

Learn and Live

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://circ.ahajournals.org/cgi/content/full/111/3/369

An erratum has been published regarding this article. Please see the attached page or: http://circ.ahajournals.org/cgi/content/full/circulationaha;111/13/1717

Subscriptions: Information about subscribing to Circulation is online at http://circ.ahajournals.org/subscriptions/

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax: 410-528-8550. E-mail: journalpermissions@lww.com

Reprints: Information about reprints can be found online at http://www.lww.com/reprints

# Cardiac Rehabilitation and Secondary Prevention of Coronary Heart Disease

# An American Heart Association Scientific Statement From the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in Collaboration With the American Association of Cardiovascular and Pulmonary Rehabilitation

Arthur S. Leon, MD, MS, Chair; Barry A. Franklin, PhD; Fernando Costa, MD; Gary J. Balady, MD; Kathy A. Berra, MSN, ANP; Kerry J. Stewart, EdD; Paul D. Thompson, MD; Mark A. Williams, PhD; Michael S. Lauer, MD

*Abstract*—This article updates the 1994 American Heart Association scientific statement on cardiac rehabilitation. It provides a review of recommended components for an effective cardiac rehabilitation/secondary prevention program, alternative ways to deliver these services, recommended future research directions, and the rationale for each component of the rehabilitation/secondary prevention program, with emphasis on the exercise training component. (*Circulation*. 2005;111:369-376.)

Key Words: AHA Scientific Statements 
rehabilitation 
exercise 
coronary disease 
prevention

This article updates the American Heart Association (AHA) 1994 scientific statement on cardiac rehabilitation.<sup>1</sup> It provides a review of the recommended components of optimal rehabilitation/secondary prevention programs, ways to deliver these services, recommended future research directions, and the rationale for these recommendations, with emphasis on the exercise training component. Secondary prevention is an essential part of the contemporary care of the patient with cardiovascular disease (CVD). The term cardiac rehabilitation refers to coordinated, multifaceted interventions designed to optimize a cardiac patient's physical, psychological, and social functioning, in addition to stabilizing, slowing, or even reversing the progression of the underlying atherosclerotic processes, thereby reducing morbidity and mortality.<sup>2</sup> As such, cardiac rehabilitation/secondary prevention programs provide an important and efficient venue in which to deliver effective preventive care. In 1994, the AHA declared that cardiac rehabilitation should not be limited to an exercise training program but also should include multifaceted strategies aimed at reducing modifiable risk factors for CVD.1 Since then, detailed guidelines have been published that clearly specify each of the core components of cardiac rehabilitation/secondary prevention programs, along with information about the evaluation, intervention, and expected outcomes in each area.3-10 Thus, cardiac rehabilitation/secondary prevention programs currently include baseline patient assessments, nutritional counseling, aggressive risk factor management (ie, lipids, hypertension, weight, diabetes, and smoking), psychosocial and vocational counseling, and physical activity counseling and exercise training, in addition to the appropriate use of cardioprotective drugs that have evidence-based efficacy for secondary prevention. Candidates for cardiac rehabilitation services historically were patients who recently had had a myocardial infarction or had undergone coronary artery bypass graft surgery, but candidacy has been broadened to include patients who have undergone percutaneous coronary interventions; are heart transplantation candidates or recipients; or have stable chronic heart failure, peripheral arterial disease with claudication, or other forms of CVD. In addition, patients

© 2005 American Heart Association, Inc.

Circulation is available at http://www.circulationaha.org

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on September 28, 2004. A single reprint is available by calling 800-242-8721 (US only) or writing the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596. Ask for reprint No. 71-0311. To purchase additional reprints: up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 410-528-4121, fax 410-528-4264, or e-mail kgray@lww.com. To make photocopies for personal or educational use, call the Copyright Clearance Center, 978-750-8400.

Expert peer review of AHA Scientific Statements is conducted at the AHA National Center. For more on AHA statements and guidelines development, visit http://www.americanheart.org/presenter.jhtml?identifier=3023366.

who have undergone other cardiac surgical procedures, such as those with valvular heart disease, also may be eligible.

Unfortunately, cardiac rehabilitation programs remain underused in the United States, with an estimated participation rate of only 10% to 20% of the >2 million eligible patients per year who experience an acute myocardial infarction or undergo coronary revascularization.7 Contributing to the vast underuse of these services are a low patient referral rate, particularly of women, older adults, and ethnic minority patients; poor patient motivation; inadequate third-party reimbursements for services; and geographic limitations to accessibility of program sites.<sup>7,11</sup> In addition, there is a lack of "visibility" and recognition by the public of the importance of cardiac rehabilitation services. To potentially rectify these concerns, alternative models to the traditional hospital- or community center-based setting for outpatient programs have been developed. These models include home-based programs for which a nurse generally serves as case manager and facilitates, supervises, and monitors patient care and progress,<sup>12,13</sup> and community-based group programs that use nurses or other nonphysician healthcare providers.14 Electronic media programs are an alternative method for providing home-based comprehensive risk-factor modification education and instruction for structured exercise.<sup>15</sup> Additional research is required to establish the effectiveness of these non-hospital-based approaches for rehabilitation and secondary prevention and to determine how to deliver these services optimally.

#### **Exercise Training Intervention**

Guidelines for prescribing aerobic and resistance exercise for patients with CVD are available elsewhere.<sup>6,9,10,16,17</sup> Specific activity recommendations also are available for women,<sup>18</sup> older adults,<sup>19</sup> patients with chronic heart failure and heart transplants,<sup>20</sup> stroke survivors,<sup>21</sup> and patients with claudication induced by peripheral arterial disease.<sup>22</sup>

# **Safety Considerations**

The relative safety of medically supervised, physiciandirected, cardiac rehabilitation exercise programs that follow these guidelines is well established. The occurrence of major cardiovascular events during supervised exercise in contemporary programs ranges from 1/50 000 to 1/120 000 patienthours of exercise, with only 2 fatalities reported per 1.5 million patient-hours of exercise.<sup>23</sup> Contemporary riskstratification procedures for the management of coronary heart disease (CHD) help to identify patients who are at increased risk for exercise-related cardiovascular events and who may require more intensive cardiac monitoring in addition to the medical supervision provided for all cardiac rehabilitation program participants.<sup>5</sup>

