Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy (Review)

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[Intervention Review]

Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

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ABSTRACT

Background

Recurrent chest pain in the absence of coronary artery disease is a common problem that sometimes leads to excess use of medical care. Although many studies examine the causes of pain in these patients, few clinical trials have evaluated treatment. The studies reviewed in this paper provide an insight into the effectiveness of psychological interventions for this group of patients.

Objectives

To update the previously published systematic review.

Search methods

We searched the Cochrane LIbrary (CENTRAL and DARE) (Issue 3 of 4 2011), MEDLINE (1966 to August Week 5, 2011), CINAHL (1982 to Sept 2011) EMBASE (1980 to Week 35 2011), PsycINFO (1887 to Sept Week 1, 2011), and Biological Abstracts (January 1980 to Sept 2011). We also searched citation lists and approached authors.

Selection criteria

Randomised controlled trials (RCTs) with standardised outcome methodology that tested any form of psychotherapy for chest pain with normal anatomy. Diagnoses included non-specific chest pain (NSCP), atypical chest pain, syndrome X, or chest pain with normal coronary anatomy (as either inpatients or outpatients).

Data collection and analysis

Two authors independently selected studies for inclusion, extracted data and assessed quality of studies. The authors contacted trial authors for further information about the RCTs included.

Main results

Six new RCTs were located and added to the existing trials, therefore, a total of 15 RCTs (803 participants) were included. There was a significant reduction in reports of chest pain in the first three months following the intervention; fixed-effect relative risk = 0.68 (95% CI 0.57 to 0.81). This was maintained from three to nine months afterwards; relative risk = 0.59 (95% CI 0.45 to 0.76). There was also a significant increase in the number of chest pain free days up to three months following the intervention; mean difference = 2.81 (95% CI 1.28 to 4.34). This was associated with reduced chest pain frequency (random-effects mean difference = -2.26 95% CI -4.41 to -0.12) but there was no evidence of effect of treatment on chest pain frequency from three to twelve months (random-effects mean difference -0.81 95% CI -2.35, 0.74). There was no effect on severity (random-effects mean difference = -4.64 (95% CI -12.18 to 2.89) up to three months after the intervention. Overall there was generally a low risk of bias, however, there was high heterogeneity and caution is required in interpreting these results. Wide variability in outcome measures made integration of studies for secondary outcome measures difficult to report on.

Authors' conclusions

This review suggests a modest to moderate benefit for psychological interventions, particularly those using a cognitive-behavioural framework, which was largely restricted to the first three months after the intervention. Hypnotherapy is also a possible alternative. The evidence for brief interventions was less clear. Further RCTs of psychological interventions for NSCP with follow-up periods of at least 12 months are needed.

PLAIN LANGUAGE SUMMARY

Cognitive-behavioural treatments for non-cardiac chest pain

Recurrent chest pain in the absence of coronary artery disease is a common, difficult to treat problem that sometimes leads to excess use of medical care. A substantial number of patients are not reassured by negative medical assessment, reporting persistent pain and limitations. Psychological factors appear to be of importance for treatment. This review included all studies of psychotherapy for non-cardiac chest pain. Due to the small number of studies, the reviewers were able to draw conclusions about cognitive-behavioural therapy only. The findings were based on 15 trials that were included in this review with a total of 803 participants. The review found that cognitive-behavioural treatments are probably effective, (in terms of reduced chest pain frequency) in the short term, for the treatment of non-cardiac related chest pain. No adverse effects of the psychotherapy were found. Hypnotherapy is also a possible alternative. A limitation of this review is the high variability of the studies included, reflected in a wide range of outcome measures, although there was an overall fairly low risk of bias.

BACKGROUND

Chest pain is one of the most frequent reasons for presentation to emergency services. Of patients admitted to the emergency department for chest pain, more than half are discharged with a diagnosis of non-cardiac chest pain or chest pain of unknown cause (Capewell 2000; Knockaert 2002). Non-specific chest pain accounts for 2-5% of all admissions to the emergency department (Eslick 2003; Knockaert 2002). Approximately 50% of new referrals to outpatient cardiac clinics with the presenting complaint of chest pain are found to have a non-cardiac basis for their pain (Mayou 1997 and Mayou 1999). The reported prevalence of non-cardiac chest pain in the community ranges from 23% to 33% (Eslick 2002; Eslick 2003). While various causes have been proposed, including micro-vascular coronary artery disease, coronary spasm, chest wall pain, oesophageal dysmotility or reflux, hyperventilation, panic disorder, and general anxiety, many patients are given a non-specific diagnosis (Mayou 1997 and Mayou 1999). In all groups of patients there is some association with psychiatric disorder, though the importance of this varies according to diagnosis.

Chest pain with normal coronary anatomy and no clear physical cause has been described by a number of terms including include non-specific chest pain (NSCP), noncardiac chest pain (NCCP), atypical chest pain, syndrome X, or chest pain with normal coronary anatomy. Syndrome X refers to a triad of angina pectoris, pos-

itive exercise electrocardiogram (ECG) for myocardial ischaemia and angiographically smooth coronary arteries (Asbury 2005). This review will use the term non-specific chest pain (NSCP). Most studies of NSCP are concerned with outpatients with normal coronary angiograms whose chest pain is chronic. In one study, 61% of patients with NSCP had psychiatric symptoms on structured interview (the Clinical Interview Schedule), compared to 23% of patients with abnormal coronary arteries (Bass 1984). The respective figures for NSCP and coronary heart disease in another study using the Diagnostic Interview Schedule were 43% & 6.5% for panic disorder, 36% & 4% for major depression, and 36% & 15% for phobias (Katon 1988). These proportions are much higher than in patients with coronary heart disease, although a possible confounding factor may have been the chronic nature of the non-specific chest pain.

There have been similar findings in inpatients. In one study of consecutive admissions to a coronary intensive care unit, 55% of patients with non-specific chest pain (n=27) had panic disorder compared to 11% of those with coronary heart disease (Carter 1992a). There was a similar but non-significant association between major depression and non-specific chest pain (22%) as opposed to coronary heart disease (11%).

The prognosis of patients with NSCP varies with the outcome measure. In contrast to patients with coronary disease, the incidence of myocardial infarction or death in patients with NSCP is zero in most long term studies (Chambers 1990). In terms of functional disability, approximately 75% of patients continue seeing a physician, 50% remain or become unemployed, and 50% regard their lives as significantly disabled. Fewer than 50% of NSCP patients appear reassured that they do not have serious heart disease. Most continue to report residual chest pain during follow-up (Chambers 1990).

A number of possible mechanisms for NSCP have been suggested. These include hyperventilation (DeGuire 1992; DeGuire 1996) or panic disorder (Mayou 1989b) and an association with alcohol and cigarette use (Kisely 1997), possibly mediated through changes in oesophageal motility (Kahrilas 1990; Matsuguchi 1984). Other potential mechanisms are less clear. There may be an interaction in which psychological factors affect the interpretation of physiological perceptions, which in turn, worsen mental state (Chambers 1990). In addition, recent life events as measured by a structured interview or personality factors such as an excess of Type A behaviour (hard driving and competitive behaviour, a potential for hostility, pronounced impatience, and vigorous speech stylistics (Hemingway 1999)) have been identified as occurring more frequently in patients with non-specific chest pain compared to physically healthy controls matched for age and sex (Roll 1987). In addition the presence of pain is associated with increased psychiatric morbidity, including psychophysiological symptoms other than pain, so exacerbating the problem (Von Korff 1988).

Treatment is known to be difficult (Klimes 1990). Some patients are reassured by negative medical assessment, but a substantial number report persistent pain and limitations. A variety of drugs have been used including anti-secretory drugs, anxiolytics, antidepressants, nitrates and calcium channel blockers (Bennett 2001). Because cognitions are of aetiological importance in NSCP and with high levels of psychiatric co-morbidity, psychological approaches have been suggested as appropriate interventions (Bass 1984; Klimes 1990; Ockene 1980) as early intervention might help prevent the pain becoming chronic. Such approaches generally use a behavioural framework and include an explanation of the nature of the pain, treatment of anxiety or depression, and cognitive behavioural psychotherapy.

The exact contributions to a successful outcome are unknown. Given the wide range of behavioural treatments in use, any systematic review would have to include a sensitivity analysis. The sensitivity analysis would identify any dilution of findings in the meta-analysis.

Both cognitive-behavioural therapy (CBT) and psychodynamic therapy are effective in treating anxiety and depressive disorders (Shapiro 1994). CBT has also been shown to be effective in the treatment of patients with unexplained physical symptoms (Speckens 1995) and chronic fatigue syndrome (Price 2008; Sharpe 1996). In a preliminary search of MEDLINE (conducted in 2002), we identified one randomised controlled trial of 34 patients with non-specific chest pain. Participants allocated to a maximum of 11 sessions of CBT with a clinical psychologist showed significant reductions in autonomic symptoms, chest pain, disruption to daily life, autonomic symptoms, distress and psychological activity (Klimes 1990). In comparison, the control group was unchanged. Controls subsequently showed comparable improvements when offered the same course of treatment. This effect was maintained at assessment four to six months later.

Given the large number of people living with chest pain and the high prevalence of psychiatric co-morbidity, it is important to identify psychological interventions that may alleviate such symptoms. Because new evidence had become apparent since the last publication of this systematic review, an update was required.

OBJECTIVES

To assess the effects of psychological interventions for chest pain, quality of life, and psychological parameters in people with non-specific chest pain

The psychological interventions included in this review are:

(1) CBT;

(2) Relaxation therapy;

(3) Hyperventilation control;

(4) Hypnotherapy;

(5) Other psychotherapy/talking /counselling therapy;

(6) Standard care, 'attention' placebo, waiting list controls, or no intervention as the control conditions.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

People presenting with chest pain who have normal anatomy as assessed on clinical history, cardiac enzymes, electrocardiograms, exercise electrocardiograms or coronary angiography. Diagnoses included NSCP, atypical chest pain, syndrome X, or chest pain with normal coronary anatomy (as either inpatients or outpatients). Psychiatric co-morbidity was included, although patients who were receiving drug therapy for psychiatric disorders were excluded.

Types of interventions

Cognitive behavioural therapy

CBT, for the purposes of this review is based on the definition employed by Jones et al (Jones 2004). In order to be classified as 'well defined' the intervention must clearly demonstrate the following components:
(1) the intervention involves the recipient establishing links between their thoughts, feelings and actions with respect to the target symptom;
(2) the intervention involves the correction of the person's misperceptions, irrational beliefs and reasoning biases related to the target symptom;
(3) the intervention should involve either or both of the following:
(a) the recipient monitoring his or her own thoughts, feelings and behaviours with respect to the target symptom;
(b) the promotion of alternative ways of coping with the target symptom.
All therapies that do not meet these inclusion criteria and are described as 'CBT' or 'cognitive therapy' were labelled as 'less-well defined' CBT. The exact nature of 'less-well defined' therapies was established through contact with study authors.

A sensitivity analysis was conducted on the primary outcomes (see type of outcomes) employed in this review to determine whether there was a difference based on the 'well-defined' or 'less-well defined' classification of cognitive-behavioural therapy.

Relaxation therapy

Relaxation therapy consists of alternating tension and relaxation of various muscle groups (Woolfolk 1983). Some studies have added imagery to the relaxation (Borkovec 1982).

Hyperventilation control

Hyperventilation control techniques consist of an explanation of how hyperventilation can contribute to symptoms (DeGuire 1992). Control of hyperventilation can be achieved by holding the breath for 20 seconds and then breathing on a six-second cycle (10 breaths per minute). Breathing should be as light as possible and preferably diaphragmatic. Additional relief can be obtained from either breathing into cupped hands or into a re-breathing bag for one to two minutes every five minutes until symptoms abate (QAP 1982).

Hypnotherapy

Hypnosis can be induced by eye closure, followed by progressive muscular relaxation and standard deepening techniques. Suggestions for normalisation of function and sensitivity are made using both imagery and conditioning techniques (Jones 2006).

Other psychotherapy/talking/counselling therapy

Any psychological intervention described as behavioural therapy such as psychosocial interventions such as non-directive counselling and supportive therapy and other 'talking therapies'.

Control interventions

Any of the above interventions compared with:

Standard care

The care that a person would normally receive had they not been included in the research trial. Standard care was considered to include no change to normal daily activities, and no care in the context of the study, but patients were free to use any health agencies (such as their general practitioner (GP) or medical specialist) on their own initiative. The category 'standard care' also incorporates 'waiting list control groups' where participants receive drug or other interventions.

'Attention' placebo

Interventions where participants are involved in education.

No intervention

Untreated control group.

Types of outcome measures

The primary outcome measure was a significant reduction in chest pain (as defined in the individual studies) following the intervention.
(1) pain intensity measured by categorical scales or visual analogue scales (VAS);
(2) pain diaries (mean difference in pain scores or recorded frequency of exacerbation of pain).
Secondary outcome measures of interest were:
(1) Psychological symptoms as defined by standardised psychiatric instruments or criteria such as the General Health Questionnaire, Beck Depression Inventory, Zung Depression Scale, Hamilton Anxiety and Depression Scales, Hospital Anxiety and Depression Scales, Present State Examination and Composite International Diagnostic Interview;
(2) Quality of life for example Short Form 36 scores;
(3) Health service use for example hospital re-admission for chest pain, outpatient contacts, visits to primary care;
(4) Non-fatal cardiovascular events (stroke, myocardial infarction, angina pectoris, pulmonary embolism, peripheral arterial embolism,);
(5) Cardiac behavioural risk factors reduction (for example smoking, exercise, and alcohol consumption);
(6) Death (cardiovascular and all-cause mortality);
(7) Health beliefs.
Outcomes were grouped into short-term (within 12 weeks of the start of therapy), medium-term (between 13 to 24 weeks after the beginning of therapy), and long-term (more than 24 weeks after the start of therapy) to ensure consistency with Cochrane Heart Group protocol (Lip 2001).

Search methods for identification of studies

Electronic searches

We searched The Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effectiveness (DARE) on *The Cochrane Library* (2011, Issue 3 of 4), MEDLINE (1966 to August Week 5, 2011), EMBASE (1980 to Week 35, 2011), CINAHL (1982 to Sept 2011), PsycINFO (1887 to Sept Week 1, 2011) and BIOSIS Previews (January 1980 to Sept 2011) to identify potentially eligible studies and review articles. Methodological filters were used to identify RCTs in MEDLINE and EMBASE (Lefebvre 2011). Appendix 1 gives details of our of our updated search from 2002 to 2008, and Appendix 2 gives details of our initial search up to 2002. Appendix 3 gives details of the 2011 updated searches.

