State of the art
CARDIAC REHABILITATION: EXPLORING NEW HORIZONS

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I have nothing to disclose.
Evolution of Cardiac Rehabilitation

• Exercise Therapy in Post-MI Patients
  (years 1960-1970s)

• Appropriate Cardiovascular Risk Stratification – Patient Assessment
  Exercise Training – Safety
  (years 1980-1990s)

• The Multifactorial – Multidisciplinary Nature of the Modern Cardiac Rehabilitation/Secondary Prevention Programs/Centres
  (present)
Physical Activity for Cardiovascular Health

Even moderate physical activity may elicit significant benefits
Survival analysis of mortality by change in level of Physical Activity in Myocardial Infarction patients

The Corpus Christi Heart Project

\[ \chi^2 = 46 \quad p < 0.001 \]
CORE COMPONENTS of CARDIAC REHABILITATION

Cardiac rehabilitation is a **multifactorial comprehensive long-term process** that includes:

- Clinical assistance and optimized therapy to relief symptoms and achieve clinical stability
- Appropriate cardiovascular risk stratification
- Exercise training
- Education and counseling regarding risk reduction and lifestyle changes
- The use of behavioural interventions, vocational counseling
- Adequate follow-up

Secondary Prevention Through Cardiac Rehabilitation

Position Paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology

P. Giannuzzi\textsuperscript{a*}, H. Saner\textsuperscript{b}, H. Björnstad\textsuperscript{c}, P. Fioretti\textsuperscript{d}, M. Mendes\textsuperscript{e}, A. Cohen-Solal\textsuperscript{f}, L. Dugmore\textsuperscript{g}, R. Hambrecht\textsuperscript{h}, I. Hellemans\textsuperscript{i}, H. McGee\textsuperscript{j}, J. Perk\textsuperscript{k}, L. Vanhees\textsuperscript{l}, G. Veress\textsuperscript{m}

The purpose of this statement is to provide specific recommendations in regard to evaluation and intervention in each of the core components of cardiac rehabilitation (CR) to assist CR staff in the design and development of their programmes; the statement should also assist health care providers, insurers, policy makers and consumers in the recognition of the comprehensive nature of such programmes. Those charged with responsibility for secondary prevention of cardiovascular disease, whether at European, at national or at individual centre level, need to consider where and how structured programmes of CR can be delivered to the large constituency of patients now considered eligible for CR.
CONTEMPORARY CR/SP PROGRAMS

1. Foster healthy behaviours
2. Promote active lifestyles
3. Reduce CV risk and event rates
Target Populations for Participation in Cardiac Rehabilitation Programs

**Ischemic heart disease**
- Post-Myocardial Infarction, coronary artery bypass graft, percutaneous transluminal coronary angioplasty
- Stable angina

**Other heart conditions**
- Chronic heart failure
- Controlled dysrhythmias
- Automatic implanted cardioverter-defibrillate/pacemaker
- Post-valve replacement
- Cardiomyopathy
- Myocardial aneurysm resection
- Pre- and post-heart transplantation
- Congenital heart defects

**Other chronic diseases**
- Stroke
- Peripheral vascular disease

**High risk of developing CVD**

EMERGING SCIENCE IN THE FIELD OF CR/SP

– Use of CR/SP services and survival benefits
– Novel exercise protocols
– Expanding applications:
  • Systolic Heart Failure
  • HF with preserved EF (Diastolic HF)
  • Diabetes Mellitus
  • Renal Dysfunction
  • Pulmonary Arterial Hypertension
  • TAVI, LVAD
  • Congenital Heart Disease
  • Peripheral Arterial Disease
USE OF CR/SP SERVICES AND SURVIVAL BENEFITS

- Despite the wealth evidence supporting the proven benefits of CR/SP programs, the services are greatly underutilized.
- Of all eligible patients, only 14% to 35% of heart attack survivors and 31% of patients after CABG participate in CR/SP programs, and the status of secondary prevention is far to be optimal.
- Addressing factors that limit participation is particularly important (inverse relationship between CR/SP program participation and adverse CV events).
Health Services and Outcomes Research

Relationship Between Cardiac Rehabilitation and Long-Term Risks of Death and Myocardial Infarction Among Elderly Medicare Beneficiaries

Bradley G. Hammill, MS; Lesley H. Curtis, PhD; Kevin A. Schulman, MD; David J. Whellan, MD, MHS

Conclusions—Among Medicare beneficiaries, a strong dose–response relationship existed between the number of cardiac rehabilitation sessions and long-term outcomes. Attending all 36 sessions reimbursed by Medicare was associated with lower risks of death and MI at 4 years compared with attending fewer sessions. (Circulation. 2010;121:63-70.)
Figure 2. Cumulative incidence of death by number of cardiac rehabilitation sessions attended.
Exercise Physiology

Impact of Cardiac Rehabilitation on Mortality and Cardiovascular Events After Percutaneous Coronary Intervention in the Community

Kashish Goel, MBBS; Ryan J. Lennon, MS; R. Thomas Tilbury, MD; Ray W. Squires, PhD; Randal J. Thomas, MD, MS

Background—Although numerous studies have reported that cardiac rehabilitation (CR) is associated with reduced mortality after myocardial infarction, less is known about its association with mortality after percutaneous coronary intervention.

Methods and Results—We performed a retrospective analysis of data from a prospectively collected registry of 2395 consecutive patients who underwent percutaneous coronary intervention in Olmsted County, Minnesota, from 1994 to 2008. The association of CR with all-cause mortality, cardiac mortality, myocardial infarction, or revascularization was assessed with 3 statistical techniques: propensity score–matched analysis (n=1438), propensity score stratification (n=2351), and regression adjustment with propensity score in a 3-month landmark analysis (n=2009). During a median follow-up of 6.3 years, 503 deaths (199 cardiac), 394 myocardial infarctions, and 755 revascularization procedures occurred in the study subjects. Participation in CR, noted in 40% (964 of 2395) of the cohort, was associated with a significant decrease in all-cause mortality by all 3 statistical techniques (hazard ratio, 0.53 to 0.55; P<0.001). A trend toward decreased cardiac mortality was also observed in CR participants; however, no effect was observed for subsequent myocardial infarction or revascularization. The association between CR participation and reduced mortality rates was similar for men and women, for older and younger patients, and for patients undergoing elective or nonelective percutaneous coronary intervention.

Conclusion—We found that CR participation after percutaneous coronary intervention was associated with a significant reduction in mortality rates. These findings add support to published clinical practice guidelines, performance measures, and insurance coverage policies that recommend CR for patients after percutaneous coronary intervention. (Circulation. 2011;123:2344-2352.)

Key Words: angioplasty ■ cardiac rehabilitation ■ exercise ■ mortality ■ prevention ■ stents
Global Secondary Prevention Strategies to Limit Event Recurrence After Myocardial Infarction

Results of the GOSPEL Study, a Multicenter, Randomized Controlled Trial From the Italian Cardiac Rehabilitation Network

Pantaleo Giannuzzi, MD; Pier Luigi Temporelli, MD; Roberto Marchioli, MD; Aldo Pietro Maggioni, MD; Gianluigi Balestrieri, PhD; Vincenzo Ceci, MD; Carmine Chieffo, MD; Marinella Gattone, MD; Raffaele Griffi, MD; Carlo Schweiger, MD; Luigi Tavazzi, MD; Stefano Urbinati, MD; Franco Valagussa, MD†; Diego Vanuzzo, MD; for the GOSPEL Investigators

Background: Secondary prevention is not adequately implemented after myocardial infarction (MI). We assessed the effect on quality of care and prognosis of a long-term, relatively intensive rehabilitation strategy after MI.

