Vascular Cognitive Impairment and Dementia (VCID)

Fifth Annual Stanford ADRC / UDall Participant Appreciation Day

11/02/2022

Kyan Younes, MD
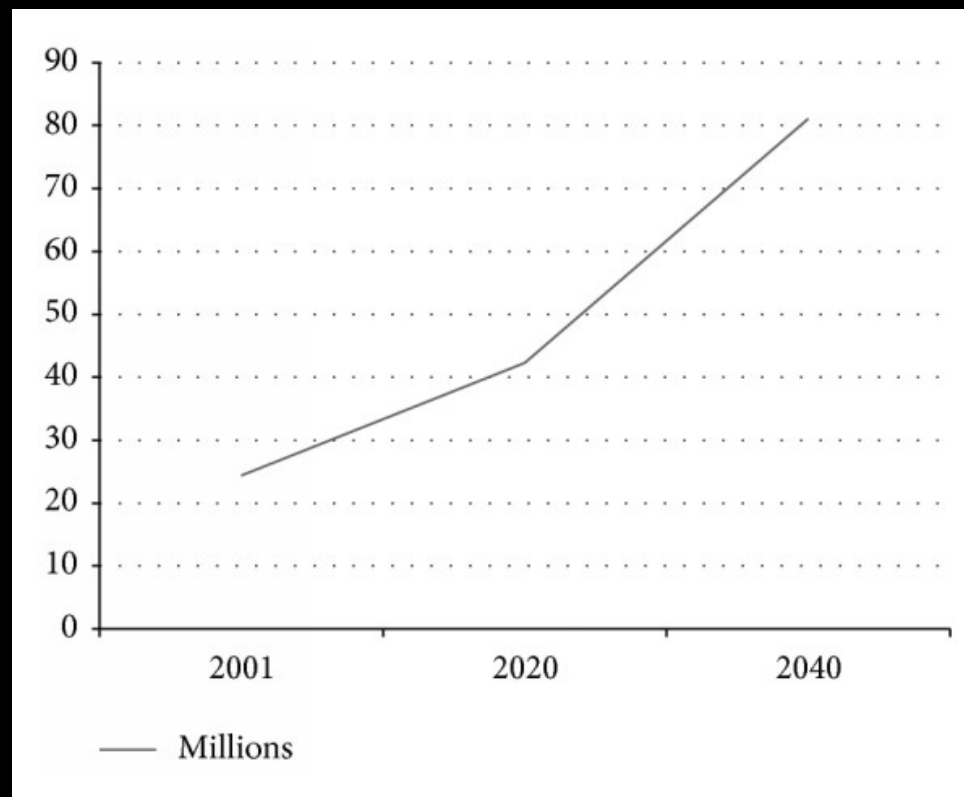
Assistant Professor

I have no disclosures

Outline

- Epidemiology of vascular risk, prevalence of vascular brain injury
- Definition of vascular disease
- Overlap between vascular disease and Alzheimer`s disease
- Impact on cognition
- Vascular imaging
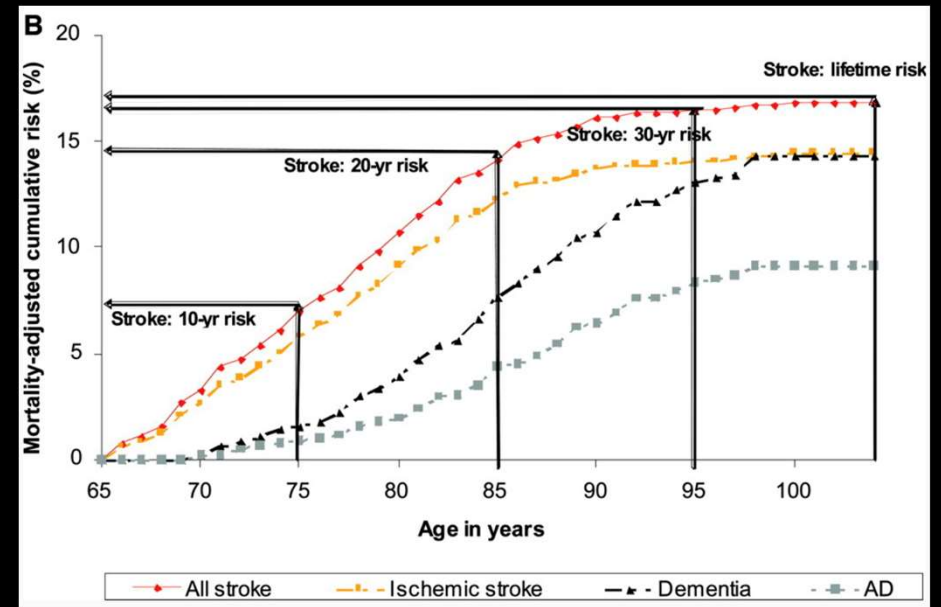
Estimated numbers of dementia patients worldwide
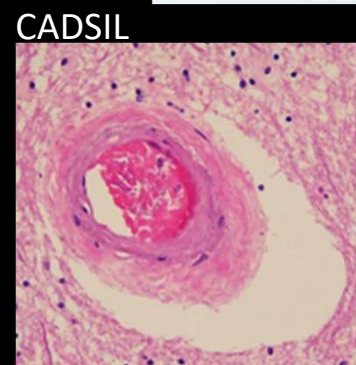
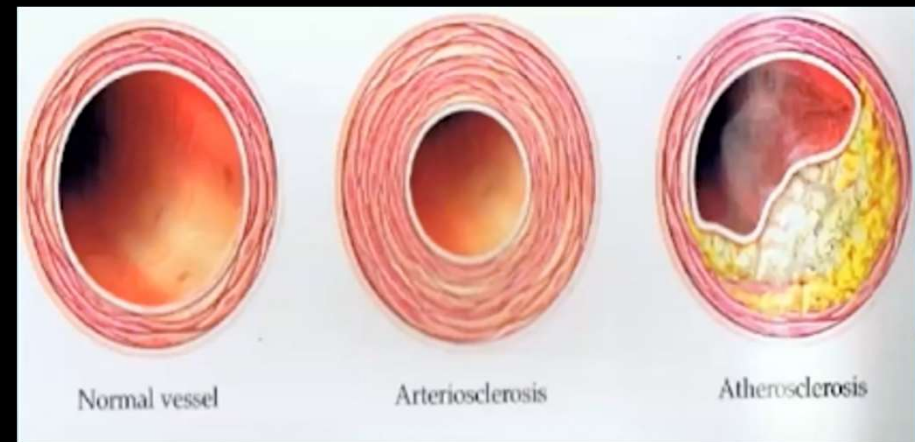# Future risk of stroke or dementia at age 65
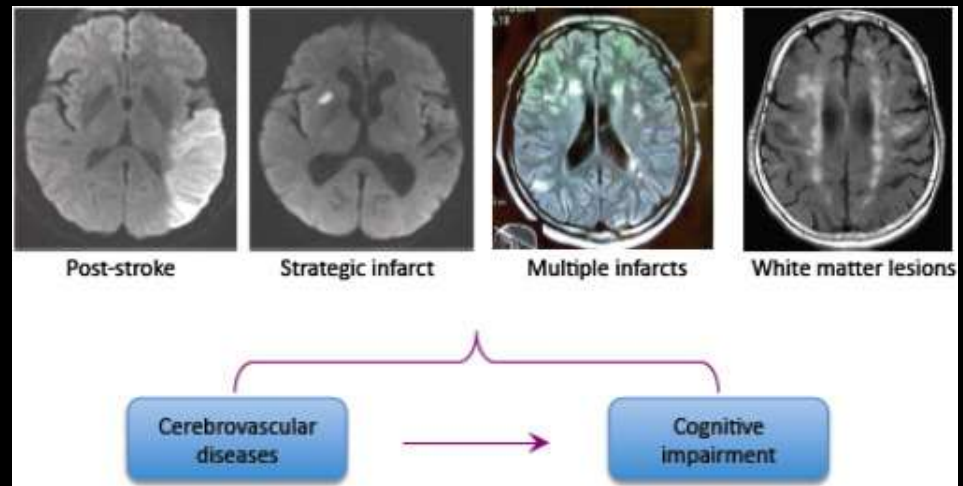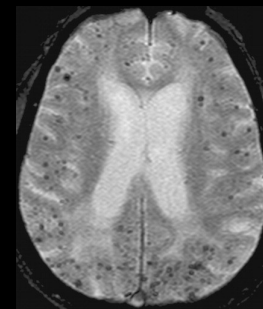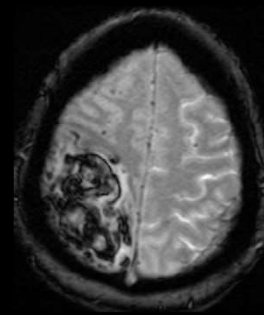
Women

