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disease risk

Alzheimer's Disease

Established Research report on 1 reported marker.

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About Alzheimer's Disease

Alzheimer's disease (AD) is a neurodegenerative condition characterized by decline in thinking and reasoning skills. Eventually, people with AD are unable to perform the basic activities of daily life. The most common cause of dementia in people over 65, AD currently affects about five million people in the United States. As the population ages, many more people are expected to develop AD; some estimate 14 million Americans will have the disease by the year 2050. There is currently no cure for AD, but scientists and physicians are working to understand how the disease develops, to improve the management of its symptoms and ultimately to develop ways of slowing or stopping its progression.

Learn more about the biology of Alzheimer's Disease...



1 of 2. Alzheimer's disease affects areas of the brain that are essential for thinking, memory, and behavior.

The information you are viewing below is based on sample data from the Mendels. When you receive your own genetic data, you will need to take additional action to unlock the corresponding information for yourself and the other individuals in your account. Before you decide whether to do this, you will be presented with a description of the implications of viewing this information.

Your Genetic Data

Show information for Lilly Mendel (Mom) assuming European ethnicity and an age range of 50-79

Lilly Mendel (Mom) has one copy of the APOE ε4 variant. APOE ε4 is not the only factor contributing to Alzheimer's disease. Although it is associated with increased risk of Alzheimer's, many people with the APOE ε4 variant never develop it. Read more in the technical report.

Lilly Mendel (Mom)

14.1 out of 100

women of European ethnicity who share Lilly Mendel (Mom)'s genotype will develop Alzheimer's Disease between the ages of 50 and 79.

Average

7.1 out of 100

women of European ethnicity will develop Alzheimer's Disease between the ages of 50 and 79.

What does the Odds Calculator show me?

Use the ethnicity and age range selectors above to see the estimated incidence of Alzheimer's Disease due to genetics for women with Lilly Mendel (Mom)'s genotype. The 23andMe Odds Calculator assumes that a person is free of the condition at the lower age in the range. You can use the name selector above to see the estimated incidence of Alzheimer's Disease for the genotypes of other people in your account.

The 23andMe Odds Calculator only takes into account effects of markers with known associations that are also on our genotyping chip. Keep in mind that aside from genetics, environment and lifestyle may also contribute to one's risk for Alzheimer's Disease.

VIDEO: The APOE Gene and Alzheimer's Disease

In this informational video, Dr. Robert C. Green describes what Alzheimer's disease is and explains the relationship between variants in the APOE gene and Alzheimer's risk. It is recommended that you watch this video prior to unlocking your results, but if you've already viewed your results, you may also find the video helpful for understanding them. You can also learn more about the APOE variants in the technical report.



Genes vs. Environment

**60-80 %
Attributable to
Genetics**

The [heritability](#) of AD is estimated to be 60-80%. This means that genetic factors contribute more to individual differences in risk for AD than [environmental factors](#) do. Genetic contributions to AD risk include known factors, such as the APOE [gene](#) variants we describe in this report. There are also rare mutations in other genes that cause early-onset (before age 65) forms of AD that run in families; this report does not currently include information on these mutations, or for additional genetic factors that have relatively weaker effects on AD risk. Non-genetic risk factors for AD include high blood pressure, high cholesterol, obesity, poorly controlled diabetes, and history of head trauma. ([sources](#))

What You Can Do

Assuming the ethnicity setting above is correct, your test results indicate you are at increased risk for AD based on genetics. However, family history, non-genetic factors, and genetic factors not covered in this report can also influence your risk for AD. Although not much is known about how to reduce your chances of developing the condition, you can use the resources below to learn more about AD and what you can do.

Know the symptoms

The early symptoms of AD can be difficult to distinguish from normal age-related changes. The [Alzheimer's Association's 10 Signs of Alzheimer's](#) guide can help you tell the difference.

Take care of your heart

Growing evidence suggests a link between heart health and brain health. Taking care of your heart by controlling your blood pressure, weight, cholesterol, and diabetes may also help decrease your risk for AD.

Exercise your body and mind

Regular exercise is associated with decreased risk of AD. And don't forget to exercise your mind too -- some studies suggest that staying mentally active throughout life can also reduce your risk.

Eat right

A healthy, low-fat diet can not only help you maintain healthy weight and cholesterol, but can also help reduce your risk of AD.

Learn your family medical history

Having a first-degree relative with AD, such as a parent or sibling, increases your chances of also being affected (see [here](#) and [here](#)). The U.S. Surgeon General's [My Family Health Portrait](#) tool can help you collect the information you need.

