

APOE variants' effect on mortality studied in 38,000

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Credit: UT Health

A new study of 38,537 persons of European ancestry suggests that a rare variation of a gene called APOE may be protective and prolong life, in sharp contrast to a more widely studied APOE variant that increases risk of death.

The findings by the E2-CHARGE consortium of investigators, led by senior investigator Sudha Seshadri, M.D., of UT Health San Antonio, suggest new research directions that "could lead to novel preventive and

[treatment options](#) for a wide variety of conditions to promote healthy aging and longevity," the team wrote.

The findings were published July 29 in the journal *PLOS ONE*. Dr. Seshadri is professor of neurology in the Joe R. and Teresa Lozano Long School of Medicine at UT Health San Antonio and founding director of the university's Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases.

APOE and its variants

APOE, a gene located on [human chromosome](#) 19, contains the instructions to make apolipoprotein E, a protein that regulates lipid transport and uptake. APOE's alleles (multiple forms of the gene that are inherited from parents or arise out of mutation) include APOE-epsilon 2 ($\epsilon 2$), APOE- $\epsilon 3$ and APOE- $\epsilon 4$.

Studies long have associated APOE- $\epsilon 4$ with increased risk of Alzheimer's disease and death. The new study confirmed this. Little was known about APOE- $\epsilon 2$, a rare variant found in only 1% of the population, however.

To learn more, E2-CHARGE examined data from six population-based studies conducted in the U.S., Iceland and the Netherlands. These included the Framingham Heart Study, for which Dr. Seshadri is senior investigator. During a mean follow-up period of 11.7 years, 17,021 individuals died. The researchers found that APOE- $\epsilon 2$ prolonged survival. Results were similar across the six study populations.

Limitations

The researchers said larger studies should be carried out to understand

this protective variant of APOE.

Because the study was conducted only in people of European ancestry, its results may not be applicable to other [ethnic groups](#), the researchers said.

Dr. Seshadri and Xianlin Han, Ph.D., professor in the Department of Medicine and the Sam and Ann Barshop Institute for Longevity and Aging Studies at UT Health San Antonio, received a grant in 2018 to understand why APOE- ϵ 2 protects a person from dementia and death.

More information: Frank J. Wolters et al, The impact of APOE genotype on survival: Results of 38,537 participants from six population-based cohorts (E2-CHARGE), *PLOS ONE* (2019). [DOI: 10.1371/journal.pone.0219668](#)

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