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Experts Reshape Treatment Guide for Cholesterol

By GINA KOLATA

The nation's leading heart organizations released new guidelines on Tuesday that will fundamentally reshape the use of cholesterol-lowering statin medicines, which are now prescribed for a quarter of Americans over 40. Patients on statins will no longer need to lower their cholesterol levels to specific numerical targets monitored by regular blood tests, as has been recommended for decades. Simply taking the right dose of a statin will be sufficient, the guidelines say.

The new approach divides people needing treatment into two broad risk categories. Those at high risk because, for example, they have diabetes or have had a heart attack should take a statin except in rare cases. People with extremely high levels of the harmful cholesterol known as LDL — 190 or higher — should also be prescribed statins. In the past, people in these categories would also have been told to get their LDL down to 70, something no longer required.

Everyone else should be considered for a statin if his or her risk of a heart attack or stroke in the next 10 years is at least 7.5 percent. Doctors are advised to use a new risk calculator that factors in blood pressure, age and total cholesterol levels, among other things.

"Now one in four Americans over 40 will be saying, 'Should I be taking this anymore?' " said Dr. Harlan M. Krumholz, a cardiologist and professor of medicine at Yale who was not on the guidelines committee.

The new guidelines, formulated by the American Heart Association and the American College of Cardiology and based on a four-year review of the evidence, simplify the current complex, five-step process for evaluating who needs to take statins. In a significant departure, the new method also counts strokes as well as heart attacks in its risk calculations, a step that will probably make some additional people candidates for the drugs.

It is not clear whether more or fewer people will end up taking the drugs under the new guidelines, experts said. Many women and African-Americans, who have a higher-

than-average risk of stroke, may find themselves candidates for treatment, but others taking statins only to lower LDL cholesterol to target levels may no longer need them.

The previous guidelines put such a strong emphasis on lowering cholesterol levels by specific amounts that patients who did not hit their target levels just by taking statins often were prescribed additional drugs like Zetia, made by Merck. But the new guidelines say doctors should no longer prescribe those extra medicines because they have never been shown to prevent heart attacks or strokes.

Zetia has been viewed with increasing skepticism in recent years since studies showed it lowered LDL cholesterol but did not reduce the risk of cardiovascular disease or death. Still, it is among Merck's top-selling drugs, earning $2.6 billion last year. Another drug, Vytorin, which combines Zetia with a statin, brought in $1.8 billion in 2012, according to company filings. And in May, Merck won approval for another drug, Liptruzet, which also contains the active ingredient in Zetia and a statin, a development that surprised many cardiologists because of questions about its effectiveness.

The new guidelines are part of a package of recommendations to reduce the risk of heart attack and stroke that includes moderate exercise and a healthy diet. But its advice on cholesterol is the flash point, arousing the ire of critics who say the authors ignored evidence that did not come from gold-standard clinical trials and should also have counted less rigorous, but compelling, data.

For example, Dr. Daniel J. Rader, the director of the preventive cardiovascular medicine and lipid clinic at the University of Pennsylvania, points to studies of people with genes giving them low LDL levels over a lifetime. Their heart attack rate is greatly reduced, he said, suggesting the benefits of long-term cholesterol reduction.

Committee members counter his view, saying that cholesterol lowered by drugs may not have the same effect.

Critics also question the use of a 10-year risk of heart attack or stroke as the measure for determining who should be treated. Many people will have a lower risk simply because they are younger, yet could benefit from taking statins for decades to keep their cholesterol levels low, they say.

Dr. Rader and other experts also worry that without the goad of target numbers, patients and their doctors will lose motivation to control cholesterol levels.

Experts say it is still unclear how much the new guidelines will change clinical practice. Dr. Rader suspects many cardiologists will still strive for the old LDL targets, at least for

patients with heart disease who are at high risk. "They are used to it and believe in it," he said.

Dr. Steven E. Nissen, a cardiologist at the Cleveland Clinic, said he thought it would take years for doctors to change their practices.

The process of developing the guidelines was rocky, taking at least twice as long as in the past. The National Heart, Lung and Blood Institute dropped out, saying that drafting guidelines was no longer part of its mission. Several committee members, including Dr. Rader, also dropped out, unhappy with the direction the committee was going.

The architects of the guidelines say their recommendations are based on the best available evidence. Large clinical trials have consistently shown that statins reduce the risk of heart attacks and strokes, but the committee concluded that there is no evidence that hitting specific cholesterol targets makes a difference. No one has ever asked in a rigorous study if a person's risk is lower with an LDL of 70 than 90 or 100, for example.

Dr. Neil J. Stone, the chairman of the committee and a professor of preventive cardiology at Northwestern University's Feinberg School of Medicine, said he was surprised by what the group discovered as it delved into the evidence. "We deliberated for several years," he said, "and could not come up with solid evidence for targets."

Dr. Nissen, who was not a member of the committee, agreed. "The science was never there" for the LDL targets, he said. Past committees "made them up out of thin air," he added.

The Department of Veterans Affairs conducted its own independent review and came to the same conclusion. About a year ago, the department, the nation's largest integrated health care system, dropped its LDL targets, said Dr. John Rumsfeld, the V.A.'s national director of cardiology.

"It is a shift," he acknowledged, "but I would argue that it is not a radical change but is a course correction."

Dr. Paul M. Ridker, the director of the center for cardiovascular disease prevention at Brigham and Women's Hospital, in Boston, said he worried the new guidelines could easily lead to overtreatment. An older man with a low LDL level who smokes and has moderately elevated blood pressure would qualify for a statin under the new guidelines. But what he really needs is to stop smoking and get his blood pressure under control.

Dr. Stone said he hoped doctors would not reflexively prescribe a statin to such a patient. Doctors are supposed to talk to their patients and realize that, with a man like the one Dr.

Ridker described, the real problem was not cholesterol.

"We are taking people out of their comfort zone," Dr. Stone said. "Instead of being reassured that reaching this number means they will be fine, we are asking, 'What is the best therapy to do the job?' "

Katie Thomas contributed reporting.