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

Kisely SR, Campbell LA, Yelland MJ, Paydar A

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2012, Issue 6

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

Steve R Kisely1, Leslie Anne Campbell2, Michael J Yelland3, Anita Paydar1

1School of Population Health, The University of Queensland, Brisbane, Australia. 2Capital District Health Authority, Halifax, Canada. 3School of Medicine, Logan Campus, Griffith University, Meadowbrook, Australia

Contact address: Steve R Kisely, School of Population Health, The University of Queensland, Brisbane, Australia. s.kisely@uq.edu.au.

Editorial group: Cochrane Heart Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 6, 2012.
Review content assessed as up-to-date: 30 November 2011.


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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 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 (Kahlilas 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 styleistics (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;

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(4) Hypnotherapy;
(5) Other psychotherapy/talking/counselling therapy;
(6) Standard care, 'attention' placebo, waiting list controls, or no intervention as the control conditions.

M E T H O D S

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.

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

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 into 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 assessor, 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 sub-group 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; Eder 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 (Potts 1999). Similarly, Eder 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%. 

Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy (Review)
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...
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 (Euler 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 (Euler 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 subscores. 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-
combined 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; Jonshu 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 participants 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 least 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.

**ACKNOWLEDGEMENTS**

The authors thank Paul Skerritt for helpful discussions and reviews of earlier versions of the manuscript.

SK is employed by the University of Queensland, and LAC by Capital District Health Authority, Halifax, Canada.

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References to studies included in this review

Ashbury 2007 [published data only]

Ashbury 2008 [published data only]

Ashbury 2011 [published data only]

DeGuire 1996 [published data only]

Esler 2001 [published data only]


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

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Carter 1992b [published data only]

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Cox 1998 [published data only]

Elder 2004 [published data only]

Elick 2004 [published data only]

Elick 2005 [published data only]

Faybush 2004 [published data only]

Fleet 1998 [published data only]

Keefe 2011 [published data only]

Klimes 1990 [published data only]

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Goodacre S, Nicholl J. A randomised controlled trial to measure the effect of chest pain unit care upon anxiety, depression, and health-related quality of life [ISRCTN85078221]. Health and Quality of Life Outcomes 2004;2:39.

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Lahmann 2010 [published data only]

Looper 2002 [published data only]

Mayou 1989a [published data only]

Mayou 1994 [published data only]

Nanke 2004 [published data only]

Nezu 2001 [published data only]

Olden 2004 [published data only]

Olden 2006 [published data only]

Palsson 2006 [published data only]

Petric 2007 [published data only]

Romeo 1993 [published data only]

Ryan 2004 [published data only]

Schey 2007 [published data only]

Schmulson 2004 [published data only]

Serlie 1995 [published data only]
Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy (Review)

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VP-Oosterbaan 1997 {published data only}

Wu 2002 {published data only}

Wulsin 2002 {published data only}

Yehuda 1999 {published data only}

Zachariae 2001 {published data only}

Zaubler 1998 {published data only}

Additional references

Bass 1984

Bennett 2001

Borkovec 1982

Capewell 2000

Chambers 1990

DeGuire 1992

Egger 1997

Eslick 2002

Eslick 2003

Hemingway 1999

Higgins 2011

Jones 2004

Kahrlas 1990

Katon 1988

Kisely 1997

Knockaert 2002

Lefebvre 2011

Matsuguchi 1984
Mayou 1989b

Ockene 1980

Price 2008

QAP 1982

Roll 1987

Shapiro 1994

Sharpe 1996

Speckens 1995

Von Korff 1988

Walker 1988

Woolfolk 1983

References to other published versions of this review

Kisely 2005

Kisely 2010

* Indicates the major publication for the study
## Characteristics of included studies

### Asbury 2007

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<th>Details</th>
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<tr>
<td><strong>Methods</strong></td>
<td>RCT</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>Fifty three female Syndrome X patients (mean +/- SD; 57.4 8.0 yrs)</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>2 groups Weekly group autogenic training (AT) sessions were supported by an individual home program and symptom diary symptom diary only control.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>The Hospital Anxiety and Depression Scale (HADS) Spielberger State-Trait Anxiety Inventory (STAI) Cardiac Anxiety Questionnaire (CAQ) and the Ferrans &amp; Powers Quality of Life Index (QLI) were completed pre- and post-intervention and at 8-week follow-up</td>
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### Asbury 2008

