

Helping Patients Improve Cardiovascular Health



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About This Supplement

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Editor's Message

Cardiovascular Benefits of Aggressive Cholesterol-Lowering Therapy

Michael B. Clearfield, DO

In the 3 articles in this supplement to *JAOA—The Journal of the American Osteopathic Association*, Drs Cruickshank,¹ Cohen,² and Smiley³ review the rationales behind the various lipid goals stipulated in the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines and the progress that has been made toward meeting those goals. In the lead article of this supplement, Dr Cruickshank highlights the progress in achieving low-density lipoprotein cholesterol (LDL-C) goals in clinical practice, citing surveys that include the Lipid Treatment Assessment Project (L-TAP) (1996-1997),⁴ the L-TAP 2 (2006-2007),⁵ and the American Osteopathic Clinical Assessment Program (AOA-CAP) (2005-2010).⁶ From 1996 to 2010, there was greater success in achieving lipid-lowering goals set by the National Cholesterol Education Panel, as noted in the NEPTUNE (National Cholesterol Education Program Evaluation Project Utilizing Novel E-Technology) trial,⁷ the L-TAP 2, and the AOA-CAP. The success rates for achieving LDL-C goals in these 3 studies were 57%, 67%, and 56%, respectively, in high-risk subjects, but only 18%, 30%, and 20%, respectively, in patients at very high risk, for whom the LDL-C goal was less than 70 mg/dL.⁵⁻⁷ Despite a substantial clinical trial database demonstrating the benefits of attaining guideline LDL-C goals, these data suggest that a considerable treatment gap still remains in many patients, especially those at the highest cardiovascular risk.

In the next article, Dr Cohen details the evidence base from clinical trials demonstrating the rationale for more aggressive lipid lowering through statin therapy.² Dr Cohen eloquently presents a case that continued lowering of LDL-C has a continuous, graded, and strong relationship to reduced cardiovascular events for patients with and patients without preexisting coronary heart disease (secondary and primary prevention, respectively). Although the article emphasizes higher-risk patients with preexisting CHD (secondary prevention), it also includes an analysis of JUPITER (Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin), which resulted in statistically significant reductions in the rate of first major cardiovascular events within a large primary prevention cohort.⁸

The concept of lifetime cardiovascular risk extends the ideas presented in Dr Cohen's article and suggests that many individuals deemed at moderate or even

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low risk over a 10-year period may very well have a high lifetime risk for a cardiovascular event.⁹ This hypothesis proposes that the risk of continued exposure to abnormal lipoproteins, even at moderately elevated levels, may be compounded over time, resulting in progressive atherosclerosis and resultant cardiovascular events. For example, in individuals with lifetime LDL-C levels reduced by approximately 28% (about 40 mg/dL) due to a nonsense mutation of *PCSK9* gene, a reduction of up to 88% in the rate of coronary heart disease events has been reported.¹⁰ This 88% reduction is quite different from the 30% reduction predicted by a similar decrease in LDL-C levels noted in a meta-analysis of statin trials.¹¹ Individuals with the *PCSK9* mutations have lower LDL-C levels throughout their entire lives, which may actually triple their risk reduction compared with those whose LDL-C levels

are lowered similarly but are measured for only a 5-year span.

In patients treated with statins for more than 5 years—which is greater than the usual duration in clinical trials—findings suggest a continuing widening of the gap between patients treated with statins and untreated patients, for both primary and secondary prevention.^{12,13} Over longer time spans, such as decades, the sustained benefit from the lower LDL-C levels achieved with continuous statin therapy may approach the 88% reductions noted with lifelong *PCSK9* mutations.

In the final article of this supplement, Dr Smiley reviews the lifestyle and the pharmacotherapeutic options available to maximize reductions in cardiovascular risk. Maximized interventions that aggressively lower LDL-C levels to less than 70 mg/dL may stabilize plaque and reduce plaque vulnerability (ie,

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plaque fractures that result in an acute event such as myocardial infarction, unstable angina, and death from thrombus formation) enough to potentially negate adverse effects from other risk factors such as elevated blood pressure and cigarette smoking. There is also potential to negate adverse effects from low levels of high-density lipoprotein cholesterol and elevated triglyceride levels, but it is theoretical and will require further studies such as the AIM-HIGH trial (Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides and Impact on Global Health Outcomes).¹⁴

In a recent editorial, William Roberts, MD, editor of the *American Journal of Cardiology*, succinctly summarized this complex issue into a simple phrase: "It's the cholesterol, stupid!"¹⁵ This opinion was recently supported by the Cholesterol Treatment Trialists' Collaboration,¹¹ a meta-analysis of 170,000 participants in 26 randomized trials, which demonstrated a 12% reduction in cardiovascular events per 1 mmol/L (39 mg/dL) decrease in LDL-C during the first year of statin therapy, followed by a consistent 25% reduction per year during each subsequent year. Extrapolating these data to primary prevention

trials, achieving LDL-C reductions of 1 to 3 mmol/L for a decade or more with statins could very well lower 10-year cardiovascular event rates to less than 2%, and possibly less than 1%.

The articles in this supplement, which were developed in part from a symposium conducted during the American Osteopathic Association's 115th Annual Osteopathic Medical Conference and Exposition on October 25, 2010, show that a model for achieving these more aggressive LDL-C reductions is clearly within our grasp and should result in astounding benefits for our patients.

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Achieving Cholesterol Targets: How Well Are We Doing?

John M. Cruickshank, DO, MBA, CPE

Elevated low-density lipoprotein cholesterol (LDL-C) levels are a modifiable risk factor for the development of coronary heart disease (CHD), the leading cause of death in the United States. Treatments to lower these levels help decrease the risk of CHD events and reduce mortality rates in patients with existing CHD and those with no history of CHD. Rates of screening and treatment for high cholesterol levels have improved somewhat in recent years, but there is still room for substantial improvement, especially in patients at high risk of CHD, who benefit most from aggressive LDL-C-lowering therapies. The American Osteopathic Association Clinical Assessment Program, a Web-based program that measures physician performance by analyzing data abstracted from patient medical records and helps guide treatment decisions, is a tool to help physicians improve outcomes in patients with elevated LDL-C levels.

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The estimated prevalence of coronary heart disease (CHD) in the United States is 17.6 million, or 7.9% of the adult population.¹ It is also the leading cause of death in the United States, accounting for more than 425,000 deaths per year—approximately 1 in 6 deaths.¹ In addition to the substantial clinical consequences, CHD is associated with a huge economic burden, costing an estimated \$177.1 billion in direct and indirect costs in 2010.¹

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Elevated cholesterol levels are a major modifiable risk factor for the development of cardiovascular disease, with a reported prevalence of approximately 25% in the United States.² In particular, epidemiologic studies have identified low-density lipoprotein cholesterol (LDL-C) as the most atherogenic lipoprotein.³ This status is evidenced by the noted acceleration of atherogenesis in genetic disorders in which serum LDL-C is markedly increased in the absence of other CHD risk factors and by the well-established benefit of lowering LDL-C levels in patients with CHD.³ In particular, such lowering is associated with a decreased risk of CHD and a reduction in mortality in patients with existing CHD (secondary prevention) and in those with no history of CHD (primary prevention). The benefit of lowering LDL-C levels is

seen regardless of whether the reduction is achieved via diet, surgery, or pharmacotherapy.³ Data from recent trials with statins indicate that a 1% decrease in LDL-C lowers the risk of CHD by approximately 1%.³ Because of this, screening patients for elevated LDL-C levels and determining appropriate management regimens are extremely important and highly effective for improving clinical outcomes.

