

How Well Do We Treat Elevated LDL-Cholesterol?

Results From A University Residents' Clinic

Peter D. R. Higgins, MD, PhD, Cheryl Russo, MS, MD, Mark Scheurer, MD, W. Lane Duvall, MD

CORONARY HEART DISEASE (CHD) is the leading cause of death in the industrialized world. In the United States alone, more than 13 million people have documented CHD, which leads to 1.5 million myocardial infarctions (MIs) and 500,000 deaths every year. Extensive clinical observations indicate that elevated blood concentrations of low density lipoprotein cholesterol (LDL-C) increase the risk of CHD and MI. Epidemiological studies indicate that every 1% increase in blood concentration of total cholesterol leads to an increase in CHD risk by 2%¹; primary and secondary prevention trials show that a 1% reduction of cholesterol decreases risk by 2-5%.^{2,3}

The National Cholesterol Education Program (NCEP) recommends intensive treatment of elevated cholesterol levels in patients with CHD (angina, documented coronary artery disease, history of MI, history of percutaneous transluminal coronary angioplasty or history of coronary artery bypass graft) because these patients have a five- to seven-fold increased risk for a CHD event. The two most recent guidelines endorsed by the NCEP^{4,5} state that patients with CHD should have their serum lipids measured at least annually, and that they should be treated to achieve an LDL-C concentration of ≤ 100 mg/dL. Nonpharmaceutical therapy (reduction of saturated fats and cholesterol in the diet, weight loss, and regular physical activity) is indicated in all patients with LDL-C > 100 mg/dL. Cholesterol-lowering medications should be used to achieve target LDL-C in patients who do not achieve goal after maximal nonpharmaceutical therapy. Clinical trials over the past 5 years⁶⁻⁸ have solidified the evidence of older trials⁹ advocating aggressive lowering of cholesterol in patients with CHD. The 4S, CARE, and

LIPID trials of secondary prevention in patients with both high and average cholesterol levels demonstrate that treatment produces a 29-34% reduction in coronary events, a 24-42% decrease in cardiac mortality, and a 24-30% reduction in total mortality.⁶⁻⁸ Despite the proven benefits of treatment, many patients with CHD do not receive therapy or are not treated to goal. We designed the present study to assess how well the current guidelines are being followed in a university outpatient clinic, and to evaluate the importance of barriers to success in patients who do not achieve these goals.

Methods

Patient Selection. We searched the Health Information System database at Duke University Medical Center to find patients who had a discharge diagnosis of CHD (ICD-9 codes 410,411,412, and 414) made before April 1, 1997, and had at least one visit to the Duke Outpatient Clinic between April 1, 1997, and April 1, 1999. A total of 513 patients were identified for further analysis.

Between 1996 and 1999, the Duke Outpatient Clinic recorded more than 47,000 patient visits. Most patients were poor and had no health insurance; 66% were women; 61% were 50 years old or older; 69% were black and 27% white. They were seen by resident physicians who spend one half-day in the clinic each week. Faculty preceptors supervise all patient encounters and frequently review established guidelines for care with house staff. The clinic has a full-time pharmacist to assist patients with medications, and two full-time social workers help patients enroll in financial and

The authors all are former residents in medicine at Duke University Medical School. Dr. Higgins is now a Fellow in Gastroenterology at the University of Michigan Hospital. Phone: 734/615-1370; email: phiggins@med.umich.edu. Dr. Russo is a Fellow in Cardiology at Duke. She can be reached at the Division of Cardiology, Box 31196 DUMC, Durham NC 27710. Dr. Scheurer is a Fellow in Pediatric Cardiology at the Medical University of South Carolina, PO Box 250915, Charleston, SC 29425. Email: scheure@musc.edu. Dr. Duvall is a Fellow in Cardiology at Mt. Sinai Hospital in New York. Phone: 212/427-1540; email: william.duvall@mssm.edu.

