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Exercise-based cardiac rehabilitation for adults after heart valve surgery (Review)

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[Intervention Review]

Exercise-based cardiac rehabilitation for adults after heart valve surgery

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ABSTRACT

Background

The impact of exercise-based cardiac rehabilitation (CR) following heart valve surgery is uncertain. We conducted an update of this systematic review and a meta-analysis to assess randomised controlled trial evidence for the use of exercise-based CR following heart valve surgery.

Objectives

To assess the benefits and harms of exercise-based CR compared with no exercise training in adults following heart valve surgery or repair, including both percutaneous and surgical procedures. We considered CR programmes consisting of exercise training with or without another intervention (such as an intervention with a psycho-educational component).

Search methods

We searched the Cochrane Central Register of Clinical Trials (CENTRAL), in the Cochrane Library; MEDLINE (Ovid); Embase (Ovid); the Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCO); PsycINFO (Ovid); Latin American Caribbean Health Sciences Literature (LILACS; Bireme); and Conference Proceedings Citation Index-Science (CPCI-S) on the Web of Science (Clarivate Analytics) on 10 January 2020. We searched for ongoing trials from ClinicalTrials.gov, Clinical-trials.com, and the World Health Organization International Clinical Trials Registry Platform on 15 May 2020.

Selection criteria

We included randomised controlled trials that compared exercise-based CR interventions with no exercise training. Trial participants comprised adults aged 18 years or older who had undergone heart valve surgery for heart valve disease (from any cause) and had received heart valve replacement or heart valve repair. Both percutaneous and surgical procedures were included.

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Data collection and analysis

Two review authors independently extracted data. We assessed the risk of systematic errors (‘bias’) by evaluating risk domains using the 'Risk of bias' (RoB2) tool. We assessed clinical and statistical heterogeneity. We performed meta-analyses using both fixed-effect and random-effects models. We used the GRADE approach to assess the quality of evidence for primary outcomes (all-cause mortality, all-cause hospitalisation, and health-related quality of life).

Main results

We included six trials with a total of 364 participants who have had open or percutaneous heart valve surgery. For this updated review, we identified four additional trials (216 participants). One trial had an overall low risk of bias, and we classified the remaining five trials as having some concerns.

Follow-up ranged across included trials from 3 to 24 months. Based on data at longest follow-up, a total of nine participants died: 4 CR versus 5 control (relative risk (RR) 0.83, 95% confidence interval (CI) 0.26 to 2.68; 2 trials, 131 participants; GRADE quality of evidence very low). No trials reported on cardiovascular mortality. One trial reported one cardiac-related hospitalisation in the CR group and none in the control group (RR 2.72, 95% CI 0.11 to 65.56; 1 trial, 122 participants; GRADE quality of evidence very low). We are uncertain about health-related quality of life at completion of the intervention in CR compared to control (Short Form (SF)-12/36 mental component: mean difference (MD) 1.28, 95% CI -1.60 to 4.16; 2 trials, 150 participants; GRADE quality of evidence very low; and SF-12/36 physical component: MD 2.99, 95% CI -5.24 to 11.21; 2 trials, 150 participants; GRADE quality of evidence very low), or at longest follow-up (SF-12/36 mental component: MD -1.45, 95% CI -4.70 to 1.80; 2 trials, 139 participants; GRADE quality of evidence very low; and SF-12/36 physical component: MD -0.87, 95% CI -3.57 to 1.83; 2 trials, 139 participants; GRADE quality of evidence very low).

Authors' conclusions

Due to lack of evidence and the very low quality of available evidence, this updated review is uncertain about the impact of exercise-CR in this population in terms of mortality, hospitalisation, and health-related quality of life. High-quality (low risk of bias) evidence on the impact of CR is needed to inform clinical guidelines and routine practice.

PLAIN LANGUAGE SUMMARY

Exercise-based cardiac rehabilitation for adults after heart valve surgery

Background

Cardiac rehabilitation (CR) that includes exercise training has been recommended as treatment for people after heart valve surgery. However, the strength of this evidence is uncertain. This updated review aimed to assess the benefits and harms of exercise-based CR for adults who have undergone heart valve surgery or repair. All types of heart valve surgery were included.

Trial characteristics

We searched for studies examining the effects of exercise-based CR compared with no exercise ('control') after heart valve surgery for adults (18 years or older) with heart valve disease (from any cause). The evidence is current to 10 January 2020.

Key results

We found six trials with a total of 364 participants. In this update, we added four new trials (216 participants) to those included in the previously published review. We are uncertain about the effects of exercise-based CR compared to control on the outcomes of all-cause mortality, health-related quality of life, and all-cause hospitalisation.

Quality of the evidence

Results from this Review should be interpreted with caution because of some concerns about risk of bias (potential for systematic error) in five out of six trials. Only one trial had low risk of bias. Additional high-quality randomised controlled trials are needed to fully assess the effects of exercise-based CR interventions.

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Summary of findings 1. Exercise compared to no exercise for adults after heart valve surgery

Exercise compared to no exercise for adults after heart valve surgery

Patient or population: adults after heart valve surgery
Setting: hospital- and home-based
Intervention: exercise
Comparison: no exercise

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no exercise	Risk with exercise				
All-cause mortality Follow-up range: 3 to 24 months	Study population 79 per 1000	66 per 1000 (21 to 213)	RR 0.83 (0.26 to 2.68)	131 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[a,b,c]	
Cardiovascular mortality	No study reported this outcome					
All-cause hospitalisation Follow-up: 6 months	Study population 0 per 1000	0 per 1000 (0 to 0)	RR 2.72 (0.11 to 65.56)	122 (1 RCT)	⊕⊖⊖⊖ VERY LOW[b,c,d]	There were 0 events in the control group
HRQoL (SF-12/36 mental component) at end of intervention Follow-up range: 2 to 3 months	Mean HRQoL range (mental component) at end of intervention was 51.3 to 53.9	MD 1.28 higher (1.60 lower to 4.16 higher)	-	150 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[b,c,d]	
HRQoL (SF-12/36 physical component) at end of intervention Follow-up range: 2 to 3 months	Mean HRQoL range (physical component) at end of intervention was 38 to 51	MD 2.99 higher (5.24 lower to 11.21 higher)	-	150 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[b,c,d,e]	
HRQoL (SF-12/36 mental component) at maximum follow-up Follow-up range: 3 to 24 months	Mean HRQoL range (mental component) at maximum follow-up was 54.9 to 55.1	MD 1.45 lower (4.70 lower to 1.80 higher)	-	139 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[b,c,d]	
HRQoL (SF-12/36 physical component) at maximum follow-up	Mean HRQoL range (physical component) at maximum follow-up was 36.9 to 52.2	MD 0.87 lower (3.57 lower to 1.83 higher)	-	139 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[b,c,d]	

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Follow-up range: 3 to 24 months

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; HRQoL: health-related quality of life; MD: mean difference; RCT: randomised controlled trial; RR: risk ratio; SMD: standardised mean difference.

GRADE Working Group grades of evidence.
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]At least one trial has some concerns for overall risk of bias. Downgraded by one level for risk of bias.
[b]Small sample size/number of events and optimal information size (OIS) criterion not reached, or OIS criterion reached but 95% CI includes RR/MD/SMD of 1/0. Downgraded by one level for inconsistency.
[c]Confidence interval includes possible benefit or harm (i.e. effect crosses RR of 0). Downgraded by one level for imprecision.
[d]All trials providing data for this outcome have an overall risk of bias judged as 'high'. Downgraded by one level for risk of bias.
[e]Substantial I^2 (between 50% and 90%). Downgraded by one level for imprecision.

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BACKGROUND

Description of the condition

Heart valve disease accounts for one-third of all heart disease and is increasing in prevalence due to an ageing population, population growth, and advances in treatment methods. Heart valve disease is mostly degenerative in nature (Nkomo 2006), and it is highly prevalent in developing countries due to rheumatic heart disease (Iung 2003; Nkomo 2006; Sibilitz 2015a; Supino 2006; Yagdir 2020).

Heart valve disease can be left-sided (aortic and mitral valve diseases), right-sided (tricuspid and pulmonary valves), or, in rare cases, a combination of both. The cause may be congenital, degenerative, or calcific, and physiological consequences may include valve insufficiency, valve stenosis, or both (Baumgartner 2017; Nkomo 2006). Heart valve disease is often asymptomatic at first. When it becomes symptomatic, the clinical presentation includes dyspnoea (difficulty breathing), fatigue, fluid retention, and decreased physical capacity. Symptomatic heart valve disease is associated with increased risks of mortality and morbidity, and it negatively impacts health-related quality of life (HRQoL) and physical capacity (Baumgartner 2017; Ben-Dor 2010; Frank 1973). Medical follow-up of valve disease includes regular clinical and echocardiographic follow-up (Baumgartner 2017; Vahanian 2012), as well as assessment of treatment indications. The treatment of choice when serious symptoms and/or haemodynamic changes occur is valve surgery with valve repair or replacement (Baumgartner 2017; Nishimura 2014; Vahanian 2012).

The changing disease pattern and expected increase in healthcare burden of patients after heart valve surgery require a well-established after-care programme to support the patient in managing postsurgical problems. These problems include physical and psychological issues and the challenge of returning to work. The large number of acute hospitalisations after valve surgery highlights the importance of follow-up (Sibilitz 2015a). One trial to date has shown that individualised follow-up programmes after surgery can reduce the risk of hospital admission (Borregaard 2019). Transcatheter aortic valve replacement (TAVR) is increasingly used for treatment of people with aortic stenosis and low surgical risk, impacting recovery following surgery. Data from the NOTION 3, PARTNER-3, and Evolut Low Risk trials show that TAVR is at least non-inferior and may be superior to surgery (Kolte 2019; Mack 2019; Popma 2019). However, the shorter stay in hospital at the time of TAVR (typically 1 to 3 days) has increased the demand for patient-centred follow-up and careful planning of rehabilitation. This is reflected in the latest (2017) European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) Guidelines, in which TAVR is recommended for patients older than 75 years of age (Baumgartner 2017); these guidelines were updated in 2020, and it is expected that results from PARTNER-3 and Evolut Low Risk trials have been integrated (Ambrosetti 2020).

Physical inactivity is a problem for heart valve surgery patients, who may experience presurgical dyspnoea and physical incapacity, immobilisation during hospitalisation, and potential postsurgical complications and restrictions due to healing of the sternum. Open heart surgery is a stressful life event (Karlsson 2010), and HRQoL is likely to be negatively affected (Hansen 2009), along with mental health; patients may require support for depressive symptoms and anxiety (Fredericks 2012). Although such problems may also occur following percutaneous procedures, recent studies suggest that after TAVR, patients have much better HRQoL within two weeks of the procedure (Lauck 2020). A Cochrane Review showed that participants who had undergone surgery for a coronary artery bypass graft might benefit from psychological interventions; however, risk of bias of included trials was considered to be high (Whalley 2011). Little is known about the effects of psychological interventions for patients after heart valve surgery.

In summary, risks of mortality and morbidity leading to hospital re-admission are increased after heart valve surgery, resulting in high potential healthcare costs. In addition, patients are likely to experience physical, mental, or social recovery problems that negatively impact their HRQoL and physical capacity. Therefore, careful postsurgical recovery programmes are needed. One key solution may be exercise-based cardiac rehabilitation (CR) (Baumgartner 2017; Butchart 2005).

Description of the intervention

CR is defined as "the coordinated sum of activities required to influence favourably the underlying cause of cardiovascular disease, as well as to provide the best possible physical, mental and social conditions, so that the participants may, by their own efforts, preserve or resume optimal functioning in their community and through improved health behaviour, slow or reverse progression of disease" (BACPR 2012). Although a central component of rehabilitation programmes is exercise training, it is recognised that CR programmes should be 'comprehensive' and combined with other interventions, particularly those with psycho-educational components (Ambrosetti 2020; Piepoli 2010).

Current European guidelines recommend that rehabilitation following heart valve surgery should include exercise training, anticoagulant therapy, and medical and echocardiographic follow-up. However, these guidelines do not explicitly state that psycho-educational interventions should be part of the rehabilitation programme (Baumgartner 2017; Butchart 2005). In contrast, American guidelines do not currently include any recommendations or information about CR after heart valve surgery (Balady 2007; Nishimura 2014).

A meta-analysis published in 2017 and including six trials showed that participation in exercise training after TAVR can increase exercise capacity within the first year after the procedure (Ribeiro 2017). This is supported by a systematic review and meta-analysis published in 2019 reporting that exercise-based CR improves exercise capacity of post-transcatheter aortic valve replacement (TAVR) and post-surgical aortic valve replacement (SAVR) patients in the short term (Anayo 2019). This review concludes that further evidence is needed to assess the clinical effects and cost-effectiveness of exercise-based CR in people with valve disease. A reported cohort trial showed that CR is associated with decreased one-year cumulative hospitalisation and mortality risk after valve surgery (Patel 2019).

The European Society of Cardiology recommends that physical activity for patients with cardiovascular disease should comprise 150 minutes per week, while others recommend three to four hours per week (Piepoli 2010). Further, recommendations state that low-risk patients should perform 30 minutes of aerobic exercise daily to achieve a weekly expenditure of 1000 kcal, whereas

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the amount of physical activity should be individually prescribed for high-risk patients (Gianuzzi 2003). Exercise training should be performed three times weekly for 12 weeks, through a local hospital or a community-based facility (Piepoli 2010). Exercise should consist of submaximal endurance training, the intensity of which is increased over time, and the programme should be expanded to include weight/resistance training. Psychological and educational interventions should offer individual and/or small group education and counselling on adjustment to heart disease, stress management, and health-related lifestyle changes (Gianuzzi 2003).

How the intervention might work

CR interventions following heart valve surgery can positively affect physical recovery, reduce blood pressure, reduce disease severity, and improve left ventricular ejection fraction (Gohlke-Bärwolf 1992; Landry 1984; Newell 1980; Pardaens 2014; Sibilitz 2016; Sire 1987). Exercise training may confer direct benefits for the heart and the coronary vasculature involving myocardial oxygen demand, endothelial function, autonomic tone, coagulation and clotting factors, inflammatory markers, and development of coronary collateral vessels (Clausen 1976; Hambrecht 2000).

We might anticipate effects of exercise-based CR after heart valve surgery similar to those seen in other cardiac populations that typically receive CR (i.e. post myocardial infarction and revascularisation and heart failure). Two Cochrane Reviews have shown that exercise-based CR has several positive effects in these latter populations (Anderson 2016; Long 2019), including reductions in hospitalisation and improvements in HRQoL. Furthermore, heart function changes due to valve dysfunction such as reduced cardiac output, stroke volume, and left ventricular ejection fraction may positively respond to exercise training. Exercise-based CR following heart valve surgery might also be expected to reduce the symptom burden, improve symptom and disease management, and decrease rates of anxiety and depression, as has been shown for patients with atrial fibrillation (Smart 2018).

Possible harmful effects of exercise-based CR after heart valve surgery include increased risk of surgery-related adverse events (e.g. arrhythmias, arterial embolism, death), as well as adverse events associated with valve disease (e.g. any arrhythmias, heart failure, death). A prospective study of patients post cardiac surgery reported a rate of adverse events (defined as chest pain with typical electrocardiographic modifications, severe ventricular arrhythmias, syncope, cardiopulmonary arrest, or a clinical condition necessitating cardiopulmonary resuscitation, immediate transfer to a coronary care unit or cardiac surgery, and/or use of intravenous drugs) of only 1 per 49,565 patient-hours of exercise training (Pavy 2006).

Why it is important to do this review

This systematic review is an update of a previous review that was undertaken to assess the benefits and harms of exercise-based CR in adults who have undergone heart valve surgery or repair (Sibilitz 2016 SR). Since the time of first publication of this review, two non-Cochrane systematic reviews and meta-analyses on this topic have been published (Anayo 2019; Ribeiro 2017).

OBJECTIVES

To assess the benefits and harms of exercise-based CR compared with no exercise training in adults following heart valve surgery or repair, including both percutaneous and surgical procedures. We considered CR programmes consisting of exercise training with or without another intervention (such as an intervention with a psycho-educational component).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) (including individual participant/cluster allocation or cross-over design) irrespective of language of publication, publication year, publication type, and publication status were eligible for inclusion in the review.

Types of participants

We included adults aged 18 years or older of both sexes and of any ethnicity who had undergone heart valve surgery for any cause of heart valve disease (i.e. aortic valve disease, mitral valve disease, tricuspid or pulmonary valve disease, or a combination) and had received heart valve replacement or heart valve repair (surgery to the valve and related anatomical areas without valve replacement, e.g. mitraclips, mitral ring, chordae rupture treatment). We included both percutaneous and surgical procedures.

Types of interventions

Exercise-based CR interventions with or without a psycho-educational intervention. Exercise-based CR interventions include supervised and unsupervised programmes conducted in an inpatient, outpatient, community, or home-based setting, including any kind of exercise training. The intervention must have included an exercise training component focused on increasing exercise capacity, and it may have included a psycho-educational intervention that focused on improving mental health and the patient's self-management skills. Patients could engage in an exercise intervention before or after discharge from the hospital for heart valve surgery (Kiel 2011). However, for inclusion in this review, the intervention must have included a postsurgical element. We applied no restriction in length, intensity, or content of the exercise training intervention.

Control interventions

We sought any of the following control interventions as long as they did not include a physical exercise element.

- Treatment as usual (e.g. standard medical care, such as drug and anticoagulant therapy; medical follow-up with echocardiography).
- No intervention.
- Any other type of CR programme.

Co-interventions

We included trials with co-interventions to CR, as long as these were delivered equally to participants in the intervention and control groups. Co-interventions could include drug, surgical (percutaneous versus transthoracic surgery), or dietary interventions.

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Types of outcome measures

Reporting one or more of the outcomes listed here for the trial is not an inclusion criterion for this review. When a published report did not appear to report one of these outcomes, we accessed the trial protocol and contacted the trial authors to ascertain whether outcomes were measured but not reported. Relevant trials that measured these outcomes but did not report the data at all, or did not provide data in a usable format, were included in the review as part of the narrative. We did not use hierarchy to choose between multiple measures of the same outcome but instead sought to report all outcome results.

Outcomes are assessed at two time points: (1) at completion of the intervention (as defined by trialists); and (2) at longest available follow-up. There was no minimum length of follow-up for trials that were eligible for inclusion in the review.

Primary outcomes

We sought the following primary outcomes.

- All-cause mortality.
- Cardiovascular mortality.
- All-cause hospitalisation.
- Health-related quality of life assessed by generic or disease-specific validated instruments (e.g. Short Form-36, EuroQoL Group Quality of Life Questionnaire based on 5 dimensions (EQ-5D) - generic measures, HeartQoL - heart disease-specific measure).

Secondary outcomes

We sought the following secondary outcomes.

- Exercise capacity: any measure of exercise capacity including direct measurement of oxygen uptake (VO_2 peak/VO_2 max) or indirect measures such as exercise time, walking distance (e.g. 6-minute walk text), etc.
- Serious adverse events: defined as any untoward medical occurrences that are life-threatening, result in death, or are persistent or lead to significant disability; or any medical events that have jeopardised the patient or required intervention to prevent them, or any hospitalisation or prolongation of existing hospitalisation (ICH-GCP 1997).
- Return to work.
- Costs and cost-effectiveness.

Search methods for identification of studies

Electronic searches

We searched the following electronic databases from their inception to 10 January 2020 (unless otherwise stated).

- Cochrane Central Register of Controlled Trials (CENTRAL; 2020, Issue 1 of 12), in the Cochrane Library.
- Database of Abstracts of Reviews of Effectiveness (DARE; 2015, Issue 1 of 4), in the Cochrane Library (last issue available, so not updated for this latest version).
- MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (Ovid) (1946 to 9 January 2020).
- Embase Classic and Embase (Ovid) (1947 to 9 January 2020).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) plus Full Text (EBSCO) (1937 to 10 January 2020).
- PsycINFO (Ovid) (1806 to January week 1 2020).
- Latin American Caribbean Health Sciences Literature (LILACS; Bireme), in English (1982 to 10 January 2020).
- Conference Proceedings Citation Index-S (CPCI-S) on Web of Science (Clarivate Analytics) (1990 to 10 January 2020).

Searches for the previous review were run on 23 March 2015, and were updated and re-run on 10 January 2020. Some additional search terms were added for each database in the latest search (Appendix 1). The RCT filter used for MEDLINE was the Cochrane sensitivity-maximising RCT filter, and for Embase, terms as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* were applied (Lefebvre 2011). RCT filters used for the other databases, except CENTRAL, were adaptations of the Cochrane RCT filter.

We applied no language restrictions. Trials written in languages that the review authors did not understand were translated professionally.

We checked the status of studies identified as ongoing (7 February 2021) to determine their current publication status. None of the 10 ongoing studies were found to have been published.

Searching other resources

We also searched the following clinical trials registers for ongoing trials on 15 May 2020.

- ClinicalTrial.gov (www.clinicaltrials.gov).
- International Standard Randomized Controlled Trials Number (ISRCTN) Registry (www.Controlled-trials.com).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (http://apps.who.int/trialsearch/).

We searched these other sources using the search terms 'heart valve surgery', 'heart valve replacement', 'exercise', and 'cardiac rehabilitation'. Several of the co-authors are experts in the field with knowledge of current unpublished trials. We searched the reference lists of previous systematic reviews and trials included in this review .

Data collection and analysis

Selection of studies

Two review authors (LA and KLS) independently assessed all titles and abstracts for inclusion, excluding trials that did not meet the inclusion criteria. We retrieved full publications of all potentially relevant trials, stored them electronically, and translated them when required. We resolved disagreements by discussion between the two review authors (LA and KLS), or, when necessary, by consultation with a third review author (RST). We detailed excluded trials and reasons for their exclusion in the Characteristics of excluded studies table.

Data extraction and management

Two review authors (LA and KLS) independently extracted data from the included trials using a standardised data extraction form. This form was used in the previous version of this review and has been adapted from previous Cochrane cardiac rehabilitation

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reviews (e.g. Anderson 2016). When not reported in the text or tables, we extracted outcome data from graphs. A third review author (RST) checked all numerical calculations and data extractions. We resolved any discrepancies by consensus. One of the included trials was available only in Chinese. Data extraction for this paper was undertaken by one of the review authors (KLS) in the presence of a translator (native Chinese speaker). Data for the Chinese article were double-checked against the English abstract (LA and KLS).

We extracted the following data.

- General information: publication status, title, authors' names, source, country, contact address, language of publication, year of publication, duplicate publication, financial conditions.
- Trial characteristics: design, duration.
- Intervention: type of exercise training, type of rehabilitation programme (comprehensive CR or only exercise training), setting (e.g. in-patient, out-patient, community, home setting, a combination), time after hospitalisation, nature of the control group.
- Participants: sampling method (e.g. convenience, random), inclusion and exclusion criteria, numbers of participants in intervention and control groups, participant demographics such as sex and age, baseline characteristics including type of valve affected and classification of heart valve disease, number of participants lost to follow-up.
- Outcomes: data sought for primary and secondary outcomes as defined earlier.
- Risk of bias: see Assessment of risk of bias in included studies below.

One review author (LA) transferred data into Review Manager 5.4 (RevMan 2020), and another review author (KLS) double-checked that data were entered correctly by checking trial characteristics for accuracy.

Assessment of risk of bias in included studies

For this review, the effect of interest is the effect of assignment to the intervention. Two review authors (LA and KS) independently assessed risk of bias using the Cochrane 'Risk of bias in randomised trials' tool (RoB2) for all primary outcomes (when data were provided) (i.e. at latest follow-up for all-cause mortality and all-cause hospitalisation, at the end of the intervention, and at latest follow-up for both exercise capacity and HRQoL outcomes) (Higgins 2019a; Sterne 2019). Secondary outcomes were not assessed for risk of bias. As all review authors but one (LA) were involved with one of the included trials (Sibilitz 2016), an independent RoB2 experienced review author Michele Hilton Boon (MHB) independently assessed all of the primary outcomes for this trial. Differences between RoB2 assessments were discussed between MHB and LA (for details, see https://www.gla.ac.uk/media/Media_775195_smxx.xlsm).

We resolved all disagreements through discussion or by consultation with a third review author (RST).

We assessed risk of bias using the following Cochrane RoB2 criteria (Higgins 2019a; Sterne 2019).

- Bias arising from the randomisation process.
- Bias due to deviations from intended interventions.
- Bias due to missing outcome data.
- Bias in measurement of the outcome.
- Bias in selection of the reported result.