Searching other resources

The reference lists of all references that were retrieved as full papers, and were potentially relevant, as well as relevant systematic reviews and literature reviews, were checked to identify other potentially relevant articles. These articles were retrieved and assessed for possible inclusion in the review.
Personal communications: we wrote to the lead author of all relevant references to ascertain if they knew of any additional published or unpublished studies that might be relevant to the review.
Abstracts from national and international cardiology, psychiatry and psychology conferences were scrutinised to identify unpublished studies. These included meetings organised by national and international medical colleges, specialty societies and professional organisations.
No language restrictions were applied and all relevant foreign language papers were translated.

Data collection and analysis

Selection of studies for inclusion/exclusion

Two reviewers (SK, LAC) independently selected suitable studies for inclusion in this review as detailed below. Where the two reviewers disagreed about the inclusion of a study, disagreements were resolved by consensus of opinion, and a third reviewer was consulted if they could not be resolved. Where resolution was not possible the author was contacted to obtain more information and clarification.
Titles and abstracts of studies identified by searching electronic databases were assessed to determine whether each article met the eligibility criteria. In order to prevent any bias, a list of all titles and abstracts was printed out excluding the author's names, institutions, and journal title. If the title and abstract contained sufficient information to determine that the article did not meet the inclusion criteria, then it was rejected. A record of all rejected papers and the reasons for rejection was documented. Reference lists of all relevant papers were scanned for published reports, conference abstracts, and citations of unpublished research;
The full papers of all remaining titles and abstracts deemed relevant were then retrieved. In addition, all other potentially relevant articles identified by the various search strategies (reference checking, personal communications etc) were also reviewed. All articles were reviewed independently by two of the reviewers, who completed a form for each study and scored the quality of the

research as defined below. The reasons for exclusion were documented. Where the same study had more than one article written about the outcomes, all articles were treated as one study and the results were presented only once.

Risk of bias

A risk of bias table was made for articles that were new in this update. The risk of bias table included random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias) using the methodology as described in the Cochrane Reviewers Handbook (Higgins 2011).

Losses to follow-up

The paper should give an adequate description of the loss of its participants in terms of the number of withdrawals, dropouts, and protocol deviations. In the protocol for this study we stated that only RCTs where less than 20% of participants originally randomised were lost to follow-up would be included in the review. In view of the limited number of trials, we relaxed these criteria to include studies that combined RCT and cross-over designs, and those that had greater losses to follow-up. In each case, we performed sensitivity analyses to assess the effect of the inclusion of these studies.

Addressing publication bias

Data from all identified and selected trials were entered in to a funnel plot (size of study versus effect size) (Egger 1997), to attempt to detect the possibility of publication bias.

Data extraction

Two reviewers (SK, LAC) completed a data extraction form for each included study to elicit the following information:

- General: published/unpublished, title, authors, source, contact address, country, language of publication, year of publication, duplicate publications, sponsoring, setting (hospital inpatients or out-patients, primary care, community);
- Trial characteristics: design, duration, randomisation and method, allocation concealment and method, blinding of outcome assessors, check of blinding;
- Interventions (frequency, timing), comparison interventions, co-medications;
- Patient characteristics - sampling, exclusion criteria number of participants, age, sex, ethnicity, marital status, educational status, duration of symptoms, number of complications, mode of referral (e.g. self-referral or via psychiatrists, psychologists, or other clinicians), similarity of groups at baseline (including any co-morbidity), withdrawals/losses to follow-up (reasons/descriptions), history of myocardial infarction (MI);
- Type of psychiatric co-morbidity - clinical diagnosis or symptomatology assessed by questionnaire;
- Type of assessment tool used to assess psychiatric co-morbidity - e.g. Beck Depression Inventory, Zung Depression Scale, Hospital Anxiety and Depression Scale, Structured interview, DSM-IV criteria;
- Cut-off used on psychiatric scale, percentage of people defined as psychiatric cases on this basis; mean (SD) symptom score;
- Type of intervention - CBT, psychotherapy, 'talking/counselling' therapy, no intervention versus psychological intervention; usual care versus psychological intervention; and 'attention' placebo versus psychological intervention; timing of intervention (early vs late);
- Type of outcomes - level of chest pain at baseline, and at subsequent follow-ups, psychiatric symptoms, quality of life, number of hospital re-admissions, non-fatal cardiovascular events, reduction of cardiovascular behavioural risk factors, death (cardiovascular and all-cause mortality), and health beliefs;
- Duration of follow-up and point from which follow-up was calculated start or end of intervention;

We stated that we would group outcomes into short term (within 12 weeks of the start of therapy), medium term (between 13 to 24 weeks after the beginning of therapy), and long-term (more than 24 weeks after the start of therapy). As interventions varied in length from one session to treatment lasting three months, we used time from the end of intervention to ensure that comparison between treatments were appropriate (i.e. an assessment made six months after baseline assessment and a three month course of treatment is the equivalent of three months after initial assessment for an intervention lasting a few days). Using this methodology, we found that it was only possible to divide outcomes into those within three months of the end of the intervention (or the equivalent time for controls), and those from 3 to 12 months after the intervention (or the equivalent time for controls). Only one study reported data on ten participants at 36 month follow-up (DeGuire 1996).

- Assessment of methodological quality - method of randomisation used, if stated; method of allocation concealment (adequate, unclear, inadequate, or allocation concealment not used); blinding of outcome assessors (yes, no, unclear); and patients lost to follow-up (cut-off of 20% attrition or more), intention-to-treat analysis.

Data Analysis

Data entry

Data were entered into RevMan software by SK and duplicated by LAC. A summary of data extracted from included studies was reported. If studies were available that were sufficiently similar and of sufficient quality we pooled those that can be grouped together and used the statistical techniques of meta-analysis. The data were synthesised using MetaView within the Cochrane Review manager software

Data types

Outcomes were assessed using continuous (for example, changes on depression scales), categorical (for example, one of three categories on a quality of life scale, such as 'better', 'worse' or 'no change'), or dichotomous (for example, either depressed or not-depressed) measures.

Continuous data

Many rating scales are available to measure outcomes in psychological trials. These scales vary in the quality of their validation and reliability. Therefore, if validation of a rating scale was not published in a peer-reviewed journal, then the data was not included in this review. In addition, the rating scale should be either self-report or completed by an independent observer or relative. Trials that have used the same instrument to measure specific outcomes were used in direct comparisons where possible. Where continuous data were presented from different scales rating the same effect both sets of data were presented and the general direction of the effect inspected. The mean and standard deviation were reported. Where standard deviations were not reported in the paper, attempts were made to obtain them from the authors or to calculate them using others measures of variation that were reported, such as the confidence intervals (CI). If possible we pooled data from different scales rating the same effect using the Standardised Mean Difference.

Dichotomous data

Continuous outcome measures were converted to dichotomous data where necessary. If the authors of the study used a designated cut-off point for determining clinical effectiveness the reviewers used this where appropriate. Otherwise, cut-offs on rating scales were identified and participants divided on the basis of whether they are 'clinically improved' or 'not clinically improved'. For dichotomous outcomes, a Mantel-Haenszel odds ratio with its associated 95% CI was estimated. As a summary measure of effectiveness, where possible, the number needed to treat statistic (NNT) was also calculated.

Initially we compared any psychological intervention to any control. Depending on the number of included studies, we compared each intervention category (1 to 4) with any control, and also subgroup according to type of control. The effect of different approaches was investigated using sensitivity analyses (see below).

Heterogeneity

Graphical representations of the data were inspected; if the CI for the results of the study did not overlap, it suggested that the differences were likely to be statistically significant (Walker 1988). In addition, differences between the results of each included trial were checked using a test of heterogeneity. As these tests usually have low statistical power, a type I error level of 0.10 rather than the customary 0.05 was used for rejecting the null hypothesis of homogeneity. If there was statistically significant heterogeneity the data were presented separately rather than pooled. Results were analysed using both the fixed-effect and random-effect methods. However, where there was significant heterogeneity, a random-effect model was used and the reviewers attempted to explore the reasons for this heterogeneity in post hoc analyses.

Sensitivity analyses

Factors, which may lead to differences between the results of individual studies, were investigated using sensitivity analyses. This review investigated differences between:

- Trials which defined psychiatric symptoms operationally e.g. clinician diagnosis or validated questionnaire and whether the questionnaire had been validated in this specific population or in other groups;
- Types of psychological interventions and types of controls;
- Route of referral for intervention e.g. referred to psychiatrists, clinical psychologists, other mental health professionals, or other clinicians for management;
- Participants with and without a family history of heart disease;
- Studies that used subject reported pain or assessments by clinicians or carers;
- Well-defined and less-well defined psychological interventions;
- Analyses involving all studies and excluding trials of low methodological quality;
- Analyses involving all studies and those that excluded comorbid psychiatric disorder;
- Participants with and without a history of myocardial infarction;
- Participants with and without coronary angiography; and
- Self referral and referral from a clinician.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The search in 2011 identified 72 references, after de-duplication, in addition to the 297 identified in 2008. From these, and the original searches, we considered 74 papers in detail for inclusion. Of these, 54 studies were excluded, and 15 studies, reported in 20 papers, were included.

Included studies

Fifteen RCTs (803 participants) were included (Asbury 2007; Asbury 2008; Asbury 2011; DeGuire 1996; Esler 2001; Jonsbu 2011; Keefe 2011; Klimes 1990; Lahmann 2008; Jones 2006; Mayou 1997 and Mayou 1999; Potts 1999; Sanders 1997; Spinhoven 2010; Tyni-Lenne 2002; VP-Oosterbaan1999). Of these, six were new to this update (Asbury 2008; Asbury 2011; Jonsbu 2011; Keefe 2011; Spinhoven 2010;). See Characteristics of included studies.

Data reporting

Two studies combined the results of the RCT and crossover designs (Klimes 1990; Potts 1999). Three studies did not report standard deviations (Klimes 1990; Potts 1999; Tyni-Lenne 2002). The authors of Potts 1999 kindly provided the missing standard deviations for the RCT component of their study, including pain episodes and pain-free days over a two weekly period.

Interventions and Analysis

Comparisons of psychological interventions included CBT, hypnotherapy, autogenic training, group support, brief intervention by a nurse, relaxation training and breathing re-training. Only two studies (Potts 1999; Asbury 2011) evaluated a group intervention. Two studies (Klimes 1990; Potts 1999) used a combined randomised controlled and crossover design where controls were offered the active treatment after the initial controlled trial. In one, controls were given an initial behavioural explanation of their symptoms before being placed on the wait-list. Although both studies reported some data of the RCT component many of the reported outcomes combine the results of the RCT and crossover designs. Where it was not possible to find data of the RCT alone, sensitivity analyses were conducted including and excluding combined data. In the other studies, controls were offered assessment only combined with either usual care (Tyni-Lenne 2002; VP-Oosterbaan1999) or no care (DeGuire 1996; Mayou 1997 and Mayou 1999). In the case of the former, no information was reported on details of usual care the controls received. Where studies had more than two arms (DeGuire 1996; Tyni-Lenne 2002); Keefe 2011), we used the control treatment that most readily allowed comparison with other studies. For DeGuire we used guided re-breathing training without physiological monitoring of diaphragmatic breathing or end-tidal CO2. For Tyni-Lenne we used relaxation as opposed to physical training. It was not possible to examine differences in the timing of the interventions. In the case of Keefe, there were four study arms: 1) placebo; 2) psychological treatment and placebo; 3) sertraline and placebo, and; 4) sertraline plus psychological treatment. We used the results of the first two arms.Timing of the intervention (early vs. late) was not described in six of the 15 studies. One study examined the differences between "immediate" and "delayed" interventions, but as per the inclusion criteria, participants may have had an angiogram within the past year (Potts 1999). Similarly, Esler 2001 conducted the intervention while the patient was in the emergency room, however, did not provide information regarding a history of chest pain. Therefore, it is not clear whether the patients were presenting for the first time or not. Therapist training was not noted in four of the studies. Adherence to a treatment manual or plan was described in nine of the studies. Keefe 2011 also assessed fidelity. Therapists met weekly for supervision with a senior psychologist (DM) who reviewed audiotapes of the sessions and provided feedback regarding treatment quality and adherence to the study protocol.

Participants

Four studies was restricted to females (Tyni-Lenne 2002; Asbury 2007; Asbury 2008; Asbury 2011). All studies were of outpatients who were either referred by treating physicians or GPs, or undergoing coronary angiography. One study (DeGuire 1996) included participants who responded to a newspaper advertisement. A sensitivity analysis excluding this study made no difference to the results. All included participants whose main symptom was chest pain and who had been investigated to some degree to exclude cardiac explanations for their pain. Only one study excluded participants who had other co-morbid medical conditions such as diabetes. Only three studies (Klimes 1990; Mayou 1997 and Mayou 1999; VP-Oosterbaan1999) excluded participants who had co-morbid psychiatric disorder such as major depression. We conducted sensitivity analyses of studies that used such exclusion criteria and those that did not.

Completion rates

Completion rates varied widely. Only nine studies reported the number of subject eligible for inclusion who agreed to participate (Jones 2006; Jonsbu 2011; Keefe 2011; Lahmann 2008; Klimes 1990; Mayou 1997 and Mayou 1999; Sanders 1997; Spinhoven 2010; VP-Oosterbaan1999). In all cases, only 40 to 60% agreed to participate. The only exception was the study of Lahmann 2008 where 90% of eligible subjects participated. Completion rates following randomisation were generally acceptable (approximately 80%), although in the case of two (DeGuire 1996; Mayou 1997 and Mayou 1999) over 35% were lost to follow-up. We conducted sensitivity analyses of studies where completion rates were less than 80%.

Outcomes

All studies reported change in frequency and severity of chest pain. Some also included the number of days when participants were free of chest pain. Studies reported a wide range of other outcomes covering psychological morbidity, quality of life, health beliefs and service use. Both observer-rated and self-report measures were included.

Duration of Follow-up

Follow-up periods varied from three to 36 months. Studies generally dated follow-up from baseline intervention rather than the end of the intervention. Duration of interventions varied from a single session, a few days or several months. We calculated duration from follow-up from the end of the intervention. For example a trial in which participants were followed up for six months dated from baseline intervention, with an intervention duration of three months was classified as followed up for three months.

Excluded studies

Fifty-five studies were excluded, see Characteristics of excluded studies. Most were reviews that did not contain primary data or were not intervention studies. Four intervention studies were excluded; three were trials of antidepressant medication (Cox 1998; Handa 1999; Wulsin 2002), and another was an uncontrolled trial of behavioural therapy (Hegel 1989). The fifth trial pooled data from 90 patients with mitral valve prolapse with 14 participants with NSCP (Cott 1992). We tried to contact the authors of this study to determine if there were any data restricted to patients with NSCP. A sixth was an evaluation of a chest pain unit where patients received up to six hours of observation and biochemical testing followed by an exercise treadmill test (Goodacre 2004). A final study was excluded (Mayou 1999) because it reported on a consecutive sample of 133 outpatients referred to cardiac outpatient clinics, and was not a randomised controlled trial.