# **Effect on Exercise Capacity**

Exercise training and regular daily physical activities (eg, working around the house and yard, climbing stairs, walking or cycling for transportation or recreation) are essential for improving a cardiac patient's physical fitness. Supervised rehabilitative exercise for 3 to 6 months generally is reported to increase a patient's peak oxygen uptake by 11% to 36%,

with the greatest improvement in the most deconditioned individuals.<sup>5,7</sup> Improved fitness enhances a patient's quality of life and even can help older adults to live independently.24 Improved physical fitness also is associated with reductions in submaximal heart rate, systolic blood pressure, and ratepressure product (RPP), thereby decreasing myocardial oxygen requirements during moderate-to-vigorous activities of daily living. Improved fitness allows patients with advanced coronary artery disease (CAD) who ordinarily experience myocardial ischemia during physical exertion to perform such tasks at a higher intensity level before reaching their ischemic ECG or anginal threshold. Furthermore, improvement in muscular strength after resistance training also can decrease RPP (and associated myocardial demands) during daily activities, such as carrying groceries or lifting moderate to heavy objects.10 In addition, improvement in cardiorespiratory endurance on exercise testing is associated with a significant reduction in subsequent cardiovascular fatal and nonfatal events independent of other risk factors.<sup>25-28</sup> These findings also apply to patients with chronic heart failure. In a recent meta-analysis of 81 studies involving 2587 patients with stable heart failure, Smart and Marwick<sup>29</sup> demonstrated a trend toward increased survival (P=0.06) associated with improved functional capacity, as well as a reduction in cardiorespiratory symptoms after aerobic and strength training.

### **Return to Work**

Although exercise training–induced improvement in functional capacity and the associated reduction in cardiorespiratory symptoms may enhance a cardiac patient's ability to perform most job-related physical tasks, factors unrelated to physical fitness appear to have a greater influence on whether a patient returns to work after a cardiac event.<sup>30</sup> These factors include socioeconomic and worksite-related issues and previous employment status. The educational and vocational counseling components of cardiac rehabilitation programs should further improve the ability of a patient to return to work.

# **Effect on CVD Prognosis**

During the past 5 decades, numerous studies have demonstrated a reduced rate of initial CHD events in physically active people.<sup>31–33</sup> These findings, along with those from studies that demonstrate biologically plausible cardioprotective mechanisms (discussed below), provide strong evidence that regular physical activity of at least moderate intensity reduces the risk of coronary events, thus leading to the conclusion that physical inactivity is a major CHD risk factor. An even greater impact is seen when the endurance exercise program is of sufficient intensity and volume to improve aerobic capacity. Data from the Health Professionals' Follow-up Study<sup>34</sup> also provide evidence that as little as 30 minutes per week of strength training may reduce the risk of an initial coronary event.

In the absence of definitive randomized controlled trials, meta-analyses of smaller studies have been used to assess the role of exercise training, alone or as part of a comprehensive cardiac rehabilitation program, on morbidity and mortality rates of CHD patients. Meta-analyses based on studies performed in the 1970s and 1980s and reviewed in the 1994 AHA scientific statement on cardiac rehabilitation programs<sup>1</sup> and the Agency for Health Care Policy and Research guidelines5 revealed a statistically significant reduction in both cardiac and total mortality after completion of cardiac rehabilitation programs that included exercise training35,36; however, the rate of nonfatal cardiovascular events was not altered significantly by rehabilitative exercise. Subjects in these earlier trials were predominately low-risk, middle-aged, white male survivors of myocardial infarction. Women, older people, ethnic minorities, and patients who underwent revascularization procedures or who had other types of cardiac conditions were excluded or markedly underrepresented in these studies. Major advances in the management of patients with CHD during the 1990s raise further questions about the relevance of findings from these earlier meta-analyses to the independent effects of the exercise component of contemporary cardiac rehabilitation programs on morbidity, mortality, and other outcome variables. These medical advances include attenuation of residual myocardial damage from acute coronary occlusion by emergent medical interventions and pharmacological therapy to reduce myocardial oxygen demands; development and use of antiplatelet and anticoagulant drugs; prompt coronary revascularization by thrombolysis or percutaneous interventions; and more frequent use of revascularization procedures. Wider prophylactic use of adjunctive cardioprotective drugs (eg, statins), as demonstrated in definitive clinical trials, has been shown to be effective for reducing cardiovascular morbidity and mortality rates. Furthermore, biotechnical advances that have improved the survival rates of cardiac patients include conventional or drug-eluting coronary stents, implantable cardioverter defibrillators, and biventricular pacing and left ventricular assist devices for treating patients with chronic heart failure. In light of these advances, the additional effect of exercise training on morbidity and mortality rates in current cardiac rehabilitation participants is unclear.

Taylor et al<sup>2</sup> reported encouraging findings in a meta-analvsis based on a review of 48 randomized trials of  $\leq 6$  months' duration that compared outcomes of exercise-based rehabilitation with usual medical care. This meta-analysis, which updated an earlier study by the same investigators,37 added >4000 more-recent subjects with CHD to the database from the earlier meta-analyses,<sup>35,36</sup> for a total of 8940 patients. Greater numbers of women (20% of the cohort), people  $\geq 65$ years of age, and patients who had undergone coronary revascularization procedures were included than in previous meta-analyses. As shown in the Table, exercise-based cardiac rehabilitation was associated with lower total and cardiac mortality rates compared with usual medical care, which was in agreement with previous reports. Subgroup analysis showed that mortality rates did not differ between programs limited to exercise and those providing more comprehensive secondary interventions, or between pre- and post-1995 studies. Favorable trends also were noted for a lower incidence of nonfatal myocardial infarction and revascularization procedures in cardiac patients who received exercise-based rehabilitation, but these trends did not achieve statistical

# Effects of Exercise-Based Cardiac Rehabilitation on Study End Points\*

Outcome	Mean Difference, %	95% Confidence Limit	Statistical Difference
Total mortality	-20	-7% to $-32%$	P=0.005
Cardiac mortality	-26	-10% to $-29%$	P=0.002
Nonfatal MI	-21	-43% to 9%	<i>P</i> =0.150
CABG	-13	-35% to 16%	P=0.400
PTCA	-19	-51% to 34%	<i>P</i> =0.400

Mean difference is the percentage of difference between exercise-trained and usual-care control group. MI indicates myocardial infarction; CABG, coronary artery bypass graft; and PTCA, percutaneous coronary angioplasty.

