The benefits and risks of exercise

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INTRODUCTION — Physical inactivity is a major health problem worldwide, particularly in developed countries. The medical literature clearly demonstrates beneficial effects of physical activity on several health outcomes, including cardiovascular disease and all-cause mortality [1]. Although there are risks associated with exercise in some patients, the benefits outweigh the risks in most patients.

Counseling patients on exercise may be challenging, as many patients have different perceived barriers to exercising. Thus, an individualized approach to the exercise prescription may be needed to effect behavioral change.

This topic will provide an overview of the benefits and risks of exercise in adults, including an evidence-based exercise prescription. Exercise recommendations for children and adolescents, as well as for specific conditions, are discussed in detail elsewhere. (See "Physical activity and strength training in children and adolescents: An overview" and "Exercise and fitness in the prevention of cardiovascular disease" and "Obesity in adults: Role of physical activity and exercise" and "Exercise in the treatment and prevention of hypertension" and "Effects of exercise in adults with diabetes mellitus" and "Exercise during pregnancy and the postpartum period: Practical recommendations".)

DEFINITIONS — Physical activity and exercise are not interchangeable terms [2].

- Physical activity is defined as bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above the basal level. Categories of physical activity include occupational, household, leisure time, and transportation.
- The term "exercise" is a form of physical activity that is planned, structured, repetitive, and purposeful with a main objective of improvement or maintenance of one or more components of physical fitness.

Physical activity may be measured in terms of METs (metabolic equivalents), units used to estimate the metabolic cost (oxygen consumption) of physical activity. One MET equals the resting metabolic rate of approximately 3.5 mL O_2/kg/min, and represents the approximate rate of oxygen consumption of a seated adult at rest. Moderate physical activity includes activity performed at an intensity of 3 to 6 METs, or the equivalent of walking briskly at approximately 5 to 8 kilometers (3 to 5 miles) per hour. Leisure cycling, moderate effort swimming, playing golf (walking), general cleaning at home, or lawn mowing also constitute moderate physical activity (figure 1) [3]. Vigorous physical activity includes activity performed at >6 METs, such as running, rope jumping, and calisthenics (eg, push-ups, pull-ups, sit-ups, jumping jacks).

Physical fitness can be described as the ability to carry out daily tasks with vigor and alertness, without undue fatigue, and with ample energy to enjoy leisure time pursuits and meet unforeseen emergencies [2]. The scope of physical fitness includes cardiorespiratory endurance, skeletal muscular endurance, skeletal muscular strength, skeletal muscular power, speed, flexibility, agility, balance, reaction time, and body composition [4]. Cardiorespiratory endurance is defined as a health related component of physical fitness that relates to the ability of the circulatory and respiratory systems to supply oxygen during sustained physical activity [2].

PHYSICAL INACTIVITY AND HEALTH — Physical inactivity is prevalent and associated with poor health outcome. Despite the widespread prevalence of physical inactivity, its associated health risks, and the potential of increasing physical activity to improve health outcomes, clinicians do not routinely screen patients for physical inactivity or provide adequate counseling. In developed countries, only 13 to 34 percent of primary care patients reported receiving advice on physical activity from their primary care physician [5-7]. The efficacy of exercise counseling is discussed below. (See 'Efficacy of exercise counseling' below.)

- **Prevalence** — Worldwide, one out of every five adults is physically inactive [8]. Physical inactivity is particularly prevalent in more developed countries and among women, older persons, and those with lower incomes. In addition to lack of regular exercise, the percentage of time spent in sedentary behaviors (watching television or in front of a computer) is increasing [9,10].

  In the United States, many Americans do not meet national guidelines for being physically active. In a sample of children and adults from the National Health and Nutrition Examination Survey (NHANES) 2003-2004, activity monitoring found that 55 percent of waking hours were spent in sedentary behaviors [11]. Subsequent NHANES data in 2005-2006 indicate that the percentage of sedentary time is increasing (58 percent), while time spent in light activity is decreasing [12]. According to the National Health Interview Survey 2008, 56.5 percent of respondents were not aerobically active, based on the 2008 Physical Activity Guidelines for Americans: 150 minutes of moderate intensity activity or 75 minutes of vigorous intensity activity weekly [2,13]. In telephone survey data from the 2007 Behavioral Risk Factor Surveillance System, 64.3 percent of adults met minimum physical activity guidelines through nonoccupational activity [14]. When occupational activity was included (mostly walking or heavy labor during work), an additional 6.5 percent of adults likely met the guidelines. However, this study was limited by a low response rate and interviews being conducted by telephone only.

- **Health effects of physical inactivity/sedentary behavior** — Large prospective cohort studies from several countries around the world have found that sedentary behavior is associated with a variety of poor health outcomes, including increased mortality [9,15-18]. One study calculated the attributable risk for premature mortality and estimated that physical inactivity worldwide causes 9 percent of premature mortality, accounting for 5.3 million deaths worldwide in 2008 [19]. A 10 percent reduction in inactivity could avert 533,000 deaths every year. Regular physical activity and higher cardiorespiratory fitness decrease overall mortality in a dose-response fashion [1,20]. (See 'Mortality' below.)

- **Health effects of extended sitting time** — Extended periods of sitting appear to be an independent risk factor for mortality [21-24]. Prolonged sitting/sedentary time has also been associated with an increased risk for diabetes, cardiovascular disease, and cancer [21,23]. In a 2015 systematic review and meta-analysis, the negative effects of prolonged sedentary time were not mitigated by participation in physical exercise, though the effects were more pronounced at lower levels of physical activity [23]. However, one study found that accounting for fitness decreased the association between extended periods of sitting and cardiometabolic biomarkers [25]. Another study including over 150,000 adults aged 59 to 82 years found that replacing sitting time with exercise was associated with a decrease in all-cause mortality [26]. For inactive adults (<2 hours of total daily activity), replacing one hour of sitting time with a variety of nonexercise activities (eg, household chores, lawn and garden work, and daily walking outside of exercise) was also associated with decreased all-cause mortality.

  Studies evaluating interventions to reduce sitting time have reported mixed results. A 2015 systematic review concluded that there was some evidence that sit-stand desks decrease sitting time but found inconsistent evidence for interventions such as counseling or computer prompts [27].

EXERCISE PHYSIOLOGY — Long-term adaptations to exercise training include effects upon the musculoskeletal, metabolic, cardiovascular, and respiratory systems. This is discussed in detail separately. (See "Exercise physiology".)

BENEFITS OF EXERCISE — Exercise favorably impacts multiple systems and health outcomes (table 1 and table 2). A graded relationship between exercise and the development of common chronic conditions (including cardiovascular disease, diabetes mellitus, chronic lung disease, chronic kidney disease, Alzheimer disease, and some cancers) has been observed, such that greater exercise in midlife was associated with compression of morbidity in later years with a decreased risk of multiple chronic conditions in the last five years of life [28].

Mortality — Most data on the benefits of exercise come from observational trials. There are no high-quality, long-term, randomized trials of exercise for prevention of cardiovascular disease or death in a healthy population. Large observational studies suggest that regular exercise reduces risk of all-cause mortality for most individuals, including men and women, as well as younger and older populations [1,29-36]. The beneficial effects appear to be dose-dependent. A 2014 meta-analysis of cohort studies in elite athletes found that compared with the general population, athletes have 67 percent lower mortality [37].

Representative studies include:

- A meta-analysis of 33 observational studies (102,980 participants) reported the risk for all-cause mortality related to cardiorespiratory fitness (CRF) [1]. CRF, based on maximal aerobic capacity, was ranked as high (≥10.9 METs), intermediate (7.9 to 10.8 METs), or low (<7.9 METs). Participants with low CRF had an increased risk of all-cause mortality compared to those with high CRF (RR 1.7, 95% CI 1.5-1.9) and intermediate CRF (RR 1.4, 95% CI 1.3-1.5). These data indicate that measured aerobic fitness, not just reported exercise, was inversely associated with mortality risk.

- In a retrospective cohort study, physical activity habits were analyzed in 10,269 Harvard College alumni over 12 years [30]. Those men who engaged in moderately vigorous sports activity had a 23 percent lower risk of death than those who were less active. The improvement in survival with exercise was equivalent and additive to other lifestyle measures such as smoking cessation, control of hypertension, and avoidance of obesity (figure 2). This highlights the importance of exercise given that the specific benefits of regular exercise persist despite individuals attempting to improve multiple lifestyle habits concurrently.

- Moderate levels of physical activity appear to confer a significant health benefit, although greater amounts of activity afford greater protection from premature death (figure 3) [33]. Progressing from lower to higher levels of physical activity has been shown to reduce overall mortality [30,32,34,36]. Vigorous exercise (at least 20 minutes three times a week) combined with regular exercise (at least 30 minutes of moderate activity most days of the week) was associated with a 50 percent decreased mortality risk in an observational study involving over 250,000 men and women aged 50 to 71 years [32]. Data from the Framingham Heart Study show that moderate and high, compared to low, physical activity levels increase life expectancy for men at age 50 by 1.3 and 3.7 years, respectively; results were similar for women (1.5 and 3.5 years) [34].

- Total daily activity energy expenditure may correlate more strongly with mortality benefit than self-reported exercise intensity. Comparing mortality among individuals in the highest versus lowest tertile for activity energy expenditure in a study of 302 high functioning volunteers (age 70 to 82 years), the hazard ratio (HR) for mortality over six years was 0.31 (95% CI 0.14-0.69); self-reported exercise intensity did not differ significantly across the energy tertiles, although frequency of paid employment and stair climbing was greater in the higher energy groups [35].

