Purpose in life and other determinants of cognitive resilience

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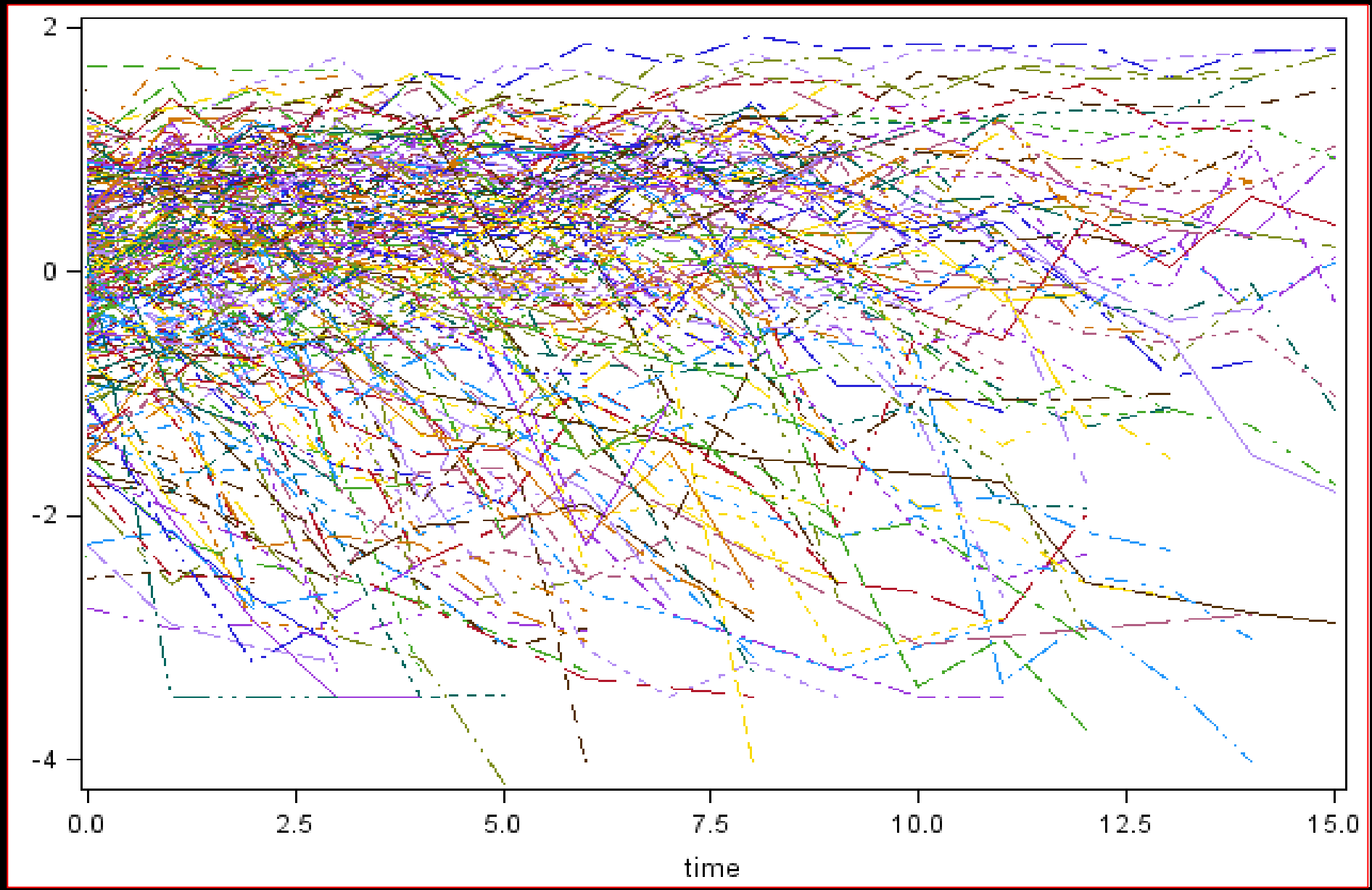
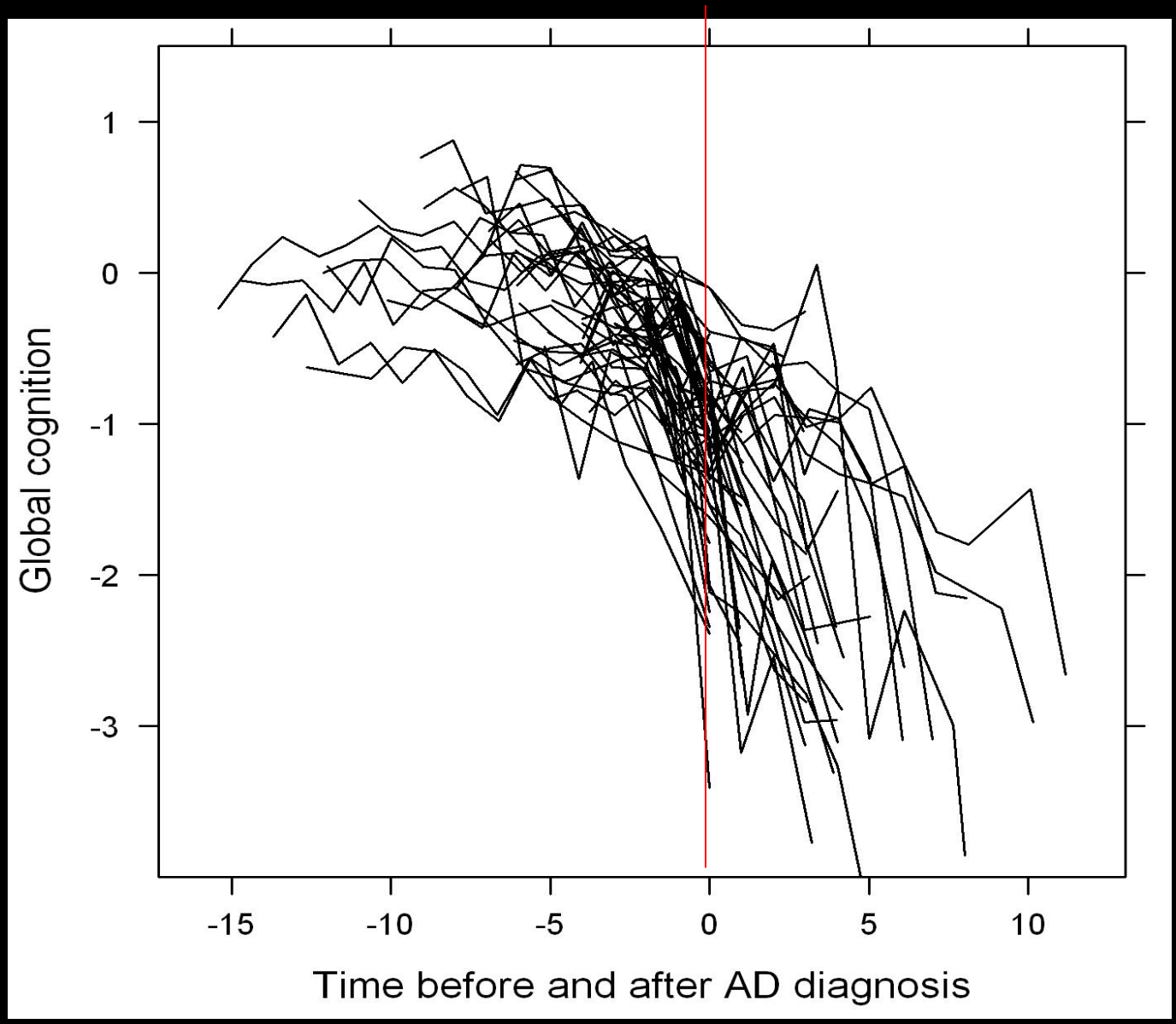
Cognitive aging

