Risk factor reduction has been the long-standing cornerstone in the prevention and treatment of coronary heart disease (CHD). Implementing healthy lifestyle behaviors including diet is a foundation for reducing CHD risk. Epidemiologic studies and controlled clinical trials consistently have demonstrated cardioprotective benefits of dietary patterns high in vegetables, fruits, legumes, whole grains, fiber, fish, lean meats and poultry, and low-fat dairy products. Other healthy lifestyle behaviors such as nonsmoking, maintaining a waist-to-hip ratio below the 75th percentile, and regular exercise, in concert with a healthy dietary pattern that includes moderate alcohol consumption, are associated with a 92% decrease in heart attack risk. Given the magnitude of the benefits that a healthy dietary pattern and lifestyle behaviors can have, these are the first steps in the prevention and treatment of CHD.

Low-density lipoprotein-cholesterol (LDL-C) is the primary target for cholesterol-lowering therapy because of strong evidence in humans and animal models that high LDL-C levels initiate and promote atherogenesis, and that LDL-C lowering reduces CHD risk. It is estimated that each 1.8 mg/dL decrease in LDL-C reduces
the risk of a cardiovascular event (heart attack, stroke, hospitalization for unstable angina, or revascularization) by 1%. Based on subsequent modifications of ATP III Guidelines, the recommended LDL-C goal for high-risk patients is less than 100 mg/dL; when risk is very high, an LDL-C goal of less than 70 mg/dL is a therapeutic option. Consistent with this recommendation is that even for very high risk patients who have a baseline LDL-C less than 100 mg/dL, an LDL-C goal of less than 70 mg/dL is a therapeutic option. In addition, an LDL-C goal of less than 100 mg/dL is a therapeutic option for moderately high-risk patients over the recommended LDL-C of less than 130 g/dL. As a result of these recommendations, the goal for LDL-C is to have levels as low as possible.

Diet and lifestyle patterns affect many CHD risk factors by a variety of mechanisms beyond LDL-C lowering. Several other major, independent lipid risk factors have been identified, including elevated triglycerides (TG) and low high-density lipoprotein-cholesterol (HDL-C). These lipid risk factors are two of the five criteria for clinically defining metabolic syndrome, and can present with normal LDL-C levels. Because metabolic syndrome is related to obesity and physical inactivity, diet and lifestyle practices also are the first line of treatment. This article discusses specific dietary factors as well as dietary patterns that affect the major CHD lipid risk factors, ie, LDL-C, HDL-C, and TG. Based on a very large evidence base, it is clear that diet and lifestyle practices can markedly affect these major CHD lipid risk factors, and consequently decrease CHD risk substantively.

DIETARY FACTORS THAT INCREASE LOW-DENSITY LIPOPROTEIN-CHOLESTEROL

**Saturated Fatty Acids**

Saturated fatty acids (SFA) raise LDL-C in a dose-dependent manner. The major sources of SFA in the United States are fatty red meats and full-fat dairy products. Tropical oils, including palm oil, palm kernel oil, and coconut oil, also are high in SFA. SFA intake has been positively correlated with CHD risk in several observational studies. In the Seven Countries Study, collective intake of the four major long-chain saturated fatty acids (eg, lauric, myristic, palmitic, and stearic acid) had a strong positive correlation with 25-year death rates from CHD ($r > 0.80$).

Meta-analyses of clinical trial data indicate that for every 1% increase in energy from SFA, LDL-C increases by 1.8 mg/dL. Reducing SFA intake to less than 7% of energy and cholesterol intake to less than 200 mg per day reduces LDL-C by 9% to 12% compared with baseline or a Western diet. In conjunction with a 3- to 6-kg weight loss, LDL-C can be reduced by 16%. The Institute of Medicine (IOM) recommendations are to consume as little SFA as possible along with a diet that is adequate in all essential nutrients. The American Heart Association (AHA) recommends that less than 7% of energy come from SFA. Substituting unsaturated fats, carbohydrates, or protein for SFA all are effective means for decreasing total- and LDL-C. Replacing SFA with unsaturated fats also lowers the total cholesterol (TC):HDL-C ratio and prevents or attenuates an increase in TG that can occur when SFA are replaced by carbohydrates. However, choosing foods high in fiber and complex carbohydrates can attenuate or prevent the TG-raising effect of increasing carbohydrate intake. Although individual SFA have different effects on LDL-C (eg, stearic acid has a neutral effect versus the other long-chain SFA), at the present time it is not appropriate to focus on specific SFA when selecting food containing a mixture of individual SFA. The presence of a variety of SFA in foods makes it challenging to emphasize or limit individual SFA. Table 1 lists simple strategies for reducing SFA in the diet.
Trans fatty acids (TFA) adversely affect serum lipid and lipoprotein levels. Compared with cis-unsaturated fatty acids, TFA raise TC and LDL-C, lower HDL-C, and increase the ratios of TC:HDL-C and LDL-C:HDL-C.

Compared with saturated fatty acids (SFA), trans fatty acids increase LDL-C similarly, but lower HDL-C. As a result, the increase in the LDL-C:HDL-C ratio following TFA consumption is twofold higher than for saturated fat (Fig. 1). Randomized clinical trials have demonstrated a positive linear relationship between TFA intake and the LDL-C:HDL-C ratio (see Fig. 1). Based on these data, each 2% increase in TFA intake raises the LDL-C:HDL-C ratio by 0.1 unit (see Fig. 1).

In prospective studies, the incidence of CHD in individuals with the highest TFA intake is greater than predicted by lipid levels alone, suggesting that there are adverse effects of TFA beyond their effects on lipids. Likewise, individuals with the highest levels of TFA in plasma phospholipids, adipose tissue, and red blood cell

<table>
<thead>
<tr>
<th>Food Category</th>
<th>Portion</th>
<th>Saturated Fat Content, g</th>
<th>Calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheese</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular cheddar cheese</td>
<td>1 oz</td>
<td>6.0</td>
<td>114</td>
</tr>
<tr>
<td>Low-fat cheddar cheese</td>
<td>1 oz</td>
<td>1.2</td>
<td>49</td>
</tr>
<tr>
<td>Ground beef</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular ground beef (25% fat)</td>
<td>3 oz (cooked)</td>
<td>6.1</td>
<td>236</td>
</tr>
<tr>
<td>Extra lean ground beef (5% fat)</td>
<td>3 oz (cooked)</td>
<td>2.6</td>
<td>148</td>
</tr>
<tr>
<td>Milk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole milk (3.25%)</td>
<td>1 cup</td>
<td>4.6</td>
<td>146</td>
</tr>
<tr>
<td>Low-fat milk (1%)</td>
<td>1 cup</td>
<td>1.5</td>
<td>102</td>
</tr>
<tr>
<td>Breads</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Croissant</td>
<td>1 medium</td>
<td>6.6</td>
<td>231</td>
</tr>
<tr>
<td>Bagel, oat bran (4&quot;)</td>
<td>1 medium</td>
<td>0.2</td>
<td>227</td>
</tr>
<tr>
<td>Frozen desserts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular ice cream</td>
<td>0.5 cup</td>
<td>4.9</td>
<td>145</td>
</tr>
<tr>
<td>Frozen yogurt, low fat</td>
<td>0.5 cup</td>
<td>2.0</td>
<td>110</td>
</tr>
<tr>
<td>Table spreads</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butter</td>
<td>1 tsp</td>
<td>2.4</td>
<td>34</td>
</tr>
<tr>
<td>Soft margarine with zero trans fats</td>
<td>1 tsp</td>
<td>0.7</td>
<td>25</td>
</tr>
<tr>
<td>Chicken</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fried chicken (leg with skin)</td>
<td>3 oz (cooked)</td>
<td>3.3</td>
<td>212</td>
</tr>
<tr>
<td>Roasted chicken (breast with no skin)</td>
<td>3 oz (cooked)</td>
<td>0.9</td>
<td>140</td>
</tr>
<tr>
<td>Fish</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fried cat fish</td>
<td>3 oz</td>
<td>2.8</td>
<td>195</td>
</tr>
<tr>
<td>Baked cat fish</td>
<td>3 oz</td>
<td>1.5</td>
<td>129</td>
</tr>
</tbody>
</table>


**Trans Fatty Acids**

Trans fatty acids (TFA) adversely affect serum lipid and lipoprotein levels. Compared with cis-unsaturated fatty acids, TFA raise TC and LDL-C, lower HDL-C, and increase the ratios of TC:HDL-C and LDL-C:HDL-C. Compared with saturated fatty acids (SFA), trans fatty acids increase LDL-C similarly, but lower HDL-C. As a result, the increase in the LDL-C:HDL-C ratio following TFA consumption is twofold higher than for saturated fat (Fig. 1). Randomized clinical trials have demonstrated a positive linear relationship between TFA intake and the LDL-C:HDL-C ratio (see Fig. 1). Based on these data, each 2% increase in TFA intake raises the LDL-C:HDL-C ratio by 0.1 unit (see Fig. 1).

