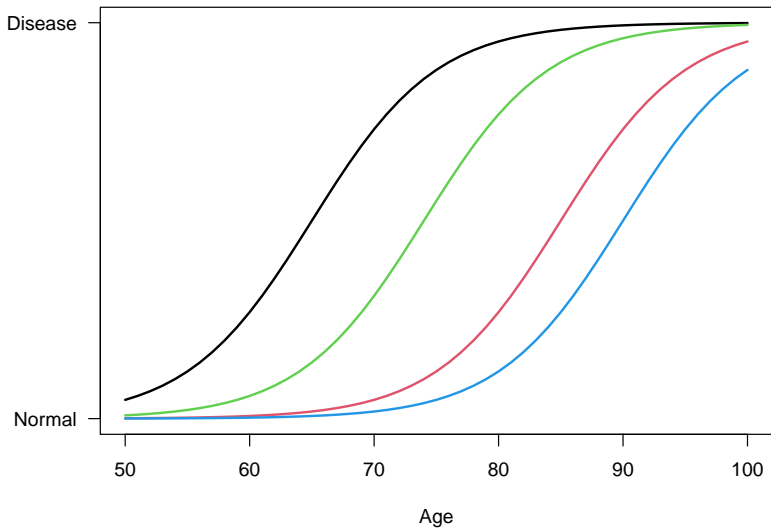


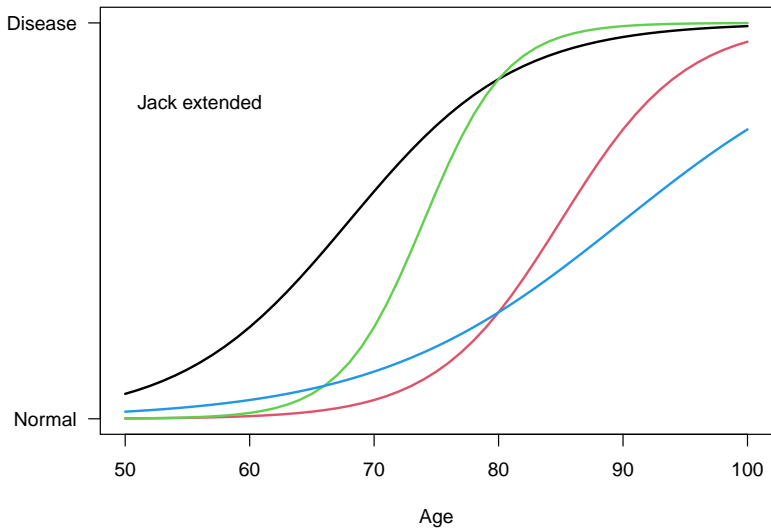
On fitting the Jack model

Terry Therneau

Mayo Clinic

Jan 2024

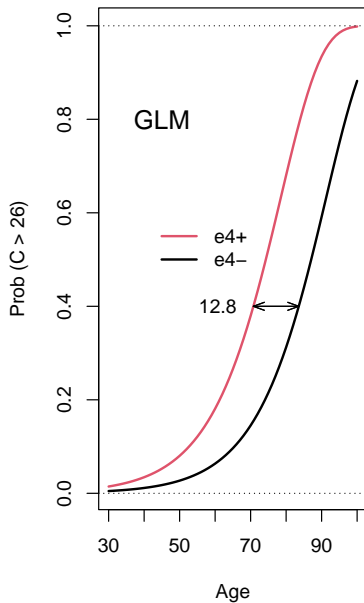
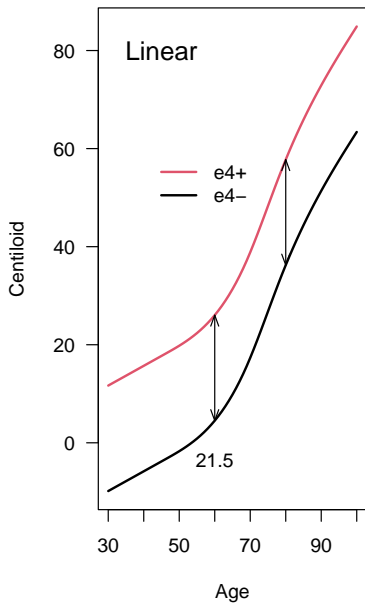