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<td><strong>Methods</strong></td>
<td>RCT</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>Sixty-four women aged 57.3 T 8.6 years (mean T SD) with cardiac syndrome X</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>8-week phase III CR exercise program or symptom monitoring control</td>
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<tr>
<td><strong>Outcomes</strong></td>
<td>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</td>
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### Risk of bias

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<td>Random sequence generation</td>
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<td>Randomly assigned using envelopes. Not described, but sounds plausible</td>
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<td>Allocation concealment</td>
<td>Low risk</td>
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<tr>
<td>personnel (performance bias)</td>
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<td>All outcomes</td>
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<td>Blinding of outcome assessment (detection bias)</td>
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<td>Patients knew what group they were in, and assessment by self reports</td>
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<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Analysed as intention to treat. One additional patient dropped out of CR arm</td>
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<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes appear to be reported on.</td>
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### Asbury 2011

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<tr>
<td>Participants</td>
<td>Forty-nine women with cardiac syndrome X (mean+standard deviation 61.8+8 years)</td>
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<tr>
<td>Interventions</td>
<td>12 monthly support group meetings or usual care control</td>
</tr>
<tr>
<td>Outcomes</td>
<td>The Health Anxiety Questionnaire (HAQ), Hospital Anxiety and Depression Scale (HADS), SF-36, York Angina Beliefs scale, ENRICH 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</td>
</tr>
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### Notes

**Risk of bias**

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<td>Patients given identical envelopes with either support group or usual care written on them</td>
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<td>High risk</td>
<td>Patients knew what group they were in, and assessment by self reports</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Analysed as intention to treat. One patient from intervention group (4%) and three (12%) from control group dropped out</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Appears that all outcomes reported on.</td>
</tr>
</tbody>
</table>
### 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  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Respiratory rate and mean end-tidal CO2 using an Ohmeda 5200 CO2 monitor</td>
</tr>
</tbody>
</table>

| 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 Disease) 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 |
### Jones 2006

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>28 patients with angina-like chest pain in whom coronary angiography was normal and oesophageal reflux was not contributory</td>
</tr>
<tr>
<td>Interventions</td>
<td>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</td>
</tr>
<tr>
<td>Outcomes</td>
<td>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</td>
</tr>
<tr>
<td>Notes</td>
<td>Of 81 eligible patients, only 28 entered the RCT</td>
</tr>
</tbody>
</table>

### Jonsbu 2011

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>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</td>
</tr>
<tr>
<td>Interventions</td>
<td>Three manualized sessions with CBT, including one physical activity exposure session. The control group received usual care from their general practitioner</td>
</tr>
<tr>
<td>Outcomes</td>
<td>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</td>
</tr>
<tr>
<td>Notes</td>
<td>Only a half of the eligible subjects entered the study</td>
</tr>
</tbody>
</table>

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>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</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Allocation conducted at an institution unrelated to study.</td>
</tr>
</tbody>
</table>
### Jonsbu 2011 (Continued)

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>Unclear risk</td>
<td>No blinding.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>High risk</td>
<td>Assessment by self-reporting and patient not blinded to treatment</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
<td>Same number of patients dropped out in both groups.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes appear to be reported on.</td>
</tr>
</tbody>
</table>

### 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 probability of 98% 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

### Risk of bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>A statistician who was not involved with the rest of the study created a randomization table to randomly assign participants</td>
</tr>
</tbody>
</table>
### Keefe 2011

<table>
<thead>
<tr>
<th>Allocation concealment (selection bias)</th>
<th>Low risk</th>
<th>Allocation concealment is described although treatment components were blinded only for the medication and not for the CST component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>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</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>Patient's outcomes were self assessed through pain scores, and pain diaries, but internal consistency was high for all tests</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>While there were many patients who did not complete therapy, there was no difference in attrition among the four treatment groups</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All stated outcomes reported on.</td>
</tr>
</tbody>
</table>