In prospective studies, the incidence of CHD in individuals with the highest TFA intake is greater than predicted by lipid levels alone, suggesting that there are adverse effects of TFA beyond their effects on lipids. Likewise, individuals with the highest levels of TFA in plasma phospholipids, adipose tissue, and red blood cell
membranes had up to a 3-fold greater increase myocardial infarction risk and approx-
imately a 1.5-fold greater risk of cardiac arrest and fatal ischemic heart disease (IHD)
compared with individuals with the lowest TFA levels.\textsuperscript{18–21} Based on data from four
prospective studies of 140,000 participants, it is estimated that a 2% increase in
energy intake from TFA increases the incidence of CHD by 23% (Pooled relative
risk [RR] 1.23; 95% confidence interval [CI] 1.11–1.37, \(P<.001\)).\textsuperscript{15} Because TFA
make up 2% to 3% of daily energy intake, a reduction in TFA in the diet to less than
1% of energy intake, as recommended by the AHA,\textsuperscript{1} can significantly reduce CHD
risk.\textsuperscript{22,23}

TFA are formed by partial hydrogenation of vegetable oils, resulting in semisolid
fats. The most common sources of TFA are margarines, shortenings, commercially
fried foods, baked goods, and savory snack foods (Table 2).\textsuperscript{2} Thus, limiting

<table>
<thead>
<tr>
<th>Food Group</th>
<th>Contribution (% of Total TFA Consumed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cakes, cookies, crackers, pies, bread</td>
<td>40</td>
</tr>
<tr>
<td>Animal products</td>
<td>21</td>
</tr>
<tr>
<td>Margarine</td>
<td>17</td>
</tr>
<tr>
<td>Fried potatoes</td>
<td>8</td>
</tr>
<tr>
<td>Potato chips, corn chips, popcorn</td>
<td>5</td>
</tr>
<tr>
<td>Household shortening</td>
<td>4</td>
</tr>
<tr>
<td>Other\textsuperscript{a}</td>
<td>5</td>
</tr>
</tbody>
</table>

The major dietary sources of TFA are listed in decreasing order. Processed foods and oils provide
approximately 80% of TFA in the diet, compared with 20% that occur naturally in food from
animal sources. The TFA content of certain processed foods has changed and is likely to continue
to change as the industry reformulates its products.\textsuperscript{2}

\textsuperscript{a} Includes breakfast cereal and candy. USDA analysis reported 0 g of TFA in salad dressing.
consumption of fried foods, commercial baked goods, and other foods made with partially hydrogenated oils are an effective means of reducing TFA intake. Naturally occurring TFA produced by biohydrogenation of fatty acids in the rumen are found in full and reduced fat milk and dairy products. In clinical trials, moderate amounts (1.5% of energy) of ruminant TFA had a neutral effect on lipids, whereas higher doses (≥ 2% of energy) had an adverse effect. In contrast, the majority of observational trials that have been conducted indicate a neutral or even protective effect of ruminant TFA. Further studies are needed to clarify the effects of ruminant TFA on CVD risk factors. In the meantime, clinicians and health professionals should focus on recommending that industrial sources of TFA be avoided to facilitate lowering total- and LDL-C. In addition, the focus on reducing TFA should not detract from efforts to decrease SFA.

**Dietary Cholesterol**

Epidemiologic studies have reported a positive or neutral relationship between dietary cholesterol intake and CHD risk. Clinical studies have shown that dietary cholesterol raises total- and LDL-C, but to a lesser extent than saturated and trans fatty acids. Consuming an additional 100 mg per day of cholesterol raises TC by about 2.4 mg/dL and LDL-C by 2.1 mg/dL. Food sources of dietary cholesterol are animal products (eg, eggs, dairy products, and meats), with eggs contributing the most cholesterol to the diet (approximately 213 mg cholesterol per egg). A decrease in dietary cholesterol is recommended to reduce LDL-C, especially in persons with elevated LDL-C levels. The AHA recommends consuming less than 300 mg of cholesterol per day and the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III recommends less than 200 mg per day to maximize cholesterol lowering with diet.

Numerous controlled clinical trials have shown that whole egg and egg yolk consumption increases total- and LDL-C. In contrast, most observational studies have not demonstrated a positive relationship between egg consumption and incidence of CHD. However, a recent, 20-year follow-up of the Physicians Health Study reported that although consumption of up to six eggs per week was not associated with incident heart failure, consumption of seven or more eggs per week was associated with an increased risk of heart failure. Compared with subjects who reported egg consumption of less than one per week, hazard ratios for heart failure risk were 1.28 (95% CI 1.02–1.61) and 1.64 (95% CI 1.08–2.49) for egg consumption of 1 per day and 2 or more per day, respectively. Two other studies have reported a twofold increased risk of CHD or CAD in individuals with diabetes who eat more than six to seven eggs per week compared with those who eat less than one egg per week. No adverse effects were associated with egg consumption in these studies in individuals without diabetes.

Because plant foods (eg, fruits, vegetables, beans, grains, nuts, and seeds) do not contain cholesterol, dietary cholesterol can be reduced by replacing meats and other animal products with plant foods. This is recommended for high-risk patients and individuals with diabetes as one dietary strategy for significantly lowering total- and LDL-C.

**DIET AND LIFESTYLE FACTORS THAT LOWER LOW-DENSITY LIPOPROTEIN-CHOLESTEROL**

**Soluble Fiber**

Dietary fiber is the nondigestible carbohydrate components of plants. Observational studies have demonstrated an inverse association between dietary fiber and CHD
risk, and clinical trials have shown an LDL-C lowering effect of dietary fiber. The primary mechanism for the reduction in LDL-C is via decreased absorption of cholesterol and bile acids. Soluble fiber is present in foods such as beans, oats, barley, and some fruits and vegetables. Based on observational and clinical trial evidence, the Food and Drug Administration (FDA) has approved a health claim that foods containing 1.7 g per serving of psyllium husk soluble fiber or 0.75 g of oat or barley soluble fiber as \( \beta \)-glucans may reduce the risk of heart disease as part of a diet low in saturated fat and cholesterol. The NCEP ATP III recommends 10 to 25 g per day of soluble fiber as a therapeutic option to enhance LDL-C lowering. Adding as little as 5 to 10 g of soluble fiber to a Therapeutic Lifestyle Change (TLC) diet (< 7% SFA, < 200 mg cholesterol per day) is expected to reduce LDL-C by approximately 5%.

The most common soluble fibers are \( \beta \)-glucan, pectin, guar gum, and psyllium. De Groot and colleagues were first to report a decrease in serum cholesterol (\(-11\%\)) following 3-week daily consumption of 300 g of bread containing 140 g of rolled oats. Davy and colleagues subsequently reported that soluble fiber also favorably affects LDL particle size. In a randomized controlled trial, 36 overweight men consumed 14 g of fiber daily for 12 weeks, including two large servings of high-fiber oat cereal (5.5 g \( \beta \)-glucan). At the end of the diet period, subjects had a 17% reduction in small LDL-C, a 5% reduction in LDL-C particle number, and a 2.5% reduction in LDL-C concentration. Similar results were reported by Shrestha and colleagues. Recently, Moreyra and colleagues reported that psyllium supplementation also reduces LDL-C in men when taken in combination with a statin. After 8 weeks of treatment, LDL-C levels in the group receiving 10 mg of simvastatin plus a fiber placebo fell by 55 mg/dL compared with 63 mg/dL in the group receiving 10 mg of simvastatin plus 15 g of psyllium (Metamucil) daily (\(P = .03\)). The popularity of \( \beta \)-glucan has led to its supplementation in other foods such as orange juice, where it also is effective in reducing LDL-C.

In a meta-analysis conducted to evaluate the efficacy of various soluble fibers to lower total- and LDL-C, Brown and colleagues reported similar effects of oats, psyllium, pectin, and guar gum. In this study, each gram of oats lowered total- and LDL-C by 1.42 mg/dL and 1.23 mg/dL, each gram of psyllium lowered total- and LDL-C by 1.10 mg/dL and 1.11 mg/dL, each gram of pectin lowered total- and LDL-C by 2.69 mg/dL and 1.96 mg/dL, and each gram of guar gum decreased total- and LDL-C by 1.13 mg/dL and 1.20 mg/dL, respectively. The similar efficacy of different soluble fibers can help achieve current recommendations for dietary fiber.

