

# Achieving Optimal Lipid Goals in Patients With Coronary Artery Disease

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Guidelines for lipid-lowering therapy recommend intensive low-density lipoprotein (LDL) cholesterol lowering for patients with coronary artery disease. Previous studies have found that many high-risk patients are not achieving their LDL cholesterol goals, and many patients, despite being treated with lipid-lowering therapy, also have elevated triglycerides or low levels of high-density lipoprotein (HDL) cholesterol. To evaluate lipid goals in a “real world” clinical setting, the electronic medical records of 10,040 patients with coronary artery disease from a large cardiology subspecialty practice from September 2008 to September 2009 were reviewed. Overall, 79% of patients achieved an LDL cholesterol goal of <100 mg/dl, while only 35% achieved the more aggressive goal of <70 mg/dl. Non-HDL cholesterol goals of <130 and <100 mg/dl were achieved in 79% and 44% of patients, respectively. Only 69% achieved normal triglyceride levels, and only 63% of men and 56% of women achieved normal levels of HDL cholesterol. Women and younger men were less likely to achieve their lipid goals. In conclusion, most patients with coronary artery disease achieve the minimal LDL cholesterol goal of 100 mg/dl, but few achieve the more aggressive goals of <70 mg/dl. Many high-risk patients have elevated levels of triglycerides or low levels of HDL cholesterol despite treatment. Combination lipid-lowering therapy is used infrequently in practice. There exists a significant opportunity for physicians to more aggressively treat lipids to achieve the levels recommended by clinical guidelines. © 2011 Elsevier Inc. All rights reserved. (Am J Cardiol 2011;107:886–890)

Previous studies have found that many patients with coronary artery disease (CAD) are not achieving their minimal recommended low-density lipoprotein (LDL) and non-high-density lipoprotein (HDL) cholesterol goals, and few achieve normal levels of HDL cholesterol and triglycerides.<sup>1–4</sup> More recent studies have found that even fewer patients with CAD are achieving an LDL cholesterol level <70 mg/dl and a non-HDL cholesterol level <100 mg/dl; however, most of these studies either evaluated patients shortly after the guidelines were updated in 2004 or focused only on LDL cholesterol goal attainment.<sup>5–8</sup> The purpose of this study was to evaluate whether patients with CAD are achieving all their lipid goals in a current, “real world” clinical practice.

## Methods

The study site was Cardiology Consultants of Philadelphia, a large cardiology subspecialty practice in the Philadelphia area. Using an electronic medical record, we identified 23,408 patients with histories of CAD who had been seen at 1 of our outpatient offices over a 12-month period from September 2008 to September 2009. Patients were

excluded if they did not have a complete lipid profile in the electronic medical record flow sheet dated within the study period or within 6 months of their last office visit. In patients with >1 complete lipid panel, the most recent lipid panel was used. Age, gender, history of current cigarette smoking, type 2 diabetes, hypertension, current lipid-lowering medications, and patient demographics were extracted from the electronic medical record. The study was approved by the Institutional Review Board of Drexel University College of Medicine.

The primary outcome measures were the percentages of patients who achieved an LDL cholesterol goal of <100 mg/dl and a non-HDL cholesterol goal of <130 mg/dl and the percentages of patients who achieved an LDL goal cholesterol of <70 mg/dl and a non-HDL cholesterol goal of <100 mg/dl. Additional outcome measures included the percentage of patients with low levels of HDL cholesterol (defined as an HDL cholesterol level of <40 mg/dl for men and <50 mg/dl for women) and the percentage of patients with high triglycerides (defined as a triglyceride level of  $\geq 150$  mg/dl).

For statistical analysis, chi-square tests were used to test differences for categorical variables and Student's *t* tests for continuous variables. Multivariate logistic regression analysis methods were applied to control confounding effects using the study outcomes (achieved vs not achieved) as the dependent variable and predictors of age, gender, cigarette smoking, body mass index, and diabetes as the independent variables. All data analyses were conducted using SAS version 9.1 (SAS Institute

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Table 1  
Patient characteristics (n = 10,040)

