MEDICINE AND SOCIETY

# A Pragmatic View of the New Cholesterol Treatment Guidelines

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On November 12, 2013, updated guidelines for the treatment of high blood cholesterol levels were released by the American College of Cardiology–American Heart Association (ACC-AHA) Task Force on Practice Guidelines.[1] This update represents the first major guideline revision since the National Cholesterol Education Program released its Adult Treatment Panel III report in 2002.[2] The previous guidelines were widely accepted and applied with relative consistency. In contrast, the new guidelines have already been the subject of controversy, with some observers arguing that some elements of the recommendations are not evidence-based.[3] Nevertheless, these recommendations may have a major effect on the clinical practice of lipid management. We therefore provide here a brief practical summary of the current cholesterol guidelines, indicating the area of dispute.

KEY FEATURES OF THE NEW GUIDELINES

The current guidelines represent a substantial departure from previous recommendations, which
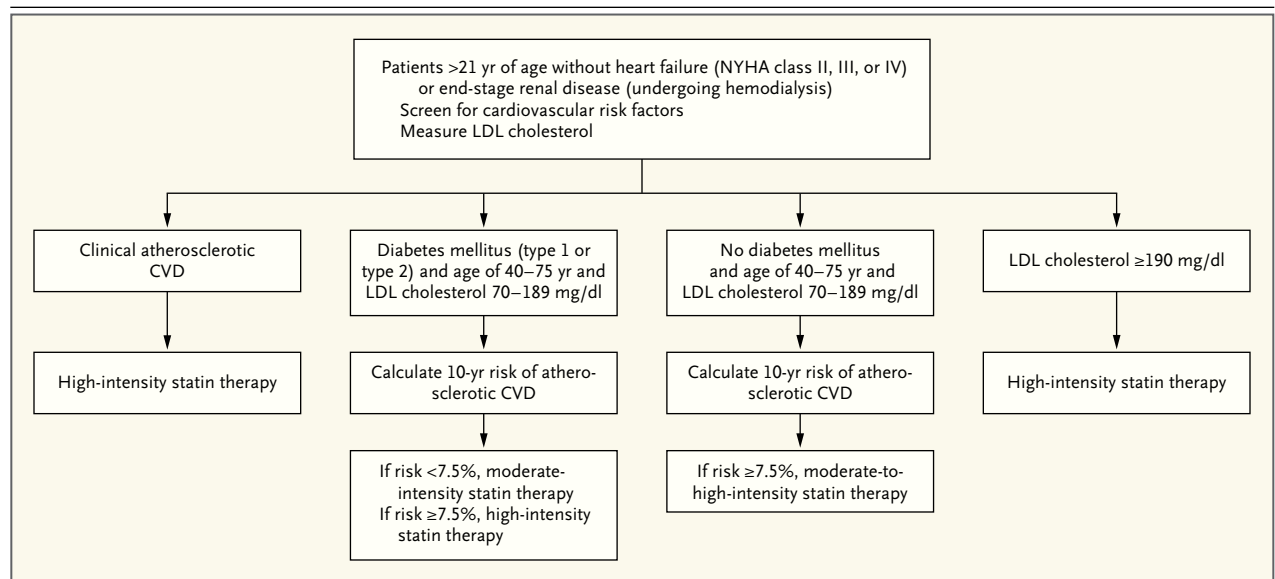
Figure 1. 2013 American College of Cardiology–American Heart Association Guidelines for Use of Statin Therapy in Patients at Increased Cardiovascular Risk.

Persons with clinical atherosclerotic cardiovascular disease (CVD) include those with an acute coronary syndrome and those with a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, or stroke, transient ischemic attack, or peripheral arterial disease that is presumed to be of atherosclerotic origin. High-intensity statin therapy is recommended for most patients meeting these criteria. Patients predisposed to adverse statin effects (including those with impaired renal or hepatic function, other serious coexisting conditions, a history of statin intolerance, concomitant use of drugs affecting statin metabolism, an age of >75 years, or unexplained elevations in alanine aminotransferase levels >3 times the upper limit of the normal range) should use moderate-intensity statin therapy when high-intensity statin therapy would otherwise be recommended. The 10-year risk of atherosclerotic CVD is calculated with the use of the new risk calculator available at http://my.americanheart.org/cvriskcalculator or at http://www.cardiosource.org/science-and-quality/practice-guidelines-and-quality-standards/2013-prevention-guideline-tools.aspx. LDL denotes low-density lipoprotein, and NYHA New York Heart Association.

Table 1. High-Intensity and Moderate-Intensity Statin Therapy, According to 2013 American College of Cardiology–American Heart Association (ACC-AHA) Cholesterol Guidelines.