**Stanols/Sterols**

Phytosterols, ie, sterols and stanols, are structurally similar to cholesterol (Fig. 2). Stanols are saturated sterols and are much less abundant in nature than sterols. Phytosterols are present in small amounts in nuts, seeds, and vegetable oils. More than 40 different phytosterols have been identified, of which \( \beta \)-sitosterol, campesterol, and stigmasterol are the most abundant. Phytoesters lower LDL-C independent of dietary cholesterol intake, and different phytosterols (ie, \( \beta \)-sitosterol versus campessterol) are equally effective in lowering LDL-C. Numerous studies have shown that phytosterols lower LDL-C in a dose-dependent fashion in amounts up to 2.5 g per day, with an LDL-C lowering effect in both normocholesterolemic and hypercholesterolemic adults. A meta-analysis of 41 trials reported that intake of 2 g per day of phytosterols reduces LDL-C by 10%, and higher intakes confer little additional benefit. The NCEP ATP III recommends 2 g per day of phytosterols to achieve about a 10% reduction in LDL-C. The typical daily intake
of phytosterols in western cultures ranges from 150 mg per day to 400 mg per day,\textsuperscript{60} making supplementation necessary to achieve the recommended intake.

Observational studies have investigated whether there is a relationship between plasma phytosterol levels and CVD risk.\textsuperscript{66–69} Most studies have not reported adverse associations. However, in the Prospective Cardiovascular Münster (PROCAM) study, there was a 1.8-fold increased risk of coronary events in subjects with sitosterol levels in the upper quartile compared with the lower three quartiles (\textit{P}<.05).\textsuperscript{66} In contrast, in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk Population study, there was a 21% reduced risk of future CAD in subjects in the highest tertile of sitosterol concentration (\textit{ns}, non-significant) after adjusting for traditional risk factors.\textsuperscript{67} The Longitudinal Aging Study Amsterdam (LASA) study reported that high plasma concentrations of sitosterol were associated with a significant 22% reduced risk of CHD (\textit{P}<.05).\textsuperscript{68} In the Dallas Heart Study, there was no relationship between plant sterol levels and family history of CHD or coronary calcium.\textsuperscript{69} Long-term randomized clinical trials will be a useful adjunct to the epidemiologic evidence base to learn about the effect of phytosterol supplementation on CVD events.

There are many products on the market that contain phytosterols for total- and LDL-C lowering. These products include orange juice, yogurt, margarine spreads, salad dressings, breads, cereals, milk, and granola bars. Phytosterols also are available in soft-gel pills. A meta-analysis of supplementation studies in familial hypercholesterolemic subjects reported that fat spreads enriched with 2.3 ± 0.5 g phytosterols per day significantly reduced TC by 7% to 11% (\textit{P}<.001) and LDL-C by 10% to 15% (\textit{P}<.001) in 6.5 ± 1.9 weeks compared with control treatment.\textsuperscript{70} Other studies using

\textbf{Fig. 2.} Structures of sterols. Cholesterol is the sterol of mammalian cells. \(\beta\)-sitosterol is the most common sterol in plants; it differs from cholesterol by having an ethyl group attached at C-24. Hydrogenation of the 5,6 double bond of \(\beta\)-sitosterol converts it into sitostanol. Campesterol and campestanol carry a methyl instead of ethyl group at C-24. \textit{(Reprinted from} Katan MB, Grundy SM, Jones P, et al. Efficacy and safety of plant stanols and sterols in the management of blood cholesterol level. Mayo Clin Proc 2003;78(8):965–78.)
foods fortified with 1.6 to 2.6 g per day of phytosterols have resulted in an LDL-C reduction of 9.4%, 71 12.4%, 72 5% to 10%, 73 9.8%, 74 and 7.8%. 75 The lowest calorie strategy for achieving maximum LDL-C lowering with phytosterols is to use soft-gel capsules that are consumed with a meal that contains fat. Alternatively, other foods including the lite margarines can be incorporated into a low calorie meal to achieve maximum LDL-C lowering.

Phytosterols inhibit cholesterol absorption by displacing cholesterol from mixed micelles. 60 This mechanism of action is different from statin drugs, which inhibit cholesterol synthesis. Consequently, phytosterols can be used in conjunction with statins for greater LDL-C lowering. 76–79 Moreover, this strategy may be more effective for LDL-C lowering than doubling the statin dose. 60 Phytosterols also elicit additional lipid lowering when combined with a heart-healthy diet using other LDL-lowering strategies. 60 Phytosterols are well tolerated, and no adverse effects have been reported. 12 A decrease in blood levels of β-carotene and other carotenoids has been reported following plant sterol consumption, 60 but does not appear to be associated with any adverse outcomes. 60 A diet high in carotenoids (high-carotenoid fruits or vegetables include carrots, pumpkin, apricots, spinach, and broccoli) can prevent this decrease in plasma levels, and is recommended when consuming phytosterols. 12,81

**Soy**

Epidemiologic studies have shown that dietary soy is inversely related to TC 82,83 and LDL-C 83 in some Asian populations. More recently, the Shanghai Women’s Health Study found that increased consumption of soy foods was associated with a significantly reduced risk of nonfatal myocardial infarction and CHD. 84 Soy protein is the major component of soybeans and typically accounts for 36% of the total bean. Nutritionally, soy protein is considered to be a complete protein because it provides all essential amino acids. A component of soy protein of interest is isoflavones, which are bioactive molecules that act as phytoestrogens. Isoflavones are present in whole soy foods in inactive forms as glucosides. Metabolism of the glucoside forms of isoflavones produces the biologically active aglycones: genistein, daidzein, and glycitein. 85 The conversion of isoflavones by intestinal flora is an area of scientific interest, as individuals with intestinal capacity to convert daidzein to equol may benefit from its greater biological activity and superior antioxidant activity. 86 The estimated prevalence of equol producers ranges between 30% and 50% of the population. 86,87

The potential for soy protein to decrease serum cholesterol levels has been studied extensively. An earlier meta-analysis (published in 1995) of 38 controlled trials reported that consumption of soy protein (average 47 g per day) significantly reduced TC (9.3%), LDL-C (12.9%), and TG (10.5%). 88 These changes in TC and LDL-C were a function of initial serum cholesterol concentrations; the greatest reductions were observed in individuals with higher levels at baseline. In 1999, the FDA approved a soy protein health claim that authorized the following label on qualified soy foods: “Diets low in saturated fat and cholesterol that include 25 g of soy protein a day may reduce the risk of heart disease.” For a food to qualify for the health claim, the FDA requires that a serving contain at least 6.25 g of soy protein, which is 25% of the recommended daily amount (25 g). 89

More recent evidence indicates that soy protein is not as effective at reducing LDL-C as initially reported. In a 2005 meta-analysis, Zhan and Ho 90 reported that soy protein with isoflavones (median 80 mg per day isoflavones) reduced TC (3.8%), LDL-C (5.3%), and TG (7.3%), and increased HDL-C (3.0%), with higher intakes of soy isoflavones (> 80 mg per day) eliciting greater effects. In a more recent
meta-analysis prepared by the Agency for Health care Research and Quality (AHRQ), Balk and colleagues,\textsuperscript{91} reported that consumption of soy protein (median intake 36 g) was associated with a modest TC (\(-5\) mg/dL, 2.5\%), LDL-C (\(-5\) mg/dL, 3\%) and TG (\(-8\) mg/dL, 6\%) lowering effect. Similar effects of soy protein on LDL-C were reported by Sacks and colleagues,\textsuperscript{92} who reviewed 22 randomized trials conducted between 1998 and 2005 as part of an AHA Science Advisory. In this analysis, intake of soy protein (25 to 135 g per day) and isoflavones (40 to 318 mg per day) varied considerably among studies; 50 g per day (average intake) of soy protein was associated with a 3\% reduction in LDL-C. These effects of soy protein on LDL-C are substantially lower than those reported by Anderson and colleagues,\textsuperscript{88} in 1995, but are consistent with more recent meta-analyses.