Variable	Value
Age (years)	71 ± 12
Men	6,650 (66%)
Women	3,390 (34%)
Diabetes mellitus	2,691 (27%)
Hypertension	6,738 (67%)
Current smokers	878 (9%)
Body mass index (kg/m <sup>2</sup> )	31 ± 6
LDL cholesterol (mg/dl)	82 ± 29
Non-HDL cholesterol (mg/dl)	109 ± 34
Triglycerides (mg/dl)	211 ± 129
HDL cholesterol (mg/dl)	39 ± 12
Statin therapy	8,727 (87%)
Pravastatin	554 (6%)
Fluvastatin	46 (0.5%)
Lovastatin	466 (5%)
Simvastatin	4,414 (44%)
Atorvastatin	1,880 (19%)
Rosuvastatin	1,367 (14%)
Ezetimibe therapy	1,577 (16%)
Bile acid sequestrant therapy	88 (0.9%)
Niacin therapy	1,051 (11%)
Fibrate therapy	914 (9%)
High-dose omega-3 fatty acid therapy	88 (0.9%)

Data are expressed as mean ± SD or as number (percentage).

Inc., Cary, North Carolina). A 2-sided p value ≤0.05 was considered statistically significant.

## Results

A total of 10,040 patients with CAD met the criteria for inclusion in the study. The clinical characteristics of the patients are listed in Table 1. Among patients prescribed ezetimibe, 88% were also taking statins, while the remaining 12% were treated with ezetimibe alone. Among patients prescribed fibrates, 61% were taking fenofibrate, 23% fenofibric acid, and 16% gemfibrozil.

Overall, 79% of patients achieved the LDL cholesterol goal of <100 mg/dl, while only 35% achieved the lower LDL cholesterol goal of <70 mg/dl. The distribution of achieved LDL cholesterol levels among the patients is depicted in Figure 1. Women compared with men were less likely to achieve an LDL cholesterol goal of <100 mg/dl (73% vs 83%,  $p < 0.001$ ) and an LDL cholesterol goal of <70 mg/dl (31% vs 38%,  $p < 0.0001$ ). Multivariate predictors of not achieving an LDL cholesterol goal of <70 mg/dl included age <65 years ( $p < 0.001$ ), female gender ( $p < 0.001$ ), and obesity, defined as body mass index ≥30 kg/m<sup>2</sup> ( $p = 0.02$ ). Among patients whose LDL cholesterol was >70 mg/dl, 51% were treated with simvastatin (average dose 42 mg), 22% were treated with atorvastatin (average dose 38 mg), and 16% were treated with rosuvastatin (average dose 19 mg). Only 11% of patients whose LDL cholesterol was >70 mg/dl were treated with bile acid sequestrants, and only 15% were taking ezetimibe.

With regard to non-HDL cholesterol, 79% of patients achieved a non-HDL cholesterol goal of <130 mg/dl, while only 44% achieved the lower non HDL cholesterol goal of

<100 mg/dl. Among those patients with triglyceride levels >200 mg/dl, a non-HDL cholesterol goal of <130 mg/dl was achieved in 72% of patients and a non-HDL cholesterol goal of <100 mg/dl in 43%.

Overall, 85% of patients achieved triglyceride levels <200 mg/dl, while only 69% achieved normal triglyceride levels of <150 mg/dl. The distribution of the patients' triglyceride levels is depicted in Figure 2. Women were less likely to achieve optimal triglyceride levels than men (66% vs 70%,  $p = 0.0004$ ). Multivariate predictors of not achieving normal triglyceride levels included age <65 years, female gender, obesity, current smoking, and diabetes ( $p < 0.001$ ). In patients with triglyceride levels >200 mg/dl only 28% were being treated with triglyceride-lowering medications. Among these patients, 18% were taking fibrates, 11% were taking niacin, and 2% were treated with high-dose prescription omega-3 fatty acids.

Overall, 63% of men and 56% of women achieved normal levels of HDL cholesterol. The mean value of HDL cholesterol for men was 36 ± 10 mg/dl and for women was 42 ± 14 mg/dl. The distribution of HDL cholesterol values for the patients is depicted in Figure 3. Multivariate predictors of not achieving normal HDL cholesterol levels included female gender, obesity, current smoking, and diabetes ( $p < 0.001$ ) as well as age <65 years ( $p = 0.002$ ). Women were less likely to achieve normal levels of HDL cholesterol than men (56% vs 63%,  $p < 0.0001$ ). Only 12% of patients with low HDL cholesterol were treated with niacin, and women were less likely than men to be treated with niacin (6% vs 16%,  $p < 0.001$ ).