Reality of cognitive decline in old age



Cognitive change before and after AD diagnosis



Objectives

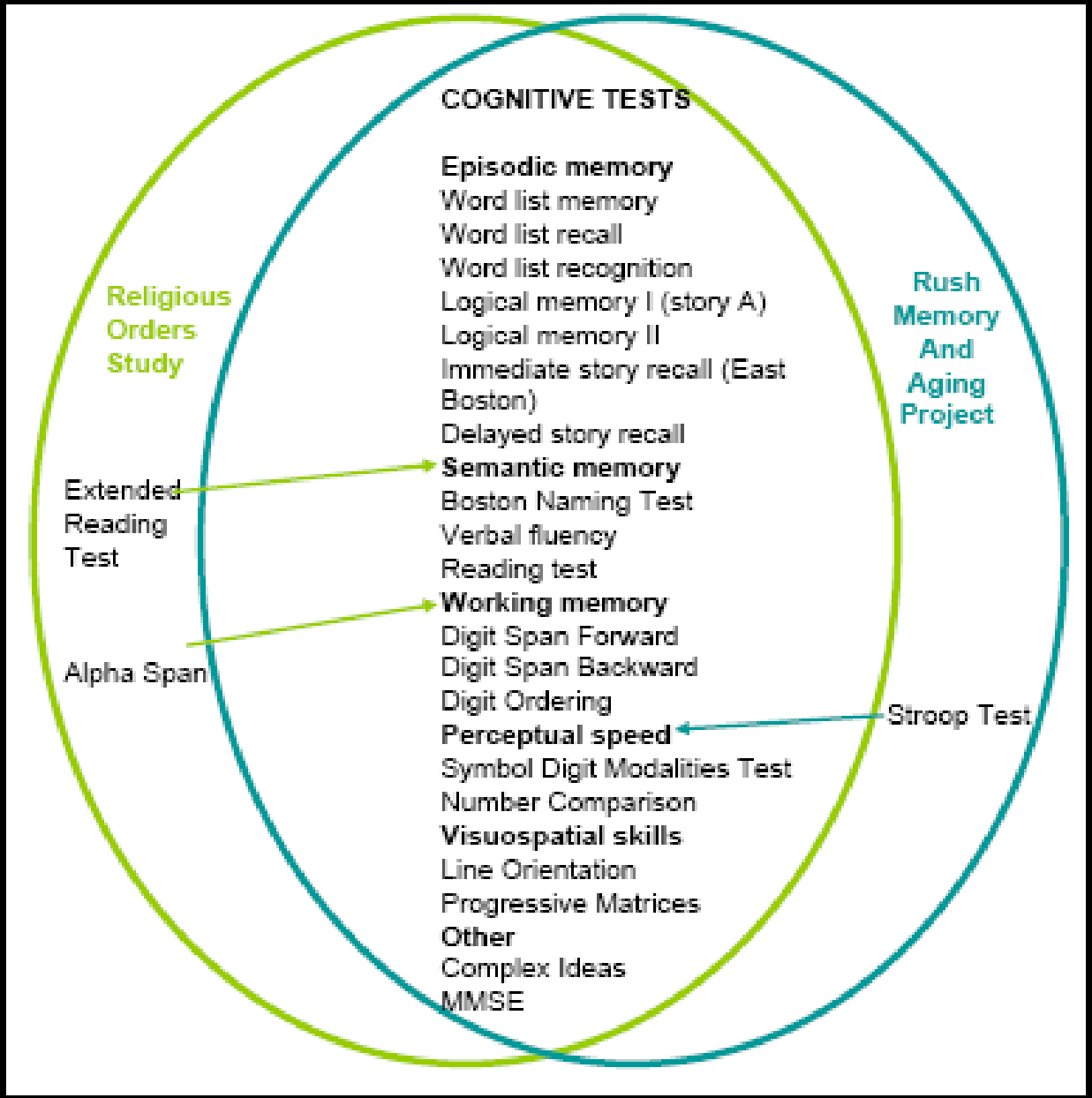
- What drives cognitive decline in old age
  - Age-related neuropathologies

- Experiential resilience factors
  - Provide protection in the face of accumulating neuropathology

The Rush Memory and Aging Project and the Religious Orders Study

- Began in 1990s
- > 3,000 older persons enrolled without dementia
- Detailed annual clinical evaluations, neuro exams, cognitive testing (up to about 23 years)
- All agreed to donate brain, spinal cord, muscle, nerve

- > 600 have developed dementia
- > 800 have developed MCI
- > 1,200 autopsies



Age-related neuropathologies

Alzheimer's disease

Cerebrovascular disease

Lewy body disease

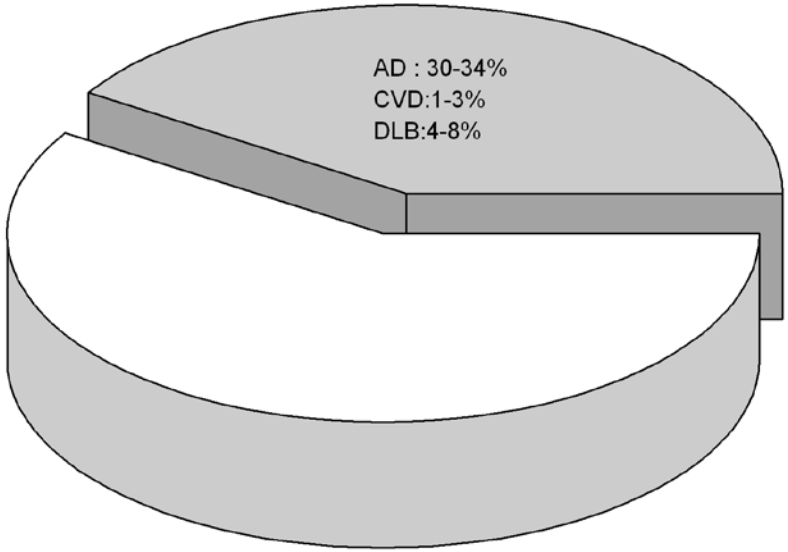
Several others

What drives cognitive decline in old age?

