

# Modeling the Transition from Cognitive Health to Dementia

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# Overview

- Categorical versus continuous outcomes
- Influences across the spectrum from intact cognition to dementia

# Data Source

## Rush Memory and Aging Project

- Annual clinical evaluations and brain autopsy at death
- Began in 1997, ongoing
- >1350 completed baseline evaluations
  - Age 80.1 (7.5)
  - Education 14.4 (3.3)
  - Women, % 72.6
  - NCI, % 67.5
  - MCI, % 27.0
  - Dementia, % 5.5
- >200 incident dementia
- >275 brain autopsies

# Data Source

## Rush Religious Orders Study

- Annual clinical evaluations and brain autopsy at death
- Began in 1994, ongoing
- >1150 completed baseline evaluations

Age	75.7 (7.5)
Education	18.1 (3.4)
Women, %	69.1
NCI, %	68.7
MCI, %	24.3
Dementia, %	7.0

- > 250 incident dementia
- > 500 brain autopsies

# Data Source

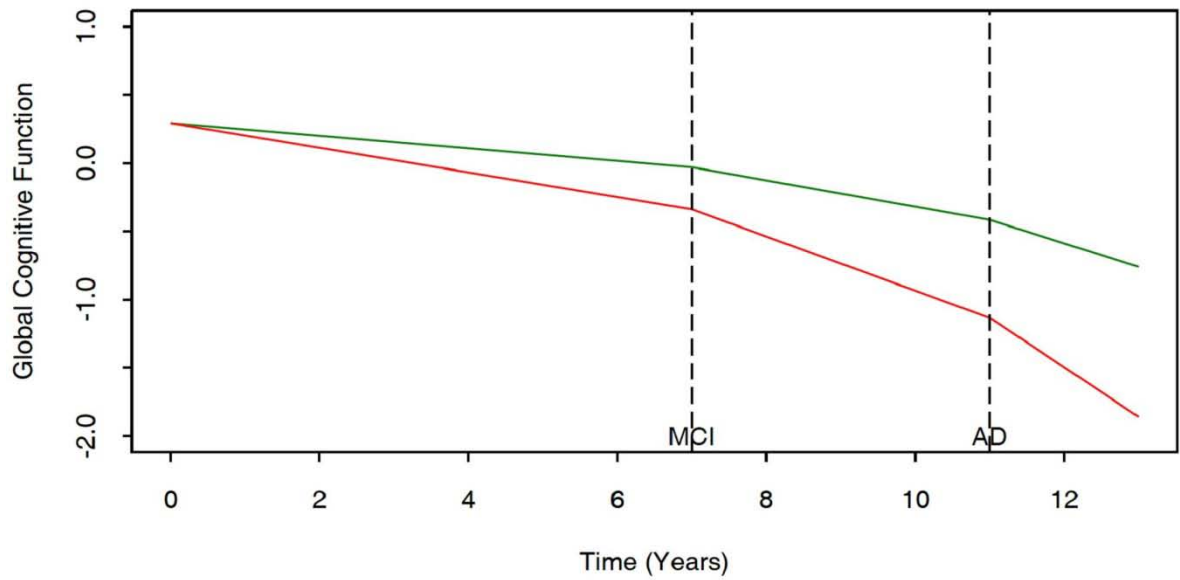
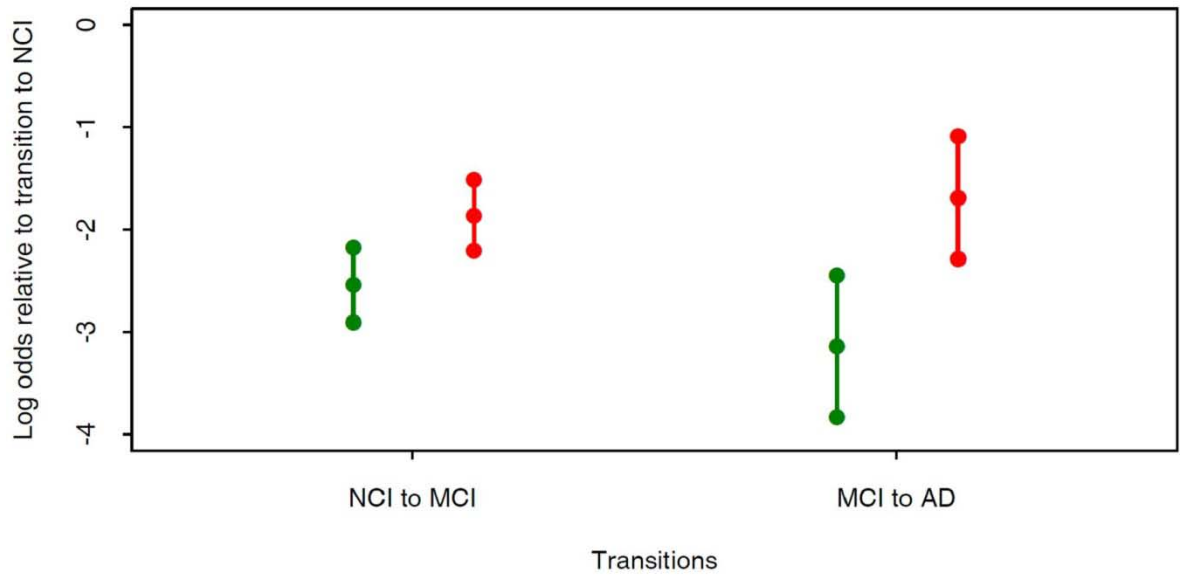
- Annual clinical evaluations
  - Battery of 17 cognitive performance tests
  - Clinical classification of MCI, dementia, and AD
- Blinding of clinical staff to previously collected data