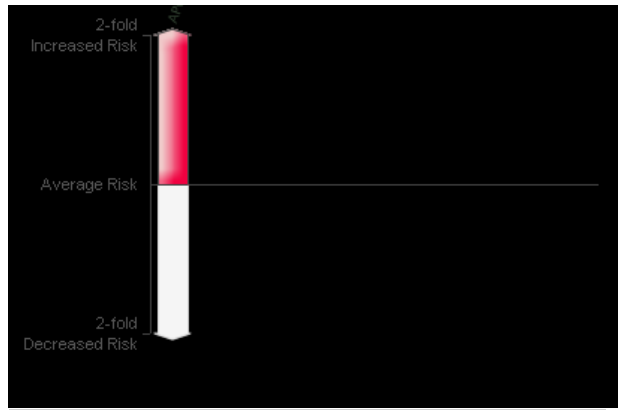
Connect with relevant groups

- [Alzheimer's Association](#)
800-272-3900
- [Alzheimer's Foundation of America](#)
866-232-8484

Talk with a genetic counselor

A genetic counselor can help you understand more about your 23andMe reports and respond to your genetic health questions. 23andMe is collaborating with Informed Medical Decisions, Inc., to give you direct access to board-certified counselors that have been specifically trained to guide you through your 23andMe results. Click [here](#) to learn more about their independent genetic counseling services.

Marker Effects



APOE Gene: **APOE**

Alzheimer's disease (AD) is a neurodegenerative condition characterized by decline in thinking and reasoning skills. Eventually, people with AD are unable to accomplish even the simplest tasks. The most common cause of dementia in people over 65, AD currently affects about five million people in the United States. As the population ages, many more people are expected to develop AD; some estimate 14 million Americans will have the disease by the year 2050. The $\epsilon 4$ variant of APOE is the strongest genetic risk factor for late-onset (after the age of 65) AD.

The APOE gene encodes the protein apolipoprotein E, a cholesterol carrier that is found in the brain and other organs. However, the protein's exact role in the development of AD is unclear. Several studies have shown that it may be involved in amyloid beta aggregation and clearance, influencing the onset of amyloid beta deposition that is believed, along with other factors, to ultimately lead to AD.

The effect of the APOE variants

Table 1. How do two SNPs determine three APOE variants?

Variant		rs429358		rs7412
$\epsilon 2$	=	T	+	T
$\epsilon 3$	=	T	+	C
$\epsilon 4$	=	C	+	C

Since the fourth combination—rs429358(C) + rs7412(T)—has never been observed, we can determine APOE variant status unambiguously from these two SNPs. For example, people with the CT genotype at both SNPs must be $\epsilon 2/\epsilon 4$, and people with CT at rs429358 and CC at rs7412 must be $\epsilon 3/\epsilon 4$. In addition, we can determine APOE variant status to varying degrees even if an individual has no data at one of the two SNPs. People with the TT genotype at rs7412 must be $\epsilon 2/\epsilon 2$ even if they have no data for rs429358. For people who have genotype data at rs429358 but no data for rs7412, we can determine how many copies of $\epsilon 4$ must be present, although we cannot always determine the exact variant combination.

The APOE gene comes in three main variants: $\epsilon 2$, $\epsilon 3$, and $\epsilon 4$ (see how the two SNPs are used to determine these variants in Table 1). APOE $\epsilon 3$ is the most common variant, APOE $\epsilon 4$ is associated with increased risk of AD, and $\epsilon 2$ is a rare variant of the gene that may have protective effects against AD. (See Table 2 below for frequencies of the different APOE variant combinations.) Studies have shown that the odds of developing AD increases with each copy of the $\epsilon 4$ variant of APOE. One copy is associated with about two times increased odds of developing AD and two copies is associated with about 11 times increased odds in populations of European ancestry, compared to average. (Note that most studies report odds relative to a reference genotype, in this case individuals who have two copies of $\epsilon 3$. The increase in odds

What does this chart show?

The chart shows the approximate effects of the selected person's genotype at the 1 reported marker. Higher, red bars indicate increased risk from the average, while lower, green bars indicate decreased risk from the average. The light gray bars show the maximum possible effects for the possible genotypes at the marker.

Mouse over individual bars to view additional information about each marker. Click on a bar to view detailed information about that marker below. You can read more about all markers in the technical report.