In total, 43% of men achieved an LDL cholesterol goal of <100 mg/dl and normal levels of triglycerides and HDL cholesterol, while only 19% achieved the more aggressive LDL cholesterol goal of <70 mg/dl along with normal levels of triglycerides and HDL cholesterol. A total of 33% of women achieved an LDL cholesterol goal of <100 mg/dl and had normal levels of triglycerides and HDL cholesterol, while only 13% achieved their more aggressive LDL cholesterol goal of <70 mg/dl along with normal levels of triglycerides and HDL cholesterol. Women were less likely to achieve normal levels of all 3 of their lipid parameters compared with men ( $p < 0.001$ ).

## Discussion

Since the National Cholesterol Education Program update published in 2004,<sup>9</sup> overall LDL goal achievement has improved. The results of our study demonstrate that most patients with CAD are achieving the minimal National Cholesterol Education Program LDL cholesterol goals,<sup>10</sup> but few patients in clinical practice are achieving the more aggressive LDL cholesterol goal of <70 mg/dl. Similarly, few are achieving the non-HDL cholesterol goal of <100 mg/dl.

In the recently published Lipid Treatment Assessment Project (L-TAP) 2 survey, conducted in 2006 and 2007, among 2,993 patients with CAD from 9 countries, the percentage of patients reaching the LDL cholesterol goal of <100 mg/dl had increased to 67%, but the percentage who achieved the more aggressive goal of <70 mg/dl, remained low at 30%.<sup>7</sup> In our study, which provides a more current

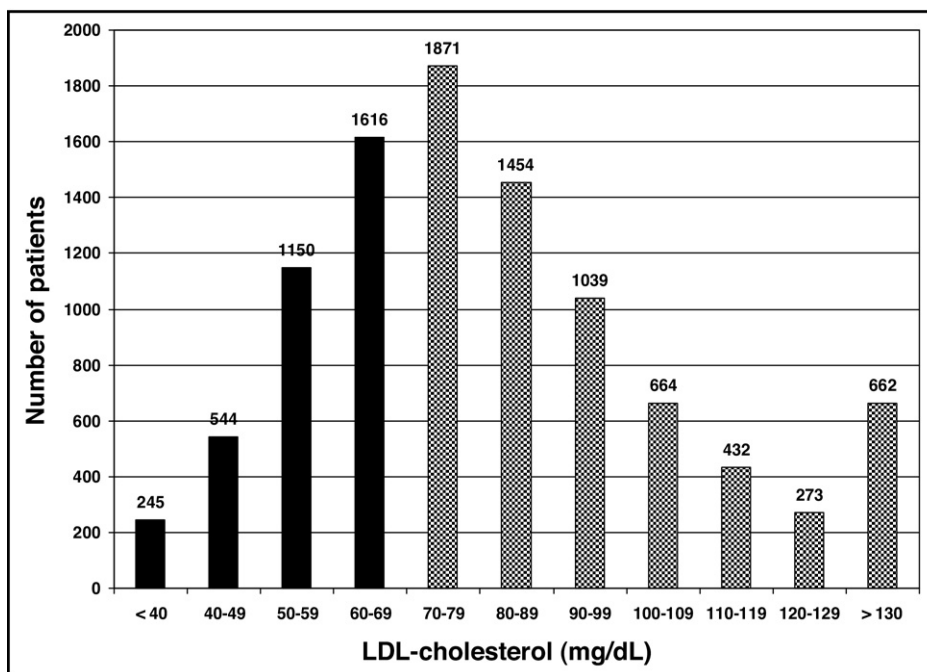


Figure 1. Distribution of achieved LDL cholesterol levels among the study patients. The shaded gray bars represent those patients who did not achieve optimal LDL cholesterol levels.

