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

Kisely SR, Campbell LA, Skerritt P

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[Intervention Review]

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

Steve R Kisely[1], Leslie Anne Campbell[2], Paul Skerritt[3]

[1]School of Medicine, Logan Campus, Griffith University, Meadowbrook, Australia. [2]Health Outcomes Research Unit, Capital Health District Authority, Halifax, Canada. [3]Suite 201, Specialist Medical Centre, Joondalup, Australia

Contact address: Steve R Kisely, School of Medicine, Logan Campus, Griffith University, Room 2.15d, Building LO3, University Drive, Meadowbrook, Qld 413, Australia. s.kisely@griffith.edu.au.

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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 trails 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 investigate psychological treatments for non-specific chest pain (NSCP) with normal coronary anatomy.

Search strategy

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2002, Issue 3), MEDLINE (1966 to 2002), CINAHL (1982 to 2002) EMBASE (1980 to 2002), PSYCH Info (1887 to 2002), the Database of Abstracts of Reviews of Effectiveness (DARE) and Biological Abstracts (January 1980 to 2002). We also searched citation lists and approached authors.

Selection criteria

RCTs with standardised outcome methodology that tested any form of psychotherapy for chest pain with normal anatomy. Diagnoses included non-specific chest pain, 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

Eight studies involving 403 randomised participants were included. There was a significant reduction in reports of chest pain in the first three months following the intervention; fixed effects relative risk = 0.68 (95% CI 0.57 to 0.81). This was maintained from 3 to 9 months afterwards; relative risk = 0.58 (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; the standardized mean difference = 0.85 (95% CI 0.38 to 1.31). However, there was high heterogeneity for this test. Wide variability in outcome measures made integration of studies for secondary outcome measures difficult.

Authors' conclusions

Review suggested 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. 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 are of some benefit 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 review found that cognitive-behavioural treatments are probably effective, in the short term, for the treatment of non-cardiac chest pain.

BACKGROUND

Chest pain is one of the most frequent reasons for presentation to emergency services. Of patients admitted to the emergency department (ED) 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). 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 microvascular 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). 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 (which is chest pain with no clear physical cause) has been described by a number of terms including include non-specific chest pain, atypical chest pain, syndrome X, or chest pain with normal coronary anatomy. This review will use the term non-specific chest pain (NSCP). Most studies of non-specific chest pain have concerned 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 non-specific chest pain 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 1989) and an association with alcohol and cigarette use (Kisely 1997), possibly mediated through changes in oesophageal motility (Kahrilas 1990; Matsuguchi 1984). Other potential mechanisms are less clear. There may be an interaction in which psychological factors affect the interpretation of physiological perceptions, which in turn, worsen mental state (Chambers 1990). In addition, recent life events as measured by a structured interview or personality factors such as an excess of Type A behaviour (hard driving and competitive behaviour, a potential for hostility, pronounced impatience, and vigorous speech stylistics (Hemingway 1999)) have been identified as occurring more frequently in patients with non-specific chest pain compared to physically healthy controls matched for age and sex (Roll 1987). In addition the presence of pain is associated with increased psychiatric morbidity, including psychophysiological symptoms other than pain, so exacerbating the problem (Von Korff 1988).

Treatment is known to be difficult (Klimes 1990). Some patients are reassured by negative medical assessment, but a substantial number report persistent pain and limitations. A variety of drugs have been used including anti-secretory drugs, anxiolytics, antidepressants, nitrates and calcium channel blockers (Bennett 2001). Because cognitions are of aetiological importance in NSCP and with high levels of psychiatric co-morbidity, psychological approaches have been suggested as appropriate interventions (Bass 1984; Klimes 1990; Ockene 1908) 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 2004; Sharpe 1996). In a preliminary search of MEDLINE, we identified one randomised controlled trial of 34 patients with non-specific chest pain. Participants allocated to a maximum of 11 sessions of cognitive-behavioural psychotherapy 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.

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) Cognitive behavioural therapy;

(2) Relaxation therapy;

(3) Hyperventilation control;

(4) Other psychotherapy/talking /counselling therapy;

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

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

People presenting with chest pain who have normal anatomy as assessed on clinical history, cardiac enzymes, electrocardiograms, exercise electrocardiograms or coronary angiography. Diagnoses

included non-specific chest pain, 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

Cognitive-behavioural therapy, for the purposes of this review is based on:

the definition employed by Cormac et al (Cormac 2001). 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 'cognitive-behavioural therapy' or 'cognitive therapy' were labelled as 'less-well defined' cognitive behavioural therapy. The exact nature of 'less-well defined' therapies was established through contact with study authors.

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

Relaxation therapy

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

Hyperventilation control

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

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 could be 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 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 e.g. Short Form 36 scores;

(3) Health service use e.g. 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, GI embolism);

(5) Cardiac behavioural risk factors reduction (e.g., 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

Initially, the Cochrane Review Group Specialised registers were checked to identify all potentially eligible studies (last searched in November 2002);

We searched electronic databases including The Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effectiveness (DARE) (on *The Cochrane Library* Issue 3, 2002), MEDLINE (1966 to 2002) (Table 1, EMBASE (1980 to 2002) (Table 2), CINAHL (1982 to 2002) (Table 3), PsychLIT (1887 to 2002) (Table 4) and Biological Abstracts BIOSIS (January 1980 to 2002) (Table 5) to identify potentially eligible studies and review articles. Methodological filters were used to identify RCTs in MEDLINE (Dickersin 1994) and EMBASE (Lefebvre 1996).