# Statistical Approach

- Logistic Markov model
  - treats outcomes as a transition between different stages
  - transition probability specified through polychotomous logistic regression
  - correlation of within-subjects measurements accounted for by random effects
- Mixed-effects model
  - rate of change in cognitive function over time is primary outcome
  - allowed rate of cognitive change to shift when MCI and AD were first diagnosed

# Summary Measure of AD Pathology

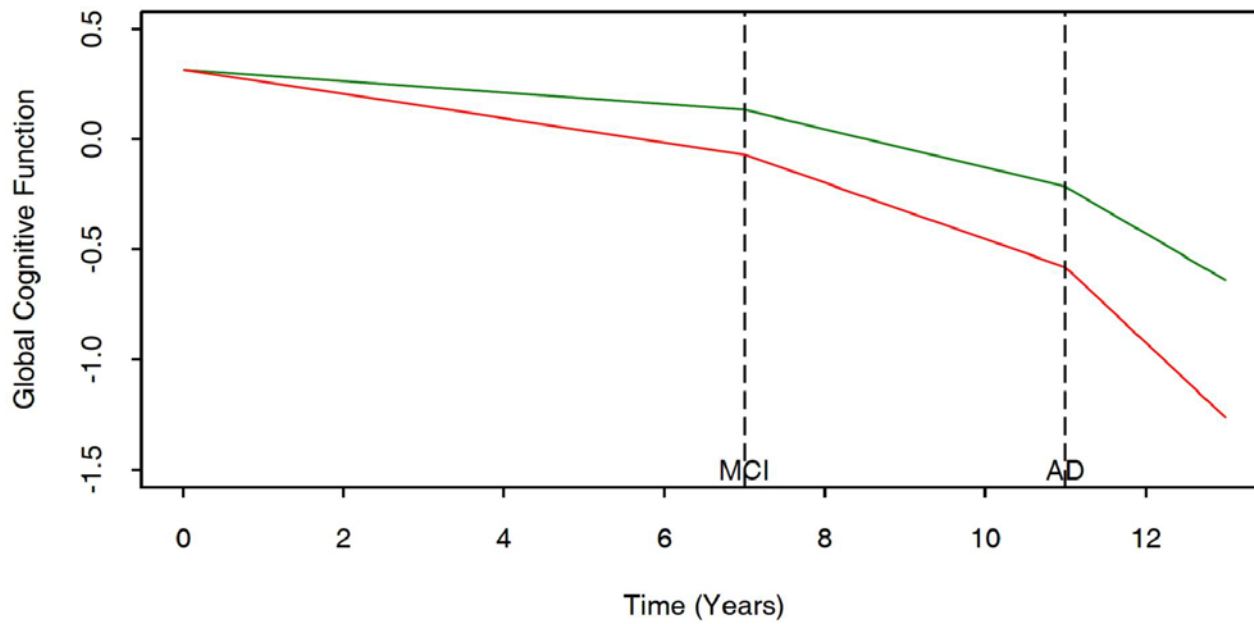
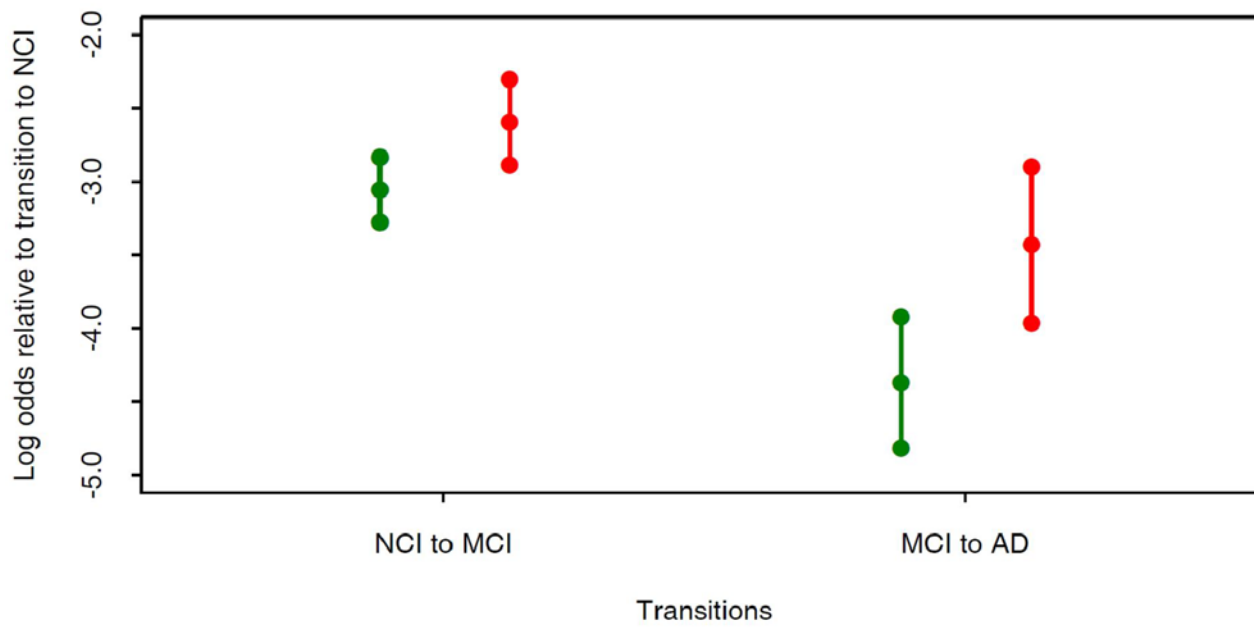
- Uniform neuropathologic examination blinded to all clinical data
- AD pathology quantified in 5 brain regions (modified Bielschowsky silver stain)
- Raw counts of neuritic plaques, diffuse plaques, and neurofibrillary tangles converted to standard scores and averaged





