Genetic testing

People often want to know if a genetic test is useful in predicting their chances of developing Alzheimer's disease. The reality in most cases is that genetic testing for Alzheimer's offers limited information about one's chances of developing the disease.

Understanding the genetics of Alzheimer's

Genetic mutations that cause Alzheimer's disease

A small percentage of Alzheimer's cases — an estimated 1% or less — are caused by specific mutations in one of three genes: the gene for the amyloid precursor protein, the gene for the presenilin 1 protein or the gene for the presenilin 2 protein. A genetic mutation is an abnormal change in the sequence of chemical pairs that make up genes. Genes with these specific mutations are considered to be "**deterministic genes,**" meaning that inheriting one of the genes virtually guarantees that an individual will develop Alzheimer's disease. In such individuals, disease symptoms tend to develop before age 65, sometimes as early as age 30, while the vast majority of individuals with Alzheimer's have late-onset disease, occurring at age 65 or later.

Apolipoprotein E (APOE)-ε4 gene

The APOE gene provides the blueprint for a protein that carries cholesterol in the blood. Everyone inherits one form of the APOE gene — e2, e3 or e4 — from each parent. The e3 form is the most common, with about 60 percent of the U.S. population inheriting e3 from both parents. The e2 and e4 forms are much less common. An estimated 20% to 30% of individuals in the United States have one or two copies of the e4 form; approximately 2 percent of the U.S. population has two copies of e4. The remaining 10% to 20% have one or two copies of e2.

Having the e3 form is believed to neither increase nor decrease risk of Alzheimer's, while having the e2 form may decrease risk. The e4 form, however, increases the risk of developing Alzheimer's disease and of developing it at a younger age. Those who inherit two e4 genes are at higher risk than those with one e4 gene. Researchers estimate that between 40% and 65% of people diagnosed with Alzheimer's have one or two copies of the APOE-e4 gene.

Unlike inheriting a deterministic gene for Alzheimer's, inheriting the e4 form of the APOE gene does not guarantee that an individual will develop Alzheimer's. For that reason, the APOE-e4 gene is considered a "**risk gene**" for Alzheimer's, There are

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several other risk genes for Alzheimer's, but they have a limited overall effect in the population because they are rare or only slightly increase risk.

Understanding genetic testing for Alzheimer's disease

Implications for testing

For the rare families that have a known genetic mutation for Alzheimer's, genetic testing could be helpful because it will show whether an individual family member carries the gene mutation and will almost certainly develop the disease. For others, a genetic test can show whether an individual has inherited the APOE-e4 risk gene.

In both cases, individuals should seek the services of a genetic counselor before and after deciding whether to undergo testing. Genetic counselors will discuss the potential emotional impact of test results and inform you of possible implications of the test, including how it may affect employment, health insurance, long-term care insurance and future plans. A genetic counselor can be located through the National Society of Genetic Counselors (**nsgc.org**).

Alzheimer's Association® position on the 23andMe Genetic Health Risk test

The 23andMe Genetic Health Risk test identifies whether an individual has genes associated with risk of 10 diseases and conditions, including late-onset Alzheimer's. Individuals are tested using saliva samples. The 23andMe test evaluates whether an individual has the APOE-e4 Alzheimer's risk gene, but not deterministic genes for Alzheimer's.

The challenge with testing is that many people who have APOE-e4 never experience Alzheimer's dementia symptoms, and many who do develop the disease do not have any copies of APOE-e4. The Alzheimer's Association is concerned that people who receive results that confirm they don't carry APOE-e4 will assume that means they won't develop Alzheimer's. The truth is that these people may still be at risk due to lifestyle and environmental factors as well as other genetic variants not considered by this test.

The Alzheimer's Association does not recommend genetic testing for Alzheimer's disease for the general population. If you are concerned about Alzheimer's disease or memory changes in yourself or a loved one, the Association encourages you to have a frank conversation with your health care provider.

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