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IV. General Approach to Treatment—Goals and Thresholds

The basic principle that guides cholesterol-lowering intervention is that the intensity of treatment is directly related to the degree of risk for CHD events. Both short-term (10-year) risk and long-term risk must be considered for treatment decisions. Persons with existing CHD (or a CHD risk equivalent) are at the highest risk; for this reason, they have the lowest goal level for LDL cholesterol and receive the most intensive treatment. For persons without CHD, classification and treatment goals are based on the category of risk, of which there are two—multiple (2+) risk factors other than LDL, and 0–1 risk factor. Persons with 2+ risk factors have an LDL goal that is not quite as low as that for persons with CHD (or CHD risk equivalents). ATP III differs from ATP II in that it distinguishes three subcategories of risk among persons with multiple (2+) risk factors: 10-year risk for hard CHD >20 percent, 10–20 percent, and <10 percent. Among the group with multiple risk factors, those at highest risk receive the most intensive LDL-lowering therapy, and those with the lowest risk receive the least intensive therapy. For persons with 0–1 risk factor, LDL goal levels are not as low as for persons with multiple risk factors, and intensive LDL-lowering therapy is not required unless LDL cholesterol levels are very high.

1. Therapeutic goals for LDL cholesterol

ATP III recommends that LDL cholesterol be the primary target of therapy. The LDL cholesterol goals for each risk category are shown in Table IV.1–1.

Table IV.1–1. LDL Cholesterol Goals for Three Risk Levels

Risk Level	LDL-C Goal
CHD and CHD Risk Equivalent	<100 mg/dL
Multiple (2+) Risk Factors	<130 mg/dL*
0–1 Risk Factor	<160 mg/dL

* LDL-C goal for multiple-risk-factor persons with 10-year risk >20 percent = <100 mg/dL.

Persons with CHD or CHD risk equivalent have an LDL cholesterol goal of <100 mg/dL. Those with multiple risk factors have an LDL cholesterol goal of <130 mg/dL; an exception is the patient with a CHD risk equivalent (>20 percent per 10 years) who has an LDL cholesterol goal <100 mg/dL. Finally, those with 0–1 risk factor have a goal LDL cholesterol of <160 mg/dL. These goals are set to maximize reduction in both short-term and long-term risk.

For persons whose LDL cholesterol levels are above the goal for the category, the goal of therapy is achieved through the judicious use of lifestyle and drug therapies. Lifestyle therapy in clinical management is designated Therapeutic Lifestyle Changes (TLC). TLC includes the following: (a) reduced intakes of saturated fats and cholesterol, (b) therapeutic dietary options to enhance LDL lowering (plant stanols/sterols and increased viscous fiber), (c) weight control, and (d) increased physical activity (see Section V). The drugs available for LDL-cholesterol-lowering are presented in Section VI.

ATP III recommends a two-step approach to cholesterol management. Priority goes to attaining the goal for LDL cholesterol; thereafter emphasis shifts to management of the metabolic syndrome and other lipid risk factors. Figure IV.1–1 shows the physician's responsibility at the first visit. Once the lipoprotein analysis is evaluated, risk factor counting and, if necessary, 10-year risk assessment are carried out to determine risk status. The patient is then started on dietary therapy or discharged with instructions for appropriate life-habit modifications. If the patient has CHD or a CHD risk equivalent, LDL-lowering drug therapy can be started simultaneously with dietary therapy if the LDL level warrants.

After an appropriate trial of dietary therapy to reduce LDL cholesterol (~ 3 months), two additional therapeutic decisions may be required. First, if the LDL cholesterol goal has not been achieved, consideration may be given to initiating drug therapy. Second, if the metabolic syndrome is present, additional lifestyle changes (i.e., weight reduction and increased physical activity) will be needed. Later, if lifestyle therapies do not alleviate the metabolic syndrome, drug therapy for treatment of the metabolic risk factors may be required.

2. Management of LDL Cholesterol

The following summarizes the ATP III approach to management of persons in the three categories of risk.

a. CHD and CHD risk equivalents

For persons with CHD and CHD risk equivalents, the type and intensity of LDL-lowering therapy are adjusted according to baseline LDL cholesterol level, i.e., whether ≥130 mg/dL, 100–129 mg/dL, or <100 mg/dL (Table IV.2–1 and Figure IV.2–1). Each subcategory of LDL cholesterol is discussed below.

1) Baseline LDL cholesterol ≥130 mg/dL

Persons with LDL cholesterol ≥130 mg/dL generally will require an LDL-lowering drug to achieve LDL cholesterol <100 mg/dL. Therefore, a cholesterol-lowering drug should be initiated simultaneously with TLC and maximal control of other risk factors. If the LDL cholesterol falls to the range of 100–129 mg/dL on cholesterol-lowering therapy, several options are available depending on circumstances:

- LDL lowering can be intensified with dietary therapy to achieve an LDL cholesterol level <100 mg/dL.
- LDL lowering can be intensified with drug therapy to achieve an LDL cholesterol level <100 mg/dL.
- If the on-treatment LDL cholesterol level is near the goal of therapy, the physician can maintain the current LDL-lowering therapy unchanged.
- If the metabolic syndrome is present, dietary therapy is intensified by increased efforts to reduce excess weight and increase physical activity.
- If the patient has elevated triglycerides or low HDL, a different lipid-lowering drug can be considered (e.g., nicotinic acid or fibric acid) for combination therapy with an LDL-lowering drug (see Section VI).

2) Baseline LDL cholesterol 100–129 mg/dL

When baseline LDL cholesterol is 100–129 mg/dL, several therapeutic options likewise are available. All approaches include TLC as initial therapy. Depending on circumstances, the following options are available:

- Inclusion of therapeutic dietary options (e.g., plant stanol/sterols and increased viscous fiber) can help to achieve the LDL goal.
- If LDL cholesterol levels remain appreciably above 100 mg/dL after 3 months of maximal dietary therapy, consideration can be given to adding an LDL-lowering drug.
- If the patient has an elevated triglyceride or low HDL cholesterol level, another lipid-lowering drug can be considered (e.g., nicotinic acid or fibric acid).
- If the LDL cholesterol level falls to near the goal on dietary therapy alone, the physician can choose to forgo use of a lipid-lowering drug for the present.

Because other risk factors may have contributed importantly to development of CHD in persons with low LDL levels, maximal control of nonlipid risk factors is necessary.

Table IV.2–1. Therapeutic Approaches to LDL Cholesterol Lowering in Persons with CHD or CHD Risk Equivalents

Subcategory of LDL Cholesterol Level	LDL Cholesterol Goal	Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)	Level at Which to Initiate LDL-Lowering Drugs
≥130 mg/dL	<100 mg/dL	≥100 mg/dL	Start drug therapy simultaneously with dietary therapy
100–129 mg/dL	<100 mg/dL	≥100 mg/dL	Consider drug options*
<100 mg/dL	<100 mg/dL	TLC & emphasize weight control and physical activity	LDL-lowering drugs not required

* Some authorities recommend use of LDL-lowering drugs in this category if an LDL cholesterol <100 mg/dL cannot be achieved by TLC. Others prefer use of drugs that primarily modify other lipoprotein fractions, e.g., nicotinic acid and fibrate. Clinical judgment also may call for withholding drug therapy in this subcategory.

3) Baseline LDL cholesterol <100 mg/dL

If baseline LDL cholesterol is below the goal of therapy, further LDL-lowering therapy is not currently recommended. Emphasis should be placed on controlling other risk factors and the metabolic syndrome. The TLC diet should be recommended to the person to help maintain a low LDL.

b. Multiple (2+) risk factors

ATP III differs from ATP II in that it distinguishes three subcategories of risk among persons with multiple risk factors, depending on 10-year risk: >20 percent, 10–20 percent, and <10 percent. Within this category of multiple (2+) risk factors, intensity of therapy is adjusted according to 10-year risk and LDL cholesterol level. The treatment approach for each subcategory is shown below in Table IV.2–2.

The following reviews the approach to each subcategory in more detail.

1) Multiple risk factors, and 10-year risk >20 percent

Persons with multiple risk factors and 10-year risk >20 percent have a CHD risk equivalent and are treated as described in the previous section (See Figure IV.2–1).

2) Multiple risk factors, and 10-year risk 10–20 percent

The goal for LDL cholesterol in this risk category is <130 mg/dL. The therapeutic aim is to reduce short-term risk as well as long-term risk for CHD. If baseline LDL cholesterol is ≥130 mg/dL, persons are started on TLC for a 3-month trial of dietary therapy, possibly augmented by options for further LDL lowering (plant stanols/sterols and increased viscous fiber). After 6 weeks and again after three months of dietary therapy, lipoprotein analysis is repeated. If LDL remains ≥130 mg/dL after three months, consideration can be given to starting an LDL-lowering drug to achieve the LDL goal <130 mg/dL. Should the LDL be less than 130 mg/dL on dietary therapy alone, it can be continued without adding drug treatment. If the metabolic syndrome is present, more attention should be given to weight control and increased physical activity. See Figure IV.2–2 for the treatment algorithm for this subcategory.

3) Multiple risk factors, 10-year risk <10 percent

The goal for LDL cholesterol in this risk category likewise is <130 mg/dL. The therapeutic aim, however, is primarily to reduce longer-term risk. If baseline LDL cholesterol is ≥130 mg/dL, persons are started on dietary therapy for reducing LDL cholesterol. Options for enhancing LDL lowering can be employed if needed to achieve the goal of therapy. After three months of dietary therapy, lipoprotein analysis is repeated. If LDL is <160 mg/dL on dietary therapy alone, the dietary therapy should be continued. LDL-lowering drugs generally are not recommended because the patient is not at high short-term risk. On the other hand, if LDL cholesterol is ≥160 mg/dL, drug therapy can be considered to achieve an LDL cholesterol <130 mg/dL. See Figure IV.2–3 for the treatment algorithm for this subcategory.

c. Zero to one risk factor

Most persons with 0–1 risk factor have a 10-year risk <10 percent. Guidelines for this category are given in Table IV.2–3.

Table IV.2–2. Management of LDL Cholesterol in Persons with Multiple (2+) Risk Factors

10-Year Risk	LDL Goal	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)	LDL Level at Which to Consider Drug Therapy (After TLC)
>20%	<100 mg/dL	≥100 mg/dL	See CHD and CHD risk equivalent
10–20%	<130 mg/dL	≥130 mg/dL	≥130 mg/dL
<10%	<130 mg/dL	≥130 mg/dL	≥160 mg/dL

Table IV.2–3. Management of LDL Cholesterol in Persons with Zero to One (0–1) Risk Factor

Risk Category	LDL Goal	LDL Level at Which to Initiate TLC	LDL Level at Which to to Consider Drug Therapy (After TLC)
0–1 Risk Factor*	<160 mg/dL	≥160 mg/dL	≥190 mg/dL†

* Most persons with 0–1 risk factor have a 10-year risk for CHD <10 percent.
† Drug therapy optional for LDL-C 160–189 mg/dL (after dietary therapy).

The goal for LDL cholesterol in this risk category is <160 mg/dL. The primary aim of therapy is to reduce long-term risk. When baseline LDL cholesterol is ≥160 mg/dL, persons are started on dietary therapy for three months. After 6 weeks, the LDL response is evaluated and dietary enhancers of LDL lowering (plant stanols/sterols and increased viscous fiber) may be added if necessary to reach the LDL goal. After 3 months, lipoprotein analysis is repeated. If LDL cholesterol is <160 mg/dL, dietary therapy is continued. For LDL cholesterol 160–189 mg/dL, drug therapy is optional depending on clinical judgment. Factors that favor use of drugs in this category include:

- A severe single risk factor (heavy cigarette smoking, poorly controlled hypertension, strong family history of premature CHD, or very low HDL cholesterol).
- Multiple life-habit risk factors and emerging risk factors (if measured).
- 10-year risk approaching 10 percent (if measured).

If LDL cholesterol is ≥190 mg/dL despite dietary therapy in persons with 0–1 risk factor, drug therapy can be considered to achieve the goal of therapy in all adults. For persons with severe elevations of LDL cholesterol (e.g., ≥220 mg/dL), drug therapy can be started together with dietary therapy. Most such patients will have genetic forms of hypercholesterolemia that cannot be adequately treated with dietary therapy alone.

d. Management of LDL cholesterol when risk assessment begins with Framingham scoring (Table IV.2–4)

If clinicians choose to begin risk assessment with Framingham risk scoring, the treatment algorithm is similar to that beginning with risk factor counting. The only difference occurs for persons whose 10-year risk is 10–20 percent and who have 0–1 risk factor; if one begins with risk factor counting, such persons would not have their 10-year risk calculated. This difference occurs in only 2.6 percent of the U.S. population that has 0–1 risk factor.

Table IV.2–4. Management of LDL Cholesterol in Persons Beginning with 10-year Risk Assessment

10-Year Risk	LDL Goal	LDL Level at Which to Initiate TLC	LDL Level at Which to Consider Drug Therapy (After TLC)
>20%	<100 mg/dL	≥100 mg/dL	See CHD and CHD risk equivalent
10–20%	<130 mg/dL	≥130 mg/dL	≥130 mg/dL
<10%:			
Multiple (2+) risk factors	<130 mg/dL	≥130 mg/dL	≥160 mg/dL
0–1 risk factor	<160 mg/dL	≥160 mg/dL	≥190 mg/dL*

* Drug therapy optional for LDL-C 160–189 mg/dL (after dietary therapy).

e. Recommendations for persons whose LDL cholesterol levels are below goal

For persons whose LDL cholesterol levels are already below goal levels upon encounter, instructions for appropriate changes in life habits, periodic follow-up, and control of other risk factors are required (upper portions of Figures IV.1–1, IV.2–2, IV.2–3, and IV.2–4). For all persons without CHD or CHD risk equivalents whose LDL is below goal, the diet for the general public and a physical activity regimen should be recommended. For those with CHD or CHD risk equivalent, the therapeutic diet (TLC diet, see Section V) should be recommended even if the LDL is below goal. Follow-up lipoprotein analysis should be carried out according to Table IV.2–5.