Men

Seshadri, et al. Stroke 2006
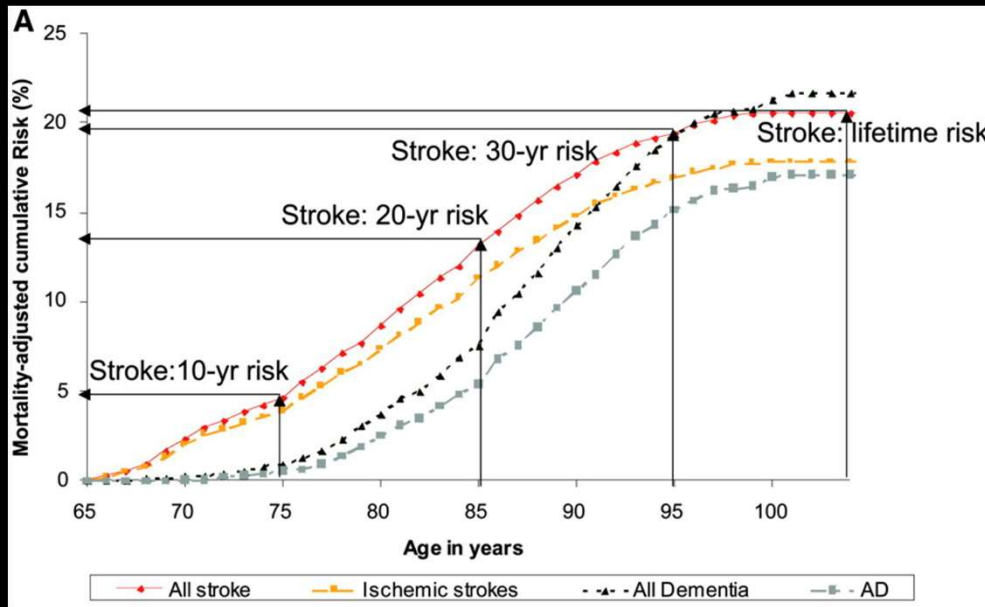
What is cerebrovascular disease?

- Any disorder of cerebral blood vessels
  - Arteriolarsclerosis
  - Atherosclerosis
  - Cerebral amyloid angiopathy
  - CADSIL

Normal vessel   Arteriosclerosis   Atherosclerosis

CAA


CADSIL

What is cerebrovascular injury

- Hemorrhage
  - Large (stroke)
  - Microbleeds (clinically silent)
- Infarction – ischemic
  - Large vessel (stroke)
  - Small vessel (clinically silent)
- White matter hyperintensities
- Dilated Perivascular spaces

Post-stroke   Strategic infarct   Multiple infarcts   White matter lesions

Cerebrovascular diseases → Cognitive impairment

What are the vascular risk factors?

- Hypertension
- Hyperlipidemia
- Diabetes Miletus
- Smoking
- Drug abuse
- Obesity
- Traumatic brain injury
- Inflammatory or infectious disorders

- Age
- Sex
- Race and ethnicity
- Family history and genetics
- Bleeding disorders/blood thinners
- Sleep apnea
- Pollution

Evolution of the concept of cognitive impairment on vascular bases

Iadecola, Neuron, 2013
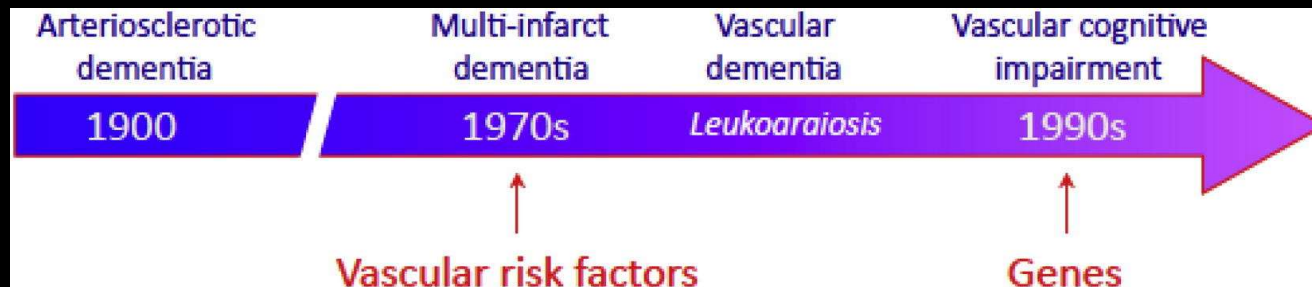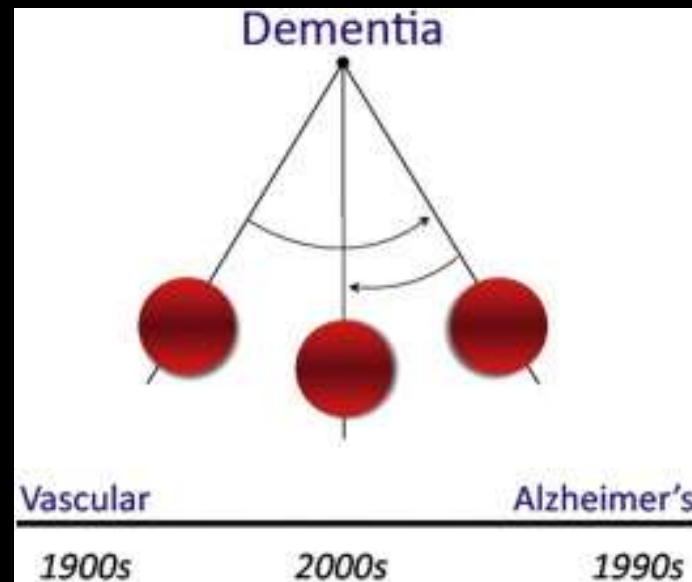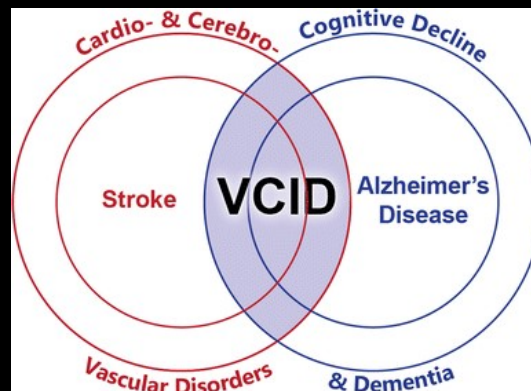
Vascular Cognitive Impairment and Dementia (VCID)
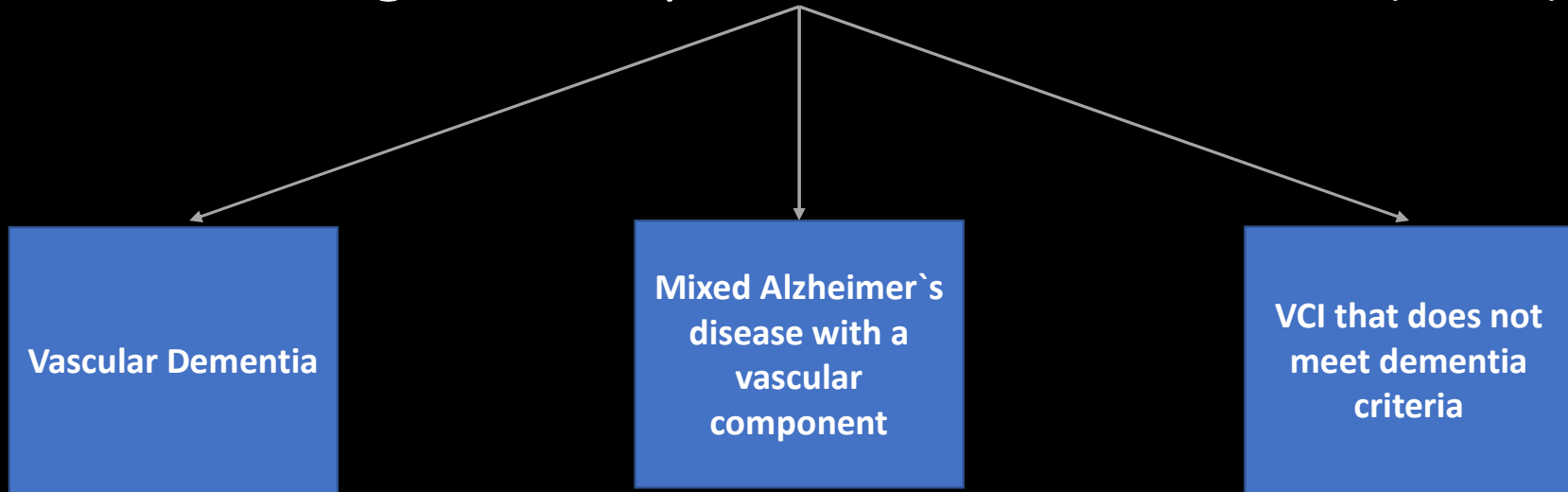
Vascular Dementia