Methods: We conducted a multicenter, randomized controlled trial in patients following standard post-MI cardiac rehabilitation, comparing a long-term, reinforced, multifactorial educational and behavioral intervention with usual care. A total of 3241 patients with recent MI were randomized to a 3-year multifactorial continued educational and behavioral program (intervention group; n=1620) or usual care (control group; n=1621). The combination of cardiovascular (CV) mortality, nonfatal MI, nonfatal stroke, and hospitalization for angina pectoris, heart failure, or urgent revascularization procedure was the primary end point. Other end points were major CV events, major cardiac and cerebrovascular events, lifestyle habits, and drug prescriptions.

Results: End point events occurred in 556 patients (17.2%). Compared with usual care, the intensive intervention did not decrease the primary end point significantly (16.1% vs 18.2%; hazard ratio [HR] 0.88; 95% confidence interval [CI], 0.74-1.04). However, the intensive intervention decreased several secondary end points: CV mortality plus nonfatal MI and stroke (3.2% vs 4.8%; HR 0.67; 95% CI, 0.47-0.95), cardiac death plus nonfatal myocardial infarction (2.5% vs 4.0%; HR 0.64; 95% CI, 0.43-0.94), and nonfatal MI (1.4% vs 2.7%; HR 0.52; 95% CI, 0.31-0.86). A marked improvement in lifestyle habits (ie, exercise, diet, psychosocial stress, less deterioration of body weight control) and in prescription of drugs for secondary prevention was seen in the intervention group.

Conclusion: The GOSPEL Study is the first trial to our knowledge to demonstrate that a multifactorial, continued reinforced intervention up to 3 years after rehabilitation following MI is effective in decreasing the risk of several important CV outcomes, particularly nonfatal MI, although the overall effect is small.

Trial Registration: ClinicalTrials.gov Identifier: NCT00421876

Arch Intern Med. 2008;168(20):2194-2204
The significant reduction of major cardiovascular events (particularly non-fatal MI), the reduction of the other clinical endpoints, the relevant improvement of lifestyle habits, cardiovascular risk factors, and prescription of pharmacological treatments all indicate the importance of an intensive, comprehensive, long-term secondary prevention program after MI, and GOSPEL is the first large-scale trial to demonstrate that such a multifactorial continued reinforced intervention following MI is possible and effective.
Mediterranean dietary habits predict prognosis in post-MI patients:

further results of the GOSPEL study
Results-1  Dietary score at baseline (N=3233)

Mean (SD) = 13.3 (2.5)
Median (25°-75°) = 14 (12-15)
Cardiovascular death, MI and stroke

Pts at risk (events)

3233 (37) 3059 (30) 2966 (15) 2887 (16) 2852 (14) 2738 (16) 2674

Q1 1.00
Q2 0.48 (0.27-0.85) p=0.012
Q3 0.55 (0.33-0.91) p=0.021
Q4 0.49 (0.28-0.88) p=0.016
Epidemiology and Prevention

Association of Diet, Exercise, and Smoking Modification With Risk of Early Cardiovascular Events After Acute Coronary Syndromes

Clara K. Chow, MBBS, FRACP, PhD; Sanjit Jolly, MD, MSc, FRCPC;
Purnima Rao-Melacini, MSc; Keith A.A. Fox, BSc (Hons), MB, ChB, FRCP, FESC, FMedSci;
Sonia S. Anand, MD, PhD, FRCPC; Salim Yusuf, DPhil, FRCPC, FRSC

Background—Although preventive drug therapy is a priority after acute coronary syndrome, less is known about adherence to behavioral recommendations. The aim of this study was to examine the influence of adherence to behavioral recommendations in the short term on risk of cardiovascular events.

Methods and Results—The study population included 18,809 patients from 41 countries enrolled in the Organization to Assess Strategies in Acute Ischemic Syndromes (OASIS) 5 randomized clinical trial. At the 30-day follow-up, patients reported adherence to diet, physical activity, and smoking cessation. Cardiovascular events (myocardial infarction, stroke, cardiovascular death) and all-cause mortality were documented to 6 months. About one third of smokers persisted in smoking. Adherence to neither diet nor exercise recommendations was reported by 28.5%, adherence to either diet or exercise by 41.6%, and adherence to both by 29.9%. In contrast, 96.1% of subjects reported antiplatelet use, 78.9% reported statin use, and 72.4% reported angiotensin-converting enzyme/angiotensin receptor blocker use. Quitting smoking was associated with a decreased risk of myocardial infarction compared with persistent smoking (odds ratio, 0.57; 95% confidence interval, 0.36 to 0.89). Diet and exercise adherence was associated with a decreased risk of myocardial infarction compared with nonadherence (odds ratio, 0.52; 95% confidence interval, 0.4 to 0.69). Patients who reported persistent smoking and nonadherence to diet and exercise had a 3.8-fold (95% confidence interval, 2.5 to 5.9) increased risk of myocardial infarction/stroke/death compared with never smokers who modified diet and exercise.

Conclusions—Adherence to behavioral advice (diet, exercise, and smoking cessation) after acute coronary syndrome was associated with a substantially lower risk of recurrent cardiovascular events. These findings suggest that behavioral modification should be given priority similar to other preventive medications immediately after acute coronary syndrome.

Clinical Trial Registration Information—URL: http://clinicaltrials.gov/ct2/show/NCT00139815. (Circulation. 2010;121:750-758.)

Key Words: acute coronary syndrome ■ cardiovascular diseases ■ diet ■ exercise ■ prevention ■ smoking
## Relationship Between Diet/Exercise Modification and Repeat Cardiovascular Events in Patients With ACS

<table>
<thead>
<tr>
<th>Category</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>OR (95% CI)</th>
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<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Diet only</td>
<td>0.93 (0.74–1.16)</td>
<td>0.5137</td>
<td>0.84 (0.54–1.31)</td>
<td>0.4357</td>
<td>0.91 (0.73–1.13)</td>
<td>0.3986</td>
<td>0.91 (0.77–1.07)</td>
<td>0.2605</td>
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<tr>
<td>Exercise only</td>
<td>0.78 (0.56–1.1)</td>
<td>0.1547</td>
<td>0.94 (0.52–1.68)</td>
<td>0.8256</td>
<td>0.61 (0.42–0.88)</td>
<td>0.0091</td>
<td>0.69 (0.54–0.89)</td>
<td>0.0037</td>
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<tr>
<td>Both diet and exercise</td>
<td>0.52 (0.40–0.69)</td>
<td>&lt;0.0001</td>
<td>0.46 (0.26–0.82)</td>
<td>0.0079</td>
<td>0.45 (0.33–0.60)</td>
<td>&lt;0.0001</td>
<td>0.46 (0.38–0.57)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Models were adjusted for age; sex; region; history of hypertension, diabetes, and prior MI; body mass index; creatinine; PCI/CABG before 30 days; and use of β-blockers, statins, antiplatelets, and ACE/ARB drugs at 30 days.

*Clara K. Chow et al, Circulation. 2010;121:750-758*
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Key Words: acute coronary syndrome ■ cardiovascular diseases ■ diet ■ exercise ■ prevention ■ smoking
Can dietary changes rapidly decrease cardiovascular mortality rates?

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The UK National Institute for Health and Clinical Excellence (NICE) recently published guidance on the prevention of cardiovascular disease (CVD) in whole populations.¹ The lukewarm government response demonstrated a surprising ignorance of the scale and rapidity of the potential benefits.