Table IV.2–5. Schedule for Follow-Up Lipoprotein Analysis for Persons Whose LDL Cholesterol Levels are Below Goal Levels

Risk Level	LDL Goal (mg/dL)	LDL Level Observed (mg/dL)	Repeat Lipoprotein Analysis
CHD or CHD risk equivalents	<100	<100	<1 year
2+ risk factors	<130	<130	≤2 years
0–1 risk factor	<160	130–159	≤2 years
0–1 risk factor	<160	<130	≤5 years

f. LDL-lowering therapy in older persons

For primary prevention in persons ≥65 years of age, clinical judgment plays an increasingly important role in decisions about LDL-lowering therapy. Framingham risk scores are less robust for predicting risk in older individuals, and measurements of subclinical atherosclerosis, when available, can assume increasing importance. Rather than routinely applying the algorithms described for persons with multiple risk factors, physician judgment may rely more heavily on the estimated NNT to achieve a reduction in CHD events for the different risk categories (Table II.7–2). Other factors including concomitant chronic diseases, social circumstances, chronological and functional age, and financial considerations must be taken into account when making decisions about therapy, especially about use of LDL-lowering drugs, in older persons.

3. Management of atherogenic dyslipidemia and the metabolic syndrome

After an adequate trial of dietary therapy for LDL lowering, attention should turn to atherogenic dyslipidemia and the metabolic syndrome. Treatment of these conditions usually begins after an initial 3-month period of dietary therapy to lower LDL cholesterol. Therapy for atherogenic dyslipidemia and metabolic syndrome thus begins after the LDL goal has been achieved with TLC alone or simultaneously with initiation of more intensive LDL-lowering therapy with drugs.

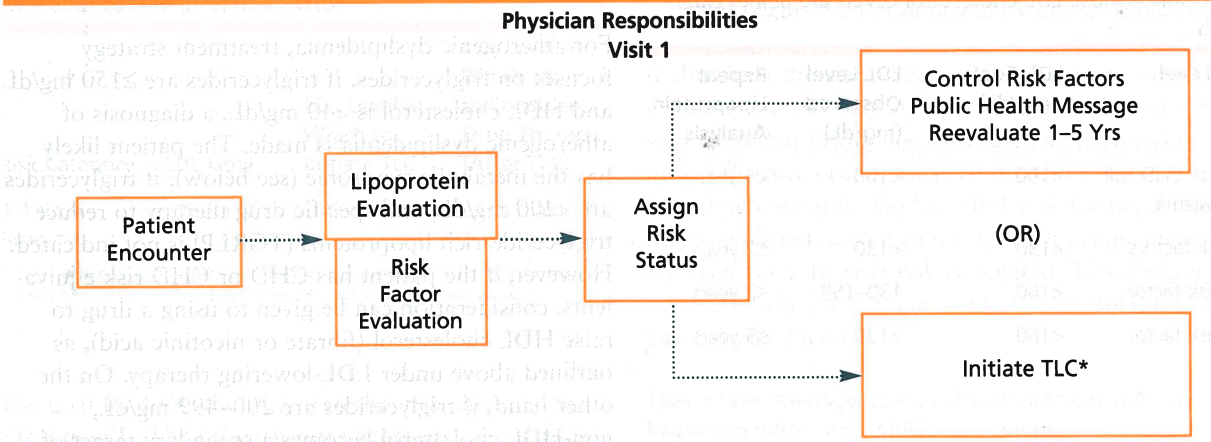
a. Atherogenic dyslipidemia

For atherogenic dyslipidemia, treatment strategy focuses on triglycerides. If triglycerides are ≥150 mg/dL and HDL cholesterol is <40 mg/dL, a diagnosis of atherogenic dyslipidemia is made. The patient likely has the metabolic syndrome (see below); if triglycerides are <200 mg/dL, and specific drug therapy to reduce triglyceride-rich lipoproteins (TGRLP) is not indicated. However, if the patient has CHD or CHD risk equivalents, consideration can be given to using a drug to raise HDL cholesterol (fibrate or nicotinic acid), as outlined above under LDL-lowering therapy. On the other hand, if triglycerides are 200–499 mg/dL, non-HDL cholesterol becomes a secondary target of therapy. Goals for non-HDL cholesterol are 30 mg/dL higher than those for LDL cholesterol. First the LDL cholesterol goal is attained, and if non-HDL remains elevated, additional therapy may be required to achieve the non-HDL goal. Alternative approaches for treatment of elevated non-HDL cholesterol that persists after the LDL goal has been achieved are (a) higher doses of statins, or (b) moderate doses of statins + triglyceride-lowering drug (nicotinic acid or fibrate) (see Sections VI and VII). If triglycerides are very high (≥500 mg/dL), attention turns first to prevention of acute pancreatitis, which is more likely to occur when triglycerides are >1000 mg/dL. Triglyceride-lowering drugs (fibrate or nicotinic acid) become first line therapy; although statins can be used to lower LDL cholesterol to reach the LDL goal, in these patients it is often difficult (and unnecessary) to achieve a non-HDL cholesterol goal of only 30 mg/dL higher than for LDL cholesterol.

b. Metabolic syndrome

Beyond treatment of elevated triglycerides, with drugs if necessary, first-line therapy for the metabolic syndrome is change in life habits, especially reducing weight and increasing physical activity. The approach to treatment of the metabolic syndrome with life-habit modification is presented in Section V.

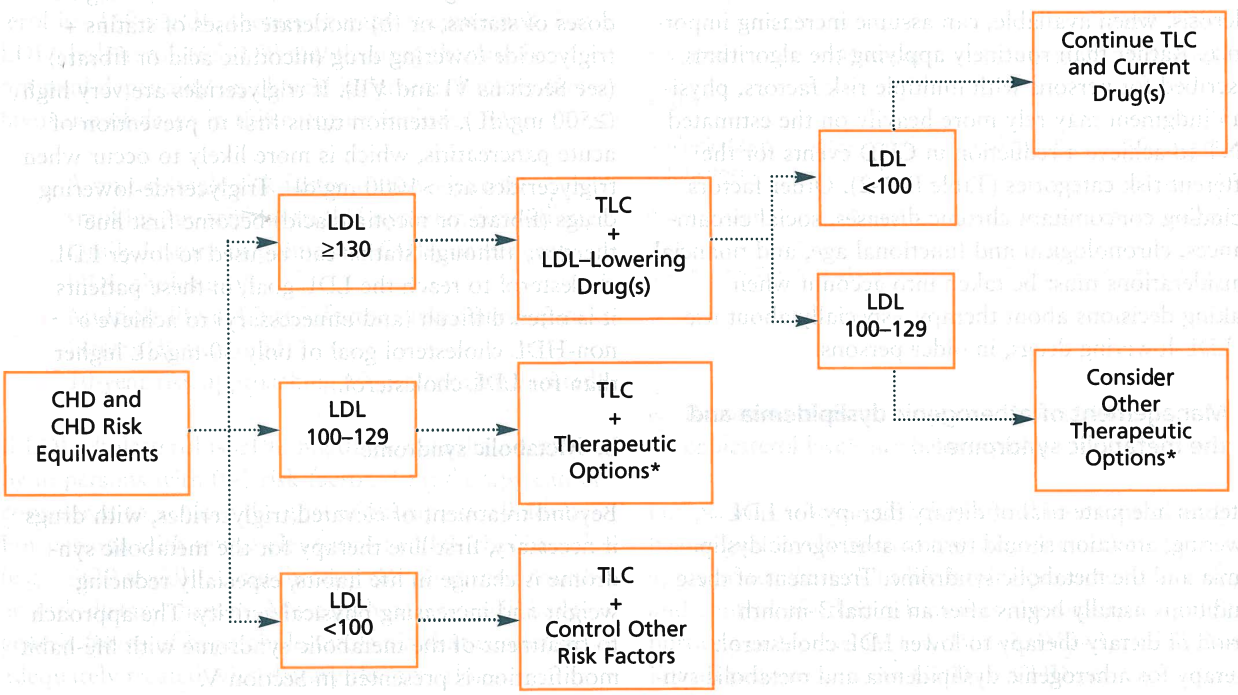
Figure IV.1–1. Physician responsibilities for Visit 1



* If CHD or CHD risk equivalent is present, drug therapy can be started simultaneously with TLC when LDL-C is ≥130 mg/dL.

Figure IV.2–1. Therapeutic approaches to persons with CHD or CHD risk equivalents

The LDL cholesterol goal is <100 mg/dL.



* Therapeutic options include intensifying LDL-lowering dietary or drug therapies, emphasizing weight reduction and increased physical activity, adding drugs to lower triglycerides or raise HDL cholesterol (nicotinic acid or fibrates), and intensifying control of other risk factors.

Figure IV.2–2. Therapeutic approaches to persons with multiple risk factors, 10-year risk 10–20 percent

The LDL cholesterol goal is <130 mg/dL. Drugs can be considered if necessary to attain the LDL cholesterol goal if the LDL cholesterol level is ≥130 mg/dL after a trial of TLC.

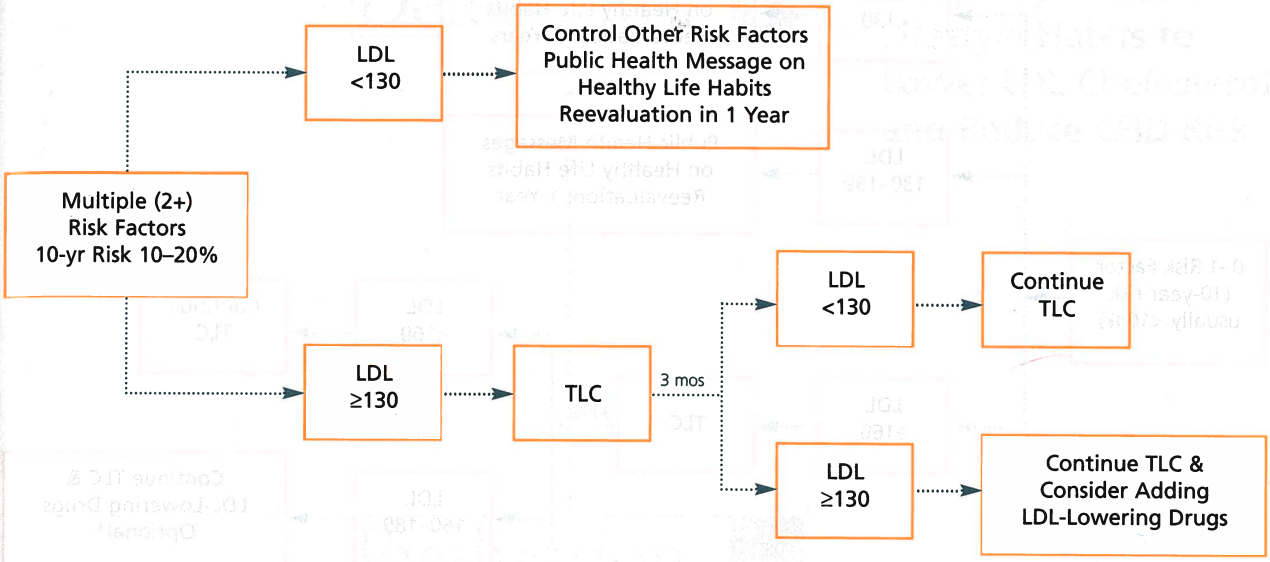


Figure IV.2–3. Therapeutic approaches to the patient with multiple (2+) risk factors, 10-year risk <10 percent

The LDL cholesterol goal is <130 mg/dL. Drug therapy can be considered if LDL cholesterol is ≥160 mg/dL after a trial of TLC.