As first reported by Anderson and colleagues,\textsuperscript{88} and illustrated in Fig. 3, baseline LDL-C concentration is an important determinant of the effectiveness of soy protein. Also evident is a dose-response relationship between changes in LDL-C and soy protein intake, but not isoflavone intake. Other factors that may influence the magnitude of changes in LDL-C include the bioavailability of isoflavones, the type and preparation of the soy foods, and the population studied (eg, hypercholesterolemic individuals).\textsuperscript{91}

The effect of isoflavones on LDL-C is less clear. Data supporting an independent cholesterol-lowering effect of soy isoflavones are inconsistent, and several meta-analyses have been conducted in an attempt to explain these differences. Weggemans and Trautwein,\textsuperscript{93} reported that daily consumption of soy protein (average 36 g)
+ isoflavones (average 52 mg) reduced LDL-C by 6.6 mg/dL (−4%) and increased HDL-C by 1.2 mg/dL (+3%). However the absence of a dose-response relationship between changes in isoflavone concentration and changes in LDL-C and HDL-C suggested that these bioactive compounds had no independent effects on lipids/lipoproteins. In comparison, another meta-analysis showed that high (96 mg per day) intakes of isoflavones were associated with greater reductions (−5.8 mg/dL) in LDL-C than lower (6 mg per day) intakes, with standard amounts of soy protein (50 g per day). This was supported by another recent meta-analysis of 11 studies that showed differential effects of the same amount of soy protein, if it were enriched or depleted of isoflavones. Isoflavone-enriched soy-protein lowered TC by 1.8% and LDL-C by 3.6% compared with isoflavone-depleted soy protein. When compared with animal protein, there is some evidence that soy protein combined with isoflavones work synergistically or additively to lower LDL-C (−4.98% for soy protein + isoflavones versus −2.77% for soy protein without isoflavones). However, both the AHRQ Report and the AHA Science Advisory on Soy Protein concluded that isoflavones have no effect on LDL-C or other lipids.

Although yet to be fully elucidated, there are animal and cell culture data supporting several mechanisms by which soy protein and isoflavones may influence lipids, including modulation of transcription factors and regulation of expression of genes involved in lipid metabolism (reviewed by Torres and colleagues and Xiao and colleagues). For example, soy protein may down-regulate the activity of sterol regulatory element binding protein (SREBP)-1, which leads to a “downstream” reduction in serum and liver TG and LDL-C. However, as discussed previously, these molecular and biochemical changes do not necessarily translate to clinically relevant benefits, particularly at doses likely to be consumed.

In conclusion, recent meta-analyses demonstrate that 30 to 50 g per day of soy protein can reduce LDL-C by 3% to 5%. For individuals trying to achieve this LDL-C lowering effect, the most concentrated sources of soy protein are isolated soy protein powders (typically 80% to 90% protein), soy nuts (40% protein), and full-fat soy flour (35% protein). Other manufactured food products such as protein bars and breakfast patties also are modest sources of soy protein, although the protein in these products is not always exclusively from soy. The following is one example of how to achieve an intake of 50 g per day of soy protein using traditional and nontraditional soy products: one breakfast patty (eg, Morningstar Farms organic soy breakfast patty, 9.8 g protein), an 8-ounce glass of soy milk (7.3 g), 3 ounces of Tofu (6 g), 1 ounce of soy nuts (11 g), and two heaping tablespoons (20 g) of soy protein powder (17 g). It is important to note that some soy protein foods are high in sodium. For example, a 70-g soy burger provides about 400 mg of sodium, and an 85-g vegan soy burger provides approximately 550 mg of sodium.

**Weight Loss**

Weight loss has favorable affects on TC, LDL-C, HDL-C, and triglycerides. Weight loss of 5% to 10% of body weight results in approximately a 15% reduction in LDL-C, a 20% decrease in triglycerides, and an 8% to 10% increase in HDL-C. Although HDL-C generally decreases during weight loss, HDL-C increases following weight maintenance in proportion to the amount of weight that is lost. The magnitude of decrease in total- and LDL-C, as well as triglycerides, is directly related to the amount of weight loss ($r = 0.89$, $0.90$, and $0.83$, respectively, all $P < .001$). In contrast, there is a weaker, indirect relationship between HDL-C and weight loss ($r = −0.31$, n.s.) (Fig. 4).
Weight loss provides health benefits beyond lipid lowering by improving glycemic control, systolic and diastolic blood pressure, inflammation, and fibrinolysis. In addition, sustained weight loss also may increase life expectancy. In a prospective analysis of 43,457 overweight, never-smoking US white women age 40 to 64, intentional weight loss of any amount was associated with a 20% reduction in all-cause mortality, a 40% to 50% reduction in mortality from obesity-related cancers, and a 30% to 40% decrease in diabetes-associated mortality.\textsuperscript{103}

Several clinical trials have reported a greater decrease in total and LDL-C cholesterol in men compared with women following a similar amount of weight loss.\textsuperscript{104} However, these sex differences are generally accounted for by differences in baseline body weight and lipid levels. Importantly, diet adherence is a strong predictor of weight loss.\textsuperscript{105} Therefore, it is important to individualize weight loss advice to match patient food preferences and lifestyle to achieve weight loss that can be sustained in the long term.\textsuperscript{105}

**Dietary Patterns That Lower Low-Density Lipoprotein-Cholesterol**

**Therapeutic Lifestyle Change Diet**

The NCEP ATP III guidelines recommend the Therapeutic Lifestyle Change (TLC) diet with therapeutic options for maximal LDL-C lowering (Table 3).\textsuperscript{4} The estimated
reduction in LDL-C for the TLC diet is shown in Table 4. Lichtenstein and colleagues evaluated the effects of the TLC diet (15% protein, 58% carbohydrate, 30% fat) versus a typical Western diet (15% protein, 47% carbohydrate, 38% fat) on lipids and lipoproteins in a controlled setting. Thirty-six participants with LDL-C higher than 130 mg/dL and not taking lipid-lowering medications were studied. The Western diet was higher in saturated fat (16% versus 7%) and monounsaturated fat (16% versus 10%) and lower in polyunsaturated fat (6% versus 10%). The TLC diet decreased LDL-C and HDL-C by 11% and 7%, respectively, over 32 days versus the Western diet. There were no significant changes in TG or the TC:HDL-C ratio.

In another study, by Welty and colleagues, combining the TLC diet with aerobic exercise (30 to 60 minutes three to six times per week) for 6 months resulted in a 9.3% reduction in LDL-C (P = .02), an 18.8% reduction in triglycerides (P < .05), and

<p>| Table 3 |</p>
<table>
<thead>
<tr>
<th>Components of a Therapeutic Lifestyle Changes diet</th>
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<tr>
<td><strong>Component</strong></td>
</tr>
<tr>
<td>LDL-raising nutrients</td>
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<tr>
<td>Saturated fat</td>
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<tr>
<td>Dietary cholesterol</td>
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<tr>
<td>Therapeutic options for LDL lowering</td>
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<tr>
<td>Plant sterols/sterols</td>
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<tr>
<td>Increased viscous (soluble) fiber</td>
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<tr>
<td>Total calories (energy)</td>
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<tr>
<td>Physical activity</td>
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</table>

**Abbreviation:** LDL, low-density lipoprotein.

* Trans fatty acids are another LDL-raising fat that should be kept at a low intake.


<p>| Table 4 |</p>
<table>
<thead>
<tr>
<th>Approximate and cumulative LDL-C reduction achievable by dietary modification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dietary Component</strong></td>
</tr>
<tr>
<td><strong>Major</strong></td>
</tr>
<tr>
<td>Saturated fat</td>
</tr>
<tr>
<td>Dietary cholesterol</td>
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<tr>
<td>Weight reduction</td>
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<tr>
<td><strong>Other LDL-lowering options</strong></td>
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<tr>
<td>Viscous fiber</td>
</tr>
<tr>
<td>Plant sterol/sterol esters</td>
</tr>
<tr>
<td><strong>Cumulative estimate</strong></td>
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</table>

**Abbreviation:** LDL-C, low-density lipoprotein cholesterol.

a 2.6% increase in HDL-C (ns). In this study, physical activity beneficially affected HDL-C and TG in subjects on a TLC diet.