Mixed Alzheimer`s disease with a vascular component

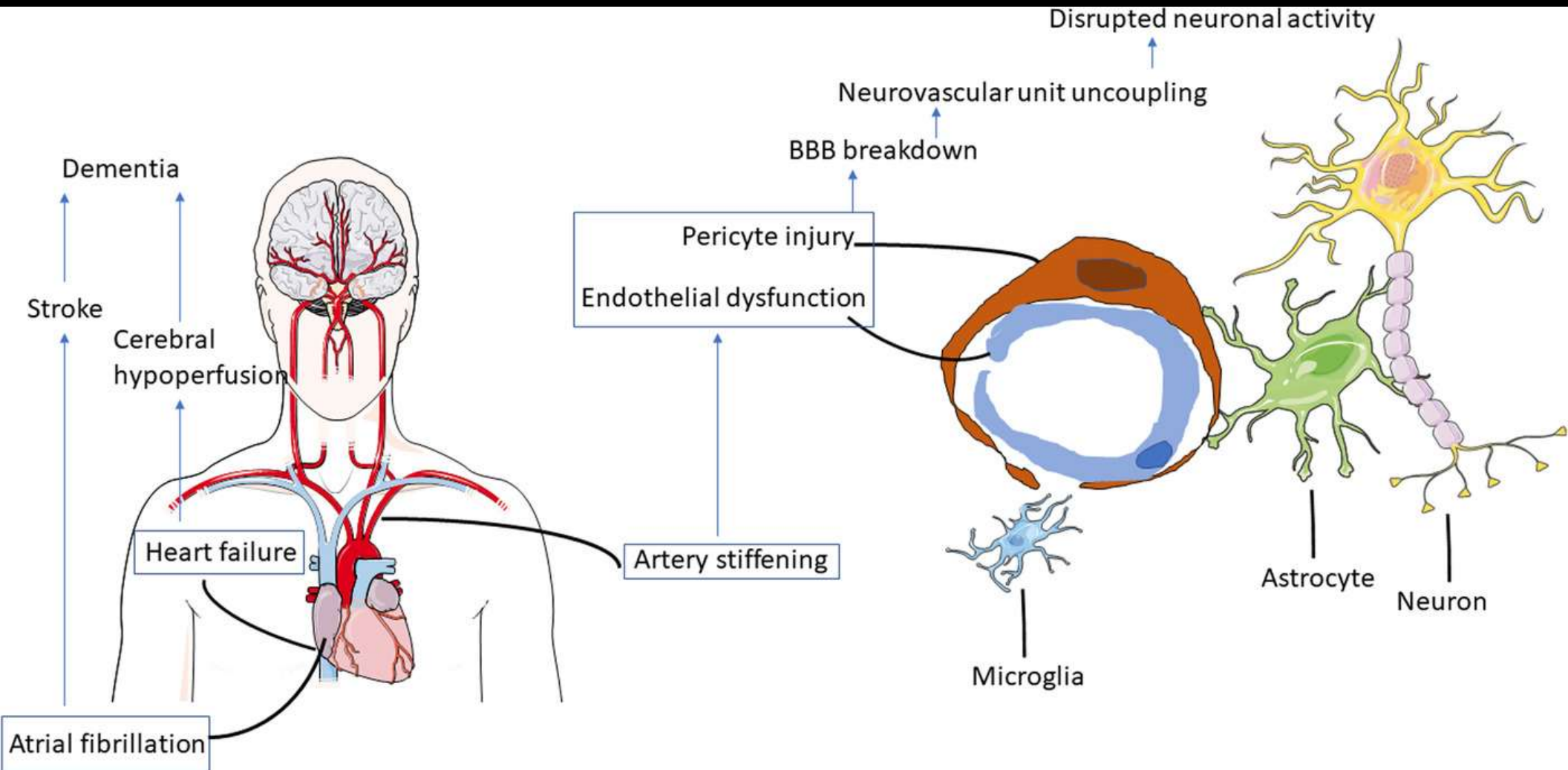**VCI that does not meet dementia criteria**

**Post-stroke dementia**

Vascular dementia without recent stroke

A group of syndromes that represent a clinicoradiologic and pathological spectrum

Disrupted neuronal activity

Neurovascular unit uncoupling

BBB breakdown

Pericyte injury

Endothelial dysfunction

Dementia

Stroke

Cerebral hypoperfusion

Heart failure

Artery stiffening

Atrial fibrillation

Microglia

Astrocyte

Neuron

Heterogenous pathology of dementia

- Multiple interacting and co-occurring pathologies
  - Neurodegenerative
    - Amyloid and tau
    - Lewy Bodies
    - TDP-43
  - Vascular
    - White matter changes
    - Infarcts
    - Microhemorrhages
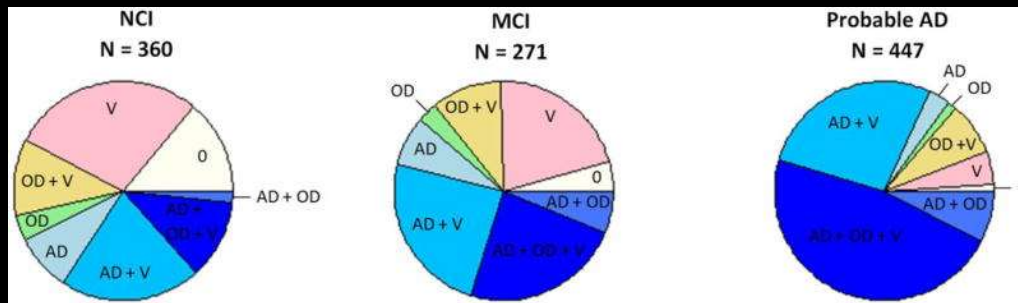
Kapasi, et al., 2017

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Attributable Risk of Alzheimer's Dementia Attributed to Age-Related Neuropathologies

