SUPPLEMENTARY MATERIAL

A Multimodal Latent Severity Axis for Alzheimer's Disease: Probabilistic PCA, Bayesian Trajectories, and Stage-Aware Timing Effects

AUTHORS:

Babak **Haji**[1], PhD and Amir Abbas **Tahami Monfared**[1,2], MD, PhD; for the Alzheimer's Disease Neuroimaging Initiative

AFFILIATIONS:

[1] Eisai Inc., 200 Metro Blvd, Nutley, NJ, USA 07110; [2] McGill University, Department of Epidemiology, Biostatistics, and Occupational Health, 2001 McGill College, Suite 1200, Montreal, QC, Canada H3A 1G1.

CORRESPONDING AUTHOR:

Amir Abbas Tahami Monfared, MD, PhD

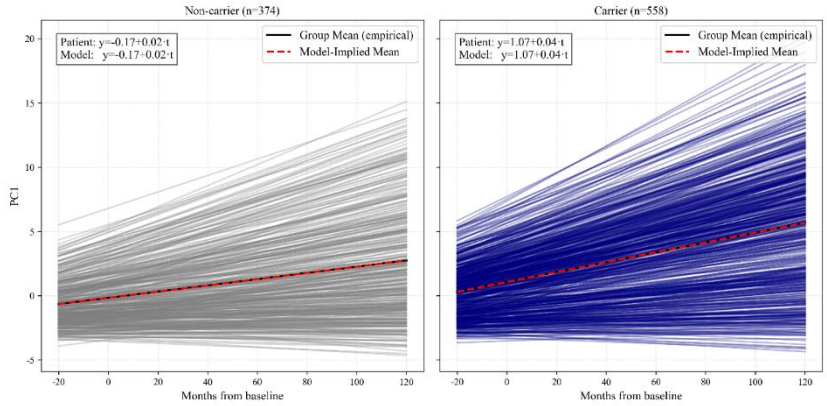
ORCID: https://orcid.org/0000-0003-4003-3192

Eisai, Inc., 200 Metro Blvd, Nutley, NJ 07110, USA

Tel.: (201) 746-2112

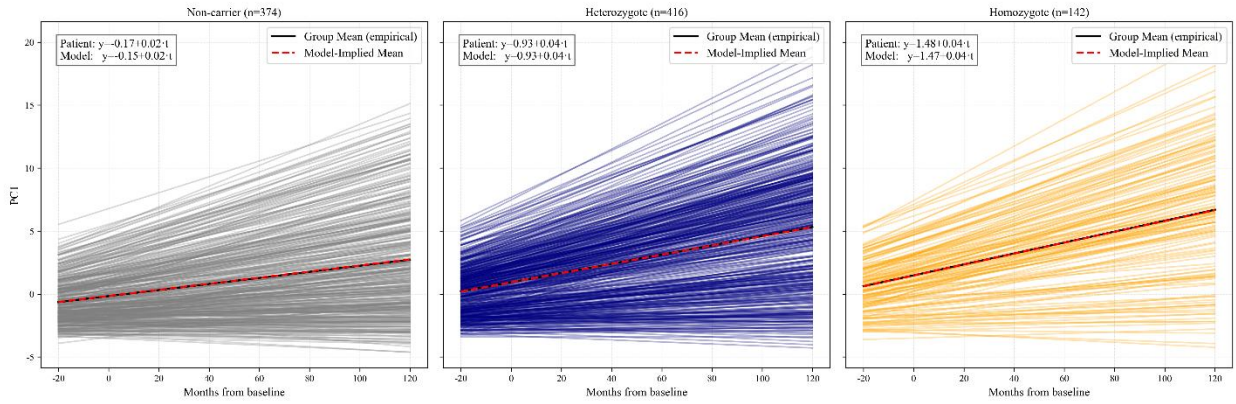
E-mail: amir.tahami@mcgill.ca

Figure S1. *APOE* ε4–stratified longitudinal trajectories along latent disease severity axis.



Individual posterior mean trajectories (thin lines) of latent PC1 are shown as a function of months from baseline for *APOE* ε4 non-carriers (left; $n = 374$) and ε4 carriers (right; $n = 558$). Solid black lines denote the empirical group-level mean trajectory obtained by averaging patient-specific posterior intercepts and slopes, while dashed red lines represent the model-implied population mean from the hierarchical Bayesian model. *APOE* ε4 carriers exhibit both a higher baseline disease burden (intercept shift) and a steeper longitudinal progression rate (slope) relative to non-carriers, indicating earlier entry onto the latent disease continuum and faster subsequent progression. The close agreement between empirical and model-implied means demonstrates good model calibration and supports a dose-dependent *APOE* effect on both disease severity at baseline and longitudinal progression along the integrated multimodal PC1 axis.

Figure S2. *APOE* ε4 dose–stratified longitudinal trajectories along latent disease severity axis.



Individual posterior mean trajectories of latent PC1 are shown as a function of months from baseline for *APOE* ε4 non-carriers (left; $n = 374$), heterozygotes (middle; $n = 416$), and homozygotes (right; $n = 142$). Thin lines represent patient-specific posterior trajectories derived from the hierarchical Bayesian model. Solid black lines denote the empirical group-level mean obtained by averaging individual posterior intercepts and slopes, while dashed red lines indicate the corresponding model-implied population means. A clear dose-dependent *APOE* effect is observed, with progressively higher baseline disease burden (intercept shifts) and steeper longitudinal progression rates (slopes) from non-carriers to heterozygotes and homozygotes. The close correspondence between empirical and model-implied means across all genotype groups demonstrates good model calibration and supports a graded influence of *APOE* ε4 dosage on both disease severity at baseline and subsequent progression along the integrated multimodal PC1 disease continuum.