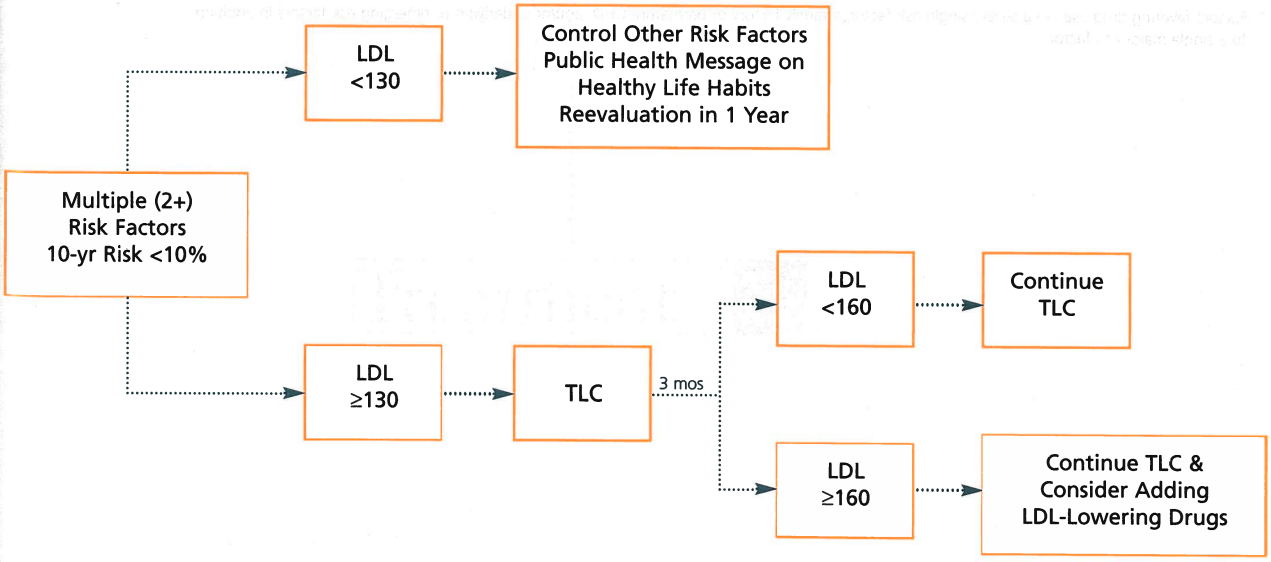
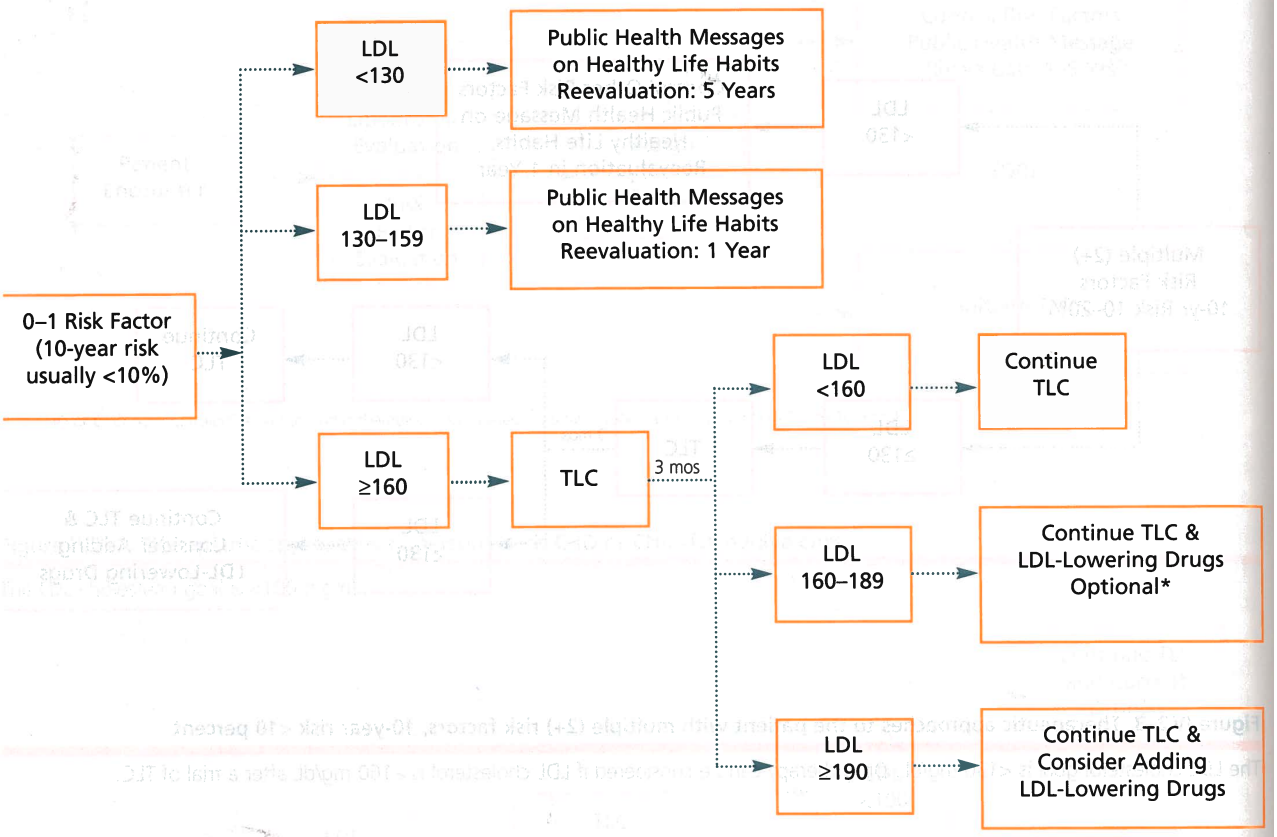


Figure IV.2–4. Therapeutic approaches to persons with 0–1 risk factor

The LDL cholesterol goal is <160 mg/dL. Drug therapy can be considered if the LDL cholesterol level is ≥190 mg/dL after a trial of TLC. If LDL cholesterol is 160–189 mg/dL, drug therapy is optional depending on clinical judgment.



* Factors favoring drug use are a severe single risk factor, a family history of premature CHD, and/or underlying or emerging risk factors in addition to a single major risk factor.

ATTACHMENT 1 (Part 5)

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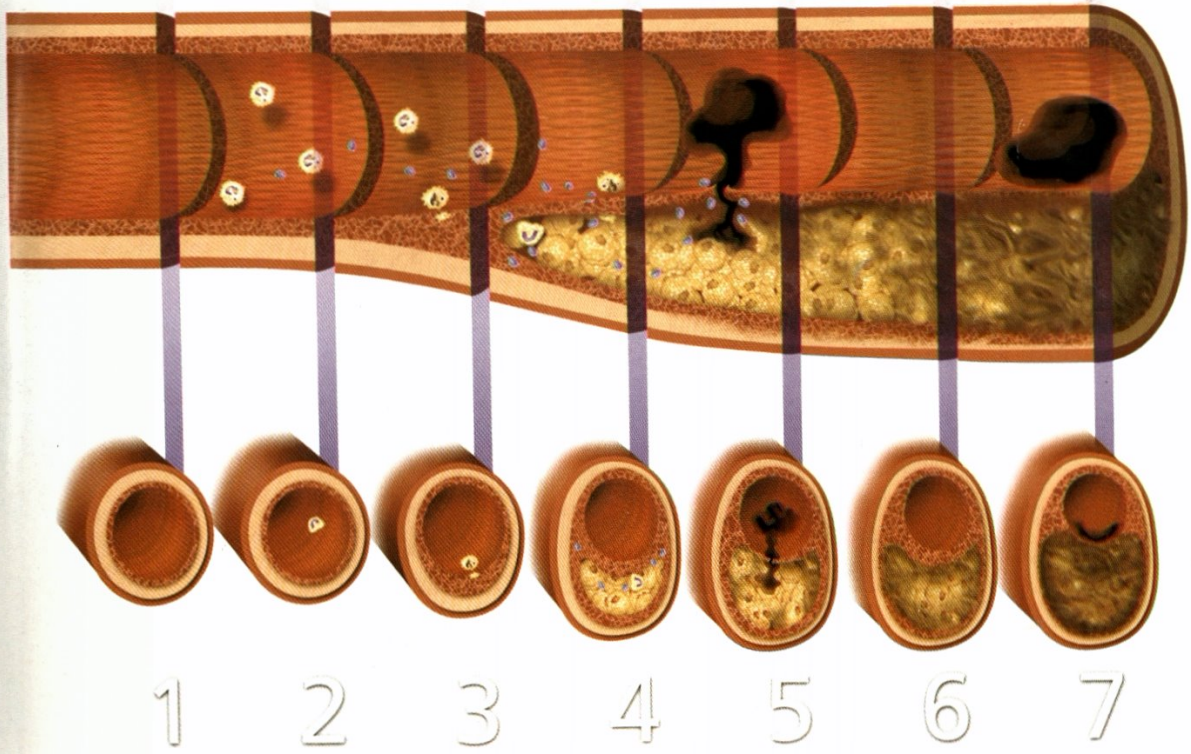

Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on

Detection

Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)

Evaluation

Final Report

Treatment

National Cholesterol Education Program

National Heart, Lung, and Blood Institute

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Contents

V. Adopting Healthful Lifestyle Habits to Lower LDL Cholesterol and Reduce CHD Risk

V. Adopting Healthful Lifestyle Habits to Lower LDL Cholesterol and Reduce CHD Risk

1. Population approach: promoting a base of healthy life habits

NCEP advocates a two-pronged approach for reducing CHD risk: the population approach and the clinical strategy. The two are closely linked. The population approach, which is outlined in the 1990 report of the Population Panel,[5,6] is designed to lower risk in the whole population through adoption of healthy life habits including a healthy diet, weight control, and increased physical activity. The clinical strategy is described in the ATP reports. This section summarizes the population approach and connects it to the clinical strategy. The clinical management team must recognize that they are an integral part of the population approach and contribute to it by providing education and guidance to the patient with high serum cholesterol and the patient's family.

The health community has provided the American public with consistent messages on cardiovascular risk reduction for the past four decades. These messages have encouraged avoidance or cessation of cigarette smoking, reduction of intakes of saturated fats and cholesterol, achieving and maintaining a healthy body weight, regular physical activity, and routine medical check-ups for blood pressure and cholesterol. Table V.1–1 (derived from the Healthy People 2010 publication)[620] reports the current status of the U.S. population on various healthy lifestyle habits and compares it with the goals for 2010.

Although progress has been made, it is clear that much more is needed to bring about the changes required to achieve the goals for 2010. The physician has an important role to play in this effort to help attain these goals.

The NHLBI, American Heart Association, and other organizations have mounted a major effort to reduce risk factors for CHD in the United States. Not only is there continuing research on improved methods for risk reduction, but national educational programs have also been put into effect. Table V.1–2 lists some of the Web sites of the programs sponsored by the U.S. Government.

Table V.1–1. Status Report on Healthy Lifestyle Habits: Healthy People 2010

Lifestyle Habit	Status in the 1990s	Goal for 2010
Healthy weight (BMI <25 kg/m^2)	42%	60%
Saturated fat intake <10% calories	36%	75%
Vegetable intake of at least 3 servings/day with at least 1/3 dark green or orange	3%	50%
Fruit intake of at least 2 servings/day	28%	75%
Grain intake of at least 6 servings/day with at least 1/3 whole grain	7%	50%
Smoking cessation by adult smokers	41%	75%
Regular physical activity of moderate intensity	15%	30%

Table V.1–2. Government-Sponsored Web Sites for Public Information: An Effective Way to Implement the Public Health Approach

Diet	www.nhlbi.nih.gov/chd www.nhlbi.nih.gov/subsites/index.htm—then click Healthy Weight www.nhlbi.nih.gov/hbp www.nutrition.gov
Physical activity	www.fitness.gov
Body weight	www.nhlbi.nih.gov/subsites/index.htm—then click Healthy Weight
Cholesterol	www.nhlbi.nih.gov/chd
Blood pressure	www.nhlbi.nih.gov/hbp
Smoking cessation	www.cdc.gov/tobacco/sgr_tobacco_use.htm

Physicians and other health professionals have the opportunity to implement the public health and clinical approaches to risk reduction through interaction with patients and their families. Even in persons who are not candidates for clinical management of high serum cholesterol, control of other risk factors and preventive efforts convey the broader public health message to the patient. The physician's advice is valued and considered more credible than mass media or non-targeted educational campaigns. The physician can affect the public health arena in many ways. Table V.1–3 compares the role of the physician and other health professionals in the implementation of the public health approach with their role in the clinical management of risk factors through lifestyle changes.

2. General approach to therapeutic lifestyle changes (TLC)

ATP III recommends a multifactorial lifestyle approach to reducing risk for CHD. This approach is designated *therapeutic lifestyle changes* (TLC) and includes the following components (see Table V.2–1):

- Reduced intakes of saturated fats and cholesterol
- Therapeutic dietary options for enhancing LDL lowering (plant stanols/sterols and increased viscous [soluble] fiber)
- Weight reduction
- Increased regular physical activity

Reduced intakes of saturated fats and cholesterol and other therapeutic dietary options for LDL-lowering (plant stanols/sterols and increased viscous fiber) are introduced first for the purpose of achieving the LDL cholesterol goal. After maximum reduction of LDL cholesterol is achieved with dietary therapy, emphasis shifts to management of the metabolic syndrome and its associated lipid risk factors (elevated triglycerides and low HDL cholesterol). A high proportion of patients with the metabolic syndrome are overweight/obese and sedentary; for them, weight reduction therapy and

Table V.1–3. The Role of the Physician and Other Health Care Professionals in Implementing the Population and Clinical Approaches to Lifestyle Modification

	Population Approach	Clinical Approach
Principles	Promote change in lifestyle habits by serving as a role model to patients.	Promote targeted changes in individual lifestyle to produce significant reductions in an individual patient's risk.
	Provide general advice and access to credible sources of information regarding healthy lifestyle habits.	Initiate outcome measurements that will be tracked during scheduled follow-up visits.
		Physicians, dietitians, and other relevant health professionals should go beyond monitoring adherence to actively helping individuals overcome barriers and promote new behaviors.
Diet	Briefly assess dietary intake of saturated fat and cholesterol.	Promote ATP III TLC diet using:
	Promote U.S. Dietary Guidelines (population diet) using pamphlets/handouts and Food Guide Pyramid.	■ Individualized diet counseling that provides acceptable substitutions for favorite foods contributing to a patient's elevated LDL level – counseling often best performed by a registered dietitian
	Provide shopping and food preparation pamphlets/handouts highlighting low saturated fat foods including reduced fat dairy products, leaner meats, lower fat ground meat, and reduced fat baked goods.	■ Reinforcement of dietary principles during follow-up visits at which LDL response to diet is assessed
	Make full use of office personnel to promote public health message.	■ Consideration of readiness to change and level of motivation
Physical activity	Promote regular physical activity by taking a physical activity history.	Follow Surgeon General recommendations for physical activity.[238]
	Provide pamphlets/advice regarding general principles of physical activity.	Promote regular physical activity for individuals using:

Table V.1–3. The Role of the Physician and Other Health Care Professionals in Implementing the Population and Clinical Approaches to Lifestyle Modification (continued)