Risk of bias in included studies

Risk of bias tables were created for the six new studies added in this update. Overall there was a low risk of random sequence generation and selection bias, with five of six studies (Asbury 2008; Asbury 2011; Jonsbu 2011; Keefe 2011; Spinhoven 2010) all having a low risk of bias, and only one study (Lahmann 2008) having unclear risk for both of these biases. Due to the nature of the interventions (normally counselling or cognitive-behaviour therapy) it was impossible to blind participants and personnel to the intervention. For this reason, all studies have an unclear risk of performance bias as it is unclear to what extent this would have biased the results. In studies where there was a medical aspect to the intervention (Keefe 2011; Spinhoven 2010), the patients were blinded to medication or placebo. Because in all studies outcomes were assessed by self-reports, and the patients were at least in part not blinded to the intervention, all studies were judged to be at high risk of outcome assessment bias. Most studies did not discuss intention to treat analysis, but most studies appeared to have analysed data based on intent to treat analysis. Two studies were thought to have a high risk of incomplete outcome bias (Asbury 2011; Spinhoven 2010) because of high loss or differential loss from baseline to follow-up. the others had low risk of bias for this domain. Two studies had unclear risk of selective reporting (Lahmann 2008; Spinhoven 2010) because they did not clearly layout the outcomes of interest.

Because the primary outcomes had two and three studies, no funnel plots were included.

Effects of interventions

The 15 included studies used very different ways of assessing outcome. For this reason, we have analysed some of them separately without attempting a quantitative integration of data (meta-analysis).

Primary outcome measures

Absence of chest pain

Studies reported either the absence of chest pain over a week (Klimes 1990; VP-Oosterbaan1999) or a month (Sanders 1997), or the number of chest-pain free days over a week (Mayou 1997 and Mayou 1999). All showed significant improvements following intervention, apart from brief CBT where the improvement failed to reach statistical significance. In the case of Klimes, the results were of the combined RCT and crossover trial. Klimes also reported the number of chest-pain free days over a week at the end of the RCT stage before the crossover trial, but did not include standard deviations (Klimes 1990). We were therefore only able to combine the studies of CBT that reported the absence of chest pain over a certain period of time (Klimes 1990; VP-Oosterbaan1999) or that included standard deviations when reporting the number of chest-pain free days (Mayou 1997 and Mayou 1999; Potts 1999). In the case of absence of chest pain (Klimes 1990; VP-Oosterbaan1999), there was a significant reduction in reports of chest pain in the first three months following the intervention. The fixed-effect model estimated the relative risk was 0.68 (95% CI 0.57 to 0.81) (Analysis 1.1), while the random-effect model gave a relative risk of 0.70 (95% CI 0.53 to 0.92). This was maintained from three to 12 months afterwards; the relative risk was 0.59 (95% CI 0.45 to 0.76) (Analysis 1.2) for both fixed or random-effects models. Exclusion of the study that reported the absence of chest pain over a month following brief CBT (Sanders 1997) made no significant difference to the results. Exclusion of the combined RCT and crossover trial (Klimes 1990) also made

no significant difference to the results. There was also a significant increase in the number of chest pain free days up to three months following intervention; the mean difference was 2.81 (95% CI 1.28 to 4.34) (Analysis 1.3), although this was largely attributable to the study reporting the results of a group intervention (Potts 1999). We found similar results with the random-effects model.

Chest pain frequency and severity

Studies reported the frequency of chest pain episodes over a week (VP-Oosterbaan1999), two weeks (DeGuire 1996; Potts 1999) or a month (Esler 2001; Mayou 1997 and Mayou 1999). Jonsbu 2011 reported frequency of symptoms of chest pain or palpitations on a scale rated as 1 ("daily"), 2 ("weekly or more often"), 3 ("rare but sometimes"), and 4 ("no symptoms for the last 6 months"). We could not therefore include this in the meta-analysis. There was a reduction in participants receiving either CBT or guided re-breathing compared to controls within the first three months of follow-up on the random-effects model; the mean difference was -2.26 [-4.41, -0.12] (Analysis 1.4). However, this was not maintained at three to nine month follow-up (mean difference -0.81 (95% CI -2.35, 0.74 Analysis 1.5). Restricting the analyses to only those studies that reported the results of CBT made little difference to any of these results.

The study of hypnotherapy reported rates of overall improvement in chest pain (Jones 2006); 80% of the hypnotherapy group improved compared to only 23% of controls (p=0.008) at 17 week follow-up. This improvement was maintained approximately two years later with 14 (93%) of the 15 patients who received hypnotherapy now classified as responders compared to only 3/13 (23%) controls (p=0.001).

Four studies reported chest pain severity (Asbury 2007; Jones 2006 ;Keefe 2011; Spinhoven 2010). Another study calculated a daily chest pain index (PI) score in which duration of chest pain activity was weighed by the intensity of the chest pain (Spinhoven 2010). At three months follow-up, there was no significant difference between intervention and control groups in the random-effects model (mean difference = -4.64 (95% CI -12.18 to 2.89) (Analysis 1.6). It is important to note that Spinhoven 2010 reported outcomes at two intervals; mid-treatment and post-treatment. The scores included in Analysis 1.6, are post-treatment outcomes.One study reported frequency of GP visits over 12 months (Asbury 2011): 29% of support patients made one or more GP visits over the duration of the study, compared with 54% of the control group (p=0.06).

Secondary outcome measures

Quality of life

Studies reported very different measures of quality of life, making quantitative integration of data difficult. Two (Potts 1999; Tyni-Lenne 2002) showed significant improvements in global quality of life following intervention using a standardised and validated instrument (the Sickness Impact Profile (SIP)) compared to controls, but reported medians and ranges instead of means and standard deviations. A further study gave the percentage of subjects reporting an improvement in global quality of life (Jones 2006): 73% of the hypnotherapy group improved compared to only 23% of controls (p=0.02) at 17 week follow-up. This improvement was maintained approximately two years later with 11 (73%) of the 15 patients who received hypnotherapy now classified as responders compared to only 3/13 (23%) controls (p=0.02). Mayou, using a non-standardised measure of social impairment, did not report significant improvement compared to controls up to three months after intervention; the mean difference was -0.33 (95% CI -1.17 to 0.51) (Analysis 1.8); or afterwards between three to nine months, the mean difference was -0.43 (95% CI -1.58 to 0.72) (Analysis 1.7) (Mayou 1997 and Mayou 1999). Five other studies reported results using some or all of the scales of the Short Form 36 including physical functioning, work problems, social functioning, and problems with role due to emotional limitations (Esler 2001; Sanders 1997; VP-Oosterbaan1999; Asbury 2008; Jonsbu 2011, but Sanders did not report standard deviations. In addition to reporting the overall percentage of patients reporting improvement in global Quality of Life (QOL), Jones et al gave MacNew scores for QOL derived from emotional, physical and social domains (Jones 2006). As with the SF36, an increase in scores indicates improvement. However, they did not report the sub scores. Asbury et al reported QoL using the Ferrans and Powers Quality of Life Index (Asbury 2007). This covers four domains (health and functioning, psychological/spiritual domain, social and economic domain, and family). Again, an increase in scores indicates improvement. We were, therefore, only able to combine data from Esler, Oosterbaan and Asbury for the following three areas: physical functioning, social functioning, and problems with role due to emotional limitations. In each case we combined these results with the global MacNew scores that incorporated emotional, physical and social domains. In the case of social functioning, we also attempted to integrate measures of social functioning and social disability by inverting the social impairment scale used by Mayou (Mayou 1997 and Mayou 1999).There were significant differences between intervention and control groups in some of the domains at short or long term follow-up (Analysis 1.8; Analysis 1.9; Analysis 1.12) except in the cases of physical or social functioning up to 3 months after the intervention(Analysis 1.7; Analysis 1.11) and role problems due to emotional limitations 3 to 12 months after the intervention (Analysis 1.10); using the random or fixed-effect model made no difference to any of these results.

Psychological measures

Again, a wide variety of measures were used that measured global outcome or the presence of depression or anxiety. The com-

bined RCT and crossover trial (Klimes 1990) reported a significant reduction in psychiatric cases compared to controls as determined by a standardised psychiatric interview following intervention; the relative risk was 0.42 (95% CI 0.22 to 0.8) (Analysis 1.15). We quantitatively analysed seven studies of self-reported depression using standardised instruments (Asbury 2007; Asbury 2008; Jonsbu 2011; Keefe 2011; Lahmann 2008; Potts 1999; VP-Oosterbaan1999), combined with a further study that reported overall morbidity including depression (Mayou 1997 and Mayou 1999). There was no significant difference between intervention and controls up to three months after the intervention (Analysis 1.13). It is worthy to once again note that Asbury 2008 reported outcomes at two intervals within the 3 month time-frame. Using one or the other made no difference in the results of Analysis 1.13. We also quantitatively analysed seven studies of self-reported anxiety using standardised instruments (Asbury 2007; Asbury 2008; ; Keefe 2011; Lahmann 2008; Potts 1999; Spinhoven 2010; VP-Oosterbaan1999), combined with a further study that reported overall morbidity including anxiety (Mayou 1997 and Mayou 1999). A ninth study reported medians and ranges rather than means and standard deviations (Jones 2006).This precluded inclusion in quantitative analyses. A further study (Asbury 2011) reported p values but no actual scores. For the eight studies where we were able to combine data, there was a significant difference between intervention and controls up to three months after the intervention; the standardised mean difference was -0.23 (95% CI -0.43 to -0.03) (Analysis 1.14). Again, Asbury 2008 reported outcomes at two intervals within the 3 month time-frame. Using one or the other made no difference in the results of this analysis.There was no significant difference between intervention and controls from three to 12 months afterwards; the standardised mean difference was -0.18 (95% CI -0.52 to -0.17) (Analysis 1.15). Four further studies reported three subscores of a scale specific to cardiac anxiety including fear, avoidance and attention to symptoms rather than generalised anxiety (Asbury 2007; Asbury 2008; Esler 2001; Spinhoven 2010). There were no significant differences in any of the domains at any time period (Analysis 1.16; Analysis 1.17; Analysis 1.18; Analysis 1.19; Analysis 1.20; Analysis 1.21). Using the random or fixed effects model made no difference to any of these results. Again, it is worthy to state that Spinhoven 2010 reported outcomes at two intervals; mid-treatment and post-treatment. The scores included in Analysis 1.14 and Analysis 1.16 are post-treatment outcomes.

Health beliefs

Studies used very different measures of changes in health beliefs, making quantitative integration of data difficult. Of the six studies examining cognitive behavioural therapies, two did not report change in health beliefs as an outcome (Esler 2001; VP-Oosterbaan1999). Klimes 1990 reported that prior to the intervention, all study patients believed their chest pain was due to a physical cause, while afterwards 69% attributed their pain to stress. They did not report the difference between intervention and control groups. One study of support groups reported that patients randomized to support showed a trend towards improved health beliefs total score (p=0.068) and threat perception (p=0.062) compared to the controls (Asbury 2011). Two studies (Mayou 1997 and Mayou 1999; Sanders 1997) reported non significant differences in health beliefs after the intervention. Only Potts 1999 reported that participants were significantly less likely to believe they had heart disease after the intervention (11/56, 20%) than before (25/56, 45%, p<0.05).

Heterogeneity

All of our analyses had a high level of heterogeneity. Our findings must therefore be treated with caution. For primary outcomes, chest pain frequency (up to and post three months) and chest pain severity had significant heterogeneity at the 0.05 level, and were therefore analysed using a random effects model. In terms of secondary outcomes, tests for heterogeneity were not statistically significant at the 0.05 level, although there was a high level of heterogeneity.

Sensitivity analyses

Because of the small number of trials in each analysis, these results are limited and should be interpreted with caution. Issues concerning the proposed sensitivity analyses are as follows:

- Differences between studies that define psychiatric symptoms operationally (clinician diagnosis or validated questionnaire (and whether validated in this specific population or in other groups): all studies included in the meta-analysis used standardised instruments;
- Differences between types of psychological interventions and types of controls: there was little change to the results when analyses were restricted to CBT or hypnotherapy only. All but two studies used individual therapy;
- Differences between routes of referral for intervention (referred to psychiatrists, clinical psychologists, other mental health professionals, or other clinicians for management): most studies did not report route of referral. There was no difference to the results when studies were excluded by route of referral;
- Differences between participants with and without a family history of heart disease: there were no studies in which this information was included;
- Differences between studies that use subject reported pain or assessments by clinicians or carers: there were no studies that used assessments by clinicians or carers;
- Differences between well defined and less-well defined psychological interventions: there was little change to the results when analyses were restricted to CBT or hypnotherapy only;
- Differences between analyses involving all studies and excluding trials of lower methodological quality: two studies

combined the results of the RCT and crossover designs (Klimes 1990; Potts 1999). There was no difference in the results when studies that combined results of a RCT and crossover trial were excluded;

- Differences between analyses involving all studies and those that excluded co-morbid psychiatric disorder: all but two of the studies (DeGuire 1996; Jones 2006) included in the meta-analysis excluded co-morbid psychiatric disorder. There was no difference to the results when these studies were excluded from the analysis;
- Differences between participants with and without a history of myocardial infarction: a history of myocardial infarction excluded in 3 studies, and not captured in the remainder. This made little change to the results;
- Differences between participants with and without coronary angiography: there was no difference to the results with this analysis;
- Differences between self referrals and referral from a clinician: one study (DeGuire 1996) included participants who responded to a newspaper advertisement. Exclusion of this study made no difference to the results.

DISCUSSION

Recurrent chest pain in the absence of coronary artery disease is a common problem that sometimes leads to excess use of medical care. Although many studies examine the causes of pain in these patients, few clinical trials have evaluated treatment. The studies reviewed in this updated review provide an insight into the effectiveness of psychological interventions for this group of patients.

We have attempted to draw modest conclusions, based on available evidence, and to highlight areas requiring further study, rather than draw conclusions that may not be based on evidence of high quality.

This review revealed limited evidence for the effective psychological treatment of NSCP. Only a small number of RCTs were identified, and two combined data from RCT and crossover trials. The identified studies were heterogeneous in terms of design, types of and implementation of interventions, outcome measurement and follow-up periods. All had small numbers of participants and questions concerning methodological quality.

Overall, the risk of bias in this study was low, however there is some risk of bias in results due to the use of outcome data that are not assessed blind to group status. For example, where participants are waiting-list controls, especially in combined RCT and crossover designs, it is not possible for the subject to be unaware of which group they are in, and many studies rely on participants' self-report assessments of outcome.

Despite these problems, it was possible to aggregate some data for short and long-term outcomes and the aggregated data support a modest to moderate benefit for psychological interventions, especially those using a cognitive-behavioural framework. The evidence for other interventions, such as brief nurse-led counselling is less clear.

