

Considering *APOE* Testing for Relatives of Patients with Alzheimer's

Some patients with early symptoms of Alzheimer's disease are getting *APOE* testing to determine if they are able to take Leqembi, a new therapy which has been found to slow cognitive decline in people with early stages of Alzheimer's disease. If your relative with Alzheimer's disease undergoes genetic testing, the results may have implications for you and other family members.

What is *APOE*?

APOE is a gene that impacts the risk for Alzheimer's disease and risks associated with some treatments, like Leqembi. Everyone has two copies of *APOE* because they inherit one from their mother and one from their father.

There are three different types of *APOE*. We refer to them as the e2, e3, and e4 types of *APOE*.

Why is a person's *APOE* results relevant to their relatives?

Everyone has two copies of the *APOE* gene: One copy is inherited from your mother and one copy from your father. These genes do not change with age. Each *APOE* gene is one of three types: e2, e3 or e4.

This means that a person's individual *APOE* gene test result will be some combination of the three types. For example, someone could have an e3 and an e4 as their *APOE* result and another person may have two copies of the e3 type (which is the most common *APOE* result).

The *APOE* e4 gene is associated with an increased risk of developing dementia due to Alzheimer's disease. Approximately one of every four people in the general population have at least one copy of this type of *APOE* gene.

Someone who has one copy of the *APOE* e4 gene is at higher risk for developing dementia due to Alzheimer's disease than someone who has no copies of e4. If an individual has two copies of *APOE* e4, their risk is further increased.

The e4 type of *APOE* gene is only one of many possible risk factors for dementia due to Alzheimer's disease. Not everyone with the e4 type will develop dementia due to Alzheimer's disease. In fact, there are people with dementia due to Alzheimer's disease who have no copies of the *APOE* e4 gene.

The e2 and e3 types of *APOE* are not considered to be risk factors for developing dementia related to Alzheimer's disease.

What can your *APOE* result actually tell you about your risk for Alzheimer's disease?

All of us have a risk of developing dementia. We each can have different risk factors like our age, other medical problems like high blood pressure or uncontrolled diabetes, and more. The general risk of developing dementia is about 10%. So, about 1 in 10 people develop dementia in their lifetime. People who have one copy of the e4 type of *APOE* have a higher risk. About 20-25% of people with one copy of *APOE* e4 will develop dementia. If a person has two copies of *APOE* e4, the risk to develop dementia increases to 30-55%. So, there are many people with one or two copies of *APOE* e4 who will not develop dementia. *APOE* is a risk factor, but cannot predict who will or will not develop Alzheimer's disease.

Should healthy people without cognitive symptoms get *APOE* Testing?

While *APOE* testing is recommended for patients considering Leqembi, genetic testing for relatives without mild cognitive impairment (MCI) or dementia is NOT currently recommended. This is because *APOE* results do not tell us whether or not you will develop Alzheimer's disease. This is just one piece of risk information. There are many factors that contribute to a person's risk of dementia. If you were found to have one or two copies of *APOE* e4, currently there would be no change to your medical care.

Relatives interested in more information about *APOE* testing should speak with a genetic counselor.

Additional resources for genetic counseling and testing include:

- Penn Neurogenetics – for genetic counseling and testing at University of Pennsylvania or via telemedicine, for those living in Pennsylvania or New Jersey
 - Contact: 215-829-6500 (call and request a neurogenetics *APOE* consult)
- Penn Telegenetics – for genetic counseling and testing via telemedicine, for those living anywhere in the US
 - Contact: 215-614-0262 (call and request a telegenetics *APOE* consult)
 - [Genetic Counseling in Your Home from Penn Medicine](#)
- NSGC find a counselor – to find a genetic counselor near you
 - Search: <https://findageneticcounselor.nsgc.org/>

What should I consider before getting *APOE* testing?

The decision whether to have *APOE* testing for individuals who don't have any cognitive symptoms is very personal.

There are many emotional and practical factors to consider. At this time there is no change to a person's medical care that would be recommended if they have no cognitive symptoms and are found to have one or two copies of e4. But, some people are interested in *APOE* testing for other reasons.

To help you with your decision, we encourage you to think about the different possible *APOE* results and how you might feel about each. You may also want to consider how learning this information might impact your family members.

What protections from genetic discrimination should I know about?

Learning your *APOE* result may have implications for decisions you make about your employment as well as life and long-term care insurance.

For example, in the United States, the Genetic Information Nondiscrimination Act (GINA) is a federal law that protects against genetic discrimination for health insurance and employment, but does not cover life insurance or long-term care/disability policies. It also does not cover those employed by the military or small workplaces.

GINA sets a minimum standard for protection against discrimination based on a genetic test result. Some states also have laws that provide additional protections. Information on state laws in the United States may be found through the National Conference of State Legislature (www.ncsl.org).

How do people respond emotionally to learning their *APOE* results?

Each person will have a unique emotional response to learning if they are at increased genetic risk for dementia due to Alzheimer's disease. Some people may experience anxiety, depression or worry when thinking about their risk.

Others may feel an urgent need to take action to reduce their risk. Some of these actions could be healthy and appropriate, for example, making positive dietary changes and committing to an exercise program. Other actions may prove to be very expensive with little or no benefit.

Still other people may feel empowered by learning this information and use it to inform their future decisions, like improving healthy behaviors or getting more involved in research.

What can learning my *APOE* results tell me about my family members?

Learning *APOE* results could also have implications for family members. Some individuals may have feelings of worry or guilt when thinking about children or siblings who may have inherited the *APOE* e4 gene.

If someone has two copies of *APOE* e4, this means that all of their biological children must have at least one copy of the *APOE* e4 gene. For someone with an *APOE* e3/e4 result, this would mean that there was a 50 percent chance of passing the e4 copy to any children, and an equal 50 percent chance of passing the e3 copy. Keep in mind that your *APOE* result is determined by inheriting one copy from your mother, and one from your father. Your results could also indicate a possible risk for *APOE* e4 in your parents and siblings. For these reasons, you may want to consider discussing your decision to learn your *APOE* results with family members.

Are there other risk factors in addition to the *APOE* e4 gene that can lead to dementia caused by Alzheimer's disease?

Yes. The greatest risk factor for developing dementia caused by Alzheimer's disease is advancing age, especially for those who are over 70 years old. However, dementia caused by Alzheimer's disease is not a normal part of aging.

Another risk factor is having a family history of dementia or Alzheimer's disease. Some studies also indicate that cardiovascular disease and conditions such as diabetes and high blood pressure are associated with a higher risk of developing dementia due to Alzheimer's disease as well as other types of dementias.

If you have any questions regarding these risk factors, please consult with your doctor.

Is the *APOE* gene associated with risk for any conditions besides Alzheimer's disease?

The *APOE* gene is also known to play a role in the cardiovascular system. Some people with different versions of the *APOE* gene can have increased risk for conditions related to the heart.

For example, people with one or two copies of e4 can have higher risk for buildup of plaque in the heart's arteries that could lead to coronary artery disease (CAD) and heart attack, also known as myocardial infarction (MI). *APOE* can also influence a person's risk for stroke and vascular dementia.

People with two copies of the *APOE* e2 gene have risk for a condition called type III hyperlipoproteinemia. There have also been associations between *APOE* and age-related hearing loss and age-related macular degeneration.

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