10. HYPERLIPIDEMIA

Beatrice Golomb, MD, PhD

The development of quality indicators for screening and treatment of hyperlipidemia was initially based on current guidelines and review articles on hyperlipidemia. Strong emphasis was placed on guidelines from the National Cholesterol Education Panel (NCEP) and American College of Physicians (ACP), which represent, respectively, more aggressive and more conservative perspectives on the management of hyperlipidemia. Additional articles identified through MEDLINE literature searches were used, with information culled from review articles, guidelines and, in particular, randomized trials and meta-analyses demonstrating significant effects of cholesterol-lowering treatment on mortality.

IMPORTANCE

Approximately seven million Americans currently have heart disease. Each year, 1.5 million people sustain heart attacks, of which roughly one-third die (McBride and Davis, 1992). The costs for care of cardiovascular disease were approximately $109 billion in 1992 (McBride and Davis, 1992). Despite a reduction in age-adjusted mortality rates over recent decades, coronary artery disease remains the leading cause of mortality in the U.S. (Harris-Hooker, 1994). Because of the prevalence of cardiovascular disease, with the attendant health and economic consequences, public health efforts have targeted modifiable risk factors such as hyperlipidemia. Data from animal studies, and from ecological, epidemiological, and clinical trials in humans indicate a relation of cholesterol to heart disease, and to initiation and progression of atherosclerotic disease (Stensvold et al., 1992; Tunstall-Pedoe, 1988; O'Keefe et al., 1995). Data also indicate a relationship between cholesterol reduction and a reduction in atherosclerotic progression (Kroon et al., 1996); release of endothelium-derived relaxing factor leading to nonspecific widening of coronary arteries (Keaney et al., 1994; van Boven et al., 1994); reduced

coronary events and reduced coronary mortality; and reduced overall mortality in high-risk populations with preexisting heart disease, as reported by the Scandinavian Simvastatin Survival Study Group (The “4S” Group, 1994).

Concerns about hyperlipidemia are compounded by the fact that it affects large segments of the population: two-thirds of middle-aged adults have lipids above the designated desirable range (Anderson et al., 1987). Cholesterol screening and treatment have substantial economic consequences; for example, among people aged 20 to 74 years who are screened, an estimated 41 percent will require a second screening test to assess lipoproteins (Sempos et al., 1989). Annual costs of screening for hyperlipidemia by NCEP guidelines have been projected at up to $10 billion (Froom, 1989). Using these same guidelines, minimal annual costs for combined screening and treatment of hypercholesterolemia in asymptomatic individuals over age 65 have been projected at $1.6 to $16.8 billion (Kaiser, 1993). For the total population aged 20 to 74, it is estimated that 36 percent, or 60 million people, would merit drug treatment if NCEP guidelines were uniformly applied (Sempos et al., 1989). In this case, expenditures for drug treatment would greatly exceed the current expenditures of $5 billion in 1995 for one class of lipid-lowering drugs alone, the HMG-CoA reductase inhibitors (Heinrichs, 1996). Therefore, decisions regarding cholesterol screening and management have potentially profound public health and economic ramifications.

SCREENING AND PREVENTION

Prevention of Hypercholesterolemia

Although recommended by many agencies, the use of diet to control cholesterol remains controversial. Diets that are tolerable to patients, and are low in total and saturated fats, do not lead to substantial reductions in serum cholesterol levels (ACP, 1996). Moreover, they do not reduce mortality from cardiovascular or other diseases. The Canadian Task Force on Periodic Health Examination (CTF) describes the evidence for general dietary advice on lowering total fat, saturated fat and cholesterol intake in the routine care of men age 30

to 69, as “fair.” It also found insufficient evidence for such advice in other populations (CTF, 1993). Due to lack of consensus in this area, there are no indicators regarding dietary treatment to lower total and saturated fat.

There are data supporting dietary advice to consume fatty fish as a secondary prevention measure; one study documented a significant 30 percent reduction in overall mortality (Burr et al., 1989) These results are comparable to those achieved with statins in the “4S” trial (The “4S” Group, 1994); however, counseling regarding fish consumption is not widespread and is not an element of most guidelines. Moreover, fish consumption does not exert its benefit through cholesterol reduction, although it is often discussed in the context of cholesterol (Harris, 1989; Simopoulos, 1990; Schmidt and Dyerberg, 1994).

