Effective Use of Statins to Prevent Coronary Heart Disease

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Primary and secondary prevention trials have shown that use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (also known as statins) to lower an elevated low-density lipoprotein cholesterol level can substantially reduce coronary events and death from coronary heart disease. In 1987 and 1993, the National Cholesterol Education Program promulgated guidelines for cholesterol screening and treatment. Thus far, however, primary care physicians have inadequately adopted these guidelines in clinical practice. A 1991 study found that cholesterol screening was performed in only 23 percent of patients. Consequently, many patients with elevated low-density lipoprotein levels and a high risk of primary or recurrent ischemic events remain unidentified and untreated. A study published in 1998 found that fewer than 15 percent of patients with known coronary heart disease have low-density lipoprotein levels at the recommended level of below 100 mg per dL (2.60 mmol per L). By identifying patients with elevated low-density lipoprotein levels and instituting appropriate lipid-lowering therapy, family physicians could help prevent cardiovascular events and death in many of their patients. (Am Fam Physician 2001;63:309-20,323-4.)

A patient information handout on goals for lowering cholesterol levels, written by the author of this article, is provided on page 323.

An elevated low-density lipoprotein (LDL) cholesterol level is a key risk factor for coronary heart disease (CHD). The National Cholesteral Education Program (NCEP) first recommended universal cholesterol screening in 1987.[1] The National Ambulatory Medical Care Survey showed that family physicians and general internists in 1990-91 screened only 23 percent of adult patients for dyslipidemias and prescribed lipid-lowering medications for only 23 percent of patients with dyslipidemias.[2] Almost one decade later, many physicians still do not routinely perform cholesterol screening. Family physicians seldom include lipid screening in well-woman visits, and lipid screening is seldom done during visits for acute illness by young-adult and middle-aged men, most of whom are unlikely to return for health maintenance visits.

Despite multiple randomized trials showing that a reduction in an elevated LDL level lowers cardiovascular morbidity and mortality,[3-5] most patients with high LDL levels remain unidentified or untreated.[2] In addition, many physicians are uncertain about when to start preventive treatment. Although dietary change can be effective in reducing the LDL level,[6] most patients are unwilling or unable to modify their eating habits sufficiently enough to achieve LDL treatment goals. In addition, patients who have no symptoms of CHD often do not perceive the need for or do not want to begin long-term drug therapy, sometimes lasting decades, to prevent future cardiovascular problems. Some are concerned about possible drug side effects, and the cost of lipid-lowering medication can also be a factor that discourages treatment.

Lipid Management: An Overview of Prevention

The family physician is uniquely positioned to detect lipid problems in multiple family members and to facilitate long-term compliance with cholesterol treatment. Prevention of cardiovascular disease ideally begins with primary interventions in persons with no known cardiovascular disease.[7] The physician's role in primary prevention is to assess CHD risk factors *(Table 1)*, urge lifestyle changes and initiate medical treatment in high-risk patients.

The goal of secondary prevention in patients with atherosclerotic disease is to lower the risk of subsequent CHD events. Clinical trials have shown that most patients with CHD are candidates for lipid-lowering medication.[8] Individuals with CHD carry a five- to sevenfold increased risk of recurrent CHD events and are most likely to benefit from lipid-lowering therapy.[4,5,9]

LIPID SCREENING GUIDELINES

NCEP guidelines recommend lipid screening in all adults by means of a lipid profile or total cholesterol and high-density lipoprotein (HDL) cholesterol determinations.[10,11] This recommendation for screening cholesterol includes the elderly population, for whom evidence of treatment benefit was lacking but is now beginning to emerge.[12] To maximize cooperation from the patient, the NCEP recommends screening with nonfasting blood specimens.[10] Random specimens often yield useful information about the postprandial rise in triglyceride levels and the related risk for atherosclerosis.[13] It should be kept in mind that acute illness can alter blood lipids, especially if the liver or thyroid is affected.