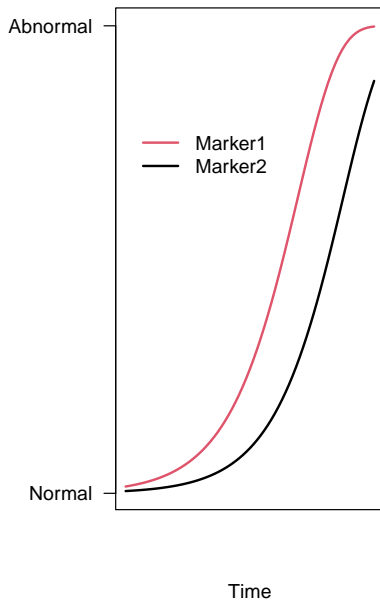
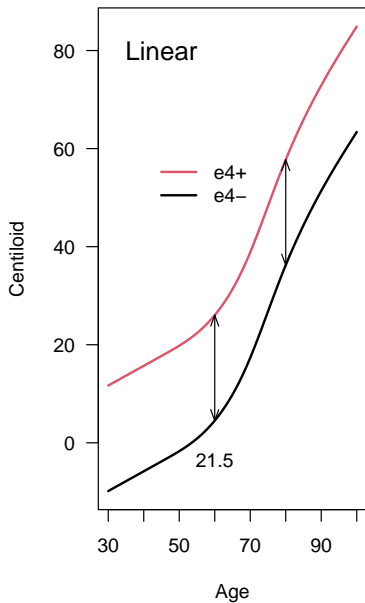


- ▶ Examples from the Mayo Clinic Study of Aging
- ▶ Age and sex stratified random sample from Olmsted County, Minn.
- ▶ 12/2004 to present

Statistical models

- ▶ Linear model (LM)
 - ▶ $y_{ij} = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \dots$
- ▶ Logistic regression, generalized linear model (GLM)
 - ▶ $y_{ij} = f(\beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \dots)$
- ▶ LME, GLME



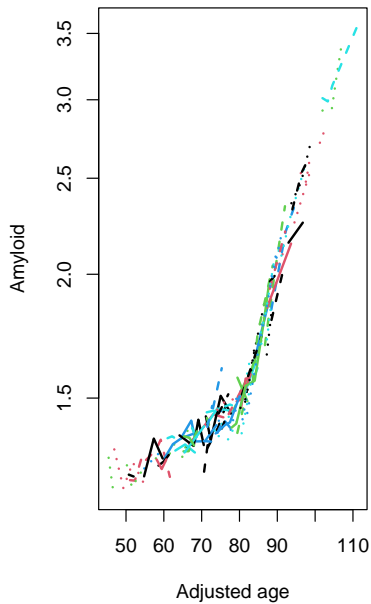
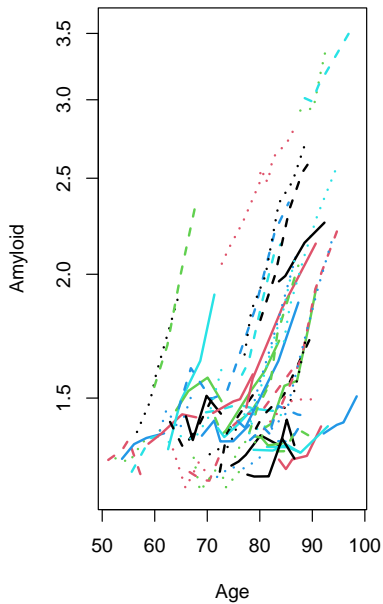


Jack model

- ▶ The Jack model is just a GLME

Jack model

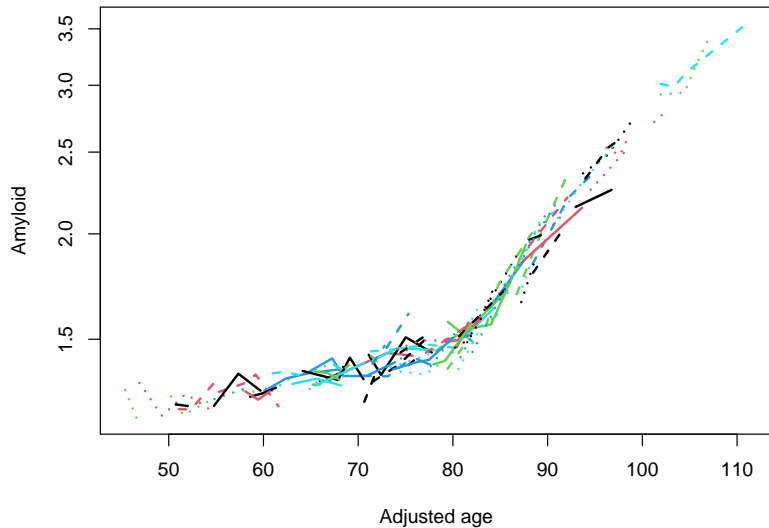
- ▶ The Jack model is just a GLME
- ▶ Except
 - ▶ we don't know f a priori (the link function)
 - ▶ a different f_k for each marker k
 - ▶ no 'out of the box' software

