depression inventory) change scores >3 months

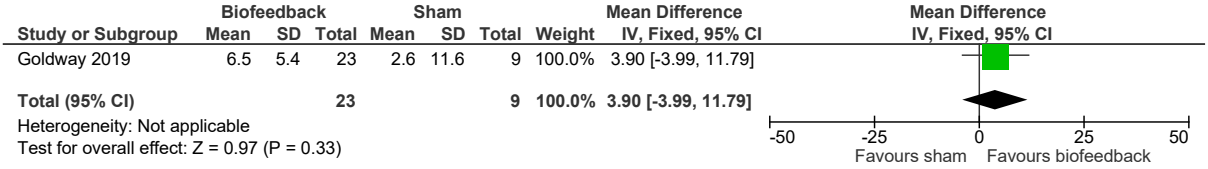


Figure 104: Psychological distress (State trait anxiety inventory - trait) change scores ≤3 months

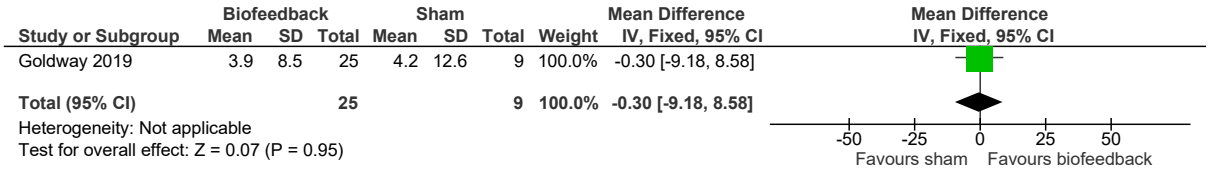


Figure 105: Psychological distress (State trait anxiety inventory - trait) change scores >3 months

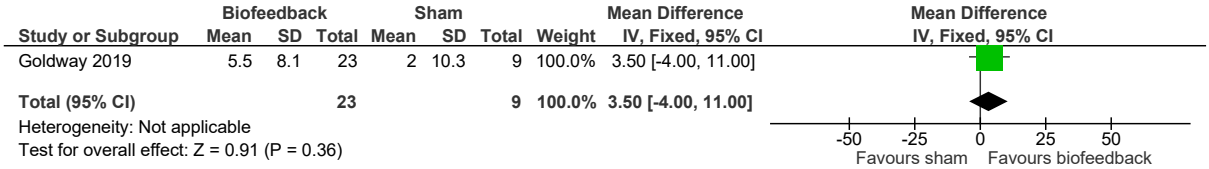


Figure 106: Sleep (Pittsburgh sleep quality index) change scores ≤3 months

Study or Subgroup	Biofeedback Mean	SD	Total	Sham Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Goldway 2019	0.4	4.4	25	1.2	4.4	9	100.0%	-0.80 [-4.15, 2.55]
Total (95% CI)			**25**			**9**	**100.0%**	**-0.80 [-4.15, 2.55]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.47 (P = 0.64)

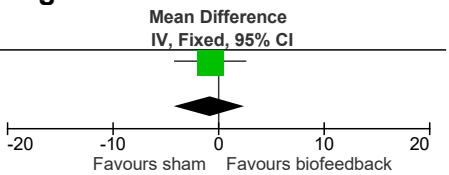


Figure 107: Sleep (Pittsburgh sleep quality index) change scores >3 months

Study or Subgroup	Biofeedback Mean	SD	Total	Sham Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Goldway 2019	1.5	4.1	23	-0.5	4.8	9	100.0%	2.00 [-1.56, 5.56]
Total (95% CI)			**23**			**9**	**100.0%**	**2.00 [-1.56, 5.56]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)

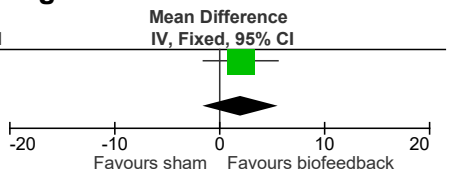


Figure 108: Discontinuation

Study or Subgroup	Biofeedback Events	Total	Sham Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Babu 2007	0	15	0	15	46.4%	0.00 [-0.12, 0.12]
Goldway 2019	6	31	3	12	53.6%	-0.06 [-0.34, 0.23]
Total (95% CI)		**46**		**27**	**100.0%**	**-0.03 [-0.19, 0.13]**
Total events	6		3			

Heterogeneity: Chi² = 0.27, df = 1 (P = 0.60); I² = 0%
Test for overall effect: Z = 0.37 (P = 0.71)

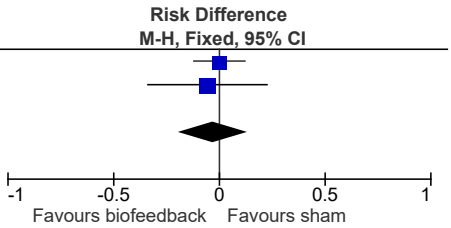


Figure 109: Pain (VAS) change scores ≤3 months - neurofeedback

Study or Subgroup	Biofeedback Mean	SD	Total	Sham Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Goldway 2019	0.2	1.6	25	1.1	1.5	9	100.0%	-0.90 [-2.06, 0.26]
Total (95% CI)			**25**			**9**	**100.0%**	**-0.90 [-2.06, 0.26]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.52 (P = 0.13)

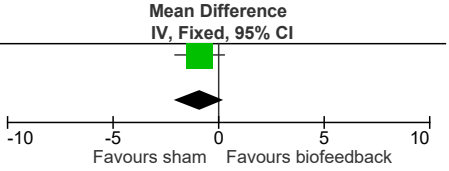


Figure 110: Pain (VAS) change scores ≤3 months

Study or Subgroup	Biofeedback Mean	SD	Total	Sham Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Babu 2007	4.3	1.976	15	2.6	3.359	15	100.0%	1.70 [-0.27, 3.67]
Total (95% CI)			**15**			**15**	**100.0%**	**1.70 [-0.27, 3.67]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.69 (P = 0.09)

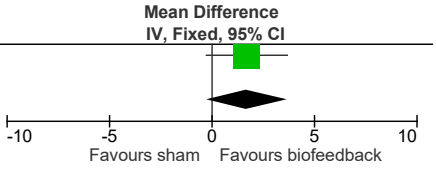
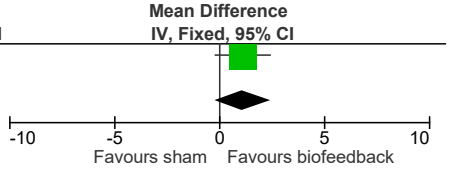


Figure 111: Pain (VAS) change scores >3 months - neurofeedback

Study or Subgroup	Biofeedback Mean	SD	Total	Sham Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Goldway 2019	1.1	2.1	23	0	1.5	9	100.0%	1.10 [-0.20, 2.40]
Total (95% CI)			**23**			**9**	**100.0%**	**1.10 [-0.20, 2.40]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.66 (P = 0.10)



E.7 Mindfulness versus Usual care

Figure 112: Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months

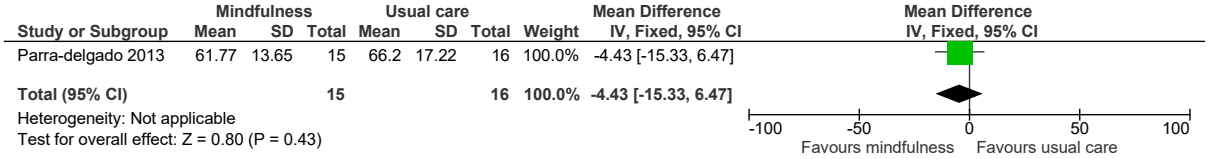


Figure 113: Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months

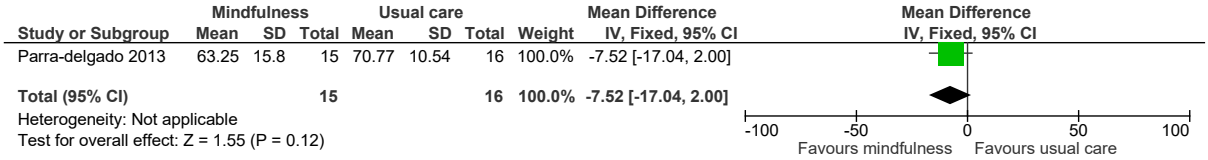


Figure 114: Psychological distress (Beck depression Inventory) final values ≤3 months

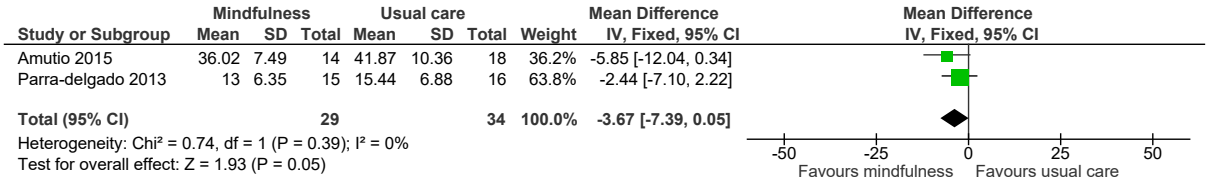


Figure 115: Psychological distress (Beck depression Inventory) final values >3 months

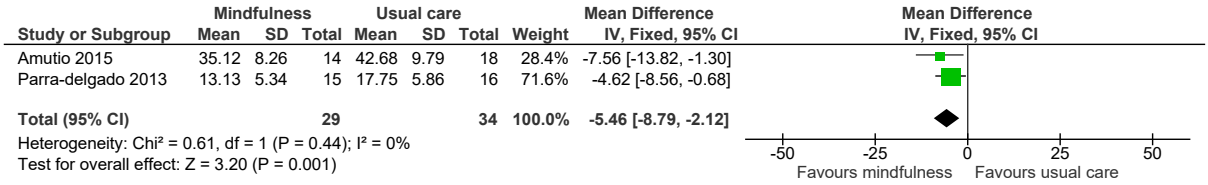


Figure 116: Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months

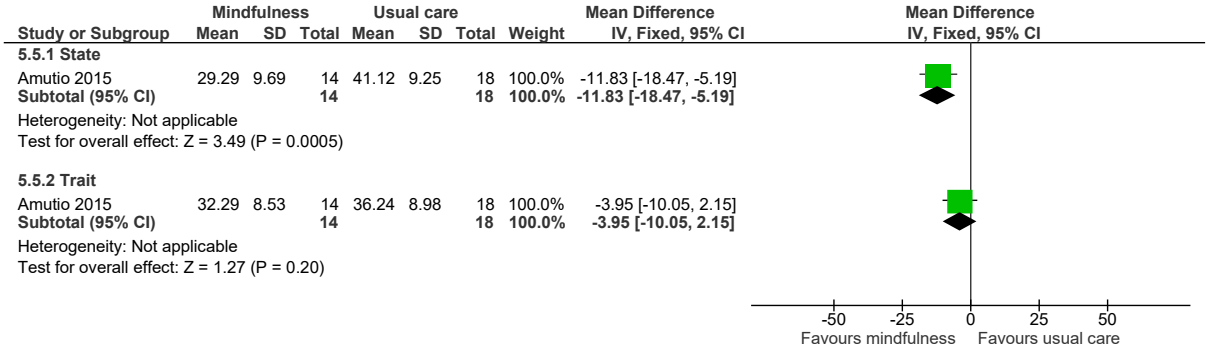


Figure 117: Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months

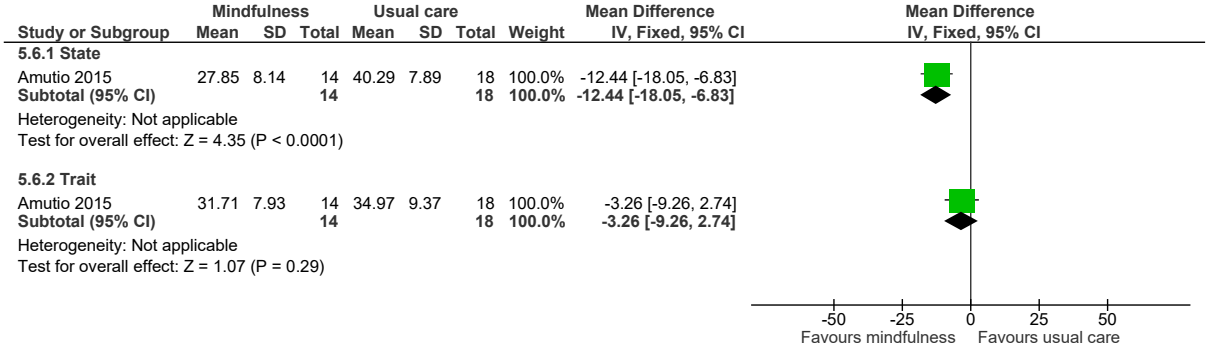


Figure 118: Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months

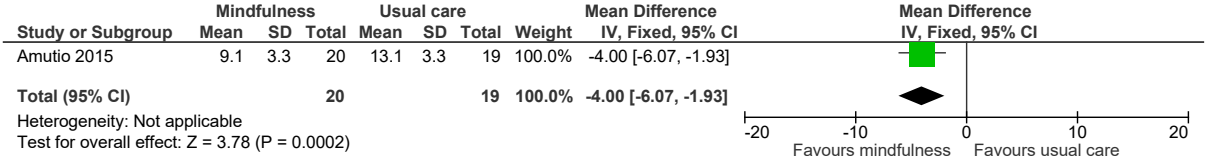


Figure 119: Sleep (Pittsburgh Sleep Quality Index) final values >3 months

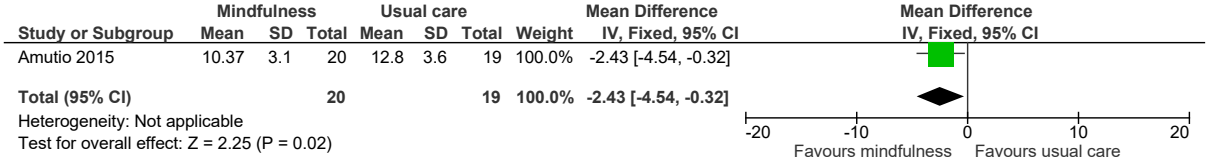
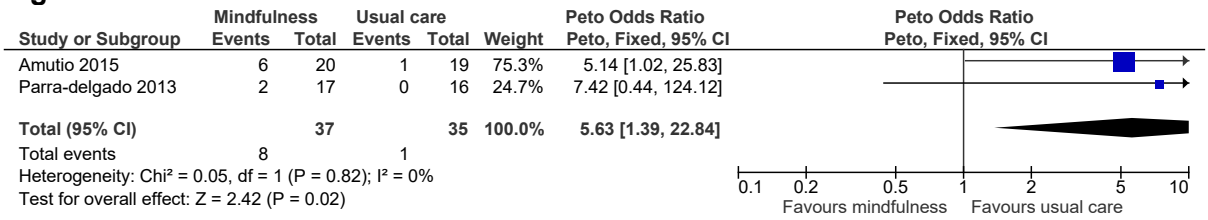


Figure 120: Discontinuation



E.8 Pain education versus Usual care

Figure 121: Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months

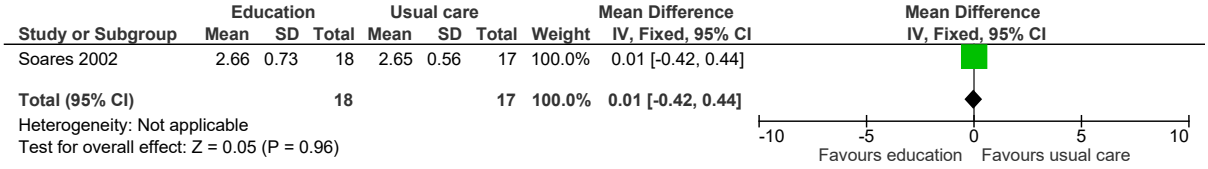


Figure 122: Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months

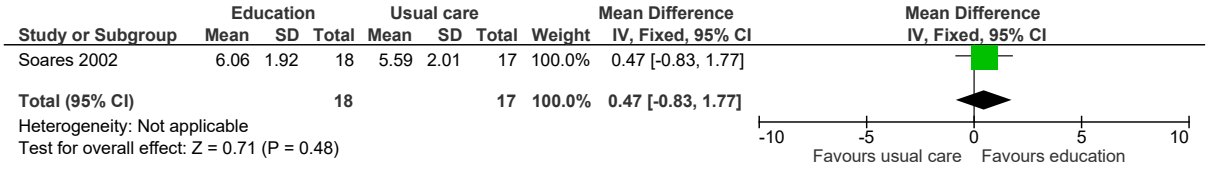


Figure 123: Sleep (Karolinska sleep questionnaire - sleep quality sub scale) final values ≤3 months

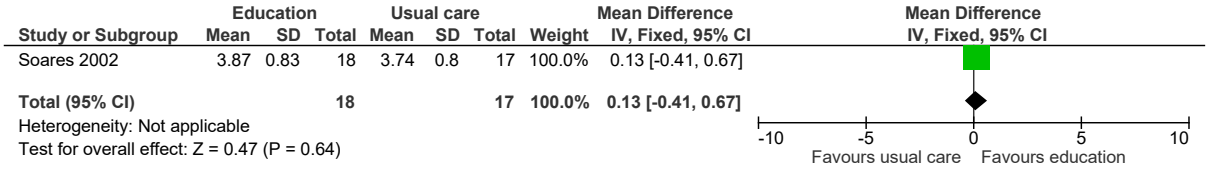
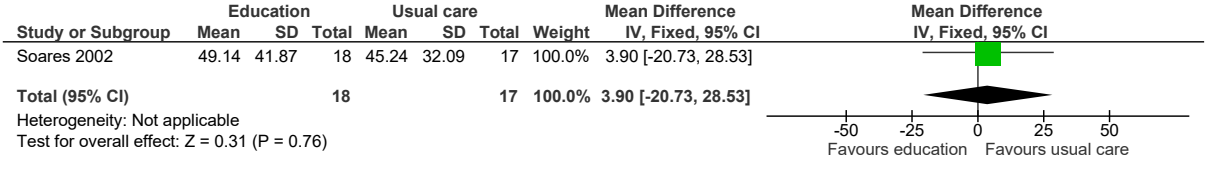


Figure 124: Pain (McGill Pain Questionnaire) final values ≤3 months



E.9 Pain education versus Attention control

Figure 125: Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months

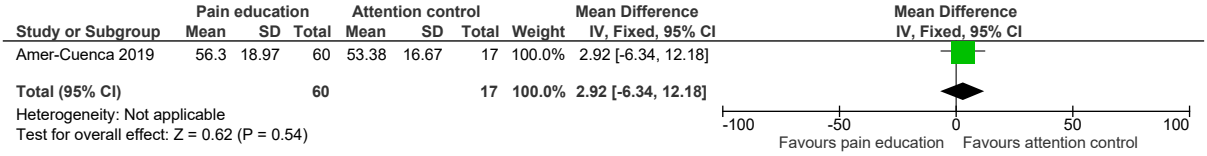


Figure 126: Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months

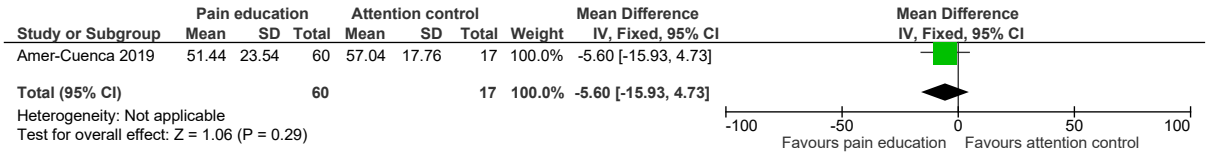


Figure 127: Psychological distress (Pain Anxiety Symptom Scale) final values ≤3 months

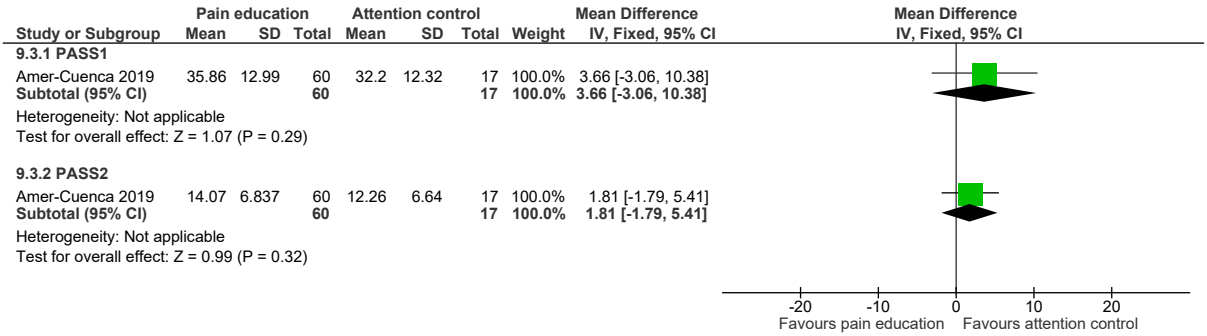


Figure 128: Psychological distress (Pain Anxiety Symptom Scale) final values >3 months

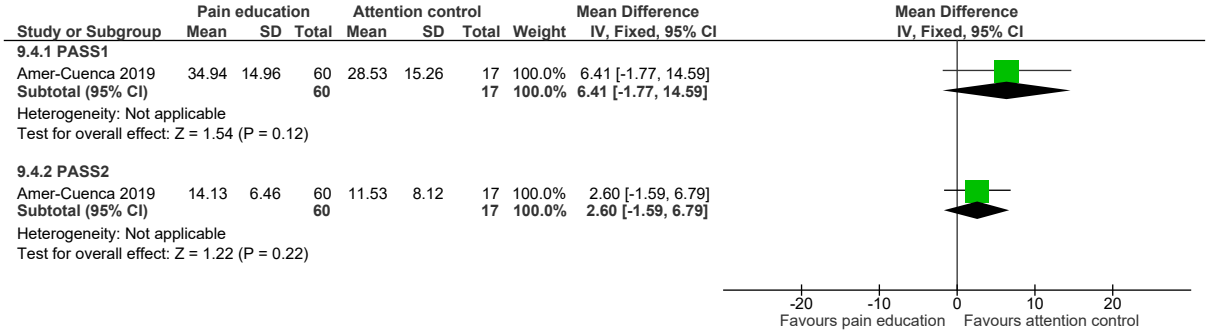


Figure 129: Pain (numeric rating scale) final values ≤3 months

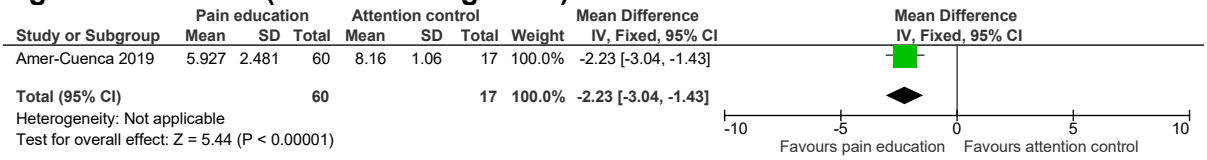


Figure 130: Pain (numeric rating scale) final values >3 months

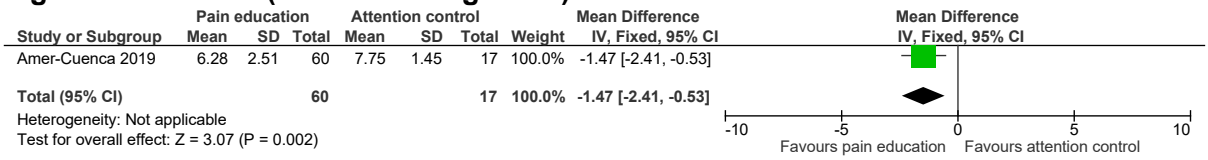
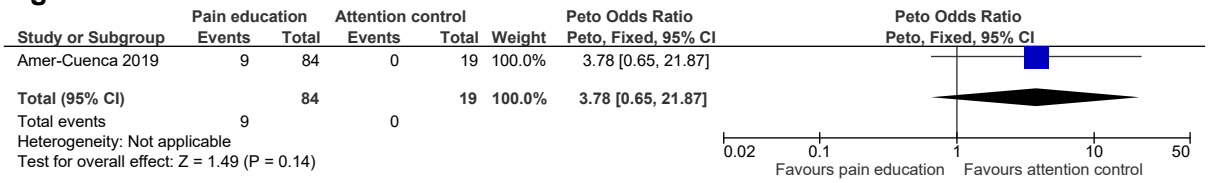


Figure 131: Discontinuation



E.10 Sleep hygiene versus Usual care

Figure 132: Quality of life (SF36 mental composite) final values ≤3 months

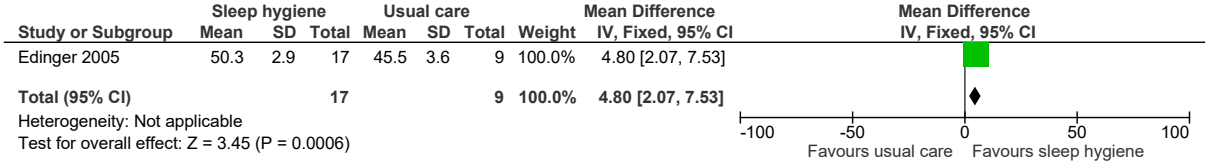


Figure 133: Quality of life (SF36 mental composite) final values >3 months

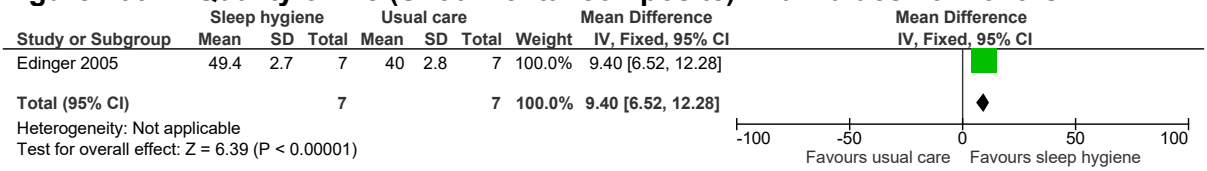


Figure 134: Sleep (Insomnia Symptom Questionnaire) final values ≤3 months

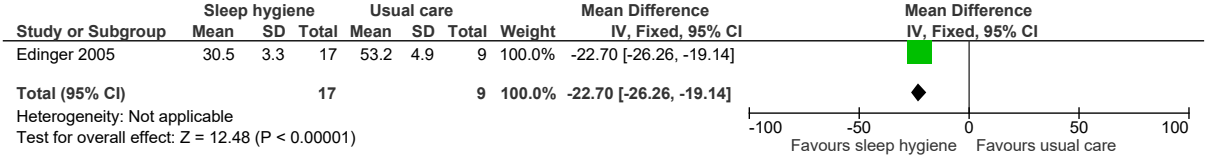


Figure 135: Sleep (Insomnia Symptom Questionnaire) final values >3 months

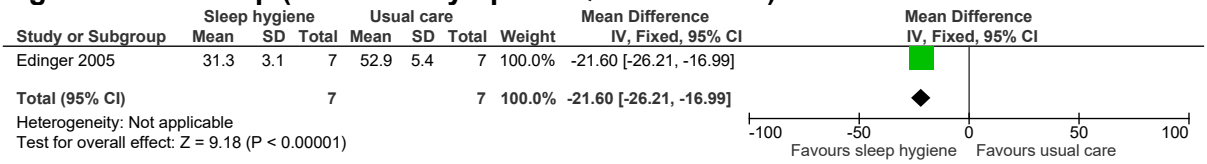


Figure 136: Discontinuation

Figure 137: Pain (McGill pain questionnaire) final values ≤3 months

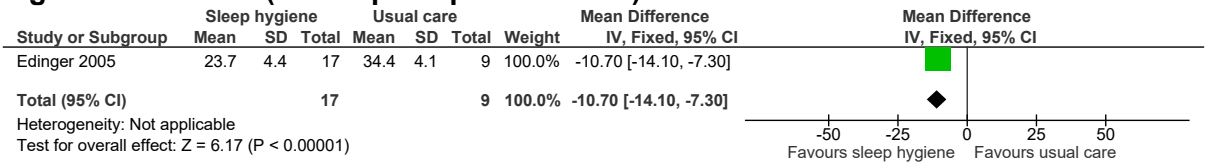
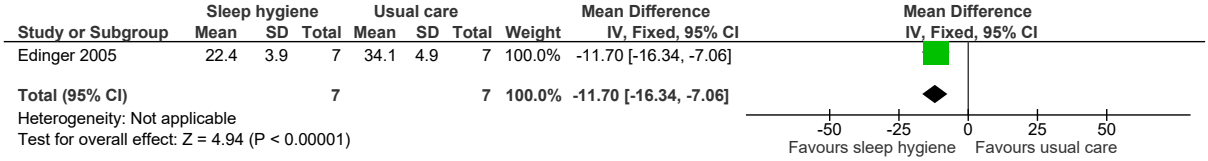


Figure 138: Pain (McGill pain questionnaire) final values >3 months



E.11 Hypnosis versus Usual care

Figure 139: Quality of life (Fibromyalgia Impact Questionnaire) change scores ≤3 months