For each domain, a series of signalling questions (with the answers yes, probably yes, no information, probably no, and no) will determine the risk of bias (low risk, some concerns, or high risk). We included text alongside the judgements to provide supporting information for our decisions (see 'Risk of bias in included trials'). We decided the risk of bias for an outcome (e.g. HRQoL) by noting its performance in each domain; if one domain was judged as 'some concerns' or 'high risk', this judgement was taken for the whole outcome. To manage the assessment of bias and to implement RoB2, we used the RoB2 Excel tool (available on the riskofbiasinfo.org website). The RoB2 tool was accessed from 18 to 20 May 2020.

Measures of treatment effect

We processed data in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019c). We expressed dichotomous data as risk ratios (RRs) with 95% confidence intervals (CIs). For continuous variables, we compared net changes (i.e. exercise-based CR minus control) to detect differences. For each trial, we sought the mean change (and the standard deviation (SD)) in outcomes between baseline and follow-up for both exercise and control groups. When not available, we used the absolute mean (and SD) outcome at follow-up for both groups. We expressed results as mean differences (MDs), except when trials used different scales or measurements, in which case we used standardised mean differences (SMDs) (Thompson 2002). We interpreted SMD as 0.2, 0.5, and 0.8, representing 'small', 'medium', and 'large' effect sizes, respectively (Higgins 2019b).

Unit of analysis issues

If any cluster-randomised controlled trials had been included, we planned to contact the trial authors to obtain an estimate of the intra-cluster correlation when appropriate adjustments for the correlation between participants within clusters had not been made, or otherwise to impute it using estimates from the other included trials, or from similar external trials. Similarly, if we had included data from cross-over trials, we would have included both periods of any cross-over trials identified, assuming that (1) there had been a washout period considered long enough to reduce carry-over, (2) no irreversible events such as mortality had occurred, and (3) appropriate statistical approaches had been used.

Dealing with missing data

As we did not obtain missing data by contacting triallists, we sought to undertake sensitivity analysis to explore the effect of this missingness. For dichotomous outcomes, we performed analyses using the intention-to-treat method (Higgins 2019c), which includes all participants according to their original random group allocation, irrespective of compliance or follow-up. For primary analyses, we assumed that participants lost to follow-up were alive and had no serious adverse events. For continuous outcomes, we performed available participant analysis and included data only on those for whom results are known (Higgins 2019c). It was possible to obtain SDs directly from the articles or by calculation (Furukawa 2006). When trials reported outcomes with medians and interquartile ranges, we calculated the means and the standard deviations by using the quantile method for estimating

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means and standard deviations. To calculate means and standard deviations, we divided the sum of the median, the first quartile range, and the third quartile range by three, and we subtracted the first quartile from the third quartile, then divided by 1.35, respectively (Higgins 2019ca; Chapter 6.5.2.5). When trials reported maximal oxygen consumption (VO_2 max) in metabolic equivalent of tasks (METS), we converted this to mL/kg/min by multiplying by 3.5. We sought to undertake two sensitivity analyses for binary primary outcomes to examine the impact of losses to follow-up.

Assessment of heterogeneity

We explored clinical heterogeneity by comparing population, intervention, and control groups across included trials. We observed statistical heterogeneity in the trials by visually inspecting forest plots, by using a standard Chi^2 value with a significance cut-off level of P = 0.10, and by using the I^2 statistic. We interpreted an I^2 estimate greater than or equal to 50% with a significant value for Chi^2 as evidence of 'substantial' statistical heterogeneity (Higgins 2019c).

Small-trial (publication) bias

We planned to construct funnel plots and to undertake Egger tests for each outcome when we identified 10 or more trials, to establish the potential influence of small-trial effects and potential publication bias (Sterne 2011; Wood 2008). However, due to the limited number of included trials (six), this was not possible.

Assessment of reporting biases

See Assessment of risk of bias in included studies and small-trial (publication) bias. There was no language bias, as relevant trials published in other languages were sought and translated.

Data synthesis

We performed data synthesis according to recommendations provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019c), using Review Manager 5.4 (RevMan 2020). We implemented RoB2 in RevMan Web, available at revman.cochrane.org. The primary analysis will include all eligible studies, irrespective of their risk of bias status.

We pooled data from each trial using a fixed-effect model, except when we identified substantial statistical heterogeneity (I^2 statistic > 50%), in which case we applied a random-effects model, which provided a more conservative statistical comparison of differences between intervention and control, because a confidence interval around a random-effects estimate is wider than a confidence interval around a fixed-effect estimate.

Subgroup analysis and investigation of heterogeneity

We planned to analyse primary outcomes using stratified meta-analysis, according to the following subgroups.

- Trials at overall low risk of bias compared to trials at overall high risk of bias based on RoB2; for trials categorised as being at overall low risk of bias, we would perform subgroup analysis on trials at overall lower risk of bias compared to trials at overall higher risk of bias.
- Trials including women only versus trials including men only.
- Trials including younger participants (< 60 years old) only versus trials including older participants (≥ 60 years old) only.
- Trials with an exercise intervention only compared to trials with an exercise intervention plus any other co-intervention, such as a psycho-educational intervention.

However, due to the small number of included trials and a limited quantity of data, it was not possible to perform these subgroup analyses.

Sensitivity analysis

For primary outcomes, we planned to perform the following sensitivity analyses.

Binary outcomes

Best/worst-case scenario: for this analysis, we would assume that all participants lost to follow-up in the intervention group have survived, and have had no serious adverse events; and that all those with missing outcomes in the control group have not survived, and have had serious adverse events.

Worst/best-case scenario: for this analysis, we would assume that all participants lost to follow-up in the intervention group have not survived, and have had serious adverse events; and that all those with missing outcomes in the control group have survived, and have had no serious adverse events.

Continuous data

Assumptions for lost data: when assumptions had been made for lost data (Dealing with missing data), we compared the findings from our assumptions with data only from those participants who completed the trials.

Summary of findings and assessment of the certainty of the evidence

One review author (LA) independently employed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to interpret study results (Schünemann 2013). We used the five GRADE considerations (overall risk of bias, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of a body of evidence as it relates to trials that contributed data to meta-analyses and narrative summaries for pre-specified outcomes. We (LA, KLS, RST) resolved any discrepancies in judgement through discussion. One review author (LA) used GRADEpro GDT software to import data from Review Manager to create a 'Summary of findings' table that included the following pre-specified outcomes: all-cause mortality; cardiovascular mortality; all-cause hospital hospitalisations; and health-related quality of life (GradePro Software; Schünemann 2013). .

RESULTS

Description of studies

The updated search results can be seen in Table 1; the trial selection process is shown in the PRISMA flow chart in Figure 1.

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Figure 1. Updated study flow diagram.

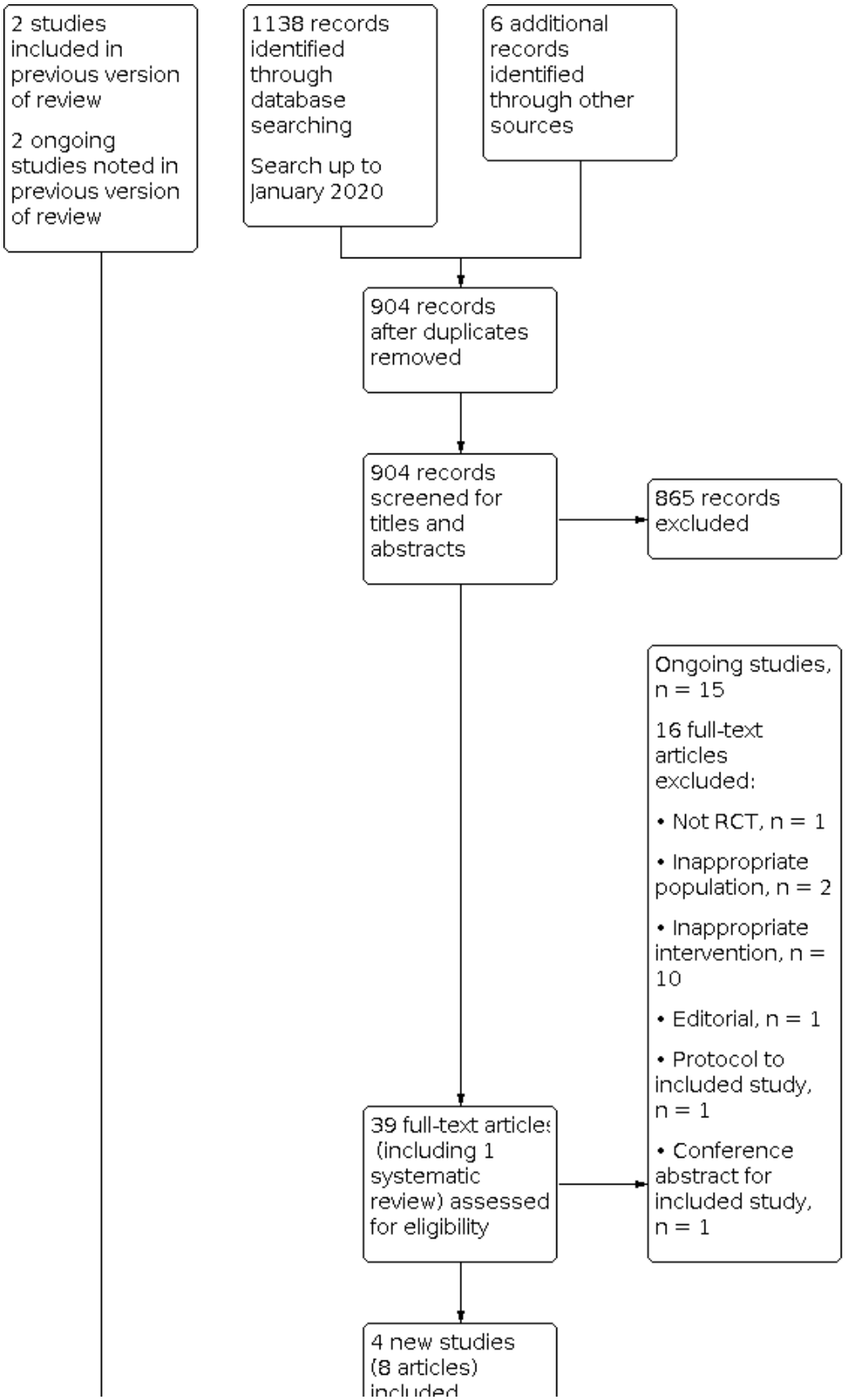

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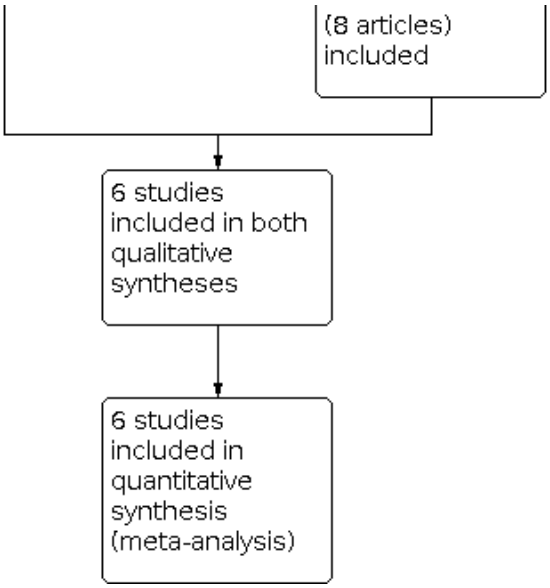
Figure 1. (Continued)



Results of the search

Through updated searches, we retrieved a total of 904 titles after de-duplication, of which 865 did not fulfil the inclusion criteria and were excluded. At full paper review stage, we excluded 16 records. One was not randomised, one was an editorial, one was a protocol for an included trial, one was a conference abstract for an included trial, two had an inappropriate population, and 10 had an inappropriate intervention.

Five records are awaiting classification, as we contacted the triallists about details of their trials but received no response, and the detail we had was insufficient to warrant inclusion in this review (Characteristics of studies awaiting classification).

We identified 10 ongoing trials from results of the electronic searches, as well as from our search of other resources. Details of these ongoing trials can be found in the section on Characteristics of ongoing studies (ACTIVE AFTER TAVR 2017; Exercise Training After TAVI; Feng 2019; HBCR-TAVR 2019; Post Cardiac Valvular Surgery Rehabilitation (PORT); PREPARE TAVR Pilot Study; REHAB-TAVR 2017; The PACO Trial; Valve-ex 2009; Wang 2019). They will be assessed during future updates of this review.

Four new trials (six publications: two from a recent systematic review - Anayo 2019) met the inclusion criteria and were therefore included in this review update. In total, this review included six trials - two from the previous version of this review.

Included studies

See Characteristics of included studies and Characteristics of excluded studies.

Population

The six included trials randomised a total of 364 participants who had undergone heart valve replacement or repair. Four trials included participants after aortic valve replacement only (Nilsson 2019; Pressler 2016; Rogers 2018; Sire 1987), one trial involved mitral valve replacement only (Lin 2004), and one trial included all heart valves (Sibilitz 2016). Some trials included participants undergoing several valve procedures at a time (e.g. two valve procedures) (Lin 2004; Sire 1987), but all trials excluded participants with other heart co-morbidities, or with other co-morbidities complicating physical activity. All trials had published abstracts in English, and all but the Lin 2004 trial (Chinese) were published in full in English. Five trials were single-centre studies. Pressler 2016 was conducted at three different centres. None of the trials were reported to be industry-sponsored.

Trial participants were predominantly male in four trials (57% - Lin 2004, 75% - Nilsson 2019, 76% - Sibilitz 2016, and 72% - Sire 1987); in the other two trials, the proportion of males was equal to the proportion of females (50% - Pressler 2016, or slightly lower (44%) - Rogers 2018). Mean participant age across trials varied from 31 years in Lin 2004 to 82 years in Rogers 2018. Although ethnicity of participants was not reported, five trials took place in Europe, and one in China. The longest reported trial follow-up time ranged from 3 months in Lin 2004 to 24 months in Pressler 2016.

Interventions

Included exercise-based interventions consisted of combined aerobic and resistance training that began one day to three months post surgery (Lin 2004; Pressler 2016). Lin 2004 also included a psychological intervention and an exercise training element, both of which were undertaken before surgery. In three trials, the intervention was provided in a combined hospital- and home-based setting (Lin 2004; Sibilitz 2016; Sire 1987), and in the other three trials, the intervention was given entirely in a hospital setting (Nilsson 2019; Pressler 2016; Rogers 2018). The dose and intensity of prescribed exercise training varied from 20 to 60 minutes per session across two to three sessions per week, except for one trial that recommended up to four hours daily (Sire 1987). The total duration of exercise programmes varied between trials from approximately one month in Sire 1987 to over three months in Lin 2004, Nilsson 2019, and Sibilitz 2016. In Rogers 2018, the dose, frequency, length, and intensity of exercise were individualised based on information gained from participants' functional capacity

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tests and discussion around their specific goals. Further details of the trials included in this review are shown under Characteristics of included studies.

Comparison

All trials compared interventions to no exercise and usual care.

Excluded studies

We excluded 16 trials and have presented reasons for their exclusion in the section Characteristics of excluded studies. The most common reason for trial exclusion was the type of intervention used, as it was not appropriate for this review.

Risk of bias in included studies

We performed risk of bias assessment using the RoB2 tool for all primary outcomes (when data were provided) and summarised results of this assessment in the results-level RoB2 tables (Higgins 2019c). Although some trials failed to give sufficient detail to enable a clear assessment of the potential risk of bias for outcomes measured (Lin 2004; Sire 1987), most trials provided sufficient information to allow for potential risk of bias assessment (for details, see https://www.gla.ac.uk/media/Media_775195_smxx.xlsm).

For all-cause mortality outcomes, we assumed an overall risk of bias with some concern, as one of the two trials was at overall high risk of bias and the other was at low risk of bias. However, no trials intended to measure mortality as a primary or secondary outcome. Only Sibilitz 2016 reported all-cause hospitalisations and was judged at high risk of bias, with short-term follow-up and few patients/events. We judged HRQoL physical and mental component outcomes to be at high risk of bias due to the small numbers of patients and the high level of missing outcome data at follow-up.

Given the nature of exercise-based CR interventions and controls, it is not possible to blind participants or people delivering the intervention. Nevertheless, blinding of outcome assessors can reduce risk of bias in measurement of outcomes that involve clinician assessment (exercise capacity) or participant self-reported outcomes (HRQoL, return to work). Three trials did not report any information on assessment of outcomes (Lin 2004; Nilsson 2019; Sire 1987).

Effects of interventions

See: **Summary of findings 1** Exercise compared to no exercise for adults after heart valve surgery

Primary outcomes

All-cause mortality

Nine deaths were reported by two trials (Lin 2004; Pressler 2016). We found lack of evidence of a difference between exercise-CR and control (risk ratio (RR) 0.83, 95% confidence interval (CI) 0.26 to 2.68; 2 trials, 131 participants; I^2 = 49%; GRADE quality of evidence very low; Analysis 1.1). In Lin 2004, two participants in the exercise-based CR group died (2/55; 3.6%) (1 sudden death, 1 brain stem death) versus none in the control group (0/49; 0%). Pressler 2016 reported seven deaths: two in the exercise-based CR arm (2/13; 15.4%) (1 intracranial bleeding, 1 unknown cause) versus five in the control arm (5/14; 35.7%) (3 pneumonia, 2 unknown cause). Sensitivity analyses (best/worst-case scenario: RR 0.44, 95% CI 0.15 to 1.32; worst/best-case scenario: RR 2.15, 95% CI 0.16 to 28.78) confirmed the lack of evidence of differences in all-cause mortality between exercise-based CR and control.

For all-cause mortality, the overall risk of bias for Pressler 2016 was 'low' and that for Lin 2004 was 'high' (see Analysis 1.1). Lin 2004 had some concerns with the randomisation process and deviations from intended interventions and was at high risk of bias for missing outcome data. Pressler 2016 led to a low risk of bias judgement for this outcome. Therefore caution should be applied when all-cause mortality results are interpreted.

Cardiovascular mortality

Cardiovascular mortality was not reported.

All-cause hospitalisations

Only one trial reported all-cause hospitalisations at six months' follow-up (Sibilitz 2016). This trial reported a cardiac-related hospitalisation in the exercise-CR group as one of the serious adverse events. No hospitalisations were reported in the control group (RR 2.72, 95% CI 0.11 to 65.56; fixed-effect model; 1 trial, 122 participants; I^2 = NA; GRADE quality of evidence very low; Analysis 1.4). We judged the trial as having overall high risk of bias, with both missing outcome data and measurement of outcomes judged at high risk of bias (see Analysis 1.4). Caution should therefore be applied when these results are interpreted.

Health-related quality of life

Pressler 2016 and Sibilitz 2016 reported HRQoL in a total of 139 participants using the 12-Item and 36-Item Short-Form Health Survey questionnaires (SF-12 and SF-36), respectively. These questionnaires were subdivided into mental component and physical component sub-scores, assessed at baseline, at completion of the intervention, and at longest follow-up. At completion of the intervention (ranging from two to three months), there was no difference between exercise-based CR and control groups in these sub-scores (mental component: mean difference (MD) 1.28, 95% CI -1.60 to 4.16; fixed-effect model; 2 trials, 150 participants; I^2 = 0%; GRADE quality of evidence very low; Analysis 1.5; physical component: MD 2.99, 95% CI -5.24 to 11.21; random-effects model; 2 trials, 150 participants; I^2 = 79%; GRADE quality of evidence very low; Analysis 1.6). At longest follow-up (six months in Sibilitz 2016 and 24 months in Pressler 2018), there was also no difference in sub-scores (mental component: MD -1.45, 95% CI -4.70 to 1.80; fixed-effect model; 2 trials, 139 participants; I^2 = 0%; GRADE quality of evidence very low; Analysis 1.7; physical component: MD -0.87, 95% CI -3.57 to 1.83; fixed-effect model; 2 trials, 139 participants; I^2 = 0%; GRADE quality of evidence very low; Analysis 1.8).

The overall risk of bias for both mental component and physical component sub-scores at completion of the intervention and at maximum follow-up was 'high' for both Sibilitz 2016 and Pressler 2016. Both trials also had some concerns for missing outcome data. Caution should therefore be applied when this outcome is interpreted; GRADE quality of evidence was very low.

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Secondary outcomes

Exercise capacity

All six trials reported exercise capacity in 321 participants assessed as VO_2 peak/max (Lin 2004; Nilsson 2019; Sire 1987), as six-minute walk test (6MWT) (Rogers 2018), or as both (Pressler 2016; Sibilitz 2016). All trials reporting VO_2 max were converted to mL/kg/min, except Sire 1987, which could not be recalculated from reported kilojoules. Due to these differences in reporting, exercise capacity is presented in three ways: (1) direct measures of VO_2 max data in mL/kg/min across four trials, (2) maximal measures (contained all peak exercise capacity data as standardised mean difference (SMD) across five trials), and (3) submaximal data based on 6MWT from three trials.

At completion of the intervention, and compared to control, exercise-based CR resulted in a moderate increase in exercise capacity for maximal measures (SMD 0.38, 95% CI 0.15 to 0.61; fixed-effect model; 5 trials, 194 participants; I^2 = 0%; Analysis 1.11) and direct measures of VO_2 max (MD 2.38 mL/kg/min, 95% CI 0.36 to 4.40; 4 trials, 250 participants; I^2 = 0%; fixed-effect model; Analysis 1.9) but not for submaximal 6MWT (MD -3.89 metres, 95% CI -58.72 to 50.95; 3 trials, 167 participants; I^2 = 85%; random-effects model; Analysis 1.13).

At longest follow-up, moderate benefit in favour of exercise was still seen for maximal measures (SMD 0.37, 95% CI 0.13 to 0.61; 5 trials, 284 participants; I^2 = 0%; fixed-effect model; Analysis 1.12) but not for direct measures of VO_2 max (MD 1.53 mL/kg/min, 95% CI -0.44 to 3.50; 4 trials, 240 participants; I^2 = 0%; fixed-effect model; Analysis 1.10) nor of 6MWT (MD -25.48 meters, 95% CI -103.04 to 52.08; 3 trials, 158 participants; I^2 = 84%; random-effects model; Analysis 1.14).

Serious adverse events

A total of 23 serious adverse events (exercise-based CR 12/164 (7.3%) versus control 11/162 (6.8%)) were reported across four trials (Lin 2004; Pressler 2016; Sibilitz 2016; Sire 1987), with no differences between groups (RR 1.07, 95% CI 0.50 to 2.27; 4 trials, 326 participants; I^2 = 0%; fixed-effect model; Analysis 1.15; Table 2).

Return to work

Only one trial reported return to work in a total of 44 participants (Sire 1987). At 12 months' follow-up, there was no difference in the proportion of participants who had returned to work in the exercise-based CR group (4/21; 19%) compared to the control group (8/23; 35%) (RR 1.24, 95% CI 0.86 to 1.79; Analysis 1.16).

Costs and cost-effectiveness

Only Sibilitz 2016 reported economic data, with cost data collected in the trial from the time of surgery to six months' follow-up and assessed from a societal perspective (Hansen 2017). Although there was no difference between exercise-CR and control in HRQoL or costs (see Table 3) driven by a trend towards cost savings with CR, trial authors reported a probability ≥ 75% that CR was cost-effective (Hansen 2017).

Subgroup analyses

Due to the small number of included trials and a limited quantity of data, it was not possible to perform any of the planned subgroup analyses.

DISCUSSION

Summary of main results

We identified six randomised trials including a total of 364 people following open or percutaneous valve surgery who received exercise-based cardiac rehabilitation (CR) or the no exercise control. Two trials reported a total of nine deaths, one trial reported one hospitalisation, and evidence of the impact on health-related quality of life (HRQoL) was of very low certainty. Exercise-based CR programmes in these trials were consistently based on aerobic exercise and were in accord with the European Society of Cardiology recommendation for physical activity for secondary prevention (Ambrosetti 2020; Corra 2010). In summary, although potentially beneficial in terms of short-term exercise capacity, data remain inadequate for definitive assessment of the impact of exercise-based CR on the key patient-related primary outcomes of mortality, hospitalisations, and HRQoL.

Overall completeness and applicability of evidence

Several issues need to be addressed when implications of the findings of this review are interpreted for daily clinical practice. First and foremost, the generalisability of the findings of this review is limited by the small quantity of data identified. Furthermore, almost all included trials recruited highly selected trial populations consisting of younger participants with low to moderate risk and few women, except for Sibilitz 2016 , which included a broad representation of participants. Throughout the last decade, novel valve repair techniques have evolved, including less invasive techniques such as percutaneous valve procedures, with resultant changes in the treatment and participant pathway following valve repair or replacement; without sternotomy, exercise-based CR programmes can start earlier and patients are older with more co-morbidities. Included trials provide few data on postsurgical complications, such as hospitalisation, atrial fibrillation, pericardial exudate, and impact on overall HRQoL. These considerations are important when postsurgery management is planned, especially after open heart surgery, and when suitable patients are selected for a rehabilitation programme after valve surgery. In summary, the applicability of the evidence in this review to current practice is limited, and the generalisability of results should be interpreted with caution.

