Risk and Protective Factors for Dementia Across the Lifespan

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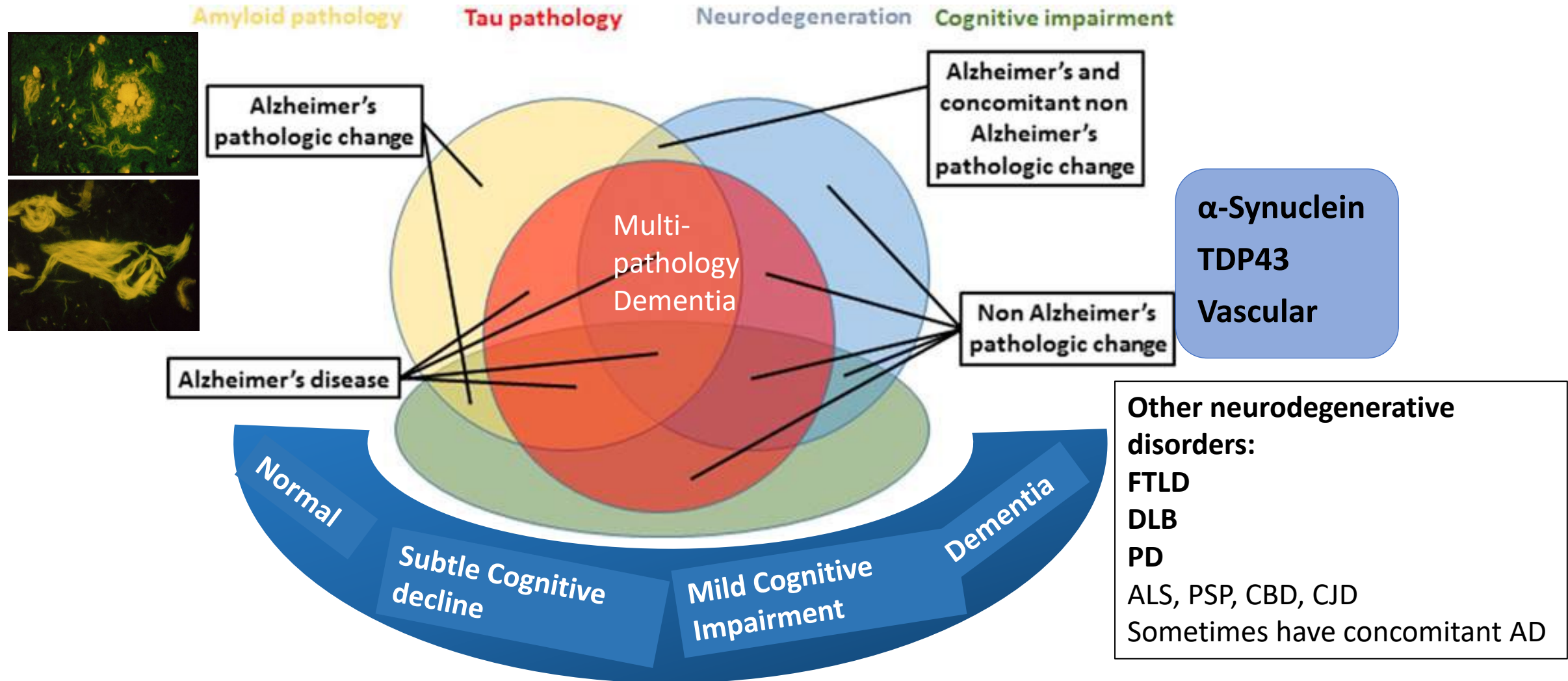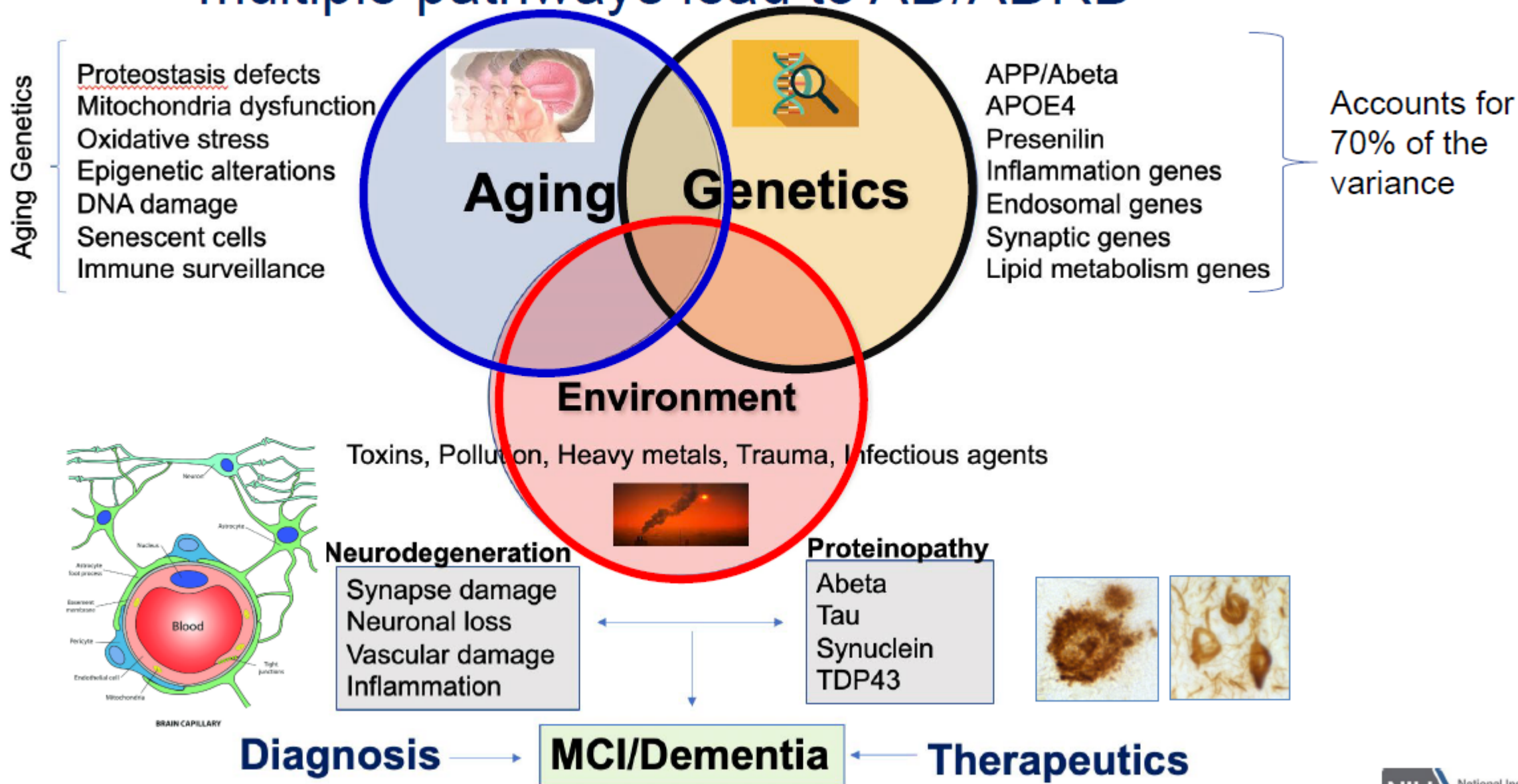
University of California, San Diego

