

Report on Rehabilitation and Palliative Care in the Management of Cardiovascular Diseases: The Evidence and the Gaps

Vicky Joshi, Lars Tang, Linda Long, Ann-Dorthe Zwisler & Rod Taylor
for the Danish Heart Foundation



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Produced by REHPA and University of Exeter Medical School for the Danish Heart Foundation

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Foreword

Today, many more people are surviving sudden cardiac events and living longer with cardiovascular diseases, thanks to improved preventative strategies and advanced treatment. Rehabilitation and palliative care has become increasingly important as the cardiac population has evolved.

This report was commissioned by the Danish Heart Foundation to map the evidence for rehabilitation and palliative care in cardiovascular diseases and to identify where gaps in the evidence might exist. The report forms part of a wider review by the Danish Heart Foundation into disease management. The results and recommendations will support the focus and prioritization of the Danish Heart Foundation over the next few years. It also summarises the evidence for cardiac rehabilitation and palliative care in one document, for clinicians and service providers working with cardiac patients. We also hope that researchers will use this report to identify research priorities and improve the quality of future research trials.

The report has been prepared by the Danish Centre on Rehabilitation and Palliative Care, Denmark, in collaboration with the Cochrane Cardiac Rehabilitation Group, University of Exeter Medical School, England. Both organisations have expertise in running, mapping and systematically reviewing evidence in relation to cardiac rehabilitation and palliative care. The report could not have been possible without the University of Exeter Evidence Synthesis & Modelling for Health Improvement team, who undertook the systematic literature searches. Thanks also go to the expert professional group for critically reviewing the report and providing feedback. Finally, we would like to thank Vicky Joshi, Lars Tang and Linda Long for their extensive contribution to analysing the literature and writing the report.

Only through mapping the existing evidence for rehabilitation and palliative care can we understand where future time, effort and resources should be focused, in order to achieve the best possible outcomes for patients living with cardiovascular diseases in the future.

Professor Ann-Dorthe Zwisler
Centre leader for REHPA

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Summary

This report summarises the evidence on the effectiveness of rehabilitation and palliative interventions in the management of cardiovascular diseases. It is based on a literature search for recent systematic reviews and meta-analyses of randomised controlled trials. The evidence is presented across cardiovascular indications under four headings: (1) exercise interventions, (2) psychological and educational intervention; (3) non-pharmacological secondary prevention (diet and smoking) and (4) palliative interventions.

We found an extensive body of evidence supporting the benefits of exercise-based rehabilitation in coronary heart disease (i.e., myocardial infarction and post-revascularisation), heart failure and intermittent claudication. Exercise capacity, health-related quality of life and risk of hospital admission were all found to improve with exercise compared to no exercise control. However, impact of exercise was uncertain in many of the less common cardiac diseases (i.e., stable angina, heart valve surgery, TAVI and pulmonary hypertension) which had small numbers of trials, with low to very low quality evidence and, for some cardiovascular diseases (i.e., infective endocarditis, cardiac arrest survivors, congenital heart disease, venous embolism and aortic syndrome), we found no systematic reviews of the effectiveness of exercise interventions.

Psychological and education-based rehabilitation involves complex, multi-element interventions. This complexity plus the heterogeneity of interventions and outcome measures may account for the low quality of evidence found for these interventions and the lack of trials in less common cardiac diseases. Overall, the majority of positive evidence is for psychological interventions for coronary heart disease post myocardial infarction and revascularisation with positive benefits also seen for heart failure, stable angina, atrial fibrillation and patients with implantable cardio-defibrillators.

The chapters on exercise and psychological and education-based rehabilitation describe interventions that include dietary and smoking cessation strategies. Hence, we only searched for reviews on secondary prevention that presented smoking or dietary interventions alone. The systematic review on smoking cessation and CHD found interventions improved abstinence rates at one year but not over a longer period. The quality of the systematic review was high but quality of the included trials was low. The systematic review on dietary-based education and heart failure found education improved sodium intake, weight monitoring and hospital readmission rates. However, the review was of low quality, involved only six trials and no information was given on the quality of included trials. No systematic reviews for dietary-based secondary prevention were identified for other CVD indications.

Palliative care has recently expanded to include the care of all individuals with life-limiting conditions, including patients diagnosed with end-stage cardiovascular disease. We found only two systematic reviews in palliative interventions limited to heart failure. They showed palliative care is associated with improvements in health-related quality of life (HRQL), symptom burden and reductions in re-hospitalisation for patients with life-limiting heart failure. However, no other systematic reviews were found in relation to palliative care for other cardiovascular disease indications.

In conclusion, there is considerable evidence for rehabilitation interventions for CHD, intermittent claudication and heart failure patients. In these areas, future research should focus on implementation, quality assurance and improving adherence. High quality research is needed to clarify the effects on smaller cardiac conditions and in patients with palliative needs, before they can be routinely included in clinical rehabilitation programmes. Future research should include well described interventions, patient-related outcomes including HRQL, function and return to work, plus healthcare system impacts including rates of hospital admission and costs.

Abbreviations

ACS	Acute coronary syndrome
AF	Atrial fibrillation
CABG	Coronary artery bypass graft
CI	Confidence interval
CAD	Coronary artery disease
CHD	Coronary heart disease
CR	Cardiac rehabilitation
CVD	Cardiovascular disease
ICD	Implantable cardioverter-defibrillators
IHD	Ischaemic heart disease
IC	Intermittent claudication
HADS	Hospital Anxiety and Depression Scale
HF	Heart failure
HFpEF	Heart failure with preserved ejection fraction
HFReEF	Heart failure with reduced ejection fraction
HR	Hazard ratio
HRQL	Health-related quality of life
MD	Mean difference
MI	Myocardial infarction
PAD	Peripheral arterial disease
PCI	Percutaneous coronary intervention
PH	Pulmonary hypertension
PRISMA	Preferred reporting items for systematic reviews and meta-analysis
R-AMSTAR	Revised a measurement tool to assess systematic reviews
RCT	Randomised controlled trial
RR	Risk Ratio
SA	Stable angina
SMD	Standardised mean difference
SVR	Surgical valve replacement
sAVR	Surgical aortic valve replacement
TAVI	Trans aortic valve implantation
VO2	Volume of oxygen
WMD	Weighted mean difference

1. Introduction

In Denmark, the prevalence of cardiovascular disease (CVD) is increasing, leading to a greater proportion of people living with problems associated with CVD and the disabilities that may follow¹.

Rehabilitation for cardiac diseases aims to address and improve the complications associated with suffering from a cardiac disease²⁻⁴. Programmes are often comprehensive in nature involving activities that improve the physical, mental and social wellbeing of patients. The aim is to allow patients, as far as possible, to return to their activities of daily living following an acute cardiac event, or to improve the well being of patients suffering from a chronic or severe CVD^{3,5-7}.

Rehabilitation for CVD includes exercise, education, psychosocial interventions and secondary prevention (smoking cessation and dietary treatment)^{4,6}. Programmes may be based on one main element while including aspects of the other two or on a single area, with exercise being the most common⁶.

Rehabilitation for CVD is a standard part of healthcare provision in Denmark. Current programmes primarily include patients following treatment for acute coronary syndrome and those with heart failure, where the effectiveness of rehabilitation has been comprehensively documented in several systematic reviews and meta-analyses⁸⁻¹⁰. Systematic reviews for other CVD diagnoses are either limited in number, do not exist or there is a lack of clinical trials on which to base them. However, collating evidence based upon systematic reviews of the literature is essential to document the effectiveness of rehabilitation for a broader range of CVD diagnoses. An overview ('review of reviews') of Cochrane systematic reviews of cardiac rehabilitation was published in 2014¹¹. However, this overview did not consider all CVD indications (i.e., excluded cardiac arrest, peripheral arterial disease) and does not include the newest published Cochrane systematic reviews within the area of rehabilitation for cardiac diseases that include atrial fibrillation, stable angina and post valve surgery¹¹. In order to plan continued research in CR (cardiac rehabilitation) and ensure effective CR is provided to all patients who will benefit, a description and mapping of evidence in all CVD groups is essential.

Having originated in the care of patients with cancer, palliative care has recently expanded to include the care of all individuals affected by life-limiting conditions, including patients diagnosed with end-stage CVD¹². Palliative care aims to improve the quality of life for these patients and their families. It is recommended that palliative care is integrated into the comprehensive treatment interventions of patients with progressive cardiac diseases. It should not be reserved for those who are expected to die within days or weeks⁷. In recent years, a number of studies have investigated palliative interventions for patients with CVD¹². An overview of this evidence is highly relevant for the implementation of palliative care in Danish healthcare services, as recommended by the Danish Society of Cardiology in a newly published position paper¹³.

Aim

The aim of this project is to provide a contemporary summary of the evidence for the effectiveness of rehabilitation and its core non-pharmacological components (i.e., exercise, education and psychological interventions) in a range of CVD conditions (see 'Table of included cardiovascular

conditions' below). Additionally, this project seeks to provide a summary of the evidence for the effectiveness of rehabilitation in relation to non-pharmacological secondary prevention and the effectiveness of palliative care for CVD.

Table of included cardiovascular conditions

Disease	Condition(s)
Coronary artery disease	myocardial infarction, acute coronary syndromes, unstable angina, post revascularisation and stable angina
Heart failure	heart failure with reduced ejection fraction and heart failure with preserved ejection fraction
Valvular heart disease	surgery for heart valve disease, transcatheter aortic valve implantation and infective endocarditis
Arrhythmia	atrial fibrillation, implantable cardioverter-defibrillators and cardiac arrest survivors
Congenital heart disease	
Aortic disease	acute aortic syndrome, aortic aneurysm
Peripheral vascular disease	intermittent claudication
Pulmonary vascular disease	pulmonary hypertension

Whilst stroke is a CVD condition, stroke rehabilitation was deemed outside the scope of this review.

Research questions

What is the effectiveness of rehabilitation across a range of CVD diagnoses?

What is the effectiveness of rehabilitation in relation to non-pharmacological secondary prevention (exercise, smoking and diet) across a range of CVD diagnoses?

What is the effectiveness of palliative care across a range of end-stage CVD diagnoses?

1.1 Organisation of the report

The methodology for the report is detailed below. In summary, the evidence for the effectiveness for rehabilitation in the management of cardiovascular disease is presented in four chapters:

1. Exercise-based rehabilitation
2. Psychological and education-based rehabilitation
3. Non-pharmacological secondary prevention (smoking cessation and dietary treatment).
4. Palliative interventions

Each chapter provides a summary of the most recent systematic review(s)/meta-analyses for each of the included CVD conditions. For each chapter, two opening statements are provided: (1) a brief overview of the evidence for efficacy of the intervention and (2) an overall statement on the quality of that evidence (based on R-AMSTAR tool (Revised- A Measurement Tool to Assess Systematic Reviews) see below).

Each summary includes a description of the following; participant demographics, length of the intervention period, length of study follow-up, a summary of the main outcome findings, limitations of the current studies or the systematic review and suggestions for future research.

The outcome findings are reported according to the following six pre-defined outcomes; mortality, morbidity (for example, hospital admission), exercise capacity, health-related quality of life (HRQL), healthcare costs and return to work. These outcomes were chosen for their relevance to patients, clinicians and policy makers. On reviewing the evidence, some additional outcomes were added that were deemed important to specific conditions, for example, 'number of shocks' for ICD patients.

The results from each of the literature searches is provided at the end of each chapter in the form of a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) flow diagram ¹⁴. This describes the number of articles included at each stage of the systematic search process and the reasons for exclusion.

The report concludes with an overarching discussion chapter that draws on the results from the four evidence summary chapters.

1.2 Methods

A separate literature search to identify systematic reviews and meta-analyses was undertaken, following the Cochrane Handbook for Systematic Reviews of Interventions methodology for each of the following six intervention groupings¹⁵.

1. 'Exercise-based interventions'
2. 'Education-based interventions'
3. 'Psychological-based interventions'
4. 'Secondary prevention' AND 'smoking'
5. 'Secondary prevention' AND 'diet'
6. 'Palliative care' OR 'palliative medicine'

Although the searches were conducted separately, given that many of the selected systematic reviews combine psychological-based rehabilitation and education-based rehabilitation, the evidence for these two interventions are presented in a single chapter. Similarly, the evidence for secondary prevention with diet and smoking were also combined into one chapter.

Full search terms are available in Appendix 1. Experienced information specialists from the University of Exeter Medical School Evidence Synthesis & Modelling for Health Improvement (ESMI) in UK, undertook the systematic literature searches and exported the results in six Endnote libraries. We contacted the Cochrane cardiac rehabilitation collaboration regarding any upcoming reviews due to be completed before 1st September 2017. As the report aimed to produce contemporary evidence for rehabilitation, only articles published after 2009 were included. Given the time and resource constraints of this project, it was not possible to undertake a separate search for individual randomised controlled trials (RCTs) or update, or undertake de novo systematic reviews.

Selection of included systematic reviews/meta-analyses

Included systematic reviews/meta-analyses were selected in a three stage process:

Stage 1 - An initial screen of the titles and abstracts was performed by one researcher (VJ). Article titles were screened on the basis of the following inclusion criteria:

- Involved one or more of the included CV conditions
- Systematic review or meta-analysis based on RCTs
- Intervention took place in the sub-acute/rehabilitation/'phase 2' time frame (except for palliative care where time frame was open)
- Published after 2009
- Effectiveness of an intervention compared to control (could include usual care, no intervention or placebo).

Depending on which library was being searched, interventions were included if there was:

1. any type of patient education intervention, as the primary intention of the intervention
2. any type of emotion-focused psychological intervention, as the primary intention of the intervention
3. any type of education or psychological intervention regarding the secondary prevention of cardiovascular diseases and smoking, as the primary intention of the intervention
4. any type of education or psychological intervention regarding the secondary prevention of cardiovascular diseases and diet, as the primary intention of the intervention
5. any type of palliative intervention, as the primary intention of the intervention.

Stage 2 - From articles shortlisted at Stage 1, a full text version was independently read by two researchers (VJ and LT). A check was done again that articles met the Stage 1 inclusion criteria listed above. In addition, as the purpose of the report was to establish overall effectiveness of rehabilitation compared to control, any systematic review or meta-analysis that assessed the components of an intervention or mode of delivery was excluded. For example, we excluded reviews comparing home versus centre-based rehabilitation. This exclusion was applied to any systematic review/meta-analysis that considered the setting, type of intervention, duration, frequency or effect on different target populations. Any disagreements on inclusion/exclusion were discussed and consensus reached with a third reviewer (RST).

Stage 3- Given the aim of this project was to produce a contemporary overarching summary of the most current evidence, we included only the most recent and highest quality review. Selection criteria applied at this third stage of review were as follows:

1. The most recent systematic review available or a Cochrane review, if this was published within two years of the more recent review.
2. If there was more than one recent systematic review available within two years, then the highest quality review was selected based on the R-AMSTAR ¹⁶.
3. We included more than one systematic review, when an individual article did not cover all the report's six pre-determined outcome measures listed above.

All papers excluded after the Stage 3 'full text review', can be found in Appendix 2.

At stage 3, the quality of each included systematic review/meta-analysis was assessed using the R-AMSTAR tool¹⁶. This scores the quality of the systematic review, with 11 being the lowest score and 44 being the highest. A copy of the R-AMSTAR tool is provided in Appendix 3.

1.3 Summary Table: Effectiveness of exercise-based rehabilitation

Condition	Number of studies =n (Study population)	Sample size, range (n)	All-cause Mortality	Cardio-vascular mortality	Morbidity (Risk of MI, CABG or PCI)	Serious adverse events during trial	Disease Specific outcome	Hospital admission	Exercise capacity	HRQL	Return to work	Healthcare costs
CHD	63 (14,486)	28-2304	∞	+	∞			+	++	+		+
Stable angina	6 (414)	12-113	∞		+		+ ^a	+	+	+		+
Heart failure HFREF	33 (4740)	19-2331	(+)					(+)	+	+		+
Heart failure HFpEF	8 (317)	28-98	∞						+	+		
Heart valve surgery	2 (148)	50-104	∞			∞			+		∞	
TAVI	5 (292)	34-76	∞						+			
Infective endocarditis												
Atrial Fibrillation	6 (421)	30-210	∞			∞			+			
ICDs	6 (1603)	35-1053				∞	+ ^b		+			
Cardiac arrest survivors												
Congenital Heart disease												
Intermittent claudication	30 (1816)	14-253	∞				∞ ^c		++	+		
Pulmonary Hypertension	5 (165)	10-87	∞			∞			+	+		
Heart transplant	10 (300)		∞					∞	+	∞		
Venous embolism												
Acute aortic syndrome												

□ White = No Data;

□ Light blue = quality of evidence graded very low or low;

■ Grey = quality of evidence graded moderate

Effect: - = Negative effect; ∞ No effect found; (+) Trend towards positive effect;

+ Positive effect

^aAngina frequency/severity

^bNumber of ICD shocks

^cAnkle brachial index

1.4 Summary Table: Effectiveness of psychological and education-based rehabilitation

Condition	Number of studies =n (Study population)	Sample size, range (n)	All-cause Mortality	Fatal/non-fatal cardio-vascular events	Morbidity (Risk of MI, CABG or PCI)	Psychological symptoms	Disease Specific outcome	Hospital admission	Exercise capacity	HRQL	Return to work	Healthcare costs
CHD Psychological	35 (10,703)	14-1,243	∞	+	∞	+				(+)	∞	+
CHD Education	22 (76,864)	43-46,606	∞	+	∞			∞		(+)		(+)
Stable angina	9 (1,282)	29-452			+	+	+ ^a			(+)		
Heart failure	32 (5,624)	42-1023						+		+		
Heart valve surgery												
TAVI												
Infective endocarditis												
Atrial Fibrillation	11 (2,246)	14-712				+	∞ ^b					
ICDs	7 (1017)	29-289				+	∞ ^c			(+)		
Cardiac arrest survivors												
Congenital Heart disease												
Intermittent claudication	6 (434)						+ ^d		(+)			
Pulmonary Hypertension												
Heart transplant												
Venous embolism												
Acute aortic syndrome												

□ White = No Data;

□ Light blue = quality of evidence graded very low or low;

■ Grey = quality of evidence graded moderate

Effect: - = negative effect

∞ No effect found

(+) Trend towards positive effect

+ Positive effect

^aAngina frequency/sublingual nitrate use

^bTime in therapeutic range/decision conflict

^cCardiac outcomes (shocks and anti-tachycardia pacing)

^dPain free walking/ step-count

2. Exercise-based rehabilitation

The following chapter will present the data from included systematic reviews on exercise-based rehabilitation. Data is presented in relation to cardiovascular diseases.