### Klimes 1990

| Methods | RCCT  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-report &amp; blind ratings</td>
<td>35 out of 56 assessed were recruited (63%) of whom 29 (83%) completed follow-up</td>
</tr>
<tr>
<td>Undetermined if treatment manual was used</td>
<td></td>
</tr>
</tbody>
</table>
| 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 3/12  
| cognitive restructuing, 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 |
Klimes 1990  *(Continued)*

| Notes | High attrition rate leading to potential follow-up bias |

**Lahmann 2008**

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>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.</td>
</tr>
<tr>
<td>Interventions</td>
<td>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.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>The Symptom Checklist of Derogatis (SCL-90) and the Giessen Inventory of Complaints (GBB), which are both self-administered tests</td>
</tr>
</tbody>
</table>

**Risk of bias**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>“randomization was carried out confidentially”-likely ok, but do not describe</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>“allocation concealment implemented by the hospital's administration department”-likely ok, but do not describe</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>No discussion of blinding, but based on intervention, most likely not blinded</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>Patients not blinded, and outcome assessment by self reports</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>All patients (22) appear to have completed trial.</td>
</tr>
<tr>
<td>All outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Study does not clearly outline outcomes of interest.</td>
</tr>
</tbody>
</table>
### 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 |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Patients undergoing coronary angiography</td>
</tr>
<tr>
<td>Interventions</td>
<td>Group CBT: 6 sessions including education, cognitive restructuring, relaxation, breathing exercises, graded exposure and light physical exercise</td>
</tr>
</tbody>
</table>
| 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,  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The Hospital Anxiety and Depression Scale (HADS), heart-focused anxiety by the Cardiac Anxiety Questionnaire (CAQ), the M.I.N.I.-Plus</td>
</tr>
</tbody>
</table>

| Notes | High attrition rate |

**Risk of bias**
### Spinhoven 2010

<table>
<thead>
<tr>
<th><strong>Bias</strong></th>
<th><strong>Authors’ judgement</strong></th>
<th><strong>Support for judgement</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Patients were randomized using random permuted blocks with a length of six</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Randomization carried out by the hospital pharmacist and the details were unknown to any of the researchers</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Medical treatment blinded, but CBT not</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>Outcome assessment by self reports</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>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</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Do not clearly state outcomes of interest.</td>
</tr>
</tbody>
</table>

### Tyni-Lenne 2002

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

---

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

*Copyright © 2012 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.*
### Methods

<table>
<thead>
<tr>
<th>RCT</th>
<th>Self-report measures some confirmed with treating doctor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Of 143 referrals who met inclusion criteria, 65 (44%) subjects entered study of whom 63 (43%) were followed-up @ 12/12</td>
</tr>
</tbody>
</table>

### Participants

<table>
<thead>
<tr>
<th>Inclusion criteria: 18-75 yrs old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal CVS according to a cardiologist</td>
</tr>
<tr>
<td>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</td>
</tr>
</tbody>
</table>

### 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 Anxiety Inventory  
BDI-Beck Depression Inventory  
SRT=Symptom Rating Test  
AS=Autonomic symptoms  
BSI= Brief symptom Inventory

