Medical News & Perspectives

What to Know About PREVENT, the AHA's New Cardiovascular Disease Risk Calculator

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After 10 years, the American Heart Association (AHA) has updated its cardiovascular disease risk calculator for all adults aged 30 to 79 years without known cardiovascular disease. The Predicting Risk of Cardiovascular Disease Events (PREVENT) calculator is based on newer data from a larger, more diverse sample than the existing tool, the commonly used Pooled Cohort Equations (PCEs), released in 2013 for non-Black Hispanic and White adults aged 40 to 79 years. The PREVENT equations also take into account other health conditions, such as kidney and metabolic diseases, for determining the 10- and 30-year chances of both atherosclerotic cardiovascular disease and heart failure.

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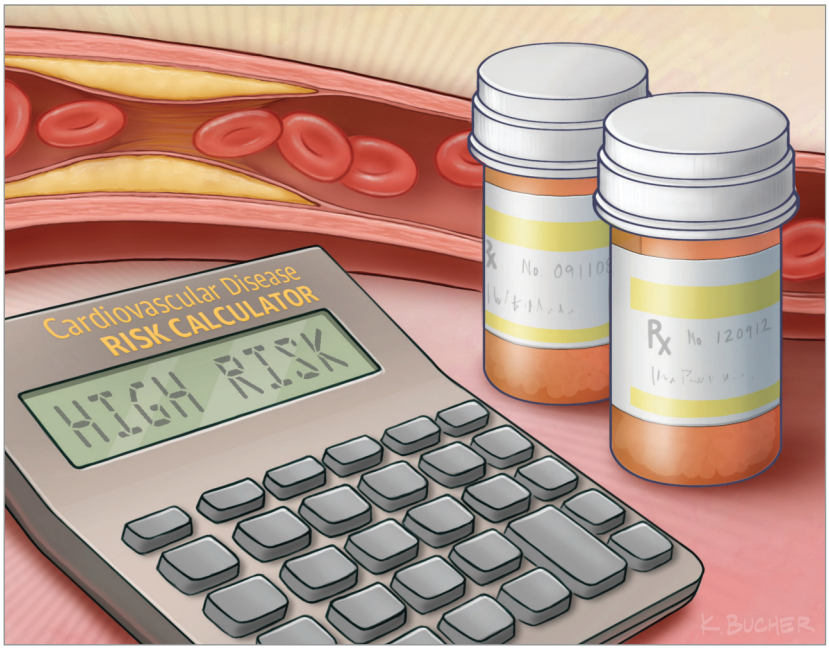

These newer risk assessment models form the basis of the new calculator, which is expected to be available online in early January 2024. The tool should be incorporated into electronic medical record systems soon after, Donald M. Lloyd-Jones, MD, ScM, coauthor of a scientific statement on the PREVENT models published in *Circulation*, said in an interview with *JAMA*.

Why update now? "Our understanding of cardiovascular disease risk has changed," the statement's lead author Sadiya S. Khan, MD, MSc, noted. Kidney disease and metabolic disease, including obesity and diabetes, multiply the odds of developing cardiovascular disease. So, researchers added these conditions along with more traditional risk factors such as smoking, blood pressure, and cholesterol levels. In addition, widespread use of statins and other treatments have lowered cardiovascular disease risks in certain groups.

For the first time, heart failure risk is included in total cardiovascular disease risk, and can be calculated separately, reflecting how often it occurs in patients with diabetes and kidney disease. And instead of only evaluating risk factors in Black and White adults, the new models eliminate race altogether and factor in social determinants of health to estimate cardiovascular disease risk.

To do that, the PREVENT models are based on data from about 6.6 million individuals from 46 datasets, including both population research studies and health system electronic medical records. The sample was much larger and more diverse than the approximately 25 000 individuals from 5 research datasets used to derive the PCEs, explained Khan, who is an associate professor of cardiology and preventive medicine at Northwestern University and a *JAMA Cardiology* associate editor. The updated models included Asian, Black, Hispanic, and White individuals with an average age of 53 years.

Together, the models' new predictor inputs and expanded outcomes can help clinicians prevent cardiovascular disease earlier and more comprehensively than before, Khan said. Clinicians will be able to recommend lifestyle changes along with treatments to modify traditional cardiovascular disease risk factors during young adulthood, as well as factor the chances of developing kidney and metabolic diseases as patients get older.

"Being able to start that conversation earlier not only requires a calculator that begins at a younger age, but also allows risks to be shared over a longer time horizon so that it is a meaningful estimate," Khan said.

