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Psychological therapies for the management of chronic neuropathic pain in adults (Review)



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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
BACKGROUND	3
OBJECTIVES	4
METHODS	2
Figure 1	6
RESULTS	7
Figure 2	ç
Figure 3	10
DISCUSSION	10
AUTHORS' CONCLUSIONS	11
ACKNOWLEDGEMENTS	12
REFERENCES	13
CHARACTERISTICS OF STUDIES	16
DATA AND ANALYSES	22
Analysis 1.1. Comparison 1: CBT versus control post-treatment, Outcome 1: Pain intensity	23
Analysis 1.2. Comparison 1: CBT versus control post-treatment, Outcome 2: Pain disability	23
Analysis 1.3. Comparison 1: CBT versus control post-treatment, Outcome 3: Anxiety	23
Analysis 2.1. Comparison 2: CBT versus control at follow up, Outcome 1: Pain intensity	24
Analysis 2.2. Comparison 2: CBT versus control at follow up, Outcome 2: Pain disability	24
Analysis 2.3. Comparison 2: CBT versus control at follow up, Outcome 3: Anxiety	24
Analysis 3.1. Comparison 3: Group psychotherapy versus placebo post-treatment, Outcome 1: No worse than mild pain	24
APPENDICES	25
HISTORY	29
CONTRIBUTIONS OF AUTHORS	29
DECLARATIONS OF INTEREST	29
SOURCES OF SUPPORT	29
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	29
NOTES	30
INDEX TERMS	30



[Intervention Review]

Psychological therapies for the management of chronic neuropathic pain in adults

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ABSTRACT

Background

Neuropathic pain is thought to arise from damage to the somatosensory nervous system. Its prevalence is increasing in line with many chronic disorders such as diabetes. All treatments have limited effectiveness. Given the evidence regarding psychological treatment for distress and disability in people with various chronic pain conditions, we were interested to investigate whether psychological treatments have any effects for those with chronic neuropathic pain.

Objectives

To assess the effects of psychological treatments on pain experience, disability, mood, and health-care use in adults with chronic neuropathic pain.

Search methods

We searched for randomised controlled trials (RCTs) published in any language in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO, from database inception to March 2015.

Selection criteria

Full publications of RCTs on psychological interventions for neuropathic pain. Trials had to have lasted at least three months, had at least 20 participants in each arm at the end of treatment, and compared a psychological intervention with any active or inactive intervention.

Data collection and analysis

We used the standard methodological procedures expected by Cochrane.

Main results

Two small studies (enrolling a total of 105 participants) met the inclusion criteria. One was a standard cognitive behavioural treatment (CBT) programme for 61 people with pain from spinal cord injury, followed up for three months, and compared with a waiting list. The other was weekly group psychotherapy for 44 people with burning mouth syndrome, compared with a daily placebo tablet. The overall risk of bias was high in both trials.

The CBT study assessed participants for pain, disability, mood, and quality of life, with improvement in treatment and control groups. However, there was no more improvement in the treatment group than in the control for any outcome, either post-treatment or at follow-



up. The group psychotherapy study only assessed pain, classifying participants by pain severity. There is a lack of evidence on the efficacy and safety of psychological interventions for people with neuropathic pain.

Authors' conclusions

There is insufficient evidence of the efficacy and safety of psychological interventions for chronic neuropathic pain. The two available studies show no benefit of treatment over either waiting list or placebo control groups.

PLAIN LANGUAGE SUMMARY

Psychological treatments for chronic pain involving damage or disease to nerves responsible for pain

Many people experience pain from an injury or disease that goes away within three months, but for some people the pain continues. When the pain involves changes to nerves we call the pain 'neuropathic'. Although the condition is increasingly common, the treatments we have help only a few people. Following unsuccessful surgical or pharmacological treatment, people with chronic pain may be offered psychologically-based rehabilitation to improve their quality of life. While we know that this can help people with other types of chronic pain, this treatment for neuropathic pain alone has received less research attention.

In this review, we were interested in finding out whether psychological treatments improve pain, distress, and disability in people with chronic neuropathic pain. We searched the academic literature to March 2015 and identified two randomised controlled trials (the gold standard design for clinical trials) on psychological interventions for chronic neuropathic pain. The two studies included 105 participants: one trial of 61 people with pain from spinal cord injury and the other of 44 people with burning mouth syndrome.

Our confidence in the results of the individual trials was limited by several potential biases in how they were conducted. We were not able to analyse the results of the two trials together because the experiences of people with spinal cord injury or burning mouth are too different from each other. On their own, the trials were too small for us to undertake any statistical analysis. However, neither trial found any clear benefit of treatment. We conclude that there is currently no evidence that will help practitioners and patients to decide whether to use these treatments. We discuss what studies are needed.



BACKGROUND

Neuropathic pain is an increasingly prevalent problem. Given the limited effectiveness of existing therapies, it is appropriate to offer psychologically based treatments that aim to rehabilitate patients despite continuing pain or to reduce pain and its effects on everyday life. This review draws on new criteria for what constitutes reliable evidence in chronic pain, established specifically for reviews of drugs for neuropathic pain (Moore 2010). We have also used material from a recent review of psychological treatments for all chronic pain in adults when developing this review (Williams 2012).

Description of the condition

The 2011 International Association for the Study of Pain defines neuropathic pain as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" (Haanpää 2011; Jensen 2011). Neuropathic pain can be a severe and complex consequence of nerve damage, which is often followed by changes in the central nervous system (Apkarian 2011; Moisset 2007; Tracey 2011). Many people with neuropathic pain conditions are significantly disabled, with moderate or severe pain for many years (Doth 2010; Smith 2012; Williams 2011).

In primary care in the UK, the estimated incidence of postherpetic neuralgia is 28 per 100,000 person-years (95% confidence interval (CI 27 to 30), while this figure stands at 27 (95% CI 26 to 29) for trigeminal neuralgia, 0.8 (95% CI 0.6 to 1.1) for phantom limb pain and 21 (95% CI 20 to 22) for painful diabetic neuropathy (Hall 2008). Because of the small numbers of cases, estimates vary between studies. In a systematic review of studies published since 2000 Moore 2014 reported the overall prevalence of neuropathic pain (all types) to be about 7%, while Haanpää 2011 reported prevalence ranging from 3.3% to 8.2%.

Neuropathic pain is difficult to treat effectively, with only a minority of individuals experiencing a clinically relevant benefit from any one intervention (Kalso 2014; Moore 2013). Thus, practitioners are increasingly taking a multidisciplinary approach that combines pharmacological treatments with physical therapy, cognitive interventions, or both. Different drugs and drug combinations are used, with efficacy varying by condition (Kalso 2014). A minority of people experience at least a 50% reduction in pain intensity, with numbers needed to treat for an additional beneficial outcome (NNT) usually falling between 4 and 10 (Moore 2013). The only Cochrane review of non-pharmacological interventions (Boldt 2014) found a single cognitive behavioural intervention (Heutink 2012).

In earlier reviews of all chronic pain except headache (Eccleston 2009; Williams 2012), we searched for all published RCTs of interventions described as psychological in nature, finding mainly trials of behavioural therapy (BT) or cognitive behavioural therapy (CBT). We excluded RCTs of interventions for headache for consistency with the previous reviews and because CBT for headache aims primarily to reduce the frequency, duration, and intensity of headache pain, rather than to rehabilitate despite ongoing pain (Eccleston 2009; Williams 2012). Readers are referred to other reviews specific to migraine and headache (Nestoriuc 2007; Nestoriuc 2008); Cochrane systematic reviews for headache are in progress (McGuire 2014). We also excluded Internet trials because they are the subject of an existing review (Eccleston 2014).