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achem 2008</td>
<td>Review article - no primary data.</td>
</tr>
<tr>
<td>Adler 2001</td>
<td>Review article - no primary data. Psychological interventions not covered</td>
</tr>
<tr>
<td>Asbury 2005</td>
<td>Review article - no primary data.</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Type</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Asbury 2005a</td>
<td>Review article - no primary data.</td>
</tr>
<tr>
<td>Carter 1992a</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Carter 1992b</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Chambers 1998</td>
<td>Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain</td>
</tr>
<tr>
<td>Cott 1992</td>
<td>An RCT that pooled data from 90 patients with mitral valve prolapse with only 14 subjects with NSCP</td>
</tr>
<tr>
<td>Cox 1998</td>
<td>RCT of antidepressant medication</td>
</tr>
<tr>
<td>Esler 2004</td>
<td>Review article - no primary data. Suggests that biopsychosocial rather than attribution models may be more effective for noncardiac chest pain</td>
</tr>
<tr>
<td>Eslick 2004</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Eslick 2005</td>
<td>Review article - no primary data.</td>
</tr>
<tr>
<td>Faybush 2004</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Fleet 1998</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Goodacre 2001</td>
<td>Not an intervention study of a psychological treatment</td>
</tr>
<tr>
<td>Goodacre 2004</td>
<td>Not an intervention study of a psychological treatment</td>
</tr>
<tr>
<td>Handa 1999</td>
<td>Non-randomised trial of antidepressant medication</td>
</tr>
<tr>
<td>Hegel 1989</td>
<td>Uncontrolled trial of behavioural therapy</td>
</tr>
<tr>
<td>Jackson 2006</td>
<td>Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain</td>
</tr>
<tr>
<td>Jeejeebhoy 2000</td>
<td>Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain</td>
</tr>
<tr>
<td>Kaski 2001</td>
<td>Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain</td>
</tr>
<tr>
<td>Katz 2000</td>
<td>Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain</td>
</tr>
<tr>
<td>Kroenke 2000</td>
<td>Review article - no primary data.</td>
</tr>
<tr>
<td>Lahmann 2010</td>
<td>No primary data</td>
</tr>
<tr>
<td>Author</td>
<td>Type</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Looper 2002</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>Mayou 1989a</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Mayou 1994</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Nanke 2004</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>Nezu 2001</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>Olden 2004</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Olden 2006</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>Palsson 2006</td>
<td>Commentary - no primary data</td>
</tr>
<tr>
<td>Petrie 2007</td>
<td>Not a study of non-specific chest pain</td>
</tr>
<tr>
<td>Romeo 1993</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Ryan 2004</td>
<td>Of the 70 subjects, only 11 had functional cardiac pain &amp; data for these were not presented separately</td>
</tr>
<tr>
<td>Schey 2007</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>Schmulson 2004</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>Serlie 1995</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>VP-Oosterbaan 1997</td>
<td>Uncontrolled trial of cognitive-behavioral therapy</td>
</tr>
<tr>
<td>Wu 2002</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>Wulsin 2002</td>
<td>Pharmacotherapy only</td>
</tr>
<tr>
<td>Yehuda 1999</td>
<td>Review article - no primary data</td>
</tr>
<tr>
<td>Zachariae 2001</td>
<td>Not an intervention study</td>
</tr>
<tr>
<td>Zaubler 1998</td>
<td>Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain</td>
</tr>
</tbody>
</table>
### Comparison 1. Psychological intervention versus no such therapy

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

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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klimes 1990</td>
<td>20/29</td>
<td>29/29</td>
<td>0.69 [0.54, 0.89]</td>
<td>37.2%</td>
<td></td>
</tr>
<tr>
<td>Sanders 1997</td>
<td>21/29</td>
<td>17/21</td>
<td>0.89 [0.66, 1.21]</td>
<td>24.9%</td>
<td></td>
</tr>
<tr>
<td>VP-Oosterbaan 1999</td>
<td>16/32</td>
<td>30/32</td>
<td>0.53 [0.37, 0.76]</td>
<td>37.9%</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>90</strong></td>
<td><strong>82</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.68 [0.57, 0.81]</strong></td>
</tr>
</tbody>
</table>