She explained that although current guidelines endorse the PCEs as the risk calculator of choice, clinicians can also use other risk calculators, including PREVENT, when appropriate. "The hope is that PREVENT will be incorporated into upcoming iterations of clinical guidelines over the next few years," she 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, Lloyd-Jones said. New cholesterol guidelines will follow, likely in 2025, and guidelines for primary prevention of cardiovascular disease after that, he added. The clinicians developing the guidelines "will certainly be taking a careful look at PREVENT," he said.

Toward a "Universal" Risk Calculator

One potential issue with including electronic medical record data in the models is that they may not be as reliable as clinical research data. To test for this, researchers compared the relationships among risk predictors and clinical outcomes in both the research and clinical care datasets. No significant differences were found. "That helped reassure us," Khan said. "Even though there may be some differences and variability in data collected for clinical care," she explained, the benefit of having a large, contemporary sample of US adults "outweighed any of those potential concerns."

As a result, PREVENT "has a very real-world flavor," said Lloyd-Jones, who is professor of preventive medicine, cardiology, and pediatrics at Northwestern University. The large sample numbers also make the calculator more precise, which should increase clinician confidence in the risk estimates it generates, he added.

"Use of a large dataset and electronic health records makes it possible to develop a risk calculator based on a wide set of characteristics" so it is potentially more accurate across more diverse patient groups, noted Ashish Sarraju, MD, a cardiologist and researcher at the Cleveland Clinic who was not involved in the PREVENT project. More current data also may better reflect the changes in disease risk as new treatments have emerged, he said.

PREVENT may be less prone than the PCEs to overestimating risk, according to an accompanying article describing its development. Early on, the PCEs proved less reliable than predicted in several cohorts, potentially leading to overtreatment or undertreatment of individuals or groups, or their inappropriate inclusion or exclusion from clinical studies.

Even though PREVENT eliminates race as a predictor, it's more accurate across racial and ethnic groups than the PCEs, Lloyd-Jones noted. Instead of race, the new models include social determinants of health as measured by the social deprivation index, which is based on a person's zip code. The index incorporates measures of income, education, employment, housing, household characteristics, and transportation, which have all been shown to influence health.

"The risk factors really work the same in everybody. That is why it was time to update to a 'universal,' if you will, risk prediction equation," Lloyd-Jones said. Doing away with race in cardiovascular risk models may help decrease inequalities in treatment and care, he added.

A recent study published in *JAMA Cardiology* found that removing race as a predictor in the PCEs didn't lessen that tool's accuracy. But adding social determinants of health didn't improve performance either.

Khan noted that racial disparities do exist in who ends up with cardiovascular disease, and that clinicians need more research to identify the causes. "Social deprivation is just the beginning of a conversation about what can contribute to increased risk."

New Inputs and Outputs

Nicholas Wettersten, MD, a cardiologist and researcher focusing on cardiorenal disease at the University of California-San Diego, praised the wider range of patients in the dataset, especially those with kidney and cardiac disease from the Chronic Renal Insufficiency Cohort Study. "Kidney disease patients are often left out of major studies, so including these individuals in developing the risk calculator can improve its accuracy and applicability," said Wettersten, who also was not involved in developing PREVENT.

The PREVENT models factor in cardiovascular-kidney-metabolic (CKM) health—recently described by the AHA—to better capture the effects of obesity, diabetes, hyperglycemia exposure, and kidney disease on cardiovascular disease risk, Lloyd-Jones said. For example, the researchers added estimated glomerular filtration rate to the calculator as a basic measure of CKM health. For higher-risk patients, clinicians can also add urine albumin-to-creatinine ratio and hemoglobin A_{1c}.

Adding albuminuria is particularly important, Wettersten said. "It has repeatedly been shown to be a strong prognostic marker of cardiovascular events in individuals with kidney disease, even if it is not severe kidney disease." Including urine albumin-to-creatinine ratio improved PREVENT's predictive power, he noted. "We have a better opportunity to discriminate risk by adding these variables."

PREVENT's developers also expanded the cardiovascular disease risk endpoint to include heart failure. "We have more opportunities now to prevent heart failure in addition to coronary disease and stroke," Lloyd-Jones said. "If we are to do that, we need to predict heart failure as an outcome." Sodium-glucose cotransporter-2 (SGLT2) inhibitors and other emerging therapies can help prevent heart failure as well as atherosclerotic disease is now treated by statins, he explained.

Still, adding new inputs and outputs can only go so far. While PREVENT's reported accuracy in the study validation sample is very high, "the true test of any calculator is external validation in other cohorts, so real world use should give us the best validation," Wettersten said. "Not everyone who goes into a registry matches who you see in the clinic." Keeping the calculator up to date also will be critical to preserving its ongoing accuracy, he said.