	Population Approach	Clinical Approach
Physical activity *(continued)*	Recommend 30 minutes of regular moderate intensity activity on most, if not all, days of the week.	■ Specific recommendations to increase physical activity based on a patient's cardiac status, age, and other factors ■ Specific advice regarding how physical activity could be integrated into the patient's lifestyle ■ Follow-up visits to monitor physical activity level, and follow-up counseling regarding barriers to daily physical activity
Body Weight	Ensure that weight, height, and waist circumference are measured at every visit. Promote prevention of weight gain: ■ Provide access to tables identifying height/weight categories for BMI in waiting room or exam room ■ Provide literature relating BMI to health outcomes ■ Provide literature explaining use of Nutrition Facts labeling to identify calorie content and recommended portion sizes of foods	Follow Obesity Education Initiative (OEI) guidelines for weight management.[78,79] Promote prevention of weight gain: ■ Calculate BMI for every patient at every visit ■ Anticipate high-risk times for weight gain (peri-menopausal years, times of significant life stress) and counsel patient on ways to prevent weight gain ■ Follow-up visits to discuss success of weight gain prevention strategies Discuss 10% weight loss goals for persons who are overweight: ■ Discuss lifestyle patterns that promote weight loss ■ Portion control ■ Daily physical activity ■ Follow-up visits to examine weight/BMI and discuss barriers to adherence
Cholesterol	Ensure that all adults age 20 and over have their blood cholesterol measured and their results explained in keeping with ATP III guidelines. Ensure children and first degree relatives of adults in whom a genetic lipoprotein disorder is suspected have cholesterol screening performed.	Follow ATP III guidelines for detection, evaluation, and treatment of persons with lipid disorders.
Blood Pressure	Ensure that all adults have their blood pressure measured and their results explained in keeping with JNC VI guidelines.	Follow JNC VI guidelines for the detection, evaluation, and treatment of persons with high blood pressure.[160,161]
Smoking Cessation	Ensure that all persons are aware of the health hazards of cigarette smoking by using posters/handouts in the waiting room. Query all persons regarding their smoking habits on every visit.	Follow U.S. Department of Health and Human Services Clinical Practice Guideline: Treating Tobacco Use and Dependence.[621] Promote smoking cessation: ■ Query regarding smoking habits ■ Provide targeted advice according to patient's knowledge base, e.g., dangers of smoking, benefits of quitting, and tips to quit ■ Schedule follow-up visits to discuss patient's progress in addressing smoking cessation

Table V.2–1. Essential Components of Therapeutic Lifestyle Changes (TLC)

Component	Recommendation
LDL-raising nutrients	
Saturated fats*	Less than 7% of total calories
Dietary cholesterol	Less than 200 mg/day
Therapeutic options for LDL lowering	
Plant stanols/sterols	2 grams per day
Increased viscous (soluble) fiber	10–25 grams per day
Total calories (energy)	Adjust total caloric intake to maintain desirable body weight/prevent weight gain
Physical activity	Include enough moderate exercise to expend at least 200 kcal per day

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

Table V.2–2. Macronutrient Recommendations for the TLC Diet

Component	Recommendation
Polyunsaturated fat	Up to 10% of total calories
Monounsaturated fat	Up to 20% of total calories
Total fat	25–35% of total calories*
Carbohydrate†	50–60% of total calories*
Dietary fiber	20–30 grams per day
Protein	Approximately 15% of total calories

* ATP III allows an increase of total fat to 35 percent of total calories and a reduction in carbohydrate to 50 percent for persons with the metabolic syndrome. Any increase in fat intake should be in the form of either polyunsaturated or monounsaturated fat.

† Carbohydrate should derive predominantly from foods rich in complex carbohydrates including grains—especially whole grains—fruits, and vegetables.

Table V.2–3. Dietary Guidelines for Americans (2000)[241]

Aim for Fitness

- Aim for a healthy weight
- Be physically active each day

Build a Healthy Base

- Let the pyramid guide your food choices
- Choose a variety of grains daily, especially whole grains
- Choose a variety of fruits and vegetables daily
- Keep foods safe to eat

Choose sensibly

- Choose a diet that is low in saturated fat and cholesterol and moderate in total fat
- Choose beverages and foods to moderate your intake of sugars
- Choose and prepare foods with less salt
- If you drink alcoholic beverages, do so in moderation

physical activity guidance is required to obtain further CHD risk reduction beyond that achieved by LDL lowering. At all stages of dietary therapy, physicians are encouraged to refer patients to registered dietitians or other qualified nutritionists for *medical nutrition therapy*, which is the term for the nutrition intervention and guidance provided by a nutrition professional.

ATP III recommendations for ranges of other macronutrient intakes in the TLC Diet are given in Table V.2–2. Note that the recommendation for total fat ranges from 25 percent to 35 percent of total calories. To improve overall health, ATP III's lifestyle therapies generally contain the recommendations embodied in the Dietary Guidelines for Americans (2000).[241]

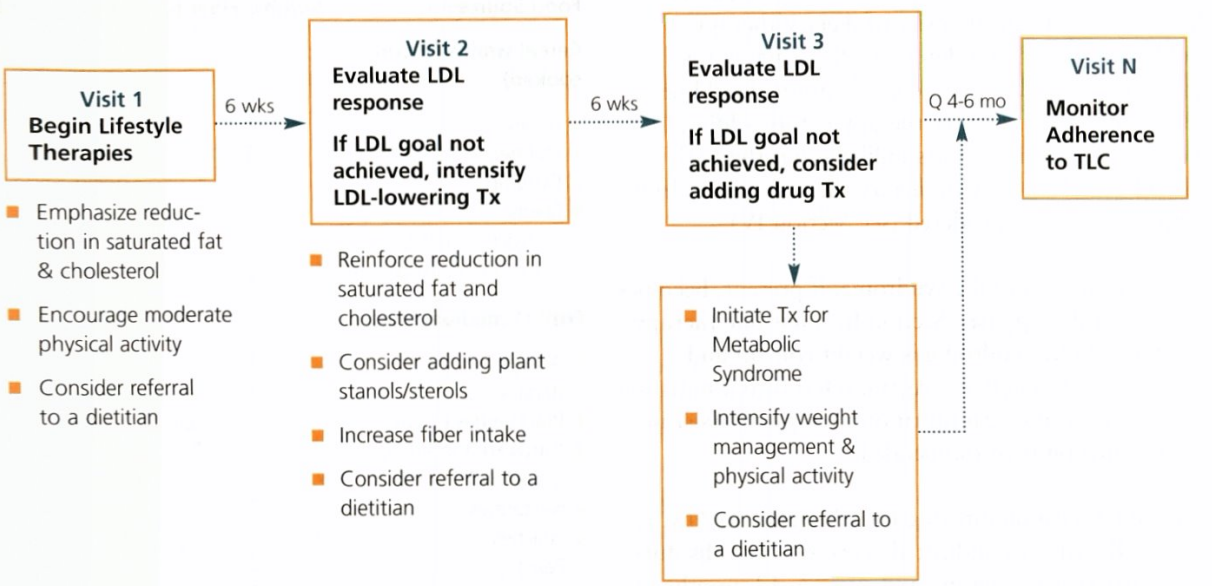
The overall composition of the TLC Diet is consistent with the recommendations of the Dietary Guidelines for Americans (2000) (Table V.2–3). The dietary principles delineated in the Dietary Guidelines need not and should not be sacrificed for the purpose of LDL lowering. Furthermore, adherence to Dietary Guidelines recommendations should contribute to a reduction in risk beyond LDL lowering.

Figure V.2–1 presents one model illustrating the general approach to dietary therapy.

During the first three months of dietary therapy, priority is given to lowering LDL cholesterol. In the first visit, the physician should address a few key questions and obtain an overall assessment of the individual's current life habits:

- Does the patient consume excess calories in the form of LDL-raising nutrients?

Figure V.2–1. A Model of Steps in Therapeutic Lifestyle Changes (TLC)



- Is the patient overweight or obese? Is abdominal obesity present?
- Is the patient physically active or inactive?
- If the patient is overweight/obese and/or physically inactive, is the metabolic syndrome present? (See Table II.6–1.)

To assess intakes of LDL-raising nutrients, the ATP III panel devised a brief Dietary CAGE that may be helpful (Table V.2–4). These questions are not a substitute for a systematic dietary assessment, which is usually carried out by a nutrition professional. CAGE questions can be used to identify the common food sources of LDL-raising nutrients—saturated fat and cholesterol—in the patient's diet. Also in the first visit, advice is given to begin moderate physical activity, but serious attempts to achieve weight loss can be delayed briefly to concentrate first on reducing intakes of LDL-raising nutrients. At any and every stage of dietary therapy, effective dietary modification will be facilitated by consultation with a registered dietitian or other qualified nutritionist for *medical nutrition therapy.* (Subsequently, the term *nutrition professional* will refer to a registered dietitian or qualified nutritionist.)

After approximately 6 weeks, the physician should evaluate the LDL cholesterol response. If the LDL cholesterol goal has been achieved, or if progress in LDL lowering has occurred, dietary therapy should be continued. If the LDL goal is not achieved, the physician has several options to enhance LDL lowering. First, dietary instructions can be reexplained and reinforced. The assistance of a nutrition professional for more formal instruction and counseling (medical nutrition therapy) is especially valuable at this time. Second, therapeutic dietary options for LDL lowering (plant stanols/sterols and increased viscous fiber) will also enhance LDL lowering. Plant stanols/sterols are currently incorporated into special margarines, which are available directly to consumers. The stanol/sterol contents are listed on the food label. They may be available in other products in the future. Viscous fiber can be increased by emphasizing certain foods: cereal grains, fruits, vegetables, and dried beans, peas, and legumes (see Table V.2–5).

Table V.2–4. Dietary CAGE Questions for Assessment of Intakes of Saturated Fat and Cholesterol

- **C**—Cheese (and other sources of dairy fats—whole milk, 2% milk, ice cream, cream, whole fat yogurt)
- **A**—Animal fats (hamburger, ground meat, frankfurters, bologna, salami, sausage, fried foods, fatty cuts of meat)
- **G**—Got it away from home (high-fat meals either purchased and brought home or eaten in restaurants)
- **E**—Eat (extra) high-fat commercial products: candy, pastries, pies, doughnuts, cookies

After another 6 weeks, the response to dietary therapy should be evaluated. If the LDL cholesterol goal is achieved, the current intensity of dietary therapy should be maintained indefinitely. If the patient is approaching the LDL goal, consideration should be given to continuing dietary therapy before adding LDL-lowering drugs. If it appears unlikely that the LDL goal will be achieved with dietary therapy alone, drug therapy should be considered (see Section IV).

Thereafter, the metabolic syndrome, if present, becomes the target of therapy (see Section II). First-line therapy for the metabolic syndrome is weight control and increased physical activity. Again, referral to a nutrition professional for medical nutrition therapy to assist in weight reduction is recommended.

Finally, long-term monitoring for adherence to TLC is required. Revisits are indicated every 4–6 months during the first year of therapy and every 6–12 months in the long term. If a person is started on drug therapy, more frequent visits are advised.

The information shown in Table V.2–6 may be helpful for the physician both for dietary and lifestyle assessment and for guidance of the patient adopting TLC recommendations. The table is compiled from current ATP III dietary recommendations, Dietary Guidelines for Americans (2000),[241] Obesity Education Initiative (OEI) guidelines for weight reduction,[78,79] and the Surgeon General's Report on Physical Activity.[238]

3. Components of the TLC Diet

a. Major nutrient components

The major LDL-raising dietary constituents are saturated fat and cholesterol. A reduction in intakes of these components is the core of the TLC Diet. The scientific foundation for the relationship between high intakes of saturated fat and increased LDL levels dates back several decades and consists of several lines of evidence: observational studies, metabolic and controlled feeding studies, and clinical studies, including randomized clinical trials. These data have been reviewed in detail in previous reports of the NCEP,[1,2,5,6] the U.S. Dietary Guidelines Committees,[241] and the American Heart Association.[393] The other major nutrients—unsaturated fats, protein, and carbohydrates—do not raise LDL cholesterol levels. In developing an LDL-lowering diet

Table V.2–5. Food Sources of Viscous (Soluble) Fiber

Food Source	Soluble Fiber (g)	Total Fiber (g)
Cereal Grains (½ cup cooked)		
■ Barley	1	4
■ Oatmeal	1	2
■ Oatbran	1	3
■ Seeds		
– Psyllium Seeds, Ground (1 Tbsp)	5	6
Fruit (1 medium fruit)		
■ Apples	1	4
■ Bananas	1	3
■ Blackberries (½ cup)	1	4
■ Citrus Fruit (orange, grapefruit)	2	2–3
■ Nectarines	1	2
■ Peaches	1	2
■ Pears	2	4
■ Plums	1	1.5
■ Prunes (¼ cup)	1.5	3
Legumes (½ cup cooked)		
■ Beans		
– Black Beans	2	5.5
– Kidney Beans	3	6
– Lima Beans	3.5	6.5
– Navy Beans	2	6
– Northern Beans	1.5	5.5
– Pinto Beans	2	7
■ Lentils (yellow, green, orange)	1	8
■ Peas		
– Chick Peas	1	6
– Black Eyed Peas	1	5.5
Vegetables (½ cup cooked)		
■ Broccoli	1	1.5
■ Brussels Sprouts	3	4.5
■ Carrots	1	2.5

Table V.2–6. Guide to Therapeutic Lifestyle Changes (TLC)