2.1 Coronary Heart Disease

Exercise based rehabilitation reduces cardiovascular mortality and hospital admissions. It improves exercise capacity and HRQL with no significant impact on overall mortality or the risk of future myocardial infarction.

The quality of evidence for each outcome was low to moderate as assessed by GRADE. Lack of reporting of methods in older trials was noted, with quality of reporting improved in more recent trials.

This summary is based on two systematic reviews;

Anderson et al. (2016) [Cochrane]⁸ R-AMSTAR score: 42

Uddin et al. (2016)¹⁷ R-AMSTAR score: 28

The Cochrane review by Anderson et al. (2016)⁸ identified 63 RCTs (14,486 patients) investigating the effectiveness of exercise-based cardiac rehabilitation in patients with CHD. Conditions included stable angina, CABG, PCI and coronary artery disease (CAD) with the main diagnosis being myocardial infarction (MI). The mean age of participants ranged from 47.5-71.0 years, with women accounting for less than 15% of those recruited. Fifty-nine percent of trials were carried out in Europe.

The intervention was comprehensive in nature (i.e., included exercise with psychological or education interventions) in 38 trials and 24 trials investigated the effect of exercise alone. The majority of programmes were in a supervised exercise setting with 15 trials being home based. Exercise was mainly aerobic with length of intervention, dose, frequency and intensity varying widely across trials. Anderson et al. (2016)⁸ presented pooled data from the longest follow-up period reported by each RCT (median 12 months).

The meta-analysis by Uddin et al (2015)¹⁷ used three systematic reviews^{8,9,18} including Anderson et al. (2016) to pool data on exercise capacity, an outcome which was not presented in the Anderson et al. (2016)⁸. They included data from 55 trials, (7553 patients) with similar patient and trial characteristics to those found in Anderson et al. (2016)⁸.

Main findings

Mortality

Anderson et al. (2016)⁸ found overall there was no reduction in total mortality with exercise-based rehabilitation (47 trials, relative risk (RR) 0.96, 95% confidence interval (CI) 0.88 to 1.04) but there was a reduction in cardiovascular related mortality compared with no exercise control (27 trials, RR 0.74, 95% CI 0.64 to 0.86)

Morbidity

The risk of hospital admissions was reduced with exercise-based rehabilitation (15 trials, RR 0.82, 95% CI 0.70 to 0.96) but there was no significant impact on the risk of MI (36 trials, RR 0.90, 95% CI 0.79 to 1.04), CABG (29 trials; RR 0.96, 95% CI 0.80 to 1.16) or PCI (18 trials; RR 0.85, 95% CI 0.70 to 1.04). There was evidence of a significant reduction in MI risk in studies with long-term follow-up (RR 0.67, 95% CI 0.50 to 0.90, 10 trials).⁸

Exercise capacity

Uddin et al. (2016)¹⁷ found pooled results for exercise capacity outcomes were on average 0.95 (53 trials, 95% CI:0.76 to 1.41) standard deviation units higher for exercise-based rehabilitation compared to control. For trials reporting VO2max, the pooled-mean exercise-control difference was 3.3 ml/kg/min in favour of exercise-based rehabilitation (95% CI 2.6 to 4.0, 41 trials).

HRQL

No meta-analysis on HRQL was undertaken in Anderson et al. (2016)⁸, due to heterogeneity in outcome measures and reporting methods. Most trials reported improved HRQL compared to baseline with improvements often found in the control group as well.

Fourteen out of twenty trials reported higher levels of quality of life in one or more sub-scales with exercise-based rehabilitation compared with control at follow up. In a quarter of trials there was evidence of significantly higher level of quality of life in half or more of the sub-scales.

Healthcare costs

Seven trials reported data on costs in Anderson et al. (2016)⁸. Three showed no difference in healthcare costs, one found rehabilitation cost less compared to control and three did not report a *p* value for their cost difference.

Four trials also reported healthcare costs, in terms of cost per quality-adjusted life year. Overall, they found rehabilitation to be cost-effective compared to usual care.

Return to work

This outcome was not included in either systematic review.

Limitations

The GRADE assessment of the quality of evidence was moderate for all outcomes except MI and hospital admission which were low. Risk of bias was low or unclear in the majority of trials. More recent trials demonstrated a higher quality of reporting and, therefore, lower risk of bias. A further limitation is that the population studied was predominantly male, young and with low cardiovascular risk.

Future research

Future RCTs are required using patient groups that are more reflective of CHD populations managed in current clinical care, for example the inclusion of higher risk population groups and those presenting with stable angina.

Future trials should include validated HRQL outcome measures and report clinical event outcomes, including mortality and hospital admissions alongside evaluating related health-care costs over follow-up periods beyond 12 months.

2.1.1 Stable Angina Pectoris

There is insufficient evidence to assess the impact of exercise-based rehabilitation on mortality, morbidity and HRQL. Exercise capacity did show a small improvement in patients with stable angina compared to control.

Quality of evidence was low to very low, with GRADE assessment indicating very low certainty of effects for mortality, morbidity and HRQL, and a low certainty of effect for exercise capacity.

This summary is based on a single systematic review
Long et al. (2017)¹⁹ R-AMSTAR score: 42

This Cochrane systematic review included six RCTs (414 patients with stable angina) comparing exercise-based rehabilitation to usual care or a no exercise comparator in their meta-analysis. The mean age of patients ranged from 50 to 66.2 years and the majority of patients were male (range 74% to 100%). Patients within three months of an acute event (MI, PCI or CABG) were excluded and those with unstable angina where revascularisation was planned. Trial populations were small ranging from 24-113 participants (median 86).

Interventions were either exercise-based alone (four trials) or combined exercise and education interventions (two trials). Studies delivering exercise-based rehabilitation in a centre setting alone (one trial), in a home setting alone (three trials) or in both a home and a centre setting (two trials) were included in the analysis. Trial interventions lasted from 6 weeks to 12 months and duration of follow-up was 6-12 months.

Main findings

Mortality

Pooled total mortality showed no difference between exercise-based rehabilitation and control (RR 1.01, 95% CI: 0.18 to 5.67; 3 trials).

Morbidity

Pooled acute MI showed no difference between exercise-based rehabilitation and control (RR: 0.33, 95% CI: 0.07 to 1.63, 3 trials). There was a reduction in revascularisation procedures (CABG or PCI) (RR: 0.27, 95% CI: 0.11 to 0.64, 3 trials) and cardiovascular-related hospital admissions (RR 0.14, 95% CI 0.02 to 1.1, 1 trial) with exercise compared to controls.

One trial showed improvement in angina frequency at six weeks ($p=0.002$) with exercise and another trial showed improvement in angina severity with exercise and an increase in the control group.

Exercise capacity

Pooled exercise capacity showed improvement compared to controls with exercise (standardised mean difference 0.45, 95% CI: 0.2 to 0.7, 5 trials).

HRQL

One trial showed improvement in emotional HRQL score at six weeks follow up ($p=0.04$) and social HRQL at six months, with exercise compared to controls.

Health care costs

One trial reported cost data in favour of exercise-based rehabilitation (\$3708 versus control: \$6086).

Return to work

We did not find a systematic review presenting evidence for this outcome.

Limitations

The effect on all outcomes is very uncertain (very low quality evidence), except exercise capacity where the effect is uncertain (low quality evidence). There were only a small number of trials with low patient numbers and many at a high risk of bias. The authors conclude that the true impact of exercise-based rehabilitation on patients with stable angina is uncertain.

Future research

Further high quality trials are needed to assess the impact of exercise-based rehabilitation on patients with stable angina. These trials should use patient specific outcome measures and evaluate the associated health-care costs. Trials should include patients that reflect the stable angina population, including a greater proportion of women.

2.2 Heart Failure

Exercise based rehabilitation reduces the risk of hospital admissions in the short term and improves exercise capacity and HRQL, for heart failure patients with reduced ejection fraction.

Overall risk of bias was moderate with high heterogeneity in outcome measures and a low representation of women and those with HFpEF.

This summary is based on three reviews;

Taylor et al. 2014⁹ R-AMSTAR score: 39

Zhang et al. 2016²⁰ R-AMSTAR score: 34

Chan et al. 2016²¹ R-AMSTAR score: 31

The Cochrane systematic review by Taylor et al. (2014)⁹ identified 33 trials (4740 participants) with HF, predominantly HF with reduced ejection fraction (HFrEF) and only 4 trials included an undefined proportion of people with preserved ejection fraction (HFpEF). Overall, most trials were small with one US multicentre trial (HF-ACTION) contributing around 50% of included participants. Overall, trials recruited mainly men (median 87%) with a mean age of 51-81 years.

All trials involved performing aerobic exercise with 11 combining this with resistance exercise, 12 trials also had elements of a comprehensive program including either psychological and/or education interventions. The majority were centre based with 5 trials being home-based.

Main findings

a. HFrEF

Mortality

Taylor et al. (2014)⁹ found there was no reduction in all-cause mortality between exercise based rehabilitation compared to an exercise control in trials with one-year follow-up (25 trials, RR 0.93; 95% CI 0.69 to 1.27). However, there was a trend towards a reduction in mortality with exercise in trials with more than one year of follow up (6 trials, RR: 0.88; 95% CI 0.75 to 1.02).

Morbidity

Compared to controls, overall admission to hospital (15 trials, RR 0.75; 95% CI 0.62 to 0.92) and HF specific admissions (12 trials: RR 0.61; 95% CI 0.46 to 0.80) was reduced at 12 months but there was no difference in trials with more than 12 months follow-up (5 trials: RR 0.92; 95% CI 0.66 to 1.29;)⁹.

Exercise capacity

The 2014 Cochrane update did not include exercise capacity hence results for this outcome will be summarised from the systematic review by Zhang et al. 2016²⁰.

The authors included 28 trials, 2533 patients enrolled in trials of short term exercise interventions (8-24 weeks) versus non-exercise control. VO₂ max (mL/min/kg) significantly increased in HF patients after exercise intervention 2.38 (95% CI 1.78-2.99). However, the meta-analysis showed a high level of heterogeneity hence subgroup analysis was performed according to age group showing the level improvement decreased with increasing age: 50-55 years old (5 trials, WMD, 3.57; 95% CI, 2.29 to

4.86, 60-65 years old (10 trials; WMD, 2.35; 95% CI, 2.04 to 2.66 to) and 69-75 years old (5 trials; WMD, 1.11; 95% CI, 0.34 to 1.88).

HRQL

Taylor et al. (2014)⁹ state 19 trials reported HRQL measures; of these, 11 showed superior HRQL with exercise at follow up, with no score lower with exercise than control.

Most trials used the Minnesota Living with Heart Failure Questionnaire, when the results were pooled they showed a clinically important improvement with exercise (13 trials, MD -5.8 points; 95% CI -9.2 to -2.4; $P < 0.001$). When all 19 trials that used HRQL measures were pooled they again show a significant improvement with exercise (MD -9.5; 95% CI -17.5 to -1.5 $P < 0.001$).

Return to work

We did not find a systematic review presenting evidence for this outcome.

Healthcare costs

Three trials investigated the cost-effectiveness of exercise based rehabilitation for HF patients. One trial reported an additional mean healthcare cost in the exercise group compared with control of \$3227/person. Another study reported the mean cost in the exercise group were lower (-GBP477.85/person) than the control group at six months follow up. The last trial indicated exercise based rehabilitation to be a potentially cost effective use of resources in terms of quality adjusted life years and life years saved.⁹ None of the between group differences in costs or outcomes across these three studies achieved statistical significance.

b. HFpEF

Taylor et al. (2014)⁹ did not analyse separately the four trials including a proportion of patients with HFpEF. Hence results from Chan et al. (2016)²¹ will be presented.

This systematic review included eight trials involving 317 patients with HFpEF. Results were similar to those described for HFrEF. Exercise based rehabilitation significantly improved exercise capacity measured as peak VO₂ (MD 2.08 mL kg⁻¹ min⁻¹, 95% C.I. 1.51 to 2.65) and 6-minute walk distance (MD 32.1m, 95% C.I. 17.2 to 47.1), and HRQL (Minnesota Living with Heart Failure Questionnaire MD -6.77 points, 95% C.I. -9.70 to -3.84 and SF-36, 11.38 points, 95% C.I. 5.28 to 17.48)²¹.

Limitations

Trials in all included systematic reviews, mainly included younger men, but this gender imbalance has lessened in more recent trials.

In Taylor et al. (2014)⁹, the overall risk of bias was moderate with some trials not reporting co-intervention details for both exercise and control groups. Heterogeneity across trials was high which may be due to the large treatment effect of HRQL outcomes in trials judged at high risk of bias, including the fact that many trials were small and follow-up was short term.

Papers in Zhang et al. (2016)²⁰ had a high risk of bias overall and the meta-analysis showed a high level of heterogeneity.

Future research

Future trials should reflect the current HF population; women, older people and people with HPpEF remain underrepresented. Trials also need to consider the maintenance of exercise training and longer follow-up periods, as well as measuring cost-effectiveness.

2.3 Interventions for Heart Valve Disease

Exercise based rehabilitation improves exercise capacity and functional capacity in both aortic valve surgery and TAVI patients.

Quality of evidence is low due to the lack of contemporary RCTs comparing exercise to a non-exercise control.

This summary is based on two reviews;

Sibiltz et al. (2016)²² – R-AMSTAR score: 43

Ribeiro et al. (2017)²³ – R-AMSTAR score: 37

2.3.1 Surgery for aortic valve replacement

Sibiltz et al. (2016)²² undertook a Cochrane systematic review and found two trials involving in total 148 patients who had undergone either aortic or mitral valve replacement surgery. Mean ages were 31 and 45 years and one took place in Norway and the other in China. Participants were mainly male: 57% and 72% respectively.

Both trials included aerobic exercise and resistance training and one included a psychological element. The setting was both home and hospital for both trials and longest follow up period were at three months and 12 months.

Main findings

Mortality

Neither trial planned to formally collect data on mortality, the trial in China reported two deaths in the exercise group and none in the control group. No deaths were reported in the Norwegian trial.

Morbidity

A total of 11 serious adverse events were seen across the two trials with no significant difference between groups (RR 1.15, 95% CI 0.37 to 3.62).

Exercise capacity

Both trials reported measures of energy expenditure during exercise (either metabolic equivalents or kilo joules). Trial results, whether presented as individual trials or pooled, showed a significant positive effect of exercise training on exercise capacity at the end of the intervention SMD 0.47 kj, 95% CI 0.13 to 0.81) and at longest follow up (three and 12 months; SMD 0.50, 95% CI 0.14 to 0.85).

HRQL

We did not find a systematic review presenting evidence for this outcome.

Healthcare costs

We did not find a systematic review presenting evidence for this outcome.

Return to work

Only the Norwegian trial reported return to work, finding a non-significant difference in the

proportion of patients in the exercise group compared to the control group returning to work at 12 months follow up (RR. 0.55, 95% CI 0.19 to 1.56. 81% exercise group v 65% in the control group had returned to work).

Limitations

In Sibilitz et al. (2016)²², the GRADE quality of evidence was moderate for exercise capacity, low for return to work and very low for mortality and morbidity.

Both trials had a high risk of bias and included young, mainly male patients. The two trials were conducted in 1987 and 2004, hence are unlikely to reflect the current heart valve population, particularly regarding anticoagulation strategy and novel, less invasive techniques, such as TAVI. Further research is needed.