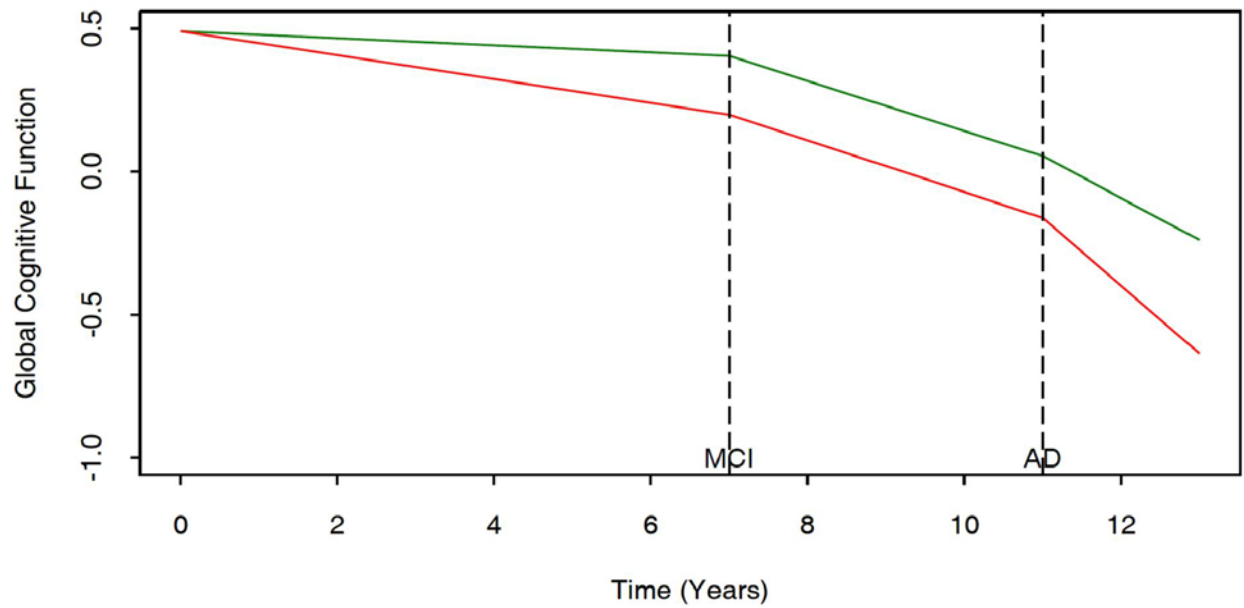
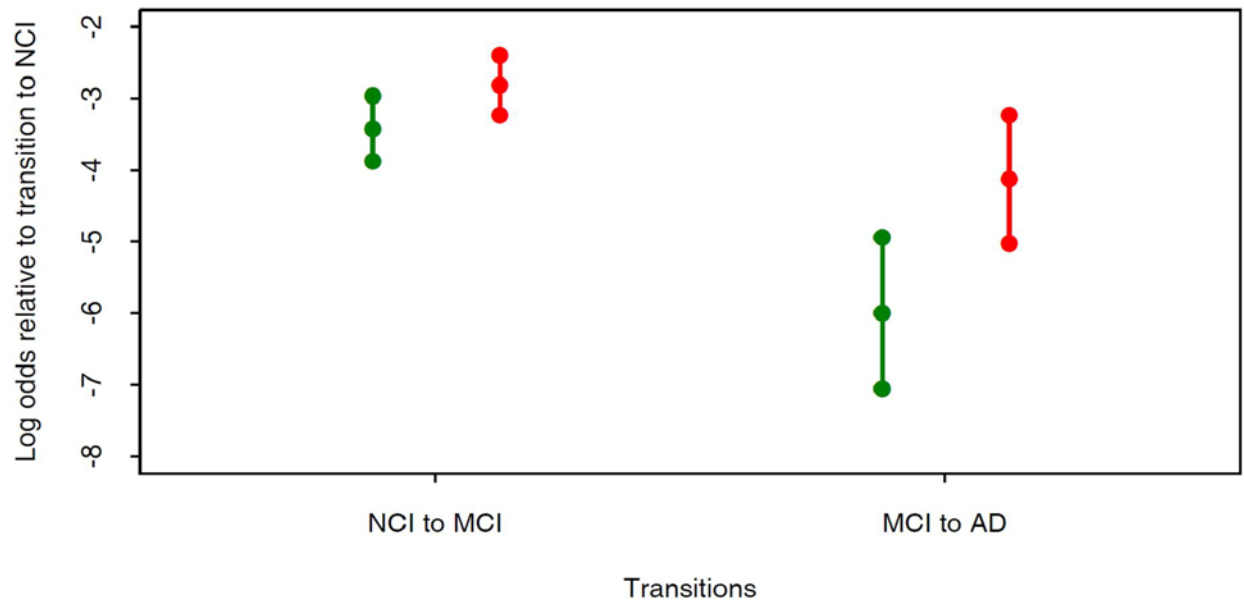
# Apolipoprotein E $\epsilon$ 4 allele