The Williams 2012 review found 42 trials, of which 35 provided data (N = 4788) for meta-analysis. CBT showed small positive effects on disability and catastrophising, but not on pain or mood, when compared with active controls. CBT showed small to moderate effects on pain, disability, mood, and catastrophising when compared with treatment as usual or waiting list. Only a small effect on mood persisted at follow-up. The only positive effect of BT was on catastrophising immediately after treatment, but there were relatively few behavioural therapy studies. The quality of trials and trial reporting is improving (Morley 2006; Williams 2012), although the quality of treatment remains variable (Williams 2012). Of the eight trials of mixed chronic pain conditions identified in that review, one identified 31% of participants with neuropathic pain, but it did not analyse this subgroup separately (Wetherell 2011); another trial described 10% of patients as having 'neurological' pain (Puder 1988).

Although combining multiple chronic pain conditions in our review made sense in terms of measuring the effect of psychological interventions, the proliferation of trials and the trend to improve participant homogeneity by selecting a single condition, such as fibromyalgia, suggests that psychological interventions for chronic pain would be best addressed by diagnostic group. This choice has the added advantage of making the results accessible to overviews that include other types of intervention, mainly pharmacological and physical. Given the ongoing Cochrane headache review (McGuire 2014) and the recent publication of a Cochrane review of CBT for fibromyalgia (Bernady 2013), we decided to focus this review on another important area: neuropathic pain.

Description of the intervention

A broad family of treatments fall under the umbrella term 'psychological'. In essence, these treatments are specifically designed to alter the psychological processes that contribute to pain, distress and disability (Eccleston 2011; Eccleston 2013; Morley 1999; Morley 2013). Specific theories relating to the aetiology of human behaviour normally underpin the design of psychological treatments, though some treatments have a more pragmatic basis in the observation and study of response to intervention (Eccleston 2013). In practice, a wide variety of interventions are used, and not all have been evaluated for their efficacy (Morley 2006; Morley 2013). The evidence base for psychological therapies stems mainly from studies of programmatic and protocolised treatments rooted in the behavioural or cognitive behavioural tradition of clinical psychology (Eccleston 2013). Practitioners may choose psychological therapies after orthodox treatments have failed, when the treatment goal shifts from removing or alleviating pain to managing pain and its myriad adverse consequences on quality of life (Lumley 2011; Morley 2006).

How the intervention might work

Most, but not all, psychological treatments consist of cognitive or behavioural therapies. A typical treatment protocol for cognitive behavioural therapy (CBT) uses methods aimed directly at assessing the thoughts and psychological biases associated with pain as well as the extent of avoiding unpleasant thoughts (Morley 1999). Behavioural methods focus on identifying behaviour that is contingent on pain or on events that suggest pain relief or comfort; interventions aim to reduce avoidance or persistence behaviour that impedes progress towards valued goals (Van Damme 2015). Most therapies involve education, and many



are incorporated within larger treatment programmes involving physical, occupational, or vocational therapy (Morley 2006). Non-CBT interventions may also be relevant to the extent that they are based on defined psychological theories and treatment methods with a foundation in the broader field of clinical psychology (Eccleston 2013).

Why it is important to do this review

Five of the 11 top-ranking conditions for years lived with disability in 2010 were chronic painful conditions (Vos 2012), which are responsible for considerable loss of quality of life, loss of employment, and increased health costs (Moore 2014). Neuropathic pain is under-recognised (see Description of the condition and Smith 2012), and some forms, such as from diabetic neuropathy and postsurgical chronic pain (often neuropathic in origin), are increasing in prevalence (Hall 2008). Neuropathic pain has a particularly severe impact on quality of life (Smith 2007), and its origins and persistence are difficult for patients to understand. For psychologically based pain management, it is not usual to distinguish between diagnoses; however, the predominant model of musculoskeletal pain may serve those with neuropathic pain rather poorly. It is time to disaggregate the compound review of psychologically based pain management for all chronic pain except headache (Williams 2012) and to instead review specific types of chronic pain, consistent with those of medical interventions. There is an increased need to evaluate psychological treatments in this field. The only existing review (Wetering 2010) is outside of Cochrane and of very poor quality (Eccleston 2010). However, there is a review of all non-pharmacological interventions, including psychological interventions, for one neuropathic pain condition: spinal cord injury (Boldt 2014).

OBJECTIVES

To assess the effects of psychological treatments on pain experience, disability, mood, and healthcare use in adults with chronic neuropathic pain.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) comparing a credible psychological treatment, or a compound treatment with primary psychological content, versus placebo, another active treatment, treatment as usual, or waiting list control. We judged a psychological treatment to be credible if it was based on an extant psychological model or framework, and if a qualified healthcare professional in psychology delivered or supervised it.

Studies were included if they:

- were available as a full publication or report of an RCT;
- had a design that considered a psychological treatment as an active treatment;
- were published (or electronically pre-published) in a peerreviewed scientific journal;
- had 20 or more participants in each treatment arm at the end of the treatment or follow-up assessment.

Types of participants

We included studies involving adult participants (≥18 years) who had been experiencing neuropathic pain for at least three months. They may have had a wide range of chronic neuropathic pain conditions, including:

- painful diabetic neuropathy (PDN);
- · postherpetic neuralgia;
- trigeminal neuralgia;
- phantom limb pain;
- postoperative or traumatic neuropathic pain;
- complex regional pain syndrome (CRPS), Types I and II;
- · cancer-related neuropathy;
- human immunodeficiency virus (HIV) neuropathy;
- spinal cord injury.

In case studies that included participants with more than one type of neuropathic pain, we planned to analyse results according to the primary condition.

Types of interventions

We included studies if at least one trial arm consisted of a psychological intervention and one comparator arm used a placebo, another active treatment, treatment as usual, or waiting list control. We define psychological intervention as using psychotherapeutic methods specifically designed to alter psychological processes believed to contribute to pain, distress, or disability (Eccleston 2013; Morley 1999; Morley 2013). We included methods underpinned by specific theories of the aetiology of human behaviour for which there is some evidence of efficacy in the broader field of clinical psychology (Eccleston 2013).

Types of outcome measures

We aimed to use outcomes in the domains of pain experience, disability, negative mood, and healthcare use as well as adverse events. We anticipated that studies would use a variety of outcome measures, with the majority of studies using standard subjective scales (numerical rating scale (NRS) or visual analogue scale (VAS)) for pain intensity, pain affect, or both. We were particularly interested in the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) definitions for moderate and substantial benefit in chronic pain studies (Dworkin 2008). This project defined moderate benefit in the domain of pain experience as at least 30% pain relief over baseline and substantial benefit as at least 50% pain relief over baseline; at least half a standard deviation, or 1 point on a 0 to 10 mean of the seven pain interference items as measured by the Brief Pain Inventory (Cleeland 1994); and at least half a standard deviation or a change of at least 5 points for depression as measured by the Beck Depression Inventory (Beck 1961; Morley 2002).

Primary outcomes

- 1. Pain experience, as measured by a self-rating of pain intensity or pain distress according to VAS or NRS.
- Mood, as measured by a standard anxiety scale such as Spielberger State/Trait Anxiety Inventory (STAI; Spielberger 1983), standard depression scale such as Beck Depression Inventory (BDI; Beck 1961), or a standard distress scale such



as the Hospital Anxiety and Depression Scale (HADS; Zigmond 1983).

