# Cardiovascular Disease: Optimal Approaches to Risk Factor Modification of Diet and Lifestyle

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## Opinion statement

Cardiovascular disease (CVD) accounts for almost 50% of all deaths in industrialized nations. As much as 70% of CVD can be prevented or delayed with dietary choices and lifestyle modifications. Western-style diets, sedentary lifestyles, and cigarette smoking are key modifiable CVD risk factors. Although CVD mortality was trending downward for almost 50 years, a resurgence, both nationally and globally, has occurred. A growing epidemic of obesity ("globesity"), decreasing physical activity, and persistent cigarette smoking are major behavioral factors underlying this change. Diet and lifestyle increase CVD risk both directly and indirectly. Direct effects include biological, molecular, and physiologic alterations, including inflammatory stimuli and oxidative stresses. Indirect effects include diabetes, dyslipidemias, and hypertension. However, trials studying links between diet and CVD remain notoriously difficult to execute and interpret. Diet interventions are typically confounded by other aspects of an overall diet as well as by lifestyle. Furthermore, benefits derived from a specific dietary or lifestyle intervention may not be proportional to the degree of risk posed by the unhealthy diet or lifestyle. Nonetheless, therapeutic rationale for diet and lifestyle are supported by basic and clinical research. Key components of a healthy aggregate diet include 1) reduced caloric intake; 2) reduced total fat, saturated fat, trans fat, and cholesterol with proportional increases in monosaturated, n-3 (omega-3), and n-6 fatty acids; 3) increased dietary fiber, fruit, and vegetables; 4) increased micronutrients (eg, folate, $B_6$, $B_{12}$); 5) increased plant protein in lieu of animal protein; 6) reduced portions of highly processed foods; and 7) adopting a more Mediterranean or "prudent" dietary pattern over the prevailing "western" dietary pattern. Key lifestyle interventions include increased physical activity and smoking cessation. Translation of the benefits of healthy diet and lifestyle to the wider population requires both individual and public health strategies targeting at-risk groups.

## Introduction

Major technological and pharmacologic advances have contributed to improved cardiovascular outcomes, but the impact of behavioral choices (ie, diet and lifestyle) remain as fundamental components to cardiovascular health. An epidemiologic perspective of cardiovascular disease (CVD) highlights the impact of such choices. CVD in the United States accounted for 5% to 10% of total mortality in the mid-1800s, but a century later CVD-

related deaths more than tripled, reaching a peak of 35% to 65% of total mortality [1]. During this period, an "epidemiologic transition" resulted in fundamental shifts in the way people ate and lived; higher consumption of western-style diets with increased saturated fats and refined carbohydrates (CHOs), less physically demanding lifestyles, and cigarette smoking were the major determinants of increased CVD prevalence [2•].

Certain behavioral risk factors, particularly dietary fat and smoking, were then targeted and modified as health care goals. In the United States, fat intake as a percentage of total daily calories fell from a high of 45% in 1965 to a low of 34% in 1995. Smoking fell from a peak prevalence of 57% and 34% among men and women, respectively, in 1955 to 26% and 21% by 2000. Major improvements in pharmacologic and cardiovascular health care technologies also accrued. The result was a substantial decline in CVD—especially heart disease and stroke—during the latter part of the 20th century. Overall, age-adjusted US deaths from CVD fell proportionately from a peak of almost 700 per 100,000 population in 1970 to 341 per 100,000 in 2000 [3••].

More recently, a rising tide of global obesity ("globesity") and increasing sedentary living are eroding these gains [4]. Widely available high-calorie convenience foods and sedentary lifestyles have led to an obesity epidemic across all socioeconomic strata, including the young and socioeconomically disadvantaged. Likewise, obesity-mediated CVD risk factors—type 2 diabetes, dyslipidemia, hypertension, and the metabolic syndrome—have also escalated [4].

In the midst of this looming threat to cardiovascular health, the importance of diet and lifestyle interventions is clear. Together, they can prevent or delay 74% to 82% of CVD in high-risk populations [5]. Whereas time and resource limitations often lead health care providers to lessen their focus on diet and lifestyle, the importance of such choices has never been greater.