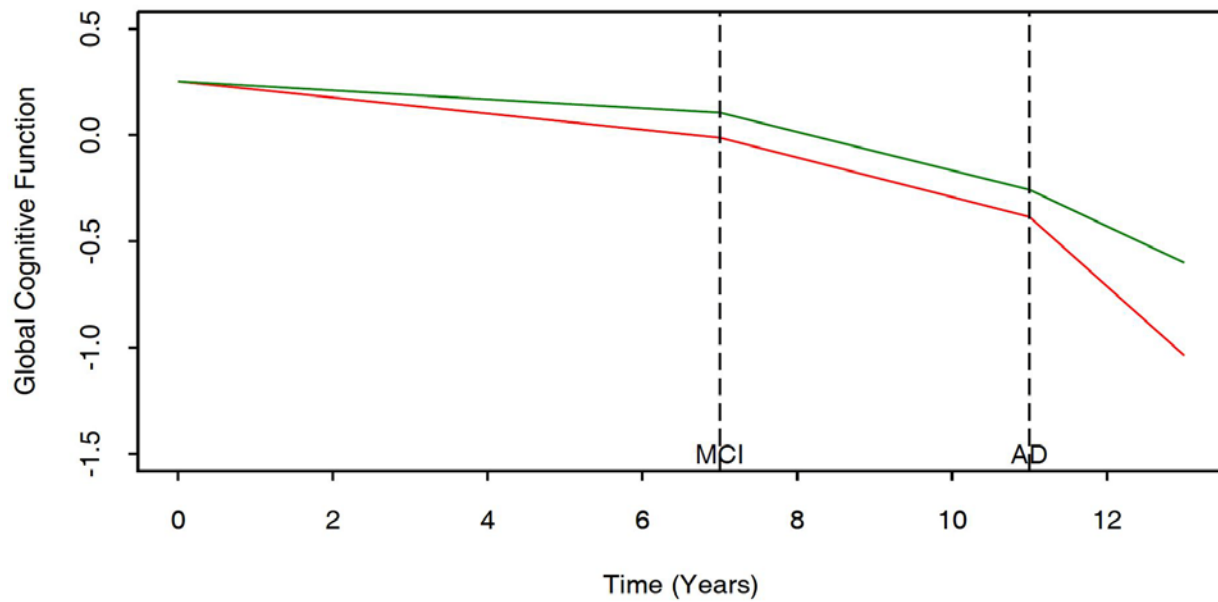
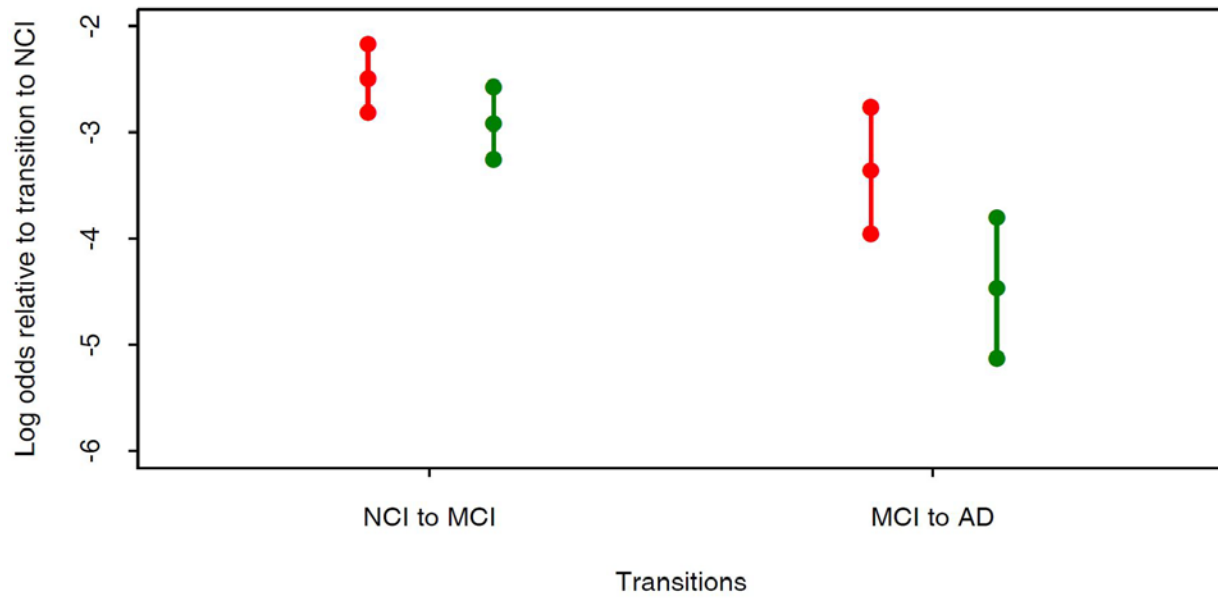
- Association with cognitive loss before and after dementia onset
- Association with cognitive impairment mediated by AD pathology