For CENTRAL we used the following search terms and adapted them for use in other databases See Table 1, Table 2, Table 3, Table 4 and Table 5):

#1 CHEST-PAIN*:ME
#2 (CHEST next PAIN)
#3 (THORAX next PAIN)
#4 (THORACIC next PAIN)
#5 SYNDROME-X*:ME
#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 CORONARY)
#11 (NORMAL near ANGIOGRAM*)
#12 (NORMAL near ANATOMY)
#13 ((#10 or #11) or #12)
#14 (#13 and #9)
#15 (#14 or #8)
#16 PSYCHOTHERAPY*:ME
#17 PSYCHOTHERAP*
#18 (COGNITIVE near THERAP*)
#19 (BEHAVIOUR* near THERAP*)
#20 (BEHAVIOR* near THERAP*)
#21 COUNSELING*:ME
#22 COUNSEL*
#23 PSYCHODYNAMIC*
#24 (RELAX* near THERAP*)
#25 PSYCHOLOGIC*
#26 HYPERVENTILATION
#27 (BREATH* near 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)

All relevant foreign language papers were translated;

(3) The reference lists of all references that were retrieved as full papers and 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.;

(4) Personal communications - The lead author of all relevant reported identified was written to in order to ascertain if they knew of any additional published or unpublished studies that might be relevant to the review;

(5) 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.

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 (PS) 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.

Critical appraisal of studies

Assessment of the quality of a particular trial were made in accordance with guidelines in the Cochrane Handbook (Clarke 2000).

Assessment of the method and adequacy of randomisation

To prevent selection bias, someone who is not responsible for recruiting the participants, such as a central trial office or someone not involved in the trial should conduct the randomisation. The method of randomisation was noted on the data extraction form.

Assessment of the degree of blinding (treatment and outcome assessment)

Allocation concealment was assessed as follows as described in the Cochrane Reviewers Handbook (Clarke 2000): (A) adequate description of the allocation procedure; (B) unclear description of the allocation procedure; (C) inadequate description of the allocation procedure; and (D) allocation concealment was not used.

If the reviewers disagreed over which category a trial is allocated to, resolution was attempted by discussion or by obtaining further information. In addition, reviewers were blinded to the author's names, institutions and journal title to prevent any bias.

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. Where more than 20% of those originally randomised have been lost to follow-up, the data were not presented in this review.

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

Addressing publication bias

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

Data extraction

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

- General: Published/unpublished, title, authors, source, contact address, country, language of publication, year of publication, duplicate publications, sponsoring, setting (hospital inpatients or out-patients, primary care, community);
- Trial characteristics: design, duration, randomisation and method, allocation concealment and method, blinding of outcome assessors, check of blinding;
- Interventions (frequency, timing), comparison interventions, co-medications;
- Patient characteristics - sampling, exclusion criteria number of participants, age, sex, ethnicity, marital status, educational status, duration of symptoms, number of complications, mode of referral (e.g. self-referral or via psychiatrists, psychologists, or other clinicians), similarity of groups at baseline (including any co-morbidity), withdrawals/losses to follow-up (reasons/ descriptions), history of myocardial infarction (MI);
- Type of psychiatric co-morbidity - clinical diagnosis or symptomatology assessed by questionnaire;
- Type of assessment tool used to assess psychiatric co-morbidity - e.g. Beck Depression Inventory, Zung Depression Scale, Hospital Anxiety and Depression Scale, Structured interview, DSM-IV criteria;
- Cut-off used on psychiatric scale, percentage of people defined as psychiatric cases on this basis; mean (SD) symptom score;
- Type of intervention - cognitive-behavioural therapy, 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 9 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 from the authors or to calculate them using others measures of variation that were reported, such as the confidence intervals. 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% confidence intervals (CI) was estimated. As a summary measure of effectiveness, where possible, the number needed to treat statistic (NNT) was also calculated.

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

Heterogeneity

Graphical representations of the data were inspected; if the confidence intervals 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 effects methods. However, where there was significant heterogeneity, a random effects 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.

See Table of Excluded Studies and Table of Included Studies.

Excluded studies

32 studies were considered for inclusion. Of these, 24 studies were excluded. Most were reviews that did not contain primary data or were not intervention studies. Four intervention studies were excluded; two were trials of antidepressant medication (Cox 1998; Handa 1999), and another was an uncontrolled trial of behavioural therapy (Hegel 1989). The fourth 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. Two papers by Oosterbaan reported different aspects of the same study. One of these (VP-Oosterbaan 1999a) was excluded because it reported data that did not concern the outcomes of interest in this review. 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.

Included studies

Eight relevant randomised controlled trials (RCTs) were identified (DeGuire 1996; Esler 2001; Klimes 1990; Mayou 1997; Potts 1999; Sanders 1997; Tyni-Lenne 2002; VP-Oosterbaan1999b).

Data reporting

Two studies combined the results of the RCT and crossover designs (Mayou 1997; 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 cognitive-behavioural therapy, brief intervention by a nurse, relaxation training and breathing re-training. Only one study (Potts 1999) 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-Oosterbaan1999b) or no care. (DeGuire 1996; Mayou 1997). In the case of the former, no information was reported on details of usual care the controls received. Only two studies had more than two arms (DeGuire 1996; Tyni-Lenne 2002) - we only used an active treatment that 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. Timing of the intervention (early v late) was not described in six of the eight studies. One study examined the differences between "immediate" and "delayed" interventions, but as per the inclusion criteria, participants may have had an angiogram within the past year (Potts 1999). Similarly, Esler 2001 conducted the intervention while the patient was in the emergency room, however, did not provide information regarding a history of chest pain. Therefore, it is not clear whether the patients were presenting for the first time or not. Therapist training was not noted in four of the studies. Adherence to a treatment manual or plan was described in seven of the studies.