The main goal of screening is to identify patients with elevated LDL levels. If screening values are abnormal, follow-up testing should be conducted in each of the following circumstances:

- Total cholesterol higher than 200 mg per dL (5.15 mmol per L) and other cardiac risk factors
- Total cholesterol higher than 240 mg per dL (6.20 mmol per L)
- HDL less than 35 mg per dL (0.90 mmol per L)

The NCEP goal for LDL levels depends on each patient's risk factor status *(Table 2)*. The NCEP recommends checking lipid levels every five years in patients without CHD risk factors and every one to two years in patients with CHD risk factors.[10] In most persons, LDL and HDL levels are relatively stable over the long term. Much expense would be saved if individuals with healthy LDL and HDL levels were rescreened less often than is recommended or than is requested by some patients.

DIETARY MODIFICATION

Dietary modification is usually the first intervention in patients with borderline-high or moderately elevated LDL levels. However, patients with elevated LDL levels despite a low-fat intake have little room for dietary change. They frequently have type IIa or IIb dyslipidemia.

A fasting lipid profile should be obtained four to six weeks after the start of dietary therapy. The change in the LDL level as a result of a

TABLE 1
NCEP Risk Factors for Coronary Heart Disease

Major positive CHD risk factors
Age: male ≥ 45 years; female ≥ 55 years or with premature menopause without estrogen replacement therapy
Family history of early CHD (male < 55 years or female < 65 years)
Tobacco use: current smoking or smoking within the preceding five years (probably also chewing tobacco or snuff)
Diabetes mellitus
Hypertension (blood pressure ≥ 140/90 mm Hg or receiving antihypertensive therapy)
Elevated LDL level (>130 mg per dL [>3.35 mmol per L])
Low HDL level (< 35 mg per dL [< 0.90 mmol per L])
Major negative CHD risk factors
High HDL level (≥60 mg per dL [≥ 1.55 mmol per L])
Other positive CHD risk factors*
Elevated apolipoprotein B (core of LDL) level
Low apolipoprotein A-1 (core of HDL) level
Elevated Lp(a) level
Elevated homocysteine and/or low folate levels
Obesity
Sedentary lifestyle
Coronary-prone (type A) personality/behavior, especially hostility component
Lack of supportive primary relationship

NCEP = National Cholesterol Education Program; CHD = coronary heart disease; LDL = low-density lipoprotein cholesterol; HDL = high-density lipoprotein cholesterol.

**—Other positive CHD risk factors are less well-proven or less acknowledged than the items listed under major positive risk factors.*

reduction in the average daily intake of saturated fat and cholesterol occurs in the first few weeks after the initiation of dietary modifications.[14] With a given amount of dietary change, lipid levels do not show further improvement as the patient continues to adhere to the low-fat diet for a longer period. Although the NCEP recommends a six-month trial of dietary therapy before drug therapy is considered in patients without CHD, patients seldom maintain dietary changes for as long as six months without receiving feedback on the response of their lipid levels to the dietary changes.

The National Cholesterol Education Program recommends dietary therapy for six months before initiating drug therapy in persons without known coronary heart disease. However, patients are seldom able to adhere to a low-fat diet for this duration without feedback on the response of their low-density lipoprotein levels to the dietary changes.

Pharmacologic Treatment for Primary Prevention of CHD

A reduction in elevated LDL levels with pravastatin has been shown to significantly reduce coronary events in individuals without CHD.[3] Lipid-lowering drug therapy for primary CHD prevention is most clearly indicated when two or more CHD risk factors are present and the LDL remains higher than 160 mg per dL (4.15 mmol per L) after an adequate dietary trial. In addition, patients with

TABLE 2
NCEP Recommendations for LDL Levels in Primary Prevention of Coronary Heart Disease

LDL levels that indicate the need for initiating dietary therapy for primary prevention

Number of CHD risk factors	*LDL level before dietary changes*
<2 other risk factors	≥160 mg per dL (4.15 mmol per L)
≥2 other risk factors	≥130 mg per dL (3.35 mmol per L)

LDL levels that indicate the need for drug therapy for primary prevention

Number of CHD risk factors	*LDL level before treatment*
<2 other risk factors	≥190 mg per dL (4.90 mmol per L) after dietary trial or ≥220 mg per dL (5.70 mmol per L) at baseline
≥2 other risk factors	≥160 mg per dL (4.15 mmol per L) after dietary trial or >190 mg per dL (4.90 mmol per L) at baseline

Goal LDL levels with dietary or drug therapy for primary prevention

Number of CHD risk factors	*Goal LDL level*
<2 other risk factors	<160 mg per dL (4.15 mmol per L)
≥2 other risk factors	<130 mg per dL (3.35 mmol per L)

NCEP = National Cholesterol Education Program; LDL = low-density lipoprotein cholesterol; CHD = coronary heart disease.