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

Heterogeneity: Chi² = 4.84, df = 2 (P = 0.09); I² = 59%

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

Test for subgroup differences: Not applicable

---

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

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

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

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.97); I² =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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Mayou 1997 and Mayou 1999</td>
<td>15</td>
<td>3.85 (2.62)</td>
<td>10</td>
<td>2.18 (2.38)</td>
<td></td>
</tr>
<tr>
<td>Potts 1999</td>
<td>32</td>
<td>9.1 (5.1)</td>
<td>24</td>
<td>4.6 (4.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>47</td>
<td>34</td>
<td></td>
<td>100.0%</td>
<td>2.81 [ 1.28, 4.34 ]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 3.16, df = 1 (P = 0.08); I² =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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>Mean difference 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>26</td>
<td>19.6 %</td>
<td>-4.45 [ -5.92, -2.98 ]</td>
<td></td>
</tr>
<tr>
<td>DeGuire 1996</td>
<td>10</td>
<td>10</td>
<td>1.4 %</td>
<td>-17.00 [ -34.75, 0.75 ]</td>
<td></td>
</tr>
<tr>
<td>Ester 2001</td>
<td>17</td>
<td>19</td>
<td>13.4 %</td>
<td>3.38 [ -0.24, 7.00 ]</td>
<td></td>
</tr>
<tr>
<td>Jonbu 2011</td>
<td>21</td>
<td>19</td>
<td>21.4 %</td>
<td>-0.09 [ -0.57, 0.39 ]</td>
<td></td>
</tr>
<tr>
<td>Mayou 1997 and Mayou 1999</td>
<td>15</td>
<td>10</td>
<td>20.6 %</td>
<td>-1.16 [ -2.15, -0.17 ]</td>
<td></td>
</tr>
<tr>
<td>Potts 1999</td>
<td>32</td>
<td>24</td>
<td>2.8 %</td>
<td>-18.30 [ -30.21, -6.39 ]</td>
<td></td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>32</td>
<td>32</td>
<td>20.8 %</td>
<td>-4.00 [ -4.88, -3.12 ]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 154 140 100.0 % -2.26 [ -4.41, -0.12 ]

Heterogeneity: Tau² = 5.56; Chi² = 95.32, df = 6 (P<0.00001); I² =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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV, Random, 95% CI</td>
</tr>
<tr>
<td>Ester 2001</td>
<td>17</td>
<td>2.06 (4.6)</td>
<td>19</td>
<td>2.68 (5.5)</td>
<td>14.0 %</td>
</tr>
<tr>
<td>Jonsbu 2011</td>
<td>21</td>
<td>2.65 (0.67)</td>
<td>19</td>
<td>2.44 (0.86)</td>
<td>36.9 %</td>
</tr>
<tr>
<td>Mayou 1997 and Mayou 1999</td>
<td>15</td>
<td>2.75 (1.59)</td>
<td>10</td>
<td>2.71 (1.8)</td>
<td>29.4 %</td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>31</td>
<td>1.46 (2.5)</td>
<td>32</td>
<td>5.54 (6.5)</td>
<td>19.8 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>84</td>
<td>80</td>
<td>100.0 %</td>
<td>-0.81 [ -2.35, 0.74 ]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 1.64; Chi² = 11.79, df = 3 (P = 0.01); I² = 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

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

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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>19.41 (5.19)</td>
<td>26</td>
<td>18.44 (7.31)</td>
</tr>
<tr>
<td>Esler 2001</td>
<td>17</td>
<td>84.4 (20.1)</td>
<td>19</td>
<td>87.6 (19.4)</td>
</tr>
<tr>
<td>Jones 2006</td>
<td>15</td>
<td>5.16 (0.81)</td>
<td>13</td>
<td>4.68 (1.07)</td>
</tr>
<tr>
<td>Jonsbu 2011</td>
<td>21</td>
<td>89.8 (10.8)</td>
<td>19</td>
<td>83.5 (16.1)</td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>32</td>
<td>82 (24)</td>
<td>32</td>
<td>75 (24)</td>
</tr>
</tbody>
</table>

**Total (95% CI)** 112 109 100.0 % 0.24 [-0.03, 0.50]

**Heterogeneity:** Chi² = 2.45, df = 4 (P = 0.65); I² =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: Psychological intervention versus no such therapy

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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td>IV,Fixed,95% CI</td>
<td></td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27 20.09 (5.47)</td>
<td>26 18.08 (7.22)</td>
<td>27.6% 0.31 [-0.23, 0.85]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esler 2001</td>
<td>17 87.4 (18.8)</td>
<td>19 86.1 (21)</td>
<td>19.0% 0.06 [-0.59, 0.72]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jonsbu 2011</td>
<td>21 88.4 (13.8)</td>
<td>19 81.9 (20.3)</td>
<td>20.7% 0.37 [-0.26, 1.00]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VP-Oosterbaan 1999</td>
<td>31 87 (19)</td>
<td>32 80 (19)</td>
<td>32.7% 0.36 [-0.13, 0.86]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>96</strong></td>
<td><strong>96</strong></td>
<td><strong>100.0 % 0.29 [0.01, 0.58]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 0.61, df = 3 (P = 0.89); I² = 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:** Psychological intervention versus no such therapy

