APOE Add-On

Nancy Drew
Sex Assigned at Birth: Female
Date of Birth: 06/15/1987

Clinic: Sample Center
Physician: Jane Doe, M.D.
Phone: 123-456-7891
NPI: 1234567890

Requisition ID:
RQ000059

Report Number:
RP000001

Report Date:
04/03/2025

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APOE GENOTYPING — ALZHEIMER'S DISEASE & CARDIOVASCULAR RISK

Increased Risk

One copy of the *APOE* ε2 allele and one copy of the *APOE* ε4 allele were detected. This genotype is associated with a modestly increased risk of late-onset Alzheimer's disease compared to the general population.

GENE	GENOTYPE	ALLELE 1	ALLELE 2	RISK CATEGORY
APOE	ε2/ε4	ε2 (C130, C176)	ε4 (R130, R176)	Increased

CLINICAL INFORMATION

This test found one copy of the *APOE* ε2 gene variant and one copy of the *APOE* ε4 gene variant, a genotype written as ε2/ε4. The *APOE* gene tells the body how to make a protein called apolipoprotein E, which helps move fats like cholesterol through the blood and is especially important in the brain. About 1 in 50 people have it.

Alzheimer's Disease Risk

Having one copy of *APOE* ε2 and one copy of *APOE* ε4 combines a protective variant with a risk-increasing variant. These opposing effects partially offset one another, resulting in a lifetime risk of late-onset Alzheimer's disease that is expected to be modestly above the general population risk of approximately 10 to 15% by age 85 (PMID: 23296339, 32015339, 21556001).

Importantly, *APOE* ε4 remains a risk factor regardless of the second variant present; ε4-associated risk estimates are based mostly on studies of people of European ancestry and may vary by ancestry (PMID: 30517106).

Risk is also affected by many additional genetic, lifestyle, and environmental factors.

Cardiovascular & Lipid Effects

APOE ε4 is associated with modestly higher LDL cholesterol levels, while *APOE* ε2 is associated with lower LDL cholesterol. The net effect of this result on cardiovascular risk is variable and should be assessed in the context of your lipid panel and overall cardiovascular risk profile.

Inheritance

Since you carry one copy of the ε2 variant and one copy of the ε4 variant, it is expected that one of your parents carries the ε2 variant and the other carries the ε4 variant, though this test cannot indicate which parent carries which. Each of your children has

a 50/50 chance of inheriting the ε2 variant or the ε4 variant from you. Full siblings have at least a 50% chance of carrying the ε2 variant, and at least a 50% chance of carrying the ε4 variant.

NEXT STEPS

- Discussing this result with your healthcare provider is recommended to help clarify what it means for your personal risk. Modifiable factors — including cardiovascular health, regular physical activity, hearing health, sleep, and cognitive and social engagement — may also be relevant to discuss (PMID: 32738937).
- If anti-amyloid antibody therapies are considered in the future, your *APOE* ε4 carrier status may affect both eligibility and the risk of a therapy-related side effect known as ARIA (amyloid-related imaging abnormalities) (PMID: 34807243); this may be a relevant discussion point with a treating neurologist.
- This result may also be relevant to your cardiovascular health; review of your lipid panel and other cardiovascular risk factors may be considered.
- Family members also have an increased chance of having these variants. Sharing these results with your family members may allow them to consider genetic counseling to better understand their own chances of carrying the same variants.
- Genetic counseling is recommended to discuss what these results mean for you and your family.
- Further information and resources may be available through the Alzheimer's Association (alz.org) and the Alzheimer's Foundation of America (alzfdn.org).

APOE GENOTYPE RISK REFERENCE

APOE produces six possible genotype combinations from three common alleles (ε2, ε3, ε4). The table below summarizes population frequencies and approximate lifetime Alzheimer's disease risk estimates for each genotype, derived primarily from European-ancestry studies.

