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Provider Guide



Understanding Test Results: *APOE* Add-On

This guide provides step-by-step guidance for interpreting patient results from the *APOE* Add-On test.

Results Overview

This test is offered as an add-on to the Curated Screen™ test and reports a patient's genotype at two common variants (rs429358 and rs7412) that define the ε2, ε3, and ε4 alleles. Each of the six possible genotypes is assigned a risk category for late-onset Alzheimer's disease relative to the general population.

Scan for more test information

Technical Overview

Product Overview

Report Walkthrough

EXAMPLE RESULT: INCREASED RISK (ε4/ε4)

APOE GENOTYPING — ALZHEIMER'S DISEASE & CARDIOVASCULAR RISK

1 **Increased Risk**

Two copies of the *APOE* ε4 allele were detected. This genotype is associated with an increased lifetime risk of late-onset Alzheimer's disease compared to the general population.

GENE (2)	GENOTYPE (2)	ALLELE 1 (3)	ALLELE 2 (3)	RISK CATEGORY
APOE	ε4/ε4	ε4 (R130, R176)	ε4 (R130, R176)	Increased

4 **CLINICAL INFORMATION**

This test found two copies of the *APOE* ε4 gene variant, a genotype written as ε4/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 2 to 3 in 100 people have it.

Alzheimer's Disease Risk

Having two copies of *APOE* ε4 is associated with the highest known lifetime risk of late-onset Alzheimer's disease among the common *APOE* genotypes. Risk is estimated at approximately 50 to 60% by age 85, compared to the general population risk of approximately 10 to 15% (PMID: 21556001). This result is also associated with an earlier average age of symptom onset.

APOE ε4 is thought to increase risk in part by reducing the brain's clearance of amyloid-beta protein, though the biology is not fully understood; ε4-associated risk estimates are based mostly on studies of people of European ancestry and may vary by ancestry (PMID: 30517106).

Importantly, ε4/ε4 status is not diagnostic and does not guarantee that a person will develop Alzheimer's disease; risk is also

1 RESULT SUMMARY
The patient's risk category (Decreased, Average, or Increased), with a one-line interpretation relative to the general population.

2 GENOTYPE
The patient's two *APOE* alleles, one inherited from each parent.

3 ALLELES
Each allele is defined by the amino acids at residues 130 and 176 (legacy numbering 112/158).

4 CLINICAL INFORMATION
Genotype-specific interpretation of Alzheimer's disease risk, cardiovascular and lipid effects, and inheritance. Next steps and a full genotype risk reference follow on page 2 of the report.

APOE Genotype Risk Reference

APOE produces six possible genotypes from three common alleles (ε2, ε3, ε4). The patient's result is highlighted in their report.

Genotype	Population Frequency	Lifetime Alzheimer's Disease Risk[§]	Risk Category
ε2/ε2	<1%	Lower than average[3]	Decreased
ε2/ε3	~10–15%	Slightly lower than average	Decreased
ε3/ε3	~60% (most common)	Population baseline (~10–15%)[1,2]	Average
ε2/ε4	~2%	Slightly higher than average	Increased
ε3/ε4	~20–25%	~20–25% by age 85[8]	Increased
ε4/ε4	~2–3%	~50–60% by age 85[8]	Increased ◀ Example above

[§]Risk estimates are derived primarily from studies of individuals of European ancestry and vary by sex and age horizon; both risk magnitude and allele frequency differ across ancestral populations.[4] Individual risk also depends on age, family history, and other genetic and environmental factors.
*Formerly offered as "Single-Gene Risk" under MyOme Proactive Health.

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Next Steps

Discussion of Risk and Modifiable Factors

ε4/ε4 is associated with the highest known lifetime risk of late-onset Alzheimer's disease among common *APOE* genotypes and an earlier average age of symptom onset, but it is not diagnostic and does not guarantee disease development.[8] Discussion may include modifiable factors associated with dementia risk, including cardiovascular health, physical activity, hearing health, and cognitive and social engagement.[6]

Cardiovascular & Lipid Assessment

APOE ε4 is associated with modestly higher LDL cholesterol, and this effect may be more pronounced with two copies. Review of the lipid panel and overall cardiovascular risk profile may be considered.[5]

Future Treatment Considerations

If anti-amyloid antibody therapy is considered in the future, ε4/ε4 status is associated with the highest known risk of ARIA (amyloid-related imaging abnormalities) and is specifically addressed in the prescribing information for these therapies.[7] This result may be a relevant discussion point with a treating neurologist.

Family Implications

Both biological parents are expected to carry at least one ε4 allele, and each biological child will inherit one. Full siblings have at least a 75% chance of carrying one or more copies. Sharing results may help relatives consider genetic counseling, though some may prefer not to learn their own risk.

Additional Support

Clinician-to-Clinician Consultation*

A clinician-to-clinician consultation to review results and management considerations is included with every report.

Patient Genetic Counseling*

Post-test genetic counseling is recommended for *APOE* results[1] and is included at no additional cost to help patients understand their result and what it may mean for them and their family.

Provider Resource Hub

Additional guides, overviews, and educational resources are available on our website.

*These optional resources are offered by our third-party provider, DNAvisit.

We're Here to Help

For additional interpretation support, fill out our Contact Us form or reach out directly to support@myome.com to set up a consultation.

1. Goldman et al. Genetic counseling and testing for Alzheimer disease: joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. Genet Med. 2011; 13(6):597-605. PMID: 21577118. 2. Liu et al. Apolipoprotein E and Alzheimer disease: risk, mechanisms and therapy. Nat Rev Neurol. 2013; 9(2):106-118. PMID: 23296339. 3. Reiman et al. Exceptionally low likelihood of Alzheimer's dementia in APOE2 homozygotes. Nat Commun. 2020; 11:667. PMID: 32015339. 4. Rajabli et al. Ancestral origin of ApoE ε4 Alzheimer disease risk in Puerto Rican and African American populations. PLoS Genet. 2018; 14(12):e1007791. PMID: 30517106. 5. Mahley et al. Pathogenesis of type III hyperlipoproteinemia (dysbetalipoproteinemia): questions, quandaries, and paradoxes. J Lipid Res. 1999; 40(11):1933-1949. PMID: 10552997. 6. Livingston et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 2020; 396(10248):413-446. PMID: 32738937. 7. Salloway et al. Amyloid-related imaging abnormalities in 2 phase 3 studies evaluating aducanumab in patients with early Alzheimer disease. JAMA Neurol. 2022; 79(1):13-21. PMID: 34807243. 8. Genin et al. APOE and Alzheimer disease: a major gene with semi-dominant inheritance. Mol Psychiatry. 2011; 16(9):903-907. PMID: 21556001.

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