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Psychological interventions for coronary heart disease: Cochrane systematic review and meta-analysis

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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 6 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: Thirty-five studies with 10,703 participants (median follow-up 12 months) were included. Psychological interventions led to a reduction in cardiovascular mortality (rfcelative 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 with different presentations of CHD.

Keywords

Cardiac morbidity, mortality, depression, anxiety, stress, psychological intervention, systematic review, randomised controlled trial

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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 USA.[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. A 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 (five 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 (eight trials, 2771 participants; SMD –0.25, 95% CI –0.35 to –0.03), although the 95% CIs 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] (see Supplementary Figure 1 for the 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 up to April 2016. We searched the World Health Organization (WHO) International Clinical Trials Registry Platform and the US ClinicalTrials.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 or 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 6 months post-randomisation and

reporting at least one of the primary outcomes (reported below).

Two reviewers (LA and SHR or CEJ) 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 and cardiovascular morbidity (non-fatal MI and revascularisation procedures [CABG and 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 (SHR or CEJ) checked the extracted data for accuracy and disagreements were resolved by discussion. Outcome data were independently extracted by two reviewers (LA and SHR). 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; and 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 SMDs 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, TX, USA).[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 (interquartile range [IQR] 73–204). The median length of follow-up was 12 months (IQR 12–29 months); longer follow-ups (over 30 months) were restricted to clinical events data extracted from routine records rather than psychological outcomes.

Table 1. Potential explanatory variables explored in univariate meta-regression.

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'

[a]First level coded '0' and second level coded '1' in regression models.

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 rates of anxiety of 32%[33,37] and 53%[38] (some papers reported both anxiety and depression). Only three excluded individuals with psychopathology at baseline and 11 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). Eleven 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), as well as 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 and 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

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

[a]The length of follow-up of clinical events; psychological outcomes were often followed up for shorter periods within the overall assessment schedule.
[b]Includes two studies in which the inclusion criterion was a confirmed psychopathology and/or another indicating condition.
[c]Clinical settings can include cardiac rehabilitation units, hospital outpatient clinics or community centres.

and stress), significant heterogeneity observed (anxiety and stress) and/or the risk of publication bias (cardiac mortality and anxiety). Thus, the GRADE ratings were moderate (total mortality and revascularisation), low (cardiac mortality, non-fatal MI, anxiety and 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 a 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. A 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, $I^2 = 69\%$; Table 4, Figure 2). Reductions in

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]

[a]Random sequence generation, allocation concealment or blinding of outcome assessors poorly described in ≥50% of included studies.
[b]Egger tests suggest evidence of asymmetry.
[c]95% CIs include both no effect and appreciable benefit or harm (i.e. 95% CI < 0.75 or >1.25).
GRADE: moderate = further research is very likely to have an important effect on confidence of the estimated effect and may change the estimate; low = further research is very likely to have an important effect on confidence in the estimated effect and is likely to change the estimate.
CABG: coronary artery bypass grafting; CI: confidence interval; GRADE: Grading of Recommendations Assessment, Development and Evaluation; MI: myocardial infarction; PCI: percutaneous coronary intervention; RR: relative risk.

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]

[a]Random sequence generation, allocation concealment or blinding of outcome assessors were poorly described in ≥50% of included studies.
[b]Moderate heterogeneity ($I^2 > 50\%$).
[c]Egger tests suggest evidence of asymmetry.
[d]95% CIs around the SMD did not include the value of a + 5 at either the lower or upper limits (indicative of clinical significance).
GRADE: moderate = further research is very likely to have an important effect on confidence of the estimated effect and may change the estimate; low = further research is very likely to have an important effect on confidence in the estimated effect and is likely to change the estimate; very low quality = the estimate is very uncertain.
CI: confidence interval; GRADE: Grading of Recommendations Assessment, Development and Evaluation; SMD: standardised mean difference.

anxiety levels (12 trials, 3161 participants; SMD –0.24, 95% CI –0.38 to –0.09, $I^2 = 47\%$; Table 4, Figure 3) and stress levels (eight trials, 1251 participants; SMD –0.56, 95% CI –0.88 to –0.24, $I^2 = 86\%$; Table 4, Figure 4) 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 mortality, depression, anxiety and 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.