There are several practical difficulties concerning the delivery of psychological interventions for NSCP. One is that participation rates in many studies were low (40-60%). It has been suggested that this is because many studies of approaches such as cognitive behavioural therapy use the Attribution Model (Esler 2004). This requires patients to complete a cardiological work up such as stress testing to definitely establish that the pain is noncardiac in origin before therapy can begin, marking one obstacle to treatment. Furthermore the Attribution Model may be incompatible with the patient's view of their symptoms. Even if patients can be convinced, this psychological attribution may still be controversial with their family and friends, and many physicians. If patients are accustomed to thinking of chest pain as a medical illness they may not be ready to attribute their symptoms to having a psychological cause. By contrast, the Biopsychosocial Model accepts that most illness, whether physical or psychiatric, is influenced and determined by biological, psychological and social phenomena. This model assumes that better patient outcomes are achieved when therapeutic interventions are based on evaluation of the relationship between biological, psychological and social variables. This approach may be more in tune with the patient's perception of their problems and does not require physical investigations to be completed before therapy can begin (Esler 2004).

There are also too few psychologists, and cardiologists or gastroenterologists have neither the time nor training necessary to provide the treatment. Furthermore, there is considerable variation in presenting physical symptomatology, concerns, needs, beliefs, and outcomes among patients. Therefore, a 'stepped' approach to the implementation of psychological interventions has been suggested (Mayou 1997 and Mayou 1999; Sanders 1997). Such an approach would include a fuller explanation of the possibility and meaning of a negative outcome of angiography as preparation for the procedure and more opportunity for discussion with cardiologists prior to discharge. There should also be follow-up for review of the findings, reinforcement of the plan for symptomatic treatment and encouragement for a return to fuller activities.

One of our objectives was to compare different psychological treatments but due to the small number of studies, we can only really draw conclusions about cognitive-behavioural therapy, and possibly hypnotherapy. We also wished to assess the association between treatment effect sizes and methodological features but were unable to do so because of the small number of participants and methodological characteristics.

One finding of our review is that we were only able to identify

15 studies. The lack of research in this area and standardisation of outcomes may mean this is a relatively new field. Alternatively, researchers may be uncomfortable with randomisation and the use of controls. A further possibility is that participants with NSCP are reluctant to accept psychological explanations and interventions for their symptoms, making this a difficult group with which to conduct such studies. The high rates of attrition in many of the studies lends support for this final explanation

AUTHORS' CONCLUSIONS

Implications for practice

Psychological treatments, especially CBT therapy and hypnotherapy, may be effective, in the short-term, for the treatment of NSCP but the evidence is limited to small trials of questionable quality.

Evidence suggests that if untreated, patients with NSCP have levels of health service use comparable to patients with chest pain of organic causes (Kisely 1997). It may be useful to detect non-cardiac chest pain early, identify individual treatment needs, and intervene before it becomes chronic. Patients in emergency departments or with recent onset of chest pain should be prepared for the possibility and meaning of negative findings. Those patients with chronic NSCP may benefit from specialist psychological intervention.

Implications for research

Further RCTs of psychological interventions for NSCP are needed. These should:

- Include a larger number of participants and be informed by explicit sample size and power analysis;
- Have follow-up periods of at last 12 months and preferably longer;
- Have adequate concealment of allocation, intention to treat analyses and at least single blind assessments of outcome;
- Use meaningful standardised outcome measurements;
- Use interventions that are explicitly described, manualised and monitored for treatment fidelity.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Asbury 2007

Methods	RCT
Participants	Fifty three female Syndrome X patients (mean +/- SD; 57.4 8.0 yrs)
Interventions	2 groups Weekly group autogenic training (AT) sessions were supported by an individual home program and symptom diary Symptom diary only control.
Outcomes	The Hospital Anxiety and Depression Scale (HADS) Spielberger State-Trait Anxiety Inventory (STAI) Cardiac Anxiety Questionnaire (CAQ) and the Ferrans & Powers Quality of Life Index (QLI) were completed pre- and post-intervention and at 8-week follow-up
Notes	

Asbury 2008

Methods	RCT
Participants	Sixty-four women aged 57.3 T 8.6 years (mean T SD) with cardiac syndrome X
Interventions	8-week phase III CR exercise program or symptom monitoring control
Outcomes	Hospital Anxiety and Depression Scale, Health Anxiety Questionnaire, and Short Form-36, energy, general health, Shuttle Walk Test, diastolic blood pressure and body mass index
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomly assigned using envelopes. Not described, but sounds plausible
Allocation concealment (selection bias)	Low risk	Patients given identical envelopes with either rehabilitation or monitoring written on them
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The use of group blinding was expressly forbidden by the local ethics committee because of issues relating to obtaining fully informed consent

Asbury 2008 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	High risk	Patients knew what group they were in, and assessment by self reports
Incomplete outcome data (attrition bias) All outcomes	Low risk	Analysed as intention to treat. One additional patient dropped out of CR arm
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported on.

Asbury 2011

Methods	RCT
Participants	Forty-nine women with cardiac syndrome X (mean+standard deviation 61.8+8 years)
Interventions	12 monthly support group meetings or usual care control
Outcomes	The Health Anxiety Questionnaire (HAQ), Hospital Anxiety and Depression Scale (HADS), SF-36, York Angina Beliefs scale, ENRICHD Social Support Instrument (ESSI) and a demographic information scale, along with hospital admissions, GP or cardiologist appointments were measured at baseline, 6 months and 12 months
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomly assigned using envelopes. Not described, but sounds plausible
Allocation concealment (selection bias)	Low risk	Patients given identical envelopes with either support group or usual care written on them
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The use of group blinding was expressly forbidden by the local ethics committee due to issues relating to obtaining fully informed consent
Blinding of outcome assessment (detection bias) All outcomes	High risk	Patients knew what group they were in, and assessment by self reports
Incomplete outcome data (attrition bias) All outcomes	High risk	Analysed as intention to treat. One patient from intervention group (4%) and three (12%) from control group dropped out
Selective reporting (reporting bias)	Low risk	Appears that all outcomes reported on.

DeGuire 1996

Methods	RCT Ratings of respiratory physiology & self-reports of cardiac symptoms 66 subjects referred/responded of whom 41 (63%) completed follow-up
Participants	Referred from physicians or responded to newspaper advertisement Inclusion criteria: Seen by physician <= 1 year before recruitment who had excluded organic causes for symptoms. Symptoms occurred at least once/week and include chest pain, palpitations, tachycardia and arrhythmias
Interventions	4 groups: 3 active treatment groups with 6 individual sessions over 3 weeks Guided breathing retraining and physiological monitoring of diaphragmatic breathing and end-tidal CO2 Guided breathing retraining and physiological monitoring of diaphragmatic breathing Guided breathing retraining No treatment (controls)
Outcomes	Chest pain: frequency & severity over 2/52 Respiratory rate and mean end-tidal CO2 using an Ohmeda 5200 CO2 monitor
Notes	High attrition rate leading to potential follow-up bias.

Esler 2001

Methods	RCT Self-report ratings of cardiac symptoms, 94 subjects referred of whom 59 (63%) were randomised. 36 of the 59 subjects (56%) completed all follow-up assessments
Participants	Referred by Accident & Emergency or observation ward physician Inclusion criteria: Chest pain as main presenting feature Adequate medical work up & ready for d/c Low suspicion of cardiac disease Over 18 years old Exclusion criteria Known/documented hx of MI, CABG, PTCA, prior angiography or stress testing indicating CAD Other significant medical illness (e.g. CCF, PE, lung Discase) or cause of chest pain (e.g. pneumonia, bronchitis, trauma)
Interventions	One brief CBT intervention lasting 1 hr including psychoeducation, cognitive restructuring & breathing exercises. Controls received treatment as usual including information, instructions and medications typically given by treating physicians to patients with -ve cardiac findings
Outcomes	Chest pain episodes over 1/12. Severity of episodes over 1/52 & 1/12 (chest pain visual analogue scale) QL: SF 36 PM: Cardiac Anxiety Questionnaire, Anx Sensitivity Index, BSI At 1/12 and 3/12 follow-up

Esler 2001 (*Continued*)

Notes	High attrition rate leading to potential follow-up bias

Jones 2006

Methods	RCT
Participants	28 patients with angina-like chest pain in whom coronary angiography was normal and oesophageal reflux was not contributory
Interventions	12 sessions of hypnotherapy or supportive therapy plus placebo medication over a 17 week period. A further paper reported results of a 2 year follow-up
Outcomes	The primary outcome measure was global assessment of chest pain improvement. Secondary variables were a change in scores for quality of life, pain severity, pain frequency, anxiety, and depression, as well as any alteration in the use of medication
Notes	Of 81 eligible patients, only 28 entered the RCT

Jonsbu 2011

Methods	RCT
Participants	Patients with persistent complaints six months after a negative evaluation at a cardiological outpatient clinic were invited to participate. Of the 94 eligible patients, 40 agreed to participate and were randomly assigned to either an intervention or control group
Interventions	Three manualized sessions with CBT, including one physical activity exposure session. The control group received usual care from their general practitioner.
Outcomes	Health-related quality of life (HRQOL) - The Body Sensations Questionnaire (BSQ) , 36-item Short-Form Health Survey (SF-36), Frequency of symptoms of chest pain or palpitations, impact of cardiac symptoms on domains of family life, social life and work, and avoidance of physical activity
Notes	Only a half of the eligible subjects entered the study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The participants were assigned to groups by a web module that offers block randomization. This was performed by a clinical research unit that is separate from the intervention location
Allocation concealment (selection bias)	Low risk	Allocation conducted at an institution unrelated to study.

Jonsbu 2011 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Assessment by self-reporting and patient not blinded to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Same number of patients dropped out in both groups.
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported on.

Keefe 2011

Methods	A randomized clinical trial of the separate and combined effects of coping skills training (CST) and antidepressant medication (sertraline) in participants with non-cardiac chest pain
Participants	Eligibility criteria for study entry were (a) presented for medical care with complaints of chest pain in the previous 6 months, (b) received a negative stress test within the past 2 years, normal coronary angiogram within the past 2 years, or had a survival probabilityP98% at 2 years (calculated from a prognostogram developed by statistical modelling from the Duke Cardiovascular Database) [33], (c) a low likelihood of significant coronary artery disease (<25%) on the National Cholesterol Education Program's (NCEP) modification of the Framingham Risk Calculator (FRC), (d) able to swallow oral medication, and (e) age 18- 85 years.38 (33%) men and 77 (67%) women.
Interventions	Random assignment to one of four treatments: (1) CST plus sertraline(CST + sertraline) , (2) CST plus placebo (CST + placebo), (3) sertraline alone, or (4) placebo alone
Outcomes	Chest pain intensity and unpleasantness from pain diaries, State-Trait Anxiety Inventory [STAI), the 13-item Pain Catastrophizing Scale [PCS), the Beck Depression Inventory [BDI), the physical disability scale of the Sickness Impact Profile [SIP), two items from Stone and Neale's Daily Coping Inventory, two items from the Coping Strategies Questionnaire were used to assess daily perceived pain control over pain
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A statistician who was not involved with the rest of the study created a randomization table to randomly assign participants

Keefe 2011 (*Continued*)

Allocation concealment (selection bias)	Low risk	Allocation concealment is described although treatment components were blinded only for the medication and not for the CST component
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Patients were blinded to the medication and not to the CST component (which is training). Medication and placebo were given in identical capsules that both investigators and participants were blind to
Blinding of outcome assessment (detection bias) All outcomes	High risk	Patient's outcomes were self assessed through pain scores, and pain diaries, but internal consistency was high for all tests
Incomplete outcome data (attrition bias) All outcomes	Low risk	While there were many patients who did not complete therapy, there was no difference in attrition among the four treatment groups
Selective reporting (reporting bias)	Low risk	All stated outcomes reported on.

Klimes 1990

Methods	RCCT Self-report & blind ratings 35 out of 56 assessed were recruited (63%) of whom 29(83%) completed follow-up Undetermined if treatment manual was used
Participants	Referred by cardiologist or GP Inclusion criteria: Chest pain as main presenting feature >= one episode weekly Normal CVS (cardiology or equivalent opinion and investigation) >= 3/12 duration Exclusion criteria: Depression on treatment Multiple somatic symptoms Investigations not completed
Interventions	Individual CBT: Max 11 sessions over 3/12cognitive restructuring, problem solving, relaxation, breathing exercises Controls: Behavioural explanation of symptoms and offered CBT after 3/12 follow-up
Outcomes	Chest pain free days and pain episodes over 1/52 QL: 5-point activity avoidance scale, 8-point distress scale 8-point disruption of everyday life scale PM: PSE, STAI-T, BDI, SRT Autonomic symptoms

Notes	High attrition rate leading to potential follow-up bias

Lahmann 2008

Methods	RCT
Participants	Patients included in the study were over the age of 18 years who presented with NSCP. 22 patients (10 men, 12 women) were eligible to take part in the study.
Interventions	Functional Relaxation and Patient Education. The study period in the functional relaxation (FR) group began with a 60-minute psychosomatic-education session, in which the development of NSCP was presented, as well as basic information relating to structure and function of the cardiovascular and autonomic nervous system. Throughout the course of the study, a total of 10 group-therapy sessions, 90 minutes each, were held during the 6-week treatment period Controls assigned to "enhanced medical care" were informed of their diagnosis and were encouraged to pass this information on without restrictions to their general-practitioner in order to initiate primary-care or specialty treatment
Outcomes	The Symptom Checklist of Derogatis (SCL-90) and the Giessen Inventory of Complaints (GBB), which are both self-administered tests
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	" randomization was carried out confidentially"-likely ok, but do not describe
Allocation concealment (selection bias)	Unclear risk	"allocation concealment implemented by the hospital's administration department"-likely ok, but do not describe
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No discussion of blinding, but based on intervention, most likely not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Patients not blinded, and outcome assessment by self reports
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients (22) appear to have completed trial.
Selective reporting (reporting bias)	Unclear risk	Study does not clearly outline outcomes of interest.