Table 1. Demographic data on 513 study patients

Age	%	Gender	%	Race	%	Insurance	%
20-29	1	Female	43	Black	60	Blue Cross	1
30-39	3	Male	57	White	37	Capitated	*
40-49	15			Indian	1	Commercial	2
50-59	27			Hispanic	1	Managed Care	3
60-69	37			Asian	*	Medicaid	13
70-79	18					Medicare	68
						Self Pay	12
						Other	2

*2 patients

medication assistance programs. The rate at which patients keep scheduled visits is low, in part because of employment constraints, difficulties with transportation, or attendance at another local low-cost clinic.

Low-Density Lipoprotein Cholesterol. The Duke University Medical Center computer database records of all 513 patients were reviewed to obtain the most recent LDL-C values; the records of those whose most recent value was ~100 were sought to ascertain whether a value >100 had been recorded in the Duke University Health System. We could locate the charts of only 50 of the 71 patients whose LDL-C was ≤100, so we randomly sampled 1/3 of the 197 charts of patients who did not meet the LDL-C goal; only 52 of 66 could be found. The database records of patients except those known to have low LDL-C were searched to identify the following possible impediments to treatment success: age, gender, follow-up rates, and the non-use of HMG-CoA reductase inhibitor (“statin”) drugs.

Statin Potency. In order to compare potency across differing dosages of different statin agents, the LDL-C-lowering potencies of various drugs were obtained from the CURVES study.¹⁰ When we encountered dosages not examined in the CURVES study, we used linear interpolation to estimate the LDL-C lowering potency.

Statistics. For comparisons of differences in categorical outcomes, we used the chi-square statistic to determine statistical significance. The percentage or mean value for the group as a whole was used to determine the expected values for each category. To compare peak LDL-C levels and statin potency, we used Students’ t statistic for mean values of groups.

Results

Patient Demographics. The 513 patients studied had an average age of 59; most were African-American men on Medicare (Table 1).

Were Goals Achieved? Only 348 (68%) of the 513 pa-

tients who had discharge diagnoses of MI or coronary artery disease (CAD) and who were seen in the Duke Outpatient Clinic during the two study years had their LDL-C levels measured even once during the two-year period (Table 2). In only 151 (43%) of the 348 did their last LDL-C measurement show that they were at the goal of ~100 mg/dL, but review of the entire database showed that 80 of these 151 patients had *never* had an LDL-C concentration above 100. Excluding those 80 patients, only 71 (27%) of the remaining 268 patients (who had at least one elevated LDL-C) had achieved the goal of ~100 mg/dL.

As shown in Table 2, LDL-C was elevated in 268 of 348 (77%) patients who had it evaluated during the study period. There is no reason to suspect that the same proportions would not hold for the 165 patients who never had their LDL-C measured, and no reason to suspect that elevated values would decrease spontaneously. This means that only 71 of about 395 (Table 2) of our patients with elevated LDL-C actually achieved the goal LDL-C—a disheartening 18%.

Identifying Barriers To Treatment. We hypothesized five reasons that might help explain why so few patients achieved LDL-C goals:

1. Elderly patients were less aggressively treated.
2. Female patients were less aggressively treated.
3. Patients who did not keep appointments were less likely to meet the goal.
4. Patients who could not afford to buy statins did not use them.
5. Patients did not have doses of statins titrated upward to meet the goal.

To assess these hypotheses, we reviewed the charts of the 268 patients who began with an elevated LDL-C, and compared the 71 who met the goal with the 197 subjects who did not.

