# Economic, social and environmental enablers of healthy brain and cognitive ageing

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# What is cognitive and normal brain ageing?

- Stable verbal ability
- More variability
- Some memory decline
- Executive function declines
- Shrinkage in frontal and hippocampal regions from age 60-70
- Decrease in cortical density due to declining synaptic connections
- Shrinkage in myelin resulting in slow processing
- Decline of chemical messenger system

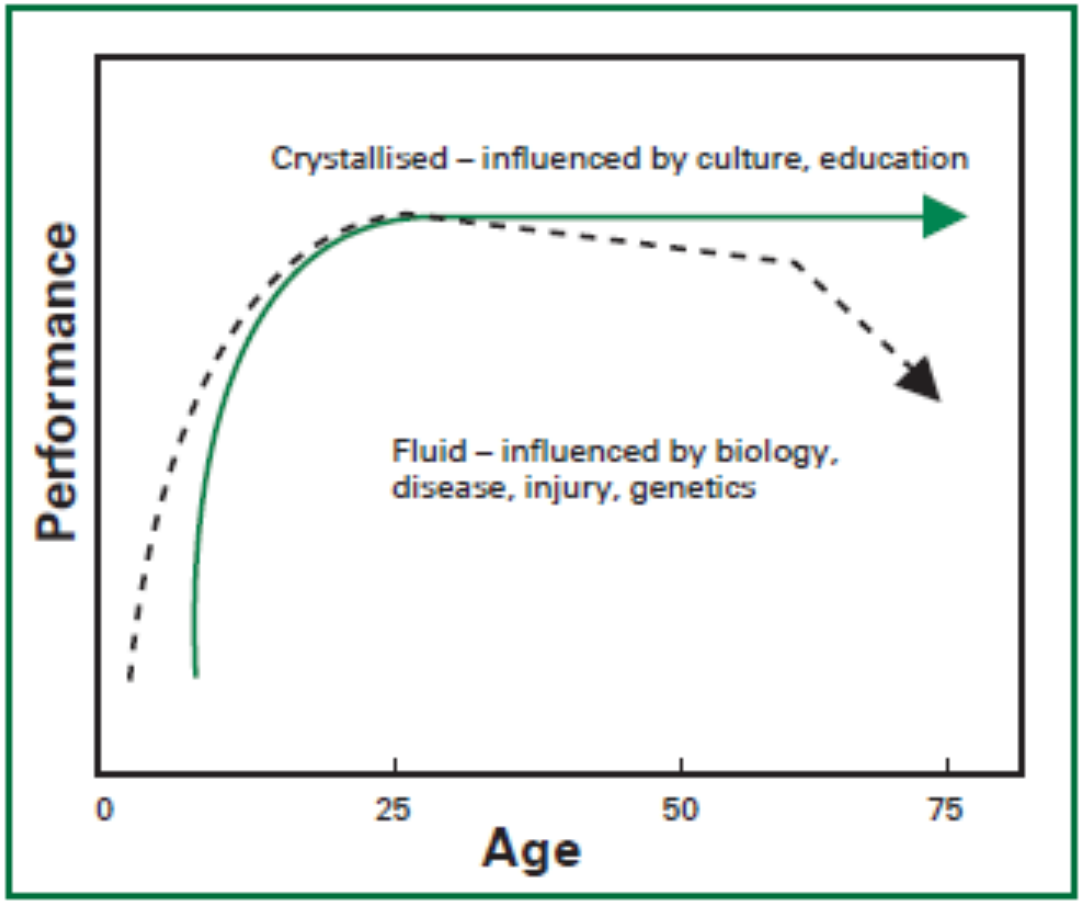
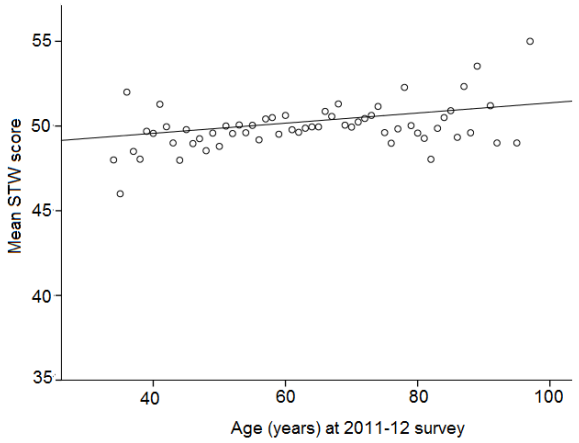
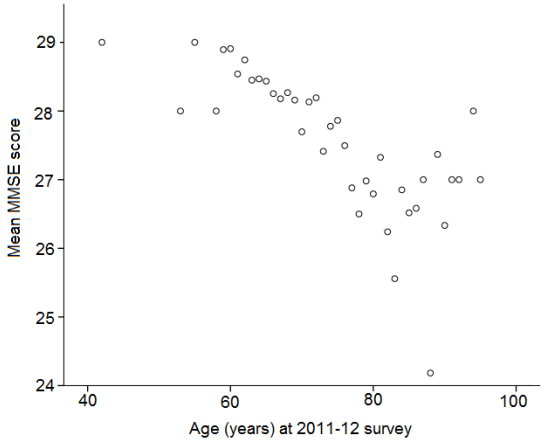
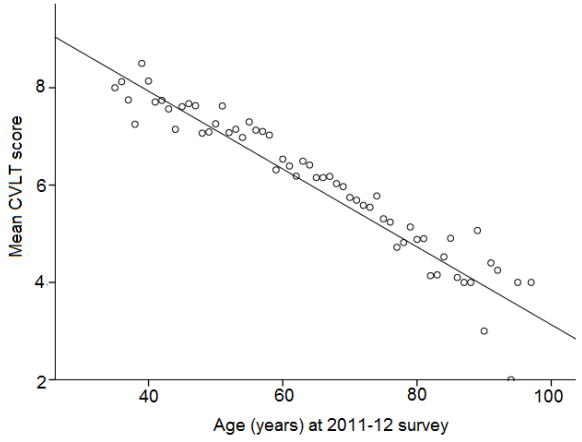


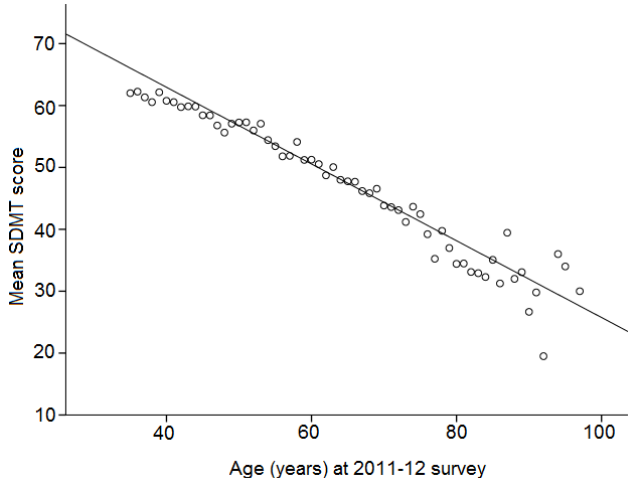

Figure 1. The change in fluid and crystallised abilities with age

# Australian Diabetes, Obesity and Lifestyle Study (AusDIAB) – National, cross-sectional data on adult cognitive performance