- 3. Disability or quality of life, as measured by the Brief Pain Inventory (BPI; Cleeland 1994) or the 36- or 12-item Short Form Health Survey (SF-36 or SF-12; Medical Outcomes Study).
- 4. Adverse events and dropouts.

Secondary outcomes

1. Healthcare use (e.g. medication use, healthcare visits, healthcare procedures, hospital stays).

Search methods for identification of studies

We searched electronic databases, journal pre-publication websites, and reference lists.

Electronic searches

We searched the following databases, with no restriction on language of publication.

- Cochrane Central Register of Controlled Trials (CENTRAL) via the CRSO to March 2015.
- MEDLINE via Ovid 1946 to March 2015.
- EMBASE via Ovid 1974 to March 2015.
- PsycINFO via Ovid 1806 to March 2015.

We describe our search strategies in Appendix 1.

At least two review authors reviewed all abstracts, consulting the third review author when necessary to decide on inclusion or exclusion.

Searching other resources

We reviewed the bibliographies of identified RCTs and review articles, and we searched the USA National Institutes of Health clinical trial database (clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (http://apps.who.int/trialsearch/) to identify additional published or unpublished data.

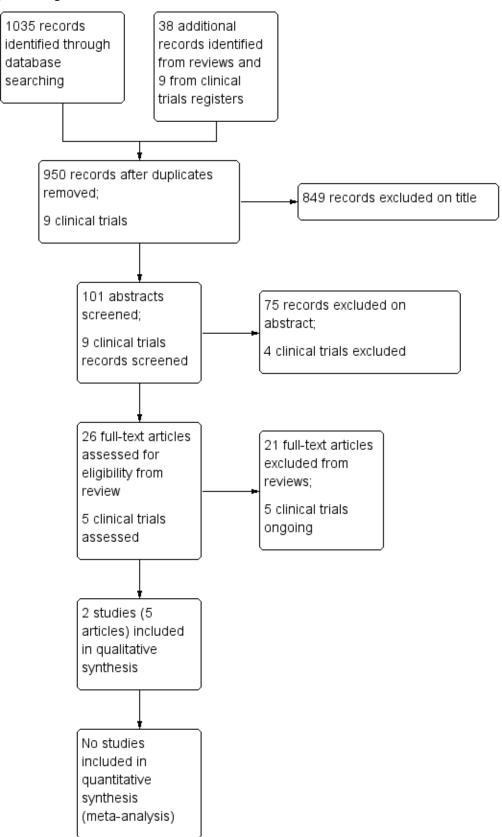
Data collection and analysis

Selection of studies

We determined eligibility by reading the abstract of each study identified in our search. We eliminated studies that clearly did not satisfy the inclusion criteria, and we obtained full copies of the remaining studies; two review authors (LH, AW) independently assessed the full text to determine eligibility, reaching agreement by discussion. We did not anonymise the studies before assessment. We created a PRISMA flow chart to describe the process (Figure 1).



Figure 1. Study flow diagram.





Data extraction and management

Two review authors (LH, AW) independently extracted data using a standard form and checked for agreement before entering data into Review Manager (RevMan 2014). We included information about the pain condition, the number of participants treated, type of intervention, study design (type of control), study duration and follow-up, outcome measures used, data for primary measure in each domain, attrition, and adverse events.

Assessment of risk of bias in included studies

We assessed risk of bias using the recommended Cochrane methods (Higgins 2011) and the five suggested 'Risk of bias' categories: random sequence generation (selection bias), allocation concealment (selection bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias). Although we included the risk 'blinding participants and personnel', it is not possible to blind therapists or patients in trials of psychologically based treatment, so we planned to follow the procedure we used in Williams 2012 of applying a quality rating scale specifically designed for psychological interventions in pain (Yates 2005).

Measures of treatment effect

Where different trials used different instruments to measure an outcome domain, we planned to analyse the effect size for continuous outcomes by calculating the standardised mean differences (SMD) with 95% confidence intervals (CI). Where appropriate, we planned to apply categories of improvement as defined by the IMMPACT group (Dworkin 2008) and analyse dichotomously. For dichotomous outcomes, we planned to calculate the odds ratio (OR) with 95% CI.

Unit of analysis issues

For trials with more than one treatment arm, we planned to combine the arms provided that the treatments were sufficiently similar.

Dealing with missing data

For continuous variables we could not assign participants who were excluded from analysis; we used the data from the published reports. We distinguished between intention-to-treat (ITT) and per protocol (PP) analyses when judging quality.

Assessment of heterogeneity

We planned to deal with clinical heterogeneity by only combining studies that examined similar conditions. We expected to assess statistical heterogeneity using the I² statistic, and where I² was greater than 50%, we would discuss possible reasons.

Assessment of reporting biases

We searched relevant reviews and the reference sections of eligible trials and planned a funnel plot if there were sufficient studies.

Data synthesis

We planned to use a random-effects model for meta-analysis, assuming significant clinical heterogeneity. We also planned a summary of findings table. However, because data synthesis of included studies was not relevant, we instead present a narrative summary.

Subgroup analysis and investigation of heterogeneity

Ideally, we hoped to be able to perform subgroup analysis by type of neuropathic pain (specifically painful diabetic neuropathy, postherpetic neuralgia, trigeminal neuralgia, phantom limb pain, postoperative or traumatic neuropathic pain, complex regional pain syndrome, cancer-related neuropathy, human immunodeficiency virus (HIV) neuropathy, and spinal cord injury), but we anticipated too few data for this on the basis of previous reviews of chronic pain. We did not plan any other subgroup analyses. We planned to use the I²statistic to test for heterogeneity.

Sensitivity analysis

We did not plan a sensitivity analysis because we knew that the evidence base was too small to allow reliable analysis. We planned to examine details of dose escalation schedules in the unlikely event that this could provide a basis for a sensitivity analysis.

RESULTS

Description of studies

Results of the search

Our database searches yielded 1035 records, which were reduced to 912 after removing duplicates. In addition, we handsearched the bibliographies of 60 reviews, three of which required translation from German and one from Japanese, and we identified 38 potentially eligible studies not previously identified. Of these 950 records, we excluded 849 based on title alone, leaving 101 abstracts to screen. Of these, we rejected 75 and obtained the full text of 26 (see Figure 1). After assessing these, we included two eligible studies (Heutink 2012; Miziara 2009) in five papers. In addition, we identified nine potentially relevant studies from the clinical trials registries, finding five relevant ongoing studies.

Included studies

Two studies met all of our inclusion criteria. Heutink 2012 consisted of a published protocol and separate short- and long-term outcome and process papers. The intervention under study was 30 hours of CBT over 10 weeks for outpatients with neuropathic pain from spinal cord injury. A drug company funded the study, which took place in the Netherlands; two-thirds of participants were male, with a mean age of 59. There were 61 participants at the start of the study, with 54 finishing treatment, but investigators were able to collect data from 59 at three-month follow-up, after which the comparator waiting list group entered treatment. A subsequent process study found some associations between changes in cognitive and practical strategies and improvements in pain and disability.

Johannsen 2016a reported a study of women who have ≥ 3 on a numeric rating scale, three months after breast cancer surgery. One hundred and twenty-nine women were randomised to mindfulness based cognitive therapy or a waiting-list control. Women in the treatment group received eight weekly sessions lasting two years in mindfulness, yoga, and cognitive exercises.