# Optimal approaches: behavioral risk factor interventions

- The American College of Cardiology categorized the data on the efficacy of diet and lifestyle interventions in modifying CVD risk. Gaziano *et al.* [6••] modified these into class 1, class 2, and class 3 categories by incorporating data from cost-efficacy studies [7]. Overall, this table highlights the benefits of diet and lifestyle interventions, but also underscores that the data on diet and lifestyle interventions remain limited.

## Diet and established CVD risk factors

- Examination of diet-CVD relationships has progressed from early basic research correlating saturated fat intake with atherosclerosis to today's broader perspectives on the total diet and lifestyle on cardiovascular health. The seven countries study by Keys *et al.* [8] pioneered research on dietary fat, serum cholesterol, and coronary heart disease (CHD) risk. The Framingham investigators coined the term "risk factors" to describe the relationship between cholesterol and CVD [8,9]. On a physiologic level, diet directly modifies CVD risk in terms of oxidative and inflammatory stresses, thrombosis, endothelial function, insulin secretion, and homocysteine metabolism [10]. Diet also exacerbates other CVD risk factors (eg, lipids, hypertension, type 2 diabetes, and obesity-mediated risk factors [ie, the metabolic syndrome]).

### Dietary fats, serum lipids, and CVD

- Pioneering work on diet and serum cholesterol by Keys *et al.* [8] established a relationship between total fat intake and serum cholesterol, but not clinical end points. Keys [11] and Hegsted *et al.* [12] devised equations that used serum cholesterol as a surrogate marker of CHD risk; these served as the standard in several metabolic studies that followed. The American Heart Association and the 1992 United States Department of Agriculture pyramid subsequently advocated diets aimed at replacing dietary fat with complex

CHOs (more starch, less simple sugars). Such diets lowered total and low-density lipoprotein (LDL) cholesterol, but they also lowered high-density lipoprotein (HDL) cholesterol with no appreciable change in the important total cholesterol:HDL ratio. Diets high in simple sugars elevated serum triglycerides. Subsequent recognition of a strong inverse relationship between HDL cholesterol and CHD, and the greater predictive power of the total cholesterol:HDL ratio (over total cholesterol) underscored that the cholesterol-heart disease story extended beyond total serum cholesterol.

- Despite the observation made in the seminal seven countries study by Keys *et al.* [8] that Crete—the country with the highest fat intake (40%, mainly olive oil) as a percentage of total energy—exhibited the lowest rate of CHD [8], fats tended to be viewed in combination, without distinguishing the differences between different subtypes. However, it subsequently became appreciated that fats vary considerably in their ability to influence serum lipids. Although all saturated fatty acids (SFAs) raise LDL cholesterol, this effect varies from one SFA to another. More significantly, substituting SFAs with monounsaturated fatty acids (MUFAs) lowers LDL without affecting HDL cholesterol. Increased MUFA also modifies blood glucose and triglyceride control. Foods high in MUFAs (eg, nuts) exert beneficial effects on serum lipid profile and are inversely proportional to CVD. Polyunsaturated fatty acids (PUFAs) lower total and LDL cholesterol, but elevate HDL cholesterol, although less so than SFAs. PUFAs may be particularly useful in reducing insulin resistance in patients with the metabolic syndrome and type 2 diabetes [10,13,14,15••].
- The structure of the lipid molecule impacts on its relationship to CVD. Most trans fats (both trans MUFAs and trans PUFAs) are formed during hydrogenation and deodorization of vegetable oils, such that they are ubiquitous in partially hydrogenated vegetable oils (eg, stick margarines, shortenings, and cooking fats), and commercial bakery products. Trans fats are also formed when vegetable oils are heated (eg, during deep frying). Lesser amounts of trans fats are consumed in cow's milk and beef—byproducts of ruminant bacterial action. Overall, trans fats average 2.6% of total daily energy intake or 7.4% of total fats consumed in the United States. Most dietary studies on trans fats involve trans MUFAs, with very few studies on trans PUFAs. Trans fats raise serum LDL cholesterol, triglycerides, and lipoprotein (a); they lower HDL cholesterol. Trans fats may inhibit the fibrinolytic pathway, impair endothelial function, and promote insulin resistance. Cohort studies uniformly show increased risk of CHD with higher trans fat intakes. Increased consumption of processed foods, fried foods, margarines, spreads, baked products, and so forth, parallels increased rates of CHD [16••].
- In contrast, diets high in fish and fish oils reduce CVD. The observation that Greenland Eskimos and the Japanese—whose diets were high in fish and fish oils—had lower rates of heart disease triggered much interest in the marine long-chain omega-3 (n-3) fatty acids and their possible impact on CVD. Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and their plant-based precursor α-linolenic acid found in flax seed, canola, and soybean oils, have consistently reduced CHD in studies ranging from population studies, cohort studies, and clinical trials, as both primary and secondary CHD prevention. In the DART (Diet and Reinfarction Trial), patients who ate fish at least twice weekly or consumed a fish oil supplement (1.5 g/d) had one third lower CHD mortality after 2 years follow-up. Likewise, in the GISSI-Prevenzione trial, 3 months of treatment with daily fish oil supplements (1 g/d of EPA and DHA) led to a 15% lower risk of death, nonfatal myocardial infarction (MI), and stroke [15••].