TABLE 3
Data on Coronary Heart Disease Prevention from Five Major Controlled Trials of Statins

Trial; drug therapy; mean duration of follow-up	*Study population*	*Mean baseline LDL level*	*Absolute and relative LDL reduction*	*Relative reduction in CHD events (%)*	*Relative reduction in CHD deaths (%)*
WOSCOPS[3]; pravastatin, 40 mg daily; 4.9 years	6,595 men without known CHD	192 mg per dL (4.95 mmol per L)	–50 mg per dL (–1.30 mmol per L); –26%	–31*	–28
AFCAPS/TexCAPS[26]; lovastatin, 20 to 40 mg daily; 5.2 years	5,608 men and 997 women without known CHD	150 mg per dL (3.90 mmol per L)	–35 mg per dL (–0.90 mmol per L); –25%	–24*	–27
4S study[4]; simvastatin, 20 to 40 mg daily; 5.4 years	4,444 men with CHD	188 mg per dL (4.85 mmol per L)	–66 mg per dL (–1.70 mmol per L); –35%	–34*	–42*
CARE study[5]; pravastatin, 40 mg daily; 5 years	3,583 men and 576 women with CHD	139 mg per dL (3.60 mmol per L)	–42 mg per dL (–1.10 mmol per L); –30%	–24*	–20
LIPID study[9]; pravastatin, 40 mg daily; 6.1 years	7,498 men and 1,516 women with CHD	150 mg per dL (3.90 mmol per L)	–35 mg per dL (–0.90 mmol per L); –25%	–23*	–24*

WOSCOPS = West of Scotland Coronary Prevention Study; AFCAPS/TexCAPS = Air Force Texas Coronary Atherosclerosis Prevention Study; 4S = Scandinavian Simvastatin Survival Study; CARE = Cholesterol and Recurrent Events trial; LIPID = Long-Term Intervention with Pravastatin in Ischaemic Disease study; LDL = low-density lipoprotein cholesterol; CHD = coronary heart disease.

**—P <0.01.*

†—In compliant subjects.

Data from references 3 through 5, 9 and 26.

LDL levels higher than 160 mg per dL and with one other strong risk factor (diabetes, smoking or a family history of early CHD) may also be candidates for drug therapy.[7]

When the LDL level is less than 220 mg per dL (5.70 mmol per L) and no other risk factors are present, NCEP guidelines recommend deferring drug therapy in men 35 years or younger and in premenopausal women.[10] Some individuals in this situation, however, do not want to defer treatment. Coronary atherosclerosis begins in adolescence or early adulthood[15] and often causes myocardial infarction or sudden death as the first symptom of coronary artery disease. Drug treatment may be beneficial in some young adults with no CHD risk factors other than an LDL level between 190 and 219 mg per dL (4.90 and 5.65 mmol per L), but such treatment in everyone with LDL levels in this range would not be cost-effective.[16] Some physicians and policy groups support lipid-lowering drug treatment for primary prevention only in patients with the highest absolute 10-year risk for CHD.[17-19]

The National Cholesterol Education Program treatment goal for patients with known diabetes or coronary heart disease is to reduce the low-density lipoprotein level to less than 100 mg per dL (2.60 mmol per L) with diet and pharmacologic therapy.

Pharmacologic Treatment for Secondary Prevention of Further CHD Events

The strongest evidence in support of lipid lowering as a means of secondary CHD pre-

	Relative reduction in total mortality (%)	*Relative reduction in revascularization procedure (%)*
	–22	–46†
	No reported end point	–33*
	–30*	–37*
	–9	–27*
	–22*	–20*

vention comes from three large trials—Scandinavian Simvastatin Survival Study (4S study), Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) study and the Cholesterol and Recurrent Events (CARE) trial—in which treatment with HMG-CoA reductase inhibitors (statins) reduced coronary events by 23 to 34 percent and reduced CHD mortality by 20 to 42 percent *(Table 3)*.[4,5,9] Cholesterol reduction prevented CHD events equally well in individuals with diabetes.[20] Aggressive treatment with simvastatin[4] and lovastatin[21] was found to produce greater benefit than that with moderate treatment.