Miziara 2009 reported their results in a single paper for a trial of group psychotherapy sessions delivered once a week for three months for outpatients with burning mouth syndrome, conceptualised as a psychosomatic disorder. The study took place in Brazil; two-thirds of participants were female, with a mean age



of 55. The study involved 44 participants and had no dropouts; the comparison group took a single placebo tablet daily for a month. Investigators did not declare the source of funding.

Excluded studies

Of the 23 studies that we excluded after reviewing the full text, two are new to this update (Johannsen 2016; Pozeg 2017). There were two (non-randomised) trials studying neuropathic pain: Edelson 1989 treated subjects with mixed neuropathic pain by hypnosis or CBT, and Perry 2010 treated subjects with neuropathic pain related to spinal cord injury with a multidisciplinary cognitive behavioural pain management programme.

Twelve studies did not assess psychological treatments. These included five of mirror therapy (Brodie 2007; Cacchio 2009a; Cacchio 2009b; Chan 2007; Michielsen 2011), three of graded motor imagery (Moseley 2004; Moseley 2005; Moseley 2006), one of lyengar yoga (Garfinkel 1998), one of 'therapeutic touch' (Blankfield 2001), one virtual reality therapy (Pozeg 2017), and one mindfulness therapy (Johannsen 2016).

Although Wetering 2010 did include Jensen 2001 in their review, this study did not focus on neuropathic pain. Jensen 2009a mixed neuropathic and non-neuropathic pain, and Kip 2014 did not ascertain neuropathic pain but estimated from pain descriptors that about 80% of their sample had it; the study objectives also included treatment for post-traumatic stress disorder, for which they considered pain to be a secondary symptom. Two more excluded studies described related RCTs of psychological treatment in HIV-positive people with neuropathic pain, but it was not clear that the neuropathic pain was chronic (lasting for more

than three months), and we received no answers from the authors on this question (Davis 2004; Evans 2003). In any case, these two studies did not meet our criterion for a minimum of 20 participants per arm at the end of treatment, so we would have excluded them regardless. One further study of sciatic pain recruited acute pain patients (Hasenbring 1999).

We also excluded three other studies due to an insufficient number of participants: Jensen 2009b treated subjects with multiple sclerosis-related pain using self-hypnosis, Meize-Grochowski 2012 treated subjects with postherpetic neuralgia by mindfulness meditation, and Rickard 2004 treated subjects with stump or phantom limb pain by hypnosis.

Ongoing studies

The trials register searches produced nine trials, of which five were potentially eligible for inclusion (NCT00829387; NCT00830011; NCT00731614; NCT02125006; NCT01884662). Three are completed, but the results are not yet available (NCT00829387; NCT00830011; NCT00731614).

Studies awaiting classification

There were no studies awaiting classification.

Risk of bias in included studies

We used the standard Cochrane methods for assessing risk of bias; because of the low number of eligible studies and their lack of amenability to meta-analysis, we did not proceed with the Yates 2005 quality rating as planned (Figure 2, Figure 3).



Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

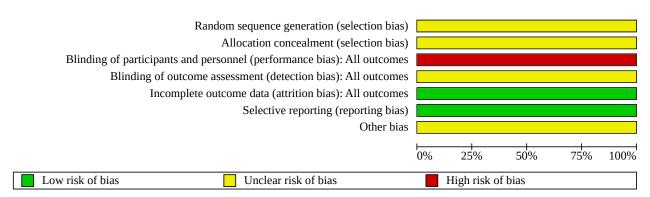
Blinding of participants and personnel (performance bias): All outcomes Blinding of outcome assessment (detection bias): All outcomes Incomplete outcome data (attrition bias): All outcomes Random sequence generation (selection bias) Allocation concealment (selection bias) Selective reporting (reporting bias) Other bias

Miziara 2009

Heutink 2012



Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

Neither study provided details on randomisation method nor information on allocation concealment, so we rated the bias for this domain as unclear.

Blinding

There was no information in either study about attempts to blind patients to allocation or to assess their expectations of benefit, and while Heutink 2012 used a waiting list control that would be unlikely to generate expectations of benefit to the active treatment, Miziara 2009 compared group psychotherapy, which might not have been very credible to patients as an intervention for pain, with a placebo tablet, which might have generated some expectation of benefit. However, neither study sampled participant expectations. Further, all assessment was by self-report, whereas a blinded assessor should ideally have evaluated the outcomes under study.

Incomplete outcome data

Heutink 2012 used ITT analysis but did not provide details about how they generated missing values; Miziara 2009 reported no attrition.

Selective reporting

Both studies reported all the outcome measures listed in their Methods. No further investigation was possible because no record of the trial protocols was found.

Other potential sources of bias

Neither control condition (waiting list for Heutink 2012, a placebo tablet for Miziara 2009) shared any general characteristics with the active treatment arm (30 hours CBT for Heutink 2012, weekly group psychotherapy for 3 months for Miziara 2009) in terms of time, therapist contact, or group support.

Effects of interventions

It was not possible to combine any of the outcomes from the two included papers.

For descriptive purposes we used RevMan to calculate the fixed-effect mean difference (MD). For the Heutink 2012 study, there were no immediate effects post-treatment on pain intensity, disability, or anxiety. Pain intensity data had an MD of -2.00 (95% CI – 9.65 to 5.65;

Analysis 1.1). Disability data had a MD of - 6.20 (95% CI - 20.37 to 7.97; Analysis 1.2). Anxiety data had a MD of -0.10 (95% CI -1.99 to 1.79; Analysis 1.3). Investigators reported the same pattern of data showing no effects at follow-up. Pain intensity data had a MD of 0.40 (95% CI - 7.69 to 8.49; Analysis 2.1). Disability data had a MD of -3.90 (95% CI - 17.79 to 9.99; Analysis 2.2). Anxiety data had a MD of 0.30 (95% CI - 1.63 to 2.23; Analysis 2.3).

For the Miziara 2009 study we were able to extract dichotomous data using the category of 'no worse than mild pain'. There was no effect of treatment compared to placebo in patients in this category at the end of treatment. The relative risk was 1.50 (95% CI 0.60 to 3.76; Analysis 3.1).

There were no data on adverse events.

We can make no conclusion on the efficacy or safety of psychological treatments for neuropathic pain from these two small, different studies.

DISCUSSION

Summary of main results

We found only two eligible studies, which we could not combine for meta-analysis because they differed in treatment method, participants, and outcomes. Neither study provided evidence supporting psychological therapy for neuropathic pain. Group therapy for burning mouth syndrome was not effective in changing pain status, but the comparison group was not a credible comparison, being placebo designed for an oral pharmacological treatment not a psychotherapy treatment (Miziara 2009). The more conventional CBT for spinal cord injury pain did not mitigate pain either, nor (using our calculations) did it improve disability or anxiety (the other two primary outcomes) by the end of treatment or at three month follow-up (Heutink 2012). Overall, we are unable to conclude anything from these two small, negative, and very different studies.

We excluded three further studies solely because there were fewer than 20 participants in each arm at the point of assessment: two used hypnosis –Jensen 2009b in people with multiple sclerosis-related pain, and Rickard 2004 with stump or phantom limb pain) – while a third used mindfulness meditation in people with postherpetic neuralgia (Meize-Grochowski 2012). These illustrate the diversity of methods and neuropathic pain populations in



the wider field. Some of the excluded trials could be eligible for inclusion in other reviews of therapies aimed at reducing pain directly: mirror therapy, used predominantly for complex regional pain syndrome (CRPS); and hypnosis, often used for spinal cord injury or phantom pain.