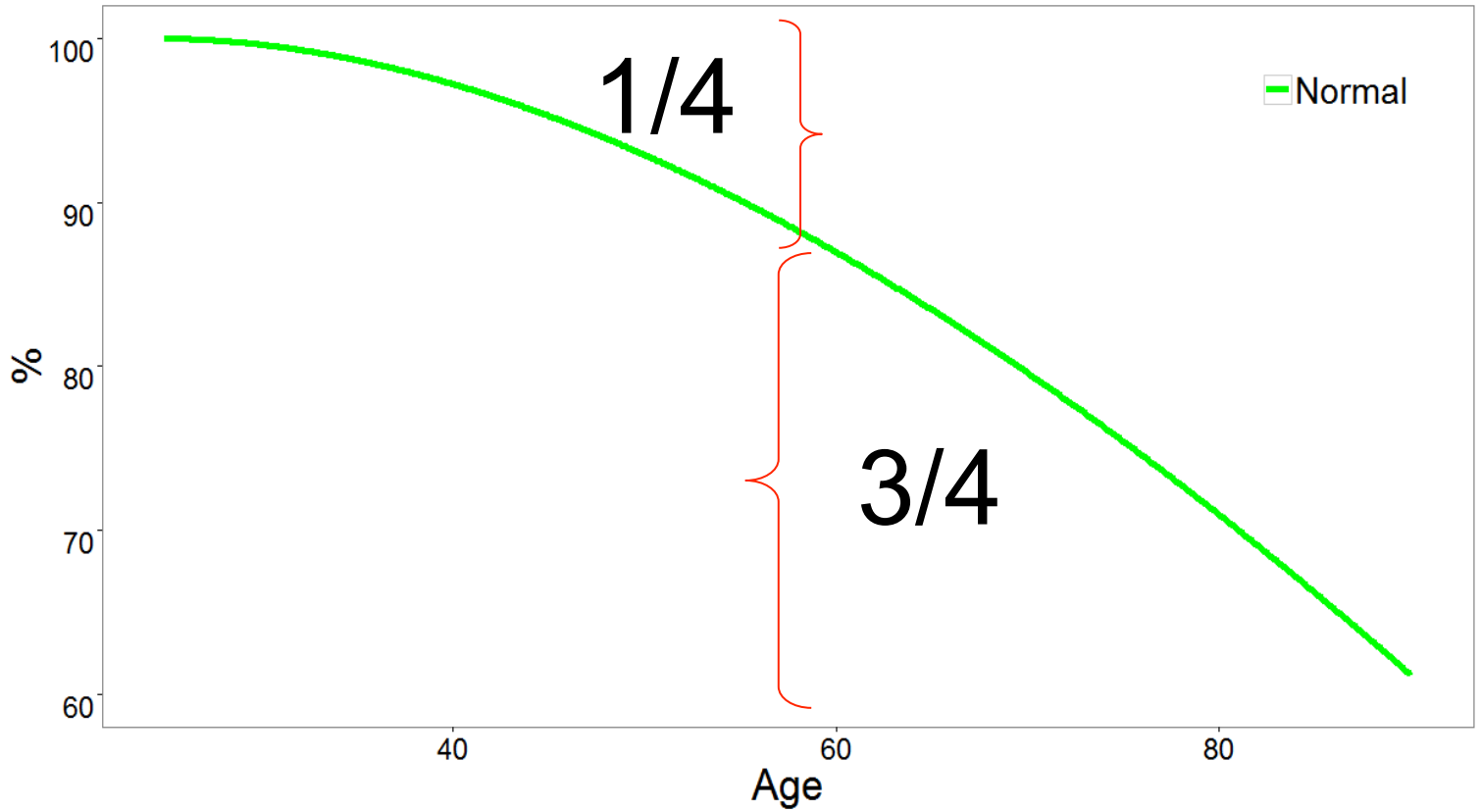


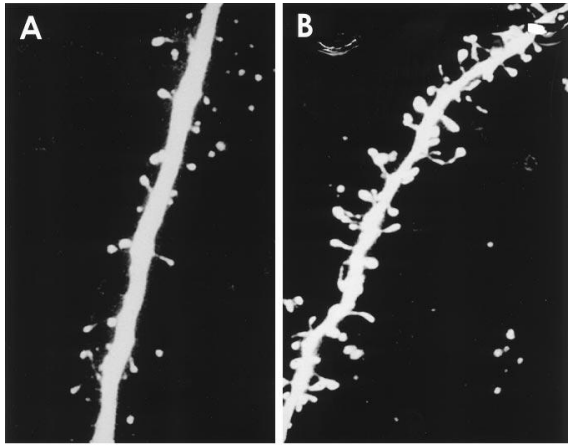



# Normal ageing : brain shrinkage occurs throughout adulthood – 25% of hippocampal shrinkage before age of 60



# Modifiability: Neuroplasticity

- Ageing brain changes, structure and function, not uniform
- Morphology of neurons and tissue density are regionally specific
- Prefrontal cortex and hippocampus atrophy faster cf reduced synaptic density
- Expression of neurotrophic factors e.g. BDNF reduces with age
- Risk and protective factors




**Increased dendritic spines on pyramidal cells of mouse brain after housing in an enriched environment.** (cited in Johansson, 2000, Stroke 31:223-231)

Rats raised in enriched environments show more dendritic spines in somatosensory cortex

# Modifiability: Cognitive reserve/resilience

137 Nursing home residents – brain autopsy

79% clinically demented of whom

- 55% Alzheimer's disease (AD) pathology
- 11% other neuropathology e.g. Parkinson's disease
- 11% no observed pathology