For patients with CHD, the NCEP recommends a treatment goal of an LDL level less than 100 mg per dL (2.60 mmol per L), with diet or drug therapy *(Table 4)*. Compared with higher LDL levels, reducing the LDL level to this extent may more effectively prevent worsening of atherosclerotic plaque and promote regression of existing lesions.[21,22] Achieving more aggressive LDL lowering (100 mg per dL or less) for five years might produce a further 15 to 20 percent reduction in CHD events and deaths beyond that achieved with drug doses used in published trials.[23] In a 1993-95 study (published in 1998), only 14 percent of patients with heart disease sampled from community family physicians' practices had LDL levels less than 100 mg per dL.[24]

The LDL treatment goal of 100 mg per dL or less may be unattainable for some patients with very high LDL levels. For such patients it is more practical to agree on an achievable goal instead of setting an unrealistic goal unrelated to the patient's LDL level before treatment.[25]

Other Lipids, Special Populations and Other Outcomes

Low HDL levels and high triglyercide levels have been identified as secondary treatment targets.[7] The combination of a borderline or mildly elevated LDL level and an HDL level of less than 45 mg per dL (1.15 mmol per L) carries a substantial risk for CHD. Individuals with this lipid combination benefit from statin therapy. In the Air Force Coronary Atherosclerosis Prevention Study (AFCAPS),[26] lovastatin was found to reduce CHD events by

TABLE 4

NCEP Recommendations for LDL Levels in Secondary Prevention of Coronary Events in Patients with Coronary Heart Disease

Baseline LDL level	*Recommendation*
100 to 129 mg per dL (2.60 to 3.35 mmol per L)	Initiate aggressive dietary therapy (Step 2 AHA diet), and consider drug therapy.
>130 mg per dL (>3.35 mmol per L)	Add drug therapy immediately to Step 2 AHA dietary therapy.

NCEP = National Cholesterol Education Program; LDL = low-density lipoprotein cholesterol; AHA = American Heart Association.

A meta-analysis of 16 studies found that lipid-lowering with statins reduced the risk of stroke by 29 percent.

40 percent in men with a mean HDL level of 36 mg per dL (0.95 mmol per L) and in women with a mean HDL level of 40 mg per dL (1.05 mmol per L).

Women with diabetes and elevated triglyceride levels (more than 200 mg per dL [2.25 mmol per L]) are at high risk for premature CHD, as are men with elevated triglyceride levels and low HDL levels. An elevated triglyceride level may be a stronger predictor of recurrent myocardial infarction after coronary artery bypass surgery than an elevated LDL level.[27] Much of the benefit from gemfibrozil in the Helsinki Heart Study[28] accrued to those with elevated triglyceride levels. Elevated triglyceride levels can be treated with statins, fibrates or niacin. Serious liver problems occur more often with fibrates and niacin.

Age is a powerful risk factor for CHD. The CARE trial[12] revealed that a reduction in borderline-high LDL levels (mean: 138 mg per dL [3.60 mmol per L]) with pravastatin in individuals 65 to 75 years of age produced relative reductions of 32 percent in major coronary events, of 45 percent in coronary deaths and of 40 percent in stroke. A meta-analysis[29] of 16 randomized studies showed that lipid-lowering with statins reduced the relative risk of stroke by 29 percent. The decision to treat LDL elevation in the elderly is best negotiated by focusing on the individual's quality of life, goals and willingness to take additional medication.

Cost-Effectiveness of Statin Treatment

Cost-benefit analyses show that lipid-lowering therapy is relatively cost-effective, compared with other interventions.[30-32] In middle-aged patients with CHD (secondary prevention), the estimated cost per year of life saved as a result of statin therapy is between $4,500 and $14,000. The cost for primary prevention of CHD with a statin in middle-aged patients is about $20,000 to $40,000 per year of life saved. These figures compare with a cost of $40,000 per year of life saved for hemodialysis and $70,000 per year of life saved for coronary artery bypass surgery for one-vessel coronary disease.