Mayou 1997 and Mayou 1999

Methods	RCT Self-report measures and observer ratings (?blinded) Of 133 referrals, 90 (67%) reached baseline assessment., of whom 56 met inclusion criteria. Of these, 37 (66%) entered the study of whom 19 (64%) completed follow-up Undetermined if treatment manual was used CBT group rated chest pain as more severe than control group
Participants	Recruited from general hospital cardiology outpatient clinic Inclusion criteria: Persisting non-cardiac chest pain >= one episode weekly for 1/12 Exclusion criteria: Subsequent cardiac diagnosis Current major depression Living outside country Unable to speak English
Interventions	Individual CBT: Max 12 sessions including cognitive restructuring, problem solving, relaxation, breathing exercises Controls: Assessment only
Outcomes	Chest pain: frequency, severity, distress over 1/12, and number of pain-free days over 1/52 QL: 4-point scales of avoidance, limitation and impairment (leisure, work, family, overall) PM: BSI Health beliefs: Whitely score
Notes	High attrition rate leading to potential follow-up bias

Potts 1999

Methods	RCCT No information on number of subjects asked to participate 60 subjects randomised of whom 56 (93%) completed follow-up
Participants	Patients undergoing coronary angiography
Interventions	Group CBT: 6 sessions including education, cognitive restructuring, relaxation, breathing exercises, graded exposure and light physical exercise
Outcomes	Chest pain free days and pain episodes over 1/52 HV score GTN dose/week Exercise duration (minutes) QL: NHP, SIP PM: HADS
Notes	Impossible to assess attrition rate as no information on number of subjects asked to participate

Sanders 1997

Methods	RCT Self-report measures & observer ratings (blinded) Of 142 referrals who met inclusion criteria, 57 (40%) entered the study of whom 50 (88%) completed follow-up, although only 41 (72%) completed psychological assessments
Participants	Patients undergoing coronary angiography
Interventions	Brief CBT intervention by nurse consisting of a single hour-long session including education, relaxation, breathing exercises, and graded exposure supplemented by a booklet and cassette tape of breathing & relaxation exercises
Outcomes	Chest pain: frequency, severity, distress, and number of pain-free days over 1/12 Associated sx i.e. palpitations and breathlessness QL: SF36 PM: SCL, STAI-T, BDI Health beliefs: Whitely score
Notes	High attrition rate leading to potential follow-up bias

Spinhoven 2010

Methods	RCT of cognitive behaviour therapy (CBT), paroxetine and placebo in the treatment of noncardiac chest pain (NCCP)
Participants	Eligible participants were cardiology outpatients of two academic and two nonacademic hospitals who had been discharged with a diagnosis of NCCP. Inclusion criteria were NCCP as main presenting complaint; NCCP occurring at least once a week, or at least once per month if accompanied by severe psychological distress; age between 18 and 75 years. An initial charts review identified 3270 patients diagnosed with NCCP. Between January 1997 and January 2002. Of these, 2367 patients (72.4%) returned a questionnaire about current symptoms, of whom 583 (24.6%) had no interest in the study, and 1310 (55.3%) did not fulfil the inclusion criteria regarding chest pain frequency. The remaining 474 potential participants received detailed information about the study and were invited for a screening and information session. After the screening session, 95 patients (20.0%) agreed to be randomized. After the intake, 26 patients had to be excluded, leaving 69 patients (37 males) who started the trial
Interventions	CBT, paroxetine and placebo
Outcomes	Frequency, duration, and intensity of chest pain, The Hospital Anxiety and Depression Scale (HADS), heart-focused anxiety by the Cardiac Anxiety Questionnaire (CAQ) , the M.I.N.I.-Plus
Notes	High attrition rate

Risk of bias

Spinhoven 2010 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were randomized using random permuted blocks with a length of six
Allocation concealment (selection bias)	Low risk	Randomization carried out by the hospital pharmacist and the details were unknown to any of the researchers
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Medical treatment blinded, but CBT not
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessment by self reports
Incomplete outcome data (attrition bias) All outcomes	High risk	Analyses conducted on intention to treat, but differences in drop outs between arms. No patients dropped out of CBT, but four (17%) dropped out of placebo group and seven (30%) dropped out of paroxetine group, mostly because of adverse effects
Selective reporting (reporting bias)	Unclear risk	Do not clearly state outcomes of interest.

Tyni-Lenne 2002

Methods	Single-blind RCT with three groups: physical training, relaxation and control groups No information on number of subjects asked to participate. 24 subjects entered study of whom 21 (88%) were followed-up Measurement of exercise capacity, peak heart rate & distance walked during 6 minutes Self-report measures of exertion & Quality of Life
Participants	Inclusion criteria: females only, limited by chest pain (Canadian Cardiovascular Society functional class II) Exclusion criteria: History of musculo-skeletal impairment, hypertension, DM or other systemic illness
Interventions	Physical training: endurance training on a cycle ergometer three times/week for 8/52 Relaxation training twice/week for 8/52 Controls: normal daily activities
Outcomes	Peak oxygen uptake, peak work rate and distance walked during 6 minutes. Rating of perceived exertion QL: SOC, SCI-93, SIP
Notes	

VP-Oosterbaan1999

Methods	RCT Self-report measures some confirmed with treating doctor Of 143 referrals who met inclusion criteria, 65 (44%) subjects entered study of whom 63 (43%) were followed-up @ 12/12
Participants	Inclusion criteria: 18-75 yrs old Normal CVS according to a cardiologist Exclusion criteria: Proven CAD of MI on coronary angiography, exercise test, laboratory results, ECG of CXR, a history of typical angina, insufficient fluency in Dutch, current psychiatric treatment for noncardiac chest pain, current diagnosis of major depression, bipolar disorder, psychoactive substance use (except nicotine) in previous 3/12
Interventions	Individual CBT: Max 12 sessions including cognitive restructuring, problem solving, relaxation, breathing exercises Controls: Assessment only and usual care
Outcomes	Chest pain free days and pain episodes including severity over 1/52 PM: HADS QL: SF-36 Health service use
Notes	High attrition rate leading to potential follow-up bias

RCCT=randomised controlled cross-over trial
RCT=randomised controlled trial
QL= Quality of life
PM=Psychological Morbidity
PSE=Present State Examination
STAI-T=State-trait Anxity Inventory
BDI-Beck Bepression Inventory
SRT=Symptom Rating Test
AS=Autonomic symptoms
BSI=Brief symptom Inventory

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Achem 2008	Review article - no primary data.
Adler 2001	Review article - no primary data. Psychological interventions not covered
Asbury 2005	Review article - no primary data.

(*Continued*)

Asbury 2005a	Review article - no primary data.
Carter 1992a	Not an intervention study
Carter 1992b	Not an intervention study
Chambers 1998	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Cott 1992	An RCT that pooled data from 90 patients with mitral valve prolapse with only 14 subjects with NSCP
Cox 1998	RCT of antidepressant medication
Esler 2004	Review article - no primary data. Suggests that biopsychosocial rather than attribution models may be more effective for noncardiac chest pain
Eslick 2004	Not an intervention study
Eslick 2005	Review article - no primary data.
Faybush 2004	Not an intervention study
Fleet 1998	Not an intervention study
Goodacre 2001	Not an intervention study of a psychological treatment
Goodacre 2004	Not an intervention study of a psychological treatment
Handa 1999	Non-randomised trial of antidepressant medication
Hegel 1989	Uncontrolled trial of behavioural therapy
Jackson 2006	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Jeejeebhoy 2000	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Kaski 2001	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Katz 2000	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Kroenke 2000	Review article - no primary data.
Lahmann 2010	No primary data

(*Continued*)

Looper 2002	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Mayou 1989a	Conference abstract - insufficient information on intervention and control groups
Mayou 1994	Not an intervention study
Nanke 2004	Review article - no primary data. Suggests that biofeedback, relaxation & cognitive-behavioural therapy are effective for somatoform symptoms including noncardiac chest pain
Nezu 2001	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Olden 2004	Not an intervention study
Olden 2006	Review article - no primary data
Palsson 2006	Commentary - no primary data
Petrie 2007	Not a study of non-specific chest pain
Romeo 1993	Not an intervention study
Ryan 2004	Of the 70 subjects, only 11 had functional cardiac pain & data for these were not presented separately
Schey 2007	Review article - no primary data. Suggests that hypnotherapy is effective for noncardiac chest pain
Schmulson 2004	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Serlie 1995	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
VP-Oosterbaan 1997	Uncontrolled trial of cognitive-behavioural therapy
Wu 2002	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Wulsin 2002	Pharmacotherapy only
Yehuda 1999	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Zachariae 2001	Not an intervention study

(*Continued*)

Zaubler 1998	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain

DATA AND ANALYSES

Comparison 1. Psychological intervention versus no such therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any chest pain up to 3 months after intervention	3	172	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.57, 0.81]
2 Any chest pain from 3 to 12 months after intervention	2	111	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.45, 0.76]
3 Chest pain free days up to 3 months after intervention	2	81	Mean Difference (IV, Fixed, 95% CI)	2.81 [1.28, 4.34]
4 Chest pain frequency up to 3 months after intervention	7	294	Mean Difference (IV, Random, 95% CI)	-2.26 [-4.41, -0.12]
5 Chest pain frequency 3 to 12 months after intervention	4	164	Mean Difference (IV, Random, 95% CI)	-0.81 [-2.35, 0.74]
6 Chest pain severity up to 3 months	4	180	Mean Difference (IV, Random, 95% CI)	-4.64 [-12.18, 2.89]
7 Quality of life - physical functioning up to 3 months after intervention	5	221	Std. Mean Difference (IV, Fixed, 95% CI)	0.24 [-0.03, 0.50]
8 Quality of life - physical functioning 3 to 12 months after intervention	4	192	Std. Mean Difference (IV, Fixed, 95% CI)	0.29 [0.01, 0.58]
9 Quality of life - role problems due to emotional limitations up to 3 months after intervention	6	284	Std. Mean Difference (IV, Fixed, 95% CI)	0.35 [0.11, 0.58]
10 Quality of life - role problems due to emotional limitations 3 to 12 months after intervention	4	192	Std. Mean Difference (IV, Fixed, 95% CI)	0.19 [-0.09, 0.48]
11 Quality of life - social functioning up to 3 months after intervention	7	310	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.04, 0.41]
12 Quality of life - social functioning 3 to 12 months after intervention	4	173	Std. Mean Difference (IV, Fixed, 95% CI)	0.43 [0.12, 0.73]
13 Psychological symptoms up to 3 months after the intervention (depression & overall)	8	377	Std. Mean Difference (IV, Fixed, 95% CI)	-0.16 [-0.37, 0.04]
14 Psychological symptoms up to 3 months after the intervention (anxiety and overall)	8	383	Std. Mean Difference (IV, Fixed, 95% CI)	-0.23 [-0.43, -0.03]
15 Psychological symptoms 3 to 12 months after the intervention	3	133	Std. Mean Difference (IV, Fixed, 95% CI)	-0.18 [-0.52, 0.17]
16 Cardiac anxiety fear up to 3 months	4	199	Std. Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.36, 0.20]
17 Cardiac anxiety fear 3 to 12 months	2	89	Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.24, 0.33]

18 Cardiac anxiety avoidance up to 3 months	3	153	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.29, 0.19]
19 Cardiac anxiety avoidance 3 to 12 months	2	89	Mean Difference (IV, Fixed, 95% CI)	0.04 [-0.31, 0.39]
20 Cardiac anxiety attention up to 3 months	3	153	Mean Difference (IV, Fixed, 95% CI)	0.17 [-0.04, 0.37]
21 Cardiac anxiety attention 3 to 12 months	2	89	Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.21, 0.27]

Analysis 1.1. Comparison 1 Psychological intervention versus no such therapy, Outcome 1 Any chest pain up to 3 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 1 Any chest pain up to 3 months after intervention

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Klimes 1990	20/29	29/29		37.2 %	0.69 [0.54, 0.89]
Sanders 1997	21/29	17/21		24.9 %	0.89 [0.66, 1.21]
VP-Oosterbaan1999	16/32	30/32		37.9 %	0.53 [0.37, 0.76]
Total (95% CI)	**90**	**82**		**100.0 %**	**0.68 [0.57, 0.81]**

Total events: 57 (Treatment), 76 (Control)

Heterogeneity: Chi^2 = 4.84, df = 2 (P = 0.09); I^2 =59%

Test for overall effect: Z = 4.27 (P = 0.000020)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Psychological intervention versus no such therapy, Outcome 2 Any chest pain from 3 to 12 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 2 Any chest pain from 3 to 12 months after intervention

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Klimes 1990	11/19	29/29		46.1 %	0.58 [0.40, 0.85]
VP-Oosterbaan1999	16/31	28/32		53.9 %	0.59 [0.41, 0.85]
Total (95% CI)	**50**	**61**		**100.0 %**	**0.59 [0.45, 0.76]**

Total events: 27 (Treatment), 57 (Control)

Heterogeneity: Chi^2 = 0.00, df = 1 (P = 0.97); I^2 =0.0%

Test for overall effect: Z = 3.96 (P = 0.000076)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Psychological intervention versus no such therapy, Outcome 3 Chest pain free days up to 3 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 3 Chest pain free days up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Mayou 1997 and Mayou 1999	15	3.85 (2.62)	10	2.18 (2.38)		59.6 %	1.67 [-0.31, 3.65]
Potts 1999	32	9.1 (5.1)	24	4.6 (4.1)		40.4 %	4.50 [2.09, 6.91]
Total (95% CI)	**47**		**34**			**100.0 %**	**2.81 [1.28, 4.34]**

Heterogeneity: Chi^2 = 3.16, df = 1 (P = 0.08); I^2 =68%

Test for overall effect: Z = 3.60 (P = 0.00032)

Test for subgroup differences: Not applicable

Analysis 1.4. Comparison 1 Psychological intervention versus no such therapy, Outcome 4 Chest pain frequency up to 3 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

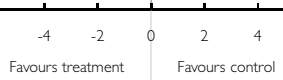
Outcome: 4 Chest pain frequency up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Asbury 2007	27	1.66 (2.19)	26	6.11 (3.17)		19.6 %	-4.45 [-5.92, -2.98]
DeGuire 1996	10	9 (12)	10	26 (26)		1.4 %	-17.00 [-34.75, 0.75]
Esler 2001	17	4.59 (7.43)	19	1.21 (1.78)		13.4 %	3.38 [-0.24, 7.00]
Jonsbu 2011	21	2.5 (0.83)	19	2.59 (0.71)		21.4 %	-0.09 [-0.57, 0.39]
Mayou 1997 and Mayou 1999	15	2.55 (1.53)	10	3.71 (0.99)		20.6 %	-1.16 [-2.15, -0.17]
Potts 1999	32	7 (9.1)	24	25.3 (28.7)		2.8 %	-18.30 [-30.21, -6.39]
VP-Oosterbaan1999	32	1.16 (1.8)	32	5.16 (1.8)		20.8 %	-4.00 [-4.88, -3.12]
Total (95% CI)	**154**		**140**			**100.0 %**	**-2.26 [-4.41, -0.12]**

Heterogeneity: $Tau^2 = 5.56$; $Chi^2 = 95.32$, df = 6 (P<0.00001); I^2 =94%

Test for overall effect: Z = 2.07 (P = 0.039)

Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1 Psychological intervention versus no such therapy, Outcome 5 Chest pain frequency 3 to 12 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 5 Chest pain frequency 3 to 12 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Esler 2001	17	2.06 (4.6)	19	2.68 (5.5)		14.0 %	-0.62 [-3.92, 2.68]
Jonsbu 2011	21	2.65 (0.67)	19	2.44 (0.86)		36.9 %	0.21 [-0.27, 0.69]
Mayou 1997 and Mayou 1999	15	2.75 (1.59)	10	2.71 (1.8)		29.4 %	0.04 [-1.34, 1.42]
VP-Oosterbaan1999	31	1.46 (2.5)	32	5.54 (6.5)		19.8 %	-4.08 [-6.50, -1.66]
Total (95% CI)	**84**		**80**			**100.0 %**	**-0.81 [-2.35, 0.74]**

