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TITLE: PSYCHOLOGICAL INTERVENTIONS FOR CORONARY HEART DISEASE: COCHRANE SYSTEMATIC REVIEW AND META-ANALYSIS

Suzanne H Richards PhD[a,b] , Lindsey Anderson PhD[c], Caroline E Jenkinson PhD[b], Ben Whalley PhD[d], Karen Rees PhD[e], Philippa Davies PhD[f], Paul Bennett PhD[g], Zulian Liu MSc[h], Robert West PhD[i], David R Thompson PhD[j], Rod S Taylor PhD[c]

[a] Leeds Institute of Health Sciences, University of Leeds, Leeds, UK

[b] Primary Care, University of Exeter Medical School, Exeter, UK

[c] Institute of Health Research, University of Exeter Medical School, Exeter, UK

[d] School of Psychology, University of Plymouth, Plymouth, UK

[e] Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, UK

[f] School of Social and Community Medicine, University of Bristol, Bristol, UK

[g] Department of Psychology, University of Swansea, Swansea, UK

[h] Nuffield Department of Population Health, University of Oxford, Oxford, UK

[i] Wales Heart Research Institute, Cardiff University, Cardiff, UK

[j] School of Nursing & Midwifery, Queen's University, Belfast, U.K.

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Address for correspondence/reprints:

Professor Suzanne Richards
Academic Unit of Primary Care
Leeds Institute of Health Research
University of Leeds
Level 10 Worsley Building
Leeds, UK
LS2 9NL
Telephone: +44(0)113 3439815
Email: S.H.Richards@leeds.ac.uk

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ABSTRACT

Background: Although psychological interventions are recommended for the management of coronary heart disease (CHD), there remains considerable uncertainty regarding their effectiveness.

Design: Systematic review and meta-analysis of randomised controlled trials (RCTs) of psychological interventions for CHD.

Methods: The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, and PsycINFO were searched to April 2016. Retrieved papers, systematic reviews, and trial registries were hand-searched. We included RCTs with at least six months of follow-up, comparing the direct effects of psychological interventions to usual care for patients following myocardial infarction or revascularisation, or with a diagnosis of angina pectoris or CHD defined by angiography. Two authors screened titles for inclusion, extracted data, and assessed risk of bias. Studies were pooled using random effects meta-analysis and meta-regression was used to explore study-level predictors.

Results: 35 studies with 10,703 participants (median follow-up 12 months) were included. Psychological interventions led to a reduction in cardiovascular mortality (relative risk 0.79, 95% confidence interval (CI) 0.63 to 0.98), although no effects were observed for total mortality, myocardial infarction, or revascularisation. Psychological interventions improved depressive symptoms (standardised mean difference (SMD) -0.27, 95% CI -0.39 to -0.15), anxiety (SMD -0.24, 95% CI -0.38 to -0.09), and stress (SMD -0.56, 95% CI -0.88 to -0.24) compared with controls.

Conclusions: We found that psychological intervention improved psychological symptoms, and reduced cardiac mortality for people with CHD. However, there remains considerable

uncertainty regarding the magnitude of these effects, and the specific techniques most likely to benefit people from different presentations of CHD.

Abstract word count: 249 words

Key words: cardiac morbidity; mortality; depression; anxiety; stress; psychological intervention; systematic review; randomised controlled trial.

INTRODUCTION

Coronary heart disease (CHD) is the single leading cause of death globally, accounting for around a third of all deaths.[1] This mortality rate is falling, and many more people are living with CHD and require support to manage their symptoms and prognosis. Cardiac events or cardiac surgery can be significant and distressing life events; mental health comorbidity is common, greatly exceeding the rates observed within the general population.[2, 3] Anxiety and depression are also independent risk factors for cardiovascular morbidity and mortality.[4, 5] Thus the need to address stress, psychosocial factors (e.g. lack of social support), and other underlying mood disorders, is recognised within conventional cardiac care in Australia,[6] Europe[7, 8] and the US.[4]