Trends in Screening and Lipid Control

Despite the proven benefit of managing hyperlipidemia, patients frequently do not receive adequate treatment.⁴ However, treatment rates have been increasing in recent years. Data from the National Committee for Quality Assurance indicate that in 2008, among patients

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aged 18 to 75 years who were discharged after admission for acute myocardial infarction or coronary angioplasty or who had a diagnosis of ischemic vascular disease, cholesterol screening was performed in 88.9% of patients enrolled in commercial health insurance plans, 88.6% of those enrolled in Medicare, and 79.6% of those enrolled in Medicaid.⁴ More notably, cholesterol control (defined as LDL-C levels <100 mg/dL) was achieved in only 59.7%, 56.7%, and 40.1%, respectively, of patients in these 3 groups.⁴ Although these rates of screening and control represent modest improvements since 2006, they also indicate that outcomes in these patients can still be substantially improved.⁴

The second Lipid Treatment Assessment Project survey was conducted between September 2006 and April 2007 in more than 10,000 patients from 9 countries in North America, South America, Europe, and Asia.⁵ The survey was designed to determine the proportion of patients achieving appropriate LDL-C goals for their given level of risk, as defined by the National Cholesterol Education Program Adult Treatment Panel III.⁵ Overall, 73% of patients achieved their LDL-C goal, including 75.7% of those in the United States.⁵ However, success was dependent on the baseline level of risk. Among patients at low risk (ie, ≤1 risk factor), moderate risk (ie, ≥2 risk factors), and high risk (ie, cardiovascular disease or diabetes mellitus), target LDL-C goals were achieved in 86%, 74%, and 67%, respectively.⁵ With more aggressive therapy to achieve an optional LDL-C level of less than 70 mg/dL for those at very high risk (ie, patients with CHD plus ≥2 risk factors), only 30% of patients achieved their goal (Figure).⁵

By comparison, the first Lipid Treatment Assessment Project survey, performed in 1996 and 1997, found that 38% of patients overall and 18% of high-risk patients achieved their LDL-C goal.⁵ These results are very similar to those reported by Kitkungvan et al⁶ for 765 patients at high or very high risk of CHD. Among the 217 patients at very high risk (defined as having a history of CHD, a CHD risk equivalent, or ≥2 risk

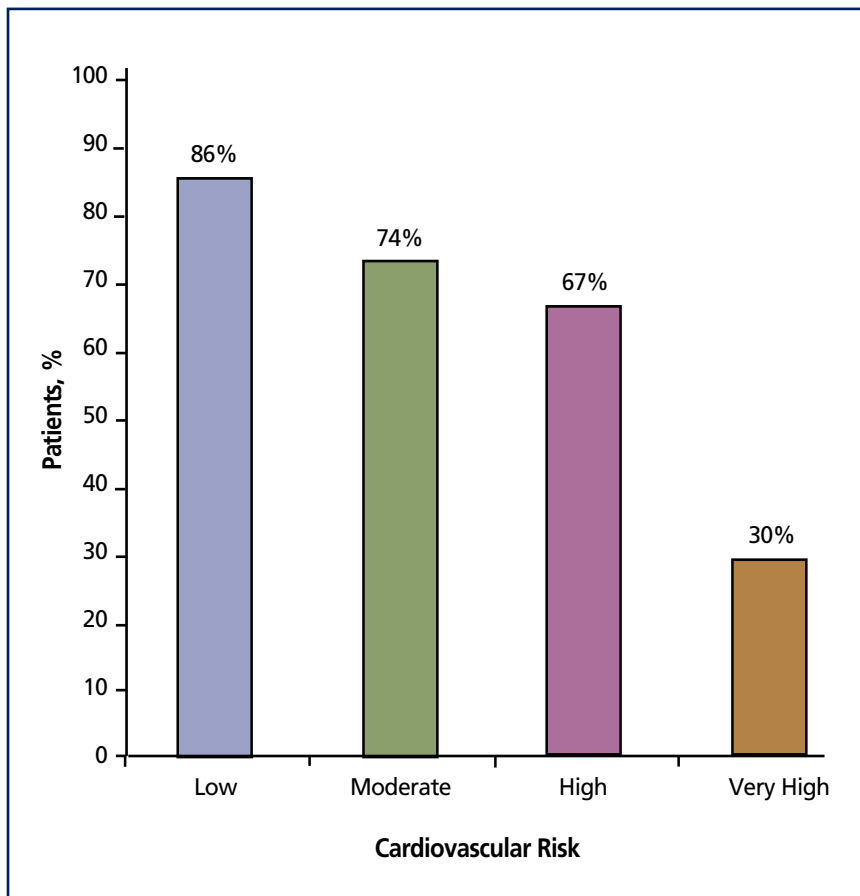


Figure. Proportions of patients who achieved target levels of low-density lipoprotein cholesterol in the second Lipid Treatment Assessment Project 2.

factors and a 10-year Framingham score of >20%), only 37% achieved their LDL-C goal of less than 70 mg/dL.⁶ Overall, these data indicate that, though there is a trend toward improvement in attaining lipid goals, a substantial proportion of patients, particularly those at highest risk, would benefit from more aggressive therapy.

American Osteopathic Association Clinical Assessment Program

The American Osteopathic Association Clinical Assessment Program (AOA-CAP) is a Web-based performance measurement program that analyzes data abstracted directly from patient medical records.⁷ The goals of the AOA-CAP are as follows⁷:

- provide a structure for quantitative evaluation of current osteopathic medical care provided individually and in

the aggregate by osteopathic physicians

- identify where quality-of-care improvements can be made in osteopathic physicians' offices and provide educational interventions to promote such improvements
- provide osteopathic physicians with information on how they are treating their populations, including patient outcomes data

This program will help physicians move beyond the recall structures that are commonly used in the office setting to a system that captures patient outcomes more objectively. The program includes 5 assessment modules—for coronary artery disease (CAD), diabetes mellitus, women's health screening, asthma, and chronic obstructive pulmonary disease.^{7,8} Data elements for each of these modules include demographic

and clinical information. Clinical indicators were developed using evidence-based guidelines that represent state-of-the-art professional standards of care. The guidelines track patient outcomes so that changes in treatment can be instituted, thereby improving the quality of patient care. The AOA-CAP is compliant with the Health Insurance Portability and Accountability Act and has been developed to avoid the collection of identifiable patient information. Physician-specific data are also confidential. Parameters that are measured in the CAD module include evaluation and control of LDL-C levels, smoking cessation counseling, appropriate use of pharmacotherapy (eg, aspirin, β -blockers, angiotensin-converting enzyme inhibitors, and warfarin in appropriate patients), assessment of kidney function, screening for depression, and osteopathic assessment of patients.⁷

Outcome Data

Since 2005, data have been collected on randomly selected patients across the program from participating family practice settings and internal medicine residencies. Data provided in the following paragraphs were provided by Sharon McGill, MPH, and Richard J. Snow, DO, MPH, from the Steering Committee of the American Osteopathic Association Clinical Assessment Program (written communication, September 2010 and April 2011).

Currently, more than 200 total programs have participated in the diabetes module, and the CAD module has 86 active programs. These data allow an assessment of outcomes and an evaluation of how physicians are responding to patient conditions. For example, among the 12,650 patients in the diabetes module, the overall rate for achieving the target LDL-C concentration (ie, ≤ 100 mg/dL) was 51.9%. Rates of control were higher for patients older than 65 years (58.8%) than for younger patients (48.8%; $P < .0001$) and slightly higher for men than for women (54.4% vs 50.0%; $P < .0001$) (Table 1). Care delivered in 2009 and 2010 was also associated with greater rates of control than that delivered between 2005 and 2008 (53.2% vs 50.9%;

Attribute	% of Patients With LDL-C Control		P Value
	With Attribute	Without Attribute	
Care delivered in 2009-2010 vs 2005-2008	53.2	50.9	<.001
Male sex	54.4	50.0	<.001
Age >65 years	58.8	48.8	<.001

* Low-density lipoprotein cholesterol (LDL-C) control was defined as LDL-C levels ≤ 100 mg/dL. The overall rate of control was LDL-C 51.9%.⁸

$P < .0001$). The rate of control was highest among patients with Medicare insurance (58.8%) and lowest among those who were self-paying (44.4%), probably reflecting a decreased ability to purchase medications in the latter group.

Physician responses to elevated LDL-C levels, as defined by the National Cholesterol Education Program Adult Treatment Panel III, were variable. The most common response was to encourage diet and weight loss (30.1%). Other documented responses included increasing the dosage of the current lipid-lowering medication (18.7%), adding a new lipid-lowering medication (15.5%), rechecking LDL-C values (14.8%), and value not available on the last visit (4.5%). Notably, no response was documented in the record in 16.5% of patients with elevated LDL-C values.

The CAD module included patients at very high risk, with acute myocardial infarction, revascularization, or stroke as the entry criterion. Among the 3463 patients in the database, 55.7% achieved an LDL-C level of 100 mg/dL or lower and 20.4% achieved the more aggressive goal of 70 mg/dL or lower (Table 2).

These results highlight opportunities for improving care. To address this need, the AOA-CAP offers an approach that supports a patient-centered medical home model, which may help achieve therapeutic goals. This model is a health-care approach that facilitates partnerships between individual patients (and their families, when appropriate) and their personal physicians. The AOA-CAP helps physicians improve the quality of

patient care by using evidence-based medicine and clinical decision support tools to guide their decision making. Another key component is the use of a registry, which allows the tracking of patients and their care. This model also takes advantage of and leverages information from systems, such as electronic health records, that support high-quality care, practice-based learning, and continuous quality improvement.