- Neuropathology very common in brains of older persons
  - Alzheimer's disease, cerebrovascular disease, Lewy bodies, other
- Frequently co-occur: nearly 2/3 have 3+
- Neuropathologies nearly always present in dementia, but also very common in older persons without dementia or any overt cognitive impairment
- Mismatch between pathology and cognition suggests that people differ in their ability to tolerate pathology (resilience)

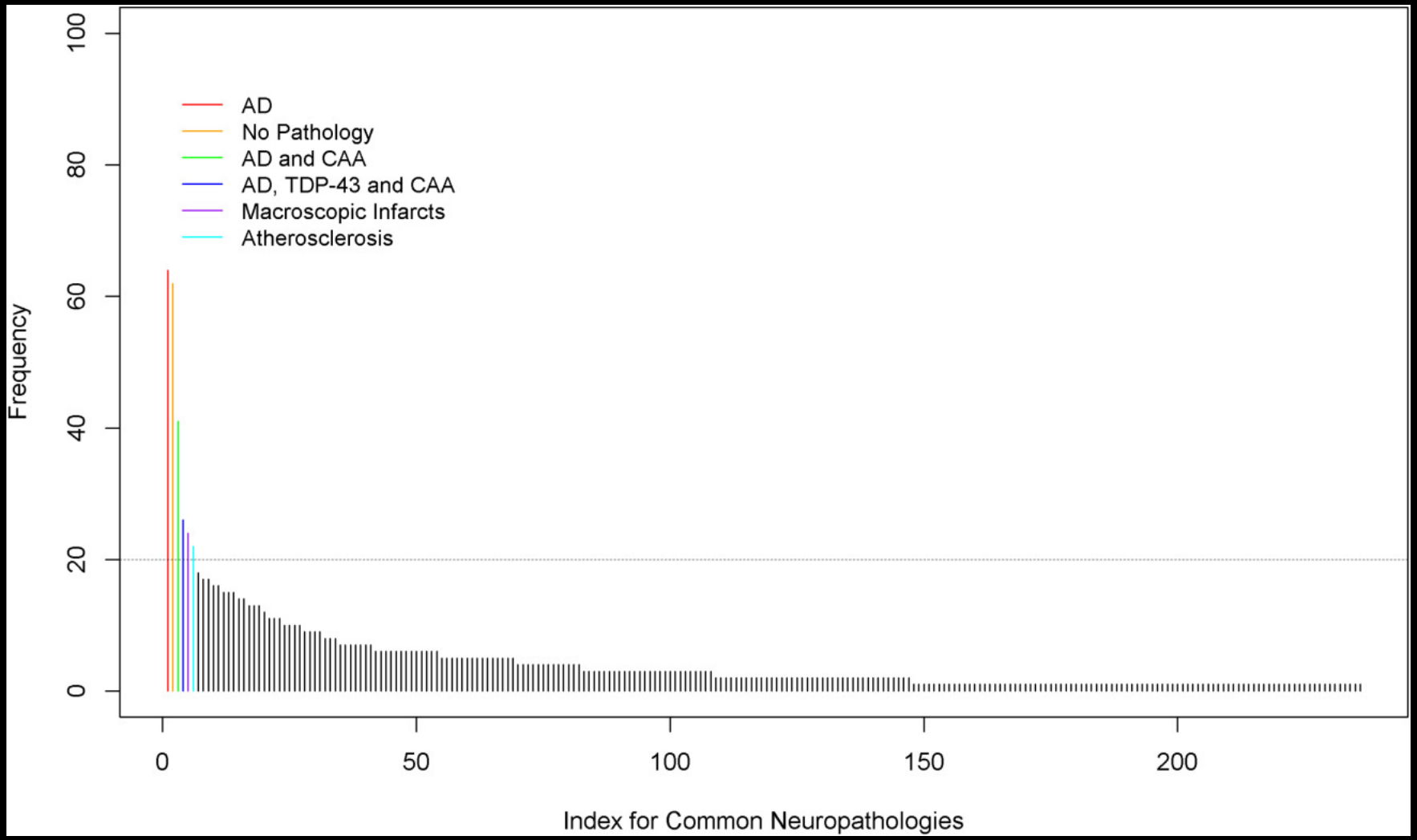
Gaps in knowledge

Variance explained by all pathologies=41%



RESIDUAL=59%

Tremendous heterogeneity in the comorbidity and impact of age-related neuropathologies