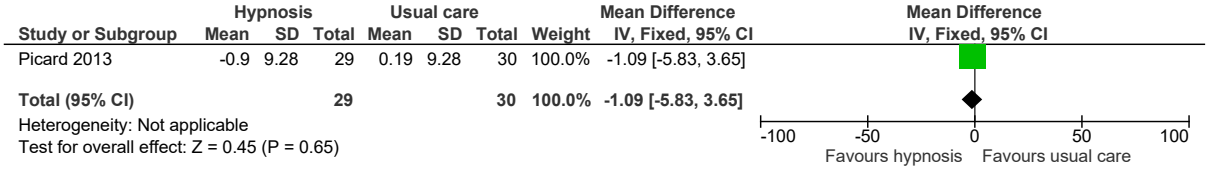


Figure 140: Quality of life (Fibromyalgia Impact Questionnaire) change scores >3 months

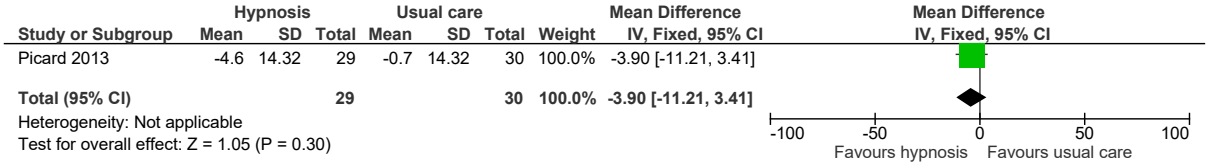


Figure 141: Psychological distress (Hospital Anxiety and Depression Scale - depression) change scores ≤3 months

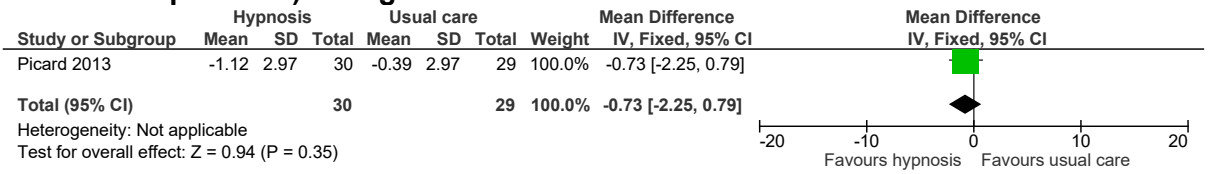


Figure 142: Psychological distress (Hospital Anxiety and Depression Scale - depression) change scores >3 months

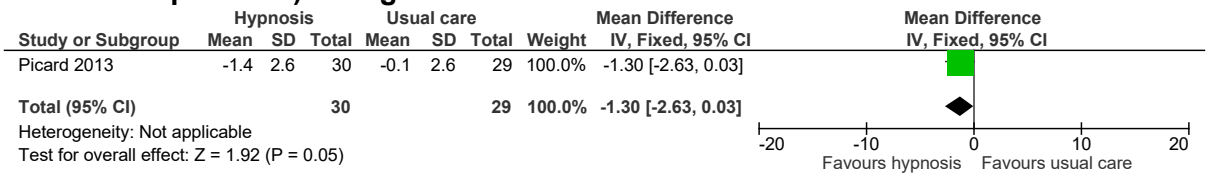


Figure 143: Psychological distress (Hospital Anxiety and Depression Scale - anxiety) change scores ≤3 months

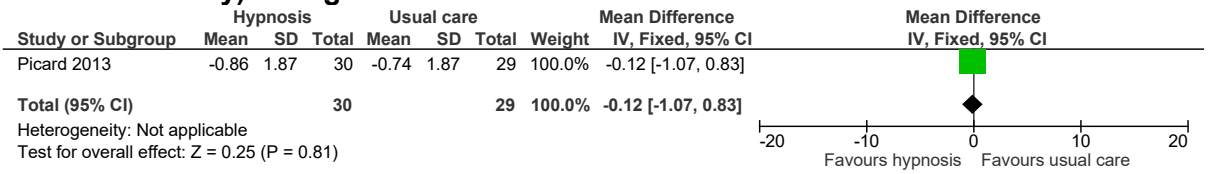


Figure 144: Psychological distress (Hospital Anxiety and Depression Scale - anxiety) change scores >3 months

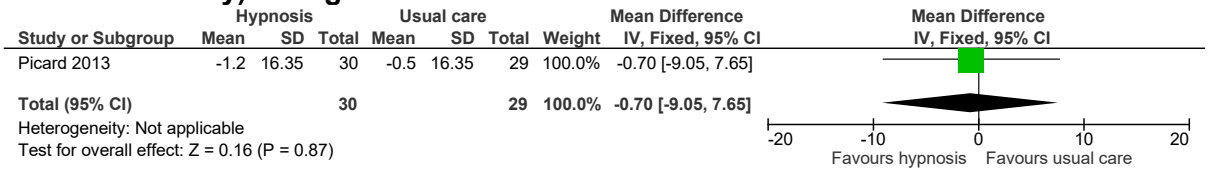


Figure 145: Sleep (Medical Outcome Sleep Scale) change scores ≤3 months

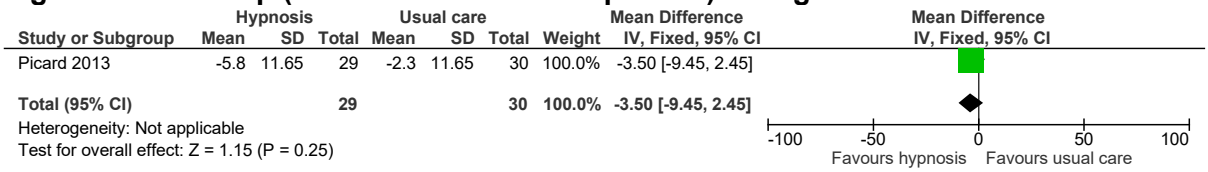


Figure 146: Sleep (Medical Outcome Sleep Scale) change scores >3 months

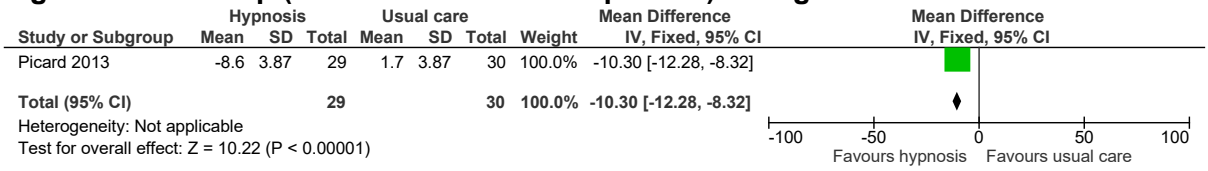


Figure 147: Discontinuation

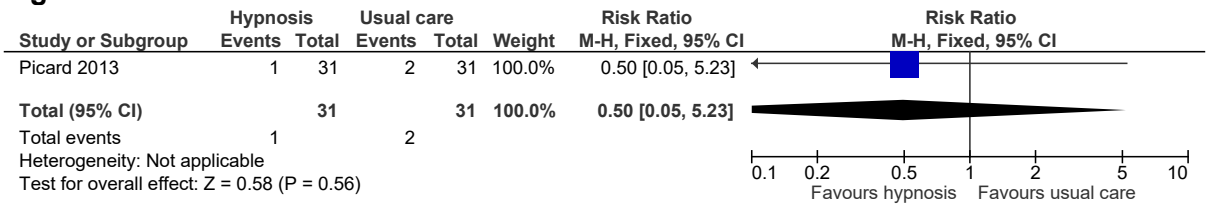
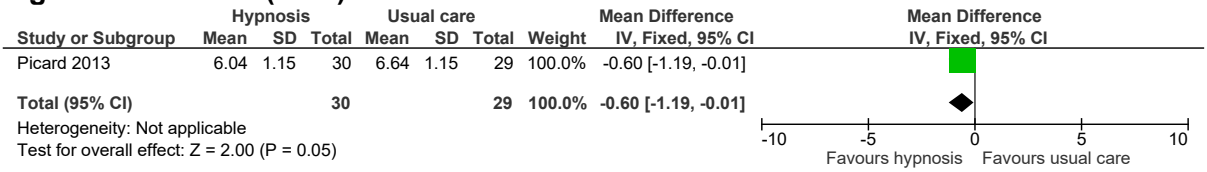


Figure 148: Pain (NRS) final values >3 months



E.12 Psychotherapy versus Usual care

Figure 149: Quality of life (SF36 physical component) final values >3 months

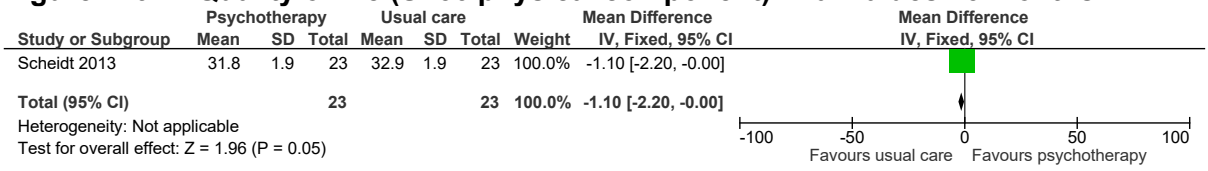


Figure 150: Quality of life (SF36 mental component) final values >3 months

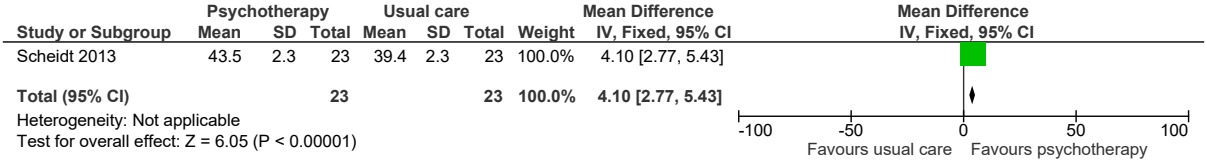


Figure 151: Physical function (Somatoform disorders-7) final values >3 months

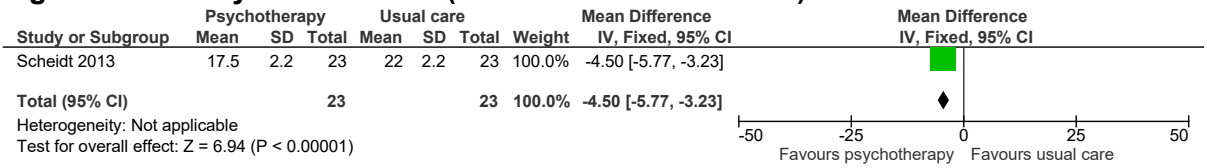


Figure 152: Psychological distress (Hospital Anxiety and Depression Scale - depression) final values >3 months

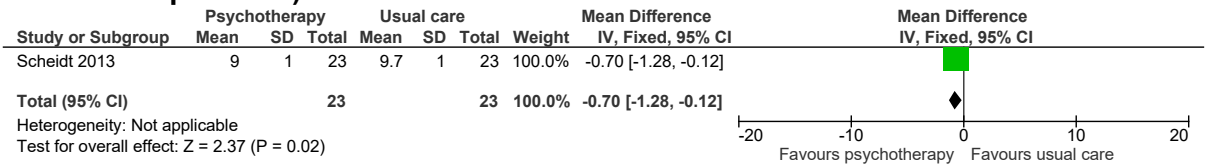


Figure 153: Psychological distress (Hospital Anxiety and Depression Scale - anxiety) final values >3 months

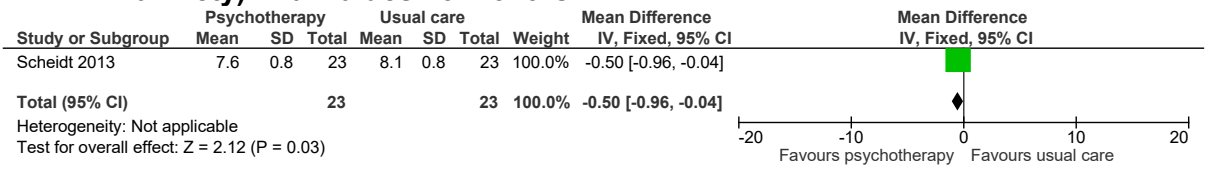


Figure 154: Pain interference (Pain disability index) final values >3 months

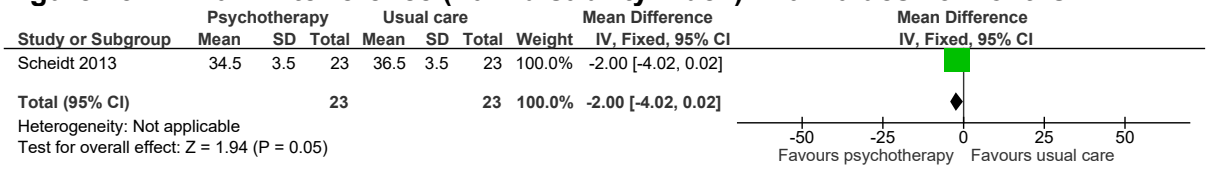
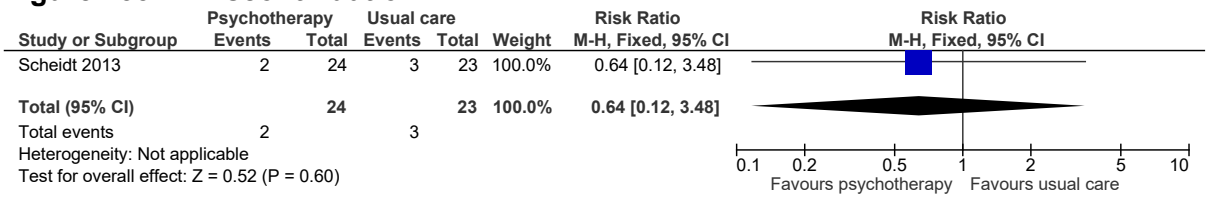


Figure 155: Discontinuation



E.13 CBT (for insomnia) versus Sleep hygiene

Figure 156: Quality of life (SF36 mental composite) final values ≤3 months

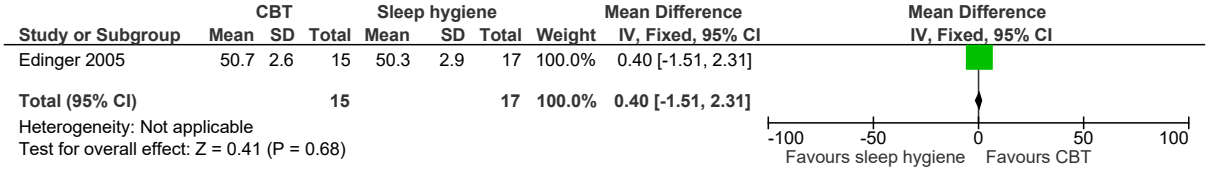


Figure 157: Quality of life (SF36 mental composite) final values >3 months

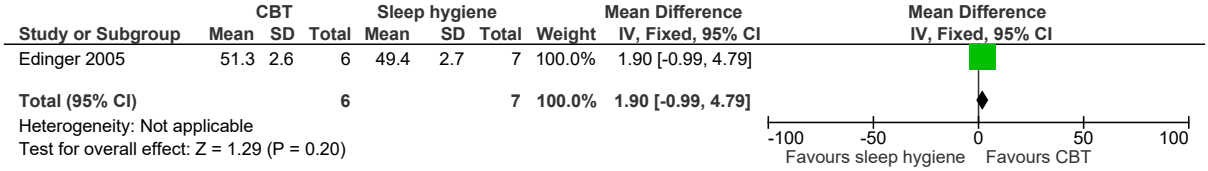


Figure 158: Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months

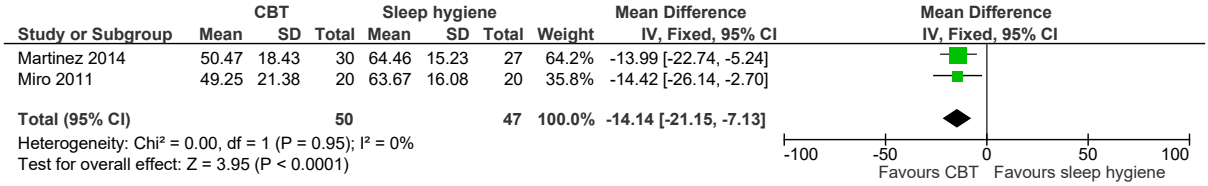


Figure 159: Psychological distress (Symptom Checklist-90-Revised - depression sub scale; Hospital Anxiety and Depression Scale - depression) final values ≤3 months

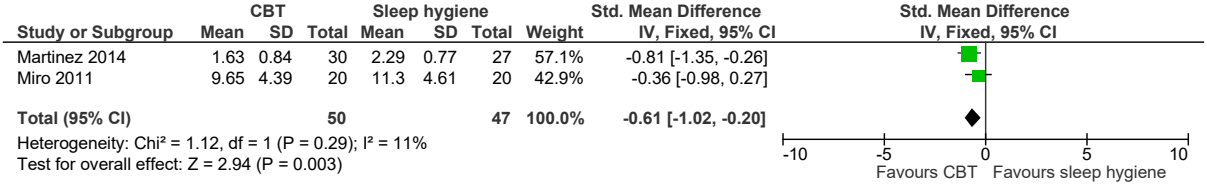


Figure 160: Psychological distress (Symptom Checklist-90-Revised - anxiety sub scale; Hospital Anxiety and Depression Scale - anxiety) final values ≤3 months

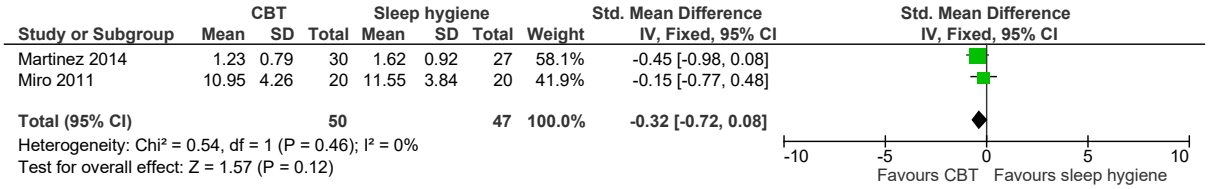


Figure 161: Pain self-efficacy (Chronic Pain Self-efficacy Scale) final values ≤3 months

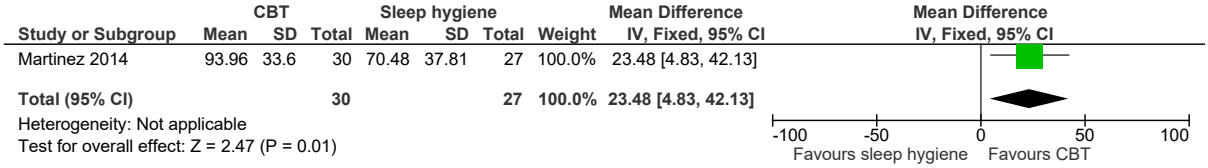
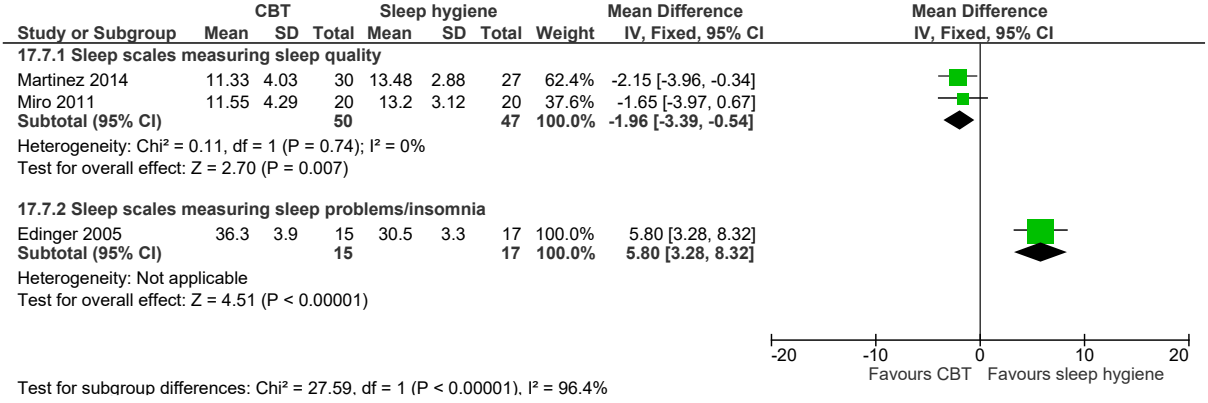


Figure 162: Sleep (Insomnia Symptom Questionnaire; Pittsburgh Sleep Quality Index) final values ≤3 months



Source/Note: *Sensitivity analysis splitting sleep scales measuring sleep quality and sleep scales measuring sleep problems/insomnia explained the heterogeneity and is presented here.*

Figure 163: Sleep (total sleep time, hours) final values ≤3 months

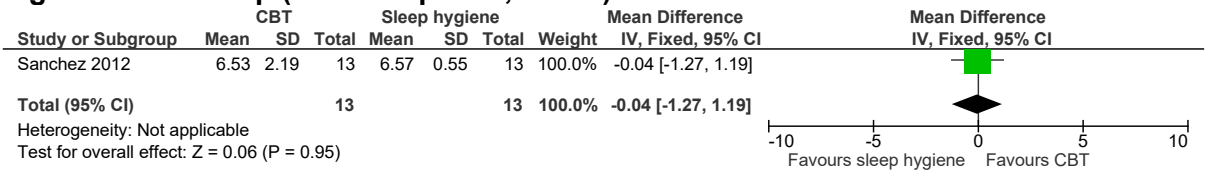


Figure 164: Sleep (Insomnia Symptom Questionnaire) final values >3 months

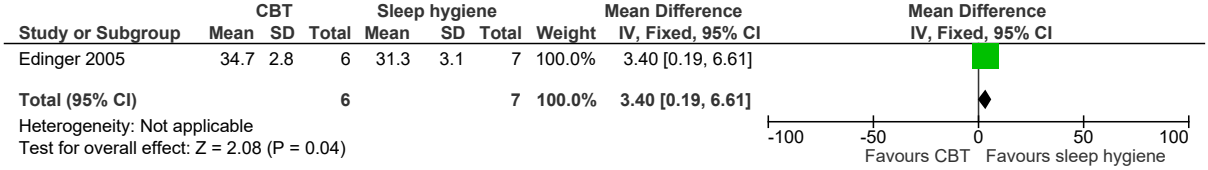


Figure 165: Discontinuation

Study or Subgroup	CBT Events	CBT Total	Sleep hygiene Events	Sleep hygiene Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Edinger 2005	3	18	1	18	39.2%	2.99 [0.38, 23.19]
Martinez 2014	2	32	3	32	50.1%	0.65 [0.11, 3.99]
Miro 2011	1	22	0	22	10.7%	7.39 [0.15, 372.38]
Total (95% CI)		**72**		**72**	**100.0%**	**1.53 [0.43, 5.53]**
Total events	6		4			

Heterogeneity: Chi² = 1.88, df = 2 (P = 0.39); I² = 0%
Test for overall effect: Z = 0.65 (P = 0.51)

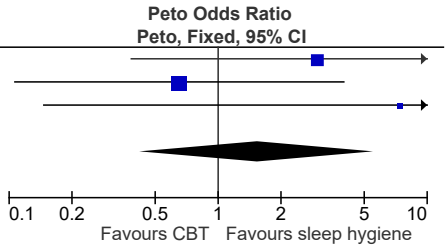


Figure 166: Pain (McGill VAS) final values ≤3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Sleep hygiene Mean	Sleep hygiene SD	Sleep hygiene Total	Weight	Mean Difference IV, Fixed, 95% CI
Martinez 2014	6.72	2.08	30	8.23	1.34	27	66.2%	-1.51 [-2.41, -0.61]
Miro 2011	6.5	2.46	20	8.26	1.48	20	33.8%	-1.76 [-3.02, -0.50]
Total (95% CI)			**50**			**47**	**100.0%**	**-1.59 [-2.33, -0.86]**

Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%
Test for overall effect: Z = 4.27 (P < 0.0001)

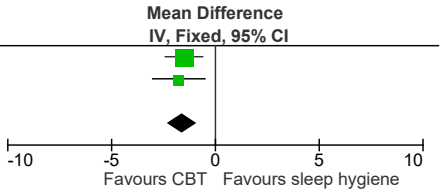


Figure 167: Pain (McGill Pain Questionnaire) final values ≤3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Sleep hygiene Mean	Sleep hygiene SD	Sleep hygiene Total	Weight	Mean Difference IV, Fixed, 95% CI
Edinger 2005	27.6	3.8	15	23.7	4.4	17	100.0%	3.90 [1.06, 6.74]
Total (95% CI)			**15**			**17**	**100.0%**	**3.90 [1.06, 6.74]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.69 (P = 0.007)

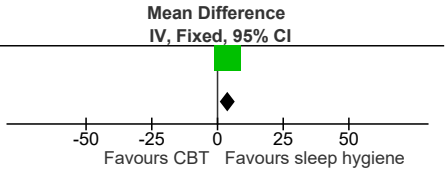
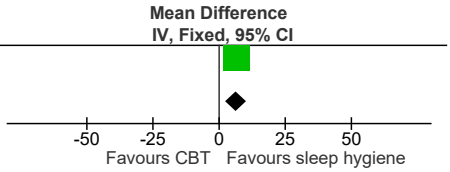


Figure 168: Pain (McGill Pain Questionnaire) final values >3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Sleep hygiene Mean	Sleep hygiene SD	Sleep hygiene Total	Weight	Mean Difference IV, Fixed, 95% CI
Edinger 2005	28.8	3.6	6	22.4	3.9	7	100.0%	6.40 [2.32, 10.48]
Total (95% CI)			**6**			**7**	**100.0%**	**6.40 [2.32, 10.48]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.07 (P = 0.002)



E.14 CBT versus Pain education

Figure 169: Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months

Study or Subgroup	CBT Mean	CBT SD	CBT Total	Pain education Mean	Pain education SD	Pain education Total	Weight	Mean Difference IV, Fixed, 95% CI
Soares 2002	2.25	0.73	18	2.66	0.73	18	100.0%	-0.41 [-0.89, 0.07]
Total (95% CI)			**18**			**18**	**100.0%**	**-0.41 [-0.89, 0.07]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.68 (P = 0.09)

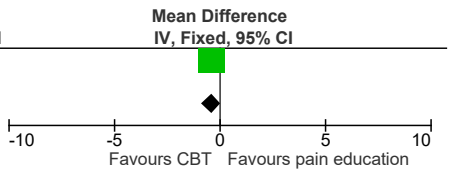


Figure 170: Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months

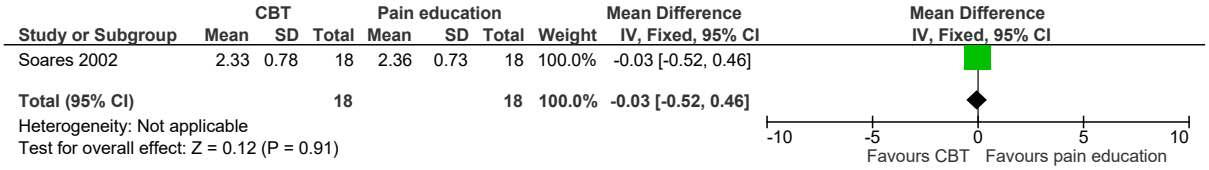


Figure 171: Quality of life (Satisfaction with life scale) final values ≤3 months

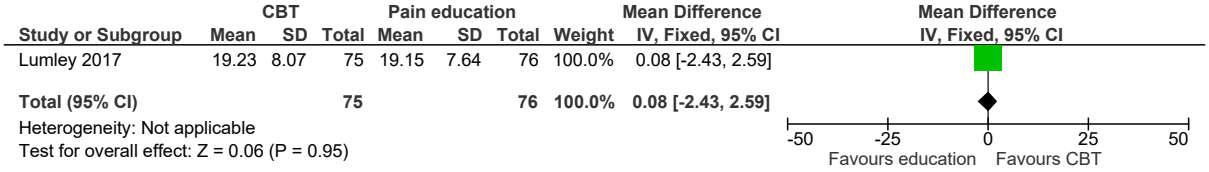


Figure 172: Quality of life (Satisfaction with life scale) final values >3 months

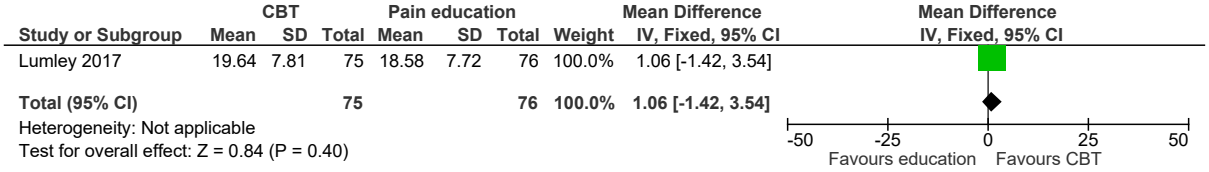


Figure 173: Physical function (SF12 physical function sub scale) final values ≤3 months

