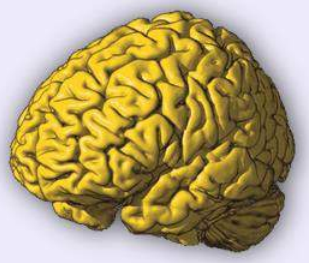
OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Alzheimer's Disease and Dementia
September 23-25, 2014 Valencia Convention Centre, Spain

Common Risk Factors in Alzheimer's Disease and Vascular Dementia



Ken Nagata, M.D.

Department of Neurology

Research Institute for Brain and Blood Vessels, Akita, Japan


Ronald W. Reagan
(1911-2004)
Margaret H. Thatcher
(1925-2013)

Ronald Reagan had Alzheimer's while president, says son.

Ed Pilkington in New York

Follow

The Guardian, Monday 17 January 2011 19.37 GMT

Jump to comments (198)

Ronald Reagan's sons have locked horns over the former president's political legacy after the younger brother, Ron, said his late father's battle with Alzheimer's began while he was in the White House.



Ronald Reagan in 1984. His son recalls how his father was 'uncharacteristically lost for words' during a presidential debate that year. Photograph: Wally McNamee/Corbis

The spat opens up a subject that has long been a talking point – when did the 40th president begin to become mentally impaired by the disease. He was formally diagnosed with Alzheimer's in 1994, five years after he left office. Reagan died 10 years later at 93.

Thatcher's struggle with dementia

Baroness Thatcher's daughter Carol has revealed details of her mother's struggle with dementia for the first time.

Last Updated: 2:28PM BST 24 Aug 2008



Baroness Thatcher has kept a low profile in recent years and her doctor advised her to stop

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Margaret Thatcher's mental decline revealed by her daughter

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Page last updated at 01:54 GMT, Sunday, 24 August 2008 02:54 UK

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Thatcher dementia fight revealed

The daughter of former UK prime minister Margaret Thatcher has spoken for the first time about her mother's struggle with dementia.



Lady Thatcher has had a series of strokes

In her new book, serialised in the Mail on Sunday, Carol Thatcher says she first noticed her mother's memory was failing over lunch in 2000.

She says she "almost fell off her chair" seeing her mother, 82, struggle.

Ms Thatcher also says Baroness Thatcher had to be reminded several times her husband, Sir Denis, had died.

Tags: Alzheimer's/Dementia | High Blood Pressure | margaret | thatcher | dementia | stroke | death

Margaret Thatcher's Battle Against Stroke-Caused Dementia

Monday, 08 Apr 2013 12:54 PM

By Charlotte Libov

British leader Margaret Thatcher likely suffered a series of small strokes over many years that went unnoticed until her legendary memory started to slip, a top neurologist tells Newsmax Health. Thatcher had an almost-photographic memory, say aides and family members, who recalled that she could often recite briefing papers and other government documents word for word after one reading.

"Small strokes are a condition known as 'multi-infract vascular dementia,' which is a major cause of dementia. Since Margaret Thatcher was known for her ability to recall monumental amounts of information, she probably had a huge reserve capacity of memory, so she might have suffered small strokes for years before it became noticeable," says Michael Sellman, M.D., chief of the neurology division at Mercy Medical Center in Baltimore. Thatcher's death from a stroke on Monday at the age of 87 came following a battle with dementia that lasted more than a dozen years. In recent years, her ill health left her so frail that she was unable to attend important events, such Prince William's wedding in 2011. Her daughter, Carol, said that she first noticed her mother's failing memory in the summer of 2000.

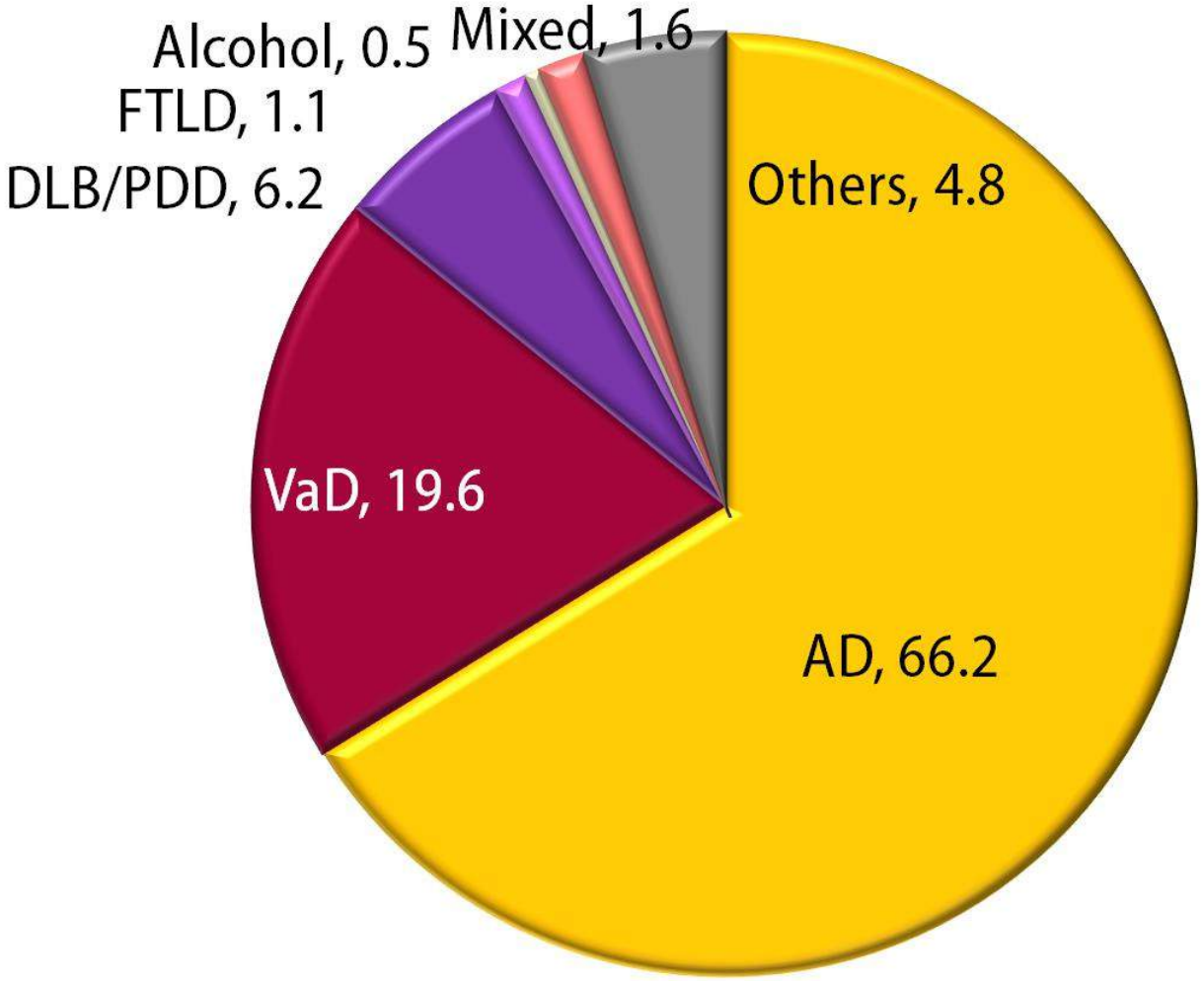
Did Baroness Thatcher die of (or with) dementia?



