

## Exercise-based cardiac rehabilitation for heart failure

### Background

The National Institute for Health and Care Excellence (NICE) identify heart failure as ‘a complex clinical syndrome of symptoms and signs that suggest impairment of the heart as a pump supporting physiological circulation’. It is caused by ‘structural or functional abnormalities of the heart’. The demonstration of objective evidence of these cardiac abnormalities is necessary for a diagnosis of heart failure to be made. Early, research into heart failure concentrated on patients with heart failure and reduced contraction of the left ventricle. The agreed description of this group of patients is heart failure with left ventricular systolic dysfunction (LVSD). It has become evident that almost half the patients with heart failure syndrome do not have LVSD.

Guidelines issued by NICE in 2010<sup>1</sup> recommend that, as part of rehabilitation, patients should be offered a supervised group exercise-based rehabilitation programme designed for patients with heart failure. Doctors should...

- Ensure the patient is stable and does not have a condition or device that would preclude an exercise-based rehabilitation programme.
- Include a psychological and educational component in the programme.
- The programme may be incorporated within an existing cardiac rehabilitation programme

The 2010 NICE guideline reviews evidence on exercise-based cardiac rehabilitation for chronic heart failure to 2009 and is included in the *reviews and overviews* section of this review.

### Summary and key findings

- exercise-based rehabilitation does not increase or decrease the risk of all-cause mortality in the short term (up to 12-months' follow-up) but reduces the risk of hospital admissions and confers important improvements in health-related quality of life.
- exercise training may reduce mortality in the longer term and the benefits of exercise training appear to be consistent across participant characteristics including age, gender and heart failure severity

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<sup>1</sup> Mant et al (2010) *Chronic Heart Failure: NICE Clinical Guideline No 108*, National Clinical Guideline Centre at The Royal College of Physicians

- exercise-based rehabilitation for patients with chronic heart failure may result in a modest reduction in depressive symptoms
- aerobic interval training (AIT) is effective for patients with heart failure and has not been associated with any adverse effects, even for patients fitted with an implantable cardioverter defibrillator.
- tai chi exercise may improve quality of life, mood, and exercise self-efficacy in patients with heart failure but has no effect on functional capabilities.
- gentle seated exercise has no effect on outcomes other than daily activity as measured by accelerometry but physical training in warm water is well tolerated and seems to improve exercise capacity as well as muscle function in small muscle groups in patients with chronic heart failure.
- home-based exercise training programmes may increase walking distance and decrease global rating of symptoms but have no effect on clinical outcomes, other than multiple rehospitalisation rates, and may not be appropriate for community-based heart failure patients.
- vitamin D supplementation does not improve functional capacity or quality of life in older patients with heart failure with vitamin D insufficiency.
- long-term exercise therapy in patients with stable chronic heart failure is cost-effective and prolongs survival by an additional 1.82 years at a cost of \$1,773 per/life-year saved – (£1,054 approx) at 2001 prices

**Review of evidence**

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The reviewed evidence is listed in reverse chronological order with the most recent evidence first.

**a) Reviews and overviews**

Study	Findings
<p>Taylor R S, Sagar V A, Davies E J, Briscoe S, Coats A J S, Dalal H, Lough F, Rees K and Singh S (2014) Exercise-based rehabilitation for heart failure, <i>The Cochrane Library 2014, Issue 4</i></p> <p>[Taylor R S, Dalal H, Jolly K, Moxham T and Zawada A (2010) Home-based versus centre-based cardiac rehabilitation, <i>The Cochrane Library 2010, Issue 1</i>]</p>	<p>This updated Cochrane review supports the conclusions of the previous version of the review that, compared with a ‘no exercise’ control, exercise-based rehabilitation does not increase or decrease the risk of all-cause mortality in the short term (up to 12-months' follow-up) but reduces the risk of hospital admissions and confers important improvements in health-related quality of life. This update provides further evidence that exercise training may reduce mortality in the longer term and that the benefits of exercise training appears to be consistent across participant characteristics including age, gender and heart failure severity</p>
<p>van der Meer S, Zwerink M, van Brussel M, van der Valk P, Wajon E and van der Palen J (2012) Effect of outpatient exercise training programmes in patients with chronic heart failure: a systematic review, <i>European Journal of Preventive Cardiology</i> 19 (4) : 795-80</p>	<p>This systematic review studies the effects of outpatient exercise training programmes compared with usual care on exercise capacity, exercise performance, quality of life, and safety in patients with chronic heart failure.</p> <p>A systematic review, with meta-analysis of randomized controlled trials of patients with chronic heart failure with a left ventricular ejection fraction not more than 40%, included. A meta-analysis was performed.</p> <p>Results: Twenty-two studies were included. VO<sub>2</sub> max, 6-min walking test, and quality of life showed significant differences in favour of the intervention group of 1.85 ml/kg/min, 47.9 m, and 6.9 points, respectively. In none of the studies was a significant relationship found between exercise training and adverse events.</p> <p>Conclusion: This meta-analysis illustrates the efficacy and safety of outpatient exercise training programmes for patients with chronic heart failure.</p>