Overall completeness and applicability of evidence

We found most but not all of the neuropathic pain groups we had $anticipated \, among \, the \, included, \, excluded, \, and \, ongoing \, studies; \, we \,$ did not find studies in people experiencing postoperative pain or cancer-related neuropathic pain. CRPS was treated most often with mirror therapy, motor imagery, or both, conceived and delivered mostly in non-psychological frameworks (although Moseley came closer to psychological methods than others; Moseley 2004; Moseley 2005; Moseley 2006). We also included a study of burning mouth syndrome, a diagnosis we had not anticipated among neuropathic pain groups. Although chronic pain is a significant problem in many of the people falling under our inclusion criteria, some of those people may receive all or most of their care within specialist services defined by the disease, such as diabetes or HIV, rather than in specialist pain services, where psychologically based treatment is more often available. Treating physicians may refer patients to specialist pain services only when they have no specific diagnosis, which is not the case for people suffering from neuropathic pain, or when they attribute patients' distress and disability to psychological factors. We do not endorse this way of implicitly dividing pain-related problems into inaccurate categories of 'organic' and 'psychological', because it is typically based on flawed science (Crombez 2009), but we recognise that it continues to guide referral in many health services.

While one of the studies reviewed used a mainstream chronic pain intervention, CBT, the other used an unconventional therapy drawn from mental health interventions and delivered within that framework, identifying burning mouth as a 'non-organic' pain problem on the basis of the lack of physical findings. Among the three studies excluded on the basis of their number of participants, two used hypnosis/self-hypnosis. Hypnosis is relatively rare in the treatment of low back or mixed chronic pain where the target of therapy is reactivation despite chronic pain; however, it is more common in neuropathic pain where the target of therapy is pain itself (Williams 2012).

The range of outcomes was adequate in Heutink 2012 but not in Miziara 2009; neither study reported adverse events, nor did they assess effects on healthcare use, our secondary outcome.

Quality of the evidence

There are no estimates of effect so a Grading of Recommendations Assessment, Development and Evaluation (GRADE) judgement of the quality of the evidence was not relevant, except by definition the quality of the evidence base was 'low' due to single small studies with extant biases.

Neither trial had sufficient information to determine selection bias, nor was it feasible (for a psychologically based trial) to blind therapists to treatment group. Both trials assessed by self-report, so they did not introduce detection bias but neither did they use third party or objective measures, such as function. Both avoided attrition bias and reporting bias, although outcomes were narrow,

particularly for Miziara 2009, and both failed to include adverse events

Potential biases in the review process

There were no obvious sources of bias in our search, but we had to assess a number full text reports to ascertain their eligibility for this review, as many abstracts did not provide sufficient information to make a firm determination. This may have introduced a bias in the representation of studies in the excluded category. We did not have difficulty applying criteria: we decided that mirror therapy and motor imagery did not constitute psychological treatment but rather education followed by intensive repeated exercises supervised by a physiotherapist, with no involvement of a psychologist. There were no discrepancies in data extraction that required the involvement of the third author.

Agreements and disagreements with other studies or reviews

Our study disagrees with the only other review we found, Wetering 2010, which included 14 studies but only three RCTs (Jensen 2001; Brodie 2007; Evans 2003). We excluded all of these: Brodie 2007 because it studied mirror therapy, with no psychological content; Evans 2003 because it focused on acute or sub-acute pain, and had fewer than 20 participants per arm; and Jensen 2001, by far the largest of the three, because the paper makes it clear that participants were experiencing musculoskeletal back and neck pain, not neuropathic pain (Wetering 2010 apparently included the study on the description of the participants as having 'spinal pain'). Wetering 2010 reported a conclusion of the positive and promising effects of psychological interventions for neuropathic pain. We believe this was based on flawed methods.

A Cochrane review of all non-pharmacological interventions for chronic pain in people with spinal cord injury included a comparison of cognitive behavioural therapy, also analysing Heutink 2012. Our results were in agreement (Boldt 2014).

Our results, such as they are, compare poorly with those from psychologically based interventions for mixed chronic pain (Williams 2012), which reported clear benefits for distress and disability in participants. The Heutink 2012 trial was certainly comparable with many of the trials included in that systematic review, but its negative findings were not offset by positive results from other trials in the present review. Our results also fall short of the general conclusions of numerous reviews of predominantly pharmacological treatments for specific neuropathic pain conditions, which find unambiguous—if not impressive—benefits for at least some patients.

AUTHORS' CONCLUSIONS

Implications for practice

The data recovered in this search and analysis do not provide any meaningful implications for individual practice or policy. Rather, our review demonstrates clearly the lack of direct evidence for or against the effectiveness of psychological interventions in altering the experience of pain, disability and impaired mood associated with chronic neuropathic pain. Thus, for now, there is still a large and growing population of people disabled by chronic neuropathic pain from diabetic neuropathy, cancer treatments, and other causes, who have limited options for treatment.



Implications for research

There is a worrying lack of trial data in this area of need. We need RCTs of specific psychological treatments tailored for neuropathic pain populations. Good candidate conditions for effective trial design and delivery are

- Peripheral Diabetic Neuropathy. An optimal treatment could be cognitive and behavioural methods aiming to increase activity and participation in society, with specific content to address mood disorder, sleep problems, and increased pain on activity. This treatment could be one component in the management of complications from diabetes.
- 2. HIV neuropathy, treated with cognitive and behavioural methods focused on social emotional functioning, compared with no treatment, aiming to address beliefs about pain, low mood, and participation in society, including work. This may be a difficult group to engage and the delivery of rehabilitative treatment might be more effective outside direct health service settings (Davis 2004).
- 3. Postherpetic neuralgia, treated with cognitive behavioural therapy incorporating some of the exposure methods used with CRPS, compared with nonspecific support and medication. Outcomes of interest might include better management of provoked pain, more engagement in valued activities, and less anxiety and depression concerning the pain (Daniel 2008).

All trials would need to be sufficiently powered (200 patients or more) and involve service users in their design, which

would include acceptable comparison groups and options for supplementary content using electronic media. Placebo comparison groups should control for patient trust and belief in therapy outcome (i.e. be equally credible), time of exposure to therapy, and general educational content. Primary endpoints should follow other neuropathic pain treatments in terms of pain, but investigators should define potential improvements in distress, disability, quality of life, pain, sleep, and acceptability/adherence in advance, also routinely reporting adverse events. See Morley 2013 for further discussion.

More generally, and to facilitate future reviews, it would be helpful if abstracts contained essential information about what treatment is used, for which pain problem, in how many participants, and what outcomes are reported, as well as whether the study was randomised and what the comparison conditions were. Reviewers can assess the studies that include this information in the abstract more effectively than those that do not.

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CHARACTERISTICS OF STUDIES

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Heutink 2012

Study characteristics

Methods

RCT, treatment versus waiting list, multicentre trial



Heutink 2012 (Continued)

Participants

Neuropathic Pain condition: NP after SCI, recruited from Dutch rehabilitation centres at least 1 year after first discharge from inpatient rehabilitation; minimum 40/100 pain score over last week; median time since SCI 5.4 years; NP for at least 6 months; median time in pain, 4.5 years

Number of participants: 61 at start of treatment, 54 at end of treatment, but data for 59 at follow-up

Mean age (SD): 59 (± 11) **Sex**: 39 men; 22 women

Interventions

Cognitive behavioural therapy versus waiting list; 10 sessions of 3 hours over 10 weeks = 30 hours.