Participants

One study was restricted to females (Tyni-Lenne 2002). 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; VP-Oosterbaan1999b) excluded participants who had comorbid 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 four studies reported the number of subject eligible for inclusion who agreed to participate (Klimes 1990; Mayou 1997; Sanders 1997; VP-Oosterbaan1999b). In all cases, only 40 to 60% agreed to participate. Completion rates following randomisation were generally acceptable (approximately 80%), although in the case of two (DeGuire 1996; Mayou 1997) over 35% were lost to follow-up. We conducted sensitivity analyses of studies where completion rates were less than 80%.

Outcomes

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

Duration of Follow-up

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

Risk of bias in included studies

The concealment of randomisation:
A - indicates adequate concealment;
B - indicates uncertainty about whether allocation was adequately concealed;
C - indicates the allocation was definitely not adequately concealed;
D - indicates the score was not assigned.
As regards concealment of the randomisation method, all trials were rated B.
The description of the randomisation method:
A - correct randomised method described;
B - randomised method described but incorrect (e.g. every alternate patient given the control treatment);
C - randomised method not described.
A correct randomisation method was described in 3 studies (Mayou 1997; Sanders 1997; VP-Oosterbaan1999b). In the remainder, a description of the randomisation method was not provided
Control of selection bias after treatment assignment:
A - intention to treat analysis;

B - analysis by treatment received only.
Only one study (Mayou 1997) controlled for selection bias by using an intention to treat analysis.
Blinding - the quality of blinding would be rated according to the following scale:
A - blinding of outcome assessor and the participant;
B - blinding of outcome assessor only;
C - blinding not done.
All of the studies used self-report measures for at least some of the outcomes, which are effectively self-blinding. Two trials (Klimes 1990; Potts 1999) used a combined RCT and crossover trial design, making blinding impossible for the controls that subsequently received the intervention, although in the case of Klimes the outcome assessor was blinded for the RCT stage. Three other studies were rated B (Mayou 1997; Sanders 1997; Tyni-Lenne 2002) when measures were not self-report.

Intervention

In those studies reporting the effect of CBT, the intervention was well-defined. (Cormac 2001). Descriptions were less clear in the case of other interventions. No study reported whether the treatment was manualised or whether any attempts were made to ensure fidelity to the intervention under study.

Effects of interventions

The eight 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-Oosterbaan1999b) or a month (Sanders 1997), or the number of chest-pain free days over a week (Mayou 1997). 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-Oosterbaan1999b) or that included standard deviations when reporting the number chest-pain free days (Mayou 1997; Potts 1999). In the case of absence of chest pain (Klimes 1990; VP-Oosterbaan1999b), there was a significant reduction in reports of chest pain in the first three months following the intervention. The fixed effects model estimated the relative risk was 0.68 (95% confidence interval 0.57 to 0.81) (Comparison 01 01), while for the random effects model, the relative risk was 0.70 (95% confidence interval 0.53 to 0.91). This was maintained from 3 to 9 months afterwards; the relative risk was 0.58 (95% confidence interval 0.45 to 0.76) (Comparison 01 02) for both fixed or random effects models. Exclusion of the study that reported the absence of chest pain over a month following brief CBT (Sanders 1997) made no significant difference to the results. Exclusion of the combined RCT and crossover trial (Klimes 1990) also made no significant difference to the results. There was also a significant increase in the number of chest pain free days up to three months following intervention; the standardized mean difference was 0.85 (95% confidence interval 0.38 to 1.31) (Comparison no 01 03), although this was largely attributable to the study reporting the results of a group intervention (Potts 1999).

Chest pain frequency

Studies reported the frequency of chest pain episodes over a week (VP-Oosterbaan1999b), two weeks (DeGuire 1996; Potts 1999) or a month (Esler 2001; Mayou 1997). All studies reported significant improvements except one study of guided re-breathing where the results failed to reach statistical significance, and another of brief CBT (Esler 2001). In the case of the four studies that reported chest pain frequency (DeGuire 1996; Esler 2001; Mayou 1997; VP-Oosterbaan1999b) there was a significant reduction in participants receiving either CBT or guided re-breathing compared to controls within the first three months of follow-up on the fixed effects model; the standardised mean difference was -0.87 (95% confidence interval -1.18 to -0.57) (Comparison 01 04). This was maintained at 3 to 9 month follow-up; the standardised mean difference was -0.43 (95% confidence interval -0.79 to -0.07) (Comparison 01 05). However, this improvement failed to reach statistical significance in the random effects model up to three months; the standardised mean difference was -0.83 (95% confidence interval -1.77 to 0.12) or at 3 to 9 month follow-up; the standardised mean difference was -0.36 (95% confidence interval -0.90 to 0.18). Restricting the analyses to only those studies that reported the results of CBT made no difference to any of these results.

