

## Medical News

## What to Know About the New Lipid Guidelines

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When it comes to “bad” cholesterol, “lower is better for longer,” says Roger Blumenthal, MD, chair of the writing committee behind new consensus guidelines for management of dyslipidemia in the US.

The updated [recommendations](#) from the American College of Cardiology (ACC) and the American Heart Association (AHA), which replace the groups’ cholesterol management



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guidance from 2018, emphasize earlier screening and intervention to reduce the risk of accumulated exposure to high levels of low-density lipoprotein cholesterol (LDL-C). “Primordial” prevention of atherosclerotic cardiovascular disease (ASCVD) should start early and continue throughout life, the guidelines say, with a heart-healthy diet, regular physical activity, a normal weight, good sleep, stress management, and avoidance of tobacco products.

Among many other reworkings, the recommendations adopt a new ASCVD risk calculator, recalibrate risk categories, push LDL-C targets lower, and advise one-time lipoprotein(a) (Lp[a]) testing for all patients. Taken together, the revised guidelines are “practice changing,” said cardiologist Neil J. Stone, MD, a professor at Northwestern Feinberg School of Medicine who led the 2013 version and vice chaired the 2018 writing committee. “New information has now allowed these guidelines to be called *dyslipidemia*,” he said, “putting emphasis not just on blood cholesterol but also on triglycerides and Lp(a). That’s a big step forward.”

Here are some of the most important takeaways.

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### Test and Treat Earlier

In recognition that cumulative exposure to elevated LDL-C levels increases heart disease risks, the new guidelines recommend lipid profiling in adults starting at age 19 years. The panel should be repeated at least every 5 years for young adults and more fre-



quently for those with additional ASCVD risk factors. As for lipid-lowering therapy, the guidelines advise starting statins at age 30 for patients with LDL-C levels at or above 160 mg/dL, a strong family history of premature ASCVD, or a high 30-year risk of ASCVD—even if their 10-year risk is low.

“If you continually refine your crystal ball so that you can more accurately identify high-risk individuals earlier in life and if you’re able to disrupt the disease process early, you’re more likely to see benefit for those patients compared to waiting,” said JAMA Associate Editor Pradeep Natarajan, MD, MMSc, a coauthor of the guideline and director of preventive cardiology at Massachusetts General Hospital.

Even before adulthood, all children should be screened with a lipid panel between the ages of 9 to 11 years to identify familial hypercholesterolemia (FH) and other lipid disorders early, according to the guidelines. For children who have close relatives with premature ASCVD, severe hypercholesterolemia, or FH, it’s reasonable to obtain a lipid profile as early as 2 years of age.

### Adopt the PREVENT Risk Calculator

For primary prevention of ASCVD in adults, the guidelines lean into the CPR concept introduced with the prior version. The model advises clinicians to calculate 10-year ASCVD risk, personalize the specific patient’s estimated risk by considering risk-enhancing factors, and possibly reclassify their risk with a coronary artery calcium (CAC) score and then reassess treatment recommendations.

As with last year’s [updated blood pressure guidelines](#), the lipid guidelines replace the pooled cohort equations (PCEs) with the AHA’s newer and more accurate PREVENT (Predicting Risk of CVD Events) risk calculator, [released in 2023](#). Guideline coauthor Donald Lloyd-Jones, MD, noted that clinicians should use the ASCVD-specific version of the PREVENT calculator to estimate atherosclerotic heart disease risk. (The other versions estimate total CVD risk, which also includes heart failure, or heart failure risk alone). For now, health professionals can find the [PREVENT online calculators](#) on the AHA site, but integration into Epic and other

electronic health record systems is coming soon, Lloyd-Jones said.

In another major shift, risk estimation using the new calculator should begin earlier, at age 30 years instead of 40. And for people in their 30s through 50s, it should include estimation of 30-year risk, which the PREVENT tool includes. For patients whose young age or female sex keeps their 10-year risk low, knowing that their longer-term risk is elevated can help spur beneficial lifestyle modifications, the guideline authors say.

Lloyd-Jones, a professor and chief of the section of preventive medicine at Boston University Chobanian & Avedisian School of Medicine, said he hopes the changes will widen the perspective of clinicians and patients—especially young ones—to think beyond just the 10-year risk. “We know this is a life course disease, that risk is accruing in our teens, 20s, and 30s, and those are the things that ultimately will lead to events in our 40s, 50s, 60s, and beyond.”