A range of psychological therapies have been employed as part of secondary prevention to improve psychological outcomes (as opposed to facilitating cardiovascular risk factor reduction). Examples include relaxation and stress management, treatments for mood disorders, or enhancing disease adjustment and coping strategies. Therapies have been used both in unselected cardiac populations, or targeted at cardiac patients with established psychopathologies. In 2011, a Cochrane review[9] synthesised 24 trials testing the direct effects of psychological interventions on cardiac and psychological outcomes compared with usual care. This review observed marked variation in the psychological interventions tested across studies. Meta-analysis found no conclusive evidence that psychological interventions had an effect on total mortality and cardiovascular morbidity, although a potential effect on cardiac mortality was observed (5 trials, 3893 participants; relative risk (RR) 0.80, 95% confidence interval (CI) 0.64 to 1.00). There was some evidence that psychological interventions improved depressive symptoms (12 trials, 5041 participants; standardised mean difference (SMD) -0.21, 95% CI -0.48 to -0.08) and anxiety (8

trials, 2771 participants; SMD -0.25, 95% CI -0.35 to -0.03), although the 95% confidence intervals were wide and estimates lacked precision. This paper is an update of this Cochrane review, which is needed now due to the publication of a number of relevant new trials, combined with the considerable uncertainties in the evidence regarding the impact of psychological interventions on clinical events, psychological outcomes and health-related quality of life.

METHODS

We conducted this third update of this Cochrane review[10] in accordance the Cochrane Handbook[11], and reported it following the PRISMA guidance[12] (Supplementary figure 1 for PRISMA flow chart). Although the protocol was first published on the Cochrane Database of Systematic Reviews in 2000, this review builds on the substantively revised protocol implemented in the second update.[9]

Data searches and sources

Search terms from the 2011 review[9] were updated and CENTRAL (Cochrane Central Register of Controlled Trials), MEDLINE (Ovid), EMBASE (Ovid), PsychINFO (Ovid) and CINAHL (EBSCO) were searched to April 2016. We searched the WHO International Clinical Trials Registry Platform and the US Clinical Trials.gov registry for active clinical trials (accessed June 2016). No language limitations were imposed on the searches (Supplementary methods 1).

Study selection

We selected randomised controlled trials (RCTs) comparing the direct effects of a psychological intervention compared with a usual care control group for adults with CHD, with or without

clinical psychopathology. Participants included those who had experienced a myocardial infarction (MI), a revascularisation procedure (coronary artery bypass grafting [CABG] or percutaneous coronary intervention [PCI]), angina pectoris, or angiographically-defined CHD. Participants could receive cardiac rehabilitation as long as this was part of usual medical care and offered routinely to both trial arms. Studies where psycho-pharmacology was offered solely or disproportionately to the treatment group in conjunction with the offer of psychological interventions were included. Studies testing psychological interventions in comorbid populations (e.g. patients with depression and either CHD or diabetes) were deemed eligible for inclusion as long as outcome data could be extracted for individuals with CHD. We excluded studies where over 50% of the sample had other cardiac conditions (e.g. heart failure), or had undergone cardiac resynchronisation therapy or received implantable defibrillators.

Eligible interventions included those addressing stress or low mood, or enhancing coping strategies, either alone or in combination. Studies evaluating interventions based on psychological principles (e.g. motivational interviewing), which were solely directed at improving adherence to other efficacious treatments (e.g. medication adherence or exercise) or the modification of cardiac risk factors (e.g. smoking, diet), were excluded. We only selected studies where the psychological interventions were delivered by health care workers who had been trained in their delivery.

Finally, we selected trials reporting outcomes for a minimum of six months post-randomisation, and reporting at least one of the primary outcomes (reported below).

Two reviewers (LA, and SR or CJ) independently assessed all identified titles/abstracts for possible inclusion, with full reports obtained and assessed for any potentially relevant references.

Any disagreements between the reviewers were resolved by discussion. Where necessary, studies were translated into English.

Data extraction and management

Event rate data were extracted for the dichotomous primary outcomes of total mortality, cardiac mortality, cardiovascular morbidity (non-fatal MI, and revascularisation procedures [CABG, PCI]). Means and standard deviations were extracted for the continuous primary outcomes of validated measures assessing symptoms of depression, anxiety or stress. In addition, data were extracted for secondary outcomes regarding other validated measures of psychological function, health-related quality of life (HRQL) and cost-effectiveness.

One reviewer (LA) extracted study and participant characteristics, intervention and comparator descriptors, and outcomes from included studies using a standardised data extraction form. A second author (SR or CJ) checked the extracted data for accuracy, and disagreements were resolved by discussion. Outcome data were independently extracted by two reviewers (LA and SR). Related publications of the same study were assessed for additional data. Authors were contacted, where necessary, to provide additional information.