# Personality

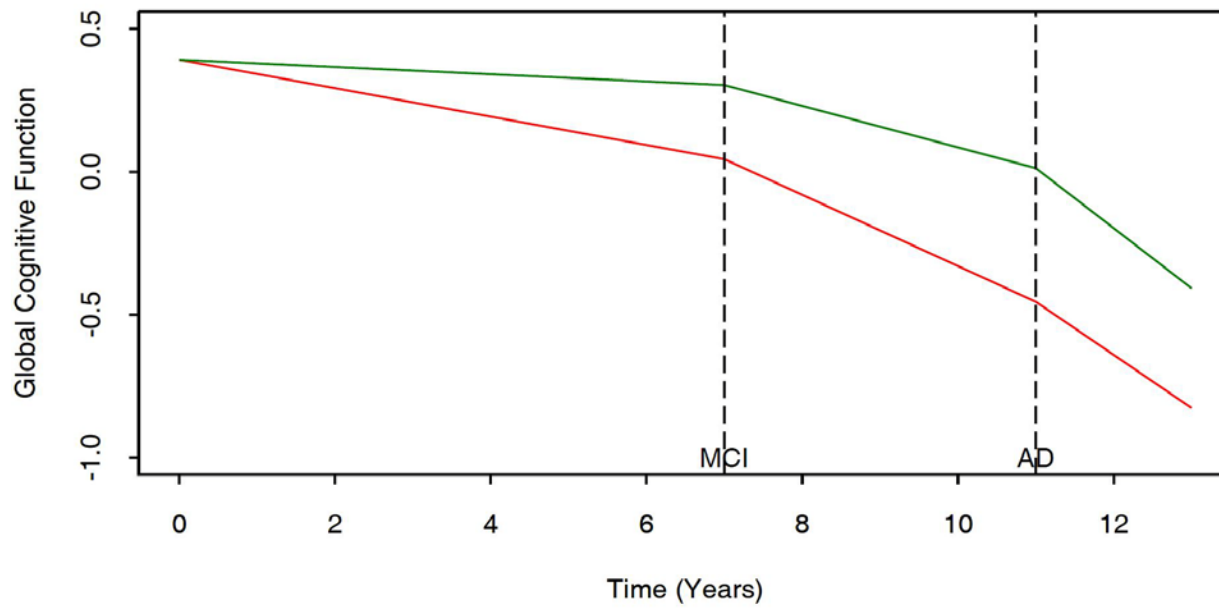
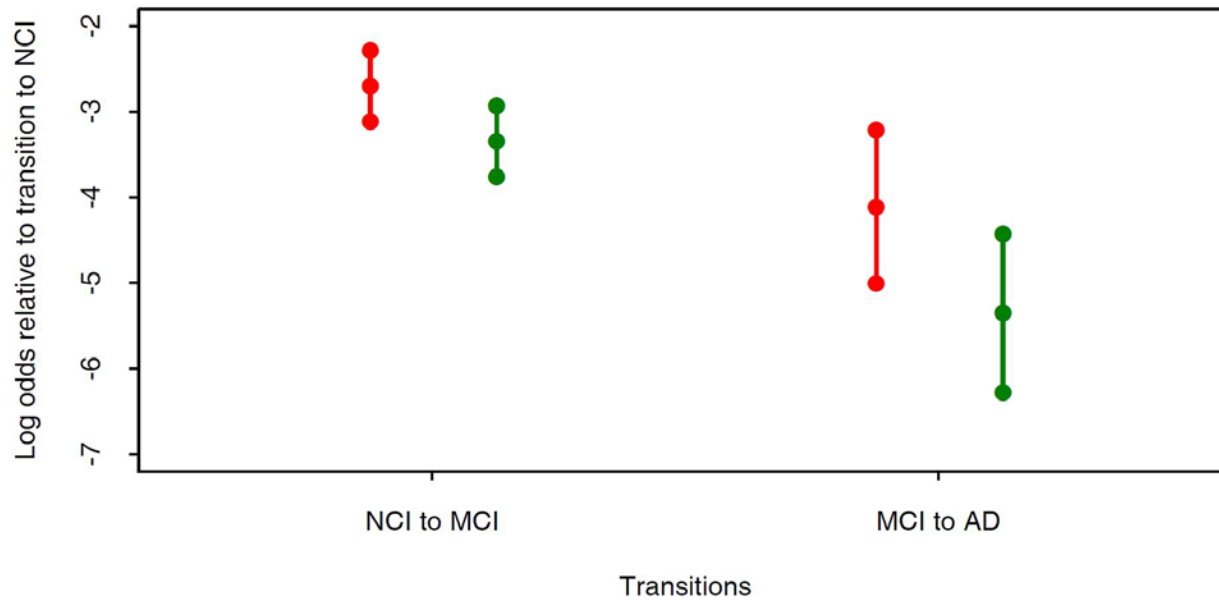
- Neuroticism
- Conscientiousness