Healthy Lifestyle Recommendations for a Healthy Heart

Food Items to Choose More Often	Food Items to Choose Less Often	Recommendations for Weight Reduction	Recommendations for Increased Physical Activity
Breads and Cereals ≥6 servings per day, adjusted to caloric needs Breads, cereals, especially whole grain; pasta; rice; potatoes; dry beans and peas; low fat crackers and cookies **Vegetables** 3–5 servings per day fresh, frozen, or canned, without added fat, sauce, or salt **Fruits** 2–4 servings per day fresh, frozen, canned, dried **Dairy Products** 2–3 servings per day Fat-free, 1/2%, 1% milk, buttermilk, yogurt, cottage cheese; fat-free & low-fat cheese **Eggs** ≤2 egg yolks per week Egg whites or egg substitute **Meat, Poultry, Fish** ≤5 oz per day Lean cuts loin, leg, round; extra lean hamburger; cold cuts made with lean meat or soy protein; skinless poultry; fish **Fats and Oils** Amount adjusted to caloric level: Unsaturated oils; soft or liquid margarines and vegetable oil spreads, salad dressings, seeds, and nuts **TLC Diet Options** Stanol/sterol-containing margarines; viscous fiber food sources: barley, oats, psyllium, apples, bananas, berries, citrus fruits, nectarines, peaches, pears, plums, prunes, broccoli, brussels sprouts, carrots, dry beans, peas, soy products (tofu, miso)	**Breads and Cereals** Many bakery products, including doughnuts, biscuits, butter rolls, muffins, croissants, sweet rolls, Danish, cakes, pies, coffee cakes, cookies Many grain-based snacks, including chips, cheese puffs, snack mix, regular crackers, buttered popcorn **Vegetables** Vegetables fried or prepared with butter, cheese, or cream sauce **Fruits** Fruits fried or served with butter or cream **Dairy Products** Whole milk/2% milk, whole-milk yogurt, ice cream, cream, cheese **Eggs** Egg yolks, whole eggs **Meat, Poultry, Fish** Higher fat meat cuts: ribs, t-bone steak, regular hamburger, bacon, sausage; cold cuts: salami, bologna, hot dogs; organ meats: liver, brains, sweetbreads; poultry with skin; fried meat; fried poultry; fried fish **Fats and Oils** Butter, shortening, stick margarine, chocolate, coconut	**Weigh Regularly** Record weight, BMI, & waist circumference **Lose Weight Gradually** Goal: lose 10% of body weight in 6 months. Lose 1/2 to 1 lb per week **Develop Healthy Eating Patterns** ■ Choose healthy foods (see Column 1) ■ Reduce intake of foods in Column 2 ■ Limit number of eating occasions ■ Select sensible portion sizes ■ Avoid second helpings ■ Identify and reduce hidden fat by reading food labels to choose products lower in saturated fat and calories, and ask about ingredients in ready-to-eat foods prepared away from home ■ Identify and reduce sources of excess carbohydrates such as fat-free and regular crackers; cookies and other desserts; snacks; and sugar-containing beverages	**Make Physical Activity Part of Daily Routines** ■ Reduce sedentary time ■ Walk, wheel, or bike-ride more, drive less; Take the stairs instead of an elevator; Get off the bus a few stops early and walk the remaining distance; Mow the lawn with a push mower; Rake leaves; Garden; Push a stroller; Clean the house; Do exercises or pedal a stationary bike while watching television; Play actively with children; Take a brisk 10-minute walk or wheel before work, during your work break, and after dinner **Make Physical Activity Part of Exercise or Recreational Activities** ■ Walk, wheel, or jog; Bicycle or use an arm pedal bicycle; Swim or do water aerobics; Play basketball; Join a sports team; Play wheelchair sports; Golf (pull cart or carry clubs); Canoe; Cross-country ski; Dance; Take part in an exercise program at work, home, school, or gym

for ATP III, consideration was given not only to these long-established factors but also to new and emerging data that support the importance of the appropriate distribution of other nutrients that are related to cardiovascular health as well as general health. Therefore, the rationale for the recommendations for each component of the TLC diet will be described briefly.

1) Saturated fatty acids

Saturated fatty acids are a major dietary determinant of LDL cholesterol level.[241] The effects of saturated fatty acids on serum total cholesterol (and LDL cholesterol) levels have been studied extensively.[622] Several meta-analyses and reviews have been carried out to estimate the impact of saturated fatty acids on cholesterol levels.[623,624] These analyses indicate that for every 1 percent increase in calories from saturated fatty acids as a percent of total energy, the serum LDL cholesterol rises about 2 percent. Conversely, a 1 percent reduction in saturated fatty acids will reduce serum cholesterol by about 2 percent. Recent trials confirm the efficacy of diets low in saturated fatty acids for lowering LDL levels. For example, the DELTA Study[625] investigated the effects of reducing dietary saturated fatty acids from 15 percent of total calories to 6.1 percent of total calories. On the diet low in saturated fatty acids, LDL cholesterol was reduced by 11 percent. Another study, beFIT,[626,627] tested effects of an NCEP therapeutic diet in individuals with hypercholesterolemia with and without hypertriglyceridemia. Compared to the participants' baseline diet, LDL cholesterol levels were reduced on the therapeutic diet by approximately 8 percent. Large-scale randomized controlled trials have been carried out to assess the safety of reduced intakes of saturated fatty acids and cholesterol in children and have found no evidence for compromised growth or development.[628,629]

Evidence statements: There is a dose response relationship between saturated fatty acids and LDL cholesterol levels. Diets high in saturated fatty acids raise serum LDL cholesterol levels (A1). Reduction in intakes of saturated fatty acids lowers LDL cholesterol levels (A1, B1).

The beneficial effects of reducing saturated fatty acids and cholesterol in the diet can be enhanced by weight reduction in overweight persons. Several studies have shown that LDL cholesterol levels can be lowered through weight reduction in overweight persons.[78,79] And most important, as shown in the MRFIT study, weight reduction will enhance serum cholesterol lowering brought about by a reduction in intakes of saturated fatty acids and cholesterol.[630,631]

Evidence statements: Weight reduction of even a few pounds will reduce LDL levels regardless of the nutrient composition of the weight loss diet (A2), but weight reduction achieved through a calorie-controlled diet low in saturated fatty acids and cholesterol will enhance and sustain LDL cholesterol lowering (A2).

Recommendation: Weight loss through reduced caloric intake and increased levels of physical activity should be encouraged in all overweight persons. Prevention of weight gain also should be emphasized for all persons.

Epidemiological studies show that populations that consume high amounts of saturated fatty acids and cholesterol have a high risk for CHD.[19,632] The evidence that lowering serum cholesterol levels by decreasing intakes of saturated fatty acids reduces the risk for CHD has been demonstrated in the meta-analysis by Gordon.[409,410] This analysis included six robust dietary trials, in aggregate including 6,356 person-years of follow up. It showed that lowering serum cholesterol levels by reducing the intake of saturated fatty acids significantly decreased the incidence of CHD by 24 percent. There was also a trend toward a decrease in coronary mortality (21 percent) and total mortality (6 percent). No increase in non-CVD mortality was found.

The data from dietary trials, in combination with the results of controlled clinical trials with cholesterol-lowering medications,[455,633] document that reducing serum cholesterol and LDL cholesterol by diet alone or with pharmacological means will reduce CHD endpoints. The current American diet contains an average of about 11 percent of total calories as saturated fatty acids. The major sources of saturated fatty acids in the diet are high-fat dairy products (whole milk, cheese,

butter, ice cream, and cream); high-fat meats; tropical oils such as palm oil, coconut oil, and palm kernel oil; and baked products and mixed dishes containing dairy fats, shortening, and tropical oils. To maximize LDL cholesterol lowering by reducing saturated fatty acid intake in the therapeutic diet, it will be necessary to lower intakes from the population mean intake of approximately 11 percent to <7 percent of total energy.

Evidence statements: High intakes of saturated fatty acids are associated with high population rates of CHD (C2). Reduction in intake of saturated fatty acids will reduce risk for CHD (A1, B1).

Recommendation: The therapeutic diet to maximize LDL cholesterol lowering should contain less than 7 percent of total calories as saturated fatty acids.

2) *Trans fatty acids*

Trans fatty acids are those in which double bonds are in the *trans* configuration. They are generally produced by hydrogenation of vegetable oils but some are found naturally in animal fats. Substantial evidence from randomized clinical trials indicates that *trans* fatty acids raise LDL cholesterol levels, compared with unsaturated fatty acids.[634-646] These studies also show that when *trans* fatty acids are substituted for saturated fatty acids, HDL cholesterol levels are lower,[647] with a dose response effect observed. Recent United States data show that the use of liquid vegetable oil or semiliquid margarine results in the most favorable total and LDL cholesterol levels and ratios of total cholesterol to HDL cholesterol, whereas the use of butter or stick margarine results in the worst lipid levels.[634] In addition, evidence from some epidemiological cohort studies suggests that high intakes of *trans* fatty acids are associated with higher risk for CHD.[648-651] Whether this association is due to adverse effects of *trans* fatty acids on lipoproteins, to other adverse actions, or to confounding variables is uncertain.

The mean U.S. level of *trans* fatty acids intake is about 2.6 percent of total energy (compared with saturated fatty acids intake of ~11 percent of energy). Major sources of *trans* fatty acids in the diet include products made from partially hydrogenated oils such as baked products including crackers, cookies, doughnuts, breads, and products like french fries or chicken fried in hydrogenated shortening. Animal sources including dairy products provide smaller amounts of *trans* fatty acids. Soft margarines, tub and liquid, and vegetable oil spreads have low amounts of *trans* fatty acids. Some margarines and spreads are now *trans*-fatty acid free. Some hydrogenation of vegetable oils is the primary technology currently used to provide form to food products, so that they can be eaten out of the hand, rather than with a spoon.

Evidence statements: *Trans* fatty acids raise serum LDL cholesterol levels (A2). Through this mechanism, higher intakes of *trans* fatty acids should increase risk for CHD. Prospective studies support an association between higher intakes of *trans* fatty acids and CHD incidence (C2). However, *trans* fatty acids are not classified as saturated fatty acids, nor are they included in the quantitative recommendations for saturated fatty acid intake of <7 percent of calories in the TLC Diet.

Recommendation: Intakes of *trans* fatty acids should be kept low. The use of liquid vegetable oil, soft margarine, and *trans* fatty acid-free margarine are encouraged instead of butter, stick margarine, and shortening.

3) *Dietary cholesterol*

Dietary cholesterol causes marked hypercholesterolemia in many laboratory animals, including nonhuman primates. High intakes of cholesterol in humans, however, do not cause such a marked increase in serum cholesterol. Nonetheless, controlled metabolic studies in humans indicate that high cholesterol intakes raise LDL cholesterol levels. The degree of rise varies from person to person, as is true for all nutrients. Meta-analyses of studies done in controlled settings confirm the LDL-raising action of dietary cholesterol.[652,653] A recent meta-analysis showed that dietary cholesterol raises the ratio of total to HDL cholesterol, adversely affecting the serum cholesterol profile.[654] A lesser effect of dietary cholesterol has been found in studies carried out in the outpatient setting;[655] in this circumstance, failure to detect the full effect of dietary cholesterol is likely related to lack of tight metabolic

control. On average, the response of serum cholesterol to dietary cholesterol as revealed in tightly controlled studies is approximately 10 mg/dL per 100 mg dietary cholesterol per 1000 kcal.[656,657]

In the past 40 years, there has been a progressive decline in intakes of dietary cholesterol. This has been the result of decreased intakes of eggs, high-fat meat, and high-fat dairy products. This reduction in cholesterol intake, along with a substantial reduction in the proportion of calories from saturated fatty acids, corresponds with the decline in serum cholesterol levels that has occurred in the U.S. population over four decades.[658] At present, the average U.S. daily consumption of cholesterol is 256 mg, higher for men (331 mg) than for women (213 mg).[659] Eggs contribute about one-third of the cholesterol in the food supply and this fraction has increased somewhat in recent years.[660] Other sources of dietary cholesterol include animal products, dairy, meats, poultry, and shellfish.

Some epidemiological data, namely the Western Electric Study, suggest dietary cholesterol increases heart disease risk independently of its effect on serum LDL cholesterol levels.[661] In contrast, data from two prospective cohort studies, the Nurses Health Study and the Health Professionals Study, found no significant association between frequency of reported egg consumption and CHD, except among diabetic women.[662]

Evidence statements: Higher intakes of dietary cholesterol raise serum LDL cholesterol levels in humans (A2, B1). Through this mechanism, higher intakes of dietary cholesterol should raise the risk for CHD. Reducing cholesterol intakes from high to low decreases serum LDL cholesterol in most persons (A2, B1).

Recommendation: Less than 200 mg per day of cholesterol should be consumed in the TLC Diet to maximize the amount of LDL cholesterol lowering that can be achieved through reduction in dietary cholesterol.

4) Monounsaturated fatty acids

The most common form of monounsaturated fatty acids is oleic acid, which occurs in the cis form. Substitution of cis-monounsaturated fatty acids for saturated fatty acids results in a fall in LDL cholesterol levels.[624] Moreover, substitution of monounsaturated fatty acids for saturated fatty acids results in little or no decrease in HDL cholesterol and does not increase triglycerides as occurs with very high intakes of carbohydrates (>60 percent of total energy).[624,663-665]

Monounsaturated fatty acids—as part of a diet that is low in saturated fatty acids and cholesterol and rich in vegetables, fruits, and grain products—have received increased attention as being potentially beneficial for risk reduction because of their association with low rates of CHD in olive-oil consuming populations of the Mediterranean basin.[19,20,632] Despite epidemiological support for higher intakes of monounsaturated fatty acids, there are no controlled clinical trials that are designed to compare effects of monounsaturated and saturated fatty acids on CHD endpoints. This lack of data contrasts with several trials that replaced saturated fat with polyunsaturated fat.

Evidence statements: Monounsaturated fatty acids lower LDL cholesterol relative to saturated fatty acids (A2, B2). Monounsaturated fatty acids do not lower HDL cholesterol nor raise triglycerides (A2, B2).

Evidence statement: Dietary patterns that are rich in monounsaturated fatty acids provided by plant sources and rich in fruits, vegetables, and whole grains and low in saturated fatty acids are associated with decreased CHD risk (C1). However, the benefits of replacement of saturated fatty acids with monounsaturated fatty acids has not been adequately tested in controlled clinical trials.

Recommendations: Monounsaturated fatty acids are one form of unsaturated fatty acid that can replace saturated fatty acids. Intake of monounsaturated fatty acids can range up to 20 percent of total calories. Most monounsaturated fatty acids should be derived from vegetable sources, including plant oils and nuts.