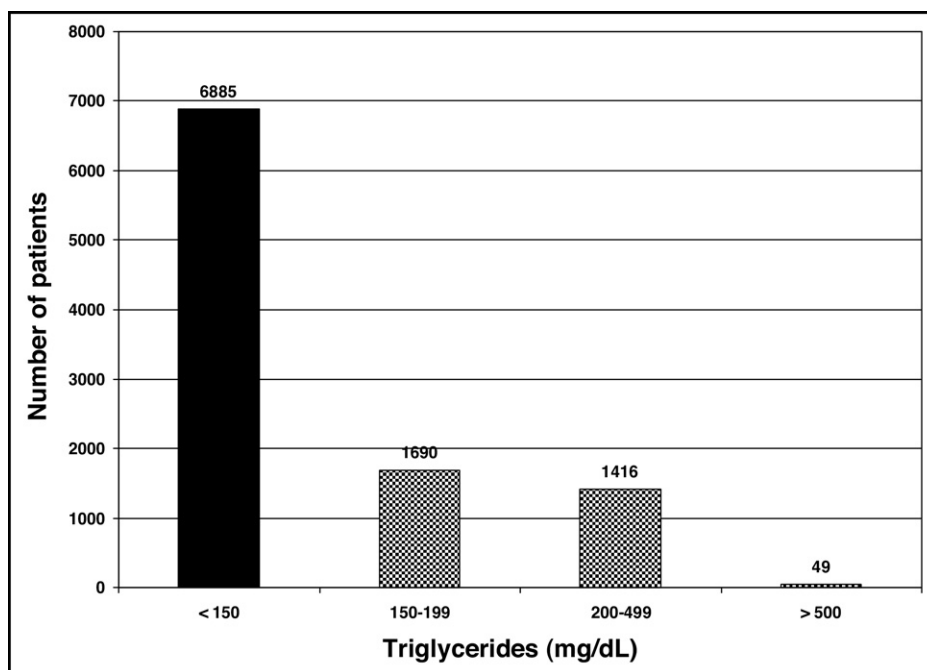


Figure 2. Distribution of achieved triglyceride levels among the study patients. The shaded gray bars represent those patients with elevated triglyceride levels.

evaluation of CAD patients' lipid goals, almost 80% of patients achieved the LDL cholesterol goal of <100 mg/dl, but achievement of the more aggressive LDL cholesterol goal of <70 mg/dl remained low at 35%. In our study, as in previous studies, success rates in achieving LDL cholesterol goals were higher in men than women and in older compared with younger subjects.<sup>1,5,11,12</sup> In a survey of a south-eastern United States managed care database, among 8,353

high-risk women followed for a period of 3 years, only 29% achieved an LDL cholesterol of <100 mg/dl, and only 32% achieved a non-HDL cholesterol of <130 mg/dl.<sup>12</sup>

Among patients who have not achieved the more aggressive LDL cholesterol goal, there is an opportunity to more aggressively treat these patients. The more potent statins atorvastatin and rosuvastatin were prescribed in <1/2 of patients who did not achieve an LDL cholesterol goal of

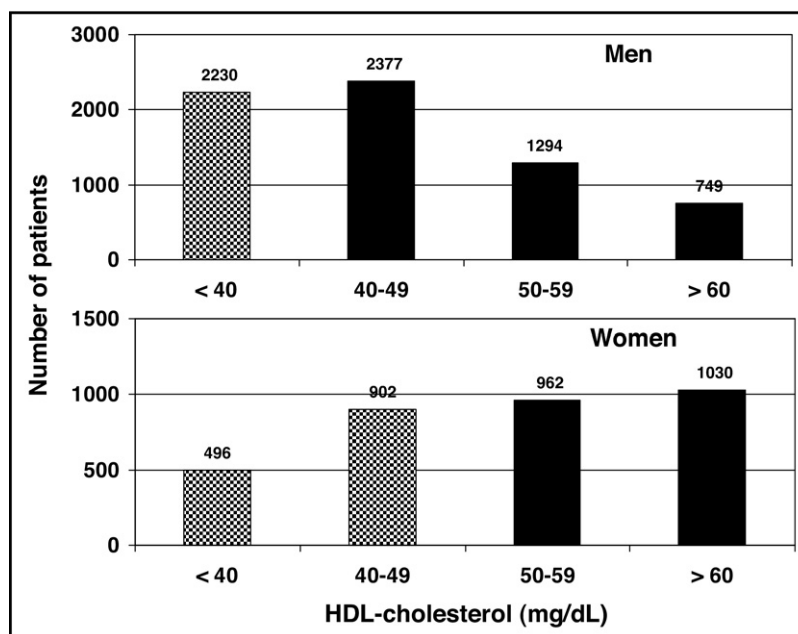


Figure 3. Distribution of achieved HDL cholesterol levels among men (*top*) and women (*bottom*) among the study patients. The shaded gray bars represent those patients with low levels of HDL cholesterol.