Quality of the evidence

We judged all primary outcomes to have 'very low' quality of evidence based on GRADE analysis. The quality of evidence for total mortality was 'very low' and was downgraded for inconsistency and small sample size/numbers of events. The quality of evidence for hospitalisation admission was 'very low' and was downgraded for risk of bias, inconsistency, and small sample size/numbers of events. The quality of evidence for HRQoL was judged to be 'very low', with downgrading due to small sample size/numbers of events, inconsistency, and lack of patient blinding (with the HRQoL physical component score at completion of the intervention also having high statistical heterogeneity).

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Potential biases in the review process

We conducted this updated review according to recommendations provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019c). We followed our peer-reviewed published protocol (Sibilitz 2013b), with its predefined participants, interventions, comparisons, and outcomes, to avoid biases during review preparation. We performed a comprehensive literature search to identify published and unpublished trials, abided by our prespecified inclusion and exclusion criteria, and conducted the meta-analysis using available data or based it on intention-to-treat when possible. However, the bias of omission of full copies of papers that may have included important data due to no response from study authors is difficult to assess.

The included trials were relatively small and had short-term follow-up and small numbers of reported events (mortality, hospitalisations, and serious adverse events). With the exception of Sibilitz 2016, none of the included trials sought to formally collect mortality or serious adverse events as outcomes, and we were able to capture these outcomes from studies based only on their reporting of losses to follow-up and dropouts. Translation of Lin 2004, which was published in Chinese, may have resulted in reporting bias.

Agreements and disagreements with other studies or reviews

Since the time this Cochrane Review was first published, two other non-Cochrane systematic reviews and meta-analyses have been published (Anayo 2019; Ribeiro 2017). The review by Ribeiro and colleagues (5 uncontrolled before-and-after studies, 862 patients) showed that the six-minute walk distance test (6MWT) significantly improved with exercise-based CR compared to control (standardised mean difference (SMD) 0.69, 95% confidence interval (CI) 0.47 to 0.91). Similarly, the Anayo et al review (3 randomised controlled trials (RCTs) and 3 non-RCTs, 255 participants) showed improvement in 6MWT favouring exercise-based CR (mean difference (MD) 22.90 metres, 95% CI −31.64 to 77.43). Although the present review found no clear evidence of improvement in 6MWT with exercise-based CR, our finding of improvement in short-term exercise capacity with CR is consistent with the findings of both of these previous reviews. In accord with this review, Anayo et al found no difference between exercise-based CR and control in 12-Item/36-Item Short-Form Health Survey questionnaire (SF-12/36) HRQoL scores (mental component: MD −0.44, 95% CI −3.43 to 2.56; physical component: MD 2.81, 95% CI −5.82 to 11.44).

AUTHORS' CONCLUSIONS

Implications for practice

Current European Society of Cardiology guidelines recommend exercise-based CR following heart valve surgery. However, this updated systematic review of randomised controlled trial evidence shows that a more cautious recommendation is needed. In particular, the impact of exercise-based CR after heart valve surgery on mortality, serious adverse events, HRQoL, return to work, and costs remains unclear. Additionally, its impact on postsurgical adverse events needs to be further investigated, and this information used to inform targeting of exercise-based CR to the most relevant heart valve patients. Nevertheless, our review supports the potential use of exercise-based CR to improve short-term exercise capacity following heart valve surgery.

The trials included in this review have investigated CR interventions based on exercise training. It is widely accepted that contemporary CR should be 'comprehensive' and should incorporate risk factor education/counselling and psychosocial interventions (Anderson 2014; Corra 2010). For use post valve surgery, CR interventions may also need to include breathing and coughing exercises and vocational evaluation advice. Moreover, due to the risk of complications and of hospitalisations, a CR programme for heart valve surgery patients also needs to address medical issues and medical stabilisation, along with anticoagulation treatment, and needs to provide thorough information about endocarditis prophylaxis. An important question for future updates on CR is whether patients could benefit from alternative modalities to centre-based CR, including home-based programmes.

Implications for research

To date, research evidence for CR has focused mainly on trials showing the benefits of CR in ischaemic heart disease (post myocardial infarction and revascularisation) and heart failure. This updated systematic review shows that further randomised controlled trial evidence at low risk of bias is needed to definitively assess the impact of exercise-based CR on patients following valve surgery. Information is especially needed on the outcomes that matter most to patients, clinicians, and policymakers (i.e. mortality, hospitalisations, HRQoL, return to work, and costs and cost-effectiveness).

We identified 10 ongoing (information from clinicaltrials.gov and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP)) randomised controlled trials, most of which are still recruiting. These trials seek to include a total of 2435 participants (with sample sizes ranging from 30 to 800 participants/trial) and report that they are collecting a range of outcomes that include mortality, exercise capacity, HRQoL, hospitalisations, and adverse events.

Critique of this new evidence should include the following considerations.

- Trial quality including consideration of sample size calculation based on participant-relevant outcomes that may include composite events (such as mortality and hospitalisation) and health-related quality of life and conduct/reporting in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines for non-pharmacological interventions (Boutron 2008).
- CR interventions that address the specific needs and preferences of heart valve patients with focus on maximising uptake, such as home-based programmes (especially given the global impact of the COVID-19 pandemic on healthcare systems).
- Routine reporting of fidelity to CR prescription delivery and patient adherence.
- Generalisability of trial populations to practice (i.e. inclusion of women, patients with baseline phenotypes including different types of valve lesions, open versus percutaneous and replacement versus repair valve surgery, inclusion of older participants).

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- Long-term follow-up (≥ 12 months) to fully assess the clinical and cost-effectiveness implications of CR.

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The Background and Methods sections of this review are based on a standard template provided by the Cochrane Heart Group.

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REFERENCES

References to studies included in this review

Lin 2004 *{published data only}*

Lin CY, He Z, Chen J, Yang B, Gu JX. Efficacy analysis of rehabilitation therapy on patients with heart valve replacement. *Chinese Journal of Clinical Rehabilitation* 2004;**8**:426-7.

Nilsson 2019 *{published data only}*

* Nilsson H, Nylander E, Borg S, Tamas E, Hedman K. Cardiopulmonary exercise testing for evaluation of a randomized exercise training intervention following aortic valve replacement. *Clinical Physiology and Functional Imaging* 2019;**39**(1):103–10.

Pressler 2016 *{published data only}*

NCT01935297. Exercise training after transcatheter aortic valve implantation (SPORT:TAVI). clinicaltrials.gov/ct2/show/NCT01935297 (first posted 5 September 2013).

Pressler A, Forschner L, Hummel J, Haller B, Christle JW, Halle M. Long-term effect of exercise training in patients after transcatheter aortic valve implantation: follow-up of the SPORT:TAVI randomised pilot study. *European Journal of Preventative Cardiology* 2018;**25**(8):794-801.

* Pressler A, Christle JW, Lechner B, Grabs V, Haller B, Hettich I, et al. Exercise training improves exercise capacity and quality of life after transcatheter aortic valve implantation: a randomized pilot trial. *American Heart Journal* 2016;**182**:44-53.

Rogers 2018 *{published data only}*

Rogers P, Al-Aidrous S, Banya W, Haley SR, Mittal T, Kabir T, et al. Cardiac rehabilitation to improve health-related quality of life following trans-catheter aortic valve implantation: a randomised controlled feasibility study RECOVER–TAVI Pilot, ORCA 4, for the Optimal Restoration of Cardiac Activity Group. *Pilot and Feasibility Studies* 2018;**13**(4):185.

Sibilitz 2016 *{published data only}*

Hansen TB, Zwisler AD, Berg SK, Sibilitz KL, Thygesen LC, Kjellberg J, et al. Cost-utility analysis of cardiac rehabilitation after conventional heart valve surgery versus usual care. *European Journal of Preventive Cardiology* 2017;**24**:698-707. [DOI: 10.1177/2047487317689908]

NCT01558765. CopenHeartVR - integrated rehabilitation of patients after heart valve surgery (CopenHeartVR). clinicaltrials.gov/ct2/show/NCT01558765 (first posted 20 March 2012).

Sibilitz KL, Berg SK, Rasmussen TB, Risom SS, Thygesen LC, Tang L, et al. Cardiac rehabilitation increases physical capacity but not mental health after heart valve surgery: a randomised clinical trial. *Heart* 2016;**102**:1995–2003.

Sire 1987 *{published data only}*

Sire S. Physical training and occupational rehabilitation after aortic valve replacement. *European Heart Journal* 1987;**8**:1215-20.

References to studies excluded from this review

Amat Santos 2012 *{unpublished data only}*

Amat Santos IJ, Duro IC, Hernandez Luis C, Alvarado M, De La Fuente L, Amado MG, et al. Benefits of cardiac rehabilitation programmes in high-risk patients with symptomatic chronic heart failure and low left ventricular ejection fraction. In: European Heart Journal. Vol. 33. 2012:1056.

Bakhshayesh 2018 *{published data only}*

IRCT20180730040643N1. The effect of IT interventions in cardiac rehabilitation patients [Home based cardiac rehabilitation after coronary angioplasty and heart surgery using booklet and mobile application: assessing the impact of interventions on health related quality of life]. en.irct.ir/trial/33791 (first received 3 November 2018).

Batra 2012 *{published and unpublished data}*

Batra AS, McElhinney DB, Wang W, Zakheim R, Garofano RP, Daniels C, et al. Cardiopulmonary exercise function among patients undergoing transcatheter pulmonary valve implantation in the US Melody valve investigational trial. *American Heart Journal* 2012;**163**:280-7.

Brosseau 1995 *{published and unpublished data}*

Brosseau R, Juneau M, Sirard A, Savard A, Marchand C, Boudreau MH, et al. Safety and feasibility of a self monitored, home-based phase II exercise program for high risk patients after cardiac surgery [La securite d'un entrainement a domicile en phase II apres une chirurgie cardiaque pour les patients a haut risque]. *Canadian Journal of Cardiology* 1995;**11**:675-85.

Cargnin 2019 *{published data only}***https://dx.doi.org/10.1097/HCR.0000000000000409**

Cargnin C, Karsten M, Guaragna JCVDC, Dal Lago P. Inspiratory muscle training after heart valve replacement surgery improves inspiratory muscle strength, lung function, and functional capacity: a randomized controlled trial. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2019;**39**(5):E1-E7.

Chambers 2005 *{published and unpublished data}*

Chambers J, Rimington H, Rajani R, Hodson F, Blauth C. Reply [2]. Journal of Heart Valve Disease 2005.

Chan 2012 *{published and unpublished data}*

Chan CL, Wang CW, Ho RT, Ho AH, Ziea ET, Taam Wong VC, et al. A systematic review of the effectiveness of qigong exercise in cardiac rehabilitation. *American Journal of Chinese Medicine* 2012;**40**:255-67.

CTRI 2017 *{published data only}*

CTRI/2017/09/009707. Effect of physiotherapy in open heart surgery patients [Maximum inspiratory pressure, functional status and quality of life of the patients after open heart surgery following physiotherapy]. www.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2017/09/009707 (first received 2017).

Copyright © 2021 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

de Charmoy 2000 *{published and unpublished data}*

de Charmoy SB, Eales CJ. The role of prophylactic chest physiotherapy after cardiac valvular surgery: is there one? *South African Journal of Physiotherapy* 2000;**56**:24-8.

Deepa 2018 *{published data only}*

CTRI/2018/02/011705. To compare the utility and efficacy of the routine exercise program and bicycle ergometer program among heart valve surgery patients [Role of bicycle ergometer training in phase one among heart valve surgery patients]. www.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2018/02/011705 (first received 2018).

Dull 1983 *{published and unpublished data}*

Dull JL, William JL. Are maximal inspiratory breathing exercises or incentive spirometry better than early mobilization after cardiopulmonary bypass? *Physical Therapy* 1983;**63**:655-9.

Editorial 2018 *{published data only}*

Francesco G, Carlo V. Editorial to 'Comparison of phase 2 cardiac rehabilitation outcomes between patients after transcatheter versus surgical aortic valve replacement'. *European Journal of Preventive Cardiology* 2018;**25**(15):1575-6.

Fang 2002 *{published and unpublished data}*

Fang W, Chen YT, Liang JJ. Effects of early rehabilitative guidance on quality of life after cardiac valve replacement. *Chinese Journal of Clinical Rehabilitation* 2002;**6**:1106-7.

Ferreira 2009 *{published and unpublished data}*

Ferreira PE, Rodrigues AJ, Evora PR. Effects of an inspiratory muscle rehabilitation program in the postoperative period of cardiac surgery. *Arquivos Brasileiros de Cardiologia* 2009;**92**:275-82.

Fontes Cerqueira 2018 *{published data only}***http://dx.doi.org/10.1097/MD.0000000000013012**

Fontes Cerqueira TC, De Cerqueira Neto ML, De Assis Pereira Cacau L, Oliveira GU, Da Silva WM, Carvalho VO, et al. Ambulation capacity and functional outcome in patients undergoing neuromuscular electrical stimulation after cardiac valve surgery: a randomised clinical trial. *Medicine (United States)* 2018;**97**(46):e13012.

Gaita 1999 *{published and unpublished data}*

Gaita D, Branea I, Dragulescu S, Gaita A, Socoteanu I, Gaspar M, et al. Benefit of Exercise Training in Patients With Valve Prostheses and Chronic Heart Failure. Bologna: Medimond S R L, 1999.

Ghalamghash 2008 *{published and unpublished data}*

Ghalamghash R, Goosheh B, Emrani A, Keyhani MR. Effect of cardiac rehabilitation program on functional capacity following valvular heart surgery. *Journal of Medical Council of Islamic Republic of Iran* 2008;**26**:292-3.

Gortner 1988 *{published and unpublished data}*

Gortner SR, Gilliss CL, Shinn JA, Sparacino PA, Rankin S, Leavitt M, et al. Improving recovery following cardiac surgery: a randomized clinical trial. *Journal of Advanced Nursing* 1988;**13**:649-61.

Green 2013 *{published and unpublished data}*

Green P, Kirtane A, Genereux P, McAndrew T, Hueter I, Alu M, et al. The impact of six-minute walk test performance on outcomes after transcatheter aortic valve replacement: insights from the PARTNER trial. *Journal of the American College of Cardiology* 2013;**62**:E1971.

Grunewald 1971 *{published and unpublished data}*

Grunewald B. Prevention and rehabilitation of rheumatic heart valve diseases. *Zeitschrift fur Allgemeinmedizin* 1971;**47**:705-9.

Ha 2011 *{published and unpublished data}*

Ha YK, Jung YY. Development and application of an early exercise program for open heart surgery patients. *Journal of Korean Critical Care Nursing* 2011;**4**:1.

Hokanson 2011 *{published and unpublished data}*

Hokanson JS, Ralphe JC. Exercise restrictions after balloon aortic valvuloplasty (Letter to the Editor). *Journal of the American College of Cardiology (JACC)* 2011;**57**:2034.

Hui 2006 *{published and unpublished data}*

Hui PN, Wan M, Chan WK, Yung PM. An evaluation of two behavioral rehabilitation programs, qigong versus progressive relaxation, in improving the quality of life in cardiac patients. *Journal of Alternative & Complementary Medicine* 2006;**12**:373-8.

Jairath 1995 *{published and unpublished data}*

Jairath N, Salerno T, Chapman J, Dornan J, Weisel R. The effect of moderate exercise training on oxygen uptake post-aortic/mitral valve surgery. *Journal of Cardiopulmonary Rehabilitation* 1995;**15**:424-30.

Johnson 1996 *{published and unpublished data}*

Johnson D, Kelm C, Thomson D, Burbridge B, Mayers I. The effect of physical therapy on respiratory complications following cardiac valve surgery. *Chest* 1996;**109**:638-44.

Kardis 2007 *{published and unpublished data}*

Kardis P, Sherman M, Barnett SD. Association of age and quality of life following phase II cardiac rehabilitation. *Journal of Nursing Care Quality* 2007;**22**:255-9.

Kassirskii 1983 *{published and unpublished data}*

Kassirskii GI, Semenovskii ML, Petrunina LV, Fomina NG. Evaluation of patient rehabilitation effectiveness after aortic valve prosthesis based on spiroergometric study data. *Kardiologiia* 1983;**23**:82-6.

Kassirskii 1991 *{published and unpublished data}*

Kassirskii GI, Grosheva TV. Physical rehabilitation using bicycle ergometry training of patients after aortic valve replacement. *Terapevticheskii Arkhiv* 1991;**63**:59-62.

Kodric 2013 *{published and unpublished data}*

Kodric M, Trevisan R, Torregiani C, Cifaldi R, Longo C, Cantarutti F, et al. Inspiratory muscle training for diaphragm dysfunction after cardiac surgery. *Journal of Thoracic & Cardiovascular Surgery* 2013;**145**:819-23.

Copyright © 2021 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Kübler 1984 *{published data only (unpublished sought but not used)}*

Kübler W, Opherk D. Angina pectoris with normal coronary arteries. *Acta Medica Scandinavica. Supplementum* 1984;**694**:55-7.

Liao 2004 *{published and unpublished data}*

Liao B, Liu H, Chen L, Guo SM, Liu AM, et al. Effect of psychological and behavioral interventions on the negative emotion of patients with heart valve replacements during perioperative period. *Chinese Journal of Clinical Rehabilitation* 2004;**8**:7360-1.

Lim 1998 *{published and unpublished data}*

Lim HY, Lee CW, Park SW, Kim JJ, Song JK, Hong MK, et al. Effects of percutaneous balloon mitral valvuloplasty and exercise training on the kinetics of recovery oxygen consumption after exercise in patients with mitral stenosis. *European Heart Journal* 1998;**19**:1865-71.

Martsinkiavichus 1980 *{published and unpublished data}*

Martsinkiavichus A, Paliushchinskaia N, Iozaitis M, Zhukauskene I, Norvilene A, et al. Physical activity and the work capacity of patients with artificial heart valves before and after rehabilitation. *Kardiologiia* 1980;**20**:28-31.

McDermott 2019 *{published data only}***10.1177/2047487319860046**

McDermott C, McCormack CM, McDermott L, O'Shea O, Kelly SM, McCarren A, et al. Comparison of selected health indices in Irish and Belgian participants commencing a home-based, technology enabled cardiac rehabilitation program. *European Journal of Preventive Cardiology* 2019;**26**:S40-S41.

Nagashio 2003 *{published and unpublished data}*

Nagashio M, Suzuki Y, Onishi Y, Tomatsu A, Shimada Y, Okamura S, et al. Post-operative cardiac rehabilitation programs for early returning to daily life activities: self-measurement of heart rate and blood pressure during staying at home trial. *Journal of Cardiology* 2003;**41**:91-5.

Nehyba 2009 *{published data only}*

Nehyba S, Chaloupka V, Soucek R, Chaloupkova S, Vysoky R, Stetka F, et al. The programme of managed ambulatory rehabilitation for patients after heart valve defect surgery. *Vnitrni Lekarstvi* 2009;**55**:1118-25.

Newell 1980 *{published and unpublished data}*

Newell JP, Kappagoda CT, Stoker JB, Deverall PB, Watson DA, Linden RJ. Physical training after heart valve replacement. *British Heart Journal* 1980;**44**:638-49.

Patel 2019 *{published data only}***https://dx.doi.org/10.1001/jamacardio.2019.4032**

Patel D, Duncan M, Shah A, Lindman B, Greevy R, Savage P, et al. Association of cardiac rehabilitation with decreased hospitalization and mortality risk after cardiac valve surgery. *JAMA Cardiology* 2019;**4**(12):1250-9.

Peng 2018 *{published data only}***http://dx.doi.org/10.1097/MD.0000000000012069**

Peng X, Su Y, Hu Z, Sun X, Li X, Dolansky MA, et al. Home-based telehealth exercise training program in Chinese patients with heart failure: a randomized controlled trial. *Medicine (United States)* 2018;**97**(35):e12069.

Petrunina 1980 *{published and unpublished data}*

Petrunina LV. Patient physical rehabilitation after mitral or aortic valve prosthesis. *Kardiologiia* 1980;**20**:50-3.

Prasciene 2019 *{published data only}***10.1177/2047487319860046**

Prasciene E, Icking N, Kisieliute E, Kubilius R, Bjarnason-Wehrens B, et al. Feasibility and short-term effectiveness of an additional resistance and balance training in cardiac rehabilitation for older patients after valve surgery: results of a pilot study. *European Journal of Preventive Cardiology* 2019;**26**:S39.

Pressler 2015 *{published data only}***10.1177/2047487315586736**

Pressler A, Lechner B, Christle J, Bleiziffer S, Mehilli J, Jochheim D, et al. Safety, applicability and outcome of regular exercise training after transcatheter aortic valve implantation: a randomized pilot trial. *European Journal of Preventive Cardiology* 2015;**22 Suppl 1**:S78.

RBR-8swgc3 2017 *{published data only}*

RBR-8swgc3. Inspiratory muscle training in patients after cardiac surgery [Inspiratory muscle training in patients undergoing cardiac surgery]. http://www.who.int/trialsearch/Trial2.aspx?TrialID=RBR-8swgc3 (first received 2019).

Rizwan 2012 *{published and unpublished data}*

Rizwan A, Jalwan J, Mukherjee S. To compare the immediate effect of deep breathing exercise and incentive spirometry on ABG after mitral valve replacement surgery. *Indian Journal of Physiotherapy & Occupational Therapy* 2012;**6**:12-7.

Rogers2018 *{published data only}*

Rogers P, Banya W, Kabir T, Panoulas V, Probert H, Prendergast C, et al. Does cardiac rehabilitation improve functional, independence, frailty and emotional outcomes following trans catheter aortic valve replacement? *European Heart Journal* 2018;**39 Suppl 1**:1121.

Roseler 1997 *{published and unpublished data}*

Roseler S, Schwartz FW, Karoff M. Evaluation of the effectiveness of an ambulatory after-care rehabilitation program. *Gesundheitswesen* 1997;**59**:236-41.

Rosenfeldt 2011 *{published and unpublished data}*

Rosenfeldt F, Braun L, Spitzer O, Bradley S, Shepherd J, Bailey M, et al. Physical conditioning and mental stress reduction - a randomised trial in patients undergoing cardiac surgery. *BMC Complementary & Alternative Medicine* 2011;**11**:20.

Royse 2015 *{published data only}*

ACTRN12615000968572. Sternal management accelerated recovery trial (S.M.A.R.T.): the efficacy of modified sternal precautions on improving physical function in patients

Copyright © 2021 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

following cardiac surgery via a midline sternal incision [A randomized controlled trial of the efficacy of modified sternal precautions versus standard care on improving physical function following cardiac surgery via a median sternotomy]. www.who.int/trialsearch/Trial2.aspx?TrialID=ACTRN12615000968572 (first received 2019).

Song 2019 *{published data only}*https://dx.doi.org/10.31083/j.rcm.2019.01.3183

Song F, Zhan H, Liang Y, He X, Guo L, et al. Cardiac rehabilitation improved oxygen uptake measured by cardiopulmonary exercise test in patients after aortic valve surgery. *Reviews in Cardiovascular Medicine* 2019;**20**(1):47-52.

Stoickov 2018 *{published data only}*10.1093/eurheartj/ehy564.P640

Stoickov V, Deljanin Ilic M, Stoickov M, Marinkovic D, Simonovic D, Golubovic M, et al. Impact of short-term exercise training on QT dispersion and double product in patients after surgical aortic valve replacement. *European Heart Journal* 2018;**39**:85-6.

Sumide 2009 *{published and unpublished data}*

Sumide T, Shimada K, Ohmura H, Onishi T, Kawakami K, Masaki Y, et al. Relationship between exercise tolerance and muscle strength following cardiac rehabilitation: comparison of patients after cardiac surgery and patients with myocardial infarction. *Journal of Cardiology* 2009;**54**:273-81.

Tang 2019 *{published data only}*https://dx.doi.org/10.1097/HCR.0000000000000416

Tang LH, Zwisler AD, Doherty P, Oldridge N, Berg SK, Christensen J. Changes in physical performance and their association with health-related quality of life in a mixed nonischemic cardiac population that participates in rehabilitation. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2020;**40**(2):102-7.

Therrien 2003 *{published and unpublished data}*

Therrien J, Fredriksen PM, Walker M, Granton J, Reid GJ, Webb G. A pilot study of exercise training in adult patients with repaired tetralogy of Fallot. *Canadian Journal of Cardiology* 2003;**19**:685-9.