Boyle et al., *Annals of Neurology* 2018

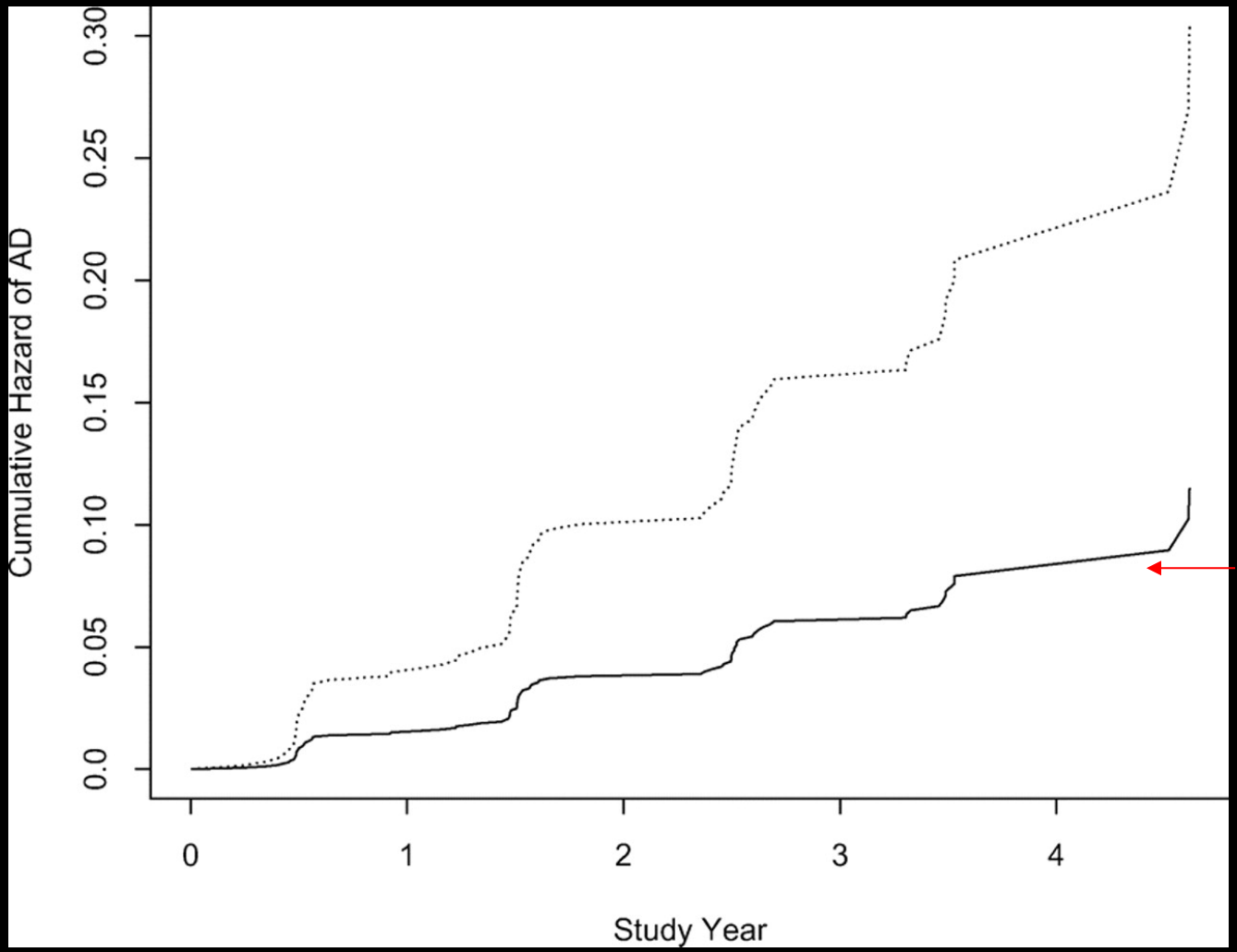
Resilience factors: experiential

Factors that protect against cognitive decline even in face of accumulating neuropathology