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. Mayou using a non-standardised measure of social impairment, did not report significant improvement compared to controls up to three months after intervention; the weighted mean difference was -0.33 (95% confidence interval -1.17 to 0.51) or afterwards between 3 to 9 months; the weighted mean difference was -0.43 (95% confidence interval 1.58 to 0.72) (Comparisons 01 06 and 01 07) (Mayou 1997). Three other studies reported results using the four scales of the Short Form 36 (physical limitations, work problems, limitations in social activities and emotional limitations) (Esler 2001; Sanders 1997;

VP-Oosterbaan1999b), but Sanders and Esler did not report standard deviations. In the case of Oosterbaan, there was no significant long-term effect on the SF36 even in the area of physical limitations where there was the most difference between intervention and control groups; the weighted mean difference was 7.00 (95% confidence interval -2.43 to 16.43) (Comparison 01 08) (VP-Oosterbaan1999b). We did attempt to integrate measures of social functioning and social disability by inverting the social impairment scale used by Mayou (Mayou 1997). We found similar results up to 3 months; the weighted mean difference was 0.33 (95% confidence interval -0.51 to 1.17) (Comparison 01 09) and at 3 to 9 months; the weighted mean difference was 0.43 (95% confidence interval -0.72 to 1.58) (Comparison 01 10). Using the random or fixed effects model made no difference to the results.

Psychological measures

Again, a wide variety of measures were used that measured global outcome or the presence of depression or anxiety. One combined RCT and CCT (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%confidence interval 0.22 to 0.8) (Comparison 01 11). We quantitatively analysed two studies of self-reported depression using standardised instruments (Potts 1999; VP-Oosterbaan1999b), combined with a further study that reported overall morbidity including depression (Mayou 1997). There was a significant difference between intervention and controls up to three months after the intervention; the standardised mean difference -0.50 (95%confidence interval -0.83 to -0.16) (Comparison 01 12). We also quantitatively analysed two studies of self-reported anxiety using standardised instruments (Potts 1999; VP-Oosterbaan1999b), combined with a further study that reported overall morbidity including anxiety (Mayou 1997). One study did not report means and standard deviations for a measurement of overall psychological morbidity, or reported three subscores of a scale specific to cardiac anxiety including fear, avoidance and attention to symptoms (Esler 2001), rather than generalised anxiety. This precluded inclusion in quantitative analyses. There was no significant difference between intervention and controls up to three months after the intervention; the standardised mean difference was -0.32 (95%confidence interval -0.65 to 0.01) (Comparison 01 13). There was also no significant difference between intervention and controls from three to nine months afterwards; the standardised mean difference was -0.02 (95%confidence interval -0.47 to 0.43) (Comparison 01 14) . Using the random or fixed effects model made no difference to the results.

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-Oosterbaan1999b). Klimes 1990 reported that prior to the intervention, all study patients believed their chest pain was due to a physical cause, while afterward 69% attributed their pain to stress. They did not report the difference between intervention and control groups. Two studies (Mayou 1997; 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 tests for heterogeneity were statistically non-significant at the p < or = 0.1 level except in the case of chest pain frequency. Furthermore, the statistically significant difference between the intervention and control groups for this variable using a fixed effects model was not maintained on the random effects model. Although we reported standardised mean differences for this variable, our findings for reduction in chest pain frequency must be treated with caution.

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 psychiatric instruments;
- differences between types of psychological interventions and types of controls: There was no change to the results when analyses were restricted to CBT only. All but one study used individual therapy. The one study that used a group intervention (Potts) could not be included in meta-analysis because means and standard deviations were not reported;
- 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 no change to the results when analyses were restricted to CBT only;
- differences between analyses involving all studies and excluding trials of low methodological quality: Two studies combined the results of the RCT and crossover designs (Klimes 1990; Potts 1999). One study (Potts 1999) could not be included in meta-analysis because means and standard deviations were not reported. There was no difference in the results when the other study that combined results of a RCT and crossover

trial (Klimes 1990) was excluded;

- differences between analyses involving all studies and those that excluded co-morbid psychiatric disorder: All but one of the studies (DeGuire 1996) included in the meta-analysis excluded co-morbid psychiatric disorder: There was no difference to the results when this study was excluded from the analysis;
- differences between participants with and without a history of myocardial infarction: History of myocardial infarction excluded in 3 studies, not captured in remainder;
- 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 trails have evaluated treatment. The studies reviewed in this paper 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.

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 wait-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. There are too few psychologists, and cardiologists 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 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, more opportunity for discussion with cardiologists prior to discharge, and follow-up for review of the findings and reinforcement of the plan for symptomatic treatment and return to fuller activities with either the primary care provider or a cardiac nurse.

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. 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 eight 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

Cognitive-behavioural treatments are probably effective, in the short-term, for the treatment of NSCP.

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). Therefore, it is important to detect non-cardiac chest pain early, identify individual treatment needs, and intervene before it becomes chronic. Patients in emergency departments or with recent onset of chest pain should be prepared for the possibility and meaning of negative findings. Those patients with chronic NSCP may benefit from specialist psychological intervention.

Implications for research

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

- Include a larger number of participants and be informed by explicit sample size and power analysis;

- Have follow-up periods of at last 12 months and preferably longer;

- Have adequate concealment of allocation, intention to treat analyses and at least single blind assessments of outcome;

- Use meaningful standardised outcome measurements;

- Use interventions that are explicitly described, manualised and monitored for treatment fidelity.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

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 weeksGuided breathing retraining and physiological monitoring of diaphragmatic breathing and end-tidal CO2 Guided breathing retraining and physiological monitoring of diaphragmatic breathing Guided breathing retraining No treatment (controls)
Outcomes	Chest pain: frequency & severity over 2/52 Respiratory rate and mean end-tidal CO2 using an Ohmeda 5200 CO2 monitor
Notes	High attrition rate leading to potential follow-up bias -

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

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 for 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 (eg CCF, PE, lung Discase) or cause of chest pain (eg pneumonia,

Esler 2001 (*Continued*)

	bronchiotis, 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
Notes	High attrition rate leading to potential follow-up bias