<70 mg/dl, and when prescribed, the average dose was below the maximal dose of either of these statins. This is despite clinical studies that have shown safety and added benefit when these drugs are prescribed at their higher doses.<sup>13–16</sup> In addition, other cholesterol-lowering drugs, such as bile acid sequestrants, ezetimibe, and niacin, which have LDL cholesterol-lowering properties, were infrequently prescribed in patients not at their optimal LDL cholesterol goals.

In addition to not achieving most patients' more aggressive LDL cholesterol goals, many patients also had persistently low levels of HDL cholesterol or high levels of triglycerides. In our study, almost 1/3 of patients had elevated levels of triglycerides, while >1/3 of men and almost 1/2 of women had low levels of HDL cholesterol. There is a high prevalence of low levels of HDL cholesterol and elevated triglyceride levels in treated CAD patients. In 1 study of 1,512 CAD or coronary heart disease risk equivalent patients, 66% had low levels of HDL cholesterol, defined as <40 mg/dl for men and <50 mg/dl for women.<sup>6</sup> In a study of 8,500 male veterans in the United States, 64% had HDL cholesterol levels <40 mg/dl.<sup>17</sup> In a more recent survey, the L-TAP 2 investigators found that 30% of high-risk men and 38% of high-risk women had low levels of HDL cholesterol, using cutoffs of <40 mg/dl for men and <50 mg/dl for women.<sup>7</sup> These findings are similar to ours and confirm previous findings that women who are being treated with cholesterol-lowering medications are more likely to have low HDL cholesterol levels on treatment compared to men.

In our study, other lipid-lowering drugs shown to be effective in lowering triglycerides or increasing HDL cholesterol were infrequently used. In 1 study in high-risk patients with low levels of HDL cholesterol, <4% of these patients were being treated with niacin, and only 4% were treated with fibrate therapy.<sup>6</sup> In a study of high-risk women

followed for a 3-year period, only 7% achieved optimal levels of LDL cholesterol, HDL cholesterol, and triglycerides.<sup>12</sup> At the end of the study period achieving optimal lipid levels for all 3 lipid parameters had increased to only 11%, and the use of niacin or fibrate therapy remained low in these women. Using observational data from a large health maintenance organization, Nichols et al<sup>18</sup> evaluated the frequency of obtaining the National Cholesterol Education Program lipid goals in patients up to 15 months after they were started on lipid-lowering therapy. Among high-risk patients, 22% had high triglyceride levels, and 59% had low levels of HDL cholesterol despite being treated with lipid-lowering therapy. As in our study, the use of nonstatin drugs in these patients was low.

There were several limitations to our study. First, our study was from a single site and only involved patients who were managed by a cardiologist. Our findings may not reflect trends in achieving lipid goals in other parts of the United States or reflect the practices of primary care physicians. Second, we only included patients who had full lipid profiles available in their electronic medical records. Patients without recent lipid profiles are more likely to be undertreated, and our findings may have underestimated the actual number of patients who are achieving their lipid goals in clinical practice.

1. Pearson TA, Laurora I, Chu H, Kafonek S. The Lipid Treatment Assessment Project (L-TAP). A multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. *Arch Intern Med* 2000;160:459–467.
2. Svilaas A, Risberg K, Thoresen M, Ose L. Lipid treatment goals achieved in patients treated with statin drugs in Norwegian general practice. *Am J Cardiol* 2000;86:1250–1253.
3. Keevil JG, Cullen MW, Gangnon R, McBride PE, Stein JH. Implications of cardiac risk, and low-density lipoprotein cholesterol distributions in the United States for the diagnosis and treatment of dyslipi-