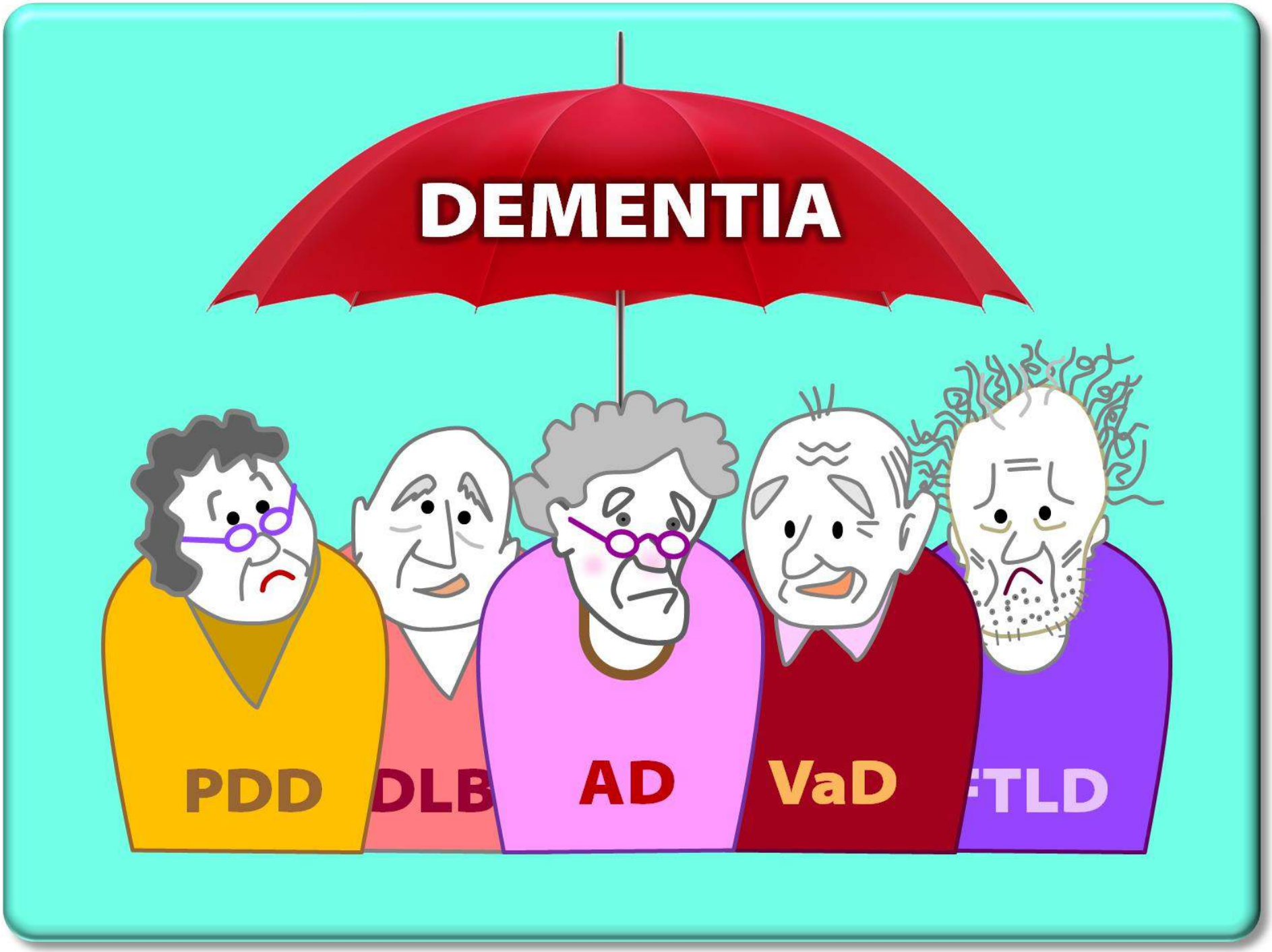
The news that Baroness Thatcher died yesterday was so breath-taking, that the underlying cause of her death really took second fiddle.