\*Data are derived from Taylor et al.<sup>2</sup>

significance. Data from a limited number of studies included in this meta-analysis also showed more favorable changes in some modifiable cardiovascular risk factors among patients who received exercise therapy. Few data were provided in these studies on the use of acute thrombolytic therapy and adjunctive cardioprotective drugs. Furthermore, quality of life was assessed, via a variety of measures, in only 25% of the clinical trials, and similar improvement was noted in both the exercise-based rehabilitation and control groups.

# **Cardioprotective Mechanisms**

Exercise training, as part of a comprehensive rehabilitation program, has been shown to slow the progression or partially reduce the severity of coronary atherosclerosis.<sup>38,39</sup> Multiple factors directly or indirectly appear to contribute to this antiatherosclerotic effect. Increased flow-mediated shear stress on artery walls during exercise results in improved endothelial function,<sup>40</sup> which is associated with enhanced synthesis, release, and duration of action of nitric oxide.<sup>41–43</sup> Nitric oxide is responsible for endothelium-dependent vaso-dilatation and inhibits multiple processes involved in atherogenesis and thrombosis.<sup>40</sup> Hambrecht et al<sup>44</sup> demonstrated a significant improvement in endothelium-dependent arterial dilatation in patients with CHD and abnormal endothelial function after only 4 weeks of vigorous endurance exercise training.

Chronic inflammation plays a major role in the pathogenesis of CAD and in plaque stability.<sup>45</sup> Plasma level of C-reactive protein, a nonspecific biomarker of inflammation, is associated with an increased risk of CHD.<sup>46</sup> Aerobic exercise training and improved cardiorespiratory endurance are associated with reduced C-reactive protein levels, which suggests that exercise training has antiinflammatory effects.<sup>47–49</sup> These observations require confirmation, however, especially in patients with CAD.

In addition, exercise training and regular physical activity can result in moderate losses in body weight and adiposity.<sup>50,51</sup> Endurance exercise also can promote decreases in blood pressure<sup>52,53</sup> and serum triglycerides, increases in high-density lipoprotein cholesterol,<sup>54–57</sup> and improvements in insulin sensitivity and glucose homeostasis,<sup>58</sup> which along with modest weight reduction have been shown to reduce the risk of type 2 diabetes mellitus in individuals with glucose intolerance.<sup>59,60</sup> Thus, aerobic exercise can favorably modify all of the components of the metabolic syndrome<sup>61</sup> and serve as a first-line therapy to combat this complex constellation of risk factors for type 2 diabetes mellitus and CVD.<sup>62</sup> In addition, the value of exercise training likely goes beyond the recognized benefits on glycemic control by improving many of the cardiovascular abnormalities associated with diabetes, such as left ventricular diastolic dysfunction, endothelial dysfunction, and systemic inflammation.<sup>63</sup>

Endurance exercise training also has potential antiischemic effects. As previously mentioned, it can reduce myocardial ischemia in patients with advanced CHD by decreasing RPP and myocardial oxygen demands during physical exertion, thereby raising the ischemic threshold.<sup>9,31,32</sup> In addition, exercise training also can increase coronary flow by improving coronary artery compliance or elasticity<sup>64,65</sup> and endothe-lium-dependent vasodilatation<sup>49</sup> and by increasing the luminal area of conduit vessels through remodeling or arteriogenesis and myocardial capillary density by angiogenesis.<sup>66</sup>

Furthermore, in the presence of advanced CAD, exercise training has been shown to induce ischemic preconditioning of the myocardium, a process by which transient myocardial ischemia during exercise enhances tolerance of the myocardium to subsequent more prolonged ischemic stress, thereby reducing myocardial damage and the risk of potentially lethal ventricular tachyarrhythmias.<sup>67,68</sup> Aerobic exercise training also may decrease the risk of sudden cardiac death due to ventricular tachyarrhythmias by reducing sympathetic and enhancing parasympathetic (vagal) activity, as evidenced by increased heart rate variability and increased baroreceptor sensitivity.<sup>69–71</sup>

Furthermore, exercise training has favorable hemostatic effects, which can reduce the risk of a thrombotic occlusion of a coronary artery after the disruption of a vulnerable plaque. These antithrombotic effects include increased plasma volume, reduced blood viscosity, decreased platelet aggregation, and enhanced thrombolytic ability.<sup>72,73</sup> Strenuous exercise training enhances fibrinolytic activity by increasing the endothelial synthesis of tissue plasminogen activator and reducing the levels of its inhibitor, plasminogen activator inhibitor-1.<sup>73</sup> Some studies also have shown that exercise training may reduce plasma levels of fibrinogen.<sup>73</sup>

# **Risk Factor Modification and Interventions**

In addition to exercise training, a comprehensive secondary prevention program for cardiac patients requires aggressive reduction of risk factors through nutritional counseling, weight management, and adherence to prescribed drug therapy.<sup>3–7</sup> Clinical trials during the past 2 decades have provided conclusive evidence of reduced mortality in patients with CHD via the reduction of individual risk factors by pharma-cological and nonpharmacological interventions.<sup>74</sup>

Previously published AHA, American College of Cardiology, US Public Health Service, and American Association of Cardiovascular and Pulmonary Rehabilitation guidelines about prevention of heart attack and death in CVD patients summarize evidence-based strategies and recommendations for controlling risk factors.<sup>3–6</sup> Nutritional counseling plays an important role in the prevention and management of obesity,

dyslipidemias, hypertension, and diabetes mellitus. Dietary recommendations for modifying these risk factors are available from the AHA.<sup>75–77</sup> National guidelines also have been published for the management of dyslipidemias,<sup>78</sup> hypertension,<sup>79</sup> obesity,<sup>80</sup> and diabetes mellitus<sup>81</sup> and for smoking cessation and the prevention of relapses.<sup>82</sup> In addition, the value of drug therapy has been well documented for secondary prevention in CVD patients with the use of aspirin or clopidogrel alone or in combination with other antiplatelet drugs,<sup>83,84</sup> HMG-coenzyme A reductase inhibitors (statins),<sup>85–87</sup> angiotensin-converting enzyme inhibitors,<sup>88,89</sup> and  $\beta$ -blockers.<sup>90–93</sup>

# **Psychosocial Interventions**

Psychosocial dysfunction is common in patients receiving cardiac rehabilitation treatment. These problems include depression, anger, anxiety disorders, and social isolation. Observational studies have demonstrated associations between psychosocial disorders and the risk of initial or recurrent cardiovascular events.94,95 A large randomized multicenter trial, Enhanced Recovery in Coronary Heart Disease Patients (ENRICHD), assessed whether morbidity (recurrent myocardial infarction) or mortality would be reduced by psychosocial interventions in 2481 people hospitalized for acute myocardial infarction associated with depression and low social support.96 Treatment for depression was provided through cognitive behavior therapy and selective serotonin reuptake inhibitors, when indicated. The ENRICHD intervention did not improve event-free survival; however, both depression and social isolation improved in the intervention and control groups. Nevertheless, even if psychosocial interventions ultimately are shown not to alter the prognosis of CHD patients, they remain an integral part of cardiac rehabilitation services to improve the psychological well-being and quality of life of cardiac patients.