Patricia A. Boyle,[1,2] Lei Yu,[1,3] Sue E. Leurgans,[1,3] Robert S. Wilson,[1,2,3] Ron Brookmeyer,[5] Julie A. Schneider,[1,3,4] and David A. Bennett[1,3]
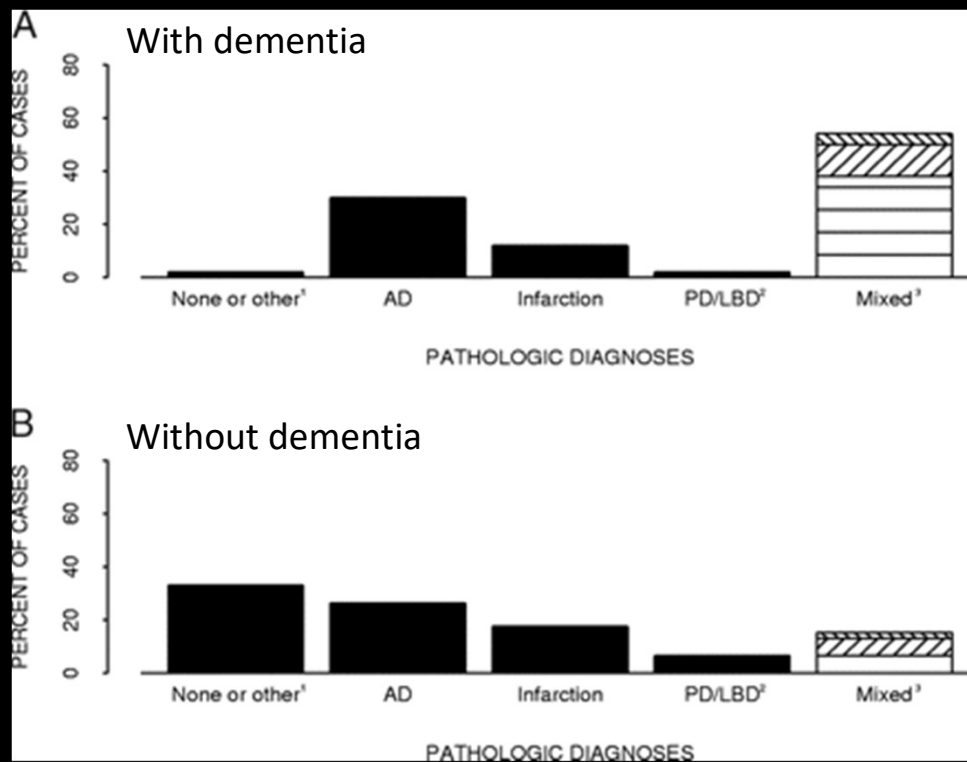
ANN NEUROL 2019;85:114–124

Neuropath	Attribution
AD (plaques/tangles)	41%
Lewy Bodies	11%
TDP-43	12%
Athero & Arteriosclerosis	11%
Infarcts	9%
CAA	8%
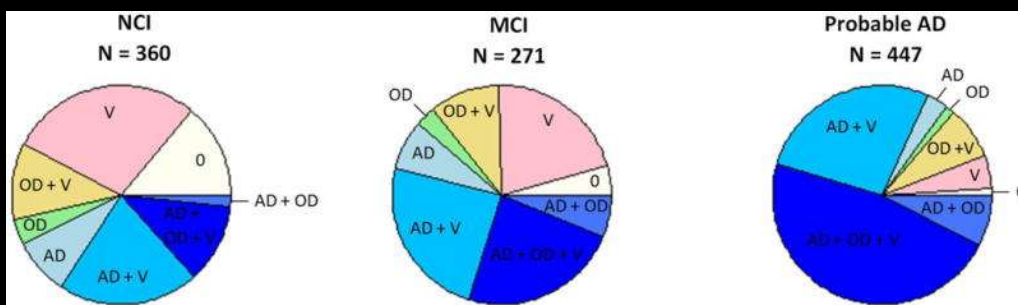
Kapasi, et al., 2017

Heterogenous pathology of dementia

Schneider 2007

Heterogenous pathology of dementia

With dementia

Without dementia
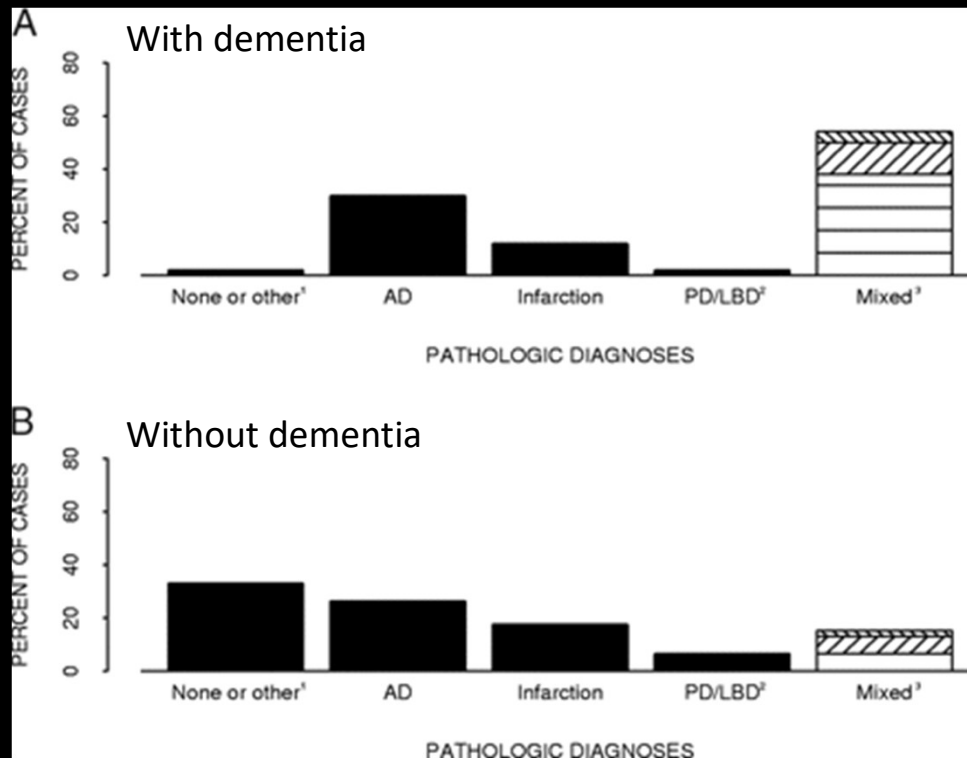
Schneider 2007

Much of Late Life Cognitive Decline Is Not due to Common Neurodegenerative Pathologies

Patricia A. Boyle, PhD,[1,2] Robert S. Wilson, PhD,[1,2,3] Lei Yu, PhD,[1,3]
Alasdair M. Barr, PhD,[4] William G. Honer, MD,[5]
Julie A. Schneider, MD,[1,3,6] and David A. Bennett, MD[1,3]
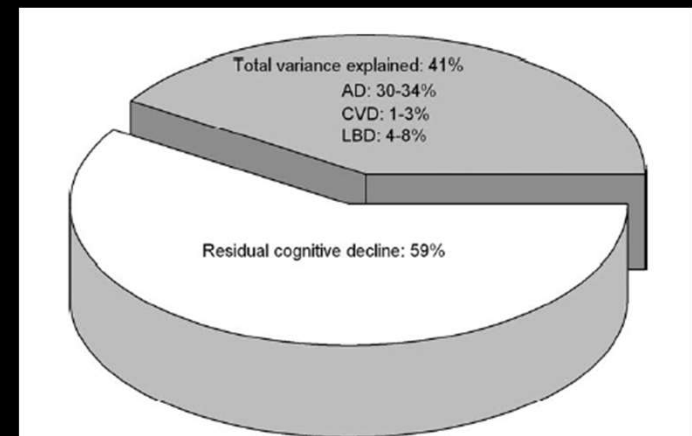
ANN NEUROL 2013;74:478–489

Total variance explained: 41%
AD: 30-34%
CVD: 1-3%
LBD: 4-8%

Residual cognitive decline: 59%

FIGURE 3: Variation in cognitive decline explained by the pathologic indices (gray) and the residual, unexplained variation in cognitive decline (white) derived from fully adjusted models. AD = Alzheimer disease; CVD = cerebrovascular disease; LBD = Lewy body disease.