The long ‘incubation period’ paradigm for cardiovascular diseases

Most heart attacks and ischaemic strokes are caused by complicated atheroma, usually compounded by thrombosis suddenly reducing blood flow in a critical artery. Extensive evidence suggests that this atheroma silently builds up over decades. Thus, early atheroma streaks were seen in classical autopsy studies on Korean war casualties and teenage traffic fatalities.² Hence, the emerging paradigm describing the temporal relationship between risk factor change and the corresponding change in CVD mortality. The time scales for this paradigm are generally perceived in terms of decades. Thus, Rose thought the ‘incubation period’ was a decade or more,³ whereas Law et al.⁴ proposed a three-decade lag time to explain the paradoxically low French CVD rates.

Reversing the CVD process following reductions in major cardiovascular risk factors has therefore also been assumed to require decades. However, this is wrong.

Cardiovascular disease mortality can change quickly

Evidence from clinical trials

Evidence in individuals and in populations actually suggests that decreases in fatal and non-fatal CVD events can rapidly follow reductions in risk. Thus, individual patients in therapeutic randomized trials often demonstrate mortality reductions within 1 or 2 years of blood pressure or cholesterol lowering.⁵ Trials in diet and lifestyle interventions also demonstrate rapid and substantial changes in multiple risk factors, notably DASH, DASH-Sodium, OMNI-Heart, and PREMIER. Even more importantly, several randomized controlled trials showed that diet interventions could have relatively rapid effects on CVD outcomes.⁶

The rapid reduction in diabetes incidence achieved with lifestyle interventions is also relevant, meaning subsequent reductions in costly diabetic care, as well as in CVD events.⁷

Even more, population level legislation like the smoking ban in Scotland and elsewhere has resulted in dramatic reductions in admissions for acute myocardial infarctions.⁸

Evidence from natural experiments and policy interventions

The natural experiments and policy interventions observed in whole populations in Cuba,⁹ Mauritius,¹⁰ Finland,¹¹ and elsewhere suggest that reductions in major factors can be quickly followed by rapid changes in CVD mortality rates. Indeed, the first clues emerged from reports of wartime Europe. Dramatic brief reductions in coronary deaths rapidly followed food rationing in the UK, and more savage ‘hunger winters’ in Holland and Norway.¹² The recent trends observed in several central European and Baltic countries were also remarkable. Thus, after steady rises through the 1970s and 1980s, CVD mortality in Poland suddenly declined sharply in the early 1990s, immediately following the profound socio-economic changes experienced after the break-up of the Soviet Union in 1989. This mortality fall was consistently attributed to diet changes. Specifically, subsidies for meat and animal fats ended and consumption fell dramatically, along with substantial increases in vegetable oils and fresh fruit.¹³ The subsequent 26% decrease in CVD deaths between 1990 and 1994 was one of the fastest declines ever observed. It could not be dismissed as a fluke, because corresponding changes were also observed in other central European and Baltic countries,¹³ many of them having experienced a profound socio-economic transformation in...
Trends in Incidence, Severity, and Outcome of Hospitalized Myocardial Infarction

Véronique L. Roger, MD, MPH; Susan A. Weston, MS; Yariv Gerber, PhD; Jill M. Killian, BS; Shannon M. Dunlay, MD; Allan S. Jaffe, MD; Malcolm R. Bell, MBBS, FRACP; Jan Kors, PhD; Barbara P. Yawn, MD, MS, MSc; Steven J. Jacobsen, MD, PhD

**Background**—In 2000, the definition of myocardial infarction (MI) changed to rely on troponin rather than creatine kinase (CK) and its MB fraction (CK-MB). The implications of this change on trends in MI incidence and outcome are not defined.

**Methods and Results**—This was a community study of 2816 patients hospitalized with incident MI from 1987 to 2006 in Olmsted County, Minnesota, with prospective measurements of troponin and CK-MB from August 2000 forward. Outcomes were MI incidence, severity, and survival. After troponin was introduced, 278 (25%) of 1127 incident MIs met only troponin-based criteria. When cases meeting only troponin criteria were included, incidence did not change between 1987 and 2006. When restricted to cases defined by CK/CK-MB, the incidence of MI declined by 20%. The incidence of non-ST-segment elevation MI increased markedly by relying on troponin, whereas that of ST-segment elevation MI declined regardless of troponin. The age- and sex-adjusted hazard ratio of death within 30 days for an infarction occurring in 2006 (compared with 1987) was 0.44 (95% confidence interval, 0.30 to 0.64). Among 30-day survivors, survival did not improve, but causes of death shifted from cardiovascular to noncardiovascular ($P=0.001$). Trends in long-term survival among 30-day survivors were similar regardless of troponin.

**Conclusions**—Over the last 2 decades, a substantial change in the epidemiology of MI occurred that was only partially mediated by the introduction of troponin. Non-ST-segment elevation MIs now constitute the majority of MIs. Although the 30-day case fatality improved markedly, long-term survival did not change, and the cause of death shifted from cardiovascular to noncardiovascular.  (*Circulation. 2010;121:863-869.*)

**Key Words:** biomarkers ■ incidence ■ mortality ■ myocardial infarction
Declining In-Hospital Mortality and Increasing Heart Failure Incidence in Elderly Patients With First Myocardial Infarction

Justin A. Ezekowitz, MBChB, MSc, Padma Kaul, PhD, Jeffery A. Bakal, PhD,† Paul W. Armstrong, MD, Robert C. Welsh, MD, Finlay A. McAlister, MD, MSc‡

Edmonton, Alberta, Canada

Objectives The purpose of this study was to examine the long-term incidence of heart failure (HF) in elderly patients with myocardial infarction (MI).

Background In-hospital HF is common after MI and is associated with poor short-term prognosis. Limited data exist concerning the long-term incidence or prognosis of HF after MI, particularly in the era of coronary revascularization.

Methods A population-based cohort of 7,733 patients ≥65 years of age hospitalized for a first MI (International Classification of Diseases-9th Revision-Clinical Modification code 410.x) and without a prior history of HF was established between 1994 and 2000 in Alberta, Canada, and followed up for 5 years.

Results During the index MI hospitalization, 2,831 (37%) MI patients were diagnosed with new HF and 1,024 (13%) died. Among hospital survivors who did not have HF during their index hospitalization (n = 4,291), an additional 3,040 patients (71%) developed HF by 5 years, 64% of which occurred in the first year. In total, 5,871 (76%) elderly patients who survived their first MI developed HF over 5 years. Among those who survived the index hospitalization, the 5-year mortality rate was 39.1% for those with HF during the index MI hospitalization compared with 26.7% among those without HF (p < 0.0001) during the index MI hospitalization. Over the study period, the 5-year mortality rate after MI decreased by 28%, whereas the 5-year rate of HF increased by 25%.

Conclusions In this large cohort of elderly patients without a history of HF, HF developed in three-quarters in the 5 years after their first MI; this proportion increased over time as peri-MI mortality rates declined. New-onset HF significantly increases the mortality risk among these patients. (J Am Coll Cardiol 2009;53:13–20) © 2009 by the American College of Cardiology Foundation
NEW ERA OF RESPONSIBILITY

Defining and Setting National Goals for Cardiovascular Health Promotion and Disease Reduction
The Stages of the Cardiovascular Disease Continuum, with Examples of Key Interventions for Prevention and Treatment of CVD

**THE WELL POPULATION**
- Campaigns to increase fruit and vegetable intake
- Regulation of tobacco sales, tax and place of use

**HIGH RISK INDIVIDUALS**
- Use of aspirin
- Absolute risk equations
- Risk factor management
- GP based screening programs

**THOSE WITH CLINICAL DISEASE**
- Coronary revascularisation
- Secondary prevention medications

**THOSE WITH CHRONIC DISEASE**
- Cardiac Rehabilitation in-Hospital CR/Secondary Prevention Programmes
- Long lasting behavioral interventions and monitoring in the Community
- Heart failure disease management programs

Reduction of salt content in processed foods

Environmental changes to increase physical activity
Remarks: The complexity and progressive nature of chronic HF requires demanding and time consuming multidisciplinary strategies that need to be integrated and coordinated in a flexible disease management that typically recalls cardiac rehabilitation deliveries and programs.