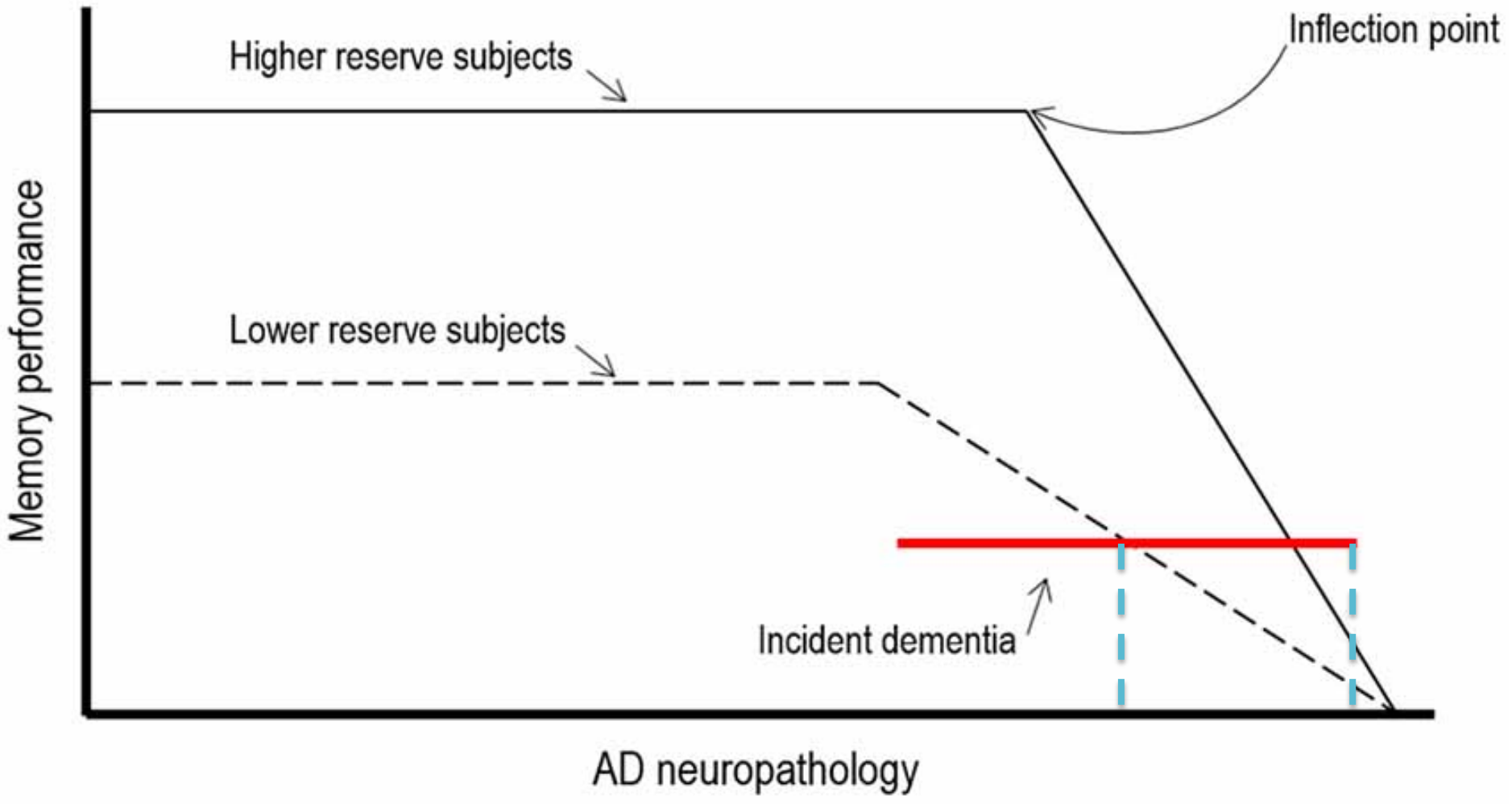
9 cognitively normal participants had a lot of AD pathology but had

- more neurones than AD patients,
- intact pyramidal neurones
- heavier brains than controls…….**'Brain Reserve'**



1988 Katzman et al Archives of Neurology

# Modifiability: Brain reserve




Brain reserve: passive, threshold model for adequate cognitive function with neuropathology



Arenaza-Urquijo et al. Frontiers in Aging Neuroscience, 2015

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# Socio-economic enablers

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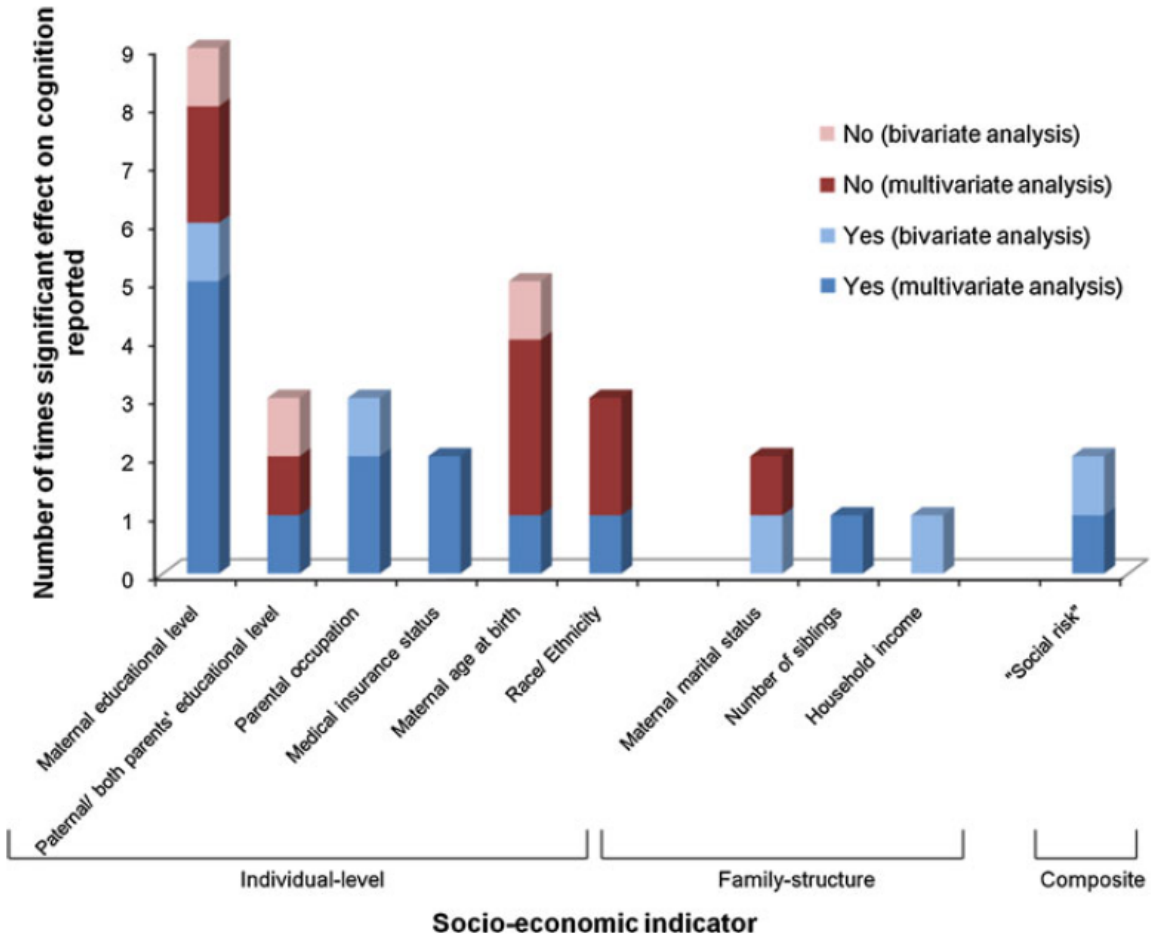
# SES and cognitive development in early life

- Systematic review of 19 longitudinal cohort studies
- 13 SES indicators including maternal education, composite social risk, medical insurance
- All but one study found significant effect for at least one indicator of SES with child cognitive outcomes






