A 2004 update to the National Cholesterol Education Program's (NCEP) clinical practice guidelines on cholesterol management advises physicians to consider new, more intensive treatment options for people at high and moderately high risk for a heart attack. These options include setting lower treatment goals for LDL ("bad") cholesterol and initiating cholesterol-lowering drug therapy at lower LDL thresholds.

The update,* published in the July 13 issue of *Circulation: Journal of the American Heart Association*, is endorsed by the National Heart, Lung, and Blood Institute (NHLBI), the American College of Cardiology, and the American Heart Association. The document is based on a review of 5 major clinical trials of statin therapy** conducted since the 2001 release of the NCEP's cholesterol guidelines known as the Adult Treatment Panel (ATP) III Report. NHLBI, a component of the National Institutes of Health, coordinates the NCEP.

"The recent trials add to the evidence that when it comes to LDL (bad) cholesterol, lower is better for persons with high risk for heart attack," said NHLBI Acting Director Barbara Alving, M.D. "These trials show a direct relationship between lower LDL cholesterol levels and reduced risk for major coronary events. So, it is important to consider more intensive treatment for people at very high risk," she added.

Major recommendations in the update include:

* **High and Very High Risk:** For high-risk patients, the overall goal remains an LDL level of less than 100 mg/dL. But for people at very high risk, a group that is considered a "sub-set" of the high-risk category, the update offers a new therapeutic option of treating to under 70 mg/dL. For very high-risk patients whose LDL levels are already below 100 mg/dL, there is also an option to use drug therapy to reach the less than 70 mg/dL goal.

For the overall category of high-risk patients, the update lowers the threshold for drug therapy to an LDL of 100 mg/dL or higher and recommends drug therapy for those high-risk patients whose LDL is 100 to 129 mg/dL. In contrast, ATP III set the threshold for drug therapy for high-risk patients at an LDL of 130 mg/dL or higher, and made drug treatment optional for LDL 100 to 129 mg/dL.

The NCEP defines high-risk patients as those who have coronary heart disease, or disease of the blood vessels to the brain or extremities, or diabetes, or multiple (2 or more) risk factors (e.g., smoking, hypertension) that give them a greater than 20 percent chance of having a heart attack within 10 years. Very high-risk patients are those who have cardiovascular disease together with either multiple risk factors (especially diabetes), or severe and poorly controlled risk factors (e.g., continued smoking), or metabolic syndrome (a constellation of risk factors associated with obesity including high triglycerides and low HDL). Patients hospitalized for acute coronary syndromes such as heart attack are also at very high risk.

* **Moderately High-Risk:** For moderately high-risk patients, the goal remains an LDL under 130 mg/dL, but the update provides a therapeutic option to set a lower LDL goal of under 100 mg/dL and to use drug therapy at LDL levels of 100 - 129 mg/dL to reach this lower goal.
For **high-risk or moderately high-risk** patients, the report advises that the intensity of LDL-lowering drug therapy be sufficient to achieve at least a 30 to 40 percent reduction in LDL levels. This can be accomplished by taking statins or by combining lower doses of statins with other drugs (bile acid resins, nicotinic acid, or ezetimibe) or with food products containing plant stanol/sterols.

* **Lower/Moderate Risk:** The update did not revise recommendations for lower risk persons: those with moderate risk (2 or more risk factors plus an under 10 percent risk of a heart attack in 10 years) or those with 0 to 1 risk factor. According to the report, the absolute benefits for people at the lower levels of risk are less clear cut and the recent clinical trials do not suggest a modification of treatment goals and cut points.

The report emphasizes the importance of therapeutic lifestyle changes (TLC -- intensive use of nutrition, physical activity, and weight control) for cholesterol management.

"Lifestyle changes continue to be an essential part of controlling cholesterol. TLC has the potential to reduce cardiovascular risk through several mechanisms beyond LDL lowering," said Scott Grundy, M.D., director of the Center for Human Nutrition at the University of Texas Southwestern Medical Center at Dallas and chair of the NCEP working group that developed the update report.