**Portfolio Diet**

The Portfolio Diet is a plant-based TLC diet that is low in saturated fat (< 7% of calories) and cholesterol (< 200 mg per day) with four LDL-C lowering components: viscous fiber (9.8 g/1000 calories), soy and other vegetable proteins (21.4 g/1000 calories), plant sterols (1.0 g/1000 calories), and almonds (14 g/1000 calories). A 35% reduction in LDL-C was predicted in response to the portfolio diet, which is similar to the reduction attainable with statin drugs. In three randomized clinical trials of the Portfolio Diet, all meals were provided to hypercholesterolemic adults (LDL-C >158 mg/dL); the portfolio diet reduced LDL-C by 29% to 35% in 4 weeks versus an 8% to 12% reduction in the control group on a traditional diet low in saturated fat and cholesterol (ATP III). The LDL-C lowering effect with the Portfolio Diet was comparable to the 31% reduction in LDL-C in participants who followed the low saturated fat and cholesterol diet with statin treatment (ie, 20 mg per day lovastatin). Participants on the portfolio diet also had a 28% reduction in C-reactive protein, which also was comparable to the effect seen with statin treatment (−33%), suggesting a similar reduction in CVD risk.

In a recent study, the efficacy of the Portfolio Diet was tested in a free-living setting with subjects on self-selected diets for 1 year. LDL-C decreased 14.0% ± 1.6% at 3 months, which was maintained at 1 year (−12.8% ± 2.0%). Although the overall reduction in LDL-C at 3 months was significantly less than in previous studies where meals were provided, 32% of participants achieved LDL-C reductions greater than 20% after 1 year. Adherence to the diet was significantly correlated with the change in LDL-C (r = −0.42, P < .001). There was also a significant increase in HDL-C (3%) and a decrease in TG (−14%) and the TC:HDL-C (−13%) and LDL-C:HDL-C (−15%) ratios after 1 year compared with baseline. This study demonstrates that the Portfolio Diet is one effective means for achieving a long-term reduction in LDL-C using diet in a free-living setting, especially for individuals who are able to adhere to this dietary pattern.

**Very Low Fat Diet**

Very low fat diets (VLFD) contain 15% or less fat and are effective in lowering total- and LDL-C. A VLFD diet frequently is accompanied by weight loss because of a reduced energy-density of the diet resulting in a negative calorie balance. Decreasing the fat content of the diet from 35% to 40% of energy to 15% to 20% of energy reduces total- and LDL-C by 10% to 20%, which reflects a decrease in saturated fat intake. There is an increase in TG and decrease in HDL-C following short-term consumption of a VLFD, regardless of whether the diet is high in simple or complex carbohydrates. These changes may be attenuated by a high fiber intake or weight loss.

The Ornish Lifestyle Heart Trial reported that a VLFD, when combined with other lifestyle changes, also reduces cardiac event rates and induces regression of atherosclerosis. In this study, 48 patients with moderate to severe CHD were randomized to receive intensive lifestyle changes or usual care. The intensive lifestyle changes included a vegetarian diet with 7% of calories from total fat, moderate aerobic exercise, stress management training, smoking cessation, and group psychosocial support. In the intensive lifestyle group, LDL-C decreased 40% at 1 year and remained 20% below baseline at 5 years. In the control group, LDL-C decreased by 1.2% at 1 year and by 19.3% at 5 years. The similar results between groups after 5 years likely reflects the fact that 9 (60%) of 15 of the control patients took lipid-lowering
medications between year 1 and year 5 of the study. Overall, 82% of the experimental group experienced lesion regression; the average percent diameter stenosis decreased 3% in the intervention group, whereas the control group showed an 11% increase. At 5 years there also was a 60% decrease in relative risk in cardiac events in the intervention group. Likewise, Esselstyn and colleagues reported disease arrest (measured by angiographic analysis) in all patients (n = 11) with severe CAD who followed a plant-based diet containing less than 10% fat after 5 years. In addition, the investigators reported regression in 8 (73%) adherent patients and no extension of clinical disease or coronary events after 12 years.

The Multisite Cardiac Lifestyle Intervention Program is a comprehensive lifestyle intervention program administered by insurance companies. Participants in an initial report were 869 nonsmoking CHD patients who attended an onsite program two times per week for 3 months for a total of 104 hours. Participants received diet instruction on a very low fat (10% of energy), plant-based, whole foods diet high in complex carbohydrates and low in simple sugars. They also were provided with demonstrations (eg, cooking), supervised exercise, stress management, and group support. Over a 3-month period, LDL-C decreased approximately 15%, and reduced dietary fat intake was the only predictor of improvement in LDL-C (P<.001). Improvements in weight, TC, TG, exercise capacity, and hemoglobin A1c also were reported. In 108 patients reporting mild angina and 174 reporting limiting angina at baseline, 74% of these patients were angina free by 12 weeks, and an additional 9% moved from limiting to mild angina.

Clinical trial evidence indicates that a VLFD is effective in reducing total- and LDL-C in the short and long term. Although shown to be effective for reducing total and LDL-C, food and nutrient intake should be monitored in certain population subgroups following a VLFD including growing children, pregnant and lactating women, and the elderly because of the relatively high nutrient and calorie needs for some individuals. More information about a very low fat diet and the Lifestyle Heart Program can be found at [www.ornish.com](http://www.ornish.com).

**DIET AND LIFESTYLE COMPONENTS THAT LOWER TRIGLYCERIDES AND RAISE HIGH-DENSITY LIPOPROTEIN-CHOLESTEROL**

**Omega 3 Fatty Acids**

Omega-3 (n-3) fatty acids are polyunsaturated fatty acids of marine (primarily eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) and plant (principally alpha-linolenic acid [ALA]) origin. Direct sources of EPA and DHA are fatty fish, fish oil, fortified foods, and more recently, DHA-rich algal oil supplements. EPA, and to some extent DHA, also can be derived from ALA. ALA is an essential fatty acid because it cannot be synthesized by humans and therefore must be consumed in the diet. Major dietary sources of ALA are vegetable oils, nuts, and seeds, with particularly high levels found in flaxseed. Other sources of ALA include canola and soybean oils, and walnuts.

ALA is the precursor to the n-3 fatty acid family and through a series of elongation and desaturation steps can be converted to EPA and DHA. However, this biochemical pathway is relatively inefficient, with low conversion of dietary ALA to EPA, and especially DHA. Metabolic conversion studies in humans estimate that 5% of ALA is converted to EPA and 0.5% to DHA. Nonetheless, there is some epidemiologic evidence of ALA having a benefit on CHD risk. The evidence to date suggests that ALA beneficially affects CVD risk via nonlipid and lipoprotein risk factors.

The Institute of Medicine of the National Academies recommends 0.6% to 1.2% of total energy from ALA (up to 10% of which can be from EPA + DHA). The lower
boundary of this range meets the adequate intake for ALA. The upper boundary corresponds to the highest intakes from foods consumed by individuals in the United States and Canada. The inclusion of 1 to 2 teaspoons per day of flaxseed oil or 1 tablespoon per day of ground flaxseed meets the current recommendations for ALA. Additionally, 500 mg per day EPA + DHA is recommended for CVD risk reduction, which is equivalent to 8 ounces or 2 servings (4 ounces) of fatty fish per week.

Numerous epidemiologic studies have demonstrated that intake of fish and marine-derived n-3 fatty acids, specifically EPA and DHA, is associated with a reduced risk of fatal and nonfatal CV events. Further evidence for a cardioprotective effect of n-3 fatty acids is provided by two secondary prevention intervention studies: the Diet and Reinfarction Trial (DART) and the Gruppo Italiano per lo Studio della Sopravvivenza nell’Infarto Miocardico (GISSI)-Prevenzione Study. The DART trial demonstrated a 29% reduction in 2-year all-cause mortality in recovered myocardial infarction (MI) patients advised to increase their intake of fatty fish to two servings per week. After 2 years, intake of EPA had increased fourfold and averaged 2.4 g per week, compared with 0.6 g per week in the control group. The GISSI Prevenzione Study was designed to investigate the independent and combined effects of fish oil and vitamin E (300 mg per day) on morbidity and mortality after a heart attack. Patients supplemented with 1 g per day of fish oil (0.85 to 0.88 mg EPA + DHA) had a 20% reduction in risk of overall mortality, a 30% reduction in risk of mortality from CVD, and 47% decrease in risk of sudden death. In the GISSI Prevenzione Study there was no benefit of vitamin E supplementation. More recently, the Japan EPA Lipid Intervention Study (JELIS) reported that combined statin + EPA treatment (1.8 g per day) in patients with existing CAD significantly reduced major coronary events (19%) and the incidence of unstable angina (28%) compared with statin-only controls. These cardioprotective benefits largely have been attributed to the antiarrhythmic effects of EPA and DHA, but also relate to improvements in other CV risk factors.