Cardiovascular disease — A number of studies have shown a strong inverse relationship between habitual exercise and the risk of coronary disease, cardiac events, and cardiovascular death for both primary and secondary prevention (figure 4) [1,38-40]. (See "Exercise and fitness in the prevention of cardiovascular disease".)

Observational studies suggest that exercise may also have the following beneficial effects:

- Aerobic training induces beneficial effects on lipoproteins (eg, decrease in very low density lipoprotein, increase in high density lipoprotein), body composition, and aerobic capacity, as well as improves hemostatic factors associated with thrombosis. (See "Effects of exercise on lipoproteins and hemostatic factors".)

- Regular physical activity is associated with decreased levels of markers of inflammation (CRP and IL6) [41]. (See "C-reactive protein in cardiovascular disease" and "Overview of the risk equivalents and established risk factors for cardiovascular disease", section on 'Inflammatory markers'.)

- Long-term aerobic exercise and resistance (strength) training have a beneficial effect upon the systemic blood pressure [42]. (See "Exercise in the treatment and prevention of hypertension".)
- Exercise may reduce the risk of stroke [43-45]. (See "Exercise and fitness in the prevention of cardiovascular disease" and "Overview of secondary prevention of ischemic stroke".)

Diabetes — Aerobic exercise may improve glycemic control, insulin sensitivity, and may prevent the development of type 2 diabetes in high-risk groups. (See "Effects of exercise in adults with diabetes mellitus" and "Prevention of type 2 diabetes mellitus", section on 'Exercise'.)

Cancer prevention and treatment — Exercise may provide modest protection against breast, intestinal, prostate, endometrial, and pancreatic cancer [46,47]. Substantial observational data suggest that regular physical activity, either occupational or leisure time, appears to be associated with protection from both proximal and distal colorectal cancer [48,49]. In a meta-analysis of 21 studies, there was a significant 27 percent reduced risk of proximal colon cancer when comparing the most versus the least active individuals (relative risk [RR] 0.73, 95% CI 0.66-0.81) [49]. An almost identical result was found for distal colon cancer (RR 0.74, 95% CI 0.68-0.80).

For patients treated for cancer, observational studies have reported a link between survival and exercise, with most of the data coming from survivors with breast, colorectal, or prostate cancers. In addition, interventional studies have shown a direct effect of exercise on other outcomes, including fatigue and quality of life. (See "The roles of diet, physical activity, and body weight in cancer survivorship" and "Cancer-related fatigue: Treatment", section on 'Exercise'.)

Obesity — Preventing or treating obesity may lead to significant health benefits over the course of a lifetime. Compared to a weight loss diet alone, diet coupled with either exercise or exercise and resistance training is associated with a greater reduction in body fat and enhanced preservation of body lean mass, compared to weight loss diet alone. (See "Obesity in adults: Role of physical activity and exercise".)

Aerobic exercise and resistance training, even in the absence of caloric restriction, may result in weight loss and a reduction in body fat [42,50,51]. Long-term (20 year) follow-up of participants in the Coronary Artery Risk Development in Young Adults (CARDIA) study found that habitual activity was associated with less weight gain at middle age, especially in women [52]. However, a 15 year longitudinal study in postmenopausal women found that a minimum of 60 minutes a day of moderate intensity activity, sustained over years, was necessary to prevent weight gain, and was effective only in women whose initial BMI was <25 kg/m2 (normal or underweight) [53].

Other health outcomes

- **Osteoporosis** — Weight-bearing exercise is associated with an increase in bone mineral density in men and women. In addition, among patients with osteoporosis, exercise is associated with a decreased risk of hip fractures. (See "Prevention of osteoporosis", section on 'Physical activity' and "Overview of the management of osteoporosis in postmenopausal women", section on 'Exercise'.)
- **Smoking cessation** — Vigorous exercise modestly facilitates short- and long-term smoking cessation in women when combined with a cognitive-behavioral smoking cessation program [54]. Vigorous exercise also delays weight gain following smoking cessation. (See "Behavioral approaches to smoking cessation".)
- **Gallstones** — Physical activity is associated with a decreased risk of symptomatic cholelithiasis. (See "Epidemiology of and risk factors for gallstones", section on 'Decreased physical activity'.)
- **Function and cognition** — Studies suggest that physical activity may reduce the risk of dementia and cognitive decline in older patients. Exercise has also been associated with improved cognitive function in young adults [55]. (See "Risk factors for cognitive decline and dementia", section on 'Lifestyle and activity' and "Prevention of dementia", section on 'Lifestyle and activity'.)
- **Psychological** — Regular exercise reduces stress, anxiety, and depression [56]. In one randomized trial, higher exercise energy expenditure led to greater improvement in measures of both physical and psychological

quality of life [57].

Exercise is recommended in the treatment of depression. (See "Unipolar major depression in adults: Choosing initial treatment", section on 'Exercise'.)

RISKS OF EXERCISE — The benefits of physical activity far outweigh the possible associated risks in the majority of patients [2]. Musculoskeletal injury is the most common risk of exercise. More serious but much less common risks include arrhythmia, sudden cardiac arrest, and myocardial infarction.

One study analyzed available data from several exercise trials in diverse patient populations (mostly sedentary at baseline and some with identified cardiovascular risk factors) and found that exercise was associated with an adverse change in one or more metabolic risk factors for cardiovascular disease in 8 to 13 percent of participants, while a similar proportion of participants experienced an unusually strong positive change in these risk factors [58]. Based upon measurements in a small sample of controls, the authors felt that these changes were larger than would be expected just with random variation; however, random variation still appears to be a likely explanation for the results. The study did not look at actual cardiovascular event rates.

Any potential risks of routine exercise do not outweigh its benefits, in the absence of a contraindication to exercise. (See 'Contraindications' below.)

Musculoskeletal injury — Acute strains and tears, inflammation of various types, chronic strain, stress fractures, traumatic fractures, nerve palsies, tendonitis, and bursitis all may occur during or as result of physical activity [59,60]. Musculoskeletal injuries vary based on a variety of factors, including age (child, adolescent, adult, older adult), type of activity (eg, contact sports, high impact exercises, walking), and intensity.

Although studies indicate that those who engage in sports activities run a higher risk of incurring minor injury, people who do not participate in sports or other physical activity on a regular basis are more likely to incur more severe injuries when engaging in such activity [61].

Many of the musculoskeletal injuries are secondary to overuse [62,63]. Two of the most common risk factors for injury among runners, for example, are longer running distances and history of previous injury [63]. (See "Musculoskeletal injury in children and skeletally immature adolescents: Overview of treatment principles for nonoperative injuries" and "Overview of running injuries of the lower extremity".)

Arrhythmia — There is an increased risk of arrhythmia during exercise in patients with underlying heart disease or a prior history of arrhythmia. Exercise training may reduce atrial and ventricular arrhythmia risk by increasing myocardial oxygen supply and by reducing sympathetic nervous system activity. (See "Arrhythmia in athletes" and "Risk of sudden cardiac death in athletes".)

A separate issue, ventricular and atrial arrhythmias occurring during exercise testing, is discussed elsewhere. (See "Exercise ECG testing to determine prognosis of coronary heart disease", section on 'Ventricular arrhythmias' and "Exercise ECG testing to determine prognosis of coronary heart disease", section on 'Atrial arrhythmias'.)

Sudden cardiac death — Sudden cardiac death (SCD) is rare, but may occur during physical or sexual activity [64,65]. The risk of SCD in athletes is discussed separately. (See "Risk of sudden cardiac death in athletes".)

The increase in risk is seen in both men and women. In the Physicians' Health Study of 21,481 males followed for 12 years, the absolute risk of SCD during any one episode of vigorous exercise was low (one death per 1.51 million episodes of exercise) [66]. In the Nurses' Health Study of 69,693 women, the absolute risk was even lower, with one death per 36.5 million hours of exertion [67]. The risk of cardiac arrest is less or may not be increased at all if there is habitual, heavy leisure-time physical activity, as noted in both the Physicians' Health Study and the Nurses' Health Study [66,67].

Mechanisms of SCD in those who exercise include coronary artery disease, arrhythmias (especially ventricular tachycardia and ventricular fibrillation), structural heart disease, and myocarditis [68]. Causes of SCD in people who exercise can be divided according to age [64]. SCD is generally a result of atherosclerotic coronary artery disease in those over age 35 years. It is more likely to be due to congenital abnormalities such as hypertrophic cardiomyopathy, coronary anomalies, or to myocarditis in younger individuals. (See "Overview of sudden cardiac arrest and sudden cardiac death", section on 'Exercise'.)

Because the increase in risk of SCD during or just after activity is low, the long-term health benefits of exercise outweigh the risks in patient with and without established heart disease [69].

Myocardial infarction — Physical or sexual activity is associated with a temporary increase in the risk of having a myocardial infarction (MI), particularly among those who exercise infrequently and have multiple cardiac risk factors [65,69,70]. In a study of 1194 patients who completed a survey within two weeks of having an MI, physical exertion at the onset of infarction was reported in 7.1 percent of the case patients compared with 3.9 percent of matched controls prior to the onset of the control event [70]. The adjusted relative risk of having engaged in strenuous physical activity at the onset of the MI was 2.1; the relative risk was much higher in patients who performed regular exercise less than four times per week and compared to those who exercised four or more times per week (relative risk 6.9 versus 1.3).