# **Future Research Recommendations**

- 1. Evaluations are needed to determine the effectiveness and safety of a variety of approaches designed to increase patient referrals, accessibility, and delivery of cardiac rehabilitation and secondary prevention services and to promote adherence to program components. These include evaluations of community-based, home-based, and Internet-based interventions and of care management by nonphysician healthcare professionals to complement physicians' services.
- 2. Because of continuously escalating medical costs, thirdparty payers demand evidence of cost-effectiveness and the cost-related benefits of healthcare services and procedures. Only a limited number of studies have examined these issues for cardiac rehabilitation and secondary prevention services.<sup>97,98</sup> These studies strongly indicate the cost-effectiveness of comprehensive rehabilitation/ secondary prevention programs and their individual components, including exercise training. Future studies should include comparisons of the cost-effectiveness of traditional supervised programs versus home-based exercise and educational services with regard to improving functional capacity, self-efficacy, independent living, risk factor

modification, long-term compliance, rehospitalization rates, and quality of life.

- 3. Additional research is required to study contributions of endurance and resistance exercise for the modification of risk factors and for their effects on pathophysiological mechanisms involved in atherogenesis, myocardial ischemia, coronary thrombosis, and ventricular tachyarrhythmias. This research should include the effects of exercise on endothelial function, vasomotor reactivity, blood-flow rheology, inflammatory and oxidative stress markers, endothelial-adhesion proteins, baroreceptor and related neurohumoral functions, and platelet aggregation and other factors involved in blood coagulation and fibrinolysis. Exercise dose–response relationships also need to be determined.
- 4. Randomized trials are needed to better define the role of exercise therapy for safely improving functional capacity, reducing cardiovascular symptoms, and enhancing the quality of life among specific subgroups of CVD patients, particularly older, female, and ethnic minority patients. Further research also is needed to clarify better the role of exercise in patients with chronic stable angina, peripheral arterial disease, diabetes, impaired left ventricular function, heart transplantation, or an implanted cardioverter defibrillator.
- 5. The feasibility of definitive randomized multicenter clinical trials should be explored to assess the independent contribution of exercise training to the morbidity and mortality of patients after myocardial infarction or coronary artery revascularization procedures and of patients with stable angina pectoris or silent myocardial ischemia. These trials should include older, female, and ethnic minority patients. A multicenter randomized trial of comprehensive cardiac rehabilitation and secondary prevention for patients with CAD in which interventions with or without an exercise component are com-

pared during a 3- to 5-year observational period is estimated to require 4000 to 4500 patients to have the power to demonstrate a statistically significant 20% reduction in cardiac mortality in the exercise group.99 Secondary end points should include nonfatal cardiovascular events, requirements for revascularization procedures, and the rate of progression or regression of disease as assessed by quantitative coronary arteriography, carotid artery ultrasound, or developing technologies such as coronary intravascular ultrasound, multislice computed tomography, and MRI.<sup>100</sup> The projected required sample size is comparable to that of several major multicenter randomized placebo-controlled trials that involve the use of statins in patients with CAD, in which a 20% to 30% reduction in many of the abovereferenced primary and secondary end points was demonstrated.99-103

- 6. The proven salutary impact of comprehensive lifestyle modification often has been overlooked and underemphasized as a first-line approach to secondary prevention. Additional studies are needed to clarify the independent and additive benefits of lifestyle modification (ie, beyond coronary revascularization and effective pharmacotherapies) individually or in combination with other interventions in preventing recurrent cardiovascular events.<sup>104</sup>
- 7. Research should be geared toward evaluating the use of cardiac rehabilitation programs as centers for intensive lifestyle management for weight loss, physical activity, nutrition, and psychosocial support for people with additional chronic medical conditions, such as type 2 diabetes mellitus, the metabolic syndrome, and other insulin-resistant states. Preventing these conditions from following their natural course into acute and chronic vascular disease would be lifesaving and economically beneficial.

### Disclosures

Writing Group Member Name	Research Grant	Speakers Bureau/Honoraria	Stock Ownership	Consultant/Advisory Board	Other
Dr Arthur S. Leon	None	None	None	None	None
Dr Barry A. Franklin	None	Merck, Pfizer, Bayer	None	None	None
Dr Fernando Costa	None	None	None	None	None
Dr Gary J. Balady	None	None	None	None	None
Dr Kathy A. Berra	None	None	None	None	None
Dr Kerry J. Stewart	None	None	None	None	None
Dr Paul D. Thompson	Otsuka, Merck, Pfizer, AstraZeneca, Bristol-Myers Squibb, Schering-Plough	Merck, Pfizer, Schering-Plough, AstraZeneca, Bristol-Myers Squibb, Reliant	Pfizer, Schering-Plough	Merck, Pfizer, AstraZeneca, Schering-Plough	None
Dr Mark A. Williams	None	None	None	None	None
Dr Michael S. Lauer	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group were required to complete and submit.

# References

- Cardiac rehabilitation programs: a statement for healthcare professionals from the American Heart Association. *Circulation*. 1994;90:1602–1610.
   Taylor PS, Provin A, Ebrahim S, Jalliffe L, Nagarri H, Para K.
- Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, Skidmore B, Stone JA, Thompson DR, Oldridge N. Exercise-based

rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized trials. Am J Med. 2004;116:682-697.

3. Balady GJ, Ades PA, Comoss P, Limacher M, Pina IL, Southard D, Williams MA, Bazzarre T. Core components of cardiac rehabilitation/ secondary prevention programs: a statement for healthcare professionals from the American Heart Association and American Association of Cardiovascular and Pulmonary Rehabilitation Writing Group. *Circulation*. 2000;102:1069–1073.