Effects of Age. Patients were divided into three groups: those aged less than 65, those aged 65-74, and those 75 and older. Table 3 shows the percentage of each group that had LDL-C measured and the percentage of those with LDL-C >100 that achieved the goal. With advancing age there was

Table 2. Low density lipoprotein cholesterol measurement and outcomes of treatment in 513 outpatients with coronary artery disease

	<i>Patients in group</i>	<i>LDL-C never high</i>	<i>At risk</i>	<i>Reached goal</i>	<i>Failed to reach goal</i>
Had LDL-C measured in clinic	348				
Never high		80			
At risk			268		
Reached goal				71	
Failed to reach goal					197
Did not have LDL-C measured	165				
Assume never high		38			
Assume at risk			127		
Assume could have reached goal, but not treated				44	
Assume would fail to reach goal					83
Totals	513	118	395	71	324

a significant decrease in percentage of subjects in whom LDL-C was measured (chi-square statistic 11.75, $p < 0.005$), but the small differences in the percentage at LDL-C goal were not statistically significant (chi-square statistic 0.022).

Effects of Gender.

The percentage of men and women patients who had LDL-C measured and the percentage of those with LDL-C >100 who met the goal are shown in Table 3. There were no significant differences in the slightly increased percentage of men who had LDL-C measured (chi-square statistic 2.96, $p = 0.09$), or the slightly decreased percentage of women who met the goal (chi-square statistic 2.75, $p = 0.10$).

Effects of Follow-up. Patients were divided into three groups based on whether their last follow-up appointment in the Duke Outpatient Clinic occurred in 1997, 1998, or 1999 (Table 3). Those with recent follow-up appointments were more likely to have had their LDL-C checked (chi-square statistic 10.19, $p < 0.01$), but not more likely to reach the goal (chi-square statistic 1.92, NS).

Table 3. Effects of age, gender, and follow-up on percentage of patients who have LDL-C screening and percentage of those at risk who reach treatment goals.

<i>Age</i>	<i>No. of patients</i>	<i>LDL-C measured</i>	<i>No. at risk*</i>	<i>At goal</i>
<65	220	74%	131	27%
65-74	130	73%	70	26%
>75	163	55%	67	27%
<i>Gender</i>				
Male	252	72%	136	34%
Female	261	64%	132	27%
<i>Year last seen</i>				
1997	109	55%	41	29%
1998	174	67%	89	24%
1999	230	76%	138	25%

*At risk = LDL-C ever >100

Effects Of Statin Use. We located 50 of the 71 charts of patients who reached LDL-C goals after having had an elevated LDL-C, and compared data from these to data from 52 located charts (of 66 sought) randomly selected from the 201 patients with elevated LDL-C who did not reach their goal. Nineteen (38%) of the 50 patients who succeeded were taking statin drugs when they achieved the goal, but 29 (56%) of the 52 of the patients who failed were also taking statins (chi-square statistic 1.713, NS). Interestingly, the highest recorded concentration of LDL-C was significantly greater in those who failed to reach the goal than in those who

succeeded (161.8 mg/dL vs 141.2 mg/dL; $p < 0.001$). This may explain the higher percentage of statin use in patients who failed to meet the goal (because those who succeeded may have been able to reach their goal with diet and exercise alone, and therefore not need statins).

Effects of Statin Potency. The LDL-C lowering percentage (LLP) potency of statins used by patients who met goals did not differ from the LLP of those who did not (LLP of 32.8 ± 7.6 [SD] vs 33.3 ± 6.5 [SD]). It is noteworthy that none of the 29 unsuccessful patients who were on statins were using the maximum recommended dose of their medication.

Discussion

Strong evidence supports the conclusion that lowering blood lipid concentrations reduces subsequent events in patients with CAD.⁶⁻⁹ In 2001 the NCEP updated its previous guidelines for screening and treatment in the primary and secondary prevention of CHD.⁵ Our retrospective study of secondary prevention in CHD patients attending a resident clinic found suboptimal adherence to NCEP screening and treatment guidelines—results similar to those found in other studies.

Screening. The NCEP recommends annual screening for secondary prevention. We found that only 348/513 (68%) of our patients with diagnosed CAD were screened for elevated LDL-C during a two-year period.