GENOTYPE	POPULATION FREQUENCY	LIFETIME ALZHEIMER'S DISEASE RISK*	RISK CATEGORY
ε2/ε2	<1%	Lower than average	Decreased
ε2/ε3	~10–15%	Slightly lower than average	Decreased
ε3/ε3	~60% (most common)	Population baseline (~10–15%)	Average
ε2/ε4	**~2%**	**Slightly higher than average**	**Increased ◀ your result**
ε3/ε4	~20–25%	~20–25% by age 85	Increased
ε4/ε4	~2–3%	~50–60% by age 85	Increased

*Lifetime Alzheimer's disease risk estimates are based on data primarily from individuals of European ancestry and are intended to support clinical interpretation only. Actual risk for an individual depends on age, sex, family history, ancestry, and other genetic and environmental factors.

MyOme, Inc.
1505 Adams Drive, Suite B1
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Report Information:
Nancy Drew
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Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

TEST METHODS

- Specimen receipt, accessioning, data analysis, and interpretation is performed by MyOme Inc., 1505 Adams Drive, Suite B1, Menlo Park, CA 94025, CLIA# 05D2203070. Whole Genome Sequencing, excluding data analysis and interpretation, is performed by Broad Clinical Labs LLC, 27 Blue Sky Dr, Burlington, MA 01803, CLIA#22D2055652.
- Genomic DNA obtained from the submitted sample was sequenced using Illumina technology. Reads were aligned to the NCBI GRCh38 reference assembly.
- *APOE* genotype is determined by characterization of two common single nucleotide variants in the *APOE* gene:
  - rs429358 — NM_000041.4(APOE):c.388T>C (p.Cys130Arg); chr19:44,908,684 T>C (NC_000019.10:g.44908684T>C)
  - rs7412 — NM_000041.4(APOE):c.526C>T (p.Arg176Cys); chr19:44,908,822 C>T (NC_000019.10:g.44908822C>T)
- The combination of alleles at these two positions defines six possible *APOE* genotypes (ε2/ε2, ε2/ε3, ε2/ε4, ε3/ε3, ε3/ε4, ε4/ε4). This assay is unable to resolve phasing for these variants which is required in order to differentiate an ε1/ε3 from an ε2/ε4. The ε1 haplotype is rare, therefore we assign the more common ε2/ε4 when an individual has a heterozygous genotype at both variants.

TEST LIMITATIONS

- This test is designed to characterize the two common *APOE* variants (rs429358 and rs7412) that define the ε2, ε3, and ε4 alleles. *APOE* genotype is one component of risk and does not constitute a diagnosis. *APOE* testing cannot predict whether, or when, an individual will develop Alzheimer's disease.
- Risk estimates reported here are derived primarily from studies of individuals of European ancestry. The magnitude of *APOE* ε4-associated Alzheimer's disease risk has been shown to vary across ancestral populations and may differ from the estimates presented in this report.
- Other genetic variants (including rare highly-penetrant variants in *APP*, *PSEN1*, and *PSEN2* associated with autosomal dominant early-onset Alzheimer's disease) are not analyzed by this test. Polygenic contributions from common variants outside *APOE* are not included in this report.
- A history of stem cell or bone marrow transplantation, or recent blood transfusion, may impact the accuracy of these results.
- Like most tests, this test carries a risk of false negative or false positive results, which may be caused by, without limitation, sample contamination from biological or non-biological sources, specimen labeling issues, rare genetic variants interfering with analysis, and other technical issues and limitations.

DISCLAIMERS

- This test was developed, and its performance characteristics were determined, by MyOme, Inc., a clinical laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and accredited by the College of American Pathologists (CAP) to perform high-complexity clinical laboratory testing. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA).
- Like most tests, this test carries a risk of false negative or false positive results. Testing is unavailable for samples damaged by human error or lost/destroyed due to weather, transit issues or other problems beyond the control of MyOme. MyOme is not responsible for the content of any third-party websites referenced in this report.
- Test results should be interpreted by a qualified healthcare professional in the context of the patient's clinical presentation, medical history, and family history. Genetic counseling may be appropriate depending on the findings reported.

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REFERENCES

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SAMPLE DETAILS

Sample ID	Source	Collected	Received
SM00232	Blood	02/01/2024	02/03/2024

REVIEWED BY

MyOme

MyOme Example Lab Director

04/03/2025

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