<p>Piepoli M F, Conraads V, Corrà U, Dickstein K, Francis D P, Jaarsma T, McMurray J, Pieske B, Piotrowicz E, Schmid J-P, Anker S D, Cohen Solal A, Filippatos G S, Hoes A W, Gielen S, Giannuzzi P and Ponikowski P P (2011) Exercise training in heart failure: from theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation, <i>European Journal of Heart Failure</i> 13 (4) : 347-357</p>	<p>The European Society of Cardiology heart failure guidelines firmly recommend regular physical activity and structured exercise training (ET), but this recommendation is still poorly implemented in daily clinical practice outside specialized centres and in the real world of heart failure clinics.</p> <p>The authors claim that exercise intolerance can be successfully tackled by applying ET. There is a need to encourage the mindset that breathlessness may be evidence of signalling between the periphery and central haemodynamic performance and regular physical activity may ultimately bring about favourable changes in myocardial function, symptoms, functional capacity, and increased hospitalization-free life span and probably survival.</p> <p>In this position paper, the authors provide practical advice for the application of exercise in heart failure and how to overcome traditional barriers, based on the current scientific and clinical knowledge supporting the beneficial effect of this intervention.</p>
<p>Mant J (Chair), Al-Mohammad A (Clinical Advisor), Davis M, Dawda P, Gilmour J, Hardman S, Leyva F, McIntyre H, Mindham R, Price A, Kirwin G, Laramie P, Newberry N, Richards A, Ritchie G, Swain S, Turner C, Foley P, Leyva F and Fuat A (2010) <i>Chronic Heart Failure: NICE Clinical Guideline No 108</i>, National Clinical Guideline Centre at The Royal College of Physicians</p>	<p>The NICE guideline on rehabilitation suggests that the person treated should be offered a supervised group exercise-based rehabilitation programme designed for patients with heart failure.</p> <ul style="list-style-type: none"> <li>• Ensure the patient is stable and does not have a condition (such as uncontrolled ventricular response to atrial fibrillation, or uncontrolled hypertension) or device (for example, a high-energy pacing device set to be activated at rates achieved during exercise) that would preclude the programme.</li> <li>• Include a psychological and educational component in the programme.</li> <li>• The programme may be incorporated within an existing cardiac rehabilitation programme.</li> </ul>

<p>Smart N and Marwick T H (2004) Exercise training for patients with heart failure: a systematic review of factors that improve mortality and morbidity, <i>American Journal of Medicine</i> 116 (10) : 693-706</p>	<p>A review to determine the efficacy of exercise training and its effects on outcomes in patients with heart failure.</p> <p>A total of 81 studies were identified: 30 randomized controlled trials, five nonrandomized controlled trials, nine randomized crossover trials, and 37 longitudinal cohort studies. Exercise training was performed in 2387 patients.</p> <p>The average increment in peak oxygen consumption was 17% in 57 studies that measured oxygen consumption directly, 17% in 40 studies of aerobic training, 9% in three studies that only used strength training, 15% in 13 studies of combined aerobic and strength training, and 16% in the one study on inspiratory training. There were no reports of deaths that were directly related to exercise during more than 60,000 patient-hours of exercise training. During the training and follow-up periods of the randomized controlled trials, there were 56 combined (deaths or adverse events) events in the exercise groups and 75 combined events in the control groups (odds ratio [OR] = 0.98; 95% confidence interval [CI]: 0.61 to 1.32; P = 0.60). During this same period, 26 exercising and 41 non-exercising subjects died (OR = 0.71; 95% CI: 0.37 to 1.02; P = 0.06).</p> <p>Conclusion</p> <p>Exercise training is safe and effective in patients with heart failure. The risk of adverse events may be reduced, but further studies are required to determine whether there is any mortality benefit.</p>
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**b) Exercise-based cardiac rehabilitation for heart failure - in general**

Study	Methods	Findings
<p>Belardinelli R, Georgiou D, Cianci G and Purcaro A (2012) 10-Year Exercise Training in Chronic Heart Failure: A Randomized Controlled Trial, <i>Journal of the American College of Cardiology</i> 60 (16)</p>	<p>This study investigated the effect of a very long-term exercise training in 123 chronic heart failure (CHF) patients whose condition was stable over the previous 3 months.</p> <p>After randomization, a trained group (T group, n = 63) underwent a supervised ET at 60% of peak oxygen consumption (Vo<sub>2</sub>), 2 times weekly for 10 years, whereas a non-trained group (NT group, n = 60) did not exercise formally. The ET program was supervised and performed mostly at a coronary club with periodic control sessions twice yearly at the hospital's gym.</p> <p>The authors had previously shown (Belardinelli et al, 1999) that long-term moderate exercise training improves functional capacity and quality of life in New York Heart Association class II and III CHF patients.</p>	<p>In the trained group (T), peak VO<sub>2</sub> was more than 60% of age- and gender-predicted maximum Vo<sub>2</sub> each year during the 10-year study (p &lt; 0.05 vs. the non-trained (NT) group). In NT patients, peak VO<sub>2</sub> decreased progressively with an average of 52 ± 8% of maximum VO<sub>2</sub> predicted. Ventilation relative to carbon dioxide output (VE/VCO<sub>2</sub>) slope was significantly lower (35 ± 9) in T patients versus NT patients (42 ± 11, p &lt; 0.01). Quality-of-life score was significantly better in the T group versus the NT group (43 ± 12 vs. 58 ± 14, p &lt; 0.05). During the 10-year study, T patients had a significant lower rate of hospital readmission (hazard ratio: 0.64, p &lt; 0.001) and cardiac mortality (hazard ratio: 0.68, p &lt; 0.001) than controls. Multivariate analysis selected peak VO<sub>2</sub> and resting heart rate as independent predictors of events.</p> <p>Conclusions: Moderate supervised ET performed twice weekly for 10 years maintains functional capacity of more than 60% of maximum VO<sub>2</sub> and confers a sustained improvement in quality of life compared with NT patients. These sustained improvements are associated with reduction in major cardiovascular events, including hospitalizations for CHF and cardiac mortality.</p>