High-intensity statin therapy

Daily dose lowers LDL cholesterol level by approximately ≥50% on average

Recommended: atorvastatin, 40 to 80 mg; rosuvastatin, 20 to 40 mg

Moderate-intensity statin therapy

Daily dose lowers LDL cholesterol level by approximately 30 to <50% on average

Recommended: atorvastatin, 10 to 20 mg; rosuvastatin, 5 to 10 mg; simvastatin, 20 to 40 mg; pravastatin, 40 to 80 mg; lovastatin, 40 mg; extended-release fluvastatin, 80 mg; fluvastatin, 40 mg twice a day; pitavastatin, 2 to 4 mg

promoted specific lipid-level goals for patients that were dependent on the level of risk. The new guidelines rely heavily on randomized, controlled trials that largely involved fixed doses of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) in patient populations that are at risk for atherosclerotic cardiovascular disease (defined as nonfatal myocardial infarction, death due to coronary heart disease, or nonfatal or fatal stroke).

Using this new approach, the expert panel identified four subgroups of patients for whom the benefit of statins clearly outweighs the risk (Fig. 1).[4] These groups are patients with

1. clinically evident atherosclerotic cardiovascular disease,

2. primary low-density lipoprotein (LDL) cholesterol levels of at least 190 mg per deciliter,

3. type 1 or type 2 diabetes and an LDL cholesterol level of 70 mg per deciliter or higher, or

4. a 10-year risk of atherosclerotic cardiovascular disease of at least 7.5%, according to the new, publicly available, pooled cohort equations,[3] and an LDL cholesterol level of at least 70 mg per deciliter.

In these patient groups, high-intensity statin therapy (designed to reduce LDL cholesterol levels by ≥50%) is generally recommended (Table 1). Moderate-intensity statin therapy (aiming for a reduction of 30 to <50% in LDL cholesterol levels) is recommended for patients who cannot tolerate high-intensity treatment or patients with diabetes and a 10-year risk of atherosclerotic cardiovascular disease of less than 7.5%. Persons receiving statin therapy should be monitored for muscle and hepatic injury and for new-onset diabetes.

An important caveat regarding the new guidelines is that they also identify patients for whom available data do not support statin therapy and for whom no recommendation is made. These groups are patients with

1. an age of more than 75 years, unless clinical atherosclerotic cardiovascular disease is present;

2. a need for hemodialysis; or

3. New York Heart Association class II, III, or IV heart failure.

Finally, the panel noted that it found no evidence to support the use of non-statin cholesterol-lowering drugs, either combined with statin therapy or in statin-intolerant patients.

KEY IMPLICATIONS FOR PRACTITIONERS

Practicing clinicians will see considerable changes in practice patterns as they follow the new cholesterol treatment guidelines, including

1. avoidance of cholesterol-lowering therapy in certain patient groups;

2. elimination of routine assessments of LDL cholesterol levels in patients receiving statin therapy, because target levels are no longer emphasized;

3. avoidance of non-statin LDL cholesterol–lowering agents in statin-tolerant patients;

4. more conservative use of statins in patients older than 75 years of age who have no clinical atherosclerotic cardiovascular disease;

5. diminished use of surrogate markers such as C-reactive protein or calcium scores; and

6. the use of a new risk calculator that is certain to target larger numbers of patients for statin treatment.

We have provided some examples of patients with various risk-factor profiles, along with the consequent recommendations for therapy based on use of the new risk calculator (Table 2).

Ridker and Cook[3] have raised concern about the new risk calculator, which is based on data derived from several large cohort studies. The risk calculator itself has not been prospectively tested for its accuracy in predicting cardiovascular risk. On the basis of comparisons with findings in several large cohorts of persons without current atherosclerotic cardiovascular disease, the new risk calculator appears to overestimate observed risks. The guideline developers, however, note that the cohorts examined by Ridker and Cook may not be appropriate for assessing