- Omega-3 fatty acids can markedly inhibit atherosclerotic plaque progression, coronary thrombosis, and post-MI cardiac arrhythmias, especially ventricular fibrillation leading to cardiac arrest. They markedly lower plasma very low density lipoprotein and triglyceride levels by suppressing hepatic triglyceride production, reducing postprandial lipemia, and preventing CHO-induced hypertriglyceridemia. These benefits appear to hold true regardless of the source of omega-3 fats—marine, or from plant-based foods or dietary supplements. Farmed fish (eg, catfish) exhibit a 50% to 75% lower concentration of EPA and DHA, but their content in farmed and wild salmon appears similar.

## Carbohydrates and dietary fiber

- Dietary CHOs are a diverse group, with a range of effects on CVD. Although it was once common to explain CHOs relative to their structures (ie, simple sugars [eg, monosaccharides and disaccharides] and complex CHOs [eg, polysaccharides]), it is more useful to discuss CHOs in terms of their physiology. Complex CHOs (starch) found in potatoes, white bread, and highly refined wheat products behave metabolically differently from complex CHO contained in oats, bread, or other foods with whole wheat grains. Dietary fiber—the complex nondigestible CHO found in many vegetables—confers distinctive differences (benefits).
- CHOs account for more than 50% of total calories in the American diet—the bulk coming from breads, sweetened beverages, baked cereals, potatoes, and sugar-laden spreads. There is a consistent association with between fiber-depleted CHO (sugar, starch, and highly refined CHO) intake and increased risk of obesity and risk for CVD [17•].
- The concept of glycemic index (GI) underscores the physiologic behaviors and effects of different types of CHO by grouping foods relative to their digestion and absorption. Lower GI foods (eg, oats, barley, and pasta) bring about smoother blood glucose absorption and insulin response. Insulin secretion following consumption of low GI foods is relatively moderated in comparison with consumption of high GI foods (eg, white bread and sugary beverages). Glycemic load (GL)—the average weighted GI times the amount of CHO consumed—is an even more meaningful concept. Foods with higher GLs raise triglycerides, lower HDL, and may worsen glycemic control and insulin resistance.
- Whole grains and dietary fiber, both low GI foods, are consistently linked to a reduced risk of CHD, independent of their cholesterol-lowering benefits. CVD risk reduction is more strongly linked to cereal fiber (especially mucinous fiber-like oats) than to vegetable fiber. Dietary fiber improves glucose physiology in patients with impaired glucose tolerance and diabetes. In general, increased fiber intake improves insulin sensitivity, assists weight control, lowers blood pressure, and modifies the overall risk profile of the metabolic syndrome. Consistently, dietary fiber intake is inversely associated with the risk of total and ischemic stroke [15••,17•,18].
- On the epidemiologic front, the dietary guidelines to replace fat with complex CHO that were particularly popular in the 1990s may have contributed to the fattening of America and today's CVD risk escalation. People are consuming more CHO calories, usually opting for highly refined CHO varieties with the least healthy implications.