Vascular risk scores

Step 1

Age, y	Points
40–46	0
47–53	3
54–55	4

Step 2

Education, y	Points
0–6	3
7–9	2
>9	0

Step 3

Sex	Points
Men	1
Female	0

Step 4

Cholesterol, mg/dL	Points
<251	0
≥251	2

Step 5

BMI, kg/m²	Points
<30	0
≥ 30	2

Step 6

Systolic blood Pressure, mm/Hg	Points
<140	0
>140	2

Predicted 40-year risk of dementia

Total points	40–Year risk, %
0–1	10
2	11
3	15
4	17
5	20
6	21
7	25
8 –14	29

Add up points from stepts 1 through 6, then look up predicted 40-years risk of dementia.

Exalto et al 2014

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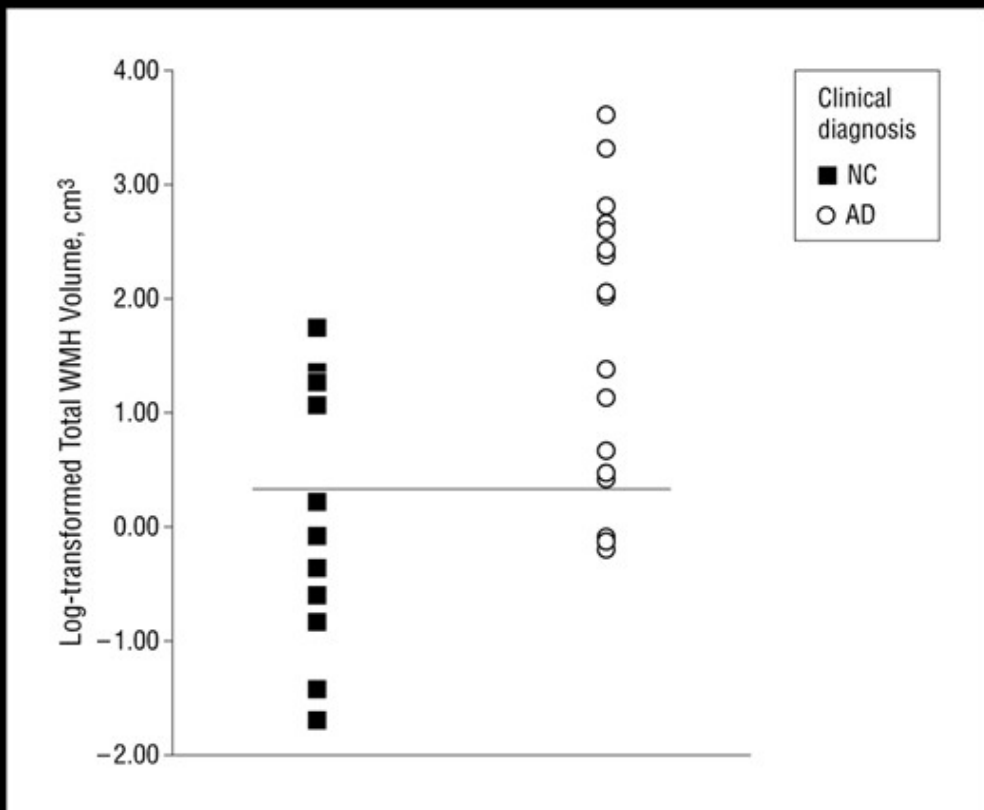Rabin et al. Annals of Neurology, 2019   Clark et al. Alzheimer's & Dementia, 2019

Rabin et al. Annals of Neurology, 2019
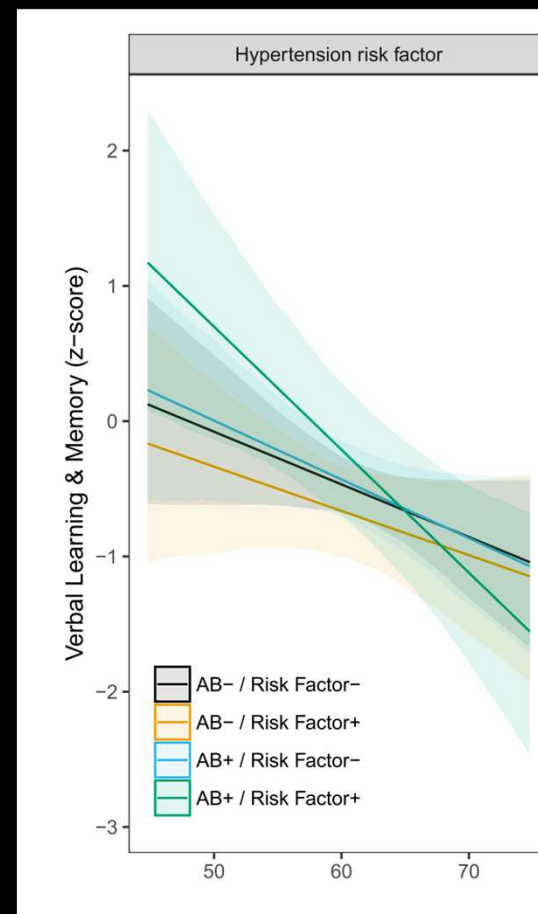
Clark et al. Alzheimer's & Dementia, 2019