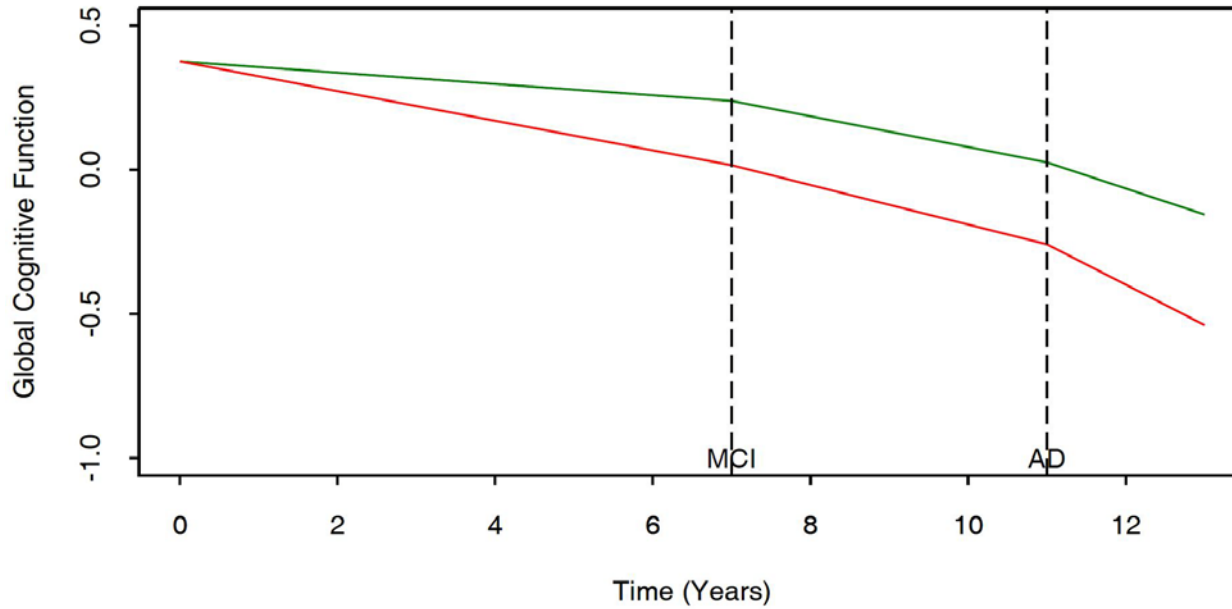
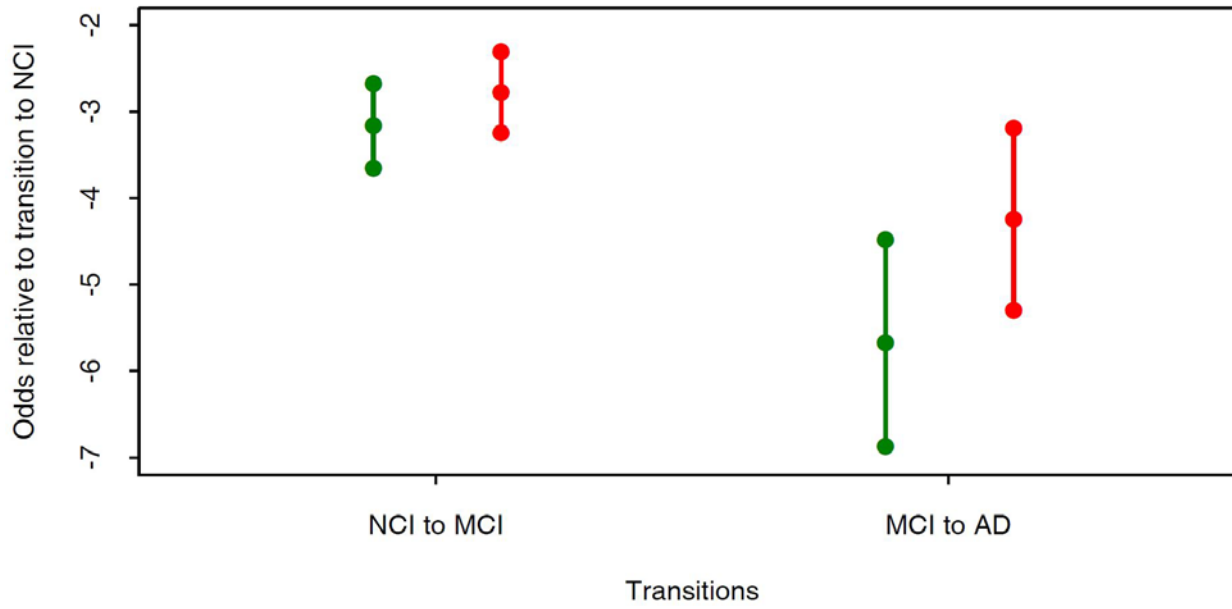




