# Successful Control of Dyslipidemia in Patients with Metabolic Syndrome: Focus on Lifestyle Changes

**Neil J. Stone, MD**
*Professor, Department of Medicine*
*Section of Cardiology*
*Feinberg School of Medicine*
*Northwestern University*
*Chicago, Illinois*



**Approaches to controlling dyslipidemia in patients with metabolic syndrome must take into consideration a patient's individual characteristics and underlying lipid disorder. Some patients will require pharmacologic therapy, whereas others can be controlled with lifestyle changes alone. The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines recommend that patients with at least 3 of the following clinical variables be designated as having metabolic syndrome: abdominal obesity as reflected in increased waist circumference; a low high-density lipoprotein cholesterol (HDL-C) level; an elevated triglyceride level; elevated blood pressure or treatment with antihypertensive medications; and/or elevated fasting plasma glucose or treatment with antidiabetic medications. Unless patients with metabolic syndrome change their lifestyle, existing cardiovascular and metabolic risk factors will worsen or new risk factors will develop. This helps explain why these patients are at increased risk for developing type 2 diabetes mellitus (DM) and coronary heart disease (CHD). The lifestyle changes recommended by NCEP ATP III for controlling dyslipidemia (ie, elevated levels of triglycerides and decreased levels of HDL-C) in patients with metabolic syndrome or type 2 DM include (1) reduced intake of saturated fats and dietary cholesterol, (2) intake of dietary options to enhance lowering of low-density lipoprotein cholesterol, (3) weight control, and (4) increased physical activity. If lifestyle changes are not successful for individuals at high risk of developing CHD, or for those who currently have CHD, a CHD risk equivalent, or persistent atherogenic dyslipidemia, then pharmacotherapy may be necessary as defined by NCEP ATP III guidelines. (*Clinical Cornerstone.* 2006;8[Suppl 1];S15–S20) Copyright © 2006 Excerpta Medica, Inc.**

Controlling dyslipidemia in patients with metabolic syndrome requires strategies appropriate to a patient's individual characteristics and underlying lipid disorder. Patients with a cluster of cardiovascular and metabolic risk factors are at increased risk for developing type 2 diabetes mellitus (DM) and coronary heart disease (CHD).[1–3]

In 2001, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III)[4] proposed that patients with at least 3 of the following clinical variables be designated as having metabolic syndrome: abdominal obesity as reflected in increased waist circumference; a low high-density lipoprotein cholesterol (HDL-C) level; an elevated triglyceride level; elevated blood pressure or treatment with antihypertensive medications; and/or elevated fasting plasma glucose (FPG) or treatment with antidiabetic medications. Elevated levels of small, dense low-density lipoprotein (sdLDL) particles also have been found to be prevalent.

However, the recent American Heart Association/ National Heart, Lung, and Blood Institute definition for

**KEY POINT**

**Controlling dyslipidemia requires strategies appropriate to a patient's individual characteristics and underlying lipid disorder.**

metabolic syndrome[5] focuses the clinician and patient on the underlying causes of the syndrome—poor diet, sedentary lifestyle, and weight gain. This focus is of clinical import because successful lifestyle changes can improve dyslipidemia (ie, elevated triglycerides and decreased levels of HDL-C), markedly reduce the risk for progression to type 2 DM,[6,7] and reduce CHD risk.[5]

**KEY POINT**

**Lifestyle changes can improve dyslipidemia, markedly reduce the risk for progression to type 2 DM, and reduce CHD risk.**

## NONPHARMACOLOGIC TREATMENT OF DYSLIPIDEMIA

### Weight Loss

The adverse effects of increasing body mass index (BMI) on total cholesterol (TC), HDL-C, and blood pressure are well documented.[8] Fot this reason, there has been great interest among clinicians in helping patients lose weight effectively. Although few long-term (≥1 year) controlled studies have been performed to assess the efficacy of dietary interventions (**Table I**),[9–12] in a long-term, randomized controlled study of a very-low-carbohydrate/high-protein (Atkins) diet in 63 obese patients, Foster et al[11] found a significantly greater mean (SD) percentage change in body weight from baseline to 6 months with the Atkins diet compared with a conventional diet (–7.0% [6.5%] vs –3.2% [5.6%]; $P = 0.02$). At 1 year, however, the difference was not significant (–4.4% [6.7%] vs –2.5% [6.3%]). Yet based on the results of a study by Dansinger et al,[12] a low-carbohydrate regimen might be associated with improvements in some glycemic indices, as well as triglyceride and HDL-C levels. When several low-carbohydrate diets (Atkins, Ornish, Weight Watchers, and Zone) were compared in a study of 160 patients with hypertension, dyslipidemia, or elevated FPG, the greatest benefit was not related to a specific diet but rather occurred in those patients with greatest adherence to the assigned regimen ($r = 0.6$; $P < 0.001$).