Failure of doctors to comply with screening recommendations is well documented in the literature, which shows cholesterol screening rates ranging from 19% to 84%. The best rate was found in a retrospective review of 1,004 managed care patients; 84% had total cholesterol and 67% had HDL-C measured during a 5 year period.¹¹ At the other end of the spectrum, Caggiula et al found that only 19% of 9,171 primary care patients were screened or properly followed for their cholesterol.¹² Primary prevention studies in the primary care setting routinely find screening rates of less than 50%.

Secondary prevention fares no better, with screening rates only up to 67%.¹³ One study of 225 patients admitted to a coronary care unit (two-thirds of whom had documented CHD) found that only 50% of those who should have had a full lipid panel actually had one.¹⁴

Multiple attempts to improve screening performance have met with little success. Lectures,^{15,16} pamphlets, and group counseling for patients,¹⁷ and chart reminders for physicians¹⁸ fail to significantly improve cholesterol screening rates. Modest improvements have been seen with direct feedback to physicians about specific patients,^{16,18} and screening rates near 90% have been achieved with a combination of feedback, peer review, and financial incentives.¹⁹ The gold standard remains the dedicated lipid clinic where screening rates exceed 99%.²⁰

Treatment. NCEP guidelines call for patients with CHD to have an LDL-C of ≤ 100 . Only 18% of the patients in our cohort achieved this goal. The literature is full of studies demonstrating the failure of doctors to treat patients to goal. The primary care literature shows that NCEP cholesterol goals were reached in 28% and 39% of outpatients treated by cardiologists, and in even smaller percentages of patients treated by primary care physicians.^{20,21} It has been estimated that 36% of all US outpatients have cholesterol levels high enough to need treatment, but only 12-20% actually get it.²² A secondary prevention study involving primary care physicians and cardiologists noted that LDL-C levels were elevated in 84% of patients, only 46% of whom received drug therapy.²⁰ And, at hospital discharge from a coronary care unit, lipid-lowering therapy was prescribed for only 36-46% of those who needed it.¹⁴

As with screening, interventions to improve the treatment efficacy have met with little success. Continuing Medical Education programs,¹⁵ pamphlets and group counseling for patients,²⁹ chart reminders,¹⁶ and intensive advice²³ have all failed to help. Dietary advice from trained dietitians, other health care providers, or from a pamphlet leads to modest reduction in cholesterol.²⁴ Computer-based systems, however, have demonstrated promising positive results in dietary management and direct lipid management.^{25,26} When specific personnel, such as nurses trained in lipid management, are added to the health care team, a higher percentage of patients reach LDL-C goal levels (26% versus 10%).²⁷ Similarly, a pharmacist working in conjunction with physicians doubled the rate of success in achieving NCEP goals after six months (43% versus 21%).⁵⁰ A dedicated lipid clinic got 93% of patients to take drug therapy, and 41% met goal levels.²⁰

Barriers to Achieving Goals. We examined five factors suspected of impeding patients' success in meeting NCEP guidelines for screening and treatment. Secondary screening rates were significantly affected by patient age (older patients were less likely to have their LDL-C measured), and regular follow-up (a recent appointment made patients more likely to have their LDL-C measured). Gender did not significantly affect secondary screening rates, and none of the five putative barriers (age, patient gender, date of last clinic appointment, statin potency, or rate of statin use) significantly affected achievement of goal LDL-C. The one variable that was significantly related to achievement of goal was the peak pretreatment level of LDL-C. Patients who failed to reach goal were much more likely to have LDL-C > 160 mg/dL. These patients need more aggressive treatment than patients with lower LDL-C, but we found only a nonsignificant trend toward use of statin medications in these patients, and at the end of two years they were no more likely to be on higher potency statin regimens than patients who had achieved goal LDL-C. This suggests that the failure of physicians to dose statins adequately, and their failure to titrate doses upward after initial failure to meet goal LDL-C, is the major

barrier to adequate lipid lowering in this patient population.