- 4. Smith SC Jr, Blair SN, Bonow RO, Brass LM, Cerqueira MD, Dracup K, Fuster V, Gotto A, Grundy SM, Miller NH, Jacobs A, Jones D, Krauss RM, Mosca L, Ockene I, Pasternak RC, Pearson T, Pfeffer MA, Starke RD, Taubert KA. AHA/ACC Scientific Statement: AHA/ACC guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular disease: 2001 update: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation*. 2001;104:1577–1579.
- 5. Wenger NK, Froelicher ES, Smith LK, Philip A. Ades PA, Berra K, Blumenthal JA, Certo CM, Dattilo AM, Davis D, DeBusk RF, Drozda JP Jr, Fletcher BJ, Franklin BA, Gaston H, Greenland P, McBride PE, McGregor CG, Oldridge NB, Piscatella JC, Rogers FJ. *Clinical Practice Guidelines No. 17: Cardiac Rehabilitation as Secondary Prevention*. Rockville, Md: US Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, National Heart, Lung and Blood Institute; 1995. AHCPR Publication 96-0672.
- American Association of Cardiovascular and Pulmonary Rehabilitation. *Guidelines for Cardiac Rehabilitation and Secondary Prevention Programs.* 4th ed. Champaign, IL: Human Kinetics; 2004.
- Ades PA. Cardiac rehabilitation and secondary prevention of coronary heart disease. N Engl J Med. 2001;345:892–902.
- Ades PA, Balady GJ, Berra K. Transforming exercise-based cardiac rehabilitation programs into secondary prevention centers: a national imperative. J Cardiopulm Rehabil. 2001;21:263–272.
- Leon AS. Exercise following myocardial infarction: current recommendations. Sports Med. 2000;29:301–311.
- 10. Pollock ML, Franklin BA, Balady GJ, Chaitman BL, Fleg JL, Fletcher B, Limacher M, Pina IL, Stein RA, Williams M, Bazzarre T. AHA Science Advisory. Resistance exercise in individuals with and without cardiovascular disease: benefits, rationale, safety, and prescription: an advisory from the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, American Heart Association; position paper endorsed by the American College of Sports Medicine. *Circulation.* 2000;101:828–833.
- Allen JK, Scott LB, Stewart KJ, Young DR. Disparities in women's referral to and enrollment in outpatient cardiac rehabilitation. J Gen Intern Med. 2004;19:747–753.
- Miller NH, Haskell WL, Berra K, DeBusk RF. Home versus group exercise training for increased functional capacity after myocardial infarction. *Circulation*. 1984;70:645–649.
- Haskell WL. Cardiovascular disease prevention and lifestyle interventions: effectiveness and efficacy. J Cardiovasc Nurs. 2003;18: 245–255.
- Harris DE, Record NB. Cardiac rehabilitation in community settings. J Cardiopulm Rehabil. 2003;23:250–259.
- Southard BH, Southard DR, Nuckolls J. Clinical trials of an Internet-based case management system for secondary prevention of heart disease. J Cardiopulm Rehabil. 2003;23:341–348.
- American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription. 6th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2000.
- Fletcher GF, Balady G, Amsterdam EA, Chaitman B, Eckel R, Fleg J, Froelicher VF, Leon AS, Pina IL, Rodney R, Simons-Morton DA, Williams MA, Bazzarre T. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation*. 2001;104:1694–1740.
- Bonzheim KA, Franklin BA. Women and heart disease: role of exercise-based cardiac rehabilitation. Am J Sports Med. 2001;3: 135–144.
- 19. Williams MA, Fleg JL, Ades PA, Chaitman BR, Miller NH, Mohiuddin SM, Ockene IS, Taylor CB, Wenger NK; American Heart Association Council on Clinical Cardiology Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention. Secondary prevention of coronary heart disease in the elderly (with emphasis on patients ≥75 years of age): an American Heart Association scientific statement from the Council on Clinical Cardiology Subcommittee on Exercise, Cardiac Rehabilitation and Prevention. 2002;105:1735–1743.
- 20. Piña IL, Epstein CS, Balady GJ, Belardinelli R, Chaitman BR, Duscha BD, Fletcher BJ, Fleg JL, Myers JN, Sullivan MJ; American Heart Association Committee on exercise, rehabilitation, and prevention. Exercise and heart failure: a statement from the American Heart Association Committee on Exercise, Rehabilitation, and Prevention. *Circulation*. 2003;107:1210–1225.