Like ATP III, the update addresses and emphasizes cholesterol lowering in older persons (age 65 or above). High-risk older persons with established cardiovascular disease are included in the recommendations for intensive LDL-lowering therapy.

"Although the update suggests that physicians use their clinical judgment to determine whether intensive LDL-lowering therapy is warranted in older persons, these people should not be excluded from the benefits of LDL-lowering treatment just because of age," said NCEP Coordinator James Cleeman, M.D.

A comparison of the key modifications in the update with the ATP III recommendations follows:

**ATP III**: The goal for high-risk patients is an LDL of <100 mg/dL.

**Update**: LDL<100 mg/dL is still an overall goal for high-risk patients; for very high-risk patients, a therapeutic option is to treat to <70 mg/dL.

**ATP III**: The threshold for cholesterol-lowering drug treatment for high-risk patients was 130 mg/dL or higher, and cholesterol-lowering drugs for LDL 100 - 129 mg/dL were "optional."

**Update**: The threshold for cholesterol-lowering drug treatment is lowered to 100 mg/dL or above, and it is recommended that patients with LDL 100 - 129 mg/dL receive cholesterol-lowering drug therapy.

**ATP III**: For moderately high-risk persons, the LDL treatment goal is <130 mg/dL and drug therapy is recommended if LDL is 130 mg/dL or higher.

**Update**: A therapeutic option is to set the treatment goal at LDL <100 mg/dL, and to use drug therapy if LDL is 100 - 129 mg/dL to reach the goal.

**ATP III**: Achieving a certain percentage lowering of LDL cholesterol was not emphasized.

**Update**: When LDL-lowering drug therapy is used in high- and moderately high-risk patients, it is advised that the intensity of therapy be sufficient to achieve at least a 30 to 40 percent reduction in LDL levels.

**ATP III**: Initiate therapeutic lifestyle changes (TLC) in patients whose LDL cholesterol numbers are above goal levels.

**Update**: In addition to patients with LDL above goal, any person at high- or moderately high-risk who has lifestyle-related risk factors is a candidate for TLC regardless of LDL level.
According to Dr. Cleeman, the update to the ATP III guidelines is not the final word on LDL goals. There are three ongoing trials in high-risk individuals, which when completed, may lead to a broader recommendation for reaching very low LDL goals in high-risk patients.


**The five clinical trials reviewed by the NCEP working group were: the Heart Protection Study (HPS), the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER), the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial-Lipid Lowering Trial (ALLHAT-LLT), the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA), and the Pravastatin or Atorvastatin Evaluation and Infection-Thrombolysis in Myocardial Infarction (PROVE IT-TIMI 22)

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Statin Use Does Not Reduce Fracture Risk in Postmenopausal Women

'Statins are one of a class of drugs used to lower blood cholesterol levels. Mevacor, Zocor, Pravachol, Lescol and Lipitor are some of the more commonly prescribed statins. 'Statin use does not appear to protect postmenopausal women from fractures, which is contrary to some early reports. The results run counter to a report presented in May that use was found to improve bone density and prevent fractures in older women. Other studies, however, have failed to uncover a beneficial anti-fracture effect for statins.
The current findings are based on a study of 93,716 postmenopausal women who participated in the Women’s Health Initiative Observational Study and were followed for a median of 3.9 years. The subjects included 7846 statin users and 85,870 nonusers.

Regardless of treatment duration, statin therapy did not appear to protect against fractures in the hip, lower arm or wrist, or other site. In fact, at most sites, statin use was actually linked with a slightly increased risk of fracture, noted lead author Dr. Andrea Z. LaCroix, from the Fred Hutchinson Cancer Research Center in Seattle. After adjusting for age and other potential confounders, the authors found no difference in bone density levels at any site between statin users and nonusers.

"A substantial reduction in fracture risk from statin use is statistically incompatible" with the new findings, the researchers conclude. "The cumulative evidence does not warrant the use of statins as agents to prevent or treat osteoporosis," they add. Ann Intern Med 2003;139:97-104.