Wong & Edwards (2012), *Maternal and Child Health Journal, 17*(9), 1689-1700

# Financial hardship and brain structure middle-aged Australians

PATH Through Life Project, 431 adults aged 44-48 years,

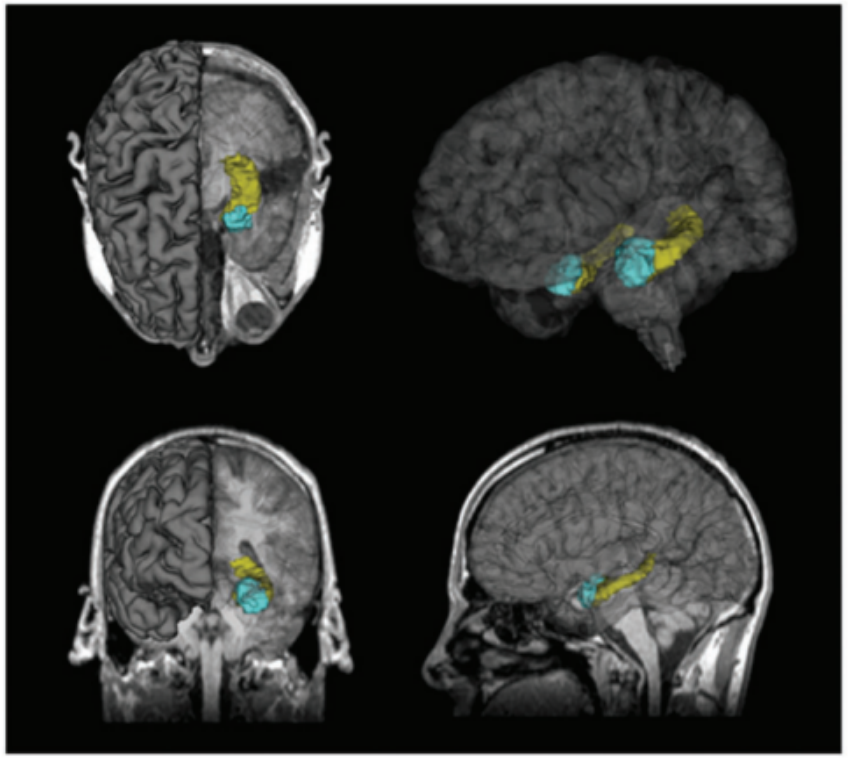


**Fig. 1** Three-dimensional model of the segmented hippocampus (yellow) and amygdala (blue) using Freesurfer and displayed in Slicer (www.slicer.org).

| | Financial hardship | | | |
|---|---|---|---|---|
| | No | Yes | Coefficient | *P*-value |
| | Full sample ($n = 384$) | ($n = 19$) | | |
| Left hippocampus[a] | 3691 (18.9) | 3619 (92.2) | −9.9 (5.00) | 0.049 |
| Right hippocampus[b] | 3981 (19.4) | 3850 (85.2) | −12.7 (5.04) | 0.012 |
| Left amygdala[c] | 1462 (11.1) | 1341 (47.3) | −7.6 (2.76) | 0.007 |
| Right amygdala[d] | 1628 (11.2) | 1527 (43.2) | −7.9 (2.59) | 0.003 |
| | Matched control group ($n = 42$) | ($n = 19$) | | |
| Left hippocampus[a] | 3756 (50.1) | 3619 (92.2) | −11.4 (6.55) | 0.087 |
| Right hippocampus[b] | 4057 (58.1) | 3850 (85.2) | −14.4 (6.22) | 0.025 |
| Left amygdala[c] | 1492 (37.7) | 1341 (47.3) | −6.19 (3.08) | 0.050 |
| Right amygdala[d] | 1664 (35.7) | 1527 (43.2) | −6.39 (2.81) | 0.027 |
| | Childhood poverty | | | |
| | No | Yes | Coefficient | *P*-value |
| | ($n = 353$) | ($n = 50$) | | |
| Left Hippocampus [a] | 3690 (20.1) | 3674 (48.4) | −2.9 (3.18) | 0.362 |
| Right Hippocampus [b] | 3968 (20.3) | 4017 (52.4) | 2.7 (3.23) | 0.401 |
| Left Amygdala [c] | 1453 (11.6) | 1476 (30.4) | 1.4 (1.78) | 0.429 |
| Right Amygdala [d] | 1620 (11.8) | 1650 (26.7) | 1.8 (1.72) | 0.289 |

Covariates in final models are:
[a]sex, years of education, labour-force status, diabetes, experience of physical assault, experienced physical abuse as child, depression and cognition.
[b]Sex, years of education, diabetes, depression and cognition.
[c]Sex, labour-force status, reported heart disease, neglect during childhood, experienced physical abuse as child, depression and cognition.
[d]Sex, diabetes, stroke, experience of sexual molestation, experience of physical assault, depression and cognition.



Butterworth, Cherbuin, Sachdev, Anstey, Soc Affective Cognitive Neuroscience, 2012

# Current financial hardship and cognitive function

| | Simple models | | Adjusted models A | | Adjusted models B | |
|---|---|---|---|---|---|---|
| Financial hardship | B | (95% CI) | B | (95% CI) | B | (95% CI) |
| Unable to heat home | -0.12* | (-0.22, -0.02) | -0.12* | (-0.22, -0.02) | **-0.11*** | (-0.21, -0.01) |
| Missed meals | -0.08 | (-0.16, 0.00) | -0.07 | (-0.15, 0.02) | -0.06 | (-0.15, 0.02) |
| Pawned items | -0.02 | (-0.09, 0.05) | -0.01 | (-0.08, 0.06) | -0.01 | (-0.08, 0.06) |
| Sought help from community welfare organisations | -0.02 | (-0.10, 0.07) | -0.01 | (-0.10, 0.08) | -0.01 | (-0.10, 0.08) |
| Went without basic needs | -0.07*** | (-0.10, -0.03) | -0.07*** | (-0.10, -0.03) | **-0.07*** ** | (-0.10, -0.03) |
| Life event: major financial crisis | -0.04 | (-0.09, 0.00) | -0.04 | (-0.09, 0.00) | -0.04 | (-0.09, 0.00) |
| | | | | | | |
| Hardship severity (count) | -0.03*** | (-0.05, -0.01) | -0.03*** | (-0.05, -0.01) | **-0.03*** ** | (-0.05, -0.01) |