Cardiac rehabilitation is the ideal comprehensive structured disease interventions, as better addresses the complex interplay between medical, psychological, and behavioral factors facing chronic HF patients and carers.
Exercise Training in Heart Failure

In patients with stable HF, exercise training can:

- Relief symptoms
- Improve exercise capacity and quality of life
- Reduce disability, hospitalizations and cardiovascular outcomes
ExTra MATCH Exercise training Meta Analysis of Trials in Chronic HF patients

Piepoli et al, ESC Wien, 2003
EXERCISE TRAINING IN PATIENTS WITH CHRONIC HEART FAILURE:

THE HF – ACTION trial

All-Cause Mortality or All-Cause Hospitalization

All-Cause Mortality

<table>
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<th>No. at risk</th>
<th>Usual care</th>
<th>Exercise training</th>
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<td></td>
<td>1172</td>
<td>1159</td>
</tr>
<tr>
<td>1 year</td>
<td>651</td>
<td>656</td>
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<tr>
<td>2 years</td>
<td>337</td>
<td>352</td>
</tr>
<tr>
<td>3 years</td>
<td>146</td>
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</table>

CI indicates confidence interval; HR, hazard ratio.

Adjusted for key prognostic factors.

JAMA, April 8, 2009.
EXERCISE TRAINING IN PATIENTS WITH CHRONIC HEART FAILURE

- THE HF – ACTION trial

Cardiovascular Mortality or Cardiovascular Hospitalization

HR, 0.92 (95% CI, 0.83-1.03); P = .14
Adjusted HR, 0.91 (95% CI, 0.82-1.01); P = .09*a

Cardiovascular Mortality or Heart Failure Hospitalization

HR, 0.87 (95% CI, 0.75-1.00); P = .06
Adjusted HR, 0.85 (95% CI, 0.74-0.99); P = .03*a

No. at risk
Usual care 1172    Exercise training 1159
Time From Randomization, y
0    1    2    3
Event Rate
0.1    0.2    0.3    0.4    0.5    0.6    0.7    0.8

CI indicates confidence interval; HR, hazard ratio.
*aAdjusted for key prognostic factors.
Exercise based rehabilitation for heart failure (Review)

Davies EJ, Moxham T, Rees K, Singh S, Coats AJS, Ebrahim S, Lough F, Taylor RS
Main results

Nineteen trials (3647 participants) met the inclusion criteria. One large trial recruited 2331 of the participants. There was no significant difference in pooled mortality between groups in the 13 trials with < 1 year follow up. There was evidence of a non-significant trend toward a reduction in pooled mortality with exercise in the four trials with > 1 year follow up. A reduction in the hospitalisation rate was demonstrated with exercise training programmes. Hospitalisations due to systolic heart failure were reduced with exercise and there was a significant improvement in health-related quality of life (HRQoL). The effect of cardiac exercise training on total mortality and HRQoL were independent of the degree of left ventricular dysfunction, type of cardiac rehabilitation, dose of exercise intervention, length of follow up, trial quality, and trial publication date.

Authors’ conclusions

The previous version of this review showed that exercise training improved exercise capacity in the short term in patients with mild to moderate heart failure when compared to usual care. This updated review provides evidence that in a similar population of patients, exercise does not increase the risk of all-cause mortality and may reduce heart failure-related hospital admissions. Exercise training may offer important improvements in patients’ health-related quality of life.
Exercise Training in HF

How does exercise training prevent heart failure and clinical deterioration?
Exercise training in patients with HF

**Neurohumoral**
- ↓ Norepinephrine
- ↓ Vasopressin
- ↓ Ang II
- ↓ Aldosterone

**Musculature**
- ↑ Oxidative enzymes
- ↑ Mitochondria content
- ↓ Oxidative stress
- ↓ Proinflammatory cytokines
- ↑ IGF-1

**Inflammatory response**
- ↓ iNOS
- ↓ TNF, IL-1β, IL-6
- ↑ IL-10
- ↓ CD40L, P-selectin
- ↓ GM-CSF, MCP-1,ICAM-1, VCAM-1

**Nervous system**
- ↓ Ang II, ↓ AT1, ↓ ROS, ↑ NO
- ↓ Sympathetic activity
- ↑ Vagal activity

**Vascular reflex**
- ↑ Arterial baroreceptors
- ↓ Chemoreceptors

**Vasculature**
- ↑ eNOS, ↑ NO
- ↑ SOD
- ↓ ROS
- ↓ Oxidative stress
- ↑ Endothelial function

**Cardiac function**
- ↑ Ca²⁺ sensitivity
- ↑ Myocyte contractility
- Improved hemodynamic restoration of ischemic preconditioning

**PATHOBILOGICAL PATHWAYS INDUCED BY EXERCISE TRAINING IN PATIENTS WITH HEART FAILURE**
Central adaptations to aerobic training in normal subjects and CHF patients

<table>
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<th>Normals</th>
<th>CHF</th>
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</tr>
<tr>
<td>Resting</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>Submaximal</td>
<td>= (\downarrow)</td>
<td>= (\uparrow)</td>
</tr>
<tr>
<td>Peak</td>
<td>(\uparrow)</td>
<td>(\uparrow)</td>
</tr>
<tr>
<td><strong>Heart rate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>= (\downarrow)</td>
<td>= (\downarrow)</td>
</tr>
<tr>
<td>Submaximal</td>
<td>(\downarrow)</td>
<td>(\downarrow)</td>
</tr>
<tr>
<td>Peak</td>
<td>=</td>
<td>(\uparrow)</td>
</tr>
<tr>
<td><strong>LVEDV</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>= (\uparrow)</td>
<td>(\downarrow)</td>
</tr>
<tr>
<td>Peak</td>
<td>= (\uparrow)</td>
<td>=</td>
</tr>
<tr>
<td><strong>Ejection Fraction</strong></td>
<td></td>
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</tr>
<tr>
<td>Resting</td>
<td>=</td>
<td>= (\uparrow)</td>
</tr>
<tr>
<td>Peak</td>
<td>(\uparrow)</td>
<td>?</td>
</tr>
<tr>
<td><strong>Mitral regurgitation fraction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting</td>
<td>/</td>
<td>(=)</td>
</tr>
<tr>
<td>Peak</td>
<td>/</td>
<td>(=)</td>
</tr>
</tbody>
</table>
PHYSICAL TRAINING AS AN ANTI-REMODELLING TREATMENT
### Function and Remodeling

**ELVD - CHF**

<table>
<thead>
<tr>
<th></th>
<th>Control Group (n=44)</th>
<th>Exercise Training Group (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>6 Months</td>
</tr>
<tr>
<td><strong>EDV ml/m²</strong></td>
<td>147 ± 41</td>
<td>156 ± 42*†</td>
</tr>
<tr>
<td><strong>EVS ml/m²</strong></td>
<td>110 ± 34</td>
<td>118 ± 34‡</td>
</tr>
<tr>
<td><strong>EF %</strong></td>
<td>25 ± 4</td>
<td>25 ± 5‡</td>
</tr>
</tbody>
</table>

* p<0.01 time effect within group; † p<0.001 interaction; ‡ p<0.01 interaction

Giannuzzi et al, Circulation 2003
Age-related effects of exercise training on diastolic function in heart failure with reduced ejection fraction: The Leipzig Exercise Intervention in Chronic Heart Failure and Aging (LEICA) Diastolic Dysfunction Study