Although patients with coronary disease are more likely to have a myocardial infarction at the time they are participating in strenuous exercise than when they are not, patients with coronary disease who exercise are overall less likely to have an MI than those with coronary disease who do not exercise. A 12 year prospective study of 2400 men found that men who were in the highest third of vigorous physical activity, compared to the lowest third, experienced a decreased risk of myocardial infarction, regardless of the presence of symptomatic, asymptomatic (EKG changes consistent with ischemia), or no coronary heart disease at baseline (HR 0.71, 0.42, and 0.60, respectively) [71].

Rhabdomyolysis — Subclinical myoglobinemia, myoglobinuria, and elevation of creatine kinase (CK) are common following physical exertion [72]. The CK level can rise several fold, particularly after intense exercise for extended periods of time (eg, marathon running). Rhabdomyolysis may occur following extreme exertion in individuals with normal muscles when the energy supply to muscle is insufficient to meet demands. Severe complications of rhabdomyolysis include renal failure, electrolyte abnormalities (eg, hyperkalemia, metabolic acidosis), and compartment syndrome. (See "Clinical manifestations and diagnosis of rhabdomyolysis".)

Massive rhabdomyolysis may arise with marked physical exertion, particularly when the following risk factors are present [73,74]:

- The individual is physically untrained.
- Exertion occurs in extremely hot, humid conditions. (See "Severe nonexertional hyperthermia (classic heat stroke) in adults".)
- Normal heat loss through sweating is impaired, such as via the use of anticholinergic medications or heavy football equipment.
- An individual with a sickle cell syndrome exercises at high altitude, a setting in which the decreased partial pressure of oxygen causes erythrocyte sickling with subsequent vascular occlusion and muscle ischemia. (See "Variant sickle cell syndromes".)
- Electrolytes abnormalities are present, particularly hypokalemia, which can be partly caused by potassium loss from sweating. (See "Causes of rhabdomyolysis", section on 'Electrolyte disorders'.)
- Metabolic or inflammatory myopathies are present. (See "Approach to the metabolic myopathies" and "Clinical manifestations of dermatomyositis and polymyositis in adults".)

However, rhabdomyolysis can also occur in trained individuals following physical exertion in the absence of these risk factors [75,76].

Bronchoconstriction — Exercise-induced bronchoconstriction occurs in the majority of patients with current symptomatic asthma [77]. The magnitude of exercise-induced bronchoconstriction is correlated with the degree of airway hyperresponsiveness.

Improving a patient's cardiovascular fitness reduces the minute ventilation required for a given level of exercise, thereby decreasing the stimulus for bronchoconstriction. Thus, regular, long-term exercise may be helpful in preventing the onset of exercise-induced bronchoconstriction. (See "Exercise-induced bronchoconstriction".)

Other effects — Hyperthermia, hypothermia, and dehydration are potential preventable risks of physical activity. Heat-related risks range from mild fatigue to death [78]. Dehydration may be a problem itself or can be related to hyperthermia.

Intense exercise can lead to amenorrhea and infertility, particularly in women with low body weight. The "female athlete triad" consists of disordered eating, amenorrhea, and osteoporosis. This is commonly seen in younger individuals, especially those who exercise regularly and intensely. (See "Amenorrhea and infertility associated with exercise".)

Urticaria and anaphylaxis can rarely occur with exercise. (See "Exercise-induced anaphylaxis: Clinical manifestations, epidemiology, pathogenesis, and diagnosis".)

Exercise-associated hyponatremia primarily occurs in athletes participating in aerobic (endurance) events, such as marathons (42.2 km), triathlons (3.8 km swim, 180 km cycling, and 42.2 km running), and ultradistance (100 km) races. (See "Exercise-associated hyponatremia".)

MEDICAL EVALUATION PRIOR TO EXERCISE — Medical evaluation prior to initiation of an exercise program focuses on risks for coronary heart disease and other potential medical comorbidities that might place the patient at risk for one of the complications above.

There is general consensus based on large observational studies that a screening medical evaluation prior to exercise is not necessary for asymptomatic patients at low risk for coronary heart disease. As an example, the Lipid Research Clinics Coronary Primary Prevention Trial found that, of 3617 asymptomatic men with hypercholesterolemia, the cumulative incidence of activity-related acute cardiac events was only 2 percent during a mean follow-up of 7.4 years [79]. Furthermore, although the risk of a cardiac event was increased 2.6-fold in patients with clinically silent, exercise induced ST-segment changes during submaximal exercise ECG testing at study entry, only 11 of the 62 men who experienced an activity-related event had a positive test at entry (sensitivity 18 percent). (See "Screening for coronary heart disease", section on 'Pre-participation testing'.)

However, there may be certain groups in which screening is warranted. Two screening tools, the American Heart Association/American College of Sports Medicine Preparticipation Questionnaire (AAPQ) [80] and the Physical Activity Readiness Questionnaire (PAR-Q) [81] have been developed as self-screening tools to identify individuals who should have a physician assessment prior to initiating a moderately intense exercise regimen. However, in one study that entered data from the National Health and Nutrition Examination Survey (NHANES) for respondents older than 40 years into the AAPQ criteria, over 90 percent would have met criteria for a physician evaluation, making this tool of questionable value [82]. The AAPQ and PAR-Q produced similar results for about 70 percent of respondents.

Although the available data are not strong enough to reach consensus on the identity of groups for which screening is appropriate, many clinicians perform periodic exercise ECG tests in asymptomatic individuals with multiple cardiovascular risk factors including hypercholesterolemia, hypertension, smoking, diabetes, and a history of premature myocardial infarction or sudden cardiac death in a first-degree relative under age 60. A positive exercise ECG test in such patients is associated with an increased risk of subsequent myocardial infarction and death. (See "Screening for coronary heart disease", section on 'Stress testing'.)

When the decision is made to screen for coronary heart disease, no single test is ideal. However, it seems reasonable to conclude, based upon the available data, easy accessibility, and cost considerations, that initial screening with exercise ECG testing is the most prudent approach in high-risk individuals who can exercise and who do not have ECG abnormalities that can limit the detection of ischemic changes.

In addition to determining whether testing should be performed to evaluate for coronary heart disease, the preexercise medical evaluation should attempt to identify other risks for the individual. Factors that may influence risk of injury include:

- Age
- General physical condition
- Exercise history
- Orthopedic history and musculoskeletal risks
- Medication use (eg, beta blockers, calcium channel blockers, digitalis, nitrates, sulfonylureas, and insulin)
- History of pulmonary disease
- Anticipated type of exercise
- Handicaps or disabilities

The clinical encounter provides an opportunity to counsel with respect to the goals of exercise, the importance of establishing and maintaining lifelong physical activity patterns, and to assess the degree of social support such as an exercise group, exercising peers, or family members.

EXERCISE PRESCRIPTION — There is no one exercise prescription for all individuals. A general weekly goal of at least 150 minutes of moderate intensity aerobic activity or 75 minutes of vigorous intensity activity is ideal for many people. As sedentary lifestyles are associated with health risks and even modest increases in physical activity are associated with improved health outcomes, it is also reasonable to advocate for a modest increase in physical activity even if the specific goals above are not met. An individualized approach should be applied toward a specific exercise prescription, injury prevention, and maximizing incentives for maintaining a consistent exercise regimen. (See 'Benefits of exercise' above.)

Exercise characteristics — Several factors are important in considering a specific exercise prescription. These include type of exercise, intensity, frequency, location, and markers indicating adequate degree of exercise during a given workout.

Types of exercise — Although a wide range of physical activities is available to patients, there are few data demonstrating superiority of one activity over another that would lead to substantially greater health benefits. In a comparison of clinical outcomes in two large cohort studies of running and walking respectively, individuals who achieved a threshold level of energy expenditure from either activity had lower rates of hypertension, diabetes, hypercholesterolemia, and possibly coronary heart disease over six years of follow-up. BMI was also reduced with both activities [83].

Patients should select activities or sports that they enjoy to maximize likelihood of continued physical activity. Examples of common lifestyle exercises are brisk walking at 4.8 to 6.4 kilometers (three to four miles) per hour for most healthy adults, active yard work, and dancing. Exercises such as bicycling, jogging, and other leisure sports can also be performed (table 3).

Resistance (strength) training appears to add to the benefits of aerobic (endurance) training for cardiovascular fitness (table 4) [42].

Deciding which type of exercise to recommend may depend on the setting in which the individual engages in exercise, as well as individual preference or exercise goals. A more structured environment with classes (eg, yoga, pilates, dancing) or in a fitness center (with a trainer or specialized equipment) may provide a variety of activities that may engage the individual, but home-based exercise (eg, jogging, using an exercise bike) may result in better adherence given low cost and convenience. Data are lacking in determining the optimal setting to perform exercise (eg, outdoors versus indoors, home versus fitness center) [84,85]. A systematic review of six trials evaluated the efficacy of home-based versus hospital (center)-based exercise programs in older adults [85]. In the short-term, center-based programs were superior to home-based programs in patients with peripheral vascular disease. However, in the long-term, home-based programs were superior to center-based programs in terms of adherence.

Intensity and frequency — Several large cohort studies have found that increasing exercise intensity is associated with a reduction in cardiovascular disease and all-cause mortality (see 'Benefits of exercise' above) [32,34,86]. Most guidelines recommend moderate to vigorous exercise intensity at least a few times per week [2,87]. However, the intensity and frequency of an exercise prescription varies based on a given individual.

One of the most important parameters of exercise is total aerobic activity. A key finding of the 2008 Physical Activity Guidelines for Americans, based on a systematic review of the evidence, was that 500 to 1000 MET-minutes per week was the necessary amount of physical activity to produce substantial health benefits, including a substantial reduction in the risk of premature death and breast cancer (figure 3) [2]. As the term METs (metabolic equivalents) is not readily understandable by many patients, these guidelines recommend the equivalent in minutes of moderate and/or vigorous exercise per week. As an example, 150 minutes of walking (3.3 METs) per week is equal to 500 MET-minutes per week and meets the weekly recommendations for exercise in most individuals.

