Healthy lifestyle may offset effects of life-shortening genes by more than 60%

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A healthy lifestyle may offset the effects of life-shortening genes by more than 60%, suggests an analysis of the findings from several large long-term studies, published online in the journal *BMJ Evidence-Based*

Medicine.

While genes and lifestyle seem to have an additive effect on a person's lifespan, an unhealthy lifestyle is independently linked to a 78% heightened risk of dying before one's time, regardless of genetic predisposition, the research indicates.

The polygenic risk score (PRS) combines multiple genetic variants to arrive at a person's overall genetic predisposition to a longer or shorter lifespan. And lifestyle—tobacco use, alcohol consumption, diet quality, sleep quota and physical activity levels—is a key factor.

But it's not clear the extent to which a healthy lifestyle might offset genetic predisposition to a shortened lifespan, say the researchers.

To explore this further, they drew on a total of 353,742 adults, recruited to the UK Biobank between 2006 and 2010, and whose health was tracked up until 2021.

A polygenic risk score was derived for long (20% of participants), intermediate (60%), and short (20%) lifespan risks, using data from the LifeGen cohort study.

And a weighted healthy lifestyle score, including no current smoking, moderate alcohol consumption, regular physical activity, healthy body shape, adequate sleep, and a healthy diet, was categorized into favorable (23% of participants), intermediate (56%), and unfavorable (22%) lifestyles, using data from the US NHANES study.

During an average tracking period of nearly 13 years, 24,239 participants died.

Those genetically predisposed to a short lifespan were 21% more likely

to die early than those genetically predisposed to a long life, regardless of their lifestyle.

Similarly, those who had an unfavorable lifestyle were 78% more likely to die before their time than those with a favorable lifestyle, irrespective of their genetic predisposition.

And those at high genetic risk of a shortened lifespan and who had an unfavorable lifestyle were twice as likely to die as those genetically predisposed to a long life and who had a favorable lifestyle.

Four factors in particular seemed to make up the optimal lifestyle combination: not smoking; regular physical activity; adequate nightly sleep; and a healthy diet.

This is an observational study, and as such, no definitive conclusions can be reached about cause and effect, added to which the researchers acknowledge various limitations to their findings.

Lifestyle was assessed at only one point in time, for example, and lifestyle choices differ by age. Participants were also all of European ancestry, which may limit the generalizability of the findings, say the researchers.

Nevertheless, they suggest that their findings indicate that the genetic risk of a shorter lifespan or premature death might be offset by a favorable lifestyle by around 62%.

Those at high genetic risk of a shortened lifespan could extend their life expectancy by nearly 5.5 years at the age of 40 with a healthy lifestyle, they suggest, adding that given how lifestyle habits tend to be cemented before middle age, steps to mitigate genetic predisposition to a shortened life are needed before then.

"This study elucidates the pivotal role of a healthy lifestyle in mitigating the impact of genetic factors on lifespan reduction," they conclude. "Public health policies for improving healthy lifestyles would serve as potent complements to conventional health care and mitigate the influence of genetic factors on human lifespan."

More information: Genetic predisposition, modifiable lifestyles, and their joint effects on human lifespan: evidence from multiple cohort studies, *BMJ Evidence-Based Medicine* (2024). DOI: 10.1136/bmjebm-2023-112583

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