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
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Requisition ID:
RQ000059

Report Number:
RP000001

Report Date:
04/03/2025

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APOE GENOTYPING — ALZHEIMER'S DISEASE & CARDIOVASCULAR RISK

Decreased Risk

One copy of the *APOE* ε2 allele was detected. This genotype is associated with a modestly decreased lifetime risk of late-onset Alzheimer's disease compared to the general population.

GENE	GENOTYPE	ALLELE 1	ALLELE 2	RISK CATEGORY
APOE	ε2/ε3	ε2 (C130, C176)	ε3 (C130, R176)	Decreased

CLINICAL INFORMATION

This test found one copy of the *APOE* ε2 gene variant and one copy of the *APOE* ε3 gene variant, a genotype written as ε2/ε3. 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 10 to 15 in 100 people have it.

Alzheimer's Disease Risk

Having one copy of *APOE* ε2 and one copy of *APOE* ε3 is associated with a lifetime risk of late-onset Alzheimer's disease that is modestly lower than the general population risk of approximately 10 to 15% (PMID: 21577118, 23296339). The protective mechanism of *APOE* ε2 is not fully understood, and *APOE* ε3 has a neutral effect on risk.

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

Cardiovascular & Lipid Effects

APOE ε2 is associated with lower LDL cholesterol levels, while *APOE* ε3 has a neutral effect on cholesterol. Overall, this result is generally associated with a modestly favorable lipid profile. Type III hyperlipoproteinemia (dysbetalipoproteinemia), a rare disorder involving elevated cholesterol and triglycerides (a type of fat in the blood), is uncommon in people with only one copy of ε2 and typically requires an additional genetic or metabolic trigger (PMID: 10552997). Review of your lipid panel is recommended as part of routine cardiovascular risk assessment.

Inheritance

Since you carry one copy of the ε2 variant and one copy of the ε3 variant, it is expected that one of your parents carries the ε2 variant and the other carries the ε3 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 ε3 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 ε3 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).
- 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 ◀ your result**
ε3/ε3	~60% (most common)	Population baseline (~10–15%)	Average
ε2/ε4	~2%	Slightly higher than average	Increased
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.

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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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