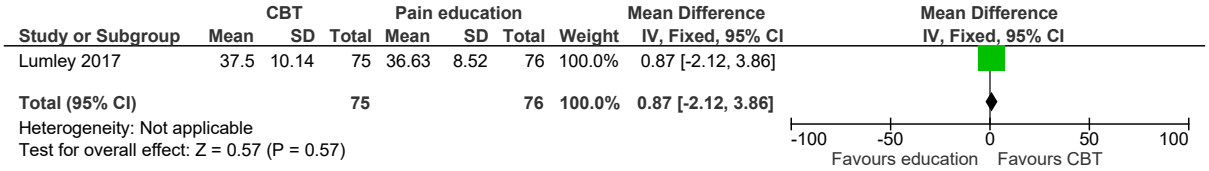


Figure 174: Physical function (SF12 physical function sub scale) final values >3 months

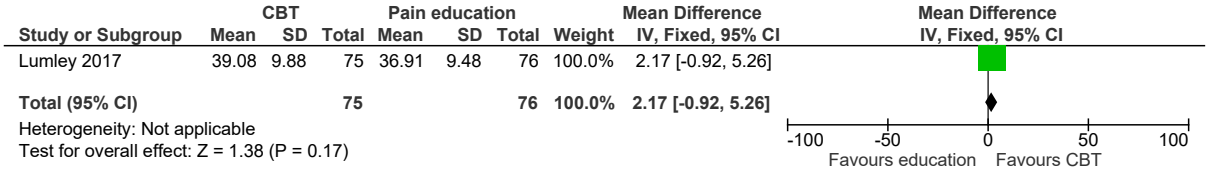


Figure 175: Psychological distress (Beck depression Inventory) change scores ≤3 months

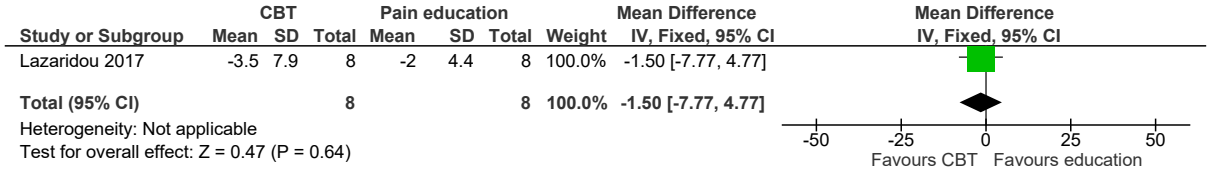


Figure 176: Psychological distress (Center for Epidemiologic Studies - depression) final values ≤3 months

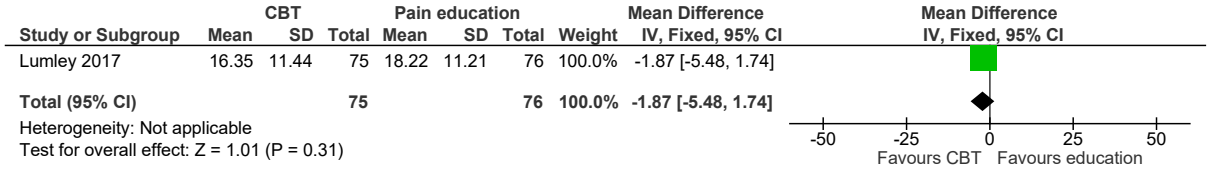


Figure 177: Psychological distress (Center for Epidemiologic Studies - depression) final values >3 months

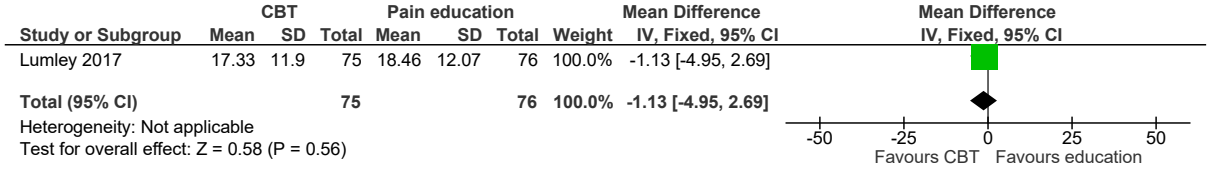


Figure 178: Psychological distress (Generalised anxiety disorder-7) final values ≤3 months

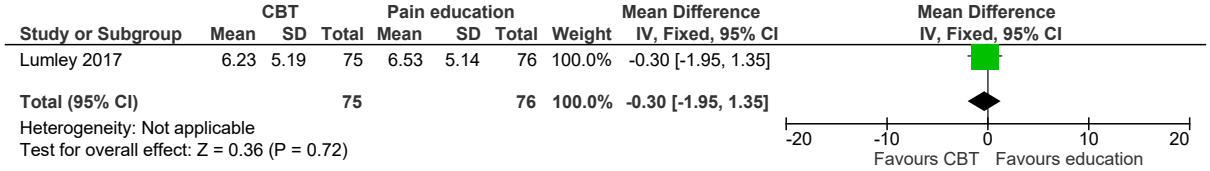


Figure 179: Psychological distress (Generalised anxiety disorder-7) final values >3 months

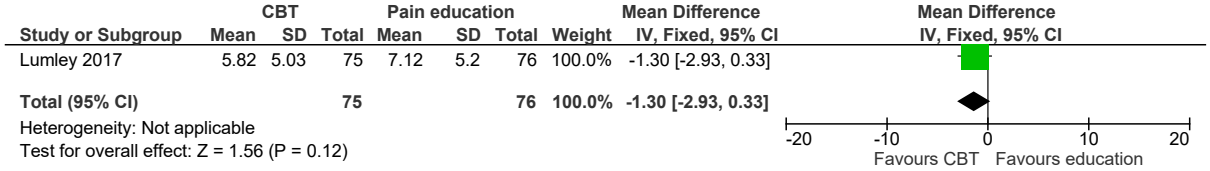


Figure 180: Pain interference (Brief Pain Inventory - interference) change scores ≤3 months

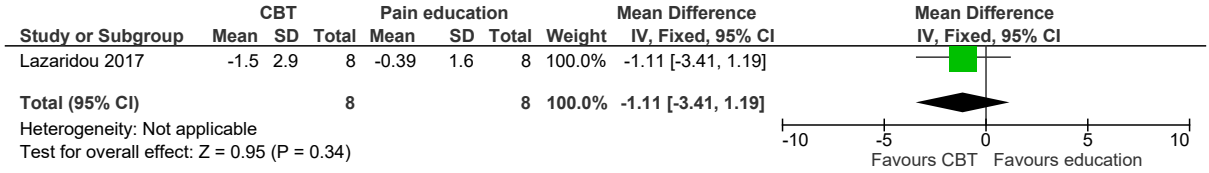


Figure 181: Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months

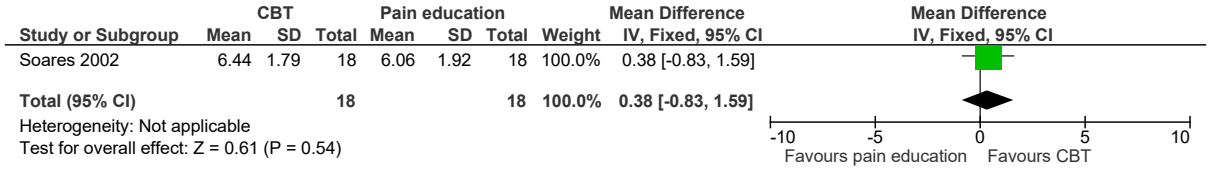


Figure 182: Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values >3 months

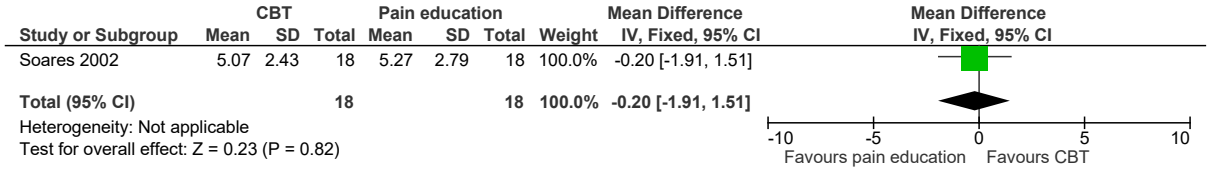
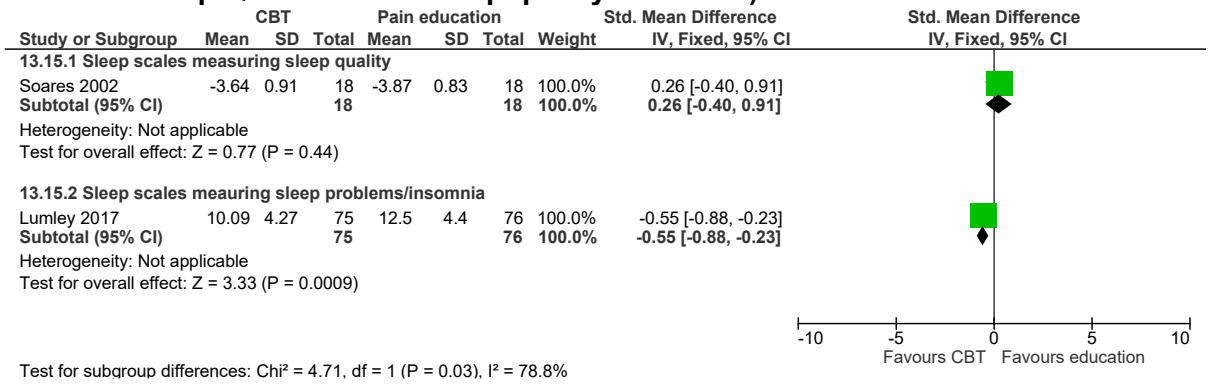
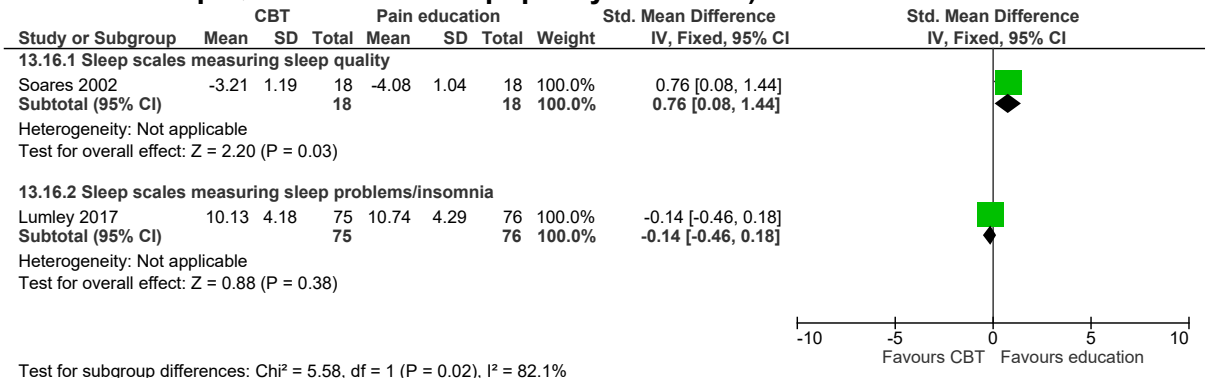


Figure 183: Sleep (Pittsburgh Sleep Quality Index - sleep problems; Karolinska Sleep Questionnaire sleep quality sub scale) final values ≤3 months



Source/Note: *Heterogeneity was observed in other comparisons when sleep quality and sleep problem/insomnia scales were combined, so they have been separated here for consistency.*

Figure 184: Sleep (Pittsburgh Sleep Quality Index - sleep problems; Karolinska Sleep Questionnaire sleep quality sub scale) final values >3 months



Source/Note: Heterogeneity was observed in other comparisons when sleep quality and sleep problem/insomnia scales were combined, so they have been separated here for consistency.

Figure 185: Use of healthcare services (physician/other health professional visits in past 3 months) final values ≤3 months

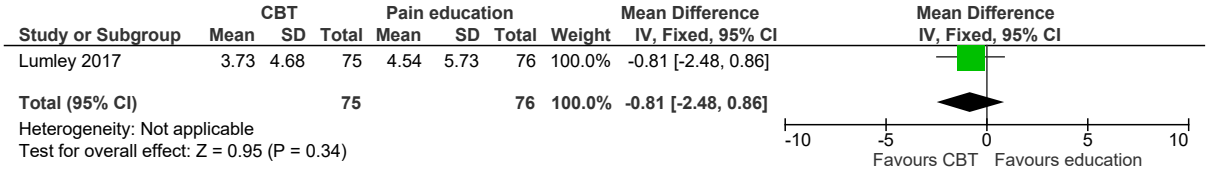


Figure 186: Use of healthcare services (physician/other health professional visits in past 3 months) final values >3 months

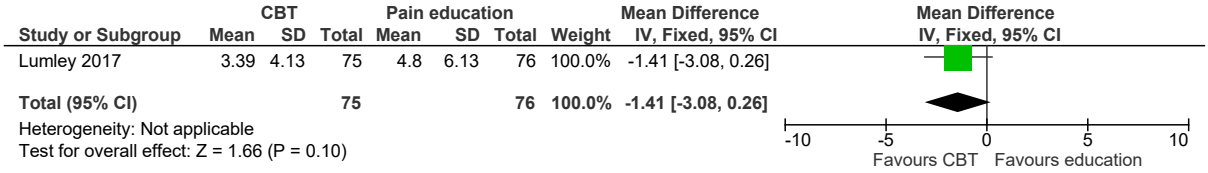


Figure 187: Discontinuation

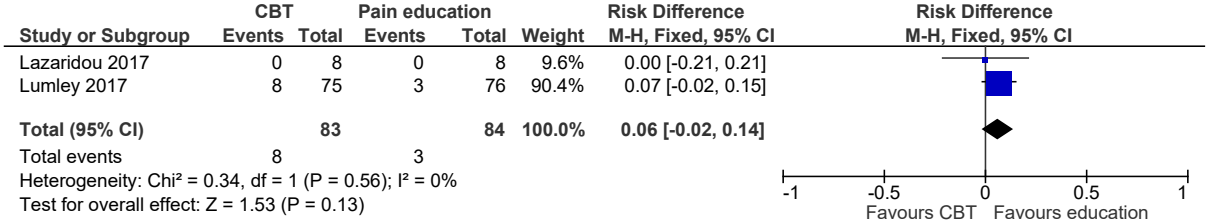


Figure 188: Pain (VAS/NRS) final values/change scores ≤3 months

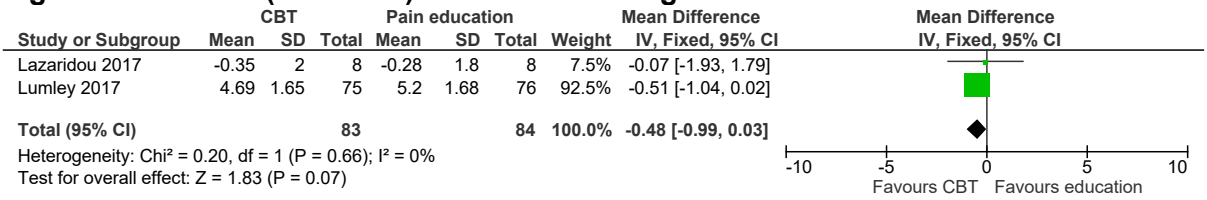


Figure 189: Pain (VAS/NRS) final values >3 months

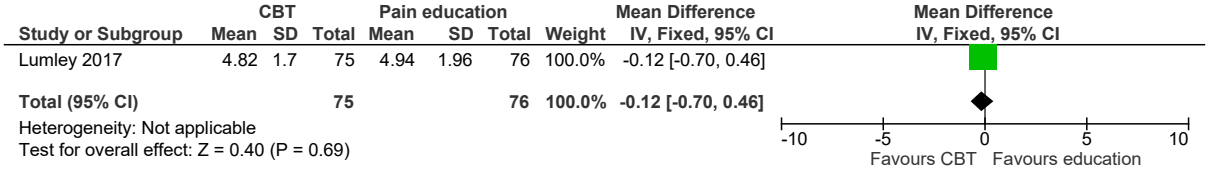


Figure 190: Pain (McGill Pain Questionnaire) final values ≤3 months

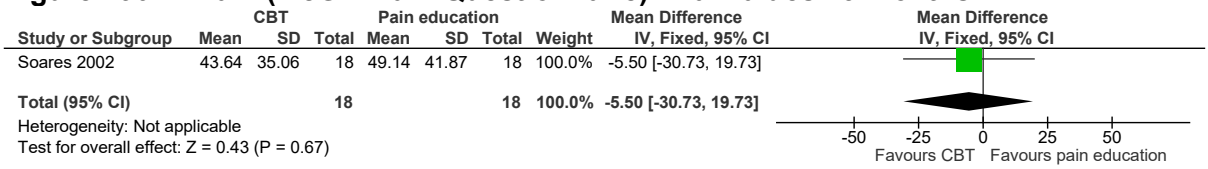
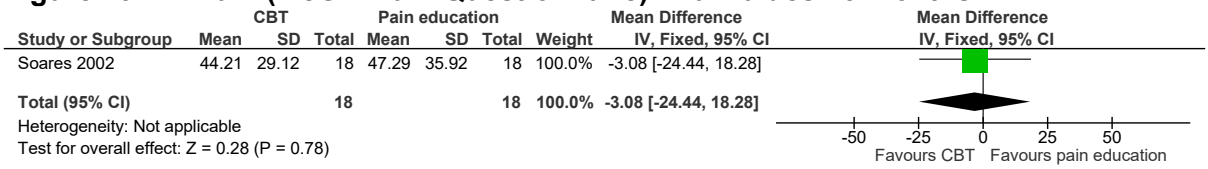


Figure 191: Pain (McGill Pain Questionnaire) final values >3 months



E.15 CBT versus Biofeedback

Figure 192: Discontinuation

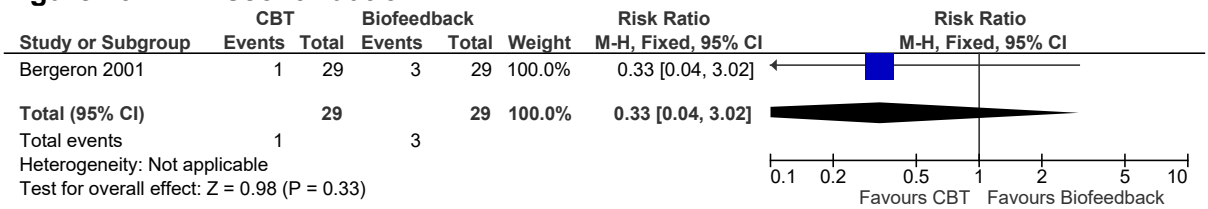


Figure 193: Pain (NRS) final values ≤3 months

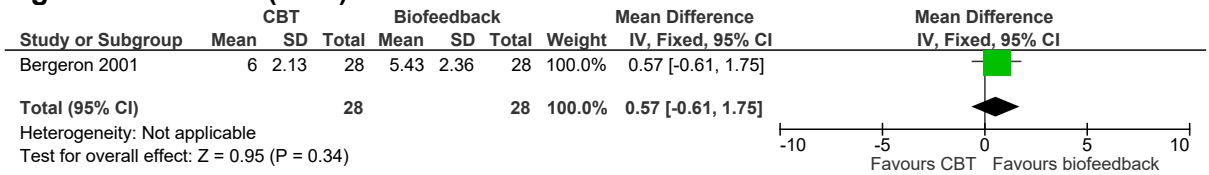
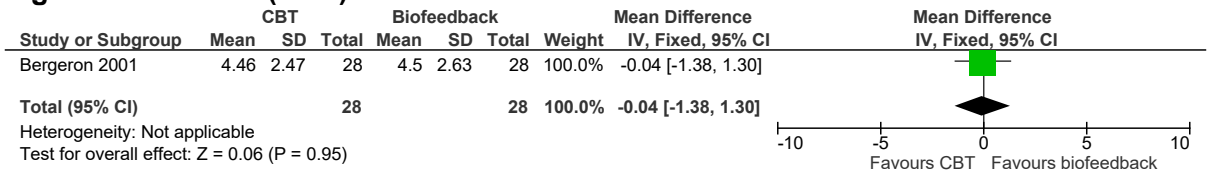


Figure 194: Pain (NRS) final values >3 months



E.16 CBT versus Psychotherapy

Figure 195: Psychological distress (Beck depression Inventory) final values ≤3 months

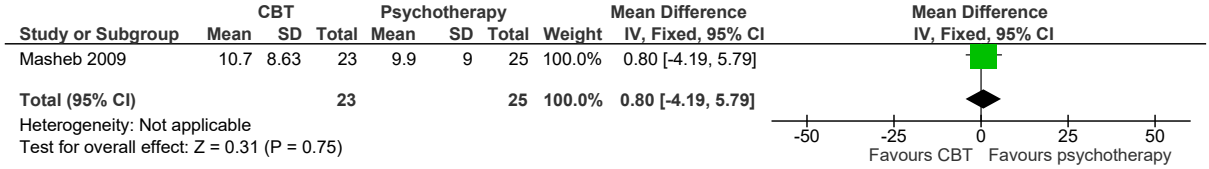


Figure 196: Psychological distress (Beck depression Inventory) final values >3 months

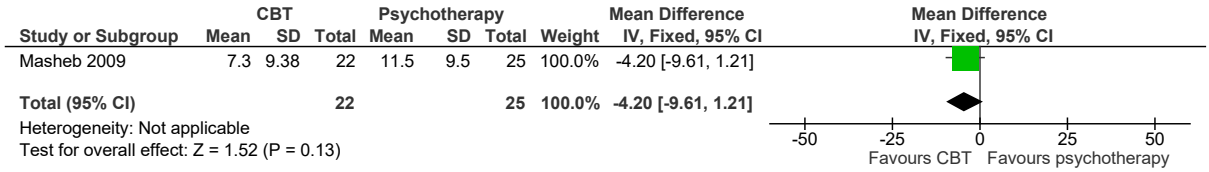


Figure 197: Psychological distress (Pain Anxiety Symptoms Scale) final values ≤3 months

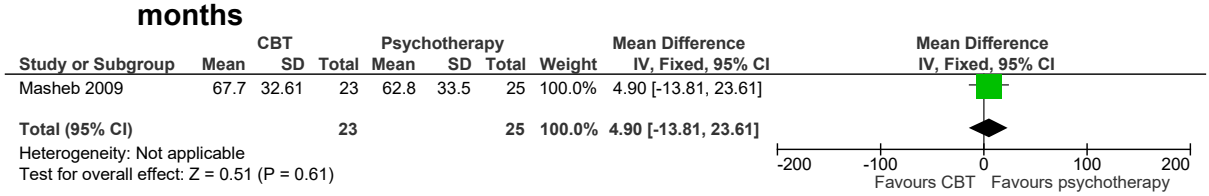


Figure 198: Psychological distress (Pain Anxiety Symptoms Scale) final values >3 months

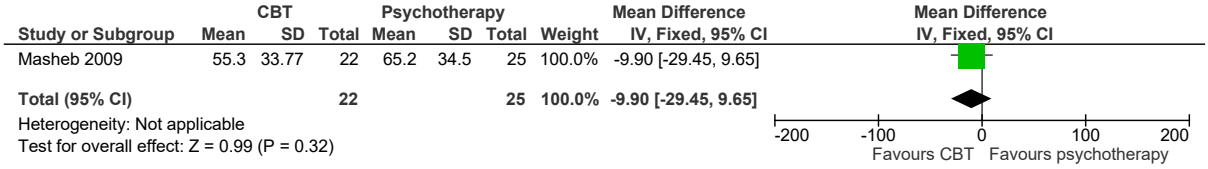


Figure 199: Discontinuation

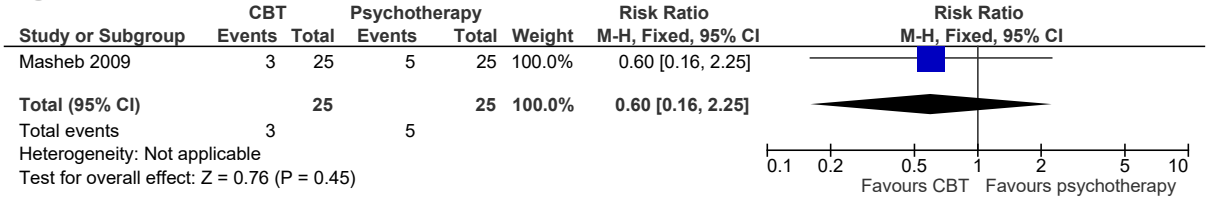


Figure 200: Pain (McGill Pain Questionnaire) final values ≤3 months

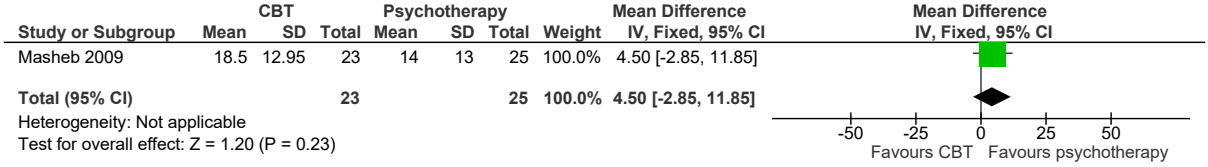
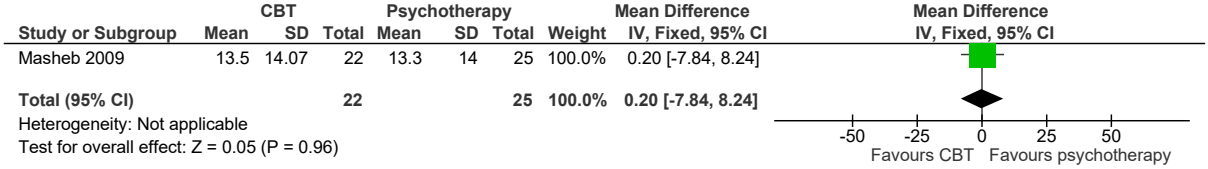


Figure 201: Pain (McGill Pain Questionnaire) final values >3 months



E.17 CBT versus Behaviour therapy

Figure 202: Physical function (Fibromyalgia Impact Questionnaire physical function sub scale) final values >3 months

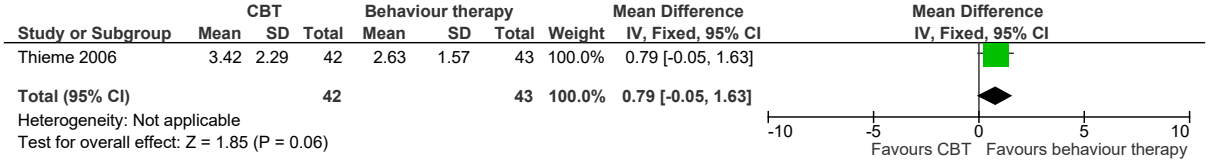


Figure 203: Use of healthcare services (Physician visits) >3 months

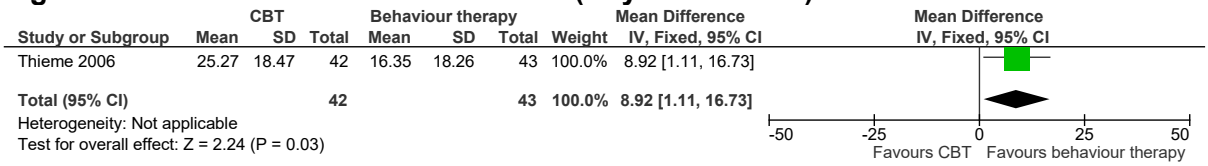


Figure 204: Discontinuation

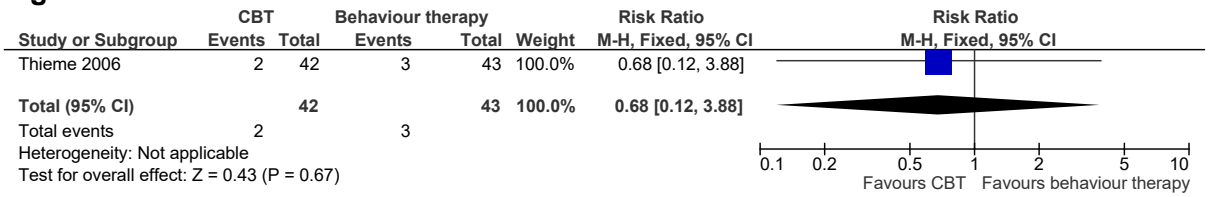
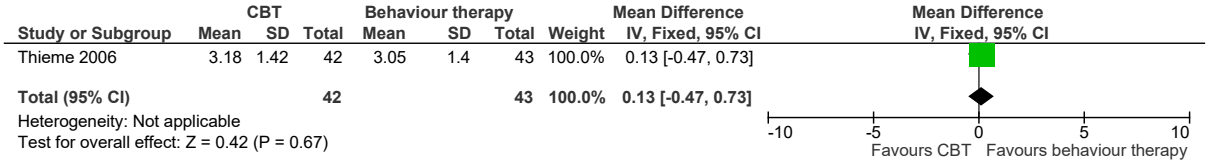
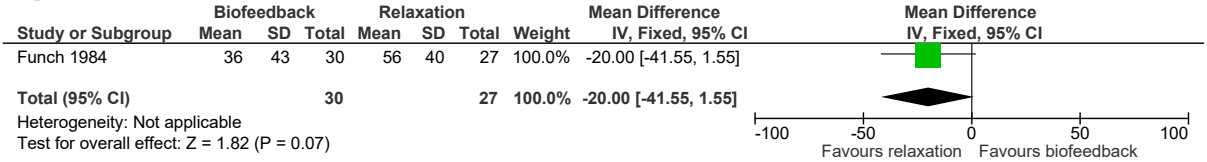