5) *Polyunsaturated fatty acids*

Polyunsaturated fatty acids, consisting mainly of n-6 linoleic acid, reduce LDL cholesterol levels when substituted for saturated fatty acids. At high intakes, linoleic acid also can produce small reductions in HDL cholesterol and triglycerides, although these responses are variable. Compared to cis-monounsaturated fatty acids, polyunsaturated fatty acids often cause a slightly greater reduction in LDL cholesterol levels.[624]

Several controlled clinical trials have compared the effects of polyunsaturated fatty acids, as a replacement for saturated fatty acids, on coronary endpoints.[657] Meta-analysis of trial results indicates that substitution of polyunsaturated fatty acids for saturated fatty acids reduces risk for CHD.[409,410,624] This positive result is supported by research in primates that indicates that polyunsaturated fatty acids are antiatherogenic when substituted for saturated fatty acids.[666]

Despite evidence of CHD risk reduction from polyunsaturated fatty acids, there are no large populations that have consumed large quantities of polyunsaturated fatty acids for long periods. Thus, high intakes have not been proven safe in large populations; this introduces a note of caution for recommending high intakes.

Evidence statements: Linoleic acid, a polyunsaturated fatty acid, reduces LDL cholesterol levels when substituted for saturated fatty acids in the diet (A1, B1). Polyunsaturated fatty acids can also cause small reductions in HDL cholesterol when compared with monounsaturated fatty acids (B2). Controlled clinical trials indicate that substitution of polyunsaturated fatty acids for saturated fatty acids reduces risk for CHD (A2, B2).

Recommendations: Polyunsaturated fatty acids are one form of unsaturated fatty acids that can replace saturated fat. Most polyunsaturated fatty acids should be derived from liquid vegetable oils, semi-liquid margarines, and other margarines low in *trans* fatty acids. Intakes of polyunsaturated fat can range up to 10 percent of total calories.

6) *Total fat*

Among the fatty acids that make up the total fat in the diet, only saturated fatty acids and *trans* fatty acids raise LDL cholesterol levels.[657] Thus, serum levels of LDL cholesterol are independent of intakes of total fat per se. ATP II[1,2] advised limiting total fat in Step I and Step II diets to ≤30 percent of calories primarily as a means of achieving lower intakes of saturated fatty acids. The focus of the dietary approach to reducing CHD risk then and now is on dietary fatty acids that raise LDL cholesterol concentrations.

Evidence statement: Unsaturated fatty acids do not raise LDL cholesterol concentrations when substituted for carbohydrates in the diet (A2, B2).

Recommendation: It is not necessary to restrict total fat intake for the express purpose of reducing LDL cholesterol levels, provided saturated fatty acids are reduced to goal levels.

For many years, other public health groups have recommended low intakes of total fat in an effort to curtail obesity and to reduce the risk for some forms of cancer. These recommendations were based largely on experiments in laboratory animals and cross-cultural studies. Several short-term studies also suggest that higher fat intakes (>35 percent of calories) modify the body's metabolism in ways that favor fat accumulation.[667-672] However, isocaloric exchange of fat for carbohydrate does not produce weight gain over a period of many months.[673,674] Further, although some prospective studies have suggested a relationship between the percentage of dietary fat and obesity,[675,676] recent prospective studies (or meta-analysis of studies) have failed to detect a causative link between them.[677,678] Evidence related to these areas is reviewed in detail in the recent rationale report of the Dietary Guidelines for Americans (2000).[241]

Studies in laboratory animals and cross-cultural studies have suggested a relationship between fat intake and risk for certain cancers.[679-682] Moreover, a major clinical trial is presently underway to determine whether low-fat diets will reduce risk for breast cancer in women; this trial is a component of the Women's Health Initiative[683] and is scheduled to end in 2005.

Even so, recent prospective studies have not confirmed an association between fat intake and cancer.[684-687] Thus, a strong recommendation to reduce fat intake for the purpose of preventing cancer does not seem warranted at this time.[241]

The Dietary Guidelines for Americans (2000)[241] noted that some investigators are concerned that recommendations that emphasize lower total fat intakes (<30 percent of energy) may have led to an overconsumption of carbohydrates, contributing to an increased prevalence of obesity. Moreover, very high intakes of carbohydrates (>60 percent of calories) in overweight/-obese persons can aggravate some of the risk factors of the metabolic syndrome.[663,664,688-691] These latter responses have led some investigators to propose that populations with a high prevalence of insulin resistance and the metabolic syndrome should avoid very high-carbohydrate diets and should consume relatively more unsaturated fatty acids.[692]

Evidence statement: The percentage of total fat in the diet, independent of caloric intake, has not been documented to be related to body weight or risk for cancer in the general population.[241] Short-term studies suggest that very high fat intakes (>35 percent of calories) modify metabolism in ways that could promote obesity (C2). On the other hand, very high carbohydrate intakes (>60 percent of calories) aggravate some of the lipid and non-lipid risk factors common in the metabolic syndrome (A2, B2, C2).

Recommendations: Dietary fat recommendations should emphasize reduction in saturated fatty acids. Further, for persons with lipid disorders or the metabolic syndrome, extremes of total fat intake—either high or low—should be avoided. In such persons, total fat intakes should range from 25–35 percent of calories. For some persons with the metabolic syndrome, a total fat intake of 30–35 percent may reduce lipid and nonlipid risk factors.

7) Carbohydrate

When carbohydrates are substituted for saturated fatty acids, the fall in LDL cholesterol levels equals that with monounsaturated fatty acids. However, compared with monounsaturated fatty acids, substitution of carbohydrate for saturated fatty acids frequently causes a fall in HDL cholesterol and a rise in triglyceride.[624,663,689,693] This effect apparently persists in the long term, as suggested by differences in population lipid levels in the presence of different habitual diets.[694,695] When carbohydrate is consumed along with high-fiber diets, however, the rise in triglycerides or fall in HDL cholesterol has been reported to be reduced.[693,696,697]

Digestible carbohydrates include starches (complex carbohydrates) and sugar. Some foods, such as whole grains, vegetables, and some fruits, contain viscous fiber that helps to lower LDL cholesterol as well (see Table V.2–5). Sugars and starches occur naturally in many foods that also supply other important nutrients. Examples of these foods include fat-free and low-fat dairy products, fruits, some vegetables, breads, cereals, and grains. Inclusion of these foods helps provide daily recommended intakes of essential nutrients.[241]

An old concept receiving recent attention is the "glycemic" potential of different foods. Glycemic index refers to the value obtained by feeding a carbohydrate load and measuring the level of blood glucose. Study of this factor is complicated because there is a wide range in the glycemic index for each group of foods, attributed to factors such as its form when eaten, the way it is processed, how it is chewed, how it is emptied from the stomach, and an individual's physiologic and metabolic responses.[698] To date the glycemic index has not been widely accepted as a practical means by which to select specific carbohydrate-containing foods for dietary therapy.[241]

Evidence statement: When carbohydrate is substituted for saturated fatty acids, LDL cholesterol levels fall (A2, B2). However, very high intakes of carbohydrate (>60 percent of total calories) are accompanied by a reduction in HDL cholesterol and a rise in triglyceride (B1, C1). These latter responses are sometimes reduced when carbohydate is consumed with viscous fiber (C2); however, it has not been demonstrated convincingly that viscous fiber can fully negate the triglyceride-raising or HDL-lowering actions of very high intakes of carbohydrates.

Recommendation: Carbohydrate intakes should be limited to 60 percent of total calories. Lower intakes (e.g., 50 percent of calories) should be considered for persons with the metabolic syndrome who have elevated triglycerides or low HDL cholesterol. Regardless of intakes, most of the carbohydrate intake should come from grain products, especially whole grains, vegetables, fruits, and fat-free and low-fat dairy products.

8) Protein

Dietary protein in general has little effect on serum LDL cholesterol level or other lipoprotein fractions. However, substituting soy protein for animal protein has been reported to lower LDL cholesterol[699] (see Section V.3.b.3). Plant sources of protein are predominantly legumes, dry beans, nuts, and, to a lesser extent, grain products and vegetables, which are low in saturated fats and cholesterol. Animal sources of protein that are lower in saturated fat and cholesterol include fat-free and low-fat dairy products, egg whites, fish, skinless poultry, and lean meats.

b. Additional dietary options for LDL lowering

1) Increasing viscous fiber in the diet

Recent reports indicate that viscous (soluble) forms of dietary fiber can reduce LDL cholesterol levels. In contrast, insoluble fiber does not significantly affect LDL cholesterol.[700] On average, an increase in viscous fiber of 5–10 grams per day is accompanied by an approximately 5 percent reduction in LDL cholesterol.[701,702] In a meta-analysis of 67 trials related to oats, pectin, guar, and psyllium, a small but significant reduction in serum total and LDL cholesterol was noted for all sources of viscous fiber in ranges of 2–10 grams per day.[703] Thus, at present, there is general agreement that viscous fiber (e.g., oats, guar, pectin, and psyllium) decreases serum cholesterol and LDL cholesterol. Because of the favorable effect of viscous fiber on LDL cholesterol levels, the ATP III panel recommends that the therapeutic diet be enriched by foods that provide a total of at least 5–10 grams of viscous fiber daily (see Table V.2–5). Even higher intakes of 10–25 grams per day can be beneficial.

Some investigators report that the consumption of viscous (soluble) fiber (provided by oats, barley, psyllium, pectin-rich fruit, and beans) produces a reduction in HDL cholesterol concentration.[699] Other reviews report little, no, or inconsistent effect on HDL cholesterol.[704,705]

Evidence statement: 5–10 grams of viscous fiber per day reduces LDL cholesterol levels by approximately 5 percent (A2, B1).

Recommendation: The use of dietary sources of viscous fiber is a therapeutic option to enhance LDL cholesterol lowering.

2) Plant stanols/sterols

Recent studies have demonstrated the LDL-lowering effect of plant sterols, which are isolated from soybean and tall pine-tree oils. Plant sterols can be esterified to unsaturated fatty acids (creating sterol esters) to increase lipid solubility. Hydrogenating sterols produces plant stanols and, with esterification, stanol esters. The efficacy of plant sterols and plant stanols is considered to be comparable.[706,707] Because lipids are needed to solubilize stanol/sterol esters, they are usually available in commercial margarines. The presence of plant stanols/sterols is listed on the food label. When margarine products are used, persons must be advised to adjust caloric intake to account for the calories contained in the products.

Data show that plant-derived stanol/sterol esters at dosages of 2–3 g/day lower LDL-C levels by 6–15 percent with little or no change in HDL cholesterol or triglyceride levels.[707-713] The more recent among these studies indicate that maximal lowering of LDL cholesterol occurs at intakes of plant stanol/sterol esters of 2 g/day. LDL reductions also occur in individuals who have both hypercholesterolemia and type 2 diabetes[714] and in children with hypercholesterolemia.[715] A greater percent lowering of LDL occurs in older people than in younger people.[716] No studies have been conducted to determine the effect of plant stanols/sterols on CHD risk, although Law[716] has recently projected that their use should double the beneficial effect on CHD risk achieved by reducing dietary saturated fatty acids and cholesterol.

Plant sterols/stanols reduce absorption of dietary carotenoids, and decreased levels of plasma beta-carotene have been observed subsequent to consumption of margarines that contain either stanol ester or sterol ester.[706] Whether carotenoid decreases are deleterious is unknown, but prudence calls for adhering to current recommendations for intakes of fruits and vegetables with consumption of plant stanols/sterols.

Evidence statement: Daily intakes of 2–3 grams per day of plant stanol/sterol esters will reduce LDL cholesterol by 6–15 percent (A2, B1).

Recommendation: Plant stanol/sterol esters (2 g/day) are a therapeutic option to enhance LDL cholesterol lowering.

3) Soy protein

Soy protein included in a diet low in saturated fatty acids and cholesterol can lower levels of total cholesterol and LDL cholesterol in individuals with hypercholesterolemia. Recent reviews[717,718] gave particular weight to 16 well-controlled trials that reported intakes of saturated fatty acids and cholesterol. More than half of the studies used more than 40 g/day soy protein in some form. One report[719] indicated that 25 g/day soy protein in a diet low in saturated fatty acids and cholesterol lowers LDL cholesterol levels by about 5 percent.

The specific processing of the soybean determines the characteristics of soy protein, such as the content of isoflavones, fiber, and saponins. There is some evidence that an LDL-lowering effect is dependent upon isoflavone content[720] but conclusive data are lacking. Since there are inconsistent findings regarding both the dose and the potential benefit of soy protein, soy protein's major role in LDL-lowering may be to help reduce the intake of animal food products with their higher content of saturated fatty acids.

Evidence statement: High intakes of soy protein can cause small reductions in LDL cholesterol levels, especially when it replaces animal food products (A2, B2).

Recommendation: Food sources containing soy protein are acceptable as replacements for animal food products containing animal fats.

c. Other dietary factors that may reduce baseline risk for CHD

Epidemiological studies strongly suggest that other nutrient factors affect baseline risk for CHD. For example, in the Mediterranean region, where the diet is rich in fruits and vegetables, whole grains, ocean fish, and unsaturated fatty acids, the risk for CHD appears to be lower than predicted by the major risk factors. In contrast, in regions without this dietary pattern, such as Eastern Europe and Russia, CHD rates are higher than predicted by the prevalence of CHD risk factors. Such observational data provide a basis for a general recommendation for a dietary pattern that is consistent with a low baseline population risk. The Dietary Guidelines for Americans (2000),[241] were crafted to facilitate reduction in baseline risk for CHD (Table V.2–3).

In addition, nutritional research has focused on several specific factors that may have unique properties to reduce risk for CHD. The status of these emerging dietary factors are reviewed below and summarized in evidence statements.

1) n-3 (omega-3) polyunsaturated fatty acids

Polyunsaturated fatty acids of the n-3 (omega-3) type occur as alpha-linolenic acid (18:3), primarily in certain vegetable sources such as soybean, canola oil and

English walnuts, and in fish oils as eicosapentaenoic acid (EPA) (20:5) and docosahexaenoic acid (DHA) (22:6) *(marine n-3 fatty acids)*.