When treating patients with metabolic syndrome and atherogenic dyslipidemia, therefore, it is important to achieve the patient's commitment and to advocate a dietary regimen that is healthful for the long term.

### Exercise

The Studies of Targeted Risk Reduction Interventions through Defined Exercise (STRRIDE)[13] trial provided insight into the qualitative and quantitative aspects of exercise in a population that had risk factors for metabolic syndrome. STRRIDE investigators reported on 111 overweight (mean BMI, 29 kg/m$^2$), sedentary men and women with mild to moderate dyslipidemia who were randomly assigned to participate in 1 of 3 exercise groups for ~8 months, or in a nonexercising control group for 6 months. Both the amount (km/wk) and the intensity (percentage of peak oxygen consumption) of exercise varied between groups as follows: the low-amount, moderate-intensity (LA-MI) group exercised the caloric equivalent of walking 19.2 km (12 miles) per week at 40% to 55% of peak oxygen consumption; the low-amount, high-intensity (LA-HI) group exercised the caloric equivalent of jogging 19.2 km (12 miles) per week at 65% to 80% peak oxygen consumption; and the high-amount, high-intensity (HA-HI) group exercised the caloric equivalent of jogging 32.0 km (20 miles) per week at 65% to 80% of peak oxygen consumption. Subjects were encouraged to maintain their baseline body weight.

Among the 76% (84/111) of subjects who complied with the program and were included in the analysis, it was the amount of exercise and not the intensity of exercise that had a positive effect on lipoproteins and lipoprotein subfractions. Importantly, the investigators found that a relatively high amount of regular exercise, even in the absence of clinically significant weight loss, improved the overall lipoprotein profile. Although exercise had no significant effect on TC or low-density lipoprotein cholesterol (LDL-C) levels in any of the 3 exercise groups, the concentrations of low-density lipoprotein (LDL) and sdLDL particles decreased significantly in the HA-HI group ($P = 0.02$ and $P = 0.016$, respectively). Additionally, the average size of LDL particles was increased significantly in all 3 exercise groups ($P = 0.03$, $P = 0.015$, $P = 0.002$ in the LA-MI, LA-HI, and HA-HI groups, respectively). Moreover, there was a significant increase in HDL-C levels in the HA-HI group ($P = 0.015$) and a significant decrease in triglyceride levels in the LA-MI and HA-HI groups ($P < 0.001$ and $P = 0.006$, respectively). The concentration of large high-density lipoprotein (HDL) particles was increased only in the

**TABLE I. SELECTED CONTROLLED STUDIES OF WEIGHT LOSS WITH A DURATION ≥1 YEAR.**

| Study | Duration, mo | Completers | Age, Mean, y | BMI, Mean, kg/m$^2$ | Interventions | Weight Δs, Comments |
|---|---|---|---|---|---|---|
| McManus et al[9] | 18 | After 18 mo, 54% in moderate-fat group still actively participating vs 20% in low-fat group ($P < 0.002$) | 44 | 33.5 | Moderate-fat diet (35% of energy) vs low-fat diet (20% of energy) | Between-group Δ in mean weight loss: 7.0 kg (95% CI, 5.3–8.7) |
| Stern et al[10] | 12 | 87/132 (66%): 44/64 (69%) in low-carbohydrate group, 43/68 (63%) in conventional group | 53 | 42.9 | Low-carbohydrate (<30 g/d) diet vs conventional/ calorie-restricted (<25% fat) diet | Weight Δs NS (mean [SD], –5.1 [8.7] vs –4.1 [8.4] kg); significant improvements in triglyceride and HDL-C levels vs conventional diet ($P = 0.044$ and $P = 0.025$, respectively) |
| Foster et al[11] | 12 | 37/63 (59%): 20/33 (61%) in study group, 17/30 (57%) in conventional group | 44 | 33 | Low-carbohydrate/ high-protein/high-fat diet vs conventional/calorie-restricted/high-carbohydrate/ low-fat (25%) diet | Weight Δs NS (mean [SD], –4.4 [6.7] vs –2.5 [6.3] kg); significant improvements in triglyceride and HDL-C levels vs conventional diet (both, $P = 0.04$) |
| Dansinger et al[12] | 12 | 93/160 (58%): 21/40 (53%) in Atkins group, 26/40 (65%) in Zone group, 26/40 (65%) in Weight Watchers group, 20/40 (50%) in Ornish group | 49 | 35 | Atkins, Zone, Weight Watchers, and Ornish diets | Weight Δ correlated with self-reported dietary adherence ($r = 0.6$; $P < 0.001$), but not with diet type ($r = 0.07$; $P = 0.40$); for all diets, ↓ TC/HDL-C, CRP, and insulin levels correlated with weight loss (mean $r = 0.36$, 0.37, and 0.39, respectively; $P$ = NS between groups) |