subscale

**Adjusted models B:** Adjusted models A + time varying Pearlin mastery scale. **p < .05, **p < .01, ** p<.001*



Kiely, Anstey, Butterworth, American Journal of Epidemiology, 2019

# SES and cognitive decline in late life

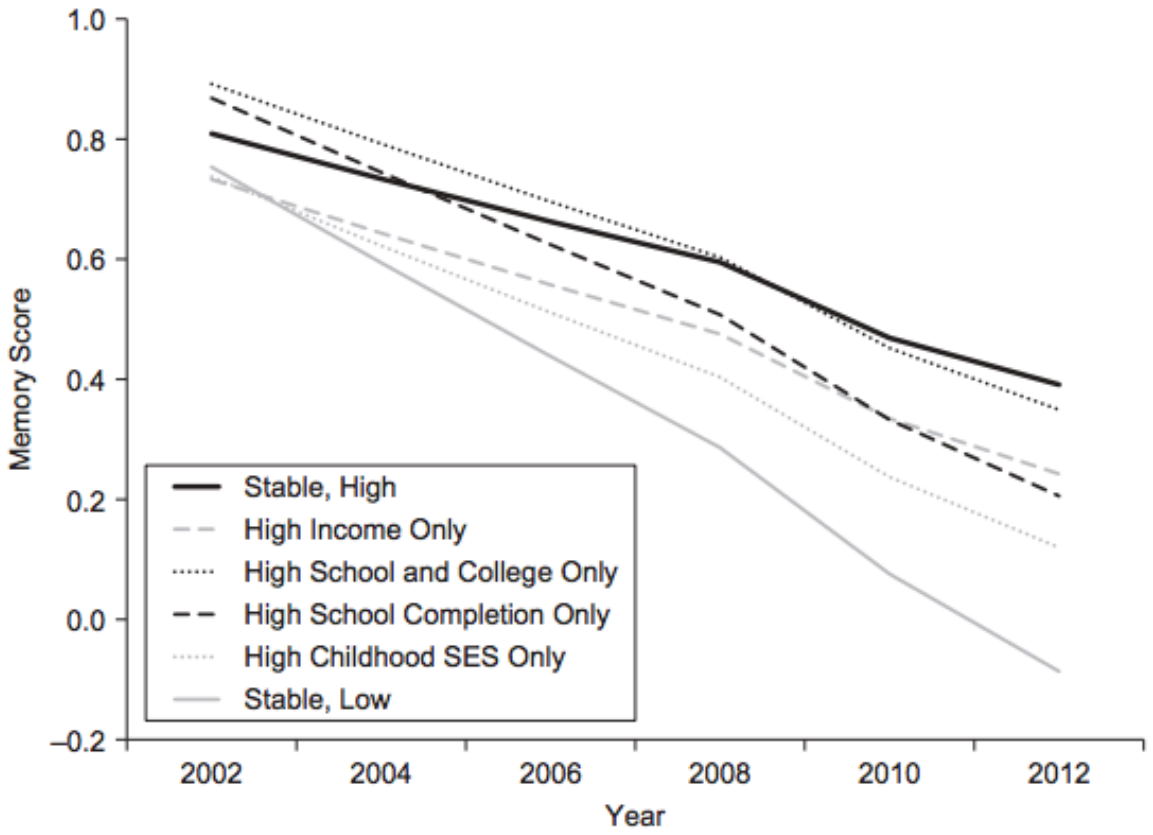



**Figure 2.** Predicted memory decline curves, Health and Retirement Study, United States, 2000–2012. Predictions were calculated from the memory decline model that included all 3 socioeconomic status (SES) measures and their interactions (Table 5, model 3).

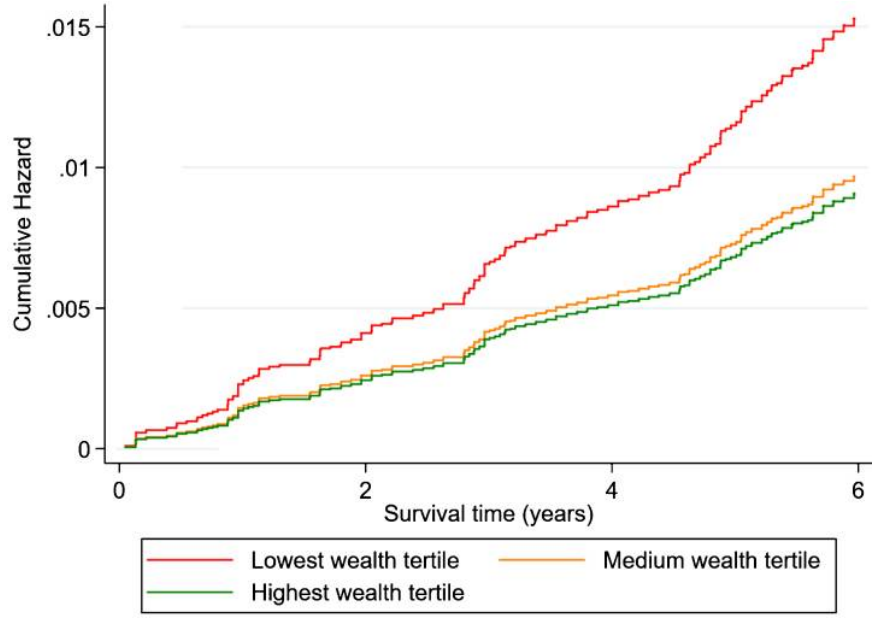
- Health and retirement study (USA)
- *N* = 10,781 (male = 4,205)
- Early-life SES determined by educational attainment
- Late-life SES determined by household income
- **Results:**
  - High childhood SES, high-school completion, college completion, and high income in late life were each associated with better memory function.
  - Higher SES generally predicted slower decline



Marden et al. (2016), *American Journal of Epidemiology, 186*(7), 805-814.

# Wealth and risk of dementia – English Longitudinal Study of Ageing

- Deckers et al., Journal of Alzheimer's Disease, 2019



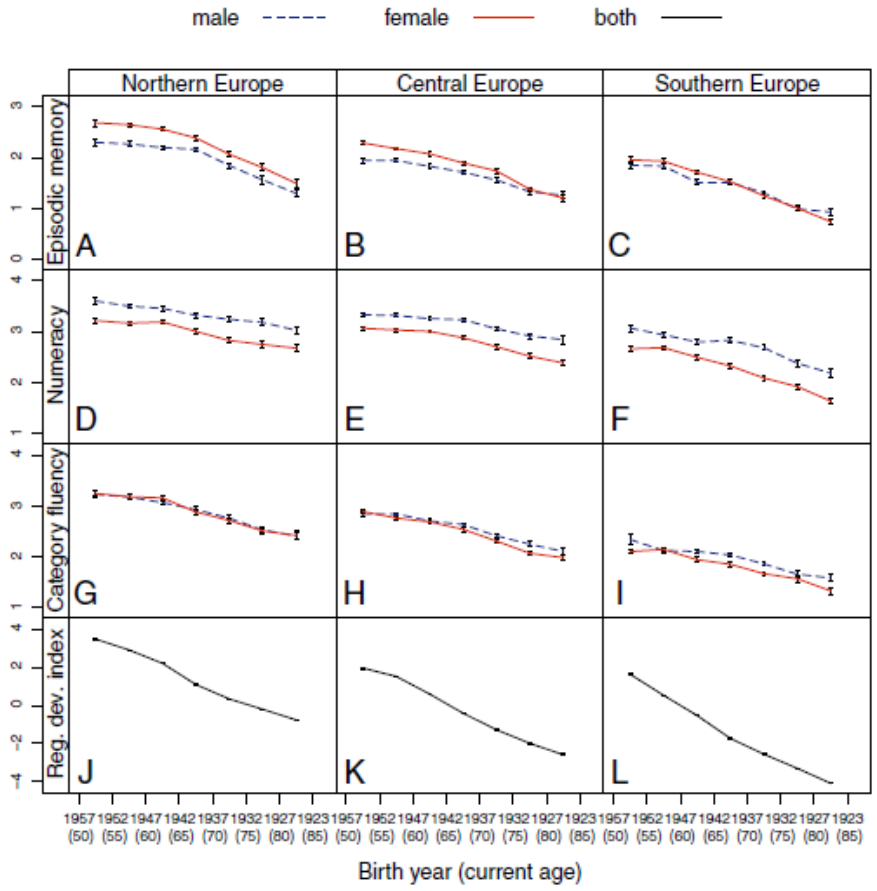

Model adjusted for age, gender, education, and clustering at the household level

N = 6346,

followed for 6 years, assessed on lifestyle risk factors and cognitive function

Risk of dementia between high and low levels of wealth was partly explained by modifiable lifestyle factors

