

# Society Guidelines and Position Statements Recommend Against ApoE Predictive Testing

American College of Medical Genetics and National Society of Genetic Counselors (2011) <sup>1</sup>	“Genetic testing for susceptibility loci (eg, ApoE) is not clinically recommended due to limited clinical utility and poor predictive value. If a patient wishes to pursue testing despite genetic counseling and recommendations to the contrary, testing may be considered at the clinician’s discretion.”
American College of Medical Genetics and Genomics lists genetic testing for ApoE alleles as 1 of 5 recommendations in the Choosing Wisely initiative (2015) <sup>2</sup>	“Don’t order ApoE genetic testing as a predictive test for Alzheimer’s disease.”
American Academy of Neurology (2001) <sup>3</sup>	“Routine use of ApoE genotyping in patients with suspected AD is not recommended at this time.”

# ApoE Testing Is Used in Some AD Preventative Studies as an Enrichment Strategy or Inclusion Criterion

## Alzheimer's Prevention Initiative Generation Study<sup>1,2</sup>

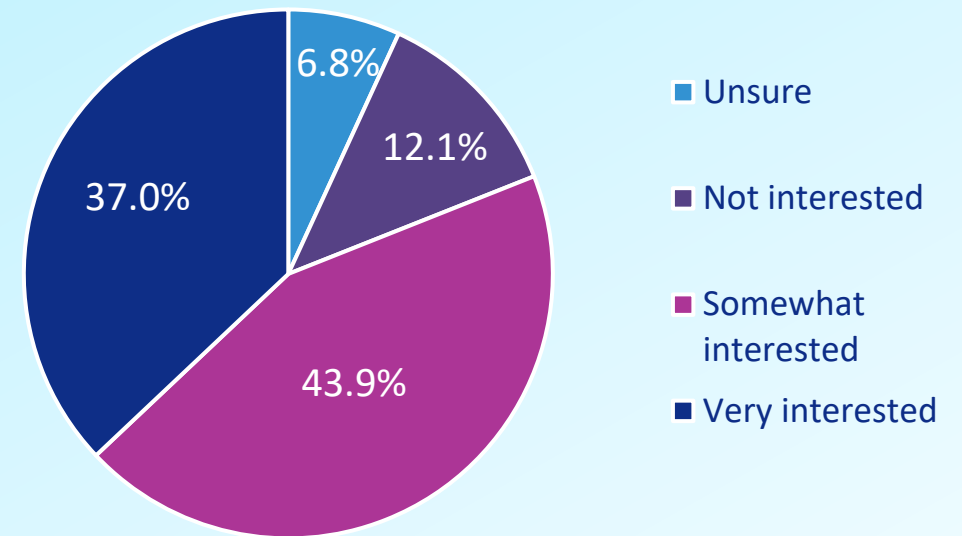
- Cognitively unimpaired participants aged 60-75 with 1 or 2 ApoE4 alleles, disclosure of ApoE status required
- Phase 2/3 trial to test amyloid-targeting therapy
- Demonstrates it is feasible to recruit, screen, and randomize cognitively unimpaired ApoE4 carriers on a large scale
- Screening context approved by the National Institute on Aging<sup>3</sup>

“The ultimate goal of identifying individuals in the preclinical stages of AD is to facilitate early intervention to delay and perhaps even prevent emergence of the clinical syndrome”<sup>5</sup>

DTC, direct-to-consumer.

1. Lopez Knop man C et al. *Alzheimers Dement (N Y)*. 2019;5:216-227; 2. National Institutes of Health, National Institute on Aging (NIH). Reviewed March 1, 2023. Accessed May 24, 2023. <https://www.nia.nih.gov/health/alzheimers-disease-genetics-fact-sheet>; 3. Langlois CM et al. *Alzheimers Dement (N Y)*. 2019;5:705-716;
4. Ryan MM et al. *Dis Assoc Disord*. 2021;35:141-147; 5. Sperling RA et al. *Nat Rev Neurol*. 2013;9:54-58.

## Interest level in learning ApoE status<sup>4</sup>



77% of 1312 survey participants were aware of DTC testing, but only 7% knew their ApoE status, less than 0.8% through a provider; 90% were willing to share their ApoE status for AD Prevention Study recruitment

# GeneMatch Is a Program to Recruit Volunteers to AD Prevention Trials Based on Their ApoE Results

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Recruitment for AD prevention research is difficult because of a lack of awareness among cognitively healthy adults coupled with a high screen fail rate due to participants not having a genetic risk factor or biomarker evidence of disease<sup>1</sup>

## GeneMatch:<sup>2</sup>

- 80% of research studies do not complete enrollment on time
- National program
- Trial-independent
- Led by Banner Alzheimer's Institute
- Uses genetic testing to accelerate prescreening and enrollment for AD prevention trials

## Patients:

- Aged 50 to 90
- Live in the United States
- Cognitively healthy
- Can opt-out at any time
- May or may not learn their results
- Testing results are confidential and secure
- Test results are not part of the medical record

# Providing and Obtaining Informed Consent for Genetic Tests Can Be Challenging, Especially in People with Early AD or MCI

Four generally accepted decision-making abilities constitute capacity:

- Understanding
- Expressing a choice
- Appreciation
- Reasoning

Genetic test limitations that may affect informed consent:<sup>1</sup>

- The specific gene may not yet be known
- All pathogenic gene changes may not yet be identified
- Knowledge about the clinical significance of the variant may be limited
- Variants of uncertain significance may be identified

**Online self-test to determine whether to get ApoE testing:**

- <https://genetestornot.org>

Many factors can influence the informed consent process; these include patients' levels of health literacy and psychosocial stress, the complexity of information conveyed, and time limitations for clinic visits<sup>1</sup>

**Tests for decisional capability<sup>2,3</sup>**

- Assessment of the Capacity for Everyday Decision Making (ACED)
- MacArthur Capacity Assessment Tool for Treatment (MacCAT-T)

AD, Alzheimer's disease; MCI, mild cognitive impairment.

1. Roberts JS et al. *Neurobiol Dis.* 2020;141:104871; 2. Grisso T, Appelbaum PS. *Assessing Competence to Consent to Treatment: A Guide for Physicians and Other Health Professionals.* Oxford University Press; 1998; 3. Lai JM et al. *Am J Geriatr Psychiatry.* 2008;16:693-696.