Disclosures

None

NIA-AA Research Framework: Towards a biological definition of Alzheimer's disease – A, T, N

Progress toward understanding the pathogenesis of AD-
multiple pathways lead to AD/ADRD

Aging Genetics

Proteostasis defects
Mitochondria dysfunction
Oxidative stress
Epigenetic alterations
DNA damage
Senescent cells
Immune surveillance

Aging

Genetics

APP/Abeta
APOE4
Presenilin
Inflammation genes
Endosomal genes
Synaptic genes
Lipid metabolism genes

Accounts for 70% of the variance

Environment

Toxins, Pollution, Heavy metals, Trauma, Infectious agents

Neurodegeneration

Synapse damage
Neuronal loss
Vascular damage
Inflammation

Proteinopathy

Abeta
Tau
Synuclein
TDP43

Diagnosis → **MCI/Dementia** ← **Therapeutics**

BRAIN CAPILLARY

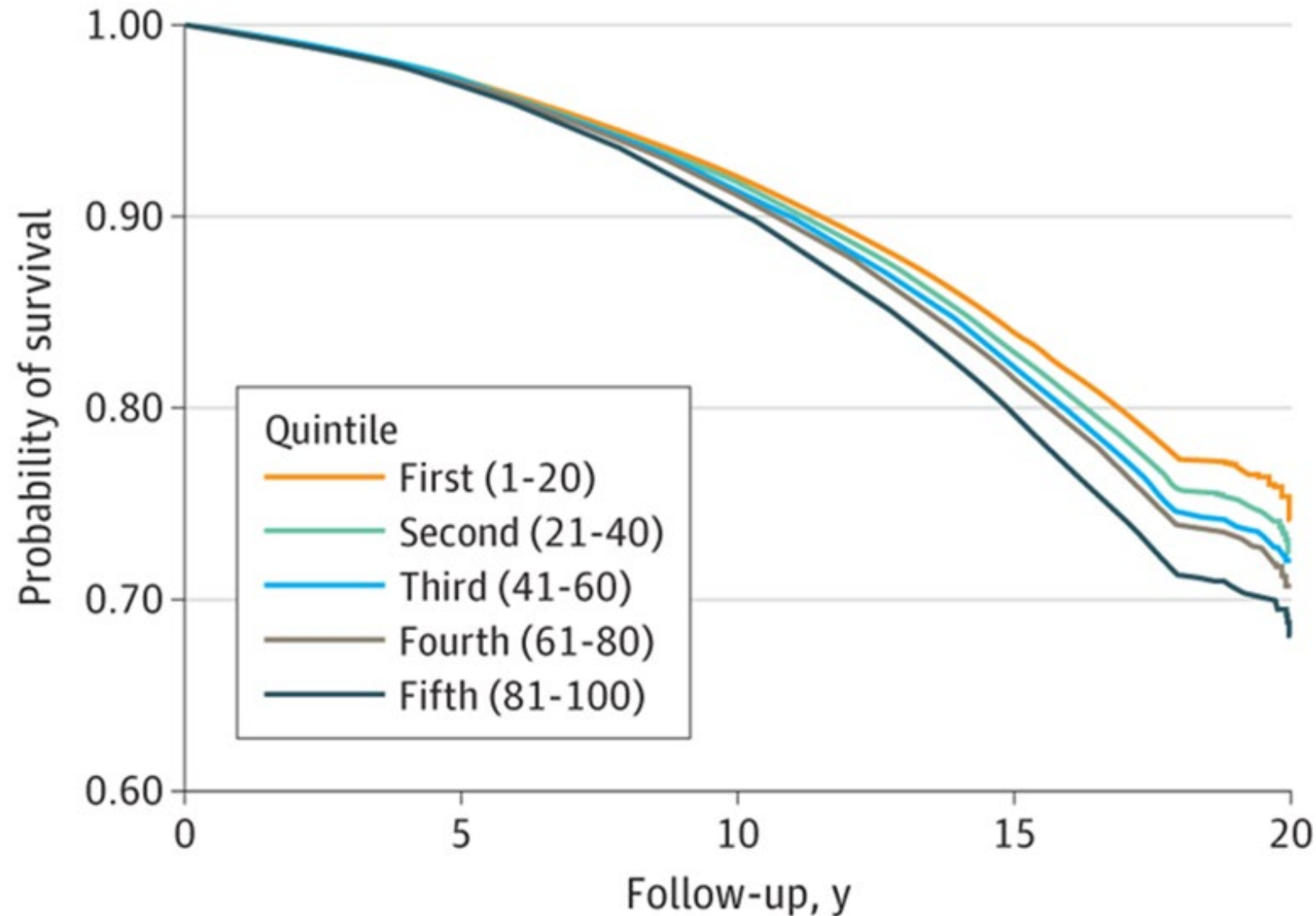# Dementia Incidence Varies Across Racial/Ethnic Groups
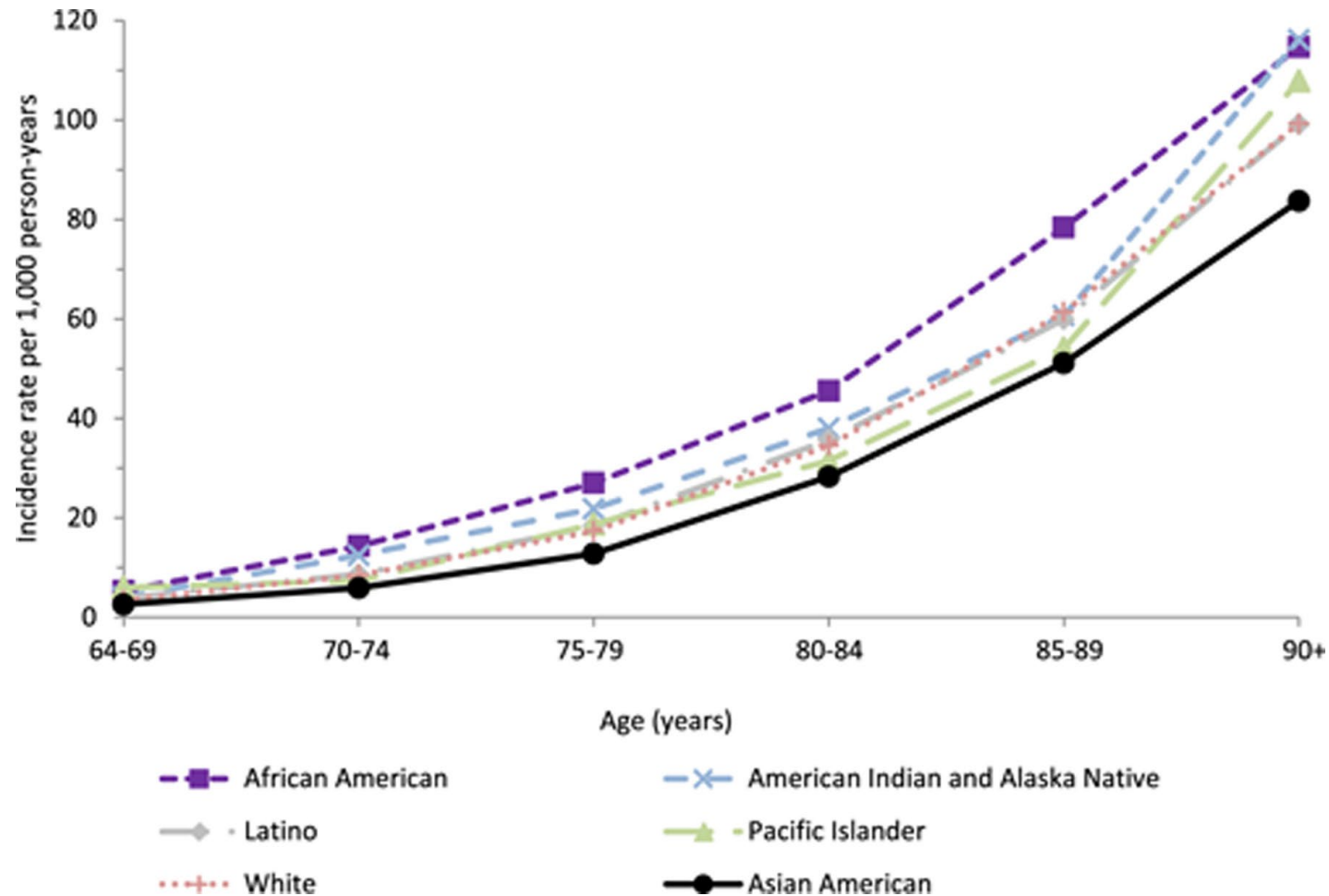
Dementia incidence rates per 1000 person-years by age and race-ethnicity, 2000–2013.