Participation

Physicians who decide to participate in the AOA-CAP can visit the AOA Web site (www.osteopathic.org), log in, and select 1 of the 5 modules.⁷ Participants are asked to abstract data from 20 patient records for chart review. The medical records are selected based on patient characteristics (eg, diagnostic criteria, inclusion or exclusion criteria) and sampling technique. The data are then entered online through the Web site. After entering the data, participants receive a performance analysis report that compares their performance with that of other participants and with national benchmarks (eg, National Committee for Quality Assurance, Healthcare Effectiveness Data and Information Set measures). For evaluation, 20 additional charts are abstracted and entered into the database to generate a comparison report. In addition, the physician can select educational interventions designed to improve clinical performance. As an incentive for participation, physicians receive 20 hours of AOA Category 1-B continuing medical education (CME)

Table 2.
LDL-C Control in Patients with Coronary Artery Disease Enrolled in the American Osteopathic Association Clinical Assessment Program (n=3463)*

Attribute	% of Patients With LDL-C Control		P Value
	With Attribute	Without Attribute	
■ Target LDL-C Level, ≤100 mg/dL			
□ Care delivered 2009-2010 vs 2005-2008	57.6	54.6	.076
□ Male sex	57.3	53.5	.026
□ Age >65 years	61.5	49.5	<.001
■ Target LDL-C Level, ≤70 mg/dL			
□ Care delivered 2009-2010 vs 2005-2008	20.6	20.3	.8
□ Male sex	21.8	18.5	.15
□ Age >65 years	23.8	16.7	<.001

* The overall rates of low-density lipoprotein cholesterol (LDL-C) control were 55.7% and 20.4% for the targets of ≤100 and ≤70 mg/dL, respectively.⁸

credit for each of the 5 modules. If a physician participates in all 5 modules, he or she is eligible for a total of 100 hours of CME credit.

Conclusion

Elevated LDL-C levels are a modifiable risk factor for the development of CHD, and there is compelling evidence that therapies to lower these levels are associated with substantial reductions in CHD events and overall mortality rates in both primary and secondary prevention settings. However, despite increased

proportions of patients achieving target LDL-C levels, there remains a treatment gap, particularly among those at highest risk. Clinical tools exist to help physicians achieve treatment goals and improve the quality of care and clinical outcomes by evaluating current practices and guiding improvements. The AOA-CAP is one such tool that can help improve outcomes for patients with dyslipidemia and promote an approach to delivering patient care that's aligned with the patient-centered medical home model.

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Partnership to Fight Chronic Disease

The American Osteopathic Association has been an active member of the Partnership to Fight Chronic Disease (PFCD) since 2007. This supplement promotes the ideals of this partnership.

The PFCD is a national and state-based coalition of hundreds of provider, patient, community, business, and labor groups committed to raising awareness of the leading causes of death, disability, and rising healthcare costs in the United States—chronic diseases such as diabetes, asthma, cancer, and heart disease. In addition, the PFCD has worked to ensure that prevention and wellness measures were incorporated into healthcare reform legislation passed by Congress in 2010.

For additional information, visit www.fightchronicdisease.org.

Rationale for Aggressive Lipid Lowering in High-Risk Patients

Jerome D. Cohen, MD

According to current guidelines from the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), the target low-density lipoprotein cholesterol (LDL-C) level for patients with established coronary heart disease (CHD) or CHD risk equivalents is less than 100 mg/dL, with an optional target of less than 70 mg/dL. More recent data suggest, however, that the physiologically normal level of LDL-C and the level at which atherogenesis is initiated is much lower. Overall, the data convincingly demonstrate that LDL-C lowering is associated with a significant reduction in CHD events, regardless of preexisting CHD. The NCEP ATP III treatment guidelines, published in 2002 and updated in 2004, do not reflect more recent findings on intensive lipid-lowering therapy, which are likely to be addressed in the NCEP ATP IV guidelines, scheduled to be released in 2011. Drug options for LDL-C lowering include statins (the drug of choice), bile acid sequestrants, nicotinic acid, fibrates, and selective cholesterol absorption inhibitors.

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Current guidelines from the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) state that the target low-density lipoprotein cholesterol (LDL-C) level for patients with established coronary heart disease (CHD) or CHD risk equivalents (eg, diabetes, peripheral or cerebral vas-

cular disease, Framingham 10-year CHD risk >20%¹) is less than 100 mg/dL, with a target of less than 70 mg/dL considered an option.¹ However, data now suggest that the physiologically normal level of LDL-C and the level at which atherogenesis is initiated is much lower.²

Although the average total cholesterol level in US adults is 200 mg/dL, mean values in individuals from hunter-gatherer societies and in wild primates range from 70 to 140 mg/dL.³ These hunter-gatherer populations show no evidence of atherosclerosis.² Thus, it has been estimated that LDL-C levels of 50 to 70 mg/dL are physiologically normal and the levels for which humans are genetically adapted.² This notion is supported by data from the MRFIT (Multiple Risk Factor Intervention Trial) study, involving more than 360,000 men

in the United States who were followed longitudinally for morbidity and mortality.⁴ As illustrated in *Figure 1*, the relationship between total serum cholesterol levels and the 10-year risk of death due to CHD in this population was strong, continuous, and graded over the entire range of total cholesterol concentrations. Thus, current target goals for LDL-C may lead to substantial undertreatment of patients at risk for CHD events.⁴

Aggressive Lowering of LDL-C Levels

Data from the Heart Protection Study⁵ conducted in the United Kingdom support the value of LDL-C lowering even in patients with relatively low LDL-C values at baseline. This study⁵ included 20,536 participants aged 40 to 80 years

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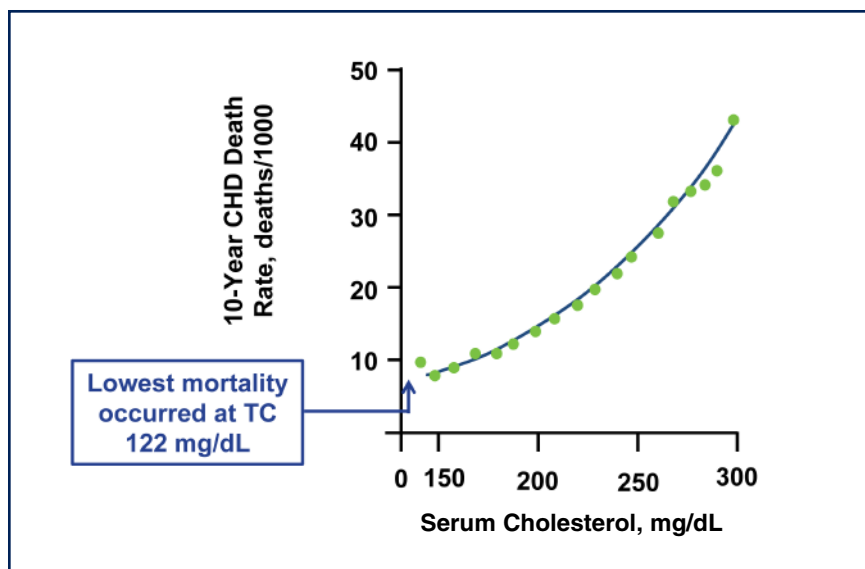


Figure 1. Relationship between total cholesterol levels and rates of death due to coronary heart disease (CHD) in 361,662 men screened for MRFIT (Multiple Risk Factor Intervention Trial).⁴

with an increased 5-year risk of CHD death due to prior disease (eg, myocardial infarction or other CHD, occlusive disease of noncoronary arteries, type 1 or type 2 diabetes, treated hypertension). Notably, the total cholesterol threshold level for entry into the study was 135 mg/dL or above, meaning that a large number of patients with “normal” cholesterol levels were allowed entry. The results indicated that vascular events (eg, total CHD, total stroke, revascularization) were reduced by 24% in patients receiving simvastatin compared with those receiving placebo ($P < .0001$). Importantly, the relative risk reduction was similar across groups when results were stratified by baseline LDL-C values. The Heart Protection Study⁵ was one of the first to demonstrate that treatment of LDL-C levels considered “normal” is associated with clinical benefit.

Cannon and colleagues⁶ conducted a meta-analysis of trials comparing intensive (high-dose) and moderate (standard-dose) statin therapy in patients with CHD or acute coronary syndromes.⁶ The analysis included data from 4 trials comparing more vs less aggressive cholesterol lowering: PROVE IT-TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy—Thrombolysis in Myocardial Infarction 22), TNT

(Treating to New Targets), A-to-Z (Aggrastat to Zocor), and IDEAL (Incremental Decrease in Endpoints Through Aggressive Lipid Lowering). A total of 27,548 patients were enrolled.