BMI = body mass index; Δ = change; NS = not significant; HDL-C = high-density lipoprotein cholesterol; TC = total cholesterol; CRP = C-reactive protein.

HA-HI group ($P = 0.05$). The results of this study suggest that sustained exercise improves the levels and concentrations of lipids, lipoproteins, and lipoprotein subfractions found in individuals with metabolic syndrome and atherogenic dyslipidemia. The investigators stressed that it was the amount and not the intensity of exercise that made the most difference in improving lipid and lipoprotein profiles.

**KEY POINT**

**Sustained exercise improves the levels and concentrations of lipids, lipoproteins, and lipoprotein subfractions.**

CHD risk is also improved with exercise. In a large, observational study,[14] 73,743 healthy postmenopausal women aged 50 to 79 years were asked to walk briskly or exercise vigorously for at least 2.5 hours per week. At a mean follow-up period of 3.2 years, the women had a mean relative risk reduction for cardiovascular disease of ~30%. This finding was observed in all of the subjects, regardless of race, BMI, or age. These findings support the endorsement of regular exercise in individuals with metabolic syndrome.

### Therapeutic Lifestyle Change

Whereas NCEP ATP II guidelines, which were published in 1994, focused primarily on limiting intake of total dietary fat (<30% of energy), saturated fat, and dietary cholesterol,[15] NCEP ATP III guidelines suggest an approach called *therapeutic lifestyle change* (TLC).[4] The TLC approach recommends (1) reduced intake of saturated fats and cholesterol; (2) intake of therapeutic dietary options (eg, plant stanols/sterols and increased viscous fiber) to enhance lowering of LDL-C levels; (3) weight control; and (4) increased physical activity. Most important, ATP III guidelines specifically recommend a range of total fat intake of 25% to 35% to emphasize the need for qualitative rather than quantitative changes in dietary fat. The TLC approach is consistent with the lifestyle regimens used in the Finnish Diabetes Prevention Study[6] and the Diabetes Prevention Program.[7] These controlled trials in overweight men and women with impaired glucose tolerance found that a regimen of regular exercise and a low-saturated-fat/high-fiber diet that resulted in mild weight loss could reduce the risk for progression to diabetes by ~60%.[6,7] This lifestyle approach worked in both men and women and in each age group included in these studies,[6,7] and it was nearly twice as effective as metformin therapy in reducing the risk for progression to type 2 DM (58% [95% CI, 48%–66%] vs 31% [95% CI, 17%–43%]).[7]

### Mediterranean-Style vs Western-Style Diet

A significant reduction in cardiac events was seen in the Lyon Diet Heart Study,[16,17] a trial in 605 male and female survivors of a first myocardial infarction (MI) who were randomized to a Mediterranean-style diet (n = 302) or a more Western-style diet typically given postinfarct (control; n = 303). The Mediterranean diet emphasizes (1) a high intake of fruits, vegetables, bread, cereal, potatoes, beans, nuts, seeds, and olive oil; (2) dairy products, fish, and poultry in low to moderate amounts; (3) eggs 0 to 4 times weekly; and (5) little red meat.[17] Thus, in contrast to the control diet, the study diet was low in saturated fat and dietary cholesterol and high in fiber, monounsaturated fats (eg, olive oil), and omega (Ω)-3 fatty acids. Participants assigned to the study diet were given a margarine with saturated fatty acid and oleic acid contents similar to olive oil but with higher linoleic acid and α-linolenic acid levels. At 46 months, subjects following the study diet had a 50% to 70% lower risk for recurrent CHD compared with subjects following the usual postinfarct diet.

