

Genetic Testing

With the growth in public awareness of Alzheimer's disease and other dementias, the proliferation of marketing communications related to research and purported treatments, and regular reports about new findings and regulatory actions, many people have questions about the genetics of Alzheimer's disease and the value of genetic testing for Alzheimer's risk – for themselves and for loved ones.

THINGS TO KNOW WHEN CONSIDERING GENETIC TESTING

The genetics of Alzheimer's disease and related dementias (such as frontotemporal dementia, Lewy Body dementia, etc.) varies from one disorder to another. At this time, genetic tests that determine susceptibility to Alzheimer's disease are primarily of value in a research setting, for example in studies investigating the role of genes in the onset and progression of the disease.

Having one or two copies the most impactful known Alzheimer's risk gene (APOE-ε4) only provides very general information about increased Alzheimer's risk. A person genuinely concerned about their dementia risk, or the risk of a loved one, based on family history, should consider making lifestyle changes regardless of genetic status. Growing evidence indicates that people can reduce their risk of cognitive decline by adopting key lifestyle habits.

Today, not only is there no effective pharmaceutical intervention to slow or stop Alzheimer's, there is no definitive research on how to prevent the disease. As such, the only actions that can be taken are making healthful lifestyle changes that may reduce risk of cognitive decline or dementia. The Alzheimer's Association offers 10 Ways to Love Your Brain; more information is at alz.org/10ways.

At-home genetic testing, or other genetic testing outside of a research setting, must be considered very carefully by an individual, in consultation with his or her family and physician. Things to think about when considering genetic testing for Alzheimer's disease may include how it could affect one's employment, health insurance and long-term care insurance. People should receive genetic counseling before a test is ordered and when the results are obtained. A genetic counselor may be found through the [National Society of Genetic Counselors \(nsgc.org\)](http://nsgc.org).

The Alzheimer's Association cautions against routine genetic testing for Alzheimer's disease risk until an individual has received proper counseling and understands the information necessary to make an informed decision, including the social and economic factors that could be impacted by having this genetic information. If and when genetic testing can productively guide medical treatment, our guidance surrounding its use will be reconsidered.

BACKGROUND INFORMATION

The cause of Alzheimer's disease remains unknown, but some risk factors – characteristics that increase the incidence of the disease – have been identified. The greatest risk factor for Alzheimer's disease is age.

Scientists have found some of the genes that contribute to the risk of Alzheimer's. They come in two major categories: risk genes and deterministic genes. Risk genes increase the likelihood of developing a disease, but do not guarantee it will happen. Deterministic genes directly cause a disease; they guarantee that anyone who inherits one will develop the disorder if they live to the estimated age of onset.

More than 100 risk genes are suspected to confer greater susceptibility for developing late-onset (old age) Alzheimer's disease, the most common form of the disease. Inheritance of a handful of these genes has been clearly linked to higher risk. The gene with the largest impact on risk is APOE (on chromosome 19), which encodes the protein apolipoprotein E. People with one copy of APOE-ε4 have a greater risk (about threefold) of getting Alzheimer's disease than people with other forms of the gene, and people with two copies of APOE-ε4 have an even greater risk. However, having one or two copies of the APOE-ε4 gene does not necessarily mean a person will develop Alzheimer's disease.

Because having one or two copies of APOE-ε4 only provides general risk information, and the scientific/medical community does not yet have an effective way to slow or stop Alzheimer's disease, the presence or absence of the ε4 form of the APOE gene is not used to determine a course of treatment either before or after the symptoms of dementia appear. Although tests for this gene are available, knowing the gene is present or not may invite other issues, such as anxiety about getting the disease or discrimination in obtaining disability or long-term care insurance.

Genetic tests to determine susceptibility to Alzheimer's disease are primarily of value in a research setting investigating the role of genes in the onset and progression of the disease. However, some persons might feel that receiving genetic test results may provide motivation for themselves to make healthful lifestyle choices that may reduce their risk of cognitive decline. More information about benefits and unexpected risks is needed on this topic. Importantly, people who choose to receive genetic test results related to Alzheimer's disease should be aware of several cautions, as described above.

A small minority of Alzheimer's disease cases are caused by deterministic genes. In general, these are of the younger-onset (sometimes called early-onset) form, in which symptoms appear in a person's 50s or earlier. A proportion of these early-onset cases are linked to mutations identified in

three genes: APP (on chromosome 21), PSEN1 (on chromosome 14) and PSEN2 (on chromosome 1). This is also referred to Dominantly Inherited or Autosomal Dominant Alzheimer's disease. If someone has one of these gene mutations, there is a high degree of certainty (approaching 99 percent) he or she will develop the disease, depending on the age of the individual. Such cases of "autosomal dominant" Alzheimer's disease are very rare, accounting for about two-tenths of one percent of dementia cases worldwide.

Families with Dominantly Inherited Alzheimer's are usually well aware of their unusual history with the disease, as about 50% of the people in the family tree get the illness before age 60. For members of these rare families, a genetic test could indicate whether an individual carries the gene mutation and will develop the disease. Some members of these families may wish to know their genetic status (for planning and decision-making), but others may not. For individuals from families in which dementia is of the late-onset type, or in which there is only one additional affected individual, screening for the deterministic genes is not recommended.

AVAILABLE GENETIC TESTS

On April 6, 2017, the U.S. Food and Drug Administration (FDA) allowed marketing of 23andMe Personal Genome Service Genetic Health Risk (GHR) tests for 10 diseases or conditions. The test includes the option to know one's status re: the APOE-e4 Alzheimer's risk gene.

Many people develop Alzheimer's dementia without having the Alzheimer's risk gene identified by this test; and many people with the gene do not develop Alzheimer's dementia. As noted above, genetic testing must be considered very carefully by an individual and his or her physician. The Alzheimer's Association strongly recommends that people receive genetic counseling before a test is ordered and when the results are obtained.

If you are concerned about Alzheimer's disease or memory changes in yourself or a loved one, the Alzheimer's Association encourages you to have a frank conversation with your healthcare provider. The Association has developed the [10 Warning Signs of Alzheimer's Disease](#). If you or a loved one are experiencing these symptoms, talk to your doctor about getting a thorough evaluation.

— Alzheimer's Association Medical and Scientific Advisory Council, reviewed June 2017