### Fruits and vegetables (including legumes)

- People with high fruit and vegetable intake have consistently shown lower rates of CVD (especially MI) and chronic disease [19]. In contrast, studies of vitamins and other isolated food nutrients from fruits and vegetables have not always demonstrated benefit. In the Physicians' Health Study, a 12-year follow-up of more than 15,000 men showed a 25% lower incidence of CHD in men who consumed greater than 2.5 or more servings of vegetables daily, compared with those who consumed less than one serving daily. Similar results were demonstrated in women, in smokers, and in those who were overweight [20]. A large prospective cohort study of 84,251 women in the Nurses' Health Study and 42,148 men in the Health Professionals Follow-up Study showed people with the highest quintile of fruit and vegetable intake had a 30% lower risk of CVD compared to those with the lowest quintile of intake. This was especially true with increased intake of green leafy vegetables and vitamin C–rich fruit. For each increase of one serving per day in fruit and vegetables, a 4% lower risk of CHD and a 6% lower risk of ischemic stroke was observed [21,22].

### Micronutrients, antioxidants, and phytochemicals

- Based on the clear benefit of increased fruit and vegetable consumption, several components of such diets (eg, vitamins, potassium, magnesium, and dietary fiber) have been investigated. Convincing inverse associations have been found between dietary folate, vitamins $B_6$ and $B_{12}$, and the development and progression of atherosclerosis. Debate over dietary antioxidants and CVD continues. Foods high in antioxidants—particularly fresh fruits, nuts, and vegetables—are linked to lower rates of CVD. Basic research supports a link between oxidative stress and CVD. However, clinical trials do not support the use of dietary antioxidants (notably vitamins C and E) for the prevention and treatment of CVD [15••,23].
- Despite these trial data, it may be premature to dismiss the role of antioxidants. Understanding of the legion of antioxidants and phytochemicals and their dietary dynamics is still incomplete. Phytochemicals, for example, have a complex physiology. It is not clear if manipulating any single phytochemical is physiologically meaningful. In contrast, fruits and vegetables deliver a complete antioxidant package that may provoke a vital synergy. Furthermore, the temporal relationships between supplementation and outcomes may extend beyond what is feasible in most clinical trials [17•].

## Dietary patterns and CVD risk

- Studies that try to isolate the value of any single dietary component are also conceptually flawed because they cannot account for the complexity of aggregate eating behaviors. People eat food—not nutrients—with inevitable food-nutrient, nutrient-nutrient, and even lifestyle-food interactions. The totality of the diet and lifestyle is greater than the contribution of any one ingredient, making diet- or nutrient-to-disease studies particularly difficult. Complex food-nutrient and nutrient-nutrient interactions occur, and the totality of the diet, although methodologically difficult to assess, should be emphasized. Compared with pharmacologic trials, food studies are far more challenging methodologically and more difficult to assess [24••].
- Dietary pattern analyses may provide a more realistic diet-disease correlate than methods examining individual nutrients or foods [25•]. They have recently become popular as alternative and complementary tools for

examining diet-disease relationships. This approach more closely reflects natural eating behavior, compared with single-nutrient studies. Dietary pattern analyses also take into account a longer-term measure of dietary habits—an important consideration in diseases (like CVD) with long latency periods. As in all dietary studies, they are also limited by deficiencies intrinsic to dietary assessment studies and food frequency questionnaires [26••].