The actual cause of Thatcher's dementia was never confirmed but it was after a series of mini-strokes in 2002 that Thatcher finally withdrew from public life. A number of small strokes commonly trigger dementia. It was in 2008 that daughter Carol broke the news that her mother had been suffering from dementia.

Late-onset Dementia

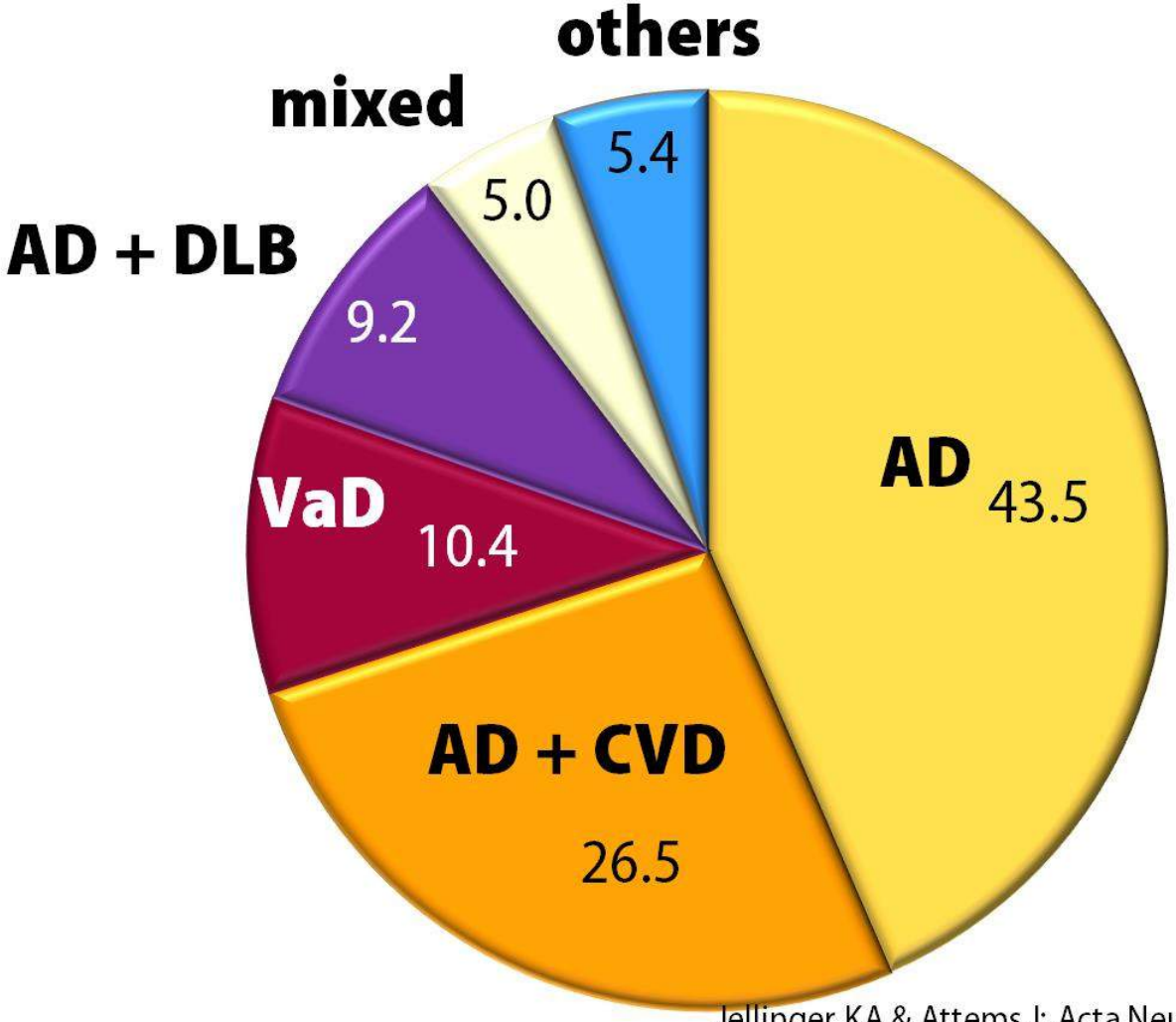


Ikejima C, et al. 2011


DEMENTIA
PDD
DLB
AD
VaD
FTLD

Pathological Diagnosis of Dementia

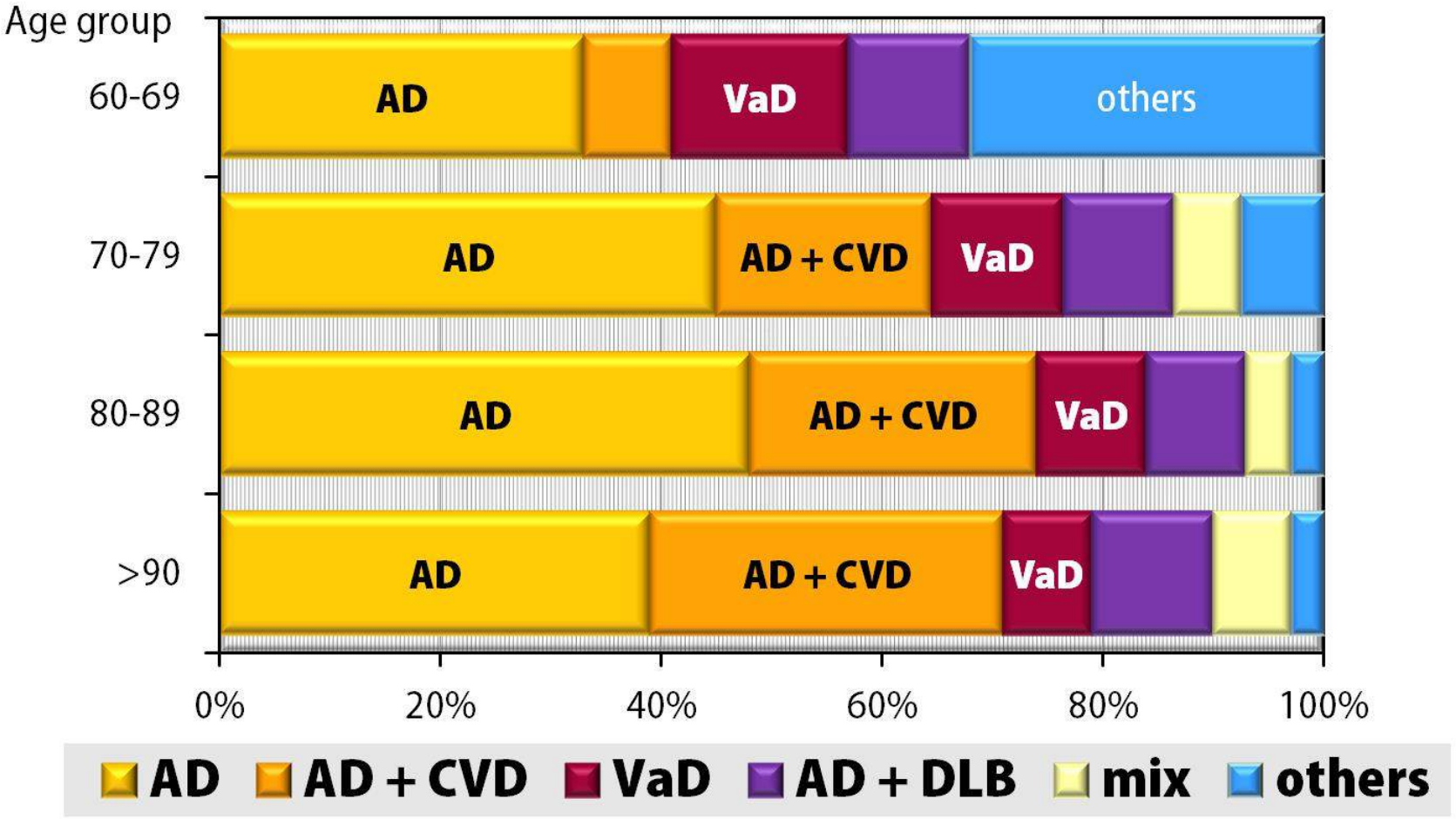
n=1,110 subjects, MMSE < 20/30, mean age: 83.3 yrs