Assessment of risk of bias and overall quality of evidence

The Cochrane Collaboration's core risk of bias items and three further items deemed relevant to this review were assessed, with each study assigned a ‘low’, ‘high’ or ‘unclear’ risk of bias for each item. A detailed description for the three additional criteria (groups balanced at baseline; use of intention-to-treat analysis; groups receiving comparable treatment except the psychological treatment) can be found elsewhere.[10] One reviewer extracted these data, and a second reviewer checked the extracted data for accuracy. For each outcome, the overall quality

of evidence was assessed by employing the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to interpret result findings, using GRADEpro GDT software.[13]

Data synthesis and analysis

Dichotomous outcomes, relating to mortality and cardiovascular morbidity, were expressed as risk ratios with 95% CIs. Continuous outcomes, relating to psychological outcomes, were expressed as standardised mean differences (SMD) with 95% CIs. For primary outcomes, data were pooled using a conservative random effects model due to the substantial clinical heterogeneity in psychological treatments and study populations identified. Heterogeneity was explored qualitatively and quantitatively (using the I^2 statistic and chi-square test of heterogeneity). Small study bias was examined through visual inspection of the funnel plot and the use of Egger tests.[14]

For secondary outcomes where there were insufficient data, or where it was inappropriate to combine studies statistically, a narrative review was presented.

Exploratory meta-regression was undertaken to examine potential treatment effect modifiers (Table 1) on the selected outcomes of total mortality, cardiac mortality, depression and anxiety. The explanatory variables were selected *a priori* following the approach outlined in the 2011 update,[9] although we restricted analyses to a smaller group of variables due to concerns over data quality. Given the relatively small ratio of trials to covariates, meta-regression was limited to univariate analysis.[15]

All statistical analyses were performed using Review Manager 5.3 Software[16] and STATA version 13.0 (StataCorp, College Station, Texas).[17]

RESULTS

Selection and inclusion of studies

The 2011 review identified 24 studies that met the inclusion criteria. On review, three studies were excluded due to either an ineligible patient population,[18] an inappropriate control group,[19] or a non-randomised trial design[20] and therefore 21 of the 24 studies were included in this update. Searches between 2009 and 2016 yielded 6359 titles and abstracts (Supplementary figure 1). A total of 123 papers were reviewed and 14 studies (2577 participants) met the inclusion criteria.[21-34] Thus a total of 35 studies (81 publications) were included, reporting data from 10,703 participants (Supplementary table 1 provides a full bibliography).

Study, participant and intervention characteristics

Studies

Most studies were published in Europe (19 studies) or North America (12 studies) (Table 2). While studies randomised between 42 and 2481 participants, most were small, with a median sample size of 123 participants (IQR 73 to 204). The median length of follow-up was 12 months (IQR range 12 to 29 months); longer follow-ups (over 30 months) were restricted to clinical events data extracted from routine records rather than psychological outcomes.

Participants

The median of study mean ages was 59.6 years, and the median proportion of males was 77% (Table 2). The most common cardiac indication upon study referral was an MI (65.7%), with around a third having undergone some form of revascularisation procedure (27.4%). Twelve

studies required participants to have a clinical psychopathology (most commonly depression) at baseline to satisfy an eligibility criterion. In unselected cardiac populations nine studies reported rates of depression of between 3.8%[35] and 53%[36] and three studies reported anxiety of 32%[33, 37] and 53%[38] (some papers reported both anxiety and depression). Only three excluded individuals with psychopathology at baseline and eleven studies either did not measure psychological outcomes at baseline, or did not report them.

Interventions

The number of contact hours in psychological interventions varied considerably, ranging from an average of 2 hours to 96 hours (31 studies; Table 2). Over half were delivered in groups (20 studies), or a mix of group and individual sessions (five studies). 11 studies reported family involvement in treatment.

Although the quality of reporting of interventions was highly variable, based on available descriptions 23 studies evaluated psychological treatments with multiple treatment aims and components. Common treatment aims included managing stress (22 studies), depression (17 studies), anxiety (16 studies) and Type A behaviour including anger and hostility (12 studies), and achieving improved disease adjustment (11 studies). Common treatment components included relaxation techniques (20 studies), self-awareness and self-monitoring (20 studies), emotional support or client led discussion (15 studies), and cognitive challenge or cognitive restructuring techniques (19 studies). Many interventions included co-interventions aimed at raising awareness of cardiac risk factors (16 studies), and the targeting of behaviours relating to cardiac risk reduction (e.g. smoking, salt intake; 19 studies). Only three studies incorporated the co-prescribing of pharmacological drugs where it was deemed clinically appropriate.[21, 29, 39]

Risk of bias and GRADE assessment

The overall risk of bias scores varied between items assessed (Supplementary table 2). The quality of reporting was highly variable, with an unclear risk of bias for over half the studies for domains relating to randomisation procedures and the blinding of outcome assessment. This limited our ability to judge risk of bias, and thus downgrading the GRADE quality of evidence across all outcomes (Tables 3 and 4).

