

APOE4 & Alzheimer's

Reducing Risk For *APOE4* Genotypes



INTRODUCTION

The *APOE4* allele confers risk for Alzheimer's disease (AZD). The current evidence suggests that *APOE4/4* genotypes (individuals homozygote for the *APOE4* allele) have a 5x greater risk of AZD, with onset occurring 15-20 years earlier than in the general population. *APOE4/4* genotypes also have a 30-40% increased risk of heart disease. It is thought that lowering the risk of heart disease reduces the risk for AZD and dementia.

The *APOE4* allele is not diagnostic of AZD. There is good evidence that lifestyle and dietary changes can lower the risk of AZD for *APOE4* genotypes to that of other *APOE* genotypes. However, any changes should be closely adhered to long-term, with minimum deviation.

There are some advantages in having the *APOE4/4* genotype. For example, children who are *APOE4/4* tend to have a better memory, suggesting that the *APOE4/4* genotype, and by exclusion the *APOE4* allele, does not necessarily cause memory problems.

What follows are recommendations according to a traffic light system. Green indicates lifestyle measures that should be followed, and for which there is strong evidence. Amber indicates interventions for which there is good evidence for the prevention of AZD, but which

apply to the general population, and are not specific to APOE4 genotypes; following such recommendations might be useful. Red are lifestyle and dietary choices that should be avoided. Evidence has been restricted to peer-reviewed, scientific studies.



GREEN

- 1 EXERCISE** This is the single most important action that APOE4 genotypes can take. Exercise interacts with the APOE4 allele to reduce the rate of hippocampal atrophy. APOE4 genotypes who engage in 30 minutes per day of exercise have amyloid plaque formation at normal levels.
- 2 BE YOUR IDEAL WEIGHT** This is the second most important action to take. Weight gain strongly interacts with the APOE4 allele, increasing triglycerides, insulin, and LDL cholesterol, leading to poor vascular health.
- 3 EAT LOTS OF VEGETABLES AND FRUITS** APOE4 genotypes often have lower levels of plasma antioxidants: consume more fruits and especially vegetables. In addition, researchers at the University of Washington found that consuming vegetable juice 3x per week reduced risk for AZD by up to 76%, especially for APOE4 genotypes.
- 4 ENGAGE IN CONSISTENT, LIFELONG LEARNING** APOE4 genotypes who engage in lifetime cognitive activity have similar amyloid-beta molecules to other APOE genotypes.
- 5 TAKE TURMERIC OR CURCUMIN** Just 80 mg per day of curcumin lowers plasma triglyceride values, lowers plasma beta amyloid protein concentrations, and increases plasma nitric oxide. The average daily consumption in areas of India that have the lowest incidents of AZD is just 125 mg per day. Mega doses are not necessary, only consistent, long-term daily doses.
- 6 IMPLEMENT WHILE YOUNG** If middle aged, implement as soon as possible. Don't wait to until old age to change your lifestyle. Amyloid plaques associated with Alzheimer's disease can start forming many years before the symptoms of the disease are apparent.
- 7 BE HAPPY AND UPBEAT** In being told you are APOE4 you've had some challenging news. However, people who are depressed are twice as likely to have dementia and 65% more likely to develop Alzheimer's disease. If you have clinical depression seek professional help, don't suffer in silence.