Screening and Primary Prevention

Guidelines for screening cholesterol are in agreement only for a restricted subset of patients at high risk. The NCEP and ACP guidelines can be taken to reflect two major divergent perspectives.

The NCEP guidelines recommend screening total cholesterol and HDL at least every five years in all adults over age 20 (Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults, 1993). This is in sharp contrast with the ACP guidelines, which do not specify any minimum age for screening in those without previously diagnosed atherosclerotic disease. The ACP's position, in which no screening is mandated in primary prevention, stems from the absence of demonstrated benefit of hyperlipidemia treatment for primary prevention of coronary artery disease (CAD).

In those without previously diagnosed atherosclerotic disease, no study to date has shown significantly increased survival with cholesterol reduction. The same is true for studies of cholesterol reduction and cardiac mortality, although one mixed secondary and high-risk primary prevention study came close to demonstrating mortality benefit (Shepherd et al., 1995). The largest primary prevention study unexpectedly showed a significant 30 percent increase in overall mortality in those assigned to treatment (Committee of Principal

Investigators, 1978). Several meta-analyses of single and multiple risk factor intervention studies involving lipids have also demonstrated a trend toward increased overall mortality in low-risk populations assigned to treatment (McCormick and Skrabanek, 1988; Muldoon et al., 1990; Davey Smith et al., 1993). One such study suggests that harm or benefit is probably a function of baseline level of risk, with those at highest risk benefiting, and those at lowest risk placed at greater risk for overall mortality, which is consistent with divergent findings for primary and secondary prevention populations (Davey et al., 1993).

With regard to cholesterol screening, guidelines of the American Academy of Family Physicians and the American College of Obstetricians and Gynecologists are similar to those of the NCEP, whereas guidelines of the CTF more closely mirror those of the ACP (CTF, 1993; U.S. Public Health Service, 1995). In New Zealand, Britain, the Netherlands, and Europe in general, printed guidelines and consensus statements favor an approach to screening and treatment that is more conservative than that of the NCEP, with none advocating universal screening, and some maintaining that drug treatment is rarely indicated unless cholesterol exceeds 300 mg/dl (Rossner et al., 1993).

While many would agree that screening of lipids in individuals (at least in men over age 35 and women over age 45) with two or more risk factors for cardiovascular disease is appropriate, even in the absence of identified atherosclerotic disease, there is no consensus that such screening is mandatory (ACP, 1996). Due to the lack of demonstrated mortality benefit with treatment of hyperlipidemia in the primary prevention population, no indicators are directed at screening in this group.

Screening for Hypercholesterolemia in Patients With Preexisting Coronary Heart Disease

In contrast to primary prevention, mortality benefit has been demonstrated for cholesterol reduction in men with preexisting heart disease. The “4S” trial (The “4S” Group, 1994) showed HMG-CoA reductase inhibitors to produce a 30 percent reduction in relative risk of overall mortality with simvastatin treatment in a high-risk secondary prevention group of 4444 patients with CAD and high cholesterol, consisting

primarily of men with prior myocardial infarction (MI). Benefit to overall mortality in the older population within this study (age 60 to 70) was smaller but remained significant (The “4S” Group, 1994). In support of the “4S” study finding, meta-analysis has shown a reduction in overall mortality with cholesterol-lowering treatment in high-risk individuals, primarily men with preexisting heart disease (Davey Smith et al., 1993). Experts agree that lipid screening -- including HDL and total cholesterol -- should be performed in men with identified atherosclerotic disease (particularly coronary disease), and perhaps also after stroke or carotid occlusion and peripheral vascular disease (ACP, 1996). It is also believed that treatment to lower cholesterol should be initiated in this group if an elevated cholesterol (LDL greater than 130) is identified. For this reason, our screening and treatment indicators are directed at screening for hyperlipidemia in men under age 70 with prior vascular disease.

Frequency of Screening

Because reductions in mortality have been shown with treatment of hyperlipidemia in men under age 70 with preexisting heart disease, men with heart disease who do not have identified hyperlipidemia should nonetheless have lipid measurements periodically to allow prompt initiation of treatment when indicated. Although there is no direct evidence supporting the opinion, a frequency of every five years is often cited as reasonable for cholesterol screening in men with heart disease who do not currently require cholesterol-lowering treatment (ACP, 1996) (Indicator 1).