<p>Kitzman D W, Brubaker P H, Morgan T M, Stewart K P and Little W C (2010) Exercise Training in Older Patients With Heart Failure and Preserved Ejection Fraction: A Randomized, Controlled, Single-Blind Trial, <i>Circulation: Heart Failure</i> 3 : 659-667</p>	<p>Heart failure (HF) with preserved left ventricular ejection fraction (HFPEF) is the most common form of HF in the older population. Exercise intolerance is the primary chronic symptom in patients with HFPEF and is a strong determinant of their reduced quality of life (QOL). Exercise training (ET) improves exercise intolerance and QOL in patients with HF with reduced ejection fraction (EF). However, the effect of ET in HFPEF has not been examined in a randomized controlled trial.</p> <p>This 16-week investigation was a randomized, attention-controlled, single-blind study of medically supervised ET (3 days per week) on exercise intolerance and QOL in 53 elderly patients (mean age, 70±6 years; range, 60 to 82 years; women, 46) with isolated HFPEF (EF =50% and no significant coronary, valvular, or pulmonary disease). Attention controls received biweekly follow-up telephone calls. Forty-six patients completed the study (24 ET, 22 controls).</p>	<p>Attendance at exercise sessions in the ET group was excellent (88%; range, 64% to 100%). There were no trial-related adverse events. The primary outcome of peak exercise oxygen uptake increased significantly in the ET group compared to the control group (13.8±2.5 to 16.1±2.6 mL/kg per minute [change, 2.3±2.2 mL/kg per minute] versus 12.8±2.6 to 12.5±3.4 mL/kg per minute [change, -0.3±2.1 mL/kg per minute]; P=0.0002). There were significant improvements in peak power output, exercise time, 6-minute walk distance, and ventilatory anaerobic threshold (all P&lt;0.002). There was improvement in the physical QOL score (P=0.03) but not in the total score (P=0.11).</p> <p>Conclusions— Exercise training (ET) improves peak and sub-maximal exercise capacity in older patients with heart failure with preserved left ventricular ejection fraction (HFPEF).</p>
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<p>O'Connor C M, Whellan D J, Lee K L, Keteyian S J, Cooper L S, Ellis S J, Leifer E S, Kraus W E, Kitzman D W, Blumenthal J A, Rendall D S, Houston Miller N, Fleg J L, Schulman K A, McKelvie R S, Zinnad F and Piña I L (2009) Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial, <i>Journal of the American Medical Association</i> 301 (14) : 1439-1450</p>	<p>To test the efficacy and safety of exercise training among patients with heart failure.</p> <p>A multi-centre randomized controlled trial of 2331 medically stable outpatients with heart failure and reduced ejection fraction. Participants in Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) were randomized from April 2003 through February 2007 at 82 centres within the United States, Canada, and France; median follow-up was 30 months.</p> <p>Interventions Usual care plus aerobic exercise training, consisting of 36 supervised sessions followed by home-based training, or usual care alone.</p> <p>Main Outcome Measures: Composite primary end point of all-cause mortality or hospitalization and pre-specified secondary end points of all-cause mortality, cardiovascular mortality or cardiovascular hospitalization, and cardiovascular mortality or heart failure hospitalization.</p> <p>The median age was 59 years, 28% were women, and 37% had New York Heart Association class III or IV symptoms. Heart failure etiology was ischemic in 51%, and median left ventricular ejection fraction was 25%.</p> <p>Exercise adherence decreased from a median of 95 minutes per week during months 4 through 6 of follow-up to 74 minutes per week during months 10 through 12. A total of 759 patients (65%) in the exercise training group died or were hospitalized compared with 796 patients (68%) in the usual care group (hazard ratio [HR], 0.93 [95% confidence interval {CI}, 0.84-1.02]; P = .13).</p>	<p>There were non-significant reductions in the exercise training group for mortality (189 patients [16%] in the exercise training group vs 198 patients [17%] in the usual care group; HR, 0.96 [95% CI, 0.79-1.17]; P = .70), cardiovascular mortality or cardiovascular hospitalization (632 [55%] in the exercise training group vs 677 [58%] in the usual care group; HR, 0.92 [95% CI, 0.83-1.03]; P = .14), and cardiovascular mortality or heart failure hospitalization (344 [30%] in the exercise training group vs 393 [34%] in the usual care group; HR, 0.87 [95% CI, 0.75-1.00]; P = .06). In pre-specified supplementary analyses adjusting for highly prognostic baseline characteristics, the HRs were 0.89 (95% CI, 0.81-0.99; P = .03) for all-cause mortality or hospitalization, 0.91 (95% CI, 0.82-1.01; P = .09) for cardiovascular mortality or cardiovascular hospitalization, and 0.85 (95% CI, 0.74-0.99; P = .03) for cardiovascular mortality or heart failure hospitalization. Other adverse events were similar between the groups.</p> <p>Conclusions</p> <p>In the protocol-specified primary analysis, exercise training resulted in non-significant reductions in the primary end point of all-cause mortality or hospitalization and in key secondary clinical end points.</p> <p>After adjustment for highly prognostic predictors of the primary end point, exercise training was associated with modest significant reductions for both all-cause mortality or hospitalization and cardiovascular mortality or heart failure hospitalization.</p>
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<p>Austin J, Williams R, Ross L, Moseley L and Hutchison S (2008) Five-year follow-up findings from a randomized controlled trial of cardiac rehabilitation for heart failure., <i>European Journal of Cardiovascular Prevention &amp; Rehabilitation</i> 15 (2) : 162-167</p>	<p>A follow-up study on the 5-year status of the surviving patients (n = 179 at 6 months) of a 24-week randomized controlled trial comparing cardiac rehabilitation (CR) with heart failure outpatient clinic care (standard care).</p> <p>In the original randomized controlled trial, 200 patients (60–89 years, 132 men) with New York Heart Association II/III heart failure confirmed by echocardiography had been randomized (2000–2001). At the 5-year follow-up, the initial trial measures (6-min walk test, Minnesota living with heart failure, EuroQol health-related quality of life, and routine biochemistry) were repeated if the patient was in a satisfactory condition. Data on deaths and admissions were obtained from the medical records department.</p>	<p>Over half of the original participants (n = 119, 59.5%) were alive at 5 years (mean age 75.2 years), and most (94%) attended the clinic for assessment. A sustained improvement from baseline for both groups in Minnesota living with heart failure, but not in EuroQol was observed, and the majority of the other measures had deteriorated. In contrast to the CR group, the standard care group showed a significant deterioration in walking distance (5 versus 11%; P [ 0.05). More patients in the CR group were taking regular exercise (71 versus 51%; P [ 0.05). No significant differences between the groups in health care utilization or survival were observed.</p> <p>Conclusion A 24-week CR programme for patients with stable heart failure showed some long-term benefit at 5 years. Differences in the mean values of most of the functional and quality of life measures were evidently to the advantage of the CR group, which also showed a better exercise profile.</p>