Ueshima 2004 *{published data only (unpublished sought but not used)}*

Ueshima K, Kamata J, Kobayashi N, Saito M, Sato S, Kawazoe K, et al. Effects of exercise training after open heart surgery on quality of life and exercise tolerance in patients with mitral regurgitation or aortic regurgitation. *Japanese Heart Journal* 2004;**45**(5):789-97.

Viana 2018 *{published data only}*

RBR-8ysb3n. Evaluation of the physiotherapy with cycle ergometer in the funcional recovery after cardiac surgery [Cycle ergometer and conventional physiotherapy in patients submitted the cardiac surgery]. www.who.int/trialsearch/Trial2.aspx?TrialID=RBR-8ysb3n (first received 2019).

Weber 2019 *{published data only}*

DRKS00017239. Use of pre- and intensified post-procedural physiotherapy in patients with symptomatic aortic stenosis undergoing transcatheter aortic valve replacement - the 4P TAVR study. www.who.int/trialsearch/Trial2.aspx?TrialID=DRKS00017239 (first received 2019).

Widimsky 2009 *{published and unpublished data}*

Widimsky P, Suryapranata H. "PRAGUE" randomized clinical trials: pride of Czech cardiology. *Cor et Vasa* 2009;**51**(10):679-83.

Yan 2016 *{published data only}*

Yan XY. Early rehabilitation mode in transcatheter domestic aortic valve implantation of perioperative implementation and effects on patient life ability. *Journal of the Hong Kong College of Cardiology* 2016;**24**:A25.

Yau 2018 *{published data only}*

ChiCTR1800016098. PREQUEL (PREhabilitation for improving QUality of recovery after ELective cardiac surgery) study: a randomised controlled trial. www.who.int/trialsearch/Trial2.aspx?TrialID=ChiCTR1800016098 (first received 2019).

References to ongoing studies

ACTIVE AFTER TAVR 2017 *{published data only}*

NCT03270124. A pragmatiC sTrategy to Promote actIVity and Enhance Quality of Life AFTER Transcatheter Aortic Valve Replacement (ACTIVE AFTER TAVR): a pilot study. https://clinicaltrials.gov/ct2/show/NCT03270124 (first received 1 September 2017).

Exercise Training After TAVI *{unpublished data only}*

NCT03966417. Exercise training after transcatheter aortic valve implantation (FitTAVI). clinicaltrials.gov/show/NCT03966417 (first received 29 May 2019).

Feng 2019 *{published data only}*

ChiCTR-IPR-17011445. The effects of I stage cardiac rehabilitation on cardiopulmonary function in patients undergoing open heart surgery: a randomized controlled study. www.who.int/trialsearch/Trial2.aspx?TrialID=ChiCTR-IPR-17011445 (first received 2019).

HBCR-TAVR 2019 *{published data only}*

NCT04166682. Impact of home-based cardiac rehabilitation on outcomes after TAVR (HBCR-TAVR). https://clinicaltrials.gov/ct2/show/NCT04166682 (first received 18 November 2019).

Post Cardiac Valvular Surgery Rehabilitation (PORT *{published data only}*

NCT03709511. Post cardiac valvular surgery rehabilitation (PORT). https://clinicaltrials.gov/ct2/show/NCT03709511 (first received 17 October 2018).

PREPARE TAVR Pilot Study *{unpublished data only}*

NCT01504737. Rehabilitation in the form of exercise training in aortic stenosis patients (RASP). http://clinicaltrials.gov/show/NCT01504737 (first received 5 January 2012).

Copyright © 2021 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

REHAB-TAVR 2017 *{published data only}*

NCT02805309. Home-based exercise program for recovery after transcatheter aortic valve replacement: a pilot study. https://clinicaltrials.gov/ct2/show/NCT02805309 (first received 20 June 2016).

The PACO Trial *{published data only}*

Vasankari V, Jari Husu PY, Henri Tokola K, Jaana Sievanen H, Vesa Airaksinen J, Tommi Hartikainen J. Personalised eHealth intervention to increase physical activity and reduce sedentary behaviour in rehabilitation after cardiac operations: study protocol for the PACO randomised controlled trial. *BMJ Open Sport & Exercise Medicine* 2019;**5**(1):e000539.

Valve-ex 2009 *{published data only}*

NCT00860678. Physical activity in patients after aortic valve replacement (Valve-ex). clinicaltrials.gov/ct2/show/NCT00860678 (first received 12 March 2009).

Wang 2019 *{published data only}*

NCT04166682. Impact of home-based cardiac rehabilitation on outcomes after TAVR (HBCR-TAVR) [A study of the impact of home-based cardiac rehabilitation on outcomes after transcatheter aortic valve replacement (TAVR)]. clinicaltrials.gov/ct2/show/NCT04166682 (first received 18 November 2019).

Additional references

Ambrosetti 2020

Ambrosetti M, Abreu A, Corra U, Davos CH, Hansen D, Frederix I, et al. Secondary prevention through comprehensive cardiovascular rehabilitation: from knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. *European Journal of Preventive Cardiology* 2020;**0**(0):1-42 [Epub ahead of print]. [DOI: 10.1177/2047487320913379] [PMID: PMID: 32223332]

Anayo 2019

Anayo L, Rogers P, Long L, Dalby M, Taylor R. Exercise-based cardiac rehabilitation for patients following open surgical aortic valve replacement and transcatheter aortic valve implant: a systematic review and meta-analysis. *Open Heart* 2019;**6**(1):e000922. [DOI: 10.1136/openhrt-2018-000922] [PMID: PMCID: PMC6519423 PMID: 31168371]

Anderson 2014

Anderson LJ, Taylor RS. Cardiac rehabilitation for people with heart disease: an overview of Cochrane systematic reviews. *International Journal of Cardiology* 2014;**177**(2):348-61. [DOI: http://dx.doi.org/10.1016/j.ijcard.2014.10.011]

Anderson 2016

Anderson L, Thompson DR, Oldridge N, Zwisler AD, Rees K, Martin N, et al. 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]

BACPR 2012

The British Association for Cardiovascular Prevention and Rehabilitation. The BACPR Standards and Core Components for Cardiovascular Disease Prevention and Rehabilitation 2012 (2nd edition). The British Cardiovascular Society 2012.

Balady 2007

Balady GJ, Williams MA, Ades PA, Bittner V, Comoss P, Foody JM, et al. Core components of cardiac rehabilitation/secondary prevention programs: 2007 update. A scientific statement from the American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee, the Council on Clinical Cardiology; the Councils on Cardiovascular Nursing, Epidemiology and Prevention, and Nutrition, Physical Activity, and Metabolism; and the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2007;**115**:2675-82.

Baumgartner 2017

Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *European Heart Journal* 2017;**38**(36):2739-91.

Ben-Dor 2010

Ben-Dor I, Pichard AD, Gonzalez MA, Weissman G, Li Y, Goldstein SA, et al. Correlates and causes of death in patients with severe symptomatic aortic stenosis who are not eligible to participate in a clinical trial of transcatheter aortic valve implantation. *Circulation* 2010;**122**(11):37-42. [DOI: 10.1161/CIRCULATIONAHA.109.926873]

Borregaard 2019

Borregaard B, Dahl JS, Riber LPS, Ekholm O, Sibilitz KL, Weiss M, et al. Effect of early, individualised and intensified follow-up after open heart valve surgery on unplanned cardiac hospital readmissions and all-cause mortality. *International Journal of Cardiology* 2019;**15**(289):30-6 [Epub 2019 Apr 11]. [DOI: 10.1016/j.ijcard.2019.02.056]

Boutron 2008

Boutron I, Moher D, Altman DG, Schultz KF, Ravaud P, CONSORT Group. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Annals of Internal Medicine* 2008;**148**(4):295-309.

Butchart 2005

Butchart EG, Gohlke-Bärwolf C, Antunes MJ, Tornos P, Caterina RD, Cormier B, et al. Recommendations for the management of patients after heart valve surgery. *European Heart Journal* 2005;**26**:2463–71.

Clausen 1976

Clausen JP, Trap-Jensen J. Heart rate and arterial blood pressure during exercise in patients with angina pectoris: effects of exercise training and of nitroglycerin. *Circulation* 1976;**53**:436-42.

Corra 2010

European Association of Cardiovascular Prevention and Rehabilitation Committee for Science Guidelines, EACPR, Corrà U, Piepoli MF, Carré F, Heuschmann P, Hoffmann U, et al.

Copyright © 2021 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Secondary prevention through cardiac rehabilitation: physical activity counselling and exercise training: key components of the position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *European Heart Journal* 2014;**31**(16):1967-74. [PMID: 20643803]

Frank 1973

Frank S, Johnson A, Ross J. Natural history of valvular aortic stenosis. *British Heart Journal* 1973;**35**:41-6.

Fredericks 2012

Fredericks S, Lapum J, Lo J. Anxiety, depression, and self-management: a systematic review. *Clinical Nursing Research* 2012;**21**(4):411-30. [DOI: 10.1177/1054773812436681]

Furukawa 2006

Furukawa TA, Barbuib C, Ciprianib A, Brambillac P, Watanabe N. Imputing missing standard deviations in meta-analyses can provide accurate results. *Journal of Clinical Epidemiology* 2006;**59**:7–10. [DOI: 10.1016/j.jclinepi.2005.06.006]

Gianuzzi 2003

Giannuzzi P, Mezzani A, Saner H, Björnstad H, Fioretti P, Mendes M, et al. Physical activity for primary and secondary prevention. Position paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. *European Journal of Cardiovascular Prevention & Rehabilitation* 2003;**10**:319–27. [DOI: 10.1097/01.hjr.0000086303.28200.50]

Gohlke-Bärwolf 1992

Gohlke-Bärwolf C, Gohlke H, Samek L, Peters K, Betz P, Eschenbruch E, et al. Exercise tolerance and working capacity after valve replacement. *Journal of Heart Valve Disease* 1992;**1**(2):189-95. [PMID: 1341626]

GradePro Software [Computer program]

GRADEpro GDT: GRADEpro Guideline Development Tool [Software]. GRADEpro, 2015 (developed by Evidence Prime, Inc.).

Hambrecht 2000

Hambrecht R, Gielen S, Linke A, Fiehn E, Yu J, Walther C, et al. Effects of exercise training on left ventricular function and peripheral resistance in patients with chronic heart failure: a randomised trial. *JAMA* 2000;**283**(23):3095–101.

Hansen 2009

Hansen L, Winkel S, Kuhr J, Bader R, Bleese N, Riess F-C. Factors influencing survival and postoperative quality of life after mitral valve reconstruction. *European Journal of Cardio-Thoracic Surgery* 2010;**37**:635-44. [DOI: 10.1016/j.ejcts.2009.07.044]

Hansen 2017

Hansen TB, Zwisler AD, Berg SK, et al. Cost-utility analysis of cardiac rehabilitation after conventional heart valve surgery versus usual care. *European Journal of Preventive Cardiology* 2017;**24**:698–707. [DOI: 10.1177/2047487317689908]

Higgins 2019a

Higgins JP, Savović J, Page MJ, Elbers RG, Sterne JA. Chapter 8. Assessing risk of bias in a randomized trial. In: Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane 2019. Available from www.training.cochrane.org/handbook.

Higgins 2019b

Higgins JP, Li T, Deeks JJ (editors). Chapter 6. Choosing effect measures and computing estimates of effect. In: Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane 2019. Available from www.training.cochrane.org/handbook.

Higgins 2019c

Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane 2019. Version 6. Available from www.training.cochrane.org/handbook.

Iung 2003

Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, et al. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease. *European Heart Journal* 2003;**24**:1231-43. [DOI: 10.1016/S0195-668X(03)00201-X]

Karlsson 2010

Karlsson AK, Mattson B, Johansson M, Lidell E. Well-being in patients and relatives after open-heart surgery from the perspective of health care professionals. *Journal of Clinical Nursing* 2010;**19**:840-6. [DOI: 10.1111/j.1365-2702.2009.03017.x]

Kiel 2011

Kiel MK. Cardiac rehabilitation after heart valve surgery. *Journal of Injury, Function and Rehabilitation* 2011;**3**(10):962-7. [DOI: 10.1016/j.pmrj.2011.06.007]

Kolte 2019

Kolte D, Vlahakes GJ, Palacios IF, Sakhuja R, Passeri JJ, Inglessis I, et al. Transcatheter versus surgical aortic valve replacement in low-risk patients. *Journal of the American College of Cardiology* 2019;**74**:1532-40.

Landry 1984

Landry F, Habel C, Desaulniers D, Dagenais GR, Moisan A, Cote L. Vigorous physical training after aortic valve replacement: analysis of 10 patients. *American Journal of Cardiology* 1984;**53**(4):562-6. [PMID: 6695785]

Lauck 2020

Lauck SB, Arnold SV, Borregaard B, Sathananthan J, Humphries KH, Baron SJ, et al, 3M TAVR Investigators. Very early changes in quality of life after transcatheter aortic valve replacement: results from the 3M TAVR trial. *Cardiovascular Revascularization Medicine* 2020;**S1553-8389**(20):30349-3. [DOI: 10.1016/j.carrev.2020.05.044]

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Lefebvre 2011

Lefebvre C, Manheimer E, Glanville J. Chapter 6. Searching for studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Long 2019

Long L, Mordi IR, Bridges C, Sagar VA, Davies EJ, Coats AJS, et al. Exercise-based cardiac rehabilitation for adults with heart failure. *Cochrane Database of Systematic Reviews* 2019, Issue 1. Art. No: CD003331. [DOI: 10.1002/14651858.CD003331.pub5]

Mack 2019

Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *New England Journal of Medicine* 2019;**380**:1695-705.

Nishimura 2014

Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin III JP, Guyton RA, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;**129**:2440-92. [DOI: 10.1161/CIR.0000000000000029]

Nkomo 2006

Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet* 2006;**368(9540)**:1005-11.

Pardaens 2014

Pardaens S, Moerman V, Willems AM, Calders P, Bartunek J, Vanderheyden M, et al. Impact of the preoperative risk and the type of surgery on exercise capacity and training after valvular surgery. *American Journal of Cardiology* 2014;**113**(8):1383-9. [DOI: 10.1016/j.amjcard.2014.01.413]

Pavy 2006

Pavy B, Iliou MC, Meurin P, Tabet JY, Corone S. Safety of exercise training for cardiac patients: results of the French registry of complications during cardiac rehabilitation. *Archives of Internal Medicine* 2006;**166**(21):2329-34. [PMID: 17130385]

Piepoli 2010

Piepoli MF, Corra U, Benzer W, Bjarnason-Wehrens B, Dendale P, Gaita D, et al. Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. European Journal of Cardiovascular Prevention & Rehabilitation 2010;**17**(1):1-17. [DOI: 10.1097/HJR.0b013e3283313592]

Popma 2019

Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *New England Journal of Medicine* 2019;**380**:1706-15.

Pressler 2018

Pressler A, Forschner L, Hummel J, et al. Long-term effect of exercise training in patients after transcatheter aortic valve implantation: follow-up of the SPORT:TAVI randomised pilot study. *European Journal of Preventative Cardiology* 2018;**25**(8):794-801.

RevMan 2020 [Computer program]

Review Manager (RevMan). Version 5.4. The Cochrane Collaboration, May 2020.

Ribeiro 2017

Ribeiro GS, Melo RD, Deresz LF, Dal Lago P, Pontes MR, Karsten M. Cardiac rehabilitation programme after transcatheter aortic valve implantation versus surgical aortic valve replacement: systematic review and meta-analysis. *European Journal of Preventive Cardiology* 2017;**24**:688-97.

Schünemann 2013

Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from guidelinedevelopment.org/handbook.

Sibilitz 2015

Sibilitz K, Berg S, Hansen T, et al. Update to the trial protocol, including statistical analysis plan for a randomized clinical trial comparing comprehensive cardiac rehabilitation after heart valve surgery with control: the CopenHeart VR trial. *Trials* 2015;**16**:38.

Sibilitz 2015a

Sibilitz KL, Berg SK, Thygesen LC, Hansen TB, Køber L, Hassager C, et al. High readmission rate after heart valve surgery: a nationwide cohort study. *International Journal of Cardiology* 2015;**189**:96-104. [DOI: 10.1016/j.ijcard.2015.04.078]

Sibilitz 2016 SR

Sibilitz KL, Berg SK, Tang LH, Risom SS, Gluud C, Lindschou J, et al. Exercise-based cardiac rehabilitation for adults after heart valve surgery. *Cochrane Database of Systematic Reviews* 2016;**Issue 3**:Art. No.: CD010876. [DOI: 10.1002/14651858.CD010876.pub2]

Smart 2018

Smart NA, King N, Lambert JD, et al. Exercise based cardiac rehabilitation improves exercise capacity and health-related quality of life in participants with atrial fibrillation: a systematic review and meta-analysis of randomised and non-randomised trials. *Open Heart* 2018;**5**:e000880. [DOI: 10.1136/openhrt-2018-000880]

Sterne 2011

Sterne JAC, Egger M, Moher D. Chapter 10. Addressing reporting biases. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

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Sterne 2019

Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898. [DOI: https://doi.org/10.1136/bmj.l4898]

Supino 2006

Supino PG, Borer JS, Preibisz J, Bornstein A. The epidemiology of valvular heart disease: a growing public health problem. *Heart Failure Clinics* 2006;**2**(4):379-93.

Thompson 2002

Thompson SG, Higgens JP. How should meta-regression analyses be undertaken and interpreted? *Statistics in Medicine* 2002;**21**(11):1559-73. [PMID: 12111920]

Vahanian 2012

Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H, et al. Guidelines on the management of valvular heart disease: the Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the Eurpoean Association for Cardio-Thoracic Surgery (EACTS). *European Heart Journal* 2012;**33**(19):2451-96. [DOI: 10.1093/eurheartj/ehs109]

Whalley 2011

Whalley B, Rees K, Davies P, Bennett P, Ebrahim S, Liu Z, et al. Psychological interventions for coronary heart disease. *Cochrane Database of Systematic Reviews* 2011, Issue 8. Art. No: CD002902. [DOI: 10.1002/14651858.CD002902.pub3]

Wood 2008

Wood L, Egger M, Gluud LL, Schulz KF, Jüni P, Altman DG, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 2008;**336**(7644):601-5. [DOI: 18316340]

Yagdir 2020

Yadgir S, Johnson CO, Aboyans V, et al. Global, regional, and national burden of calcific aortic valve and degenerative mitral valve diseases, 1990-2017. *Circulation* 2020;**121**:1670–80. [DOI: 10.1161/CIRCULATIONAHA.119.043391] [PMID: PMID: 32223336]

References to other published versions of this review

Sibilitz 2013b

Sibilitz KL, Berg SK, Tang LH, Risom SS, Gluud C, Lindschou J, et al. Exercise-based cardiac rehabilitation for adults after heart valve surgery. *Cochrane Database of Systematic Reviews* 2013, Issue 12. Art. No: CD010876. [DOI: 10.1002/14651858.CD010876]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Lin 2004

Study characteristics	
Methods	**Study design:** parallel-group randomised controlled trial **No of centres:** 1 **Country:** China **Dates patients recruited:** NR **When randomised:** NR **Maximum follow-up (from baseline):** 3 months
Participants	**Inclusion criteria:** 20 to 45 years of age who have undergone single or double heart valve replacement **Exclusion criteria:** comorbidities including pathological changes associated with coronary arteries, re-operations for valve replacement surgeries (patients who have undergone valve replacement before), severe pathological changes associated with other organs **N Randomised: total:** 104**; intervention:** 55**; comparator:** 49 Number of participants lost to follow-up: 7 Number of dropouts: 3 (2 due to irregular heart rhythm, 1 for delayed pericardial tamponade) Number with complications: 4 (rehabilitation group: 1 sudden death, 1 brain stem disease; control group: 1 paravalvular leakage, 1 endocarditis)

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Lin 2004 *(Continued)*

Diagnosis (% of pts):

e.g.

Aetiology: the kind of valve disease is not specified; we assume that all kinds of valve diseases are included

Kind of surgery: mechanical valve replacement of any kind

NYHA **:** NR

LVEF: NR

Case mix: NR

Age (mean ± SD): total: NR; **intervention:** 32.8 ± 12.1;**comparator:** 29.8 ± 9.4

Percentage male: total: 56.73%; **intervention:** 56.36%;**comparator:** 57.14%

Ethnicity: NR

Interventions	**Intervention (exercise-based CR)** **Description** Type of rehabilitation programme: combined physical exercise, breathing exercises, and psychological intervention Setting: hospital-based and home-based. At hospital and at home before and after surgery Time after hospitalisation: the day after surgery, and continuing until 3 months after surgery Total duration: starting the week before surgery with breathing exercises and psychological intervention, and the day after surgery with physical exercise • Psychological intervention Conducted before surgery, to prevent anxiety and mental pressure before surgery. Introduction to the surgery in detail, and information about safety of the surgery • Breathing and coughing exercises Conducted before and after surgery Frequency and duration: 2 times a day 1 week before surgery and after surgery Before surgery Breathing exercises: lie down or sit up, pillow under knees, relax muscles in stomach, breathe in through the nose so stomach puffs up, breathe out through the nose. 10 to 12 times per minute. Patients monitor themselves Coughing exercises: after deep breath, use chest and stomach power to cough as much as possible, 2 times daily, 20 times each session, the week before surgery. Breathing machine (Sherwood Voldyne) controls frequency. The patient can look over the results during exercises. Exercises are to be performed both sitting up and half lying down After surgery Day 1: stomach breathing exercise, coughing exercise to get rid of mucus, half lying down, relaxing whole body Day 2: both breathing and coughing exercises • Physical exercise

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Lin 2004 *(Continued)*

	Conducted after surgery. Includes limb stretch/joint exercises and aerobic exercises Frequency: limb stretch/joint exercises: patients were advised to do this whenever they felt like it at home; aerobic exercise 2 to 3 times per week Duration: 3 to 5 minutes limb stretch/joint exercises and 20 to 30 minutes aerobic exercise/session Purpose: the purpose of the training is to increase endurance and increase pulmonary and cardiac capacity At hospital (after surgery) Day 2: joint exercises with passive arms and switch exercises Day 3: joint exercises including both arm and leg exercises Day 4: going out of the hospital, sitting, standing, getting out of bed, walking exercises. Aerobic exercises At home (after discharge) Resistance training: stretch arms and legs 3 to 5 minutes equivalent to 5 to 7 metabolic equivalents (METs) each session. Patients were encouraged to do the exercises whenever possible. The purpose of the exercises was to increase joint mobility, warm up the body, and relieve chest pressure Aerobic exercise: consisted of walking slowly uphill, using treadmill or exercise bike at home. Goal of 5 to 7 METs per session Intensity: not reported Modality: not relevant **Both groups**: follow regular principles and normal procedure for surgery. During surgery, the same equipment is used for all patients. After surgery, all patients receive the same quantities of analgesics, antibiotics, and anticoagulants **Comparator** **Description:** usual care by the hospital's heart doctor **Co-interventions:** NR
Outcomes	**Outcomes (scale measured in)** Postoperative incidence of pulmonary complications after surgery: measured once in all patients in % of control group and rehabilitation group, respectively, during the 3-month period Duration of hospitalisation for surgery: days of hospitalisation calculated once after all patients have been discharged after surgery. The number of days between groups was compared Body activity energy level: measured at baseline and after 3 months in METs spent, using low strenuous physical exercises to test pulmonary and cardiac capacity Besides outcome measurement, the purpose of the test was to determine for which patients the exercise could include potential risk and thus tailor the exercise plan in the most appropriate way **Other outcomes measured**
Notes	Follow-up: 3 months from procedure First author involved in patient selection, not in randomisation. Study authors emphasise that cardiac rehabilitation including physical exercise should be tailored and concrete, based on different patients' needs, and adjusted if necessary

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Nilsson 2019

Study characteristics	
Methods	**Study design:** RCT **No of centres:** 1 **Country:** Sweden **Dates patients recruited:** August 2011 and December 2014 **When randomised:** after surgery **Maximum follow-up (from baseline):** 1 year
Participants	**Inclusion criteria:** all adult patients undergoing AVR due to AS **Exclusion criteria:** any other concomitant cardiac disease, symptomatic lung disease, or mental or physical disability possibly limiting participation in the study **N Randomised: total:** 12;**intervention:** 6;**comparator:** 6 **Diagnosis (% of pts):** **e.g.** *Aetiology:* (total): HR at rest TG (50 to 93), UC (48 to 91); SBP at rest TG (110 to 145), UC (110 to 170); DBP at rest (mmHg) TG (60 to 90), UC (70 to 95) *NYHA* **:** NR *LVEF* **:** NR **Case mix:** NR **Age (mean ± SD): total:** 62.5 (39 to 75); **intervention: 58.5 (**39 to 75);**comparator:** 65.5 (60 to 71) **Percentage male: total:** 75%; **intervention:** 83.33%;**comparator:** 66.67% **Ethnicity:** NR
Interventions	**Intervention (exercise-based CR)** **Description:** the exercise training protocol was designed according to the most recent European position paper concerning exercise training in cardiac patients in addition to feasibility over a large span of age and fitness. Heart rate, workload (Watts), and perceived exertion (Borg RPE scale) were recorded every 5 minutes, and the workload was adjusted to preserve HR within the given interval according to the protocol **Time of start after event:** 5 to 6 weeks postoperatively **Components:** aerobic exercise **Detail of exercise:** patients allocated to EX performed heart rate-guided supervised exercise training on a bicycle ergometer **Modality:** bicycle ergometer **Dose of exercise** (**calculated as overall no. of weeks of training multiplied by mean number of sessions per week multiplied by mean duration of sessions in minutes):** 12 x 3 x 20 vigorous aerobic activity ± 12 x 5 x 30 light to moderate physical activity **Length of session:** not clearly stated but about 45 to 60 minutes