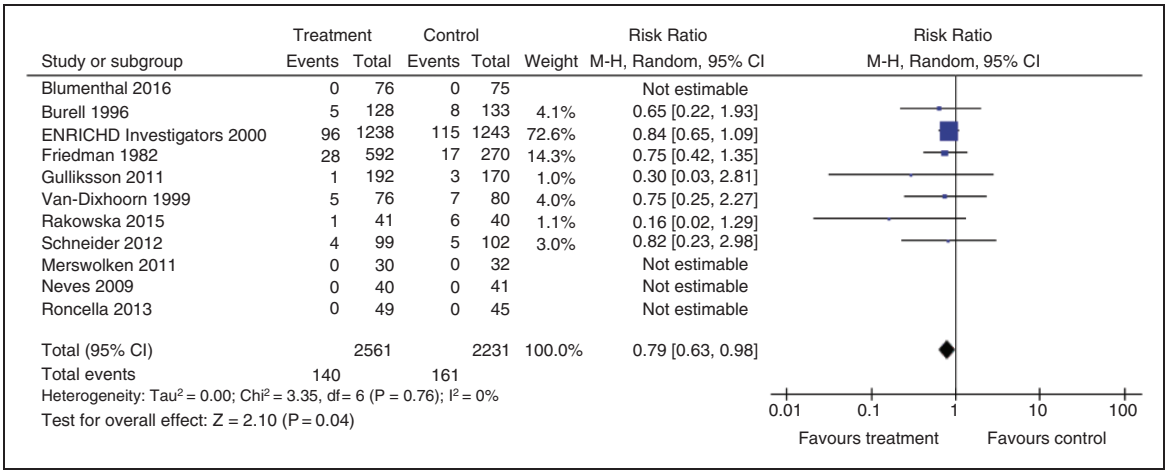

Figure 1. Forest plot of psychological intervention versus usual care: cardiovascular mortality.
CI: confidence interval; df: degrees of freedom; M-H: Mantel-Haenszel method.
Reproduced from Richards et al.[10]

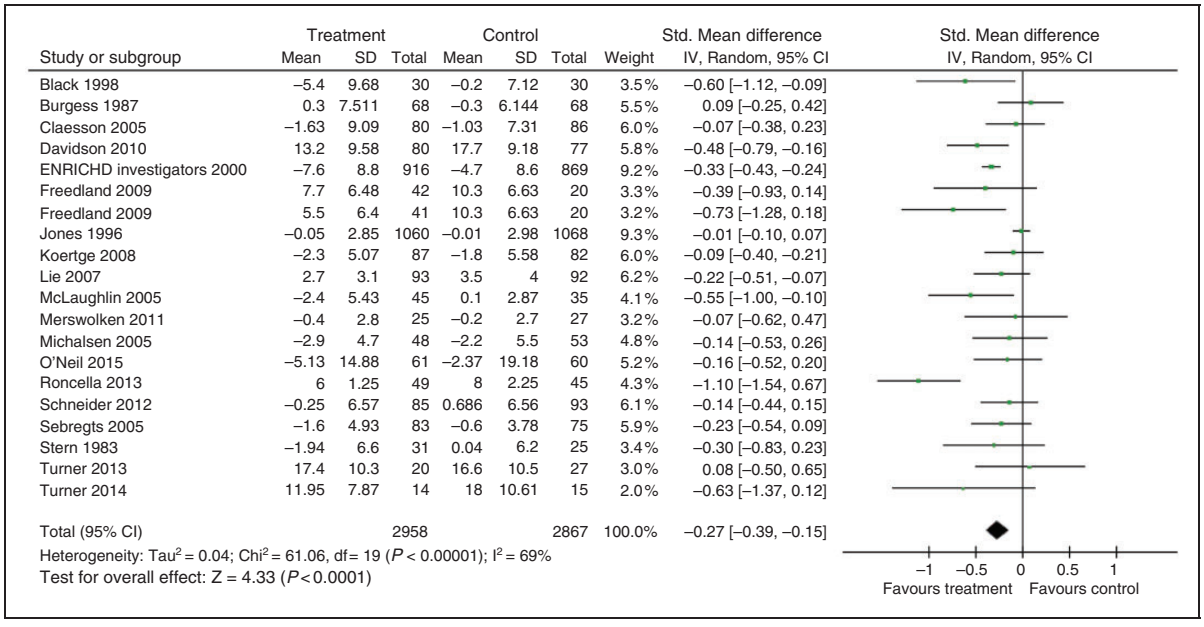

Figure 2. Forest plot of psychological intervention versus usual care: depression.
CI: confidence interval; df: degrees of freedom; IV: inverse variance method.
Reproduced from Richards et al.[10]

