Medical News & Perspectives

New Cholesterol Guidelines Personalize Risk and Add Treatments

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Last November, more than 15 000 clinicians alighted on Chicago for the American Heart Association (AHA) Scientific Sessions, the group's annual flagship conference. The meeting featured the release of the federal government's physical activity guidelines and results from several high-profile clinical trials, like VITAL and REDUCE-IT and DECLARE-TIMI 58. The announcements also included new cholesterol clinical practice guidelines from the AHA, the American College of Cardiology (ACC), and several other organizations, the first update since 2013.

According to the guidelines, people with clinical atherosclerotic cardiovascular disease (ASCVD) should use maximally tolerated statin therapy to lower their low-density lipoprotein cholesterol (LDL-C) levels by at least 50%. But the big news in secondary prevention was the addition of nonstatin drugs in combination with statin therapy for certain patients, including those who are at very high risk of ASCVD, which includes a history of multiple major ASCVD events or 1 major event and multiple high-risk conditions.

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These patients who also have LDL-C levels of 70 mg/dL or higher despite maximally tolerated statins can be considered for ezetimibe, which prevents the intestines from absorbing cholesterol. For those whose LDL-C levels still don't drop lower than the 70 mg/dL threshold or whose non–HDL-C levels are 100 mg/dL or higher, adding a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor is an option, although the high cost of these drugs is an important consideration.

Physicians can also consider adding ezetimibe or a PCSK9 inhibitor to high-intensity statin therapy for primary prevention for patients with very high cholesterol—LDL-C levels of 190 mg/dL or higher—that doesn't drop lower than 100 mg/dL.

According to *JAMA* Senior Editor Philip Greenland, MD, a professor of cardiology at the Northwestern University Feinberg School of Medicine in Chicago, this year's update was met with considerably less controversy than the last incarnation, which deemphasized LDL-C treatment targets and introduced the AHA/ACC ASCVD risk calculator.

In the new guidelines, statin treatment targets are back for both primary and secondary prevention. Patients whose 10-year risk of ASCVD is 20% or more should try to reduce LDL-C levels by at least 50%, the same goal as for people with clinical ASCVD. Those with more intermediate risk should aim for at least a 30% decrease.

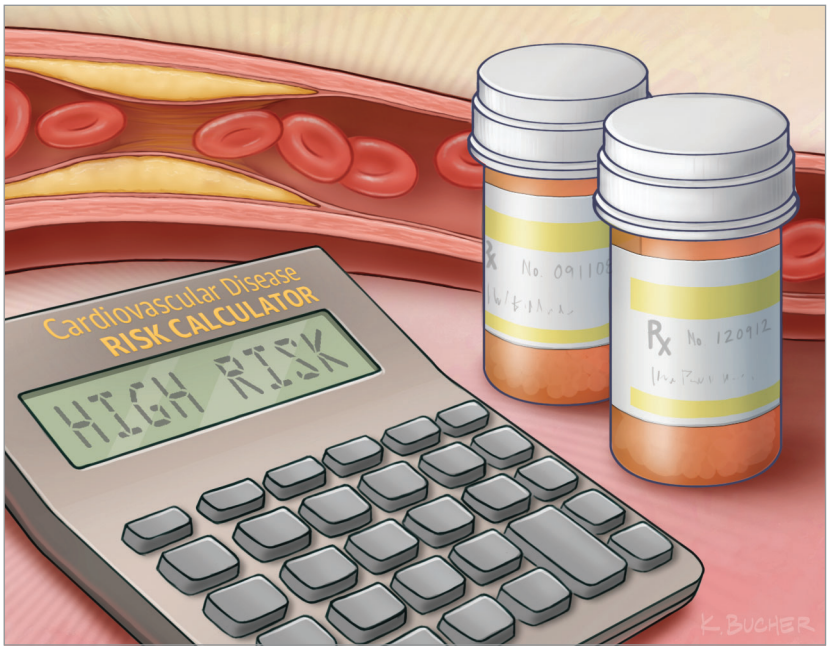
Personalizing Risk in Primary Prevention

When the 2013 guidelines were released, the risk calculator was swiftly criticized for overestimating risk in several populations, potentially leading to overtreatment with statins. Since then, the calculator's risk-prediction algorithm—known as the pooled cohort equations—has been further validated, putting to rest some objections, Greenland said. A growing understanding among the clinical community that guidelines aren't hard-and-fast rules has also quieted the debate, he said.

The updated guidelines and a companion AHA/ACC special report on risk assessment tools acknowledge that the calculator estimates risk for an average person in the US population and may overestimate—or underestimate—a given person's chances of having an ASCVD event within 10 years.

At the conference, researchers presented at least 2 alternate calculators, including 1 using machine learning that more accurately estimated risk in a specific cohort than did the ACC's calculator. A recent report in *JAMA Cardiology* also found that using long-term cumulative systolic blood pressure instead of single blood pressure measurements could make the pooled cohort equations more accurate.

Greenland emphasized that no risk calculator is perfect: "Doctors have hunches about patients based on a variety of clinical factors, and what these calculators are intended to do is to make your hunch a little more accurate," he said. For



now, the guidelines reaffirm the use of the pooled cohort equations for the US population, and state that they should be used as a "starting point, not as the final arbiter, for decision-making in primary prevention of ASCVD."

To address the uncertainties and to help provide more information to patients who are on the fence about statins, there's new advice for people with LDL-C levels of 70 mg/dL or higher and a 10-year ASCVD risk of 7.5% through 19.9%.

Among these intermediate-risk patients, "risk-enhancing" factors can tip the decision-making scales in favor of statins, according to Scott M. Grundy, MD, PhD, of the University of Texas Southwestern Medical Center, who chaired the guideline writing committee.

These factors include a family history of premature ASCVD, persistently elevated LDL-C levels or triglycerides, metabolic syndrome, chronic kidney disease, a history of preeclampsia or premature menopause, chronic inflammatory disorders, and high-risk ethnicities (like South Asian). If measured, apolipoprotein B, high-sensitivity C-reactive protein, ankle-brachial index, and lipoprotein(a) are additional risk factors to consider. "There are abundant epidemiologic data showing that risk-enhancing factors correlate significantly with ASCVD," Grundy said.

If there's still uncertainty about patients at intermediate risk, clinicians can also use coronary artery calcium (CAC) testing. Although no trial has been done to show that CAC testing improves selection of patients for treatment, "it's the best test for helping define risk beyond the standard risk factors," Greenland said.

A CAC score of 0 allows a delay of statin treatment except in cigarette smokers, patients with diabetes, and those with a family history of premature ASCVD. "Low levels of coronary calcium defer to clinical judgment, whereas high levels strongly support use of statin therapy," Grundy said.

Another new feature of the guidelines is that clinicians are now encouraged to have a comprehensive risk discussion with patients before initiating statin therapy, which should include a consideration of potential adverse effects and drug interactions, costs, and patient preferences and values. "The guideline places importance on a process of shared decision-making," said *JAMA* Deputy Editor Gregory Curfman, MD.

Meanwhile, a new AHA scientific statement released in December may help quell patient fears about statins. The report found that statin-related muscle aches and pains, the drugs' most common adverse effects, occur in no more than 1% of patients. The statement concluded that statins have a low risk of adverse effects and that, for most people, their benefits outweigh the risks. ■

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