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Nilsson 2019 *(Continued)*

	Frequency/no. of sessions: 3 sessions per week **Intensity:** workload was adjusted to preserve HR within the given interval according to the protocol **Resistance training included?** NR **Total duration:** 12 weeks **Setting:** hospital **Supervision:** yes, heart rate-guided supervised **Intermittent nurse or exercise specialist support?** NR **Co-interventions:** NR **Comparator** **Description:** patients in CON received the same general physical activity recommendations as those in EX at discharge and were contacted on 3 occasions during the 12 weeks to encourage them to follow these recommendations and to give them the opportunity to ask any questions connected to recovery and physical activity **Co-interventions:** NR
Outcomes	**Outcomes (scale measured in):** peak VO_2 measured during maximal exercise test on a cycle ergometer using cardiopulmonary exercise testing with oxygen uptake **Other outcomes measured** Effect on submaximal cardiopulmonary variables including oxygen uptake kinetics (tau), oxygen uptake efficiency slope (OUES), and ventilatory efficiency (VE/VCO_2 slope)
Notes	Follow-up: baseline (i.e. 5 to 6 weeks postoperatively), at the end of the 12-week intervention (i.e. 3 months from baseline), and 1 year hereafter Study was supported by the Medical Research Council of Southeast Sweden (FORSS) and ALF Grants, Region Östergötland Study authors have no conflicts of interest

Pressler 2016

Study characteristics	
Methods	**Study design:** randomised controlled pilot trial **No of centres:** 3 **Country:** Germany **Dates patients recruited:** October 2012 to April 2014 **When randomised:** 83 ± 34 days (range 42 to 132) after intervention **Maximum follow-up (from baseline):** 24 ± 6 months
Participants	**Inclusion criteria:** TAVI within previous 6 months, physically able and clinically stable to perform regular exercise as judged by study investigators, optimal medical treatment for cardiac and concomitant diseases, written informed consent. Only patients living within a reasonable distance from the exercise centre were contacted and were consecutively included in the screening process **Exclusion criteria:** patients' decision to undergo TAVI despite receiving a recommendation for SAVR by the heart team (to avoid inclusion of atypical, low-risk TAVI patients), physical disabilities making regu-

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Pressler 2016 *(Continued)*

lar exercise impossible, unstable cardiac conditions (e.g. decompensated heart failure, New York Heart Association (NYHA) Class IV, severe rhythm disorders), uncontrolled hypertension or diabetes, severe obstructive pulmonary disease (forced expiratory volume in 1 second b50%). Patients were not included in cases of echocardiographic signs of prosthesis dysfunction according to the Valve Academic Research Consortium (valve orifice area of b1.2 cm^2 plus mean transaortic pressure gradient ≥ 20 mmHg, or velocity ≥ 3 m/s, at least moderate paravalvular regurgitation, signs of ischaemia, severe arrhythmias, or haemodynamic deterioration during the initial exercise test)

N Randomised: total: 30;**intervention:** 13;**comparator:** 14

Diagnosis (% of pts)

e.g.

Aetiology: (total): aortic regurgitation (TG = 53%, UC = 73%), coronary artery disease (TG = 69%, UC = 71%), previous myocardial infarction (TG = 15%, UC = 35%), coronary artery bypass graft (TG = 23%, UC = 14%), atrial fibrillation (TG = 54%, UC = 36%), pacemaker/ICD (TG = 15%, UC = 21%), previous cerebrovascular event (TG = 8%, UC = 21%)

NYHA: TG: Class I: 1 (8), Class II: 10 (77), Class III: 2 (15); UC: Class I: 4 (29), Class II: 6 (42), Class III: 4 (29)

LVEF: TG: 58 ± 8%; UC: 57 ± 10%

Case mix: NR

Age (mean ± SD): total: 81 ± 6; **intervention:** 81 ± 7;**comparator:** 81 ± 5

Percentage male: 15/30 (50%): intervention: 47% (N = 7/15);**comparator:** 53% (8/15)

Ethnicity: NR

Interventions

Intervention (exercise-based CR)

Description: the training group received combined endurance and resistance exercise starting with 2 exercise sessions during the first week, followed by 3 sessions per week during Weeks 2 to 8. Resistance training started in Week 2 and was conducted subsequent to the endurance exercise portion in 2 of the 3 weekly workouts

Time of start after event: 81 days ± 27 days post TAVI in the exercise group;

84 days ± 41 days post TAVI in the usual care group

Components: exercise

Detail of exercise: exercise consisted of endurance training on cycle ergometers at moderate intensities, starting with 20 minutes and gradually increasing to 45 minutes by Week 8. Resistance training occurred after endurance training twice weekly from Week 2

Modality: cycle ergometer

Dose of exercise: (**calculated as overall no. of weeks of training multiplied by mean number of sessions per week multiplied by mean duration of sessions in minutes):** NR

Length of session: 20 to 45 minutes/session

Frequency/no. of sessions: Week 1: 2/week; Weeks 2 to 8: 2 to 3/week

Intensity : 45% to 70% VO_2 peak

Resistance training included: yes + muscular endurance (bench press, rowing, shoulder press, pull-down, leg press) 1 to 3 sets at 50% to 60% 1 RM

Total duration: 8 weeks

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Pressler 2016 *(Continued)*

	Setting: hospital **Supervision:** Supervised **Intermittent nurse or exercise specialist support?** NR **Co-interventions:** NR **Comparator** **Description:** usual care. Not receiving structured exercise **Co-interventions:** both groups received usual medical care
Outcomes	**Outcomes (scale measured in):** exercise tolerance assessed by cardiopulmonary testing (VO_2 peak), exercise capacity (6-minute walk distance), HRQoL (KCCQ and SF-12), mortality, all-cause or cardiovascular **Other outcomes measured** Muscular strength with 1 repetition maximum testing, prosthetic aortic valve function with echocardiography
Notes	Follow-up: baseline, 8 weeks after baseline visit, 24 ± 6 months after baseline This study received grant support from the German Heart Foundation/German Foundation of Heart Research (Frankfurt, Germany; F/14/12). Author BL received financial support from the German Cardiac Society (Düsseldorf, Germany) via the Otto-Hess-Research-Grant Conflict of interest: none declared There were 3 dropouts: 2 from the training group that were unrelated to the intervention (1 had an accident, 1 had a lethal cerebral haemorrhage) and 1 from the usual care group who was not willing to continue in the study

Rogers 2018

Study characteristics	
Methods	**Study design:** pilot RCT **No of centres:** 1 **Country:** UK **Dates patients recruited:** June 2016 to March 2017 **When randomised:** 4 weeks after TAVI **Maximum follow-up (from baseline):** 6 months post randomisation
Participants	**Inclusion criteria:** severe symptomatic aortic stenosis accepted for TAVI in our institutional Multidisciplinary Team Meeting, age ≥ 75 years, able to give written informed consent, in the Investigator's opinion able to comply with all study requirements **Exclusion criteria:** CR deemed inappropriate due to comorbidity or frailty, life expectancy < 1 year due to comorbidity, previous AVR or TAVI, predominant aortic regurgitation **N Randomised: total:** 27;**intervention:** 14;**comparator:** 13 **Diagnosis (% of pts)**

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Rogers 2018 *(Continued)*

e.g.

Aetiology: (total): previous MI, n (%), UC 2 (14.3), TG 3 (23.1); history of pulmonary disease, n (%), UC 4 (28.6), TG 3 (23.1); preoperative arrhythmia, n (%), UC 7 (50.0), TG 8 (61.5); previous cardiac surgery, n (%), UC 3 (21.4), TG 4 (30.8); previous PCI, n (%), UC 5 (35.7), TG 6 (46.2)

NYHA: NR

LVEF: ≥ 50% UC 12 (85.7%), TG 9 (69.2%); 30% to 49% UC 2 (14.3%), TG 3 (23.1%); < 30% UC 0, TG 1 (7.7%)

Case mix: NR

Age (mean ± SD): total: 82.04 ± 4.8; **intervention:** 82.92 ± 6.0;**comparator:** 81.21 ± 3.6

Percentage male: total: 44.4%; **intervention:** 46.2%;**comparator:** 42.9%

Ethnicity: NR

Interventions

Intervention (exercise-based CR)

Description: patients randomised to the intervention group underwent a comprehensive biopsychosocial assessment with a member of the exercise team, initiated 1 month post procedure and comprising once-weekly sessions for 60 to 90 minutes for 6 sessions. An individualised programme was prescribed for each patient based on information gained from his/her functional capacity test and discussion around his/her specific goals

Time of start after event: 1 month post procedure

Components: exercise

Details of exercise: comprehensive biopsychosocial assessment comprising once-weekly sessions for 60 to 90 minutes for 6 sessions. An individualised programme was then prescribed for each patient based on information gained from his/her functional capacity test and discussion around his/her specific goals. After each exercise session, each individual's prescription was reviewed and was altered appropriately for the subsequent session. The intensity of the exercise was progressively increased based on self-reported BORG intensity. Patients were offered further sessions if able to attend, in line with our institutional programme and British Association for Cardiovascular Prevention and Rehabilitation (BACPR) recommendations

Modality: exercise prescription consisted of graduated cardiovascular training and resistance training (both upper body and lower body) using cardiovascular exercise machines (treadmill and bike) as well as functional exercise such as 'sit to stand'

Dose of exercise: (**calculated as overall no. of weeks of training multiplied by mean number of sessions per week multiplied by mean number of sessions per week multiplied by mean duration of sessions in minutes):** individualised

Length of session: individualised (avg ± SD: 7.5 ± 4.25) (77% completed 6 sessions; 3 participants completed 15, 13, and 12 sessions, respectively)

Frequency/no. of sessions: individualised

Intensity: individualised

Resistance training included? yes, + cardiovascular training

Total duration: individualised

Setting: hospital

Supervision: supervised

Intermittent nurse or exercise specialist support? NR

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Rogers 2018 *(Continued)*

	Co-interventions: both control and intervention groups received routine medical care, which included an outpatient clinic follow-up appointment, appropriate drug therapy, and concomitant medical management of co-morbidities according to local practice **Comparator** **Description:** patients randomised to the control group received SOC according to our institutional protocols **Co-interventions:** both control and intervention groups received routine medical care, which included an outpatient clinic follow-up appointment, appropriate drug therapy, and concomitant medical management of co-morbidities according to local practice
Outcomes	**Outcomes (scale measured in):** exercise capacity measured by 6-minute walk test (6MWT), Nottingham Activities of Daily Living (ADL; scale of 0 for least activity to 22 for most activity), FRIED Frailty score (0 = not frail, 1 to 2 = pre-frail, 3 = frail), Edmonton Frailty Score (9 domains, scale of 0 for non-frail to 17 for severely frail), and Hospital Anxiety and Depression Scores (HADS, 0 to 7 normal, 8 to 10 borderline, 11 to 21 abnormal) score **Other outcomes measured** Thirty-eight separate post-TAVI patients completed the KCCQ with mean clinical summary score in a substudy
Notes	Follow-up: baseline (pre-randomisation), 3 months and 6 months post randomisation The RECOVER-TAVI trial was funded through a pump priming grant from the Royal Brompton & Harefield NHS Foundation Trust Biomedical Research Unit Conflicts of Interest: MD has received research grants, consultancy and proctorship fees from Astra Zeneca, Eli Lilly, Abbott Vascular, Daiichi Sankyo, Daiichi Sankyo, Lilly Alliance, Abbott Vascular, Sanofi, Medtronic, Boston Scientific, Edwards Lifesciences. NM has received honoraria, consultancy and proctorship fees from Abbott Vascular, Medtronic, and Edwards Lifesciences. MS has received research grants, consultancy and proctorship fees from Medtronic, Edwards Lifesciences, St Jude (now Abbott Vascular), and Boston Scientific. RST is the lead for the ongoing portfolio of Cochrane Reviews of cardiac rehabilitation. RST is a named scientific advisor for ongoing National Institutes of Health and Care Excellence (NICE) updated clinical guidelines for management of heart failure (CG108). HP is a member of the British Association for Cardiovascular Prevention and Rehabilitation (BACPR) and the Association of Chartered Physiotherapists in Cardiac Rehabilitation (ACPICR). HP chaired the referenced ACPICR Working Group for the national standards document Thirteen control group patients completed the study assessment. Ten in the 13 intervention group completed the CR and assessment; 3 were too unwell to do so; and all patients were followed up

Sibilitz 2016

Study characteristics	
Methods	**Study design:** randomised controlled trial **No of centres:** 1 **Country:** Denmark **Dates patients recruited:** 17 February 2012 and 7 May 2014 **When randomised:** after baseline outcome assessment **Maximum follow-up (from baseline):** 24 months (but data for 12 and 24 months recorded elsewhere)
Participants	**Inclusion criteria:** elective right-sided or left-sided heart valve surgery, age ≥ 18 years, able to speak and understand Danish, ability to provide informed written consent

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Sibilitz 2016 *(Continued)*

Exclusion criteria: known ischaemic heart disease before surgery, current recruitment to other rehabilitation trials or participating in trials precluding patients from participating, expected to not cooperate according to trial instructions, diseases in the musculoskeletal system, comorbidity complicating physical activity, competitive sports, and pregnancy and/or breastfeeding

N Randomised: total: 147;**intervention:** 72;**comparator:** 75

Diagnosis (% of pts)

e.g.

Aetiology: (total): atrial fibrillation 21% (intervention), 85% (control); symptoms before surgery are self-reported and include dyspnoea, angina pectoris, palpitations, and decreased physical activity level – 92% (intervention), 92% (control)

NYHA: intervention NYHA Class I to II: 74%, Class III to IV: 26%; control NYHA Class I to II: 69%, Class III to IV: 31%

LVEF: intervention 55 ± 9.6 (89%); control 54 ± 10.2 (85%) ADD

Case mix: cardiac rehab group – aortic valve surgery 46 (64%), mitral valve surgery 27 (38%), pulmonal and tricuspid valve surgery 1 (1.4%)

Control group – aortic valve surgery 45 (60%), mitral valve surgery 26 (35%), pulmonal and tricuspid valve surgery 2 (3%)

Age (mean ± SD): total: 62; **intervention:** 62.0 ± 11.5;**comparator:** 61.0 ± 9.9

Percentage male: total: 76% (112/147); **intervention:** 82% (59/82);**comparator:** 71% (53/75)

Ethnicity: NR

Interventions	**Intervention (exercise-based CR)** **Description:** exercise comprising 3 weekly exercise sessions for 12 weeks **Time of start after event:** 1 month after surgery **Components:** exercise **Detail of exercise:** the programme consisted of graduated cardiovascular training (based on intensity on the Borg Scale, with progressively increasing intensity during the 12 weeks) and strength exercises (lower body exercises) **Modality:** exercise training combining aerobic and resistance training **Dose of exercise:** (**calculated as overall no. of weeks of training multiplied by mean number of sessions per week multiplied by mean duration of sessions in minutes):** NR **Length of session:** 40 minutes/session (including 10-minute warm-up/10-minute cool-down) **Frequency/no. of sessions:** 3 sessions/week **Intensity :** 13 to 17 on Borg Scale **Resistance training included?** yes, strength training for lower body (60% to 70% 1 RM) **Total duration:** 12 weeks **Setting:** home and hospital or local study protocol-certified supervised facility **Supervision:** hospital supervised, home unsupervised (had contact with a physiotherapist when indicated)

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Sibilitz 2016 *(Continued)*

	Intermittent nurse or exercise specialist support? NR **Co-interventions:** monthly psychoeducational consultations **Comparator** **Description:** all patients were provided early mobilisation immediately following surgery as part of usual care. Participants were not allowed to participate in a physical exercise programme **Co-interventions:** none
Outcomes	**Outcomes (scale measured in):** exercise capacity (measured by VO_2 peak) and self-reported mental health (measured by Short Form-36), 6MWT **Other outcomes measured**
Notes	Follow-up: baseline; then 1, 4, and 6 months after randomisation The Danish Strategic Research Foundation (10-092790); the Heart Centre Research Council, Rigshospitalet; Familien Hede Nielsen Foundation (2013-1226); National Institutes of Public Health, University of Southern Denmark; Region Zealand Health Research Foundation, Denmark (12-000095/jun2014). Funders had no influence on trial design, execution of the trial, nor interpretation of data Conflicts of interest: none declared Due to pitfalls (such as calibration errors, flow errors, and mask leakage), 16 tests were estimated, with no overrepresentation in either randomisation group, using the following estimation equation: VO_2 = 10.8 × (Watt max/weight) + 3.5. Estimation was validated on all measurements and was compared with non-estimated values; the equation generally underestimated the VO_2 peak value Two serious adverse events were reported in the intervention group versus 1 in the control group at 6 months. Serious adverse events in the intervention group were evaluated as not caused by the intervention (1 with postsurgical cardiac tamponade and 1 with heart failure-related re-admission). Eleven of 72 (15.3%) in the intervention group versus 3 of 75 (4.0%) in the control group had self-reported non-serious adverse events (P = 0.02). These events were caused primarily by musculoskeletal problems and were related to exercise training in general 7 patients dropped out of the intervention group, and 11 dropped out of the control group due to complications after surgery and withdrawal of consent

Sire 1987

Study characteristics	
Methods	**Study design:** prospective randomised study **No of centres:** 1 trial centre but 2 patients received training at local hospital **Country:** Norway **Dates patients recruited:** NR **When randomised:** 2 months after operation **Maximum follow-up (from baseline):** 12 months
Participants	**Inclusion criteria:** had isolated aortic valve replacement and could tolerate and perform a physical training programme **Exclusion criteria:** signs and symptoms of other heart disease, over 60 years of age, disease in the locomotor system, obvious mental ailments or social disturbances (e.g. alcoholics). Male patients with heart volumes exceeding 750 mL m^{-2} BSA and females with hearts larger than 650 mL m^{-2} BSA were also excluded

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Sire 1987 *(Continued)*

N Randomised: total: 44;**intervention:** 21;**comparator:** 23

Diagnosis (% of pts)

e.g.

Aetiology: (total): 27.3% due to aortic stenosis (n = 12), 31.8% due to aortic insufficiency (n = 14), 40.9% due to combined aortic stenosis and insufficiency (n = 18)

NYHA: NR

LVEF: NR

Case mix

Age (mean ± SD): total: NR; **intervention:** 45.5 ± 11.7;**comparator:** 45.5 ± 12.2

Percentage male: total: male 36, female 8; **intervention:** male 18, female 3; **comparator:** male 18, female 3

Ethnicity: NR

Interventions	**Intervention (exercise-based CR)** **Description:** exercise was divided into 2 phases: centre-based training (consisting of several types of exercise + 30-minute cooling down period at the end), and home-based training (consisting of a few simple daily exercises) **Time of start after event:** 2 months after surgery **Components:** exercise **Detail of exercise:** started with 15-minute bicycle warm-up session, then short programme of 30 minutes (with 20 different arm and leg exercises of 1 to 2 minutes each). Calisthenics of alternative heavy (e.g. jogging, jumping) or light (e.g. rocking sit-ups, arm flinging at slow speeds) exercises were then carried out for 1 hour, followed by playing volleyball for 30 minutes and a 1-hour break. Selected exercises from the above were then repeated, before the session concluded with a 30-minute cooling down period **Modality:** bicycle ergometer + aerobics + calisthenics **Dose of exercise:** (**calculated as overall no. of weeks of training multiplied by mean number of sessions per week multiplied by mean duration of sessions in minutes):** NR (centre) + NR (home) **Length of session:** 3 to 4 hours **Frequency/no. of sessions:** daily **Intensity:** individualised to patient (upper pulse limit during training was adjusted to 85% to 90% of maximal heart rate obtained at initial exercise test) **Resistance training included:** yes, isometric arm and leg exercises **Total duration:** 4 weeks **Setting: home/hospital/Internet delivery or combination:** hospital + home **Supervision: supervised/unsupervised/not reported:** centre-based supervised, home-based not supervised **Intermittent nurse or exercise specialist support?** NR **Co-interventions:** NR

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Sire 1987 *(Continued)*

	Comparator **Description:** patients were not encouraged to start any systematic training (no patients started this). Patients reported moderate daily physical activity at each control visit **Co-interventions:** NR
Outcomes	**Outcomes (scale measured in):** return to work, exercise capacity (cumulated work, i.e. work performed + workload) **Other outcomes measured** Physical work capacity
Notes	Follow-up at 2, 6, and 12 months • In training group, 3 patients did not perform the exercise test at the end of the training period (i.e. at 3 months after surgery) for non-medical reasons, and 1 patient did not attend the 12-month control • In the control group, 2 patients were unable to participate 7.5 and 8 months following surgery due to a non-fatal thromboembolic episode, and 1 patient did not come to the 12-month review for non-medical reasons • Only 15 male participants from the training group and 16 male participants from the control group were included in the exercise capacity assessments, as females could not reach the highest comparable workload (100W)

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

Study	Reason for exclusion
Amat Santos 2012	Patient population not appropriate. Conference paper
Bakhshayesh 2018	Population
Batra 2012	Not a randomised trial
Brosseau 1995	Patient population not appropriate
Cargnin 2019	Inappropriate intervention
Chambers 2005	Letter to the Editor; not a randomised trial
Chan 2012	Not a randomised trial (systematic review of effectiveness of qigong in cardiac rehabilitation)
CTRI 2017	Inappropriate Intervention
de Charmoy 2000	Intervention not appropriate (chest physiotherapy)
Deepa 2018	Not an RCT
Dull 1983	Patient population not appropriate
Editorial 2018	Editorial to paper that compares CR referral and outcomes in TAVR vs SAVR patients
Fang 2002	Inappropriate intervention (rehabilitation guidance at 24 hours after surgery and QoL measure) and unclear patient population (including both patients with rheumatic heart disease and patients after valve replacement)

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Study	Reason for exclusion
Ferreira 2009	Intervention not appropriate (inspiratory breathing exercises)
Fontes Cerqueira 2018	Inappropriate intervention
Gaita 1999	Patient population not appropriate (randomisation method and study population unclear)
Ghalamghash 2008	Not a randomised trial
Gortner 1988	Intervention not appropriate (nursing intervention, no physical exercise)
Green 2013	Not a randomised trial
Grunewald 1971	Not a randomised trial
Ha 2011	Not a randomised trial. Not possible to obtain full paper
Hokanson 2011	Letter to the Editor; not a randomised trial
Hui 2006	Patient population not appropriate
Jairath 1995	Not a randomised trial (non-randomised cluster trial)
Johnson 1996	Intervention not appropriate (physical intervention in control group)
Kardis 2007	Not a randomised trial (a randomised case control study)
Kassirskii 1983	Not a randomised trial (an observational study)
Kassirskii 1991	Not a randomised trial
Kodric 2013	Patient population not appropriate (patients after all kinds of major cardiac surgery)
Kübler 1984	Patient population not appropriate
Liao 2004	Intervention not eligible (no physical intervention, only psychological and behavioural interventions)
Lim 1998	Patient population not appropriate
Martsinkiavichus 1980	Not a randomised trial
McDermott 2019	Inappropriate intervention
Nagashio 2003	Patient population not appropriate
Nehyba 2009	Not a randomised trial (a non-randomised cluster trial); patient population including patients with coronary artery bypass surgery
Newell 1980	Not a randomised trial (a non-randomised cluster trial)
Patel 2019	Investigators were looking into the rate of CR enrolment in the studied population
Peng 2018	Inappropriate population
Petrunina 1980	Not a randomised trial

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Study	Reason for exclusion
Prasciene 2019	Inappropriate intervention
Pressler 2015	Conference abstract for included study
RBR-8swgc3 2017	Inappropriate intervention
Rizwan 2012	Not a randomised trial
Rogers2018	Conference abstract for included study
Roseler 1997	Not a randomised trial and inappropriate patient population
Rosenfeldt 2011	Patient population not appropriate (patients with valve surgery and coronary artery bypass graft surgery)
Royse 2015	Inappropriate intervention
Song 2019	Non-RCT
Stoickov 2018	Outcomes
Sumide 2009	Not a randomised trial
Tang 2019	The only RCT of interest in this study is the one that has been updated
Therrien 2003	Patient population not appropriate (repaired tetralogy of Fallot)
Ueshima 2004	Not a randomised trial
Viana 2018	Not an RCT
Weber 2019	Inappropriate intervention
Widimsky 2009	Patient population not appropriate (patients with acute myocardial infarction)
Yan 2016	Not an RCT
Yau 2018	Inappropriate intervention

CR: cardiac rehabilitation.
QoL: quality of life.
RCT: randomised controlled trial.
SAVR: surgical aortic valve replacement.
TAVR: transcatheter aortic valve replacement.