Health-related quality of life. HRQL was reported in ten studies (Supplementary Table 3). A 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] and 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 two studies reported any form of economic evaluation alongside trial data. Van-Dixhoorn and Duivenvoorden[44] limited the economic evaluation to an examination of hospital costs arising

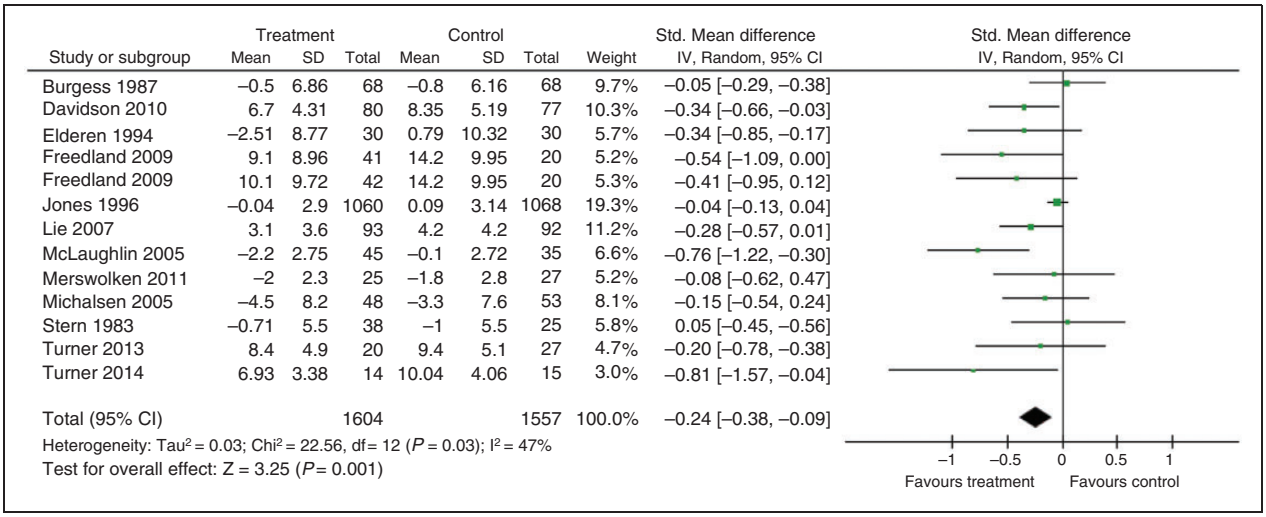

Figure 3. Forest plot of psychological intervention versus usual care: anxiety.
CI: confidence interval; df: degrees of freedom; IV: inverse variance method.
Reproduced from Richards et al.[10]

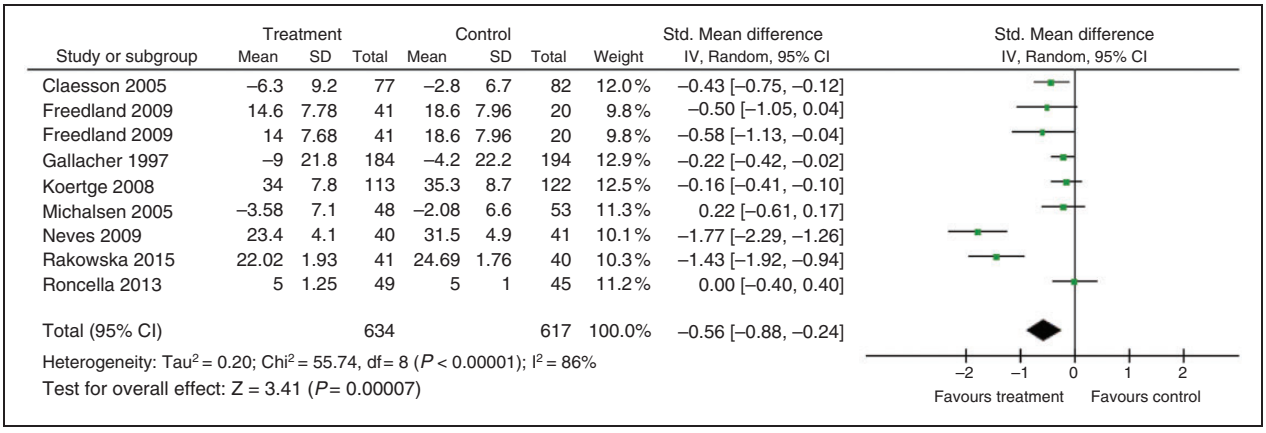

Figure 4. Forest plot of psychological intervention versus usual care: stress.
CI: confidence interval; df: degrees of freedom; IV: inverse variance method.
Reproduced from Richards et al.[10]

from cardiac-related hospital readmissions across a 5-year follow-up. The authors reported that 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 et al.[21] (see Ladapo et al.[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 and hospitalisations) were $1857 for the intervention group and $2797 for the usual care group (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.