Higher intensity activity may lead to additional gains in aerobic fitness. As an example, high-intensity interval walking (repeated alternating three minute sets of high and low intensity walking), compared to moderate-intensity continuous walking, resulted in greater improvements in blood pressure and muscle strength in one study [88]. Another popular form of exercise is high-intensity interval training, which involves repeated, brief sessions of high-intensity exercise over short periods of time. Although there is no standard regimen, one program for high-intensity interval training includes 30 seconds of "all-out" effort cycling or running repeated four to six times and separated by four minutes of recovery for a total of two to three minutes of intense training weekly for several weeks [89]. High-intensity interval training is found to have several short-term physiologic benefits, including improved cardiorespiratory fitness [90]. However, the long-term health effects of high-intensity interval training are not known. The potential for greater compliance and duration of exercise with moderate activity and increased injury with high intensity exercise should be factored in to determining an appropriate exercise prescription.

A sedentary person should begin physical activity with short duration of low- or moderate-intensity activity and gradually increase the duration and intensity until the goal is reached. The greatest health benefits appear to be in those who move from sedentary to moderate-level activity [91]. Exercise can be performed for short periods several times a day and integrated into the course of one's daily life. In one randomized trial of previously sedentary healthy adults, subjects who engaged in 30 minutes of moderate-intensity physical activity on most days of the week had similar cardiovascular and blood pressure benefits as those who underwent a structured exercise program involving three or more sessions of supervised vigorous physical activity per week [92]. In one large prospective cohort study, individuals who engaged in brief physical activity (15 minutes daily or 90 minutes weekly) had a 14 percent reduction in all-cause mortality and a three year longer life expectancy compared to those who were inactive [36]. Using less vigorous recommendations for exercise may help more patients increase their activity level and accrue health benefits.

Resistance training can supplement aerobic exercise [93]. One common regimen includes free weights or exercise equipment consisting of 10 to 15 repetitions of each exercise for arms, shoulders, chest, trunk, back, hips, and legs performed two to three times a week.

Markers indicating an adequate degree of exercise include:

- Breathlessness
- Fatigue
- Sweating

Achievement of goal heart rate is **not** necessary [94]. (See "Exercise and fitness in the prevention of cardiovascular disease", section on 'The exercise prescription'.)

Several national and international guidelines have similar goals of exercise intensity and frequency. The World Health Organization and the 2008 Physical Activity Guidelines for Americans recommend at least 150 minutes of moderate intensity aerobic activity or 75 minutes of vigorous intensity activity weekly for all adults [2,87]. Patients with sedentary lifestyles should start with small amounts of physical activity and gradually increase duration, frequency, and intensity over time. Adults with poor mobility should stay as physically active as their condition allows and, if possible, perform physical activity to enhance balance and prevent falls on three or more days weekly. Muscle-strengthening activities that involve major muscle groups should be done on two or more days a week to provide additional benefit. Guidelines from the American Heart Association and the American College of Sports Medicine are similar, recommending either moderate intensity exercise for 30 minutes for a minimum of five days a week, or strenuous exercise for 20 minutes three days a week, or a combination of these activities [95].

Contraindications — Despite the benefits of an exercise program, there are risks as noted above, even in trained athletes (see 'Risks of exercise' above). As a result, the American Heart Association (AHA) published a summary outlining the absolute and relative contraindications for exercise testing and training (table 5). The absolute contraindications include severe cardiac disease (eg, unstable angina, uncontrolled symptomatic heart failure) and acute noncardiac disease (eg, infection, renal failure). (See "Exercise and fitness in the prevention of cardiovascular disease".)

Injury prevention — There are no clear data that indicate which physical activities or sports are safest, nor what degree of activity is optimal to prevent injury. Recommendations for injury prevention should be tailored to specific populations. As an example, older populations may be at risk for falls. As the older population may injure more easily and recover more slowly, some patients will need to have supervised exercise. (See "Falls: Prevention in community-dwelling older persons".)

Strategies to reduce running injuries are discussed separately. (See "Overview of running injuries of the lower extremity", section on 'Training suggestions to reduce injury risk'.)

- **Stretching** — Observational studies and randomized trials have found conflicting results on whether stretching prior to exercise is helpful for preventing injuries [96-98]. Systematic reviews have found that muscle stretching does not reduce delayed-onset muscle soreness after exercise [99,100].

  There is little downside to the warm-up, and we still believe it is reasonable to recommend it prior to exercise. The warm-up can include stretching exercises, walking, or calisthenics; a period of five minutes should be adequate. Stretching exercises should be a slow dynamic movement followed by static stretch that is sustained for approximately 30 seconds. There should be no bouncing into the stretch or during the stretch.

- **Cool-down** — "Cool-down" after exercise for a period of approximately five minutes may facilitate lactate removal from muscles, the slow return from vasodilation, and gradual return of blood to the central circulation [101]. Cooling down leads to an increase in cardiac vagal tone and a reduction in resting heart rate, compared to complete rest without cool-down [102]. The cool-down exercises may include slow walking, calisthenics, or stretching exercises.

Maximizing incentives — The individual should perceive a net health benefit from his or her physical activity. The activity should be enjoyable and the person should feel both competent and safe while active. The activity should be readily accessible on a regular basis, and it should fit easily into the individual's daily schedule. The activity should not generate unbearable financial or social costs. Parents, other family members, and peers can provide a positive influence for initiating and maintaining physical activity.

Physical activity in childhood predicts a continued active lifestyle into and through adulthood [103]. Physically active parents can serve as role models for their children. Schools are also a major community resource to foster increased physical activity and promote a physically active lifestyle in children.

The use of a pedometer may help motivate individuals to increase physical activity. A systematic review found that use of a pedometer worn throughout the day, combined with a specific goal for number of steps taken per day, increased physical activity by 27 percent, and was associated with modest decline in body mass index and blood pressure [104].

Efficacy of exercise counseling — Several systematic reviews have evaluated whether exercise counseling impacts levels of physical activity or secondary outcomes of increased activity (eg, physical fitness or metabolic parameters). Results have mostly supported some effectiveness for increasing self-reported activity levels, but less impact on more objective outcomes. Results of these systematic reviews include the following:

- A 2012 systematic review of randomized trials of primary care promotion of physical activity for sedentary individuals found a small to medium positive effect on self-reported increased activity over 12 months and a nonsignificant positive effect on cardiorespiratory fitness (odds ratio [OR] 1.38, 95% CI 0.98-1.95) [105]. The number needed to treat with an intervention for one additional sedentary adult to achieve recommended minimal levels of activity at 12 months was 12 (7 to 33).
- An updated 2010 systematic review for the United States Preventive Services Task Force (USPSTF) reviewed trials of counseling for exercise and/or dietary change and found that moderate to intensive counseling was associated with small improvements in secondary outcomes (weight, blood pressure, lipids) and self-reported physical activity [106]. Effective interventions were delivered by trained health educators (nutritionists, nurses, or exercise physiologists) and not by primary care clinicians.
- A 2007 systematic review of randomized and non-randomized studies found that counseling targeted to motivated sedentary patients, and tailored to patient's needs, could increase walking up to 30 to 60 minutes weekly at short-term follow-up (6 weeks to 12 months) [107].
- A 2005 systematic review that included only randomized studies with a minimum follow-up of six months found that interventions aimed at increasing physical activity had a moderate impact on self-reported activity (standardized mean difference 0.31, 95% CI 0.12-0.50), but achievement of predetermined goal levels of activity did not meet statistical significance [108].

Recommendations to promote physical activity — The US Preventive Services Task Force (USPSTF) revised earlier recommendations in 2012 and recommends that primary care clinicians may choose to selectively counsel patients to promote a healthful diet and physical activity, targeting patients with increased risk for CVD who exhibit readiness to change and for whom support is available to promote lifestyle changes [109]. This recommendation is based upon the small benefit observed from counseling in the primary care setting, and the time involved in providing the counseling that may otherwise be used to provide services of greater benefit. Nevertheless, the potential health benefits of even modest increases in exercise suggest that counseling to increase physical activity is likely warranted.

More intensive, individualized counseling with scheduled follow-up may be effective [106,110], including a personalized exercise prescription from primary care clinicians [111] or through an exercise referral program [112]. The American Heart Association (AHA) prepared a listing of the most effective strategies to promote exercise, as well as healthy diet, based on a systematic review of studies published between 1999 and 2009 (table 6) [113]. The AHA also prepared a set of population-based strategies to promote physical activity, as well as diet and smoking cessation [114]. For physical activity, strategies include prompts to encourage use of stairs, incentives to commute by active means, increased opportunities, structured programs, and time set aside for physical activity in the school and workplace.

The AHA has also prepared a guide for determining how best to assess the exercise level of a patient or a group of patients, including questionnaires, logs, heart rate monitoring, pedometers, accelerometers, or methodology appropriate in the research setting [115].

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient information: Exercise (The Basics)" and "Patient information: Arthritis and exercise (The Basics)" and "Patient information: Rhabdomyolysis (The Basics)")
- Beyond the Basics topics (See "Patient information: Exercise (Beyond the Basics)" and "Patient information: Arthritis and exercise (Beyond the Basics)".)