Jellinger KA & Attems J: Acta Neuropathol 119:421-433, 2010

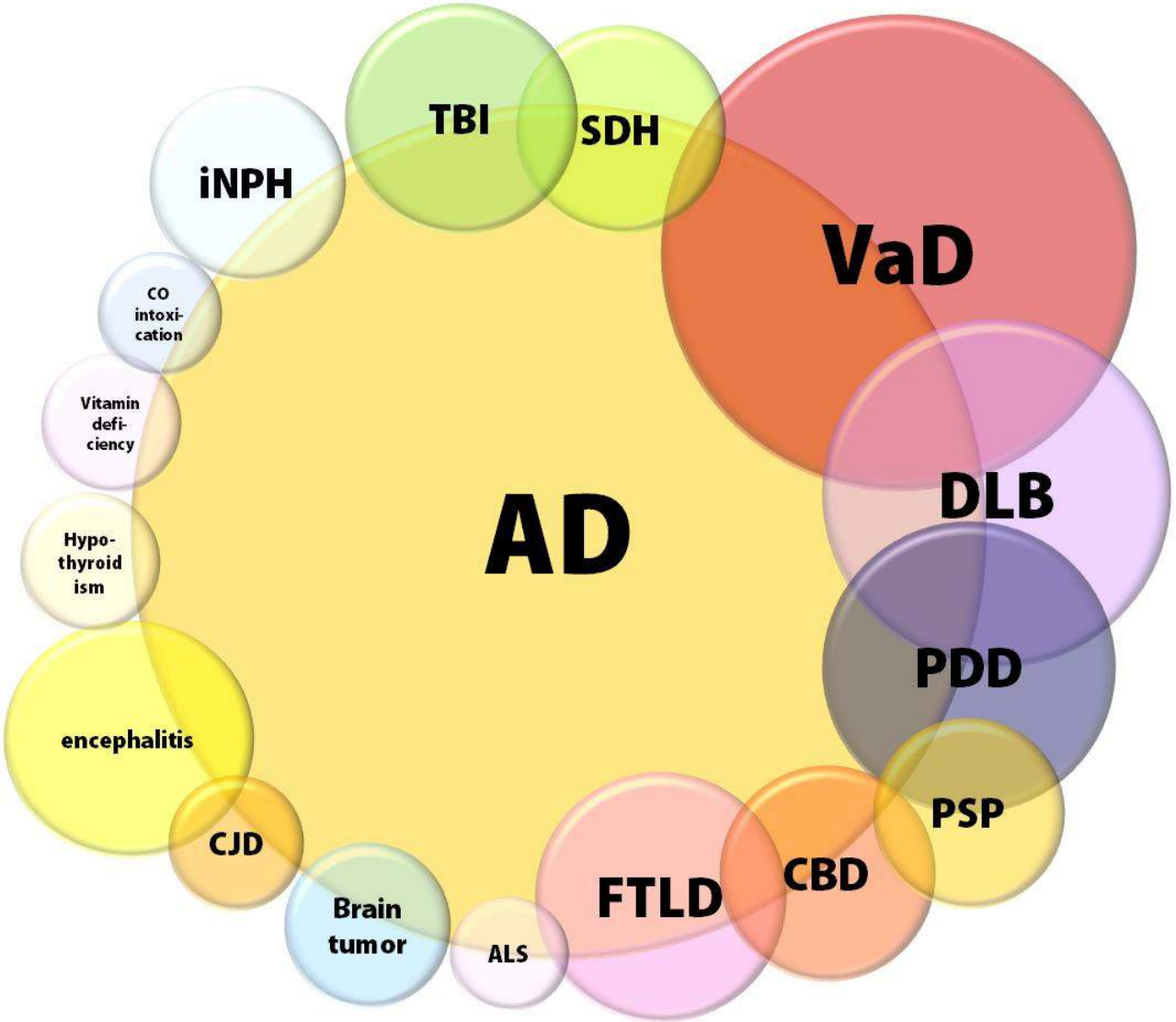
Pathological Diagnosis of Dementia

n=1,110 subjects, MMSE < 20/30, mean age: 83.3 yrs



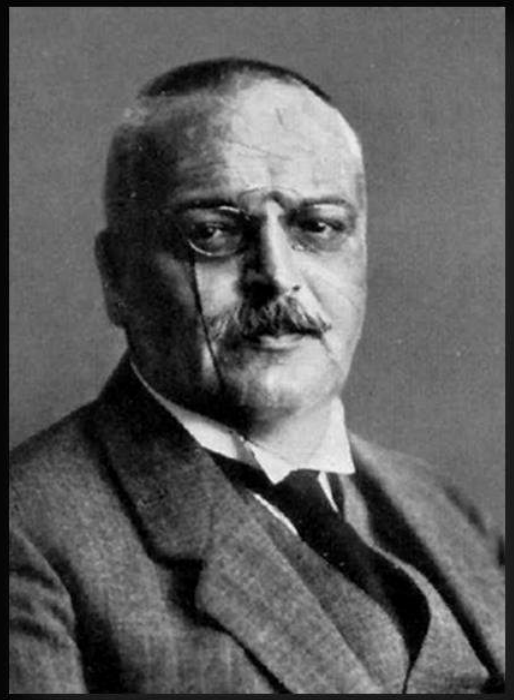
Jellinger KA & Attems J: Acta Neuropathol 119:421-433, 2010

Overlapping Etiology of Dementia



Vascular Dementia





Alois Alzheimer
(1864-1915)



Otto Binswanger
(1852-1929)

"In 1894, Binswanger and Alzheimer first described arteriosclerotic brain atrophy and emphasized the need to differentiate it from [syphilitic] paralysis."

Alzheimer 1902

PSYCHIATRIE

Ein Lehrbuch

für

Studirende und Aerzte

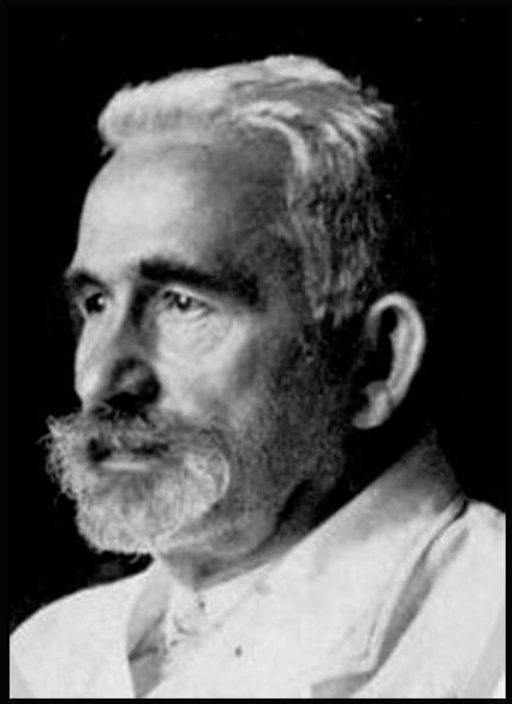
von

Dr. Emil Kraepelin
Professor in Heidelberg

Fünfte, vollständig umgearbeitete Auflage

Mit 10 Lichtdrucktafeln, 13 Curven und 13 Schriftproben

Leipzig
Verlag von Johann Ambrosius Barth
1896



Emil Kraepelin
(1856-1926)

"Ein Lehrbuch für Studierende und Ärzte"