- 21. Gordon NF, Gulanick M, Costa F, Fletcher G, Franklin BA, Roth EJ, Shephard T; American Heart Association Council on Clinical Cardiology, Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention; the Council on Cardiovascular Nursing; the Council on Nutrition, Physical Activity, and Metabolism; and the Stroke Council. Physical activity and exercise recommendations for stroke survivors: an American Heart Association scientific statement from the Council on Clinical Cardiology, Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention; the Council on Cardiovascular Nursing; the Council on Nutrition, Physical Activity, and Metabolism; and the Stroke Council on Nutrition, Physical Activity, and Metabolism; and the Stroke Council on Nutrition, Physical Activity, and Metabolism; and the Stroke Council *Circulation*. 2004;109:2031–2041.
- Stewart KJ, Hiatt WR, Regensteiner JG, Hirsch AT. Exercise training for claudication. N Engl J Med. 2002;347:1941–1951.
- Franklin BA, Bonzheim K, Gordon S, Timmis GC. Safety of medically supervised cardiac rehabilitation exercise therapy: a 16-year follow-up. *Chest.* 1998;114:902–906.
- Stewart KJ, Turner KL, Bacher AC, DeRegis JR, Sung J, Tayback M, Ouyang P. Are fitness, activity, and fatness associated with healthrelated quality of life and mood in older persons? *J Cardiopulm Rehabil*. 2003;23:115–121.
- Mark DB, Lauer MS. Exercise capacity: the prognostic variable that doesn't get enough respect. *Circulation*. 2003;108:1534–1536.
- Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality of men referred for exercise testing. *N Engl J Med.* 2002;346:793–801.
- Kavanagh T, Mertens DJ, Hamm LF, Beyene J, Kennedy J, Corey P, Shephard RJ. Prediction of long-term prognosis in 12 169 men referred for cardiac rehabilitation. *Circulation*. 2002;106:666–671.
- Kavanagh T, Mertens DJ, Hamm LF, Beyene J, Kennedy J, Corey P, Shephard RJ. Peak oxygen intake and cardiac mortality in women referred for cardiac rehabilitation. J Am Coll Cardiol. 2003;42: 2139–2143.
- 29. Smart N, Marwick TH. Exercise training for patients with heart failure: a systematic review of factors that improve mortality and morbidity. *Am J Med.* 2004;116:693–706.
- 20th Bethesda Conference: insurability and employability of the patient with ischemic heart disease. October 3–4, 1988, Bethesda, Maryland. *J Am Coll Cardiol.* 1989;14:1003–1044.
- 31. Thompson PD, Buchner D, Piña IL, Balady GJ, Williams MA, Marcus BH, Berra K, Blair SN, Costa F, Franklin B, Fletcher GF, Gordon NF, Pate RR, Rodriguez BL, Yancey AK, Wenger NK; American Heart Association Council on Clinical Cardiology Subcommittee on Exercise, Rehabilitation, and Prevention; American Heart Association Council on Nutrition, Physical Activity, and Metabolism Subcommittee on Physical Activity. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation*. 2003;107: 3109–3116.
- 32. Shephard RJ, Balady GJ. Exercise as cardiovascular therapy. *Circulation*. 1999;99:963–972.
- Lakka TA, Venäläinen JM, Rauramaa R, Salonen R, Tuomilehto J, Salonen JT. Relation of leisure-time physical activity and cardiorespiratory fitness to the risk of acute myocardial infarction. *N Engl J Med.* 1994;330:1549–1554.
- Tanasescu M, Leitzmann MF, Rimm EB, Willett WC, Stampfer MJ, Hu FB. Exercise type and intensity in relation to coronary heart disease in men. JAMA. 2002;288:1994–2000.
- O'Connor GT, Buring JE, Yusuf S, Goldhaber SZ, Olmstead EM, Paffenbarger RS Jr, Hennekens CH. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. *Circulation*. 1989;80:234–244.
- Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction: combined experience of randomized clinical trials. *JAMA*. 1988;260:945–950.
- Jolliffe JA, Rees K, Taylor RS, Thompson D, Oldridge N, Ebrahim S. Exercise-based rehabilitation for coronary heart disease. *Cochrane Database Syst Rev.* 2001;CD001800.
- Niebauer J, Hambrecht R, Velich T, Hauer K, Marburger C, Kalberer B, Weiss C, von Hodenberg E, Schlierf G, Schuler G, Zimmermann R, Kubler W. Attenuated progression of coronary artery disease after 6 years of multifactorial risk intervention: role of physical exercise. *Circulation*. 1997;96:2534–2541.

- 39. Haskell WL, Alderman EL, Fair JM, Maron DJ, Mackey SF, Superko HR, Williams PT, Johnstone IM, Champagne MA, Krauss RM, et al. Effects of intensive multiple risk factor reduction on coronary atherosclerosis and clinical cardiac events in men and women with coronary artery disease. The Stanford Coronary Risk Intervention Prevention Project (SCRIP). *Circulation*. 1994;89:975–990.
- Niebauer J, Cooke JP. Cardiovascular effects of exercise: role of endothelial shear stress. J Am Coll Cardiol. 1996;28:1652–1660.
- Dimmeler S, Zeiher AM. Exercise and cardiovascular health: get active to "AKTivate" your endothelial nitric oxide synthase. *Circulation*. 2003; 107:3118–3120.
- 42. Hambrecht R, Adams V, Erbs S, Linke A, Krankel N, Shu Y, Baither Y, Gielen S, Thiele H, Gummert JF, Mohr FW, Schuler G. Regular physical activity improves endothelial function in patients with coronary artery disease by increasing phosphorylation of endothelial nitric oxide synthase. *Circulation*. 2003;107:3152–3158.
- Fukai T, Siegfred MR, Ushio-Fukai M, Cheng Y, Kojda G, Harrison DG. Regulation of the vascular extracellular superoxide dismutase by nitric oxide and exercise training. *J Clin Invest.* 2000;105:1631–1639.
- 44. Hambrecht R, Wolf A, Gielen S, Linke A, Hofer J, Erbs S, Schoene N, Schuler G. Effect of exercise on coronary endothelial function in patients with coronary artery disease. *N Engl J Med.* 2000;342: 454–460.
- Maseri A. Inflammation, atherosclerosis, and ischemic events exploring the hidden side of the moon. N Engl J Med. 1997;336: 1014–1016.
- Ridker PM. High-sensitivity C-reactive protein: potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. *Circulation*. 2001;103:1813–1818.
- Mattusch HF, Dufaux B, Heine O, Mertens I, Rost R. Reduction of the plasma concentration of C-reactive protein following nine months of endurance training. *Int J Sports Med.* 1999;20:21–24.
- Church TS, Barlow CE, Earnest CP, Kampert JB, Priest EL, Blair SN. Association between cardiorespiratory fitness and C-reactive protein in men. Arterioscler Thromb Vasc Biol. 2002;22:1869–1876.
- LaMonde MJ, Durstine JL, Yanowitz FG, Lim T, DuBose KD, Davis P, Ainsworth BE. Cardiorespiratory fitness and C-reactive protein among a tri-ethnic sample of women. *Circulation*. 2002;106:403–406.
- 50. Ross R, Janssen I. Physical activity, total and regional obesity: doseresponse considerations. *Med Sci Sports Exerc*. 2001;33:S521–S527.
- 51. Jakicic JM, Clark K, Coleman E, Donnelly JE, Foreyt J, Melanson E, Volek J, Volpe SL; American College of Sports Medicine. American College of Sports Medicine position stand: appropriate intervention strategies for weight loss and prevention of weight regain for adults. *Med Sci Sports Exerc.* 2001;33:2145–2156.
- Fagard RH. Exercise characteristics and the blood pressure response to dynamic physical training. *Med Sci Sport Exerc*. 2001;33:S484–S492.
- Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA; American College of Sports Medicine. American College of Sports Medicine position stand: exercise and hypertension. *Med Sci Sports Exerc*. 2004;36:533–553.
- 54. Leon AS, Rice T, Mandel S, Despres JP, Bergeron J, Gagnon J, Rao DC, Skinner JS, Wilmore JH, Bouchard C. Blood lipid response to 20 weeks of supervised exercise in a large biracial population: the HERITAGE Family Study. *Metabolism.* 2000;49:513–520.
- Leon AS, Sanchez OA. Response of blood lipids to exercise training alone or combined with dietary intervention. *Med Sci Sports Exerc*. 2001;33:S502–S515.
- Durstine JL, Grandjean PW, Davis PG, Ferguson MA, Alderson NL, DuBose KD. Blood lipid and lipoprotein adaptations to exercise: a quantitative analysis. *Sports Med.* 2001;31:1033–1062.
- 57. Kraus WE, Houmard JA, Duscha BD, Knetzger KJ, Wharton MB, McCartney JS, Bales CW, Henes S, Samsa GP, Otvos JD, Kulkarni KR, Slentz CA. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med.* 2002;347:1483–1492.
- Kelley DE, Goodpaster BH. Effects of exercise on glucose homeostasis in type 2 diabetes mellitus. *Med Sci Sports Exerc*. 2001;33:S495–S501, S528–S529.
- 59. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by change in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med.* 2001; 344:1343–1350.