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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>22.01 (4.81)</td>
<td>26</td>
<td>19.92 (6.05)</td>
<td>18.7 %</td>
</tr>
<tr>
<td>Asbury 2008</td>
<td>32</td>
<td>72.6 (38.5)</td>
<td>32</td>
<td>70.1 (40.1)</td>
<td>23.0 %</td>
</tr>
<tr>
<td>Esler 2001</td>
<td>17</td>
<td>88.3 (26)</td>
<td>19</td>
<td>79 (33.7)</td>
<td>12.8 %</td>
</tr>
<tr>
<td>Jones 2006</td>
<td>15</td>
<td>5.16 (0.81)</td>
<td>13</td>
<td>4.68 (1.07)</td>
<td>9.7 %</td>
</tr>
<tr>
<td>Jonath 2011</td>
<td>21</td>
<td>87.3 (26.8)</td>
<td>19</td>
<td>66.7 (39.1)</td>
<td>13.7 %</td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>32</td>
<td>80 (36)</td>
<td>31</td>
<td>63 (43)</td>
<td>22.1 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>144</strong></td>
<td><strong>140</strong></td>
<td></td>
<td></td>
<td><strong>100.0 %</strong></td>
</tr>
</tbody>
</table>

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:** Psychological intervention versus no such therapy

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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
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<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>22.54 (5.76)</td>
<td>26</td>
<td>18.04 (6.64)</td>
<td>26.4 %</td>
</tr>
<tr>
<td>Esler 2001</td>
<td>17</td>
<td>84.3 (35.6)</td>
<td>19</td>
<td>91.3 (18.7)</td>
<td>19.0 %</td>
</tr>
<tr>
<td>Jonsbu 2011</td>
<td>21</td>
<td>76.7 (36)</td>
<td>19</td>
<td>77.8 (32.3)</td>
<td>21.2 %</td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>31</td>
<td>79 (38)</td>
<td>32</td>
<td>72 (42)</td>
<td>33.4 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>96</strong></td>
<td><strong>96</strong></td>
<td></td>
<td></td>
<td><strong>100.0 %</strong></td>
</tr>
</tbody>
</table>