Emil Kraepelin 1910

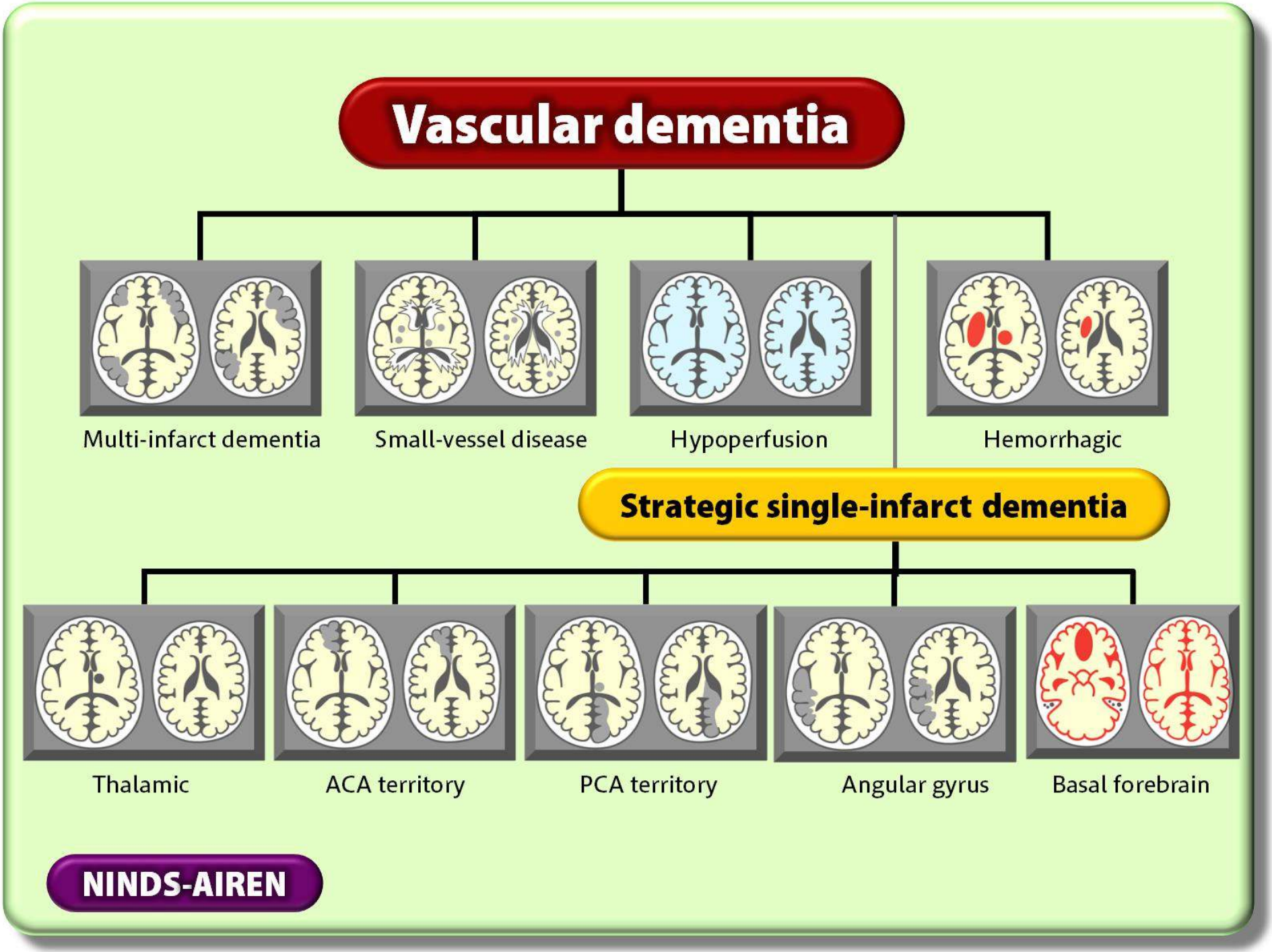
- ***Pre-senile dementia*** = Alzheimer's disease
- ***Arteriosclerotic psychosis***= Vascular dementia
  - ***Dementia post-apoplexiam***

    = post-stroke dementia
  - ***Arteriosclerotic brain degeneration:***

    = multiple lacunar lesions and état criblé
  - ***Senile vascular cortical atrophy:***

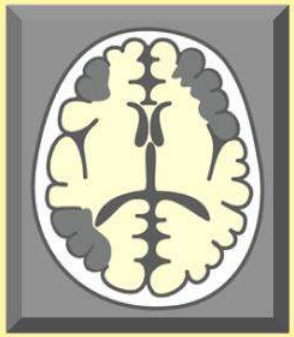
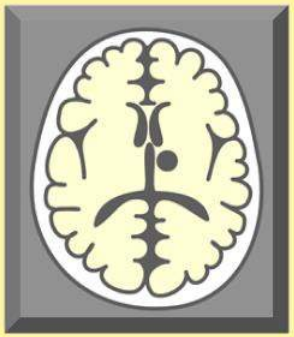
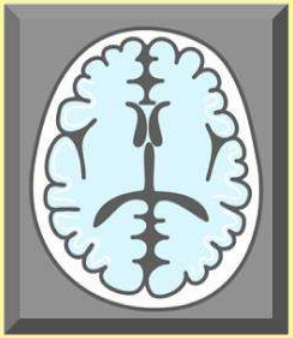
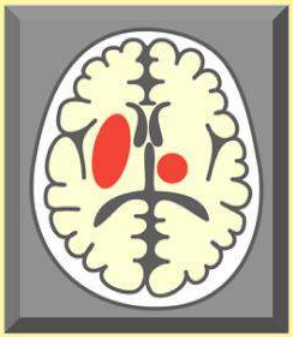
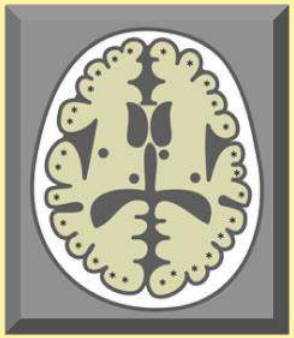
    = granular atrophy and laminar necrosis
  - ***Chronic progressive subcortical encephalitis***