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

ACTIVE AFTER TAVR 2017

Study name	A pragmatiC sTrategy to Promote actIVity and Enhance Quality of Life AFTER Transcatheter Aortic Valve Replacement (ACTIVE AFTER TAVR): a pilot study
Methods	Parallel-assignment RCT

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ACTIVE AFTER TAVR 2017 *(Continued)*

Participants	Subjects who have been treated commercially with TAVR with a SAPIEN 3 valve and are being discharged to home
Interventions	Active comparator: no resistance exercise and no activity goal arm; blinded use of Fitbit with no daily activity goal and no resistance exercises Experimental: resistance exercise and activity goal arm; unblinded use of Fitbit with daily activity goal (steps per day) and resistance exercises
Outcomes	Primary outcome measures • Average daily steps [Time Frame: randomization to 6 weeks, average daily steps over the intervention period] • Short physical performance battery score [Time Frame: 6-week value, adjusted for baseline value, combination of gait speed, balance test, and chair-to-stand test at end of intervention] • Quality of life as measured with KCCQ Overall Summary Score [Time Frame: 6-week value, adjusted for baseline value, KCCQ overall summary score] Secondary outcome measures • 5-meter gait time at end of intervention period [Time Frame: randomisation to 6 weeks, 5-meter gait time at end of intervention period, adjusted for baseline] • Chair sit-to-stand test [Time Frame: 6-week value, adjusted for baseline value, time to complete 5 chair stands] • Balance test score at end of intervention period [Time Frame: randomisation to 6 weeks, balance test score at end of intervention period, adjusted for baseline] • 6-minute walk [Time Frame: 6-week value, adjusted for baseline value, 6-minute walk distance at end of intervention period] • Handgrip [Time Frame: 6-week value, adjusted for baseline value, handgrip strength' • Average number of hours per day with 250 or more steps [Time Frame: randomisation to 6 weeks, average number of hours per day with 250 or more steps over intervention period] • Average global physical health as assessed by PROMIS Global Health 10 Short Form [Time Frame: randomisation to 6 weeks, average global physical health as assessed by PROMIS Global Health 10 Short Form over intervention period] • Average global mental health as assessed by PROMIS Global Health 10 Short Form [Time Frame: randomisation to 6 weeks, average global mental health as assessed by PROMIS Global Health 10 Short Form over intervention period] • Physical function as assessed by NIH PROMIS computerised adaptive test [Time Frame: randomisation to 6 weeks, physical function as assessed by NIH PROMIS computerised adaptive test, adjusted for baseline] • Depression as assessed by NIH PROMIS computerised adaptive test [Time Frame: randomisation to 6 weeks, depression as assessed by NIH PROMIS computerised adaptive test, adjusted for baseline] • Fatigue as assessed by NIH PROMIS computerised adaptive test [Time Frame: randomisation to 6 weeks, fatigue as assessed by NIH PROMIS computerised adaptive test, adjusted for baseline] • Dyspnoea as assessed by NIH PROMIS computerised adaptive test [Time Frame: randomisation to 6 weeks, dyspnoea as assessed by NIH PROMIS computerised adaptive test, adjusted for baseline] • Daily active minutes (total) [Time Frame: randomisation to 6 weeks, average daily active minutes (total) • Daily active minutes of moderate to high intensity [Time Frame: randomisation to 6 weeks, average daily minutes of moderate to high intensity] • Sedentary minutes [Time Frame: randomisation to 6 weeks, average daily sedentary minutes] • Daily steps [Time Frame: 6 weeks post baseline to end of study, average daily steps] • Daily active minutes (total) [Time Frame: 6 weeks post baseline to end of study, average daily active minutes (total)] • Daily active minutes of moderate to high intensity [Time Frame: 6 weeks post baseline to end of study, average daily active minutes of moderate to high intensity]

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ACTIVE AFTER TAVR 2017 *(Continued)*

	• Daily sedentary minutes [Time Frame: 6 weeks post baseline to end of study, average daily sedentary minutes] • KCCQ Overall Summary Score [Time Frame: 6 weeks post baseline to end of study, KCCQ overall summary score, adjusted for baseline] • Global physical health [Time Frame: 6 weeks post baseline to end of study, global physical health as assessed by PROMIS Global Health 10 Short Form, adjusted for baseline] • Global mental health [Time Frame: 6 weeks post baseline to end of study, global mental health as assessed by PROMIS Global Health 10 Short Form, adjusted for baseline]
Starting date	7 November 2017
Contact information	Brian Lindman, Associate Professor, Vanderbilt University Medical Center
Notes	Estimated enrolment: 85 participants. Estimated study completion date: August 2020 Location: Massachusetts General Hospital, Dartmouth-Hitchcock Medical Center, Atlantic Health - Morristown Medical Center, Vanderbilt University Medical Center, University of Utah

Exercise Training After TAVI

Study name	Exercise training after transcatheter aortic valve implantation
Methods	Parallel-assignment RCT
Participants	Patients after transcatheter aortic valve replacement (TAVI)
Interventions	Continuous exercise training 2 times per week for a period of 12 weeks Patients will undergo moderate continuous exercise training at 75% of VO_2 max
Outcomes	Primary • Change in maximal oxygen uptake during exercise [Time Frame: 3 months, mL/kg/min] Secondary • Change in flow-mediated dilatation (FMD) of the brachial artery [Time Frame: 3 months, % flow-mediated dilatation and arterial stiffness] • Change in arterial stiffness coefficient [Time Frame: 3 months, coefficient] • Change in value of blood N terminal-proBNP [Time Frame: 3 months, ng/L] • Change in value of blood D-dimer [Time Frame: 3 months, microg/L] • Change in value from questionnaire-obtained quality of life [Time Frame: 3 months, points] • Change in ECG waves [Time Frame: 3 months, estimated with digital high-resolution ECG] • Change in result of the 6-minute walking test [Time Frame: 3 months, metres] • Change in heart rate variability [Time Frame: 3 months, estimated with digital high-resolution ECG] Other outcome measures • Change in heart rate recovery [Time Frame: 3 months, beats/min]
Starting date	18 June 2019
Contact information	luka.vitez@gmail.com borut.jug@kclj.si
Notes	Estimated enrolment: 40 participants. Estimated study completion date: December 2020

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Exercise Training After TAVI *(Continued)*

	Location: UMC Ljubljana Slovenia

Feng 2019

Study name	The effects of stage I cardiac rehabilitation on cardiopulmonary function in patients undergoing open heart surgery: a randomized controlled study.
Methods	Randomised parallel controlled trial
Participants	Adults after open heart surgery
Interventions	General exercise rehabilitation group: general exercise rehabilitation Intensive exercise rehabilitation group: intensive exercise rehabilitation
Outcomes	Primary • PVO_2 Secondary • Peak cardiac output • Resting cardiac output • Cardiac NYHA grading • Echocardiography
Starting date	1 July 2017
Contact information	29611290@qq.com; liubomiao424@sina.cn
Notes	Estimated enrolment: general exercise rehabilitation group: 60; intensive exercise rehabilitation group: 60 Estimated study finish date: 31 March 2020 Location: Fuwai Hospital; Chinese Academy of Medical Sciences, Beijing, China

HBCR-TAVR 2019

Study name	Impact of home-based cardiac rehabilitation on outcomes after TAVR (HBCR-TAVR)
Methods	Parallel-assignment RCT
Participants	Chinese patients after transcatheter aortic valve replacement (TAVR)
Interventions	Placebo comparator: control group: routine care Experimental: intervention group: home-based cardiac rehabilitation
Outcomes	Primary outcome measures • 6-minute walk test [Time Frame: 6 weeks, total distance walked in meters during 6 minutes] Secondary outcome measures

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HBCR-TAVR 2019 *(Continued)*

- Number of participants to die [Time Frame: 6 weeks, 12 months, number of participants who die during the study due to cardiovascular or non-cardiovascular causes]
- Number of participants re-hospitalised [Time Frame: 6 weeks, 12 months, number of participants re-hospitalised during the study]
- Number of participants completing home-based cardiac rehabilitation [Time Frame: 6 weeks, number of participants completing home-based cardiac rehabilitation]
- Cardiac function [Time Frame: 12 months, ejection fraction estimated by echocardiography]
- Aortic valve function [Time Frame: 12 months, aortic valve function estimated by echocardiography]
- Number of participants injured [Time Frame: 6 weeks, number of participants injured or dying during the course of home-based cardiac rehabilitation]
- Time spent performing activities [Time Frame: 6 weeks, 12 months, number of minutes in a typical week that participants spent performing activities]
- 6-minute walk test [Time Frame: 12 months, total distance walked in meters during 6 minutes]

Starting date	9 May 2020
Contact information	Xiaoya Wang, 15715702712 wxyonce@zju.edu.cn
Notes	Estimated enrolment: 300 participants. Estimated study completion date: 31 December 2023 Locations: Second Affiliated Hospital of Zhejiang University, School of Medicine, Hangzhou, Zhejiang, China, 310000

Post Cardiac Valvular Surgery Rehabilitation (PORT

Study name	Post Cardiac Valvular Surgery Rehabilitation (PORT)
Methods	Parallel-assignment RCT
Participants	Chinese patients after heart valve surgery
Interventions	No intervention: conventional treatment group: this arm will receive usual care Cardiac rehabilitation: cardiac rehabilitation consists of exercise rehabilitation, psychological counselling, and dietary guidance Rehabilitation starts preoperatively with education and exercise management. After screening with cardiopulmonary exercise test, the participant will receive daily preoperative exercise rehabilitation till surgery. This lasts for 20 minutes per day, starting with a 40% to 60% anaerobic threshold and gradually advancing to 80%. Each patient was motivated to adhere to the basic protocol, but individual adjustments were allowed in case of slower progress. Physical exercise starts 1 month postoperatively after the first cardiopulmonary exercise testing and comprises the following 3 elements: individual planning of physical exercise, a specially trained physiotherapist conduction, and integrating of detailed information concerning medical treatment and diet. The exercise diary and the heart rate monitor recordings are essential for monitoring during the whole intervention
Outcomes	Primary outcomes • Composite endpoint of in-hospital all-cause death, pulmonary complications, and ratio of postoperative hospitalisation longer than 7 days [Time Frame: through hospitalisation (up to 2 months), composite of in-hospital all-cause death and pulmonary complications, such as pulmonary infection, postoperative hospitalisation days] • Postoperative duration of hospitalisation [Time Frame: through hospitalisation (up to 2 months), length of hospital stay]

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Post Cardiac Valvular Surgery Rehabilitation (PORT *(Continued)*

	Secondary outcomes • Incidence of all-cause death in 3 months [Time Frame: 3 months, incidence of all-cause death at 3-month follow-up] • Incidence of pulmonary complications in 3 months [Time Frame: 3 months, incidence of pulmonary complications, such as pulmonary infection at 3-month follow-up] • Individualised Short Form-36 (SF-36) living quality scores in 3 months [Time Frame: 3 months, scores from self-administered SF-36 living quality questionnaire are measured. Higher mean scores reflect better outcomes] • VO_2 peak in 3 months [Time Frame: 3 months, peak oxygen consumption at cardiopulmonary exercise test is measured through a metabolic cart during a graded exercise test on a treadmill at 3 months' follow-up] • Length of ICU treatment [Time Frame: through hospitalisation (up to 2 months), total length of treatment at intensive care unit] • Total length of in-hospital stays [Time Frame: through hospitalisation (up to 2 months), total length of in-hospital stays] • Length of bed rest [Time Frame: through hospitalisation (up to 2 months), length of bed rest] Description: postoperative duration of bed rest until off-bed activity supervised by rehabilitation therapists • Total postoperative cost of medical expenses [Time Frame: through hospitalisation (up to 2 months), total postoperative cost of medical expenses] • Incidence of treatment-emergent adverse events [Emerging Arrhythmia or/and Muscle Injury or/and Acute Heart Failure] [Time Frame: through hospitalisation (up to 2 months), evaluation of treatment-emergent adverse events during hospitalisation: Emerging Arrhythmia or/and Muscle Injury or/and Acute Heart Failure]
Starting date	1 January 2018
Contact information	Jiyan Chen, MD; 02083827812; chenjiyandr@126.com
Notes	Estimated enrolment: 800 participants. Estimated study completion date: 30 December 2021 Locations: Guangdong General Hospital, China

PREPARE TAVR Pilot Study

Study name	Physiological reconditioning program administered remotely in patients undergoing transcatheter aortic valve replacement pilot study
Methods	Parallel-assignment RCT
Participants	Frail adults undergoing transcatheter aortic valve replacement (TAVR) procedures
Interventions	Patients assigned to intervention arm will be provided a personalised, tailored, and graduated exercise programme to improve physical strength and conditioning
Outcomes	Primary • Quality of life (QoL) [Time Frame: 1 year] Quality of life as assessed by the Kansas City Cardiomyopathy Questionnaire (KCCQ). KCCQE is a 23-item self-administered questionnaire developed to independently measure patients' perceptions of their health status, which includes heart failure symptoms, impact on physical and social function, and how their heart failure impacts their quality of life (QoL) within a 2-week recall period. KCCQ responses are provided along a rating scale continuum with equal spacing from worst to best

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PREPARE TAVR Pilot Study *(Continued)*

	Secondary • LOS [Time Frame: index hospitalisation, length of stay post TAVR] • MACE [Time Frame: 1 year, composite of mortality and repeat hospitalisation]
Starting date	1 February 2019
Contact information	Syed Ishba; syedi@smh.ca
Notes	Estimated enrolment: 160 participants. Estimated study finish date: 31 March 2021 Location: St. Michael's Hospital, Toronto

REHAB-TAVR 2017

Study name	Home-based exercise program for recovery after transcatheter aortic valve replacement: a pilot study
Methods	Parallel-assignment RCT
Participants	Older adults after TAVR
Interventions	Experimental: exercise and cognitive-behavioural intervention. A physical therapist will make home visits, beginning within 1 week of discharge, to deliver an individualised exercise programme and cognitive-behavioural interventions Experimental: exercise alone. A physical therapist will make home visits, beginning within 1 week of discharge, to deliver an individualised exercise programme, without cognitive-behavioural interventions Active comparator: attention control education programme. Participants will receive telephone-based education sessions from a study health professional
Outcomes	Primary outcome measure • Change in Late-Life Function and Disability Instrument (LLFDI) score [Time Frame: at baseline and at Week 8, LLFDI is a validated patient-reported outcome questionnaire that measures both functional limitations (inability to perform physical tasks) and disability (inability to perform major life tasks and social roles) (range 0 to 100)] Secondary outcome measures • Change in Short Physical Performance Battery (SPPB) summary score [Time Frame: at baseline and at Week 8, summary score is calculated based on chair stands, walking speed, and standing balance (range 0 to 12)] • Change in 2-minute walk distance (meters) [Time Frame: at baseline and at Week 8, 2-minute walk distance measures endurance] • Change in dominant handgrip strength (kg) [Time Frame: at baseline and at Week 8, dominant handgrip strength measures upper extremity strength] • Number of participants who experienced adverse events [Time Frame: at Week 8] Other outcome measures • Change in Mini-Mental State Examination (MMSE) score [Time Frame: at baseline and at Week 8, MMSE is an instrument that assesses general cognitive function] • Change in New York Heart Association (NYHA) functional class [Time Frame: at baseline and at Week 8, NYHA assesses the extent of physical activity limitation due to heart failure]

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REHAB-TAVR 2017 *(Continued)*

	• Change in Self-Efficacy Scale for Exercise (SEE) [Time Frame: at baseline and at Week 8, SEE Scale measures self-efficacy about exercise (range 0 to 90)] • Change in Outcome Expectation Scale for Exercise (OEE) [Time Frame: at baseline and at Week 8, OEE Scale measures outcome expectation about exercise (range 1 to 5)] • Adherence to home-based exercise programme [Time Frame: at Week 8, proportion of days with completed daily task during entire study period will be measured]
Starting date	1 August 2017
Contact information	Dae Hyun Kim, Associate Physician, Brigham and Women's Hospital
Notes	Estimated enrolment: 60 participants. Estimated study completion date: 31 May 2020 Location: United States, Massachusetts

The PACO Trial

Study name	Personalized intervention to increase physical activity and reduce sedentary behaviour in rehabilitation after cardiac operations (the PACO trial)
Methods	Parallel-assignment RCT
Participants	Coronary artery disease, aortic valve stenosis, and mitral valve insufficiency patients preparing for elective coronary artery bypass grafting (CABG), aortic valve replacement (AVR), or mitral valve repair (MVR)
Interventions	The group of aortic valve stenosis patients receiving the PACO intervention for AVR/MVR patients besides the standard postoperative rehabilitation of Kuopio and Turku University Hospitals after aortic valve replacement. The PACO intervention includes activity guidance (i.e. goals to improve daily steps and physical activity levels, while reducing prolonged sitting) provided to patients with the novel combination of ExSed application, MoveSense accelerometer, and cloud system. In addition, exercise guidance (short video files) and regular mobile phone contacts from physiotherapist will be included in the intervention
Outcomes	Primary outcome • Improvement in mean daily number of steps [Time Frame: improvement between baseline (during last preoperative month) and first 3 (and 12) months after discharge] Improvement in mean daily number of steps after 3 months from discharge. In addition, follow-up will be continued until 12 months after discharge. Baseline values of mean daily number of steps will be determined in a 7-day accelerometer measurement conducted for patients before elective cardiac operation. Mean daily number of steps after the first 3 and 12 months of postoperative rehabilitation at home will be also determined in 7-day (24-hour) accelerometer measurements. Raw accelerometer data will be analysed with mean amplitude deviation and angle for posture estimation algorithms to recognise daily steps for the 7 days for which average will be calculated for each study patient Secondary outcomes • Change in mean daily accumulated total time of light PA and MVPA [Time Frame: change between baseline (during last preoperative month) and first 3 months after discharge, postoperative change in patient's mean daily accumulated total time of light and moderate to vigorous physical activity] • Change in mean daily total time of sedentary behaviour (SB) [Time Frame: change between baseline (during last preoperative month) and first 3 months after discharge, postoperative change in patient's mean daily total time of SB]

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The PACO Trial *(Continued)*

- Change in maximal oxygen consumption [Time Frame: change between first and third months after discharge, evolvement of patient's maximal oxygen consumption (VO_2 peak) will be determined in 6-minute walking test, conducted for patients twice (after 1 and 3 months) postoperatively. Only some of the randomised patients coming from city areas of Kuopio and Turku will be included for measurements of maximal oxygen consumption
- Improvement in self-perceived quality of life (QoL) assessed with SAQ-7 questionnaire [Time Frame: improvement between baseline (during last preoperative month) and first 3 months after discharge, improvement in patient's postoperative quality of life after 3 months of rehabilitation; quality of life will be determined with Seattle Angina Questionnaire 7 (SAQ-7)]
- Improvement in self-perceived quality of life (QoL) assessed with SF-36 questionnaire [Time Frame: change between baseline (during last preoperative month) and first 3 months after discharge, improvement in patient's postoperative quality of life after 3 months of rehabilitation; quality of life will be determined with SF-36 questionnaire]
- Improvement in self-perceived quality of life (QoL) assessed with 15 D questionnaire [Time Frame: improvement between baseline (during last preoperative month) and first 3 months after discharge, improvement in patient's postoperative quality of life after 3 months of rehabilitation; quality of life will be determined with 15 D questionnaire]
- Improvement in self-perceived quality of life (QoL) assessed with PHQ-2 questionnaire [Time Frame: improvement between baseline (during last preoperative month) and first 3 months after discharge, improvement in patient's postoperative quality of life after 3 months of rehabilitation; quality of life will be determined with PHQ-2 questionnaire]
- Improvement in self-perceived quality of life (QoL) assessed with Rose Dyspnoea Index [Time Frame: improvement between baseline (during last preoperative month) and first 3 months after discharge, improvement in patient's postoperative quality of life after 3 months of rehabilitation; quality of life will be determined with Rose Dyspnoea Index]
- Incidence of major cardiovascular events [Time Frame: first 12 postoperative months, major cardiovascular events include all-cause mortality, any re-hospitalisations due to CVD, repeat coronary re-vascularisation, non-operational myocardial infarction, and stroke. The incidence of major cardiovascular events will be monitored from patient records at the hospitals and from HILMO database during the first 12 postoperative months. In addition, patients will be asked about cardiovascular events during research telephone contact (after 12 months of rehabilitation)]
- Change in accelerometer-derived portion of deep sleep [Time Frame: change between baseline (during last preoperative month) and first 3 months after discharge, change in patient's deep sleep portion after cardiac operations. Deep sleep will be recognised with accelerometer attached to patient's wrist during sleep. Accelerometer will be used during 7 days]
- Change in heart rate variability [Time Frame: change between baseline (during last preoperative month) and first 3 months after discharge, change in heart rate variability]

Starting date	6 April 2018
Contact information	villevas@uef.fi ; jari.halonen@kuh.fi
Notes	Specific operation groups (CABG, AVR, and MVR) will be analysed separately Estimated enrolment: 540 participants. Estimated study completion date: 1 March 2028 Location: Kuopio University Hospital, Kuopio, Finland, 70029

Valve-ex 2009

Study name	Physical activity in patients after aortic valve replacement (Valve-ex) [influence of regular physical activity on exercise capacity, cardiac remodeling and endothelial function in patients after aortic valve replacement]
Methods	Parallel-assignment RCT

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Valve-ex 2009 *(Continued)*

Participants	Patients after aortic valve replacement due to severe stenosis
Interventions	Active comparator: training group: physical activity B controls: no intervention
Outcomes	Maximum oxygen uptake
Starting date	12 March 2009
Contact information	Technische Universität München
Notes	Estimated enrolment: 30 participants. Estimated study completion date: not reported Location: Department of Prevention and Sports Medicine, Technische Universität München, München, Bavaria, Germany, 80802

Wang 2019

Study name	A study of the impact of home-based cardiac rehabilitation on outcomes after transcatheter aortic valve replacement (TAVR)
Methods	Parallel-assignment RCT
Participants	Adult Chinese patients after transcatheter aortic valve replacement (TAVR)
Interventions	Placebo comparator; control group: routine care; experimental group/interventional group: home-based cardiac rehabilitation
Outcomes	Primary outcomes • 6-minute walk test [Time Frame: 6 weeks, total distance walked in meters during 6 minutes] Secondary outcomes • Number of participants who will die [Time Frame: 6 weeks, 12 months, number of participants who die during the study due to cardiovascular or non-cardiovascular causes] • Number of participants re-hospitalised [Time Frame: 6 weeks, 12 months, number of participants re-hospitalised during the study] • Number of participants completing home-based cardiac rehabilitation [Time Frame: 6 weeks, number of participants completing home-based cardiac rehabilitation] • Cardiac function [Time Frame: 12 months, ejection fraction estimated by echocardiography] • Aortic valve function [Time Frame: 12 months, aortic valve function estimated by echocardiography] • Number of participants injured [Time Frame: 6 weeks, number of participants injured or who die during the course of home-based cardiac rehabilitation] • Time spent performing activities [Time Frame: 6 weeks, 12 months, number of minutes in a typical week that participants spent performing activities] • 6-minute walk test [Time Frame: 12 months, total distance walked in meters during 6 minutes]
Starting date	1 January 2020
Contact information	wxyonce@zju.edu.cn
Notes	Estimated enrolment: 300 participants. Estimated study finish date: 31 December 2023

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Wang 2019 *(Continued)*

Location: Second Affiliated Hospital, School of Medicine, Zhejiang University

AVR: aortic valve replacement.
CABG: coronary artery bypass graft.
ECG: electrocardiogram.
KCCQ: Kansas City Cardiomyopathy Questionnaire.
LOS: length of stay.
MACE: major adverse cardiovascular event.
MVR: mitral valve replacement.
NYHA: New York Heart Association.
PVO_2: mixed venous oxygen tension.
RCT: randomised controlled trial.
TAVR: transaortic valve replacement.
VO_2: maximal oxygen consumption.