- 60. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* 2002;346:393–403.
- 61. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C; American Heart Association; National Heart, Lung, and Blood Institute. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*. 2004;109:433–438.
- 62. Grundy SM, Hansen B, Smith SC Jr, Cleeman JI, Kahn RA; American Heart Association; National Heart, Lung, and Blood Institute; American Diabetes Association. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. *Circulation*. 2004;109:551–556.
- 63. Stewart KJ. Exercise training and the cardiovascular consequences of type 2 diabetes and hypertension: plausible mechanisms for improving cardiovascular health. JAMA. 2002;288:1622–1631.
- Tanaka H, Dinenno FA, Monahan KD, Clevenger CM, DeSouza CA, Seals DR. Aging, habitual exercise, and dynamic arterial compliance. *Circulation*. 2000;102:1270–1275.
- Joyner MJ. Effect of exercise on arterial compliance. *Circulation*. 2000; 102:1214–1215.
- Laughlin MH, Oltman C, Bowles DK. Exercise training-induced adaptations in the coronary circulation. *Med Sci Sports Exerc.* 1998;30: 352–360.
- Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. *Circulation*. 1986; 74:1124–1136.
- 68. Bolli R. The late phase of preconditioning. Circ Res. 2000;87:972-983.
- Leitch JW, Newling RP, Basta M, Inder K, Dear K, Fletcher PJ. Randomized trial of a hospital-based exercise training program after acute myocardial infarction: cardiac autonomic effects. J Am Coll Cardiol. 1997;29:1263–1268.
- Iellamo F, Legramante JM, Massaro MA, Raimondi G, Galante A. Effects of residential exercise training on baroreflex sensitivity and heart rate variability in patients with coronary artery disease: a randomized, controlled study. *Circulation*. 2000;102:2588–2592.
- Kingwell BA, Dart AM, Jennings GL, Korner PI. Exercise training reduces the sympathetic component of the blood pressure-heart rate baroreflex in man. *Clin Sci.* 1992;82:357–362.
- Church TS, Lavie CJ, Milani RV, Kirby GS. Improvements in blood rheology after cardiac rehabilitation and exercise training in patients with coronary heart disease. *Am Heart J.* 2002;143:349–355.
- Rauramaa R, Li G, Vaisanen SB. Dose-response and coagulation and hemostatic factors. *Med Sci Sports Exerc*. 2001;33:S516–S520, S528–S529.
- Mukherjee D, Fang J, Chetcuti S, Moscucci M, Kline-Rogers E, Eagle KA. Impact of combination evidence-based medical therapy on mortality in patients with acute coronary syndromes. *Circulation*. 2004;109: 745–749.
- 75. Krauss RM, Eckel RH, Howard B, Appel LJ, Daniels SR, Deckelbaum RJ, Erdman JW Jr, Kris-Etherton P, Goldberg IJ, Kotchen TA, Lichtenstein AH, Mitch WE, Mullis R, Robinson K, Wylie-Rosett J, St Jeor S, Suttie J, Tribble DL, Bazzarre TL. AHA Dietary Guidelines: revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. *Circulation*. 2000;102: 2284–2299.
- Kris-Etherton P, Harris WS, Appel LJ. American Heart Association. Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation*. 2002;106:2747–2757.
- 77. Kris-Etherton P, Eckel RH, Howard BV, St. Jeor S, Bazzarre TL; Nutrition Committee Population Science Committee and Clinical Science Committee of the American Heart Association. AHA Science Advisory: Lyon Diet Heart Study: benefits of a Mediterranean-style, National Cholesterol Education Program/American Heart Association Step I dietary pattern on cardiovascular disease. *Circulation*. 2001;103: 1823–1825.
- 78. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106:3143–3421.

- 79. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC7 Report. JAMA. 2003;289:2560–2572. [Published erratum in: JAMA. 2003;290:197.]
- NHLBI Obesity Education Initial Expert Panel. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report. Rockville, Md: National Heart, Lung and Blood Institute in cooperation with the National Institutes of Diabetes and Digestive and Kidney Diseases; September 1998. NIH Publication 98–4083.
- American Diabetes Association. Clinical practice recommendations 2004. Diabetes Care. 2004;27:S1–S145.
- Murray EW. Smoking cessation clinical practice guideline update and Agency for Healthcare Research and Quality tobacco resources. *Tobacco Control.* 2000;172–173.
- Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomized trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ*. 2002;324: 71–86.
- Randomised double-blind trial of fixed low-dose warfarin with aspirin after myocardial infarction. Coumadin Aspirin Reinfarction Study (CARS) Investigators. *Lancet.* 1997;350:389–396.
- Vaughan CJ, Gotto AM Jr, Basson CT. The evolving role of statins in the management of atherosclerosis. J Am Coll Cardiol. 2000;35:1–10.
- Maron DJ, Fazio S, Linton MF. Current perspectives on statins. *Circulation*. 2000;101:207–213.
- Libby P, Aikawa M. Mechanisms of plaque stabilization with statins. *Am J Cardiol.* 2003;91:4B–8B.
- Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med. 2000;342:145–153. [Published errata in: N Engl J Med. 2000;342:1376; N Engl J Med. 2000;342:748.]
- 89. Fox KM; EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). *Lancet*. 2003;362:782–788.
- Yusuf S, Peto R, Lewis J, Collins R, Sleight P. Beta blockade during and after myocardial infarction: an overview of the randomized trials. *Prog Cardiovasc Dis.* 1985;27:335–371.
- Goldstein S. Beta-blockers in hypertensive and coronary heart disease. Arch Intern Med. 1996;156:1267–1276.