Citations

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Naj AC et al. (2011) . "Common variants at MS4A4/MS4A6E, CD2AP, CD33 and EPHA1 are associated with late-onset Alzheimer's disease." *None None(None):None.*

Hollingworth P et al. (2011) . "Common variants at ABCA7, MS4A6A/MS4A4E, EPHA1, CD33 and CD2AP are associated with Alzheimer's disease." *None None(None):None.*

associated with one and two copies of $\epsilon 4$ reported in those studies will therefore be slightly higher than the odds reported here, which are adjusted relative to the average person.)

Carrying a copy of the $\epsilon 4$ variant of APOE does not mean that a person will definitely develop AD. Many people who carry the $\epsilon 4$ variant never develop AD and more than half of the people with AD have no copies of APOE $\epsilon 4$ at all. But people with one copy of APOE $\epsilon 4$ who do get AD tend to get it earlier than patients with no copies of $\epsilon 4$ and people with two copies of APOE $\epsilon 4$ tend to get AD earlier still.

The effect of APOE $\epsilon 4$ is not well-established in non-European ethnicities

Compared to its effect in Europeans, the APOE $\epsilon 4$ variant seems to have weaker and less consistent effects in African American and Hispanic populations. Studies in both of these ethnicities have provided conflicting results ranging from the APOE $\epsilon 4$ variant having effects similar to those in Europeans to no effect at all. These differences may be due to the smaller sizes of studies in these populations, AD being more prevalent in these populations regardless of APOE $\epsilon 4$ status, or the effect of other genetic and [environmental factors](#) in the development of AD in these populations. The $\epsilon 4$ variant may have a slightly stronger effect in Asian populations, but more studies are needed to confirm this.

Risk for Alzheimer's changes significantly with age

Most people who develop Alzheimer's are diagnosed after age 80. In fact, the number of people who are diagnosed with Alzheimer's doubles between age 79 and age 84, and doubles again between age 85 and age 90. Keep in mind that the risk estimates provided in this report are calculated up to age 80 (the approximate average life expectancy in the U.S.).

In contrast, residual risk, or the risk of developing AD by a certain age starting at one's current age, decreases as an individual gets older. If an individual has reached a specific age—such as 70—without developing AD, his or her remaining risk for developing AD by age 80 will be lower than his or her lifetime risk would have been at age 50.

This report does not include information on variants other than APOE

In addition to APOE variants, there are some rare genetic mutations that are linked to early-onset forms of familial AD. 23andMe does not provide data about these mutations.

Recent studies have also identified additional common variants—including variants in the CLU, PICALM, CR1, MS4A, CD2AP, CD33, BIN1 and ABCA7 genes—that influence risk for AD, but their effects are relatively weak compared to the influence of the APOE $\epsilon 4$ variant. Recent studies have also shown that variants in TOMM40, a gene located near the APOE gene, may modify the age of onset of AD in those carrying the APOE $\epsilon 4$ variant. This report only includes information about the main APOE variant associated with AD.

This report does not include risk estimates for other health conditions

Many studies have also investigated the relationship between APOE variants and cardiovascular conditions, and while there is evidence that the APOE $\epsilon 4$ variant may associate with higher LDL cholesterol levels, consistent associations have not been demonstrated for coronary heart disease or response to statins.

Family history is also a significant risk factor for Alzheimer's disease

Although the APOE $\epsilon 4$ variant is the single strongest risk factor for late-onset AD, having a first-degree relative (such as a parent or sibling) with AD can more than double an individual's risk of also developing AD. Individuals with a first-degree relative with AD are at higher risk of

developing AD if that relative carries the APOE $\epsilon 4$ variant.

What should you do if you are concerned about your risk for Alzheimer's?

It is important for individuals concerned about their risk for AD to know their family history and to discuss their concerns with a medical professional or a genetic counselor. 23andMe is collaborating with Informed Medical Decisions, Inc., to give you direct access to board-certified genetic counselors that have been specifically trained to guide you through your 23andMe results. Click [here](#) to learn more about their independent genetic counseling services.

Table 2. APOE variant frequencies in Europeans

Genotype	Frequency
$\epsilon 2/\epsilon 2$	0.4%
$\epsilon 2/\epsilon 3$	13.7%
$\epsilon 3/\epsilon 3$	63.9%
$\epsilon 2/\epsilon 4$	1.3%
$\epsilon 3/\epsilon 4$	19.0%
$\epsilon 4/\epsilon 4$	1.7%

Data from Lahoz et al (2001).

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