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Klimes 1990

Methods	RCCT Self-report & blind ratings 35 out of 56 assessed were recruited (63%) of whom 29(83%) completed follow-up Undetermined if treatment manual was used
Participants	Referred by cardiologist or GP Inclusion criteria: Chest pain as main presenting feature >= one episode weekly Normal CVS (cardiology or equivalent opinion and investigation) >= 3/12 duration Exclusion criteria: Depression on treatment Multiple somatic symptoms Investigations not completed
Interventions	Individual CBT: Max 11 sessions over 3/12cognitive restructuring, problem solving, relaxation, breathing exercisesControls: 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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Mayou 1997

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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Potts 1999

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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

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

Risk of bias

Sanders 1997 (*Continued*)

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Tyni-Lenne 2002

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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	D - Not used

VP-Oosterbaan1999b

Methods	RCT Self-report measures some confirmed with treating doctor Of 143 referrals who met inclusion criteria, 65 (44%) subjects entered study of whom 63 (43%) were followed-up @ 12/12
Participants	Inclusion criteria: 18-75 yrs old Normal CVS according to a cardiologist Exclusion criteria: Proven CAD of MI on coronary angiography, exercise test, laboratory results, ECG of CXR, a hx 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

VP-Oosterbaan1999b (*Continued*)

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

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

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

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

Study	Reason for exclusion
Adler 2001	Review article - no primary data. Psychological interventions not covered
Carter 1992a	Not an intervention study
Chambers 1998	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Cott 1992	An RCT that pooled data from 90 patients with mitral valve prolapse with only 14 subjects with NSCP
Cox 1998	RCT of antidepressant medication

(*Continued*)

Fleet 1998	Not an intervention study
Goodacre 2001	Not an intervention study
Handa 1999	Non-randomised trial of antidepressant medication
Hegel 1989	Uncontrolled trial of behavioural therapy
Jeejeebhoy 2000	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Kaski 2001	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Katz 2000	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Looper 2002	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Mayou 1994	Not an intervention study
Mayou 1999	Reports the same data as Mayou 1997
Nezu 2001	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Romeo 1993	Not an intervention study
Serlie 1995	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
VP-Oosterbaan 1997	Uncontrolled trial of cognitive-behavioural therapy
VP-Oosterbaan 1999a	Did not report the main outcomes of interest (i.e. pain and/ or function), rather, it reported cognitive change
Wu 2002	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Yehuda 1999	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain
Zachariae 2001	Not an intervention study
Zaubler 1998	Review article - no primary data. Suggests that cognitive-behavioural therapy is effective for noncardiac chest pain

DATA AND ANALYSES

Comparison 1. Psychological intervention versus no such therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any chest pain up to 3 months after intervention	3	172	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.57, 0.81]
2 Any chest pain from 3 to 9 months after intervention	2	111	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.45, 0.76]
3 Chest pain free days up to 3 months	2	81	Std. Mean Difference (IV, Fixed, 95% CI)	0.85 [0.38, 1.31]
4 Chest pain frequency up to 3 months after intervention	5	201	Std. Mean Difference (IV, Fixed, 95% CI)	-0.87 [-1.18, -0.56]
5 Chest pain frequency 3 to 9 months after intervention	3	124	Std. Mean Difference (IV, Fixed, 95% CI)	-0.43 [-0.79, -0.07]
6 Quality of life - social functioning up to 3 months after intervention	2	89	Mean Difference (IV, Fixed, 95% CI)	0.38 [-0.45, 1.22]
7 Quality of life - social functioning up to 3 to 9 months after intervention	2	80	Mean Difference (IV, Fixed, 95% CI)	0.55 [-0.60, 1.69]
8 Physical functioning	1	63	Mean Difference (IV, Fixed, 95% CI)	7.00 [-2.38, 16.38]
9 Social impairement up to 3 months after intervention	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
10 Social impairment up to 3 to 9 months after intervention	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11 Psychiatric case up to 3 months after intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
12 Psychological symptoms up to 3 months after the intervention (depression & overall)	3	145	Std. Mean Difference (IV, Fixed, 95% CI)	-0.50 [-0.83, -0.16]
13 Psychological symptoms up to 3 months after the intervention (anxiety and overall)	3	145	Std. Mean Difference (IV, Fixed, 95% CI)	-0.32 [-0.65, 0.01]
14 Psychological symptoms up 3 to 9 months after the intervention	2	80	Std. Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.47, 0.42]

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

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

Comparison: 1 Psychological intervention versus no such therapy

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

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

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

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

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

Analysis 1.2. Comparison 1 Psychological intervention versus no such therapy, Outcome 2 Any chest pain from 3 to 9 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

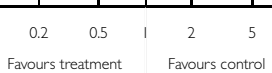
Outcome: 2 Any chest pain from 3 to 9 months after intervention

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

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

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

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



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

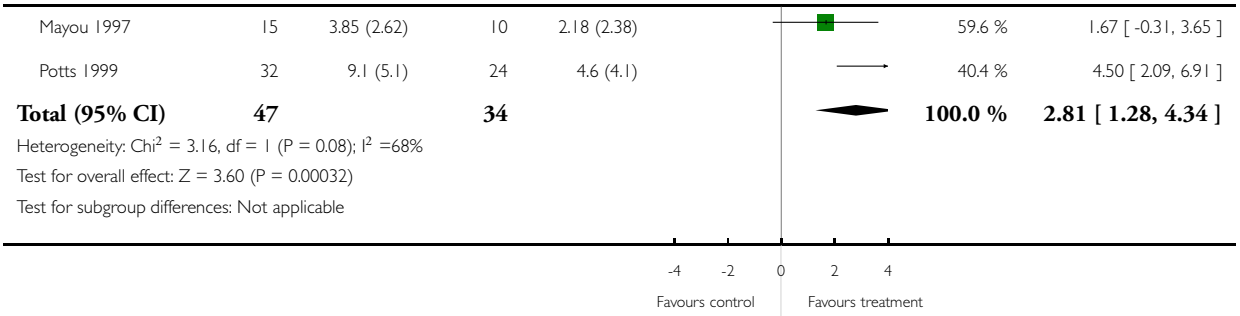
Outcome: 3 Chest pain free days up to 3 months after intervention