# Regional development index (RDI), gender and cognition - SHARE




- In countries with higher RDI there is better performance on tests of episodic memory
- Authors suggest that women benefit from economic improvement more than men

Weber et al, Proceedings of the National Academy of Science, 2014.

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# Social enablers

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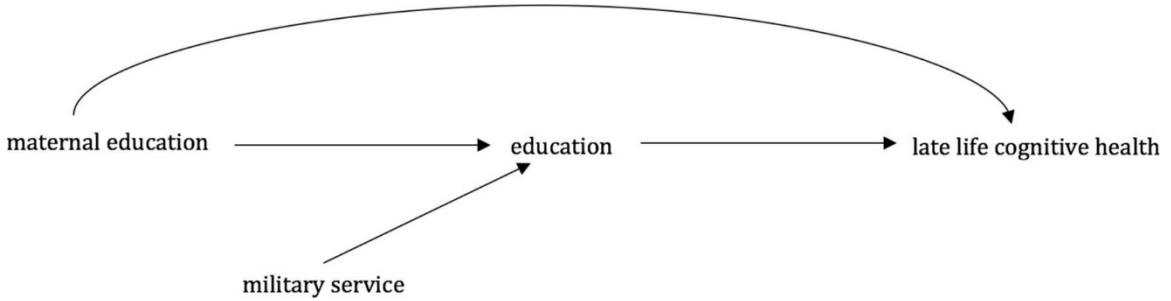
# Occupational opportunities – US Health & Retirement Study

Vable et al, Journal of Epidemiology and Community Health, 2018

Hypothesis: military service in the Korean (US involvement: 1950–1953) or Vietnam Wars (US involvement: 1964–1975) will offset the effects of low maternal education (a marker of SES) on late-life memory or dementia risk among US men;




N = 7916,  16% maternal low education, 33% medium and 51% high

Low maternal education predicted poorer memory performance

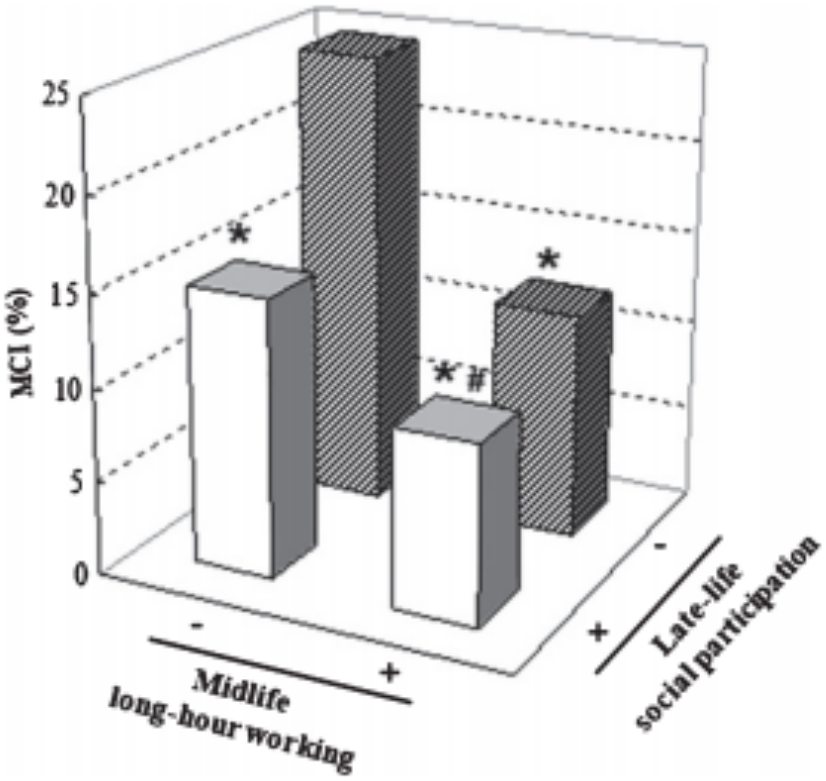
# Results

**Table 3** Childhood SES, veteran status and dementia

| | Model 1: main effects model | | Model 2: interaction model | |
|---|---|---|---|---|
| | OR (95% CI) | P values | OR (95% CI) | P values |
| Odds in the reference category (high cSES non-veteran) | 0.01 (0.00 to 0.82) | 0.040 | 0.01 (0.00 to 0.72) | 0.035 |
| Maternal education (high=ref) | | | | |
| Low | 1.72 (1.36 to 2.18) | <0.0005 | 2.09 (1.53 to 2.83) | <0.0005 |
| Middle | 1.41 (1.15 to 1.72) | 0.001 | 1.60 (1.22 to 2.09) | 0.001 |
| Veteran | 0.72 (0.61 to 0.86) | <0.0005 | 0.91 (0.67 to 1.23) | 0.524 |
| Interaction terms | | | | |
| Low cSES * veteran | | | 0.64 (0.41 to 1.01) | 0.057 |
| Middle cSES * veteran | | | 0.76 (0.51 to 1.14) | 0.183 |

Model 1 includes age (linear and quadratic terms), year of outcome assessment, a practice effect, race and childhood self-reported health.
Model 2 adds interaction terms for maternal education * veteran status.
cSES is childhood socioeconomic status; SES, socioeconomic status.

