The New ACC/AHA Cardiovascular Risk Guidelines: Impact and Controversies

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The new American College of Cardiology/American Heart Association (ACC/AHA)2 guidelines for cardiovascular disease (CVD) risk assessment and treatment (1), released >6 months ago, have engendered much controversy. A recent New England Journal of Medicine article (2) has estimated the impact of the new guidelines on the use of statins in the US. Extrapolating from the National Health and Nutrition Examination Survey population, the new guidelines could result in treating approximately 56 million Americans with statins, or 12.8 million more people than would have been treated according to the older Adult Treatment Panel III (ATP-III) guidelines (3). Approximately half the population between the ages of 40 and 75 years would be eligible for statins under the new guidelines, compared with about 37.5% under ATP-III. Given that CVD accounts for about a third of all mortality, and that the lifetime incidence of CVD is about 60%, treating more patients with statins is perhaps reasonable. Furthermore, it is estimated that the new guidelines may reduce CVD by about a half million events every 10 years (2). So why are the new ACC/AHA guidelines controversial?

Three of the four major identified patient groups that could benefit from statins are similar between the ACC/AHA and ATP-III guidelines. The first statin benefit group for both sets of guidelines includes individuals with known CVD. In contrast to the ATP-III guidelines, which recommend statin therapy for individuals with LDL cholesterol (LDL-C) ≥100 mg/dL (2.59 mmol/L), the ACC/AHA guidelines no longer use LDL-C as a statin treatment criterion for this patient group. In the second statin benefit group, which includes individuals with LDL-C ≥190 mg/dL (4.92 mmol/L), the recommended treatment is identical in both guidelines. For the third statin benefit group, which includes those with diabetes, the two guidelines slightly differ in their LDL-C inclusion criteria, LDL-C ≥70 mg/dL (1.81 mmol/L) for ACC/AHA and LDL ≥100 mg/dL (2.59 mmol/L) for ATP-III. Another difference is that in contrast with the ATP-III guidelines, the ACC/AHA guidelines do not recommend statin treatment for as many diabetic patients, including those with type 1 diabetes, until after age 40 years, an issue that has raised concern among endocrinologists.

The major difference between the two guidelines, however, is how the fourth statin benefit group, which includes patients at intermediate risk, is defined. In ATP-III, a risk calculator based on the Framingham population was used to calculate a 10-year risk. Three levels of risk were defined (<10%, 10%–20%, ≥20%) that, along with LDL-C, were used to determine the treatment approach, whether lifestyle changes and/or statin therapy. The risk equation for ACC/AHA is based on a larger pool of individuals from multiple studies and is more representative of the general US population. It includes a separate calculation for African Americans, whose risk was underestimated with the Framingham risk equation. Importantly, the new equation, unlike that of ATP-III, also includes the risk of stroke and hence is called an Atherosclerotic CVD risk calculator. The new risk equation uses parameters similar to those of the old calculator, namely total cholesterol, HDL-C, systolic blood pressure, use of blood pressure medication, diabetes (not in ATP-III risk equation), sex, age, and smoking status, but does not consider family history of premature CVD or any other parameter as a risk modifier. The other difference is that the new risk equation is easier to interpret. Simply, any patient between age 40 and 75 years with a 10-year risk ≥7.5% and a LDL-C ≥70 mg/dL (1.81 mmol/L) is recommended for statin therapy with the new risk equation. Approximately 30% of the overall US population would fall into this category, and because age is such an important determinant of CVD risk, approximately 77% of adults between the ages of 60 and 75 years would now be recommended for statin therapy. Similarly, race and sex have a major impact on CVD risk, which accounts for the fact that the vast majority of African American men over the age of 60 years would now be recommended for statin therapy. Exam-

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Disclaimer: The opinions expressed in this article are from the authors and do not necessarily represent those of the National Heart, Lung, and Blood Institute.

Received May 21, 2014; accepted May 23, 2014.

Previously published online at DOI: 10.1373/clinchem.2014.224964

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2 Nonstandard abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; CVD, cardiovascular disease; ATP, Adult Treatment Panel; LDL-C, LDL cholesterol.
infection of other test populations besides those used in the new guidelines has raised a major concern about whether the new risk calculator is overestimating CVD risk in some groups (4), thereby leading to unnecessary statin use. At this time, it is not known if factors such as ascertainment bias, prevalence of statin use, inclusion of revascularization procedures as a CVD event, and follow-up time could account for differences in the CVD risk estimates between the different population studies.

The new guidelines are also controversial in regard to their impact on laboratory test utilization. Overall, there is less emphasis on using LDL-C for identifying patients at risk, and there is also a major change in how LDL-C is used for monitoring therapy. The ATP-III guidelines had specific LDL-C treatment goals, namely LDL-C <100 mg/dL (2.59 mmol/L) for primary prevention and LDL-C <70 mg/dL (1.81 mmol/L) for secondary prevention. Since the new guidelines were mostly on the basis of randomized clinical trials that used a fixed statin dose, there is limited evidence supporting the clinical value of treating toward a LDL-C goal. The ACC/AHA guidelines instead recommend that patients be treated with either high-intensity statin therapy, which is defined as the dose and type of statin expected to reduce LDL-C to less than 50% of baseline value, or moderate-intensity statin therapy (30 to <50% LDL-C reduction) for those with diabetes and low CVD risk, moderate-risk patients (5% to <7.5% risk) who opt for statin treatment, or any patient who cannot tolerate high-dose statins. The new guidelines discourage, in most cases, the use of alternative lipid-lowering drugs. This is, in part, because of recent randomized clinical trials that have failed to show clinical outcome benefits for drugs such as niacin, ezetimibe, and fibrates, although many of these trials have been faulted for their design. Many have expressed concern, however, that simply using percentage LDL-C reduction as a goal may still leave many patients at high residual risk, if they start out with a very high baseline LDL-C.