A 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 underpowered compared with individual patient data meta-analysis. More importantly, however, this form of analysis is prone to ecological fallacy (or 'aggregation bias').

Meta-regression failed to identify any predictor variables for 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 that 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 the 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 6 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 showing 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] suggesting 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 was moderate, low or very low across outcomes.

From the information reported, the majority of participants were men recruited post-MI and so our findings may be less generalisable 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 tested the effectiveness of single-component therapies (e.g. Van-Dixhoorn and Duivenvoorden[44] and Blumenthal et al.[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 (e.g. 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 sizes (in terms of both psychological and cardiac benefit) of any psychological interventions targeted at a population with no obvious psychopathology, testing the effectiveness of interventions for people with established psychopathology 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 and lifestyle change); this was essential in order to reduce the clinical heterogeneity of the compared interventions, but as a consequence, our findings do not inform the wider evidence base on the contribution of psychological techniques to optimising 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 the psychological status of the 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 regarding 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 subgroup analysis) in order 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.

Author contribution

RST and SHR contributed to the conception and design of this review, building on the work undertaken by the authors of the two previous versions (see below). SHR, LA and CEJ undertook study selection, data acquisition, data extraction and risk of bias assessment. SHR, LA and RST 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. RST, PD, ZL and DRT were co-authors on the second version of this review. All authors edited the manuscript, gave final approval and agree to be accountable for all aspects of the work ensuring integrity and accuracy.

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Declaration of conflicting interests

The authors declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: SHR 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 the authors of the first version (2004) of this review. BW, KR, PD, PB, ZL, RW, DRT and RST were the authors of the second version (2011) of this review. KR, DRT, LA and RST are the authors of 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.

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References

1. World Health Organisation. The top 10 causes of death, 2014. http://www.who.int/mediacentre/factsheets/fs310/en.
2. Tully PJ, Cosh SM and Baumeister H. The anxious heart in whose mind? A systematic review and meta-regression of factors associated with anxiety disorder diagnosis, treatment and morbidity risk in coronary heart disease. *J Psychosom Res* 2014; 77: 439–448.
3. Dickens C. Depression in people with coronary heart disease: Prognostic significance and mechanisms. *Curr Cardiol Rep* 2015; 17: 83.
4. Lichtman JH, Froelicher ES, Blumenthal JA, et al. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: Systematic review and recommendations: A scientific statement from the American Heart Association. *Circulation* 2014; 129: 1350–1369.
5. Gale CR, Batty D, Osborn DPJ, et al. Mental disorders across the adult life course and future coronary heart disease. *Circulation* 2014; 129: 186–193.
6. Woodruffe S, Neubeck L, Clark RA, et al. Australian Cardiovascular Health and Rehabilitation Association (ACRA) core components of cardiovascular disease secondary prevention and cardiac rehabilitation 2014. *Heart Lung Circ* 2015; 24: 430–441.
7. Piepoli MF, Corrà U, Adamopoulos S, et al. Secondary prevention in the clinical management of patients with cardiovascular diseases. Core components, standards and outcome measures for referral and delivery. A policy statement from the Cardiac Rehabilitation Section of the European Association for Cardiovascular Prevention & Rehabilitation. *Eur J Prev Cardiol* 2014; 21: 664–681.
8. Authors/Task Force Members; Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur J Prev Cardiol* 2016; 23: NP1–NP96.
9. Whalley B, Rees K, Davies P, et al. Psychological interventions for coronary heart disease. *Cochrane Database Syst Rev* 2011; 8: CD002902.
10. Richards SH, Anderson L, Jenkinson CE, et al. Psychological interventions for coronary heart disease. *Cochrane Database Syst Rev* 2017; 4: CD002902.
11. Higgins J and Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available at www.handbook.cochrane.org.
12. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *BMJ* 2009; 339: b2535.