2.3.2 Contemporary trials in heart valve intervention

Due to the age of trials included in Sibilitz et al. (2016)²², we have chosen to include a further systematic review by Ribeiro et al. (2017)²³. They looked for contemporary evidence for cardiac rehabilitation following surgical aortic valve replacement (sAVR) and TAVI.

This systematic review identified five observational trials that examined the effect of exercise based cardiac rehabilitation on a total of 292 TAVI and 570 sAVR patients. One trial reported findings for only TAVI patients while the others reported results separately for both TAVI and sAVR patients. In general, patients in the trials were older and mainly women and they all took place between 2014-15. All patients underwent supervised exercise for two to three weeks.

Main findings

a. TAVI

Mortality

There is no data on the effect of exercise based rehabilitation on mortality.

From a safety perspective, in general, the TAVI group was older and frailer than those undergoing surgery and showed a higher level of mortality in one trial overall. However, no patients died during the rehabilitation period suggesting exercise based rehabilitation during the post-operative period is safe.

Morbidity

No included trial in this systematic review reported on morbidity.

HRQL

Data on HRQL was found but the results were not reported in this systematic review.

Exercise capacity/functional independence

All five trials included the 6-minute walk test (6MWD). The meta-analysis showed exercise based rehabilitation was associated with a significant improvement in 6MWD (standardised mean improvement 0.69 (0.47 to 0.91); $p < 0.001$). The mean walked distance before exercise based rehabilitation was 186m +_86m, increasing to 257m+_111m after rehabilitation.

The Barthel index was scored in three trials (190 patients) and showed a significant improvement from 77points \pm 19 points increasing to 90 points \pm 14 points after exercise based rehabilitation (significant standardised mean improvement 0.80 (95% CI 0.29 to 1.30); P=0.002)

b. sAVR

Exercise capacity/functional independence

Four trials measured 6MWD and found the mean distance walked before exercise based rehabilitation was 228m \pm 94m, increasing to 315m \pm 122m after rehabilitation. In the pooled analysis, sAVR was associated with a significant 6MWD standardised mean improvement (0.79 (95% CI 0.43, to1.15); p<0.001).

Two trials reported Barthel Index, 80 points 0.93 (0.81, 1.05);21 points before exercise based rehabilitation and 95 points \pm 9 points after rehabilitation (standardised mean improvement (0.93 95% CI 0.67 to 1.18); p<0.001).

Limitations

Although the review by Ribeiro et al. (2017)²³ itself is of high quality (R-AMSTAR score: 37), all included trials were rated low by the authors on methodological quality. This was partly because none of the trials were RCTs and partly due to a lack of detail in the reporting of the trials.

All trials were carried out in Europe and none involved a cardiopulmonary exercise test to give a more precise measure for the effects of exercise on exercise capacity.

Future research

Future trials investigating exercise based rehabilitation following interventions for heart valve disease should be RCTs reflecting the current population with heart valve disease. This tends to be older patients, with more woman and with a higher rate of co-morbidities.

Future trials should also include validated HRQL and exercise capacity outcome measures and report clinical event outcomes, including mortality, hospital admissions and health-care costs over a longer follow up period.

2.4 Arrhythmias

2.4.1 Atrial Fibrillation

Exercise-based rehabilitation for atrial fibrillation (AF) indicates a positive effect on exercise capacity but no clinically relevant effect on HRQL.

GRADE quality of evidence for exercise capacity was moderate and low to very low for all remaining outcomes due to the small number of trials and participants included in the review.

This summary is based on a single review;
Risom et al. (2017)²⁴ - R-AMSTAR score: 41

This Cochrane systematic review identified six RCTs studying exercise-based cardiac rehabilitation for AF with a total of 421 patients, with various types of AF (including those with permanent and non-permanent AF). On average, 71% were male and mean age within trials was 56 to 73 years. Sample sizes ranged from 30 to 210 participants.

The exercise-based programmes in four trials consisted of both aerobic exercise and resistance training, in one trial consisted of Qi-gong (slow and graceful movements) and in another respiratory muscle training. One trial provided an education to both the intervention and control groups and another trial included a psycho-educational element in addition to exercise. Length of intervention ranged from eight to 16 weeks and trial follow up period from eight weeks to six months.

Main findings

Mortality

There were two deaths reported in one of the six trials, one death in each group, judged to be unrelated to the trial.

Morbidity

Only one trial reported serious adverse events as an outcome, however five trials reported a total of eight serious adverse events. There was a very low-quality finding of no clear difference between groups in the number of patients with serious adverse events (RR for non-events was 1.01, 95% CI 0.98 to 1.05).

Exercise capacity

Pooled data from two trials showed exercise-based rehabilitation increased VO₂ peak compared to no exercise (MD 3.76, 95% CI 1.37 to 6.15).

Four trials, with very low quality evidence, showed an increase in the 6MWD in favour of the exercise-based rehabilitation group (MD 75.76, 95% CI 14.00 to 137.53).

Combining data from all six trials showed very low-quality evidence that exercise-based rehabilitation improved exercise capacity (SMD 0.86, 95% CI 0.46 to 1.26).

HRQL

Four trials reported HRQL measured by the SF-36. Results from two trials could be pooled and no difference was found between the exercise and non-exercise groups for physical (MD 1.96, 95% CI -2.50 to 6.42) or mental components (MD 1.99, 95% CI -0.48 to 4.46) measured by the SF-36.

One trial used the Minnesota Living with Heart Failure questionnaire and found no significant difference between groups. Another trial used the Hospital Anxiety and Depression (HADS) questionnaire and, again, found no difference between groups.

Healthcare costs

We did not find a systematic review presenting evidence for this outcome.

Return to work

We did not find a systematic review presenting evidence for this outcome.

Limitations

GRADE quality of evidence was moderate for exercise capacity measured with VO2 peak but this included only two trials. All other outcomes were graded low or very low. Risk of bias was mainly low for most trials.

Due to the small number of trials, small number of participants and a lack of reporting of outcomes the real impact of exercise-based rehabilitation on mortality or serious adverse events cannot not be evaluated from this review.

Future research

Future high-quality RCTs are needed to assess the efficacy of exercise-based cardiac rehabilitation for adults with AF using patient-relevant outcomes, including morbidity, return to work, health-care costs and using disease specific HRQL instruments.

2.4.2 Implantable Cardioverter-defibrillations

Exercise-based rehabilitation improves exercise capacity and reduces the likelihood of implantable cardioverter-defibrillations (ICD) shocks.

Quality of evidence is moderate, due to the small number of included trials with a moderate risk of bias and in the systematic review a lack of clarity about the included patient population.

This summary is based on a single review;
Pandey et al. (2017)²⁵ – R-AMSTAR score: 32

This systematic review included six trials involving 1,603 patients in total (five RCTs and one non-RCT) comparing an exercise-based intervention with a control group in patients with an ICD. The majority of patients had HF with a depressed left ventricular ejection fraction and the most common reason for implantation was primary prevention. Seventeen percent of participants were women.

The mean duration of exercise training was 12 weeks (8-24 weeks) and mean follow up was 15 months (two to 26 months). Five out of six trials involved supervised exercise, with one trial based at home using telemonitoring.

Main findings

Mortality

We did not find a systematic review presenting evidence for this outcome.

Morbidity/disease specific outcome

Five out of six trials reported no exercise-associated ICD shocks (the sixth did not report this outcome).

All trials reported on the number of ICD shocks during the follow-up period. In pooled analyses exercise-based training following ICD implantation was associated with a significantly lower possibility of ICD shocks (pooled odds ratio: 0.47; 95% CI 0.24 to 0.91). When the analyses was limited to RCT (5 trials) pooled OR: 0.45; 95% CI: 0.21 to 0.97..

Exercise capacity

All trials reported peak exercise oxygen uptake. Pooled analyses showed that exercise-based participants had a significant improvement in peak oxygen uptake, compared to those in the control group (weighted mean difference: 1.98 ml/kg/min; 95% CI 0.58 to 3.38). A similar result was found when only analysing the five RCTs.

HRQL

We did not find a systematic review presenting evidence for this outcome.

Return to work

We did not find a systematic review presenting evidence for this outcome.

Healthcare costs

We did not find a systematic review presenting evidence for this outcome.

Limitations

Pandey et al. (2017)²⁵ provide an up to date systematic review on the efficacy of exercise following ICD implantation, however it is unclear in the paper if their focus is solely on HF patients with ICDs or on all patients with ICDs. Some of the included RCTs just include HF and some include all ICD patients, hence the outcomes are unclear.

Trials had a mainly low or unclear risk of bias. Most of the Trials were small with one trial accounting for nearly two thirds of total participants. Pandey et al. (2017)²⁵ included one non-RCT, but this was the smallest trial. Longest follow-up was 26 months, so it is not possible to state the long-term impact of exercise-based rehabilitation.

Future research

Larger trials are required to evaluate the long-term impact of exercise-based rehabilitation on exercise capacity and other clinical outcomes important to patients such as mortality, hospital re-admission and HRQL. Number of ICD shocks are an important outcome in this patient group but this needs to be recorded over a longer follow period.

Currently, there is a systematic review being conducted into exercise-based cardiac rehabilitation for adult patients with an ICD (Cochrane protocol), Kim Nielsen, Ann–Dorthe Zwisler Rod Taylor, Jesper Svenson Jane Lindschou, Lindsey Anderson, Selina Berg (*aniticpated completion date 15/08/17.*)

2.5 Intermittent Claudication

Exercise based rehabilitation, compared with placebo or usual care and medication, significantly improves walking time and distance in people with leg pain from intermittent claudication (IC).

Quality of evidence was moderate, mainly due to the absence of relevant information and the small number of participants in most trials.

This summary is based on a single review;
Lane et al. 2014²⁶ – R-AMSTAR score: 41

This Cochrane systematic review identified 30 trials (1816 patients), comparing an exercise-based rehabilitation with a placebo or usual care (20 trials). Trials, comparing exercise to percutaneous transluminal angioplasty or surgery, were excluded. Patients all had stable leg pain caused by IC. They were diagnosed by questionnaire or clinically by scoring <0.9 on the ankle-brachial index or evidence of peripheral arterial disease (PAD) on ultrasound. Mean age and sex of participants was not given in this review.

The exercise interventions lasted in general from three to 12 months and all included at least twice weekly sessions. All trials used supervised exercise, except the earliest trial from 1966. Types of exercise varied from strength training to pole striding, cycling and upper and lower limb exercises. The majority of trials were small with less than 50 participants with the rest being between 50 and 200. Earliest follow up was at 14 days and the latest at two years.

Main findings

Mortality

Five trials reported mortality. Pooled analysis did not show a significant difference in mortality (risk ratio of 0.71, 95% CI 0.28 to 1.78, $p=0.47$).

Morbidity/disease specific outcome

Overall, there was a small significant difference found in ankle brachial index between the exercise and control groups (12 trials) (MD 0.05, 95%CI -0.00 to 0.09; $P < 0.00001$).

The systematic review found no data on non-fatal cardiovascular events.

Exercise capacity and pain free walking

Maximal walking time was measured in 12 trials. There was a highly significant overall improvement in walking time for those who underwent exercise compared to controls (MD 4.51 minutes, 95% CI 3.11 to 5.92; $P < 0.001$), with an overall improvement in walking ability of 50% to 200% after exercise rehabilitation.

Ten trials reported pain-free walking time, demonstrating a combined improvement of MD 2.87 minutes (95% CI 1.65 to 4.10; $P < 0.001$). Pain-free walking distance also improved by MD 108.99m (95% CI 38.20 to 179.78) (8 trials), after exercise-based rehabilitation compared to control.

The above results were taken from the trials first time point but were maintained up to two years later.

HRQL

Quality of life was measured using the SF-36. Two trials reported three domains which all improved significantly with exercise at three months ('physical function' (MD 6.60 points, 95% CI 2.37 to 10.83), 'vitality' (MD 5.55 points, 95% CI 1.54 to 9.56) and role physical (MD 10.31 points, 95% CI 3.64 to 16.98).

At six months, five trials reported significant improvements of the SF-36 physical components score (MD 2.15 points, 95% CI 1.26 to 3.04) and mental components score (MD 3.76 points 95% CI 2.70 to 4.82).

Return to work

We did not find a systematic review presenting evidence for this outcome.

Healthcare costs

We did not find a systematic review presenting evidence for this outcome.

Limitations

No data was given on non-fatal cardiovascular events and the mortality data is inconclusive. Only a small number of trials considered quality of life and the outcomes varied making comparison difficult.

Quality of evidence was moderate, mainly due to missing relevant information. Risk of bias was low in 11 trials with a further 11 being unclear due to small sample sizes, unclear sequence generation and allocation among other reasons.

Patients with existing co-morbidities where exercise could be unsafe or impractical were excluded and this may be the case for up to a third of patients with IC.

Future research

Future trials are required that use consistent quality of life measures and record fatal and non-fatal cardiovascular events. Another area would be to consider the benefits of exercise in an asymptomatic population or those with multiple co-morbidities which more closely reflects the current IC population.

Health related costs require investigation to determine if the cost of exercise rehabilitation offsets the cost of surgery, hospital admission or other medical complications.

Combined exercise-based rehabilitation and revascularisation

Exercise-based rehabilitation for IC has been demonstrated to significantly improve walking time and distance. In a recent systematic review by Meneses et al. (2016)²⁷, combining exercise and revascularisation was found to be superior to exercise or revascularisation alone. The authors included eight trials with 726 patients with PAD. Combined therapy led to greater improvement in pain-free (mean difference range 38-408m) and maximal walking distances (mean difference range 82-321m), compared to supervised exercise or revascularisation alone. Combined therapy was superior to exercise alone, when measuring ankle brachial index but not in comparison to revascularisation.

The authors suggest that further research is needed to determine the optimum exercise programmes for patients post-revascularisation surgery and methods to improve compliance with exercise programmes²⁷.

2.6 Heart Transplant

Exercise-based rehabilitation improves exercise capacity but has no impact on HRQL in the short term.

The quality of evidence for each outcome was low to moderate as assessed by GRADE. The follow up period was short and trials only included clinically stable patients.

This summary is based on a single review;
Anderson et al. (2017a)²⁸ – R-AMSTAR score: 39

This Cochrane systematic review included ten RCTs comparing exercise-based rehabilitation to no exercise following heart transplant. Participants in the trials were all medically stable and between 0.5 and 61 months post heart transplant (mean 12 months). There were 300 participants in total whose mean age was 54.4 years (45 to 60.6 years) and under 25% were women. Trials were relatively small with between 16 and 52 participants.

Eight trials compared an exercise-based intervention to no exercise, one trial involved exercise with education in the intervention group only and another trial compared high-intensity interval training with moderate-intensity training (hence this trial was not included in the data analysis). Duration of exercise intervention lasted from 8-52 weeks. Settings, dose, intensity and frequency of exercise intervention varied but all included aerobic exercise. Two trials also included resistance training. Trials had a mean follow up period of 12 weeks (range 8 to 52).

Main findings

Mortality

Six studies reported that there were no deaths in either the intervention or the comparator groups.

Six trials reported cardiovascular mortality, with no deaths reported for either the intervention or control groups.

Morbidity

Six trials reported no adverse events. A seventh trial reported one adverse non-fatal event in the control group (a MI).

Six trials did not report data on hospital admissions. Two trials had one cardiovascular related admission in the intervention group and one further trial reported no admissions to hospital.

Exercise capacity

A pooled analysis of the nine trials showed that exercise capacity and maximum oxygen uptake or VO_2 peak improved after exercise based rehabilitation, compared to the non-exercise participants (2.49 mL/kg/min 95% CI 1.63 to 3.36).

HRQL

Three trials reported on the effect of exercise-based rehabilitation on HRQL. Due to the variation in

outcomes, meta-analysis was not possible but the authors looked at whether individual domain results between groups showed significant changes at follow up. When considering all three trial results together, 18 out of 21 HRQL domains showed no difference between the exercise and non-exercise groups.

Healthcare costs

We did not find a systematic review presenting evidence for this outcome.

Return to work

We did not find a systematic review presenting evidence for this outcome.

Limitations

The included exercise interventions were short in duration and the trials had short follow up time (median 12 weeks). The evidence was assessed as moderate in quality, due to incomplete reporting of data and the small sample sizes. Patients were all defined as healthy and medically stable hence they may have a higher baseline quality of life and motivation than the general heart transplant population.

Future research

Larger trials are required to determine the effects of exercise-based rehabilitation following heart transplant over a longer follow up period. They should include measures of HRQL, mortality, risk of readmission and healthcare costs. Future trials could also consider the impact of exercise in the first few weeks and months following heart transplant and in those with ongoing health problems.

2.7 Pulmonary Hypertension

Exercise-based rehabilitation for pulmonary hypertension (PH) showed significant improvements in exercise capacity and to a lesser extent HRQL.

The quality of evidence for all outcomes was low as assessed by GRADE, due to a small number of trials and low number of participants.

