

Guidelines for Genetic Counseling

ACMG/NSGC 2011 Guidelines, reaffirmed in 2018

- Obtain informed consent
- Provide genetic counseling and risk evaluation before ordering genetic testing
- Do not recommend direct-to-consumer ApoE testing
- Discuss informed decision-making, how results cannot be rescinded once learned, and the advantages and disadvantages of sharing results
- Discuss the implications of ApoE test results for family, finances, and insurance
- Conduct a baseline neurologic and neuropsychological evaluation before requesting genetic testing
- Offer patients the option of not learning genetic test results
- Ensure patients with cognitive impairment are accompanied by a caregiver

The API Genetic Counseling and Disclosure Process Provides a Framework for Large-Scale ApoE Genotype Disclosure to Clinical Trial Participants

Review family history with a focus on AD/dementia

Describe AD, MCI, and dementia clinical findings

Illustrate the impact of ApoE on AD risk

Describe ApoE inheritance patterns

Review implications of learning genetic information: psychological, familial, and clinical research impact

Address concerns: GINA protections

Provide options: proceed with disclosure, postpone disclosure, or decline disclosure

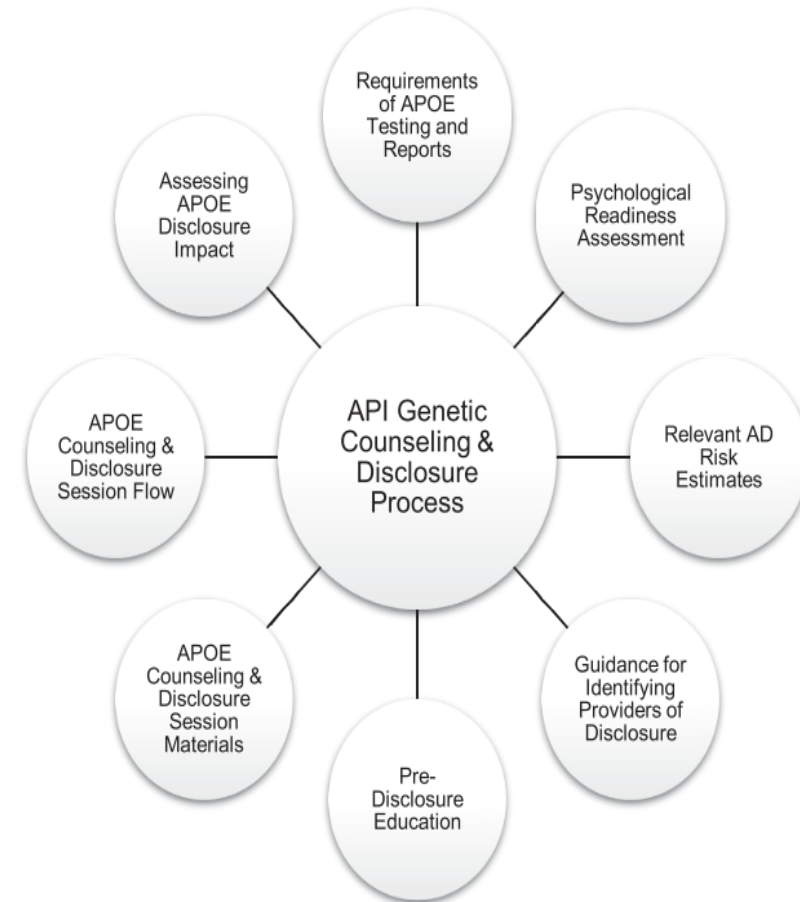


Fig. 1. Alzheimer's Prevention Initiative Genetic Counseling and Disclosure Process components. Abbreviations: APOE, apolipoprotein E; API, Alzheimer's Prevention Initiative; AD, Alzheimer's disease.

Obtain at Least 3 Generations of Family History; AD Risk Increases Even When Only Distant Relatives Have AD

Estimated relative risks for specific 1 st -degree relatives, ignoring 2 nd and 3 rd degree relatives	
Affected relative	Relative risk
mother	1.72
father	2.54
≥1 daughter	1.57
≥1 son	2.32
≥1 sister	1.74
≥1 brother	1.92

More research is needed. Previous studies suggested a higher risk when female relatives had AD

Relative risk of LOAD based on family history					
Number of 1st-degree relatives with AD	Odds ratio (2nd and 3 rd degree relatives ignored)	Number of 2 nd degree relatives with AD	Odds ratio (no 1 st degree relatives with AD, 3 rd degree relatives ignored)	Number of 3 rd degree relatives with AD	Odds ratio (no 1 st or 2 nd degree relatives with AD)
0	0.94 (n = 252,324)	0	0.93 (n = 225,137)	0	0.90 (n = 158,501)
≥1	1.73 (n = 18,494)	≥1	1.06 (n = 27,187)	≥1	0.99 (n = 66,636)
≥2	3.98 (n = 1394)	≥2	1.25 (n = 4162}	≥2	1.17 (n = 19,188)
≥3	2.48 (n = 154)	≥3	2.46 (n = 849)	≥3	1.43 (n = 5320)
≥4	14.77 (n = 21)	≥4	2.69 (n = 200)	≥4	1.44 (n = 1640)

270,818 people with at least 12 ancestors each; 4436 with AD