Mayeda et al., 2016. Inequalities in dementia incidence between six racial and ethnic groups over 14 years. *Alzheimer's & Dementia.*

Neighborhood Disadvantage Increases Risk of Dementia

Dintica et al., 2023. Dementia Risk and disadvantaged neighborhoods. *JAMA Neurology*

Dementia prevention, intervention, and care: 2024 report of the *Lancet* standing Commission

Gill Livingston, Jonathan Huntley, Kathy Y Liu, Sergi G Costafreda, Geir Selbæk, Suvarna Alladi, David Ames, Sube Banerjee, Alistair Burns, Carol Brayne, Nick C Fox, Cleusa P Ferri, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Noeline Nakasujja, Kenneth Rockwood, Quincy Samus, Kokoro Shirai, Archana Singh-Manoux, Lon S Schneider, Sebastian Walsh, Yao Yao, Andrew Sommerlad*, Naaheed Mukadam*

Population attributable fraction of potentially modifiable risk factors for dementia -Lancet Commission 2024
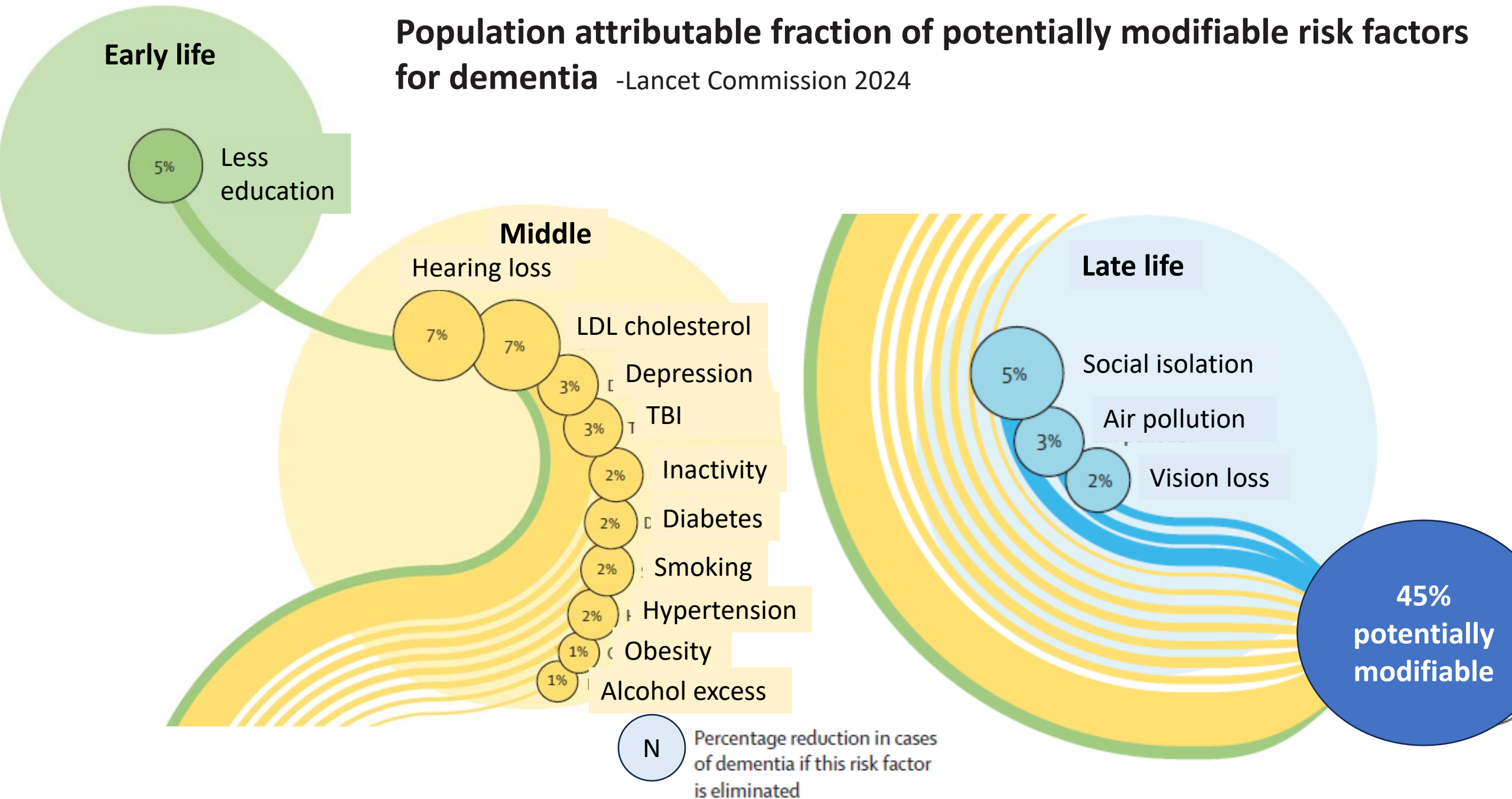
Insufficient or unclear data regarding risk