SUMMARY AND RECOMMENDATIONS

- Physical inactivity is a major health problem worldwide, particularly in developed countries and among women, older persons, and those with lower incomes. (See 'Physical inactivity and health' above.)
- Sedentary behavior is also prevalent and is associated with a variety of poor health outcomes, including increased mortality, and increased risk for diabetes and cardiovascular disease. These risks do not appear to be mitigated by participation in physical activity. (See 'Physical inactivity and health' above.)
- Moderate and/or vigorous exercise is associated with several beneficial health outcomes, including a decreased risk of obesity, coronary heart disease, stroke, certain types of cancer, and all-cause mortality (table 1). Exercise may also increase the likelihood of stopping tobacco use; reduce disability for activities of daily living in older persons; delay cognitive decline in older adults; and reduce stress, anxiety, and depression. (See 'Benefits of exercise' above.)
- Musculoskeletal injury is the most common risk of exercise. More serious, but less common, risks include arrhythmia, sudden cardiac arrest, and myocardial infarction. However, the benefits of exercise outweigh the potential risks. (See 'Risks of exercise' above.)
- A screening medical evaluation for coronary heart disease prior to starting exercise is not necessary for asymptomatic, low-risk patients. (See 'Medical evaluation prior to exercise' above and "Screening for coronary heart disease".)
- We suggest that all healthy adults incorporate moderate to vigorous exercise into their lifestyle (**Grade 2C**). One option is moderate intensity exercise for 150 minutes a week, vigorous intensity exercise for 75 minutes a week, or an equivalent combination of these activities. Adults with limited exercise capacity due to comorbidity should stay as physically active as their condition allows. Even modest increases in exercise are associated with health benefits. (See 'Exercise prescription' above.)
- The effectiveness of counseling for exercise has not been demonstrated. However, the potential health benefits of exercise suggest that clinicians should counsel patients to increase physical activity on a case-by-case basis. (See 'Exercise prescription' above.)

REFERENCES

1. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA 2009; 301:2024.
2. US Department of Health and Human Services. 2008 physical activity guidelines for Americans. Hyattsville, MD: US Department of Health and Human Services 2008. Available at: www.health.gov/PAGuidelines/guidelines/default.aspx (Accessed on October 17, 2011).
3. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. JAMA 1995; 273:402.
4. U.S. Department of Health and Human Services. Physical Activity and Health: A Report of the Surgeon General. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention,

National Center for Chronic Disease Prevention and Health Promotion, Atlanta, GA 1996.

5. Wee CC, McCarthy EP, Davis RB, Phillips RS. Physician counseling about exercise. JAMA 1999; 282:1583.
6. Eakin E, Brown W, Schofield G, et al. General practitioner advice on physical activity--who gets it? Am J Health Promot 2007; 21:225.
7. Croteau K, Schofield G, McLean G. Physical activity advice in the primary care setting: results of a population study in New Zealand. Aust N Z J Public Health 2006; 30:262.
8. Dumith SC, Hallal PC, Reis RS, Kohl HW 3rd. Worldwide prevalence of physical inactivity and its association with human development index in 76 countries. Prev Med 2011; 53:24.
9. Owen N, Sparling PB, Healy GN, et al. Sedentary behavior: emerging evidence for a new health risk. Mayo Clin Proc 2010; 85:1138.
10. Rey-López JP, Vicente-Rodriguez G, Ortega FB, et al. Sedentary patterns and media availability in European adolescents: The HELENA study. Prev Med 2010; 51:50.
11. Matthews CE, Chen KY, Freedson PS, et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol 2008; 167:875.
12. Centers for Disease Contr9ol and Prevention, National Health and Nutrition Examination Survey Data, 2005-2006. http://www.cdc.gov/nchs/nhanes.htm.
13. Carlson SA, Fulton JE, Schoenborn CA, Loustalot F. Trend and prevalence estimates based on the 2008 Physical Activity Guidelines for Americans. Am J Prev Med 2010; 39:305.
14. Centers for Disease Control and Prevention (CDC). Contribution of occupational physical activity toward meeting recommended physical activity guidelines: United States, 2007. MMWR Morb Mortal Wkly Rep 2011; 60:656.
15. Proper KI, Singh AS, van Mechelen W, Chinapaw MJ. Sedentary behaviors and health outcomes among adults: a systematic review of prospective studies. Am J Prev Med 2011; 40:174.
16. Pavey TG, Peeters GG, Brown WJ. Sitting-time and 9-year all-cause mortality in older women. Br J Sports Med 2015; 49:95.
17. León-Muñoz LM, Martínez-Gómez D, Balboa-Castillo T, et al. Continued sedentariness, change in sitting time, and mortality in older adults. Med Sci Sports Exerc 2013; 45:1501.
18. Matthews CE, Cohen SS, Fowke JH, et al. Physical activity, sedentary behavior, and cause-specific mortality in black and white adults in the Southern Community Cohort Study. Am J Epidemiol 2014; 180:394.
19. Lee IM, Shiroma EJ, Lobelo F, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet 2012; 380:219.
20. Gupta S, Rohatgi A, Ayers CR, et al. Cardiorespiratory fitness and classification of risk of cardiovascular disease mortality. Circulation 2011; 123:1377.
21. van der Ploeg HP, Chey T, Korda RJ, et al. Sitting time and all-cause mortality risk in 222 497 Australian adults. Arch Intern Med 2012; 172:494.
22. Gennuso KP, Gangnon RE, Matthews CE, et al. Sedentary behavior, physical activity, and markers of health in older adults. Med Sci Sports Exerc 2013; 45:1493.
23. Biswas A, Oh PI, Faulkner GE, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. Ann Intern Med 2015; 162:123.
24. Chau JY, Grunseit A, Midthjell K, et al. Sedentary behaviour and risk of mortality from all-causes and cardiometabolic diseases in adults: evidence from the HUNT3 population cohort. Br J Sports Med 2015; 49:737.
25. Shuval K, Finley CE, Barlow CE, et al. Sedentary behavior, cardiorespiratory fitness, physical activity, and cardiometabolic risk in men: the cooper center longitudinal study. Mayo Clin Proc 2014; 89:1052.
26. Matthews CE, Moore SC, Sampson J, et al. Mortality Benefits for Replacing Sitting Time with Different Physical Activities. Med Sci Sports Exerc 2015; 47:1833.
27. Shrestha N, Ijaz S, Kukkonen-Harjula KT, et al. Workplace interventions for reducing sitting at work. Cochrane Database Syst Rev 2015; 1:CD010912.
28. Willis BL, Gao A, Leonard D, et al. Midlife fitness and the development of chronic conditions in later life. Arch Intern Med 2012; 172:1333.
29. Andersen LB, Schnohr P, Schroll M, Hein HO. All-cause mortality associated with physical activity during

leisure time, work, sports, and cycling to work. Arch Intern Med 2000; 160:1621.

30. Paffenbarger RS Jr, Hyde RT, Wing AL, et al. The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. N Engl J Med 1993; 328:538.
31. Gregg EW, Cauley JA, Stone K, et al. Relationship of changes in physical activity and mortality among older women. JAMA 2003; 289:2379.
32. Leitzmann MF, Park Y, Blair A, et al. Physical activity recommendations and decreased risk of mortality. Arch Intern Med 2007; 167:2453.
33. Manson JE, Hu FB, Rich-Edwards JW, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. N Engl J Med 1999; 341:650.
34. Franco OH, de Laet C, Peeters A, et al. Effects of physical activity on life expectancy with cardiovascular disease. Arch Intern Med 2005; 165:2355.
35. Manini TM, Everhart JE, Patel KV, et al. Daily activity energy expenditure and mortality among older adults. JAMA 2006; 296:171.
36. Wen CP, Wai JP, Tsai MK, et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. Lancet 2011; 378:1244.
37. Garatachea N, Santos-Lozano A, Sanchis-Gomar F, et al. Elite athletes live longer than the general population: a meta-analysis. Mayo Clin Proc 2014; 89:1195.
38. Wessel TR, Arant CB, Olson MB, et al. Relationship of physical fitness vs body mass index with coronary artery disease and cardiovascular events in women. JAMA 2004; 292:1179.
39. Myers J, Kaykha A, George S, et al. Fitness versus physical activity patterns in predicting mortality in men. Am J Med 2004; 117:912.
40. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364:937.
41. Hamer M, Sabia S, Batty GD, et al. Physical activity and inflammatory markers over 10 years: follow-up in men and women from the Whitehall II cohort study. Circulation 2012; 126:928.
42. Strasser B, Siebert U, Schobersberger W. Resistance training in the treatment of the metabolic syndrome: a systematic review and meta-analysis of the effect of resistance training on metabolic clustering in patients with abnormal glucose metabolism. Sports Med 2010; 40:397.
43. Wendel-Vos GC, Schuit AJ, Feskens EJ, et al. Physical activity and stroke. A meta-analysis of observational data. Int J Epidemiol 2004; 33:787.
44. Armstrong ME, Green J, Reeves GK, et al. Frequent physical activity may not reduce vascular disease risk as much as moderate activity: large prospective study of women in the United Kingdom. Circulation 2015; 131:721.
45. Howard VJ, McDonnell MN. Physical activity in primary stroke prevention: just do it! Stroke 2015; 46:1735.
46. Michaud DS, Giovannucci E, Willett WC, et al. Physical activity, obesity, height, and the risk of pancreatic cancer. JAMA 2001; 286:921.
47. Kushi LH, Doyle C, McCullough M, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin 2012; 62:30.
48. Wolin KY, Yan Y, Colditz GA, Lee IM. Physical activity and colon cancer prevention: a meta-analysis. Br J Cancer 2009; 100:611.
49. Boyle T, Keegel T, Bull F, et al. Physical activity and risks of proximal and distal colon cancers: a systematic review and meta-analysis. J Natl Cancer Inst 2012; 104:1548.
50. Irwin ML, Yasui Y, Ulrich CM, et al. Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. JAMA 2003; 289:323.
51. Slentz CA, Duscha BD, Johnson JL, et al. Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE--a randomized controlled study. Arch Intern Med 2004; 164:31.
52. Hankinson AL, Daviglus ML, Bouchard C, et al. Maintaining a high physical activity level over 20 years and weight gain. JAMA 2010; 304:2603.
53. Lee IM, Djoussé L, Sesso HD, et al. Physical activity and weight gain prevention. JAMA 2010; 303:1173.
54. Marcus BH, Albrecht AE, King TK, et al. The efficacy of exercise as an aid for smoking cessation in women: a

randomized controlled trial. Arch Intern Med 1999; 159:1229.