In the clinical trials known as the Diet And Reinfarction Trial (DART)[18] and the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardio (ie, the Italian Group for the Study of Survival of MI, or GISSI),[19] which studied survivors of MI, an early beneficial effect on mortality was seen in patients who consumed fish or fish oil. In the GISSI trial, triglyceride and LDL-C levels were significantly improved ($P < 0.001$ and $P = 0.002$, respectively) in patients who received Ω-3 fatty acid supplementation; HDL-C levels also improved but not significantly.[19]

A careful review[20] of the GISSI trial suggested that the clinical benefits of low-dose Ω-3 supplementation were most likely due not to a lipid effect but rather to the Ω-6/Ω-3 fatty acid ratio produced. The Mediterranean diet replaces plant seed oils, which are 70% Ω-6 fatty acids/0% Ω-3 fatty acids, with very-low Ω-6 olive oil, and it is this substitution that may enhance the effects of Ω-3 supplementation.

In his review, Leaf[20] indicates that the Ω-6/Ω-3 fatty acid ratio can be further understood as the ratio of Ω-6 arachidonic acid (AA) to the Ω-3 eicosapentaenoic + docosahexaenoic acids (EPA+DHA). AA is the source of prostaglandins, leukotrienes, lipoxins, and epoxygenase products, many of which are potent regulators of cell functions. Several of the products of EPA have actions that prevent or oppose the equivalent products of AA. Excess Ω-6 AA unbalanced by Ω-3 EPA+DHA may increase the possibility of coronary atherosclerosis and sudden cardiac arrhythmic death, whereas reducing Ω-6 fatty acids and decreasing the AA/EPA+DHA ratio should promote the antiarrhythmic effects of Ω-3 fatty acids and reduce total cardiovascular mortality. The optimal Ω-6/Ω-3 ratio appears to be about 1/1; however, the ratio estimated to be prevalent in the United States today is 15/1 to 20/1 or higher.

### Importance of Behavioral Change in Affecting Lifestyle Modification

A review by Manson et al[21] emphasized the importance of behavioral change in affecting lifestyle modification and offered a modification to the stages-of-change model that might help patients understand where they are on the continuum of change. According to the stages-of-change model, behavioral change occurs in 5 steps: (1) precontemplation; (2) contemplation; (3) preparation; (4) action; and (5) maintenance. The reviewers offered a modification to this model—a "patient-stage," whereby clinicians would provide information, support, or tools—that might help patients (1) understand where they are in the continuum of change and (2) move to the next stage. In the author's opinion, asking patients how likely they are to change is useful in understanding whether expectations are realistic, and in planning future interventions.

Wing[22] has emphasized the need not only to focus on treating overweight individuals and effectively maintaining weight loss but also on preventing obesity and weight gain. There is growing evidence that efforts to prevent weight gain must begin early in life, as lower birth weight followed by rapid excess weight gain in childhood and adolescence increases the risk for the development of insulin resistance and CHD.[23,24] Clearly, the potential to reduce the burden of diabetes and CHD later in life is great.

**KEY POINT**

**Asking patients how likely they are to change is useful in understanding whether expectations are realistic.**

## CONCLUSION

In individuals with metabolic syndrome and atherogenic dyslipidemia, approaches to treatment must consider the patient's individual characteristics and underlying lipid disorder. Emphasis must be placed on lifestyle modification, including dietary changes, weight control, and increased physical activity. For those who do not have CHD or a CHD risk equivalent, these approaches may be all that is required. However, for those individuals at higher risk of developing CHD, or who currently have CHD, a CHD risk equivalent, or persistent atherogenic dyslipidemia, pharmacotherapy may also be necessary to help patients attain appropriate lipid goals.

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**Address correspondence to:** Neil J. Stone MD, Professor, Department of Medicine, Section of Cardiology, Feinberg School of Medicine, Northwestern University, 211 E. Chicago Avenue, STE 1050, Chicago, IL 60611 E-mail: n-stone@northwestern.edu