Marcus Sandri¹, Irina Kozarez¹, Volker Adams¹, Norman Mangner¹, Robert Höllriegel¹, Sandra Erbs¹, Axel Linke¹, Sven Möbius-Winkler¹, Joachim Thiery², Jürgen Kratzsch², Daniel Teupser², Meinhard Mende³, Rainer Hambrecht⁴, Gerhard Schuler¹, and Stephan Gielen¹*
A Meta-Analysis of the Effect of Exercise Training on Left Ventricular Remodeling in Heart Failure Patients

The Benefit Depends on the Type of Training Performed

Mark J. Haykowsky, PhD,* Yuanyuan Liang, PhD,† David Pechter, BA,* Lee W. Jones, PhD,§ Finlay A. McAlister, MD, MSC,|| Alexander M. Clark, PhD‡

Edmonton, Alberta, Canada; and Durham, North Carolina
Exercise training and End-Diastolic Volume: meta-analysis

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>N</th>
<th>Exercise Mean (SD)</th>
<th>N</th>
<th>Control Mean (SD)</th>
<th>WMD (random) 95% CI</th>
<th>Weight %</th>
<th>WMD (random) 95% CI</th>
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<tr>
<td><strong>AEROBIC TRAINING</strong></td>
<td></td>
<td></td>
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<tr>
<td>Belardinelli 1999</td>
<td>50</td>
<td>-7.00 (18.52)</td>
<td>49</td>
<td>-1.00 (18.52)</td>
<td>57.23 -8.00 [-13.30, 1.30]</td>
<td>100.00</td>
<td>-11.49 [-19.96, -3.02]</td>
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<tr>
<td>Hambrecht 2000</td>
<td>36</td>
<td>-22.00 (80.47)</td>
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<td>11.00 (67.02)</td>
<td>-33.00 [-67.02, 1.02]</td>
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<tr>
<td>Myers 2002</td>
<td>12</td>
<td>-0.70 (50.48)</td>
<td>12</td>
<td>-18.00 (96.02)</td>
<td>17.30 [44.08, 78.68]</td>
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<tr>
<td>Giannuzzi 2003</td>
<td>45</td>
<td>-7.00 (26.00)</td>
<td>45</td>
<td>9.00 (41.51)</td>
<td>-16.00 [-30.31, -1.69]</td>
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<tr>
<td>Passino 2006</td>
<td>44</td>
<td>-16.00 (47.83)</td>
<td>41</td>
<td>4.00 (48.34)</td>
<td>-19.00 [-39.46, 1.46]</td>
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<tr>
<td>Subtotal (95%CI)</td>
<td>187</td>
<td></td>
<td></td>
<td></td>
<td>93.29 -11.49 [-19.96, -3.02]</td>
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<tr>
<td>Test for heterogeneity: Chi²=5.07, df = 4 (P=0.28), I²=21.1%</td>
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</tr>
<tr>
<td>Test for overall effect: Z= 2.66 (P= 0.008)</td>
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<td></td>
</tr>
<tr>
<td><strong>STRENGTH TRAINING</strong></td>
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<tr>
<td>Subtotal (95%CI)</td>
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<tr>
<td>Test for overall effect: not applicable</td>
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<td><strong>AEROBIC &amp; STRENGTH TRAINING</strong></td>
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<td></td>
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<tr>
<td>Mickelvie 2002</td>
<td>80</td>
<td>27.00 (205.72)</td>
<td>80</td>
<td>5.00 (125.22)</td>
<td>1.68 22.00 [-30.77, 74.77]</td>
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<td></td>
</tr>
<tr>
<td>Jonsdottir 2006</td>
<td>20</td>
<td>-10.50 (43.04)</td>
<td>18</td>
<td>-3.80 (51.12)</td>
<td>5.03 -6.70 [-36.92, 23.52]</td>
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<tr>
<td>Subtotal (95%CI)</td>
<td>100</td>
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<td></td>
<td></td>
<td>8.71 0.39 [-25.84, 26.62]</td>
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<tr>
<td>Test for heterogeneity: Chi²=0.86, df = 1(P=0.36), I²=0%</td>
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<td></td>
<td></td>
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<tr>
<td>Test for overall effect: Z= 0.03 (P= 0.96)</td>
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<tr>
<td>Total (95%CI)</td>
<td>287</td>
<td></td>
<td></td>
<td></td>
<td>100.00 -9.75 [-16.64, -2.86]</td>
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<tr>
<td>Test for heterogeneity: Chi²=8.45, df = 6 (P=0.37), I²=7.0%</td>
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<tr>
<td>Test for overall effect: Z= 2.77 (P= 0.008)</td>
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</table>

Exercise training and Ejection Fraction: metanalysis

**AEROBIC TRAINING**

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>N</th>
<th>Exercise Mean (SD)</th>
<th>N</th>
<th>Control Mean (SD)</th>
<th>VMD (random) 95% CI</th>
<th>Weight %</th>
<th>VMD (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beraraini 1995</td>
<td>36</td>
<td>0.15 (5.75)</td>
<td>19</td>
<td>-0.30 (4.50)</td>
<td>10.42</td>
<td>0.45</td>
<td>[-2.31, 3.21]</td>
</tr>
<tr>
<td>Belardinelli 1996</td>
<td>29</td>
<td>1.00 (8.18)</td>
<td>14</td>
<td>-2.00 (5.29)</td>
<td>6.99</td>
<td>3.00</td>
<td>[-1.07, 7.07]</td>
</tr>
<tr>
<td>Killamouri 1996</td>
<td>12</td>
<td>1.00 (8.17)</td>
<td>15</td>
<td>1.00 (8.71)</td>
<td>3.87</td>
<td>0.00</td>
<td>[-6.20, 6.20]</td>
</tr>
<tr>
<td>Belardinelli 1999</td>
<td>50</td>
<td>2.30 (6.56)</td>
<td>49</td>
<td>-1.90 (5.21)</td>
<td>11.84</td>
<td>4.20</td>
<td>[1.87, 6.53]</td>
</tr>
<tr>
<td>Hambrecht 2000</td>
<td>36</td>
<td>6.00 (8.54)</td>
<td>37</td>
<td>3.00 (9.00)</td>
<td>7.09</td>
<td>2.00</td>
<td>[-2.02, 6.02]</td>
</tr>
<tr>
<td>Myers 2002</td>
<td>12</td>
<td>4.50 (10.54)</td>
<td>12</td>
<td>2.20 (10.00)</td>
<td>2.43</td>
<td>2.30</td>
<td>[-5.92, 10.52]</td>
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<tr>
<td>Giannuzzi 2003</td>
<td>45</td>
<td>4.00 (4.00)</td>
<td>45</td>
<td>0.00 (4.58)</td>
<td>13.80</td>
<td>4.00</td>
<td>[2.22, 5.78]</td>
</tr>
<tr>
<td>Kloczek 2006</td>
<td>28</td>
<td>-0.05 (3.68)</td>
<td>14</td>
<td>-1.00 (3.36)</td>
<td>12.20</td>
<td>0.95</td>
<td>[-1.28, 3.18]</td>
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<tr>
<td>Passino 2006</td>
<td>44</td>
<td>3.00 (13.27)</td>
<td>41</td>
<td>-1.00 (12.81)</td>
<td>4.59</td>
<td>4.00</td>
<td>[-1.55, 9.55]</td>
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<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>292</td>
<td></td>
<td>248</td>
<td></td>
<td>73.24</td>
<td>2.58</td>
<td>[1.44, 3.74]</td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 9.86, df = 8 (P = 0.29), I² = 17.2%
Test for overall effect: Z = 4.41 (P < 0.0001)