Patients were randomly assigned to receive standard-dose or high-dose statin. The following regimens were used in these studies⁶:

- PROVE IT-TIMI 22: pravastatin (40 mg) vs atorvastatin (80 mg)
- TNT: atorvastatin (10 mg vs 80 mg)
- A-to-Z: placebo followed by simvastatin (20 mg) vs simvastatin alone (40 mg increased to 80 mg)
- IDEAL trial: simvastatin (20 mg titrated to 40 mg) vs atorvastatin (80 mg)

More aggressive therapy was associated with a statistically significant greater reduction in LDL-C levels and an improvement in clinical outcomes compared with less aggressive therapy. Mean LDL-C concentrations during treatment ranged from 97 to 104 mg/dL in the standard therapy arms and from 65 to 81 mg/dL in the intensive therapy groups. Overall in the pooled analysis, mean LDL-C concentrations decreased from 130 mg/dL at baseline to a mean of 101 mg/dL in the standard-dose group

and 75 mg/dL in the intensive therapy group. Overall, intensive treatment with statins was associated with a 16% reduction in these clinical events ($P = .00003$). Similarly, the pooled analysis found a 16% reduction in coronary death or any cardiovascular event among those receiving high-dose rather than standard-dose statin therapy.⁶

Another analysis of the PROVE IT-TIMI study evaluated the relationship between achieved LDL-C concentrations and clinical events among patients in the intensive therapy arm.⁷ Patients were stratified into subgroups by the LDL-C concentration achieved at 4 months: >80 to 100 mg/dL, >60 to 80 mg/dL, >40 to 60 mg/dL, or ≤ 40 mg/dL.⁷ The results indicated that there was a relationship between the achieved LDL-C levels and the rates of the primary composite end point, which included instances of any of the following outcomes: death, myocardial infarction, stroke, revascularization, and unstable angina requiring hospital admission.⁷ The rates of the primary composite end point were 26.1%, 22.2%, 20.4%, and 20.4%, respectively, in the 4 LDL-C categories, showing that lower LDL-C levels were associated with progressively lower risk.⁷ A multivariable analysis found that the 2 groups with the lowest LDL-C levels had significantly lower end point rates than the >80 to 100 mg/dL group (the referent group against which hazard ratios were calculated) (Figure 2). Patients in the >40 to 60 mg/dL group achieved 33% risk reduction, compared with 39% in the ≤ 40 mg/dL group.⁷

Data from the TNT trial also support intensive lipid-lowering therapy.⁸ Overall, these data suggest that further clinical benefit is achieved by lowering LDL-C concentrations to very low levels.⁸ The study⁸ included patients with established CHD who had mean LDL-C levels less than 130 mg/dL after an 8-week open-label run-in period during which they were treated with atorvastatin at 10 mg/d.⁸ During this period, LDL-C levels were reduced to a mean of 98 mg/dL. At the completion of this phase, patients were randomized to continue atorvastatin at 10 mg/d or to receive aggressive therapy (atorvastatin, 80 mg/d).⁸ Results indicated that aggressive therapy was

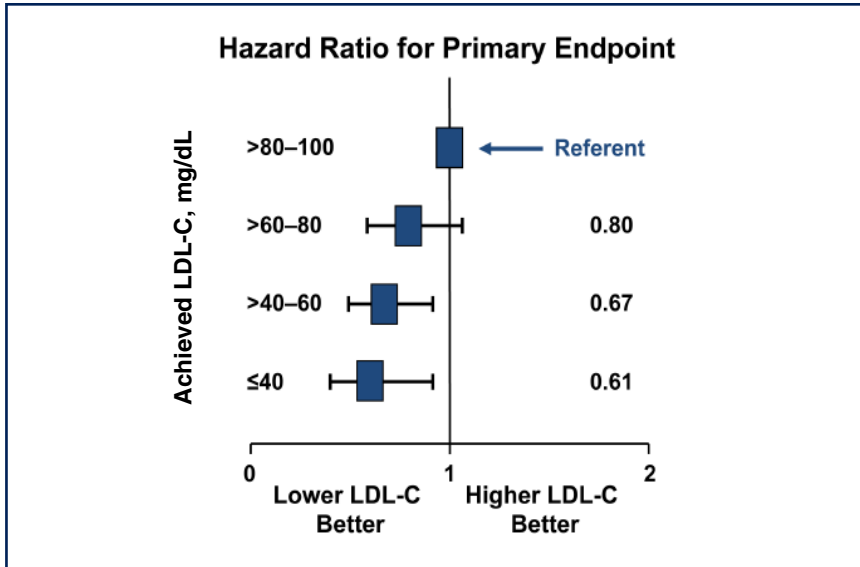


Figure 2. Coronary heart disease event rate by achieved low-density lipoprotein cholesterol (LDL-C) levels from the PROVE IT-TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy—Thrombolysis in Myocardial Infarction 22) study.⁶

associated with significantly lower LDL-C concentrations than standard therapy (77 vs 101 mg/dL).⁸ Aggressive therapy was also associated with a 22% reduction in the composite clinical outcome of death from CHD, nonfatal non-procedure-related myocardial infarction, resuscitation after cardiac arrest, or fatal or nonfatal stroke ($P<.001$).⁸

Overall, the results of these studies demonstrate that there is a relationship between reduced LDL-C levels and reduced CHD risk in the secondary prevention setting (ie, in patients with pre-existing CHD). *Figure 3* summarizes the relationship between LDL-C levels during statin therapy and clinical event rates in secondary prevention trials. Notably, the relationship is relatively linear and extends down to LDL-C concentrations substantially below 100 mg/dL.⁸

Although aggressive lowering of LDL-C levels appears to reduce CHD risk, the safety of this approach needs to be considered. In the TNT trial, significantly more patients receiving intensive therapy (atorvastatin, 80 mg/day) experienced treatment-related adverse events (8.1% vs 5.8%; $P<.001$) or discontinued therapy because of treatment-related adverse events (7.2% vs 5.3%; $P<.001$), compared with those in the standard

therapy group (atorvastatin, 10 mg/d).⁸ There was also a small but significant increase in the rate of persistently elevated liver transaminase levels in the intensive therapy vs the standard therapy group (1.2% vs 0.2%; $P<.001$). However, there were no statistically significant differences between treatment groups in the rates of myalgia (4.8% vs 4.7%; $P=.72$)

or any indication that intensive therapy was associated with an increase in persistently elevated creatinine kinase levels or with the development of rhabdomyolysis.⁸

In the PROVE IT-TIMI trial, there was no apparent relationship between the LDL-C level achieved and the development of adverse events. These events included muscle side effects (eg, myalgia, myositis, elevated creatinine kinase levels), elevated liver enzyme levels, other adverse events (eg, hemorrhagic stroke, retinal events, suicide or death due to trauma), or treatment discontinuation related to adverse events.⁷ Overall, the benefit-risk ratio of more vs less aggressive lipid-lowering therapy is favorable for secondary prevention.

Primary Prevention

Data from the primary care setting (ie, patients with no preexisting CHD) also indicate that there is a continuous and positive relationship between LDL-C concentrations and the risk of CHD events (*Table 1*); these studies include WOSCOPS (West of Scotland Coronary Prevention Study), AFCAPS (Air Force Coronary Atherosclerosis Prevention Study), and ASCOT (Anglo-Scandinavian Cardiac Outcome Trial).² For example, the lipid-lowering arm of the

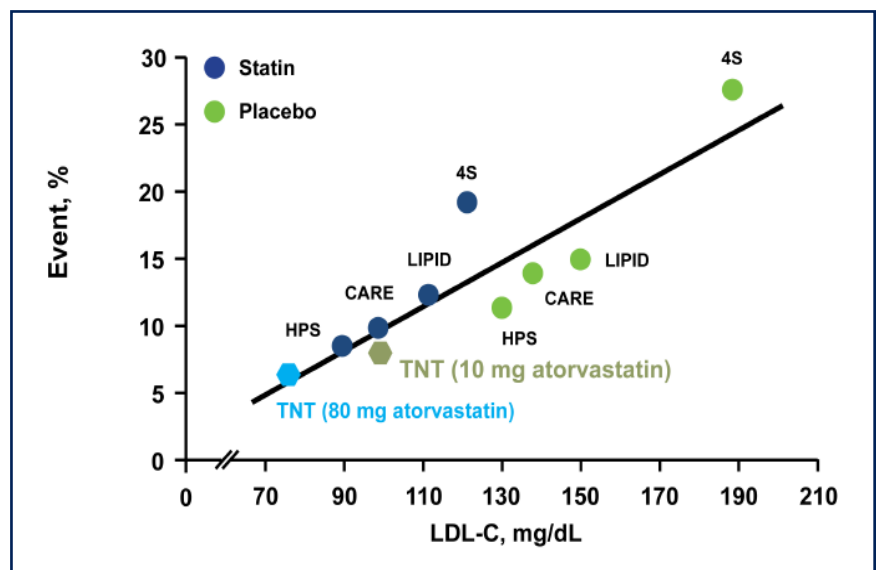


Figure 3. Relationship between low-density lipoprotein cholesterol (LDL-C) levels and coronary heart disease (CHD) events in patients with existing CHD (ie, secondary prevention). Reprinted with permission from LaRosa et al.⁸ **Abbreviations:** 4S, Scandinavian Simvastatin Survival Study; CARE, Cholesterol and Recurrent Events Trial; HPS, Heart Protection Study; LIPID, Long-Term Intervention With Pravastatin in Ischaemic Disease; TNT, Treating to New Targets trial.