Some outcomes were also downgraded due to a lack of precision around the estimated effect (non-fatal MI, stress), significant heterogeneity observed (anxiety, stress) and/or the risk of publication bias (cardiac mortality, anxiety). Thus the GRADE ratings were moderate (total mortality, revascularisation), low (cardiac mortality, non-fatal MI, anxiety, depression) or very low (stress) for all outcomes.

Outcome results

For mortality and cardiovascular morbidity data, the attrition at follow-up was low with, for example, 1.7% of total mortality data missing from the pooled analysis of 23 studies. In contrast, the overall level of attrition of studies contributing to the pooled analyses was 17.7% for depression, 9.1% for anxiety, and 9.4% for stress.

Mortality

Pooled analysis of 23 studies (Table 3, Supplementary figure 2) found no evidence that psychological therapies reduced the risk of total mortality (7776 participants; RR 0.90, 95% CI 0.77 to 1.05, I^2=2%). However, there was evidence that psychological interventions reduced the risk of cardiac mortality (Table 3, Figure 1) when pooling data from 11 studies (4792

participants, RR 0.79, 95% CI 0.63 to 0.98, I^2=0%), although there is some uncertainty in this finding as the quality of evidence is low.

Cardiovascular morbidity

There was no evidence of risk reduction for revascularisation procedures (Table 3, Supplementary figure 3) (13 studies, 6822 participants; RR 0.94, 95% CI 0.81 to 1.11, I^2=8%) or for an occurrence of a subsequent non-fatal MI (Table 3, Supplementary figure 4) (13 studies, 7845 participants; 0.82, 95% CI 0.64 to 1.05, I^2=41%).

Psychological outcomes

Meta-analysis of 19 studies (5825 participants) found evidence that psychological interventions reduced depression symptoms compared with the comparator group (SMD -0.27, 95% CI -0.39 to -0.15, I^2=69%). Reductions in anxiety levels (12 trials, 3161 participants; SMD -0.24, 95% CI -0.38 to -0.09, I^2=47%) and stress levels (8 trials, 1251 participants; SMD -0.56, 95% CI -0.88 to -0.24, I^2=86%) in favour of the intervention group were also observed. However, there remains considerable uncertainty regarding treatment effects for all comparisons as the quality of evidence was either low or very low (Table 4).

Statistical heterogeneity and small study bias

Inspection of I^2 tests found significant levels of statistical heterogeneity in the meta-analyses of all psychological outcomes, but not mortality or morbidity data. Visual inspection of the funnel plots (data reported elsewhere[10]) shows some evidence of asymmetry for cardiac and depression, anxiety, stress, but not total mortality or other measures of cardiovascular morbidity. The Egger tests for funnel plot asymmetry were non-significant for the majority of primary outcomes, with the exceptions of cardiovascular mortality (P=0.04) and anxiety (P=0.012). This asymmetry

appeared to be due to an absence of small- to medium-sized studies with negative results regarding psychological interventions.

Health-related quality of life

HRQL was reported in ten studies (Supplementary table 3). Narrative review found statistically significant improvements in at least one dimension of HRQL in favour of psychological interventions in four studies,[22, 28, 29, 40] while six studies[26, 33, 35, 41-43] reported no between group differences. Of studies reporting significant treatment effects, two observed improvements restricted to mental health and/or life satisfaction components of HRQL,[22, 40] a third study found improvements restricted to the physical health component,[29] while the fourth study reported improvements in both physical and mental health components.[28]

Cost effectiveness

Only 2 studies reported any form of economic evaluation alongside trial data. Van-Dixhoorn 1999[44] limited the economic evaluation to an examination of hospital costs arising from cardiac-related hospital readmissions across a five-year follow-up. The authors reported the extra costs of individual relaxation training sessions (the intervention) were outweighed by the benefits (30% reduction in the number of days in hospital and 46% reduction in costs due to reduced readmissions for cardiac surgery). Davidson 2010[21] (see Ladapo 2012[45]) examined HRQL, health care utilisation and costs of the intervention compared to usual physician care. The mean total health care costs (psychotropic medicines, ambulatory care, hospitalisations) was $1857 for the intervention group and $2797 for usual care (adjusted difference -$1229 per patient, 95% CI -$2652 to $195, P=0.09), with a 98% probability that this approach would be considered cost effective if a willingness-to-pay threshold of $30,000 per quality-adjusted life-year gained was applied.