Timing of Screening in Secondary Prevention

The timing of cholesterol measurement in secondary prevention is complicated by the fact that MI and surgery, including bypass surgery, can lower the serum cholesterol concentration substantially, giving a false impression that treatment of hyperlipidemia is not warranted. In most cases, the cholesterol begins to drop the first 48 hours after the event (Ryder et al., 1984), and then returns to baseline levels three months later (Brugada et al., 1996). Thus, a cholesterol level below the treatment threshold cannot exclude the need for lipid-lowering treatment if the measurement was done more than 48 hours and less than

three months after the cardiac event. Because it may take three months for a sound cholesterol value to be determined after the diagnosis of CAD (particularly if CAD is discovered through a cardiac event or is concurrent with a need for surgery), our indicator permits a four-month window after the diagnosis of CAD in which cholesterol measurement may be done (Indicator 2).

Women

No study or meta-analysis has independently shown a reduction in overall mortality in any category of women assigned to cholesterol-lowering treatment (ACP, 1996). Although women were included in the "4S" study, independent mortality benefit for this group was not demonstrated (The "4S" Group, 1994). In the absence of demonstrated treatment benefit, guidelines from both the CTF and the ACP view the evidence for care of hyperlipidemia in women as insufficient (CTF, 1993; Garber et al., 1996). Therefore, although treatment of high cholesterol in women at high risk may be appropriate, because of lack of consensus and lack of evidence of mortality benefit with cholesterol lowering treatment for women, neither screening nor treatment for high cholesterol in women will be included as an indicator.

The Elderly

In men age 60 to 70 with existing heart disease (primarily those with a prior MI), overall mortality was shown to decline with cholesterol reduction using HMG-CoA reductase inhibitors in the "4S" study; however, the benefit was less pronounced than that for younger individuals (The "4S" Group, 1994). This finding cannot be extrapolated to older individuals. Cholesterol alone is a weak predictor of coronary heart disease mortality in the elderly and not consistently predictive after age 75 (U.S. Preventive Services Task Force, 1995). Indeed, higher cholesterol values appear to be associated with *increased* survival in individuals over age 80 (CTF, 1993; Kaiser, 1993; Kronmal et al., 1993). For this reason we restrict our screening and treatment indicators to the population in whom benefit has been demonstrated, that is, men under age 70.

DIAGNOSIS

Screening for hyperlipidemia focuses on levels of serum total cholesterol and HDL; however, treatment is currently predominantly guided by the LDL cholesterol level (Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults, 1993). In men under age 70 with preexisting coronary disease, for whom treatment would be clearly indicated in the presence of high LDL, a measurement of LDL should be done within three months after a total serum cholesterol value exceeding 200 mg/dl is documented, unless an earlier measure of LDL is documented within the prior two years (Indicator 3).

Marked fluctuations in cholesterol result from differences in laboratory technique, and from such types of biological variability as infection, surgery, emotional stress, or parturition, as well as diurnal variation, postural variation, and variation with the time of tourniquet placement. For this reason, the ACP (1996) recommends that the pharmacological treatment of a patient for hyperlipidemia be based on the average of at least two cholesterol or LDL measurements, to prevent the side effects and economic costs associated with unnecessary treatment (Indicator 4).

Although our indicator requires a record of at least two cholesterol measurements before initiating anti-hyperlipidemic treatment, an exception is made for patients with identified heart disease. For these patients, prompt initiation of treatment may be more important than the need to confirm a cholesterol value with a second measurement. Nonetheless, absence of a second measurement will complicate assessment of the true effect of the treatment for hyperlipidemia, even in those with previously identified heart disease.

TREATMENT

Dietary and Pharmacological Treatment in Patients With Preexisting Coronary Disease

Dietary Treatment

If cholesterol is elevated, the NCEP recommends initiation of a Step I diet. In such a diet, total and saturated fat consumption accounts for no more than 30 percent and ten percent, respectively, of

all caloric intake. If this is not effective, a Step II diet is recommended before beginning pharmacological therapy to reduce cholesterol. The exception to this is individuals with established heart disease, in whom a Step II diet should be tried only briefly before pharmacological therapy is initiated. However, studies have shown that a low-fat diet alone leads to limited cholesterol reductions in patients assigned to dietary treatment as compared with controls. Because diets, such as a Step I diet, reduce cholesterol by an average of only two percent, recommendations for dietary treatment are not universal (ACP, 1996). For this reason we do not propose an indicator requiring that dietary treatment precede initiation of drug treatment.