Participants were randomly assigned to either:

Experimental arm: "educational, cognitive and behavioral elements" with detailed protocol and one day's training

Duration: 10 sessions of 3 h over 10 weeks = 30 h

Treatment protocol: refer to biopsychosocial model and model linking events, beliefs, and consequences

Therapists: psychologist and physiotherapist in 3 centres, nurse-practitioner and physiotherapist in 1 centre

Comparator arm: waiting list, after which invited to join treatment programme

Outcomes

Primary outcomes

- Pain intensity: Chronic Pain Grade Questionnaire, 0-10 over last week
- Pain-related disability: Chronic Pain Grade Questionnaire, (0-100 with larger number meaning more disability)

Secondary outcomes

- Anxiety: HADS (0-21 with larger numbers meaning more anxiety)
- Participation in activities: Utrecht Activities List
- Quality of life: Life Satisfaction Questionnaire

Timepoints for assessment: baseline, end of treatment (3 months), 3-month follow-up

Notes

Data available for all outcomes, all 3 time points

Study period: unknown but probably in 2010

Country: Netherlands

Funding source: unrestricted grant from Pfizer

Declarations of interest among the primary researchers: no competing interests

Dutch Trial Register NTR1580

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Participants were randomly allocated to the intervention group or to the waiting list control group within each participating rehabilitation center."
Allocation concealment (selection bias)	Unclear risk	No information



Heutink 2012 (Continued)		
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	None
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessment all by self-report
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis: no information on how investigators generated data for missing participants - EF: shouldn't this be high?
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	No further information on therapist qualifications; one day training and detailed protocol, and one of authors attended 2 sessions at each of 4 centres to ensure adherence to protocol
		No information on therapist allegiance

Miziara 2009

Study characteristics	
Methods	RCT, treatment versus daily placebo medication
Participants	Neuropathic Pain condition: Burning mouth syndrome, no identifiable organic cause
	Number of participants: 44 (recruited from 64 consecutive outpatients); no dropouts
	Mean age (SD) : 55 (± 7)
	Sex : 15 men; 29 women
Interventions	Group psychotherapy, 1 session per week for 3 months
	Participants were randomly assigned to either:
	Experimental arm: 24 participants, psychotherapy sessions in groups of 4
	Duration: once weekly for 3 months
	Treatment protocol: no information
	Therapist: psychologist
	Comparator arm: 20 participants
	Duration: 30 days
	Treatment protocol: one placebo capsule per day
	Therapist: none
	No data on adherence
Outcomes	Pain : short-form McGill Pain Questionnaire PPI, classified as improved versus not improved, and in 5 groups at assessment (no pain, mild, discomforting, distressing, horrible)
avala al a si a al Albaya mi a a fav	the management of chronic neuronathic pain in adults (Peview)



Miziara 2009	(Continued)
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Timepoints for assessment: before randomisation and at end of treatment (3 months for treatment group, 1 month for control group)

Notes **Study period**: 2002-2007

Country: Brazil

Funding source: none declared

Declarations of interest among the primary researchers: none declared

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"The other 44 patients with primary BMS were randomized and distributed into two groups."
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	None
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Assessment by self-report
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Single outcome reported
Other bias	Unclear risk	No information on therapist training, instructions with placebo, therapist allegiance, or treatment fidelity

BMS: burning mouth syndrome; **HADS**: Hospital anxiety and depression scale; **NP**: neuropathic pain; **PPI**: present pain intensity;**RCT**: randomised controlled trial; **SCI**: spinal cord injury.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Blankfield 2001	Not a psychological intervention (therapeutic touch works by 'energy exchange')
Brodie 2007	Not a psychological intervention (mirror therapy)
Cacchio 2009a	Not a psychological intervention (mirror therapy)
Cacchio 2009b	Not a psychological intervention (mirror therapy)
Chan 2007	Not a psychological intervention (mirror therapy)



Study	Reason for exclusion
Davis 2004	N < 20 at end of treatment
	Unclear if NP > 3 months
Edelson 1989	Not RCT
Evans 2003	N < 20 at end of treatment
	Unclear if NP > 3 months
Garfinkel 1998	Not a psychological intervention (Iyengar yoga)
Hasenbring 1999	N < 20 at end of treatment
	Unclear if NP > 3 months
Jensen 2001	Not NP (spinal pain)
Jensen 2009a	Exclusions: N < 20 at start of treatment
	Not clear if all NP
Jensen 2009b	N < 20
Johannsen 2016	Insufficient psychotherapeutic content
Kip 2014	80% thought to be NP by pain descriptors
	Treatment aimed at PTSD not pain: pain was secondary outcome
Meize-Grochowski 2012	Exclusions: N < 20
	Data not yet published
Michielsen 2011	Not a psychological intervention (mirror therapy)
Moseley 2004	Not a psychological intervention (graded motor imagery)
Moseley 2005	Not a psychological intervention (graded motor imagery)
Moseley 2006	Not a psychological intervention (graded motor imagery)
Perry 2010	Not RCT
Pozeg 2017	
Rickard 2004	N < 20

NP: neuropathic pain; **PTSD**: post-traumatic stress disorder; **RCT**: randomised controlled trial.

Characteristics of ongoing studies [ordered by study ID]

NCT00731614

Study name	Cognitive behavior therapy (CBT) and mirror training for phantom limb pain	
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NCT00731614 (Continued)	
Methods	RCT
Participants	Phantom limb pain
Interventions	CBT + mirror therapy versus supportive care
Outcomes	Phantom Limb Pain Questionnaire
	SF-12
Starting date	November 2008
Contact information	John McQuaid: John.McQuaid@va.gov

NCT00731614. Closed December 2012. Results not expected to be published until late 2015.

NCT00829387

Notes

Study name	Cognitive behavioral therapy for diabetic neuropathic pain
Methods	RCT
Participants	Diabetic peripheral NP
Interventions	Brief CBT + pharmacotherapy versus education + pharmacotherapy
Outcomes	Pain (NRS); pain interference (MPI)
Starting date	Completed but no results
Contact information	Alicia Heapy: alicia.heapy@va.gov
Notes	NCT00829387

NCT00830011

Methods RCT Participants Diabetic NP of lower limb(s) Interventions CBT + standard medical care versus standard medical care Outcomes Pain intensity (NRS); pain-related disability (MPI) Starting date 2004-2011	Study name	Cognitive behavioral therapy for painful diabetic neuropathy
Interventions CBT + standard medical care versus standard medical care Outcomes Pain intensity (NRS); pain-related disability (MPI) Starting date 2004-2011	Methods	RCT
Outcomes Pain intensity (NRS); pain-related disability (MPI) Starting date 2004-2011	Participants	Diabetic NP of lower limb(s)
Starting date 2004-2011	Interventions	CBT + standard medical care versus standard medical care
	Outcomes	Pain intensity (NRS); pain-related disability (MPI)
	Starting date	2004-2011
Contact information Robert Kerns: robert.kerns@va.gov	Contact information	Robert Kerns: robert.kerns@va.gov
Notes NCT00830011 completed but not yet published	Notes	NCT00830011 completed but not yet published



