

Genetic Testings Interpretation Guide

Single nucleotide polymorphisms (SNPs) are found in chromosome in genes that have variations that determine up-regulation or down-regulation of the protein enzyme activity determined by the gene activity.

APOE Status and Alzheimer's risk

Genotype	E2/ E2	E2/ E3	E2/ E4	E3/ E3	E3/ E4	E4/ E4
Disease risk	40% less likely	40% less likely	2.6 X more likely	Average risk	3.2 times more likely	14.9 times more likely

→ Clinical: Evaluate ApoE4 status

- 0 copies (e.g., ApoE3/3 or 2/3) → 9% lifetime risk.
- 1 copy ApoE4 (heterozygous) → 30% lifetime risk (75 million Americans).
- 2 copies (homozygous) → 50-90% lifetime risk (7 million Americans).
- Increases inflammation, thus increases risk for AD but reduces risk for parasite-associated dementia, and also may reduce risk for type 3 AD.
- Affects Rx regarding diet, fasting time, fat absorption, lipid profile effects, treatment of inflammation, etc.
- Critical to identify early and prevent or reverse cognitive decline of AD.

APO E : Apolipoprotein E : CHOLESTEROL REGULATION

Location:
Chromosome 19
APOE
APO E2: cys / cys
APO E3: cys / arg
APO E4: arg / arg
Your Genotype:

Apolipoprotein E (ApoE) is an essential protein for the metabolism of cholesterol and triglycerides. It is a major component of plasma lipoproteins including chylomicrons, VLDL, IDL, HDL. There are 3 common genetic variants of ApoE: E2, E3, E4 leading to 3 different conformations of the protein that affect its ability to perform its function. Because each person carries 2 copies of the ApoE gene, there are 6 possible ApoE genotypes.

E3/E3: The most common ApoE genotype (55% of the population carries this genotype). It is considered to be normal with no associated risk factors. Treatment should be based on lipid profile.

E2/E3: Common, (10-15% of most populations)

ApoE2 is associated with lower LDL cholesterol and higher HDL-C, but higher triglycerides (as found in Metabolic Syndrome) compared to the other genotypes. ApoE2 also confers a lower risk of atherosclerosis, myocardial infarction, stroke, and osteoporosis with higher antioxidant activity.

Treatment Options:

- The cholesterol-lowering effect of a low saturated fat and low cholesterol diet is least effective with E2 individuals.
- Minimize high-glycemic index foods, which produce the largest triglyceride (TG) response in E2 carriers.
- Dietary fiber, fish oils, and exercise generally improve the lipid profile in this genotype; fish oils reduce TGs most effectively in E2 individuals.
- Alcohol may reduce LDL-C in men (neutral in women)
- E2 individuals generally respond the most favorably to statins and would therefore likely respond to statin mimetics such as inositol hexaniacinate, red rice yeast, and policosanol. Gemfibrozil may be particularly effective at lowering TGs and total cholesterol
- HRT improves the lipid profile in this genotype, although oral estrogen may significantly increase TGs

E3/E4 :>25% in most populations.

ApoE4 confers a tendency toward higher total- and LDL cholesterol, lower HDL-C.

Increased risk of stroke (esp. among Asians), hypertension, and MI;

Increased risk of cognitive impairment after stroke

Independent predictor of CAD and type 2 diabetes, especially in obese individuals and smokers.

Increased risk of low BMD, oxidative stress, also easier toxicity by heavy metals such as lead and mercury

ApoE4 may increase risk and disease severity of multiple sclerosis

Clinical Management Considerations:

- Stress management: ApoE4 is associated with poor response to life stressors; prolonged stress contributes to memory decline.
- Restriction of saturated fat and cholesterol lowers total- and LDL cholesterol and CAD risk the most effectively in E4 individuals, also reduces risk of MI. (Instead of Ketogenic diet, consider modified mediterranean diet
- Avoid smoking and minimize high-glycemic index foods, both of which augment E4-associated risk of CHD.

- Alcohol may raise LDL-C in men (neutral effect in women), increase IL-6 levels, and fail to raise HDL-C.
- Reduce excess weight, which synergizes with effects of E4 on insulin and lipids.
- Antioxidants may help to counteract low antioxidant tissue levels
- Anti-inflammatory agents help preserve cognitive function.
- Lipid response to statins, and triglyceride response to fibrates, are usually the most positive in E2 > E3 > E4; studies are mixed.
- Estrogen therapy is particularly efficacious for both cholesterol and bone in postmenopausal E4 carriers.