This summary is based on a single review;
Morris et al. (2017) – R-AMSTAR score: 42

This Cochrane systematic review included six RCTs but was only able to take data from five (165 patients in total). The majority of participants had Group 1 pulmonary artery hypertension. Mean age of participants was 47-56 years and sample sizes ranged from 10-87 participants.

Interventions ranged in duration from three to 15 weeks and included both in-patient and out-patient exercise rehabilitation programs. Exercise programmes all involved aerobic exercise with some including resistance training and one including an education element for both the intervention and control group. Mean trial follow up was at 12 weeks.

Main findings

Mortality

Mortality was not formally reported but the systematic review does state that there were no deaths recorded during the intervention period of any of the included trials.

Morbidity

Only one trial had one participant who stopped training in one session due to light headedness. No other morbidity outcomes were reported.

Exercise Capacity

The mean 6MWD following exercise-based rehabilitation was 60.12m higher than in the control group (5 trials, 95% CI 30.17m to 90.07m).

Four trials reported peak exercise capacity. There was a significant increase in VO₂ peak in the intervention group after exercise 2.41 ml/kg/min higher (95% CI 1.38 to 3.44 higher) compared to the control group.

The mean exercise capacity, measured as peak power, also increased in the exercise group, MD 16.44 (95% CI 10.90 to 21.99) watts higher after exercise compared to the control group.

HRQL

Two trials reported the SF-36 physical and mental component scores. After exercise, the intervention group's physical component score was 4.63 points higher than the control group (95% CI 0.80-8.47 points) and the mental component score was 4.17 points higher (95% CI: 0.01-8.34 points).

Four trials reported changes in HRQL using the domains of the SF-36 questionnaire. Exercise-based rehabilitation showed substantial improvements for 'role physical', 'vitality' and 'social function' but not for the other domains.

Health-care costs

We did not find a systematic review presenting evidence for this outcome.

Return to work

We did not find a systematic review presenting evidence for this outcome.

Limitations

The GRADE quality of evidence was low for all outcomes with most trials found to be at high risk of bias. It was only possible to report results from five trials as the sixth was an abstract. Trials used a mix of in-patient and out-patient exercise programmes with small numbers of participants with less severe disease.

Future research

Larger RCTs are required looking at the full range of people with PH including those with more severe disease. Trials also require longer follow up periods to ascertain the durability of exercise capacity improvements and the effect of exercise-based rehabilitation on mortality and morbidity.

2.8 Congenital Heart Disease

Adult congenital heart disease

At present, there are no systematic reviews on the efficacy of exercise-based rehabilitation and adult congenital heart disease.

Children and young adults

There exists one systematic review by Duppen et al. (2013) on the effects of physical exercise training programmes in children and young adults with congenital heart disease. The review finds exercise has a significant positive effect on exercise capacity and activity levels. A future systematic review is required that examines evidence for exercise in the adult population with congenital heart disease.

2.9 Cardiac conditions with no current systematic reviews

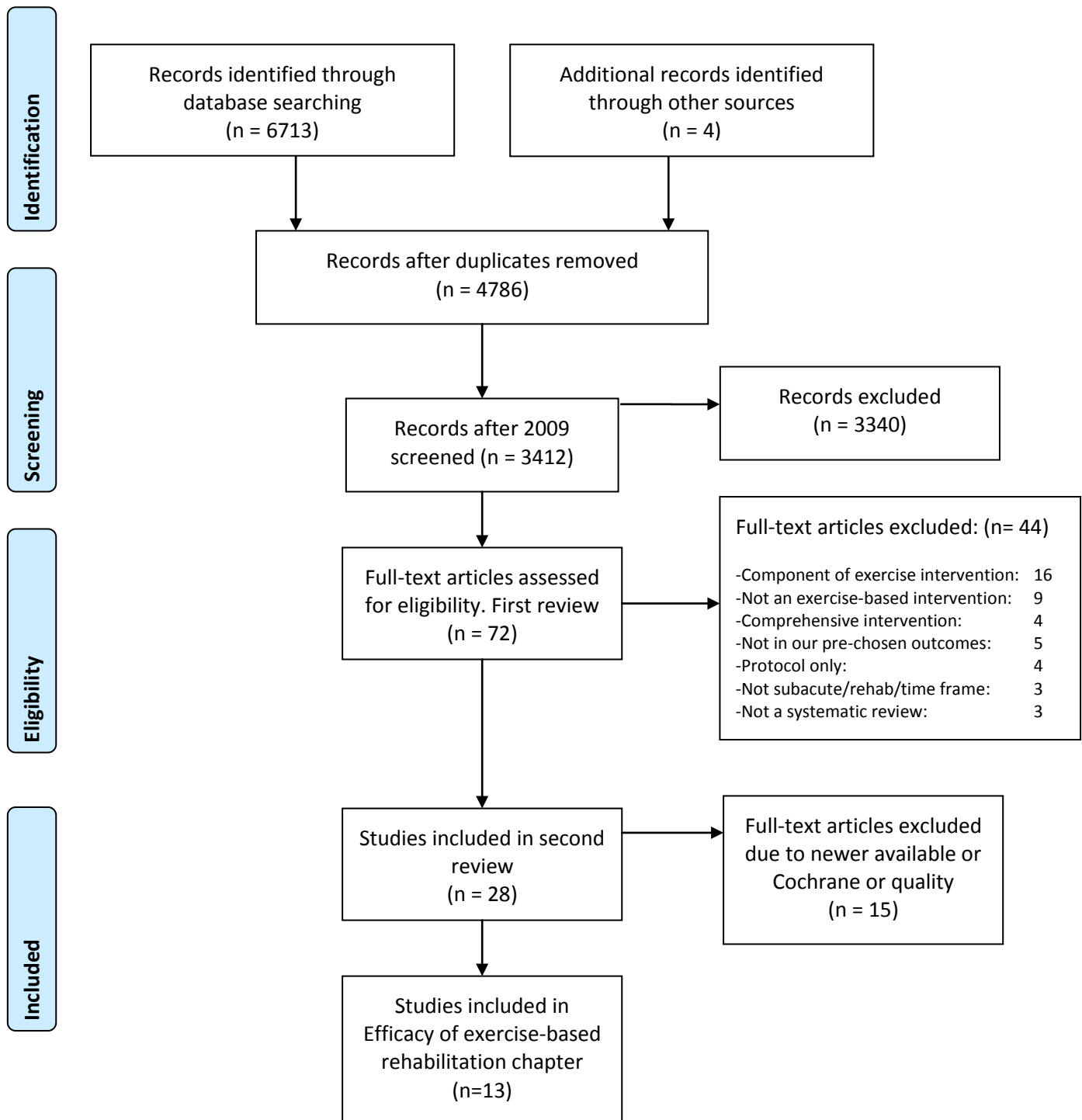
There are several cardiac conditions which are included in the original scope of this report but no systematic reviews were found on efficacy of exercise-based rehabilitation: infective endocarditis, venous embolism, acute aortic syndrome and cardiac arrest survivors.

PROSPERO was searched to discover if there are any systematic reviews planned in these conditions or as updates to the systematic reviews outlined above. Three reviews were found:

Proposed review	Anticipated completion date
Effectiveness of rehabilitation following acute pulmonary embolism: A systematic review Nanna Rolving and Barbara C. Brocki	02/0/17
Effect of acute and chronic exercise on cardiovascular function and haemodynamics parameter in peripheral artery disease patients: a systematic review and meta-analysis Kate Goessler, Bruno Calvacante, Natalia Cunha	04/04/17
Exercise-based cardiac rehabilitation for adult patients with an implantable cardioverter defibrillator (Cochrane protocol), Kim Nielsen, Ann–Dorthe Zwisler Rod Taylor, Jesper Svenson Jane Lindschou, Lindsey Anderson, Selina Berg	15/08/17

2.10 Exercise-based rehabilitation PRISMA flow diagram

The PRISMA flow diagram describes the number of articles included at each stage of the systematic search process and the reasons for exclusion.



3. Psychological and Education-based rehabilitation

The following chapter will present the data from included systematic reviews within Psychological and Education-based rehabilitation. Data is presented in relation to heart conditions. Where there are contemporary reviews for both education and psychology these are both presented.

3.1 Coronary Heart Disease

There exist separate Cochrane reviews for psychological-based and education-based rehabilitation and CHD, hence results for both will be presented separately.

3.1.1 Coronary Heart Disease - psychological-based

Psychological interventions for CHD have no effect on total mortality, rate of non-fatal MI or the risk of revascularisation but does reduce cardiac mortality and psychological symptoms.

GRADE reported that the quality of evidence was moderate for mortality and revascularisation but low for cardiac mortality and psychological symptoms.

This summary is based on a single review:

Richards et al. 2017²⁹ – R-AMSTAR score: 43

This Cochrane systematic review identified 35 trials which randomised 10,703 people with CHD to either psychological-based interventions or usual care. They were mostly men (77%), with a median age of 59.6 years and mostly post MI (65.7%). 27% had undergone a revascularisation procedure (CABG or PCI). Ten trials only recruited patients with psychopathology: primarily depression.

The selected trials evaluated a range of interventions including relaxation, self-awareness, emotional support/client-led discussion and cognitive restructuring techniques. Twenty trials focused on group therapy sessions while 11 trials explicitly involved patients' families. The dose of treatment varied across trials from two to 96 hours (median 12 hours) spent in treatment. The length of follow-up ranged from six months to 10.7 years (median 12 months).

Main findings

Mortality

There was no evidence for risk reduction for total-mortality, (risk ratio (RR) 0.90 CI 0.77 to 1.05) (23 trials).

Cardiac mortality was reduced by 21% (RR 0.79, 95% CI 0.63 to 0.98) (11 trials), following psychological-based interventions compared with control group.

Morbidity

There was no reduction found in revascularisation procedures (RR 0.94, 95% CI 0.81 to 1.11) (13 trials) or for non-fatal infarction (RR 0.79 CI 0.63 to 0.98) (13 trials) following psychological-based interventions.

Psychological outcomes

Depressive symptoms were reduced in the psychological-based intervention group, compared to

controls (SMD -0.27, CI -0.39 to -0.15) (19 trials). Reductions were also found in anxiety (12 trials) and stress (eight trials) in favour of the intervention group.

Exercise Capacity

We did not find a systematic review presenting evidence for this outcome.

HRQL

Ten trials reported HRQL but, due to the variety in outcomes measures, meta-analysis was not possible.

Four trials found statistically significant improvements in at least one dimension of HRQL in the psychologically-based intervention group compared with the comparator group, while six trials reported no difference.

Return to work

Three early trials (1987, 1985, 1983) reported return to work data. Two trials found no difference in the numbers of people returning to work in the intervention and control groups. The third trial found 90% of the intervention group versus 56% of the control group returned to work, but no *P* value was reported in this very small trial.

Healthcare costs

Only two trials reported an economic evaluation as part of their trial data. Both found the additional cost of the intervention was outweighed by the reduction in medical consumption (readmission to hospital, medication, surgery).

Limitations

The GRADE quality of evidence was rated moderate for total mortality and revascularisation and low/very low for morbidity, cardiac mortality and psychological outcomes. This was mainly due to the variability in quality and detail of reporting of interventions in included trials. Anxiety and cardiac mortality outcomes also showed evidence of small study bias.

Risk of bias was high for a quarter of trials, due to incomplete reporting of outcome data. Half of the trials also had unclear methods of randomisation, allocation concealment and blinding of outcome assessors.

Return to work has not been assessed in any contemporary trials and HRQL data was only present in ten out of 35 trials.

Future research

Due to the clinical and statistical heterogeneity of the included trials and the low quality of evidence, future trials are needed to determine the impact of psychologically-based interventions on CHD patients particularly around the impact on psychological outcomes.

These trials should include outcomes that assess the impact on HRQL, cost-effectiveness and return to work. The authors of the systematic review also suggest that new trials should focus on the effect of specific psychological interventions on sub-groups of patients at high risk of poor outcomes, for example those with pre-existing psychopathology.

3.1.2 Coronary Heart Disease - Education-based

Educational-based interventions for CHD showed no reduction in total mortality, MI or hospitalisation, but may reduce the number of cardiac related events and improve HRQL.

Quality of evidence was moderate for both mortality and HRQL, and low or very low for all other outcomes.

This summary is based on a single review;
Anderson et. al (2017b)³⁰ – R-AMSTAR score: 42

This systematic review identified 22 trials randomising 76,864 patients with CHD to either an education intervention, or usual medical care. The mean age of participants was 51.0 to 72.2 years and 25% were women. Most trials were small (range 64-46,606 participants) with the two largest trials contributing 85% of participants.

The educational interventions were a mix of face-to-face, telephone, individual and group sessions. They ranged from one 40-minute face-to-face session with one follow up to a four-week residential stay with follow-up sessions over 11 months. Mean duration of trial intervention was six months and mean trial follow-up was 12 months.

Main outcomes

Mortality

There was no difference in effect of education-based interventions on total number of deaths (189/5187 (3.6%) versus 222/4888 (4.6%); RR 0.80, 95% CI 0.60 to 1.05, outcome at median follow-up 18 months (13 trials).

Morbidity

There was no difference in effect of education-based interventions on fatal or non-fatal MI (7/107 (6.5%) versus 12/102 (11.8%), RR 0.63, 95% CI 0.26 to 1.48, 2 trials, 209 participants). There was a reduction in fatal and non-fatal cardiovascular events (21/152 (13.8%) versus 61/158 (38.6%) in favour of the intervention group) (RR 0.36, 95% CI 0.23 to 0.56), (two trials).

There was no evidence of a reduction in re-vascularisation (three trials 5/228 (2.2%) versus 8/228 (3.5%) RR 0.58, 95% CI 0.19 to 1.71) or in hospitalisations (656/10048 (6.5%) versus 381/4801 (7.9%) RR 0.93, 95% CI 0.71 to 1.21 (five trials).

Exercise capacity

We did not find a systematic review presenting evidence for this outcome.

HRQL

Fifteen trials reported HRQL using a wide range of outcome measures, hence meta-analysis could not be performed. There was some evidence of higher HRQL in some domain scores but overall there was no consistent evidence of HRQL improvement in the education group compared to control.

Return to work

We did not find a systematic review presenting evidence for this outcome.

Healthcare costs

Healthcare utilisation and cost were reported in five trials ranging from £49 GB pounds to \$453 US Dollars for the intervention group. Two trials reported an overall net saving of \$965 USD and \$1420 USD per patient. One trial found an increase in costs of \$52 USD per patient and two trials found no difference in net costs between the groups.

Limitations

Most trials were found to have a low risk of bias but educational interventions were very heterogeneous in the way they were carried out and the types of interventions that were included under the description of education.

Individual causes of death were not reported, so it is not possible to determine how many people died from cardiovascular causes and only two trials reported the number of MI or other cardiovascular events.

Quality of evidence for mortality and HRQL was moderate, for all other outcomes it was low or very low.

Future research

Future research should include longer follow-up periods to allow assessment of the effect on mortality, morbidity and hospital admissions. Trials should include assessment of health-care costs and impact on return to work, as well as ensuring they represent the current population with CHD in terms of gender and age.

3.1.3 Stable Angina

Self-management significantly improves angina frequency, perception of physical limitation, anxiety, depression and reduces silver nitrate use.

Included trials were small with a high risk of bias in several studies. No GRADE analysis was performed and no key characteristics table was included in the systematic review.

This summary is based on a single review:
McGillion et. al, 2014³¹ – R-AMSTAR score: 32

This systematic review and meta-analysis included nine trials involving 1,282 participants with ischaemic heart disease (IHD) with Class I-IV stable angina symptoms for at least three months. Sample sizes ranged from 29 to 452.

Interventions included a combination of cognitive and behavioural angina self-management techniques such as coaching, anxiety management and counselling, along with education on exercise, nutrition, medication, relaxation and energy conservation. Controls received routine or usual care. Five trials included small group sessions. Maximum trial follow-up time was 24 weeks.

Main findings

Mortality

We did not find a systematic review presenting evidence for this outcome.

Morbidity

Angina frequency was measured by counting angina attacks in the last week (three trials) and Seattle Angina Questionnaire (four trials). Pooled overall effect following self-management training showed a significant improvement in angina frequency (SMD: 0.30 (95% CI 0.14, 0.47. $p < 0.001$ (seven trials,)).

Self-management interventions demonstrated a significant reduction in sublingual nitrate use compared to the control group, SMD: -0.45 (95% CI -0.77, -0.20. $p < 0.001$) (two trials).

Exercise capacity

We did not find a systematic review presenting evidence for this outcome.

Psychological outcomes

Three trials reported the HADs. When results were pooled, this showed no significant difference in anxiety scores after the intervention, with a high level of heterogeneity across trials. When a trial with very wide confidence interval was removed, there was an overall significant reduction in HADS-Anxiety scores following self-management training (SMD: -0.27 (95% CI -0.47, -0.06. $p = 0.01$).

HADS-Depression showed a significant reduction after self-management training (SMD: -1.38 (95% CI -2.46, -0.30. $p = 0.01$).