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

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

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.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27 24.18 (4.53)</td>
<td>26 21.81 (5.32)</td>
<td>31.0 % 0.47 [-0.07, 1.02]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jonbu 2011</td>
<td>21 81.3 (25.8)</td>
<td>19 72.2 (30.8)</td>
<td>23.7 % 0.32 [-0.31, 0.94]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mayou 1997 and Mayou 1999</td>
<td>12 1.55 (1.1)</td>
<td>5 1.12 (1.11)</td>
<td>84 % 0.37 [-0.68, 1.42]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>31 87.6 (19)</td>
<td>32 77.6 (23)</td>
<td>36.9 % 0.47 [-0.03, 0.97]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>91 82</td>
<td>100.0 % 0.43 [0.12, 0.73]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 0.19, df = 3 (P = 0.98); I² =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)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td></td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27 4.36 (3.48)</td>
<td>26 4.21 (3.26)</td>
<td>14.5 % 0.04 [-0.49, 0.58]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asbury 2008</td>
<td>32 4.8 (3.3)</td>
<td>32 3.8 (2.2)</td>
<td>17.2 % 0.34 [-0.15, 0.84]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jonsbu 2011</td>
<td>21 5.9 (6.5)</td>
<td>19 8.8 (7.2)</td>
<td>10.6 % -0.42 [-1.04, 0.21]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Keefe 2011</td>
<td>29 7.26 (8.6)</td>
<td>24 5.16 (6.03)</td>
<td>14.2 % 0.27 [-0.27, 0.82]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lahmann 2008</td>
<td>11 51.6 (6.6)</td>
<td>11 56.1 (8.2)</td>
<td>5.7 % -0.58 [-1.44, 0.28]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mayou 1997 and Mayou 1999</td>
<td>15 0.35 (0.37)</td>
<td>10 0.47 (0.31)</td>
<td>6.5 % -0.33 [-1.14, 0.47]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potts 1999</td>
<td>32 4.3 (3.2)</td>
<td>24 6.4 (4.1)</td>
<td>14.4 % -0.57 [-1.11, -0.03]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>32 4.26 (3.2)</td>
<td>32 5.96 (3.6)</td>
<td>16.9 % -0.49 [-0.99, 0.00]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>199 178</td>
<td></td>
<td>100.0 % -0.16 [-0.37, 0.04]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>6.78 (4.15)</td>
<td>26</td>
<td>8 (3.42)</td>
<td>14.0 %</td>
</tr>
<tr>
<td>Asbury 2008</td>
<td>32</td>
<td>6.7 (3.3)</td>
<td>32</td>
<td>6.2 (3.3)</td>
<td>17.1 %</td>
</tr>
<tr>
<td>Keefe 2011</td>
<td>29</td>
<td>33.96 (13.19)</td>
<td>24</td>
<td>31.89 (9.89)</td>
<td>14.0 %</td>
</tr>
<tr>
<td>Lahmann 2008</td>
<td>11</td>
<td>53.5 (5.5)</td>
<td>11</td>
<td>60.5 (10.1)</td>
<td>5.3 %</td>
</tr>
<tr>
<td>Mayou 1997 and Mayou 1999</td>
<td>15</td>
<td>0.35 (0.37)</td>
<td>10</td>
<td>0.47 (0.31)</td>
<td>6.3 %</td>
</tr>
<tr>
<td>Potts 1999</td>
<td>32</td>
<td>6.2 (3)</td>
<td>24</td>
<td>8.4 (5.1)</td>
<td>14.2 %</td>
</tr>
<tr>
<td>Spinhoeven 2010</td>
<td>23</td>
<td>4.9 (3.9)</td>
<td>23</td>
<td>7 (3.3)</td>
<td>11.8 %</td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>32</td>
<td>6.66 (3.3)</td>
<td>32</td>
<td>7.16 (3.6)</td>
<td>17.1 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>201</strong></td>
<td><strong>182</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td><strong>-0.23 [ -0.43, -0.03 ]</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 9.02, df = 7 (P = 0.25); I² = 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: Psychological intervention versus no such therapy

Outcome: Psychological symptoms 3 to 12 months after the intervention

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
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<td>N</td>
<td>Mean(SD)</td>
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</tr>
<tr>
<td>IV,Fixed,95% CI</td>
<td>IV,Fixed,95% CI</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>26</td>
<td>11.05 (7.41)</td>
<td>40.3%</td>
</tr>
<tr>
<td>Mayou 1997 and Mayou 1999</td>
<td>12</td>
<td>5</td>
<td>0.37 (0.33)</td>
<td>10.9%</td>
</tr>
<tr>
<td>VP-Oosterbaan1999</td>
<td>31</td>
<td>32</td>
<td>6.96 (3.1)</td>
<td>48.9%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>70</td>
<td>63</td>
<td>100.0%</td>
<td>-0.18 [-0.52, 0.17]</td>
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</tbody>
</table>

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: Psychological intervention versus no such therapy