Meta-regression findings

We found no significant predictors of intervention effects for total or cardiovascular mortality (Supplementary table 4) for any of the population or intervention characteristics explored in univariate meta-regression models. Meta-regression of psychological outcomes yielded only two statistically significant predictor variables. Psychological interventions combined with pharmacology for an underlying psychological disorder (P=0.003) were more effective at alleviating depression than interventions that were not (Supplementary table 4). Interventions recruiting participants with an underlying psychological disorder were more effective at alleviating anxiety than those delivered to unselected populations (P=0.03).

DISCUSSION

Main findings

We updated a systematic review of the direct effects of psychological interventions for people with CHD. We found a reduction in cardiovascular mortality (7.3% to 5.5%, number needed to treat 56) with psychological interventions compared with usual care controls. No between group differences were observed for the rates of total mortality, non-fatal MI, or revascularisation procedures. Psychological interventions were found to achieve small to moderate improvements in depressive symptoms, anxiety and stress compared with controls, although there remains some uncertainty in these estimates.

Narrative synthesis found some evidence of a positive effect on HRQL, although direct comparisons are problematic due to methodological differences between studies, such as the use of different HRQL measures. Only two studies conducted economic evaluations, with both

concluding that psychological therapies were likely to be cost effective, although this evidence requires replication in future research.

We undertook an exploratory analysis seeking to identify potential effect modifiers from a range of population and intervention characteristics. In contrast to the previous update,[9] we elected not analyse some the patient characteristics of study populations (e.g. sex or age) previously explored using meta-regression. Recent methodological guidance for systematic reviews of cardiac prevention studies,[46] cautions against the analysis of patient characteristics in meta-regression when aggregated at the study level. Statistically, study-level analysis is under-powered compared with individual patient data meta-analysis. More importantly, however, this analysis is prone to ecological fallacy (or 'aggregation bias').

Meta-regression failed to identify any predictor variables for the total and cardiovascular mortality, although this was not unexpected given the lack of statistical heterogeneity in the pooled analysis. Meta-regression for the outcomes of depression and anxiety, where considerably greater statistical heterogeneity was observed in pooled analysis, found only two predictor variables. For depression, the adjunct use of pharmacological therapy for the underlying psychological condition (where deemed clinically appropriate) may increase intervention effectiveness compared with interventions that did not. For anxiety, psychological interventions which recruited participants with CHD and an underlying psychological disorder appeared more effective than those delivered to unselected CHD populations.

Findings in context

Our study has further clarified findings from the 2011 update,[9] with the precision of the effect estimates improving across all outcomes through the inclusion of new data from 14 studies (2577 participants). We also present pooled data on stress levels for the first time. However, the meta-

regression failed to replicate the effect modifiers (e.g. interventions targeting Type A behaviours, or involving family members) previously identified for the outcome of depression. This is likely to be attributable to the inclusion of a number of new studies, combined with the exclusion of data from two studies that had previously contributed data to these analyses.[19, 47]

Although other systematic reviews have sought to explore effectiveness of psychological interventions for people with CHD,[48, 49] direct comparisons are problematic due to important differences in study selection. For example, Welton et al.[48] included studies testing both the direct and indirect effects of psychological interventions for people with CHD, whilst Dickens et al.[49] included studies with a follow-up period of less than six months. In contrast to our findings, Welton et al.[48] found no evidence that psychological interventions reduced cardiovascular mortality, although consistent with our findings no effect on total mortality was observed. There is also consistent evidence emerging across a body of empirical evidence that psychological interventions have small but consistent effects at alleviating symptoms of depression[48, 49] and anxiety[48] for people with CHD. Notwithstanding the uncertainty regarding the optimal methods of providing psychological care, this review lends further support to the international guidelines[4, 6-8] that addressing psychological health should be a core component of conventional cardiac prevention services.

Study limitations

The level of reporting of key risk of bias domains relating to randomisation procedures and the blinding of outcome assessment was poor, limiting our ability to judge risk of bias. Some outcomes were also downgraded due to a lack of precision around the estimated effect, significant heterogeneity observed and/or the risk of publication bias. Thus the GRADE quality of evidence ranged from moderate, low or very low across outcomes.

From the information reported, the majority of participants were men recruited post-MI, and our findings may be less generalizable to more diverse populations of women, or to individuals with other cardiac conditions using secondary prevention services.