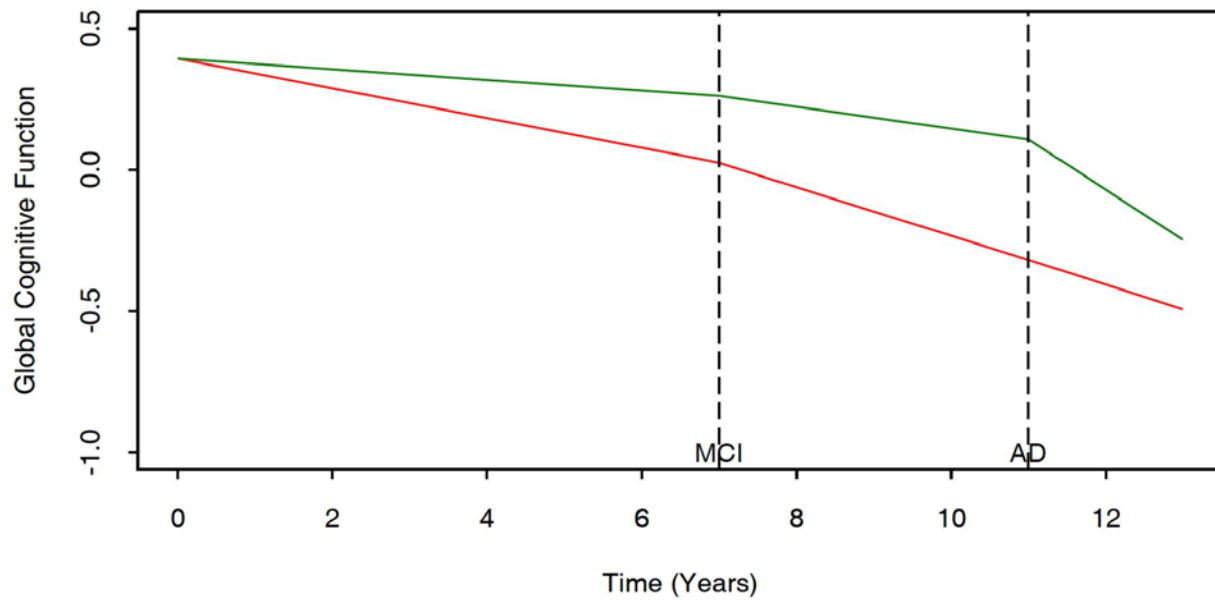
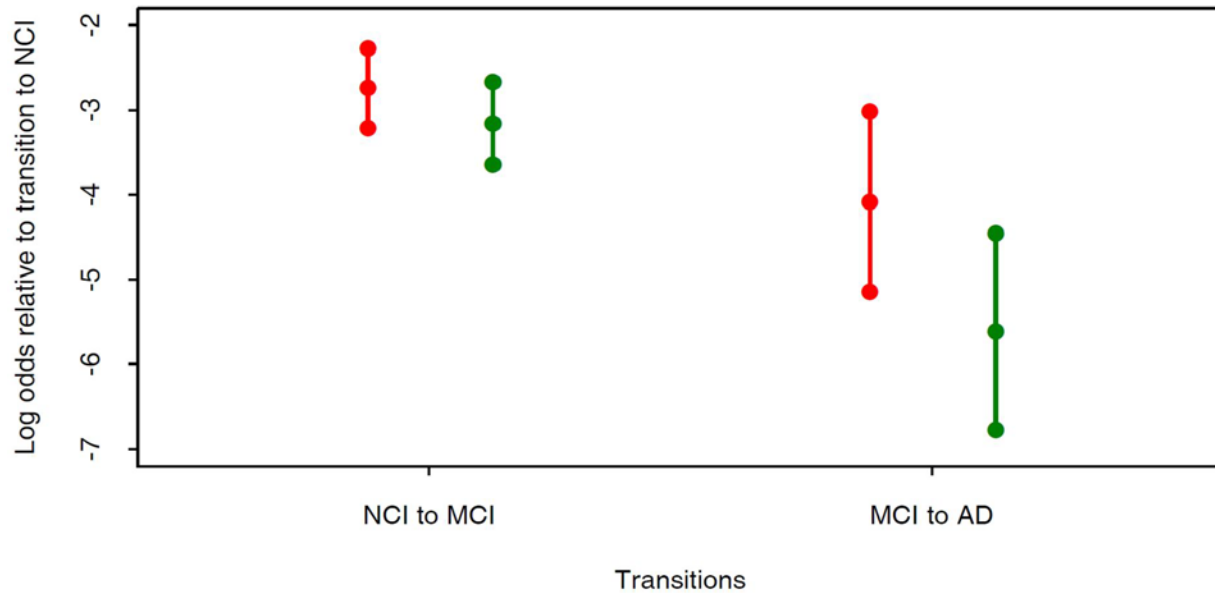
# Social Engagement

- Frequency of social interaction
- Perceived connectedness
- Purpose in life









# Conclusions

- Categorical vs continuous outcome
- No cognitive impairment – dementia spectrum
  - AD pathologic burden
  - APOE  $\epsilon$ 4 allele
  - Psychosocial variables

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- Disclosures: None