Table 1.
Relationship Between Low-Density Lipoprotein Cholesterol (LDL-C) Levels and Coronary Heart Disease (CHD) Events in the Primary Care Setting²

Study	CHD Events, %	LDL-C, mg/dL
■ Statin		
□ ASCOT	2	90
□ AFCAPS	3.8	120
□ WOSCOPS	5.9	135
■ Placebo		
□ ASCOT	3.5	124
□ AFCAPS	5.8	153
□ WOSCOPS	8.2	195

Abbreviations: AFCAPS, Air Force Coronary Atherosclerosis Prevention Study; ASCOT, Anglo-Scandinavian Cardiac Outcome Trial; WOSCOPS, West of Scotland Coronary Prevention Study.

ASCOT study included 10,305 patients aged 40 to 79 years who had hypertension and at least 3 other risk factors for cardiovascular disease but were not considered hyperlipidemic by standard guidelines (ie, total cholesterol <251 mg/dL).⁹ Patients were randomly assigned to receive atorvastatin 10 mg (n=5168) or placebo (n=5137), and the primary end point was nonfatal myocardial infarction or fatal CHD. The trial was stopped early after 3.3 years (instead of continuing to the planned 5-year duration) because significantly fewer primary events had occurred in the atorvastatin group (n=100) than in the placebo group (n=154).⁹ Rates for the primary end point were 1.9% and 3.0%, respectively, for the atorvastatin and placebo groups, amounting to a 36% risk reduction for atorvastatin-treated patients ($P=.0005$).⁹

Significant reductions in risk were also achieved for individual components of the primary end point, including fatal or nonfatal stroke (27%; $P=.024$), total cardiovascular events (21%; $P=.0005$), and total coronary events (29%; $P=.0005$). There were fewer deaths in the atorvastatin group than in the placebo group (185 vs 212 deaths), although the difference was not statistically significant.⁹ Notably, the reduction in clinical events was evident early in the study, and the difference between groups continued to

widen over time. Given that the trial was discontinued early, the long-term benefits of lipid-lowering therapy may be even greater than the early results indicate.

The most recent study evaluating statin therapy in the primary prevention setting was JUPITER (Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin),¹⁰ which included 17,802 healthy men and women with LDL-C levels less than 130 mg/dL and high-sensitivity C-reactive protein (CRP) levels of at least 2.0 mg/L. Participants were randomly assigned to receive either rosuvastatin (20 mg/d) or placebo, with a primary end point of a first major cardiovascular event (ie, nonfatal myocardial infarction, nonfatal stroke, hospitalization for unstable angina, arterial revascularization procedure, or confirmed death from cardiovascular causes).¹⁰ The trial was stopped after 1.9 years because of a statistically significant benefit in favor of rosuvastatin-treated patients.

Patients receiving rosuvastatin experienced a 50% reduction in LDL-C concentrations (median at 12 months, 55 mg/dL) and a 37% reduction in high-sensitivity CRP levels (median at 12 months, 2.2 mg/L).¹⁰ The rates for the primary end point in the rosuvastatin and placebo groups were 0.77 and 1.36 per 100 person-years of follow-up, respectively, a 44% risk reduction for rosuvastatin-treated individuals.¹⁰

Rosuvastatin was also associated with significant reductions in the individual components of the primary end point, including fatal or nonfatal myocardial infarction (54%), fatal or nonfatal stroke (48%), arterial revascularization or unstable angina (47%), and nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes (47%).¹⁰ Other adverse events, such as myopathy, hepatic injury, and cancer, did not occur more frequently in the rosuvastatin group, even though LDL-C concentrations were less than 55 mg/dL in half of patients and less than 44 mg/dL in 25%. As with secondary prevention, the benefit-risk ratio for primary prevention is also very favorable.

In addition to these trials, the benefit of lipid-lowering for reducing clinical

events has also been demonstrated in nonpharmacologic intervention studies. For example, the POSCH (Program on the Surgical Control of the Hyperlipidemias) trial compared diet plus partial ileal bypass with diet alone in adults with a prior myocardial infarction and a plasma cholesterol level of at least 220 mg/dL.¹¹ At 5 years, ileal bypass was associated with a number of clinical benefits, including reductions in overall mortality, mortality from atherosclerotic CHD, and confirmed or suspected myocardial infarction and unstable angina.¹¹ Regression analysis demonstrated a linear relationship between LDL-C levels and clinical end points.¹²

Overall, the results of these studies convincingly demonstrate that LDL-C lowering is associated with a significant reduction in CHD events, both in patients with and patients without pre-existing CHD. Although the absolute benefit is greater in patients with CHD (because they have a higher baseline risk), the benefit is also clearly evident in otherwise healthy individuals. Indeed, there are few therapeutic areas in which the proof of clinical benefit has been demonstrated as clearly and convincingly as in lipid-lowering therapy.

Treatment Recommendations

Current NCEP ATP III treatment guidelines were published in 2002 (with an update in 2004)¹ and therefore do not reflect the more recent findings demonstrating the benefit of intensive lipid-lowering therapy. The studies discussed in the present report and others will most likely be addressed in the ATP IV guidelines, scheduled to be released in 2011. Experts have speculated that ATP IV will address several issues, such as lowering goals for LDL-C in primary and secondary prevention, the routine use of CRP levels in risk stratification, the use of other secondary targets (eg, high-density lipoprotein cholesterol [HDL-C], non-HDL-C, apolipoprotein B, and LDL particle concentrations), and the use of lifetime risk instead of 10-year risk estimates.

The current recommendations are summarized in *Table 2*. For high-risk patients (ie, those with CHD or CHD

Table 2.
NCEP ATP III Goals and Initiation Levels for Therapeutic Lifestyle Changes (TLC)
and Drug Therapy by Risk Category¹³

Risk Category	LDL-C, mg/dL		
	Goal	Initiation Level for TLC	Initiation Level for Drug Therapy
High risk: CHD or CHD risk equivalents (10-year risk, >20%)	<100 (optional: <70)	≥100	≥100 (<100: consider drug options)
Moderately high risk: ≥2 risk factors (10-year risk, 10%-20%)	<130 (optional: 100)	NA	≥130 (100-129: consider drug options)
Moderate risk: ≥2 risk factors (10-year risk, <10%)	<130	NA	≥160
Lower risk: 0-1 risk factor	<160	NA	≥190 (160-189: drug therapy optional)

Abbreviations: CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol; NA, not applicable; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III.

risk equivalents), the recommended LDL-C goal is less than 100 mg/dL. An LDL-C goal of less than 70 mg/dL is a therapeutic option for these patients and should be encouraged, particularly in patients at very high risk. If the LDL-C level is 100 mg/dL or greater in high-risk patients, a lipid-lowering drug should be administered in conjunction with therapeutic lifestyle changes (TLC).¹³ For moderately high-risk patients (ie, those with ≥2 risk factors), the LDL-C goal is less than 130 mg/dL, with an optional target of 100 mg/dL. When the LDL-C level in these patients is between 100 and 129 mg/dL at baseline or with TLC, an LDL-C-lowering agent designed to lower concentrations to less than 100 mg/dL is a therapeutic option.¹³ More recent guidelines from the American Heart Association and American College of Cardiology (AHA/ACC), published in 2006, recommend an LDL-C goal of less than 100 mg/dL for all patients with CHD.¹⁴ These guidelines further state that an LDL-C level of less than 70 mg/dL is a reasonable goal for all patients with CHD.