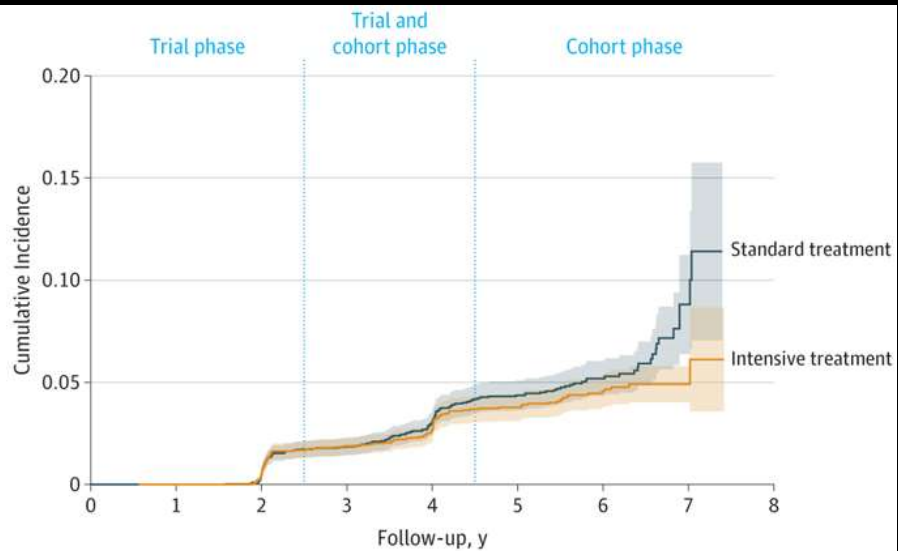# White matter hyperintensities

White matter hyperintensity
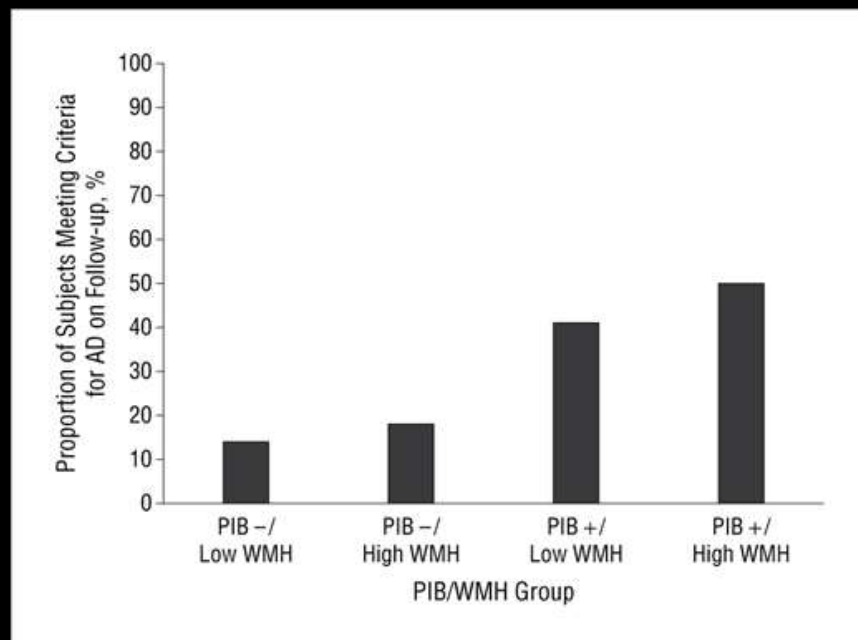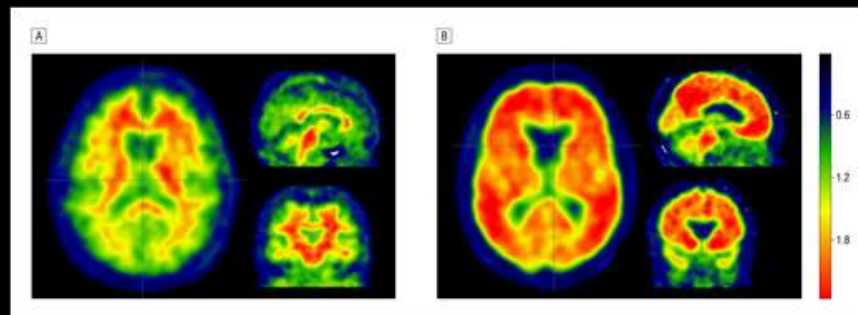
Provenzano 2013

White matter hyperintensity
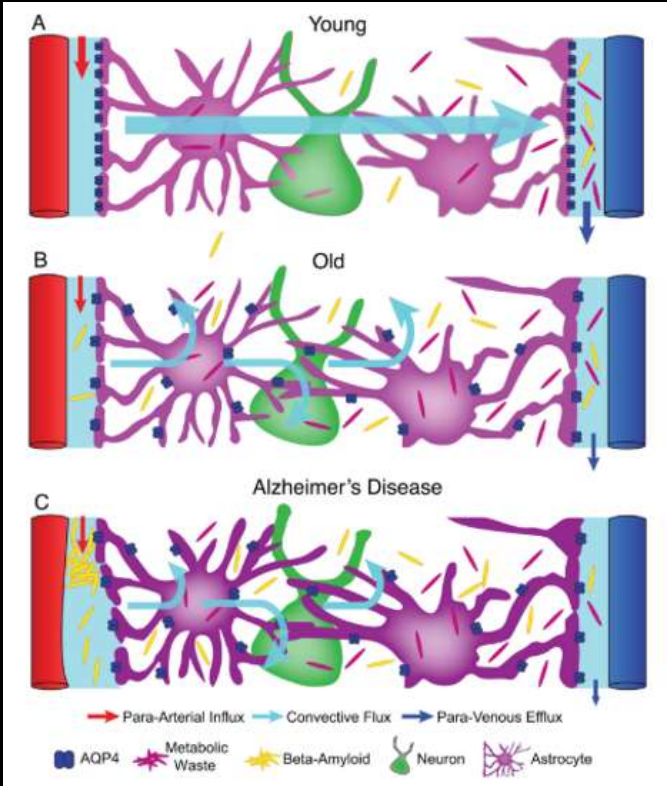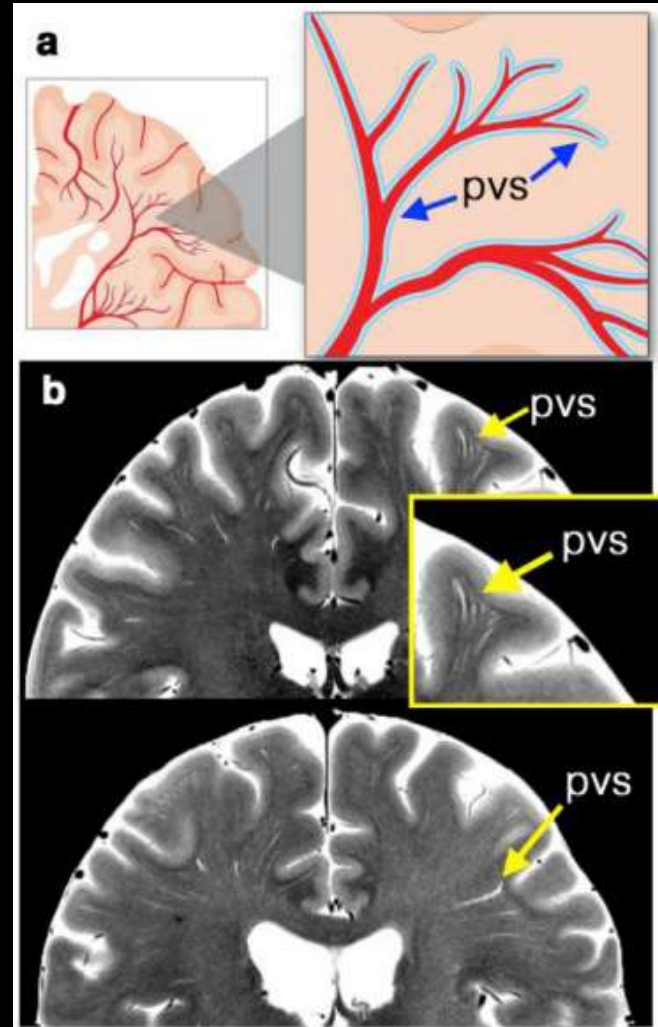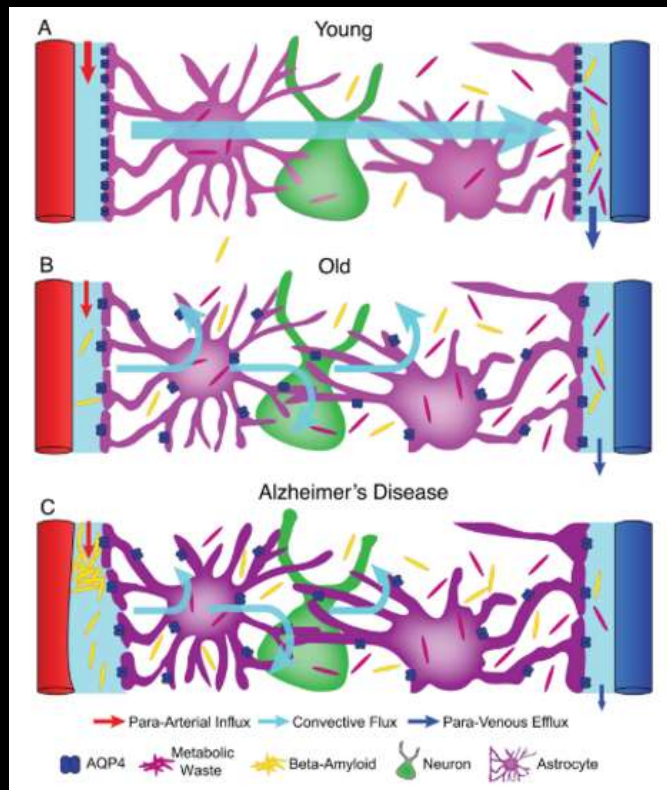
Clinical Trials
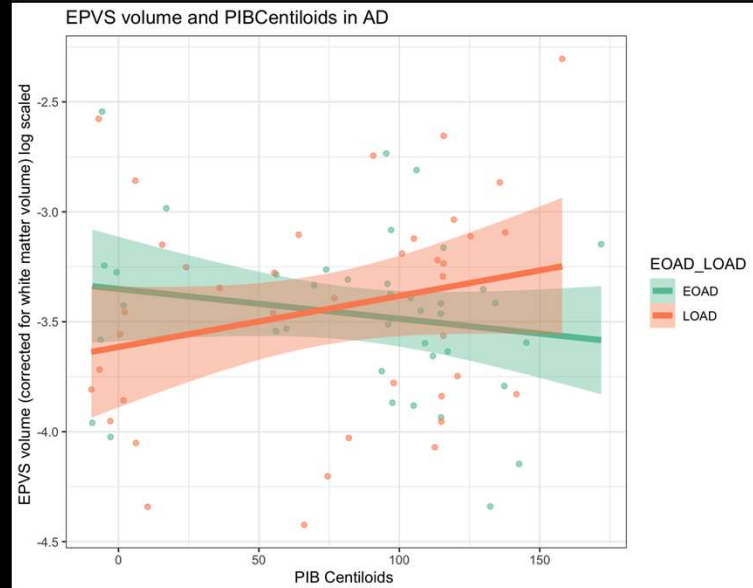
SPRINT-MIND