55. Loprinzi PD, Kane CJ. Exercise and cognitive function: a randomized controlled trial examining acute exercise and free-living physical activity and sedentary effects. Mayo Clin Proc 2015; 90:450.
56. Herring MP, O'Connor PJ, Dishman RK. The effect of exercise training on anxiety symptoms among patients: a systematic review. Arch Intern Med 2010; 170:321.
57. Martin CK, Church TS, Thompson AM, et al. Exercise dose and quality of life: a randomized controlled trial. Arch Intern Med 2009; 169:269.
58. Bouchard C, Blair SN, Church TS, et al. Adverse metabolic response to regular exercise: is it a rare or common occurrence? PLoS One 2012; 7:e37887.
59. Conn JM, Annest JL, Gilchrist J. Sports and recreation related injury episodes in the US population, 1997-99. Inj Prev 2003; 9:117.
60. Falvey EC, Eustace J, Whelan B, et al. Sport and recreation-related injuries and fracture occurrence among emergency department attendees: implications for exercise prescription and injury prevention. Emerg Med J 2009; 26:590.
61. Diener-Martin E, Bruegger O, Martin B. Physical activity promotion and safety prevention: what is the relationship in different population groups? Br J Sports Med 2011; 45:332.
62. Burns J, Keenan AM, Redmond AC. Factors associated with triathlon-related overuse injuries. J Orthop Sports Phys Ther 2003; 33:177.
63. Wen DY. Risk factors for overuse injuries in runners. Curr Sports Med Rep 2007; 6:307.
64. Corrado D, Migliore F, Basso C, Thiene G. Exercise and the risk of sudden cardiac death. Herz 2006; 31:553.
65. Dahabreh IJ, Paulus JK. Association of episodic physical and sexual activity with triggering of acute cardiac events: systematic review and meta-analysis. JAMA 2011; 305:1225.
66. Albert CM, Mittleman MA, Chae CU, et al. Triggering of sudden death from cardiac causes by vigorous exertion. N Engl J Med 2000; 343:1355.
67. Whang W, Manson JE, Hu FB, et al. Physical exertion, exercise, and sudden cardiac death in women. JAMA 2006; 295:1399.
68. Cheitlin MD, MacGregor J. Congenital anomalies of coronary arteries: role in the pathogenesis of sudden cardiac death. Herz 2009; 34:268.
69. Thompson PD, Franklin BA, Balady GJ, et al. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. Circulation 2007; 115:2358.
70. Willich SN, Lewis M, Löwel H, et al. Physical exertion as a trigger of acute myocardial infarction. Triggers and Mechanisms of Myocardial Infarction Study Group. N Engl J Med 1993; 329:1684.
71. Yu S, Patterson CC, Yarnell JW. Is vigorous physical activity contraindicated in subjects with coronary heart disease? Evidence from the Caerphilly study. Eur Heart J 2008; 29:602.
72. Sayers SP, Clarkson PM. Exercise-induced rhabdomyolysis. Curr Sports Med Rep 2002; 1:59.
73. Santos J Jr. Exertional rhabdomyolysis. Potentially life-threatening consequence of intense exercise. JAAPA 1999; 12:46.
74. Guron G, Marcussen N, Friberg P. Urinary acidification and net acid excretion in adult rats treated neonatally with enalapril. Am J Physiol 1998; 274:R1718.
75. Lonka L, Pedersen RS. Fatal rhabdomyolysis in marathon runner. Lancet 1987; 1:857.
76. Alpers JP, Jones LK Jr. Natural history of exertional rhabdomyolysis: a population-based analysis. Muscle Nerve 2010; 42:487.
77. Randolph C. An update on exercise-induced bronchoconstriction with and without asthma. Curr Allergy Asthma Rep 2009; 9:433.
78. Périard JD, Caillaud C, Thompson MW. Central and peripheral fatigue during passive and exercise-induced hyperthermia. Med Sci Sports Exerc 2011; 43:1657.
79. Siscovick DS, Ekelund LG, Johnson JL, et al. Sensitivity of exercise electrocardiography for acute cardiac events during moderate and strenuous physical activity. The Lipid Research Clinics Coronary Primary Prevention Trial. Arch Intern Med 1991; 151:325.

80. Balady GJ, Chaitman B, Driscoll D, et al. Recommendations for cardiovascular screening, staffing, and emergency policies at health/fitness facilities. Circulation 1998; 97:2283.
81. Shephard RJ, Bailey DA, Mirwald RL. Development of the Canadian Home Fitness Test. Can Med Assoc J 1976; 114:675.
82. Whitfield GP, Pettee Gabriel KK, Rahbar MH, Kohl HW 3rd. Application of the American Heart Association/American College of Sports Medicine Adult Preparticipation Screening Checklist to a nationally representative sample of US adults aged >=40 years from the National Health and Nutrition Examination Survey 2001 to 2004. Circulation 2014; 129:1113.
83. Williams PT, Thompson PD. Walking versus running for hypertension, cholesterol, and diabetes mellitus risk reduction. Arterioscler Thromb Vasc Biol 2013; 33:1085.
84. Foley A, Hillier S, Barnard R. Effectiveness of once-weekly gym-based exercise programmes for older adults post discharge from day rehabilitation: a randomised controlled trial. Br J Sports Med 2011; 45:978.
85. Ashworth NL, Chad KE, Harrison EL, et al. Home versus center based physical activity programs in older adults. Cochrane Database Syst Rev 2005; :CD004017.
86. Wannamethee SG, Shaper AG, Alberti KG. Physical activity, metabolic factors, and the incidence of coronary heart disease and type 2 diabetes. Arch Intern Med 2000; 160:2108.
87. World Health Organization. Global recommendations on physical activity for health. http://www.who.int/dietphysicalactivity/pa/en/index.html (Accessed on May 03, 2011).
88. Nemoto K, Gen-no H, Masuki S, et al. Effects of high-intensity interval walking training on physical fitness and blood pressure in middle-aged and older people. Mayo Clin Proc 2007; 82:803.
89. Gibala MJ, McGee SL. Metabolic adaptations to short-term high-intensity interval training: a little pain for a lot of gain? Exerc Sport Sci Rev 2008; 36:58.
90. Wisløff U, Ellingsen Ø, Kemi OJ. High-intensity interval training to maximize cardiac benefits of exercise training? Exerc Sport Sci Rev 2009; 37:139.
91. Blair SN, Kohl HW 3rd, Barlow CE, et al. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. JAMA 1995; 273:1093.
92. Dunn AL, Marcus BH, Kampert JB, et al. Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: a randomized trial. JAMA 1999; 281:327.
93. Ciccolo JT, Pettee Gabriel KK, Macera C, Ainsworth BE. Association between self-reported resistance training and self-rated health in a national sample of U.S. men and women. J Phys Act Health 2010; 7:289.
94. Bosquet L, Merkari S, Arvisais D, Aubert AE. Is heart rate a convenient tool to monitor over-reaching? A systematic review of the literature. Br J Sports Med 2008; 42:709.
95. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation 2007; 116:1081.
96. McHugh MP, Cosgrave CH. To stretch or not to stretch: the role of stretching in injury prevention and performance. Scand J Med Sci Sports 2010; 20:169.
97. Woods K, Bishop P, Jones E. Warm-up and stretching in the prevention of muscular injury. Sports Med 2007; 37:1089.
98. Small K, Mc Naughton L, Matthews M. A systematic review into the efficacy of static stretching as part of a warm-up for the prevention of exercise-related injury. Res Sports Med 2008; 16:213.
99. Herbert RD, de Noronha M. Stretching to prevent or reduce muscle soreness after exercise. Cochrane Database Syst Rev 2007; :CD004577.
100. Henschke N, Lin CC. Stretching before or after exercise does not reduce delayed-onset muscle soreness. Br J Sports Med 2011; 45:1249.
101. American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. Med Sci Sports Exerc 1998; 30:975.
102. Takahashi T, Okada A, Hayano J, Tamura T. Influence of cool-down exercise on autonomic control of heart rate during recovery from dynamic exercise. Front Med Biol Eng 2002; 11:249.
103. Salonen MK, Kajantie E, Osmond C, et al. Prenatal and childhood growth and leisure time physical activity in

adult life. Eur J Public Health 2011; 21:719.