- demia. Data from the National Health and Nutrition Survey 1999 to 2002. *Circulation* 2007;115:1363–1370.
4. Ghandehari H, Kamal-Bahl S, Wong ND. Prevalence and extent of dyslipidemia and recommended lipid levels in US adults with and without cardiovascular comorbidities: the National Health and Nutrition Examination Survey 2003–2004. *Am Heart J* 2008;156:112–119.
  5. Davidson MH, Maki KC, Pearson TA, Pasternak RC, Deedwania PC, McKenney JM, Fonarow GC, Maron DJ, Ansell BJ, Clark LT, Balantyne CM. Results from the National Cholesterol Education (NCEP) Program Evaluation Project Utilizing Novel E-Technology (NEPTUNE) II Survey and implications for treatment under the recent NCEP writing group recommendations. *Am J Cardiol* 2005;96:556–563.
  6. Alsheikh-Ali AA, Lin JL, Abourjaily P, Ahearn D, Kuvin JT, Karas RH. Prevalence of low-density lipoprotein cholesterol in patients with documented coronary heart disease or risk equivalent and controlled low-density lipoprotein cholesterol. *Am J Cardiol* 2007;100:1499–1501.
  7. Waters DD, Brotons C, Chiang CW, Ferrieres J, Foody J, Jukema JW, Santos RD, Verdejo J, Messig M, McPherson R, Seung KB, Tarasenko L, for the Lipid Treatment Assessment Project 2 Investigators. Lipid Treatment Assessment Project 2. A multinational survey to evaluate the proportion of patients achieving low-density lipoprotein cholesterol goals. *Circulation* 2009;120:28–34.
  8. Kauffman AB, Olson KL, Youngblood ML, Zadvorny EB, Delate T, Merenich JA, for the Clinical Pharmacy Cardiac Risk Service Study Group. Attainment of low-density lipoprotein goals in coronary artery disease. *J Clin Lipidol* 2010;4:173–180.
  9. Grundy SM, Cleeman JI, Merz NB, Brewer B, Clark LT, Hunninghake DB, Pasternak RC, Smith SC, Stone NJ, for the Coordinating Committee of the National Cholesterol Education Program. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004;110:227–239.
  10. 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;285:2486–2497.
  11. Yan AT, Yan RT, Tan M, Hackam DG, Leblanc KL, Kertland H, Tsang JL, Jaffer S, Kates ML, Leiter LA, Fitchett DH, Langer A, Goodman SG, for the Vascular Protection (VP) and Guidelines Oriented Approach to Lipid Lowering (GOALL) Registries Investigators. Contemporary management of dyslipidemia in high-risk patients: targets still not met. *Am J Med* 2006;119:676–683.
  12. Mosca L, Merz NB, Blumenthal RS, Cziraky MJ, Fabunmi RP, Sarawate C, Watson KE, Willey VJ, Stanek EJ. Opportunity for intervention to achieve American Heart Association guidelines for optimal lipid levels in high-risk women in a managed care setting. *Circulation* 2005;111:488–493.
  13. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM, for the Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis In Myocardial Infarction 22 Investigators. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;350:1495–1504.
  14. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, Gotto AM, Greten H, Kastelein JJP, Shepher J, Wenger N, for the Treating to New Targets (TNT) Investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med* 2005;352:1425–1435.
  15. Nissen SE, Nicholls SJ, Sipahi I, Libby P, Raichlen JS, Ballantyne CM, Davignon J, Erbel R, Fruchart JC, Tardif JC, Schoenhagen P, Crowe T, Cain V, Wolski K, Goormastic M, Tuzcu EM, for the ASTEROID Investigators. Effect of very high-intensity statin therapy in regression of coronary atherosclerosis. The ASTEROID trial. *JAMA* 2006;295:1556–1565.
  16. Crouse JR, Raichlen JS, Riley WA, Evans GW, Palmer MK, O’Leary DH, Grobbee DE, Bots ML, for the METEOR Study Group. Effect of rosuvastatin on progression of carotid intima-media thickness in low risk individuals with subclinical atherosclerosis. The METEOR trial. *JAMA* 2007;297:1344–1353.
  17. Rubins HB, Robins SJ, Collins D, Iranmanesh A, Wilt TJ, Mann D, Mayo-Smith M, Faas FH, Elam MB, Rutan GH, Anderson JW, Kashyap ML, Schectman G, for the Department of Veterans Affairs HDL Intervention Trial Study Group. Distribution of lipids in 8,500 men with coronary artery disease. *Am J Cardiol* 1995;75:1196–1201.
  18. Nichols GA, Ambegaonkar BM, Sazonov V, Brown JB. Frequency of obtaining National Cholesterol Education Program Adult Treatment Panel III goals for all major serum lipoproteins after initiation of lipid altering therapy. *Am J Cardiol* 2009;104:1689–1694.