The NCEP ATP III guidelines recommend intensive LDL-C lowering with TLC in all patients who have elevated levels. For patients with CHD or CHD risk equivalents, a cholesterol-lowering drug should be added to TLC in all patients with LDL-C levels of 100 mg/dL or higher and is an option for those LDL-C levels in the range of 70 to 99 mg/dL.¹

Patients without CHD but with multiple risk factors and a 10-year risk of more than 20% should be treated similarly. Based on their demonstrated ability to reduce LDL-C levels and improve clinical outcomes, statins are generally considered the drug of first choice.¹ The relative degrees of LDL-C-lowering potential for different statins are summarized in *Figure 4*.¹⁵

If LDL-C goals are not achieved within 6 weeks with initial drug therapy, treatment should be intensified, either by increasing the statin dose or by adding another lipid-lowering agent.¹ The major

classes of drugs in addition to statins include bile acid sequestrants, nicotinic acid, fibrates, and selective cholesterol absorption inhibitors, with each having advantages and therapeutic niches.¹ Bile acid sequestrants have additive lipid-lowering effects relative to statins and lack systemic toxicity because they are not absorbed. Nicotinic acid is effective for reducing LDL-C and triglyceride levels, and for raising HDL-C levels, but its long-term use can be limited by adverse events, particularly flushing.¹ Fibrates are generally used for lowering elevated levels of triglycerides, because their potential to lower LDL-C levels is modest.¹ Selective cholesterol absorption inhibitors have shown moderate reductions (<20%) in LDL-C levels when used as monotherapy and may be used in combination with statins (enabling statin doses to be reduced) or in place of them in statin-intolerant patients.¹

Conclusion

There are now convincing data that aggressive lipid lowering is effective for reducing the risk of CHD events and overall mortality in various populations. The benefit is greatest in patients at high risk (ie, those with CHD or CHD risk equivalents) but has also been demonstrated in otherwise healthy individuals. Evidence indicates that there is a linear relationship between lipid levels and the

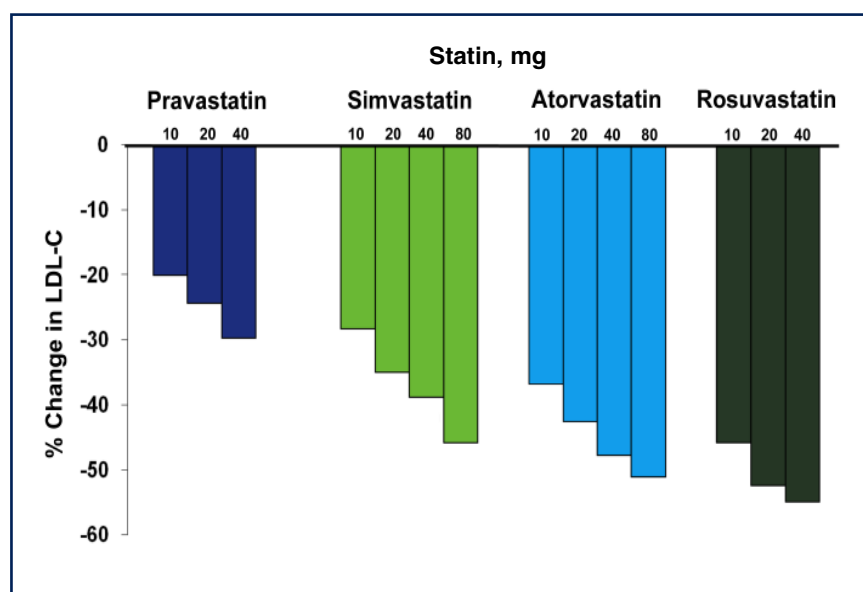


Figure 4. Low-density lipoprotein (LDL) cholesterol lowering potential of various statins at different doses.¹⁵

risk of CHD events, suggesting that LDL-C concentrations below 70 mg/dL are optimal. New NCEP ATP guidelines, to be published in 2011, are likely to reflect this more aggressive approach. Fortunately, a variety of therapeutic options are allowing a greater proportion of patients to achieve their LDL-C treatment goals.

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JAOA Peer Reviewer Seminar

On Tuesday, November 1, 2011, JAOA—*The Journal of the American Osteopathic Association* will host a peer reviewer seminar during the American Osteopathic Association's 116th Annual Osteopathic Medical Conference and Exposition in Orlando, Florida. Osteopathic physicians, researchers, and others interested in best practices in peer review are invited to attend this event, which will be held from 1:15 PM to 3:15 PM. The room will be announced at a later date. Contact JAOA staff at jaoa@osteopathic.org for more information.

Getting Patients to Their Lipid Targets: A Practical Approach to Implementing Therapeutic Lifestyle Changes

William H. Smiley III, DO

Improving clinical outcomes in patients at high risk for coronary heart disease (CHD) requires a multimodal approach, especially in patients with the metabolic risk factors that constitute the metabolic syndrome, which is associated with an elevated risk of CHD at all levels of low-density lipoprotein cholesterol (LDL-C). Achieving optimal clinical outcomes requires a comprehensive and aggressive therapeutic plan that includes pharmacotherapy and lifestyle changes. Effective pharmacotherapy for components of the metabolic syndrome (eg, hypertension, elevated LDL-C levels, prothrombotic state) is important in improving clinical outcomes, as is pharmacotherapy for glycemic control in patients with diabetes. Therapeutic lifestyle changes recommended for treatment of metabolic syndrome include smoking cessation, exercise programs, nutritional counseling, and weight control. Patient questionnaires are an effective way to help tailor recommendations to individual patients and thereby increase compliance. Clinicians can also help motivate patients by offering practical tips for modifying diet and eating habits and explaining all the benefits of exercise. These combined approaches can be used to help more patients achieve their lipid goals, and new pharmacologic therapies currently under investigation may further expand available treatment options.

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Improving clinical outcomes in patients at high risk for coronary heart disease (CHD) requires a multimodal approach. This is especially important in patients with the constellation of metabolic risk factors that are generally considered to constitute the metabolic syndrome¹:

- abdominal obesity
- atherogenic dyslipidemia
- hypertension
- insulin resistance
(with or without glucose intolerance)
- prothrombotic state
- proinflammatory state

The metabolic syndrome is closely related to the generalized metabolic disorder of insulin resistance, although the mechanistic links between the two are complex.¹ The syndrome is associated with an elevated risk of CHD at all levels of low-density lipoprotein cholesterol (LDL-C), a risk considered equal in magnitude to that of cigarette smoking.¹ Because of this risk level, treatment guidelines increasingly focus on management of metabolic syndrome.¹

For example, the Clinical Outcomes

Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial² established therapeutic goals for all of the major components of the metabolic syndrome (*Table 1*). This study was a randomized trial of patients in stable condition who had objective evidence of myocardial ischemia and significant coronary artery disease. The study compared optimal medical therapy (ie, intensive pharmacologic therapy and lifestyle intervention) alone with optimal medical therapy plus percutaneous coronary intervention for reducing the risk of cardiovascular events. The study found that, as an initial management strategy in patients with stable coronary artery disease, percutaneous coronary intervention did not reduce the risk of death, myocardial infarction, or other major cardiovascular events when added to

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optimal medical therapy.² The results underscored the importance of targeting components of the metabolic syndrome with pharmacologic therapy and therapeutic lifestyle changes (TLC).

Pharmacotherapeutic Considerations

Effective pharmacotherapy for the components of the metabolic syndrome is important in improving clinical outcomes. In particular, lowering blood pressure with antihypertensive agents, lowering LDL-C levels with statins, and managing the prothrombotic state with aspirin are well-established methods of reducing the risk of CHD.¹ Although a full review of pharmacologic management of the metabolic syndrome is beyond the scope of the present review, a few general considerations are important.

For the management of hypertension in patients with diabetes mellitus, agents that target the renin-angiotensin system, such as angiotensin-converting enzyme inhibitors (ACEIs), are preferred (or angiotensin receptor blockers when ACEIs are not tolerated).³ When combination therapy is required, combining an ACEI with a calcium channel blocker is a reasonable choice. This recommendation is based partly on the results of the Avoiding Cardiovascular Events in Combination Therapy in Patients Living With Systolic Hypertension (ACCOMPLISH) trial, in which the combination of benazepril plus amlodipine was superior to benazepril plus hydrochlorothiazide for reducing cardiovascular events in patients with diabetes and hypertension.⁴

Pharmacotherapy for glycemic control in patients with diabetes is another important component of care and is associated with a decreased risk of diabetes-related complications.³ Guidelines from the American Diabetes Association recommend the initiation of metformin therapy in combination with TLC at diagnosis and supplementation with additional agents to achieve the target glycosylated hemoglobin level of less than 7% in most patients.³ These guidelines state that the choice of specific glucose-lowering agents should be individualized for each patient, taking into account the ability of the agent to lower glycosylated

hemoglobin, safety and tolerability, ease of use, long-term adherence, cost, and nonglycemic effects.³ Metformin remains the cornerstone of therapy and is one of the few agents that has been clearly shown to be effective for diabetes prevention.^{3,5} Several classes of drugs are associated with weight loss (eg, glucagon-like peptide-1 agonists, pramlintide) or to be weight neutral (metformin, dipeptidyl peptidase-4 inhibitors).⁵ In contrast, other agents, such as thiazolidinediones, sulfonylureas, and insulin, are associated with weight gain⁵ (Table 1). In addition, thiazolidinediones are associated with fluid retention, increased risk of congestive heart failure, and possibly myocardial infarction (rosiglitazone).⁵