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<p>Sarullo F M, Gristina T, Brusca I, Milia S, Raimondi R, Sajeva M, La Chiusa S M, Serio G, Paterna S, Di Pasquale P and Castello A (2006) Effect of physical training on exercise capacity, gas exchange and N-terminal pro-brain natriuretic peptide levels in patients with chronic heart failure, <i>European Journal of Cardiovascular Prevention &amp; Rehabilitation</i> 13 (5) : 812-817</p>	<p>To evaluate the effect of exercise training on functional capacity and on changes in N-terminal pro-brain natriuretic peptide (NT pro-BNP) levels and to assess the effect of exercise training on quality of life.</p> <p>Sixty patients (45 men/15 women, mean age 52.7 years; <math>\pm 5.3</math> SD), with stable heart failure (45 ischaemic/hypertensive and 15 idiopathic patients), in New York Heart Association (NYHA) functional class II (n = 35) to III (n = 25), with an ejection fraction less than 40%, were randomly assigned to a training (n = 30) and a control group (n = 30).</p> <p>The training group (30 patients) performed 3 months of supervised physical training programme using a bicycle ergometer for 30 min three times a week at a load corresponding to 60–70% of their oxygen consumption (<math>V_{O_2}</math>) peak.</p> <p>The control group did not change their previous physical activity. A graded maximal exercise test with respiratory gas analysis and an endurance test with constant workload corresponding to 85% of the peak oxygen load at the baseline and after 3 months were performed, and at the same times NT pro-BNP levels were measured.</p>	<p>The exercise capacity increased from 15.8 (<math>\pm 2.3</math> SD) to 29.9 (<math>\pm 2.1</math> SD) min (<math>P &lt; 0.0001</math>) and the peak <math>VO_2</math> tended to improve from 14.5 (<math>\pm 1.4</math> SD) to 17.7 (<math>\pm 2.6</math> SD) ml/kg per min (<math>P &lt; 0.0001</math>) during the supervised training period. <math>VO_2</math> at the anaerobic threshold increased from 12.9 (<math>\pm 1.0</math> SD) to 15.5 (<math>\pm 1.7</math> SD) ml/kg per min (<math>P &lt; 0.0001</math>). NT pro-BNP levels decreased from 3376 (<math>\pm 3133</math> SD) to 1434 (<math>\pm 1673</math> SD) pg/ml (<math>P = 0.043</math>). The positive training effects were associated with an improvement in the NYHA functional class.</p> <p>Conclusion Physical training of moderate intensity significantly improves the exercise capacity and neuro-hormonal modulation in patients with chronic heart failure. This is associated with an alleviation of symptoms and improvement in quality of life.</p>
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<p>Austin J, Williams R, Ross L, Moseley L and Hutchison S (2005) Randomised controlled trial of cardiac rehabilitation in elderly patients with heart failure, <i>European Journal of Heart Failure</i> 7 (3) : 411-417</p>	<p>Cardiac rehabilitation, the main focus of which is exercise, is integral to most cardiology departments. The aim of this study was to determine whether a cardiac rehabilitation programme improved on the outcomes of an outpatient heart failure clinic (standard care) for patients, over 60 years of age, with chronic heart failure.</p> <p>Two hundred patients (60–89 years, 66% male) with New York Heart Association (NYHA) II or III heart failure confirmed by echocardiography were randomised. Both standard care and experimental groups attended clinic with a cardiologist and specialist nurse every 8 weeks. Interventions included exercise prescription, education, dietetics, occupational therapy and psychosocial counselling.</p> <p>The main outcome measures were functional status (NYHA, 6-min walk), health-related quality of life (MLHF and EuroQol) and <i>hospital admissions</i>.</p>	<p>There were significant improvements in MLHF and EuroQol scores, NYHA classification and 6-min walking distance (metres) at 24 weeks between the groups (<math>p &lt; 0.001</math>). The experimental group had fewer admissions (11 vs. 33, <math>p &lt; 0.01</math>) and spent fewer days in hospital (41 vs. 187, <math>p &lt; 0.001</math>).</p> <p>Conclusions: Cardiac rehabilitation, already widely established in the UK, offers an effective model of care for older patients with heart failure.</p>
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<p>Collins E, Langbein W E, Dilan-Koetje J, Bammert C, Hanson K, Reda D and Edwards L (2004) Effects of exercise training on aerobic capacity and quality of life in individuals with heart failure., <i>Heart &amp; Lung</i> 33 (3) : 154-161</p>	<p>To determine whether subjects with chronic heart failure, who completed a 12-week rehabilitation program, would have significantly greater quality of life, better aerobic fitness, less difficulty with symptoms of heart failure, greater self-efficacy for exercise, and higher daily activity levels when compared with subjects in a control group. Thirty-one males, aged 64 ± 10 years with left ventricular ejection fraction of 29 ± 7%, were randomized to a moderate intensity supervised aerobic exercise program (n = 15) or a control group (n = 16). Twenty-seven subjects completed at least 1 follow-up assessment.</p>	<p>After 12 weeks there were significant differences in the change scores for perceived physical function (using RAND Corporation's 36-item short form) (P = .025) and peak oxygen uptake (P = .019) between the exercise and control groups with the exercise group experiencing improved physical function and fitness. Conclusions: Exercise training in adults with heart failure increases exercise tolerance and perceived physical function. Improved heart failure symptoms, self-efficacy for exercise, or increased physical activity may not be associated with enhancement of exercise tolerance.</p>
<p>Belardinelli R, Georgiou D, Cianci G and Purcaro A (1999) Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: effects on functional capacity, quality of life, and clinical outcome, <i>Circulation</i> 99 (9) : 1173-1182</p>	<p>To determine whether long-term moderate exercise training (ET) improves functional capacity and quality of life in patients with CHF and whether these effects translate into a favourable outcome, 110 patients with stable CHF were initially recruited, and 99 (59±14 years of age; 88 men and 11 women) were randomized into 2 groups. One group (group T, n=50) underwent ET at 60% of peak VO<sub>2</sub>, initially 3 times a week for 8 weeks, then twice a week for 1 year. Another group (group NT, n=49) did not exercise. At baseline and at months 2 and 14, all patients underwent a cardiopulmonary exercise test, while 74 patients (37 in group T and 37 in group NT) with ischemic heart disease underwent myocardial scintigraphy. Quality of life was assessed by questionnaire. Ninety-four patients completed the protocol (48 in group T and 46 in group NT).</p>	<p>In group T—both peak VO<sub>2</sub> and thallium activity score improved at 2 months (18% and 24%, respectively; P&lt;0.001 for both) and did not change further after 1 year. Quality of life also improved and paralleled peak VO<sub>2</sub>. Exercise training was associated both with lower mortality (n=9 versus n=20 for those with training versus those without; relative risk (RR)=0.37; 95% CI, 0.17 to 0.84; P=0.01) and hospital readmission for heart failure (5 versus 14; RR=0.29; 95% CI, 0.11 to 0.88; P=0.02). Independent predictors of events were ventilatory threshold at baseline (β-coefficient=0.378) and post-training thallium activity score (β-coefficient -0.165). Conclusions—Long-term moderate ET determines a sustained improvement in functional capacity and quality of life in patients with CHF. This benefit seems to translate into a favourable outcome.</p>

