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New Cardiovascular Disease Risk Calculator Could Eliminate the Need for Statins for Millions

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Roughly 45 million people in the US take statins, the cholesterol-lowering medications used to prevent cardiovascular disease. Many patients without heart disease, though, are taking them based on older estimates of their risk of developing it. Now, research suggests that millions of them may no longer qualify for statins because of a newer prediction model that estimates the 10-year risk of atherosclerotic cardiovascular disease (ASCVD).

The researchers compared risk estimates for ASCVD using the older pooled cohort equations (PCEs), released in 2013, and the new Predicting Risk of Cardiovascular Disease Events (PREVENT) equations. PREVENT, developed by the American Heart Association (AHA) and released in 2023, marks a major revision from the PCEs because it's based on newer data from a much larger and more diverse sample of people. It also accounts for additional health conditions, such as kidney and metabolic diseases, when determining the 10- and 30-year chances of both ASCVD and heart failure.

The new study, published in *JAMA Internal Medicine*, was based on data from 3785 US adults who participated in the National Health and Nutrition Examination Study (NHANES) from 2017 to March 2020, roughly 21% of whom reported taking statins. Data were weighted to be more representative of the population to produce national estimates.

When they compared the results from both calculators, the researchers found that the PREVENT model lowered the average ASCVD risk estimates across all demographic groups by roughly half, with the largest differences among Black people and among older adults.

Nationally, that would cut the number of people eligible to take statins for primary prevention from about 45.4 million to about 28.3 million. This includes about 4.1 million currently taking the drugs, setting up important but potentially challenging conversations with patients, said study lead author Timothy S. Anderson, MD, MAS, an assistant professor of medicine at the University of Pittsburgh and the Pittsburgh Veterans Administration.

Comparing the 2 Models

Overall, the average 10-year estimated ASCVD risk was 8% using the PCEs but only 4.3% using the PREVENT equations, the researchers found. The differences between the calculators' risk estimates were greatest for Black adults (10.9% vs 5.1%, respectively) and those aged 70 to 75 years (22.8% vs 10.2%).

These findings parallel the AHA's assessment of how well the 2 models reflect the prevalence and distribution of ASCVD in recent years, said Sadiya S. Khan, MD, MSc, chair of the AHA committee that developed the PREVENT equations. When the AHA's researchers applied the PCEs and the PREVENT model to more recent patient datasets, the PCEs overestimated ASCVD risk by about a factor of 2, which is largely consistent with the current study findings, she noted.

"Some of the data for the PCEs comes from the 1990s or earlier," Khan said, explaining the difference. "We know that rates of ASCVD death have decreased since then." In part, this could be because more people are using preventive measures and therapies, including statins.

In the new analysis, the researchers didn't use the PREVENT model's optional zip code–level social deprivation index (SDI) data because those data are not reported in NHANES. The SDI factors the effects of poverty, education, housing, and employment conditions on health outcomes rather than factoring race as the PCEs did.

Not including SDI data may account for some of the difference in the PCEs and PREVENT risk estimates for Black adults in the study by leaving out groups that may have higher poverty rates and other SDI factors, said Khan, who is also an associate professor of cardiology and preventive medicine at Northwestern University and a *JAMA Cardiology* associate editor. In addition, the SDI data would be available in clinical practice, "and I think this is important," she added.

There were other limitations to the study. For example, it didn't compare 30-year ASCVD risk using the 2 equations or

10-year risks for patients younger than 40 or older than 75. It also didn't examine total cardiovascular disease risk estimates, which include heart failure, or estimates for heart failure alone.

More importantly, the study does not assess if either model's risk estimates are more accurate in current clinical practice, Khan noted—something that the study's authors also acknowledge.

Despite that caveat, Anderson thinks that the PCEs needed to be updated and "PREVENT fits that." For one thing, "the PREVENT equations were developed based on more contemporary cohorts and thus are likely to be more reflective of current populations than the PCEs," Anderson said.

For another, as Khan points out, the PREVENT model "has been vetted and demonstrated good accuracy across age groups, different race and ethnic groups, and people with chronic kidney disease."

That said, risk calculators are tools best used by clinicians to start important conversations, said Anderson. "They cannot provide highly customized predictions. That is where patient-doctor discussions come into play, both to consider other factors that might impact risk—family history, for example—and other important considerations, like other chronic conditions and patient preferences."

An Individualized Decision

Using the PREVENT equations instead of the PCEs would mean that millions of patients without known ASCVD would now be reclassified into lower risk levels. Among the 29.3 million people in the US who are currently classified as having intermediate risk for developing the disease, about a quarter would now be considered low risk and 46% as having borderline risk.

Changes in cardiovascular disease risk evaluation could also lead to different recommendations for other types of preventive therapies, including medications like low-dose aspirin. This could potentially reduce polypharmacy, the researchers wrote. A switch to PREVENT could also change recommendations for running more tests for risk-enhancing factors, like lipoprotein(a) and coronary artery calcium. And that could possibly reduce the cost and stress of unneeded procedures.

But statin adherence is also key—as is improving it. The researchers found that only about 44% of patients in the study group eligible for primary preventive statin therapy based on the PREVENT equations reported using the drugs—meaning more than half of US adults who probably should be taking statins aren't.

Improving uptake of primary prevention statin therapy means addressing systemic factors. That includes lack of access to primary care and insurance, which are the most important drivers of low statin use, Anderson noted. Individual factors such as reluctance to take preventive medications also must be dealt with, he said. "Some prefer not to take statins and others have misunderstandings about statin risks. Health education helps."

So too can clarifying the guidelines for "patients who are already taking a statin but for whom updated risk calculators indicate they may actually now be below the risk threshold for which we'd normally recommend a statin," said Anderson, who is a primary care physician.

For those patients, he noted, it's important to remind them that risk generally goes up with age. "We need to help patients understand that this does not mean they were incorrectly treated in the past, but that medical evidence accumulates, and recommendations change. Maybe we started [statins] early and maybe we continue or stop and then start again in a couple of years."

For patients at higher risk, quantifying that risk can help inform the discussion of whether to wait or start preventive medication, Anderson said. "There isn't much difference between 4% and 6%, but 5% is very different from 25%," he noted. He also finds the 10-year risk estimate more valuable than the 30-year one: "If you talk to someone at age 30 about risk at age 60, they may think 'I've got 30 years to lose 20 pounds vs taking a medication every day,' and they may not want to do it."

Not everyone agrees. Ashish Sarraju, MD, a cardiologist and researcher at the Cleveland Clinic who was not involved in developing PREVENT or with the current study, finds the 30-year estimates valuable for younger patients. "When you have a 35- or 45-year-old, their risk at 55 is not the only question," he said. In his view, having the longer-term estimates helps start the conversation on a range of preventive strategies that include lifestyle changes as well as medication.

"Prevention is often a very individualized decision," Sarraju said. For patients without a definitive indication for statins, like a family history of high cholesterol, "it comes down to a discussion of risks and benefits, and that is where the risk estimates come in handy."

Given their development by the AHA, the PREVENT equations may soon be incorporated into practice guidelines, Anderson said. This could begin by the end of 2024 or early 2025, when the AHA and the American College of Cardiology release new hypertension guidelines now being developed. New cholesterol guidelines will follow, likely in 2025, and guidelines for primary prevention of cardiovascular disease after that.

In the meantime, the AHA will continue to monitor the new model's performance in larger and more diverse populations, including with a database of more than 100 million individuals, Khan said, which should further improve the calculator's reliability. "Accuracy is important. It's got to be an ongoing or living approach." ■

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