Based on their proven ability to substantially lower LDL-C levels and to reduce the risk of clinical events, statins are the drug of choice for patients with hyperlipidemia. In patients who do not achieve lipid treatment goals with initial statin therapy, there are a number of options (Table 2). Doubling the dose of the statin produces a modest additional improvement in lipid parameters, but the benefit may not be sufficient to get patients to their goal. Bile acid sequestrants lower LDL-C levels additively in combination with statins and lack systemic toxicity, but they are associated with gastrointestinal symptoms and tend to raise serum triglyceride levels.¹ Niacin produces a favorable effect across the entire lipid profile, raising high-density lipoprotein cholesterol levels and decreasing levels of LDL-C, lipoprotein(a), and triglycerides. However, compliance is a problem because of adverse effects (eg, flushing, gastrointestinal symptoms).¹ Fibrates are especially effective for lowering triglyceride concentrations.¹ The addition of ezetimibe to a statin is also an effective option. For example, the combination of rosuvastatin plus ezetimibe significantly increases the likelihood of achieving LDL-C goals.⁸ However, because such combinations are associated with increased costs and might decrease compliance, the use of a fixed-dose statin combination (eg, simvastatin-ezetimibe) is a reasonable option.⁸

Therapeutic Lifestyle Changes

Therapeutic lifestyle changes (TLC) are important elements of treatment for patients with most major components of the metabolic syndrome (eg, dyslipidemia, hypertension, insulin resistance). Therapeutic lifestyle changes have 4 major constituents, as follows:

- smoking cessation
- exercise programs
- nutritional counseling
- weight control

These components can be simplified for patients into an easy-to-remember sound bite: "Eat smart, eat less, and move more." Weight loss achieved through TLC is associated with improvements in diabetes control, hypertension, and lipid parameters.⁹ "Eating smart" also means eating the right kinds of food, and the Mediterranean diet is a good option for decreasing cardiovascular risk.^{10,11} For example, the Lyon Diet Heart Study was a secondary prevention study designed to evaluate whether a Mediterranean-type diet could reduce the rate of recurrence after a first myocardial infarction, compared with a prudent Western-style diet.¹⁰ After a mean follow-up of approximately 4 years, patients in the Mediterranean diet group achieved statistically significant reductions in all-cause and cardiovascular mortality ($P=.01$) and in the combination of recurrent myocardial infarction and cardiac death ($P=.0001$).¹⁰ There was an absolute 32% reduction (14 vs 44 events) for the combined end point of recurrent myocardial infarction and cardiac death.¹⁰ This dramatic reduction in risk exceeds that achieved in statin trials and underscores the value of TLC in the therapeutic regimen.

Figure 1 illustrates the differences between the Mediterranean diet pyramid and the United States Department of Agriculture food pyramid. The most important difference between these pyramids is the increased importance of fish consumption in the Mediterranean pyramid. In addition, there is a big emphasis in the Mediterranean pyramid on increasing the intake of fruits and vegetables. This increase is supported by results from the Nurses' Health Study

Table 1.
Risk Factor Goals From the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial²

Variable	Goal
■ Smoking	Cessation
■ Total dietary fat/saturated fat	<30%/<7% of calorie intake
■ Dietary cholesterol	<200 mg/d
■ LDL-C (primary goal)	60-85 mg/dL
■ HDL-C (secondary goal)	>40 mg/dL
■ Triglycerides (secondary goal)	<150 mg/dL
■ Physical activity	30-45 min of moderate-intensity activity, 5 times per week
■ Body mass index (BMI)	
□ Initial, 25-27	<25
□ Initial, >27.5	10% relative weight loss
■ Blood pressure	<130/85 mm Hg
■ Diabetes	HbA _{1c} <7.0%

Abbreviations: HbA_{1c}, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 2.
Drug Effects of Therapeutic Options for Patients Who Do Not Achieve Lipid Goals With Statin Monotherapy^{1,6,7}

Drug Class	Decrease in LDL-C, %	Decrease in Triglycerides, %	Increase in HDL-C, %
Double statin dose	6	2-12	2% decrease to 2% increase
Ezetimibe	25	14	NS
Niacin	5-25	20-50	15-35
Bile acid sequestrant	15-30	No effect	3-5
Fibrate	5-20	20-50	10-35

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NS, not significant.

and the Health Professionals' Follow-up Study,¹² which evaluated 84,251 women aged 34 to 59 years, followed for 14 years, and 42,148 men aged 40 to 75 years, followed for 8 years. Increased intake of fruits and vegetables was associated with a progressive decrease in the risk for CHD, with a 20% risk reduction in the highest quintile compared with the lowest quintile.¹² Each serving of fruits or vegetables was associated with a 4%

lower risk for CHD, with green leafy vegetables and vitamin C-rich fruits and vegetables having the greatest benefit. Dietary whole grains and fiber have also been demonstrated to reduce CHD events. A pooled analysis of 10 clinical trials found that each 10-g incremental increase in total dietary fiber intake was associated with a 14% decreased relative risk for all coronary events and a 27% decreased risk of coronary death.¹³

Achieving Maximal Reductions in Cardiovascular Risk

Achieving optimal clinical outcomes requires a comprehensive and aggressive therapeutic plan. In other words, pharmacotherapy and TLC both need to be used, with both components being approximately equally important. Failure to implement all the components of the plan will result in failure to achieve maximal reductions in future cardiovascular events.

Despite the conservative recommendations of the National Cholesterol Education Program ATP III, treatment should be considered in all men older than 45 years and all women older than 55 years.¹ Treatment goals should also be aggressive because, as discussed earlier, there is a clear relationship between lower concentrations of LDL-C and improved clinical outcomes. Another major impetus for overcoming the clinical inertia for initiating aggressive therapy is the likelihood that insurance and governmental reimbursement rates in the future will be tied to quality-of-care markers. Physician reimbursements will be affected by the ability of clinicians to get their patients to targets established by national guidelines.

Enhancing the Likelihood of Successful TLC Implementation Questionnaires

Persuading patients to embrace an effective TLC program is challenging; simply telling them to eat better and exercise more is usually not effective. Patient questionnaires are an effective way to increase patient acceptance of TLC programs by allowing the recommendations to be tailored to individual patients. Potential questions to be asked of patients are listed in *Figure 2*.

Patient Education: Clinical Pearls

It is important to discuss the patient's eating schedule and to emphasize the value of eating breakfast. Skipping breakfast drives nighttime eating, which can cause patients to skip breakfast. When breakfast is skipped, lunch becomes breakfast, dinner becomes lunch, and the late-night snack becomes dinner, causing the cycle to continue. The importance of