## c) Aerobic interval training

Study	Methods	Findings
Isaksen K, Munk P S, Valborgland T and Larsen A I (2014) Aerobic interval training in patients with heart failure and an implantable cardioverter defibrillator: a controlled study evaluating feasibility and effect, <i>European Journal of Preventive Cardiology: Published online before print January 8, 2014, doi: 10.1177/2047487313519345</i>	See: patients with an implantable cardioverter defibrillator	
Nilsson B B, Westheim A and Risberg M A (2008) Effects of group-based high-intensity aerobic interval training in patients with chronic heart failure, <i>American Journal of Cardiology</i> 102 (10) : 1361-1365	To evaluate the effectiveness of a novel group-based aerobic interval training of high intensity on functional capacity and quality of life in patients with chronic heart failure (CHF) and examine the relation between changes in functional capacity and quality of life. Eighty patients with stable CHF (63 men, 17 women; mean age 70.1 ± 7.9 [SD] years; left ventricular ejection fraction 30 ± 8.5%) on optimal medical treatment were randomly assigned to either a 16-week group-based aerobic high-intensity interval training model twice weekly for 65 to 80 minutes/day (n = 40) or a control group (n = 40) that received standard care. Functional capacity was measured using the 6-minute walk test and cycle ergometer test. Quality of life was measured using the Minnesota Living with Heart Failure Questionnaire.	After 16 weeks, functional capacity improved significantly in the exercise group compared with the control group measured using the 6-minute walk test (+58 vs -15 metres; p <0.001) and for both workload and time measured using the bicycle ergometer test (+10 vs -1 W; p < 0.001; + 57 vs -8 seconds; p <0.001). Quality of life improved significantly in the exercise group compared with the control group (p = 0.03), and a significant inverse correlation was found between quality of life and functional capacity (r = - 0.49, p <0.05). Conclusion: This exercise model significantly improved functional capacity and quality of life compared with the control group in patients with CHF. Improvements in quality of life were significantly related to functional capacity.

<p>Nilsson B B, Westheim A and Risberg M A (2008) Long-term effects of a group-based high-intensity aerobic interval-training program in patients with chronic heart failure, <i>American Journal of Cardiology</i> 102 (9) : 1220-1224</p>	<p>The aim of this study was to evaluate the long-term effects of group-based, high-intensity interval training on functional capacity and the quality of life in 80 patients with stable CHF (mean age 70.1 ± 7.9 years) in New York Heart Association classes II to IIIB. Patients were randomized to either an exercise group (n = 40) or a control group (n = 40). The mean ejection fractions at baseline were 31 ± 8% in the exercise group and 31 ± 1% in the control group. The exercise group exercised twice a week for 4 months in addition to 4 consultations with a CHF nurse. Six-minute walking distance, workload and exercise time on a cycle ergometer test, and the quality of life were measured at baseline and 4 and 12 months after enrolment.</p>	<p>After 4 months, functional capacity (6-minute walking distance +58 vs -15 m, p &lt;0.001) and the quality of life (Minnesota Living With Heart Failure Questionnaire score +10 vs -1 point, p &lt;0.005) improved significantly in the exercise group compared with the control group. After 12 months, the improvements were still significant in the exercise group compared with the control group for all parameters (6-minute walking distance +41 vs -20 m, p &lt;0.001; workload +10 vs -1 W, p = 0.001; exercise time +53 vs -6 seconds, p = 0.003; quality of life +10 vs -6 points, p = 0.003). Conclusion: The results support the implementation of a group-based aerobic interval training program to improve long-term effects on functional capacity and the quality of life in patients with CHF.</p>
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## d) Seated exercise

Study	Methods	Findings
Witham M D, Gray J M, Argo I S, Johnston D W, Struthers A D and McMurdo M E T (2005) Effect of a seated exercise program to improve physical function and health status in frail patients [greater-than or equal to]70 years of age with heart failure, <i>American Journal of Cardiology</i> 95 (9) : 1120-1124	Eighty-two patients aged at least 70 years with heart failure were randomized to a gentle, seated exercise program or to usual care.	Six-minute walk distance and quality of life did not change between groups, but daily activity as measured by accelerometry increased in the exercise group relative to the control group.