Outcome: Cardiac anxiety fear up to 3 months

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
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<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>1.35 (0.56)</td>
<td>26</td>
<td>1.27 (0.63)</td>
<td>26.7 %</td>
</tr>
<tr>
<td>Asbury 2008</td>
<td>32</td>
<td>1.2 (0.5)</td>
<td>32</td>
<td>1.2 (0.5)</td>
<td>32.3 %</td>
</tr>
<tr>
<td>Esler 2001</td>
<td>17</td>
<td>1.4 (0.42)</td>
<td>19</td>
<td>1.49 (0.25)</td>
<td>18.0 %</td>
</tr>
<tr>
<td>Spinhoven 2010</td>
<td>23</td>
<td>12.8 (7.8)</td>
<td>23</td>
<td>15.1 (7.5)</td>
<td>23.0 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>99</strong></td>
<td><strong>100</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>-0.08 [ -0.36, 0.20 ]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 1.51, df = 3 (P = 0.68); I² = 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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
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<tr>
<td></td>
<td>N Mean(SD)</td>
<td>N Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
<td>%</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27 1.3 (0.67)</td>
<td>26 1.31 (0.58)</td>
<td>-0.01 [-0.35, 0.33]</td>
<td>73.4 %</td>
<td></td>
</tr>
<tr>
<td>Ester 2001</td>
<td>17 1.46 (0.87)</td>
<td>19 1.26 (0.84)</td>
<td>0.20 [-0.36, 0.76]</td>
<td>26.6 %</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>44</strong></td>
<td><strong>45</strong></td>
<td><strong>0.05 [-0.24, 0.33]</strong></td>
<td><strong>100.0 %</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 0.40, df = 1 (P = 0.53); I² =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: Psychological intervention versus no such therapy

Outcome: Cardiac anxiety avoidance up to 3 months

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

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

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

Heterogeneity: Chi² = 2.39, df = 1 (P = 0.12); I² =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

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>1.37 (0.66)</td>
<td>26</td>
<td>1.16 (0.57)</td>
<td>39.3 %</td>
</tr>
<tr>
<td>Asbury 2008</td>
<td>32</td>
<td>1.4 (0.6)</td>
<td>32</td>
<td>1.2 (0.7)</td>
<td>42.3 %</td>
</tr>
<tr>
<td>Ester 2001</td>
<td>17</td>
<td>1.06 (0.74)</td>
<td>19</td>
<td>1.07 (0.74)</td>
<td>18.4 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>76</td>
<td>77</td>
<td>100.0 %</td>
<td>0.17 [-0.04, 0.37]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: \( \chi^2 = 0.62, \text{ 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: Psychological intervention versus no such therapy

Outcome: Cardiac anxiety attention 3 to 12 months

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>IV,Fixed,95% CI</td>
</tr>
<tr>
<td>Asbury 2007</td>
<td>27</td>
<td>1.28 (0.13)</td>
<td>26</td>
<td>1.25 (0.71)</td>
<td>75.8 %</td>
</tr>
<tr>
<td>Ester 2001</td>
<td>17</td>
<td>1.01 (0.75)</td>
<td>19</td>
<td>0.98 (0.75)</td>
<td>24.2 %</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>44</td>
<td>45</td>
<td><strong>100.0 %</strong></td>
<td><strong>0.03 [-0.21, 0.27]</strong></td>
<td></td>
</tr>
</tbody>
</table>

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
Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy (Review)  Copyright © 2012 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy (Review)

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

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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.

---

Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy (Review)  
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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 exp "Mind-Body and Relaxation Techniques"/
27 (relaxation adj5 (treat$ or therap$ or technique$)).tw.
28 or/18-27
29 17 and 28

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

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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$.tw.
20 (behavior$ adj3 therap$).tw.
21 (cognitive$ 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 (behavior* therap*) or (counsel*) or (psychotherap*) or (explode "Counseling-" in DE) or (explode "Psychotherapy-" in DE))
#22 (relaxation) or (psychodynamic*) or (behavior* therap*) or (counsel*) or (psychotherap*) or (explode "Counseling-" in DE) or (explode "Psychotherapy-" in DE)
#21 behavior* 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

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

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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. psychoterap*
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/

Psychological interventions for symptomatic management of non-specific chest pain in patients with normal coronary anatomy (Review) 59

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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.
13. (normal adj5 angiogram*).tw.
15. or/12-14
16. 10 or 11
17. 15 and 16
18. 9 or 17
19. exp Psychotherapy/
20. exp Counseling/
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.
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.

<table>
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<th>Date</th>
<th>Event</th>
<th>Description</th>
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<td>30 November 2011</td>
<td>New search has been performed</td>
<td>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</td>
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</table>
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

<table>
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<th>Date</th>
<th>Event</th>
<th>Description</th>
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<td>9 September 2008</td>
<td>Amended</td>
<td>Converted to new review format.</td>
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<tr>
<td>1 November 2004</td>
<td>New citation required and conclusions have changed</td>
<td>First version of the review</td>
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**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