- A summary of noteworthy studies on dietary patterns and CVD is presented in Table 1 [27–37]. From a historical and nutritional standpoint, because dietary patterns studies are helpful considering the whole diet, they should be especially helpful in devising dietary guidelines. Generally, dietary pattern studies highlight the benefits of more traditional or healthy dietary patterns—replete with fruit, vegetables, nuts, fish, and whole grains—over a more western dietary pattern. The latter pattern—characterized by increased consumption of red and processed meats, deep fried foods, baked snacks, and highly refined grains—are associated with higher risks of CVD, obesity, and type 2 diabetes. Mediterranean diets, with moderate amounts of healthier lipids and unrefined CHOs, also provide conspicuous cardiovascular benefits.
- Consistently, diet influences physiology underlying CVD. In one example, the western dietary pattern in combination with sedentary lifestyle has been demonstrated to elevate serum C-reactive protein (CRP), a marker of inflammation, whereas dietary patterns that include omega-3 fats, MUFA, and PUFA fats lower CRP [38]. In other studies, outcome measurements of lipoprotein (a), small dense LDL, homocysteine, hemostatic factors, and other novel risk factors for CVD have also been modified by diet.

## Overweight, obesity, and CVD

- Excess weight (body mass index [BMI] 25.0 to 29.9 kg/m$^2$) and obesity (BMI > 30.0 kg/m$^2$) are mounting threats to public health in the United States. Almost 120 million or 64.5% of US adults are either overweight or obese, and the prevalence of obesity rose from approximately 12% to almost 24.5% of the US population from 1978 to 1990. Based on current projections, 73% of US adults could be overweight or obese by 2008. Annual deaths from obesity may reach 300,000 US adults, with CVD being the leading cause of death among this population [39,40•].
- The detrimental effects of increased consumption of convenience and fast foods have been compounded by larger portion sizes and a sedentary ("couch potato") environment [41]. The lopsided campaign waged against all dietary fat in the 1990s was accompanied by a rather cavalier attitude toward CHOs. The US Department of Agriculture's 1992 food guide pyramid recommendation of six to 11 servings daily and the advice to choose more complex CHOs (starch) over simple sugars did not help, and may have accelerated the fattening of America. Excess caloric intake—regardless of the source—is directly linked to increased BMI. A calorie is a calorie [17•].
- Excessive body weight is a risk factor for hypertension, stroke, and type 2 diabetes. The evidence for obesity as an independent risk factor for CHD is compelling. Obesity, especially central obesity, mediates excess cardiovascular risk via multiple mechanisms, including increased insulin resistance, impaired glucose tolerance, hypertension, dyslipidemia, and inflammation—all fundamental components of the metabolic syndrome. Obesity-mediated CVD may be aggravated via additional mechanisms (eg, the obesity-hypoventilation [obstructive sleep apnea] syndrome), and the accompanying sedentary lifestyle, and psychosocial pressures.