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

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

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

Test for subgroup differences: Not applicable



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

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

Comparison: 1 Psychological intervention versus no such therapy

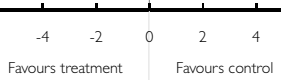
Outcome: 4 Chest pain frequency up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Asbury 2007	26	1.23 (1.36)	26	1.95 (1.19)		46.4 %	-0.72 [-1.41, -0.03]
DeGuire 1996	10	9 (12)	10	26 (26)		0.1 %	-17.00 [-34.75, 0.75]
Esler 2001	17	4.59 (7.43)	19	1.21 (1.78)		1.7 %	3.38 [-0.24, 7.00]
Mayou 1997	15	2.55 (1.53)	10	3.71 (0.99)		22.9 %	-1.16 [-2.15, -0.17]
Potts 1999	32	7 (9.1)	24	25.3 (28.7)		0.2 %	-18.30 [-30.21, -6.39]
VP-Oosterbaan1999	32	1.16 (1.8)	32	5.16 (1.8)		28.8 %	-4.00 [-4.88, -3.12]
Total (95% CI)	**132**		**121**			**100.0 %**	**-1.73 [-2.21, -1.26]**

Heterogeneity: Chi^2 = 52.78, df = 5 (P<0.00001); I^2 =91%

Test for overall effect: Z = 7.18 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1 Psychological intervention versus no such therapy, Outcome 5 Chest pain frequency 3 to 9 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

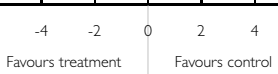
Outcome: 5 Chest pain frequency 3 to 9 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Esler 2001	17	2.06 (4.6)	19	2.68 (5.5)		11.6 %	-0.62 [-3.92, 2.68]
Mayou 1997	15	2.75 (1.59)	10	2.71 (1.8)		66.8 %	0.04 [-1.34, 1.42]
VP-Oosterbaan1999	31	1.46 (2.5)	32	5.54 (6.5)		21.6 %	-4.08 [-6.50, -1.66]
Total (95% CI)	**63**		**61**			**100.0 %**	**-0.93 [-2.05, 0.20]**

Heterogeneity: Chi^2 = 8.46, df = 2 (P = 0.01); I^2 =76%

Test for overall effect: Z = 1.62 (P = 0.11)

Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1 Psychological intervention versus no such therapy, Outcome 6 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

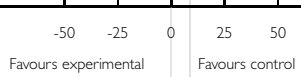
Outcome: 6 Chest pain severity up to 3 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Asbury 2007	26	1.66 (2.19)	26	8.04 (10.08)		95.9 %	-6.38 [-10.34, -2.42]
Jones 2006	15	29.13 (25.31)	13	47.31 (26.55)		4.1 %	-18.18 [-37.48, 1.12]
Total (95% CI)	**41**		**39**			**100.0 %**	**-6.86 [-10.74, -2.97]**

Heterogeneity: Chi^2 = 1.38, df = 1 (P = 0.24); I^2 =27%

Test for overall effect: Z = 3.46 (P = 0.00054)

Test for subgroup differences: Not applicable



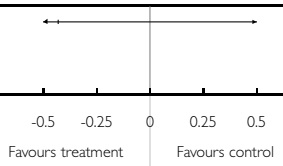
Analysis 1.7. Comparison 1 Psychological intervention versus no such therapy, Outcome 7 Quality of life - social functioning up to 3 to 9 months after intervention.

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 Social impairment up to 3 to 9 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Mayou 1997	12	1.45 (1.1)	5	1.88 (1.11)		-0.43 [-1.58, 0.72]



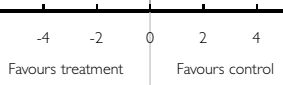
Analysis 1.8. Comparison 1 Psychological intervention versus no such therapy, Outcome 8 Physical functioning.

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

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 8 Social impairment up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Mean Difference IV,Fixed,95% CI
Mayou 1997	15	1.55 (0.95)	10	1.88 (1.11)		-0.33 [-1.17, 0.51]



Analysis 1.9. Comparison 1 Psychological intervention versus no such therapy, Outcome 9 Social impairement up to 3 months after intervention.

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

Comparison: 1 Psychological intervention versus no such therapy

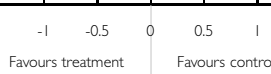
Outcome: 9 Quality of life - physical functioning up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	22	19.4 (5.19)	24	18.44 (7.31)		26.7 %	0.15 [-0.43, 0.73]
Esler 2001	17	84.4 (20.1)	19	87.6 (19.4)		20.8 %	-0.16 [-0.81, 0.50]
Jones 2006	15	5.16 (0.81)	13	4.68 (1.07)		15.7 %	0.50 [-0.26, 1.25]
VP-Oosterbaan1999	32	82 (24)	32	75 (24)		36.9 %	0.29 [-0.20, 0.78]
Total (95% CI)	**86**		**88**			**100.0 %**	**0.19 [-0.11, 0.49]**

Heterogeneity: Chi^2 = 1.89, df = 3 (P = 0.60); I^2 =0.0%

Test for overall effect: Z = 1.25 (P = 0.21)

Test for subgroup differences: Not applicable



Analysis 1.10. Comparison 1 Psychological intervention versus no such therapy, Outcome 10 Social impairment up to 3 to 9 months after intervention.