- Gheorghiade M, Colucci WS, Swedberg K. Beta-blockers in chronic heart failure. *Circulation*. 2003;107:1570–1575.
- Gottlieb SS, McCarter RJ, Vogel RA. Effect of beta-blockade on mortality among high-risk and low-risk patients after myocardial infarction. *N Engl J Med.* 1998;339:489–497.
- Franklin BA. Psychosocial considerations in heart disease. J Hong Kong Coll Cardiol. 2001;9:16–22.
- Rozanski A, Blumenthal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation*. 1999;99:2192–2217.
- 96. Berkman LF, Blumenthal J, Burg M, Carney RM, Catellier D, Cowan MJ, Czajkowski SM, DeBusk R, Hosking J, Jaffe A, Kaufmann PG, Mitchell P, Norman J, Powell LH, Raczynski JM, Schneiderman N; Enhancing Recovery in Coronary Heart Disease Patients Investigators (ENRICHD). Effects of treating depression and low perceived social support on clinical events after myocardial infarction: the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial. JAMA. 2003;289:3106–3116.
- Ades PA, Huang D, Weaver SO. Cardiac rehabilitation participation predicts lower rehospitalization costs. Am Heart J. 1992;123:916–921.
- Ades PA, Pashkow FJ, Nestor JR. Cost-effectiveness of cardiac rehabilitation after myocardial infarction. J Cardiopulm Rehabil. 1997;17: 222–231.
- Thompson PD. Exercise for patients with coronary artery and/or coronary heart disease. In: Thompson PD, ed. *Exercise and Sports Cardiology*. New York, NY: McGraw Hill; 2001:354–370.
- Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet*. 1994;344:1383–1389.
- 101. Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, Brown L, Warnica JW, Arnold JM, Wun CC, Davis BR, Braunwald E. The effects of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. N Engl J Med. 1996;335:1001–1009.
- 102. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. N Engl J Med. 1998;339:1349–1357.
- 103. Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, Zeiher A, Chaitman BR, Leslie S, Stern T; Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) Study Investigators. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. JAMA. 2001;285:1711–1718.
- 104. Franklin BA, Kahn JK, Gordon NF, Bonow RO. A cardioprotective "polypill"? Independent and additive benefits of lifestyle modification. *Am J Cardiol.* 2004;94:162–166.

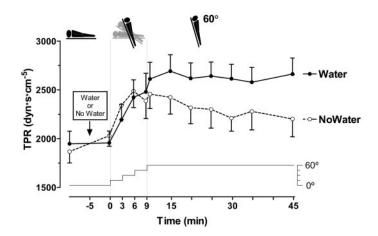
# Corrections

In the article by Leon et al, "Cardiac Rehabilitation and Secondary Prevention of Coronary Heart Disease: An American Heart Association Scientific Statement From the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in Collaboration With the American Association of Cardiovascular and Pulmonary Rehabilitation," which appeared in the January 25, 2005, issue of the journal (*Circulation*. 2005;111:369–376), an error appears on page 372. In the paragraph that begins, "Furthermore, in the presence of advanced CAD. . .," the last sentence of the paragraph should read, "Aerobic exercise training also may decrease the risk of sudden cardiac death due to ventricular tachyarrhythmias by reducing sympathetic and enhancing parasympathetic (vagal) activity, as evidenced by increased heart rate variability and increased baroreceptor sensitivity.<sup>69–71</sup>"

The corrected version of this article is available online at http://circ.ahajournals.org/cgi/content/ full/111/3/369. (The previous version, if needed, can be accessed by selecting the "Previous Version of This Article" link.)

#### DOI: 10.1161/01.CIR.0000163615.58440.7A

In the article by Lu et al, "Water Ingestion as Prophylaxis Against Syncope," which appeared in the November 25, 2003, issue of the journal (*Circulation*. 2003;108:2660–2665), Figure 4 was not the correct figure; a duplicate of Figure 5 was inadvertently placed above the Figure 4 legend. The correct Figure 4 appears below. Its legend was correct as originally printed. We regret this error.



**Figure 4.** Total peripheral resistance (TPR) during head-up tilt. Water ingestion accentuated the increasing TPR during tilt-table testing. P<0.001.

#### DOI: 10.1161/01.CIR.0000163621.17775.A8

In the March 21, 2005, online posting of the article by Bennett et al, "The Use of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): A Science Advisory From the American Heart Association" (*Circulation*. 2005;111:1713–1716; DOI: 10.1161/01.CIR.0000160005.90598.41), the discussion of the Adenoma Prevention with Celecoxib (APC) trial contained some unclear text about the results of the trial. The printed version as it appears in this issue has been changed to improve clarity, as has the online version.

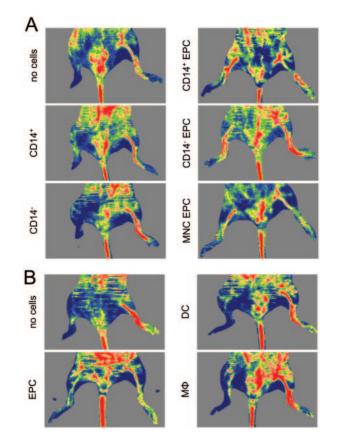
### DOI: 10.1161/01.CIR.0000164587.06064.83

(*Circulation.* 2005;111:1717–1718.) © 2005 American Heart Association, Inc.

*Circulation* is available at http://www.circulationaha.org

# **Corrections**

In the article by Urbich et al, "Relevance of Monocytic Features for Neovascularization Capacity of Circulating Endothelial Progenitor Cells," which appeared in the November 18, 2003, issue of the journal (*Circulation*. 2003;108:2511–2516), the authors have identified incorrect representative laser Doppler images in Figure 4. The representative images were inadvertently mixed up during electronic compilation of the original laser Doppler recordings for composition of the representative figure. The quantitative data shown in the analysis are not affected because quantitative analysis was performed using the original recordings. The corrected images for Figure 4A and 4B appear below. The authors regret this error.



DOI: 10.1161/01.CIR.0000163618.00600.26