# Mid-life working hours and late life social engagement



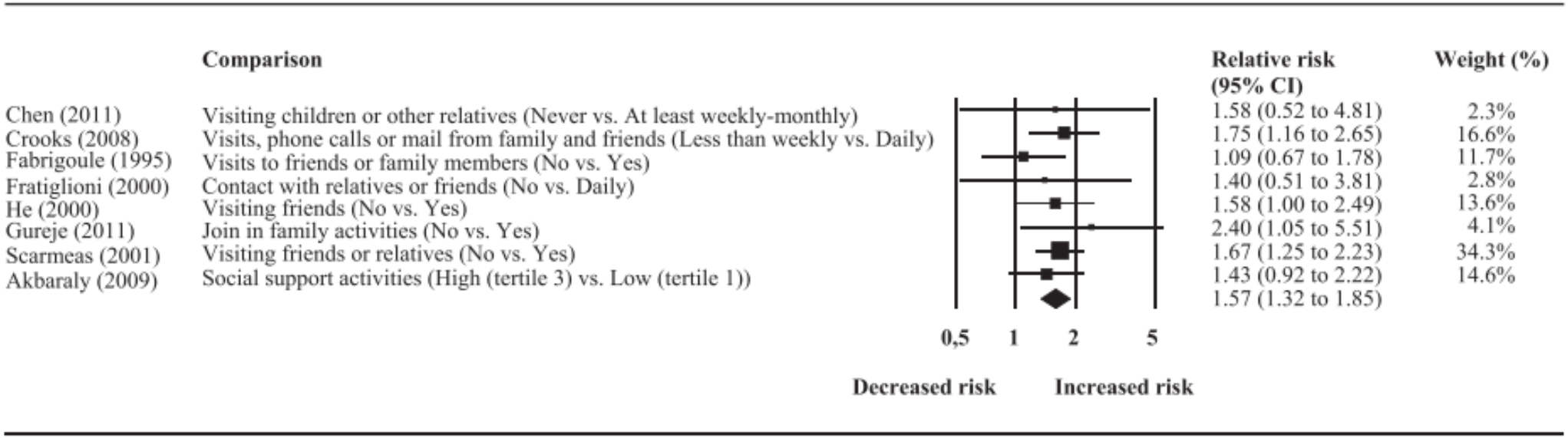

Diet and Healthy Ageing Study
Singapore (N = 751)

- 119 diagnosed with MCI
- Adults with longest working hours in mid-life had reduced risk of MCI
- Adults with higher level of social engagement in late life had lower rates of MCI

Deng et al, J Alz Dis, 2019

# Social engagement, loneliness and cognitive decline

Systematic review  of evidence is that social engagement is protective against risk of dementia but mechanism is not understood



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# Environmental en(dis)ablers

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# Proximity to Roads associated with dementia risk

| | Main model ‡ | | Indirectly adjusted for smoking | | Further indirectly adjusted for BMI, physical activity | | Further indirectly adjusted for education | |
|---|---|---|---|---|---|---|---|---|
| | Hazard ratio | 95% CI | Hazard ratio | 95% CI | Hazard ratio | 95% CI | Hazard ratio | 95% CI |
| Distance† by category | | | | | | | | |
| <50 m | 1·07 | 1·06–1·08 | 1·06 | 1·05–1·08 | 1·06 | 1·05–1·08 | 1·06 | 1·05–1·08 |
| 50–100 m | 1·04 | 1·02–1·05 | 1·03 | 1·02–1·05 | 1·03 | 1·02–1·05 | 1·04 | 1·02–1·06 |
| 101–200 m | 1·02 | 1·01–1·03 | 1·01 | 1·00–1·02 | 1·01 | 1·00–1·03 | 1·02 | 1·01–1·04 |
| 201–300 m | 1·00 | 0·99–1·01 | 1·00 | 0·98–1·01 | 1·00 | 0·99–1·02 | 1·01 | 0·99–1·03 |
| >300 m | Reference | .. | Reference | .. | Reference | .. | Reference | .. |
| Log (distance)§ | 0·91 | 0·89–0·92 | 0·92 | 0·90–0·93 | 0·92 | 0·90–0·93 | 0·92 | 0·90–0·93 |

Indirect adjustment for smoking, body-mass index (BMI), physical activity, and attained education. Data of smoking, BMI, physical activity, and educational attainment were obtained from Ontario respondents to the 1996 cycle of National Population Health Survey and the 2000–01, 2003 cycles of Canadian Community Health Survey, and who were 50 to 85 years old at the time of the surveys (n=16 441). †Major traffic roads include primary urban roads and arterial roads whereas highways include expressways and primary and secondary highways, as defined by Ontario Government Road Network Data Standards. ‡Cox proportional hazards model with age as time axis, stratified by an indicator for living in the Greater Toronto Area or not, adjusted for sex, history of diabetes, hypertension, coronary heart disease, stroke, congestive heart failure, arrhythmia, and traumatic brain injury, income quintile, urban/rural indicator, census division-level unemployment, education, and recent immigrants, as well as the subtraction of these variables at the census dissemination level from their census division. §Distance was fitted as a continuous variable, using natural logarithm of distance. The hazard ratios were expressed per interquartile-range increase in distance (310 m).

***Table 3*: Hazard ratios and 95% CI for associations between residential proximity to major roadways in 1996 and the risk of incident dementia in Ontario during the follow-up period 2001–12**

**Chen et al., Lancet, 2017**

## Sample:

Adults aged  aged 55–85 years (about 2·2 million; dementia or Parkinson's disease cohort) who resided in Ontario, Canada on April 1, 2001.

Major traffic roads include primary urban roads and arterial roads (ie, a major thoroughfare with medium to large traffic capacity with a combination of controlled access and intersections at grade level) whereas highways include expressways and primary and secondary highways, according to Ontario Government Road Network Data Standards. Consistent with previous studies,