Other studies have examined these same barriers to achievement of NCEP goals. Only 24% of a group of Veterans Administration patients being treated for secondary prevention met LDL-C goal, and only 2 of 90 patients were maximally medicated.¹³ However, Schectman and Hiatt showed that medications are effective when used diligently. They studied 244 patients with CHD and found that 75% of those with LDL-C ~160 could achieve goal with medications.²⁹ A study of the effect of age found that only 7% of patients aged 60-80 with a recent MI and LDL-C >125 were being treated with medication.³⁰

Socioeconomic status was felt to be a barrier in one self-report study,³² but another study comparing public and private cardiology clinics found socioeconomic status to be less of a factor than individual physician practices.³³ Two studies have associated minority racial status (African-American and Latino patients) with poor physician compliance with guidelines.^{32,34} Two studies that looked comprehensively at factors associated with achieving LDL-C goal found that use of lipid-lowering agents was higher in patients who were married, better educated, had fewer risk factors, and maintained dietary compliance; it was lower when patients were elderly, of minority race, did not exercise, drank alcohol, and smoked.^{29,31}

Our resident clinic's performance in achieving NCEP goals for lipid management in secondary prevention of CAD was similar to or better than what is reported in the literature. Unfortunately, the most effective solutions for improving compliance are also the most expensive: augmenting the healthcare team with nurses, pharmacists, or a consultant from a dedicated lipid clinic. Computer-based adjuncts may be more economical, but are not yet proven to be as effective as human consultants. Our study suggests that, despite the enormous recent educational focus on the large contribution of serum lipid levels to CHD and the relative ease of treatment with well tolerated medications, doctors still need to improve their practice patterns.

Acknowledgements. Much thanks goes to Al Stone for his help accessing the Duke University Medical Center's computer databases.

REFERENCES

- 1 Stamier I, Wentworth D, Neaton ID. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). *JAMA* 1986;256:2823-8.
- 2 Yusuf S, Wittes I, Friedman L. Overview of results of randomized clinical trials in heart disease: II. Unstable angina, heart failure, primary prevention with aspirin, and risk factor modification. *JAMA* 1988;260:2259-63.
- 3 Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischemic heart disease? *BMJ* 1994;308:367-72.
- 4 Anonymous. National Cholesterol Education Program: Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment panel II). *Circulation* 1994;89:1333-445.
- 5 Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285(19):2486-7.
- 6 Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994;344:1383-9.
- 7 Sacks PM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *N Engl J Med* 1996;335:1001-9.
- 8 Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. *N Engl J Med* 1998;339:1349-57.
- 9 Rossouw IE, Lewis B, Rifkind BM. The value of lowering cholesterol after myocardial infarction. *N Engl J Med* 1990;323:1112-9.
- 10 Jones P, Kafonek S, Laurora I, Hunninghake D. Comparative dose efficacy of atorvastatin versus simvastatin, pravastatin, lovastatin, and fluvastatin in patients with hypercholesterolemia (the CURVES study). *Am J Cardiol* 1998;81:582-7.
- 11 Davis, KC, Cogswell ME, Rothenberg SL, Koplan JP. Lipid screening in a managed care population. *Public Health Rep* 1998;113:346-50.
- 12 Caggiula AW, Watson JE, Milas NC, et al. Evaluating the efficacy of the National Cholesterol Education Program adult treatment guidelines: cholesterol lowering intervention program. *Prev Med* 1995;24:485-91.
- 13 Marcelino II and Feingold KR. Inadequate treatment with HMG-CoA reductase inhibitors by health care providers. *Am J Med* 1996;100:605-10.
- 14 Frolkis JP, Zyzanski SJ, Schwartz JM, Suhan PS. Physician noncompliance with the 1993 National Cholesterol Education Program (NCEP-ATPII) guidelines. *Circulation* 1998;98:851-5.
- 15 Browner WS, Baron RB, Solkowitz S, et al. Physician management of hypercholesterolemia. A randomized trial of continuing medical education. *West J Med* 1994;161:772-8.
- 16 Headrick LA, Speroff T, Pelecanos HI, Cebul RD. Efforts to improve compliance with the National Cholesterol Education Program Guidelines. Results of a randomized controlled trial. *Arch Intern Med* 1992;152:2490-6.
- 17 Reid C, McNeil JJ, Williams F, Powles J. Cardiovascular Risk Reduction: a randomized trial of two health promotion strategies for lowering risk in a community with low socioeconomic status. *J Cardiovasc Risk* 1995;2:155-63.
- 18 Boekeloo BO, Becker DM, Levine DM, et al. Strategies for increasing house staff management of cholesterol with inpatients. *Am J Prev Med* 1990;6(2 Suppl):51-9.
- 19 Morrow RW, Gooding AD, Clark C. Improving physicians'