Heterogeneity: $Tau^2 = 1.64$; $Chi^2 = 11.79$, df = 3 (P = 0.01); $I^2 = 75\%$

Test for overall effect: Z = 1.02 (P = 0.31)

Test for subgroup differences: Not applicable

Analysis 1.6. Comparison 1 Psychological intervention versus no such therapy, Outcome 6 Chest pain severity up to 3 months.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 6 Chest pain severity up to 3 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Asbury 2007	27	1.23 (1.36)	26	2.08 (1.03)		42.6 %	-0.85 [-1.50, -0.20]
Jones 2006	15	29.13 (25.31)	13	47.31 (26.55)		11.2 %	-18.18 [-37.48, 1.12]
Keefe 2011	29	15.13 (23.61)	24	11.66 (20.58)		20.7 %	3.47 [-8.43, 15.37]
Spinhoven 2010	23	11.9 (14)	23	23.5 (18.5)		25.5 %	-11.60 [-21.08, -2.12]
Total (95% CI)	**94**		**86**			**100.0 %**	**-4.64 [-12.18, 2.89]**

Heterogeneity: $Tau^2 = 34.60$; $Chi^2 = 8.51$, df = 3 (P = 0.04); $I^2 = 65\%$

Test for overall effect: Z = 1.21 (P = 0.23)

Test for subgroup differences: Not applicable

Analysis 1.7. Comparison 1 Psychological intervention versus no such therapy, Outcome 7 Quality of life - physical functioning up to 3 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

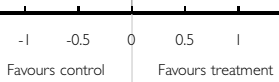
Outcome: 7 Quality of life - physical functioning up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	27	19.41 (5.19)	26	18.44 (7.31)		24.3 %	0.15 [-0.39, 0.69]
Esler 2001	17	84.4 (20.1)	19	87.6 (19.4)		16.4 %	-0.16 [-0.81, 0.50]
Jones 2006	15	5.16 (0.81)	13	4.68 (1.07)		12.4 %	0.50 [-0.26, 1.25]
Jonsbu 2011	21	89.8 (10.8)	19	83.5 (16.1)		17.8 %	0.46 [-0.17, 1.08]
VP-Oosterbaan1999	32	82 (24)	32	75 (24)		29.1 %	0.29 [-0.20, 0.78]
Total (95% CI)	**112**		**109**			**100.0 %**	**0.24 [-0.03, 0.50]**

Heterogeneity: Chi^2 = 2.45, df = 4 (P = 0.65); I^2 =0.0%

Test for overall effect: Z = 1.75 (P = 0.081)

Test for subgroup differences: Not applicable



Analysis 1.8. Comparison 1 Psychological intervention versus no such therapy, Outcome 8 Quality of life - physical functioning 3 to 12 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 8 Quality of life - physical functioning 3 to 12 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	27	20.09 (5.47)	26	18.08 (7.22)		27.6 %	0.31 [-0.23, 0.85]
Esler 2001	17	87.4 (18.8)	19	86.1 (21)		19.0 %	0.06 [-0.59, 0.72]
Jonsbu 2011	21	88.4 (13.8)	19	81.9 (20.3)		20.7 %	0.37 [-0.26, 1.00]
VP-Oosterbaan1999	31	87 (19)	32	80 (19)		32.7 %	0.36 [-0.13, 0.86]
Total (95% CI)	**96**		**96**			**100.0 %**	**0.29 [0.01, 0.58]**

Heterogeneity: Chi^2 = 0.61, df = 3 (P = 0.89); I^2 =0.0%

Test for overall effect: Z = 2.02 (P = 0.044)

Test for subgroup differences: Not applicable

Analysis 1.9. Comparison 1 Psychological intervention versus no such therapy, Outcome 9 Quality of life - role problems due to emotional limitations up to 3 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

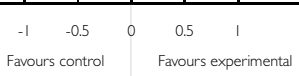
Outcome: 9 Quality of life - role problems due to emotional limitations up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	27	22.01 (4.81)	26	19.92 (6.05)		18.7 %	0.38 [-0.17, 0.92]
Asbury 2008	32	72.6 (38.5)	32	70.1 (40.1)		23.0 %	0.06 [-0.43, 0.55]
Esler 2001	17	88.3 (26)	19	79 (33.7)		12.8 %	0.30 [-0.36, 0.96]
Jones 2006	15	5.16 (0.81)	13	4.68 (1.07)		9.7 %	0.50 [-0.26, 1.25]
Jonsbu 2011	21	87.3 (26.8)	19	66.7 (39.1)		13.7 %	0.61 [-0.03, 1.24]
VP-Oosterbaan1999	32	80 (36)	31	63 (43)		22.1 %	0.42 [-0.08, 0.92]
Total (95% CI)	**144**		**140**			**100.0 %**	**0.35 [0.11, 0.58]**

Heterogeneity: Chi^2 = 2.21, df = 5 (P = 0.82); I^2 =0.0%

Test for overall effect: Z = 2.90 (P = 0.0037)

Test for subgroup differences: Not applicable



Analysis 1.10. Comparison 1 Psychological intervention versus no such therapy, Outcome 10 Quality of life - role problems due to emotional limitations 3 to 12 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

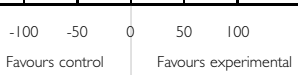
Outcome: 10 Quality of life - role problems due to emotional limitations 3 to 12 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	27	22.54 (5.76)	26	18.04 (6.64)		26.4 %	0.71 [0.16, 1.27]
Esler 2001	17	84.3 (35.6)	19	91.3 (18.7)		19.0 %	-0.24 [-0.90, 0.41]
Jonsbu 2011	21	76.7 (36)	19	77.8 (32.3)		21.2 %	-0.03 [-0.65, 0.59]
VP-Oosterbaan1999	31	79 (38)	32	72 (42)		33.4 %	0.17 [-0.32, 0.67]
Total (95% CI)	**96**		**96**			**100.0 %**	**0.19 [-0.09, 0.48]**

Heterogeneity: $Chi^2 = 5.58$, df = 3 (P = 0.13); $I^2 = 46\%$

Test for overall effect: Z = 1.32 (P = 0.19)

Test for subgroup differences: Not applicable



Analysis 1.11. Comparison 1 Psychological intervention versus no such therapy, Outcome 11 Quality of life - social functioning up to 3 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

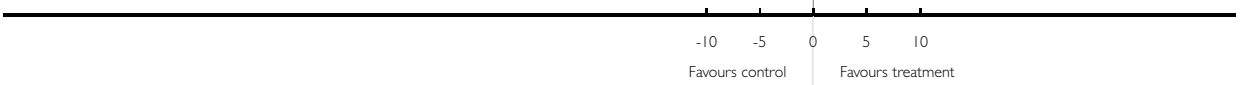
Outcome: 11 Quality of life - social functioning up to 3 months after intervention

Study or subgroup	Favours control N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Asbury 2007	27	22.8 (4.31)	26	23.08 (4.8)		17.4 %	-0.06 [-0.60, 0.48]
Asbury 2008	32	70.5 (26.8)	32	69.8 (23.7)		21.0 %	0.03 [-0.46, 0.52]
Esler 2001	17	80.9 (28.2)	19	83.1 (24.2)		11.8 %	-0.08 [-0.74, 0.57]
Jones 2006	15	5.16 (0.81)	13	4.68 (1.07)		8.8 %	0.50 [-0.26, 1.25]
Jonsbu 2011	21	86.3 (19.7)	19	75 (27.2)		12.7 %	0.47 [-0.16, 1.10]
Mayou 1997 and Mayou 1999	15	1.45 (0.95)	10	1.12 (1.11)		7.8 %	0.31 [-0.49, 1.12]
VP-Oosterbaan1999	32	85.6 (16)	32	78.6 (22)		20.6 %	0.36 [-0.13, 0.85]
Total (95% CI)	**159**		**151**			**100.0 %**	**0.19 [-0.04, 0.41]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.85$, df = 6 (P = 0.70); $I^2 = 0.0\%$

Test for overall effect: Z = 1.64 (P = 0.10)

Test for subgroup differences: Not applicable



Analysis 1.12. Comparison 1 Psychological intervention versus no such therapy, Outcome 12 Quality of life - social functioning 3 to 12 months after intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

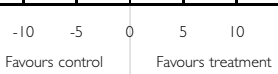
Outcome: 12 Quality of life - social functioning 3 to 12 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	27	24.18 (4.53)	26	21.81 (5.32)		31.0 %	0.47 [-0.07, 1.02]
Jonsbu 2011	21	81.3 (25.8)	19	72.2 (30.8)		23.7 %	0.32 [-0.31, 0.94]
Mayou 1997 and Mayou 1999	12	1.55 (1.1)	5	1.12 (1.11)		8.4 %	0.37 [-0.68, 1.42]
VP-Oosterbaan1999	31	87.6 (19)	32	77.6 (23)		36.9 %	0.47 [-0.03, 0.97]
Total (95% CI)	**91**		**82**			**100.0 %**	**0.43 [0.12, 0.73]**

Heterogeneity: Chi^2 = 0.19, df = 3 (P = 0.98); I^2 =0.0%

Test for overall effect: Z = 2.74 (P = 0.0062)

Test for subgroup differences: Not applicable



Analysis 1.13. Comparison 1 Psychological intervention versus no such therapy, Outcome 13 Psychological symptoms up to 3 months after the intervention (depression & overall).

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

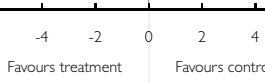
Outcome: 13 Psychological symptoms up to 3 months after the intervention (depression % overall)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	27	4.36 (3.48)	26	4.21 (3.26)		14.5 %	0.04 [-0.49, 0.58]
Asbury 2008	32	4.8 (3.3)	32	3.8 (2.4)		17.2 %	0.34 [-0.15, 0.84]
Jonsbu 2011	21	5.9 (6.5)	19	8.8 (7.2)		10.6 %	-0.42 [-1.04, 0.21]
Keefe 2011	29	7.26 (8.6)	24	5.16 (6.03)		14.2 %	0.27 [-0.27, 0.82]
Lahmann 2008	11	51.6 (6.6)	11	56.1 (8.2)		5.7 %	-0.58 [-1.44, 0.28]
Mayou 1997 and Mayou 1999	15	0.35 (0.37)	10	0.47 (0.31)		6.5 %	-0.33 [-1.14, 0.47]
Potts 1999	32	4.3 (3.2)	24	6.4 (4.1)		14.4 %	-0.57 [-1.11, -0.03]
VP-Oosterbaan1999	32	4.26 (3.2)	32	5.96 (3.6)		16.9 %	-0.49 [-0.99, 0.00]
Total (95% CI)	**199**		**178**			**100.0 %**	**-0.16 [-0.37, 0.04]**

Heterogeneity: Chi^2 = 12.69, df = 7 (P = 0.08); I^2 =45%

Test for overall effect: Z = 1.54 (P = 0.12)

Test for subgroup differences: Not applicable



Analysis 1.14. Comparison 1 Psychological intervention versus no such therapy, Outcome 14 Psychological symptoms up to 3 months after the intervention (anxiety and overall).

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

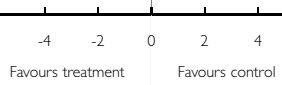
Outcome: 14 Psychological symptoms up to 3 months after the intervention (anxiety and overall)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	27	6.78 (4.15)	26	8 (3.42)		14.0 %	-0.32 [-0.86, 0.23]
Asbury 2008	32	6.7 (3.3)	32	6.2 (3.3)		17.1 %	0.15 [-0.34, 0.64]
Keefe 2011	29	33.96 (13.19)	24	31.89 (9.89)		14.0 %	0.17 [-0.37, 0.71]
Lahmann 2008	11	53.5 (5.5)	11	60.5 (10.1)		5.3 %	-0.83 [-1.71, 0.05]
Mayou 1997 and Mayou 1999	15	0.35 (0.37)	10	0.47 (0.31)		6.3 %	-0.33 [-1.14, 0.47]
Potts 1999	32	6.2 (3)	24	8.4 (5.1)		14.2 %	-0.54 [-1.08, 0.00]
Spinhoven 2010	23	4.9 (3.9)	23	7 (3.3)		11.8 %	-0.57 [-1.16, 0.02]
VP-Oosterbaan1999	32	6.66 (3.3)	32	7.16 (3.6)		17.1 %	-0.14 [-0.63, 0.35]
Total (95% CI)	**201**		**182**			**100.0 %**	**-0.23 [-0.43, -0.03]**

Heterogeneity: Chi^2 = 9.02, df = 7 (P = 0.25); I^2 =22%

Test for overall effect: Z = 2.20 (P = 0.028)

Test for subgroup differences: Not applicable



Analysis 1.15. Comparison 1 Psychological intervention versus no such therapy, Outcome 15 Psychological symptoms 3 to 12 months after the intervention.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 15 Psychological symptoms 3 to 12 months after the intervention

Study or subgroup	Treatment		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Asbury 2007	27	11.05 (7.41)	26	14 (6.89)		40.3 %	-0.41 [-0.95, 0.14]
Mayou 1997 and Mayou 1999	12	0.37 (0.33)	5	0.29 (0.22)		10.9 %	0.25 [-0.80, 1.30]
VP-Oosterbaan1999	31	6.96 (3.1)	32	7.26 (4)		48.9 %	-0.08 [-0.58, 0.41]
Total (95% CI)	**70**		**63**			**100.0 %**	**-0.18 [-0.52, 0.17]**

Heterogeneity: Chi² = 1.46, df = 2 (P = 0.48); I² =0.0%

Test for overall effect: Z = 1.00 (P = 0.32)

Test for subgroup differences: Not applicable

Analysis 1.16. Comparison 1 Psychological intervention versus no such therapy, Outcome 16 Cardiac anxiety fear up to 3 months.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

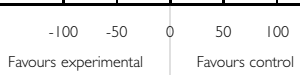
Outcome: 16 Cardiac anxiety fear up to 3 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	27	1.35 (0.56)	26	1.27 (0.63)		26.7 %	0.13 [-0.41, 0.67]
Asbury 2008	32	1.2 (0.5)	32	1.2 (0.5)		32.3 %	0.0 [-0.49, 0.49]
Esler 2001	17	1.4 (0.42)	19	1.49 (0.25)		18.0 %	-0.26 [-0.92, 0.40]
Spinhoven 2010	23	12.8 (7.8)	23	15.1 (7.5)		23.0 %	-0.30 [-0.88, 0.29]
Total (95% CI)	**99**		**100**			**100.0 %**	**-0.08 [-0.36, 0.20]**