**STRENGTH TRAINING**

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Exercise Mean (SD)</th>
<th>N</th>
<th>Control Mean (SD)</th>
<th>VMD (random) 95% CI</th>
<th>Weight %</th>
<th>VMD (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koch 1992</td>
<td>12</td>
<td>0.80 (10.00)</td>
<td>13</td>
<td>5.30 (12.00)</td>
<td>2.23</td>
<td>2.23</td>
<td>-4.50 [-13.14, 4.14]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>12</td>
<td></td>
<td>13</td>
<td></td>
<td>2.23</td>
<td>2.23</td>
<td>-4.50 [-13.14, 4.14]</td>
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</tbody>
</table>

Test for heterogeneity: not applicable
Test for overall effect: Z = 1.02 (P = 0.31)

**AEROBIC & STRENGTH TRAINING**

<table>
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<tr>
<th>Study</th>
<th>N</th>
<th>Exercise Mean (SD)</th>
<th>N</th>
<th>Control Mean (SD)</th>
<th>VMD (random) 95% CI</th>
<th>Weight %</th>
<th>VMD (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>McKelvie 2002</td>
<td>80</td>
<td>0.20 (8.26)</td>
<td>81</td>
<td>1.60 (8.30)</td>
<td>13.22</td>
<td>13.40</td>
<td>[-3.34, 0.54]</td>
</tr>
<tr>
<td>Roveda 2003</td>
<td>7</td>
<td>2.40 (5.05)</td>
<td>9</td>
<td>-0.10 (5.98)</td>
<td>4.76</td>
<td>2.50</td>
<td>[-2.91, 7.91]</td>
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<tr>
<td>Sabelis 2004</td>
<td>16</td>
<td>3.20 (8.00)</td>
<td>13</td>
<td>-0.40 (9.40)</td>
<td>3.65</td>
<td>3.60</td>
<td>[-2.84, 10.04]</td>
</tr>
<tr>
<td>Jonasdottir 2006</td>
<td>21</td>
<td>4.10 (12.22)</td>
<td>22</td>
<td>2.00 (12.64)</td>
<td>2.81</td>
<td>2.10</td>
<td>[-6.30, 6.80]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>124</td>
<td></td>
<td>125</td>
<td></td>
<td>24.63</td>
<td>0.37</td>
<td>[-2.23, 2.97]</td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chisq = 4.04, df = 3 (P = 0.26), I² = 25.7%
Test for overall effect: Z = 0.28 (P = 0.78)

**Total (95% CI)**

<table>
<thead>
<tr>
<th>Total</th>
<th>428</th>
<th>384</th>
</tr>
</thead>
</table>

Test for heterogeneity: Chi² = 25.59, df = 13 (P = 0.02), I² = 49.2%
Test for overall effect: Z = 2.50 (P = 0.009)
High-Intensity Interval Training to Maximize Cardiac Benefits of Exercise Training?

Ulrik Wisløff\textsuperscript{1,2}, Øyvind Ellingsen\textsuperscript{1,2}, and Ole J. Kemi\textsuperscript{3}

\textsuperscript{1}Department of Circulation and Medical Imaging, Norwegian University of Science and Technology; \textsuperscript{2}Department of Cardiology, St. Olavs Hospital, Trondheim, Norway; and \textsuperscript{3}Institute of Biomedical and Life Sciences, University of Glasgow, Scotland, United Kingdom
Superior Cardiovascular Effect of Aerobic Interval Training Versus Moderate Continuous Training in Heart Failure Patients
A Randomized Study

Ulrik Wisløff, PhD; Asbjørn Støylen, MD, PhD; Jan P. Loennechen, MD, PhD; Morten Bruvoidt, MSc; Øivind Rognmo, MSc; Per Magnus Haram, MD, PhD; Arnt Erik Tjønna, MSc; Jan Helgerud, PhD; Stig A. Sørdahl, MD, PhD; Sang Jun Lee, PhD; Vibeke Videm, MD, PhD; Anja Bye, MSc; Godfrey L. Smith, PhD; Sonia M. Najjar, PhD; Øyvind Ellingsen, MD, PhD; Terje Skjærpe, MD, PhD

High Intensity Interval Training in Heart Failure

MCT = Moderate Continuous Training
AIT = Aerobic Interval Training

Probability values inside figures indicate within-group differences.
§ different from control and MCT, \( P<0.01 \);
‡ different from control, \( P<0.01 \).
## High Intensity Interval Training in Heart Failure

### LV REMODELING AND RESTING HEMODYNAMICS

<table>
<thead>
<tr>
<th></th>
<th>Control Baseline</th>
<th>Control Follow-Up</th>
<th>MCT Baseline</th>
<th>MCT Follow-Up</th>
<th>AIT Baseline</th>
<th>AIT Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVDD, mm</td>
<td>67.2±8.1</td>
<td>67.8±12.5</td>
<td>69.1±8.6</td>
<td>68.2±6.5</td>
<td>66.7±6.8</td>
<td>59.0±6.8*†</td>
</tr>
<tr>
<td>LVSD, mm</td>
<td>56.2±9.2</td>
<td>56.7±13.7</td>
<td>56.6±8.8</td>
<td>53.9±7.4</td>
<td>53.9±6.7</td>
<td>46.1±8.2*†</td>
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<tr>
<td>LVEDV, mL</td>
<td>250.5±64.4</td>
<td>242.1±62.3</td>
<td>245.5±53.1</td>
<td>230.3±41.0</td>
<td>248.1±79.6</td>
<td>202.9±72.0*†</td>
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<tr>
<td>LVESV, mL</td>
<td>187.8±53.0</td>
<td>186.6±58.6</td>
<td>172.9±48.7</td>
<td>160.6±34.3</td>
<td>177.4±72.1</td>
<td>133.9±57.8*†</td>
</tr>
<tr>
<td>HR at rest, bpm</td>
<td>60±11</td>
<td>59±11</td>
<td>55±10</td>
<td>54±12</td>
<td>65±14</td>
<td>61±13</td>
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<tr>
<td>SV, mL</td>
<td>53.4±15.3</td>
<td>55.0±13.7</td>
<td>63.5±12.7</td>
<td>63.1±15.7</td>
<td>57.1±14.3</td>
<td>67.0±19.9*†</td>
</tr>
<tr>
<td>CO, L/min</td>
<td>3.1±0.6</td>
<td>3.2±0.5</td>
<td>3.5±0.9</td>
<td>3.4±1.1</td>
<td>3.5±0.5</td>
<td>3.9±0.6*</td>
</tr>
<tr>
<td>EF, %</td>
<td>26.2±8.0</td>
<td>26.6±9.7</td>
<td>32.8±4.8</td>
<td>33.5±5.7</td>
<td>28.0±7.3</td>
<td>38.0±9.8*†</td>
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</tbody>
</table>

\[\dot{V}_O^{2peak}\] = 13.2±1.9  

<table>
<thead>
<tr>
<th></th>
<th>Control Baseline</th>
<th>Control Follow-Up</th>
<th>MCT Baseline</th>
<th>MCT Follow-Up</th>
<th>AIT Baseline</th>
<th>AIT Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>13.4±2.0</td>
<td>13.0±1.1</td>
<td>14.9±0.9*</td>
<td>13.0±1.6</td>
<td>19.0±2.1*†</td>
<td></td>
</tr>
</tbody>
</table>

MCT = Moderate Continuous Training,  AIT = Aerobic Interval Training

* different from baseline, $P<0.01$;  † different from controls and MCT, $P<0.02$.  