Figure 205: Pain (West Haven-Yale Multidimensional Pain Inventory – pain intensity) final values >3 months



E.18 Biofeedback versus Relaxation

Figure 206: Pain (% reduction in pain from baseline) ≤3 months



E.19 ACT versus Relaxation

Figure 207: Quality of life (SF12 mental component) final values ≤3 months

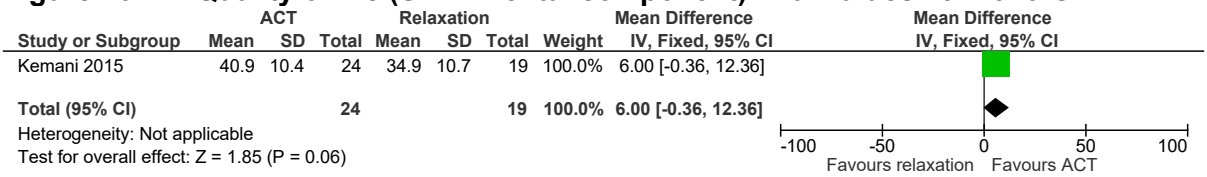


Figure 208: Quality of life (SF12 mental component) >3 months

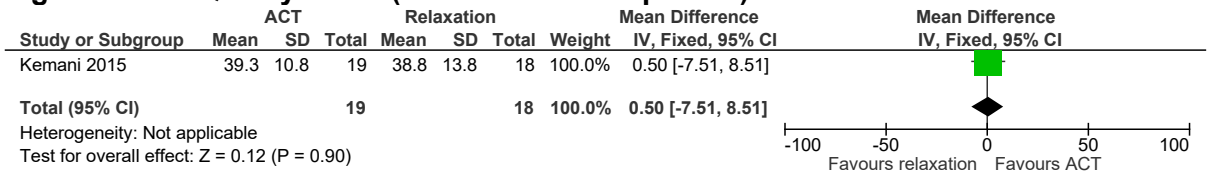


Figure 209: Quality of life (SF12 physical component) final values ≤3 months

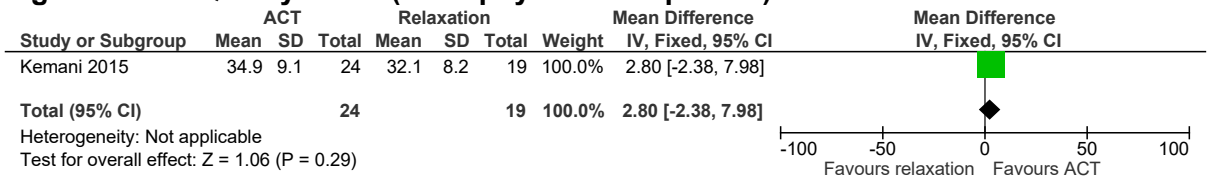


Figure 210: Quality of life (SF12 physical component) final values >3 months

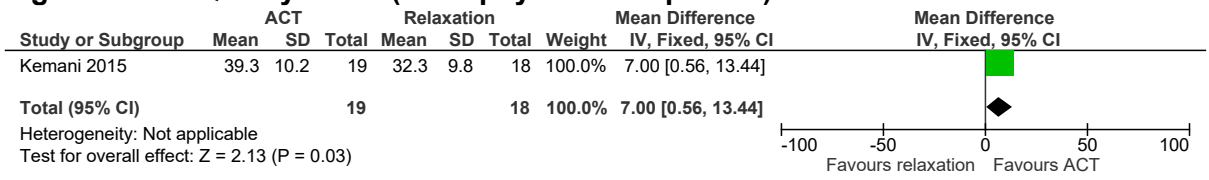


Figure 211: Pain interference (Pain disability index) final values ≤3 months

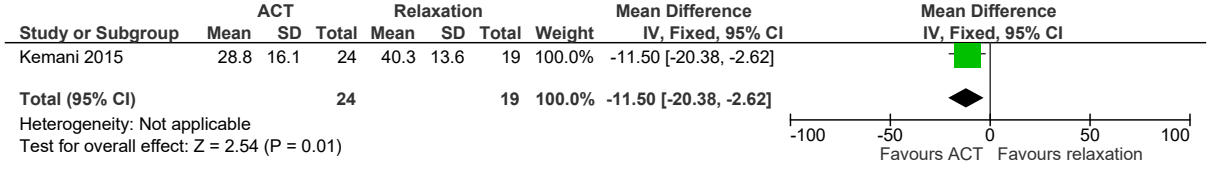


Figure 212: Pain interference (Pain disability index) final values >3 months

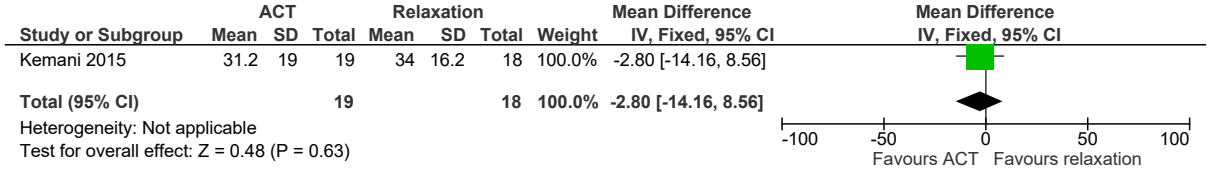


Figure 213: Psychological distress (Hospital Anxiety and Depression Scale depression) final values ≤3 months

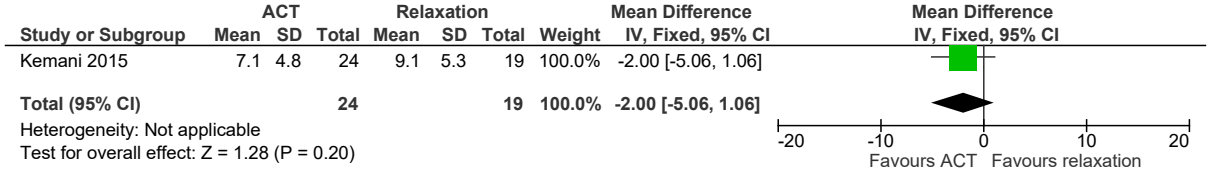


Figure 214: Psychological distress (Hospital Anxiety and Depression Scale depression) final values >3 months

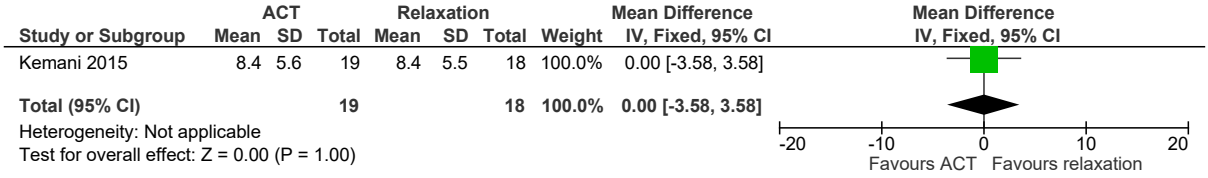


Figure 215: Psychological distress (Hospital Anxiety and Depression Scale anxiety) final values ≤3 months

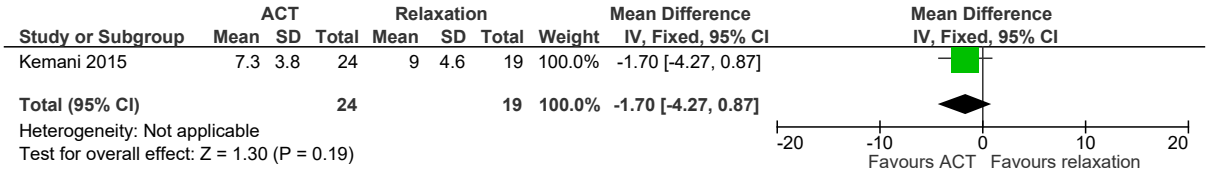


Figure 216: Psychological distress (Hospital Anxiety and Depression Scale anxiety) final values >3 months

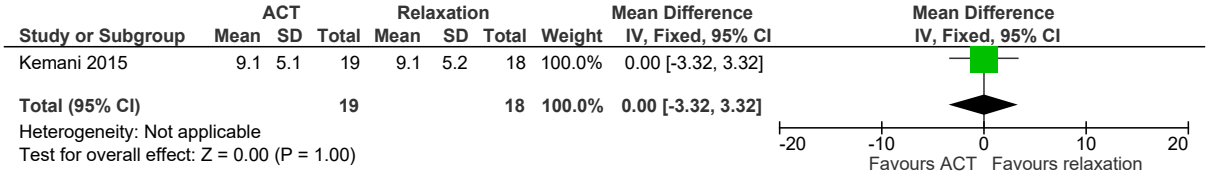


Figure 217: Discontinuation

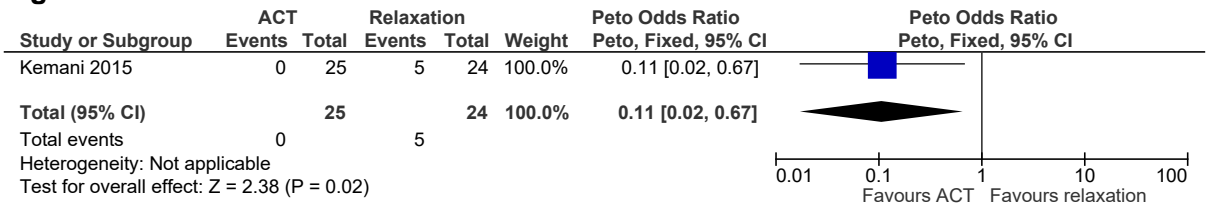


Figure 218: Pain (NRS 0-6) final values ≤3 months

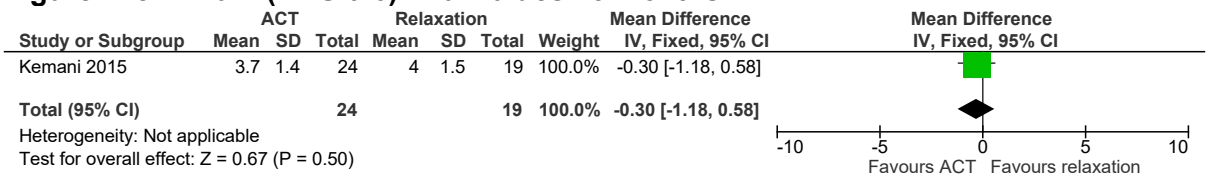
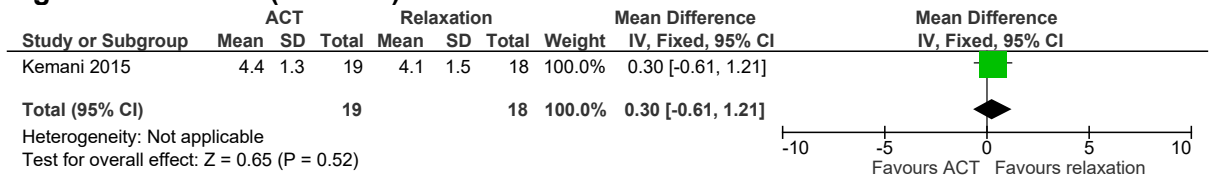


Figure 219: Pain (NRS 0-6) final values >3 months



Appendix F: GRADE tables

Table 31: Clinical evidence profile: CBT versus Usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT versus Usual care		Relative (95% CI)	Absolute		
Quality of life (EQ-5D) final values ≤3 months (follow-up 10 weeks; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	70	70	-	MD 0.16 higher (0.06 to 0.26 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (EQ-5D) final values >3 months (follow-up 6-9 months; range of scores: 0-1; Better indicated by higher values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	124	132	-	MD 0.1 higher (0.03 to 0.16 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (EuroQoL VAS) final values ≤3 months (follow-up 9 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[4]	serious[3]	none	57	56	-	MD 6.96 higher (1.23 to 12.69 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months - CBT for pain (follow-up 9-10 weeks; range of scores: 0-100; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	46	53	-	MD 2.43 lower (6.17 lower to 1.31 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months - CBT for pain + insomnia (follow-up 9 weeks; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	27	36	-	MD 0.37 higher (7.38 lower to 8.12 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months - CBT for pain (follow-up 5 months; range of scores: 0-100; Better indicated by lower values)												

2	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	40	33	-	MD 0.91 lower (8.74 lower to 6.92 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months - CBT for pain + insomnia (follow-up 5-9 months; range of scores: 0-100; Better indicated by lower values)												
2	randomised trials	very serious[1]	very serious[6]	serious[2]	very serious[3]	none	56	56	-	MD 7.78 lower (28.65 lower to 13.08 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36 mental composite) final values ≤3 months (follow-up 6 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	6	7	-	MD 5.2 higher (1.82 to 8.58 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36 mental composite) final values >3 months - CBT for pain + insomnia (follow-up 8 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15	9	-	MD 11.3 higher (9.05 to 13.55 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Functional capacity (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	48	45	-	MD 3.8 higher (4.15 lower to 11.75 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Physical limitations (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	48	45	-	MD 8.9 higher (0.95 to 16.85 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - General health (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	48	45	-	MD 9.1 higher (0.96 to 17.24 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Pain (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	48	45	-	MD 0.7 higher (6.26 lower to 7.66 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Vitality (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	48	45	-	MD 6.8 higher (1 lower to 14.6 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Social aspects (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	48	45	-	MD 5.3 higher (3.04 lower to 13.64 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Emotional limitations (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	48	45	-	MD 11.1 higher (0.97 lower to 23.17 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Mental health (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	48	45	-	MD 5 higher (3.29 lower to 13.29 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF12 physical component) final values ≤3 months (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 1.88 higher (2.2 lower to 5.96 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF12 mental component) final values ≤3 months (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 0.67 higher (4.51 lower to 5.85 higher)	⊕⊕OO LOW	CRITICAL
Physical function (WHO Disability Assessment Schedule) final values ≤3 months (follow-up 10 weeks; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	70	70	-	MD 16.19 lower (22.1 to 10.28 lower)	⊕⊕OO LOW	CRITICAL
Physical function (Fibromyalgia Impact Questionnaire physical impairment sub scale) final values ≤3 months (follow-up 8 weeks; range of scores: 0-27; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	112	50	-	MD 2.69 lower (4.6 to 0.78 lower)	⊕OOO VERY LOW	CRITICAL
Physical function (FIQ physical function sub scale) change scores ≤3 months (follow-up 6 weeks; range of scores: 0-10; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	15	13	-	MD 0.5 lower (1.95 lower to 0.95 higher)	⊕OOO VERY LOW	CRITICAL
Physical function (SF36 physical function sub scale) final values >3 months (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	59	59	-	MD 2.2 higher (0.92 lower to 5.32 higher)	⊕OOO VERY LOW	CRITICAL
Physical function (FIQ physical function sub scale) change scores >3 months (follow-up 3 months; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	15	13	-	MD 1.1 lower (2.43 lower to 0.23 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hamilton Rating Scale for Depression; Hospital Anxiety and Depression Scale depression; Patient Health Questionnaire-9; Symptoms Checklist 90-R depression; Beck depression inventory) final values ≤3 months - CBT for pain (follow-up 8-10 weeks; Better indicated by lower values)												
6	randomised trials	serious[1]	very serious[5]	serious[2]	serious[3]	none	327	270	-	SMD 0.35 lower (0.74 lower to 0.05 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Symptoms Checklist 90-R depression; Beck Depression Inventory) final values ≤3 months - CBT for pain + insomnia (follow-up 8-9 weeks; Better indicated by lower values)												
2	randomised trials	very serious[1]	very serious[5]	serious[2]	very serious[3]	none	54	64	-	SMD 0.19 lower (1.28 lower to 0.89 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hamilton Rating Scale for Depression; Symptoms Checklist 90-R depression; Hospital Anxiety and Depression Scale depression; Center for Epidemiological Studies Depression Scale; Beck depression Inventory) final values >3 months - CBT for pain (follow-up 5-12 months; Better indicated by lower values)												
5	randomised trials	very serious[1]	serious[5]	serious[2]	no serious imprecision	none	198	196	-	SMD 0.05 lower (0.39 lower to 0.29 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Symptoms Checklist 90-R depression; Beck Depression Inventory) final values >3 months - CBT for pain + insomnia (follow-up 5-6 months; Better indicated by lower values)												
2	randomised trials	serious[1]	very serious[5]	serious[2]	very serious[3]	none	46	49	-	SMD 0.02 higher (1.13 lower to 1.17 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Patient Health Questionnaire 8-item depression) change scores >3 months (follow-up 3 months; range of scores: 0-24; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	15	13	-	MD 0.9 lower (4.35 lower to 2.55 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hamilton Anxiety Rating Scale; Hospital Anxiety and Depression Scale anxiety; Symptoms checklist 90-R anxiety; State-Trait Anxiety Inventory) final values ≤3 months - CBT for pain (follow-up 8-9 weeks; Better indicated by lower values)												
5	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	257	200	-	SMD 0.10 lower (0.29 lower to 0.09 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Symptoms checklist 90-R anxiety; State-Trait Anxiety Inventory) final values ≤3 months - CBT for pain + insomnia (follow-up 8-9 weeks; Better indicated by lower values)												
2	randomised trials	very serious[1]	very serious[5]	serious[2]	very serious[3]	none	54	64	-	SMD 0.17 lower (1.15 lower to 0.8 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hamilton Anxiety Rating Scale; Symptoms Checklist 90-R anxiety; Hospital Anxiety and Depression Scale anxiety; State-Trait Personality Inventory anxiety) final values >3 months - CBT for pain (follow-up 5-12 months; Better indicated by lower values)												
5	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	198	196	-	SMD 0.01 lower (0.2 lower to 0.19 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Symptoms Checklist 90-R anxiety; State-Trait Personality Inventory anxiety) final values >3 months - CBT for pain + insomnia (follow-up 5-6 months; Better indicated by lower values)												
2	randomised trials	serious[1]	very serious[5]	serious[2]	very serious[3]	none	46	49	-	SMD 0.05 higher (0.86 lower to 0.97 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Multiple Pain Inventory-affective distress) final values >3 months (follow-up 6 months; range of scores: 0-6; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	23	24	-	MD 0.02 higher (0.34 lower to 0.38 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Brief Pain inventory - pain interference) final values ≤3 months (follow-up 8 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	30	-	MD 1.86 lower (2.8 to 0.92 lower)	⊕⊕⊕O MODERATE	CRITICAL
Pain interference (Pain disability index) final values ≤3 months - CBT for pain (follow-up 8 weeks; range of scores: 0-70; Better indicated by lower values)												

1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	30	28	-	MD 2.35 higher (6.09 lower to 10.79 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Pain disability index) final values ≤3 months - CBT for insomnia (follow-up 8 weeks; range of scores: 0-70; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	27	28	-	MD 7.83 lower (16.72 lower to 1.06 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Pain disability index) final values >3 months -CBT for pain (follow-up 6 months; range of scores: 0-70; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	27	23	-	MD 1.5 higher (8.33 lower to 11.33 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Pain disability index) final values >3 months -CBT for insomnia (follow-up 6 months; range of scores: 0-70; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	24	23	-	MD 7.11 lower (17.42 lower to 3.2 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Multiple Pain Inventory - pain interference) final values >3 months (follow-up 6 months; range of scores: 0-6; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	23	24	-	MD 0.62 higher (0.14 to 1.1 higher)	⊕OOO VERY LOW	CRITICAL
Pain self-efficacy (Pain Self-efficacy Questionnaire; Chronic Pain Self-efficacy Scale; Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months - CBT for pain (follow-up 8-10 weeks; Better indicated by higher values)												
3	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	76	84	-	SMD 0.48 higher (0.16 to 0.8 higher)	⊕OOO VERY LOW	CRITICAL
Pain self-efficacy (Pain Self-efficacy Questionnaire; Chronic Pain Self-efficacy Scale) final values ≤3 months - CBT for pain + insomnia (follow-up 9 weeks; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	27	36	-	SMD 0.19 higher (0.31 lower to 0.69 higher)	⊕OOO VERY LOW	CRITICAL
Pain self-efficacy (Chronic Pain Self-efficacy scale) final values >3 months - CBT for pain (follow-up 5 months; Better indicated by higher values)												

1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	24	26	-	MD 3.43 lower (25.7 lower to 18.84 higher)	⊕OOO VERY LOW	CRITICAL
Pain self-efficacy (Chronic Pain Self-efficacy scale) final values >3 months - CBT for pain + insomnia (follow-up 5 months; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	22	26	-	MD 8.62 higher (13.06 lower to 30.3 higher)	⊕OOO VERY LOW	CRITICAL
Sleep (Pittsburgh Sleep Quality Index; Karolinska Sleep Questionnaire sleep quality sub scale; self-reported sleep quality rating) final values ≤3 months - CBT for pain (follow-up 9-10 weeks; Better indicated by lower values)												
3	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision[3]	none	76	81	-	SMD 0.03 higher (0.29 lower to 0.34 higher)	⊕⊕OO LOW	IMPORTANT
Sleep (Insomnia Severity Index) final values ≤3 months - CBT for pain (follow-up 10 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	70	70	-	SMD 0.44 lower (0.77 to 0.10 lower)	⊕⊕OO LOW	IMPORTANT
Sleep (Pittsburgh Sleep Quality Index; self-reported sleep quality rating) final values ≤3 months - CBT for pain + insomnia (follow-up 6-9 weeks; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	54	64	-	SMD 0.08 lower (0.44 lower to 0.28 higher)	⊕OOO VERY LOW	IMPORTANT
Sleep (Insomnia Severity Index) final values ≤3 months - CBT for pain + insomnia (follow-up 6-9 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15	9	-	SMD 3.8 lower (5.24 to 2.36 lower)	⊕⊕OO LOW	IMPORTANT
Sleep (Pittsburgh Sleep Quality Index; Sleep Scale; self-reported sleep quality rating) final values >3 months - CBT for pain (follow-up 5-9 months; Better indicated by lower values)												
3	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	142	147	-	SMD 0.04 lower (0.27 lower to 0.2 higher)	⊕OOO VERY LOW	IMPORTANT
Sleep (Medical Outcomes Study Sleep Problems Index (scale inverted for analysis)) final values >3 months - CBT for pain (follow-up 5-9 months; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	59	59	-	SMD 0.26 higher (0.11 lower 0.62 higher)	⊕OOO VERY LOW	IMPORTANT

Sleep (Pittsburgh Sleep Quality Index; self-reported sleep quality rating) final values >3 months - CBT for pain + insomnia (follow-up 5-6 months; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	46	49	-	SMD 0.11 higher (0.3 lower to 0.51 higher)	⊕OOO VERY LOW	IMPORTANT
Sleep (Medical Outcomes Study Sleep Problems Index (scale inverted for analysis); Insomnia Symptom Questionnaire) final values >3 months - CBT for pain + insomnia (follow-up 6 months; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	40	37	-	SMD 6.37 lower (7.56 to 5.18 lower)	⊕OOO VERY LOW	IMPORTANT
Use of healthcare services (GP visits for non-cardiac chest pain) >3 months (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	2/31 (6.5%)	12.5%	RR 0.52 (0.1 to 2.62)	60 fewer per 1000 (from 112 fewer to 202 more)	⊕OOO VERY LOW	IMPORTANT
Use of healthcare services (referral to a specialist for non-cardiac chest pain) >3 months (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	1/31 (3.2%)	3.1%	RR 1.03 (0.07 to 15.79)	1 more per 1000 (from 29 fewer to 458 more)	⊕OOO VERY LOW	IMPORTANT
Use of healthcare services (use of additional psychological services) >3 months (follow-up 12 months)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	0/31 (0%)	18.8%	OR 0.12 (0.02 to 0.62)	161 fewer per 1000 (from 62 fewer to 183 fewer)	⊕OOO VERY LOW	IMPORTANT
Discontinuation - CBT for pain (follow-up 2-6 months)												
13	randomised trials	serious[1]	serious[6]	very serious[2,7]	no serious imprecision	none	96/667 (14.4%)	5.4%	OR 1.99 (1.36 to 2.89)	48 more per 1000 (from 18 more to 88 more)	⊕OOO VERY LOW	IMPORTANT
Discontinuation - CBT for pain + insomnia (follow-up 6-14 weeks)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	10/94 (10.6%)	3.3%	OR 2.06 (0.68 to 6.21)	33 more per 1000 (from 10 fewer to 142 more)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain (follow-up 6-10 weeks; range of scores: 0-10; Better indicated by lower values)												

8	randomised trials	very serious[1]	very serious[5]	serious[2]	no serious imprecision	none	376	307	-	MD 0.57 lower (1.14 lower to 0 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain + insomnia (follow-up 9 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	27	36	-	MD 0.11 lower (0.8 lower to 0.58 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS) final values and change scores >3 months - CBT for pain (follow-up 3-6 months; range of scores: 0-10; Better indicated by lower values)												
4	randomised trials	very serious[1]	no serious inconsistency	serious[4]	no serious imprecision	none	155	154	-	MD 0.39 lower (0.67 to 0.11 lower)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS) final values and change scores >3 months - CBT for pain + insomnia (follow-up 5-6 months; range of scores: 0-10; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	56	56	-	MD 1.07 lower (1.27 to 0.88 lower)	⊕OOO VERY LOW	IMPORTANT
Pain (30% reduction in pain from baseline) ≤3 months (follow-up 3 months)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	25/38 (65.8%)	5.3%	RR 12.5 (3.18 to 49.11)	610 more per 1000 (from 116 more to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Pain (30% reduction in pain from baseline) >3 months (follow-up 9 months)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	24/38 (63.2%)	2.6%	RR 24 (3.42 to 168.55)	598 more per 1000 (from 63 more to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values ≤3 months - CBT for pain (follow-up 8-10 weeks; range of scores: 0-78; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	48	45	-	MD 1.81 lower (8.82 lower to 5.21 higher)	⊕⊕OO LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values ≤3 months - CBT for insomnia (follow-up 6-8 weeks; range of scores: 0-78; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	42	37	-	MD 6.31 lower (9.35 to 3.28 lower)	⊕OOO VERY LOW	IMPORTANT
Pain (Multiple Pain Inventory - pain severity) final values >3 months - CBT for pain (follow-up 6 months; range of scores: 0-6; Better indicated by lower values)												

1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	23	24	-	MD 0.21 higher (0.31 lower to 0.73 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill pain questionnaire) final values >3 months - CBT for pain (follow-up 6 months; range of scores: 0-78; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	27	23	-	MD 5.69 higher (2.97 lower to 14.35 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values >3 months - CBT for pain + insomnia (follow-up 6 months; range of scores: 0-78; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	31	30	-	MD 4.22 lower (8.26 to 0.17 lower)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[4] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect comparisons
[5] Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis
[6] Downgraded by 1 or 2 increments because the point estimate varies widely across studies, unexplained by subgroup analysis
[7] Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes

Table 32: Clinical evidence profile: ACT versus Usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**ACT versus Usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life (SF36 physical component) final values ≤3 months (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	20	16	-	MD 1.7 lower (7.69 lower to 4.29 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36 physical component) final values >3 months (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	14	-	MD 2.7 lower (9.5 lower to 4.1 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36 mental component) final values ≤3 months (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	20	16	-	MD 8.8 higher (1.42 to 16.18 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36 mental component) final values >3 months (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	19	14	-	MD 11.3 higher (3.64 to 18.96 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (EQ-5D VAS) final values ≤3 months (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[3]	no serious imprecision	none	51	53	-	MD 15.2 higher (11.47 to 18.93 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (EQ-5D) final values >3 months (follow-up 6 months; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[3]	no serious imprecision	none	51	53	-	MD 0.23 higher (0.18 to 0.28 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months (follow-up 2 months; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3,4]	no serious imprecision	none	30	31	-	MD 16.23 lower (22.69 to 9.77 lower)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months (follow-up 5 months; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3,4]	no serious imprecision	none	30	31	-	MD 21.87 lower (28.83 to 14.91 lower)	⊕OOO VERY LOW	CRITICAL
Physical function (6 minute walk test) final values ≤3 months (follow-up 2 months; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3,4]	serious[2]	none	30	31	-	MD 6.39 lower (62.01 lower to 49.23 higher)	⊕OOO VERY LOW	CRITICAL

Physical function (6 minute walk test) final values >3 months (follow-up 5 months; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3,4]	serious[2]	none	30	31	-	MD 34.51 higher (26.32 lower to 95.34 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Geriatric Depression Scale; Beck Depression Inventory; HADS depression; Center for Epidemiologic Studies depression scale) final values ≤3 months (follow-up 9-12 weeks; Better indicated by lower values)												
4	randomised trials	very serious[1]	serious[5]	serious[3]	serious[2]	none	128	126	-	SMD 0.92 lower (1.62 to 0.23 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Beck Depression Inventory; HADS depression; Center for Epidemiologic Studies depression scale) final values >3 months (follow-up 5-6 months; Better indicated by lower values)												
3	randomised trials	very serious[1]	serious[5]	serious[3]	serious[2]	none	100	98	-	SMD 0.88 lower (1.5 to 0.26 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - State (follow-up 12 weeks; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	20	16	-	MD 6.8 lower (15.68 lower to 2.08 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - Trait (follow-up 12 weeks; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	20	16	-	MD 8.7 lower (16.73 to 0.67 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Pain Anxiety Symptoms Scale; HADS anxiety) final values ≤3 months (follow-up 8-9 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	serious[5]	serious[3]	serious[2]	none	78	79	-	SMD 0.73 lower (1.24 to 0.21 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - State (follow-up 6 months; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	14	-	MD 5.6 lower (13.11 lower to 1.91 higher)	⊕OOO VERY LOW	CRITICAL

Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - Trait (follow-up 6 months; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	14	-	MD 8 lower (15.59 to 0.41 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital anxiety and depression scale - anxiety) final values >3 months (follow-up 6 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[3]	no serious imprecision	none	51	53	-	MD 3.42 lower (4.68 to 2.16 lower)	⊕⊕OO LOW	CRITICAL
Pain interference (Brief Pain inventory - pain interference) final values ≤3 months - General activity (follow-up 9 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[4]	very serious[2]	none	27	26	-	MD 0.19 lower (2.19 lower to 1.81 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Brief Pain inventory - pain interference) final values ≤3 months - Mood (follow-up 9 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[4]	serious[2]	none	27	26	-	MD 1.03 lower (3.06 lower to 1 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Brief Pain inventory - pain interference) final values ≤3 months - Walking ability (follow-up 9 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[4]	serious[2]	none	27	26	-	MD 1.38 lower (3.21 lower to 0.45 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Brief Pain inventory - pain interference) final values ≤3 months - Relations with other people (follow-up 9 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[4]	serious[2]	none	27	26	-	MD 1.47 lower (3.31 lower to 0.37 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Brief Pain inventory - pain interference) final values ≤3 months - Sleep (follow-up 9 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[4]	serious[2]	none	27	26	-	MD 2.64 lower (4.7 to 0.58 lower)	⊕OOO VERY LOW	CRITICAL
Pain interference (Pain disability index) final values ≤3 months (follow-up 12 weeks; range of scores: 0-70; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	20	16	-	MD 10.6 lower (20.19 to 1.01 lower)	⊕OOO VERY LOW	CRITICAL
Pain interference (Pain disability index) final values >3 months (follow-up 6 months; range of scores: 0-70; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	14	-	MD 10 lower (19.83 to 0.17 lower)	⊕OOO VERY LOW	CRITICAL
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months (follow-up 8 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3,4]	serious[2]	none	30	31	-	MD 2.76 lower (4.54 to 0.98 lower)	⊕OOO VERY LOW	IMPORTANT
Sleep (Pittsburgh Sleep Quality Index) final values >3 months (follow-up 5 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3,4]	serious[2]	none	30	31	-	MD 2.51 lower (4.89 to 0.13 lower)	⊕OOO VERY LOW	IMPORTANT
Use of health care services (costs in euros) final values >3 months - primary health care service costs (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3]	no serious imprecision	none	45	47	-	MD 99.3 lower (113.85 to 84.75 lower)	⊕OOO VERY LOW	IMPORTANT
Use of health care services (costs in euros) final values >3 months - specialised health care service costs (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3]	serious[2]	none	45	47	-	MD 1446 lower (2323.7 to 568.3 lower)	⊕OOO VERY LOW	IMPORTANT
Discontinuation (follow-up 8-12 weeks)												
4	randomised trials	serious[1]	no serious inconsistency	serious[4]	serious[2]	none	37/160 (23.1%)	7.4%	RR 1.64 (1.03 to 2.6)	47 more per 1000 (from 2 more to 118 more)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS; McGill pain questionnaire) final values ≤3 months (follow-up 8-12 weeks; Better indicated by lower values)												

3	randomised trials	very serious[1]	serious[5]	serious[3]	serious[2]	none	101	100	-	SMD 0.84 lower (1.31 to 0.37 lower)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS; McGill pain questionnaire) final values >3 months (follow-up 5-6 months; Better indicated by lower values)												
3	randomised trials	very serious[1]	serious[5]	serious[3]	serious[2]	none	100	98	-	SMD 0.67 lower (1.32 to 0.02 lower)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
[4] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect comparisons
[5] Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis

Table 33: Clinical evidence profile: Relaxation versus Usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relaxation versus Usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months (follow-up 4-10 weeks; Better indicated by lower values)												
2	randomised trials	very serious[1]	very serious[2]	no serious indirectness	very serious[3]	none	91	82	-	SMD 1.46 lower (4.69 lower to 1.77 higher)	⊕OOO VERY LOW	CRITICAL
Physical function (Neck disability index) final values ≤3 months (follow-up 12 weeks; range of scores: 0-80; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	128	130	-	MD 0 higher (3.21 lower to 3.21 higher)	⊕⊕⊕O MODERATE	CRITICAL
Physical function (Neck disability index) final values >3 months (follow-up 12 months; range of scores: 0-80; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	128	130	-	MD 2 higher (1.47 lower to 5.47 higher)	⊕⊕⊕O MODERATE	CRITICAL

Psychological distress (Hospital Anxiety and Depression Scale depression; Center for Epidemiologic Studies depression scale) final values ≤3 months (follow-up 4-10 weeks; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	97	92	-	SMD 0.26 lower (0.54 lower to 0.03 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale anxiety) final values ≤3 months (follow-up 4 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	58	-	MD 0.27 higher (1.03 lower to 1.57 higher)	⊕⊕OO LOW	CRITICAL
Pain interference (Brief Pain Inventory - interference) final values ≤3 months (follow-up 10 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	30	34	-	MD 0.7 lower (2.05 lower to 0.65 higher)	⊕OOO VERY LOW	CRITICAL
Pain self-efficacy (Arthritis Self-efficacy Scale - pain sub scale) final values ≤3 months (follow-up 10 weeks; range of scores: 10-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	24	24	-	MD 14.9 higher (12.3 to 17.5 higher)	⊕⊕⊕O MODERATE	CRITICAL
Pain self-efficacy (Arthritis Self-efficacy Scale - self-efficacy for managing other symptoms sub scale) final values ≤3 months (follow-up 10 weeks; range of scores: 10-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	30	34	-	MD 10.6 higher (0.12 to 21.08 higher)	⊕OOO VERY LOW	CRITICAL
Sleep (Medical Outcome Sleep Scale sleep problems index) final values ≤3 months (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	67	58	-	MD 9.27 lower (14.35 to 4.19 lower)	⊕OOO VERY LOW	IMPORTANT
Discontinuation (follow-up 4-12 weeks)												
3	randomised trials	serious[1]	serious[2]	no serious indirectness	very serious[3]	none	19/231 (8.2%)	8.5%	RR 0.66 (0.19 to 2.29)	29 fewer per 1000 (from 69 fewer to 110 more)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS) final values ≤3 months (follow-up 4-12 weeks; range of scores: 0-10; Better indicated by lower values)												
4	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	249	236	-	MD 0.49 lower (0.71 to 0.28 lower)	⊕⊕OO LOW	IMPORTANT

Pain (VAS/NRS) final values >3 months (follow-up 12 months; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	128	130	-	MD 0.1 higher (0.52 lower to 0.72 higher)	⊕⊕⊕O MODERATE	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because the point estimate varies widely across studies, unexplained by subgroup analysis
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[4] Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis

Table 34: Clinical evidence profile: Relaxation versus Attention control

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relaxation versus Attention control**	**Control**	**Relative (95% CI)**	**Absolute**		
Pain reduction (follow-up 5 days; measured with: Brief pain inventory pain severity sub scale (VAS); range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	13	10	-	MD 1.35 lower (2.88 lower to 0.18 higher)	⊕OOO VERY LOW	IMPORTANT
Discontinuation (follow-up 4 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/13 (0%)	28.6%	OR 0.11 (0.01 to 0.91)	244 fewer per 1000 (from 19 fewer to 282 fewer)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 35: Clinical evidence profile: Biofeedback versus Usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Biofeedback versus Usual care	Control	Relative (95% CI)	Absolute		
Quality of life (SF36) final values ≤3 months - Physical functioning (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	19	-	MD 4.9 lower (18.88 lower to 9.08 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Role physical (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	19	-	MD 19.2 lower (40.39 lower to 1.99 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Bodily pain (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	19	-	MD 6.3 higher (4.16 lower to 16.76 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - General health (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	19	-	MD 8.2 lower (20.19 lower to 3.79 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Vitality (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	19	19	-	MD 13.5 lower (23.81 to 3.19 lower)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Social functioning (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	19	-	MD 10.4 lower (26.16 lower to 5.36 higher)	⊕OOO VERY LOW	CRITICAL

Quality of life (SF36) final values ≤3 months - Role emotional (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	19	-	MD 9.5 lower (38.48 lower to 19.48 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Mental health (follow-up 8 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	19	-	MD 9.3 lower (22.53 lower to 3.93 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Physical functioning (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	10	-	MD 8 higher (2.34 lower to 18.34 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Role physical (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 9.6 higher (24.3 lower to 43.5 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Bodily pain (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 13.4 higher (12.83 lower to 39.63 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - General health (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 2.9 higher (17.7 lower to 23.5 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Vitality (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 9.5 higher (12.88 lower to 31.88 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Social functioning (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 8.1 higher (8.25 lower to 24.45 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Role emotional (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 0 higher (25.49 lower to 25.49 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values ≤3 months - Mental health (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 0.7 lower (17.72 lower to 16.32 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values >3 months - Physical functioning (follow-up 5 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 0.7 higher (10.91 lower to 12.31 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values >3 months - Role physical (follow-up 5 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 5.2 lower (24.28 lower to 13.88 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values >3 months - Bodily pain (follow-up 5 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 0.7 higher (8.14 lower to 9.54 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values >3 months - General health (follow-up 5 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 0.9 lower (12.28 lower to 10.48 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values >3 months - Vitality (follow-up 5 months; range of scores: 0-100; Better indicated by higher values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	18	18	-	MD 10.2 lower (20.62 lower to 0.22 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values >3 months - Social functioning (follow-up 5 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 7.4 lower (24.19 lower to 9.39 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values >3 months - Role emotional (follow-up 5 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 23.9 lower (53.64 lower to 5.84 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36) final values >3 months - Mental health (follow-up 5 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	18	-	MD 6.4 lower (18.26 lower to 5.46 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Arthritis Impact Measurement Scale) change scores >3 months (follow-up 6 months; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3]	serious[2]	none	38	27	-	MD 0.4 lower (1.34 lower to 0.54 higher)	⊕OOO VERY LOW	CRITICAL
Physical function (Neck disability index) final values ≤3 months (follow-up 10 weeks; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	10	-	MD 6.6 lower (17.17 lower to 3.97 higher)	⊕OOO VERY LOW	CRITICAL
Physical function (Maximal Watt bicycle ergometer) change scores >3 months (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3]	serious[2]	none	38	27	-	MD 14.1 higher (4.46 to 23.74 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Beck Depression Inventory) final values ≤3 months (follow-up 8 weeks; range of scores: 0-63; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	19	-	MD 3.2 higher (1.94 lower to 8.34 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale - depression) final values ≤3 months (follow-up 10 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	10	-	MD 2.49 lower (5.65 lower to 0.67 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Beck Depression Inventory) final values >3 months (follow-up 5 months; range of scores: 0-63; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	18	18	-	MD 4.6 higher (0.21 lower to 9.41 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Symptoms Checklist-90-revised) change scores >3 months (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[3]	very serious[2]	none	38	27	-	MD 1.3 lower (19.16 lower to 16.56 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale anxiety) final values ≤3 months (follow-up 10 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 0.95 lower (3.77 lower to 1.87 higher)	⊕OOO VERY LOW	CRITICAL
Discontinuation (follow-up 2-6 months)												
3	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[2]	none	19/88 (21.6%)	7.4%	OR 2.65 (1.01 to 6.97)	101 more per 1000 (from 1 more to 284 more)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS) final values ≤3 months (follow-up 10 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 0.3 lower (1.62 lower to 1.02 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS) change scores >3 months (follow-up 6 months; range of scores: 0-10; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	serious[3]	serious[2]	none	38	27	-	MD 1.9 lower (10.18 lower to 6.38 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions

Table 36: Clinical evidence profile: Biofeedback versus Sham biofeedback

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Biofeedback versus Sham**		**Relative (95% CI)**	**Absolute**		
Quality of life (Fibromyalgia impact questionnaire) changes scores<3 months (follow-up 6 days; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	15	-	MD 9.6 lower (20.14 lower to 0.94 higher)	⊕⊕OO LOW	CRITICAL
Physical function (6 minute walk test) change scores <3 months (follow-up 6 days; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	15	-	MD 53 higher (4.18 lower to 110.18 higher)	⊕⊕OO LOW	CRITICAL
Psychological distress (Beck depression inventory) change scores ≤3 months (follow-up 5 weeks; range of scores: 0-63; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	25	9	-	MD 0.7 lower (7.71 lower to 6.31 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Beck depression inventory) change scores >3 months (follow-up mean 16.2 months; range of scores: 0-63; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	9	-	MD 3.9 higher (3.99 lower to 11.79 higher)	⊕⊕OO LOW	CRITICAL
Psychological distress (State trait anxiety inventory - trait) change scores ≤3 months (follow-up 5 weeks; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	25	9	-	MD 0.3 lower (9.18 lower to 8.58 higher)	⊕OOO VERY LOW	CRITICAL

Psychological distress (State trait anxiety inventory - trait) change scores >3 months (follow-up mean 16.2 months; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	9	-	MD 3.5 higher (4 lower to 11 higher)	⊕⊕OO LOW	CRITICAL
Sleep (Pittsburgh sleep quality index) change scores ≤3 months (follow-up 5 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	25	9	-	MD 0.8 lower (4.15 lower to 2.55 higher)	⊕OOO VERY LOW	IMPORTANT
Sleep (Pittsburgh sleep quality index) change scores >3 months (follow-up mean 16.2 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	9	-	MD 2 higher (1.56 lower to 5.56 higher)	⊕⊕OO LOW	IMPORTANT
Discontinuation												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	6/46 (13%)	0%	RD 0 (-0.19 to 0.13)	-	⊕⊕⊕O MODERATE	IMPORTANT
Pain (VAS) change scores ≤3 months - neurofeedback (follow-up 5 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	25	9	-	MD 0.9 lower (2.06 lower to 0.26 higher)	⊕⊕OO LOW	IMPORTANT
Pain (VAS) change scores ≤3 months (follow-up 6 days; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	15	-	MD 1.7 higher (0.27 lower to 3.67 higher)	⊕⊕OO LOW	IMPORTANT
Pain (VAS) change scores >3 months - neurofeedback (follow-up mean 16.2 months; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	9	-	MD 1.10 higher (0.2 lower to 2.4 higher)	⊕⊕OO LOW	IMPORTANT

Table 37: Clinical evidence profile: Mindfulness versus Usual care

Quality assessment							No of patients		Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Mindfulness versus Usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months (follow-up 12 weeks; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	16	-	MD 4.43 lower (15.33 lower to 6.47 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months (follow-up 6 months; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	16	-	MD 7.52 lower (17.04 lower to 2 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Beck depression Inventory) final values ≤3 months (follow-up 7-12 weeks; range of scores: 0-63; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	29	34	-	MD 3.67 lower (7.39 lower to 0.05 higher)	⊕⊕OO LOW	CRITICAL
Psychological distress (Beck depression Inventory) final values >3 months (follow-up 5-6 months; range of scores: 0-63; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	29	34	-	MD 5.46 lower (8.79 to 2.12 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - State (follow-up 7 weeks; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14	18	-	MD 11.83 lower (18.47 to 5.19 lower)	⊕⊕OO LOW	CRITICAL
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - Trait (follow-up 7 weeks; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	14	18	-	MD 3.95 lower (10.05 lower to 2.15 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - State (follow-up 5 months; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14	18	-	MD 12.44 lower (18.05 to 6.83 lower)	⊕⊕OO LOW	CRITICAL

Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - Trait (follow-up 5 months; range of scores: 20-80; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	14	18	-	MD 3.26 lower (9.26 lower to 2.74 higher)	⊕OOO VERY LOW	CRITICAL
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months (follow-up 7 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20	19	-	MD 4 lower (6.07 to 1.93 lower)	⊕⊕OO LOW	IMPORTANT
Sleep (Pittsburgh Sleep Quality Index) final values >3 months (follow-up 5 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	20	19	-	MD 2.43 lower (4.54 to 0.32 lower)	⊕OOO VERY LOW	IMPORTANT
Discontinuation (follow-up 7-12 weeks)												
2	randomised trials	serious[1]	no serious inconsistency	serious[3]	no serious imprecision	none	8/37 (21.6%)	2.6%	OR 5.63 (1.39 to 22.84)	105 more per 1000 (from 10 more to 353 more)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] Downgraded by 1 or 2 increments because the majority of the evidence had indirect outcomes

Table 38: Clinical evidence profile: Pain education versus Usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Pain education versus Usual care**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months (follow-up 10 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	17	-	MD 0.01 higher (0.42 lower to 0.44 higher)	⊕OOO VERY LOW	CRITICAL

Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months (follow-up 10 weeks; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	18	17	-	MD 0.47 higher (0.83 lower to 1.77 higher)	⊕⊕OO LOW	CRITICAL
Sleep (Karolinska sleep questionnaire - sleep quality sub scale) final values ≤3 months (follow-up 10 weeks; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	17	-	MD 0.13 higher (0.41 lower to 0.67 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values ≤3 months (follow-up 10 weeks; range of scores: 0-78; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18	17	-	MD 3.9 higher (20.73 lower to 28.53 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 39: Clinical evidence profile: Pain education versus Attention control

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Pain education**	**Attention control**	**Relative (95% CI)**	**Absolute**		
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months (follow-up unclear; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	60	17	-	MD 2.92 higher (6.34 lower to 12.18 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months (follow-up unclear; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	60	17	-	MD 5.6 lower (15.93 lower to 4.73 higher)	⊕OOO VERY LOW	CRITICAL

Psychological distress (Pain Anxiety Symptom Scale) final values ≤3 months - PASS1 (follow-up unclear; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	60	17	-	MD 3.66 higher (3.06 lower to 10.38 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Pain Anxiety Symptom Scale) final values ≤3 months - PASS2 (follow-up unclear; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	60	17	-	MD 1.81 higher (1.79 lower to 5.41 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Pain Anxiety Symptom Scale) final values >3 months - PASS1 (follow-up unclear; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	60	17	-	MD 6.41 higher (1.77 lower to 14.59 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Pain Anxiety Symptom Scale) final values >3 months - PASS2 (follow-up unclear; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	60	17	-	MD 2.6 higher (1.59 lower to 6.79 higher)	⊕OOO VERY LOW	CRITICAL
Pain (numeric rating scale) final values ≤3 months (follow-up unclear; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	60	17	-	MD 2.23 lower (3.04 to 1.43 lower)	⊕⊕OO LOW	IMPORTANT
Pain (numeric rating scale) final values >3 months (follow-up unclear; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	60	17	-	MD 1.47 lower (2.41 to 0.53 lower)	⊕OOO VERY LOW	IMPORTANT
Discontinuation (follow-up unclear)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/84 (10.7%)	0%	Peto OR 3.78 (0.65 to 21.87)	110 more per 1000 (from 10 to 200 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 40: Clinical evidence profile: Sleep hygiene versus Usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sleep hygiene versus Usual care	Control	Relative (95% CI)	Absolute		
Quality of life (SF36 mental composite) final values ≤3 months (follow-up 6 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	17	9	-	MD 4.8 higher (2.07 to 7.53 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36 mental composite) final values >3 months (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7	7	-	MD 9.4 higher (6.52 to 12.28 higher)	⊕⊕OO LOW	CRITICAL
Sleep (Insomnia Symptom Questionnaire) final values ≤3 months (follow-up 6 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17	9	-	MD 22.7 lower (26.26 to 19.14 lower)	⊕⊕OO LOW	IMPORTANT
Sleep (Insomnia Symptom Questionnaire) final values >3 months (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7	7	-	MD 21.6 lower (26.21 to 16.99 lower)	⊕⊕OO LOW	IMPORTANT
Discontinuation (follow-up 6 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/18 (5.6%)	18.2%	RR 0.31 (0.03 to 2.99)	126 fewer per 1000 (from 177 fewer to 362 more)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill pain questionnaire) final values ≤3 months (follow-up 6 weeks; range of scores: 0-78; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17	9	-	MD 10.7 lower (14.1 to 7.3 lower)	⊕⊕OO LOW	IMPORTANT
Pain (McGill pain questionnaire) final values >3 months (follow-up 6 months; range of scores: 0-78; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7	7	-	MD 11.7 lower (16.34 to 7.06 lower)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 41: Clinical evidence profile: Hypnosis versus Usual care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hypnosis versus Usual care	Control	Relative (95% CI)	Absolute		
Quality of life (Fibromyalgia Impact Questionnaire) change scores ≤3 months (follow-up 12 weeks; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	29	30	-	MD 1.09 lower (5.83 lower to 3.65 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) change scores >3 months (follow-up 6 months; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	29	30	-	MD 3.9 lower (11.21 lower to 3.41 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale - depression) change scores ≤3 months (follow-up 12 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	30	29	-	MD 0.73 lower (2.25 lower to 0.79 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale - depression) change scores >3 months (follow-up 6 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	30	29	-	MD 1.3 lower (2.63 lower to 0.03 higher)	⊕OOO VERY LOW	CRITICAL

Psychological distress (Hospital Anxiety and Depression Scale - anxiety) change scores ≤3 months (follow-up 12 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	30	29	-	MD 0.12 lower (1.07 lower to 0.83 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale - anxiety) change scores >3 months (follow-up 6 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	30	29	-	MD 0.7 lower (9.05 lower to 7.65 higher)	⊕OOO VERY LOW	CRITICAL
Sleep (Medical Outcome Sleep Scale) change scores ≤3 months (follow-up 12 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	29	30	-	MD 3.5 lower (9.45 lower to 2.45 higher)	⊕OOO VERY LOW	IMPORTANT
Sleep (Medical Outcome Sleep Scale) change scores >3 months (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	29	30	-	MD 10.3 lower (12.28 to 8.32 lower)	⊕⊕OO LOW	IMPORTANT
Discontinuation (follow-up 6 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/31 (3.2%)	6.5%	RR 0.5 (0.05 to 5.23)	32 fewer per 1000 (from 62 fewer to 275 more)	⊕OOO VERY LOW	IMPORTANT
Pain (NRS) final values >3 months (follow-up 6 months; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	29	-	MD 0.6 lower (1.19 to 0.01 lower)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 42: Clinical evidence profile: Psychotherapy versus Usual care

Quality assessment							No of patients		Effect		Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Psychotherapy versus Usual care	Control	Relative (95% CI)	Absolute		
Quality of life (SF36 physical component) final values >3 months (follow-up 12 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	23	-	MD 1.1 lower (2.2 lower to 0 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36 mental component) final values >3 months (follow-up 12 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	23	-	MD 4.1 higher (2.77 to 5.43 higher)	⊕OOO VERY LOW	CRITICAL
Physical function (Somatoform disorders-7) final values >3 months (follow-up 12 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	23	23	-	MD 4.5 lower (5.77 to 3.23 lower)	⊕⊕OO LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale - depression) final values >3 months (follow-up 12 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	23	-	MD 0.7 lower (1.28 to 0.12 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale - anxiety) final values >3 months (follow-up 12 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	23	-	MD 0.5 lower (0.96 to 0.04 lower)	⊕OOO VERY LOW	CRITICAL
Pain interference (Pain disability index) final values >3 months (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	23	23	-	MD 2 lower (4.02 lower to 0.02 higher)	⊕OOO VERY LOW	CRITICAL
Discontinuation (follow-up 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/24 (8.3%)	13%	RR 0.64 (0.12 to 3.48)	47 fewer per 1000 (from 114 fewer to 322 more)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 43: Clinical evidence profile: CBT versus Sleep hygiene

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT versus Sleep hygiene	Control	Relative (95% CI)	Absolute		
Quality of life (SF36 mental composite) final values ≤3 months (follow-up 6 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15	17	-	MD 0.4 higher (1.51 lower to 2.31 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36 mental composite) final values >3 months (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6	7	-	MD 1.9 higher (0.99 lower to 4.79 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months (follow-up 6-7 weeks; range of scores: 0-100; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[2]	none	50	47	-	MD 14.14 lower (21.15 to 7.13 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Symptom Checklist-90-Revised - depression sub scale; Hospital Anxiety and Depression Scale - depression) final values ≤3 months (follow-up 6-7 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[2]	none	50	47	-	SMD 0.61 lower (1.02 to 0.2 lower)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Symptom Checklist-90-Revised - anxiety sub scale; Hospital Anxiety and Depression Scale - anxiety) final values ≤3 months (follow-up 6-7 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[2]	none	50	47	-	SMD 0.32 lower (0.72 lower to 0.08 higher)	⊕OOO VERY LOW	CRITICAL

Pain self-efficacy (Chronic Pain Self-efficacy Scale) final values ≤3 months (follow-up 6 weeks; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[2]	none	30	27	-	MD 23.48 higher (4.83 to 42.13 higher)	⊕OOO VERY LOW	CRITICAL
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months (follow-up 6-7 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	50	47	-	MD 1.96 lower (3.39 to 0.54 lower)	⊕⊕OO LOW	IMPORTANT
Sleep (Insomnia Symptom Questionnaire) final values ≤3 months (follow-up 6 weeks; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15	17	-	MD 5.8 higher (3.28 to 8.32 higher)	⊕⊕OO LOW	IMPORTANT
Sleep (total sleep time, hours) final values ≤3 months (follow-up 6 weeks; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	13	13	-	MD 0.04 lower (1.27 lower to 1.19 higher)	⊕OOO VERY LOW	IMPORTANT
Sleep (Insomnia Symptom Questionnaire) final values >3 months (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6	7	-	MD 3.4 higher (0.19 to 6.61 higher)	⊕OOO VERY LOW	IMPORTANT
Discontinuation (follow-up 6 weeks)												
3	randomised trials	serious[1]	no serious inconsistency	serious[3]	very serious[2]	none	6/72 (8.3%)	5.6%	OR 1.53 (0.43 to 5.53)	27 more per 1000 (from 31 fewer to 191 more)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill VAS) final values ≤3 months (follow-up 6-7 weeks; range of scores: 0-10; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[3]	no serious imprecision	none	50	47	-	MD 1.59 lower (2.33 to 0.86 lower)	⊕⊕OO LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values ≤3 months (follow-up 6 weeks; range of scores: 0-78; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15	17	-	MD 3.9 higher (1.06 to 6.74 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values >3 months (follow-up 6 months; range of scores: 0-78; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6	7	-	MD 6.4 higher (2.32 to 10.48 higher)	⊕⊕OO LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
[4] Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis

Table 44: Clinical evidence profile: CBT versus Pain education

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT versus Pain education**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life (Fibromyalgia Impact Questionnaire) final values ≤3 months (follow-up 10 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	18	18	-	MD 0.41 lower (0.89 lower to 0.07 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Fibromyalgia Impact Questionnaire) final values >3 months (Copy) (follow-up 6 months; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	18	18	-	MD 0.03 lower (0.52 lower to 0.46 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (Satisfaction with life scale) final values ≤3 months (follow-up 10 weeks; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 0.08 higher (2.43 lower to 2.59 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (Satisfaction with life scale) final values >3 months (follow-up 6 months; Better indicated by higher values)												

1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 1.06 higher (1.42 lower to 3.54 higher)	⊕⊕OO LOW	CRITICAL
Physical function (SF12 physical function sub scale) final values ≤3 months (follow-up 10 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 0.87 higher (2.12 lower to 3.86 higher)	⊕⊕OO LOW	CRITICAL
Physical function (SF12 physical function sub scale) final values >3 months (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	75	76	-	MD 0.87 higher (2.12 lower to 3.86 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Beck depression Inventory) change scores ≤3 months (follow-up 4 weeks; range of scores: 0-63; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	8	8	-	MD 1.5 lower (7.77 lower to 4.77 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Center for Epidemiologic Studies - depression) final values ≤3 months (follow-up 10 weeks; range of scores: 0-60; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 1.87 lower (5.48 lower to 1.74 higher)	⊕⊕OO LOW	CRITICAL
Psychological distress (Center for Epidemiologic Studies - depression) final values >3 months (follow-up 6 months; range of scores: 0-60; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 1.13 lower (4.95 lower to 2.69 higher)	⊕⊕OO LOW	CRITICAL
Psychological distress (Generalised anxiety disorder-7) final values ≤3 months (follow-up 10 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 0.3 lower (1.95 lower to 1.35 higher)	⊕⊕OO LOW	CRITICAL
Psychological distress (Generalised anxiety disorder-7) final values >3 months (follow-up 6 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	75	76	-	MD 1.3 lower (2.93 lower to 0.33 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Brief Pain Inventory - interference) change scores ≤3 months (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	8	8	-	MD 1.11 lower (3.41 lower to 1.19 higher)	⊕OOO VERY LOW	CRITICAL
Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months (follow-up 10 weeks; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	18	18	-	MD 0.38 higher (0.83 lower to 1.59 higher)	⊕OOO VERY LOW	CRITICAL
Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values >3 months (Copy) (follow-up 6 months; Better indicated by higher values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	18	18	-	MD 0.20 lower (0.91 lower to 1.51 higher)	⊕OOO VERY LOW	CRITICAL
Sleep (Karolinska Sleep Questionnaire sleep quality) final values ≤3 months (follow-up 10 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	18	18	-	SMD 0.26 higher (0.40 lower to 0.91 higher)	⊕OOO VERY LOW	IMPORTANT
Sleep (Pittsburgh Sleep Quality Index - sleep problems) final values ≤3 months (follow-up 10 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	75	76	-	SMD 0.55 lower (0.88 to 0.23 lower)	⊕OOO VERY LOW	IMPORTANT
Sleep (Karolinska Sleep Questionnaire sleep quality) final values >3 months (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	18	18	-	SMD 0.76 higher (0.08 to 1.44 higher)	⊕OOO VERY LOW	IMPORTANT
Sleep (Pittsburgh Sleep Quality Index - sleep problems) final values >3 months (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	SMD 0.14 lower (0.46 lower to 0.18 higher)	⊕⊕OO LOW	IMPORTANT
Use of healthcare services (physician/other health professional visits in past 3 months) final values ≤3 months (follow-up 10 weeks; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 0.81 lower (2.48 lower to 0.86 higher)	⊕OOO VERY LOW	IMPORTANT
Use of healthcare services (physician/other health professional visits in past 3 months) final values >3 months (follow-up 6 months; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 1.41 lower (3.08 lower to 0.26 higher)	⊕OOO VERY LOW	IMPORTANT
Discontinuation (follow-up 4-10 weeks)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	8/83 (9.6%)	2%	See comment	34 more per 1000 (from 11 fewer to 78 more)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS) final values/change scores ≤3 months (follow-up 4-10 weeks; range of scores: 0-10; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	83	84	-	MD 0.48 lower (0.99 lower to 0.03 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS/NRS) final values >3 months (follow-up 6 months; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	75	76	-	MD 0.12 lower (0.7 lower to 0.46 higher)	⊕⊕OO LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values ≤3 months (follow-up 10 weeks; range of scores: 0-78; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	18	18	-	MD 5.5 lower (30.73 lower to 19.73 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values >3 months (follow-up 6 months; range of scores: 0-78; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	18	18	-	MD 3.08 lower (24.44 lower to 18.28 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[4] Downgraded by 1 or 2 increments because heterogeneity, I2=50%, p=0.04, unexplained by subgroup analysis