Heterogeneity: Chi^2 = 1.51, df = 3 (P = 0.68); I^2 =0.0%

Test for overall effect: Z = 0.56 (P = 0.58)

Test for subgroup differences: Not applicable



Analysis 1.17. Comparison 1 Psychological intervention versus no such therapy, Outcome 17 Cardiac anxiety fear 3 to 12 months.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

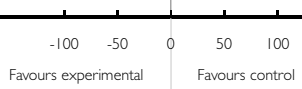
Outcome: 17 Cardiac anxiety fear 3 to 12 months

Study or subgroup	Treatment		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Asbury 2007	27	1.3 (0.67)	26	1.31 (0.58)		73.4 %	-0.01 [-0.35, 0.33]
Esler 2001	17	1.46 (0.87)	19	1.26 (0.84)		26.6 %	0.20 [-0.36, 0.76]
Total (95% CI)	**44**		**45**			**100.0 %**	**0.05 [-0.24, 0.33]**

Heterogeneity: $Chi^2 = 0.40$, df = 1 (P = 0.53); $I^2 = 0.0\%$

Test for overall effect: Z = 0.31 (P = 0.76)

Test for subgroup differences: Not applicable



Analysis 1.18. Comparison 1 Psychological intervention versus no such therapy, Outcome 18 Cardiac anxiety avoidance up to 3 months.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

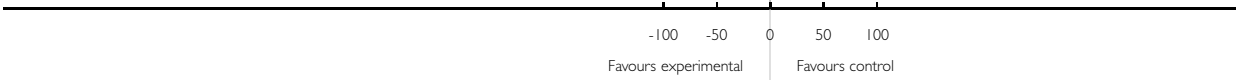
Outcome: 18 Cardiac anxiety avoidance up to 3 months

Study or subgroup	Treatment		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Asbury 2007	27	1.16 (0.74)	26	1.24 (0.89)		29.9 %	-0.08 [-0.52, 0.36]
Asbury 2008	32	1.3 (0.6)	32	1.5 (0.8)		48.5 %	-0.20 [-0.55, 0.15]
Esler 2001	17	0.94 (0.86)	19	0.62 (0.71)		21.6 %	0.32 [-0.20, 0.84]
Total (95% CI)	**76**		**77**			**100.0 %**	**-0.05 [-0.29, 0.19]**

Heterogeneity: Chi^2 = 2.69, df = 2 (P = 0.26); I^2 =26%

Test for overall effect: Z = 0.42 (P = 0.67)

Test for subgroup differences: Not applicable



Analysis 1.19. Comparison 1 Psychological intervention versus no such therapy, Outcome 19 Cardiac anxiety avoidance 3 to 12 months.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

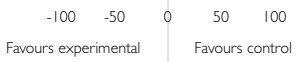
Outcome: 19 Cardiac anxiety avoidance 3 to 12 months

Study or subgroup	Treatment		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Asbury 2007	27	1.29 (0.66)	26	1.46 (0.95)		62.6 %	-0.17 [-0.61, 0.27]
Esler 2001	17	0.93 (1.01)	19	0.53 (0.69)		37.4 %	0.40 [-0.17, 0.97]
Total (95% CI)	**44**		**45**			**100.0 %**	**0.04 [-0.31, 0.39]**

Heterogeneity: $Chi^2 = 2.39$, df = 1 (P = 0.12); $I^2 = 58\%$

Test for overall effect: Z = 0.24 (P = 0.81)

Test for subgroup differences: Not applicable



Analysis 1.20. Comparison 1 Psychological intervention versus no such therapy, Outcome 20 Cardiac anxiety attention up to 3 months.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 20 Cardiac anxiety attention up to 3 months

Study or subgroup	Treatment		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Asbury 2007	27	1.37 (0.66)	26	1.16 (0.57)		39.3 %	0.21 [-0.12, 0.54]
Asbury 2008	32	1.4 (0.6)	32	1.2 (0.7)		42.3 %	0.20 [-0.12, 0.52]
Esler 2001	17	1.06 (0.74)	19	1.07 (0.74)		18.4 %	-0.01 [-0.49, 0.47]
Total (95% CI)	**76**		**77**			**100.0 %**	**0.17 [-0.04, 0.37]**

Heterogeneity: Chi^2 = 0.62, df = 2 (P = 0.73); I^2 =0.0%

Test for overall effect: Z = 1.56 (P = 0.12)

Test for subgroup differences: Not applicable

Analysis 1.21. Comparison 1 Psychological intervention versus no such therapy, Outcome 21 Cardiac anxiety attention 3 to 12 months.

Review: Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy

Comparison: 1 Psychological intervention versus no such therapy

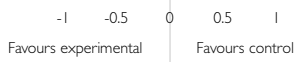
Outcome: 21 Cardiac anxiety attention 3 to 12 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Asbury 2007	27	1.28 (0.13)	26	1.25 (0.71)		75.8 %	0.03 [-0.25, 0.31]
Esler 2001	17	1.01 (0.75)	19	0.98 (0.75)		24.2 %	0.03 [-0.46, 0.52]
Total (95% CI)	**44**		**45**			**100.0 %**	**0.03 [-0.21, 0.27]**

Heterogeneity: Chi² = 0.0, df = 1 (P = 1.00); I² =0.0%

Test for overall effect: Z = 0.24 (P = 0.81)

Test for subgroup differences: Not applicable



APPENDICES

Appendix 1. 2008 search strategies

CENTRAL on The Cochrane LIbrary

#1 MeSH descriptor chest pain this term only
#2 chest next pain in All Text
#3 thorax next pain in All Text
#4 thoracic next pain in All Text
#5 MeSH descriptor Microvascular Angina explode all trees
#6 cardiac next syndrome* in All Text
#7 microvascular next angina in All Text
#8 ((((((#1 or #2) or #3) or #4) or #5) or #6) or #7)
#9 angina in All Text
#10 (normal in All Text near/6 coronary in All Text)
#11 (normal in All Text near/6 angiogram* in All Text)
#12 (normal in All Text near/6 anatomy in All Text)
#13 ((#10 or #11) or #12)
#14 (#13 and #9)
#15 (#14 or #8)
#16 MeSH descriptor PSYCHOTHERAPY explode all trees

#17 psychotherap* in All Text
#18 (cognitive in All Text near/6 therap* in All Text)
#19 (behaviour* in All Text near/6 therap* in All Text)
#20 (behavior* in All Text near/6 therap* in All Text) 7551
#21 MeSH descriptor COUNSELING explode all trees
#22 counsel* in All Text
#23 psychodynamic* in All Text
#24 (relax* in All Text near/6 therap* in All Text)
#25 psychologic* in All Text
#26 hyperventilation in All Text
#27 (breath* in All Text near/6 control* in All Text)
#28 (#16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27)
#29 (#15 and #28) 148

MEDLINE on Ovid

1 Chest Pain/ (6468)
2 exp Microvascular Angina/ (727)
3 "syndrome x".tw. (1275)
4 microvascular angina.tw. (150)
5 cardiac syndrome$.tw. (339)
6 chest pain$.tw. (16817)
7 ((thorax or thoracic) adj1 pain$).tw. (731)
8 cardiac syndrome$.tw. (339)
9 or/1-8 (21108)
10 Angina Pectoris/ (28905)
11 angina.tw. (37131)
12 (normal adj5 coronary).tw. (6979)
13 (normal adj5 angiogram$).tw. (1260)
14 (normal adj5 anatomy).tw. (4111)
15 or/12-14 (11535)
16 10 or 11 (49340)
17 15 and 16 (1725)
18 9 or 17 (22123)
19 exp Psychotherapy/ (122234)
20 exp Counseling/ (26136)
21 psychotherap$.tw. (24990)
22 counsel$.tw. (44851)
23 psychodynamic$.tw. (4079)
24 (behavio$ adj3 therap$).tw. (9026)
25 (cognitiv$ adj3 therap$).tw. (5666)
26 psychologic$.tw. (93626)
27 exp "Mind-Body and Relaxation Techniques"/ (33980)
28 (relaxation adj5 (treat$ or therap$ or technique$)).tw. (3240)
29 cbt.tw. (2105)
30 guided imagery.tw. (330)
31 (hyperventilat$ adj3 control$).tw. (235)
32 (hyperventilat$ adj5 (treat$ or therap$ or technique$)).tw. (404)
33 (talk$ adj3 (therap$ or treat$)).tw. (180)
34 or/19-33 (282622)
35 34 and 18 (414)
36 randomized controlled trial.pt. (269477)
37 controlled clinical trial.pt. (80776)

38 Randomized controlled trials/ (58509)
39 random allocation/ (63710)
40 double blind method/ (101566)
41 single-blind method/ (12762)
42 or/36-41 (454816)
43 exp animal/ not humans/ (3412892)
44 42 not 43 (425364)
45 clinical trial.pt. (460981)
46 exp Clinical Trials as Topic/ (215116)
47 (clin$ adj25 trial$).ti,ab. (155757)
48 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab. (98377)
49 placebos/ (28390)
50 placebo$.ti,ab. (115404)
51 random$.ti,ab. (435396)
52 research design/ (55352)
53 or/45-52 (961765)
54 53 not 43 (892832)
55 44 or 54 (919159)
56 35 and 55 (70)
57 limit 56 to yr="2002 - 2008" (30)

EMBASE on Ovid < to 2008 Week 49>

1 Thorax Pain/ (19589)
2 Syndrome X/ (1145)
3 "syndrome x".tw. (1187)
4 microvascular angina.tw. (151)
5 cardiac syndrome$.tw. (245)
6 chest pain$.tw. (14796)
7 ((thorax or thoracic) adj1 pain$).tw. (611)
8 cardiac syndrome$.tw. (245)
9 or/1-8 (27777)
10 Angina Pectoris/ (25627)
11 angina.tw. (29619)
12 (normal adj5 coronary).tw. (6060)
13 (normal adj5 angiogram$).tw. (1075)
14 (normal adj5 anatomy).tw. (3182)
15 or/12-14 (9561)
16 10 or 11 (40997)
17 15 and 16 (1485)
18 9 or 17 (28598)
19 exp Psychiatric treatment/ (115676)
20 exp Counseling/ (46367)
21 psychotherap$.tw. (22346)
22 counsel$.tw. (36138)
23 psychodynamic$.tw. (4102)
24 (behavio$ adj3 therap$).tw. (9850)
25 (cognitiv$ adj3 therap$).tw. (7174)
26 psychologic$.tw. (79410)
27 (relaxation adj5 (treat$ or therap$ or technique$)).tw. (2922)
28 cbt.tw. (2504)
29 guided imagery.tw. (233)
30 (hyperventilat$ adj3 control$).tw. (175)

31 (hyperventilat$ adj5 (treat$ or therap$ or technique$)).tw. (317)
32 (talk$ adj3 (therap$ or treat$)).tw. (143)
33 or/19-32 (242638)
34 33 and 18 (717)
35 controlled clinical trial/ (54279)
36 random$.tw. (384980)
37 randomized controlled trial/ (163469)
38 follow-up.tw. (346476)
39 double blind procedure/ (70681)
40 placebo$.tw. (108133)
41 placebo/ (120719)
42 factorial$.ti,ab. (8024)
43 (crossover$ or cross-over$).ti,ab. (38882)
44 (double$ adj blind$).ti,ab. (83559)
45 (singl$ adj blind$).ti,ab. (7337)
46 assign$.ti,ab. (106482)
47 allocat$.ti,ab. (33672)
48 volunteer$.ti,ab. (97667)
49 Crossover Procedure/ (20766)
50 Single Blind Procedure/ (7842)
51 or/35-50 (1002039)
52 34 and 51 (218)

PsycINFO on Ovid < to December Week 1 2008

1 Thorax/ (220)
2 Pain/ (10982)
3 1 and 2 (124)
4 "syndrome x".tw. (34)
5 microvascular angina.tw. (1)
6 cardiac syndrome$.tw. (7)
7 chest pain$.tw. (588)
8 ((thorax or thoracic) adj1 pain$).tw. (18)
9 or/3-8 (644)
10 Angina Pectoris/ (228)
11 angina.tw. (614)
12 (normal adj5 coronary).tw. (58)
13 (normal adj5 angiogram$).tw. (9)
14 (normal adj5 anatomy).tw. (58)
15 or/12-14 (121)
16 10 or 11 (632)
17 15 and 16 (8)
18 9 or 17 (644)
19 exp Psychotherapy/ (134584)
20 exp Counseling/ (54251)
21 psychotherap$.tw. (79096)
22 counsel$.tw. (69295)
23 psychodynamic$.tw. (15557)
24 (behavio$ adj3 therap$).tw. (20467)
25 (cognitiv$ adj3 therap$).tw. (13689)
26 psychologic$.tw. (208058)
27 (relaxation adj5 (treat$ or therap$ or technique$)).tw. (3337)
28 cbt.tw. (3295)

29 guided imagery.tw. (795)
30 (hyperventilat$ adj3 control$).tw. (29)
31 (hyperventilat$ adj5 (treat$ or therap$ or technique$)).tw. (91)
32 (talk$ adj3 (therap$ or treat$)).tw. (562)
33 or/19-32 (428634)
34 33 and 18 (171)
35 clinical trials/ (2481)
36 "Empirical Study".md. (1109008)
37 random$.tw. (77684)
38 groups.tw. (261176)
39 (double adj3 blind).tw. (12272)
40 (single adj3 blind).tw. (818)
41 experimental design/ (7154)
42 controlled.tw. (49420)
43 (clinical adj3 study).tw. (5165)
44 trial.tw. (41661)
45 or/35-44 (1267552)
46 34 and 45 (109)
47 limit 46 to yr="2002 - 2008" (40)

CINAHL on EBSCO

((MH "Clinical Trials+") or (random* or rct or groups or trial or "clinical study")) and ((MH "Syndrome X") or (MH "Chest Pain") or ("chest pain" or "microvascular angina")) and ((MH "Psychology, Applied+") or (MH "Psychotherapy+") or (psychol* or counsel* or talk* or relaxation or hyperventilat* or CBT or cognitive or behavio*))

BIOSIS on ISI Web of Knowledge

# 3 52 #1 and #2 AND Taxa Notes=(Humans)
Databases=PREVIEWS Timespan=2002-2008

# 2 715 (ts=(angina and ((normal same angiogram*) or (normal same coronary) or (normal same anatomy))) or ts= ("microvascular angina" or "chest pain")) and TS=(random* or trial or RCT or groups or controlled or (double same blind) or (single same blind)) AND Taxa Notes=(Humans)
Databases=PREVIEWS Timespan=2002-2008

# 1 989 ts=(psychotherap* or counsel* or psychologic* or psychodynamic* or talk or talking or (behavio* same therap*) or (cognitive same therap*) or CBT or hyperventilat*) and ts=(chest or angina or thora*)
Databases=PREVIEWS Timespan=2002-2008

Appendix 2. 2002 search strategies

MEDLINE

1 Chest Pain/
2 Syndrome X/
3 "syndrome x".tw.
4 microvascular angina.tw.
5 cardiac syndrome$.tw.
6 chest pain$.tw.
7 ((thorax or thoracic) adj1 pain$).tw.