Another feature of the studies synthesised was the clinical heterogeneity, as studies often tested complex psychological interventions with multiple treatment targets and components; only a minority test the effectiveness of single component therapies (e.g. Van-Dixhoorn 1999[44] and Blumenthal 2016[34] tested a stress management intervention). The poor reporting of intervention components (e.g. the training received, or any ongoing supervision provided) and participant characteristics (for example, a third of studies did not report the presence of psychopathology at baseline) limited a detailed examination of the active ingredients of psychological techniques through meta-regression. While meta-analysis found evidence of small effects on a number of outcomes, there remains considerable uncertainty regarding which type of psychological techniques are most effective and for whom. The effectiveness of emerging, and potentially more beneficial psychological interventions has yet to be addressed: mindfulness, for example, may be more effective than traditional stress management approaches for individuals with high levels of health anxiety.[50] In addition, given the likely low effect size (in terms of both psychological and cardiac benefit) of any psychological intervention targeted at a population with no obvious psychopathology, the latter is an important issue to address in future studies. A number of ongoing trials appear to be directly assessing some of these uncertainties.[51-53]

Our review also excluded psychological interventions designed specifically to improve adherence to cardiac risk factor modification (e.g. medicines, lifestyle change); this was essential to reduce the clinical heterogeneity of interventions compared, but as a consequence our findings do not inform the wider evidence-base on the contribution of psychological techniques to optimise risk factor management.

While we were able to pool data for a number of important clinical and psychological outcomes, the breadth of outcome measures reported was often limited within studies. For example, while around two-thirds of studies (23/35) reported total mortality, less than a third of studies reported stress levels (8/35) or cardiovascular mortality (11/35) in a way that could be pooled. In addition, the reporting of psychological status of study populations at baseline was often omitted, and only a minority of studies reported other important outcomes, such as HRQL, or data that could be used to support health economic evaluation.

Conclusions

This updated Cochrane review found that psychological treatments had important health benefits among people with CHD, reducing the rate of cardiac mortality and alleviating the psychological symptoms of depression, anxiety, and stress. However, according to the GRADE methodology there remains uncertainty in these benefits and large-scale trials are still warranted. Future trials must provide a clearer reporting of their methods and interventions (perhaps following similar taxonomies of intervention components to those encouraged in health behaviour interventions[54]), assess a broader range of outcomes, and undertake health economic evaluation. There also remains uncertainty regarding who benefits most from treatment, and which types of psychological intervention yield the greatest benefit. Future trials that test the efficacy of specific psychological techniques are still needed, although this may prove challenging in real-world settings where patients may present with complex psychological needs that alter across the course of their recovery. Pragmatic trials of multifactorial interventions, delivered in a blended fashion, are also justified, but should be accompanied by pre-planned process evaluations (e.g. using sub-group analysis) to better understand the active ingredients of such complex

interventions.[55] Future trials should also explore the optimal targeting of interventions for people with CHD with or without psychopathologies.

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Declaration of conflicting interests

SR is currently a co-investigator on the CADENCE study (funded by the UK NHIR HTA 12/189/06). This study is a feasibility and pilot study aimed at developing enhanced psychological care for people with new onset depression using cardiac rehabilitation services (ISRCTN34701576). KR, PB and RW were authors of the first version (2004) of this review. BW, KR, PD, PB, ZL, RW, DRT and RST were authors of the second version (2011) of this review. KR, DRT, LA and RST are authors on a number of other Cochrane cardiac rehabilitation reviews. RST is currently the co-chief investigator on the programme of research with the overarching aims of developing and evaluating a home-based cardiac rehabilitation intervention for people with heart failure and their carers (UK NIHR PGfAR RP-PG-0611-12004). RST is

also currently a co-investigator on the CADENCE study (funded by the UK NHIR HTA 12/189/06). The other authors declare no other conflicts of interest.

Author contributions

RT and SR contributed to the conception and design of this review, building on the work undertaken by authors of the two previous versions (see below). SR, LA and CJ undertook study selection, data acquisition, data extraction, and risk of bias assessment. SR, LA and RT undertook data analysis. KR was the lead author on the first version (2004) of this review, and a co-author on the second version (2011). BW was the lead author on the second version (2011) of this review, and in this third update advised with study selection and analyses, and provided advice on classifying study interventions. PB and RW were co-authors on both the first and second versions of this review. RT, PD, ZL, DRT were co-authors on the second version of this review. All authors edited the manuscript and gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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List of Tables

Variable	Levels[a]
Targeting of psychological interventions	'non-selected population (including not reported)', 'population with clinically established psychological disorder'
Mode of intervention delivery	'individual (including not reported)', 'group or mix of individual & group'
Family involvement in intervention	'no (including not reported)', 'yes'
Cardiac risk factor education included as part of the intervention	'no (including not reported)', 'yes'
Behaviour change for cardiac risk factors included as part of the intervention	'no (including not reported)', 'yes'
Psychological treatment targets	
Depression	'no (including not reported)', 'yes'
Anxiety	'no (including not reported)', 'yes'
Stress management	'no (including not reported)', 'yes'
Type A behaviour	'no (including not reported)', 'yes'
Psychological components	
Relaxation	'no (including not reported)', 'yes'
Cognitive techniques	'no (including not reported)', 'yes'
Emotional support and/or client-led discussion	'no (including not reported)', 'yes'
Adjunct pharmacology	'no (including not reported)', 'yes'