Choosing Among the Statins

Because of their effectiveness, tolerability and safety, the statins have become the first-line agents for primary and secondary prevention of CHD in patients with elevated LDL levels. Available statins (in order of labeling by the U.S. Food and Drug Administration) include lovastatin (Mevacor), pravastatin (Pravachol), simvastatin (Zocor), fluvastatin (Lescol), atorvastatin (Lipitor) and cerivastatin (Baycol). The choice of statin is usually based on the clinician's judgment of the relative importance of three factors: evidence of beneficial clinical outcomes, efficacy for lowering LDL and cost.

Evidence for benefits in clinical outcome is strong for simvastatin,[4] pravastatin[3,5,9] and lovastatin[26] *(Table 3)*. Coronary angiographic evidence of benefit is available for atorvastatin[22] and fluvastatin.[33] The preventive effect of statins appears to be a class effect that is partly mediated by effects on nonlipid factors, including stabilization of arterial plaques.[34] Simvastatin may be more likely than pravastatin to produce additional reduction of CHD risk by reducing the LDL level to less than 125 mg per dL (3.25 mmol per L).[35]

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The statins differ in their efficacy in reducing the LDL level *(Table 5)*.[36-38] The starting dosages of the two most efficacious statins—simvastatin (20 mg) and atorvastatin (10 mg)—reduce LDL levels an average of 35 percent and 38 percent, respectively. At these starting dosages, LDL levels drop to below the NCEP treatment goal in a higher proportion of patients than the proportion of patients receiving the starting dosages of cerivastatin, lovastatin, pravastatin and fluvastatin.

The cost of the statins varies widely *(Tables 6 and 7)*. Use of a highly efficacious statin can reduce the number of return visits and blood tests conducted for dose titration. The least costly drug, fluvastatin, may be best suited for patients who require a moderate LDL reduction (less than 25 percent). The choice of statin often is constrained by cost-oriented managed care formularies and differential copayment levels. Comparative analyses suggest that fluvastatin or atorvastatin may be the most cost-effective agent in patients with mild or moderate LDL elevation.[39,40] For patients with severe LDL elevation, atorvastatin may be cost effective. Future cost-benefit analyses may show that cerivastatin is the most cost-effective statin because of its favor-

The decision to treat an elevated low-density lipoprotein level in an elderly patient is best negotiated by focusing on the patient's quality of life, goals and willingness to take additional medication.

TABLE 5
Average Percentage of the Reduction in LDL Levels with Different Efficacy of Statin Drugs

Statin	*10-mg dosage*	*20-mg dosage*	*40-mg dosage*	*80-mg dosage*
Lovastatin (Mevacor)	—	29%*†	31%	48%
Pravastatin (Pravachol)	19%	24%*†	34%	40%
Simvastatin (Zocor)	28%	35%*†	40%	48%
Fluvastatin (Lescol)	—	17%*†	23%	33%
Atorvastatin (Lipitor)	38%*	46%	51%	54%
Cerivastatin (Baycol)	0.2-mg dosage: 25%	0.3-mg dosage: 30%*‡	0.4-mg dosage: 36%	0.8-mg dosage: 44%§

LDL = low-density lipoprotein.

**—A daily dosage of 10 mg is the recommended starting dose for atorvastatin.*

†—*A daily dosage of 20 mg is the recommended starting dose for lovastatin, pravastatin, simvastatin and fluvastatin.*

‡—*A daily dosage of 0.3 mg is the recommended starting dose for cerivastatin.*

§—*The 0.8-mg dose of cerivastatin is not yet on the market.*

Drugs are listed in descending order based on labeling by the U.S. Food and Drug Administration.

Information from Jones P, Kafonek S, Laurora I, Hunninghake D. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia (the CURVES study). Am J Cardiol 1998;81:582-7 [Published erratum appears in Am J Cardiol 1998;82:128], and Sasaki J, Arakawa K, Yamamoto K, Kobori S, Ageta M, Kono S. A long-term comparative trial of cerivastatin sodium, a new HMG-CoA reductase inhibitor, in patients with primary hypercholesterolemia. Clin Ther 1998;20:539-48.