When considering effects on lipids and lipoproteins, marine-derived n-3 fatty acids are known for their hypotriglyceridemic effects. A comprehensive review by Harris summarized the results of placebo-controlled trials administering less than 7 g per day of n-3 fatty acids (EPA + DHA) from fish oil in individuals with normal (TG < 177 mg/dL) and elevated (TG ≥ 177 mg/dL) TG. Omega-3 fatty acid supplementation (from fish oil) consistently lowered TG in both populations; approximately 4 g per day of EPA + DHA decreased serum TG by 25% to 30%. Furthermore, other studies conducted during this time showed that fish oil lowers TG in a dose-dependent manner (Fig. 5), with the greatest reductions in TG occurring in individuals with higher TG levels at baseline. The results from these early studies are supported by data from numerous clinical trials. In a systematic analysis of 21 studies, Balk and colleagues reported an average reduction in TG of 15% with n-3 fatty acid supplementation from fish oil (0.045 to 5.9 g per day EPA + DHA). A dose-dependent relationship also was apparent; every 1 g per day increase in fish oil (EPA + DHA not reported) resulted in an 8 mg/dL reduction in TG.

In comparison to their effects on TG, the extent to which marine-derived n-3 fatty acids induce clinically significant changes in LDL-C and HDL-C is still under question. Generally, fish oil supplementation is associated with small increases in LDL-C and HDL-C. This LDL-C and HDL-C response typically is seen in response to high doses of marine-derived n-3 fatty acids that are used to treat hypertriglyceridemia. Harris reported that daily supplementation with approximately 4 g per day n-3 fatty acids (EPA + DHA) was associated with a 5% to 10% increase in LDL-C and a 1% to 3% increase in HDL-C. The observed increase in LDL-C was greater in
hypertriglyceridemic patients (TG ≥ 177 mg/dL), and in those with the greatest TG-lowering response. Similarly, Balk and colleagues\textsuperscript{139} concluded that n-3 fatty acids from fish oil (0.045 to 5.9 g per day EPA + DHA) increased HDL-C and LDL-C by 1.6 mg/dL and 6 mg/dL, respectively. In a meta-analysis of 27 studies, Robinson and Stone\textsuperscript{140} summarized and updated the findings of an AHRQ commissioned review of the CV effects of n-3 fatty acids. They reported a 10 mg/dL net increase in LDL-C, with smaller changes in HDL-C (3 to 5 mg/dL), following supplementation with n-3 fatty acids from fish oil (0.045 to 5.4 g per day EPA + DHA). It has been suggested that the increase in LDL-C with fish oil supplementation is because of an increase in LDL-C particle size,\textsuperscript{141,142} although not all studies have reported such an effect.\textsuperscript{143} Although marine-derived n-3 fatty acids have modest effects on total HDL-C, there is some evidence that they also alter HDL subfractions toward a more favorable, cardioprotective profile (increased HDL-2, decreased HDL-3).\textsuperscript{141,144}

**Monounsaturated Fatty Acids**

There is evidence from both epidemiologic and clinical studies that dietary monounsaturated fatty acids (MUFA) have a protective effect on CVD risk. Compared with saturated fats, MUFA have a small total- and LDL-C lowering effect, and relative to carbohydrate, they increase HDL-C and decrease TG.\textsuperscript{145} In a study by Kris-Etherton and colleagues\textsuperscript{146} comparing high-MUFA diets (34% to 36% fat, 17% to 21% MUFA) with a low-fat, Step 2 diet (25% fat, 12% MUFA) and an average American diet (AAD) (34% fat, 11% MUFA), TG were 13% lower in subjects consuming the high-MUFA diets compared with the AAD. In contrast, TG were 11% higher following the low-fat, Step 2 diet compared with the AAD. The high-MUFA diet did not lower HDL-C compared with the AAD, whereas the low-fat diet lowered HDL-C by 4%. Both the high-MUFA diets and low-fat Step 2 diet lowered LDL-C by 10% to 15%. Likewise, a recent study by Berglund and colleagues\textsuperscript{147} compared an AAD (36% fat) with two diets in which 7% of energy from SFA was replaced with either carbohydrate (CHO) or MUFA. Relative to the AAD, LDL-C decreased similarly after the CHO

![Fig. 5. Dose-dependent hypotriglyceridemic effect of omega-3 fatty acids.](image)
(−7.0%) and MUFA (−6.3%) diets. However, the decrease in HDL-C was less during the MUFA diet (−4.3%) versus the CHO diet (−7.2%) (P<.01). In addition, TG were not affected by the MUFA diet compared with the AAD; however, compared with the AAD and the MUFA diet, they were higher on the CHO diet (7.4% and 12%, respectively, P<.01 for both).

These reports that MUFA are more effective than carbohydrates at maintaining HDL-C and lowering TG are consistent with other studies comparing a low-fat versus a moderate-fat diet. A 2008 meta-analysis by Cao and colleagues of 30 controlled feeding studies reported that moderate-fat (MF) and low-fat (LF) blood cholesterol–lowering diets decreased LDL-C similarly. However, although both blood cholesterol–lowering diets decreased HDL-C, the MF diet decreased HDL-C less than the LF diet (difference 2.28 mg/dL, 95% CI 1.66, 2.90, P<.001). The MF diet decreased TG versus the LF diet (−9.36 mg/dL, 95% CI −12.26, −6.08, P<.001 for MF versus LF).

The OmniHeart study compared a diet high in MUFA (37% fat, 21% MUFA) with a carbohydrate-rich (58% carbohydrate, 27% fat, 13% MUFA) and protein-rich (25% protein, 27% fat, 13% MUFA) diet in a randomized, crossover design. HDL-C significantly decreased on the high-carbohydrate and high-protein blood cholesterol–lowering diets (−1.4, and −2.6 mg/dL), but not on the high-MUFA diet (−0.3 mg/dL). In addition, TG significantly decreased following the high-MUFA and high-protein diets (−9.3 and −16.4 mg/dL), but not on the high-carbohydrate diet (+0.1 mg/dL). LDL-C decreased similarly on all three blood cholesterol-lowering diets (−13.1, −14.2 mg/dL, and −11.6, respectively).

Although human studies have reported a favorable effect of MUFA on the lipid profile, a primate study has demonstrated an adverse effect of MUFA on atherosclerosis progression. In this report by Rudel and colleagues, monkeys fed MUFA developed equivalent amounts of coronary artery atherosclerosis (measured by intimal area) as those fed saturated fat, whereas coronary artery atherosclerosis was less in monkeys fed polyunsaturated fat. Further human studies with long-term CVD end points are needed to conclusively determine the effect of MUFA on CVD risk. Long-term studies of a Mediterranean diet, which is high in MUFA and described later in this article, suggests there is, in fact, a favorable effect of a dietary pattern that emphasizes a high-MUFA vegetable oil (ie, olive oil).

Physical Activity

Several notable studies provided early evidence for an association between increased physical activity and reduced total mortality. Since then, epidemiologic studies have sought to clarify the relationship between physical activity and CHD, and have confirmed a reduced risk of overall and/or CVD mortality in physically active compared with sedentary individuals. The Framingham Study provides additional support for the prevention of CVD and an increase in life expectancy in physically active individuals. In this longitudinal study, data collected over 12 years of follow-up showed that men and women in the highest tertile for physical activity had 3.7 and 3.5 years more total life expectancy, respectively, than those with a low physical activity level. Furthermore, men who had a high level of physical activity lived 3.2 more years without CV disease and women 3.3 more years than those in the lowest tertile. More objective measures of physical activity, ie, physical or cardiorespiratory fitness (CRF), also are associated with a reduced incidence of all-cause and CVD mortality. An increase in energy expenditure of 1000 kcal per week (equivalent to 30 minutes of moderate-intensity walking on most days of the week) is associated with a 20% to 30% reduction in risk of all-cause mortality. It is probable that this risk reduction
is influenced by improvements in CVD risk factors, including plasma lipids and lipoproteins.

The effects of regular aerobic exercise training on lipids and lipoproteins have been reviewed in several meta-analyses. Carroll and Dudfield reported that regular aerobic exercise was effective in reducing TG (−18.7 mg/dL, −12%) and increasing HDL-C (1.6 mg/dL, +4.1%) in overweight and obese, sedentary adults with dyslipidemia. Although not clinically significant, exercise was associated with a small reduction in body weight (range −1.5 to 1.9 kg). Similar changes in HDL-C (+4.6%) were reported by Leon and Sanchez, primarily because of an increase in HDL-2. However, they noted that the effect of regular exercise on other parameters such as TG, total- and LDL-C, and body weight was far less consistent and induced only modest improvements (−3.7%, −1.0% (ns), −5.0%, and −0.82 kg, respectively). A meta-analysis by Kelley and colleagues concluded that regular aerobic exercise was effective in reducing TG (−11%) and TC (−2%), but had no significant effects on LDL-C or HDL-C in previously sedentary, overweight, and obese adults. Exercise training was associated with a small reduction in body weight (−1.6 kg).