The Long View

The PREVENT scientific statement includes a framework for integrating the model in a more holistic way, so it can be used by a wide range of clinicians.

"It's a step forward in actually applying something that has been known—that we can't look at one organ in isolation, we have to look at the interplay," Wettersten said. "We'll have to see how well this calculator and future calculators incorporate that interplay."

The statement also recommends that clinicians start screening and staging for cardiovascular risk factors much earlier than before.

So, for instance, pediatricians can screen and stage CKM risks beginning at birth. They can even include prenatal factors because an infant's risk of CKM syndrome goes up if their birthing parent had gestational diabetes or hypertension during pregnancy. The hope is that this early staging could encourage modifications to social, behavioral, and biological risk factors for CKM from infancy on.

Then when patients reach 30 years old, clinicians can start screening for cardiovascular disease risk, and if needed, begin guideline-based heart protective therapies with an eye toward also lowering the CKM stage. These therapies may include statins, SGLT2 inhibitors, glucagon-like peptide 1 receptor agonists, and blood pressure control medications.

Because few 30-year-olds have a high 10-year risk of cardiovascular disease—overall, in the US the risk is less than 1% at that age—including 30-year risk estimates beginning at age 30 is especially helpful for

early patient counseling and prevention, Lloyd-Jones said.

For younger patients "we need that longer-term risk assessment, so we are not saying 'Oh, you're good if your 10-year risk is fine' when you are not fine longer term," Lloyd-Jones noted. However, the 10-year absolute risk score, along with the relative risk reduction with specific treatments, is still critical for older patients to assess treatment benefits and risks and guide cost-effective decisions, he said.

"It's well understood that starting prevention earlier is better," added Sarraju. "Waiting for someone to reach a threshold of 10-year risk may not be aggressive enough," he said, noting that their risk over the next decade may not reflect their 30-year risk.

Wettersten agreed. A 30-year perspective, he said, "helps most with young individuals who may struggle to see the benefits of initiating certain therapies and lifestyle changes." He sometimes counsels patients, "I am giving you a medication for 40 years that may have some minor side effects to prevent you from having a stroke in 20 years that will have major side effects."

Rollout and Beyond

At press time, the PREVENT online calculator was being finalized, Khan said. Integrating it with electronic medical records so that it can be automatically populated likely will follow quickly, Lloyd-Jones added: "The goal is to make this as easy to use as possible. Let the electronic health record do the work; that's what it's there for."

Down the road, PREVENT could become the practice standard, ultimately replacing the PCEs. "For now, it is really an opportunity to start the conversation with patients about risk, and start it earlier and more comprehensively," said Khan.

The models will also be developed further, Khan said. The scientific statement highlights several areas for additional research. These include:

- Identifying individual- and place-based social determinants of health with greater predictive power and exploring how to identify and address them in clinical practice.
- Investigating novel predictors and outcomes, including chronic kidney disease progression risk; subclinical cardiovascular disease risk factors, such as coronary artery calcium; and genomic, metabolomic, and other "-omic" data.
- Interventional and implementation questions, including the risk thresholds at which each cardioprotective therapy shows a net benefit for treating cardiovascular risk; strategies for implementing the AHA's Life's Essential 8 framework that promotes healthier living to measure, modify, and monitor CKM; and randomized clinical trials of interventions to prevent onset of cardiovascular clinical risk factors or subclinical disease in younger patients.

Seeing how the models perform among Hispanic and, especially, South Asian subpopulations that weren't well represented in the PREVENT sample is also critical to improve their performance over time, Lloyd-Jones said.

He emphasized that PREVENT is a tool for patients who have not yet had a cardiovascular event, including heart attack, stroke, or heart failure. It can help clinicians identify patients at higher odds of experiencing these outcomes so they can decide how to intervene, especially with medications that carry their own hazards and costs.

Because the calculator is intended for general use, it does not consider less-common tests, such as coronary artery calcium levels. It also doesn't factor in a family history of gestational diabetes or cardiovascular disease, Khan said. She explained that clinicians can consider these variables as necessary to personalize risk profiles after calculating an initial estimate.

"As a clinician, I will implement it," Lloyd-Jones said. "It provides more and better information on the outcomes I am interested in." ■

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Conflict of Interest Disclosures: Dr Lloyd-Jones reported being a member of the AHA national board of directors. No other disclosures were reported.

Note: Source references are available through embedded hyperlinks in the article text online.