TABLE 6
Suggestions for Prescribing Statin Drugs in a Cost-Effective Manner

	Goal LDL level and dosage, cost and efficacy of different statins*	
Baseline LDL level	*<130 mg per dL (patients without CHD or diabetes)*	*<100 mg per dL (patients with CHD or diabetes)*
130 to 159 mg per dL (3.35 to 4.10 mmol per L)	Cerivastatin (Baycol), one 0.3-mg tablet daily; $40 per month; lowers LDL 30% *or* Pravastatin (Pravachol), one half of a 20-mg tablet daily; $34 per month; lowers LDL 19% *or* Atorvastatin, one half of a 20-mg tablet daily; $45 per month; lowers LDL 38% *or* Fluvastatin (Lescol), 20-mg or 40-mg tablet daily; $40 per month; lowers LDL 17% to 23%	Cerivastatin, 0.4-mg tablet daily; $40 per month; lowers LDL 36% *or* Atorvastatin (Lipitor), one half of a 20-mg tablet daily; $45 per month; lowers LDL 38% *or* Atorvastatin, 10-mg tablet daily; $55 per month; lowers LDL 38% *or* Simvastatin (Zocor), one half of a 40-mg tablet daily; $57 per month; lowers LDL 35%
160 to 189 mg per dL (4.15 to 4.90 mmol per L)	Cerivastatin, 0.4-mg tablet daily; $40 per month; lowers LDL 36% *or* Atorvastatin, one half of a 20-mg tablet daily; $45 per month; lowers LDL 38% *or* Atorvastatin, 10-mg tablet daily; $55 per month; lowers LDL 38% *or* Simvastatin, one half of a 40-mg tablet daily; $57 per month; lowers LDL 35% *or* Simvastatin, 20-mg tablet daily; $114 per month; lowers LDL 35%	Atorvastatin, one half of a 40-mg tablet daily; $53 per month; lowers LDL 46% *or* Simvastatin, one half of an 80-mg tablet daily; $57 per month; lowers LDL 40% *or* Atorvastatin, 20-mg tablet daily; $90 per month; lowers LDL 46% *or* Pravastatin, two 40-mg tablets daily; $224 per month; lowers LDL 40%
≥190 mg per dL (4.90 mmol per L)	Atorvastatin, one half or one 40-mg tablet daily; $53 to $105 per month; lowers LDL 46% to 51% *or* Simvastatin, one half to one 80-mg tablet daily; $57 to $114 per month; lowers LDL 40% to 48%	Atorvastatin, one or two 40-mg tablets or one 80-mg tablet daily; $105 to $210 per month; lowers LDL 51% to 54% *or* Simvastatin, 80-mg tablet daily; $114 per month; lowers LDL 48%

LDL = low-density lipoprotein cholesterol; CHD = coronary heart disease.

**—Estimated cost to the pharmacist based on average wholesale prices (rounded to the nearest dollar) in Red Book. Montvale, N.J.: Medical Economics Data, 1999. Cost to the patient may be greater, depending on prescription filling fee.*

Information from Jones P, Kafonek S, Laurora I, Hunninghake D. Comparative dose efficacy study of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia (the CURVES study). Am J Cardiol 1998;81:582-7 [Published erratum appears in Am J Cardiol 1998;82:128], and Sasaki J, Arakawa K, Yamamoto K, Kobori S, Ageta M, Kono S. A long-term comparative trial of cerivastatin sodium, a new HMG-CoA reductase inhibitor, in patients with primary hypercholesterolemia. Clin Ther 1998;20:539-48.

able combination of efficacy and relatively economical price.

The statins are well tolerated, with less than a 5 percent discontinuation rate related to perceived side effects.[38] Clinically significant liver enzyme elevations (which usually appear in the first 12 weeks of therapy) occur in fewer than 1 percent of patients taking any statin.[38] It is not necessary to recheck liver enzymes after 12 weeks unless the dose is increased.

Simvastatin increases HDL levels more than the other statins[41]; whether this effect is clinically important is unknown. All statins lower an elevated triglyceride level by approximately 25 percent at low doses and by approximately 40 percent at high doses.[42] Some patients with high triglyceride, low HDL and normal LDL levels may receive most benefit from treatment with a fibrate, such as gemfibrozil (Lopid) or fenofibrate (Tricor).[28] Either drug may be combined with a statin,[43] but patients must be cautioned about a rise in the very low absolute risk of myositis and rhabdomyolysis when a statin is taken with gemfibrozil, fenofibrate or niacin.