Pharmacological Therapy

The section on screening describes the data on mortality benefit and indications for both screening and treatment with cholesterol-lowering treatment. To recapitulate, mortality benefit from cholesterol-lowering treatment has been demonstrated in men under age 70 with preexisting coronary disease who have “high” cholesterol. While the LDL cutoff at which benefit is derived from cholesterol-lowering treatment is a subject of continued study, it is generally agreed that cholesterol-lowering treatment should be initiated within three months of an LDL measurement exceeding 130 mg/dl in those who are not already on dietary or pharmacological treatment (Indicator 5). Evidence of mortality benefit has only been demonstrated with pharmacological therapy. Therefore, men under age 70 with preexisting heart disease who continue to have an LDL above 130 mg/dl after six months of dietary treatment should begin receiving pharmacological treatment or have LDL rechecked promptly (Indicator 6).

We define “pharmacological therapy” as any approved drug for treatment of hyperlipidemia. We have chosen not to generate indicators restricting drug choice on the grounds that expert agreement would likely be possible only for selected lipid profiles that refer to a minority of patients, limiting the utility of the indicator.

FOLLOW-UP

All patients for whom cholesterol-lowering pharmacological treatment has been initiated, or for whom the dose has been modified, should have their cholesterol value rechecked after four months to ensure that cholesterol is being successfully reduced (Indicator 7). Based on the repeat measurements, the medication dose may be further modified, or a different lipid-lowering drug may be substituted to achieve the desired lipid reduction. There are no firm data to indicate the optimum timing of reevaluation, which may vary with the pharmacological agent used. We have allowed four months for retesting in our indicator (Indicator 8).

REFERENCES

American College of Physicians. 1996. Guidelines for using serum cholesterol, high-density lipoprotein cholesterol, and triglyceride levels as screening tests for preventing coronary heart disease in adults. *Archives of Internal Medicine* 124: 515-517.

Anderson K, W Castelli, et al. 1996. Cholesterol and mortality: 30 years of follow-up from the Framingham study. *Journal of the American Medical Association* 257 (16): 2176-80.

Brugada R, N Wenger, et al. 1996. Changes in plasma cholesterol levels after hospitalization for acute coronary events. *Cardiology* 87 (3): 194-9.

Burr M, A Fehily, et al. 1989. Effects of changes in fat, fish and fibre intakes on death and myocardial reinfarction: Diet and Reinfarction Trial (DART). *Lancet* II: 757-61.

Canadian Task Force on the Periodic Health Examination. Periodic health examination, 1993 update: 2. Lowering the blood total cholesterol level to prevent coronary heaert disease. *Canadian Medical Association Journal* 148 (4): 521-538.

Committee of Principal Investigators. 1989. WHO Clofibrate Trial: A cooperative trial in the primary prevention of ischaemic heart disease using clofibrate. *British Heart Journal* 40: 1069-1118.

Davey Smith G, F Song, et al. 1993. Cholesterol lowering and mortality: the importance of considering initial level of risk. *British Medical Journal* 306: 1367-73.

Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults. 1993. Summary of the Second Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). *Journal of the American Medical Association* 269 (23): 3015-20.

Froom J. 1989. Selections from current literature: The cholesterol controversy. *Family Practice* 6 (3): 232-7.

Garber A, W Browner, et al. 1996. Cholesterol screening in asymptomatic adults, revisited. *Archives of Internal Medicine* 124 (5): 518-531.

Harris W. 1989. Fish oils and plasma lipid and lipoprotein metabolism in humans -- a critical review. *J Lipid Res* 30: 785-807.

Harris-Hooker S, and S GL. Lipids, lipoproteins and coronary heart disease in minority populations. *Atherosclerosis* 108 (Suppl): S83-104.

Kaiser F. Cholesterol and the older adult. *Southern Medical Journal* 86 (10): 2S11-2S14.

Keaney JJ, J Gaziano, et al. Low-dose alpha-tocopherol improves and high-dose alpha-tocopherol worsens endothelial vasodilator function in cholesterol-fed rabbits. *Journal of Clinical Investigation* 93 (2): 844-5.