13. GRADEpro GTD. GRADEpro Guideline Development Tool [software], 2015. www.gradepro.org.
14. Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple graphical test. *BMJ* 1997; 315: 629–634.
15. Deeks JJ, Higgins JPT and Altman DG. Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins J and Green S (eds) *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available at www.handbook.cochrane.org.
16. The Cochrane Community. *Review Manager (RevMan). 5.3 Edition*. Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014..
17. StataCorp LP. *STATA Software (Version 14.1)*. College Station, TX, USA: StataCorp, 2016.
18. Cowan MJ, Pike KC and Budzynski HK. Psychosocial nursing therapy following sudden cardiac arrest: Impact on two-year survival. *Nurs Res* 2001; 50: 68–76.
19. Hofman-Bang C, Lisspers J, Nordlander R, et al. Two-year results of a controlled study of residential rehabilitation for patients treated with percutaneous transluminal coronary angioplasty. A randomized study of a multifactorial programme. *Eur Heart J* 1999; 20: 1465–1474.
20. Ibrahim MA, Feldman JG, Sultz HA, et al. Management after myocardial infarction: A controlled trial of the effect of group psychotherapy. *Int J Psychiatry Med* 1974; 5: 253–268.
21. Davidson KW, Rieckmann N, Clemow L, et al. Enhanced depression care for patients with acute coronary syndrome and persistent depressive symptoms: Coronary psychosocial evaluation studies randomized controlled trial. *Arch Intern Med* 2010; 170: 600–608.
22. Freedland KE, Skala JA, Carney RM, et al. Treatment of depression after coronary artery bypass surgery: A randomized controlled trial. *Arch Gen Psychiatry* 2009; 66: 387–396.
23. Gulliksson M, Burell G, Wessby B, et al. Randomized controlled trial of cognitive behavioral therapy vs standard treatment to prevent recurrent cardiovascular events in patients with coronary heart disease. *Eur Heart J* 2011; 32: 390.
24. Merswolken M, Siebenhuener S, Orth-Gomer K, et al. Treating anxiety in patients with coronary heart disease: A randomized controlled trial. *Psychother Psychosom* 2011; 80: 365–370.
25. Neves A, Alves AJ, Ribeiro F, et al. The effect of cardiac rehabilitation with relaxation therapy on psychological, hemodynamic, and hospital admission outcome variables. *J Cardiopulm Rehabil Prev* 2009; 29: 304–309.
26. O'Neil A, Taylor B, Hare DL, et al. Long-term efficacy of a tele-health intervention for acute coronary syndrome patients with depression: 12-month results of the MoodCare randomized controlled trial. *Eur J Prev Cardiol* 2015; 22: 1111–1120.
27. Oranta O, Luutonen S, Salokangas RK, et al. The outcomes of interpersonal counselling on depressive symptoms and distress after myocardial infarction. *Nord J Psychiatry* 2010; 64: 78–86.
28. Rakowska JM. Brief strategic therapy in first myocardial infarction patients with increased levels of stress: A randomized clinical trial. *Anxiety Stress Coping* 2015; 28: 687–705.
29. Roncella A, Pristipino C, Cianfrocca C, et al. One-year results of the randomized, controlled, short-term psychotherapy in acute myocardial infarction (STEP-IN-AMI) trial. *Int J Cardiol* 2013; 170: 132–139.
30. Schneider RH, Grim CE, Rainforth MV, et al. Stress reduction in the secondary prevention of cardiovascular disease: Randomized, controlled trial of transcendental meditation and health education in blacks. *Circ Cardiovasc Qual Outcomes* 2012; 5: 750–758.
31. Turner A, Murphy BM, Higgins RO, et al. An integrated secondary prevention group programme reduces depression in cardiac patients. *Eur J Prev Cardiol* 2014; 21: 153–162.
32. Turner A, Hambridge J, Baker A, et al. Randomised controlled trial of group cognitive behaviour therapy versus brief intervention for depression in cardiac patients. *Aust N Z J Psychiatry* 2013; 47: 235–243.
33. Lie I, Arnesen H, Sandvik L, et al. Effects of a home-based intervention program on anxiety and depression 6 months after coronary artery bypass grafting: A randomized controlled trial. *J Psychosom Res* 2007; 62: 411–418.
34. Blumenthal JA, Sherwood A, Smith PJ, et al. Enhancing cardiac rehabilitation with stress management training. A randomized, clinical efficacy trial. *Circulation* 2016; 133: 1341–1350.
35. Michalsen A, Grossman P, Lehmann N, et al. Psychological and quality-of-life outcomes from a comprehensive stress reduction and lifestyle program in patients with coronary artery disease: Results of a randomized trial. *Psychother Psychosom* 2005; 74: 344–352.
36. Koertge J, Janszky I, Sundin O, et al. Effects of a stress management program on vital exhaustion and depression in women with coronary heart disease: A randomized controlled intervention study. *J Intern Med* 2008; 263: 281–293.
37. Jones DA and West RR. Psychological rehabilitation after myocardial infarction: Multicentre randomised controlled trial. *BMJ* 1996; 313: 1517–1521.
38. McLaughlin T, Aupont O, Bambauer K, et al. Improving psychologic adjustment to chronic illness in cardiac patients: The role of depression and anxiety. *J Gen Intern Med* 2005; 20: 1084–1090.
39. Black JL, Allison TG, Williams DE, et al. Effect of intervention for psychological distress on rehospitalization rates in cardiac rehabilitation patients. *Psychosomatics* 1998; 39: 134–143.
40. The ENRICHD Investigators. Enhancing recovery in coronary heart disease patients (ENRICHD): Study design and methods. *Am Heart J* 2000; 139: 1–9.
41. Appels A, Bär F, van der Pol G, et al. Effects of treating exhaustion in angioplasty patients on new coronary events: Results of the randomized exhaustion intervention trial (EXIT). *Psychosom Med* 2005; 67: 217–223.
42. Claesson M, Birgander L, Lindahl B, et al. Women's hearts: Stress management for women with ischemic