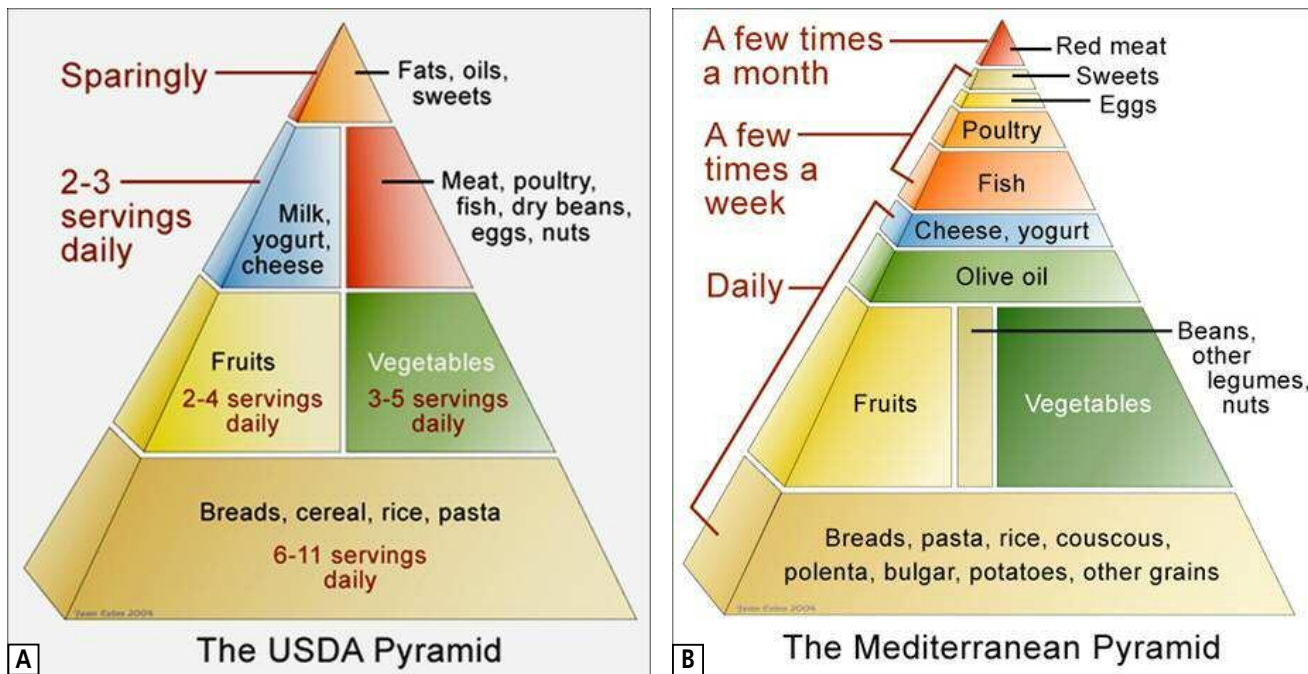


Figure 1. Dietary recommendations from United States Department of Agriculture (USDA) food pyramid (A) vs the Mediterranean food pyramid (B).

breakfast should be stressed—based on my expertise, eating breakfast is clearly associated with weight loss. It is also important to educate patients on the role of visceral obesity in the development of metabolic manifestations. Patients should understand that visceral fat cells are involved in the production of inflammatory proteins and the development of insulin resistance, elevated blood sugar, hypertension, and dyslipidemia and that, based on my expertise, relatively modest reductions in weight (eg, 10%) can result in a 33% reduction in visceral fat and have a very positive effect on the lipid profile and insulin resistance.

Patients also need to understand that the calories consumed in liquids can often be substantial. A dietary diary that lists the time, location, portion size, and calories of everything consumed—including liquids—can be an excellent approach. Downloadable Internet applications (eg, www.myplate.com) can also be used to determine the caloric content of specific food portions.

Specific eating tips for patients include having an apple before lunch, which will decrease the number of calories consumed during the meal. Fiber intake can be increased by sprinkling a

high-fiber breakfast cereal (eg, Fiber One) on low-fat yogurt as a bedtime snack. Patients should also be encouraged to eat only in a designated spot. Refraining from eating in other places can help break a number of bad eating habits.

Explaining the benefits of exercise to patients can help motivate them. Most patients are aware of the benefits of exercise for reducing cardiovascular risk, but emphasizing other benefits can be helpful. The effect of exercise on metabolic abnormalities—rather than as the key to weight reduction—should be stressed. Most patients do not know that, beginning at about age 45 years, they lose almost 1% in muscle mass per year.¹⁴ Patients should also be reminded of the potential benefits of exercise for maintaining cognitive function and reducing the risk of osteoporosis. Furthermore, exercise is helpful for maintaining flexibility and is a good stress reducer.

It is important to discuss pharmacotherapy and TLC at each office visit to underscore the importance of these treatments, and there are a number of specific things patients can be told to help improve their compliance with therapy. Patients should be reminded that their medications are not necessarily pre-

scribed to make them feel better but to reduce their risk potential for heart attack and stroke. The establishment of target levels and the use of “report cards” (with smiley face stickers for good results) are important morale boosters. Relating personal experiences with successful therapy and stressing that the benefits of pharmacotherapy far outweigh the risk are also useful ways to motivate patients. Finally, recognize that cost is an important factor in patient compliance.

Future Therapies

A wide range of pharmacologic therapies are currently under clinical investigation. These include agents that work at different points in cholesterol synthesis (eg, squalene synthase inhibitors), affect intestinal lipid transport (eg, microsomal triglyceride transfer protein inhibitors), stimulate hepatic LDL receptors and potentially amplify several steps in reverse cholesterol transport (eg, thymimetics), or target apolipoprotein B production genetic determinants (eg, antisense oligonucleotides), as well as bile acid transport inhibitors, anti-inflammatory agents, immunizations against oxidized LDL, and selective D prostanoid 1 inhibitors. The

Question	Plan of Action
Are you ready to change your lifestyle?	If not, do not prescribe therapy; rather, focus on increasing the patient's awareness of his or her risk.
Is cost an issue?	If so, low-cost options are available (eg, WeightWatchers, Cardiometabolic Support Network [https://www.cmsnonline.com]).
Do you have time to plan and prepare meals?	If so, any plan is an option; if not, consider meal replacements (eg, Jenny Craig, lean frozen entrees).
Do you eat for emotional reasons?	If yes, Overeaters Anonymous or working with a therapist or registered dietitian will be more effective.
Do you have access to a local track, mall, or gym?	A safe, accessible, and affordable place to be active is important.
Do you have internet access and feel comfortable using it?	Internet weight-loss support programs (eg, LivestrongTM.com, chat rooms, Weight Watchers online, CMSNonline, eDiets) are useful.
Do you prefer working in groups or individually?	For a group setting, programs such as Weight Watchers are good; a registered dietitian may be a good choice for individualized help.

Figure 2. Potential questions physicians can ask patients and corresponding recommendations to more effectively increase patient acceptance of programs related to therapeutic lifestyle changes.

development of these newer agents will increase the available treatment options and may help more patients achieve their lipid goals.

Conclusion

The benefit and importance of lowering LDL-C levels is increasingly clear; therefore, LDL-C target goals should be aggressive. To achieve these goals, multifactorial interventions—not just a pharmacologic approach—are required to realize maximal reductions in cardiovascular risk. However, getting patients to their goals requires a concerted and systematic effort. Patient education is the key to changing behavior and improving compliance with prescribed therapeutic regimens. Questionnaires are a useful tool to help create individualized plans for patients to successfully implement TLC, and using easy-to-remember “sound bites” at every patient visit can also help drive home impor-

tant concepts. By incorporating these approaches into everyday clinical practice, the attainment of target LDL-C concentrations can be improved, helping to optimize clinical outcomes.

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The purpose of this quiz is to provide a convenient means for osteopathic physicians to assess their understanding of the scientific content in the April 2011 supplement to *JAOA—The Journal of the American Osteopathic Association*.

To apply for 2 hours of Category 1-B continuing medical education (CME) credit, AOA members may take this quiz online at <http://www.osteopathic.org/quiz>, where this and other *JAOA* quizzes can be accessed. Quizzes that are completed online will be graded and credited to members' CME activity reports.

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For each of the questions below, place a checkmark in the box provided next to your answer so that you can easily verify your answers against the correct answers, which will be published in the May 2011 issue of the *JAOA*.

1. Current target goals for low-density lipoprotein cholesterol (LDL-C) may lead to _____ of patients at risk for coronary heart disease (CHD) events.

- (a) slight overtreatment
- (b) slight undertreatment
- (c) substantial overtreatment
- (d) substantial undertreatment

2. According to recent evidence, LDL-C concentrations less than which of the following are considered optimal:

- (a) 50 mg/dL
- (b) 60 mg/dL
- (c) 70 mg/dL
- (d) 80 mg/dL

3. The increased risk of CHD in patients with the metabolic syndrome is equivalent to that of patients with which of the following characteristics:

- (a) cigarette smoking
- (b) obesity
- (c) prior myocardial infarction
- (d) prior stroke

4. Based on their proven ability to substantially lower LDL-C and to reduce clinical events, which of the following medications is most appropriate for the treatment of patients with hyperlipidemia:

- (a) bile acid sequestrants
- (b) calcium channel blockers
- (c) niacin
- (d) statins

5. Which of the following therapeutic lifestyle changes is important for most of the major components of the metabolic syndrome:

- (a) exercise
- (b) smoking cessation
- (c) weight control
- (d) all of the above

6. Which of the following tools is an effective way to increase patient acceptance of therapeutic lifestyle change programs:

- (a) discussion of pharmacotherapy and lifestyle at each visit
- (b) food diaries
- (c) specific eating tips
- (d) questionnaires

7. Which of the following patients is likely to be considered at very high risk for CHD:

- (a) a patient with a history of CHD
- (b) a patient with 2 or more risk factors
- (c) a patient with a 10-year Framingham score of greater than 20%
- (d) all of the above

8. According to data from the American Osteopathic Association Clinical Assessment Program, what is the most common physician response to patients with elevated LDL-C levels?

- (a) add a new lipid-lowering medication
- (b) encourage diet and weight loss
- (c) increase dose of the existing lipid-lowering medication
- (d) recheck of the LDL-C value ♦