HRQL

Pooled data from four trials using the Seattle Angina Questionnaire found a significant improvement in physical limitation scores at follow-up (SMD: 0.38 (95% CI 0.20, 0.55 $p < 0.0001$). No improvements in disease perception (3 trials) or treatment satisfaction (4 trials) were found.

Exercise capacity

We did not find a systematic review presenting evidence for this outcome.

Healthcare costs

We did not find a systematic review presenting evidence for this outcome.

Return to work

We did not find a systematic review presenting evidence for this outcome.

Limitations

This systematic review did not include a summary of key characteristics for included trials, hence we do not have full details of demographics, trial lengths etc.

Risk of bias for included trials ranged from low to high with only five out of nine trials blinding outcome assessors. Trials were also small and longest follow up was 24 months, hence long term benefits of self-management are not currently known.

Future research

High quality trials are required that include blinding of the assessor, long-term follow up and the inclusion of measures of HRQL, return to work and healthcare costs.

3.2 Heart Failure

Self-management interventions improve time to HF-related hospitalisation or all-cause death and HF-related hospitalisation alone while having a minimal effect on HF related quality of life.

The systematic review did not include risk of bias data or a quality of evidence analysis but a reasonable number of trials and participants were included suggesting that results may be credible.

This summary is based on a single review:
Jonkman et al. (2016)³² –R-AMSTAR score: 26

This systematic review and individual patient data meta-analysis examined the use of self-management interventions for HF patients. The authors identified 32 trials and were able to include data from 20 trials in the analysis (5624 patients diagnosed with HF). Fifty-seven percent were male, the mean age was 69.7 years (SD 12.4). Mean left-ventricular ejection fraction was 39.2% (SD 18.2) and 26% of patients had a preserved ejection fraction. Median time since diagnosis was 1.6 years (Interquartile range 0.1-5.4). Sample size ranged from 42-1023 participants.

The interventions included home visits and telephone calls mostly by specialist nurses, while two trials used group education. The duration of the intervention was between two weeks and 18 months. The control groups all received usual care apart from in two trials, in which some education was given, but this was deemed marginal and in-line with usual care received generally by HF patients.

Main findings

Mortality

The authors used a combined end-point of time to first HF-related hospitalisation or all-cause death. They found self-management interventions significantly reduced risk of time to HF-related hospitalisation or all-cause death, hazard ratio, 0.80 (95% CI, 0.71-0.89, 10 trials).

Morbidity

Self-management interventions reduced risk of time to HF-related hospitalisation HR 0.80 (95%CI, 0.69-0.92, 10 trials).

No effect was found for total length of hospital stay (five trials).

Exercise capacity

We did not find a systematic review presenting evidence for this outcome

HRQL

There was a very small improvement in HRQL at 12 months following self-management interventions compared with control standardised mean difference, 0.15 points; 95% CI 0.00-0.30) (11 trials).

Health care costs

We did not find a systematic review presenting evidence for this outcome

Return to work

We did not find a systematic review presenting evidence for this outcome

Limitations

The authors did assess the risk of bias of included trials and then conducted a sensitivity analysis that showed those trials with a high risk of bias did not alter the overall results. However, as the risk of bias results are not presented we cannot know the general quality of included trials. Two trials included education in their control group, which the authors state was marginal compared to the education in the intervention group, but it may still have impacted on the result.

This systematic review and meta-analyses scored low on the R-AMSTAR, due to missing information on trial selection, excluded trials, quality of evidence and publication bias. The authors gave extensive details on their definition of 'self-management' and at least two components needed to be present for trials to be included, but they did not say which components were included in the trials that were subsequently selected. Hence, it is unknown how similar the trials were when considering the pooled data.

Future research

Future research is required to investigate the effect of self-management interventions on HF patients, particularly in the areas of health care cost and return to work. Trials should include standardised measures for HRQL and follow patients over a long enough period, in order to establish the effect on clinical outcomes such as mortality and readmission rates.

3.3 Arrhythmias

3.3.1 Atrial Fibrillation

Education and behavioural interventions may improve psychological outcomes and decision confidence but the impact of time spent in therapeutic INR¹ range and other outcomes was inconclusive.

Quality of evidence was low to very low, with GRADE assessment indicating uncertainty of effect for all outcome measures.

This summary is based on a single review:

Clarksmith et al. 2017³³ – R-AMSTAR score: 43

This Cochrane systematic review considers the evidence for educational and behavioural interventions to improve patients' ability to maintain their INR control. This is important since patients with AF, with one or more risk factors for stroke, are prescribed anticoagulants to prevent stroke.

The authors included 11 trials with 2,246 participants. Six trials included only AF patients and the rest recruited a mix of patients on anticoagulant therapy (for example, venous thromboembolism, CVD, heart valve prosthesis and MI). Trial size was from 14 to 712 participants and mean age ranged from 59-75 years.

The trial interventions included education alone, decision-support aids and self-monitoring plus education, compared to usual care. Four trials used a one-off session, three used three-four sessions and three trials did not report length of the intervention.

Due to the variation in outcome measures, follow-up periods and type of interventions, only a few outcomes could be included in a meta-analysis. Most results could not be pooled to present conclusive results, hence only the pooled results will be presented below.

Main findings

We did not find a systematic review presenting evidence for the following outcomes; mortality, morbidity, exercise capacity, HRQL, health care costs or return to work.

Time in therapeutic range (TTR)

The effect of self-monitoring in combination with education on TTR was uncertain compared with usual care (MD 6.31, 95% CI -5.63 to 18.25) (two trials).

¹ INR: International normalized ratio: A system established by the World Health Organization (WHO) and the International Committee on Thrombosis and Homeostasis for reporting the results of blood coagulation (clotting) tests.

Psychological outcomes

Two trials (587 participants) compared education to usual care and found education had a small, but positive impact on anxiety (MD -0.62, 95% CI -1.21 to 0.04, $p=0.04$) and depression (MD -0.74, 95% CI -1.34 to -0.14, $P=0.02$).

Decision conflict

The effect of decision aids on decision conflict favoured usual care (MD -0.1, 95% CI -0.17 to -0.02, 2 trials, 721 participants).

Limitations

This is a high quality contemporary systematic review, however the included trials are of low quality and the findings very difficult to pool, due to heterogeneity in interventions and outcomes, hence the authors suggest the results are inconclusive and further studies are required.

Future research

High quality RCTs are required to investigate the impact of education on AF patients' ability to maintain their INR control. However, it should also be considered that as drug management of AF changes maintenance of INR may not be as important. The focus of education interventions may change to primary and secondary prevention. Other outcome measures for this patient group may also be considered, such as adherence to medication in general, HRQL and healthcare costs.

3.3.2 Implantable cardioverter defibrillators

Psycho-educational interventions significantly reduce anxiety and depression in ICD patients and significantly improved the physical component but not the mental component of HRQL.

Quality of evidence was high in the majority of included studies but further systematic reviews are required to establish the evidence for outcomes beyond psychological distress and HRQL.

This summary is based on two reviews:

Habibovic et al. (2013)³⁴ - R-AMSTAR score: 16

Kao et al. (2016)²⁰ - R-AMSTAR score: 34

Habibovic et al. (2013)³⁴ focused their systematic review on anxiety and depression outcomes. They found 17 randomised control trials and present the data for the five most recent trials because they felt the results were comparable to previous trials. Sample sizes were mostly small, with less than 35 participants in either intervention or control groups.

Patients received psycho-educational interventions including education on ICDs, coping skills, cognitive behavioural therapy and relaxation exercises. The control groups received usual care in three trials and two trials used waiting list controls, who received the intervention at the end of the trial. Follow up ranged from one to 12 months.

Habibovic et al. (2013)³⁴ only focused on trials with psychological distress outcomes, hence a further by Kao et al. (2016)³⁵ will be presented.

The systematic review by Kao et al. (2016)³⁵ searched for HRQL evidence for psycho-educational

interventions in patients with an ICD. They included seven randomised control trials, 1017 participants, all adults with an ICD. Mean age of participants in the trials was 55.9 to 64.4 years and 80.4 % were male.

The interventions included ICD education, cognitive behavioural techniques, relaxation and psychological treatment. The interventions were provided via on-line courses, written material, cognitive behavioural techniques, group support and one trial provided psycho-education as part of comprehensive cardiac rehabilitation. The intervention period lasted for between four and 52 weeks (mean 18 weeks) and outcome data was collected for between one and 12 months.

Main findings

Mortality

We did not find a systematic review presenting evidence for this outcome.

Morbidity

We did not find a systematic review presenting evidence for this outcome.

Habibovic et al. (2013)³⁴ present data from one trial that found no difference in cardiac outcomes (shocks and anti-tachycardia pacing) between groups.

Psychological distress

Four out of five trials in Habibovic et al. (2013)³⁴ showed significant improvement in psychological distress (anxiety, depression and post-traumatic stress disorder), while one trial found no difference between control and intervention group after psychological interventions. Effect sizes in these trials ranged from 0.10 to 0.72 for anxiety and 0.23 to 0.61 for depression, indicating a low to moderate-large effect.

Exercise capacity

We did not find a systematic review presenting evidence for this outcome.

HRQL

Kao et al. (2016)³⁵ only searched for and extracted data from trials that included the SF-12 and SF-36. Quality of life was measured in four trials with the SF-12 and in three trials using the SF-36. Data for time points under six months were pooled for analysis.

The psycho-educational interventions improved physical component summary scores in the intervention groups compared to the control groups (mean difference 2.08 points, 95% CI 0.86 to 3.29, $p < 0.001$). However, the interventions did not significantly affect mental component summary scores (mean difference 0.84 points, 95% CI -1.68 to 3.35, $p = 0.52$).

Healthcare costs

We did not find a systematic review presenting evidence for this outcome.

Return to work

We did not find a systematic review presenting evidence for this outcome.

Limitations

Habibovic et al. (2013)³⁴ presents a brief summary of their systematic review and included papers, with a focus on discussing future research. They do not present full participant demographic information or consider the quality of evidence (R-AMSTAR score: 16).

Kao et al. (2016)³⁵ used the Jadad scale to assess quality of the trials. Five achieved high quality scores, however the trials included difference psycho-educational interventions and the majority had less than one hundred participants in each group. Kao et al. (2016) is a 'moderate' quality review, however there are no details on the timeframe, the reason for ICD implantation, or the type of control used in the trials.

Future research

Future larger trials with longer follow-up periods are required, in order to determine the effect of psycho-educational interventions in patients with ICDs.

High quality systematic reviews are needed, in order to establish the evidence for outcomes other than anxiety, depression and HRQL.

3.4 Intermittent Claudication

The evidence for behaviour change techniques to improve walking in people with IC is currently inconclusive.

The evidence was of limited quality due to the small number of trials, small numbers of participants and the high risk of bias in included trials.

This summary is based on a single review;

Galea, 2013³⁶ – R-AMSTAR score: 34

This systematic review included six RCTs evaluating behaviour change techniques explicitly aimed at improving walking in people with IC. Improving walking ability is a key component of managing IC³⁷. There was a total of 434 participants, whose mean age was 67.3 years and 64% were male. Sample sizes ranged from 23 to 145.

From the trials, the authors identified 11 different behaviour-change techniques, most frequently barrier identification with problem solving, self-monitoring and feedback on performance that were given in conjunction with walking advice. Control groups received walking advice in four trials and walking advice plus usual care or an attention placebo in two trials. Number of sessions ranged from one to seven and two of the trials gave the intervention in a group. Intervention setting varied, with one given by telephone and another in the patients' own home with the rest in being centre-based.

Main findings

Mortality

We did not find a systematic review presenting evidence for this outcome.

Morbidity

One high quality trial found greater improvement in pain free walking ability in the intervention group compared to control (MD 150.0 seconds; 95% CI 65.5 to 234.5; $p < 0.001$). Two other low quality trials found no difference between groups.

One high quality trial showed the change in mean 6-day step count (the mean number of steps taken by the patient over six days) was greater in the intervention group (MD 1,674.2 steps; 95% CI; 156.0 to 3,188.4; $p = 0.03$), versus walking advice and attention placebo alone. A second, high quality trial and a small pilot trial showed no change in mean 7-day activity time following behaviour change techniques compared to control.

Exercise capacity

Due to the heterogeneity in findings no meta-analysis was performed.

Four trials reported maximal walking ability. One high quality trial reported significantly greater improvements in maximal walking ability at three months in the intervention versus control groups (Mean Difference 134 seconds; 95% CI: 39.7 to 228.3; $p = 0.005$). Improvements were also found in a low quality trial, while two found no difference (one at three months the other at six months follow-up).

HRQL

We did not find a systematic review presenting evidence for this outcome

Health care costs

We did not find a systematic review presenting evidence for this outcome

Return to work

We did not find a systematic review presenting evidence for this outcome

Limitations

Risk of bias was high in the majority of studies, mainly due to inadequate allocation concealment and none of the studies blinded outcome assessment. Studies were small with two being pilot studies. Reported outcomes were too heterogeneous to complete a meta-analysis and interventions varied in type, frequency and setting making comparison of trials difficult.

Future research

Larger RCTs are required to determine if behaviour change techniques improve walking in people with IC. The review authors suggest that the low number of sessions in some of the studies maybe responsible for the equivocal results and that further studies should investigate whether increased dose would effect the outcome.

None of the studies used specific psychosocial outcomes to investigate the effects of behavioural change techniques or considered outcomes such as HRQL or the impact on health-care costs. These should also be included in any future trials.

3.5 Congenital heart disease

Lane et al. (2013)³⁸ conducted a Cochrane systematic review to assess the efficacy of non-pharmacological treatments for treating depression and improving quality of life for adults and young adults with congenital heart disease. This was a high quality systematic review but it did not find any RCTs within the condition Congenital heart disease.

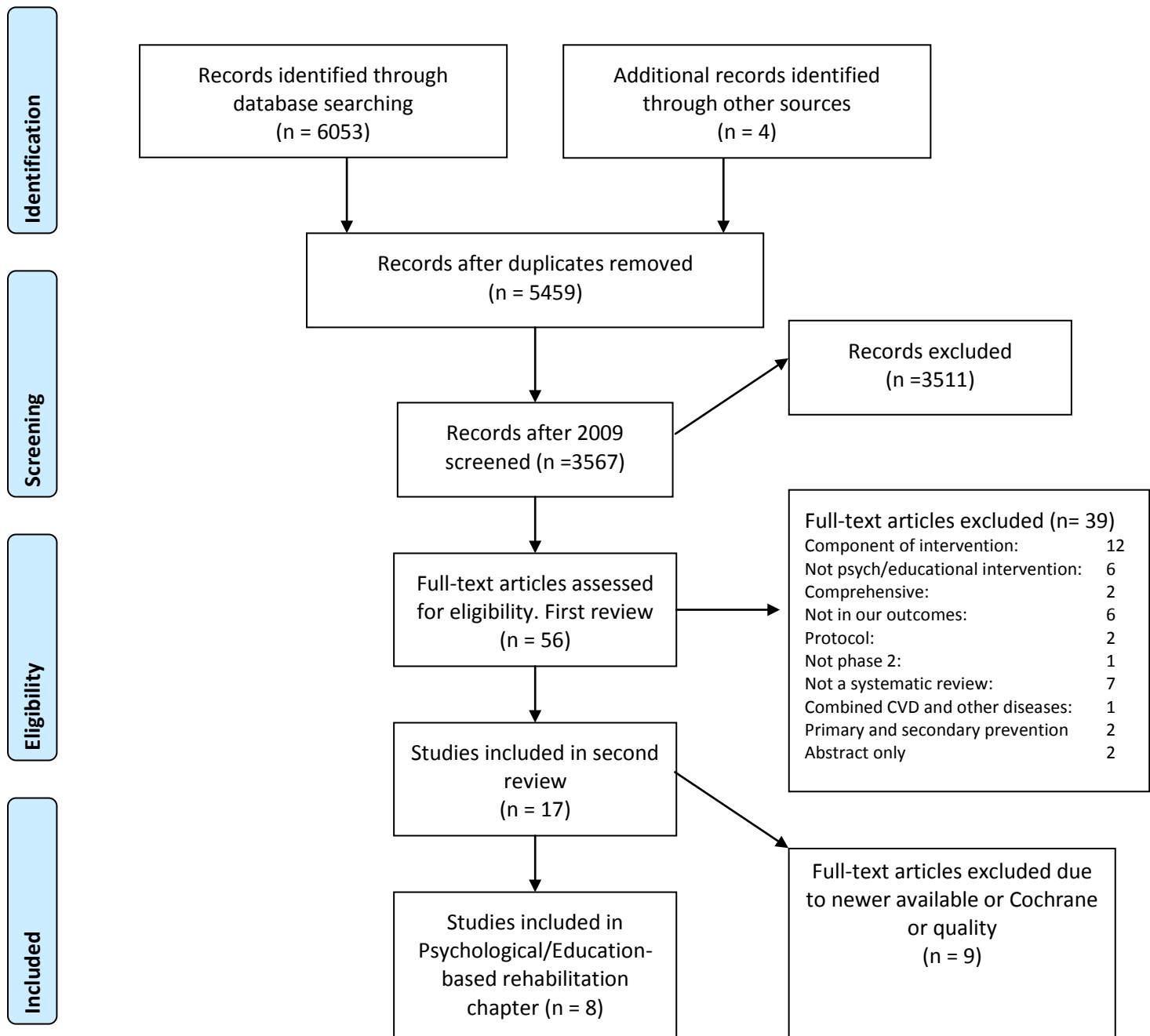
3.6 Cardiac conditions with no current systematic reviews

For the remaining cardiac conditions, that are included in the original scope of this report, no systematic reviews were found on efficacy of psychological and education-based rehabilitation interventions for heart valve disease, PH, heart transplant, infective endocarditis, venous embolism, acute aortic syndrome and cardiac arrest survivors.