    = Binswanger's disease


Vascular dementia
Multi-infarct dementia
Small-vessel disease
Hypoperfusion
Hemorrhagic
Strategic single-infarct dementia
Thalamic
ACA territory
PCA territory
Angular gyrus
Basal forebrain
NINDS-AIREN

Classification of VaD

Newcastle Categorization of the Major CV lesions Associated with Cognitive Impairment

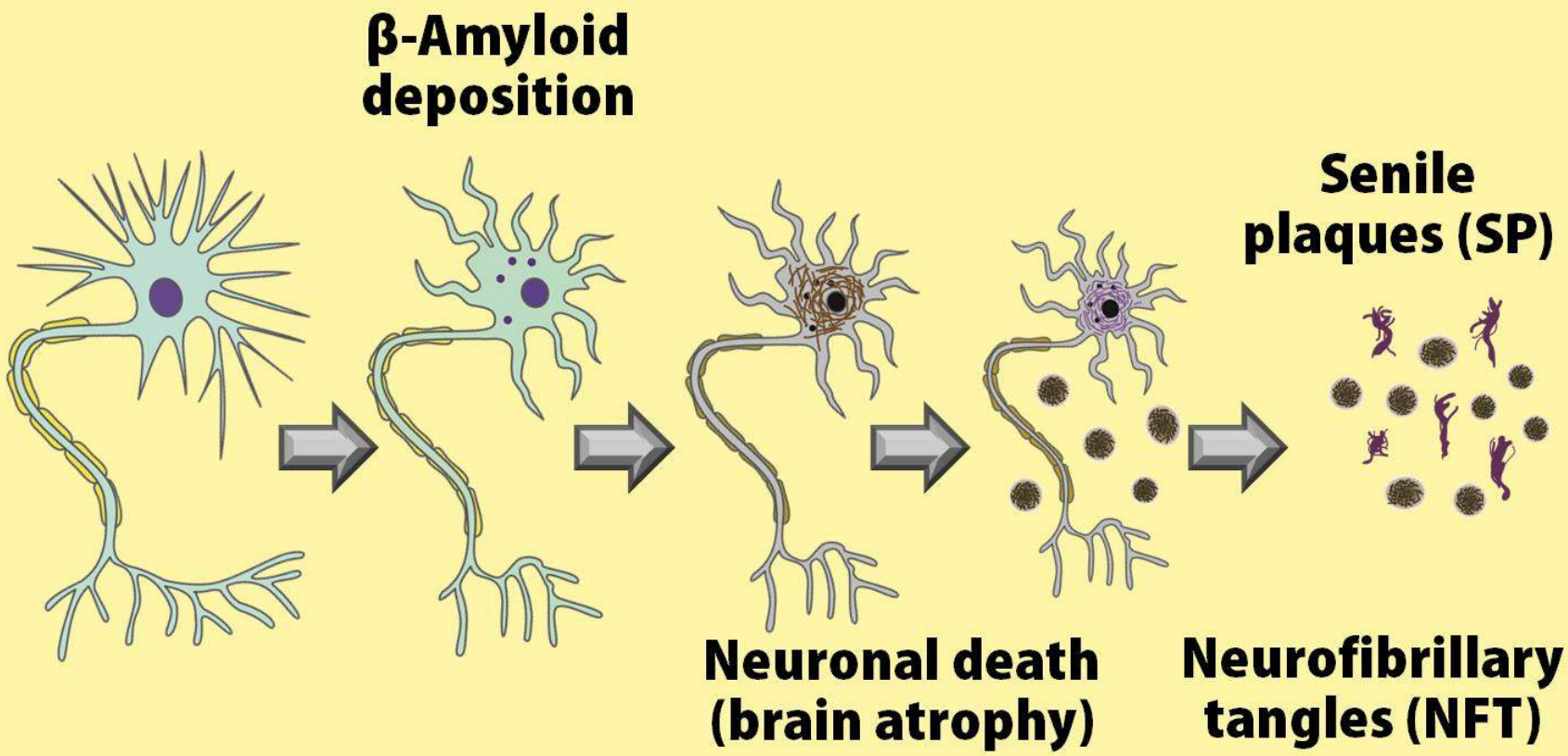
I	II	III	IV	V	VI
					
large infarct or several infarcts	multiple small or microinfarcts	strategic infarcts	cerebral hypoperfusion	cerebral hemorrhage	CV lesions with AD pathology
multi-infarct dementia	white matter lesions	thalamus hippocampus basal forebrain	hippocampal sclerosis	lobar ICH SAH	mixed dementia AD with CVD