## e) Hydrotherapy

Study	Methods	Findings
<p>Cider Å, Schaufelberger M, Sunnerhagen K S and Andersson B (2003) Hydrotherapy—a new approach to improve function in the older patient with chronic heart failure, <i>European Journal of Heart Failure</i> 5 (4) : 527-535</p>	<p>Hydrotherapy, i.e. exercise in warm water, as a rehabilitation program has been considered potentially dangerous in patients with chronic heart failure (CHF) due to the increased venous return caused by the hydrostatic pressure. However, hydrotherapy has advantages compared to conventional training. This study tested the applicability of an exercise programme in a temperature-controlled swimming pool, with specific reference to exercise capacity, muscle function, quality of life and safety.</p> <p>Twenty-five patients with CHF (NYHA II–III, age 72.1±6.1) were randomised into either 8 weeks of hydrotherapy (n=15), or into a control group (n=10).</p>	<p>The training program was well tolerated with no adverse events. Patients in the hydrotherapy group improved their maximal exercise capacity (+6.5 vs. -5.9 W, P=0.001), isometric endurance in knee extension (+4 vs. -9 s, P=0.01) together with an improvement in the performance of heel-lift (+4 vs. -3 n.o., P=&lt;0.01), shoulder abduction (+12 vs. -8 s, P=0.01) and shoulder flexion (+6 vs. +4, P=0.01) in comparison to patients in the control group.</p> <p>Conclusion: Physical training in warm water was well tolerated and seems to improve exercise capacity as well as muscle function in small muscle groups in patients with CHF.</p>

## f) Tai Chi

Study	Methods	Findings
<p>Yeh G Y, McCarthy E P, Wayne P M, Stevenson L W, Wood M J, Forman D, Davis R B and Phillips R S (2011) Tai Chi Exercise in Patients With Chronic Heart Failure: A Randomized Clinical Trial, <i>JAMA Internal Medicine (formerly Archives of Internal Medicine)</i> 171 (8) : 750-757</p>	<p>To investigate whether tai chi, as an adjunct to standard care, improves functional capacity and quality of life in patients with heart failure. A single-blind, multisite, parallel-group, randomized controlled trial evaluated 100 outpatients with systolic HF (New York Heart Association class I-III, left ventricular ejection fraction =40%) who were recruited between May 1, 2005, and September 30, 2008. A group-based 12-week tai chi exercise program (n = 50) or time-matched education (n = 50, control group) was conducted. Outcome measures included exercise capacity (6- minute walk test and peak oxygen uptake) and disease-specific quality of life (Minnesota Living With Heart Failure Questionnaire).</p> <p>Mean (SD) age of patients was 67 (11) years; baseline values were left ventricular ejection fraction, 29% (8%) and peak oxygen uptake, 13.5 mL/kg/min; the median New York Heart Association class of HF was class II.</p>	<p>At completion of the study, there were no significant differences in change in 6-minute walk distance and peak oxygen uptake (median change [first quartile, third quartile], 35 [-2, 51] vs 2 [-7, 54] metres, P = .95; and 1.1 [-1.1, 1.5] vs -0.5 [-1.2, 1.8] mL/kg/min, P = .81) when comparing tai chi and control groups; however, patients in the tai chi group had greater improvements in quality of life (Minnesota Living With Heart Failure Questionnaire, -19 [-23, -3] vs 1 [-16, 3], P = .02). Improvements with tai chi were also seen in exercise self-efficacy (Cardiac Exercise Self-efficacy Instrument, 0.1 [0.1, 0.6] vs -0.3 [-0.5, 0.2], P &lt; .001) and mood (Profile of Mood States total mood disturbance, -6 [-17, 1] vs -1 [-13, 10], P = .01).</p> <p>Conclusion: Tai chi exercise may improve quality of life, mood, and exercise self-efficacy in patients with heart failure.</p>

**g) Home-based exercise programmes**

Study	Methods	Findings
<p>Jolly K, Taylor R S, Lip G Y H, Davies M, Davis R, Mant J, Singh S, Greenfield S, Ingram J, Stubley J, Bryan S and Stevens A (2009) A randomized trial of the addition of home-based exercise to specialist heart failure nurse care: the Birmingham Rehabilitation Uptake Maximisation study for patients with Congestive Heart Failure (BRUM-CHF) study., <i>European Journal of Heart Failure</i> 11 (2) : 205-213</p>	<p>To assess the effectiveness of a home-based exercise programme in addition to specialist heart failure nurse care.</p> <p>A randomized controlled trial of a home-based walking and resistance exercise programme plus specialist nurse care (n = 84) compared with specialist nurse care alone (n = 85) in a heart failure population in the West Midlands, UK.</p> <p>Primary outcome: Minnesota Living with Heart Failure Questionnaire (MLwHFQ) at 6 and 12 months.</p> <p>Secondary outcomes: composite of death, hospital admission with heart failure or myocardial infarction; psychological well-being; generic quality of life (EQ-5D); exercise capacity.</p>	<p>There was no statistically significant difference between groups in the MLwHFQ at 6 month (mean, 95% CI) (-2.53, -7.87 to 2.80) and 12 month (-0.55, -5.87 to 4.76) follow-up or secondary outcomes with the exception of a higher EQ-5D score (0.11, 0.04 to 0.18) at 6 months and lower Hospital Anxiety and Depression Scale score (-1.07, -2.00 to -0.14) at 12 months, in favour of the exercise group. At 6 months, the control group showed deterioration in physical activity, exercise capacity, and generic quality of life.</p> <p>Conclusion: home-based exercise training programmes may not be appropriate for community-based heart failure patients</p>

