Traditional risk factors predict heart disease as well as genetic test

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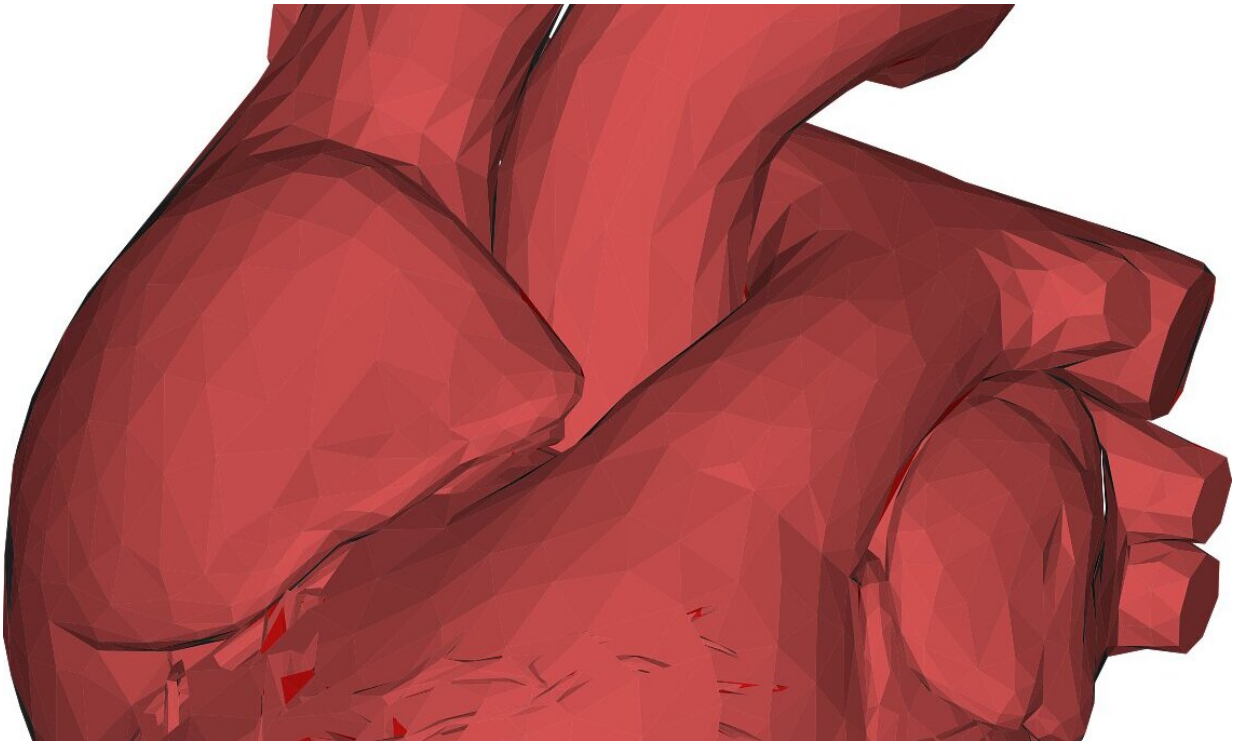

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Traditional cardiovascular risk factors often assessed in an annual physical, such as blood pressure, cholesterol levels, diabetes, and smoking status, are at least as valuable in predicting who will develop coronary heart disease (CHD) as a sophisticated genetic test that surveys millions of different points in DNA, a study led by a UT Southwestern

Medical Center researcher suggests. The findings, published Feb. 18, 2020, in *JAMA*, support the utility of these tried-and-true methods.

Identifying elevated risk for CHD as early as possible can help patients avoid potentially fatal events, such as heart attacks, through lifestyle changes and preventive treatments like cholesterol-lowering statins, explains study leader Thomas J. Wang, M.D., the Donald W. Seldin Distinguished Chair in Internal Medicine at UT Southwestern. Toward that end, the American College of Cardiology and the American Heart Association collaboratively developed a risk calculator known as the 2013 ACC/AHA Pooled Cohort Equations that's based on traditional cardiovascular risk factors. However, Wang says, many individuals calculated with this tool to be at low risk still develop CHD, and, conversely, only a minority of those calculated to be high risk end up having heart attacks and other cardiac events.

Some studies have explored the utility of DNA to predict risk more accurately. In August 2018, researchers published a widely cited study in *Nature Genetics* that showed that variations among individuals at more than 6 million points in their DNA were accurately associated with who had already had a heart attack.

However, says Wang, it's unclear whether this association with cardiac events that had already taken place could translate into predictive value for future events, as well as how this predictive value compared with calculations made using traditional risk factors.

To answer these questions, he and his colleagues used data from two long-running studies that follow heart health in thousands of volunteers: the Atherosclerosis Risk in Communities (ARIC) study and the Multi-Ethnic Study of Atherosclerosis (MESA). Because the polygenic risk calculator had been developed using individuals of European descent, Wang and his colleagues included only this population in their own

analysis, extracting data on traditional CHD risk factors and genetics from 7,306 individuals ages 45-79. They ran this information through both the ACC/AHA tool and the polygenic risk calculator for these study volunteers at baseline, then checked how these scores compared with which individuals experienced cardiac events over an average of about 15 years.

Their results showed a strong association between polygenic risk scores and CHD, with those scoring highest on this calculator at baseline most likely to experience cardiac events over the follow-up period. However, these results were roughly the same using the ACC/AHA calculator. Although the polygenic risk calculator reclassified about 5% of individuals to a higher or lower risk category, many of these classifications didn't match who developed CHD or not.

The bottom line, says Wang, is that the polygenic risk score didn't add much information beyond the ACC/AHA score that could help doctors more accurately predict CHD risk.

"Genetics is an important determinant of familial diseases and a key tool for understanding human biology, and the idea that genetics may also be important for predicting common diseases has been a source of excitement over the past several years. But as an everyday clinical tool for predicting cardiovascular risk, human genetics isn't there yet," Wang says. "We should not lose sight of traditional risk factors for assessing risk of cardiovascular disease, counseling about that risk, and strategizing on reducing it."

CHD is the leading cause of death worldwide, killing an estimated 3.8 million men and 3.4 million women each year.

More information: Jonathan D. Mosley et al. Predictive Accuracy of a Polygenic Risk Score Compared With a Clinical Risk Score for

Incident Coronary Heart Disease, *JAMA* (2020). DOI: 10.1001/jama.2019.21782