AMBER

- 1 CONSUME FLAVONOID-RICH FOODS** Berries, citrus fruit, coffee (in moderation and if caffeine is tolerated), cocoa, red wine (in moderation), tea, concord grape juice or blueberry juice.
- 2 WALK AND STAND** Leading a non-sedentary lifestyle by walking and standing (as opposed to sitting on a chair for long periods) improves cardiovascular health, mortality, and reduces the risk of AZD and dementia.
- 3 OMEGA-3 FATTY ACIDS** There is strong evidence associating omega-3 fat consumption from fish with a reduction in risk for dementia and AZD. However, APOE4 genotypes should proceed with caution, as omega-3 fatty acids may not be as helpful for these genotypes. High amounts of DHA fatty acids worsen LDL cholesterol for APOE4 genotypes. Moreover, DHA fatty acid consumption has consistently been shown to be unhelpful for APOE4 genotypes. More research is needed on this. Eating oily fish two or three times a week may be more helpful than taking fish oil supplements.
- 4 LOWERING TOTAL CHOLESTEROL** is inconclusive.
- 5 MAINTAIN OPTIMAL VITAMIN D LEVELS** There is evidence that optimal vitamin D levels protects against dementia. The emphasis here is 'optimal'. Do not take large doses. Have vitamin D levels monitored.
- 6 CONSIDER VITAMIN B12** Vitamin B12 interacts with the APOE4 genotype to positively modify cognitive performance.
- 7 CONSIDER LOW DOSE (60 MG PER DAY) OF VITAMIN C** In APOE4 genotypes vitamin C reduces the pro-inflammatory effects of smoking.
- 8 CONSIDER LUTEIN** 12 mg of Lutein with 800 mg of DHA significantly improved verbal and memory scores in older women. However, high DHA consumption (>3g per day) increased LDL cholesterol.



RED

- 1 AVOID ANYTHING THAT CAUSES INFLAMMATION** The APOE4 genotypes are associated with a pro-inflammatory state. Numerous studies have reshaped our understanding of AZD such that it is now considered as much as a vascular/inflammatory disease as it is a brain/neuronal disease. As a general rule, APOE4 genotypes should avoid pro-inflammatory lifestyle choices.
- 2 AVOID SATURATED FAT** Researchers with Finland's Cardiovascular Risk Factors, Aging and Dementia study found that a high intake of saturated fat more than doubled the risk of mild cognitive impairment. Among APOE4 genotypes, a fatty diet increased the risk fivefold. While saturated fat is no longer the villain once thought, numerous studies over the last decade have shown a negative association between APOE4 genotypes and saturated fat.
- 3 AVOID SMOKING AND SMOKE-FILLED ENVIRONMENTS.**
- 4 AVOID STRESS** Prolonged exposure to stress combined with the APOE4 allele leads to memory decline.
- 5 AVOID TRANS-FATS** These are found in margarine, spreads, processed and fast food.
- 6 AVOID EXCESS IRON** University of Chicago researchers found people who had haemoglobin levels around 14 grams per deciliter maintained their mental functioning into old age. Much lower or higher levels of haemoglobin resulted in poorer brain function.
- 7 AVOID EXCESS COPPER** Older people with excess copper in their blood score more poorly in memory tests and have a higher chance of developing Alzheimer's disease.
- 8 AVOID ALCOHOL** Alcohol magnifies the association between the APOE4 allele and poor vascular health.

THE TRADITIONAL DIET

Pima Indians have a high incidence of the *APOE4* allele. When removed from their natural environment they have high rates of obesity, type2 diabetes, and AZD. It is thought that this increase in disease is due to the adoption of a non-traditional, western diet coupled with a sedentary lifestyle. In contrast, Pima Indians who consume their traditional diet of maize, beans, squash, deer, jackrabbits, fish, and desert fruits have low rates of AZD despite carrying the *APOE4* allele.



Similarly, Nigerians who carry the *APOE4* allele, and who consume their traditional diet, which is low in high-glycemic carbohydrates and sugar, low fat, low calorie, and predominantly made up of grains, yams, vegetables, and some fish, also have a low incidence of dementia.

In sub-Saharan Africans the *APOE4* allele does not confer an increased risk of Alzheimer's disease.

These groups of traditional peoples who carry the *APOE4* allele give tremendous hope to *APOE4* genotypes. It suggests that if *APOE4* genotypes apply the scientific dietary and lifestyle principles outlined above, combine it with the traditional foods from their culture that are in harmony with those principles, then the risk of Alzheimer's disease could be significantly reduced.

WEBSITES

- ➔ <http://alzheimer.neurology.ucla.edu/mission.html>
- ➔ <http://www.alzheimers.org.uk/site/scripts/documents.php?categoryID=200422>

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