Kronmal R, K Cain, et al. 1993. Total serum cholesterol levels and mortality risk as a function of age: A report based on the Framingham data. *Archives of Internal Medicine* 153: 1065-1073

Kroon A, W Aengevaeren, et al. 1996. LDL-Apheresis Atherosclerosis Regression Study (LAARS). Effect of aggressive versus conventional lipid lowering treatment on coronary atherosclerosis. *Circulation* 93 (10): 1826-35.

McBride P, and J Davis. 1992. Cholesterol and cost-effectiveness: Implications for practice, policy, and research. *Circulation* 85 (5): 1939-41.

McCormick J, and P Skrabanek. 1988. Coronary heart disease is not preventable by population interventions. *Lancet* ii: 839-41.

Muldoon M, S Manuck, et al. 1990. Lowering cholesterol concentrations and mortality: a review of primary prevention trials. *Br Med J* 301: 309-14.

O'Keefe JJ, CJ Lavie, et al. 1995. Insights into the pathogenesis and prevention of coronary artery disease. *Mayo Clinic Proceedings* 70 (1): 69-79.

Rossner W, W Palmer, et al. 1993. An international perspective on the cholesterol debate. *Family Practice* 10 (4): 431-438.

Ryder R, T Hayes, et al. 1984. How soon after myocardial infarction should plasma lipid values be assessed? *British Medical Journal* 289: 1651-3.

Scandinavian Simvastatin Survival Study Group. 1994. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S). *Lancet* 344: 1383-9.

Schmidt E, and J Dyerberg. 1994. Omega-3 fatty acids: current status in cardiovascular medicine. *Drugs* 47: 405-24.

Sempos C, R Fulwood, et al. 1989. The prevalence of high blood cholesterol levels among adults in the United States. *J Am Med Assoc* 262: 45-52.

Shepherd J, S Cobbe, et al. 1995. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *New England Journal of Medicine* 333 (20): 1301-7.

Simopoulos A. 1990. Diet and new lesions of the coronary arteries. *Journal of the American Medical Association* 254: 1251.

Stensvold I, P Urdal, et al. 1992. High-density lipoprotein cholesterol and coronary, cardiovascular and all cause mortality among middle-aged Norwegian men and women. *European Heart Journal* 13 (9): 1155-63.

Tunstall-Pedoe H. 1988. Epidemiology and pathogenesis of ischaemic heart disease. *Current Opinion in Cardiology* 3: 550-60.

US Preventive Services Task Force Screening for high blood cholesterol and other lipid abnormalities. 15-37.

US Public Health Service. 1995. Cholesterol screening in adults. *American Family Physician* 51 (1): 129-136.

Van Boven A, J Jukema, et al. 1994. Endothelial dysfunction and dyslipidemia: possible effects of lipid lowering and lipid modifying therapy. *Pharmacological Research* 29 (3): 261-72.

RECOMMENDED QUALITY INDICATORS FOR HYPERLIPIDEMIA

These indicators apply to men and women age 18 and older, except where otherwise noted.

Indicator	Quality of Evidence	Literature	Benefits	Comments
Screening				
1. Men under age 70 with preexisting heart disease[2] who are not on pharmacological therapy for hyperlipidemia[5] should have cholesterol level documented at least every 5 years.	III	4S, 1994	Improve survival.	Cholesterol lowering reduces mortality in hyperlipidemic men under age 70 with identified heart disease (4S, class I evidence). Identification of hyperlipidemia in these men is therefore important, and screening should be repeated periodically. A 5-year period is often cited as reasonable interval for rescreening, although no data support any particular interval.
2. Men under age 70 with newly diagnosed coronary disease[1] should have had total cholesterol documented within 2 years before or within 4 months after the diagnosis is first noted in the medical record.	III	ACP, 1996	Decrease mortality.	Mortality benefit has been shown with cholesterol reduction in hyperlipidemic men under age 70 with prior heart disease (4S, 1994). Because MI or surgery can lower the cholesterol value, thereby obscuring a true high cholesterol, some recommend against measurement within the first 3 months after MI or surgery. A high value in this time will dictate need for treatment; thus an expanded 4 month window is given.
Diagnosis				
3. Men under age 70 with preexisting coronary disease[2] who have a total cholesterol level exceeding 200 mg/dl should have a measure of their LDL cholesterol[3] documented within 2 years before or 3 months after the 200 mg/dl level.	III	NCEP, 1993	Decrease mortality.	LDL cholesterol is used to guide need for treatment.