<p>Dracup K, Evangelista L S, Hamilton M A, Erickson V, Hage A, Moriguchi J, Canary C, MacLellan W R and Fonarow G C (2007) Effects of a home-based exercise program on clinical outcomes in heart failure, <i>American Heart Journal</i> 154 (5) : 877-883</p>	<p>To determine the effects of a home-based exercise program on clinical outcomes. This study randomized 173 patients with systolic HF to control (n = 87) or home-based exercise (n = 86). The primary end point was a composite of all-cause hospitalizations, emergency department admissions, urgent transplantation, and death at 12 months. Functional performance (as assessed by cardiopulmonary exercise testing and the 6-minute walk test), quality of life, and psychological states were measured at baseline, 3 months, and 6 months.</p>	<p>There was no significant difference between experimental and control groups in the combined clinical end point at 12 months and in functional status, quality of life, or psychological states over 6 months. Patients in the exercise group had a lower incidence of multiple (2 or more) hospitalizations compared with the control group: 12.8% versus 26.6%, respectively (P = .018). Conclusions: A home-based walking program that incorporated aerobic and resistance exercise did not result in improved clinical outcomes at 1-year follow-up in this cohort of patients with systolic HF. However, the exercise program resulted in reduced rehospitalisation rates.</p>
<p>Corvera-Tindel T, Doering L V, Woo M A, Khan S and Dracup K (2004) Effects of a home walking exercise program on functional status and symptoms in heart failure, <i>American Heart Journal</i> 147 (2) : 339-346</p>	<p>A randomized controlled trial comparing a 12-week progressive home walking exercise program (n = 42) to a “usual activity” control group (n = 37) was conducted in patients with heart failure (78 [99%] male; mean age 62.6 ± 10.6 years; ejection fraction 27% ± 8.8%; 63 [80%] New York Heart Association class II; 15[20%] New York Heart Association class III–IV) from a Veterans Affairs medical centre and a university-affiliated medical centre. Functional status (peak oxygen consumption via cardiopulmonary exercise testing, 6-minute walk test, the Heart Failure Functional Status Inventory), and symptoms (Dyspnea-Fatigue Index score with a post-global rating of symptoms) were measured at baseline and 12 weeks. Compliance=(Actual/Recommended)x100</p>	<p>No adverse events related to exercise training occurred. Overall mean compliance to training was 74 ± 37%. Peak oxygen consumption and the Heart Failure Functional Status Inventory were unchanged with training. Compared to the usual activity group, the training group had significantly longer walking distances measured by the 6-minute walk test (1264 ± 255 vs 1337 ± 272 feet, P = .001), and improved post-global rating of symptoms (P = .03). Conclusion: In patients with heart failure, a progressive home walking exercise program is acceptable, increases walking distance, and decreases global rating of symptoms.</p>

**h) The effect on depression**

Study	Methods	Findings
<p>Blumenthal J A, Babyak M A, O'Connor C, Keteyian S, Landzberg J, Howlett J, Kraus W, Gottlieb S, Blackburn G, Swank A and Whellan D J (2012) Effects of Exercise Training on Depressive Symptoms in Patients With Chronic Heart Failure: The HF-ACTION Randomized Trial, <i>Journal of the American Medical Association</i> 308 (5)</p>	<p>To determine whether exercise training will result in greater improvements in depressive symptoms compared with usual care among patients with heart failure, a multi-centre randomized controlled trial involving 2322 stable patients treated for heart failure at 82 medical clinical centres in the United States, Canada, and France. Patients who had a left ventricular ejection fraction of 35% or lower, had New York Heart Association class I to IV heart failure, and had completed the Beck Depression Inventory II (BDI-II) score were randomized (1:1) between April 2003 and February 2007. Depressive scores ranged from 0 to 59; scores of 14 or higher are considered clinically significant. Participants were randomized either to supervised aerobic exercise (goal of 90 min/wk for months 1-3 followed by home exercise with a goal of =120 min/wk for months 4-12) or to education and usual guideline-based heart failure care. Main Outcome Measures Composite of death or hospitalization due to any cause and scores on the BDI-II at months 3 and 12.</p>	<p>Over a median follow-up period of 30 months, 789 patients (68%) died or were hospitalized in the usual care group compared with 759 (66%) in the aerobic exercise group (hazard ratio [HR], 0.89; 95% CI, 0.81 to 0.99; P = .03). The median BDI-II score at study entry was 8, with 28% of the sample having BDI-II scores of 14 or higher. Compared with usual care, aerobic exercise resulted in lower mean BDI-II scores at 3 months (aerobic exercise, 8.95; 95% CI, 8.61 to 9.29 vs usual care, 9.70; 95% CI, 9.34 to 10.06; difference, -0.76; 95% CI, -1.22 to -0.29; P = .002) and at 12 months (aerobic exercise, 8.86; 95% CI, 8.67 to 9.24 vs usual care, 9.54; 95% CI, 9.15 to 9.92; difference, -0.68; 95% CI, -1.20 to -0.16; P = .01).</p> <p>Conclusions: Compared with guideline-based usual care, exercise training resulted in a modest reduction in depressive symptoms, although the clinical significance of this improvement is unknown.</p>

## i) The effect of vitamin D supplementation

Study	Methods	Findings
<p>Witham M D, Crighton L J, Gillespie N D, Struthers A D, and McMurdo M E T (2010) The Effects of Vitamin D Supplementation on Physical Function and Quality of Life in Older Patients With Heart Failure: A Randomized Controlled Trial, <i>Circulation: Heart Failure</i> 3 : 195-201</p>	<p>Low 25-hydroxyvitamin D levels, commonly found in older patients with heart failure, may contribute to the chronic inflammation and skeletal myopathy that lead to poor exercise tolerance. This study tested whether vitamin D supplementation of patients with heart failure and vitamin D insufficiency can improve physical function and quality of life.</p> <p>In a randomized, parallel group, double-blind, placebo-controlled trial, patients with systolic heart failure aged =70 years with 25-hydroxyvitamin D levels &lt;50 nmol/L (20 ng/mL) received 100 000 U of oral vitamin D2 or placebo at baseline and 10 weeks.</p> <p>Outcomes measured at baseline, 10 weeks, and 20 weeks were 6-minute walk distance, quality of life (Minnesota score), daily activity measured by accelerometry, Functional Limitations Profile, B-type natriuretic peptide, and tumour necrosis factor-<math>\alpha</math>.</p>	<p>Participants in the vitamin D group had an increase in their 25-hydroxyvitamin D levels compared with placebo at 10 weeks (22.9 versus 2.3 nmol/L [9.2 versus 0.9 ng/mL]; <math>P&lt;0.001</math>) and maintained this increase at 20 weeks. The 6-minute walk did not improve in the treatment group relative to placebo. No significant benefit was seen on timed up and go testing, subjective measures of function, daily activity, or tumor necrosis factor. Quality of life worsened by a small, but significant amount in the treatment group relative to placebo. B-type natriuretic peptide decreased in the treatment group relative to placebo (-22 versus +78 pg/mL at 10 weeks; <math>P=0.04</math>).</p> <p>Conclusions— Vitamin D supplementation did not improve functional capacity or quality of life in older patients with heart failure with vitamin D insufficiency.</p>