Table 2. Study, participant, and intervention characteristics

Study characteristics (35 studies)	n Studies
Study location	
Europe	19
North America	12
Australia	4
China	1
Duration of follow-up, months (range)[a]	12 (6, 128)
Median sample size (range)	123 (42, 2481)
Median duration of follow-up, months (range)[a]	12 (6, 128)
Population characteristics	
Median of study mean ages, years (range)	59.6 (53–67)
Median proportion of males (range)	77 (0–100)
Cardiac indication on referral, %	
Myocardial infarction	65.7
Revascularisation procedure	27.4
Psychological disorder present at baseline	
All sample (inclusion criterion)	12
Mixed (observed, not required)[b]	11
None (exclusion criterion)	3
Not reported	11
Intervention characteristics	
Setting[c]	
Hospital	9
Clinic	7
Home-based	4
Mixed (inpatient, other support)	2
Not reported	13
Median treatment contact hours (range)	12 (2–96)
Mode of delivery	
Group	20
Individual (including not reported)	10
Mixed (group/individual)	5
Family involvement with treatment	
Yes	11
Not reported	24
Psychological treatment aims/components	
Multiple aims/components	23
Single aim/component	12
Treatment aims	
Stress	22
Depression	17
Anxiety	16
Type A behaviour (including anger/hostility)	12
Improving disease adjustment	11
Treatment components	
Relaxation techniques	20
Self-awareness and self-monitoring	20
Cognitive challenge or restructuring	19
Emotional support or client-led discussion	15
Treatment co-interventions	
Behavioural change for cardiac risk factors	19
Awareness of cardiac risk factors	16
Psycho-pharmacological prescribing	3

Table 3. Results from the pooled analysis of mortality and cardiovascular morbidity

Outcome (median follow-up)	Number of participants (studies)	Number of events		RR (95% CI)	Statistical heterogeneity I^2 (*p*-value)	GRADE quality of evidence
		Intervention	Comparator			
Total mortality (13 months)	7776 (23)	319/3899	352/3877	0.90 (0.77, 1.05)	2% (0.43)	Moderate[a]
Cardiovascular mortality (57 months)	4792 (11)	140/2561	161/2231	0.79 (0.63, 0.98)	0% (0.76)	Low[a,b]
Revascularisation (CABG/PCI) (12 months)	6822 (13)	395/3429	412/3393	0.94 (0.81, 1.11)	8% (0.36)	Moderate[a]
Non-fatal MI (30 months)	7845 (13)	340/4114	355/3731	0.82 (0.64, 1.05)	41% (0.07)	Low[a,c]

Table 4. Results from the pooled analysis psychological outcomes

Outcome (median follow-up)	Number of participants (studies)	SMD (95% CI) (intervention – comparator)	Statistical heterogeneity I^2 (*p*-value)	GRADE quality of evidence
Depression (12 months)	5829 (19)	–0.27 (–0.39, –0.15)	69% (<0.001)	++– Low[a,b]
Anxiety (12 months)	3165 (12)	–0.24 (–0.38, –0.09)	47% (0.03)	++– Low[a,c]
Stress (12 months)	1255 (8)	–0.56 (–0.88, –0.24)	86% (<0.001)	+— Very low[a,b,d]

List of figures

Figure 1. Forest plot of psychological intervention versus usual care: cardiac mortality

