Using precision cardiovascular medicine to prevent the development of heart diseases

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Nearly half of all American adults have elevated blood pressure or hypertension. High blood pressure contributes to 65% of cardiovascular deaths in the United States. Exponential advances in genomic sequencing technology have enabled scientists to read the 3.4 billion letters that make up an individual's DNA in a short period of time and utilize this information for research purposes.

Researchers are now using the information from a patient's DNA to identify their genetic risk of developing hypertension and potentially fatal cardiovascular events over a lifetime—a concept known as precision medicine.

A recent study led by investigators at the University of Alabama at Birmingham Division of Cardiovascular Disease, and published in the journal *Circulation: Genomics & Precision Medicine*, could play a pivotal role in the era of precision cardiovascular medicine.

This study used genomic information from nearly a half-million individuals from multiple racial and ethnic backgrounds to create a blood pressure "genetic risk score" that captures an individual's genetic risk for high blood pressure.

"Commonly occurring changes in our DNA form the composite genetic risk score for hypertension in an individual," said Vibhu Parcha, M.D., first author of the study and researcher at the UAB Division of Cardiovascular Disease. "Since we are born with these commonly occurring DNA changes, we carry the risk for hypertension and heart conditions throughout our lifetime, and genetic risk score determines this."

The investigator team applied this score to over 21,000 American adult research participants who contributed to the Trans-Omics for Precision Medicine, or TOPMed, program, sponsored by the National Institutes of

Health and National Heart, Lung and Blood Institute as part of the Precision Medicine Initiative.

They found that the genetic risk score identified individuals at a higher risk of hypertension and was able to predict an individual's risk of developing heart failure, stroke and heart attacks even when accounting for their traditional cardiovascular risk factors such as obesity, smoking, diabetes, lipid profile and blood pressure. This genetic risk score also provides an improvement in the prediction of an individual's risk of these fatal events, especially among younger individuals.

"DNA is not your destiny," Parcha said. "We can potentially mitigate our genetic risk for heart diseases by improving our lifestyle by reducing weight, increasing physical activity and stopping smoking and by controlling diabetes, blood pressure and cholesterol levels."

According to Pankaj Arora, M.D., associate professor in the UAB Marnix E. Heersink School of Medicine's Division of Cardiovascular Disease and the director of the UAB Cardiogenomics Clinic, the aim of the study is to advance precision cardiovascular medicine that helps understand how an individual's lifestyles, behavior, environment and genetic risk profile interact to affect their risk of developing hypertension, heart failure, stroke and heart attacks.

"In the current era of precision cardiovascular medicine, we want to have an individualized assessment of a person's risk of fatal cardiac events," Arora said. "This allows us to focus our efforts on preventing fatal heart events through a personalized approach based on their genetic risk."

Arora says, generally, genomic medicine does not have a good history of including individuals from minoritized populations in research. Incorporating participants from marginalized populations is one of the biggest strengths of this research. The future implications of this study

include further investigations into the role of disseminating the genetic risk score results to improve blood pressure control and to motivate sustained lifestyle changes among younger individuals with high genetic risk of cardiac events.

The findings of the study were cross-verified in more than 50,000 participants of the National Institutes of Health-sponsored All of Us Research Program and the Action to Control Cardiovascular Risk in Diabetes trial database.

More information: Vibhu Parcha et al, Association of a Multiancestry Genome-Wide Blood Pressure Polygenic Risk Score With Adverse Cardiovascular Events, *Circulation: Genomic and Precision Medicine* (2022). DOI: 10.1161/CIRCGEN.122.003946

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