104. Bravata DM, Smith-Spangler C, Sundaram V, et al. Using pedometers to increase physical activity and improve health: a systematic review. JAMA 2007; 298:2296.
105. Orrow G, Kinmonth AL, Sanderson S, Sutton S. Effectiveness of physical activity promotion based in primary care: systematic review and meta-analysis of randomised controlled trials. BMJ 2012; 344:e1389.
106. Lin JS, O'Connor E, Whitlock EP, Beil TL. Behavioral counseling to promote physical activity and a healthful diet to prevent cardiovascular disease in adults: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2010; 153:736.
107. Ogilvie D, Foster CE, Rothnie H, et al. Interventions to promote walking: systematic review. BMJ 2007; 334:1204.
108. Hillsdon M, Foster C, Thorogood M. Interventions for promoting physical activity. Cochrane Database Syst Rev 2005; :CD003180.
109. Moyer VA, U.S. Preventive Services Task Force. Behavioral counseling interventions to promote a healthful diet and physical activity for cardiovascular disease prevention in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2012; 157:367.
110. Lawton BA, Rose SB, Raina Elley C, et al. Exercise on prescription for women aged 40-74 recruited through primary care: two year randomised controlled trial. Br J Sports Med 2009; 43:120.
111. Grandes G, Sanchez A, Sanchez-Pinilla RO, et al. Effectiveness of physical activity advice and prescription by physicians in routine primary care: a cluster randomized trial. Arch Intern Med 2009; 169:694.
112. Pavey TG, Taylor AH, Fox KR, et al. Effect of exercise referral schemes in primary care on physical activity and improving health outcomes: systematic review and meta-analysis. BMJ 2011; 343:d6462.
113. Artinian NT, Fletcher GF, Mozaffarian D, et al. Interventions to promote physical activity and dietary lifestyle changes for cardiovascular risk factor reduction in adults: a scientific statement from the American Heart Association. Circulation 2010; 122:406.
114. Mozaffarian D, Afshin A, Benowitz NL, et al. Population approaches to improve diet, physical activity, and smoking habits: a scientific statement from the American Heart Association. Circulation 2012; 126:1514.
115. Strath SJ, Kaminsky LA, Ainsworth BE, et al. Guide to the assessment of physical activity: Clinical and research applications: A scientific statement from the American Heart Association. Circulation 2013; 128:00.

Topic 2786 Version 58.0

GRAPHICS

Examples of moderate physical activity

- Washing and waxing a car for 45-60 minutes
- Washing windows or floors for 45-60 minutes
- Playing volleyball for 45 minutes
- Playing touch football for 30-45 minutes
- Gardening for 30-45 minutes
- Wheeling self in wheelchair for 30-40 minutes
- Walking 1 3/4 miles in 35 minutes (20 min/mile)
- Basketball (shooting baskets) for 30 minutes
- Bicycling 5 miles in 30 minutes
- Dancing fast (social) for 30 minutes
- Pushing a stroller 1.5 miles in 30 minutes
- Raking leaves for 30 minutes
- Walking 2 miles in 30 minutes (15 min/mile)
- Water aerobics for 30 minutes
- Swimming laps for 20 minutes
- Wheelchair basketball for 20 minutes
- Basketball (playing a game) for 15-20 minutes
- Bicycling 4 miles in 15 minutes
- Jumping rope for 15 minutes
- Running 1.5 miles in 15 min (10 min/mile)
- Shoveling snow for 15 minutes
- Stairwalking for 15 minutes

A moderate amount of physical activity is roughly equivalent to physical activity that uses approximately 150 calories (kcal) of energy per day, or 1000 calories per week. Some activities can be performed at various intensities; the suggested durations correspond to the expected intensity of effort.

Graphic 73838 Version 3.0

Benefits of regular physical activity

Reduces the risk of dying prematurely
Reduces the risk of dying from heart disease
Reduces the risk of stroke
Reduces the risk of developing diabetes
Reduces the risk of developing high blood pressure
Helps reduce blood pressure in people who already have high blood pressure
Reduces the risk of developing colon cancer
Reduces feelings of depression and anxiety
Helps control weight
Helps build and maintain healthy bones, muscles and joints
Helps older adults become stronger and better able to move about without falling
Promotes psychological well-being

Graphic 51565 Version 1.0

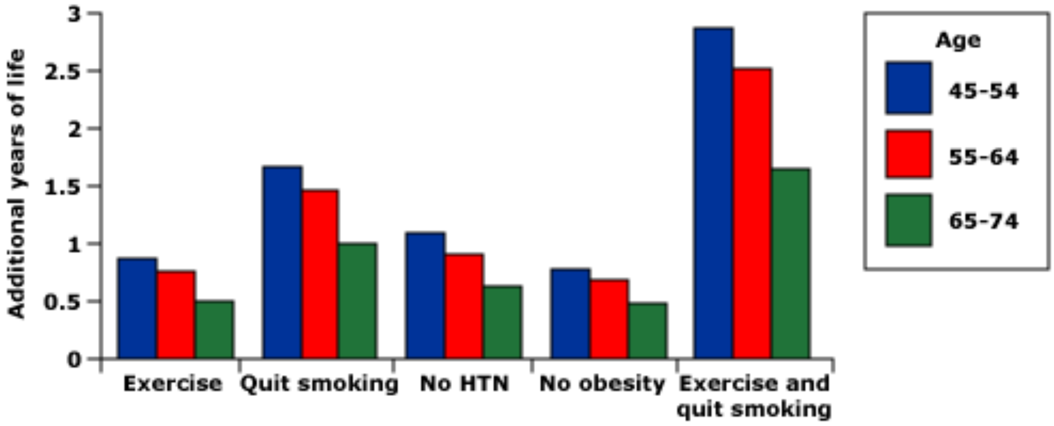
Evidence for health benefits associated with regular physical activity (2008 Physical Activity Guideline)

Adults and older adults
Strong evidence
Lower risk of early death
Lower risk of coronary heart disease
Lower risk of stroke
Lower risk of high blood pressure
Lower risk of adverse blood lipid profile
Lower risk of type 2 diabetes
Lower risk of metabolic syndrome
Lower risk of colon cancer
Lower risk of breast cancer
Prevention of weight gain
Weight loss, particularly when combined with reduced calorie intake
Improved cardiorespiratory and muscular fitness
Prevention of falls
Reduced depression
Better cognitive function (for older adults)
Moderate to strong evidence
Better functional health (for older adults)
Reduced abdominal obesity
Moderate evidence
Lower risk of hip fracture
Lower risk of lung cancer
Lower risk of endometrial cancer
Weight maintenance after weight loss
Increased bone density
Improved sleep quality

US Department of Health & Human Services. 2008 Physical Activity Guidelines for Americans.

Graphic 59285 Version 1.0

Lifestyle factors and survival



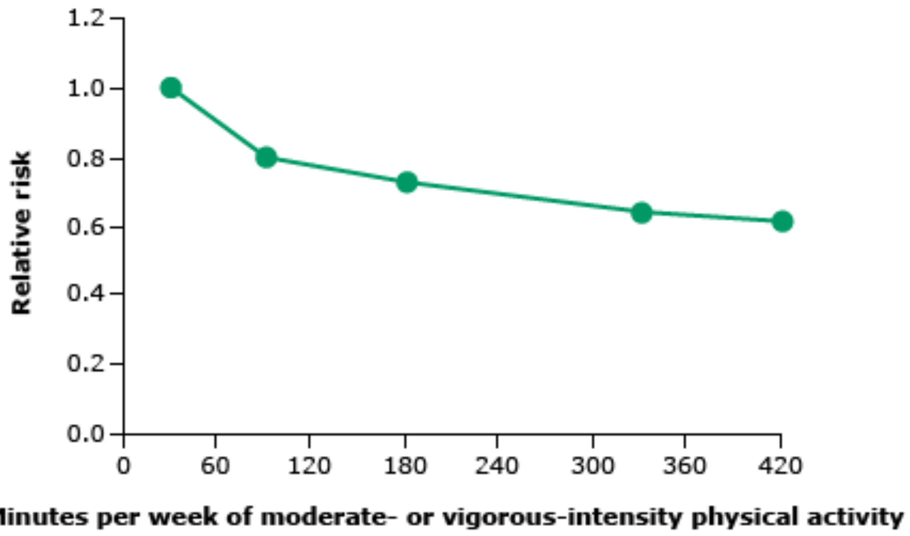
Additional years of life according to age associated with adoption or maintenance of a favorable physical-activity (≥4.5 metabolic equivalents, or METS) level and other characteristics between 1962 or 1966 and 1977, as estimated from mortality rates among 10,269 male Harvard alumni from 1977 through 1985. Prolongation of life was greater in younger men and with cessation of smoking, alone or particularly with exercise. The effect of each individual factor was adjusted for differences in other factors.

HTN: hypertension.

Data from Paffenberger RS Jr, Hyde RT, Wing AL, et al. N Engl J Med 1993; 328:538.

Graphic 56864 Version 2.0

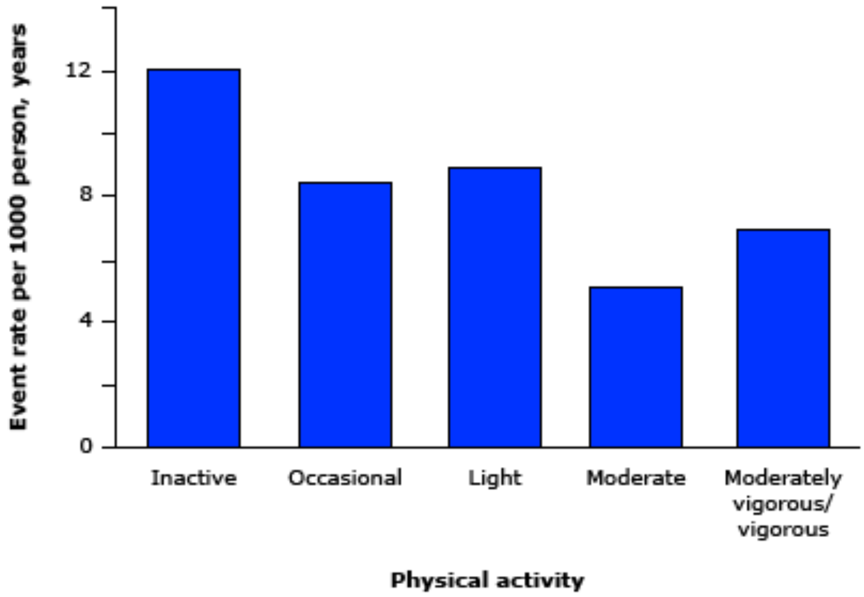
The risk of dying prematurely declines as people become physically active



Reproduced from: Physical Activity Guidelines for Americans. US Department of Heath and Human Services. Available at http://www.health.gov/paguidelines/pdf/paguide.pdf.