A search of the PROSPERO database found one planned systematic review about cardiac arrest survivors and psychological interventions: A rapid review of psychological interventions following out of hospital arrest, Rosalind Case, Susie Cartledge, Janet Bray Dion Stub (*anticipated completion 23/03/17*).

3.7 Psychological and education-based rehabilitation PRISMA flow diagram

The PRISMA flow diagram describes the number of articles included at each stage of the systematic search process and the reasons for exclusion.



4. Rehabilitation and non-pharmacological secondary prevention

The previous chapter on psychological and educational-based rehabilitation, presented the evidence for interventions that includes advice on smoking and diet. Hence, in this chapter, we will consider only systematic reviews that have looked at the evidence for rehabilitation interventions that promote adherence to smoking cessation and dietary treatment.

There have been few trials that have investigated the efficacy of dietary education alone in the secondary prevention of cardiac disease and almost no systematic reviews. However, there is one trial that specifically reviewed nutritional interventions in heart failure.

4.1 Smoking cessation

Psychosocial interventions for smoking cessation in CHD show improved abstinence rates at one year compared to controls but not over a longer period of time.

Quality of evidence is low due to the high risk of bias, poor reporting of trials, use of non-validated outcomes and high heterogeneity in interventions.

This summary is based on a single review:

Barth et al. 2015³⁹ – R-AMSTAR score: 42

This Cochrane systematic review included 40 RCTs (7682 patients) involving patients with CHD, who received either usual care or a specific smoking cessation intervention. Mean age was 50-60 years, 70-90% of the patients were male, and the majority were post-MI.

The interventions had to include a psychological element, but were delivered in a variety of methods and settings and either as stand-alone or as part of a comprehensive programme of CR.

An important consideration before considering the evidence for this intervention is that after a cardiac event 30% to 50% of smokers with CHD quit without professional help.

Effect of a psychosocial intervention on smoking abstinence

Overall, there was a positive effect of interventions on abstinence after 6-12 months (risk ratio 1.22, 95% CI 1.13 to 1.32, abstinence rate treatment group =46% and in the control group =37.4%). Brief interventions of less than one month or with no supporting follow up contact were not effective. Seven trials collected abstinence data past 12 months, but found that the short-term benefits were not sustained.

Limitations

Trials had a low risk of selection bias, but high risk of detection bias due to many being unblinded or using a non-validated assessment of smoking status

There was high heterogeneity among the trials, in terms of interventions used and some trials included the use of nicotine patches. The authors also note that greater effects were found in trials of lower quality, this may cause an overestimation of the effectiveness of psychosocial smoking interventions on CHD patients.

Future research

Future trials should include cost-effectiveness, continue follow up beyond 12 months and include a validated measure of abstinence.

Improved reporting of trial methods, including whether medications were used to assist with quitting, are also required.

4.2 Diet and heart failure

Dietary based educational interventions for HF may improve sodium intake, weight monitoring, mortality and readmission rates.

Included trials were small with heterogeneous outcome measures, no measure of quality was provided and the quality of the systematic review itself was low.

This summary is based on a single review:

Abshire et al. (2015) – R-AMSTAR score: 24

The evidence for specific dietary treatment and CVD is presented in the National Clinical Guidelines for Cardiac rehabilitation report by Sundhedsstrelsen (2013)¹. This report also systematically reviewed the evidence for the effectiveness of diet and rehabilitation interventions. Hence, our report only searched for systematic reviews after 2013.

This systematic review considered the effectiveness of both educational interventions and specific prescriptive nutritional interventions, but only the educational intervention data will be presented.

Seven trials were included focusing on educational interventions to improve nutritional knowledge and compliance with dietary recommendations in HF patients. All were RCTs with a mean age from 51-75 years with most trials including <40% women. All patients had stable or compensated HF. Sample sizes were small in six studies (range 46-117) with the seventh trial involving 1,518 participants.

All control groups received usual care and in five trials the control group received written dietary material. All the intervention groups received the written information and either face-to-face counselling or telephone education, but it is not clear which interventions were individual or group-based. Other educational interventions included; nurse/dietician-led sessions, sodium goals, individualized education/planning, food diary review with participant, family involvement and published materials or online resources available. The intervention timeframe ranged from 14 days to 36 months with trial follow up lasting from six months to 36 months.

Main outcomes

Educational interventions resulted in significant improvement in urine sodium excretion (two trials), self-reported sodium intake (four trials) and daily weight monitoring (two trials).

One trial delivering dietary education over the telephone showed decreased mortality and readmission rates.

No meta-analysis of data was performed.

Limitations

In five of the trials both control and intervention participants received written information on recommended diet and both groups showed some improvement. No recognised tool was used to measure quality of the trials, quality of evidence or risk of bias.

All but one of the trials were small pilot trials suggesting results could be under powered. Outcome measures were heterogeneous hence meta-analysis was not performed.

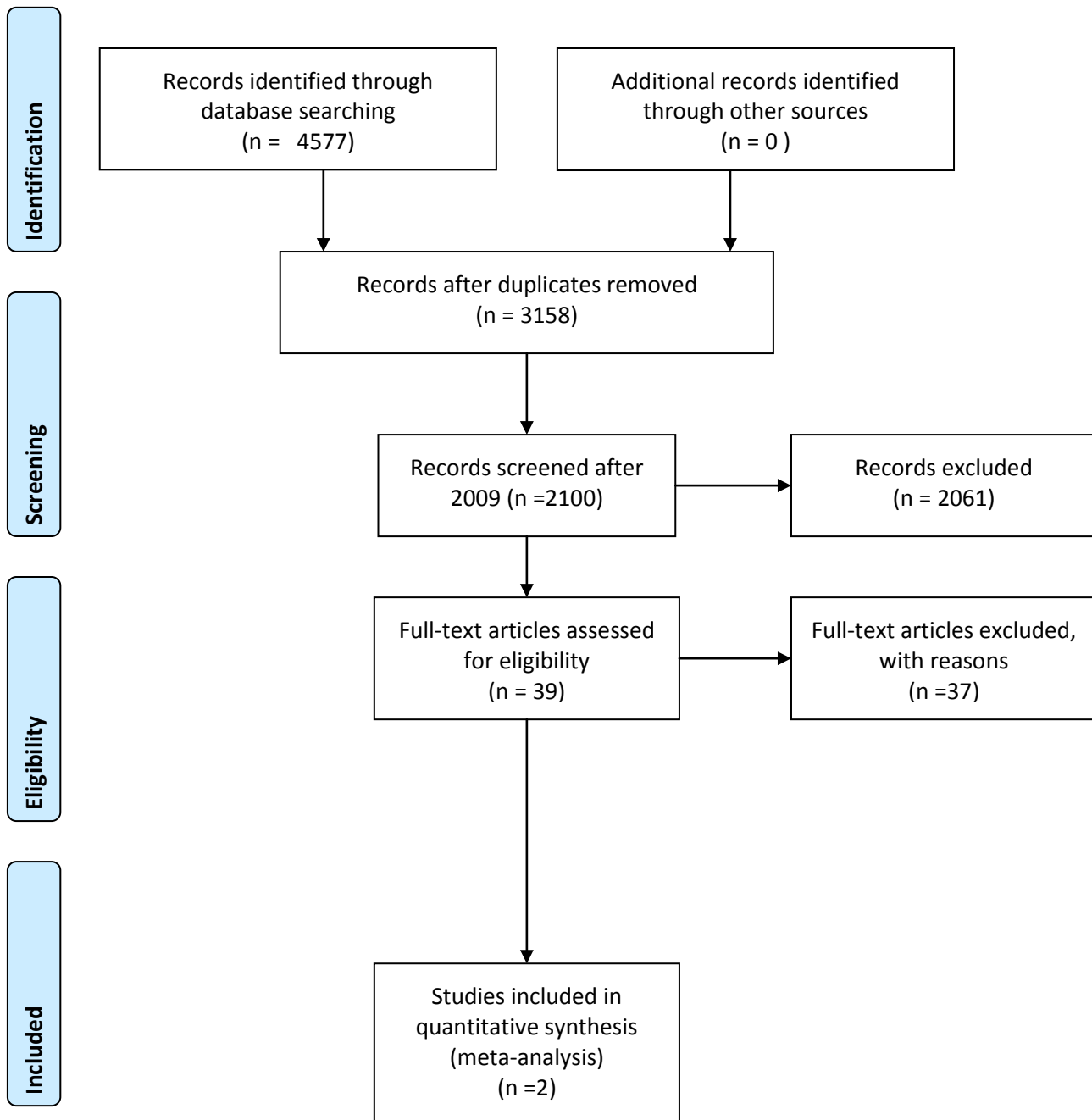
The overall quality of the systematic review was low.

Future research

Future trials should fully describe interventions with published protocols and with the educational materials fully available. Cost-effectiveness and feasibility of interventions should be determined and follow-up time frames should reflect current healthcare resources. In future trials, adherence to advice should be collected via a validated objective measure and trials should consider the involvement of family in any nutritional educational intervention.

4.3 Secondary prevention PRISMA flow diagram

The PRISMA flow diagram describes the number of articles included at each stage of the systematic search process and the reasons for exclusion.



5. Palliative care for cardiovascular diseases

There are very few systematic reviews in palliative interventions and CVD. There are currently no reviews considering the evidence for palliative care in the rare CVD conditions with high mortality or shortened life-expectancy, for example acute aorta dissection, endocarditis and severe congenital conditions. Palliative interventions and HF have been investigated and RCT evidence from two recently conducted systematic reviews is presented below.

5.1 Palliative interventions and heart failure

Palliative care is associated with improvements in HRQL, symptom burden and reductions in re-hospitalisation for patients with a life-limiting primary diagnosis of HF.

However, the quality of this evidence is low as it is based on a small number of RCTs with a high risk or unclear risk of bias and high levels of statistical heterogeneity.

This summary is based on two reviews:

Kavalieratos et al. (2016)⁴⁰ – R-AMSTAR score: 30

Diop et al. (2017)⁴¹ – R-AMSTAR score: 22

Both reviews conducted searches within one month of each other and both report analyses for HF patients. Because of significant differences in the quality of the systematic reviews, as assessed using R-AMSTAR, we focus on evidence from the higher quality review (Kavalieratos et al (2016)⁴⁰), this aimed to determine the association of palliative care interventions with HRQL, symptom burden and other outcomes for people with life-limiting illness, including HF patients.

Kavalieratos et al (2016)⁴⁰ identified 14 RCTs of HF patients treated with a wide spectrum of interventions consistent with the philosophy or components of palliative care. Interventions ranged from interdisciplinary specialised palliative care to those in which palliative care domains were delivered by a non-palliative care specialist. Interventions addressed a range of palliative care components such as structure, physical, psychological, social, spiritual and legal elements; however, no interventions described cultural assessment as an aspect of the intervention or reported using culturally sensitive materials.

Main findings

HRQL

Improvements in HRQL are reported in individual trials. Pooled data from three RCTs (assessed as being at high risk of bias and including 603 HF patients suffering advanced end stage chronic HF (NYHA stage III or IV) or hospitalised for acute HF) found a non-significant association (SMD: 1.98 (95% CI 0.56 to 4.51 p=0.11) between palliative care and control group patients HRQL at one to three months follow-up.

Diop et al (2017)⁴¹ noted improvements in HRQL in five of six studies (in a total of 589 HF patients, and including four RCTs) in their review. Assessments utilised include the Chronic Heart Failure Questionnaire and Minnesota Living with Heart Failure Questionnaire. Diop et al (2017)⁴¹ stated that heterogeneity among trials including the use of multiple instruments to assess HRQL prevented them from undertaking meta-analysis.

Symptom relief

Improvements in HRQL are reported in individual trials. Pooled data from three RCTs (two RCTs assessed as being at high risk of bias and including 251 HF patients (acute and end stage e.g. NYHA stage III or IV); one RCT of multiple sclerosis patients) found no association between palliative care and improvement in patient burden at one to three months follow-up (SMD: -1.95 (95% CI - 4.4, 0.49 $p=0.12$) (Kavalieratos et al (2016)⁴⁰).

Diop et al (2017) report that six of seven studies (in a total of 620 HF patients and including four RCTs) reported improvements in symptoms. Improvement was most frequently seen with dyspnoea and sleep quality, depression and anxiety⁴¹. The assessments used to gather information about symptoms varied across studies. Tools that assessed a range of symptoms included the Edmonton Symptom Assessment Scale and Kansas City Cardiomyopathy Questionnaire, but other assessments, such as the Profile of Mood States and Brief Pain Inventory measured individual symptoms. Diop et al (2017)⁴¹ stated that heterogeneity among trials including the use of multiple instruments to assess HRQL prevented them from undertaking meta-analysis.

Hospital re-admissions

Diop et al. (2017)⁴¹ report reduced rehospitalisation among home-based palliative interventions for HF patients. Pooled data from three RCTs (assessed to be of either high or unclear risk of bias and including 253 HF patients (chronic and end-stage)) found that home-based palliative care consultations in HF patients lowered the risk of rehospitalisation by 42% (relative risk (RR): 0.58; 95% CI 0.44 to 0.77). There was no evidence of statistical heterogeneity ($I^2=0\%$; p =not clearly reported)⁴⁰.

Kavalieratos et al (2016)⁴⁰ report that five trials, all of these were home-based interventions involving either HF or mixed-disease samples, reported significant reductions in hospital utilisation; of these four were judged of high risk of bias and one as unclear risk.

Limitations

Whilst both systematic reviews undertook searches at similar times and both reviews included (although Diop et al (2017)⁴¹ was not limited to) RCTs, these studies were rated differently in overall quality as assessed using R-AMSTAR. Only one of the systematic reviews (Kavalieratos et al (2016)⁴⁰) performed a risk of bias assessment of included trials and discussed their review findings in relation to quality of evidence. Differences between reviews regarding trial inclusion, data extraction and reporting were also noted, for example, Kavalieratos et al (2016)⁴⁰ did not extract HRQL outcomes (measured using SF-36) from a trial while Diop et al (2017)⁴⁰ did; and Diop et al (2017)⁴¹ did not include a relevant trial containing outcome data for HRQL in HF patients, while Kavalieratos et al (2016)⁴⁰ did. There was minimal information from included studies in both systematic reviews on severity of HF, social determinants of health, types of caregiver involvement and patient's attitudes towards care and this limited performance of meta-analyses of the impact of these factors on the effectiveness of palliative care interventions for patients with advanced HF.

No GRADE analysis was performed.