**Table 1. Selected whole diet studies (dietary patterns) and CVD risk**

| Study | Population | Design or method | Dietary patterns | Comment |
|---|---|---|---|---|
| Kerver *et al.* [27] | 13,130 healthy US adults | Cross-sectional study FFQ; NHANES III | 1) American healthy, 2) western pattern | Western pattern positive relation with CVD risk factor biomarkers. American healthy pattern showed significant positive differences |
| van Dam *et al.* [28] | 19,750 Dutch men and women | Cross-sectional study FFQ | 1) Cosmopolitan, 2) traditional, 3) refined foods | Cosmopolitan diet score associated with lower SBP and higher HDL; refined foods pattern associated with higher cholesterol |
| Esposito *et al.* [29] | 180 Italian men and women | RCT; single-blind; 30-month FU | Mediterranean diet ($n$ = 90) vs AHA-style diet ($n$ = 90) | Marked reduction in the prevalence of the metabolic syndrome and associated CVD risk—lower body weight, hs-CRP, insulin resistance, and endothelial function score |
| Singh *et al.* [30] | 1000 Indians > age 25 y | RCT; single-blind; 2-y FU | Indo-Mediterranean diet ($n$ = 499) vs control (local) diet ($n$ = 501) | Reduction in fatal MI by 1/3, reduced nonfatal MI; reduction in SCD by 2/3. Fewer total cardiac end points in the intervention group |
| Appel *et al.* [31] | 459 US adults, 49% women, 60% black | RCT; 11-wk feeding study | American DASH diet vs control/typical American diet vs combination diet | Marked lowering of SBP and DBP in all individuals on DASH diet; effects seen after 2 wk on DASH diet—more marked in hypertensive patients |
| Renaud *et al.* [32] | 605 post-MI patients, setting: Crete, Greece | RCT; 1- to 4-y FU—mean 27 mo | Cretan Greek Mediterranean diet vs usual prescribed diet | Recurrent MI, all CVD events, and cardiac and total death significantly decreased by 70% to 80% in the Mediterranean diet group |
| de Lorgeril *et al.* [33] | 302 MI patients, mainly French men | RCT; single-blind; 46-mo FU | Mediterranean diet enriched with ALA vs control diet | Mediterranean-style diet showed 50% to 70% lower risk of recurrent CHD and death; for nonfatal MI |
| Singh *et al.* [34] | 204 immediate post-MI patients, setting: India | RCT; single-blind; 1-y FU | Semi-vegetarian South Asian diet vs control diet | Dietary changes and weight loss immediately post-MI reduce complications and death—41% reduction in deaths from CHD; 38% reduction in nonfatal MI |
| Trichopoulou *et al.* [25•] | 22,043 Greek men and women | Validated FFQ; prospective cohort study; 44-mo FU | Traditional Greek Mediterranean diet categorized by Mediterranean diet scores | 25% drop in total mortality; more marked for CHD than cancer; totality of diet more effective than individual foods. Adherence inversely associated with deaths from CHD |
| Osler *et al.* [35] | 3698 Danish men and 3618 women | FFQ; prospective cohort study; 15-y FU; factor analysis | 1) Prudent pattern, 2) western pattern | Healthy food index/prudent pattern shows inverse association with all-cause mortality; no significant association with western pattern |
| Fung *et al.* [36] | 69,017 US women, mainly white | FFQ; prospective cohort study; 13-y FU; factor analysis | 1) Prudent pattern, 2) western pattern | Prudent pattern lowers CVD risk; western pattern increases risk |
| Stampfer *et al.* [5] | 84,129 US women, mainly white | FFQ 1980—updated 1984, 1986, 1990; prospective cohort study; 14-y FU | Healthy diet and lifestyles | Adherence to healthy guidelines: nonsmokers, recommended diet, and exercise showed 80% less coronary events compared with those who did not |
| Hu *et al.* [37] | 44,875 US men, mainly white | FFQ; prospective cohort study; 8-y FU; factor analysis | 1) Prudent pattern, 2) western pattern | Western pattern higher CHD risk; prudent pattern lower risk. Risks independent of other lifestyle variables |

AHA—American Heart Association; ALA—α-linolenic acid; BP—blood pressure; CHD—coronary heart disease; CVD—cardiovascular disease; DASH—Dietary Approaches to Stop Hypertension; DBP—diastolic blood pressure; FFQ—food frequency questionnaire; FU—follow-up; HDL—high-density lipoprotein; hs-CRP—high-sensitivity C-reactive protein; MI—myocardial infarction; NHANES III—Third National Health and Nutrition Examination Survey; RCT—randomized controlled trial; SBP—systolic blood pressure; SCD—sudden cardiac death.

- Excess mortality from CVD has been shown with BMIs greater than 26.5 kg/m$^2$ in men and BMIs greater than 25 kg/m$^2$ in women. In the Health Professionals Follow-up Study and Nurses' Health Study, middle-aged men and women who gained between 11 and 22 pounds after age 20 were up to three times more likely to develop CHD, hypertension, and type 2 diabetes [42].
- Although definitive data on the CVD effects of weight loss are not yet available, smaller trials indicate that modest weight loss (< 10% of original body weight) by whatever means (dietary, lifestyle, and pharmacologic interventions) can substantially lower blood pressure, improve lipid profile, and modify propensity to the metabolic syndrome, lessening CHD and stroke risks [43].