Ulrik Wisløff, Circulation June 19, 2007

#esc2012  www.escardio.org
Exercise training has the potential to prevent the progression of LV dysfunction, the hemodynamic and clinical deterioration;

In this regard, central adaptations (hemodynamic and morpho-functional) to exercise training seem to play a major role;

The intensity of exercise may be also an important factor for reversing LV remodeling, improving aerobic capacity and quality of live: even moderate exercise training may induce significant peripheral and central adaptations;

Larger studies are needed to compare the results of different exercise training intensity and modality, to establish whether the benefits of exercise can be maintained over time and will lead to substantial clinical benefits.
Controlled study of myocardial recovery after interval training in heart failure: SMARTEX-HF – rationale and design

Asbjørn Støylen¹,², Viviane Conraads³, Martin Halle⁴, Axel Linke⁵, Eva Prescott⁶ and Øyvind Ellingsen¹,²,⁷

Study design: In a three-armed randomized multicentre study of stable heart failure patients with left ventricular ejection fraction ≤35%, the effects of a 12-week programme of high-intensity interval training (HIT; 85–90% of peak oxygen uptake, VO₂peak) will be compared to actual practice in Europe, represented by either an isocaloric programme of moderate continuous training (MCT; 50–60% of VO₂peak) and a recommendation of regular exercise (RE) of the individual patients’ own preference based on clinical practice at the local centre. The primary endpoint is reverse remodelling, defined as change in left ventricular end-diastolic diameter assessed by echocardiography. Secondary endpoints include peak oxygen uptake (VO₂peak), biomarkers, quality of life, and level of physical activity assessed by questionnaires. In addition, long-term maintenance of effects after the supervised training period will be determined. Assessments will be made at baseline, after the 12-week intervention programme, and at 1-year follow up. A total number of 200 patients on treatment per protocol, randomized to the three groups in a 1:1:1 manner, is estimated to detect clinically relevant differences in effect with HIT vs. MCT and RE (p < 0.05; statistical power 0.90) for the primary endpoint. Inclusion of patients started May 2009 and will run until total number has been reached.
EXPANDING EXPERIENCES in HF

- Patients with advanced systolic HF or after acute decompensation
- HF with preserved EF
Exercise Training in Patients With Advanced Chronic Heart Failure (NYHA IIIb) Promotes Restoration of Peripheral Vasomotor Function, Induction of Endogenous Regeneration, and Improvement of Left Ventricular Function

Sandra Erbs, MD; Robert Höllriegel, MD; Axel Linke, MD; Ephraim B. Beck, MD; Volker Adams, PhD; Stephan Gielen, MD; Sven Möbius-Winkler, MD; Marcus Sandri, MD; Nicolle Kränkel, PhD; Rainer Hambrecht, MD; Gerhard Schuler, MD

**Conclusions**—Twelve weeks of ET in patients with advanced CHF is associated with augmented regenerative capacity of CPCs, enhanced flow-mediated dilation suggestive of improvement in endothelial function, skeletal muscle neovascularization, and improved LV function.

*(Circ Heart Fail. 2010;3:486-494.)*
EARLY-START EXERCISE TRAINING AFTER ACUTE DECOMPENSATION IN PATIENTS WITH CHRONIC HEART FAILURE: FEASIBILITY AND IMPACT ON FUNCTIONAL CAPACITY, NEUROHUMORAL ACTIVATION AND QUALITY OF LIFE.

A pilot Study
Chairman: Alessandro Mezzani
Exercise Training in Older Patients With Heart Failure and Preserved Ejection Fraction
A Randomized, Controlled, Single-Blind Trial

Dalane W. Kitzman, MD; Peter H. Brubaker, PhD; Timothy M. Morgan, PhD;
Kathryn P. Stewart, RT, RDMS; William C. Little, MD

Conclusions—ET improves peak and submaximal exercise capacity in older patients with HFPEF.

(Circ Heart Fail. 2010;3:659-667.)
Exercise Training Improves Exercise Capacity and Diastolic Function in Patients With Heart Failure With Preserved Ejection Fraction

Results of the Ex-DHF (Exercise training in Diastolic Heart Failure) Pilot Study

Frank Edelmann, MD,* Götz Gelbrich, PhD,§ Hans-Dirk Düngen, MD,¶ Stefan Fröhling, MD,* Rolf Wachter, MD,* Raoul Stahrenberg, MD,* Lutz Binder, MD,† Agnieszka Töpper, MD,¶ Diana Jahanar Lashki, MD,¶ Silja Schwarz, MD,# Christoph Herrmann-Lingen, MD,‡ Markus Löffler, MD, PhD,§|| Gerd Hasenfuss, MD,* Martin Halle, MD,# Burkert Pieske, MD**

Göttingen, Leipzig, Berlin, and Munich, Germany; and Graz, Austria
EXPANDING APPLICATIONS OF CR/SP

- Diabetes Mellitus, Impaired glucose tolerance/metabolic syndrome
- Chronic Kidney disease
- Pulmonary Hypertension
- TAVI and LVAD patients
- Congenital heart diseases
DIABETES MELLITUS

- Rising epidemic of DM due to the growing prevalence of obesity and overweight

- Beneficial effects of exercise training include:
  - improved glycemic control
  - reduction of body fat and BMI
  - reduced hypoglicemic medication requirement
  - and improved exercise capacity

Marwick et al. Circulation 2009
Short and long-term effects of regular physical exercise training on diastolic function in pre-diabetic, adipose patients with coronary artery disease

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EXPANDING APPLICATIONS OF CR/SP

- Diabetes Mellitus, Impaired glucose tolerance/metabolic syndrome
- Chronic Kidney disease
- Pulmonary Hypertension
- TAVI and LVAD patients
- Congenital heart diseases
Effect of Exercise & Lifestyle Intervention on Left Ventricular and Vascular Function in Patients with Chronic Kidney Disease: a Randomised Controlled Trial

Authors: Erin Howden¹,², Jeff Coombes¹, Rodel Leano², Nicole Isbel³, Thomas Marwick⁴

Schools of Human Movement Studies¹, & Medicine², The University of Queensland, & Department of Renal Medicine³, Princess Alexandra Hospital, Brisbane, Queensland, Australia, The Cleveland Clinic⁴, Ohio, US.
EXPANDING APPLICATIONS OF CR/SP

• Diabetes Mellitus, Impaired glucose tolerance/metabolic syndrome
• Chronic Kidney disease
• Pulmonary Hypertension
• TAVI and LVAD patients
• Congenital heart diseases
Exercise and Respiratory Training Improve Exercise Capacity and Quality of Life in Patients With Severe Chronic Pulmonary Hypertension

Derliz Mereles, MD*, Nicola Ehlken*, Sandra Kreuscher*, Stefanie Ghofrani, MD; Marius M. Hoeper, MD; Michael Halank, MD; F. Joachim Meyer, MD; Gabriele Karger, MD; Jan Buss, MD; Jana Juenger, MD; Nicole Holzapfel, MA; Christian Opitz, MD; Jörg Winkler, MD; Felix F.J. Herth, MD; Heinrike Wilkens, MD; Hugo A. Katus, MD; Horst Olschewski, MD; Ekkehard Grünig, MD

Background—Pulmonary hypertension (PH) is associated with restricted physical capacity, limited quality of life, and a poor prognosis because of right heart failure. The present study is the first prospective randomized study to evaluate the effects of exercise and respiratory training in patients with severe symptomatic PH.