Table 45: Clinical evidence profile: CBT versus Biofeedback

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT versus Biofeedback	Control	Relative (95% CI)	Absolute		
Discontinuation (follow-up 12 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	31/29 (106.9%)	3.5%	RR 0.33 (0.04 to 3.02)	23 fewer per 1000 (from 34 fewer to 71 more)	⊕OOO VERY LOW	IMPORTANT
Pain (NRS) final values ≤3 months (follow-up 12 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	28	28	-	MD 0.57 higher (0.61 lower to 1.75 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (NRS) final values >3 months (follow-up 6 months; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	28	28	-	MD 0.04 lower (1.38 lower to 1.3 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 46: Clinical evidence profile: CBT versus Psychotherapy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT versus Psychotherapy	Control	Relative (95% CI)	Absolute		
Psychological distress (Beck depression Inventory) final values ≤3 months (follow-up 10 weeks; range of scores: 0-63; Better indicated by lower values)												

1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	23	25	-	MD 0.8 higher (4.19 lower to 5.79 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Beck depression Inventory) final values >3 months (follow-up 12 months; range of scores: 0-63; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	22	25	-	MD 4.2 lower (9.61 lower to 1.21 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Pain Anxiety Symptoms Scale) final values ≤3 months (follow-up 10 weeks; range of scores: 0-200; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	23	25	-	MD 4.9 higher (13.81 lower to 23.61 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Pain Anxiety Symptoms Scale) final values >3 months (follow-up 12 months; range of scores: 0-200; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	22	25	-	MD 9.9 lower (29.45 lower to 9.65 higher)	⊕OOO VERY LOW	CRITICAL
Discontinuation (follow-up 10 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	3/25 (12%)	20%	RR 0.6 (0.16 to 2.25)	80 fewer per 1000 (from 168 fewer to 250 more)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values ≤3 months (follow-up 10 weeks; range of scores: 0-78; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	23	25	-	MD 4.5 higher (2.85 lower to 11.85 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (McGill Pain Questionnaire) final values >3 months (follow-up 12 months; range of scores: 0-78; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	22	25	-	MD 0.2 higher (7.84 lower to 8.24 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 47: Clinical evidence profile: CBT versus Behaviour therapy

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CBT versus Behaviour therapy	Control	Relative (95% CI)	Absolute		
Physical function (Fibromyalgia Impact Questionnaire physical function sub scale) final values >3 months (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	42	43	-	MD 0.79 higher (0.05 lower to 1.63 higher)	⊕OOO VERY LOW	CRITICAL
Use of healthcare services (Physician visits) >3 months (follow-up 12 months; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	42	43	-	MD 8.92 higher (1.11 to 16.73 higher)	⊕OOO VERY LOW	IMPORTANT
Discontinuation (follow-up 15 weeks)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	2/42 (4.8%)	7%	RR 0.68 (0.12 to 3.88)	22 fewer per 1000 (from 62 fewer to 202 more)	⊕OOO VERY LOW	IMPORTANT
Pain (West Haven-Yale Multidimension Pain Inventory) final values >3 months (follow-up 12 months; Better indicated by lower values)												

1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	42	43	-	MD 0.13 higher (0.47 lower to 0.73 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 48: Clinical evidence profile: Biofeedback versus Relaxation

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Biofeedback versus Relaxation**	**Control**	**Relative (95% CI)**	**Absolute**		
Pain (% reduction in pain from baseline) ≤3 months (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	30	27	-	MD 20 lower (41.55 lower to 1.55 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 or 2 increments because the majority of the evidence was based on indirect interventions
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 49: Clinical evidence profile: ACT versus Relaxation

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**ACT versus Relaxation**	**Control**	**Relative (95% CI)**	**Absolute**		
Quality of life (SF12 mental component) final values ≤3 months (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												

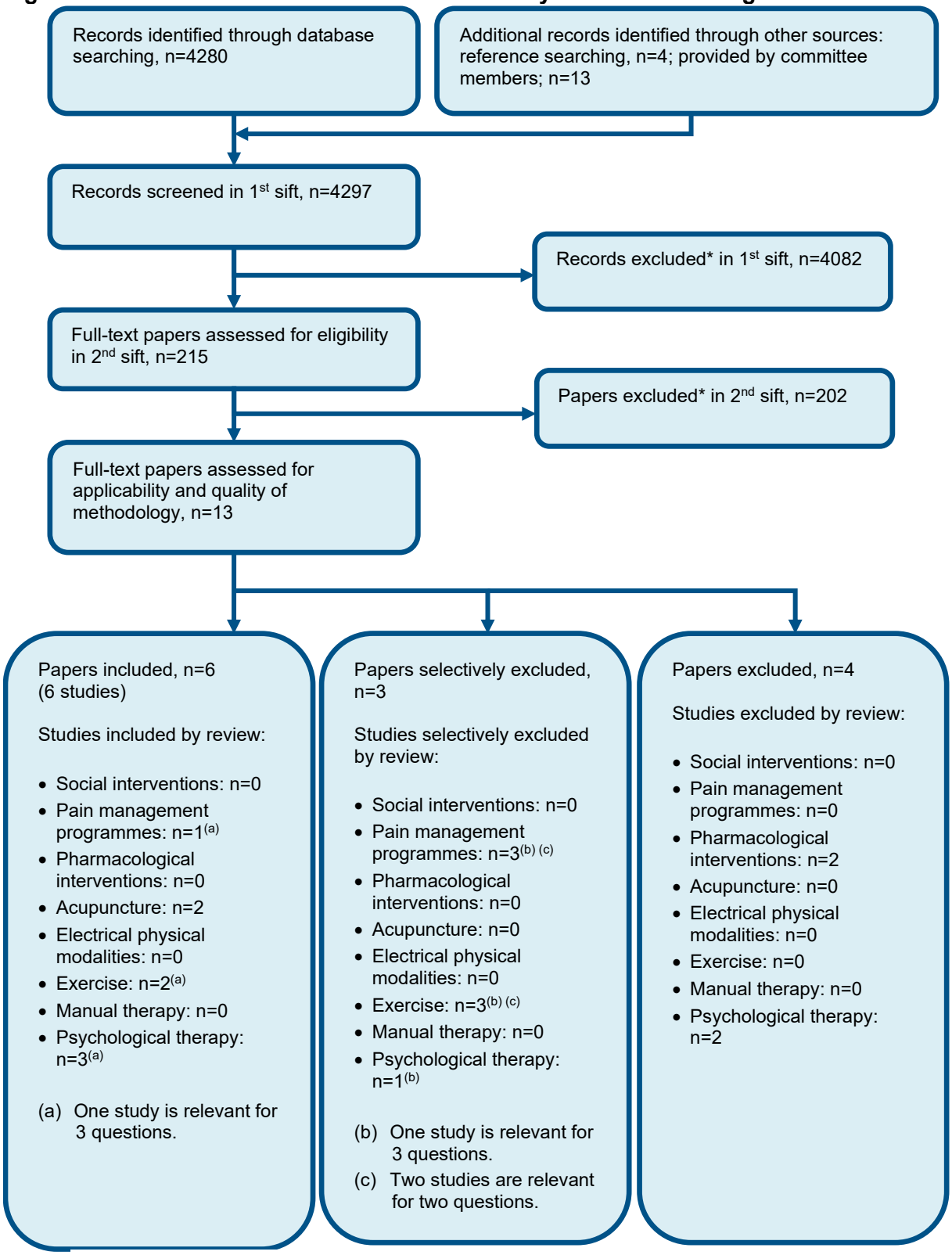
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	19	-	MD 6 higher (0.36 lower to 12.36 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF12 mental component) >3 months (follow-up 9 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	18	-	MD 0.5 higher (7.51 lower to 8.51 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF12 physical component) final values ≤3 months (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	19	-	MD 2.8 higher (2.38 lower to 7.98 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF12 physical component) final values >3 months (follow-up 9 months; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	18	-	MD 7 higher (0.56 to 13.44 higher)	⊕OOO VERY LOW	CRITICAL
Pain interference (Pain disability index) final values ≤3 months (follow-up 12 weeks; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	19	-	MD 11.5 lower (20.38 to 2.62 lower)	⊕OOO VERY LOW	CRITICAL
Pain interference (Pain disability index) final values >3 months (follow-up 9 months; range of scores: 0-100; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	18	-	MD 2.8 lower (14.16 lower to 8.56 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale depression) final values ≤3 months (follow-up 12 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	19	-	MD 2 lower (5.06 lower to 1.06 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale depression) final values >3 months (follow-up 9 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	18	-	MD 0 higher (3.58 lower to 3.58 higher)	⊕OOO VERY LOW	CRITICAL
Psychological distress (Hospital Anxiety and Depression Scale anxiety) final values ≤3 months (follow-up 12 weeks; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	19	-	MD 1.7 lower (4.27 lower to 0.87 higher)	⊕OOO VERY LOW	CRITICAL

Psychological distress (Hospital Anxiety and Depression Scale anxiety) final values >3 months (follow-up 9 months; range of scores: 0-21; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19	18	-	MD 0 higher (3.32 lower to 3.32 higher)	⊕OOO VERY LOW	CRITICAL
Discontinuation (follow-up 12 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/25 (0%)	20.8%	OR 0.11 (0.02 to 0.67)	180 fewer per 1000 (from 58 fewer to 203 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Pain (NRS 0-6) final values ≤3 months (follow-up 12 weeks; range of scores: 0-6; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	19	-	MD 0.3 lower (1.18 lower to 0.58 higher)	⊕OOO VERY LOW	IMPORTANT
Pain (NRS 0-6) final values >3 months (follow-up 9 months; range of scores: 0-6; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	18	-	MD 0.3 higher (0.61 lower to 1.21 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Appendix G: Health economic evidence selection

Figure 220: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix H: Health economic evidence tables

<table>
<tr><th>Study</th><th colspan="4">Beasley (2015);[41]</th></tr>
<tr><th>Study details</th><th>Population & interventions</th><th>Costs</th><th>Health outcomes</th><th>Cost effectiveness</th></tr>
<tr>
<td>Economic analysis: CUA (health outcome: QALYs)

Study design: Within-trial analysis (RCT – clinical results in same paper)

Approach to analysis: Analysis of individual data for EQ-5D (adjusted for baseline differences in utility) and resource use. Unit costs applied.

Perspective: UK NHS

Follow-up: 30 months*

Treatment effect duration:[(a)] 6 months</td>
<td>Population:
People aged 25 years and over with chronic widespread pain according to the definition in the American College of Rheumatology (ACR) 1990 criteria for fibromyalgia, for which they have consulted their general practitioner in the previous year.

Patient characteristics:
N = 442 (in all four arms)
Age: 56.3
Male: 30.5%

Intervention 1:
Treatment as usual (from GP – precise care delivered not recorded)

Intervention 2:
Telephone-delivered cognitive behaviour therapy (TCBT): initial assessment (45-60mins)</td>
<td>Incremental costs (mean per patient):

Intervention 1 is the reference.

<u>Complete cases</u>
Intervention 1: £0
Intervention 2: £574
Intervention 3: £1,924
Intervention 4: £1,778

<u>Multiple imputations</u>
Intervention 1: £0
Intervention 2: £554
Intervention 3: £1,256
Intervention 4: £1,453

Currency & cost year:
2010 UK pounds</td>
<td>Incremental QALYs (mean per patient):

Intervention 1 is the reference.

<u>Complete cases</u>
Intervention 1: 0
Intervention 2: 0.097
Intervention 3: 0.025
Intervention 4: 0.047

<u>Multiple imputations</u>
Intervention 1: 0
Intervention 2: 0.140
Intervention 3: 0.071
Intervention 4: 0.096</td>
<td>ICER:
Full incremental analysis (complete cases, adjusted) (pa):
<table>
<tr><th>Int</th><th>Inc cost</th><th>Inc QALY</th><th>ICER</th><th>ICER (ruled out dominated options)</th></tr>
<tr><td>1</td><td>£0</td><td>£0</td><td>Reference</td><td>-</td></tr>
<tr><td>2</td><td>£574</td><td>0.097</td><td>£5,917</td><td>£5,917</td></tr>
<tr><td>3</td><td>£1,924</td><td>0.025</td><td>£76,960</td><td>Dominated</td></tr>
<tr><td>4</td><td>£1,778</td><td>0.047</td><td>£37,830</td><td>Dominated</td></tr>
</table>
Probability Intervention 2 cost effective (£20K threshold): approx. 75% (read off graph)

Full incremental analysis (multiple imputations, adjusted) (pa):
<table>
<tr><th>Int</th><th>Inc cost</th><th>Inc QALY</th><th>ICER</th><th>ICER (ruled out dominated options)</th></tr>
<tr><td>1</td><td>£0</td><td>0</td><td>Reference</td><td>-</td></tr>
<tr><td>2</td><td>£554</td><td>0.140</td><td>£3,957</td><td>£3,957</td></tr>
<tr><td>3</td><td>£1,256</td><td>0.071</td><td>£17,690</td><td>Dominated</td></tr>
<tr><td>4</td><td>£1,453</td><td>0.096</td><td>£15,135</td><td>Dominated</td></tr>
</table>
</td>
</tr>
</table>

Discounting: Costs: 3.5%; Outcomes: 3.5%	followed by 7 weekly sessions (30-45mins each), 1 session at three months, and 1 session at 6 months. Intervention delivered by 4 therapists accredited by the British Association for Behaviour and Cognitive Psychotherapies. Therapists conducted a patient-centred assessment, developed shared understanding and formulation of the participants' problem(s) and identified two to three patient-defined goals. Patients also received a self-management CBT manual that included: behavioural activation, cognitive restructuring, unhelpful thinking and lifestyle changes. **Intervention 3:** Exercise therapy: leisure-facility-and-gym-based exercise program consistent with American College of Sport Medicine (ACSM) guidelines for improving cardiorespiratory fitness. Following an induction sessions, patients were offered 6 fitness	**Cost components incorporated:** • Intervention costs (for exercise this includes gym membership) • Routine health service (GP, nurse, physio, community visits, outpatient, inpatient, admission, primary care).		Probability Intervention 2 cost effective (£20K/30K threshold): NR **Analysis of uncertainty:** Used non-parametric bootstrapping. Multiple imputation was also used to assess the sensitivity of findings to missing data.

	instructor-led monthly appointments. Experienced fitness instructors delivered the intervention following a 1-day training session on exercise prescription for people with CWP. The specific exercises are negotiated between fitness instructor and patient, and can be changed while maintaining goal of improving cardio-respiratory fitness. Initial intensity was low to moderate, patients were free to engage in additional exercises to those prescribed. Recommended session duration was 20-60 mins, patients were advised to attend at least twice a week and engage in 'everyday' activities on non-gym days. **Intervention 4:** Combination of Interventions 2 and 3.			

Data sources
*The follow up is 24 months post treatment, and given that the exercise and CBT interventions were about 6 months in length then that equates to a 30 month follow up. Also has an exercise and combination arm (TCBT + exercise) but these are not reported here as are not relevant to the question.

Analyses were adjusted for age, sex, baseline pain score, baseline psychological distress score, study centre, and baseline scores of outcome of interest (e.g. EQ-5D). **Health outcomes:** Resource use was reported to 3 months post treatment, and at months 18-24 post treatment. Linear interpolation between reported health service costs at 3 and 24 months post treatment was used to impute an average cost per quarter for the 5 quarters not covered by data collection (i.e. months 3-6, 6-9, 9-12, 12-15 and 15-18 post treatment). **Quality-of-life weights:** EQ-5D UK tariff. QALYs calculated using patient response to EQ-5D at 24 months post-treatment. Additional QALYs accrued between 3 and 24 months post treatment were calculated for each person assuming a linear change in utility. **Cost sources:** Cost sources were the same as those used for the original McBeth 2012 economic evaluation that this paper is also based on, which are PSSRU 2010, and NHS reference costs 2008/9. TCBT delivered by 4 therapists accredited by the British Association for Behaviour and Cognitive Psychotherapies. Exercise delivered by experienced fitness instructors.	
Comments	
Source of funding: Arthritis Research UK. **Limitations:** Participation in study based on self-reported symptoms and recruited through primary care, may not necessarily be representative of general population with chronic widespread pain caused by fibromyalgia. Treatment as usual not defined, usual care provided by GP was not restricted and may not be the same across all participants in that group. Within-study analysis which may not reflect full body of evidence. **Other:** Analyses were adjusted for: age, sex, baseline pain on CPG (chronic pain grade) scale, baseline GHQ (general health questionnaire) score and study centre.	
Overall applicability:[(b)] Directly applicable	**Overall quality:**[(c)] Potentially serious limitations

Abbreviations: 95% CI: 95% confidence interval; CUA: cost–utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.as follow up was longer tan duration of trial then could be longer than 6 months if there is still a treatment effect remaining.

(b) Directly applicable / Partially applicable / Not applicable

(c) Minor limitations / Potentially serious limitations / Very serious limitations

Study	**Luciano 2014[289]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Within-trial analysis (RCT) **Approach to analysis:**	**Population:** Patients with fibromyalgia **Patient characteristics:** N = 112 Age: 47	**Total costs (mean per patient, complete case analysis):** Intervention 1: £2,346 Intervention 2: £1,354 Incremental (2−1) (adjusted, bootstrapped): -£1,560	**QALYs (mean per patient, complete case analysis):** Intervention 1: 0.24 Intervention 2: 0.25 Incremental (2−1) (adjusted, bootstrapped): 0.01	**ICER (Intervention 2 versus Intervention 1):** CBT dominant (pa) 95% CI: NR Probability Intervention 2 cost effective (£20K/30K threshold): NR

EQ-5D data collected and combined with unit costs applied to resource use. **Perspective:** Spanish healthcare perspective **Time horizon/Follow-up:**6 months **Treatment effect duration:**[(a)] 6 months **Discounting:** Costs: NA; Outcomes: NA	Male: 46% **Intervention 1:** Treatment as usual **Intervention 2:** CBT group based (9 sessions). Homework assigned outside of classes. 8 patients per group.	(95% CI: NR; p=NR) **Currency & cost year:** 2011 Euros[(b)] **Cost components incorporated:** Staff running the intervention, emergency services (total days), inpatient admissions (total days), outpatient healthcare services (total visits to GP, nurse, social worker, psychologist, and other community healthcare professionals), diagnostic tests, medications. Indirect costs of lost productivity also included but are reported separately and can be excluded from results reported here.	(95% CI: NR; p=NR)	**Analysis of uncertainty:** 1,000 bootstrap replications. Sensitivity analysis: • Intention to treat analysis. Where missing data was imputed. • Per protocol analysis where excluded 14 patients who did not attend the 9 sessions. Both of these analyses also showed CBT remained dominant.
Data sources				
Health outcomes: Clinical outcomes based on the Alda 2011 trial[6] included in the clinical review. Note there is a third arm of drug treatment but that is not a relevant comparator in this review and has not been included here. The clinical trial says 10 sessions of the intervention but the economic evaluation says 9. Certain analgesics were not allowed in the CBT group so as to assess the effect of CBT alone. Treatment as usual group were treated based on GP's having a guide on the treatment of fibromyalgia in primary care, and got some exercise counselling, but no psychological intervention. **Quality-of-life weights:** Spanish version of EQ-5D used as an outcome in the trial. **Cost sources:** Resource use collected from self-reports from the patient using a questionnaire. Medication costs were from the Vademecum international (Red book edition 2011) and included value added tax. Medical tests and service use cost was from the SOIKOS database of heath care costs which contains information about the Spanish healthcare service costs and is derived by systematic review of the literature. The cost of the intervention was based on the price per hour of a clinical psychologist established by the Official College of Psychologists of Spain.				
Comments				
Source of funding: Spanish Ministry of Health. **Limitations:** Non-UK cost perspective. Drug costs include VAT, UK costs wouldn't. Based on one trial. Self-reported resource use. Only minor medication was allowed to be continued in the CBT arm so it is not in addition to usual care and therefore costs of				

CBT arm might be underestimated without medication. **Other:** Incremental marginal costs and incremental effects were estimated using the seemingly unrelated regression model (SUR). The regression controlled for the following variables at baseline; age gender, marital status, education level, living arrangement, employment status, minimum wage, duration of illness, baseline costs and outcomes. The complete case data analysis used in the base case was missing 16 people who could not be followed up at 6 months.

Overall applicability: Partially applicable(c) **Overall quality: Potentially serious limitations**(d)

Abbreviations: 95% CI= 95% confidence interval; CUA= cost–utility analysis; da= deterministic analysis; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER= incremental cost-effectiveness ratio; NR= not reported; pa= probabilistic analysis; QALYs= quality-adjusted life years.

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2011 purchasing power parities[442]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Study	**Luciano et al 2017** [290]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design: RCT** Within-trial analysis **Approach to analysis:** EQ-5D data collected and combined with unit costs applied to resource use. **Perspective:** Spanish healthcare **Time horizon/Follow-up**: 6 Months	**Population:** People aged 18-65 years with fibromyalgia with no pharmacological or psychological treatment during the previous year. **Cohort settings:** N: 156 **Intervention 1:** Waiting list - no active treatment and offered preferred intervention at study conclusion **Intervention 2:** Group acceptance and commitment therapy	**Total costs (mean per patient, complete case analysis):** Intervention 1: £2,597 Intervention 2: £869 Incremental (2−1) (adjusted bootstrapped estimates): -£1,897 (95% CI: £-2,996--£801; p=NR) **Currency & cost year:** 2014 Spanish Euros (c) **Cost components incorporated:** All direct healthcare costs; medication, medical test, use of health-related	**QALYs (mean per patient, complete case analysis):** Intervention 1: 0.28 Intervention 2: 0.34 Incremental (2−1) (adjusted bootstrapped estimates): 0.05 (95% CI: 0.04-0.07; p=NR)	**ICER (Intervention 2 versus Intervention 1):** GACT dominant 95% CI: NR Probability Intervention 2 cost effective (£20K/30K threshold): NR **Analysis of uncertainty:** Regression model was bootstrapped with 1000 replications. Sensitivity analyses: • Intention to treat (imputing outcomes) • Per protocol analysis (excluding patients who didn't attend the sessions) Both of these analyses also showed GACT remained dominant.

Treatment effect duration:[(a)] 6 months **Discounting:** n/a	(GACT), 8 x 2.5 hour weekly group sessions; 10-15 patients; covering exercises and topics within the context of ACT practice and training; including various types of formal mindfulness practice; daily homework assignments of 15-30 minutes; led by a clinical psychologist . Duration 8 weeks	services (emergency services, inpatient admissions, outpatient services), and cost of the staff running the GACT intervention. The paper also includes Spanish government perspective which includes indirect healthcare costs such as lost productivity costs, but this is reported separately and can be excluded from results reported here.		

Data sources

Health outcomes: Based on the EFFIGACT trial[291]. **Quality-of-life weights:** EQ-5D-3L Spanish tariff. **Cost sources:** Medication costs were from Vademecum international (red book; edition 2014), unit cost data for medical tests and health services was the SOIKOS database of health care costs, this database contains Spanish healthcare costs derived from systematic literature. Costs of the GACT was from the Official College of Psychologist of Spain, with cost of sessions resources assumed to be consistent across all sessions and groups but number of participants attending each sessions varied, and so intervention costs were dependent on number of sessions attended by each patient. Incremental costs and effects were estimated with unrelated regression models, whereby costs and QALYs were predicted based on assignment to each intervention, and controlling for variables such as age, gender, education level and baseline costs and outcomes depending on equation considered, and bootstrapped using 1000 replications. Imputation of missing data for intention to treat analysis based on chained equations to impute EQ-5D data and costs of non-responders.

Comments

Source of funding: Intituto de Salud Carlos III through the network for prevention and health promotion in primary care. **Limitations:** Non UK. Drug costs include VAT, UK costs wouldn't. Based on one trial. Self-reported resource use. Co-medication not allowed in ACT arm so it is not in addition to usual care and therefore costs of ACT arm might be underestimated without medication. **Other:**

Overall applicability:[(c)] Partially applicable **Overall quality:**[(d)] Potentially serious limitations

Abbreviations: CUA= cost–utility analysis; da= deterministic analysis; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER= incremental cost-effectiveness ratio; NR= not reported; QALYs= quality-adjusted life years; RCT= Randomised control trial

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. Intervention was 8 weeks long but study had a time horizon of 6 months. Treatment effect could have continued beyond intervention if people continue to use the techniques learnt.