Clinical Trials

SPRINT-MIND
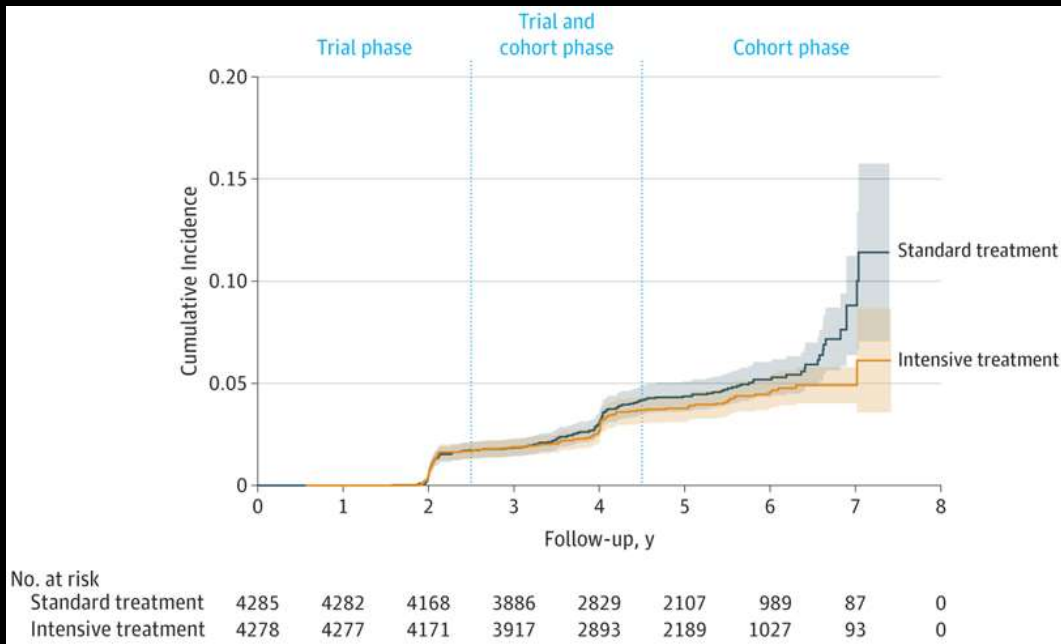
FINGER
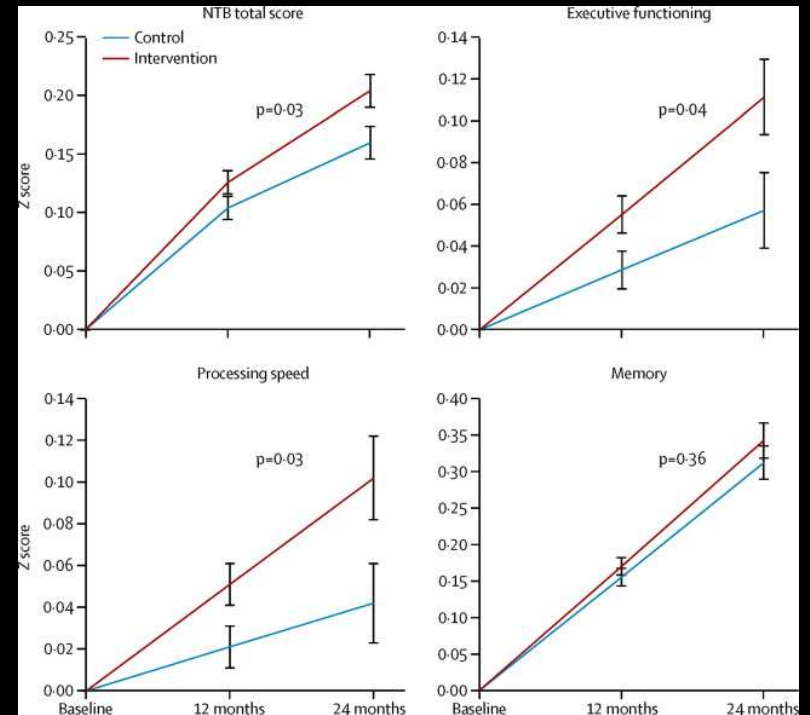
The glymphatic system