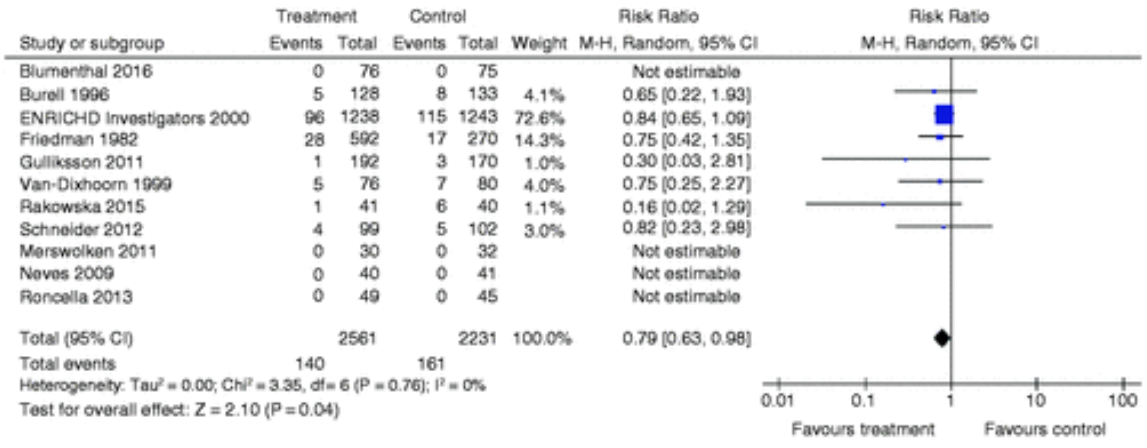

Figure 2. Forest plot of psychological intervention versus usual care: depression

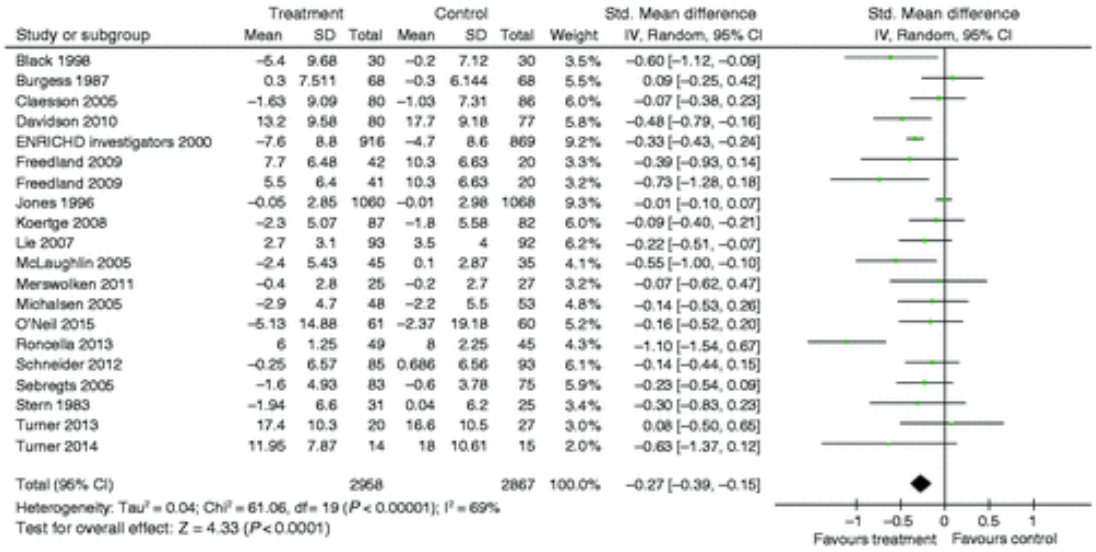

Figure 3. Forest plot of psychological intervention versus usual care: anxiety

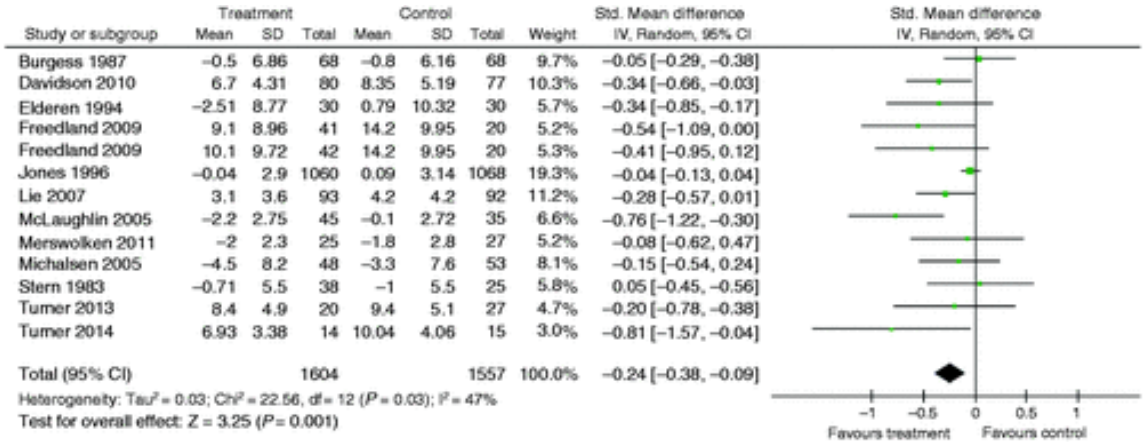

Figure 4. Forest plot of psychological intervention versus usual care: stress