- Sleep
- Diet
- Inflammation or infection
- Major Psychiatric Disease
- PTSD
- Anxiety
- Hormone replacement therapy
- Multimorbidity and frailty
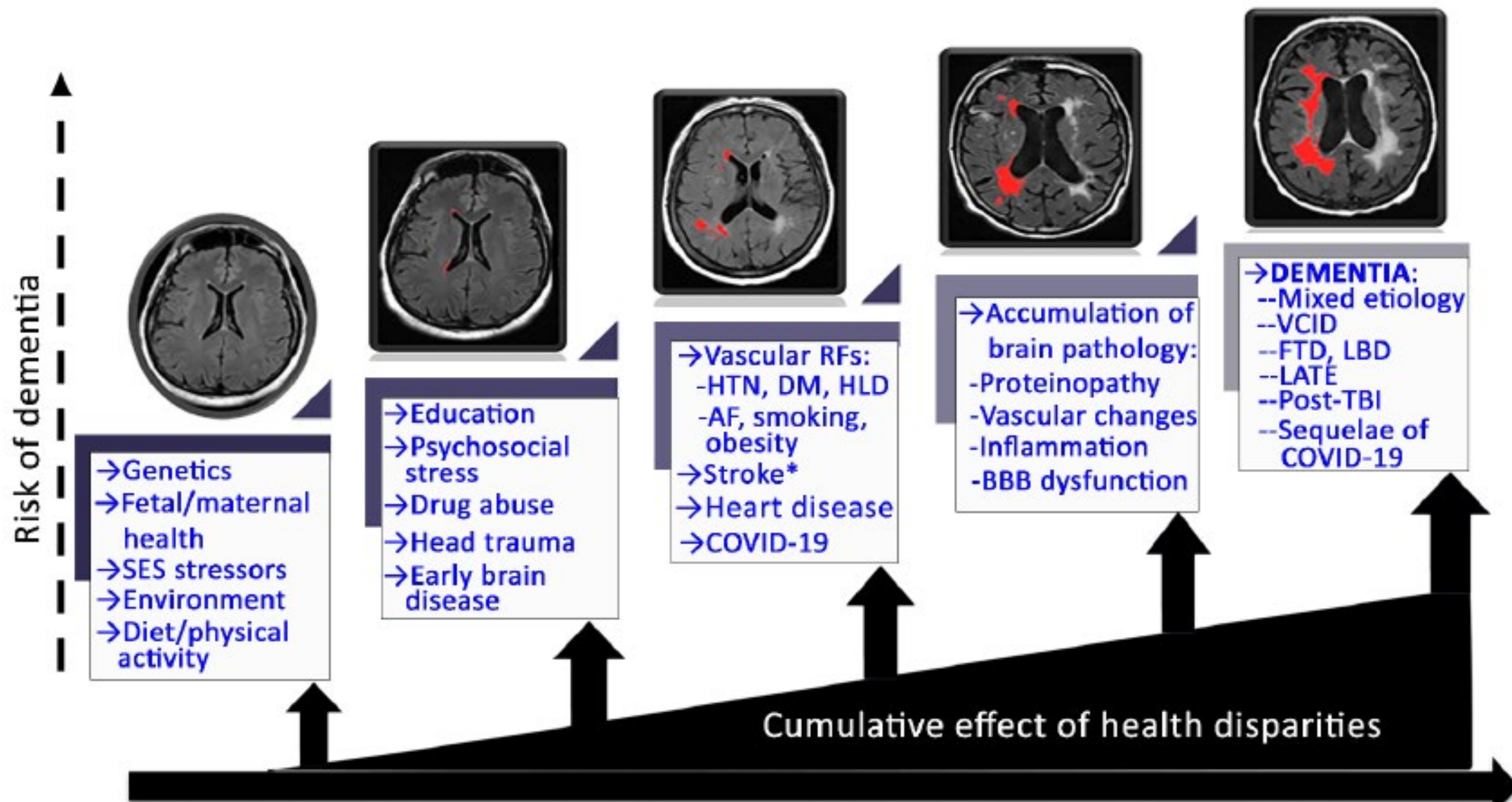
Lancet Commission 2024