Table 2. Case Examples of Application of 2013 ACC-AHA Cholesterol Guidelines.*

High-Intensity Statin Therapy Recommended	Moderate-Intensity Statin Therapy Recommended	Statin Therapy Not Recommended
Black man with low HDL cholesterol level 62 yr of age Total cholesterol, 140 mg/dl HDL cholesterol, 35 mg/dl Systolic blood pressure, 130 mm Hg Not taking antihypertensive medication Not diabetic Nonsmoker Calculated 10-yr risk of CHD or stroke, 9.1% Comment: Total cholesterol is quite low, but age is >60 yr; HDL is also low.	**White woman with diabetes** 48 yr of age Total cholesterol, 180 mg/dl HDL cholesterol, 55 mg/dl Systolic blood pressure, 130 mm Hg Not taking antihypertensive medication Diabetic Nonsmoker Calculated 10-yr risk of CHD or stroke, 1.8% Comment: Patient qualifies because she has diabetes but has a 10-yr risk of <7.5%.	**White man with high cholesterol** 57 yr of age Total cholesterol, 255 mg/dl HDL cholesterol, 45 mg/dl Systolic blood pressure, 110 mm Hg Not taking antihypertensive medication Not diabetic Nonsmoker Calculated 10-yr risk of CHD or stroke, 7.2% Comment: Total cholesterol is high, but patient has no other risk factors.
White male smoker with high cholesterol 42 yr of age Total cholesterol, 250 mg/dl HDL cholesterol, 40 mg/dl Systolic blood pressure, 130 mm Hg Not taking antihypertensive medication Not diabetic Smoker Calculated 10-yr risk of CHD or stroke, 9.0% Comment: Total cholesterol is high, and patient also smokes.	**White man with a history of statin intolerance** 61 yr of age Total cholesterol, 200 mg/dl HDL cholesterol, 35 mg/dl Systolic blood pressure, 145 mm Hg Taking antihypertensive medication Not diabetic Nonsmoker History of previous statin intolerance Calculated 10-yr risk of CHD or stroke, 17% Comment: Patient qualifies because he has a 10-yr risk of >7.5% but has a history of statin intolerance.	**Black male smoker** 42 yr of age Total cholesterol, 180 mg/dl HDL cholesterol, 40 mg/dl Systolic blood pressure, 130 mm Hg Not taking antihypertensive medication Not diabetic Smoker Calculated 10-yr risk of CHD or stroke, 6.3% Comment: Patient smokes but has no other risk factors.
White female smoker with diabetes 50 yr of age Total cholesterol, 180 mg/dl HDL cholesterol, 50 mg/dl Systolic blood pressure, 135 mm Hg Taking antihypertensive medication Diabetic Smoker Calculated 10-yr risk of CHD or stroke, 9.8% Comment: Total cholesterol and HDL are within desirable ranges, but patient has diabetes and hypertension and smokes.	**Elderly black man** 79 yr of age Total cholesterol, 150 mg/dl HDL cholesterol, 40 mg/dl Systolic blood pressure, 120 mm Hg Not taking antihypertensive medication Not diabetic Nonsmoker Calculated 10-yr risk of CHD or stroke, 13.7% Comment: Patient qualifies because he has a 10-yr risk of >7.5% but is >75 yr of age.	**Black woman in her 60s** 64 yr of age Total cholesterol, 190 mg/dl HDL cholesterol, 45 mg/dl Systolic blood pressure, 125 mm Hg Not taking antihypertensive medication Not diabetic Nonsmoker Calculated 10-yr risk of CHD or stroke, 6.9% Comment: HDL cholesterol is low for a woman (<50 mg/dl), but patient has no other risk factors.
Elderly black woman 73 yr of age Total cholesterol, 170 mg/dl HDL cholesterol, 50 mg/dl Systolic blood pressure, 110 mm Hg Not taking antihypertensive medication Not diabetic Nonsmoker Calculated 10-yr risk of CHD or stroke, 9.5% Comment: Total cholesterol is low, but age is >70 yr.	**Black woman taking amiodarone** 54 yr of age Total cholesterol, 182 mg/dl HDL cholesterol, 45 mg/dl Systolic blood pressure, 135 mm Hg Taking antihypertensive medication Not diabetic Smoker Taking amiodarone Calculated 10-yr risk of CHD or stroke, 12.1% Comment: Patient qualifies because she has a 10-yr risk of >7.5% but is taking a drug that affects statin metabolism.	**White woman with hyperlipidemia and hypertension** 46 yr of age Total cholesterol, 230 mg/dl HDL cholesterol, 55 mg/dl Systolic blood pressure, 150 mm Hg Taking antihypertensive medication Not diabetic Nonsmoker Calculated 10-yr risk of CHD or stroke, 2.0% Comment: Total cholesterol is high and blood pressure is not controlled, but patient has no other risk factors.

* CHD denotes coronary heart disease, and HDL high-density lipoprotein.

the accuracy of the risk calculator for two reasons. First, these cohorts include volunteers, who are likely to be healthier than the population as a whole. Second, patients in these cohorts have received modern therapies for reducing cardiovascular risk, thus altering the natural history of the disease.

Overall, the current ACC-AHA recommendations regarding lowering cholesterol levels will move treatment toward statins and deemphasize other agents for a broader range of patients than the previous recommendations did. There is likely to be considerable interest in prospectively testing the new risk calculator in multiple groups

of various ethnic backgrounds to substantiate its relevance as a foundation for the primary prevention of atherosclerotic cardiovascular disease.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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