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

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 10 Quality of life - physical functioning up to 3 to 9 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	22	20.09 (5.47)	24	18.08 (7.22)		31.7 %	0.31 [-0.28, 0.89]
Esler 2001	17	87.4 (18.8)	19	86.1 (21)		25.1 %	0.06 [-0.59, 0.72]
VP-Oosterbaan1999	31	87 (19)	32	80 (19)		43.3 %	0.36 [-0.13, 0.86]
Total (95% CI)	**70**		**75**			**100.0 %**	**0.27 [-0.06, 0.60]**

Heterogeneity: Chi² = 0.53, df = 2 (P = 0.77); I² =0.0%

Test for overall effect: Z = 1.62 (P = 0.11)

Test for subgroup differences: Not applicable

Analysis 1.11. Comparison 1 Psychological intervention versus no such therapy, Outcome 11 Psychiatric case 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 - role problems due to emotional limitations up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	22	22.01 (4.81)	24	19.92 (6.05)		26.7 %	0.37 [-0.21, 0.96]
Esler 2001	17	88.3 (26)	19	79 (33.7)		21.0 %	0.30 [-0.36, 0.96]
Jones 2006	15	5.16 (0.81)	13	4.68 (1.07)		15.9 %	0.50 [-0.26, 1.25]
VP-Oosterbaan1999	32	80 (36)	31	63 (43)		36.4 %	0.42 [-0.08, 0.92]
Total (95% CI)	**86**		**87**			**100.0 %**	**0.40 [0.09, 0.70]**

Heterogeneity: Chi^2 = 0.17, df = 3 (P = 0.98); I^2 =0.0%

Test for overall effect: Z = 2.57 (P = 0.010)

Test for subgroup differences: Not applicable

Analysis 1.12. Comparison 1 Psychological intervention versus no such therapy, Outcome 12 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

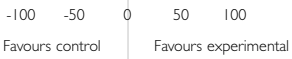
Outcome: 12 Quality of life - role problems due to emotional limitations 3 to 9 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	22	22.54 (5.76)	24	18.04 (6.64)		30.4 %	0.71 [0.11, 1.31]
Esler 2001	17	84.3 (35.6)	19	91.3 (18.7)		25.2 %	-0.24 [-0.90, 0.41]
VP-Oosterbaan1999	31	79 (38)	32	72 (42)		44.4 %	0.17 [-0.32, 0.67]
Total (95% CI)	**70**		**75**			**100.0 %**	**0.23 [-0.10, 0.56]**

Heterogeneity: Chi² = 4.53, df = 2 (P = 0.10); I² =56%

Test for overall effect: Z = 1.37 (P = 0.17)

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 (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

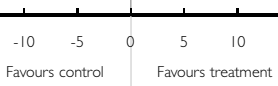
Outcome: 13 Quality of life - social functioning up to 3 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Asbury 2007	22	22.8 (4.31)	24	23.08 (4.8)		23.5 %	-0.06 [-0.64, 0.52]
Esler 2001	17	80.9 (28.2)	19	83.1 (24.2)		18.4 %	-0.08 [-0.74, 0.57]
Jones 2006	15	5.16 (0.81)	13	4.68 (1.07)		13.8 %	0.50 [-0.26, 1.25]
Mayou 1997	15	1.45 (0.95)	10	1.12 (1.11)		12.1 %	0.31 [-0.49, 1.12]
VP-Oosterbaan1999	32	85.6 (16)	32	78.6 (22)		32.2 %	0.36 [-0.13, 0.85]
Total (95% CI)	**101**		**98**			**100.0 %**	**0.19 [-0.09, 0.47]**

Heterogeneity: Chi² = 2.56, df = 4 (P = 0.63); I² =0.0%

Test for overall effect: Z = 1.35 (P = 0.18)

Test for subgroup differences: Not applicable



Analysis 1.14. Comparison 1 Psychological intervention versus no such therapy, Outcome 14 Psychological symptoms up 3 to 9 months after the intervention.

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

Comparison: 1 Psychological intervention versus no such therapy

Outcome: 14 Quality of life - social functioning up to 3 to 9 months after intervention

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Asbury 2007	22	24.18 (4.53)	24	21.81 (5.32)		37.3 %	0.47 [-0.12, 1.06]
Mayou 1997	12	1.55 (1.1)	5	1.12 (1.11)		11.6 %	0.37 [-0.68, 1.42]
VP-Oosterbaan1999	31	87.6 (19)	32	77.6 (23)		51.2 %	0.47 [-0.03, 0.97]
Total (95% CI)	**65**		**61**			**100.0 %**	**0.46 [0.10, 0.82]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.03$, df = 2 (P = 0.99); $I^2 = 0.0\%$

Test for overall effect: Z = 2.50 (P = 0.012)

ADDITIONAL TABLES

Table 1. Search strategy for MEDLINE

1999 to week 5 2002
1 Chest Pain/
2 Syndrome X/
3 “syndrome x”.tw.
4 microvascular angina.tw.
5 cardiac syndrome$.tw.
6 chest pain$.tw.
7 ((thorax or thoracic) adj1 pain$).tw.
8 or/1-7
9 Angina Pectoris/
10 angina.tw.
11 (normal adj5 coronary).tw.
12 (normal adj5 angiogram$).tw.
13 (normal adj5 anatomy).tw.
14 or/11-13
15 9 or 10
16 14 and 15
17 8 or 16
18 exp Psychotherapy/