### Use New Risk Category Ranges

Using the PREVENT-ASCVD calculator, the 10-year risk categories have been recalibrated:

- Low risk: less than 3% (previously less than 5% based on the PCEs)
- Borderline risk: 3% to less than 5% (previously 5% to less than 7.5%)
- Intermediate risk: 5% to less than 10% (previously 7.5% to less than 20%)
- High risk: 10% or higher (previously 20% or higher)

For primary prevention, the guidelines say lipid-lowering therapy can be considered for patients with borderline risk based on PREVENT-ASCVD and should be considered for those with intermediate risk.

“Starting at 5%, the evidence is really there that these are groups of people that will benefit” from statins, Lloyd-Jones said. “We are much more likely to prevent a heart attack or stroke than we are to see any adverse effect from starting drug therapy.”

### Set Cholesterol Goals

Although the recommendations continue to stress the importance of percentage reductions in LDL-C levels, specific LDL-C goals are fully back in the new guidelines, thanks to informative findings from recent clinical trials that targeted specific numbers. The targets are based on accumulating evidence that

lower is better for reducing risk. The LDL-C goals are

- less than 100 mg/dL for patients without clinical ASCVD who have low, borderline, or intermediate risk based on PREVENT-ASCVD
- less than 70 mg/dL for patients without clinical ASCVD who have high risk based on PREVENT-ASCVD and for the small number of patients with clinical ASCVD who do not have very high risk
- less than 55 mg/dL for most patients with clinical ASCVD

The recommendations also incorporate guidance for lipid-lowering therapies that can be added on to statins, including the newer drugs ezetimibe, bempedoic acid, and proprotein convertase subtilisin/kexin type 9 (PCSK9) monoclonal antibodies.

“I think it’s important to remember, cardiovascular disease is still the number one cause of death and disability in the world and in this country,” Lloyd-Jones said. “Diet and exercise are absolutely critically important, and we don’t abandon those when we start drug therapy, but a lot of patients can’t get there with diet and exercise.”

### Test Lp(a) Once for Everyone

“The big, exciting news is that the science base now is strong enough that Lp(a), which was considered a risk-enhancing factor and still is, now should be measured in everyone, because some people have extraordinarily high levels and we would not be able to guess it,” said Stone, who served as a peer reviewer on the new guidelines.

Elevated Lp(a) levels are associated with enhanced cardiovascular risks. Patients with Lp(a) levels at or above 125 nmol/L (50 mg/dL) have a 1.4-fold increased risk of ASCVD, and the risk doubles at values at or above 250 nmol/L (100 mg/dL) and quadruples at values at or above 430 nmol/L (180 mg/dL).

That’s why the guidelines now recommend Lp(a) testing for all patients to identify those at greater risk of ASCVD. (Repeating the test generally isn’t necessary because Lp[a] levels are mostly genetically determined and tend to be stable over time.) Although Lp(a)-lowering treatments aren’t yet available, patients with elevated levels should have more intense LDL-C-lowering treatments and tighter control of additional risk factors.

Trials testing the effects of lowering Lp(a) levels on heart attacks and strokes are expected to start reporting out later this year. Depending on the results, an update to the

guidelines could come as soon as next year. Going forward, individual sections will be updated annually as needed. “It really is a living document that we will plug and play when there’s new evidence that merits a change,” Lloyd-Jones said.

### Consider ApoB Testing and CAC Scoring

The updated guidelines are more supportive of apolipoprotein B (apoB) testing and CAC scoring to help refine risk and guide treatment in certain patients.

“ApoB adds real power to a clinician’s ability to predict future events and whether or not there’s a potential for genetic abnormality,” Stone explained. A patient’s apoB level represents their total number of atherogenic lipoprotein particles—LDL, very-low-density lipoprotein, and Lp(a)—and it’s not affected by fasting.

The guidelines note that apoB testing can help identify residual lipoprotein-related risk in patients who have met their LDL-C and non-high-density lipoprotein cholesterol goals, and that it can be particularly useful in those with ASCVD, elevated triglycerides, type 2 diabetes, or **cardiovascular-kidney-metabolic (CKM) syndrome**.