(b) Converted using 2014 purchasing power parities[442]

(c) Directly applicable / Partially applicable / Not applicable
(d) Minor limitations / Potentially serious limitations / Very serious limitations

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 50: Studies excluded from the clinical review

Study	Exclusion reason
Abrahamsen 2008[1]	Inappropriate comparison
Abrahamsen 2009[2]	Inappropriate comparison
Adachi 2014[3]	Systematic review is not relevant to review question or unclear PICO
Aggarwal 2010[4]	Systematic review is not relevant to review question or unclear PICO
Alberts 2018[5]	Not review population
Alonso 2013[8]	Not review population
Alparslan 2016[9]	Incorrect interventions. music therapy
Alvarez-nemegyei 2007[10]	Article not in English
Amris 2014[13]	Incorrect interventions
Anderson 2018 [16]	Systematic review is not relevant to review question or unclear PICO
Andersson 2012[17]	Not review population
Ang 2013[19]	Incorrect interventions. all received exercise sessions and purpose of the intervention is to increase exercise participation
Anonymous 1996[20]	Incorrect study design
Anonymous 2011[21]	Erratum
Anonymous 2012[22]	Erratum
Anvari 2014[23]	Article not in English
Aragones 2019 [25]	Incorrect interventions
Ardigo 2016[26]	Inappropriate comparison
Astin 2003[27]	Incorrect interventions
Baad-hansen 2013[28]	No relevant outcomes
Baker 2018[31]	Not review population
Bakker 1995[32]	No relevant outcomes
Bakker 1995[33]	No relevant outcomes
Ball 2017[35]	Systematic review is not relevant to review question or unclear PICO
Ball 2018[34]	Study protocol
Barefoot 2012[36]	Not review population
Bassett 1985[37]	Unclear population ('chronic pain' no further details)
Baumuller 2009[39]	Not available (thesis)
Bawa 2015[40]	Systematic review is not relevant to review question or unclear PICO
Bennett 2011[42]	Systematic review is not relevant to review question or unclear PICO
Bergdahl 1995[43]	Inappropriate comparison
Berglund 2018 [45]	No relevant outcomes; not guideline condition
Berman 2009[46]	Not review population

Study	Exclusion reason
Bernardy 2011[47]	Systematic review is not relevant to review question or unclear PICO
Bernardy 2018[48]	Systematic review is not relevant to review question or unclear PICO
Bernardy 2019 [49]	Systematic review is not relevant to review question or unclear PICO. duplicate
Berry 2014[50]	Unclear population
Berry 2015[51]	Not review population
Bhimani 2017[52]	Study protocol
Bissett 1985[53]	Not review population
Bland 2010[54]	Editorial
Blodt 2014[55]	Study protocol
Boersma 2019 [56]	Inappropriate comparison
Bohra 2013[57]	Systematic review is not relevant to review question or unclear PICO
Bonnert 2019 [58]	Not review population
Bosch romero 2002[59]	Article not in English
Bourgault 2015[60]	Incorrect interventions
Bowering 2013[61]	Systematic review is not relevant to review question or unclear PICO
Boyle 1994[62]	Non-randomised study
Braden 2016[63]	Not review population
Brattberg 2006[64]	Not review population
Bravo 2019 [65]	Incorrect interventions
Brooke 1983[66]	Inappropriate comparison
Brotto 2015[67]	Non-randomised study
Brotto 2019 [68]	Not all participants were randomised
Brown 2013[69]	Incorrect interventions
Buchanan 2002[70]	Incorrect study design
Buckelew 1998[71]	Incorrect interventions
Buhrman 2004[72]	Not review population
Buhrman 2011[74]	Not review population
Buhrman 2013[75]	Inappropriate comparison
Buhrman 2013[73]	Inappropriate comparison
Buhrman 2015[76]	Not review population
Burckhardt 1994[78]	Incorrect interventions
Burckhardt 2005[77]	Literature review
Burgstaller 2014[79]	Systematic review is not relevant to review question or unclear PICO
Burns 2015[80]	Not review population
Busch 2011[81]	Not review population
Cadth 2013[82]	Incorrect study design
Cantero-braojos 2019 [83]	Article not in English
Carleton 2011[85]	Incorrect intervention
Carleton 2019 [84]	Incorrect intervention
Carmody 2013[86]	Not review population
Carnes 2013[87]	Not review population

Study	Exclusion reason
Carrico 2008[88]	No extractable outcomes
Carroll 1998[89]	Systematic review is not relevant to review question or unclear PICO
Carville 2008[90]	incorrect study design
Cash 2015[91]	Incorrect interventions
Castel 2007[93]	Incorrect interventions
Castillo-bueno 2010[95]	Systematic review protocol
Cederbom 2014[99]	Incorrect interventions
Cederbom 2017[97]	Incorrect interventions
Cederbom 2019 [98]	Incorrect intervention. Not review population
Cedraschi 2004[100]	Incorrect interventions
Chadi 2016[101]	Not review population
Champaneria 2012[102]	Systematic review is not relevant to review question or unclear PICO
Chang 2015[103]	Not available
Chavooshi 2016[104]	Letter
Chen 2010[105]	Not review population
Cherkin 2014[106]	Not review population
Chiauzzi 2010[107]	Not review population
Chiesa 2011[108]	Systematic review is not relevant to review question or unclear PICO
Christiansen 2010[109]	Not review population
Cook 1998[110]	Not review population
Corrado 1999[111]	Unclear population ('chronic pain' no further details)
Corrado 2003[112]	Unclear population ('chronic pain' no further details)
Cossins 2013[113]	Incorrect interventions
Cour 2015[114]	Incorrect interventions
Crawford 2014[115]	Systematic review: methods are not adequate/unclear
Currie 2000[116]	Not review population
Cusens 2010[119]	Not review population
Dahl 2004[120]	Unclear population
Dalen 1986[121]	Not review population
Davis 2013[122]	No extractable outcome data
Day 2011[123]	Incorrect study design
De 1999[126]	Inappropriate comparison
De Barros Pascoal 2019 [124]	Incorrect study design (non-randomised)
De boer 2014[125]	Inappropriate comparison
De jong 2016[127]	Not review population
De jong 2018[128]	Not review population
Dear 2013[131]	Not review population
Dear 2015[130]	Not review population
Dear 2017[129]	Unclear population (mixed chronic pain, location but not causes reported)
Den hollander 2016[132]	Inappropriate comparison
Dionne 2013[134]	Article not in English
Dohrmann 1976[135]	Study abstract

Study	Exclusion reason
Dowd 2015[136]	Not review population
Drks 2018 [137]	Trial registry record
Duggan 2015[138]	Not review population
Dura-ferrandis 2017[139]	No relevant outcomes
Dworkin 1994[141]	Incorrect interventions
Dworkin 2002[140]	Incorrect interventions
Eccleston 2014[142]	Systematic review is not relevant to review question or unclear PICO
Eccleston 2014[144]	Systematic review is not relevant to review question or unclear PICO
Eccleston 2017[143]	Systematic review is not relevant to review question or unclear PICO
Edelson 1989[145]	Incorrect study design (non-randomised)
Elbers 2018[147]	Systematic review is not relevant to review question or unclear PICO
Ersek 2003[150]	Not review population
Ersek 2004[148]	Incorrect interventions
Ersek 2008[149]	Inappropriate comparison
Esler 2003[151]	Not review population
Estergard 2009[152]	Not available (thesis)
Eyer 2016[153]	Study protocol
Falcao 2008[154]	Inappropriate comparison
Fales 2015[155]	Not review population
Feliu-soler 2016[156]	Study protocol
Fernandez 2008[157]	Incorrect interventions
Ferrando 2012[158]	Not review population
Ferrari 2006[159]	Article not in English
Flor 1993[160]	Not review population
Forbes 2020 [161]	Unclear population (chronic pelvic pain with identifiable or unidentifiable cause with no further detail)
Fors 2002[162]	Inappropriate comparison
Franco 2018[163]	Systematic review is not relevant to review question or unclear PICO
Gale 2002[167]	Not review population
Gallagher 2013[168]	Incorrect interventions. unclear population
Garaigordobil 2016[169]	Inappropriate comparison
Garcia 2006[172]	No relevant outcomes
Garcia-palacios 2015[171]	Incorrect interventions
Gardner-nix 2008[173]	Study design (non-randomised)
Gardner-nix 2014[174]	Not review population
Garland 2013[177]	Not review population
Garland 2014[179]	Not review population
Garland 2014[178]	Not review population
Garland 2015[175]	Not review population
Garland 2019 [176]	No extractable outcome data
Garmon 2014[180]	Systematic review is not relevant to review question or unclear PICO

Study	Exclusion reason
Geneen 2015[181]	Systematic review is not relevant to review question or unclear PICO
Gerhardt 2016[182]	Not review population
Glombiewski 2010[184]	Not review population
Glombiewski 2010[185]	Systematic review is not relevant to review question or unclear PICO
Glombiewski 2013[183]	Systematic review is not relevant to review question or unclear PICO
Goldenberg 1994[186]	Incorrect study design
Gomez-perez 2018 [188]	Study protocol
Goossens 1996[189]	Incorrect interventions
Green 2009[190]	Incorrect study design
Grondahl 2008[191]	No relevant outcomes
Gross 2012[192]	Systematic review is not relevant to review question or unclear PICO
Grossman 2017[193]	No relevant outcomes
Guarino 2018[194]	Not review population. unclear population
Guillet 2019 [195]	Incorrect interventions
Gustavsson 2006[196]	no extractable outcomes
Hadhazy 2000[197]	Systematic review is not relevant to review question or unclear PICO
Haines 2009[199]	Systematic review is not relevant to review question or unclear PICO
Haines 2009[198]	Systematic review is not relevant to review question or unclear PICO
Haldorsen 1998[200]	Incorrect interventions
Hann 2014[202]	Systematic review is not relevant to review question or unclear PICO
Hartwich-tersek 2008[203]	Article not in English
Hatchard 2014[204]	Review protocol
Haugli 2000[205]	Incorrect interventions
Haugli 2001[206]	Incorrect interventions
Haugli 2003[207]	Incorrect interventions
Haugmark 2019 [208]	Systematic review is not relevant to review question or unclear PICO
Haugstad 2006[209]	Incorrect interventions
Haugstad 2008[210]	Incorrect interventions
Hauser-Ulrich 2020 [211]	Not review population
Hayes 2014[212]	study protocol
Heapy 2015[213]	Systematic review is not relevant to review question or unclear PICO
Heapy 2017[214]	Inappropriate comparison
Henriksson 2016[217]	Not review population. (Not chronic primary pain)
Herbert 2017[218]	Not review population
Hijzen 1986[219]	No relevant outcomes
Hilton 2017[220]	Systematic review is not relevant to review question or unclear PICO
Howarth 2016[221]	Study protocol

Study	Exclusion reason
Howarth 2019 [222]	Not review population
Hsu 2010[223]	Incorrect interventions
Hughes 2017[224]	Systematic review is not relevant to review question or unclear PICO
Hutting 2013[226]	Study protocol
Hutting 2015[225]	Incorrect interventions
Igna 2011[227]	Not available
Igna 2014[228]	Not review population. unclear population
Iwasaki 2018[229]	Systematic review is not relevant to review question or unclear PICO
Jackson 2019 [230]	Systematic review is not relevant to review question or unclear PICO
Jamison 2010[231]	Not review population
Jensen 2001[232]	Not review population
Jeon 2014[234]	Incorrect interventions
Jerjes 2007[235]	Not review population
Johnston 2010[236]	Not review population. unclear population
Jonbozorgi 2013[237]	Article not in English
Jones 2006[238]	Not review population
Jprn 2018 [239]	Trial registry record
Jungquist 2010[240]	Not review population
Jungquist 2012[241]	Not review population
Kabat-zinn 1985[242]	Incorrect study design
Kanter 2016[243]	Incorrect interventions
Kanzler 2018[244]	Study protocol
Kayiran 2010[246]	Inappropriate comparison
Kerns 2014[249]	Not review population
Kerns jr 1985[248]	Not review population
Khazraee 2018 [250]	Not review population
Khoo 2019 [251]	Systematic review is not relevant to review question or unclear PICO
King 2002[252]	Inappropriate comparison
King 2002[253]	No relevant outcomes
Kisely 2015[254]	Systematic review is not relevant to review question or unclear PICO
Klimes 1990[255]	No useable outcomes
Kollner 2012[256]	Article not in English
Kristjánsdóttir ó 2013[257]	Incorrect interventions
Kroenke 2013[258]	Commentary
Kwok 2016[259]	Incorrect interventions
Lami 2013[261]	Systematic review is not relevant to review question or unclear PICO
Large 1983[262]	incorrect study design
Lauche 2013[263]	Systematic review is not relevant to review question or unclear PICO
Lauche 2016[264]	Inappropriate comparison

Study	Exclusion reason
Lee 2014[267]	Systematic review is not relevant to review question or unclear PICO
Lee 2014[266]	Systematic review is not relevant to review question or unclear PICO
Lee 2018 [268]	Incorrect study design (non-randomised)
Lefort 1998[269]	Incorrect population
Leung 2015[270]	Review protocol
Lewandowski 2004[271]	Not review population
Liedl 2011[272]	Retracted paper. Not review population
Liegl 2016[273]	Systematic review is not relevant to review question or unclear PICO
Lin 2010[277]	Inappropriate comparison
Lin 2015[275]	Study protocol
Lin 2017[276]	Not review population
Lin 2018[274]	Not available
Linden 2014[278]	Not review population
Linton 1983[281]	Not review population. unclear population
Linton 1984[279]	Not review population
Linton 1985[282]	Not review population
Linton 1997[280]	Not review population. unclear population
Litt 2009[284]	Inappropriate comparison
Litt 2010[285]	Inappropriate comparison
Litt 2013[283]	Inappropriate comparison
Lorig 2002[286]	Not review population
Louw 2011[287]	Systematic review is not relevant to review question or unclear PICO
Louw 2016[288]	Systematic review is not relevant to review question or unclear PICO
Luciano 2011[292]	Incorrect interventions
Luciano 2013[293]	Incorrect interventions
Lunde 2009[295]	Systematic review is not relevant to review question or unclear PICO
Macea 2010[296]	Systematic review is not relevant to review question or unclear PICO
Malfliet 2018[297]	Not review population
Martinez-valero 2008[298]	No extractable outcomes
Mawani 2014[301]	Not review population
Mayou 1989[302]	Study abstract
Mayou 1997[303]	Inappropriate comparison
Mcclintock 2019 [305]	Systematic review is not relevant to review question or unclear PICO
Mccracken 2002[308]	Incorrect study design
Mccracken 2013[306]	Not review population
Mccracken 2014[307]	Not review population
Mccrae 2018 [309]	No relevant outcomes (subset of participants from McCrae 2018 with MRI outcomes)
Mccrae 2019 [311]	Duplicate

Study	Exclusion reason
Mendez-rebolledo 2017[312]	Systematic review is not relevant to review question or unclear PICO
Menga 2014[313]	Inappropriate comparison. unclear comparator (online educational information about FM, no further details)
Mertens 2013[316]	Study protocol
Miller 2013[317]	Not review population
Minelli 2012[318]	Systematic review is not relevant to review question or unclear PICO
Mishra 2000[320]	Not review population
Miziara 2009[321]	Inappropriate comparison
Molinari 2018 [322]	Incorrect interventions
Montero-marin 2018 [323]	Incorrect interventions
Monticone 2015[324]	Systematic review is not relevant to review question or unclear PICO
Moore 2000[325]	Not review population
Morales-fernandez 2016[326]	Study protocol
Moseley 2004[327]	Incorrect interventions
Mourad 2016[328]	Not review population
Mulder 2019 [329]	Not guideline condition
Mundt 2016[330]	No useable outcomes
Musekamp 2016[332]	Study protocol
Musekamp 2019 [331]	Inappropriate comparison
Myers 2002[333]	Systematic review is not relevant to review question or unclear PICO
Naylor 2008[335]	Not review population. unclear population
Naylor 2010[336]	Not review population
Nct 2000[337]	web page citation only
Nct 2001[338]	web page citation only
Nct 2003[339]	web page citation only
Nct 2003[340]	web page citation only
Nct 2004[341]	web page citation only
Nct 2005[342]	web page citation only
Nct 2005[343]	web page citation only
Nct 2005[344]	web page citation only
Nct 2006[345]	web page citation only
Nct 2006[347]	web page citation only
Nct 2006[346]	web page citation only
Nct 2007[348]	web page citation only
Nct 2007[349]	web page citation only
Nct 2007[350]	web page citation only
Nct 2008[351]	web page citation only
Nct 2008[352]	web page citation only
Nct 2008[353]	web page citation only
Nct 2008[354]	web page citation only
Nct 2008[355]	web page citation only
Nct 2009[356]	web page citation only
Nct 2010[359]	web page citation only

Study	Exclusion reason
Nct 2010[357]	web page citation only
Nct 2010[358]	web page citation only
Nct 2011[360]	web page citation only
Nct 2011[361]	web page citation only
Nct 2011[362]	web page citation only
Nct 2011[363]	web page citation only
Nct 2011[364]	web page citation only
Nct 2012[365]	web page citation only
Nct 2012[366]	web page citation only
Nct 2012[368]	web page citation only
Nct 2012[367]	web page citation only
Nct 2012[369]	web page citation only
Nct 2012[370]	web page citation only
Nct 2013[371]	web page citation only
Nct 2013[431]	web page citation only
Nct 2014[373]	web page citation only
Nct 2014[375]	web page citation only
Nct 2014[376]	web page citation only
Nct 2014[377]	web page citation only
Nct 2014[372]	web page citation only
Nct 2014[374]	web page citation only
Nct 2015[378]	web page citation only
Nct 2015[379]	web page citation only
Nct 2015[380]	web page citation only
Nct 2015[381]	web page citation only
Nct 2015[382]	web page citation only
Nct 2015[383]	web page citation only
Nct 2015[384]	web page citation only
Nct 2016[385]	web page citation only
Nct 2016[388]	web page citation only
Nct 2016[389]	web page citation only
Nct 2016[390]	web page citation only
Nct 2016[391]	web page citation only
Nct 2016[392]	web page citation only
Nct 2016[393]	web page citation only
Nct 2016[395]	web page citation only
Nct 2016[394]	web page citation only
Nct 2016[396]	web page citation only
Nct 2016[397]	web page citation only
Nct 2016[398]	web page citation only
Nct 2016[399]	web page citation only
Nct 2016[386]	web page citation only
Nct 2016[387]	web page citation only
Nct 2017[400]	web page citation only
Nct 2017[401]	web page citation only

Study	Exclusion reason
Nct 2017[402]	web page citation only
Nct 2017[403]	web page citation only
Nct 2017[404]	web page citation only
Nct 2017[405]	web page citation only
Nct 2017[406]	web page citation only
Nct 2017[407]	web page citation only
Nct 2017[408]	web page citation only
Nct 2017[409]	web page citation only
Nct 2017[410]	web page citation only
Nct 2017[411]	web page citation only
Nct 2017[414]	web page citation only
Nct 2017[415]	web page citation only
Nct 2017[412]	web page citation only
Nct 2017[413]	web page citation only
Nct 2018[417]	web page citation only
Nct 2018[418]	web page citation only
Nct 2018[421]	web page citation only
Nct 2018[422]	web page citation only
Nct 2018[424]	web page citation only
Nct 2018[425]	web page citation only
Nct 2018[426]	web page citation only
Nct 2018[427]	web page citation only
Nct 2018[429]	web page citation only
Nct 2018[430]	web page citation only
Nct 2018[416]	web page citation only
Nct 2018[420]	web page citation only
Nct 2018[423]	web page citation only
Nct 2018[428]	web page citation only
Nct 2018[419]	web page citation only
Nicassio 1997[432]	Incorrect interventions
Nicholas 2013[433]	Not review population
Nicholas 2017[434]	Not review population
Niknejad 2018[435]	Systematic review is not relevant to review question or unclear PICO
Oakley 1994[436]	Incorrect study design
Olason 2018[437]	Not review population
Oliver 2001[438]	Incorrect interventions
Olson 1987[439]	Inappropriate comparison
Onieva-zafra 2015[440]	Inappropriate comparison
Onieva-zafra 2019 [441]	Inappropriate comparison
Paganini 2019 [443]	Not review population
Palsson 2006[444]	Commentary
Peniston 1985[446]	Not review population
Pereira pernambuco 2018 [447]	Incorrect interventions
Perez-Aranda 2019 [449]	Incorrect interventions
Perez-Aranda 2019 [448]	Incorrect interventions

Study	Exclusion reason
Persson 2008[450]	Systematic review is not relevant to review question or unclear PICO
Pervane vural 2016[451]	Not review population
Philips 1987[454]	Not review population
Pigeon 2012[456]	Not review population. unclear population
Pike 2016[457]	Systematic review is not relevant to review question or unclear PICO
Plews-ogan 2005[458]	No useable outcomes
Plumb vilardaga 2012[459]	Not review population
Plumbe 2016[460]	Withdrawn Cochrane review
Poirier-bisson 2013[461]	Incorrect study design
Posadzki 2011[462]	Systematic review is not relevant to review question or unclear PICO
Posadzki 2012[463]	Systematic review is not relevant to review question or unclear PICO
Potts 1999[464]	Incorrect interventions
Puder 1988[465]	Not review population
Racine 2018 [466]	Inappropriate comparison
Raftery 2013[467]	Study protocol
Ramke 2016[468]	Not review population
Ray 2002[469]	Incorrect study design
Rochester 2011[470]	Study protocol
Rogers 1989[471]	Incorrect study design
Roldan-barraza 2014[472]	Systematic review is not relevant to review question or unclear PICO
Rucco 1995[473]	Not available
Ruehlman 2012[474]	Not review population
Rutten-van molken 1994[475]	No relevant outcomes
Sagula 1999[476]	Not available
Sander 2017[478]	Study protocol
Santoro 2014[479]	Systematic review is not relevant to review question or unclear PICO
Scheidt 2014[481]	Erratum
Schmidt 2011[482]	Incorrect interventions
Schofield 1998[484]	Inappropriate comparison
Schofield 1998[486]	Inappropriate comparison
Schofield 2000[485]	Inappropriate comparison
Schofield 2002[483]	Inappropriate comparison
Schroeder 2020 [487]	Not review population
Schultz 2018 [488]	Incorrect interventions
Scott 2018 [489]	Not review population
Sephton 2007[490]	Incorrect interventions
Shennan 2009[491]	Abstract
Sherman 1997[492]	Intervention: single 30 minute session
Sielski 2017[493]	Systematic review is not relevant to review question or unclear PICO

Study	Exclusion reason
Simpson 2017[495]	Systematic review is not relevant to review question or unclear PICO
Slattery 2019 [496]	Study protocol
Sleptsova 2013[497]	Inappropriate comparison
Smallwood 2016[498]	Not review population
Smith 2014[499]	Guideline summary
Spaeth 2006[501]	Incorrect study design
Spence 1989[502]	Not review population
Spence 1991[503]	Not review population
Steen 2000[504]	Incorrect study design
Steiner 2013[505]	No relevant outcomes
Steiro 2012[506]	Not available
Stenn 1979[507]	Incorrect study design
Stones 2000[508]	Withdrawn
Stuifbergen 2010[509]	Incorrect interventions
Stuve 2015[510]	Not review population
Subramanian 1988[511]	Not review population
Tang 2012[512]	Not review population. unclear population
Tang 2020 [513]	No useable outcome data
Taylor 2016[514]	Not guideline condition
Tefft 2016[515]	Systematic review is not relevant to review question or unclear PICO
Ter kuile 2006[516]	Incorrect study design
Tesarz 2013[517]	Study protocol
Tesarz 2014[518]	Systematic review is not relevant to review question or unclear PICO
Theadom 2015[519]	Systematic review is not relevant to review question or unclear PICO
Thieme 2003[521]	Inappropriate comparison
Thieme 2016[523]	No relevant outcomes
Thompson 2019 [524]	Systematic review is not relevant to review question or unclear PICO
Thorn 2007[525]	incorrect study design
Thorn 2011[526]	Not review population
Thorn 2018[527]	Not review population
Thorsell 2011[528]	Not review population. unclear population
Timmerman 2016[529]	Not review population
Tomas-carus 2018 [530]	No description of 'control' condition
Tomas-carus 2019 [531]	No extractable outcome data
Trompetter 2015[534]	Not review population
Trompetter 2015[532]	Not review population
Trompetter 2016[533]	Not review population
Turner 2005[537]	Incorrect interventions
Turner 2018[536]	Not review population
Turner 2018[535]	Not review population
Tyrer 2015[539]	Study protocol
Tyrer 2017[540]	Not review population

Study	Exclusion reason
Ussher 2014[541]	Not review population
Vallejo 2015[542]	No relevant outcomes
Van der maas 2015[544]	Incorrect interventions
Van der maas 2016[543]	No relevant outcomes
Van Dyke 2019 [545]	Not review population. unclear population
Van gordon 2017[546]	Inappropriate comparison
Van ittersum 2014[547]	Inappropriate comparison
Van oosterwijck 2013[548]	Inappropriate comparison
Van peski-oosterbaan 1999[550]	Duplicate
Vanbuskirk 2014[552]	Not review population
Veehof 2016[553]	Systematic review is not relevant to review question or unclear PICO
Verkaik 2014[554]	Inappropriate comparison
Vieira 2018 [555]	Trial registry record
Vlaeyen 1996[557]	Incorrect interventions
Wang 2018[558]	Inappropriate comparison
Watson 2019 [559]	Systematic review is not relevant to review question or unclear PICO
Weissbecker 2002[560]	No relevant outcomes
Wetherell 2011[561]	Not review population
Wetherell 2016[562]	Not review population
Whitney 2014[563]	Incorrect study design
Wigers 1996[565]	Incorrect interventions
Williams 1996[566]	Comment
Williams 2002[569]	No relevant outcomes
Williams 2006[568]	Synopsis
Williams 2012[567]	Systematic review is not relevant to review question or unclear PICO
Wilson 2015[572]	Not review population
Wilson 2018[571]	Not review population
Winocur 2002[573]	Incorrect study design
Winstead 2020 [574]	Unclear population (unclear if chronic primary pain)
Wong 2009[576]	Systematic review is not relevant to review question or unclear PICO
Wong chi 2011[575]	Not review population
Yarns 2020 [578]	Not review population
Zangi 2017[579]	Incorrect study design
Zech 2017[580]	Systematic review is not relevant to review question or unclear PICO

I.2 Excluded health economic studies

Studies that meet the review protocol population and interventions, and the economic study inclusion criteria but have not been included in the review based on applicability and/or methodological quality are summarised below with reasons for exclusion.

Table 51: Studies excluded from the health economic review

Reference	Reason for exclusion
Kemani 2015[247]	This study was assessed as partially applicable with very serious limitations. This study had methodological limitations (such as the post treatment bootstrapped incremental cost seeming very different to the crude mean (by about $2,000), and there was a large amount of imputed data in cost effectiveness analysis (32.8%)). The committee therefore judged that other available evidence was of greater applicability and methodological quality and therefore this study was selectively excluded.
McBeth 2012[304]	This study was assessed as partially applicable with potentially serious limitations. The committee judged that other available evidence was of greater applicability and methodological quality and therefore this study was selectively excluded. This is the same study as the included economic evaluation but has shorter follow up period.
Hedman-Lagerlof 2019 [216]	This study was assessed as partially applicable with very serious limitations. This study had methodological limitations (such as how the incremental costs were calculated is potentially unclear and the time horizon is also unclear). The committee therefore judged that other available evidence was of greater applicability and methodological quality and therefore this study was selectively excluded.

Appendix J: Research recommendations

J.1 Mindfulness

Research question: What is the clinical and cost effectiveness of mindfulness therapy for managing chronic primary pain in people aged 16 years and over?

Why this is important:

Chronic primary pain is a common disorder with substantial personal and societal impact. Mindfulness therapy is sometimes offered as part of pain management programmes or as stand-alone treatment. There is some evidence for benefits of mindfulness therapy in people with pain, but the best way to deliver mindfulness therapy, and the clinical and cost effectiveness of mindfulness therapy in people with chronic primary pain remain uncertain.

In the review of evidence for the use of mindfulness in the treatment of chronic primary pain the committee found weak evidence for benefits of mindfulness meditation on psychological distress and quality of life, however there was no cost-effectiveness data available. The clinical experience of the committee was that as Mindfulness Meditation is a widely available treatment with perceived limited harms, often taught and practiced within local communities or NHS environments, with a developing evidence base suggesting positive involvement in neuroplasticity, it is important to better understand its role in chronic primary pain.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults with chronic primary pain Intervention(s): mindfulness training Comparison: group treatment vs individual treatment vs usual care. Outcome(s): Sleep, Pain, Health related quality of Life, Physical Function, Psychological Distress, Use of healthcare services, Medication Use.
Importance to patients or the population	Mindfulness therapy is well tolerated and likely to be acceptable. It is also implicated in pain research studying neuroplasticity, and the potential effect of reducing central nervous system sensitisation and pain.
Relevance to NICE guidance	To understand whether to offer mindfulness therapy as a stand-alone intervention, alongside other interventions, or not at all would inform future updates of this guideline.
Relevance to the NHS	Mindfulness therapy is sometimes offered as a stand-alone treatment or in combination with other therapies. Better understanding of the effectiveness of mindfulness therapy will allow the most rational use of it. If shown to be cost-effective, it will be an intervention that can be delivered in the NHS without major investment. Conversely, if shown not to be cost effective, discontinuing could free resources for other more effective treatments.
National priorities	None
Current evidence base	Current evidence is limited by poor quality and low numbers of participants. A weak signal exists for improvements in psychological distress and quality of life.
Equality	No relevance to protected characteristics as defined in the Equality Act.
Study design	Adequately powered randomised controlled trial(s) in population of adults with chronic primary pain from a range of diagnostic subgroups. Mindfulness therapy should be considered as stand-alone and in combination with other treatments. Effect of time-limited vs ongoing intervention should be assessed. Use of specialist vs non-specialist staff to deliver. Will need post intervention follow up of adequate duration – 12 months is reasonable.

Feasibility	Feasible – population easy to access and studies do not require special equipment to deliver. Main costs will be staff time and training. Large studies will be needed in assessing mindfulness as a stand-alone intervention in this population (as distinct from mindfulness offered within other treatment modalities, for example pain management programmes).
Other comments	Mindfulness therapy is already part of the NHS armamentarium for people with chronic primary pain, and its utility needs better stablishing. Mindfulness therapy may form part of a pain management programme and therefore its effectiveness in combination with other treatments would be of benefit to help inform the design of such programmes.
Importance	High: the research is essential to inform future updates of key recommendations in the guideline.

J.2 CBT for insomnia

Research question: What is the clinical and cost effectiveness of Cognitive Behavioural Therapy for insomnia or hybrid Cognitive Behaviour Therapy for Insomnia and pain for the management of chronic primary pain in people aged 16 years and over?

Why this is important:

Many people who have chronic primary pain report difficulties with sleeping which affect their quality of life. Insomnia is the most common form of sleep disturbance. There are reciprocal relationships between sleep disturbance and pain which suggest that sleep disturbance can be both a consequence and a factor contributing to the development and maintenance of persistent pain.

The effectiveness of non-pharmacological interventions for primary insomnia (such as Cognitive Behaviour Therapy CBT-I) is well established. Non-pharmacological interventions are favoured over medications both because of sustained treatments effects and the lack of side effects. However insomnia co-morbid with persistent pain is overlooked as a target for intervention and non-pharmacological treatments for co-morbid insomnia are not widely available currently.

CBT-I has been trialled in for insomnia co-morbid with persistent pain conditions, both as a stand-alone treatment and in hybrid forms with CBT for pain (hybrid CBT-I/P). There are promising results for improved sleep and function, but the impact on pain outcomes is inconsistent. Identifying the impact of these treatments on pain outcomes may require studies with a lengthy follow-up period. Establishing the effectiveness and cost effectiveness of interventions for insomnia co-morbid with chronic primary pain may improve the quality of life of people with both pain and insomnia.

This research recommendation has been written to guide the design of studies so that the evidence generated is of sufficient, high quality for inclusion in future guidance.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults with chronic primary pain and insomnia Intervention(s): Cognitive Behaviour Therapy for Insomnia and Hybrid Cognitive Behaviour Therapy for Insomnia and Pain Comparison: Usual Care or attention control. Each other. Outcome(s): Sleep outcomes, Pain, Pain Interference, Health related quality of Life, Physical Function, Psychological Distress, Use of healthcare services, Medication Use.