## Diet trends

- A discussion of diet and CVD in America would be incomplete without reference to the impact of popular diets (eg, the Atkin's diet) on CVD risk. A proliferation of popular diets often contradict one another because each lays claim to a superior weight loss strategy, including diets with low fat, moderate fat, and high fat parameters. In general, popular diets are all oriented to weight loss, but they vary on how weight loss occurs (water weight vs body tissue), durability of weight loss, the effects on insulin levels and micronutrients, and effects on appetite and energy. Although most popular diets lead to short-term weight loss, impact on long-term weight maintenance and CVD risks is much less clear. Critics of the Atkin's high fat, low CHO diet point particularly to the fact that early weight loss correlates in large part to water loss that occurs with a ketogenic diet [44•]. Moreover, concerns have been raised that CVD and diabetes may increase with high fat intake.

## Physical inactivity

- Recent studies have shown that increased levels of physical activity and fitness are associated with a decreased incidence of heart disease and hypertension. Ironically, almost 75% of US adults and 50% of youth lead sedentary lifestyles. Inactivity has been demonstrated to increase CVD as an independent risk factor, and also because it compounds risks of obesity, and type 2 diabetes. Sedentary living has become more prevalent than excess weight and cigarette smoking, and is therefore the leading behavioral risk factor for CVD [45].
- Increasing physical activity improves lipid metabolism, autonomic balance, endothelial function, myocardial work efficiency, and even modifies fundamental inflammatory factors that underlie propensity to CVD. Likewise, increased physical activity lowers blood pressure, increases insulin sensitivity, and lowers appetite—all key in ameliorating the metabolic syndrome.
- In primary prevention studies, a strong inverse relationship is seen between physical activity and CHD development and mortality in men, women, ethnic minorities, and the elderly. In the Harvard alumni cohort of 10,269 men, those who were moderately active (> 4200 kJ or 1000 cal/wk) had a 23% lower risk of death compared with less active alumni [46]. Among women, the Nurses' Health Study of 72,488 women between ages 50 and 79 showed an inverse relationship between the risk of coronary events and exercise. In the Health Professionals Follow-up Study of 44,452 men, brisk walking ≥ 30 minutes daily, running ≥ 1 hour weekly, weight lifting ≥ 30 minutes weekly, and rowing ≥ 1 hour weekly all reduced the risk of CHD. Furthermore, higher levels of fitness and physical activity were associated with the greatest health benefit. Peak exercise capacity and physical fitness are the strongest predictors of CVD and mortality in both men and women [47].

- In secondary prevention, cardiac rehabilitation trials, physical activity, and exercise also benefit people with established CHD, including those with a history of MI. Exercise training studies and rehabilitation programs reduce CVD mortality, but not recurrent coronary events or the rates of revascularization procedures in post-MI patients [48].
- Overall, increased physical activity and exercise lowers CVD incidence and CVD deaths, especially from CHD. A dose-response relationship with increasing levels of activity occurs, with a halving of CHD risk in those most active compared with those less active. Maximal cardiovascular benefit is seen when moderate physical activity replaces sedentary lifestyles, in both men and women [49]. Nonetheless, there have been no controlled trials to clarify optimal intensity, duration, frequency, or type of exercise.

### Cigarette smoking

- The evidence linking cigarette smoking to increased CVD risk is firmly established. Smoking doubles the risk of CVD and is an independent risk factor for CHD, cerebrovascular disease, peripheral vascular disease, and sudden cardiac death. It is still considered the leading cause of preventable death in the industrialized world, and increasingly so in emerging economies and the developing world. Smoking causes in excess of 400,000 deaths annually in the United States, of which 40% is due to CVD; passive smoking causes in excess of 40,000 deaths. There is no convincing evidence that smoking cigars is safer than smoking cigarettes, and habitual use of smokeless tobacco products is associated with increased risk [50,51].
- Smoking exerts deleterious effects on the cardiovascular system via a legion of mechanisms, including increased free radical–mediated oxidative stress on several blood components, including platelets, lipids, and the endothelium, acceleration of inflammation, and stimulation of the sympathetic nervous system stimulation.
- Complete smoking cessation is always beneficial. Benefits begin soon after smoking cessation and CVD risks continue to fall with time. There is a 50% reduction in risk after 1 year, reaching a CVD risk equivalent to that of nonsmokers 10 to 15 years later [52].

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