Table 1. Search strategy for MEDLINE (*Continued*)

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

Table 2. Search strategy for EMBASE

1998 to week 46 2002
1 Thorax Pain/
2 Syndrome X/
3 "syndrome x".tw.
4 microvascular angina.tw.
5 cardiac syndrome$.tw.
6 chest pain$.tw.
7 ((thorax or thoracic) adj1 pain$).tw.
8 or/1-7
9 Angina Pectoris/
10 angina.tw.
11 (normal adj5 coronary).tw.
12 (normal adj5 angiogram$).tw.
13 (normal adj5 anatomy).tw.
14 or/11-13
15 9 or 10
16 14 and 15
17 8 or 16
18 exp Psychiatric treatment/
19 exp Counseling/
20 psychotherap$.tw.
21 counsel$.tw.
22 psychodynamic$.tw.
23 (behavio$ adj3 therap$).tw.
24 (cognitiv$ adj3 therap$).tw.
25 psychologic$.tw.
26 (relaxation adj5 (treat$ or therap$ or technique$)).tw.
27 or/18-26
28 17 and 27

Table 3. Search strategy for CINAHL

1982 to Week 2, 2002
1 Chest Pain/
2 "syndrome x".tw.
3 microvascular angina.tw.
4 cardiac syndrome$.tw.
5 chest pain$.tw.
6 ((thorax or thoracic) adj1 pain$).tw.
7 Angina Pectoris/
8 angina.tw.
9 (normal adj5 coronary).tw.
10 (normal adj5 angiogram$).tw.
11 (normal adj5 anatomy).tw.
12 or/9-11
13 7 or 8
14 12 and 13
15 exp Psychotherapy/
16 exp Counseling/
17 psychotherap$.tw.
18 counsel$.tw.
19 psychodynamic$.tw.
20 (behavio$ adj3 therap$).tw.
21 (cognitiv$ adj3 therap$).tw.
22 psychologic$.tw.
23 (relaxation adj5 (treat$ or therap$ or technique$)).tw.
24 or/1-6,14
25 or/15-23
26 24 and 25

Table 4. Search strategy for PsycLIT

From 1872 to 2002
#23 ((((thorax or thoracic) next pain) or (cardiac syndrome*) or (microvascular angina) or (chest pain)) or (((angina) or (explode "Angina-Pectoris" in DE)) and ((normal near anatomy) or (normal near angiogram*) or (normal near coronary)))) and ((relaxation) or (psychodynamic*) or (behavio?r* therap*) or (counsel*) or (psychotherap*) or (explode "Counseling-" in DE) or (explode "Psychotherapy-" in DE))
#22 (relaxation) or (psychodynamic*) or (behavio?r* therap*) or (counsel*) or (psychotherap*) or (explode "Counseling-" in DE) or (explode "Psychotherapy-" in DE)
#21 behavio?r* therap*
#20 relaxation
#19 psychodynamic*
#18 counsel*
#17 psychotherap*
#16 explode "Counseling-" in DE
#15 explode "Psychotherapy-" in DE
#14 (((thorax or thoracic) next pain) or (cardiac syndrome*) or (microvascular angina) or (chest pain)) or (((angina) or (explode "Angina-Pectoris" in DE)) and ((normal near anatomy) or (normal near angiogram*) or (normal near coronary)))

Table 4. Search strategy for PsycLIT (*Continued*)

#13 ((angina) or (explode "Angina-Pectoris" in DE)) and ((normal near anatomy) or (normal near angiogram*) or (normal near coronary))
#12 (normal near anatomy) or (normal near angiogram*) or (normal near coronary)
#11 normal near anatomy
#10 normal near angiogram*
#9 normal near coronary
#8 (angina) or (explode "Angina-Pectoris" in DE)
#7 angina
#6 explode "Angina-Pectoris" in DE
#5 ((thorax or thoracic) next pain) or (cardiac syndrome*) or (microvascular angina) or (chest pain)
#4 (thorax or thoracic) next pain
#3 cardiac syndrome*
#2 microvascular angina
#1 chest pain

Table 5. Search strategy for BIOSIS

From 1985 to 2002
((al: (relaxation)) or (al: ((behavio* w therap*) or (cognitiv* w therap*) or psychotherap* or counsel* or psychologic* or psychodynamic*))) and ((((al: ((normal w angiogram*) or (normal with coronary) or (normal w anatomy))) and al: (angina)) or (al: ((chest w pain) or (microvascula* w angina) or (cardiac w syndrome)))) and (al: ((clin* n3 trial*) or random* or singl* or doubl* or blind* or mask* or placebo* or (clin* n3 study) or controlled)))

WHAT'S NEW

Last assessed as up-to-date: 31 October 2004.

Date	Event	Description
9 September 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 1, 2003

Review first published: Issue 1, 2005

Date	Event	Description
1 November 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Two reviewers (SK, LAC) will independently select suitable studies for inclusion in this review as detailed below. Where the two reviewers disagree about the inclusion of a study, disagreements will be resolved by consensus of opinion, and a third reviewer (PS) consulted if they cannot be resolved. SK and LAC will complete the extraction of data from the papers. Data will be 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.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

Behavior Therapy; Chest Pain [psychology; *therapy]; Cognitive Therapy; Psychotherapy [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Humans