## j) Patients with an implantable cardioverter defibrillator

Study	Methods	Findings
<p>Isaksen K, Munk P S, Valborgland T and Larsen A I (2014) Aerobic interval training in patients with heart failure and an implantable cardioverter defibrillator: a controlled study evaluating feasibility and effect, <i>European Journal of Preventive Cardiology: Published online before print January 8, 2014, doi: 10.1177/2047487313519345</i></p>	<p>Aerobic interval training (AIT) has been shown to be superior to moderate continuous exercise training in improving exercise capacity and endothelial function in patients with both coronary artery disease and heart failure (HF). The objective of this study was to evaluate this training modality in patients with HF and an implantable cardioverter defibrillator (ICD) with regard to feasibility, safety, and effect.</p> <p>Methods: 38 patients with an ICD were prospectively included: 26 patients participated in an AIT programme for 3 months, while 12 patients served as controls. At baseline and 12-week follow up, patients were assessed with a maximal ergospirometry stress test, echocardiography, endothelial function testing, and ICD interrogation.</p>	<p>No exercise-related adverse events occurred during or soon after the training sessions. ICD interrogation revealed no sustained arrhythmias, antitachycardia pacing, or ICD discharge related to exercise sessions. The AIT programme led to a significant increase in peak oxygen uptake, cycle ergometer workload, and endothelial function compared to the control group. The training programme was safe and not associated with any adverse events or ICD-related complications.</p> <p>Conclusions: An AIT programme is feasible and seems safe in a well-treated, stable ICD population. Further, AIT for 3 months results in significantly increased aerobic capacity and endothelial function in this population.</p>

<p>Piccini J P, Hellkamp A S, Whellan D J, Ellis S J, Keteyian S J, Kraus W E, Hernandez A F, Daubert J P, Piña I L and O'Connor C M for the HF-ACTION Investigators (2013) Exercise training and implantable cardioverter defibrillator shocks in patients with heart failure: Results from HF-ACTION, <i>JACC: Heart Failure</i> 1 (2) : 142-148</p>	<p>To determine if exercise training is associated with an increased risk of implantable cardioverter defibrillator (ICD) therapies in patients with heart failure (HF).</p> <p>A Controlled Trial Investigating Outcomes of Exercise TraiNing (HFACTION) randomized 2331 outpatients with HF and an ejection fraction (EF) .35% to exercise training or usual care. 'Cox proportional hazards modelling' was used to examine the relation between exercise training and ICD shocks.</p> <p>The study identified 1053 patients (45%) with an ICD at baseline randomized to exercise training (n=546) or usual care (n=507). The median age was 61 and the median EF was 24%.</p>	<p>Over a median 2.2 years of follow-up, 20% (108) of the exercise patients had a shock versus 22% (113) of the control patients. A history of sustained ventricular tachycardia/fibrillation (HR 1.93 [1.47-2.54]), prior atrial fibrillation/flutter (HR 1.63 [1.22-2.18]), exercise induced dysrhythmia (HR 1.67 [1.23-2.26]), lower diastolic blood pressure (HR for 5 mmHg decrease &lt; 60: 1.35 [1.12-1.61]), and non-white race (HR 1.50 [1.13-2.00]) were associated with an increased risk of ICD shocks. Exercise training was not associated with the occurrence of ICD shocks (HR 0.90 [0.69-1.18], p=0.45). The presence of an ICD was not associated with the primary efficacy composite endpoint of death or hospitalization (HR 0.99 [0.86-1.14], p=0.90).</p> <p>Conclusions: The study found no evidence of increased ICD shocks in patients with HF and reduced LV function who underwent exercise training. Exercise therapy should not be prohibited in ICD recipients with HF.</p>
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**k) Cost effectiveness**

Study	Methods	Findings
<p>Georgiou D, Chen Y, Appadoo S, Belardinelli R, Greene R, Parides M K and Glied S (2001) Cost-effectiveness analysis of long-term moderate exercise training in chronic heart failure, <i>The American Journal of Cardiology</i> 87 (8) : 984-988</p>	<p>To perform a cost-effectiveness analysis of long-term moderate exercise training (ET) in patients with stable chronic heart failure. In particular, the study focuses on the survival analysis and cost savings from the reduction in the hospitalization rate in the exercise group.</p> <p>The study examined the cost-effectiveness of a 14-month long-term training in patients with stable chronic heart failure. The estimated increment cost for the training group, \$3,227/patient, was calculated by subtracting the averted hospitalization cost, \$1,336/patient, from the cost of ET and wage lost due to ET, estimated at \$4,563/patient.</p>	<p>For patients receiving ET, the estimated increment in life expectancy was 1.82 years/person in a time period of 15.5 years, compared with patients in the control group. The cost-effectiveness ratio for long-term ET in patients with stable heart failure was thus determined at \$1,773/life-year saved, at a 3% discount rate. Long-term ET in patients with stable chronic heart failure is cost-effective and prolongs survival by an additional 1.82 years at a low cost of \$1,773 per/life-year saved.</p>

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