heart disease: Explanatory analyses of a randomized controlled trial. *J Cardiopulm Rehabil* 2005; 25: 93–102.
43. Mayou R, Thompson D, Clements A, et al. Guideline-based early rehabilitation after myocardial infarction: A pragmatic randomised controlled trial. *J Psychosom Res* 2002; 52: 89–95.
44. Van-Dixhoorn JJ and Duivenvoorden HJ. Effect of relaxation therapy on cardiac events after myocardial infarction: A 5-year follow-up study. *J Cardiopulm Rehabil* 1999; 19: 178–185.
45. Ladapo JA, Shaffer JA, Fang Y, et al. Cost-effectiveness of enhanced depression care after acute coronary syndrome: Results from the Coronary Psychosocial Evaluation Studies randomized controlled trial. *Arch Intern Med* 2012; 172: 1682–1684.
46. Rao G, Lopez-Jimenez F, Boyd J, et al. Methodological standards for meta-analyses and qualitative systematic reviews of cardiac prevention and treatment studies: A scientific statement from the American Heart Association. *Circulation* 2017; 136: e172–e194.
47. Peng J and Jiang LJ. Psychotherapy on negative emotions for the incidence of ischemia-related events in patients with coronary heart disease. *Chinese J Clin Rehabil* 2005; 9: 38–39.
48. Welton NJ, Caldwell DM, Adamopoulos E, et al. Mixed treatment comparison meta-analysis of complex interventions: Psychological interventions in coronary heart disease. *Am J Epidemiol* 2009; 169: 1158–1165.
49. Dickens C, Cherrington A, Adeyemi I, et al. Characteristics of psychological interventions that improve depression in people with coronary heart disease: A systematic review and meta-regression. *Psychosom Med* 2013; 72: 211–221.
50. McManus F, Surawy C, Muse K, et al. A randomized clinical trial of mindfulness-based cognitive therapy versus unrestricted services for health anxiety (hypochondriasis). *J Consult Clin Psychol* 2012; 80: 817–828.
51. Norlund F, Olsson EM, Burell G, et al. Treatment of depression and anxiety with internet-based cognitive behavior therapy in patients with a recent myocardial infarction (U-CARE Heart): Study protocol for a randomized controlled trial. *Trials* 2015; 16: 154.
52. Richards SH, Dickens C, Anderson R, et al. Assessing the effectiveness of enhanced psychological care for patients with depressive symptoms attending cardiac rehabilitation compared with treatment as usual (CADENCE): Study protocol for a pilot cluster randomised controlled trial. *Trials* 2016; 17: 1.
53. Spatola CA, Manzoni GM, Castelnuovo G, et al. The ACTonHEART study: Rationale and design of a randomized controlled clinical trial comparing a brief intervention based on acceptance and commitment therapy to usual secondary prevention care of coronary heart disease. *Health Qual Life Outcomes* 2014; 12: 22.
54. Michie S, Richardson M, Johnston M, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: Building an international consensus for the reporting of behavior change interventions. *Ann Behav Med* 2013; 46: 81–95.
55. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ* 2015; 350: h1258.