Another useful indicator is the CAC score. “It’s the best tiebreaker we have,” said Blumenthal, who is a professor of cardiology at Johns Hopkins Hospital in Baltimore and director of the Johns Hopkins Ciccarone Center for the Prevention of Heart Disease.

The guidelines here focus on men aged 40 years or older and women aged 45 years or older—the ages at which CAC typically emerges—who are at intermediate risk or at borderline risk with no prior ASCVD. If it’s unclear whether they should initiate lipid-lowering therapy, the recommendation is to use a CAC score to further stratify their risk and help guide the decision. The scores can also be helpful for refining treatment goals and determining whether to intensify lipid-lowering therapy in patients with intermediate or high risk with no prior ASCVD. Even incidental findings of coronary artery calcification on general chest computed tomography should be considered, according to the guidance.

### Factor in New Risk Enhancers

The 2018 cholesterol guidelines introduced the idea of risk-enhancing factors, and the new version adds to the list of these considerations, which can be especially infor-

mative for patients with borderline 10-year ASCVD risk.

Of note, the guidelines expand the reproductive risk markers that should be factored in when assessing ASCVD risk, including early menarche, early menopause before the age of 45, polycystic ovary syndrome, and adverse pregnancy outcomes such as hypertensive disorders of pregnancy, gestational diabetes, and preterm delivery. "Clinicians really need to be fastidious and consistent about asking about those historical features," Lloyd-Jones said.

Additionally, Filipino ethnicity joins South Asian ethnicity as a higher-risk ancestry, based on recent research. "More and more data had accrued showing that people of Filipino descent seem to have a significantly higher risk of cardiovascular disease," Blumenthal said.

Other risk enhancers include having a parent or sibling with premature heart disease or having CKM syndrome, elevated Lp(a), persistently elevated LDL-C or triglyceride levels, high polygenic risk (if measured), elevated high-sensitivity C-reactive protein levels (if measured), or a chronic inflammatory condition. According to Natarajan, there's a much stronger recommendation to ascertain that inflammation. "Calling that out is critical because that's not part of the standard risk assessment in cardiology and primary care," he said.

### Use Lipid-Lowering Therapy in Chronic Kidney Disease and HIV

In addition to preexisting recommendations for diabetes, the guidelines now recommend that all patients aged 40 to 75

years with stage 3 or 4 chronic kidney disease or HIV should be prescribed statins for primary prevention, regardless of their LDL-C levels. In patients older than 75 years with these conditions, lipid-lowering therapy can be considered alongside lifestyle interventions to reduce cardiovascular risks. Blumenthal noted that for HIV, the persuasive data come from the REPRIEVE trial, which found that pitavastatin decreased cardiovascular events by 35% in this population.

### For High Triglycerides, Consider Dietitians

For patients with high triglycerides, although a fibrate drug or icosapent ethyl may be added on, statins are still the mainstays of pharmacotherapy. "We still want to have a statin on board," Blumenthal said.

He noted that lifestyle modification remains the gold standard for trying to reduce triglycerides. To aid in this, the guidelines now recommend that clinicians refer patients with fasting triglycerides at or above 1000 mg/dL or 150 to 999 mg/dL and features of CKM syndrome to a registered dietitian nutritionist for counseling. Nutrition professionals can help these patients improve their lipoprotein levels and reduce their risk of pancreatitis.

The authors acknowledge that insurance coverage for medical nutrition therapy provided by registered dietician nutritionists is lacking in the US. "By getting recommendations like this in the guidelines, we're trying to move the needle and get more payers to pay for something that's incredibly helpful to patients," Lloyd-Jones said.

### Know the Data on Dietary Supplements

For the first time, dietary supplements such as nonprescription fish oil are directly addressed. The guidelines do not recommend the use of supplements to lower LDL-C or triglycerides in people with ASCVD. They cite limited and inconsistent data and lack of benefit in randomized clinical trials.

"We have tons of evidence that supplements do nothing," Lloyd-Jones said. "It's not the absence of evidence, it's the evidence of absence of benefit. They're a distraction from where we should be focused, which is on diet, on healthy lifestyle, and for patients who need it, medication." ■

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