Moderate fish consumption has been associated with reduced sudden cardiac death or reduced CHD mortality in several prospective cohort studies[721-723] but not in others.[724,725] One study found a trend toward increased relative risk of CHD death with marine n-3 fatty acids. A nested, case-control study found an inverse relationship between risk for sudden cardiac death and both reported intake of marine n-3 fatty acids and red blood cell n-3 fatty acid level.[726] Postulated mechanisms for the effects of marine n-3 fatty acids on CHD risk include favorable effects on cardiac rhythm, platelet aggregation, inflammatory responses, and serum triglyceride levels. High intakes of marine n-3 fatty acids reduce triglyceride levels;[727] this effect appears to be secondary to decreased VLDL production.[728] Generally, marine n-3 fatty acids have no effect on LDL cholesterol levels, but large doses have been shown to reciprocally increase LDL cholesterol levels in persons with hypertriglyceridemia.[729] Recent data indicate that some fish have a high mercury content and the toxic effects of mercury could attenuate protective effects of fish.[730,731]

Four clinical trials suggest that n-3 fatty acids from marine or plant sources reduce sudden death and overall death in populations with pre-existing cardiovascular disease. The DART trial[732] was a relatively large secondary prevention trial in which subjects advised to eat fatty fish had a 29 percent reduction in 2-year all-cause mortality compared with those not so advised, although myocardial infarction and coronary death were not specifically reduced. The Lyon Heart Trial[733] included increased intakes of alpha-linolenic acid as part of a "Mediterranean" diet. Compared to the control group, subjects consuming the Mediterranean diet had fewer coronary events. The authors attributed some of the benefit to higher intakes of n-3 fatty acids. In a small supplement trial, Singh et al.[734] treated patients with suspected acute myocardial infarction with fish oil capsules (EPA 1.08 g/day) or mustard oil (alpha-linolenic acid 2.9 g/day) or placebo. After one year, total cardiac events were significantly less in the groups on fish oil and mustard seed oil supplements. Further, the large placebo-controlled, but unblinded Italian GISSI Prevention trial[735] administered fish oil supplements containing n-3 fatty acids (1 g/day fish oil, n = 2836 subjects) and compared coronary outcomes to controls (n = 2828). The group receiving fish-oil supplements had a 14 percent reduction in total death and a 17 percent reduction in cardiovascular death. Other clinical trials are less suggestive of benefit from n-3 fatty acids. Angiographic data fail to show that marine n-3 fatty acids modify coronary lumen size.[736,737] Also, fish oil administration apparently does not prevent restenosis after coronary angioplasty.[738] Additional studies are underway to determine the effect of n-3 fatty acids on CHD risk in the U.S. population.[241]

Based on these findings, the Dietary Guidelines for Americans (2000)[241] noted that some fish, such as salmon, tuna, and mackerel, contain omega-3 fatty acids that are being studied to determine if they offer protection against heart disease. No quantitative recommendations for n-3 fatty acids were made for the general public.

Evidence statement: The mechanisms whereby n-3 fatty acids might reduce coronary events are unknown and may be multiple. Prospective data and clinical trial evidence in secondary CHD prevention suggest that higher intakes of n-3 fatty acids reduce risk for coronary events or coronary mortality (A2, C2).

Recommendation: Higher dietary intakes of n-3 fatty acids in the form of fatty fish or vegetable oils are an option for reducing risk for CHD. This recommendation is optional because the strength of the evidence is only moderate at present. ATP III supports the American Heart Association's recommendation that fish be included as part of a CHD risk-reduction diet. Fish in general is low in saturated fat and may contain some cardioprotective n-3 fatty acids. However, a dietary recommendation for a specific amount of n-3 fatty acids is not being made (See Section VI for ATP III recommendations on n-3 supplements for reducing risk for CHD.)

2) *Vitamins/antioxidants*

a) Folic acid and vitamins B_6 and B_{12}

Folic acid and vitamins B_6 and B_{12} play a role in the metabolism of homocysteine, and levels of these vitamins correlate inversely with homocysteine levels. Data from the Framingham Heart Study suggest that the mandated fortification of cereal grains with folic acid has lowered population mean homocysteine levels as well as the prevalence of hyperhomocysteinemia.[307] Many cross-sectional case-control studies and some prospective cohort studies show a positive association between plasma homocysteine levels and CVD risk[297,739-743] but other prospective cohort studies do not.[300,744-746]

Despite the fact that homocysteine levels can be reduced with supplements of folate, B_6, and B_{12}, it is not known whether reduction of plasma homocysteine levels by diet and/or vitamin supplements will reduce CVD risk.[743] Several randomized trials are underway to determine if folic acid, vitamin B_6, and vitamin B_{12} will be effective in reducing the risk of heart disease.[304]

The Institute of Medicine has recently published dietary recommendations for folate for the general population.[747] The recommended dietary allowance (RDA) for folate is 400 micrograms per day. This level of intake was deemed adequate to provide any reduction in risk for cardiovascular disease that can be obtained from dietary folate. An upper limit for folate derived from fortified food or supplements was estimated to be 1000 micrograms per day.

Evidence statement: According to the Institute of Medicine, the RDA for folate for adults is 400 micrograms per day, and the upper limit is 1000 micrograms per day. There are no published randomized controlled clinical trials to show whether lowering homocysteine levels through dietary intake or supplements of folate and other B vitamins will reduce the risk for CHD.

Recommendation: ATP III endorses the Institute of Medicine RDA for dietary folate, namely, 400 micrograms per day. Folate should be consumed largely from dietary sources.

b) Antioxidants

Oxidative stress is a putative cause of atherosclerotic disease. In experimental studies, oxidation of LDL is an important step in the development and progression of CHD. Thus, a large body of research has been directed towards the potential of antioxidants for reducing CHD risk. Antioxidants under investigation include ascorbic acid (vitamin C), alpha-tocopherol (vitamin E), beta-carotene, ubiquinone (coenzyme Q10), bioflavonoids, and selenium.

Several studies in laboratory animals support the concept that antioxidants are antiatherogenic.[748] Some, but not all, epidemiological data lend additional support to the concept that dietary antioxidants can reduce risk for CHD.[748] Generally, in populations that consume a dietary pattern rich in fruits and vegetables and other foods high in antioxidants, there is a reduced risk of CHD.

Several controlled clinical trials have been carried out to determine whether supplementation with antioxidants reduces risk for CHD. The Linxian study in China found that supplements of beta-carotene (15 mg/d), vitamin E (30 mg/d), and selenium (15 mcg/d), given at levels obtained from foods, were associated with a non-significant 10 percent decrease in CVD mortality.[749] In the Alpha-Tocopherol, Beta Carotene Cancer Prevention Study, supplementation with beta-carotene had no beneficial effect on the incidence of myocardial infarction.[750] Another trial,[751] found no benefit (or harm) for CHD incidence after 12 years of beta-carotene supplementation in 22,071 male physicians. Finally, in the CARET study, a non-significant 26 percent increase in cardiovascular mortality was reported in a group supplemented with beta-carotene.[752]

In the Alpha-Tocopherol, Beta Carotene Cancer Prevention Study, supplementation with small doses of vitamin E in Finnish male smokers had only a marginal effect on incidence of fatal CHD, whereas it had no effect on incidence of nonfatal myocardial infarction.[750] In a secondary prevention trial among patients with CHD, vitamin E supplementation (400 or 800 IU per day during 1.5 years) in the Cambridge Heart Antioxidant Study (CHAOS), significantly reduced the risk for recurrent MI (77 percent). No effect was demonstrated for CVD mortality. A non-significant increase in total mortality was observed in the vitamin E group.[753] Two large-scale clinical trials in patients

with established CHD failed to demonstrate a protective effect of vitamin E supplementation on subsequent cardiovascular events.[510,735,754]

Thus, in spite of the theoretical benefits of antioxidant vitamins for reducing risk for CHD, this potential has so far not been found in controlled clinical trials that have used a variety of antioxidant mixtures and doses. The failure to demonstrate benefit in controlled trials does not eliminate the possibility of benefit. It does, however, dilute confidence in benefit and stands in the way of a solid recommendation for high intakes of antioxidants for CHD prevention.

The Institute of Medicine has recently released recommendations for Dietary Reference Intakes (DRIs) for antioxidant vitamins. A specific recommendation was not made for beta-carotene because it has not been shown to be an essential nutrient nor have clinical trials demonstrated benefit for reduction in risk for either cardiovascular disease or cancer. The RDA for vitamin C was increased to 75 mg/day for women and 90 mg/day for men. The RDA for Vitamin E was set at 15 mg/day. Vitamin E supplementation was not recommended for prevention of chronic disease because of a lack of convincing evidence of benefit.

Evidence Statement: Oxidative stress and LDL oxidation appear to be involved in atherogenesis. However, clinical trials to date have failed to demonstrate that supplementation of the diet with antioxidants will reduce risk for CHD (A2).

Recommendation: Evidence of CHD risk reduction from dietary antioxidants is not strong enough to justify a recommendation for antioxidant supplementation to reduce CHD risk in clinical practice. ATP III supports current recommendations of the Institute of Medicine's RDAs for dietary antioxidants, i.e., 75 mg and 90 mg per day for women and men, respectively, for vitamin C and 15 mg per day for vitamin E.

3) Moderate intakes of alcohol

Observational studies consistently show a J-shaped relation between alcohol consumption and total mortality. Moderate alcohol consumption is associated with lower mortality, and higher consumption with higher mortality. The lower mortality appears to be related to CHD death, because CHD accounts for a significant proportion of total deaths. Case-control, cohort, and ecological studies indicate lower risk for CHD at low to moderate alcohol intake.[755] A moderate amount of alcohol can be defined as no more than one drink per day for women and no more than two drinks per day for men.[756,757] This gender distinction takes into account differences in both weight and metabolism. Moreover, any cardiovascular benefit occurs not in the young age groups but in middle-aged adults, men 45 years of age or older and women 55 years of age or older.[758] Mechanisms of putative risk reduction from moderate alcohol consumption are unknown; however, it could be due to an increase in HDL cholesterol and apo A-1 and modestly to an improvement in hemostatic factors.[759] Prospective cohort studies suggest a similar relationship with CHD regardless of the type of alcoholic beverages consumed.[760]

The dangers of overconsumption of alcohol are well known. At higher levels of intake, adverse effects include elevated blood pressure, arrhythmia, and myocardial dysfunction.[755,757] Alcohol excess also predisposes to acute pancreatitis. Rarely it can precipitate pancreatitis by accentuating a pre-existing hypertriglyceridemia and chylomicronemia.[761] A pooled analysis shows that alcohol intake increases the risk of breast cancer in women.[762] Since up to 10 percent of U.S. adults misuse alcohol, advice about alcohol intake should be given carefully with both advantages and negatives presented.[763] For some persons, the negatives of alcohol consumption will outweigh any advantage.

Evidence Statement: Moderate intakes of alcohol in middle-aged and older adults may reduce risk for CHD (C2). However, high intakes of alcohol produce multiple adverse effects (C1).

Recommendation: No more than two drinks per day for men and no more than one drink per day for women should be consumed. A drink is defined as 5 ounces of wine, 12 ounces of beer, or 1½ ounces of 80 proof whiskey. Persons who do not drink should not be encouraged to initiate regular alcohol consumption.

4) Dietary sodium, potassium, and calcium

Many individuals with hypercholesterolemia also have hypertension (see Section VII.6). Evidence suggests that even those with normal blood pressure levels can reduce their chances of developing high blood pressure by consuming less salt.[160,161,657] Studies in diverse populations have shown that a high sodium intake is associated with higher blood pressure.[764] Also, a high salt intake increases the amount of calcium excreted in the urine, and has been independently associated with bone loss at the hip.[764] The Dietary Approaches to Stop Hypertension (DASH) trial has provided evidence that a dietary pattern high in fruits, vegetables, low-fat dairy products, whole grains, poultry, fish, and nuts and low in fats, red meat, and sweets—foods that are good sources of potassium, calcium, and magnesium–favorably influences blood pressure even when sodium levels are held constant,[765] but when these nutrients are consumed in combination with a low sodium intake, 2400 mg or 1800 mg, blood pressure is lowered even more.[766]

Evidence statement: JNC VI[160,161] provides a review of the evidence to support the concept that lower salt intake lowers blood pressure or prevents its rise. One clinical trial further shows that the effects of a dietary pattern high in fruits, vegetables, low-fat dairy products, whole grains, poultry, fish, and nuts and low in fats, red meat, and sweets—foods that are good sources of potassium, calcium, and magnesium—to reduce blood pressure are enhanced by a diet low in salt (A2).

Recommendation: The Diet and Health report[657] and JNC VI recommend a sodium intake of <2400 mg/d (no more than 100 mmol/day, 2.4g sodium or 6.4g sodium chloride). JNC VI further recommends maintaining adequate intakes of dietary potassium (approximately 90 mmol per day) and enough dietary calcium and magnesium for general health. ATP III affirms these recommendations for persons undergoing cholesterol management in clinical practice.

5) Herbal or botanical dietary supplements

The 10 top-selling herbal or botanical dietary supplements are cranberry, echinacea, evening primrose, garlic, ginkgo, ginseng, goldenseal, grape seed extract, St. John's wort, and saw palmetto.[767] These botanical supplements are available in health food stores, pharmacies, and many supermarkets. Several of the compounds have been promoted as agents to reduce the risk of CHD. Data from controlled trials regarding efficacy and safety are limited, in part because existing food and drug laws do not require demonstration of safety and efficacy to support legal marketing of dietary supplements. Dietary supplements are regulated according to different standards than are drugs. In addition to concerns about efficacy and safety, there is a lack of standardization among brands of botanical supplements. As a result, the amount of bioactive constituent, by which the supplements are hypothesized to influence disease, can differ widely among brands. In the case of garlic, a few randomized controlled studies are available, but the preponderance of available evidence fails to establish that garlic reduces LDL cholesterol levels. Biological plausibility supports use of some supplements, but there are few controlled clinical trials to document benefit. Studies designed to evaluate efficacy for disease endpoints, long-term safety, and drug interaction have not been reported.

Evidence statement: Despite widespread promotion of several herbal or botanical dietary supplements for prevention of CHD, a paucity of data exists on product standardization, controlled clinical trials for efficacy, and long-term safety and drug interactions. Clinical trial data are not available to support the use of herbal and botanical supplements in the prevention or treatment of heart disease.