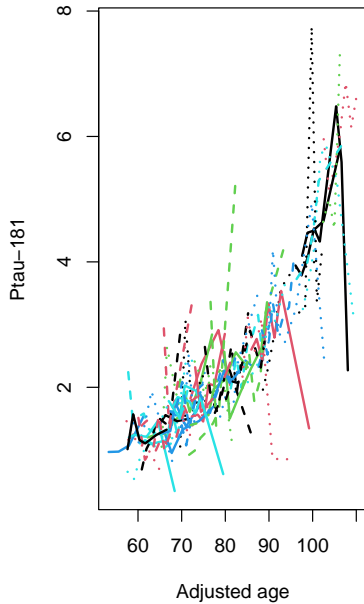
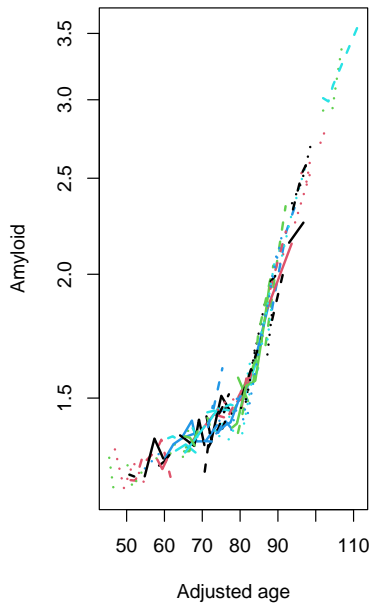


Solution

- ▶ Components
 - ▶ Coefficients β_1, β_2, \dots
 - ▶ Per subject random effects α_i
 - ▶ Per marker transform $f_k(\text{age} + \beta_1 APOE + \dots + \alpha)$
- ▶ All at once (Therneau): slow, touchy
- ▶ First get approximate α values (Koscik, Betthausen)
- ▶ First get an approximate f (Jedynak, Donohue)

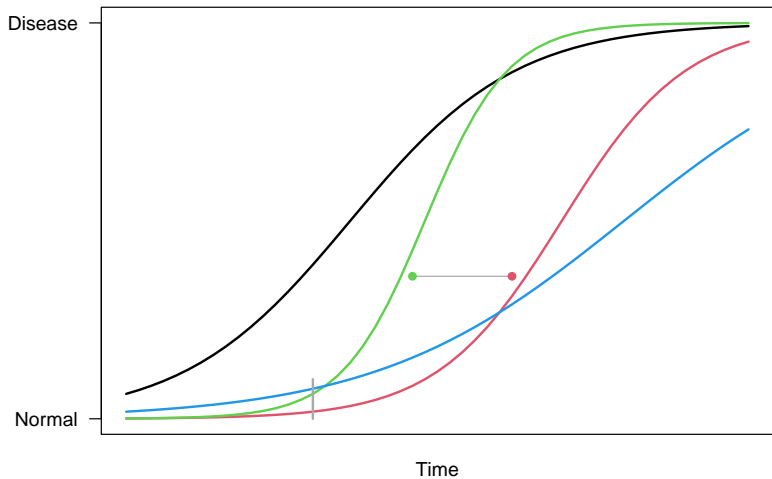
The real problem





What to do?

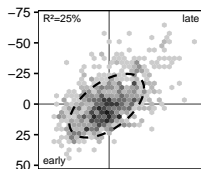
- ▶ More data
 1. Longer follow-up
 2. Less noisy markers
- ▶ Multiple markers + joint analysis



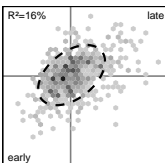
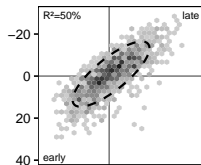
Challenge

- ▶ Multiple markers
 - ▶ Which ones, how many?
 - ▶ Longer delay times (pathology, cognition)
- ▶ Joint analysis across markers
 - ▶ GLM + shared random effects
 - ▶ Other models
 - ▶ Sensible constraints

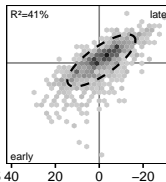
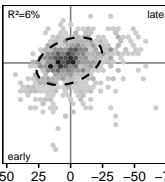
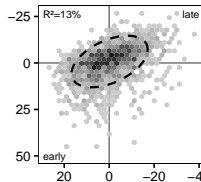
Amyloid
onset
adjustment



Tau
onset
adjustment



P-tau217
onset
adjustment



P-tau181
onset
adjustment

Summary

- ▶ Many models doing essentially the same thing.
- ▶ More information per participant
 - ▶ Multiple markers. Which ones, how many?
- ▶ Comprehensive analysis across markers
 - ▶ GLM
 - ▶ Shared random effect
 - ▶ Correlated random effects
 - ▶ More comprehensive models
 - ▶ Co-pathology
 - ▶ Latent traits (HMM)