Importance to patients or the population	Sleep disturbance is a common and distressing problem for people with chronic primary pain. Pharmacological approaches are the main treatment available currently. The identification of benefit from CBT for insomnia would be a new treatment approach which could potentially improve quality of life for people with insomnia co-morbid with chronic primary pain, in the context of a paucity of other effective treatments.
Relevance to NICE guidance	Further high quality research in this area would generate new evidence and may enable future updates of this guidance to make recommendations on the use of CBT-I and hybrid CBT-I/P for the management of insomnia co-morbid with chronic primary pain. If studies investigate different methods of delivering the treatment then it may be possible to make recommendations regarding method and/or intensity and/or delivery methods for the intervention.
Relevance to the NHS	CBT-I and hybrid CBT-I/P are not currently widely available on the NHS. Any impact on future service delivery or finances is dependent on the clinical and cost effectiveness of the intervention.
National priorities	No
Current evidence base	All studies included in the guideline evidence review for CBT-I were in people with fibromyalgia, but no other chronic primary pain conditions. Several potentially relevant studies were not included because of ineligible populations (for example, other types of chronic pain). Three relatively small studies of CBT-I and one hybrid CBT-I/P were identified, and although results were promising, the committee considered the evidence too limited to make a recommendation. There was a lack of cost effectiveness data.
Equality	No effect on 'protected characteristics' as defined in the Equality Act.
Study design	Randomised control trial of CBT-I, or hybrid CBT-I/P in addition to usual care or an attention control. Method of delivery might include 1:1, group or internet delivered. Study duration 18 months or more. Population should be defined by assessment of both the chronic primary pain condition (for example Fibromyalgia) and insomnia. Inclusion criteria should include a cut-off to identify participants with higher levels of pain and disability. Post-intervention follow up of adequate duration is required, suggest at least 12 months.
Feasibility	This is considered feasible as similar trials have already been carried out or are underway in other conditions.
Other comments	It is suggested that different types of chronic primary pain should be considered as subgroups within the review as there is the potential for different efficacy in different conditions.
Importance	High: the research is essential to inform future updates of key recommendations in the guideline.

J.3 Psychotherapy

Research question: What is the clinical and cost effectiveness of psychodynamic psychotherapy for managing chronic primary pain in people aged 16 years and over?

Why this is important:

People with chronic primary pain report a higher than expected prevalence of early life disadvantage. Psychodynamically-informed psychotherapy has been used as an approach for the management of people with chronic primary pain, but to uncertain outcome. Its use throughout the NHS is inconsistent and unstandardised.

The evidence reviewed for this guideline for psychodynamic psychotherapy showed some benefit. Evidence on quality of life was conflicting, with one outcome measure showing a benefit and one showing no difference after three months. Evidence showed a benefit for physical function, psychological distress, pain interference and discontinuation at the time points after three months. The committee considered that although there was an overall benefit of psychotherapy, the evidence was of low to very low quality and based on a single study. Therefore, it was decided that a practice recommendation for psychotherapy could not be made without further research.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults with chronic primary pain Intervention(s): Psychodynamic psychotherapy Comparison: usual care or attention control. Outcome(s): Sleep, Pain, Health related quality of Life, Physical Function, Psychological Distress, Use of healthcare services, Medication Use.
Importance to patients or the population	Psychodynamic psychotherapy is a potentially important intervention to a large group of people with substantial physical, social and psychological difficulties.
Relevance to NICE guidance	A brief report on the evidence meeting the criteria for the chronic primary pain guidance is given above.
Relevance to the NHS	Psychodynamic psychotherapy is sometimes offered as a stand-alone treatment or in combination with other therapies. Better understanding of the effectiveness of psychotherapy will allow the most rational use of it.
National priorities	None
Current evidence base	The evidence base for psychotherapy meeting inclusion for review in this guideline was limited to one study, on which no definitive recommendation could be made.
Equality	Psychotherapy may need to be specially adapted for people of limited cognitive ability. It may also need to be delivered in a different language for people who do not have English as a first language.
Study design	Adequately powered randomised controlled trial(s) in population of adults with chronic primary pain from a range of diagnostic subgroups. Should consider psychodynamic psychotherapy as stand-alone and in combination with other treatments as part of a pain management programme. Effect of time- limited versus ongoing intervention should be assessed. This will require a post intervention follow up of adequate duration, suggested 12 months minimum.
Feasibility	Feasible – population easy to access and studies do not require special equipment to deliver. Main costs will be staff time and training. Large studies will be needed in assessing psychotherapy as part of a pain management programme and would probably be best done after studies looking at psychotherapy as a stand-alone intervention in this population.
Other comments	Psychotherapy is already part of the NHS armamentarium for people with chronic primary pain, and its utility needs better stablishing.
Importance	Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates.

J.4 Relaxation therapy

Research question: What is the clinical and cost effectiveness of relaxation therapies for managing chronic primary pain in people aged 16 years and over?

Why this is important:

Relaxation training is sometimes offered as part of pain management programmes or as stand-alone treatment. There is some evidence for benefits of relaxation training in people with pain but the best way to deliver relaxation training, and the clinical effectiveness and cost-benefit of relaxation training in people with chronic primary pain remain uncertain.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults (aged 16 or over) with chronic primary pain Intervention(s): Relaxation training Comparison: usual care or attention control. Outcome(s): Sleep, Pain, Health related quality of life, Physical Function, Psychological Distress, Use of healthcare services, Medication Use.
Importance to patients or the population	Relaxation training is well tolerated and is likely to be highly acceptable, therefore if there is good evidence of benefit it could be a useful treatment option.
Relevance to NICE guidance	Better evidence on this topic to help understand relaxation training as a stand-alone intervention, alongside other interventions, or not at all would inform future updates of this guideline.
Relevance to the NHS	Relaxation training is sometimes offered as a stand-alone treatment or in combination with other therapies. Better understanding of the effectiveness of relaxation training will allow the most rational use of it. If shown to be cost-effective, it will be an intervention that can be delivered in the NHS without major investment.
National priorities	No
Current evidence base	There was a limited amount of evidence identified in the current review comparing relaxation to usual care or attention control. Although there was a suggestion of a benefit in terms of quality of life and sleep at short-term follow up, there was no evidence for long term, and no difference in physical function, psychological distress, pain interference or pain reduction. There was also a lack of cost-effectiveness evidence. This evidence was therefore insufficient to base a practice recommendation on.
Equality	No particular relevance to protected characteristics as defined in the Equality Act.
Study design	An adequately powered randomised controlled trial in a population of adults with chronic primary pain from a range of diagnostic subgroups. Should consider relaxation training as stand-alone and in combination with other treatments. Effect of time-limited versus ongoing intervention should be assessed. Use of specialist versus non-specialist staff to deliver would be a helpful comparison to include. Method of delivery might include 1:1, group or internet delivered. Post-intervention follow up of adequate duration is required, suggest at least 12 months.
Feasibility	Feasible – population easy to access and studies do not require special equipment to deliver. Main costs will be staff time and training.
Other comments	None.
Importance	Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates.

Appendix K: MIDs for continuous outcomes

Table 52: MID for continuous outcomes (0.5 x SD): CBT versus usual care

Outcomes	MID
Quality of life (EuroQoL VAS) final values ≤3 months Scale from: 0 to 100.	7.2
Quality of life (FIQ) final values ≤3 months - CBT for pain Scale from: 0 to 100.	5.6
Quality of life (FIQ) final values ≤3 months - CBT for pain + insomnia Scale from: 0 to 100.	8.4
Quality of life (FIQ) final values >3 months - CBT for pain Scale from: 0 to 100.	8.85
Quality of life (FIQ) final values >3 months - CBT for pain + insomnia Scale from: 0 to 100.	5.07
Quality of life (SF12 physical component) final values ≤3 months Scale from: 0 to 100.	4.1
Quality of life (SF12 mental component) final values ≤3 months Scale from: 0 to 100.	4.58
Physical function (WHO Disability Assessment Schedule) final values ≤3 months Scale from: 0 to 100.	8.98
Physical function (FIQ physical impairment sub scale) final values ≤3 months Scale from: 0 to 27.	2.93
Physical function (FIQ physical function sub scale) change scores ≤3 months Scale from: 0 to 10.	0.85
Physical function (FIQ physical function sub scale) change scores >3 months Scale from: 0 to 10.	0.6
Psychological distress (Hamilton Rating Scale for Depression; HADS depression; Patient Health Questionnaire-9; Symptoms Checklist 90-R depression; BDI) final values ≤3 months - CBT for pain	0.5 (SMD)
Psychological distress (Symptoms Checklist 90-R depression; BDI) final values ≤3 months - CBT for pain + insomnia	0.5 (SMD)
Psychological distress (Hamilton Rating Scale for Depression; Symptoms Checklist 90-R depression; HADS depression; Center for Epidemiological Studies Depression Scale; BDI) final values >3 months - CBT for pain	0.5 (SMD)
Psychological distress (Symptoms Checklist 90-R depression; BDI) final values >3 months - CBT for pain + insomnia	0.5 (SMD)
Psychological distress (Patient Health Questionnaire 8-item depression) change scores >3 months Scale from: 0 to 24.	2.05
Psychological distress (Hamilton Anxiety Rating Scale; HADS anxiety; Symptoms checklist 90-R anxiety; State-Trait Anxiety Inventory) final values ≤3 months - CBT for pain	0.5 (SMD)

Outcomes	MID
Psychological distress (Symptoms checklist 90-R anxiety; State-Trait Anxiety Inventory) final values ≤3 months - CBT for pain + insomnia	0.5 (SMD)
Psychological distress (Hamilton Anxiety Rating Scale; Symptoms Checklist 90-R anxiety; HADS anxiety; State-Trait Personality Inventory anxiety) final values >3 months - CBT for pain	0.5 (SMD)
Psychological distress (Symptoms Checklist 90-R anxiety; State-Trait Personality Inventory anxiety) final values >3 months - CBT for pain + insomnia	0.5 (SMD)
Psychological distress (Multiple Pain Inventory-affective distress) final values >3 months Scale from: 0 to 6.	0.29
Pain interference (BPI - pain interference) final values ≤3 months Scale from: 0 to 10.	0.79
Pain interference (Pain Disability Index) final values ≤3 months – CBT for pain Scale from: 0 to 70.	8.4
Pain interference (Pain Disability Index) final values ≤3 months – CBT for insomnia Scale from: 0 to 70.	8.4
Pain interference (Pain Disability Index) final values >3 months – CBT for pain Scale from: 0 to 70.	9.04
Pain interference (Pain Disability Index) final values >3 months – CBT for insomnia Scale from: 0 to 70.	9.04
Pain interference (Multiple Pain Inventory - pain interference) final values >3 months Scale from: 0 to 6.	0.41
Pain self-efficacy (Pain Self-efficacy Questionnaire; Chronic Pain Self-efficacy Scale; Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months - CBT for pain	0.5 (SMD)
Pain self-efficacy (Pain Self-efficacy Questionnaire; Chronic Pain Self-efficacy Scale) final values ≤3 months - CBT for pain + insomnia	0.5 (SMD)
Pain self-efficacy (Chronic Pain Self-efficacy scale) final values >3 months - CBT for pain	19.41
Pain self-efficacy (Chronic Pain Self-efficacy scale) final values >3 months - CBT for pain + insomnia	19.41
Sleep (Pittsburgh Sleep Quality Index; Karolinska Sleep Questionnaire sleep quality sub scale; self-reported sleep quality rating) final values ≤3 months - CBT for pain	0.5 (SMD)
Sleep (Insomnia Severity Index) final values ≤3 months - CBT for pain	0.5 (SMD)
Sleep (Pittsburgh Sleep Quality Index; self-reported sleep quality rating) final values ≤3 months - CBT for pain + insomnia	0.5 (SMD)
Sleep (Insomnia Symptoms Questionnaire) final values ≤3 months - CBT for pain + insomnia	0.5 (SMD)
Sleep (Pittsburgh Sleep Quality Index; Sleep Scale; self-reported sleep quality rating) final values >3 months - CBT for pain	0.5 (SMD)
Sleep (MOS Sleep Problems Index (scale inverted for analysis)) final values >3 months - CBT for pain	0.5 (SMD)

Outcomes	MID
Sleep (Pittsburgh Sleep Quality Index; self-reported sleep quality rating) final values >3 months - CBT for pain + insomnia	0.5 (SMD)
Sleep (MOS Sleep Problems Index (scale inverted for analysis; Insomnia Symptom Questionnaire) final values >3 months - CBT for pain + insomnia	0.5 (SMD)
Pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain Scale from: 0 to 10.	0.64
Pain (VAS/NRS) final values and change scores ≤3 months - CBT for pain + insomnia Scale from: 0 to 10.	0.65
Pain (VAS/NRS) final values and change scores >3 months - CBT for pain Scale from: 0 to 10.	0.77
Pain (VAS/NRS) final values and change scores >3 months - CBT for pain + insomnia Scale from: 0 to 10.	0.5
Pain (McGill Pain Questionnaire) final values ≤3 months – CBT for pain Scale from: 0 to 78.	11.66
Pain (McGill Pain Questionnaire) final values ≤3 months – CBT for insomnia Scale from: 0 to 78.	4.66
Pain (Multiple Pain Inventory - pain severity) final values >3 months - CBT for pain Scale from: 0 to 6.	0.38
Pain (McGill Pain Questionnaire) final values >3 months - CBT for pain Scale from: 0 to 78.	8.01
Pain (McGill Pain Questionnaire) final values >3 months - CBT for pain +/ insomnia Scale from: 0 to 78.	5.23

Table 53: MID for continuous outcomes (0.5 x SD): ACT versus usual care

Outcomes	MID
Quality of life (EQ-5D VAS) final values ≤3 months Scale from: 0 to 100.	5.35
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 100.	6.33
Quality of life (FIQ) final values >3 months Scale from: 0 to 100.	6.96
Physical function (6 minute walk test) final values ≤3 months	54.26
Physical function (6 minute walk test) final values >3 months	60.15
Psychological distress (Geriatric Depression Scale; BDI; HADS depression; Center for Epidemiologic Studies depression scale) final values ≤3 months	0.5 (SMD)
Psychological distress (BDI; HADS depression; Center for Epidemiologic Studies depression scale) final values >3 months	0.5 (SMD)

Outcomes	MID
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - State Scale from: 20 to 80.	7.2
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - Trait Scale from: 20 to 80.	6.75
Psychological distress (Pain Anxiety Symptoms Scale; HADS anxiety) final values ≤3 months	0.5 (SMD)
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - State Scale from: 20 to 80.	6.4
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - Trait Scale from: 20 to 80.	5.9
Psychological distress (HADS - anxiety) final values >3 months Scale from: 0 to 21.	2.1
Pain interference (BPI - pain interference) final values ≤3 months - General activity Scale from: 0 to 10.	1.8
Pain interference (BPI - pain interference) final values ≤3 months - Mood Scale from: 0 to 10.	2.02
Pain interference (BPI - pain interference) final values ≤3 months - Walking ability Scale from: 0 to 10.	1.61
Pain interference (BPI - pain interference) final values ≤3 months - Relations with other people Scale from: 0 to 10.	1.92
Pain interference (BPI - pain interference) final values ≤3 months - Sleep Scale from: 0 to 10.	2.04
Pain interference (Pain disability index) final values ≤3 months Scale from: 0 to 70.	7.8
Pain interference (Pain disability index) final values >3 months Scale from: 0 to 70.	7.7
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months Scale from: 0 to 21.	1.74
Sleep (Pittsburgh Sleep Quality Index) final values >3 months Scale from: 0 to 21.	2.38
Pain (VAS/NRS; McGill pain questionnaire) final values ≤3 months	0.5 (SMD)
Pain (VAS/NRS; McGill pain questionnaire) final values >3 months	0.5 (SMD)

Table 54: MID for continuous outcomes (0.5 x SD): Relaxation versus usual care

Outcomes	MID
Quality of life (FIQ) final values ≤3 months	0.5 (SMD)
Physical function (Neck disability index) final values ≤3 months Scale from: 0 to 80.	6.9

Outcomes	MID
Physical function (Neck disability index) final values >3 months Scale from: 0 to 80.	6.85
Psychological distress (HADS depression; Center for Epidemiologic Studies depression scale) final values ≤3 months	0.5 (SMD)
Psychological distress (HADS anxiety) final values ≤3 months Scale from: 0 to 21.	1.67
Pain interference (BPI - interference) final values ≤3 months Scale from: 0 to 10.	1.37
Pain self-efficacy (Arthritis Self-efficacy Scale - pain sub scale) final values ≤3 months Scale from: 10 to 100.	2.25
Pain self-efficacy (Arthritis Self-efficacy Scale - self-efficacy for managing other symptoms sub scale) final values ≤3 months Scale from: 10 to 100.	10.67
Sleep (MOS sleep problems index) final values ≤3 months	7.36
Pain (VAS/NRS) final values ≤3 months Scale from: 0 to 10.	0.96
Pain (VAS/NRS) final values >3 months Scale from: 0 to 10.	1.25

Table 55: MID for continuous outcomes (0.5 x SD): Relaxation versus attention control

Outcomes	MID
Pain reduction Brief pain inventory pain severity sub scale (VAS). Scale from: 0 to 10.	1

Table 56: MID for continuous outcomes (0.5 x SD): Biofeedback versus usual care

Outcomes	MID
Quality of life (Arthritis Impact Measurement Scale) change scores >3 months Scale from: 0 to 10.	1.06
Physical function (Neck disability index) final values ≤3 months Scale from: 0 to 100.	7.2
Physical function (Maximal Watt bicycle ergometer) change scores >3 months	10.21
Psychological distress (BDI) – EMG biofeedback final values ≤3 months Scale from: 0 to 63.	3.65
Psychological distress (HADS - depression) – HRV biofeedback final values ≤3 months Scale from: 0 to 21.	2.23
Psychological distress (BDI) – EMG biofeedback final values >3 months Scale from: 0 to 63.	3.15
Psychological distress (Symptoms Checklist-90-revised) change scores >3 months	15.51

Outcomes	MID
Psychological distress (HADS anxiety) – HRV biofeedback final values ≤3 months Scale from: 0 to 21.	1.8
Pain (VAS/NRS) final values ≤3 months Scale from: 0 to 10.	0.85
Pain (VAS) change scores >3 months Scale from: 0 to 10.	7.69

Table 57: MID for continuous outcomes (0.5 x SD): Biofeedback versus sham biofeedback

Outcomes	MID
Quality of life (FIQ) changes scores<3 months	8.2
Physical function (6 minute walk test) change scores <3 months	39.95
Psychological distress (BDI) change scores ≤3 months Scale from: 0 to 63.	5.05
Psychological distress (BDI) change scores >3 months Scale from: 0 to 63.	5.8
Psychological distress (State trait anxiety inventory - trait) change scores ≤3 months Scale from: 20 to 80.	6.3
Psychological distress (State trait anxiety inventory - trait) change scores >3 months Scale from: 20 to 80.	5.15
Sleep (Pittsburgh sleep quality index) change scores ≤3 months Scale from: 0 to 21.	2.2
Sleep (Pittsburgh sleep quality index) change scores >3 months Scale from: 0 to 21.	2.4
Pain (VAS) change scores ≤3 months - neurofeedback Scale from: 0 to 10.	0.75
Pain (VAS) change scores ≤3 months Scale from: 0 to 10.	1.68
Pain (VAS) change scores >3 months - neurofeedback Scale from: 0 to 10.	0.75

Table 58: MID for continuous outcomes (0.5 x SD): Mindfulness versus usual care

Outcomes	MID
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 100.	8.61
Quality of life (FIQ) final values >3 months Scale from: 0 to 100.	5.27
Psychological distress (BDI) final values ≤3 months Scale from: 0 to 63.	4.31
Psychological distress (BDI) final values >3 months Scale from: 0 to 63.	3.91

Outcomes	MID
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - State Scale from: 20 to 80.	4.63
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values ≤3 months - Trait Scale from: 20 to 80.	4.49
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - State Scale from: 20 to 80.	3.95
Psychological distress (Spielberger Trait-State Anxiety Inventory) final values >3 months - Trait Scale from: 20 to 80.	4.69
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months Scale from: 0 to 21.	1.65
Sleep (Pittsburgh Sleep Quality Index) final values >3 months Scale from: 0 to 21.	1.8

Table 59: MID for continuous outcomes (0.5 x SD): Pain education versus usual care

Outcomes	MID
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 10	0.28
Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months	1.01
Sleep (Karolinska sleep questionnaire - sleep quality sub scale) final values ≤3 months	0.4
Pain (McGill Pain Questionnaire) final values ≤3 months Scale from: 0 to 78.	16.05

Table 60: MID for continuous outcomes (0.5 x SD): Pain education versus attention control

Outcomes	MID
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 100.	8.34
Quality of life (FIQ) final values >3 months Scale from: 0 to 100.	8.88
Psychological distress (Pain Anxiety Symptom Scale) final values ≤3 months - PASS1	6.16
Psychological distress (Pain Anxiety Symptom Scale) final values ≤3 months - PASS2	3.32
Psychological distress (Pain Anxiety Symptom Scale) final values >3 months - PASS1	7.63
Psychological distress (Pain Anxiety Symptom Scale) final values >3 months - PASS2	4.6
Pain (NRS) final values ≤3 months Scale from: 0 to 10.	0.53

Outcomes	MID
Pain (NRS) final values >3 months Scale from: 0 to 10.	0.73

Table 61: MID for continuous outcomes (0.5 x SD): Sleep hygiene versus usual care

Outcomes	MID
Sleep (Insomnia Symptom Questionnaire) final values ≤3 months	2.45
Sleep (Insomnia Symptom Questionnaire) final values >3 months	2.7
Pain (McGill pain questionnaire) final values ≤3 months Scale from: 0 to 78.	2.05
Pain (McGill pain questionnaire) final values >3 months Scale from: 0 to 78.	2.45

Table 62: MID for continuous outcomes (0.5 x SD): Hypnosis versus usual care

Outcomes	MID
Quality of life (FIQ) change scores ≤3 months Scale from: 0 to 100.	4.64
Quality of life (FIQ) change scores >3 months Scale from: 0 to 100.	7.16
Psychological distress (HADS - depression) change scores ≤3 months Scale from: 0 to 21.	1.49
Psychological distress (HADS - depression) change scores >3 months Scale from: 0 to 21.	1.3
Psychological distress (HADS - anxiety) change scores ≤3 months Scale from: 0 to 21.	0.94
Psychological distress (HADS - anxiety) change scores >3 months Scale from: 0 to 21.	8.18
Sleep (MOS Sleep Scale) change scores ≤3 months	5.83
Sleep (MOS Sleep Scale) change scores >3 months	1.94
Pain (NRS) final values >3 months Scale from: 0 to 10.	0.58

Table 63: MID for continuous outcomes (0.5 x SD): Psychotherapy versus usual care

Outcomes	MID
Physical function (Somatoform disorders-7) final values >3 months Scale from: 0 to 100.	1.1
Psychological distress (HADS - depression) final values >3 months Scale from: 0 to 21.	0.5
Psychological distress (HADS - anxiety) final values >3 months Scale from: 0 to 21.	0.4
Pain interference (Pain disability index) final values >3 months	1.75

Table 64: MID for continuous outcomes (0.5 x SD): CBT (for insomnia) versus sleep hygiene

Outcomes	MID
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 100.	7.83
Psychological distress (Symptom Checklist-90-Revised - depression sub scale; HADS - depression) final values ≤3 months	0.5 (SMD)
Psychological distress (Symptom Checklist-90-Revised - anxiety sub scale; HADS - anxiety) final values ≤3 months	0.5 (SMD)
Pain self-efficacy (Chronic Pain Self-efficacy Scale) final values ≤3 months	18.91
Sleep (Pittsburgh Sleep Quality Index) final values ≤3 months	1.5
Sleep (Insomnia Symptom Questionnaire) final values ≤3 months	1.65
Sleep (total sleep time, hours) final values ≤3 months	0.28
Sleep (Insomnia Symptom Questionnaire) final values >3 months	1.55
Pain (McGill VAS) final values ≤3 months Scale from: 0 to 10.	0.71
Pain (McGill Pain Questionnaire) final values ≤3 months Scale from: 0 to 78.	2.2
Pain (McGill Pain Questionnaire) final values >3 months Scale from: 0 to 78.	1.95

Table 65: MID for continuous outcomes (0.5 x SD): CBT versus pain education

Outcomes	MID
Quality of life (FIQ) final values ≤3 months Scale from: 0 to 10	0.37
Quality of life (FIQ) final values >3 months Scale from: 0 to 10	0.37
Quality of life (Satisfaction with life scale) final values ≤3 months	3.82
Quality of life (Satisfaction with life scale) final values >3 months	3.86
Physical function (SF12 physical function sub scale) final values ≤3 months Scale from: 0 to 100.	4.26
Physical function (SF12 physical function sub scale) final values >3 months Scale from: 0 to 100.	4.74
Psychological distress (BDI) change scores ≤3 months Scale from: 0 to 63.	2.2
Psychological distress (Center for Epidemiologic Studies - depression) final values ≤3 months Scale from: 0 to 60.	5.61
Psychological distress (Center for Epidemiologic Studies - depression) final values >3 months Scale from: 0 to 60.	6.04
Psychological distress (Generalised anxiety disorder-7) final values ≤3 months Scale from: 0 to 21.	2.57

Outcomes	MID
Psychological distress (Generalised anxiety disorder-7) final values >3 months Scale from: 0 to 21.	2.6
Pain interference (BPI - interference) change scores ≤3 months Scale from: 0 to 10.	0.8
Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values ≤3 months	0.96
Pain self-efficacy (Coping Skills Questionnaire self-efficacy sub scale) final values >3 months	1.4
Sleep (Karolinska Sleep Questionnaire sleep quality) final values ≤3 months	0.5 (SMD)
Sleep (Pittsburgh Sleep Quality Index - sleep problems) final values ≤3 months	0.5 (SMD)
Sleep (Karolinska Sleep Questionnaire sleep quality) final values >3 months	0.5 (SMD)
Sleep (Pittsburgh Sleep Quality Index - sleep problems) final values >3 months	0.5 (SMD)
Use of healthcare services (physician/other health professional visits in past 3 months) final values ≤3 months	2.87
Use of healthcare services (physician/other health professional visits in past 3 months) final values >3 months	3.07
Pain (VAS/NRS) final values/change scores ≤3 months Scale from: 0 to 10.	0.87
Pain (VAS/NRS) final values >3 months Scale from: 0 to 10.	0.98
Pain (McGill Pain Questionnaire) final values ≤3 months Scale from: 0 to 78	20.94
Pain (McGill Pain Questionnaire) final values >3 months Scale from: 0 to 78	17.96

Table 66: MID for continuous outcomes (0.5 x SD): CBT versus biofeedback

Outcomes	MID
Pain (NRS) final values ≤3 months Scale from: 0 to 10.	1.18
Pain (NRS) final values >3 months Scale from: 0 to 10.	1.32

Table 67: MID for continuous outcomes (0.5 x SD): CBT versus psychotherapy

Outcomes	MID
Psychological distress (BDI) final values ≤3 months Scale from: 0 to 63.	4.5
Psychological distress (BDI) final values >3 months Scale from: 0 to 63.	4.75

Outcomes	MID
Psychological distress (Pain Anxiety Symptoms Scale) final values ≤3 months Scale from: 0 to 200.	16.75
Psychological distress (Pain Anxiety Symptoms Scale) final values >3 months Scale from: 0 to 200.	17.25
Pain (McGill Pain Questionnaire) final values ≤3 months Scale from: 0 to 78.	6.5
Pain (McGill Pain Questionnaire) final values >3 months Scale from: 0 to 78.	7

Table 68: MID for continuous outcomes (0.5 x SD): CBT versus behaviour therapy

Outcomes	MID
Physical function (FIQ physical function sub scale) final values >3 months	0.79
Use of healthcare services (Physician visits) >3 months	9.13
Pain (West Haven-Yale Multidimensional Pain Inventory) final values >3 months	0.7

Table 69: MID for continuous outcomes (0.5 x SD): Biofeedback versus relaxation

Outcomes	MID
Pain (% reduction in pain from baseline) ≤3 months Scale from: 0 to 100.	20

Table 70: MID for continuous outcomes (0.5 x SD): ACT versus relaxation

Outcomes	MID
Quality of life (SF12 mental component) final values ≤3 months Scale from: 0 to 100.	5.35
Quality of life (SF12 mental component) >3 months Scale from: 0 to 100.	6.9
Quality of life (SF12 physical component) final values ≤3 months Scale from: 0 to 100.	4.1
Quality of life (SF12 physical component) final values >3 months Scale from: 0 to 100.	4.9
Pain interference (Pain disability index) final values ≤3 months Scale from: 0 to 70.	6.8
Pain interference (Pain disability index) final values >3 months Scale from: 0 to 70.	8.1
Psychological distress (HADS depression) final values ≤3 months Scale from: 0 to 21.	2.65
Psychological distress (HADS depression) final values >3 months Scale from: 0 to 21.	2.75

Outcomes	MID
Psychological distress (HADS anxiety) final values ≤3 months Scale from: 0 to 21.	2.3
Psychological distress (HADS anxiety) final values >3 months Scale from: 0 to 21.	2.6
Pain (NRS 0-6) final values ≤3 months Scale from: 0 to 6.	0.75
Pain (NRS 0-6) final values >3 months Scale from: 0 to 6.	0.75