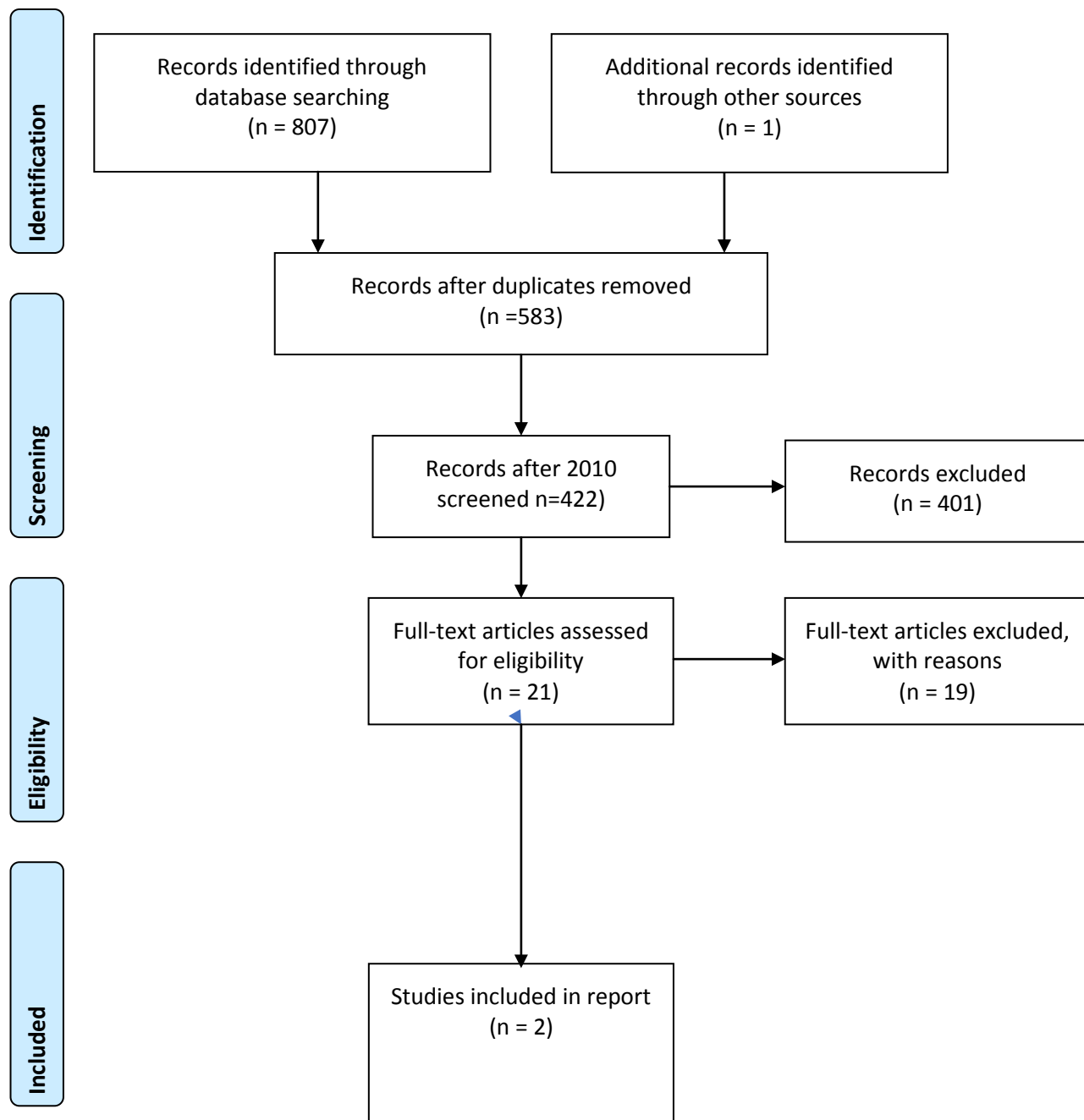
Future research

Additional high quality RCTs are needed to evaluate the role of palliative care in HF and other CVD indications. Future studies should assess patient-reported outcomes using a core set of standardised and validated measures appropriate for seriously ill patients at similar time points.

Future studies should aim to identify the efficacious component(s) of palliative care. A research gap exists to address the link between social determinants of health and patient-centred outcomes, such as symptom relief and HRQL. Future studies should consider the impact of the patients' social environment, services offered and timing of interventions when designing palliative care programmes to maximise the efficiency and quality of care delivered to patients with HF. Finally, trials are needed to establish optimal modes of palliative care delivery that help caregivers in addition to patients.

5.2. Palliative care for cardiovascular diseases PRISMA flow diagram

The PRISMA flow diagram describes the number of articles included at each stage of the systematic search process and the reasons for exclusion.



6. Discussion

6.1 Limitations of the report

There are several limitations that should be considered. First, given the wide scope of the review, we only focused on the effectiveness of rehabilitation and palliative interventions for CVD relative to control. We did not consider the relative effectiveness of different components of interventions (for example, type, duration, frequency of exercise training) or settings.

Second, we focused on existing systematic reviews and meta-analyses of RCTs, as these are recognised as the highest level of evidence. Given the time and resource constraints, it was not possible to directly search for RCTs or undertake an update or de novo primary systematic review to include this evidence. However, where possible, we sought to identify the most recent and comprehensive systematic reviews.

Third, we excluded systematic reviews on interventions that specifically targeted interventions aimed at improving adherence to rehabilitation for CVD. However, adherence was included as an outcome in the chapter evaluating the evidence for rehabilitation interventions that promote strategies to follow dietary or smoking advice. We also excluded systematic reviews of rehabilitation interventions where exercise, psychological, education and medication management are all included as it was not possible to assess the effectiveness of individual interventional components.

Finally, we used the R-AMSTAR tool to determine the quality of included systematic reviews. As this tool effectively assessed the quality of reporting, we recognise that it may be positively biased towards the lengthier Cochrane reviews. Given the constraints of the project, we did not have time to contact the authors of included systematic reviews to clarify missing aspects other their reporting. The R-AMSTAR tool assesses the quality of the systematic review and not the quality of the RCTs. Some of the included systematic reviews provided a summary of the quality of the included trials, and, in many cases, assessed the certainty of effect on outcomes using the GRADE tool.

6.2 Summary of Findings

This summary of finding section draws on the results presented in each of the four evidence summary chapters. An overview of the results is also shown in Tables 2 and 3.

Exercise-based rehabilitation

The largest amount of evidence for exercise-based rehabilitation exists for patients with CHD. The two included systematic reviews showed positive effects for cardiovascular mortality, hospital admission, exercise capacity and HRQL. These reviews included a total of 63 RCTs, primarily in post-MI and revascularisation patients. The systematic reviews for HF and IC included 33 and 30 trials, respectively, and found positive results, in terms of hospital admission, exercise capacity and HRQL. The majority of evidence for exercise rehabilitation in HF is limited to HF with reduced ejection fraction.

A systematic review was identified for each of the six following conditions: stable angina, heart valve implantation, PH, AF, ICD and heart transplant. Whilst these reviews are based on smaller numbers of trials than CHD, they all showed positive improvements in exercise capacity with exercise-based rehabilitation. However, only a total of three trials from across these six reviews included HRQL. They trials found a positive effect on HRQL for stable angina and PH patients, with no effect shown in heart transplant patients.

Furthermore, only three systematic reviews included disease-specific outcomes related to patient symptoms; angina frequency/severity measured in patients with SA, number of ICD shocks in ICD patients and ankle brachial index in patients with IC. Both angina frequency/severity and ICD shocks reduced with exercise but there was no change to ankle brachial index in patients with IC.

Healthcare costs were only reported in CHD, HF and SA. They showed positive results but involved a small number of trials (seven, three and one, respectively). Return to work data was only presented in the heart valve surgery systematic review and showed positive effect of rehabilitation on return to work. The two included trials were old and no effect on healthcare cost was found.

No systematic reviews of exercise-based rehabilitation were found for infective endocarditis, cardiac arrest survivors, congenital heart disease, venous embolism and acute aortic syndrome.

The overall quality of the included systematic reviews was low to moderate, with the highest quality evidence for CHD and HF. None of the included systematic reviews included all six of our pre-determined outcome measures.

Psychological and education-based rehabilitation

Systematic reviews for the effectiveness of psychological and education-based rehabilitation were found for six CVD indications; CHD, SA, HF, AF, ICDs and IC. There were no systematic reviews identified for heart valve disease, PH, heart transplant, infective endocarditis, venous embolism, acute aortic syndrome and cardiac arrest survivors

There are two separate systematic reviews on psychological and education-based rehabilitation for CHD, including a total of 57 trials. Psychological-based rehabilitation for CHD showed positive benefits in fatal/non-fatal cardiovascular events, psychological symptoms, HRQL and healthcare costs. Education-based rehabilitation for CHD was shown to improve fatal/non-fatal cardiovascular events

and, in two trials, to be cost-effective. The CHD psychological review was the only review to include return to work and healthcare costs, while the CHD education review included only healthcare costs.

The systematic reviews for the other five CVDs all combined psychological and education rehabilitation interventions. The systematic review for HF contained 32 trials. The review combined psychological and education-based rehabilitation under the term 'self-management'. It showed positive benefits in all-cause mortality, hospital admission and HRQL but the quality of the review was low (R-AMSTAR = 26) and there was no information on the quality of included trials.

The systematic reviews for the other four CVDs all had small number of trials, ranging from six to 11 trials. Psychological and education-based rehabilitation improved psychological outcomes for SA, AF and ICD patients but was not reported for IC. HRQL was only reported for SA and ICD and showed only a trend towards a positive effect.

All four reviews reported disease specific outcomes. Self-management interventions were found to positively affect angina frequency/sublingual nitrate use for SA patients and behaviour change techniques to improve pain free walking ability for IC. There was no effect found for AF (time in therapeutic range/decision conflict) and ICD (number of shocks and anti-tachycardia pacing).

Overall, the quality of evidence was low. Only the CHD systematic review found moderately graded evidence level, for mortality, morbidity and HRQL. No systematic reviews were found for nine of the included CVD conditions (heart valve surgery, TAVI, infective endocarditis, cardiac arrest survivors, congenital heart disease, PH, heart transplant, venous embolism and acute aortic syndrome). Only the CHD review found evidence for return to work and healthcare costs, in relation to psychological and education-based rehabilitation.

Secondary prevention

The chapters on exercise and psychological and education-based rehabilitation describe interventions that include dietary and smoking cessation strategies. Hence, we only searched for reviews on secondary prevention that presented smoking or dietary interventions alone.

The systematic review on smoking cessation and CHD found interventions improved abstinence rates at one year but not over a longer period. The quality of the systematic review was high but quality of the included trials was low.

The systematic review on dietary-based education and HF found education improved sodium intake, weight monitoring and hospital readmission rates. However, the review was of low quality, involved only six trials and no information was given on the quality of included trials.

No systematic reviews for secondary prevention were identified for other CVD indications.

Palliative care for CVD

Two systematic reviews were found investigating palliative care interventions for HF. They found palliative interventions were associated with improvements in HRQL and reductions in symptom burden and re-hospitalisation for patient with a life-limiting primary diagnosis of HF. No GRADE analysis was performed in either review.

No systematic reviews of palliative care interventions were identified for other CVD indications.

6.3 Recommendations for Future Research

1.	Avoid duplication of previous studies where evidence is well established, for example, in CHD and HF.
2.	Instead, prioritise RCTS that establish the effectiveness of rehabilitation in CVD indications where there is currently little or no evidence.
3.	Where effectiveness of CR is well established, RCTs should focus on real-world implementation, quality assurance and overcoming barriers to participation or adherence.
4.	RCTS are needed involving innovative delivery models where the content and components of an intervention, for example, the setting, type or frequency of an intervention are examined.
5.	Future RCTs need to target populations that are more representative of clinical practice (for example, higher risk, older and more female groups).
6.	RCTs should reflect the typical clinical setting, for example avoiding highly selective inclusion criteria, using community locations and designing interventions and timeframes that are feasible in routine practice.
7.	Where interventions are very complex, studies should follow clinical guidelines on CR, so that most of the intervention design is based on established evidence and the effectiveness of the innovative element can be clearly identified.
8.	RCTs should use agreed definitions for outcomes and should include reporting of events (especially death and hospitalisations), socio-economic outcomes (return to work and costs), patient reported outcomes and disease specific outcomes tailored to the symptoms of specific CVDs.
9.	Future RCTs need to be better reported and conform to current agreed reporting guidelines for example CONSORT or TIDiER.
10.	Future RCTs should focus on sub-groups of patients at high risk of poor outcomes, for example, those with pre-existing psychopathology and screen patients to identify those who would most benefit from the intervention.
11.	High quality RCTs are required to evaluate the efficacy of dietary and smoking interventions in CVD indications.

12.	High quality RCTs are needed to evaluate the role of palliative care in HF and other CVD indications and identify the efficacious components. Future studies should assess patient-reported outcomes using a core set of standardised and validated measures appropriate for seriously ill patients, taken at similar time points.
13.	Trials are needed to establish optimal modes of palliative care delivery for both patients and caregivers. Future studies should consider impact of factors such as social environment, services offered and timing of interventions to maximise efficiency and quality of care.

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Appendices

Appendix 1: Full search terms for the six systematic reviews

Cardiovascular disease terms used in combination with specific search area (1-6 see below)

- #1 MeSH descriptor: [Heart Arrest] explode all trees 1484
- #2 (cardiac near/3 arrest*):ti,ab 1970
- #3 (heart near/3 arrest*):ti,ab 91
- #4 (cardiopulmonary near/3 arrest*):ti,ab 138
- #5 (sudden near/3 death):ti,ab 1500
- #6 asystole*:ti,ab 177
- #7 (myocard* near/2 contract*):ti,ab 427
- #8 MeSH descriptor: [Intermittent Claudication] explode all trees 837
- #9 claudica*:ti,ab 1536
- #10 MeSH descriptor: [Peripheral Vascular Diseases] explode all trees 2507
- #11 MeSH descriptor: [Vascular Diseases] this term only 482
- #12 (peripher* near/3 (occlu* or arteri* or vascular)):ti,ab 3541
- #13 (arterial near/3 (obstruct* or occlus*)):ti,ab 1058
- #14 MeSH descriptor: [Arteriosclerosis Obliterans] this term only 76
- #15 MeSH descriptor: [Atherosclerosis] this term only 688
- #16 MeSH descriptor: [Arterial Occlusive Diseases] this term only 858
- #17 ((leg or limb) near/3 (isch*emia or occlusi*)):ti,ab 858
- #18 (arteriosclerosis or atherosclerosis):ti,ab 5084
- #19 MeSH descriptor: [Femoral Artery] this term only 919
- #20 MeSH descriptor: [Popliteal Artery] this term only 335
- #21 MeSH descriptor: [Iliac Artery] this term only 171
- #22 ((femoral or renal or iliac) near/3 artery):ti,ab 1278
- #23 #19 or #20 or #21 or #22 2065
- #24 (occlu* or obstruct*):ti,ab 27002
- #25 #23 and #24 414
- #26 MeSH descriptor: [Heart Failure] explode all trees 6801
- #27 MeSH descriptor: [Myocardial Ischemia] explode all trees 24444
- #28 myocard*:ti,ab 26770
- #29 MeSH descriptor: [Ventricular Dysfunction] explode all trees 2111
- #30 (ventricular near/2 failure):ti,ab 403
- #31 revascular*:ti,ab 6938
- #32 (isch*mi* near/3 heart):ti,ab 2586
- #33 coronary:ti,ab 34354
- #34 MeSH descriptor: [Angioplasty] explode all trees 4782
- #35 (PTCA or angioplast*):ti,ab 4475
- #36 MeSH descriptor: [Myocardial Revascularization] this term only 949
- #37 stenocardia*:ti,ab 59
- #38 (heart near/3 decompensation):ti,ab 34
- #39 MeSH descriptor: [Myocardial Infarction] explode all trees 9828
- #40 MeSH descriptor: [Acute Coronary Syndrome] this term only 1210
- #41 "coronary syndrome":ti,ab 3622
- #42 "unstable coronary":ti,ab 186
- #43 "heart arrhythmia":ti,ab 5
- #44 "without st segment":ti,ab 121
- #45 "non st segment":ti,ab 552
- #46 "non-q-wave":ti,ab 304
- #47 NSTEMI:ti,ab 234

#48 (heart near/3 infarc*):ti,ab 546
 #49 (heart near/3 failure):ti,ab 14674
 #50 cardiac*:ti,ab 34439
 #51 CABG:ti,ab 3175
 #52 MeSH descriptor: [Coronary Artery Bypass] explode all trees 5492
 #53 (heart near/3 bypass):ti,ab 118
 #54 MeSH descriptor: [Heart Valve Diseases] explode all trees 1490
 #55 (valve near/2 (disease* or stenosis* or insufficiency*)):ti,ab 420
 #56 MeSH descriptor: [Heart Valve Prosthesis Implantation] this term only 677
 #57 MeSH descriptor: [Heart Valve Prosthesis] this term only 548
 #58 (valve near/2 (surg* or replace* or repair* or prosthesis*)):ti,ab 2043
 #59 MeSH descriptor: [Defibrillators, Implantable] this term only 1043
 #60 (implantable near/2 defibrillator*):ti,ab 1140
 #61 (cardioverter near/2 defibrillator*):ti,ab 1084
 #62 ICD:ti,ab 1829
 #63 ICD-CRT:ti,ab 19
 #64 MeSH descriptor: [Endocarditis] this term only 33
 #65 endocarditis:ti,ab 314
 #66 MeSH descriptor: [Thrombosis] this term only 1429
 #67 MeSH descriptor: [Thromboembolism] this term only 1146
 #68 MeSH descriptor: [Venous Thromboembolism] this term only 553
 #69 MeSH descriptor: [Venous Thrombosis] explode all trees 2510
 #70 (thrombus* or thrombotic* or thrombotic* or thromboembolism* or thrombosis* or embolism*):ti,ab 16974
 #71 MeSH descriptor: [Pulmonary Embolism] explode all trees 1011
 #72 (PE or DVT or VTE):ti,ab 3512
 #73 ((vein* or ven*) near/6 thromb*):ti,ab 6747
 #74 (blood near/3 clot*):ti,ab 620
 #75 (pulmonary near/3 clot*):ti,ab 13
 #76 (lung near/3 clot*):ti,ab 1
 #77 MeSH descriptor: [Hypertension, Pulmonary] this term only 631
 #78 "pulmonary arterial hypertension":ti,ab 773
 #79 MeSH descriptor: [Atrial Fibrillation] this term only 3352
 #80 "atrial fibrillation*":ti,ab 6645
 #81 "auricular fibrillation*":ti,ab 12
 #82 "atrium fibrillation*":ti,ab 2
 #83 "ventricular fibrillation":ti,ab 878
 #84 "ventricular tachycardia":ti,ab 1128
 #85 MeSH descriptor: [Heart Defects, Congenital] explode all trees 1805
 #86 (congenital* near/6 heart):ti,ab 942
 #87 (congenital* near/6 cardiac):ti,ab 160
 #88 (heart near/6 malform*):ti,ab 20
 #89 (cardiac near/6 malform*):ti,ab 24
 #90 (heart near/6 defect*):ti,ab 227
 #91 (cardiac near/6 defect*):ti,ab 83
 #92 (coarctation near/6 aorta*):ti,ab 64
 #93 (septal near/6 defect*):ti,ab 333
 #94 (septum near/6 defect*):ti,ab 13
 #95 (patent next ductus next arteriosus):ti,ab 502
 #96 (transposition near/6 arteries):ti,ab 88
 #97 (transposition near/6 vessels):ti,ab 3
 #98 guch:ti,ab 1
 #99 (fallot* near/6 tetralogy):ti,ab 161
 #100 "unstable angina":ti,ab 2031

#101 MeSH descriptor: [Angina Pectoris] explode all trees 4288

#102 angina:ti,ab 8282

#103 "angor pectoris":ti,ab 7

1.Exercise

Sourced from: Anderson L, Thompson DR, Oldridge N, Zwisler AD, Rees K, Martin N, Taylor RS.