# Other environmental factors

Proximity to green space probably protective

Air pollution increases risk

Pesticides increase risk

Other toxins – data are lacking

Noise – does not appear to affect cognition

Urban vs rural setting – limited data

Environmental complexity – limited data

Occupational complexity - enabling

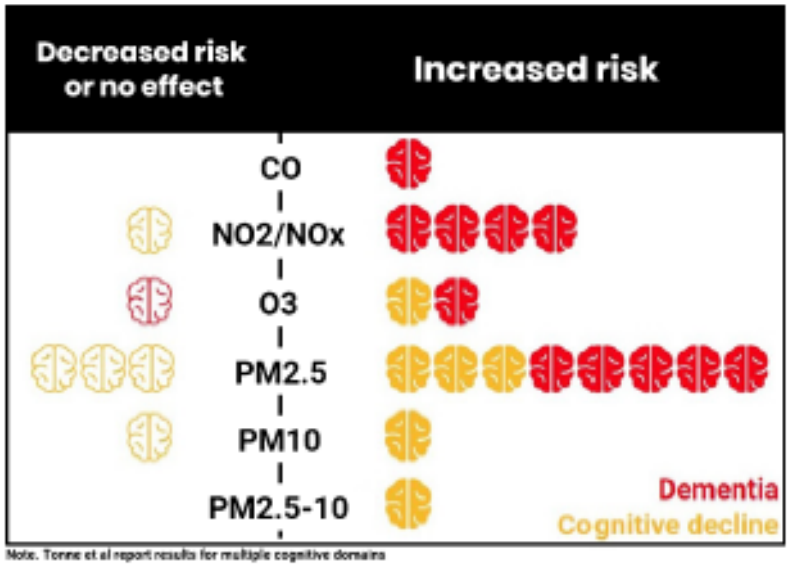
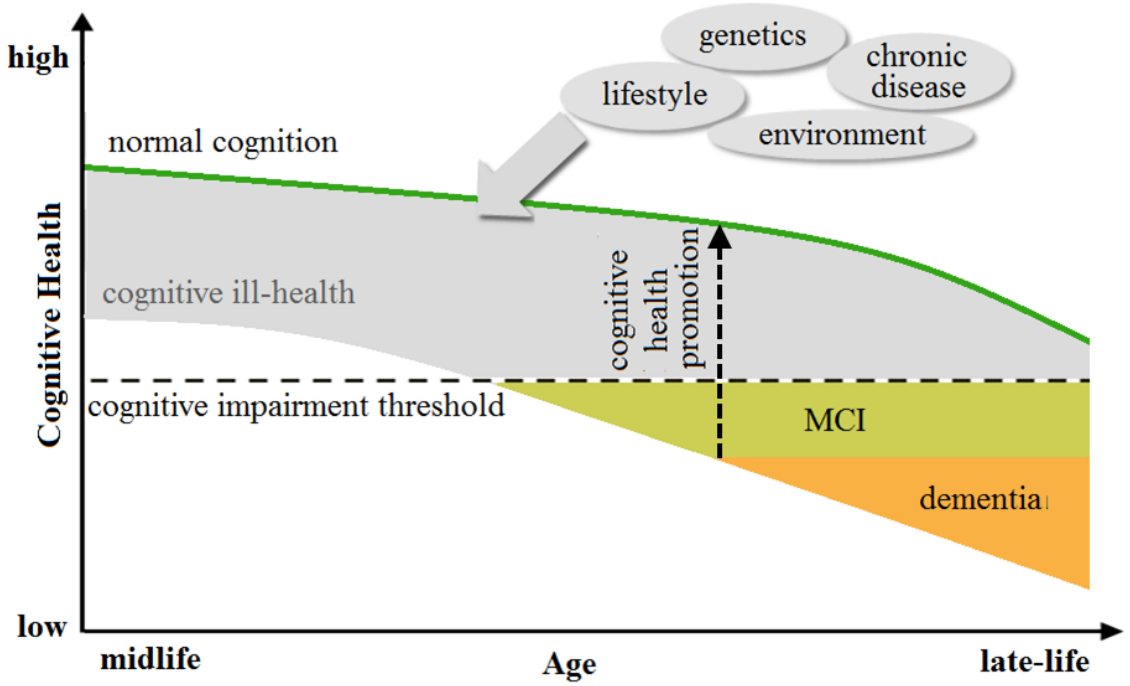



Fig. 2. Number of studies investigating relationship between exposure to pollutants and cognitive function or dementia.

**Figure from Peters et al, Journal of Alzheimer's Disease, 2019**

# Multi-Domain Life Course Model is Required

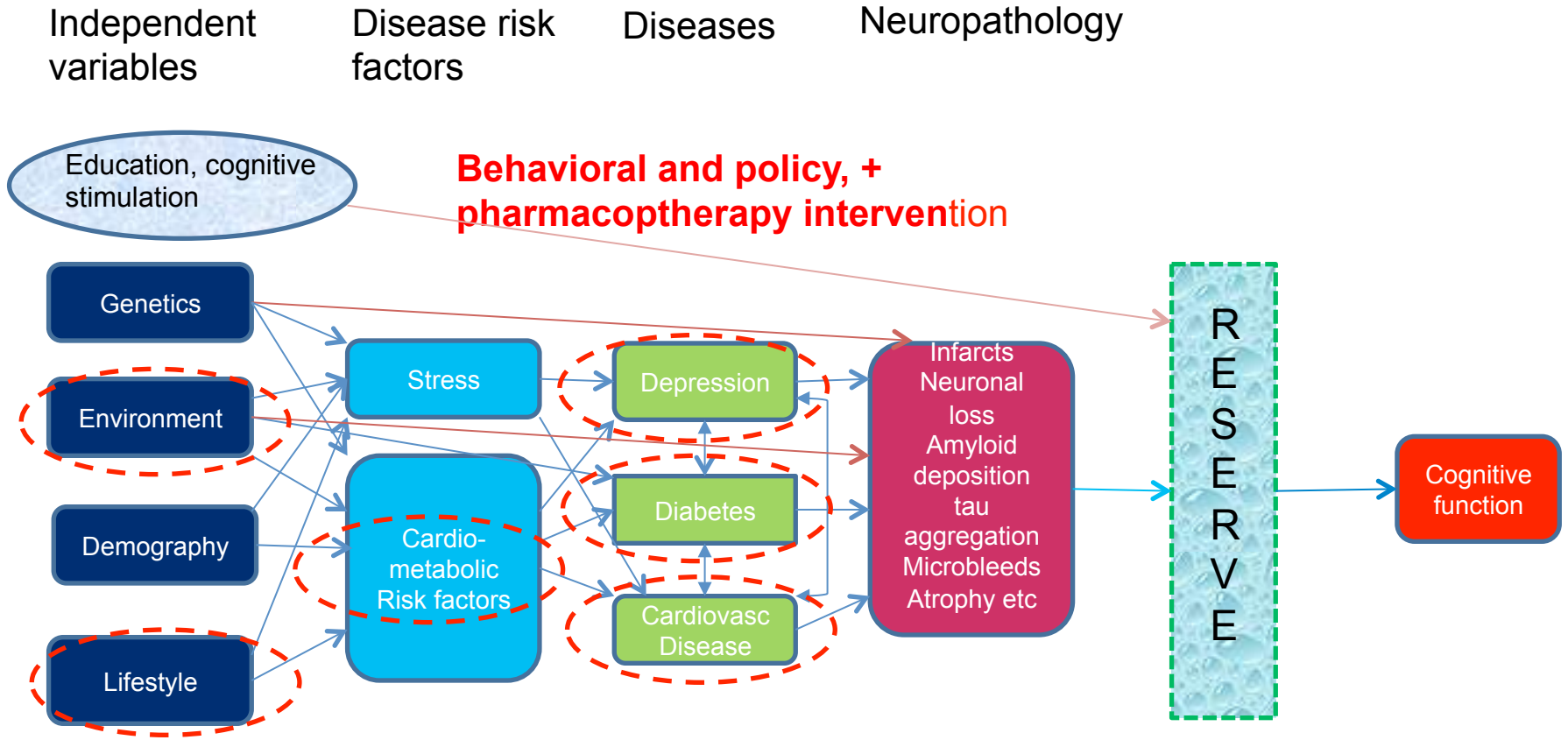
- Early life experience impacts on cognitive reserve and brain development
- Lifestyle, environmental and medical risk factor effects accumulate
- Benefits of protective behaviour may accumulate






Whalley et al, Lancet Neurology, 2009; Anstey, K.J International Journal of Behavioral Development, 2014

# Cognitive Health Environment Life Course Model




**Anstey, K.J.**, *Optimizing cognitive development over the life course and preventing cognitive decline: Introducing the Cognitive Health Environment Life Course Model.* Int J Behav Dev, 2014. 38: 1-10.

# Summary and conclusion

Enablers of healthy cognitive ageing draw from economic, social and environmental domains, as well as medical and lifestyle

Life-course perspective is required

A multi-level approach is required to enable healthy cognitive ageing

- healthy start to life, addressing poverty and disadvantage
- enriched education in childhood with continuing opportunities
- clean physical environment
- social capital and engagement
- healthy lifestyle
- medical management of chronic disease

# Acknowledgements

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