Graphic 74679 Version 3.0

Beneficial effects of any physical activity on coronary heart disease



Coronary events are less frequent among those who exercise. In a study of 5159 men, aged 40 to 49 years, followed for an average of almost 19 years, the age-adjusted coronary heart disease event rate per 1000 person-years is lower in those who perform any physical activity compared to inactive subjects.

Data from: Wannamethee SG, Shaper AG, Alberti KG. Arch Intern Med 2000; 160:2108.

Graphic 81608 Version 2.0

Leisure activity energy expenditure in metabolic equivalents (METs)

Activity	Mean	Range
Archery	3.9	3-4
Backpacking	--	5-11
Badminton	5.8	4-9+
Basketball		
Gameplay	8.3	7-12+
Non-game	--	3-9
Billiards	2.5	--
Bowling	--	2-4
Boxing		
In-ring	13.3	--
Sparring	8.3	--
Canoeing, rowing, kayaking	--	3-8
Conditioning exercise	--	3-8+
Climbing hills	7.2	5-10+
Cricket	5.2	4.6-7.4
Croquet	3.5	--
Cycling		
Pleasure or to work	--	3-8+
10 mph	7.0	--
Dancing (social, square, tap)	--	3.7-7.4
Dancing (aerobic)	--	6-9
Fencing	--	6-10+
Field hockey	8.0	--
Fishing		
From bank	3.7	2-4
Wading in stream	--	5-6
Football (touch)	7.9	6-10
Golf		
Power cart	--	2-3
Walking (carrying bag or pulling cart)	5.1	4-7
Handball	--	8-12+
Hiking (cross country)	--	3-7
Horseback riding		
Galloping	8.2	--

Trotting	6.6	--
Walking	2.4	--
Horseshoe pitching	--	2-3
Hunting (bow or gun)		
Small game (walking, carrying light load)	--	3-7
Big game (dragging carcass, walking)	--	3-14
Judo	13.5	--
Mountain climbing	--	5-10+
Music playing	--	2-3
Paddleball, raquetball	9	8-12
Rope jumping	11	--
60-80 skips/min	9	--
120-140 skips/min	--	11-12
Running		--
12 min/mile	8.7	--
11 min/mile	9.4	--
10 min/mile	10.2	--
9 min/mile	11.2	--
8 min/mile	12.5	--
7 min/mile	14.1	--
6 min/mile	16.3	--
Sailing	--	2-5
Scuba diving	--	5-10
Shuffleboard	--	2-3
Skating, ice and roller	--	5-8
Skiing, snow		
Downhill	--	5-8
Cross country	--	6-12+
Skiing, water	--	5-7
Sledding, tobogganing	--	4-8
Snowshoeing	9.9	7-14
Squash	--	8-12+
Soccer	--	5-12+
Stairclimbing	--	4-8
Swimming	--	4-8+
Table tennis	4.1	3-5
Tennis	6.5	4-9+
Volleyball	--	3-6

Adapted from: American College of Sports Medicine, Guidelines for Exercise Testing and Prescription, 3rd Ed, Lea and Febiger, Philadelphia 1986, p.20.

Graphic 66344 Version 2.0

Exercise prescription for endurance and resistance training for cardiovascular fitness

Endurance training	
Frequency	3 to 5 days/wk
Intensity	55 to 90 percent maximum HR OR
	40 to 85 percent maximum VO2 OR HRR
Duration	20 to 60 min
Modality	
Lower extremity	Walking
	Jogging/running
	Stairclimber
Upper extremity	Arm ergometry
Combined	Rowing
	Cross-country ski machine
	Combined arm/leg cycle
	Swimming
	Aerobics
Resistance training	
Frequency	2 to 3 days/wk
Intensity	1 to 3 sets of 8 to 15 RM for each muscle group
Modality	
Lower extremity	Leg extensions, curls, presses
	Adductors/abductors
Upper extremity	Biceps curls
	Triceps extensions
	Bench/overhead presses
	Lateral pulldowns/raises
	Benchovers/seated rowing

Modalities listed here are not all-inclusive.
Maximum heart rate (HR) indicates 220 minus age or peak HR on exercise test.
Heart rate reserve (HRR) = (Peak HR - Resting HR); goal intensity is 40 to 85 percent of the HRR added to the resting HR.

VO2: measured oxygen intake; RM: maximum number of times a load can be lifted before fatigue.

Data from: Shepard RJ, Balady GJ. Circulation 1999; 99:963.

Graphic 75107 Version 7.0

Absolute and relative contraindications to exercise treadmill testing

Absolute
Acute myocardial infarction (within two days)
Unstable angina
Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise
Symptomatic severe aortic stenosis
Uncontrolled symptomatic heart failure
Acute pulmonary embolus or pulmonary infarction
Acute myocarditis or pericarditis
Active endocarditis
Acute aortic dissection
Acute noncardiac disorder that may affect exercise performance or be aggravated by exercise (eg, infection, renal failure, thyrotoxicosis)
Inability to obtain consent
Relative*
Left main coronary stenosis or its equivalent
Moderate stenotic valvular heart disease
Electrolyte abnormalities
Severe hypertension (systolic ≥200 mmHg and/or diastolic ≥110 mmHg)
Tachyarrhythmias or bradyarrhythmias, including atrial fibrillation with uncontrolled ventricular rate
Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
Mental or physical impairment leading to inability to cooperate
High-degree atrioventricular block

* Relative contraindications can be superseded if benefits outweigh risks of exercise.

Data from Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. Circulation 2001; 104:1694; and Gibbons, RJ, Balady, GJ, Bricker, JT, et al. ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). Circulation 2002; 106:1883.

Graphic 80110 Version 3.0

American Heart Association (AHA) recommendations for counseling to promote dietary and physical activity changes

Cognitive-behavioral strategies for promoting behavior change
Class I
Design interventions to target dietary and physical activity behaviors with specific, proximal goals. (Level of evidence: A)
Provide feedback on progress toward goals. (Level of evidence: A)
Provide strategies for self-monitoring. (Level of evidence: A)
Establish a plan for frequency and duration of follow-up contacts (eg, in-person, oral, written, electronic) in accordance with individual needs to assess and reinforce progress toward goal achievement. (Level of evidence: A)
Utilize motivational interviewing strategies, particularly when an individual is resistant or ambivalent about dietary and physical activity behavior change. (Level of evidence: A)
Provide for direct or peer-based long-term support and follow-up, such as referral to ongoing community-based programs, to offset the common occurrence of declining adherence that typically begins at 4-6 months in most behavior change programs. (Level of evidence: B)
Incorporate strategies to build self-efficacy into the intervention. (Level of evidence: A)
Use a combination of 2 of the above strategies (eg, goal setting, feedback, self-monitoring, follow-up, motivational interviewing, self-efficacy) in an intervention. (Level of evidence: A)
Class II
Use incentives, modeling, and problem solving strategies. (Level of evidence: B)
Intervention processes and/or delivery strategies
Class I
Use individual- or group-based strategies. (Level of evidence: A)
Use individual-oriented sessions to assess where the individual is in relation to behavior change, to jointly identify the goals for risk reduction or improved cardiovascular health, and to develop a personalized plan to achieve it. (Level of evidence: A)
Use group sessions with cognitive-behavioral strategies to teach skills to modify the diet and develop a physical activity program, to provide role modeling and positive observational learning, and to maximize the benefits of peer support and group problem solving. (Level of evidence: A)
For appropriate target populations, use Internet- and computer-based programs to target dietary and physical activity change; adding a form of electronic-counseling improves outcomes. (Level of evidence: B)
Class IIa
Use individualized rather than nonindividualized print- or media-only delivery strategies. (Level of evidence: A)
Addressing cultural and social context variables that influence behavioral change

Class IIa
Utilize church, community, work, or clinic settings for delivery of interventions. (Level of evidence: B)
Use a multiple-component delivery strategy that includes a group component rather than individual-only or group-only approaches. (Level of evidence: A)
Use culturally-adapted strategies, including use of peer or lay health advisors to increase trust; tailor health messages and counseling strategies to be sensitive to the cultural beliefs, values, language, literacy, and customs of the target population. (Level of evidence: A)
Use problem solving to address barriers to physical activity and dietary change, such as transportation barriers, poor local safety, and lack of access to affordable healthier foods and physical activity. (Level of evidence: B)

PA: physical activity; Class I: evidence of effectiveness; Class II: conflicting evidence; Class IIa: weight of evidence in favor; Level of evidence A: data derived from multiple randomized clinical trials; Level of evidence B: data derived from a single randomized trial or nonrandomized studies; Level of evidence C: expert opinion or case studies.

Reprinted with permission from: Artinian NT, Fletcher GF, Mozaffarian D, et al. Interventions to promote physical activity and dietary lifestyle changes for cardiovascular risk factor reduction in adults: a scientific statement from the American Heart Association. Circulation 2010; 122:406.

Graphic 59899 Version 9.0

Disclosures

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