Exercise-based cardiac rehabilitation for coronary heart disease.

Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD001800.

DOI: 10.1002/14651858.CD001800.pub3.

Central

#23 MeSH descriptor: [Exercise Therapy] explode all trees

#24 MeSH descriptor: [Sports] explode all trees

#25 MeSH descriptor: [Physical Exertion] explode all trees

#26 rehabilitat*:ti,ab,kw (Word variations have been searched)

#27 (physical* near (fit* or train* or therap* or activit*)):ti,ab,kw (Word variations have been searched)

#28 MeSH descriptor: [Exercise] explode all trees

#29 (train*) near (strength* or aerobic* or exercise*):ti,ab,kw (Word variations have been searched)

#30 ((exercise* or fitness) near/3 (treatment or intervent* or program*)):ti,ab,kw (Word variations have been searched)

#31 MeSH descriptor: [Rehabilitation] explode all trees

#32 kinesiotherap*:ti,ab,kw (Word variations have been searched)

#33 MeSH descriptor: [Physical Education and Training] explode all trees

Medline

23. exp Exercise Therapy/

24. Sports/

25. Physical Exertion/

26. rehabilitat*.mp.

27. (physical* adj5 (fit* or train* or therap* or activit*)).mp.

28. exp Exercise/

29. (train* adj5 (strength* or aerobic* or exercise*)).tw.

30. ((exercise* or fitness) adj3 (treatment or intervent* or program*)).tw.

31. exp Rehabilitation/

32. kinesiotherap*.tw.

33. "Physical Education and Training"/

34. Patient Education as Topic/

EMBASE

23. exp Kinesiotherapy/

24. Sport/

25. rehabilitat*.mp.

26. (physical* adj5 (fit* or train* or therap* or activit*)).mp.

27. exp Exercise/

28. (train* adj5 (strength* or aerobic* or exercise*)).tw.

29. ((exercise* or fitness) adj3 (treatment or intervent* or program*)).tw.

30. exp Rehabilitation/

31. kinesiotherap*.tw.

32. Physical Education/

CINAHL

S21 (MH "Physical Education and Training")

S20 kinesiotherap*

S19 (MH "Rehabilitation+")

S18 ((exercise* or fitness) N3 (treatment or intervent* or program*))

S17 (train* N5 (strength* or aerobic* or exercise*))

S16 (MH "Exercise+")

S15 (physical* N5 (fit* or train* or therap* or activit*))
S14 rehabilitat*
S13 (MH "Physical Activity")
S12 (MH "Sports")
S11 (MH "Therapeutic Exercise+")

2. Education

Sourced from: Anderson L, Brown JP, Clark AM, Dalal H, Rossau HK, Bridges C, Taylor RS. Patient education in the management of coronary heart disease. Taylor RS, ed. *Cochrane Database Syst Rev* Chichester, UK: John Wiley & Sons, Ltd; 2017;6:CD008895.

Central

#30 MeSH descriptor: [Patient Education as Topic] this term only
#31 MeSH descriptor: [Health Education] this term only
#32 MeSH descriptor: [Telemedicine] this term only
#33 (patient* near/6 (educat* or communicat* or interacti* or inform* or advi*)):ti,ab,kw (Word variations have been searched)
#34 (educat* near/6 (intervention* or rehabilitation* or program*)):ti,ab,kw (Word variations have been searched)
#35 (education near/6 (service* or group* or program* or session*)):ti,ab,kw (Word variations have been searched)
#36 (education near/6 prevent*):ti,ab,kw (Word variations have been searched)
#37 ((rehabilitati* or educat*) near/6 (literature or audiovisual or av or audio visual or internet or web* or telecare or telemedicine or telephone* or phone* or teleconference* or telehealth or transtelephonic* or podcast* or email* or email*)):ti,ab,kw (Word variations have been searched)
#38 ((educat* or intervent*) near/6 (communit* or famil* or spouse* or nurs*)):ti,ab,kw (Word variations have been searched)

3. Psychology

Sourced from: Richards SH, Anderson L, Jenkinson CE, Whalley B, Rees K, Davies P, Bennett P, Liu Z, West R, Thompson DR, Taylor RS.

Psychological interventions for coronary heart disease.

Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD002902.

DOI: 10.1002/14651858.CD002902.pub3.

Central

#39 MeSH descriptor: [Psychotherapy] explode all trees
#40 psychotherap*
#41 psycholog* near intervent*
#42 relax*
#43 MeSH descriptor: [Relaxation Therapy] explode all trees
#44 MeSH descriptor: [Counseling] explode all trees
#45 counsel*ing
#46 MeSH descriptor: [Cognitive Therapy] explode all trees
#47 MeSH descriptor: [Behavior Therapy] explode all trees
#48 (behavio*r*) near/4 (modif* or therap* or rehab* or change)
#49 MeSH descriptor: [Stress, Psychological] explode all trees
#50 stress near manage*
#51 cognitive* near therap*
#52 MeSH descriptor: [Meditation] explode all trees
#53 meditat*
#54 MeSH descriptor: [Anxiety] explode all trees
#55 (manage*) near (anxiety or depres*)
#56 CBT

#57 hypnotherap*
 #58 goal near/3 setting
 #59 (psycho-educat*) or (psychoeducat*)
 #60 motivat* near interv*
 #61 MeSH descriptor: [Psychopathology] explode all trees
 #62 psychopathol*
 #63 MeSH descriptor: [Autogenic Training] explode all trees
 #64 autogenic*
 #65 self near (manage* or care or motivat*)
 #66 distress*
 #67 psychosocial* or psycho-social

4. Smoking

21. Smoking Cessation/
 22. (smok* adj6 cessation).tw.
 23. (smok* adj6 cease*).tw.
 24. (smok* adj6 quit*).tw.
 25. antismoking.tw.
 26. anti-smoking.tw.
 27. (smok* adj6 giv*).tw.
 28. (smok* adj6 stop*).tw.

5. Diet

16. exp Weight Loss/
 17. weight loss*.mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]
 18. 16 or 17
 19. exp Diet Therapy/
 20. (diet therap* or caloric restriction or low calorie diet* or liquid diet* or fat* or protein* or carbohydrate* or fibre).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

6. Palliative Care (MeSH)

21. exp Palliative Care/
 22. "Hospice and Palliative Care Nursing"/
 23. Terminal Care/
 24. "end of life".ti,ab.
 25. palliative.ti,ab.
 26. (dying adj3 (care or comfort or relief or strateg* or plan or intervention or pain)).ti,ab.

Appendix 2: Papers that met the report inclusion criteria but were excluded based on age or quality (full text review 2).

Exercise-based rehabilitation

Author, date	Condition	Title	Reason for exclusion
Rauch, 2016	ACS/CAB G/CAD	The prognostic effect of cardiac rehabilitation in the era of acute revascularisation and statin therapy: A systematic review and meta-analysis of randomized studies –The Cardiac Rehabilitation Outcome Study (CROS)	Newer review available
Fakuta, 2016	HFpEF	The effects of drug and exercise intervention on functional capacity and quality of life in heart failure with preserved ejection fraction: A meta-analysis of randomised controlled trials	Lower R-AMSTAR than Chan et al. (2016)
Elliott, 2016	ICD	Effects of aerobic exercise training in patients with an implantable cardioverter defibrillator: A meta-analysis	Newer review available
Yuan, 2015	PH	Exercise training for pulmonary hypertension: A systematic review and meta-analysis	Newer review available
Vemulapalli, 2015	IC	Comparative effectiveness of medical therapy, supervised exercise, and revascularization for patients with intermittent claudication: A network Meta-analysis	Cochrane review available
Parmenter, 2015a	PAD	Exercise training for health-related quality of life in peripheral artery disease: A systematic review and meta-analysis	Cochrane review available
Parmenter, 2015b	PAD	Exercise training for management of peripheral arterial disease: A systematic review and meta-analysis	Cochrane review available
Parashar, 2015	ICD	Exercise training in patients with ICD: A meta-analysis of efficacy and safety outcomes	Cochrane review available
Pandey, 2015	HFpEF	Exercise training with heart failure and preserved ejection fraction meta-analysis of randomised controlled trials	Cochrane review available
Lewinter, 2015	HF	Exercise-based cardiac rehabilitation in patients with heart failure: A meta-analysis of randomised controlled trials 1999-2013	Cochrane review available
Reiter, 2014	HF	The role of exercise in heart failure: a systematic review	Cochrane review available
Parashar, 2014	HFpEF	Exercise training in patients with heart failure and preserved ejection fraction: A meta-analysis of randomised control trials	Cochrane review available
Giacomanotoni, 2013	AF	A systematic Review of the health benefits of Exercise Rehabilitation in persons living with atrial fibrillation	Newer available
Isaksen et. al, 2012	ICD	Exercise training and cardiac rehabilitation in patients with implantable cardioverter defibrillators: a review of current literature focusing on safety, effects of exercise training and the psychological impact of programme participation	Cochrane review available
Van der Meer, 2012	HFrEF	Effect of outpatient exercise training programmes in patients with chronic heart failure: A systematic review	Cochrane review available

ACS: Acute coronary syndrome, CABG: Coronary artery bypass graft, CAD: Coronary artery disease, PAD: Peripheral artery disease, HFpEF: Heart failure with preserved ejection fraction, ICD: Implantable cardioverter-defibrillation, PH: Pulmonary hypertension, IC: Intermittent claudication, AF: Atrial fibrillation, HFrEF: Heart failure with reduced ejection fraction

Education and psychology-based rehabilitation

Author, date	Condition	Title	Reason exclusion
Klanin-Yobas, 2016	CHD	Efficacy of psychosocial interventions on psychological outcomes among people with cardiovascular diseases: A systematic review and meta-analysis	Newer review available
Casimir, 2014	HF	The effectiveness of patient centred self-care for adults with heart failure on knowledge, self-care behaviours, quality of life, and readmissions: a systematic review	Newer review available
Akdeniz, 2014	HF	Effects of planned patient education on symptoms management on the patients diagnosed with heart failure	Newer review available
Spatola, 2013	HF	Educational interventions in patients with heart failure: a review of the literature	Newer review available
Sookhoo, 2013	HF	The experiences of heart failure patients following their participation in self-management patient education programmes: A systematic review	Newer review available
Samrtziz, 2013	HF	Effect of psychological interventions on quality of life in patients with chronic heart failure: A meta-analysis of randomised controlled trials	Newer review available
Reese, 2012	CHD	Psychological interventions in the rehabilitation of patients with coronary heart disease	Newer review available
Brown, 2011	CHD	Patient education in the management of coronary heart disease	Newer review available
Boyde, 2011	HF	Educational interventions for patients with heart failure: a systematic review of randomised controlled trials	Newer review available

HF: Heart failure, CHD: Coronary heart disease

Appendix 3: R-AMSTAR

How to use the R-AMSTAR tool?

The tool contains 11 questions with regard to the quality of the review. These questions are in the left column. Based on the criteria mentioned in the right column, every question should be assigned a score from 1 to 4. The sum of all scores is the overall quality score of the systematic review.

AMSTAR items	Criteria
1. Was an “a priori” design provided? The research question and inclusion criteria should be established before the conduct of the review.	A A clearly focused (PICO-based) question B Description of inclusion criteria C Study protocol is published and/or registered in advance 3 criteria!4, 2!3, 1!2, 0!1
Explanation: A. It should be explicitly mentioned that a protocol was published or registered, for example in PROSPERO an online international prospective register of systematic reviews. C. The question contains P opulation, I ntervention/exposure, C omparator/control and O utcome.	
2. Was there duplicate study selection and data extraction? There should be at least two persons who independently extracted data and a consensus procedure for disagreements should be in place.	A At least two persons independently extracted the data, explicitly stated B Statement of consensus procedure for disagreements C Disagreements among extractors resolved properly as stated or implied 3 criteria!4, 2!3, 1!2, 0!1
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated, and where feasible, the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	A At least two electronic sources are searched B Years and databases used are mentioned C Key words and/or MESH terms are stated and where feasible the search strategy outline is provided D Searches should be supplemented by consulting current contents, reviews, textbooks, registers and by reviewing the references in the studies found E Journals are hand-searched or manual searched 4 or 5 criteria!4, 3!3, 2!2, 1 or 0!1
Explanation: E. hand-searched means identifying highly relevant journals and conducting a manual, page-by-page search of their contents looking for potentially eligible studies.	
4. Was the status of publication (i.e., grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	A The authors state that they searched for reports regardless of their publication type. B The authors state whether or not they excluded any reports based on their publication status, language etc. C “Non-English papers were translated” or readers sufficiently trained in foreign language D No language restriction or recognition of non-English articles 3 or 4 criteria!4, 2!3, 1!2, 0!1

AMSTAR items	Criteria
5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.	A Table/list/figure of included studies, a reference list does not suffice B Table/list/figure of excluded studies either in the article or in a supplemental source C Satisfactory/sufficient statement of the reason for exclusion of the seriously considered studies D Reader is able to retrace the included and the excluded studies anywhere in the article bibliography, reference or supplemental source 4 criteria!4, 3!3, 2!2, 1!1
Explanation: "Excluded studies" refers to those studies seriously considered on the basis of title and/or abstract, but rejected after reading the body of the text.	
6. Were the characteristics of the included studies provided? In an aggregated form, such as a table, data from the original studies should be provided on the participants, interventions/exposure, and outcomes. The ranges of characteristics in all the studies analyzed, e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.	A In an aggregated form such as a table, data from the original studies are provided on the participants, interventions/exposure and outcomes B Ranges are provided of the relevant characteristics in the studies analyzed C The information provided appears to be complete and accurate 3 criteria!4, 2!3, 1!2, 0!1
7. Was the scientific quality of the included studies assessed and documented? "A priori" methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo-controlled studies, or allocation concealment as inclusion criteria); for other types of studies, alternative items will be relevant.	A 'A priori' methods are provided B The scientific quality of the included studies appears to be meaningful C Discussion/recognition/awareness of level of evidence is present D Quality of evidence is rated/ranked base on characterized instruments 4 criteria!4, 3!3, 2!2, 1 or 0!1
Explanation: D. A characterized instrument is a created instrument that ranks the level of evidence, e.g. GRADE [Grading of Recommendations Assessment, Development and Evaluation].	
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	A The scientific quality is considered in the analysis and the conclusions of the review B The scientific quality is explicitly stated in formulating recommendations C Conclusions integrated/drives towards practice guidelines D Clinical consensus statement drives toward revision or confirmation of practice guidelines 4 criteria!4, 3!3, 2!2, 1 or 0!1
9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists, a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?).	A Statement of criteria that were used to decide that the studies analyzed were similar enough to be pooled B For the pooled results, a test is done to ensure the studies were combinable, to assess their homogeneity C a recognition of heterogeneity or lack of thereof is present D If heterogeneity exists a 'random effects model' is used and/or the

AMSTAR items	Criteria
	<p>rationale of combining is taken into consideration</p> <p>E If homogeneity exists, author state a rationale or a statistical test</p> <p>4 or 5 criteria!4, 3!3, 2!2, 1 or 0!1</p>
<p>10. Was the likelihood of publication bias assessed?</p> <p>An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).</p>	<p>A Recognition of publication bias or file-drawer effect</p> <p>B Graphical aids (e.g. funnel plot)</p> <p>C Statistical tests (e.g. Egger regression test)</p> <p>3 criteria!4, 2!3, 1!2, 0!1</p>
<p>11. Was the conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.</p>	<p>A Statement of sources of support</p> <p>B No conflict of interest. This is subjective and may require some deduction or searching.</p> <p>C An awareness/statement of support or conflict of interest in the primary inclusion studies</p> <p>3 criteria!4, 2!3, 1!2, 0!1</p>

Maximum quality score sum: 44

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