Worldwide Clinical Trials

Infographic

# Global APOE4 Prevalence & Implications for Alzheimer's Disease Research

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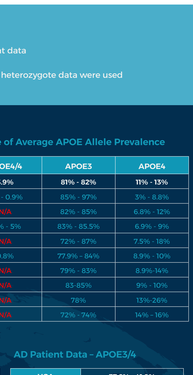
Understanding the global prevalence of APOE 3 and 4 genotypes based on country is essential for Alzheimer's disease (AD) research, as the APOE3 variant is neutral, yet the APOE4 variant is associated with late-onset AD. This is particularly because of the increased attention given to the amyloid hypothesis, which posits that the accumulation of amyloid beta (Aβ) protein in the brain is a key driver of AD progression and symptomology. Thus, understanding the prevalence and global distribution of APOE4 variants informs country and site selection, especially in Phase III/IV AD trials. This infographic explores the reported global APOE variant prevalence rates, including the prevalence differences between Northern, Central, and Southern Europe, to help guide and optimize trial operation decisions. In addition, these data allow trials to target geographic locations with high volumes of undiagnosed, genotypically vulnerable individuals to allow for more meaningful early or preventative interventions.

## Methods

For the global analysis, we performed a literature review for APOE3/4, and 4/4 frequency for the following 12 regions:


United States of America
China
Japan
South Korea
Singapore
Taiwan
India
Australia
New Zealand
Eastern Europe
(composite of Czech Republic, Hungary, Poland)

Within Europe specifically, we analyzed by northern, central, and southern regions.




**Northern**
Finland, Netherlands, Norway, Sweden, and United Kingdom

**Central**
Austria, Belgium, France, Germany, Hungary, Poland, Slovakia, and Switzerland

**Southern**
Israel, Italy, Portugal, Spain, Tunisia, and Turkey

### Additional Search Criteria:

- Included general healthy population data and AD patient data
- No lookback period
- If APOE3/4 allele frequency data were not available, E-/4 heterozygote data were used

## Findings

### Global

- If multiple APOE prevalence studies were found for a country, APOE frequencies were listed as a range (lowest to highest).
- APOE frequencies varied by region, sex, and race/ethnicity in each country.
- Different allele frequencies are reported in different studies of the same population.
- APOE3 and 4 were more accessible, data for APOE3/4 and 4/4 were less accessible per country.
- APOE4 prevalence tended to be higher in Australia, New Zealand, and North America, and lower in Asia; supported by published reviews listed in the references below.

**General Population Data – Range of Average APOE Allele Prevalence**

| | APOE3/4 | APOE4/4 | APOE3 | APOE4 |
|---|---|---|---|---|
| **USA** | **25.4%** | **3.9%** | **81% - 82%** | **11% - 13%** |
| India | 0% - 15% | 0% - 0.9% | 85% - 97% | 3% - 8.8% |
| Taiwan | N/A | N/A | 82% - 85% | 6.8% - 12% |
| China | 12% | 1.2% - 5% | 83% - 85.5% | 6.9% - 9% |
| Singapore | N/A | N/A | 72% - 87% | 7.5% - 18% |
| Japan | 16% | 0.8% | 77.9% - 84% | 8.9% - 10% |
| Eastern Europe | N/A | N/A | 79% - 83% | 8.9%-14% |
| South Korea | N/A | N/A | 83-85% | 9% - 10% |
| Australia | N/A | N/A | 78% | 13%-26% |
| New Zealand | N/A | N/A | 72% - 74% | 14% - 16% |

**AD Patient Data – APOE4/4**

| | |
|---|---|
| **USA** | **12.9%** |
| India | 4.1% |
| Taiwan | 6.1% |
| China | 5.65% |
| Singapore | N/A |
| Japan | 9.3% |
| Eastern Europe | 6.3% - 13.9% |
| South Korea | 1.4% |
| Australia | 13.4% |
| New Zealand | N/A |

**AD Patient Data – APOE3/4**

| | |
|---|---|
| **USA** | **37.6% - 41.8%** |
| India | 37.1% |
| Taiwan | 28.4% |
| China | 38% |
| Singapore | N/A |
| Japan | 31.3% - 38.8% |
| Eastern Europe | 36% - 48% |
| South Korea | 39.1% |
| Australia | N/A |
| New Zealand | 48.2% |

## Comparing Northern, Central, & Southern Europe

- If E3/E4 data were unavailable, we used E4 heterozygote data (APOE-/4).
- Allele frequency data displayed significant heterogeneity between studies of the same population and region.

### General Population Data

**APOE3/4**
Finland (Northern Europe proxy): 34.8%
Italy (Southern Europe proxy): 13.6%

**APOE4/4**
Finland (Northern Europe proxy): 5.8%
Italy (Southern Europe proxy): 1.6%

### AD Patient Data

**APOE-/E4**
Northern Europe: 61.25%
Central Europe: 51.74%
Southern Europe: 40.45%

**APOE4/4**
Northern Europe: 14.1%
Central Europe: 11.85%
Southern Europe: 4.56%

## Takeaways

Our research indicates that while APOE4 prevalence varies significantly by region and population, there are useful patterns to help guide strategy and research initiatives.

### APOE3/4 Genotype in the General Population

- In the general, undiagnosed population, this indicates vulnerability.
- Selecting countries with high populations of E3/4 variants that are not diagnosed with Alzheimer's Disease (AD) provides promise for:
  - Developing novel early intervention treatments.
  - Creating preventative treatments, which are critical in AD.
- The highest reported levels of E3/4 variants are found in:
  - The U.S. and Finland.

### APOE4/4 & APOE4 Genotypes

- These genotypes represent significantly increased vulnerability to late-onset Alzheimer's disease (AD).
- They are frequently reported in individuals already diagnosed with AD.
- The highest general population levels of these genotypes are found in:
  - Australia, Singapore, New Zealand, and Eastern Europe

### Already Diagnosed

- Those with AD and the APOE4/4 allele are the most populous in the U.S.
- Those with APOE3/4 are more widespread, including:
  - The U.S., and India, Taiwan, China, Japan, Eastern Europe, South Korea, and New Zealand.

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