How do they work? independent, interaction, direct effects

Cognitive activity and risk of AD

Reading, playing games, going to museums, learning new things

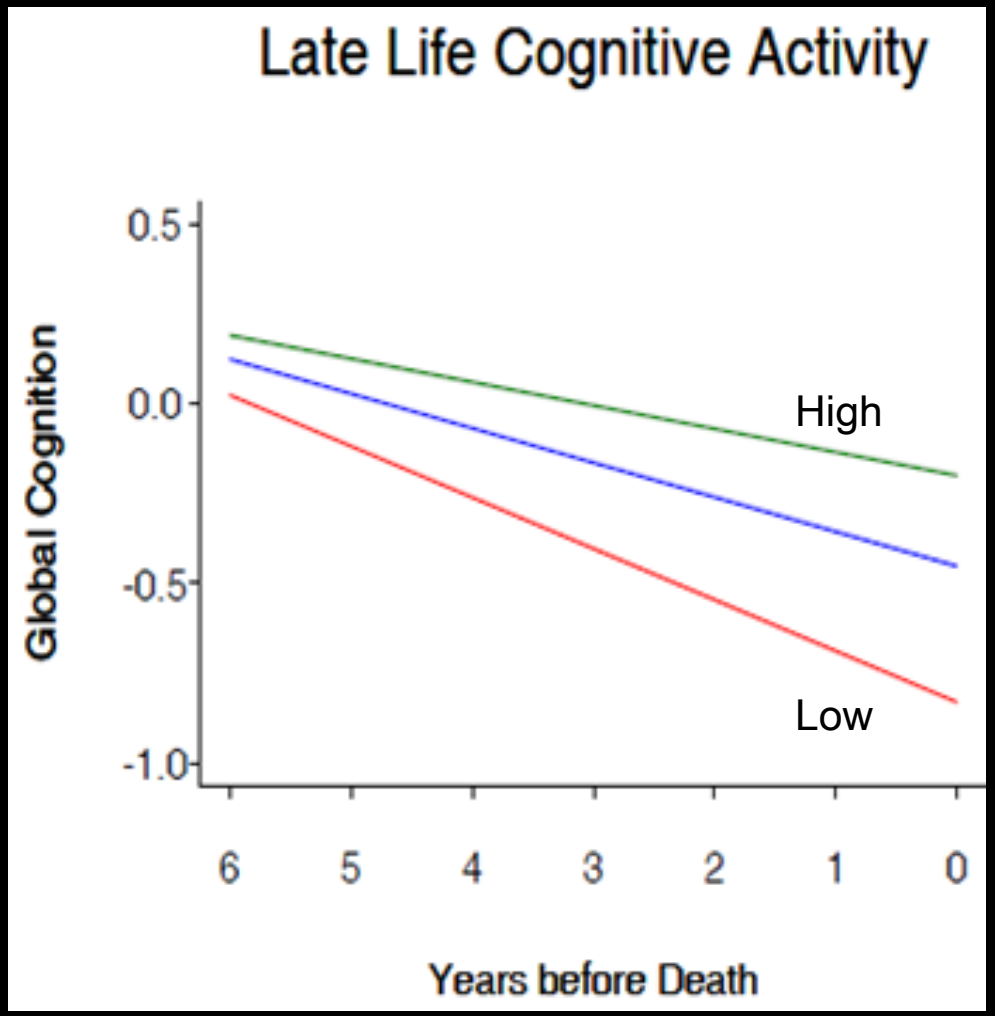


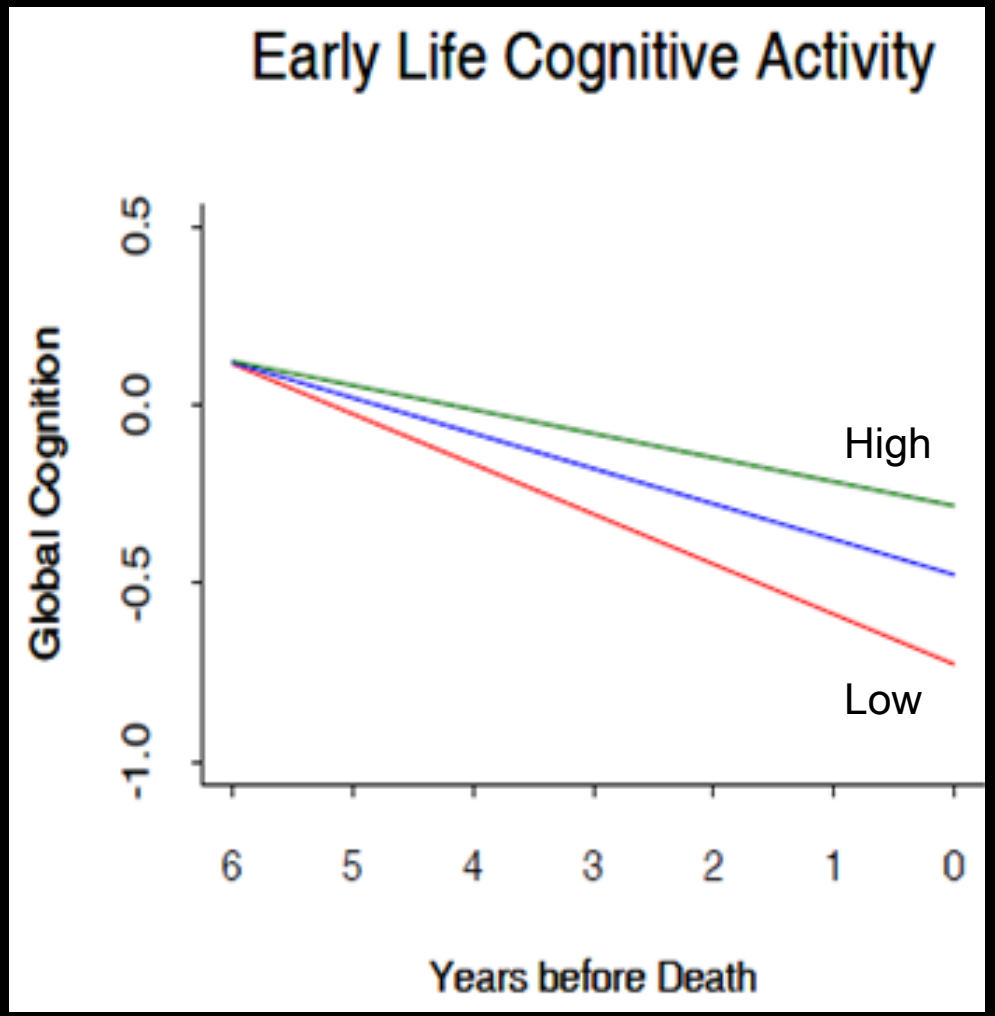
HR = 0.58; 95% CI: 0.44, 0.77

Cognitively active person 2x less likely to develop AD

Wilson et al. Neurology 2007;69:1911-1920

Lifespan cognitive activity is related to cognitive decline after controlling for common pathologies (independent effect)





