We assigned participating countries to 7 global regions:

- **North America (NA)**: Canada, US, Mexico
- **South America (SA)**: Brazil, Chile, Peru
- **Europe**: Western (WE), Eastern (EE), Russia, Turkey
- **Asia (AS)**: China, Japan (JP), Korea, Malaysia, Philippines, Singapore, Thailand, Vietnam
- **Northwest Europe (NW)**: Belgium, France, Germany, Italy, Norway, Netherlands, Sweden, Switzerland, UK
- **Eastern Europe (EE)**: Bulgaria, Croatia, Estonia, Greece, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, Slovenia, Ukraine
- **South America (SA)**: Argentina, Brazil, Colombia, Ecuador, Peru, Uruguay

These regions were chosen as they are generally recognized and encompass the majority of the study participants. The results are presented in Table 1, which includes demographic and disease-related summaries of the participants at baseline. The table shows the mean age, sex, disease duration, and other variables across regions.

### Results

- **We examined data from 4694 participants. More participants were enrolled in North America than any other region.**
- **We observed significant effects of global region (p<0.01) for every variable we examined (Table 1, Figure 2).**

### Discussion

- **Most (86%) participants took approved AD therapies; anti-AD drug use was lower in SA, WE, and JP.** Recruiting treatment-naive AD patients will be difficult, even if enrolling globally.
- **NA, WE, and AU were similar in the proportions of male participants, apolipoprotein ε4 carriers, and participants enrolling with a spouse study partner.** AD, SE, and SA had lower proportions for these variables.
- **NA, WE, and AU had milder scores for the ADCS-Cog11 and MMSE scales (p<0.01 vs all other regions).** EE had worse ADAS-cog11 scores than all other regions.
- **NE and SA had more severe scores for the ADRD-ADL and the CDR-SB.** Mean scores in AS were milder than all regions except JP for the CDR-SB. NPI scores were highest in WP and SA, and lower in all other regions.
- **Several not mutually exclusive factors may contribute to the observed heterogeneity.** Regional differences in demographic and ethnogenetic factors; differences in drug development; differences in disease progression; differences in treatment availability; differences in disease awareness; differences in patient self-care and social activities; differences in healthcare infrastructure; and differences in healthcare access.

### Conclusions

- **Despite strict protocols, ample site training, and substantial trial monitoring—significant heterogeneity exists among global AD trial populations.**
- **Consistent regional patterns were observed when comparing scores on trial outcomes at screen and baseline, but seemed dependent upon whether the outcome measure was based on informant report.**
- **Sponsors should consider this heterogeneity when planning multinational AD trials.**

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