The glymphatic system

Jessen et al, Neurochem Res 2015
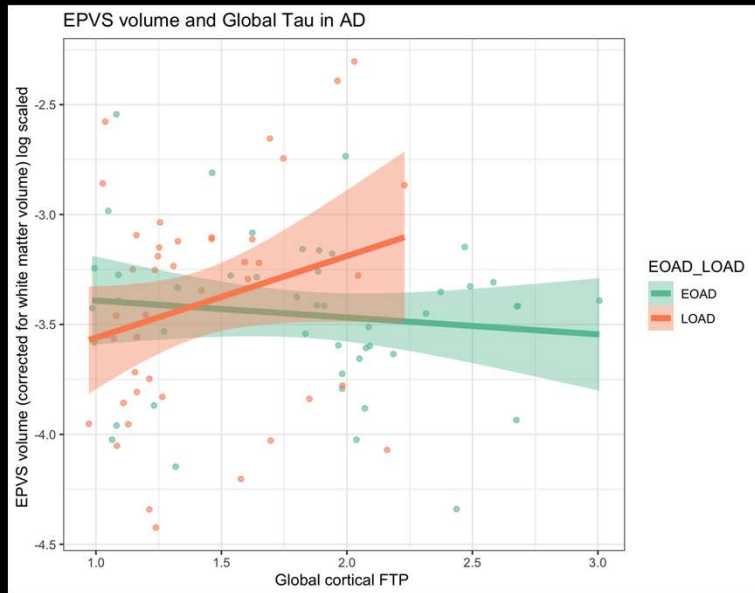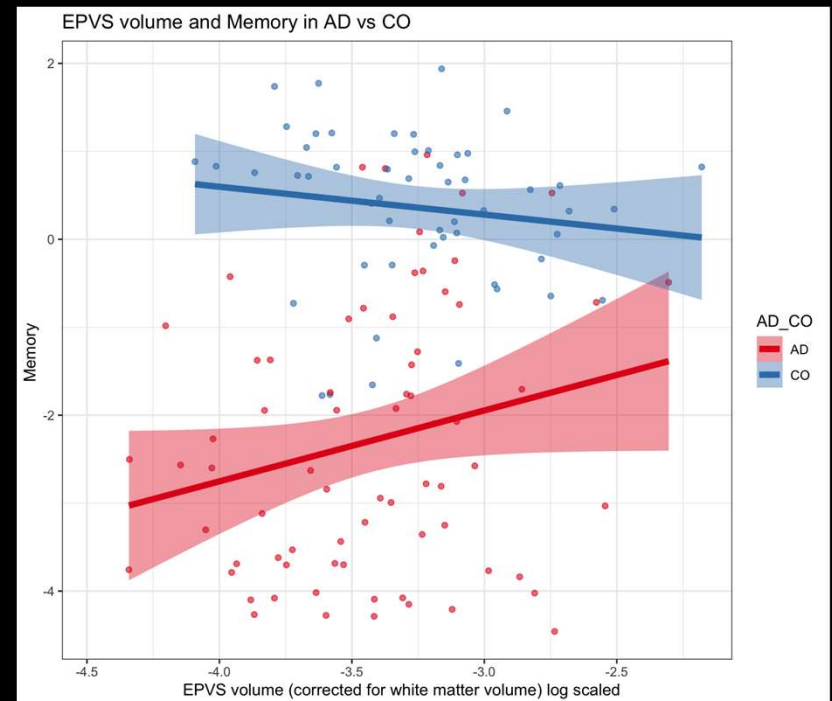
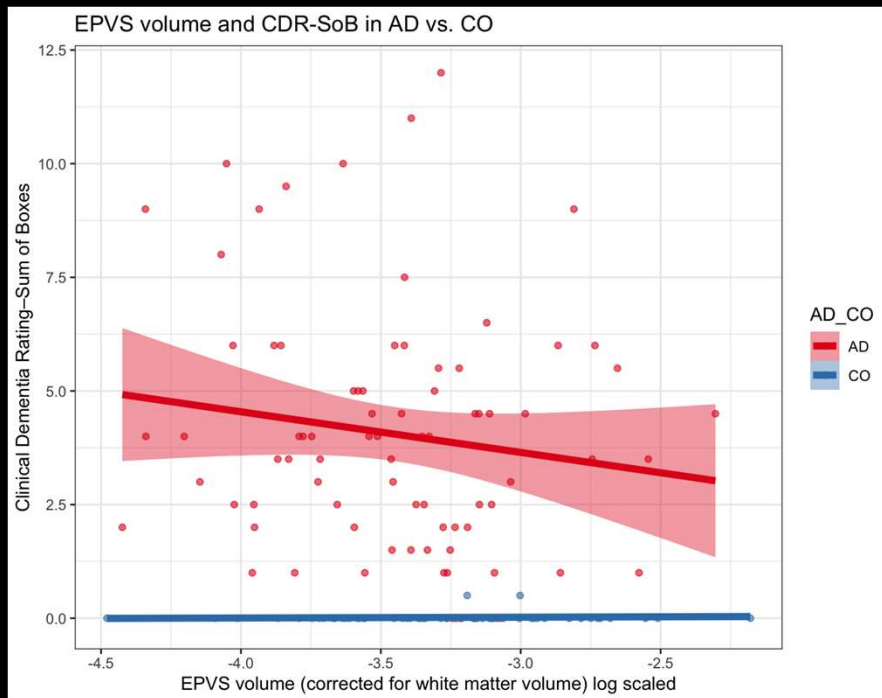Expanded perivascular spaces (EPVS)
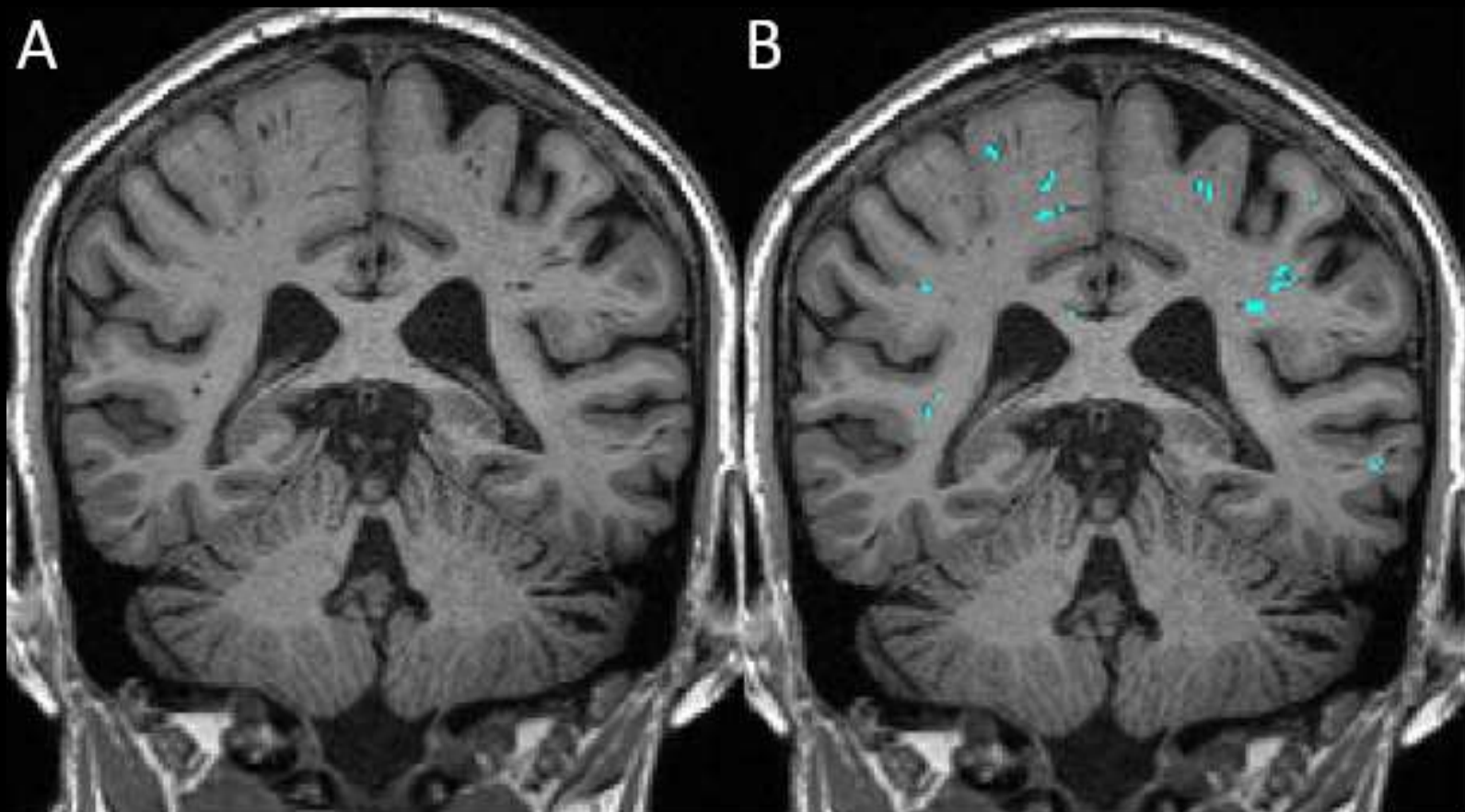
EPVS in Early and Late Age-of-onset AD
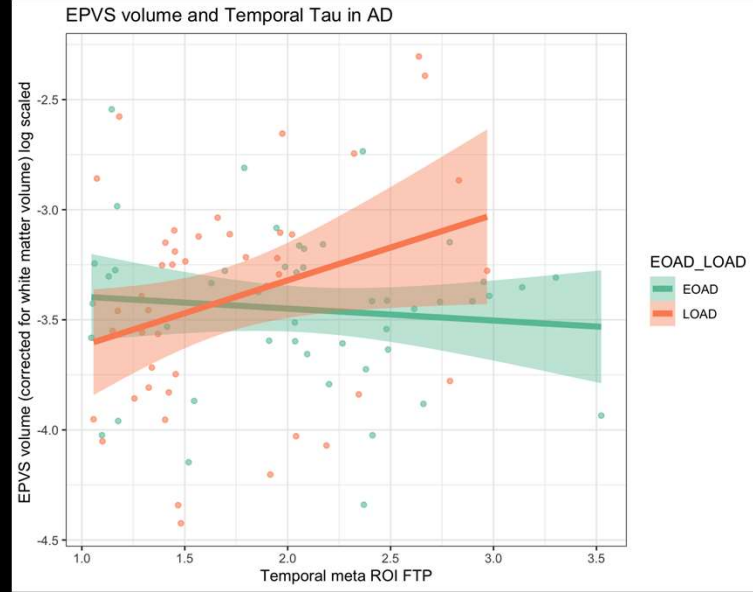
In prep

Function and cognition in AD and CO

In prep

Treatment of vascular cognitive impairment and dementia

- Antihypertensive therapy
- Diabetes management
- Statins
- Antithrombotic therapy
- Cholinesterase inhibitors
- Memantine
- Nonpharmacologic therapy

Cardiovascular Disease Deaths: 1950 to 2010

Nabel and Braunwald, NEJM 2012