- preventive health care behavior through peer review and financial incentives. *Arch Fam Med* 1995;4:165-9.
- 20 Bramlet DA, King H, Young L, et al. Management of hypercholesterolemia: practice patterns for primary care providers and cardiologists. *Am J Cardiol* 1997;80(8B):39H-44H.
 - 21 Allison TG, Squires RW, Johnson BD, Gau GT. Achieving National Cholesterol Education Program goals for low-density lipoprotein cholesterol in cardiac patients: importance of diet, exercise, weight control, and drug therapy. *Mayo Clin Proc* 1999;74:466-73.
 - 22 Giles WH, Anda RF, Jones DH, et al. Recent trends in the identification and treatment of high blood cholesterol by physicians: Progress and missed opportunities. *JAMA* 1993;269:1133-8.
 - 23 Lindholm LH, Ekblom T, Dash C, et al. Changes in cardiovascular risk factors by combined pharmacological and nonpharmacological strategies: the main results of the CELL study. *J Intern Med* 1996;240:13-22.
 - 24 Neil HA, Roe L, Godlee RJ, et al. Randomized trial of lipid lowering dietary advice in general practice: the effects on serum lipids, lipoproteins, and antioxidants. *BMJ* 1995;310:569-73.
 - 25 Clark M, Ghandour G, Miller NH, et al. Development and evaluation of a computer-based system for dietary management of hyperlipidemia. *J Am Diet Assoc* 1997;97:146-50.
 - 26 Tsui FC, Wagner M, Thompson ME. Implementing NCEP guidelines in a Web-based disease-management system. *Proceedings AMIA Annual Fall Symposium* 1997:764-8.
 - 27 Becker DM, Raqueno JV, Yook RM, et al. Nurse-mediated cholesterol management compared with enhanced primary care in siblings of individuals with premature coronary disease. *Arch Intern Med* 1998;158:1533-9.
 - 28 Bogden PF, Koontz LM, Williamson P, Abbott RD. The physician and pharmacist team. An effective approach to cholesterol reduction. *J Gen Int Med* 1997;12:158-64.
 - 29 Schectman G, Hiatt J. Drug therapy for hypercholesterolemia in adults with cardiovascular disease: factors limiting achievement of lipid goals. *Am J Med* 1996;100:197-204.
 - 30 Aronow WS. Underutilization of lipid-lowering drugs in older persons with prior myocardial infarction and a serum low-density lipoprotein cholesterol >125 mg/ dl. *Am J Cardiol* 1998;82:668-9.
 - 31 Brown AS, Cofer LA. Lipid management in a private cardiology practice (The Midwest Heart experience). *Am J Cardiol* 2000;85:18A-22A.
 - 32 Davis SK, Ahn DK, Fortmann SP, Farquhar JW. Determinants of cholesterol screening and treatment patterns. Insights for decision-makers. *Am J Prev Med* 1998;15:178-86.
 - 33 Harnick DJ, Cohen JL, Schechter CB, et al. Effects of practice setting on quality of lipid-lowering management in patients with coronary artery disease. *Am J Cardiol* 1998;81:1416-20.
 - 34 Naumburg EH, Franks P, Bell B, et al. Racial differentials in the identification of hypercholesterolemia. *J Fam Pract* 1993;36:425-30.