RISK OF BIAS

Legend: Low risk of bias | High risk of bias | Some concerns

Risk of bias for analysis 1.1 All-cause mortality at longest follow-up

	Bias					
Study	**Randomisation process**	**Deviations from intended interventions**	**Missing outcome data**	**Measurement of the outcome**	**Selection of the reported results**	**Overall**
Lin 2004	~	~	✗	✓	✓	✗
Pressler 2016	✓	✓	✓	✓	✓	✓

Risk of bias for analysis 1.4 All-cause hospitalisation at longest follow-up

	Bias					
Study	**Randomisation process**	**Deviations from intended interventions**	**Missing outcome data**	**Measurement of the outcome**	**Selection of the reported results**	**Overall**
Sibilitz 2016	✓	✓	~	✓	✓	~

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Risk of bias for analysis 1.5 HRQoL (mental component) at end of intervention

	Bias					
Study	**Randomisation process**	**Deviations from intended interventions**	**Missing outcome data**	**Measurement of the outcome**	**Selection of the reported results**	**Overall**
Pressler 2016	✓	✓	✓	✗	✓	✗
Sibilitz 2016	✓	✓	~	✗	✓	✗

Risk of bias for analysis 1.6 HRQoL (physical component) at end of intervention

	Bias					
Study	**Randomisation process**	**Deviations from intended interventions**	**Missing outcome data**	**Measurement of the outcome**	**Selection of the reported results**	**Overall**
Pressler 2016	✓	✓	✓	✗	✓	✗
Sibilitz 2016	✓	✓	~	✗	✓	✗

Risk of bias for analysis 1.7 HRQoL (mental component) at maximum follow-up

	Bias					
Study	**Randomisation process**	**Deviations from intended interventions**	**Missing outcome data**	**Measurement of the outcome**	**Selection of the reported results**	**Overall**
Pressler 2016	✓	✓	~	✗	✓	✗
Sibilitz 2016	✓	✓	~	✗	✓	✗

Risk of bias for analysis 1.8 HRQoL (physical component) at maximum follow-up

	Bias					
Study	**Randomisation process**	**Deviations from intended interventions**	**Missing outcome data**	**Measurement of the outcome**	**Selection of the reported results**	**Overall**
Pressler 2016	✓	✓	~	✗	✓	✗

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	Bias					
Study	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Sibilitz 2016						

DATA AND ANALYSES

Comparison 1. Exercise versus no exercise

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 All-cause mortality at longest follow-up	2	131	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.26, 2.68]
1.2 All-cause mortality: best/worst-case scenario	2	131	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.15, 1.32]
1.3 All-cause mortality: worst/best-case scenario	2	131	Risk Ratio (M-H, Random, 95% CI)	2.15 [0.16, 28.78]
1.4 All-cause hospitalisation at longest follow-up	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.5 HRQoL (mental component) at end of intervention	2	150	Mean Difference (IV, Fixed, 95% CI)	1.28 [-1.60, 4.16]
1.6 HRQoL (physical component) at end of intervention	2	150	Mean Difference (IV, Random, 95% CI)	2.99 [-5.24, 11.21]
1.7 HRQoL (mental component) at maximum follow-up	2	139	Mean Difference (IV, Fixed, 95% CI)	-1.45 [-4.70, 1.80]
1.8 HRQoL (physical component) at maximum follow-up	2	139	Mean Difference (IV, Fixed, 95% CI)	-0.87 [-3.57, 1.83]
1.9 Exercise capacity (direct: VO_2 max) at end of intervention	4	250	Mean Difference (IV, Fixed, 95% CI)	2.38 [0.36, 4.40]
1.10 Exercise capacity (direct: VO_2 max) at longest follow-up	4	240	Mean Difference (IV, Fixed, 95% CI)	1.53 [-0.44, 3.50]
1.11 Exercise capacity (maximum measures) at end of Intervention	5	294	Std. Mean Difference (IV, Fixed, 95% CI)	0.38 [0.15, 0.61]
1.12 Exercise capacity (maximum measures) at longest follow-up	5	284	Std. Mean Difference (IV, Fixed, 95% CI)	0.37 [0.13, 0.61]
1.13 Exercise capacity (indirect/submaximal: 6MWT) at end of Intervention	3	167	Mean Difference (IV, Random, 95% CI)	-3.89 [-58.72, 50.95]

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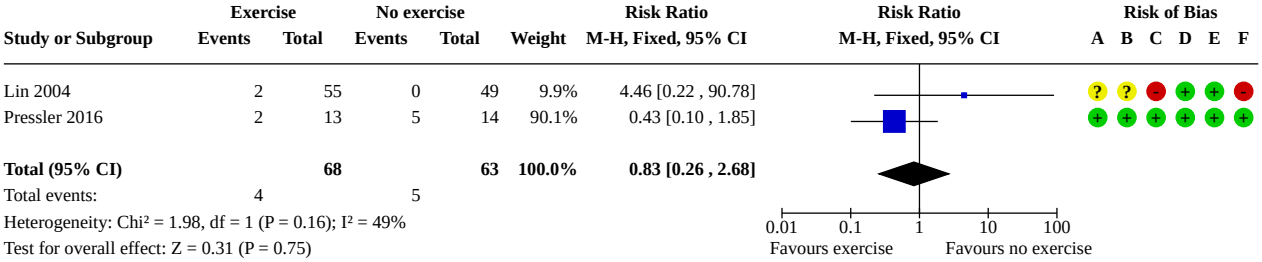
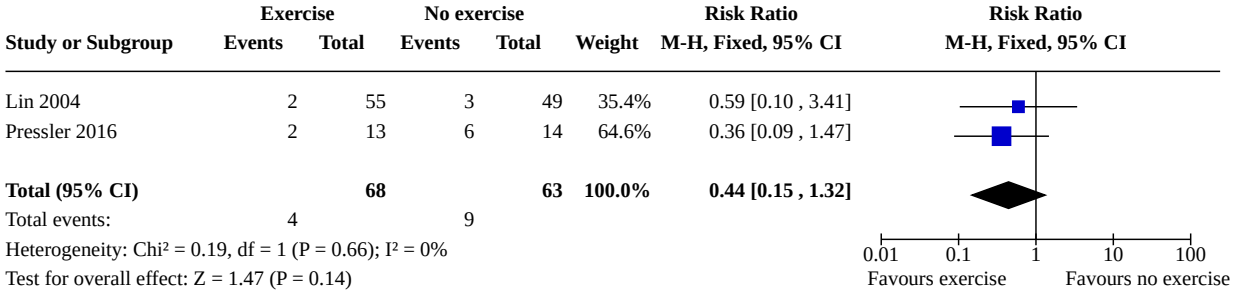
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.14 Exercise capacity (indirect/submaximal: 6MWT) at longest follow-up	3	157	Mean Difference (IV, Random, 95% CI)	-25.48 [-103.04, 52.08]
1.15 Serious adverse events	4	326	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.50, 2.27]
1.16 Return to work	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1: Exercise versus no exercise, Outcome 1: All-cause mortality at longest follow-up



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions: All-cause mortality at longest follow-up
(C) Bias due to missing outcome data: All-cause mortality at longest follow-up
(D) Bias in measurement of the outcome: All-cause mortality at longest follow-up
(E) Bias in selection of the reported result: All-cause mortality at longest follow-up
(F) Overall bias: All-cause mortality at longest follow-up

Analysis 1.2. Comparison 1: Exercise versus no exercise, Outcome 2: All-cause mortality: best/worst-case scenario



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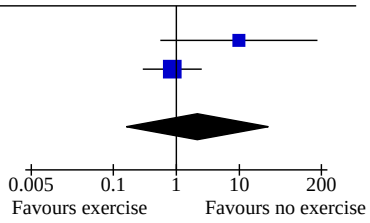
Analysis 1.3. Comparison 1: Exercise versus no exercise, Outcome 3: All-cause mortality: worst/best-case scenario

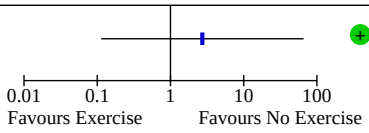
Study or Subgroup	Exercise Events	Exercise Total	No exercise Events	No exercise Total	Weight	Risk Ratio M-H, Random, 95% CI
Lin 2004	5	55	0	49	37.6%	9.82 [0.56 , 173.19]
Pressler 2016	4	13	5	14	62.4%	0.86 [0.29 , 2.53]
Total (95% CI)		**68**		**63**	**100.0%**	**2.15 [0.16 , 28.78]**
Total events:	9		5			

Heterogeneity: Tau² = 2.50; Chi² = 3.05, df = 1 (P = 0.08); I² = 67%
Test for overall effect: Z = 0.58 (P = 0.56)
Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1: Exercise versus no exercise, Outcome 4: All-cause hospitalisation at longest follow-up

Study or Subgroup	Exercise Events	Exercise Total	No exercise Events	No exercise Total	Risk Ratio M-H, Fixed, 95% CI	Risk of Bias A	B	C	D	E	F
Sibilitz 2016	1	64	0	58	2.72 [0.11 , 65.56]	+	+	?	+	+	?

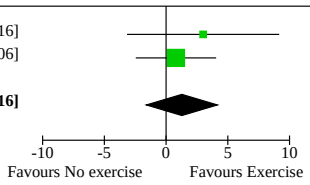


Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions: All-cause hospitalisation at longest follow-up
(C) Bias due to missing outcome data: All-cause hospitalisation at longest follow-up
(D) Bias in measurement of the outcome: All-cause hospitalisation at longest follow-up
(E) Bias in selection of the reported result: All-cause hospitalisation at longest follow-up
(F) Overall bias: All-cause hospitalisation at longest follow-up

Analysis 1.5. Comparison 1: Exercise versus no exercise, Outcome 5: HRQoL (mental component) at end of intervention

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A	B	C	D	E	F
Pressler 2016	54.3	8.4	13	51.3	7.9	14	21.8%	3.00 [-3.16 , 9.16]	+	+	+	-	+	-
Sibilitz 2016	54.7	8.2	65	53.9	10	58	78.2%	0.80 [-2.46 , 4.06]	+	+	?	-	+	-
Total (95% CI)			**78**			**72**	**100.0%**	**1.28 [-1.60 , 4.16]**						

Heterogeneity: Chi² = 0.38, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 0.87 (P = 0.38)
Test for subgroup differences: Not applicable



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions: HRQoL (mental component) at end of intervention
(C) Bias due to missing outcome data: HRQoL (mental component) at end of intervention
(D) Bias in measurement of the outcome: HRQoL (mental component) at end of intervention
(E) Bias in selection of the reported result: HRQoL (mental component) at end of intervention
(F) Overall bias: HRQoL (mental component) at end of intervention

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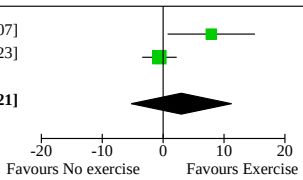
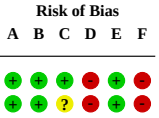
Analysis 1.6. Comparison 1: Exercise versus no exercise, Outcome 6: HRQoL (physical component) at end of intervention

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Mean Difference IV, Random, 95% CI
Pressler 2016	45.9	8.9	13	38	10.1	14	42.2%	7.90 [0.73 , 15.07]
Sibilitz 2016	50.4	8.4	65	51	7.6	58	57.8%	-0.60 [-3.43 , 2.23]
Total (95% CI)			**78**			**72**	**100.0%**	**2.99 [-5.24 , 11.21]**

Heterogeneity: Tau² = 28.39; Chi² = 4.67, df = 1 (P = 0.03); I² = 79%
Test for overall effect: Z = 0.71 (P = 0.48)
Test for subgroup differences: Not applicable



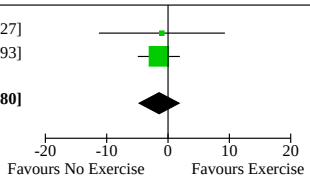


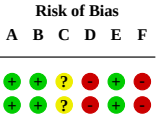
Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions: HRQoL (physical component) at end of intervention
(C) Bias due to missing outcome data: HRQoL (physical component) at end of intervention
(D) Bias in measurement of the outcome: HRQoL (physical component) at end of intervention
(E) Bias in selection of the reported result: HRQoL (physical component) at end of intervention
(F) Overall bias: HRQoL (physical component) at end of intervention

Analysis 1.7. Comparison 1: Exercise versus no exercise, Outcome 7: HRQoL (mental component) at maximum follow-up

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Mean Difference IV, Fixed, 95% CI
Pressler 2016	53.9	12.8	10	54.9	8.8	7	10.0%	-1.00 [-11.27 , 9.27]
Sibilitz 2016	53.6	10.5	64	55.1	8.8	58	90.0%	-1.50 [-4.93 , 1.93]
Total (95% CI)			**74**			**65**	**100.0%**	**-1.45 [-4.70 , 1.80]**

Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%
Test for overall effect: Z = 0.87 (P = 0.38)
Test for subgroup differences: Not applicable



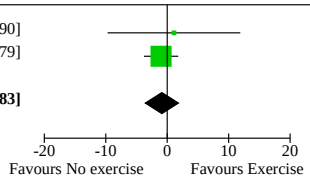


Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions: HRQoL (mental component) at maximum follow-up
(C) Bias due to missing outcome data: HRQoL (mental component) at maximum follow-up
(D) Bias in measurement of the outcome: HRQoL (mental component) at maximum follow-up
(E) Bias in selection of the reported result: HRQoL (mental component) at maximum follow-up
(F) Overall bias: HRQoL (mental component) at maximum follow-up

Analysis 1.8. Comparison 1: Exercise versus no exercise, Outcome 8: HRQoL (physical component) at maximum follow-up

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Mean Difference IV, Fixed, 95% CI
Pressler 2016	38	10.7	10	36.9	11.5	7	6.2%	1.10 [-9.70 , 11.90]
Sibilitz 2016	51.2	8.3	64	52.2	7.4	58	93.8%	-1.00 [-3.79 , 1.79]
Total (95% CI)			**74**			**65**	**100.0%**	**-0.87 [-3.57 , 1.83]**

Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0%
Test for overall effect: Z = 0.63 (P = 0.53)
Test for subgroup differences: Not applicable



Risk of bias legend
(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions: HRQoL (physical component) at maximum follow-up
(C) Bias due to missing outcome data: HRQoL (physical component) at maximum follow-up
(D) Bias in measurement of the outcome: HRQoL (physical component) at maximum follow-up
(E) Bias in selection of the reported result: HRQoL (physical component) at maximum follow-up
(F) Overall bias: HRQoL (physical component) at maximum follow-up

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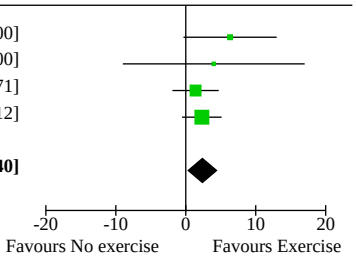
Analysis 1.9. Comparison 1: Exercise versus no exercise, Outcome 9: Exercise capacity (direct: VO_2 max) at end of intervention

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Mean Difference IV, Fixed, 95% CI
Lin 2004	30.345	18.305	50	24.01	14.945	46	9.2%	6.33 [-0.33 , 13.00]
Nilsson 2019	28	14.81	6	24	6.67	6	2.4%	4.00 [-9.00 , 17.00]
Pressler 2016	15.9	5	13	14.5	3.6	14	37.3%	1.40 [-1.91 , 4.71]
Sibilitz 2016	25.5	7.3	63	23.2	8	52	51.1%	2.30 [-0.52 , 5.12]
Total (95% CI)			**132**			**118**	**100.0%**	**2.38 [0.36 , 4.40]**

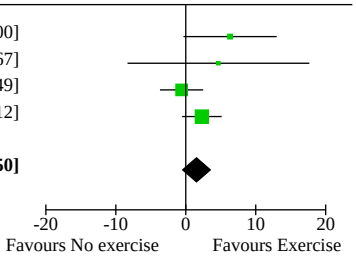
Heterogeneity: Chi² = 1.75, df = 3 (P = 0.63); I² = 0%
Test for overall effect: Z = 2.31 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 1.10. Comparison 1: Exercise versus no exercise, Outcome 10: Exercise capacity (direct: VO_2 max) at longest follow-up

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Mean Difference IV, Fixed, 95% CI
Lin 2004	30.345	18.305	50	24.01	14.945	46	8.7%	6.33 [-0.33 , 13.00]
Nilsson 2019	28.67	14.81	6	24	6.67	6	2.3%	4.67 [-8.33 , 17.67]
Pressler 2016	13.9	3.9	10	14.5	2.6	7	40.5%	-0.60 [-3.69 , 2.49]
Sibilitz 2016	25.5	7.3	63	23.2	8	52	48.5%	2.30 [-0.52 , 5.12]
Total (95% CI)			**129**			**111**	**100.0%**	**1.53 [-0.44 , 3.50]**

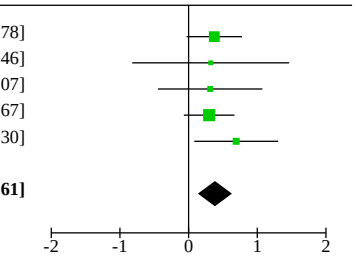
Heterogeneity: Chi² = 4.33, df = 3 (P = 0.23); I² = 31%
Test for overall effect: Z = 1.53 (P = 0.13)
Test for subgroup differences: Not applicable



Analysis 1.11. Comparison 1: Exercise versus no exercise, Outcome 11: Exercise capacity (maximum measures) at end of Intervention

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Lin 2004	30.345	18.305	50	24.01	14.945	46	32.9%	0.37 [-0.03 , 0.78]
Nilsson 2019	28	14.81	6	24	6.67	6	4.1%	0.32 [-0.82 , 1.46]
Pressler 2016	15.9	5	13	14.5	3.6	14	9.3%	0.31 [-0.45 , 1.07]
Sibilitz 2016	25.5	7.3	63	23.2	8	52	39.3%	0.30 [-0.07 , 0.67]
Sire 1987	111.6	47	21	84	30.2	23	14.4%	0.69 [0.08 , 1.30]
Total (95% CI)			**153**			**141**	**100.0%**	**0.38 [0.15 , 0.61]**

Heterogeneity: Chi² = 1.23, df = 4 (P = 0.87); I² = 0%
Test for overall effect: Z = 3.24 (P = 0.001)
Test for subgroup differences: Not applicable



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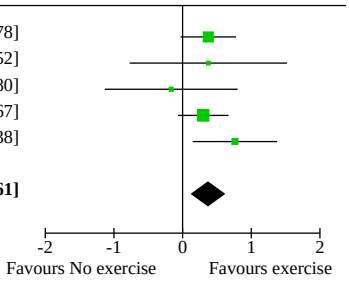
Analysis 1.12. Comparison 1: Exercise versus no exercise, Outcome 12: Exercise capacity (maximum measures) at longest follow-up

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Lin 2004	30.345	18.305	50	24.01	14.945	46	34.2%	0.37 [-0.03 , 0.78]
Nilsson 2019	28.67	14.81	6	24	6.67	6	4.2%	0.38 [-0.77 , 1.52]
Pressler 2016	13.9	3.9	10	14.5	2.6	7	6.0%	-0.17 [-1.13 , 0.80]
Sibilitz 2016	25.5	7.3	63	23.2	8	52	40.9%	0.30 [-0.07 , 0.67]
Sire 1987	123.9	50.6	21	91.4	32	23	14.8%	0.76 [0.15 , 1.38]
Total (95% CI)			**150**			**134**	**100.0%**	**0.37 [0.13 , 0.61]**

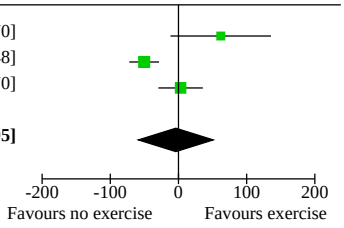
Heterogeneity: Chi² = 2.88, df = 4 (P = 0.58); I² = 0%
Test for overall effect: Z = 3.06 (P = 0.002)
Test for subgroup differences: Not applicable



Analysis 1.13. Comparison 1: Exercise versus no exercise, Outcome 13: Exercise capacity (indirect/submaximal: 6MWT) at end of Intervention

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Mean Difference IV, Random, 95% CI
Pressler 2016	392	100	13	330	95	14	23.9%	62.00 [-11.70 , 135.70]
Rogers 2018	319.7	24.5	13	370	33	14	39.5%	-50.30 [-72.12 , -28.48]
Sibilitz 2016	597.4	97	61	594.3	79.8	52	36.6%	3.10 [-29.50 , 35.70]
Total (95% CI)			**87**			**80**	**100.0%**	**-3.89 [-58.72 , 50.95]**

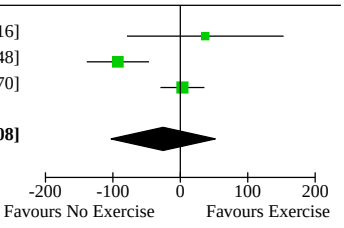
Heterogeneity: Tau² = 1859.93; Chi² = 13.23, df = 2 (P = 0.001); I² = 85%
Test for overall effect: Z = 0.14 (P = 0.89)
Test for subgroup differences: Not applicable



Analysis 1.14. Comparison 1: Exercise versus no exercise, Outcome 14: Exercise capacity (indirect/submaximal: 6MWT) at longest follow-up

Study or Subgroup	Exercise Mean	Exercise SD	Exercise Total	No exercise Mean	No exercise SD	No exercise Total	Weight	Mean Difference IV, Random, 95% CI
Pressler 2016	333	150	10	296	94	7	22.0%	37.00 [-79.16 , 153.16]
Rogers 2018	292.9	24.5	13	385.5	84.3	14	37.7%	-92.60 [-138.72 , -46.48]
Sibilitz 2016	597.4	97	61	594.3	79.8	52	40.3%	3.10 [-29.50 , 35.70]
Total (95% CI)			**84**			**73**	**100.0%**	**-25.48 [-103.04 , 52.08]**

Heterogeneity: Tau² = 3604.95; Chi² = 12.20, df = 2 (P = 0.002); I² = 84%
Test for overall effect: Z = 0.64 (P = 0.52)
Test for subgroup differences: Not applicable



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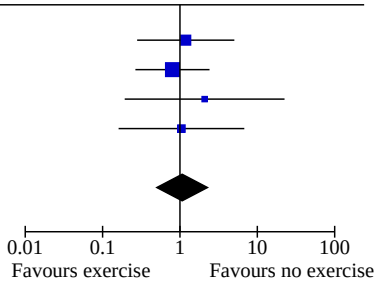
Analysis 1.15. Comparison 1: Exercise versus no exercise, Outcome 15: Serious adverse events

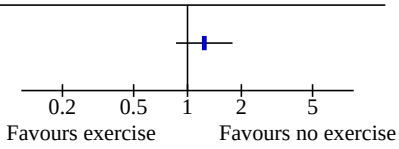
Study or Subgroup	Exercise Events	Exercise Total	No exercise Events	No exercise Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lin 2004	4	55	3	49	28.6%	1.19 [0.28 , 5.05]
Pressler 2016	4	15	5	15	45.0%	0.80 [0.27 , 2.41]
Sibilitz 2016	2	72	1	75	8.8%	2.08 [0.19 , 22.48]
Sire 1987	2	22	2	23	17.6%	1.05 [0.16 , 6.79]
Total (95% CI)		**164**		**162**	**100.0%**	**1.07 [0.50 , 2.27]**
Total events:	12		11			

Heterogeneity: Chi² = 0.59, df = 3 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.17 (P = 0.87)
Test for subgroup differences: Not applicable



Analysis 1.16. Comparison 1: Exercise versus no exercise, Outcome 16: Return to work

Study or Subgroup	Exercise Events	Exercise Total	No exercise Events	No exercise Total	Risk Ratio M-H, Fixed, 95% CI
Sire 1987	17	21	15	23	1.24 [0.86 , 1.79]



ADDITIONAL TABLES

Table 1. Updated search results

Database searched	Date searched	February 2019	October 2019	January 2020	Total number of results
CENTRAL (January 2020; Issue 1 of 12), in the Cochrane Library	10/01/2020	211	132	28	371
MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (Ovid, 1946 to 9 January 2020)	10/01/2020	242	46	27	315
Embase Classic + Embase (Ovid, 1947 to 9 January 2019)	10/01/2020	121	17	12	150
CINAHL Plus with Full Text (EBSCO, 1937 to 10 January 2020)	10/01/2020	160	31	16	207
PsycINFO (Ovid, 1806 to January week 1 2020)	10/01/2020	27	8	3	38
LILACS (Bireme, 1982 to 10 January 2020) in English	10/01/2020	38	6	1	45

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Table 1. Updated search results *(Continued)*

Conference Proceedings Citation Index - Science (CPCI-S) on Web of Science (Clarivate Analytics, 1990 to 10 January 2020)	10/01/2020	10	0	2	12
DARE (2015, Issue 1 of 4), in the Cochrane Library	No longer updated since March 2015	0	0	0	0
Total		**809**	**240**	**89**	**1138**
After de-duplication		**606**	**216**	**76**	**898**

Exercise-based cardiac rehabilitation for adults after heart valve surgery: updated search results

Table 2. Description of severe adverse events

	Lin 2004	Sire 1987	Pressler 2018	Sibilitz 2016	Total events
No exercise group	**3 patients:** 1 pericardial effusion 1 paravalvular leakage 1 endocarditis	**2 patients:** 2 non-fatal thromboembolism	**5 patients:** 5 died before 24 months' follow-up	**1 patient:** Not reported	11
Exercise group	**4 patients:** 2 heart arrhythmias 1 sudden death 1 brain stem death	**2 patients:** 1 haematoma in abdominal muscle 1 angina pectoris	**4 patients:** **(but not due to exercise)** 1 fell due to icy conditions leading to severe cerebral trauma 1 lethal cerebral haemorrhage due to oral anticoagulant 2 died before 24 months' follow-up	**2 patients:** **(but not due to exercise)** 1 postsurgical cardiac tamponade 1 heart failure-related re-admission	12

Table 3. Mean total societal cost

Exercise group	Control group	Group difference (95% CI)	Statistical Significance
14,185 Euros/patient	17,448 Euros/patient	-1609 Euros/patient (-6162 to 2942)	NS

Table showing mean total societal cost between exercise-CR and control groups from Sibilitz 2016. NS: not statistically significant.