In terms of monitoring, the new guidelines recommend that a fasting lipid panel (total cholesterol, triglycerides, HDL-C, and a calculated LDL-C) be performed 4–12 weeks after starting statin therapy and then every 3–12 months thereafter. Alanine aminotransferase should also be periodically monitored for assessing liver toxicity, but creatine kinase is no longer routinely recommended unless the patient is suspected of having myopathy or has a history of statin intolerance. Because of the recent finding that statin therapy may slightly increase the risk of diabetes, physicians should be alert to the development of diabetes. Patients at low CVD risk should be screened with a fasting lipid panel every 4–6 years. Unfortunately, the new guidelines did not address the issue of test accuracy or standardization, which is still an important problem that can negatively impact the effectiveness of CVD risk assessment (5).

For the most part, the new guidelines were either neutral or deferred making a recommendation on the use of alternative or emerging cardiovascular risk biomarkers. Unlike ATP-III, triglycerides and non-HDL-C are no longer used to identify a subset of hypertriglyceridemic patients who may require a different therapy, such as fibrates, or different treatment goals. On the basis of only expert opinion, owing to limited evidence, ACC/AHA states that high-sensitivity C-reactive protein >2 mg/L may be considered as a criterion for selecting a patient for statin therapy, who may otherwise not fall into 1 of the 4 statin benefit groups. Similarly, on the basis of expert opinion, family history, ankle brachial index, and coronary artery calcium score can also be considered. No opinion, pro or con, was made for apolipoprotein B or albuminuria, and many other old and new markers, such as lipoprotein(a) and LDL particle number, were not fully evaluated. Articles from only a limited number of studies (n = 13) were used in the development of the CVD biomarker guidelines, which has raised concern about whether the selection criteria were too rigorous in the evidence-collection part of the process.

Another point of controversy pertains to patients who may be excluded from statin therapy under the new guidelines. Although ACC/AHA overall would treat more people with a statin, many middle-aged individuals with only moderately increased LDL-C would no longer be candidates for treatment. For example, a 36-year-old obese white man with systolic blood pressure of 120 mmHg, a strong family history of premature CVD, total cholesterol of 210 mg/dL (5.44 mmol/L), HDL-C of 35 mg/dL (0.9 mmol/L), and LDL-C of 165 mg/dL (4.27 mmol/L) would not be recommended for statin therapy with the ACC/AHA guidelines but would be with ATP-III. The new risk equation is applicable only for individuals between the ages of 40 and 75 years and does not include family history. This particular patient’s 10-year risk would not exceed 7.5% until 20 years later when he reaches the age of 56 years, although his lifetime risk is estimated at 46%. Because we know that it takes several decades for atherosclerosis to develop and manifest clinically, many would argue that it would be best to treat this patient early on to prevent him from developing atherosclerosis and getting a myocardial infarction before the age of 56 years. The new guidelines do state that patient preference and other extenuating circumstances, such as family history, can be considered in making any treatment decision, but do not provide more specific guidance on this issue. The ACC/AHA
guidelines also state, on the basis of relatively weak evidence, that it may be reasonable to consider treating patients 40–75 years of age with a 5%–7.5% 10-year risk and LDL-C 70–189 mg/dL (1.81–4.9 mmol/L) with moderate-intensity statin therapy. This particular patient, however, would not cross this threshold until age 51 years by the new calculator.

On balance, the new ACC/AHA guidelines are estimated to reduce more CVD events than ATP-III (2), so they are viewed as an important advance. The ACC/AHA guidelines are also easier to follow, which could lead to better compliance. Undoubtedly, there will also be updates to the new guidelines, such as addition of risk equations for Hispanics and possibly other ethnic groups. Finally, it is important to emphasize that the identification of a patient at risk for CVD is only a starting point. Ultimately, it is a discussion between the patient and the physician that is pivotal in deciding the course of any therapy. During this time, they can weigh together the risks and benefits of statin therapy, as well as discuss lifestyle changes. The physician can then practice the “art of medicine” in creating an optimized personal treatment plan. As Dr. William Osler once said, “The good physician treats the disease; the great physician treats the patient who has the disease.”

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

Authors’ Disclosures or Potential Conflicts of Interest: Upon manuscript submission, all authors completed the author disclosure form. Disclosures and/or potential conflicts of interest:

Employment or Leadership: None declared.
Consultant or Advisory Role: None declared.
Stock Ownership: None declared.
Honoraria: None declared.
Research Funding: This work was supported by the Intramural Research program of the NIH, National Heart, Lung, and Blood Institute.
Expert Testimony: None declared.
Patents: None declared.

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