Can we modify these risk factors?

- Good quality education; midlife stimulation
- Hearing aids and decrease noise exposure
- Treat depression
- Helmets in contact sports and for cyclists
- Encourage exercise
- Reduce smoking

- Treat hypertension
- LDL cholesterol
- Healthy weight
- Reduce alcohol
- Age-friendly communities, decrease isolation
- Screen for vision loss and treat
- Reduce air pollution exposure

Potentially modifiable risk factors and possible mechanisms for protection from dementia

Lancet Commission, 2024
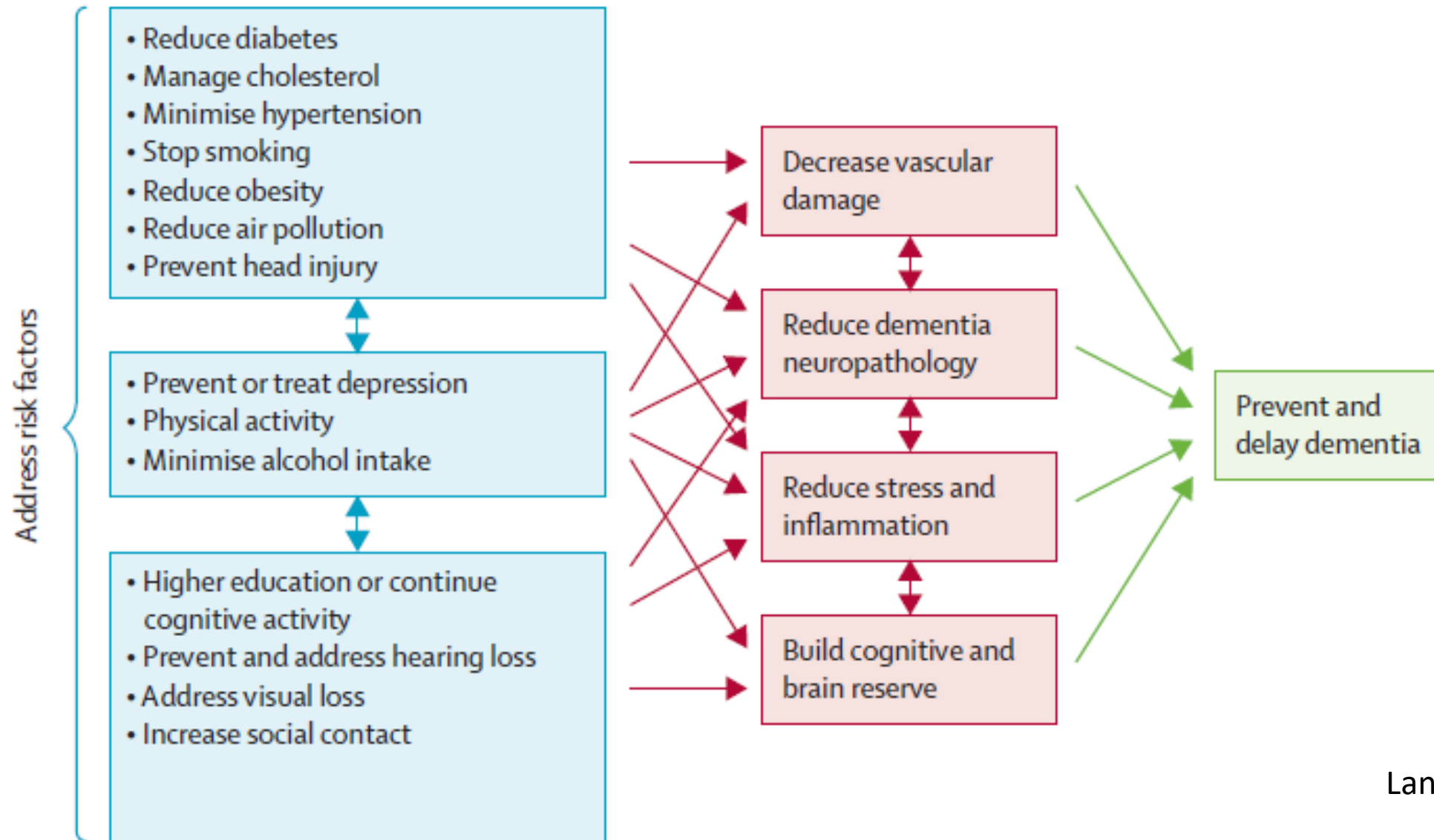
Health disparities may influence dementia risk

The Lancet Commission and different populations at risk

The Commission tried to assemble worldwide data, although the majority of data comes from well-educated White populations.

Social determinants of health may vary among communities.

"There may be greater potential for modifying risk factors in low to middle income countries and among minoritized and lower socio-economic groups."

Questionnaires and information we collect

- UDS 4.0 is a standardized assessment that all 34 ADRCs will be completing

- Questions about Social Determinants of Health are now included
  - Self-completed questionnaire
  - Will be administered to participants who are cognitively unimpaired
  - One-time assessment
  - Take about 10-15 minutes

Form A1a: SDOH

Purpose

- Collect data on social conditions of our participants
- Represent risk/protective factors beyond what can be gathered from ADI or other public databases

Constructs

- Section 1: Transportation
- Section 2: Financial Security
- Section 3: Social connections, activities, and environment
- Section 4: Experiences with healthcare system
- Section 5: Experiences of discrimination

Why a new form on SDOH?

Social Determinants of Health

conditions in the environments where people are born, live, learn, work, play, and age

Non-medical factors that influence health outcomes

Education Access and Quality

Health Care Access and Quality

Economic Stability

Neighborhood and Built Environment

Social and Community Context