

Higher cardiovascular health may partially offset increased genetic risk for stroke

July 20 2022



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Genes and lifestyle factors together play a role in stroke risk. However, even for people at high risk for stroke, adopting a healthy cardiovascular lifestyle may significantly lower the risk of stroke in their lifetime, according to new research published today in the *Journal of the American Heart Association*.



"We know that well-managed, modifiable <u>risk factors</u>, especially treatment of hypertension, can noticeably lower an individual's risk of <u>stroke</u>," said senior study author Myriam Fornage, Ph.D., FAHA, professor of molecular medicine and <u>human genetics</u> at the Institute of Molecular Medicine at The University of Texas Health Science Center at Houston.

"Our study confirmed that we may be able to mitigate the lifetime risk of stroke by modifying other risk factors, and that regardless of genetics—whether you have a high <u>polygenic risk score</u> or low polygenic risk score—maintaining good cardiovascular health decreases the lifetime risk of stroke. So, <u>modifiable risk factors</u> are crucial in preventing stroke."

For the study, researchers reviewed data from the Atherosclerosis Risk in Communities (ARIC) Study, a community-based study of more than 11,500 white and Black adults over the age of 45, who had no history of stroke at enrollment. Study participants were followed for 28 years; 45% were men, and 55% were women.

Researchers estimated the lifetime risk of a first stroke according to levels of genetic risk based on a stroke polygenic risk score. Polygenic risk scores were derived from over 3 million genetic variants, or single-nucleotide polymorphisms, across the whole genome. Participants were categorized as having either low, intermediate or high genetic risk based on an analysis of how many stroke-related single-nucleotide polymorphisms they had. The number of SNPs related to stroke was standardized at more than 2.7 million for white adults and more than 2.2 million SNPs for Black adults. The researchers investigated the potential impact of the American Heart Association's Life's Simple 7 recommendations and whether higher Life's Simple 7 cardiovascular score (equating to better cardiovascular health) lessened the negative impact of a high genetic risk on the lifetime risk of stroke.



Life's Simple 7 scores are a composite measure of seven modifiable cardiovascular disease risk factors: smoking status, <u>physical activity</u>, <u>healthy diet</u>, body mass index, total cholesterol, blood pressure and glucose levels. Cardiovascular health is categorized as optimal, average or inadequate based on each participants' total score of ideal cardiovascular health components according to Life's Simple 7. For this analysis, Life's Simple 7 scores were combined with the polygenic risk score to estimate lifetime stroke risk.

Please note, this study used the American Heart Association's Life's Simple 7 metrics, which were established in 2010. On June 29, 2022, the organization expanded and relaunched the recommendations to Life's Essential 8, adding sleep as an additional component of heart health.

The study found:

- At age 45, study participants with the lowest polygenic risk scores had the lowest lifetime risk of stroke, 9.6%. The lifetime risk of stroke was 13.8% for participants with an intermediate polygenic risk score and 23.2% for participants with a high polygenic risk score.
- Those with both high genetic risk for stroke and low cardiovascular health had the highest lifetime risk of stroke score of 24.8%.
- Across all polygenic risk score categories (low, intermediate and high), people with optimal cardiovascular health had the most significant reduction in lifetime risk of stroke. Participants who had a high polygenic risk and optimal cardiovascular health were observed to mitigate their <u>lifetime</u> risk of stroke by up to 43%, compared to those with inadequate cardiovascular health. This translated into to about six additional years without a stroke.

"This is the first step in using genetic information to identify people who



may be at higher risk for stroke, and also in motivating people to make lifestyle changes for cardiovascular disease prevention," Fornage said. "This type of study shows us the possibilities for the future. Polygenic risk scores are not used clinically at this point; however, this may be the first step towards achieving personalized risk information to be used in lifestyle and health change. Having optimal cardiovascular health is crucial in stroke prevention."

The authors note that one major limitation of the study is that the polygenic risk score is a tool that needs improvement before it can be used broadly. The tool was developed and validated only among people who are white, which means it cannot be used to predict <u>stroke risk</u> accurately in people from diverse racial or ethnic backgrounds.

More information: Emy A. Thomas et al, Polygenic Risk, Midlife Life's Simple 7, and Lifetime Risk of Stroke, *Journal of the American Heart Association* (2022). DOI: 10.1161/JAHA.122.025703

Donald M. Lloyd-Jones et al, Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health: A Presidential Advisory From the American Heart Association, *Circulation* (2022). DOI: 10.1161/CIR.00000000000001078

Provided by American Heart Association

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