Recommendation: ATP III does not recommend use of herbal or botanical dietary supplements to reduce risk for CHD. However, health care professionals should query patients to establish whether such products are being used because of the potential for drug interaction.

6) High protein, high total fat and saturated fat weight loss regimens

Periodically, weight-loss diets high in protein and fat and low in carbohydrate surge in popularity. Such diets will result in weight loss within a few weeks or months if calories are restricted. However, such diets have not been demonstrated to produce long-term weight loss in controlled trials. Although clinical trial data are lacking, several concerns have been expressed about the use of these diets in clinical weight reduction:

- Short-term, extreme diets rarely produce long-term weight reduction.
- High intakes of saturated fats can raise LDL cholesterol.
- Low intakes of fruits, vegetables, and grains can deprive persons of healthful nutrients and are not conducive to long-term health.

Diets popularized as low-carbohydrate, high-fat, high-protein regimens for rapid weight loss should not be confused with ATP III's easing restriction of the percentage of dietary fat for persons with the metabolic syndrome. The latter allows dietary fat to rise to 35 percent of total calories, provided it remains low in saturated fatty acids (<7 percent of total energy) and includes mostly unsaturated fats. This will reduce carbohydrate intake somewhat to prevent the actions of high-carbohydrate diets to raise triglycerides and reduce HDL cholesterol levels. The ATP III recommendation allows for the dietary variety outlined in the Dietary Guidelines for Americans (2000).[241]

Evidence statement: High protein, high total fat and saturated fat weight loss regimens have not been demonstrated in controlled clinical trials to produce long-term weight reduction. In addition, their nutrient composition does not appear to be conducive to long-term health.

Recommendation: High protein, high total fat and saturated fat weight loss regimens are not recommended for weight reduction in clinical practice.

4. Management of the metabolic syndrome through life habit changes

a. Weight control

ATP II[1,2] recommended increased emphasis on weight reduction as part of LDL-lowering therapy for overweight/obese persons who enter clinical guidelines for cholesterol management. ATP III confirms this recommendation. However, in ATP III, emphasis on weight reduction is delayed until after other dietary measures are introduced for LDL lowering (reduced intakes of saturated fatty acids and cholesterol and possibly other options for LDL lowering [plant stanols/sterols and increased dietary fiber]) (see Figure V.2–1). The delay in emphasizing weight reduction is to avoid overloading new patients with a multitude of dietary messages and to concentrate first on LDL reduction. After an adequate trial of LDL-lowering measures, attention turns to other lipid risk factors and the metabolic syndrome (see Figure V.2–1). Weight reduction then becomes a major focus of TLC. In 1998, the NHLBI published Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults from the Obesity Education Initiative (OEI).[78,79] This is an evidence-based report, and its recommendations for techniques of weight reduction are accepted by ATP III for persons undergoing management for cholesterol disorders. The ATP III report does not independently develop evidence statements beyond those in the OEI report. ATP III endorses the importance of weight control described in the OEI report. Indeed, weight control alone, in addition to lowering LDL cholesterol, favorably influences all of the risk factors of the metabolic syndrome.

b. Increased regular physical activity

ATP II also recommended increased emphasis on regular physical activity. In ATP III, the emphasis is reinforced with particular attention to its benefits for management of the metabolic syndrome. The recommendation for increased physical activity is introduced when TLC is initiated and the recommendation is reinforced when emphasis shifts to management of the metabolic syndrome (see Figure V.2–1). Physical inactivity is a major risk factor for CHD.[237,238] It raises risk for CHD in several ways, notably by augmenting the lipid and nonlipid risk factors of the metabolic

syndrome. It further enhances risk by impairing cardiovascular fitness and coronary blood flow. Regular physical activity can help reverse these adverse effects. It can have favorable effects on the metabolic syndrome and can reduce VLDL levels, raise HDL cholesterol and, in some persons, lower LDL levels. Regular physical activity lowers blood pressure and reduces insulin resistance. It also has been reported to reduce risk for CHD independently of standard risk factors. The evidence base for the recommendation of increased physical activity as part of cholesterol management is presented in the U.S. Surgeon General's Report on Physical Activity[238] and will not be detailed in this report. The purposes of regular exercise are to promote energy balance to maintain healthy body weight, to alleviate the metabolic syndrome, and to independently reduce baseline risk for CHD. In certain circumstances, a physician has the option of referring a patient to an exercise specialist for prescription and guidance in exercise training. Exercise specialists can complement nutrition professionals in implementation of TLC by guiding individuals in a healthy exercise program.

5. Practical approach to life habit changes

a. Role of the physician

The physician is crucial to initiating and maintaining the patient's dietary adherence. Physician knowledge, attitude, and motivational skills will strongly influence the success of dietary therapy. A positive attitude combined with effective dietary assessment, initiation of therapy, and followup are essential for initial and long-term adherence. The physician should try to determine the patient's attitude towards acceptance of and commitment to TLC. The physician's key responsibilities include: assessment of CHD risk, dietary assessment, explanation of the problem for the patient, decision about appropriate therapeutic plan, and description of the plan to the patient. The multiple benefits of lifestyle changes should be emphasized. The need for lifestyle change, even when drugs are prescribed, should be stressed. In this section, one model for the role of the physician in the institution and followup of dietary therapy will be described. This model can be modified according to the constraints of the practice setting. The key feature of this model is the introduction of dietary therapy in a stepwise manner, beginning with an emphasis on lowering LDL cholesterol and followed by a shift in emphasis to management of the metabolic syndrome, if the latter is present. The essential steps in this model are shown in Figure V.2–1.

1) *Visit 1: Risk assessment, diet assessment, and initiation of therapeutic lifestyle change*

Some persons do not qualify for immediate clinical management to lower LDL because their LDL level is not above the goal for their category of risk for CHD (see Section III). Nonetheless, the physican should appropriately control other risk factors, provide a public health message on overall risk reduction, and prescribe subsequent lipoprotein reevaluation as needed. Suggestions to assist the physician in conveying the public health message are outlined in Table V.1–3.

For persons who require dietary therapy, the first step is assessment of lifestyle habits. CAGE questions provide the physician with a way to rapidly assess current intakes of LDL-raising nutrients (Table V.2–4). A more detailed tool for both assessment and as a guide to TLC is available in Table V.2–6. Therapeutic change in the first visit should begin with the TLC diet. If the patient demonstrates a lack of basic knowledge of the principles of the TLC diet, the physician should consider referral to a nutrition professional for medical nutrition therapy.

2) *Visit 2: Intensifying the TLC diet for LDL cholesterol lowering*

Approximately 6 weeks after starting the TLC diet, lipoprotein analysis is repeated and assessed. If the LDL cholesterol goal is achieved by 6 weeks, the patient should be commended for his/her adherence and encouraged to continue lifestyle changes (Figure V.2–1). If the LDL goal has not been achieved, the LDL-lowering TLC should be intensified. Depending upon the patient's level of dietary adherence, various options exist. More vigorous reduction in saturated fats and cholesterol, adding plant stanols/sterols (2 g/day), increasing viscous fiber (see Table V.2–5), and referral to a nutrition professional can all enhance LDL lowering.

The physician should not ignore the power of TLC to reduce CHD risk. Despite the marked advances in drug therapy for elevated LDL cholesterol level,

ATP III places increased emphasis on nutrition and physical activity for cholesterol management and overall risk reduction. The low prevalence of CHD in populations that consume low intakes of saturated fats and cholesterol and high intakes of other healthful nutrients, and who maintain desirable body weight through balanced caloric intake and output, illustrate what can be achieved without drug therapy.[632] Moreover, specifically for LDL cholesterol reduction, the combination of several dietary modifications can produce a reduction in LDL levels that rivals reductions produced by standard doses of statins. LDL cholesterol responses shown in Table V.5–2 represent conservative estimates based on the literature. Although cumulative responses have not been documented by clinical trial, a sizable summed response from the multiple components of TLC is likely.

Table V.5–2. Approximate and Cumulative LDL Cholesterol Reduction Achievable By Dietary Modification

Dietary Component	Dietary Change	Approximate LDL Reduction
Major		
Saturated fat	<7% of calories	8–10%
Dietary cholesterol	<200 mg/day	3–5%
Weight reduction	Lose 10 lbs	5–8%
Other LDL-lowering options		
Viscous fiber	5–10 g/day	3–5%
Plant sterol/ stanol esters	2g/day	6–15%
Cumulative estimate		20–30%

Adapted From Jenkins et al.[768]

3) Visit 3: Decision about drug therapy; initiating management of the metabolic syndrome

If the LDL cholesterol goal has not been achieved after 3 months of TLC, a decision must be made whether to consider adding drug therapy. If drugs are started, TLC should be continued indefinitely in parallel with drug treatment. Although the apparent ease of drug use is appealing, the additive effect of TLC to drug therapy in LDL cholesterol lowering is substantial and should not be overlooked. For example, Hunninghake et al.[769] reported an extra 5 percent lowering of LDL cholesterol when lovastatin therapy was combined with dietary therapy. This additional LDL cholesterol lowering equates to doubling the dose of the statin, due to the log-dose characteristics of statin usage. Other studies revealed a much greater LDL reduction when dietary therapy plus plant stanols were combined with statin therapy.[709,770] These dietary options, if successfully implemented, are preferable to progressively increasing doses of LDL-lowering drugs.

A second purpose of Visit 3 is to initiate lifestyle therapies for the metabolic syndrome, if it is present. Emphasis in TLC shifts to weight control and increased physical activity. The principles of weight control are described in the Obesity Education Initiative report.[78,79]

Because of the complexities and frequent failures of long-term weight control in clinical practice, consideration should be given to referring overweight or obese individuals to a qualified nutrition professional for medical nutrition therapy.

A second element of treatment of the metabolic syndrome is to increase physical activity. The physician should provide specific recommendations for physical activity depending on the patient's physical well-being and social circumstances. Consideration also can be given to referral to an exercise specialist for guidance if this resource is available. Moderate, sustained exercise can cause a significant reduction in baseline risk for CHD. Examples of moderate intensity exercise that may be useful to individuals are listed in Tables V.2–6 and V.5–3. Moderate intensity physical activity should be promoted for most people. Moderate amounts of vigorous activity also can be beneficial for some individuals, provided safety is ensured. Suggestions to incorporate more exercise into daily life are shown in Table V.5–4.

Table V.5–3. Examples of Moderate* Physical Activity in Healthy Adults†

- Brisk walking (3–4 mph) for 30–40 minutes
- Swimming—laps for 20 minutes
- Bicycling for pleasure or transportation, 5 miles in 30 minutes
- Volleyball (noncompetitive) for 45 minutes
- Raking leaves for 30 minutes
- Moderate lawn mowing (push a powered mower) for 30 minutes
- Home care—heavy cleaning
- Basketball for 15–20 minutes
- Golf—pulling a cart or carrying clubs
- Social dancing for 30 minutes

* Moderate intensity defined as 4–7 kcal/minute or 3–6 METS. METS (work metabolic rate/resting metabolic rate) are multiples of the resting rates of oxygen consumption during physical activity. One MET represents the approximate rate of oxygen consumption of a seated adult at rest, or about 3.5 mL per min per kg.

† This table was adapted from the recommendations of the Surgeon General's Report on Physical Activity and Health[238] and the Centers for Disease Control and Prevention and American College of Sports Medicine.[771]

Table V.5–4. Suggestions to Incorporate More Physical Activity into the Day

- Walk more—look for opportunities!
  - Park farther away in parking lots near a mall so you have a longer walk
  - Walk or bike if your destination is just a short distance away
  - Walk up or down 1–2 flights of stairs instead of always taking the elevator
  - Walk after work for 30 minutes before getting in the car and sitting in traffic
  - Walk home from the train or bus—take a longer route so it takes 20 minutes instead of 5–10 minutes
  - Walk with a colleague or friend at the start of your lunch hour for 20 minutes
- Do heavy house cleaning, push a stroller, or take walks with your children
- Exercise at home while watching television
- Go dancing or join an exercise program that meets several times per week
- If wheelchair bound, wheel yourself for part of every day in a wheelchair

4) Visit N: Long-term follow-up and monitoring adherence to therapeutic lifestyle changes (TLC)

The patient who has achieved the goal LDL cholesterol as a result of TLC must be monitored for the long term. TLC is maintained indefinitely and reinforced by the physician and, as appropriate, by a nutrition professional if medical nutrition therapy is necessary. The patient can be counseled quarterly for the first year of long-term monitoring and twice yearly thereafter.

LDL cholesterol is measured prior to each visit, and the results are explained at the counseling session. When no lipoprotein abnormalities other than elevated LDL cholesterol are present, monitoring at 6-month intervals is appropriate. If elevated cholesterol level redevelops, the procedure outlined above for diet therapy of elevated LDL cholesterol should be reinstituted.

Persons who fail to achieve their goal LDL cholesterol by dietary therapy can be classified as having an inadequate response to diet. Such responses fall into four categories:

- *Poor adherence.* Some persons adhere poorly to diet modification despite intensive and prolonged dietary counseling. They are not ready to change for various reasons. Physician endorsement of the importance of diet is essential for facilitating increased interest on the part of the patient. If the patient admits a lack of willingness to change diet or other life habits, drug therapy may be the only reasonable option to effectively lower LDL.
- *Gradual change.* Some individuals modify eating habits only gradually. They may adhere poorly to diet in the first few months but eventually will modify their eating habits to meet the goals of therapy. Up to a year of instruction and counseling may be required for these persons. This is especially true for persons who are following a weight reduction plan. Ongoing follow-up and reinforcement is crucial for developing long-term adherence. A continued effort to achieve adherence to life-habit changes should not be abandoned if drug therapy is started.
- *Poor responders.* A minority of persons are non-responders to dietary therapy and will have high LDL cholesterol levels that are inherently resistant to dietary modification despite good