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APPENDICES

Appendix 1. Search strategies for review update

CENTRAL

#1 MeSH descriptor: [Exercise] explode all trees

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

#3 MeSH descriptor: [Exercise Tolerance] this term only

#4 MeSH descriptor: [Sports] explode all trees

#5 MeSH descriptor: [Physical Exertion] this term only

#6 exercis*

#7 sport*

#8 MeSH descriptor: [Physical Fitness] this term only

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

#10 (fitness or fitter or fit)

#11 muscle* near/3 (train* or activ*)

#12 train* near/5 (strength* or aerobic* or exercise*)

#13 (aerobic or resistance) near/3 (train* or activ*)

#14 physical* near/5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)

#15 (exercise* or fitness) near/3 (treat* or interven* or program* or train* or physical or activ*)

#16 MeSH descriptor: [Rehabilitation] this term only

#17 MeSH descriptor: [Rehabilitation Centers] this term only

#18 rehabilitat*

#19 MeSH descriptor: [Dance Therapy] this term only

#20 kinesiotherap*

#21 danc*

#22 ("lifestyle" or life-style) near/5 activ*

#23 ("lifestyle" or life-style) near/5 physical*

#24 walk*

#25 run*

#26 jog*

#27 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26

#28 MeSH descriptor: [Heart Valve Diseases] explode all trees

#29 valve near/2 (disease* or stenos* or insufficien*)

#30 MeSH descriptor: [Heart Valve Prosthesis Implantation] this term only

#31 MeSH descriptor: [Heart Valve Prosthesis] this term only

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#32 (valve near/2 (surg* or replace* or repair* or prosthe* or implant* or procedure*))

#33 MitraClip

#34 MeSH descriptor: [Transcatheter Aortic Valve Replacement] this term only

#35 TAVI

#36 #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35

#37 #27 and #36

MEDLINE Ovid

1 exp Exercise/

2 exp Exercise Therapy/

3 Exercise Tolerance/

4 exp Sports/

5 Physical Exertion/

6 exercis*.tw.

7 sport*.tw.

8 Physical Fitness/

9 exp "Physical Education and Training"/

10 (fitness or fitter or fit).tw.

11 (muscle* adj3 (train* or activ*)).tw.

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

13 ((aerobic or resistance) adj3 (train* or activ*)).tw.

14 (physical* adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)).tw.

15 ((exercise* or fitness) adj3 (treat* or interven* or program* or train* or physical or activ*)).tw.

16 Rehabilitation/

17 Rehabilitation Centers/

18 rehabilitat*.tw.

19 Dance Therapy/

20 kinesiotherap*.tw.

21 danc*.tw.

22 (("lifestyle" or life-style) adj5 activ$).tw.

23 (("lifestyle" or life-style) adj5 physical$).tw.

24 walk*.tw.

25 run*.tw.

26 jog*.tw.

27 or/1-26

28 exp Heart Valve Diseases/

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29 (valve adj2 (disease* or stenos* or insufficien*)).tw.

30 Heart Valve Prosthesis Implantation/

31 Heart Valve Prosthesis/

32 (valve adj2 (surg* or replace* or repair* or prosthe* or implant* or procedure*)).tw.

33 MitraClip.tw.

34 Transcatheter Aortic Valve Replacement/

35 TAVI.tw.

36 or/28-35

37 27 and 36

38 randomized controlled trial.pt.

39 controlled clinical trial.pt.

40 randomized.ab.

41 placebo.ab.

42 drug therapy.fs.

43 randomly.ab.

44 trial.ab.

45 groups.ab.

46 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45

47 exp animals/ not humans.sh.

48 46 not 47

49 37 and 48

Embase Ovid

1 exp exercise/

2 exp kinesiotherapy/

3 exercise tolerance/

4 exp sport/

5 exercis*.tw.

6 sport*.tw.

7 fitness/

8 physical education/

9 (fitness or fitter or fit).tw.

10 (muscle* adj3 (train* or activ*)).tw.

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

12 ((aerobic or resistance) adj3 (train* or activ*)).tw.

13 (physical* adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)).tw.

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14 ((exercise* or fitness) adj3 (treat* or interven* or program* or train* or physical or activ*)).tw.

15 Rehabilitation/

16 rehabilitation center/

17 rehabilitat*.tw.

18 dance therapy/

19 kinesiotherap*.tw.

20 danc*.tw.

21 (("lifestyle" or life-style) adj5 activ$).tw.

22 (("lifestyle" or life-style) adj5 physical$).tw.

23 walk*.tw.

24 run*.tw.

25 jog*.tw.

26 or/1-25

27 exp valvular heart disease/

28 (valve adj2 (disease* or stenos* or insufficien*)).tw.

29 exp heart valve replacement/

30 exp heart valve prosthesis/

31 (valve adj2 (surg* or replace* or repair* or prosthe* or implant* or procedure*)).tw.

32 MitraClip.tw.

33 transcatheter aortic valve implantation/

34 TAVI.tw.

35 or/27-34

36 26 and 35

37 random$.tw.

38 factorial$.tw.

39 crossover$.tw.

40 cross over$.tw.

41 cross-over$.tw.

42 placebo$.tw.

43 (doubl$ adj blind$).tw.

44 (singl$ adj blind$).tw.

45 assign$.tw.

46 allocat$.tw.

47 volunteer$.tw.

48 crossover procedure/

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49 double blind procedure/

50 randomized controlled trial/

51 single blind procedure/

52 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51

53 (animal/ or nonhuman/) not human/

54 52 not 53

55 36 and 54

56 limit 55 to embase

CINAHL

S50 S31 AND S49

S49 S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48

S48 TX cross-over*

S47 TX crossover*

S46 TX volunteer*

S45 (MH "Crossover Design")

S44 TX allocat*

S43 TX control*

S42 TX assign*

S41 TX placebo*

S40 (MH "Placebos")

S39 TX random*

S38 TX (doubl* N1 mask*)

S37 TX (singl* N1 mask*)

S36 TX (doubl* N1 blind*)

S35 TX (singl* N1 blind*)

S34 TX (clinic* N1 trial?)

S33 PT clinical trial

S32 (MH "Clinical Trials+")

S31 S22 AND S30

S30 S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29

S29 TAVI

S28 transcatheter aortic valve replacement*

S27 MitraClip

S26 valve N2 (surg* or replace* or repair* or prosthe* or implant* or procedure*)

S25 (MH "Heart Valve Prosthesis")

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S24 valve N2 (disease* or stenos* or insufficien*)

S23 (MH "Heart Valve Diseases+")

S22 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21

S21 walk* or run* or jog*

S20 (("lifestyle" or life-style) N5 physical*)

S19 (("lifestyle" or life-style) N5 activ*)

S18 kinesiotherap* or danc*

S17 (MH "Dance Therapy")

S16 rehabilitat*

S15 (MH "Rehabilitation Centers")

S14 (MH "Rehabilitation")

S13 (exercise* or fitness) N3 (treat* or interven* or program* or train* or physical or activ*)

S12 physical* N5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)

S11 (aerobic or resistance) N3 (train* or activ*)

S10 train* N5 (strength* or aerobic* or exercise*)

S9 muscle* N3 (train* or activ*)

S8 fitness or fitter or fit

S7 (MH "Physical Education and Training+")

S6 (MH "Physical Fitness")

S5 exercis* or sport*

S4 (MH "Sports+")

S3 (MH "Exercise Tolerance+")

S2 (MH "Therapeutic Exercise+")

S1 (MH "Exercise+")

PsycINFO

1 exp Exercise/

2 exp Sports/

3 exercis*.tw.

4 sport*.tw.

5 physical fitness/

6 physical education/

7 (fitness or fitter or fit).tw.

8 (muscle* adj3 (train* or activ*)).tw.

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

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10 ((aerobic or resistance) adj3 (train* or activ*)).tw.

11 (physical* adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)).tw.

12 ((exercise* or fitness) adj3 (treat* or interven* or program* or train* or physical or activ*)).tw.

13 rehabilitation/

14 rehabilitation centers/

15 rehabilitat*.tw.

16 dance therapy/

17 kinesiotherap*.tw.

18 danc*.tw.

19 (("lifestyle" or life-style) adj5 activ*).tw.

20 (("lifestyle" or life-style) adj5 physical*).tw.

21 walk*.tw.

22 run*.tw.

23 jog*.tw.

24 or/1-23

25 (valve adj2 (disease* or stenos* or insufficien*)).tw.

26 prostheses/

27 (valve adj2 (surg* or replace* or repair* or prosthe* or implant* or procedure*)).tw.

28 MitraClip.tw.

29 TAVI.tw.

30 25 or 26 or 27 or 28 or 29

31 24 and 30

32 random$.tw.

33 factorial$.tw.

34 crossover$.tw.

35 cross-over$.tw.

36 placebo$.tw.

37 (doubl$ adj blind$).tw.

38 (singl$ adj blind$).tw.

39 assign$.tw.

40 allocat$.tw.

41 volunteer$.tw.

42 control*.tw.

43 "2000".md.

44 or/32-43

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45 31 and 44

LILACS

(exercis$ or sport$ or fit$ or train$ or activ$ or aerobic$ or rehabilit$ or walk$ or jog$ or run$) [Words] and ("heart valve$" or "heart prosthe $") [Words]

CPCI-S

18 #17 AND #16

17 TS=(random* or blind* or allocat* or assign* or trial* or placebo* or crossover* or cross-over*)

16 #15 AND #10

15 #14 OR #13 OR #12 OR #11

14 TS=TAVI

13 TS=MitraClip

12 TS=(valve and (surg* or replace* or repair* or prosthe* or implant* or procedure*))

11 TS=(valve and (disease* or stenos* or insufficien*))

10 #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1

9 TS=(("lifestyle" or life-style) and physical*)

8 TS=(("lifestyle" or life-style) and activ*)

7 TS=(rehabilitat* or danc* or kinesiotherap* or walk* or run* or jog*)

6 TS=((exercise* or fitness) and (treat* or interven* or program* or train* or physical or activ*))

5 TS=(physical* and (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*))

4 TS=((aerobic or resistance) and (train* or activ*))

3 TS=(train* and (strength* or aerobic* or exercise*))

2 TS=(muscle* and (train* or active*))

1 TS=(exercis* or sport* or fitness or fitter or fit)

Appendix 2. Previous search strategies

Cochrane Library

#1MeSH descriptor: [Exercise] explode all trees
#2MeSH descriptor: [Exercise Therapy] explode all trees
#3MeSH descriptor: [Exercise Tolerance] this term only
#4MeSH descriptor: [Sports] explode all trees
#5MeSH descriptor: [Physical Exertion] this term only
#6exercis*
#7sport*
#8MeSH descriptor: [Physical Fitness] this term only
#9MeSH descriptor: [Physical Education and Training] explode all trees
#10(fitness or fitter or fit)
#11muscle* near/3 (train* or activ*)
#12train* near/5 (strength* or aerobic* or exercise*)
#13(aerobic or resistance) near/3 (train* or activ*)
#14physical* near/5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)
#15(exercise* or fitness) near/3 (treat* or interven* or program* or train* or physical or activ*)
#16MeSH descriptor: [Rehabilitation] this term only
#17MeSH descriptor: [Rehabilitation Centers] this term only
#18rehabilitat*

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#19MeSH descriptor: [Dance Therapy] this term only
#20kinesiotherap*
#21danc*
#22("lifestyle" or life-style) near/5 activ*
#23("lifestyle" or life-style) near/5 physical*
#24walk*
#25run*
#26jog*
#27#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
#28MeSH descriptor: [Heart Valve Diseases] explode all trees
#29valve near/2 (disease* or stenos* or insufficien*)
#30MeSH descriptor: [Heart Valve Prosthesis Implantation] this term only
#31MeSH descriptor: [Heart Valve Prosthesis] this term only
#32valve near/2 (surg* or replace* or repair* or prosthe*)
#33#28 or #29 or #30 or #31 or #32
#34#27 and #33

MEDLINE

1 exp Exercise/
2 exp Exercise Therapy/
3 Exercise Tolerance/
4 exp Sports/
5 Physical Exertion/
6 exercis*.tw.
7 sport*.tw.
8 Physical Fitness/
9 exp "Physical Education and Training"/
10 (fitness or fitter or fit).tw.
11 (muscle* adj3 (train* or activ*)).tw.
12 (train* adj5 (strength* or aerobic* or exercise*)).tw.
13 ((aerobic or resistance) adj3 (train* or activ*)).tw.
14 (physical* adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)).tw.
15 ((exercise* or fitness) adj3 (treat* or interven* or program* or train* or physical or activ*)).tw.
16 Rehabilitation/
17 Rehabilitation Centers/
18 rehabilitat*.tw.
19 Dance Therapy/
20 kinesiotherap*.tw.
21 danc*.tw.
22 (("lifestyle" or life-style) adj5 activ$).tw.
23 (("lifestyle" or life-style) adj5 physical$).tw.
24 walk*.tw.
25 run*.tw.
26 jog*.tw.
27 or/1-26
28 exp Heart Valve Diseases/
29 (valve adj2 (disease* or stenos* or insufficien*)).tw.
30 Heart Valve Prosthesis Implantation/
31 Heart Valve Prosthesis/
32 (valve adj2 (surg* or replace* or repair* or prosthe*)).tw.
33 or/28-32
34 27 and 33
35 randomized controlled trial.pt.
36 controlled clinical trial.pt.
37 randomized.ab.
38 placebo.ab.
39 drug therapy.fs.
40 randomly.ab.
41 trial.ab.
42 groups.ab.

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43 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42
44 exp animals/ not humans.sh.
45 43 not 44
46 34 and 45

Embase

1. exp exercise/
2. exp kinesiotherapy/
3. exercise tolerance/
4. exp sport/
5. exercis*.tw.
6. sport*.tw.
7. fitness/
8. fitness/
9. physical education/
10. (fitness or fitter or fit).tw.
11. (muscle* adj3 (train* or activ*)).tw.
12. (train* adj5 (strength* or aerobic* or exercise*)).tw.
13. ((aerobic or resistance) adj3 (train* or activ*)).tw.
14. (physical* adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)).tw.
15. ((exercise* or fitness) adj3 (treat* or interven* or program* or train* or physical or activ*)).tw.
16. rehabilitation/
17. rehabilitation center/
18. rehabilitat*.tw.
19. dance therapy/
20. kinesiotherap*.tw.
21. danc*.tw.
22. (("lifestyle" or life-style) adj5 activ$).tw.
23. (("lifestyle" or life-style) adj5 physical$).tw.
24. walk*.tw.
25. run*.tw.
26. jog*.tw.
27. or/1-26
28. exp valvular heart disease/
29. (valve adj2 (disease* or stenos* or insufficien*)).tw.
30. exp heart valve replacement/
31. exp heart valve prosthesis/
32. (valve adj2 (surg* or replace* or repair* or prosthe*)).tw.
33. or/28-32
34. 27 and 33
35. random$.tw.
36. factorial$.tw.
37. crossover$.tw.
38. cross over$.tw.
39. cross-over$.tw.
40. placebo$.tw.
41. (doubl$ adj blind$).tw.
42. (singl$ adj blind$).tw.
43. assign$.tw.
44. allocat$.tw.
45. volunteer$.tw.
46. crossover procedure/
47. double blind procedure/
48. randomized controlled trial/
49. single blind procedure/
50. 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49
51. (animal/ or nonhuman/) not human/
52. 50 not 51
53. 34 and 52
54. limit 53 to embase

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CINAHL

S47 S28 AND S46
S46 S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45
S45 TX cross-over*
S44 TX crossover*
S43 TX volunteer*
S42 (MH "Crossover Design")
S41 TX allocat*
S40 TX control*
S39 TX assign*
S38 TX placebo*
S37 (MH "Placebos")
S36 TX random*
S35 TX (doubl* N1 mask*)
S34 TX (singl* N1 mask*)
S33 TX (doubl* N1 blind*)
S32 TX (singl* N1 blind*)
S31 TX (clinic* N1 trial?)
S30 PT clinical trial
S29 (MH "Clinical Trials+")
S28 S22 AND S27
S27 S23 OR S24 OR S25 OR S26
S26 valve N2 (surg* or replace* or repair* or prosthe*)
S25 (MH "Heart Valve Prosthesis")
S24 valve N2 (disease* or stenos* or insufficien*)
S23 (MH "Heart Valve Diseases+")
S22 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21
S21 walk* or run* or jog*
S20 (("lifestyle" or life-style) N5 physical*)
S19 (("lifestyle" or life-style) N5 activ*)
S18 kinesiotherap* or danc*
S17 (MH "Dance Therapy")
S16 rehabilitat*
S15 (MH "Rehabilitation Centers")
S14 (MH "Rehabilitation")
S13 (exercise* or fitness) N3 (treat* or interven* or program* or train* or physical or activ*)
S12 physical* N5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)
S11 (aerobic or resistance) N3 (train* or activ*)
S10 train* N5 (strength* or aerobic* or exercise*)
S9 muscle* N3 (train* or activ*)
S8 fitness or fitter or fit
S7 (MH "Physical Education and Training+")
S6 (MH "Physical Fitness")
S5 exercis* or sport*
S4 (MH "Sports+")
S3 (MH "Exercise Tolerance+")
S2 (MH "Therapeutic Exercise+")
S1 (MH "Exercise+")

PsycINFO

1. exp Exercise/
2. exp Sports/
3. exercis*.tw.
4. sport*.tw.
5. physical fitness/
6. physical education/
7. (fitness or fitter or fit).tw.
8. (muscle* adj3 (train* or activ*)).tw.
9. (train* adj5 (strength* or aerobic* or exercise*)).tw.
10. ((aerobic or resistance) adj3 (train* or activ*)).tw.

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11. (physical* adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*)).tw.
12. ((exercise* or fitness) adj3 (treat* or interven* or program* or train* or physical or activ*)).tw.
13. rehabilitation/
14. rehabilitation centers/
15. rehabilitat*.tw.
16. dance therapy/
17. kinesiotherap*.tw.
18. danc*.tw.
19. (("lifestyle" or life-style) adj5 activ*).tw.
20. (("lifestyle" or life-style) adj5 physical*).tw.
21. walk*.tw.
22. run*.tw.
23. jog*.tw.
24. or/1-23
25. (valve adj2 (disease* or stenos* or insufficien*)).tw.
26. prostheses/
27. (valve adj2 (surg* or replace* or repair* or prosthe*)).tw.
28. or/25-27
29. 24 and 28
30. random$.tw.
31. factorial$.tw.
32. crossover$.tw.
33. cross-over$.tw.
34. placebo$.tw.
35. (doubl$ adj blind$).tw.
36. (singl$ adj blind$).tw.
37. assign$.tw.
38. allocat$.tw.
39. volunteer$.tw.
40. control*.tw.
41. "2000".md.
42. or/30-41
43. 29 and 42

LILACS

(exercis$ or sport$ or fit$ or train$ or activ$ or aerobic$ or rehabilit$ or walk$ or jog$ or run$) [Words] and ("heart valve$" or "heart prosthe $") [Words]

CPCI-S

16 #15 AND #14
15 TS=(random* or blind* or allocat* or assign* or trial* or placebo* or crossover* or cross-over*)
14 #13 AND #10
13 #12 OR #11
12 TS=(valve and (surg* or replace* or repair* or prosthe*))
11 TS=(valve and (disease* or stenos* or insufficien*))
10 #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
9 TS=(("lifestyle" or life-style) and physical*)
8 TS=(("lifestyle" or life-style) and activ*)
7 TS=(rehabilitat* or danc* or kinesiotherap* or walk* or run* or jog*)
6 TS=((exercise* or fitness) and (treat* or interven* or program* or train* or physical or activ*))
5 TS=(physical* and (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit*))
4 TS=((aerobic or resistance) and (train* or activ*))
3 TS=(train* and (strength* or aerobic* or exercise*))
2 TS=(muscle* and (train* or active*))
1 TS=(exercis* or sport* or fitness or fitter or fit)

WHAT'S NEW

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Date	Event	Description
9 July 2020	New search has been performed	Four new studies added in updated review with evidence current to January 2020
6 July 2020	New citation required but conclusions have not changed	We conducted an update of the previous systematic review and meta-analysis to assess randomised clinical trial evidence for the use of exercise-based CR following heart valve surgery

HISTORY

Protocol first published: Issue 12, 2013
Review first published: Issue 3, 2016

CONTRIBUTIONS OF AUTHORS

KLS and ADZ initiated and raised funding for the initial review. KLS drafted the initial review. LA, KLS, and RST contributed to updating of the text. LA and KLS carried out trial selection, data extraction, and RoB2 analysis, with RST confirming all data extractions and resolving any disagreements. LA carried out meta-analysis with supervision from RST. All review authors have revised and contributed to drafting of the review, and all have approved the final version of the review for publication.

DECLARATIONS OF INTEREST

Lizette Abraham declares no conflict of interest.

Kirstine L Sibilitz, Selina K Berg, Lars H Tang, Signe S Risom, Britt Borregaard, Jane Lindschou, Rod Taylor, and Ann-Dorthe Zwisler are involved in conducting previous and/or current randomised clinical trials (including the included trial of Sibilitz et al) investigating the effects of cardiac rehabilitation for different cardiac populations. None of these trials were or are industry sponsored, but studies were sponsored by private and public funding. None of the founders had any involvement in analyses, collection of data, or interpretation of trial results.

Kirstine L Sibilitz and Ann-Dorthe Zwisler are currently co-authoring other Cochrane Reviews of cardiac rehabilitation.

Rod S Taylor is an author on previous Cochrane Reviews on cardiac rehabilitation and is the Chief Investigator for ongoing trials (REACH-HFpEF, SCOT:REACH-HF, DK:REACH-HF) assessing the clinical effectiveness and cost-effectiveness of home-based self-directed exercise-based cardiac rehabilitation interventions for patients with heart failure and their carers.

Ann-Dorthe Zwisler declares financial support for expert testimony as part of her employment as professor.

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Internal sources

- No sources of support supplied

External sources

- NIHR, UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This updated review included the RoB2 assessment, which was not included in the last review, nor in the protocol. The protocol has now been updated to account for RoB2 and MECIR guidance. The RoB2 assessment for all primary outcomes and secondary outcomes of exercise capacity has been included.

Given their importance to policymakers, this update added the following secondary outcomes to the review: (1) return to work, (2) costs, and (3) cost-effectiveness.

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We deleted the outcomes of NYHA classification and LVEF as we considered them to be population characteristics rather than outcomes of interventions, and we therefore did not believe it was important to include them.

INDEX TERMS

Medical Subject Headings (MeSH)

Aortic Valve [surgery]; Cardiac Rehabilitation [*methods]; Exercise; *Exercise Tolerance; Heart Valve Prosthesis Implantation [mortality] [*rehabilitation]; Mitral Valve [surgery]; Physical Conditioning, Human [*methods]; Randomized Controlled Trials as Topic; Resistance Training; Return to Work; Time Factors

MeSH check words

Adult; Female; Humans; Male; Middle Aged

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