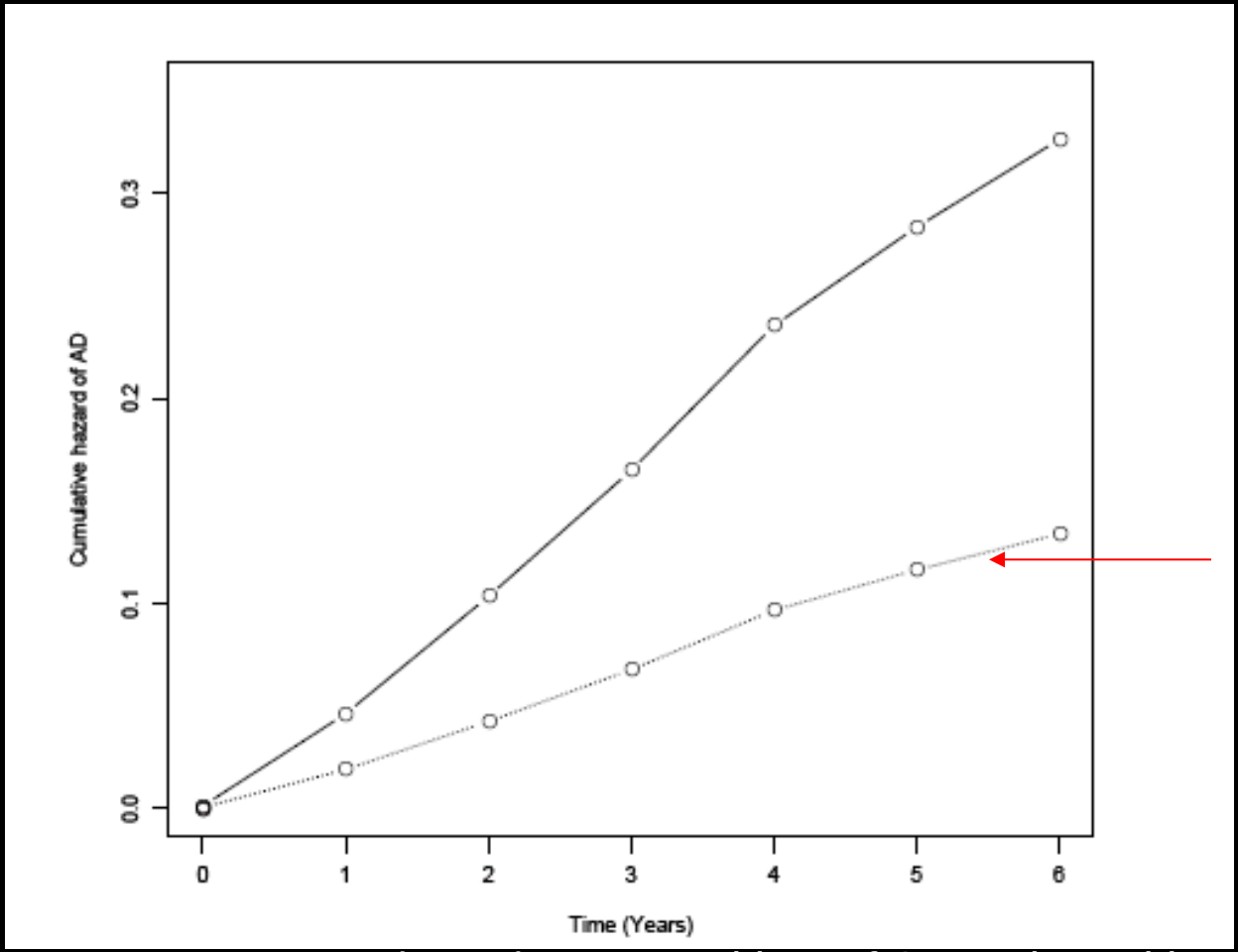
Early + late life cognitive activity=14% of variability in decline (additive effects)

Wilson et al. *Neurology* 2014

Purpose in life and risk of AD

Tendency to have a sense that life is meaningful, be goal focused and driven

Ex: “I enjoy making plans for the future and working them to a reality”