8 or/1-7
9 Angina Pectoris/
10 angina.tw.
11 (normal adj5 coronary).tw.
12 (normal adj5 angiogram$).tw.
13 (normal adj5 anatomy).tw.
14 or/11-13
15 9 or 10
16 14 and 15
17 8 or 16
18 exp Psychotherapy/
19 exp Counseling/
20 psychotherap$.tw.
21 counsel$.tw.
22 psychodynamic$.tw.
23 (behavio$ adj3 therap$).tw.
24 (cognitiv$ adj3 therap$).tw.
25 psychologic$.tw.
26 exp "Mind-Body and Relaxation Techniques"/
27 (relaxation adj5 (treat$ or therap$ or technique$)).tw.
28 or/18-27
29 17 and 28

EMBASE

1 Thorax Pain/
2 Syndrome X/
3 "syndrome x".tw.
4 microvascular angina.tw.
5 cardiac syndrome$.tw.
6 chest pain$.tw.
7 ((thorax or thoracic) adj1 pain$).tw.
8 or/1-7
9 Angina Pectoris/
10 angina.tw.
11 (normal adj5 coronary).tw.
12 (normal adj5 angiogram$).tw.
13 (normal adj5 anatomy).tw.
14 or/11-13
15 9 or 10
16 14 and 15
17 8 or 16
18 exp Psychiatric treatment/
19 exp Counseling/
20 psychotherap$.tw.
21 counsel$.tw.
22 psychodynamic$.tw.
23 (behavio$ adj3 therap$).tw.
24 (cognitiv$ adj3 therap$).tw.
25 psychologic$.tw.
26 (relaxation adj5 (treat$ or therap$ or technique$)).tw.
27 or/18-26
28 17 and 27

CINAHL on Ovid

1 Chest Pain/
2 "syndrome x".tw.
3 microvascular angina.tw.
4 cardiac syndrome$.tw.
5 chest pain$.tw.
6 ((thorax or thoracic) adj1 pain$).tw.
7 Angina Pectoris/
8 angina.tw.
9 (normal adj5 coronary).tw.
10 (normal adj5 angiogram$).tw.
11 (normal adj5 anatomy).tw.
12 or/9-11
13 7 or 8
14 12 and 13
15 exp Psychotherapy/
16 exp Counseling/
17 psychotherap$.tw.
18 counsel$.tw.
19 psychodynamic$.tw.
20 (behavio$ adj3 therap$).tw.
21 (cognitiv$ adj3 therap$).tw.
22 psychologic$.tw.
23 (relaxation adj5 (treat$ or therap$ or technique$)).tw.
24 or/1-6,14
25 or/15-23
26 24 and 25

PsycLIT

#23 ((((thorax or thoracic) next pain) or (cardiac syndrome*) or (microvascular angina) or (chest pain)) or (((angina) or (explode "Angina-Pectoris" in DE)) and ((normal near anatomy) or (normal near angiogram*) or (normal near coronary)))) and ((relaxation) or (psychodynamic*) or (behavio?r* therap*) or (counsel*) or (psychotherap*) or (explode "Counseling-" in DE) or (explode "Psychotherapy-" in DE))
#22 (relaxation) or (psychodynamic*) or (behavio?r* therap*) or (counsel*) or (psychotherap*) or (explode "Counseling-" in DE) or (explode "Psychotherapy-" in DE)
#21 behavio?r* therap*
#20 relaxation
#19 psychodynamic*
#18 counsel*
#17 psychotherap*
#16 explode "Counseling-" in DE
#15 explode "Psychotherapy-" in DE
#14 (((thorax or thoracic) next pain) or (cardiac syndrome*) or (microvascular angina) or (chest pain)) or (((angina) or (explode "Angina-Pectoris" in DE)) and ((normal near anatomy) or (normal near angiogram*) or (normal near coronary)))
#13 ((angina) or (explode "Angina-Pectoris" in DE)) and ((normal near anatomy) or (normal near angiogram*) or (normal near coronary))
#12 (normal near anatomy) or (normal near angiogram*) or (normal near coronary)
#11 normal near anatomy
#10 normal near angiogram*
#9 normal near coronary
#8 (angina) or (explode "Angina-Pectoris" in DE)
#7 angina

#6 explode "Angina-Pectoris" in DE
#5 ((thorax or thoracic) next pain) or (cardiac syndrome*) or (microvascular angina) or (chest pain)
#4 (thorax or thoracic) next pain
#3 cardiac syndrome*
#2 microvascular angina
#1 chest pain

BIOSIS (EDINA)

((al: (relaxation)) or (al: ((behavio* w therap*) or (cognitiv* w therap*) or psychotherap* or counsel* or psychologic* or psychodynamic*))) and ((((al: ((normal w angiogram*) or (normal with coronary) or (normal w anatomy))) and al: (angina)) or (al: ((chest w pain) or (microvascula* w angina) or (cardiac w syndrome)))) and (al: ((clin* n3 trial*) or random* or singl* or doubl* or blind* or mask* or placebo* or (clin* n3 study) or controlled)))

Appendix 3. 2011 search strategies

CENTRAL AND DARE (The Cochrane Library)

#1	MeSH descriptor Chest Pain, this term only
#2	chest next pain
#3	thorax next pain
#4	thoracic next pain
#5	MeSH descriptor Microvascular Angina, this term only
#6	cardiac next syndrome*
#7	microvascular next angina
#8	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9	angina
#10	normal near/6 coronary
#11	normal near/6 coronary
#12	normal near/6 anatomy
#13	(#10 OR #11 OR #12)
#14	(#9 AND #13)
#15	(#8 OR #14)
#16	MeSH descriptor Psychotherapy explode all trees
#17	psychotherap*
#18	cognitive near/6 therap*
#19	behaviour* near/6 therap*
#20	behavior* near/6 therap*
#21	MeSH descriptor Counseling explode all trees
#22	counsel*
#23	psychodynamic*
#24	relax* near/6 therap*
#25	psychologic*
#26	hyperventilation
#27	breath* near/6 control*
#28	(#16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27)
#29	(#15 AND #28)

MEDLINE (OVID)

1. Chest Pain/

2. exp Microvascular Angina/
3. "syndrome x".tw.
4. microvascular angina.tw.
5. cardiac syndrome*.tw.
6. chest pain*.tw.
7. ((thorax or thoracic) adj1 pain*).tw.
8. cardiac syndrome*.tw.
9. or/1-8
10. Angina Pectoris/
11. angina.tw.
12. (normal adj5 coronary).tw.
13. (normal adj5 angiogram*).tw.
14. (normal adj5 anatomy).tw.
15. or/12-14
16. 10 or 11
17. 15 and 16
18. 9 or 17
19. exp Psychotherapy/
20. exp Counseling/
21. psychotherap*.tw.
22. counsel*.tw.
23. psychodynamic*.tw.
24. (behavio* adj3 therap*).tw.
25. (cognitiv* adj3 therap*).tw.
26. psychologic*.tw.
27. exp Mind-Body Therapies/
28. (relaxation adj5 (treat* or therap* or technique*)).tw.
29. cbt.tw.
30. guided imagery.tw.
31. (hyperventilate* adj3 control*).tw.
32. (hyperventilate* adj5 (treat* or therap* or technique*)).tw.
33. (talk* adj3 (therap* or treat*)).tw.
34. or/19-33
35. 34 and 18
36. randomized controlled trial.pt.
37. controlled clinical trial.pt.
38. randomized.ab.
39. placebo.ab.
40. drug therapy.fs.
41. randomly.ab.
42. trial.ab.
43. groups.ab.
44. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43
45. exp animals/ not humans.sh.
46. 44 not 45
47. 35 and 46
48. (2008121* or 2008122* or 2008123* or 2009* or 2010* or 2011*).ed.
49. 47 and 48

EMBASE (OVID)

1. thorax pain/
2. Syndrome X/

3. “syndrome x”.tw.
4. microvascular angina.tw.
5. cardiac syndrome*.tw.
6. chest pain*.tw.
7. ((thorax or thoracic) adj1 pain*).tw.
8. cardiac syndrome*.tw.
9. or/1-8
10. angina pectoris/
11. angina.tw.
12. (normal adj5 coronary).tw.
13. (normal adj5 angiogram*).tw.
14. (normal adj5 anatomy).tw.
15. or/12-14
16. 10 or 11
17. 15 and 16
18. 9 or 17
19. exp psychiatric treatment/
20. exp counseling/
21. psychotherap*.tw.
22. counsel*.tw.
23. psychodynamic*.tw.
24. (behavio* adj3 therap*).tw.
25. (cognitiv* adj3 therap*).tw.
26. psychologic*.tw.
27. (relaxation adj5 (treat* or therap* or technique*)).tw.
28. cbt.tw.
29. guided imagery.tw.
30. (hyperventilat* adj3 control*).tw.
31. (hyperventilat* adj5 (treat* or therap* or technique*)).tw.
32. (talk* adj3 (therap* or treat*)).tw.
33. or/19-32
34. 33 and 18
35. random$.tw.
36. factorial$.tw.
37. crossover$.tw.
38. cross over$.tw.
39. cross-over$.tw.
40. placebo$.tw.
41. (doubl$ adj blind$).tw.
42. (singl$ adj blind$).tw.
43. assign$.tw.
44. allocat$.tw.
45. volunteer$.tw.
46. crossover procedure/
47. double blind procedure/
48. randomized controlled trial/
49. single blind procedure/
50. 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49
51. (animal/ or nonhuman/) not human/
52. 50 not 51
53. 34 and 52
54. limit 53 to embase
55. (2008121* or 2008122* or 2008123* or 2009* or 2010* or 2011*).dd.

56. 54 and 55

PsycINFO (OVID)

The RCT filter has been amended as an adaption of the Cochrane RCT filters used for MEDLINE and EMBASE.

1. Thorax/
2. Pain/
3. 1 and 2
4. "syndrome x".tw.
5. microvascular angina.tw.
6. cardiac syndrome*.tw.
7. chest pain*.tw.
8. ((thorax or thoracic) adj1 pain*).tw.
9. or/3-8
10. Angina Pectoris/
11. angina.tw.
12. (normal adj5 coronary).tw.
13. (normal adj5 angiogram*).tw.
14. (normal adj5 anatomy).tw.
15. or/12-14
16. 10 or 11
17. 15 and 16
18. 9 or 17
19. exp Psychotherapy/
20. exp Counseling/
21. psychotherap*.tw.
22. counsel*.tw.
23. psychodynamic*.tw.
24. (behavio* adj3 therap*).tw.
25. (cognitiv* adj3 therap*).tw.
26. psychologic*.tw.
27. (relaxation adj5 (treat* or therap* or technique*)).tw.
28. cbt.tw.
29. guided imagery.tw.
30. (hyperventilat* adj3 control*).tw.
31. (hyperventilat* adj5 (treat* or therap* or technique*)).tw.
32. (talk* adj3 (therap* or treat*)).tw.
33. or/19-32
34. 33 and 18
35. random$.tw.
36. factorial$.tw.
37. crossover$.tw.
38. cross-over$.tw.
39. placebo$.tw.
40. (doubl$ adj blind$).tw.
41. (singl$ adj blind$).tw.
42. assign$.tw.
43. allocat$.tw.
44. volunteer$.tw.
45. control*.tw.
46. "2000".md.
47. or/35-46
48. 34 and 47

49. (2008121* or 2008122* or 2008123* or 2009* or 2010* or 2011*).up.
50. 48 and 49

CINAHL Plus (EBSCO)

S17 S15 and S16
S16 EM 20081210-20110909
S15 S11 and S14
S14 S12 or S13
S13 (random* or rct or groups or trial or "clinical study")
S12 (MH "Clinical Trials+")
S11 S5 and S10
S10 S6 or S7 or S8 or S9
S9 AB (psychol* or counsel* or talk* or relaxation or hyperventilat* or CBT or cognitive or behavio*)
S8 TI (psychol* or counsel* or talk* or relaxation or hyperventilat* or CBT or cognitive or behavio*)
S7 (MH "Psychotherapy+")
S6 (MH "Psychology, Applied+")
S5 S1 or S2 or S3 or S4
S4 (TI "microvascular angina") or (AB "microvascular angina")
S3 (TI "chest pain") or (AB "chest pain")
S2 (MH "Chest Pain")
S1 (MH "Syndrome X")

BIOSIS (ISI Web of Knowledge)

#6 #5 AND #4 AND #3
#5 TS=(random* or trial or RCT or groups or controlled or (double same blind) or (single same blind))
#4 TS=(angina and ((normal same angiogram*) or (normal same coronary) or (normal same anatomy)))
#3 #2 AND #1
#2 TS=(psychotherap* or counsel* or psychologic* or psychodynamic* or talk or talking or (behavio* same therap*) or (cognitive same therap*) or CBT or hyperventilat*)
#1 TS=(chest or angina or thora*)

WHAT'S NEW

Last assessed as up-to-date: 30 November 2011.

Date	Event	Description
30 November 2011	New search has been performed	Search strategies were updated and searches re-run to September 2011. Five new studies, and an additional paper to an already included study were identified and included. The conclusions are essentially unchanged

(*Continued*)

21 September 2009	New search has been performed	Search strategies were updated and searches reran to December 2008. Two new studies, and an additional paper to an already included study were identified and included. Twenty-one new studies were assessed in detail and excluded. The conclusions are essentially unchanged
21 September 2009	New citation required but conclusions have not changed	New author added.

HISTORY

Protocol first published: Issue 1, 2003

Review first published: Issue 1, 2005

Date	Event	Description
9 September 2008	Amended	Converted to new review format.
1 November 2004	New citation required and conclusions have changed	First version of the review

CONTRIBUTIONS OF AUTHORS

Two reviewers (SK, LAC) independently selected suitable studies for inclusion in this review as detailed below. Where the two reviewers disagreed about the inclusion of a study, disagreements were resolved by consensus of opinion, or a third and fourth reviewer (PS, MY) consulted if they could not be resolved. SK and LAC completed the extraction of data from the papers. Data was entered into RevMan software by SK and duplicated by LAC

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Health Outcomes Unit, Capital District Health Authority, Halifax, Canada.
- Dalhousie University, Halifax, Canada.
- University of Western Australia, Australia.
- Fremantle Hospital, Australia.
- University of Queensland, School of Population Health, Australia.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

Behavior Therapy; Chest Pain [*psychology; therapy]; Cognitive Therapy [*methods]; Coronary Vessels [*anatomy & histology]; Hypnosis; Microvascular Angina [psychology; therapy]; Psychotherapy [methods]; Randomized Controlled Trials as Topic; Recurrence

MeSH check words

Humans