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Study name	Virtual walking for neuropathic pain in spinal cord injury
Methods	RCT
Participants	People with traumatic spinal cord injury with neuropathic pain
Interventions	Virtual reality walking versus tape of wheeling (wheelchair)
Outcomes	Change in pain (NRS); change in pain interference (NRS); change in neuropathic pain (NPS); cortical somatosensory plasticity (fMRI)
Starting date	2012-2016
Contact information	John S Richards, University of Alabama at Birmingham
Notes	NCT01884662

NCT02125006

Study name	The effect of an inter-disciplinary program, including MBSR, in breast cancer survivors with chronic neuropathic pain (in depth)
Methods	RCT
Participants	Breast cancer survivors
Interventions	Medical treatment and MSBR versus waitlist
Outcomes	Pain interference (BPI); pain intensity (NPSI); pain severity (BPI); mood (POMS); depression (PHQ); catastrophising (PCS); mindfulness; stress; quality of life (SF-12); cortisol; immune function; white matter integrity; brain volume; patient global impression of change
Starting date	2013-2016
Contact information	Patricia Poulin, Ottawa Hospital Research Institute
Notes	NCT02125006

BPI: brief pain inventory; **CBT**: cognitive behavioural therapy;**fMRI**: functional magnetic resonance imaging; **MBSR**: mindfulness-based stress reduction;**MPI**: multidimensional pain inventory; **NP**: neuropathic pain; **NPS**: neuropathic pain scale; **NPSI**: neuropathic pain symptom inventory; **NRS**: numerical rating scale; **PCS**: pain catastrophising scale; **PQ**: patient health questionnaire; **POMS**: profile of mood states; **RCT**: randomised controlled trial; **SF-12**: 12-item Short Form Health Survey.

DATA AND ANALYSES



Comparison 1. CBT versus control post-treatment

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1.1 Pain intensity	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.2 Pain disability	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.3 Anxiety	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1: CBT versus control post-treatment, Outcome 1: Pain intensity

Study or Subgroup	Mean	CBT SD	Total	Mean	WLC SD	Total	Mean Difference IV, Fixed, 95% CI	Mean IV, Fix	Differe		
Heutink 2012	65.2	12.7	24	67.2	16	30	-2.00 [-9.65 , 5.65]		+		
								-100 -50 Favours CBT	0 Fa	50	100 Vaiting List

Analysis 1.2. Comparison 1: CBT versus control post-treatment, Outcome 2: Pain disability

Study or Subgroup	Mean	CBT SD	Total	Mean	WLC SD	Total	Mean Difference IV, Fixed, 95% CI		ifference I, 95% CI
Heutink 2012	38	25.4	24	44.2	27.6	30	-6.20 [-20.37 , 7.97]	-+	
								-100 -50 Favours CBT	50 100 Favours Waiting List

Analysis 1.3. Comparison 1: CBT versus control post-treatment, Outcome 3: Anxiety

Study or Subgroup	Mean	CBT SD	Total	Mean	WLC SD	Total	Mean Difference IV, Fixed, 95% CI				erence 95% CI	
Heutink 2012	5.6	3.6	24	5.7	3.4	30	-0.10 [-1.99 , 1.79]					
								-100	-50	0	50	100
								Fa	vours CBT		Favours	Waiting List

Comparison 2. CBT versus control at follow up

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
2.1 Pain intensity	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.2 Pain disability	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.3 Anxiety	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected



Analysis 2.1. Comparison 2: CBT versus control at follow up, Outcome 1: Pain intensity

		CBT			WLC		Mean Difference		Mean	Diff	erence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI		IV, Fix	ked, 9	95% CI	
Heutink 2012	66.7	13	24	66.3	17.3	30	0.40 [-7.69 , 8.49]			+		
								-100 Favo	-50 ours CBT	0	50 Favours	100 Waiting List

Analysis 2.2. Comparison 2: CBT versus control at follow up, Outcome 2: Pain disability

Study or Subgroup	Mean	CBT SD	Total	Mean	WLC SD	Total	Mean Difference IV, Fixed, 95% CI		ifference I, 95% CI
Heutink 2012	38.9	24.5	24	42.8	27.5	30	-3.90 [-17.79 , 9.99]		
								-100 -50 Favours CBT	0 50 100 Favours Waiting List

Analysis 2.3. Comparison 2: CBT versus control at follow up, Outcome 3: Anxiety

		CBT			Control		Mean Difference		Mean	Diff	erence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Fixed, 95% CI		IV, Fix	ed, 9	95% CI	
Heutink 2012	5.9	3.6	24	5.6	3.6	30	0.30 [-1.63 , 2.23]					
								-100 Far	-50	0	50 Favours	100 Waiting List

Comparison 3. Group psychotherapy versus placebo post-treatment

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
3.1 No worse than mild pain	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 3.1. Comparison 3: Group psychotherapy versus placebo post-treatment, Outcome 1: No worse than mild pain

	Experin	nental	Cont	rol	Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Miziara 2009	9	24	5	20	1.50 [0.60 , 3.76]	
						0.1 0.2 0.5 1 2 5 10 Favours Placebo Favours Psychotherapy



APPENDICES

Appendix 1. Search strategies

CENTRAL (CRSO)

MESH DESCRIPTOR Psychotherapy EXPLODE ALL TREES

MESH DESCRIPTOR Behavior Therapy

MESH DESCRIPTOR cognitive therapy EXPLODE ALL TREES

MESH DESCRIPTOR Biofeedback, Psychology EXPLODE ALL TREES

(behavio?r therap*):TI,AB,KY

(cognitive therap*):TI,AB,KY

((relax* near3 therap*)):TI,AB,KY

((relax* near3 technique*)):TI,AB,KY

meditat*:TI,AB,KY

psychotherap*:TI,AB,KY

((psychological near2 (treatment* or therap*))):TI,AB,KY

("group therapy"):TI,AB,KY

("self-regulation training"):TI,AB,KY

("coping skill*"):TI,AB,KY

("pain-related thought*"):TI,AB,KY

((behavio?r* near3 rehabilitat*)):TI,AB,KY

((psychoeducation near2 group*)):TI,AB,KY

((psycho-education near2 group*)):TI,AB,KY

(("mind and body relaxation technique*" or "mind-body relaxation technique*")):TI,AB,KY

MESH DESCRIPTOR mind-body therapies EXPLODE ALL TREES

MESH DESCRIPTOR relaxation therapy

#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

MESH DESCRIPTOR Neuralgia EXPLODE ALL TREES

MESH DESCRIPTOR Chronic Pain

((neuralgia* or neurodynia)):TI,AB,KY

(((neuropathic or nerve*) near3 pain*)):TI,AB,KY

#23 OR #24 OR #25 OR #26

#22 AND #27

MEDLINE (OVID)

1 exp Psychotherapy/

2 behavior therapy/ or cognitive therapy/

3 exp Biofeedback, Psychology/

4 behavio#r therap*.tw.