Indicator	Quality of Evidence	Literature	Benefits	Comments
4. Patients without preexisting coronary disease[2] who are started on pharmacological treatment for hyperlipidemia should have had at least 2 measurements of their cholesterol (total or LDL) documented in the year before the start of pharmacological treatment.	III	ACP, 1996	Prevent morbidity associated with unnecessary treatment.	High variability in cholesterol measurements renders unjustified pharmacological treatment of hyperlipidemia based on a single measurement. Ideally, two measurements should exceed the physician's treatment threshold prior to institution of lipid-lowering treatment, though some will accept the average of the two. For subjects with identified cardiac disease, prompt initiation of treatment may be viewed as a higher priority than the need to corroborate a cholesterol value with a second measurement. This could be justified on the grounds that benefit of cholesterol reduction to cardiac outcomes has been shown in those with heart disease even in the presence "normal" cholesterol.
Treatment				
5. Men under age 70 with preexisting coronary disease[2] who have an untreated LDL cholesterol level >130 mg/dl should begin diet[4] or drug therapy[5] within 3 months of the high LDL measurement.	I	NCEP, 1993; 4S, 1994; ACP, 1996	Reduce mortality.	Mortality benefit with pharmacological therapy has been shown in this group. Treatment with HMG-CoA reductase inhibitors is preferred, since significant mortality benefit during the time of treatment has been demonstrated only with simvastatin.
6. Men under age 70 with preexisting coronary disease[2] who have an LDL level >130 mg/dl after 6 months of dietary cholesterol-lowering treatment[4] should receive one of the following within 2 months: • pharmacological therapy[5] for hyperlipidemia; or • a repeat LDL measurement.	III	4S, 1994; ACP 1996	Reduce mortality.	In patients with preexisting coronary disease, a maximum of 6 months of dietary treatment is recommended before drug treatment is started, unless cholesterol is brought below 130 mg/dl with diet alone. Drug treatment has been shown to reduce mortality in this group (4S, class I evidence), whereas dietary therapy has not.

Indicator	Quality of Evidence	Literature	Benefits	Comments
Follow-up				
7. Patients in whom pharmacological therapy for hyperlipidemia[5] has been initiated should have their cholesterol rechecked within 4 months.	III	4S, 1994	Prevent morbidity from treatment side effects. Improve survival.	Ineffective cholesterol-lowering treatment poses risks without benefits. Therefore cholesterol measurements should be obtained after adding or changing a cholesterol-lowering drug to ensure that treatment is effective and to allow treatment modification if it is not. Additionally, effective lipid reduction improves mortality in men under age 70 with heart disease (class I evidence, 4S). Therefore mortality may be improved by assuring that therapy given is effective.
8. Patients receiving pharmacological therapy for hyperlipidemia[5] who have had a dosage or medication change should have cholesterol rechecked within 4 months of the change.	III	4S, 1994	Prevent morbidity from treatment side effects. Improve survival.	Ineffective cholesterol-lowering treatment poses risks without benefits. Therefore cholesterol measurements should be obtained after adding or changing a cholesterol-lowering drug to ensure that treatment is effective and to allow treatment modification if it is not. Additionally, effective lipid reduction improves mortality in men under age 70 with heart disease (class I evidence, 4S). Therefore mortality may be improved by assuring that therapy given is effective.

Definitions and Examples

[1] Newly diagnosed coronary disease: New diagnosis of CAD mentioned in chart, admission for myocardial infarction, admission for unstable angina.
[2] Prexisting heart disease: History of myocardial infarction, angioplasty, cardiac bypass surgery, or a physician's note of CAD or angina.
[3] Either LDL cholesterol or both HDL and triglycerides to allow calculation of LDL.
[4] Dietary therapy: Includes any mention of diet counseling in the medical record (either by a physician, nurse, physician assistant, dietitian or nutritionist).
[5] Pharmacological (drug) therapy: May include HMG-CoA reductase inhibitors (simvastatin, lovastatin, fluvastatin, pravastatin, atorvastatin or other statins), niacin, gemfibrozil, cholestyramine, colestipol, or a combination of agents.

Quality of Evidence Codes

I	RCT
II-1	Nonrandomized controlled trials
II-2	Cohort or case analysis
II-3	Multiple time series
III	Opinions or descriptive studies