Interestingly, there is evidence that regular moderate exercise changes LDL-C particle size without any change in total LDL-C concentration. Other reviews have suggested that changes in lipids are dependent on training volume, which can be determined by the number calories expended during physical activity. Durstine and colleagues reported that a regular training program with a minimum expenditure of 1200 kcal per week reduces TG by 4% to 22% and increases HDL-C by 4% to 37%, but has limited effects on LDL-C and TC. Kodama and colleagues recently reported that a minimum energy expenditure of 900 kcal per week (or 120 min/wk) from physical activity was required to elicit changes in HDL-C. For energy expended above this threshold, there existed a dose-response relationship; every 10-minute prolongation of exercise per session (ie, above 120 min/wk) was associated with a 1.4-mg/dL increase in HDL-C.

Although variable, these reviews indicate that regular aerobic exercise can induce favorable changes in TG and HDL-C, but is less effective in lowering total- and LDL-C. Without concomitant energy restriction, exercise training produces only small changes in body weight (generally 1 to 2 kg), and therefore the associated improvements in TG and HDL-C are relatively independent of weight loss. Regular physical activity is recognized by the AHA as an effective therapeutic strategy for the management of abnormal blood lipids, particularly for reducing TG and increasing HDL-C. The exercise-induced improvements in TG and HDL-C are likely mediated by changes in the activity of lipoprotein lipase (LPL), which is increased following aerobic exercise. Interestingly, there is emerging evidence that LPL also is strongly influenced by inactivity. Studies have shown that reducing normal spontaneous standing and ambulatory time (ie, increased sitting) suppresses LPL activity more than it is increased by a bout of vigorous exercise (reviewed by Hamilton and colleagues).

With this in mind, individuals aiming to improve their TG and HDL-C levels should increase their participation in regular structured physical activity and reduce their time spent in sedentary activities. The recently updated physical activity guidelines from the AHA and American College of Sports Medicine recommend that adults spend a minimum of 30 minutes, 5 days per week engaged in moderate aerobic activity, or 20 minutes, 3 days per week in vigorous aerobic activity (a combination of the two is also acceptable) to promote and maintain health. Such aerobic activity is in addition to other light physical tasks such as household chores, gardening, and activities lasting less than 10 minutes. Individuals also are advised to perform muscle strength and endurance activities on 2 days per week.
Population and cohort studies have reported an inverse relationship between daily consumption of one to two alcoholic beverages and CVD risk.\textsuperscript{169–171} One mechanism by which alcohol reduces CVD risk is by lowering fibrinogen levels and increasing protein tissue type plasminogen activator, thereby decreasing blood clot formation.\textsuperscript{172} In addition, moderate alcohol consumption (one to two drinks per day) is associated with higher levels of HDL–C.\textsuperscript{173} The AHA defines a drink as 12 ounces of beer, 4 ounces of wine, 1.5 ounces of 80-proof spirits, or 1 ounce of 100-proof spirits.\textsuperscript{1} The Dietary Guidelines for Americans, 2005 similarly defines alcoholic beverages, however, a serving of wine is defined as 5 ounces.\textsuperscript{2} A meta-analysis of 26 retrospective and prospective observational studies reported a lower risk of CVD for wine and beer drinkers who consume one to two alcoholic beverages daily.\textsuperscript{174} The RR for wine drinkers was 0.68 (95% CI 0.59–0.77) and 0.78 (95% CI 0.70–0.86) for beer drinkers compared with nondrinkers.

A cross-sectional analysis of data from the Third National Health and Nutrition Examination Survey (NHANES III) evaluated the relationship between alcohol consumption and the prevalence of the metabolic syndrome and its components in the US population.\textsuperscript{175} This analysis was performed on 8125 men and women age 20 or older, of which 22% met the NCEP criteria for metabolic syndrome. After adjusting for age, sex, race/ethnicity, education, income, tobacco use, physical activity, and diet, a lower prevalence of metabolic syndrome was observed with mild to moderate alcohol consumption, as was more favorable lipid levels, waist circumference, and fasting insulin (Table 5).

Randomized clinical trials consistently have demonstrated an HDL-raising effect of alcohol. In a randomized crossover study performed by Baer and colleagues,\textsuperscript{176} 51 postmenopausal women were given a controlled diet with zero, one (15 g), or two (30 g) alcoholic drinks per day for 8 weeks. The alcohol, Everclear, was provided with orange juice and participants were instructed to consume their beverage with their evening snack. When compared with the control diet, the alcohol-consuming

### Table 5

<table>
<thead>
<tr>
<th>Alcohol Consumption</th>
<th>Metabolic Syndrome</th>
<th>Low Serum HDL-C</th>
<th>Elevated Triglycerides</th>
<th>Increased Waist Circumference</th>
<th>Elevated Fasting Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 Alcoholic Drink/d</td>
<td>1.0</td>
<td>0.65 (0.54–0.79)</td>
<td>0.73 (0.62–0.87)</td>
<td>0.74 (0.62–0.89)</td>
<td>0.64 (0.46–0.88)</td>
</tr>
<tr>
<td>1–19 Alcoholic Drinks/Month</td>
<td>0.65 (0.54–0.79)</td>
<td>0.73 (0.62–0.87)</td>
<td>0.74 (0.62–0.89)</td>
<td>0.64 (0.46–0.88)</td>
<td>0.46 (0.28–0.88)</td>
</tr>
<tr>
<td>≥ 20 Alcoholic Drinks/Month</td>
<td>0.34 (0.26–0.47)</td>
<td>0.22 (0.16–0.29)</td>
<td>0.56 (0.43–0.74)</td>
<td>0.41 (0.32–0.52)</td>
<td>0.39 (0.24–0.62)</td>
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**Abbreviations:** HDL-C, high-density lipoprotein-cholesterol; NHANES III, Third National Health and Nutrition Examination Survey.

\textsuperscript{a} Meet at least three of five National Cholesterol Education Program Adult Treatment Panel III criteria for metabolic syndrome.

\textsuperscript{b} Men < 40 mg/dL, Women < 50 mg/dL.

\textsuperscript{c} Triglycerides ≥ 150 mg/dL.

\textsuperscript{d} Men >102 cm, Women >88 cm.

\textsuperscript{e} Fasting serum insulin ≥ 90th percentile (116 pmol/L).

groups exhibited a small decrease in triglycerides (−6% to −10%) and LDL-C (−3% to −5%). In addition, HDL-C increased with increasing alcohol consumption: mean HDL-C levels were 54.1 mg/dL with no alcohol intake, 55.3 mg/dL (2.1% increase, ns) with one drink per day, and 57.2 mg/dL (5.7% increase, \( P = .02 \)) with two drinks per day (\( P < .05 \)). Likewise, in a study by Naissides and colleagues, consumption of red wine for 4 weeks decreased LDL-C by 8% and increased HDL-C by 17%, whereas there were no significant changes in the control group. Hansen and colleagues randomized 69 men and women to one of four groups: (1) red wine (males 300 mL per day, females 200 mL per day), (2) water + red grape extract tablets (wine-equivalent dose), (3) water + red grape extract tablets (half dose), or (4) water + placebo tablets for a period of 4 weeks. An increase in HDL-C (+6%) was observed only in the red wine group. Finally, Sierksma and colleagues conducted a randomized crossover study with 18 healthy postmenopausal women. The study participants consumed 24 g of white wine or white grape juice daily for 3 weeks, resulting in a 5% increase in HDL-C in the white wine group (\( P < .05 \)).

In summary, multiple studies have demonstrated a beneficial influence of alcohol on HDL-C and CVD risk. As a result, the AHA supports moderate alcohol consumption (one to two drinks per day for men and one drink per day for women) in persons who routinely consume alcohol responsibly. However, the AHA acknowledges that drinking larger quantities of alcohol increases the risk of alcoholism, high blood pressure, obesity, stroke, breast cancer, suicide, and accidents, and cautions people not to start drinking if they do not already drink alcohol.