Methods and Results—Thirty patients with PH (21 women; mean age, 50±13 years; mean pulmonary artery pressure, 50±15 mm Hg; mean World Health Organization [WHO] class, 2.9±0.5; pulmonary arterial hypertension, n=23; chronic thromboembolic PH, n=7) on stable disease-targeted medication were randomly assigned to a control (n=15) and a primary training (n=15) group. Medication remained unchanged during the study period. Primary end points were the changes from baseline to week 15 in the distance walked in 6 minutes and in scores of the Short Form Health Survey quality-of-life questionnaire. Changes in WHO functional class, Borg scale, and parameters of echocardiography and gas exchange also were assessed. At week 15, patients in the primary and secondary training groups had an improved 6-minute walking distance; the mean difference between the control and the primary training group was 111 m (95% confidence interval, 65 to 139 m; P<0.001). Exercise training was well tolerated and improved scores of quality of life, WHO functional class, peak oxygen consumption, oxygen consumption at the anaerobic threshold, and achieved workload. Systolic pulmonary artery pressure values at rest did not change significantly after 15 weeks of exercise and respiratory training (from 61±18 to 54±18 mm Hg) within the training group.

Conclusions—This study indicates that respiratory and physical training could be a promising adjunct to medical treatment in severe PH. The effects add to the beneficial results of modern medical treatment. (Circulation. 2006;114:1482-1489.)
Safety and efficacy of exercise training in various forms of pulmonary hypertension

E. GRÜNIG ET AL.

Eur Respir J 2012; 40: 84–92

mean 68±46 m   p<0.001   mean 78±49.5 m   p<0.001

Change in 6MWD m

Baseline
(n=183)

3 weeks
(n=183)

15 weeks
(n=103)
Exercise training in pulmonary arterial hypertension associated with connective tissue diseases

Ekkehard Grünig, Felicitas Maier et al.  

*Arthritis Research & Therapy* 2012, **14:**R148

**Figure 1** Individual changes in six-minute-walking distance (6MWD) after 3 and 15 weeks exercise training. Using the Wilcoxon rank test, $P < 0.001$ was obtained for the comparisons with baseline at week 3 ($n = 21$) and $P = 0.003$ for comparison to week 15 ($n = 11$). The dashed line indicates the mean change from baseline in 6MWD ($67 \pm 52$ meters and $72 \pm 35$ meters).
TAVI (Transcatheter aortic valve implantation) patients: safety and outcome of cardiac rehabilitation compared to biological aortic valve replacement for aortic stenosis (AVR)

Franco Tarro Genta  M.D.
Cardiovascular Rehabilitation Division
Fondazione Salvatore Maugeri
Presidio Major – Turin
Italy
Ventricular assist device patients on the horizon of cardiovascular prevention and rehabilitation. Can we convert challenges into opportunities?

Ugo Corrà¹, Massimo Pistono¹, Massimo F Piepoli² and Pantaleo Giannuzzi¹

European Journal of Preventive Cardiology 2012
Exercise Testing and Training in Children With Congenital Heart Disease
Jonathan Rhodes, Ana Ubeda Tikkanen and Kathy J. Jenkins

*Circulation. 2010;122:1957-1967*

Table 2. Cardiac Rehabilitation Studies in Patients With CHD

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Diagnosis</th>
<th>Program Duration, wk</th>
<th>Sessions per Week</th>
<th>Time per Session, min</th>
<th>Type</th>
<th>Control</th>
<th>Impact on Peak (\dot{V}O_2) (mL/kg per Minute), %</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldberg(^7)</td>
<td>26</td>
<td>16 TOF, 10 VSD</td>
<td>6</td>
<td>3</td>
<td>&lt;45</td>
<td>Home-based</td>
<td>No</td>
<td>Unchanged</td>
<td>Other parameters improved</td>
</tr>
<tr>
<td>Ruttenberg(^4)</td>
<td>12</td>
<td>3 TOF, 3 TGA, 1 AVC, 5 AS</td>
<td>9</td>
<td>3</td>
<td>45</td>
<td>Facility-based</td>
<td>No</td>
<td>Unchanged</td>
<td>Large (50%) dropout rate; other parameters improved</td>
</tr>
<tr>
<td>Bradley(^7)</td>
<td>9</td>
<td>5 TGA, 9 TOF</td>
<td>12</td>
<td>2</td>
<td>60</td>
<td>Facility-based</td>
<td>No</td>
<td>↑ 20</td>
<td>Internally inconsistent data; RER not measured; improvements may be effort related</td>
</tr>
<tr>
<td>Balfour(^7)</td>
<td>6</td>
<td>1 Fontan, 5 other</td>
<td>12</td>
<td>3</td>
<td>60</td>
<td>Facility-based and home-based</td>
<td>No</td>
<td>↑ 20</td>
<td>Large (&gt;50%) dropout rate</td>
</tr>
<tr>
<td>Fredriksen(^5)</td>
<td>55</td>
<td>12 TGA, 8 ASD/VSD, 11 LVOTO, 3 RVOTO, 10 TOF, 4 Fontan, 7 other</td>
<td>20</td>
<td>2</td>
<td>NA</td>
<td>Facility-based and home-based</td>
<td>Yes</td>
<td>Unchanged</td>
<td>Large program variability; other parameters improved</td>
</tr>
<tr>
<td>Minsmisawa(^6)</td>
<td>11</td>
<td>Fontan</td>
<td>8–12</td>
<td>2–3</td>
<td>30</td>
<td>Home-based</td>
<td>No</td>
<td>↑ 7</td>
<td>Rehabilitation patients’ improvement was sustained 7 mo after the program and was significantly superior to that of control subjects</td>
</tr>
<tr>
<td>Opocher(^7)</td>
<td>10</td>
<td>Fontan</td>
<td>32</td>
<td>2</td>
<td>30–45</td>
<td>Facility-based and home-based</td>
<td>No</td>
<td>↑ 11</td>
<td></td>
</tr>
<tr>
<td>Rhodes(^9,11)</td>
<td>16</td>
<td>12 Fontan, 4 other</td>
<td>12</td>
<td>2</td>
<td>60</td>
<td>Facility-based</td>
<td>Yes</td>
<td>↑ 16</td>
<td></td>
</tr>
</tbody>
</table>

TOF indicates tetralogy of Fallot; VSD, ventricular septal defect; TGA, transposition of the great arteries; AVC, atrioventricular canal; AS, aortic stenosis; LVOTO, left ventricular outflow tract obstruction; and RVOTO, right ventricular outflow tract obstruction.
A call for adult congenital heart disease patient participation in cardiac rehabilitation

Tanya M. Holloway\textsuperscript{a,b,*}, Caroline Chesssex \textsuperscript{a,d}, Sherry L. Grace \textsuperscript{a,c}, Erwin Oechslin \textsuperscript{d,e}, Lawrence L. Spriet \textsuperscript{b}, Adrienne H. Kovacs \textsuperscript{d,e}

International Journal of Cardiology 2011
Secondary prevention in the clinical management of patients with cardiovascular diseases. Core components, standards and outcome measures for referral and delivery

A Policy Statement from the Cardiac Rehabilitation Section of the European Association for Cardiovascular Prevention & Rehabilitation. Endorsed by the Committee for Practice Guidelines of the European Society of Cardiology

Massimo F Piepoli¹,², Ugo Corrà³, Stamatis Adamopoulos⁴, Werner Benzer⁵, Birna Bjarnason-Wehrens⁶, Margaret Cupples⁷, Paul Dendale⁸, Patrick Doherty⁹, Dan Gaita¹⁰, Stefan Höfer¹¹, Hannah McGee¹², Miguel Mendes¹³, Josef Niebauer¹⁴, Nana Pogosova¹⁵, Esteban Garcia-Porrero¹⁶, Bernhard Rauch¹⁷, Jean Paul Schmid¹⁸ and Pantaleo Giannuzzi³