HR=0.48

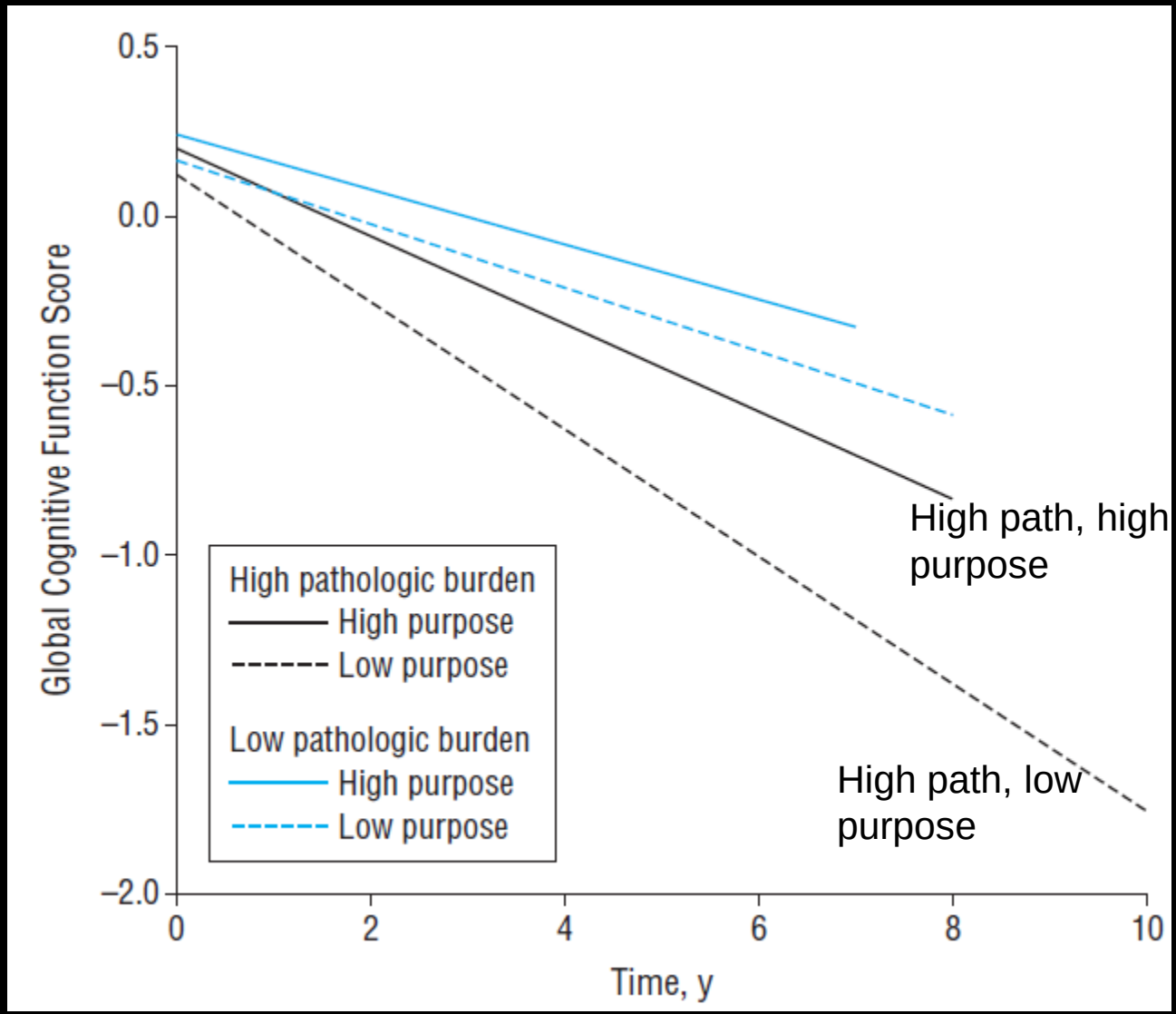
95% CI: 0.33, 0.69

High purpose 2.4x more likely to remain free of AD

Boyle et al. 2009, *Archives of General Psychiatry*

Purpose in life modifies the association of AD pathology with cognitive decline (interaction)

High purpose, slower decline despite burden of pathology



Boyle et al. *Arch General Psychiatry.* 2012;69:499-506.

Direct effects on pathology

- Purpose in life lowers the risk of macroscopic infarcts in the brain by almost 50%
  - OR = 0.535, 95% CI = 0.346-0.826, *p*=0.005

- Behavioral/psychological interventions to improve purpose may help prevent cerebrovascular disease

Yu et al., *Stroke* 2016

- Education
- Early life music/language instruction
- Social engagement
- Physical activity
- Positive affect
- Conscientiousness
- Lifespace

**mostly independent effects, many factors and mechanisms unknown

Conclusions

Age-related neuropathologies are important drivers of cognitive decline but there is tremendous heterogeneity in their comorbidity and impact

Cognitive aging is a complex function of neuropathology and resilience factors

Focus on factors that provide protection in the face of accumulating neuropathology may facilitate novel interventions to reduce the burden of cognitive decline

Can be more broadly applied and may have major public health benefit

Acknowledgements

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