**DIETARY PATTERNS THAT LOWER TRIGLYCERIDES AND RAISE HIGH-DENSITY LIPOPROTEIN-CHOLESTEROL**

**Very Low Carbohydrate Diet**

Some scientists have begun advocating a very low carbohydrate diet (VLCD) for treatment of dyslipidemia because it is effective in lowering TG and raising HDL-C (Fig. 6). In contrast, a low-fat, high-carbohydrate diet tends to raise TG and lower HDL-C. There generally is a small decrease or no change in total- or LDL-C following a VLCD; however, there is a shift in the distribution of LDL particle size resulting in a decreased number of atherogenic small, dense LDL particles, and an increase in the number of large, buoyant LDL particles, which are considered to be less atherogenic.

A VLCD generally provides 50 g or less per day of carbohydrate or has less than 10% of total energy from carbohydrate. The consumption of protein and fat is thus increased in a VLCD to compensate for the limited amount of carbohydrate. This results in an average intake of 60% to 65% of calories from fat and 20% to 25% of calories from protein. Food choices compatible with this level of carbohydrate intake include vegetables, beef, poultry, fish, oils, nuts, seeds, and cheese. Despite a high intake of dietary fat on a VLCD, there are few reported adverse effects on lipid levels. The adverse effects that have been reported for VLCDs in the short term (1 year) include constipation, headaches, muscle cramps, diarrhea, weakness, and skin rash. In addition, a VLCD limits fruits, whole grains, and skim milk dairy products, all of which provide important nutrients, and are specific food groups recommended in the Dietary Guidelines for Americans, 2005.

Following a VLCD typically leads to a reduced calorie intake because of appetite suppression and hunger reduction that is the result of the satiating effects of protein and/or ketosis from the high intake of fat. In clinical trials, a VLCD consistently results in a greater amount of weight loss than a low-fat diet over 6 months.
but at 12 months weight loss is similar.\textsuperscript{187,189,192} A decrease in TG and increase in HDL-C also is reported with a VLCD in the absence of weight loss.\textsuperscript{193}

In summary, a VLCD diet appears to be as effective in reducing body weight over the long term (ie, 1 year) as a low-fat diet. With respect to effects on the lipid profile, a VLCD diet appears to confer benefits on TG lowering. However, achieving nutrient adequacy via food-based dietary recommendations is not possible for a VLCD because of limitations in foods allowed (eg, milk, fruits, and whole grains). Thus, long-term safety studies of this dietary pattern are needed before recommendations can be made.

**Mediterranean Diet**

There are many countries in the Mediterranean region that have distinct dietary patterns. Nonetheless, there are a number of similar characteristics of diets in this region. The Mediterranean diet is associated with a low incidence of CHD, which is attributed in part to a high consumption of MUFA (primarily from olive oil) and low consumption of saturated fat. The International Conference on the Diet of the Mediterranean summarized the key dietary components in 1993. They are:

1. An abundance of plant foods (eg, fruits, vegetables, potatoes, breads, grains, beans, nuts, and seeds)
2. Minimally processed and, whenever possible, seasonally fresh foods
3. Fresh fruits as the typical daily dessert
4. Olive oil as the principal source of dietary fat
5. Dairy, poultry, and fish in low to moderate amounts
6. Less than five eggs per week
7. Red meat in low frequency and amounts
8. Wine in low to moderate amounts (one to two glasses per day for men and one glass per day for women)

The Mediterranean diet, being largely plant based, also includes a high intake of fiber and phytosterols (~400 mg per day). The Mediterranean diet is effective in reducing triglycerides and increasing HDL-C in randomized clinical trials. The Prevención con Dieta Mediterránea (PREDIMED) study is a large (n = 9000) randomized, clinical trial that is being conducted in Spain and will be completed in 2010. The aim is to evaluate the effects of the Mediterranean diet on the primary prevention of CVD by comparing three diets: a low-fat diet that meets AHA Guidelines, a Mediterranean diet with virgin olive oil (1 L per week), and a Mediterranean diet with nuts (30 g per day). A subgroup of 772 asymptomatic subjects ages 55 to 80 were followed for 3 months. LDL-C decreased significantly in both Mediterranean diet groups (−3.8 to −5.8 mg/dL) but not in the low-fat group. Both Mediterranean diets increased HDL-C relative to the low-fat diet (1.6 to 2.5 mg/dL, P<.001). In addition, triglycerides decreased significantly in the Mediterranean diet with nuts group (−7.6 mg/dL) compared with baseline, but not in the Mediterranean diet with virgin olive oil (−3.0 mg/dL) or low-fat diet (−2.4 mg/dL) groups.

In a randomized, single-blind trial by Esposito and colleagues, 180 men and women with metabolic syndrome were randomized to a control or Mediterranean style diet for 2 years. The intervention group received detailed advice about how to increase daily consumption of whole grains, fruits, vegetables, nuts, and olive oil; the control group followed a prudent diet (50% to 60% carbohydrate; 15% to 20% proteins, <30% fat). Compared with the control group, the Mediterranean diet group had a significant decrease in triglycerides (−19 mg/dL; 95% CI −6 to −32; P = .001) and a significant increase in HDL-C (3 mg/dL; 95% CI 0.8 to 5.2; P = .03).

The benefits of the Mediterranean diet go beyond its effects on HDL-C and triglycerides, as it has also been shown to reduce inflammatory markers and body weight, and improve endothelial function. In addition, the Lyon Diet Heart Study reported a dramatic decrease in recurrent heart disease in patients following a Mediterranean diet. The Lyon Diet Heart Study was a randomized, controlled trial in which patients who survived a first myocardial infarction were randomized to a Mediterranean-style diet (30% fat, high in alpha-linolenic acid, 13% MUFA, 8% SFA) or

### Table 6

<table>
<thead>
<tr>
<th>Eating Pattern</th>
<th>DASH</th>
<th>TLC</th>
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</thead>
<tbody>
<tr>
<td>Grains</td>
<td>6–8 sv/d</td>
<td>7 sv/d</td>
</tr>
<tr>
<td>Vegetables</td>
<td>4–5 sv/d</td>
<td>5 sv/d</td>
</tr>
<tr>
<td>Fruits</td>
<td>4–5 sv/d</td>
<td>4 sv/d</td>
</tr>
<tr>
<td>Fat-free or low-fat dairy</td>
<td>2–3 sv/d</td>
<td>2–3 sv/d</td>
</tr>
<tr>
<td>Lean meats, poultry and</td>
<td>&lt;6 oz./d</td>
<td>≤5 oz./d</td>
</tr>
<tr>
<td>fish</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuts, seeds, legumes</td>
<td>4–5 sv/wk</td>
<td>Counted in vegetable servings</td>
</tr>
<tr>
<td>Fats and oils</td>
<td>2–3 sv/d</td>
<td>Amount depends on calorie level</td>
</tr>
<tr>
<td>Sweets and added sugars</td>
<td>5 or less sv/wk</td>
<td>No recommendation</td>
</tr>
</tbody>
</table>

*Abbreviations: AHA, American Heart Association; DASH, dietary approaches to stop hypertension; TLC, Therapeutic Lifestyle Changes; sv, serving.*
a prudent Western diet for an average of 46 months. Subjects following the Mediterranean-style diet had a 50% to 70% lower risk of recurrent heart disease, despite no change in lipids and lipoproteins during the study period. Collectively, there is considerable evidence that a Mediterranean-style diet favorably affects HDL-C, TG, and CVD risk. The ongoing PREDIMED study will provide new data on the long-term CV effects of a Mediterranean diet.

SUMMARY

Food-based dietary guidelines have been issued that meet the recommended levels of nutrients described herein (Table 6). Adhering to these guidelines is expected to lower TC, LDL-C, and TG, and increase HDL-C, and, thereby reduce CVD risk. This dietary pattern is low in SFA, TFA, and dietary cholesterol, and emphasizes unsaturated fats. It also promotes consumption of fruits, vegetables, whole grains, low-fat/skim dairy products, lean meats, poultry, and fish (ie, two servings per week with emphasis on fatty fish), and liquid vegetable oils, nuts, and seeds. For maximum LDL-C reduction, emphasis on viscous fiber is recommended, as well as inclusion of plant sterols/stanols. In addition, weight loss and a program of regular physical activity will beneficially affect these major lipid and lipoprotein CVD risk factors. Adhering to a healthy diet is an important tool for combating heart disease through lipid and lipoprotein modulation. Major public health efforts are needed to help people adhere to this dietary pattern with recommended lifestyle behaviors to markedly reduce CVD risk.

REFERENCES


191. Volek JS, Feinman RD. Carbohydrate restriction improves the features of metabolic syndrome. Metabolic syndrome may be defined by the response to carbohydrate restriction. Nutr Metab (Lond) 2004;2:1.