- 5 cognitive therap*.tw.
- 6 (relax* adj3 technique*).tw.
- 7 (relax* adj3 (technique* or therap*)).tw.
- 8 meditat*.tw.
- 9 psychotherap*.tw.
- 10 (psychological adj2 (treatment* or therap*)).tw.
- 11 "group therapy".tw.
- 12 "self-regulation training".tw.
- 13 "coping skill*".tw.
- 14 "pain-related thought*".tw.
- 15 (behavio#r* adj3 rehabilitat*).tw.
- 16 (psychoeducation adj2 group*).tw.
- 17 (psycho-education adj2 group*).tw.
- 18 ("mind and body relaxation technique*" or "mind-body relaxation technique*").tw.
- 19 exp mind-body therapies/ or relaxation therapy/
- 20 or/1-19
- 21 exp Neuralgia/
- 22 Chronic Pain/
- 23 (neuralgia* or neurodynia).tw.
- 24 ((neuropathic or nerve*) adj3 pain*).tw
- 25 or/21-24
- 26 20 and 25
- 27 randomized controlled trial.pt.
- 28 controlled clinical trial.pt.
- 29 randomized.ab.
- 30 placebo.ab.
- 31 drug therapy.fs.
- 32 randomly.ab.
- 33 trial.ab.
- 34 or/27-33
- 35 exp animals/ not humans.sh.
- 36 34 not 35
- 37 26 and 36

EMBASE (OVID)

- 1. exp Psychotherapy/
- 2. behavior therapy/ or cognitive therapy/
- 3. exp Biofeedback, Psychology/
- 4. behavio#r therap*.tw.
- 5. cognitive therap*.tw.
- 6. (relax* adj3 technique*).tw.
- 7. (relax* adj3 (technique* or therap*)).tw.
- 8. meditat*.tw.
- 9. psychotherap*.tw.
- 10. (psychological adj2 (treatment* or therap*)).tw.
- 11. "group therapy".tw.
- 12. "self-regulation training".tw.
- 13. "coping skill*".tw.
- 14. "pain-related thought*".tw.
- 15. (behavio#r* adj3 rehabilitat*).tw.



- 16. (psychoeducation adj2 group*).tw.
- 17. (psycho-education adj2 group*).tw.
- 18. ("mind and body relaxation technique*" or "mind-body relaxation technique*").tw.
- 19. exp mind-body therapies/ or relaxation therapy/
- 20. or/1-19
- 21. exp Neuralgia/
- 22. Chronic Pain/
- 23. (neuralgia* or neurodynia).tw.
- 24. ((neuropathic or nerve*) adj3 pain*).tw.
- 25. or/21-24
- 26. 20 and 25
- 27. random\$.tw.
- 28. factorial\$.tw.
- 29. crossover\$.tw.
- 30. cross over\$.tw.
- 31. cross-over\$.tw.
- 32. placebo\$.tw.
- 33. (doubl\$ adj blind\$).tw.
- 34. (singl\$ adj blind\$).tw.
- 35. assign\$.tw.
- 36. allocat\$.tw.
- 37. volunteer\$.tw.
- 38. Crossover Procedure/
- 39. double-blind procedure.tw.
- 40. Randomized Controlled Trial/
- 41. Single Blind Procedure/
- 42. or/27-41
- 43. (animal/ or nonhuman/) not human/
- 44. 42 not 43
- 45. 26 and 44

PsycINFO (OVID)

- 1. exp Psychotherapy/
- 2. behavior therapy/ or cognitive therapy/
- 3. exp Biofeedback/
- 4. behavio#r therap*.tw.



- 5. cognitive therap*.tw.
- 6. (relax* adj3 technique*).tw.
- 7. (relax* adj3 (technique* or therap*)).tw.
- 8. meditat*.tw.
- 9. psychotherap*.tw.
- 10. (psychological adj2 (treatment* or therap*)).tw.
- 11. "group therapy".tw.
- 12. "self-regulation training".tw.
- 13. "coping skill*".tw.
- 14. "pain-related thought*".tw.
- 15. (behavio#r* adj3 rehabilitat*).tw.
- 16. (psychoeducation adj2 group*).tw.
- 17. (psycho-education adj2 group*).tw.
- 18. ("mind and body relaxation technique*" or "mind-body relaxation technique*").tw.
- 19. exp mind-body therapies/ or relaxation therapy/
- 20. or/1-19
- 21. exp Neuralgia/
- 22. Chronic Pain/
- 23. (neuralgia* or neurodynia).tw.
- 24. ((neuropathic or nerve*) adj3 pain*).tw.
- 25. or/21-24
- 26. 20 and 25
- 27. clinical trials/
- 28. (randomis* or randomiz*).tw.
- 29. (random\$ adj3 (allocat\$ or assign\$)).tw.
- 30. ((clinic\$ or control\$) adj trial\$).tw.
- 31. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (blind\$ or mask\$)).tw.
- 32. (crossover\$ or "cross over\$").tw.
- 33. random sampling/
- 34. Experiment Controls/
- 35. Placebo/
- 36. placebo\$.tw.
- 37. exp program evaluation/
- 38. treatment effectiveness evaluation/
- 39. ((effectiveness or evaluat\$) adj3 (stud\$ or research\$)).tw.



40. or/27-39

41. 26 and 40

HISTORY

Protocol first published: Issue 8, 2014 Review first published: Issue 10, 2015

Date	Event	Description		
22 June 2020	Review declared as stable	See Published notes.		
30 September 2019	Amended	Clarification added to Declarations of interest.		
13 November 2018	Review declared as stable	See Published notes		
12 November 2018	Amended	See Published notes		
26 September 2017	Review declared as stable	See Published notes.		

CONTRIBUTIONS OF AUTHORS

CE directed the project and is responsible for updates. CE, LH, and AW all contributed to conceptualising and authoring the review.

DECLARATIONS OF INTEREST

Christopher Eccleston (CE) receives funding support from the UK National Institute for Health Research for work on a series of reviews informing the unmet need of chronic pain and providing the evidence for treatments of pain. This title is part of this research programme. Since CE is an author as well as the PaPaS Co-ordinating Editor at the time of writing, we acknowledge the input of Andrew Moore who acted as Sign Off Editor for this review. CE had no input into the editorial decisions or processes for this review.

Leslie Hearn: none known.

Amanda Williams: none known.

SOURCES OF SUPPORT

Internal sources

· None, Other

External sources

• The National Institute for Health Research (NIHR), UK

NIHR Cochrane Programme Grant: 13/89/29 - Addressing the unmet need of chronic pain: providing the evidence for treatments of pain.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- 1. We used a fixed-effects rather than a random-effects model to extract an effect size from the single study in the analysis; likewise, we presented mean rather than standardised mean difference.
- 2. We reported a relative risk rather than an odds ratio for the single study in the analysis that offered dichotomous data.
- 3. We dropped the adverse events outcome in order to specify a single aim.
- 4. Because of the low number of eligible studies and their lack of amenability to meta-analysis, we did not proceed with the Yates 2005 scale as planned.
- 5. There is no 'Summary of findings' table as there are insufficient data to create one.



NOTES

2018

A restricted search in June 2018 did not identify any potentially relevant studies likely to change the conclusions. Therefore, this review has now been stabilised for two years following discussion with the authors and editors. If appropriate, we will update the review earlier if new evidence likely to change the conclusions is published, or if standards change substantially which necessitate major revisions.

2020

We performed another restricted search in May 2020 which did not identify any potentially relevant studies likely to change the conclusions. This is not an active area of research and so this review has now been stabilised following discussion with the authors and editors. If appropriate, we will update the review if new evidence likely to change the conclusions is published, or if standards change substantially which necessitate major revisions.

INDEX TERMS

Medical Subject Headings (MeSH)

Chronic Pain [*therapy]; *Cognitive Behavioral Therapy; Neuralgia [*therapy]; *Psychotherapy, Group; Randomized Controlled Trials as Topic

MeSH check words

Adult; Female; Humans; Male; Middle Aged