TABLE 7
Estimated Cost of Different Dosages of Statin Drugs

Statin	*Daily dosage (mg)*	*Estimated monthly cost**
Atorvastatin (Lipitor)	10	$ 55
	20	87
	40	105
	80 (two 40-mg tablets)	210
Cerivastatin (Baycol)	0.2	40
	0.3	40
	0.4	40
	0.6 (two 0.3-mg tablets)	80
Fluvastatin (Lescol)	20	40
	40	40
	60 (40-mg + 20-mg tablet)	80
	80 (two 40-mg tablets)	80
Lovastatin (Mevacor)	20	70
	40	126
	60 (three 20-mg tablets)	210
	80 (two 40-mg tablets)	251
Pravastatin (Pravachol)	20	68
	40	112
	80 (two 40-mg tablets)	224
Simvastatin (Zocor)	20	114
	40	114
	80	114

**—Estimated cost to the pharmacist based on average wholesale prices (rounded to the nearest dollar) in Red Book. Montvale, N.J.: Medical Economics Data, 1999. Cost to the patient may be greater, depending on prescription filling fee.*

Improving the Cost-Effectiveness of Lipid-Lowering Therapy

Key factors that influence cost-effectiveness of lipid-lowering therapy include the cost of the drug itself, the LDL-lowering efficacy of the agent and the need for return visits to the physician's office for dosage titration. Appreciable cost savings can be realized by prescribing creatively. For example, using one-half tablet instead of whole tablets can generate a large savings. Although no statin tablets are scored, 20-mg and 40-mg tablets of pravastatin, simvastatin and atorvastatin, as well as 80-mg tablets of simvastatin, usually can be cut in half accurately with a pill splitter. The 10-mg tablets of simvastatin and atorvastatin cannot be accurately halved easily or consistently. It should be noted that no information is available on how pill-splitting affects bioavailability and pharmacokinetics. Of course, a reduction in drug prices could greatly improve the cost-effectiveness of statin therapy for primary prevention in high-risk individuals.

Ingesting grapefruit juice with statins can greatly increase drug absorption and serum levels.[44] This may make it feasible to achieve therapeutic drug levels with smaller doses in

patients willing to drink grapefruit juice when they take their medication.

Patient Education

Many patients discontinue lipid-lowering therapy for long periods of time without informing their physician.[45] Some do not understand the benefits or hold mistaken beliefs about the risks of treatment. One technique with potential for improving long-term compliance is to have the patient read (and perhaps sign) a patient education form that provides information about the benefits and risks of taking a statin.

WAYS TO IMPROVE TREATMENT

Family physicians could more fully realize the potential of statin therapy for preventing CHD if they would routinely do the following:

- Screen for dyslipidemias more often during visits for acute minor illness (especially in men) and well-woman visits.
- Encourage high-risk patients with elevated LDL levels that cannot be controlled with dietary measures to consider taking a statin.
- Prescribe the lowest dose of the least expensive medication needed to lower the LDL level to below the treatment goal.
- Consider prescribing half-pill doses or recommending ingestion of grapefruit juice when the drug is taken to increase drug absorption.
- Negotiate an explicit plan to continue long-term cholesterol medication (perhaps with a written patient education form), if the patient is willing.
- Modify the medication or dose to reduce the LDL to below the appropriate target level—130 or 100 mg per dL (3.35 or 2.60 mmol per L), depending on whether or not the patient has CHD or diabetes.
- Ask patients at each follow-up visit or by telephone about side effects and about their understanding of treatment benefits.
- Explain the need to take cholesterol medication every day indefinitely to maximize benefit, noting that the LDL level returns to the pretreatment level soon after the medication is discontinued.

Family physicians can do a much better job of preventing heart disease by using methodical, cost-effective approaches for identifying high-risk patients and implementing preventive interventions. Incorporating systematic prevention programs into the office practice could help many patients avoid the problems of atherosclerotic disease throughout their lives and could help many other patients with CHD enjoy healthier lives with less disability from the disease.

A patient education form that provides information about the benefits and risks of statins is available from the author on request.

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