Kalaria, RN, et al. J Neuro Sci 226: 75-80, 2004

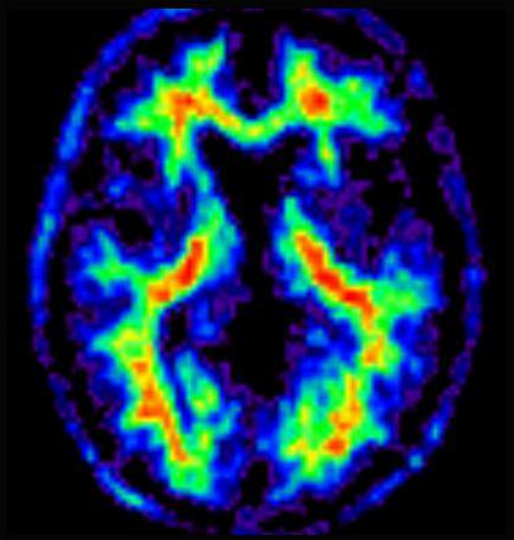
Alzheimer's Disease

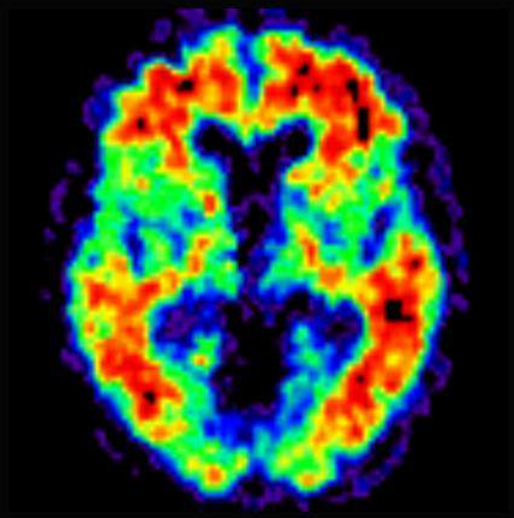


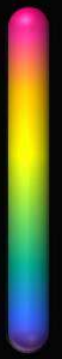
Neuropathological Hallmarks for AD



Amyloid Imaging with ^{18}F-AV-45







HC: 74-year-old woman
MMSE 30/30

AD: 77-year-old woman
MMSE 24/30

SUVR (normalized to cerebellum) 10 min acquisition, 50 min post-injection

New Diagnostic Criteria by NIA-AA



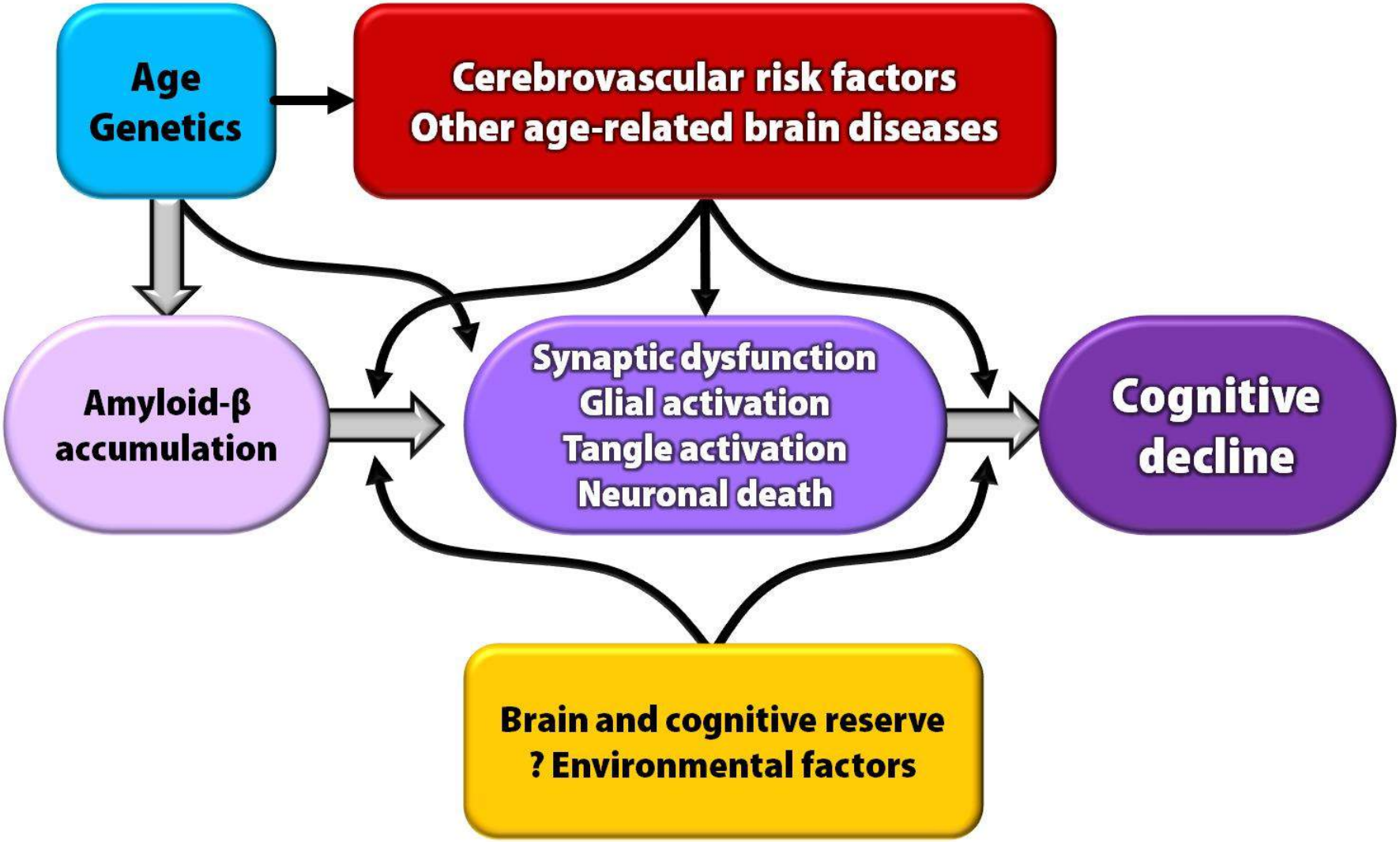
Alzheimer's & Dementia 7 (2011) 263–269

Alzheimer's & Dementia

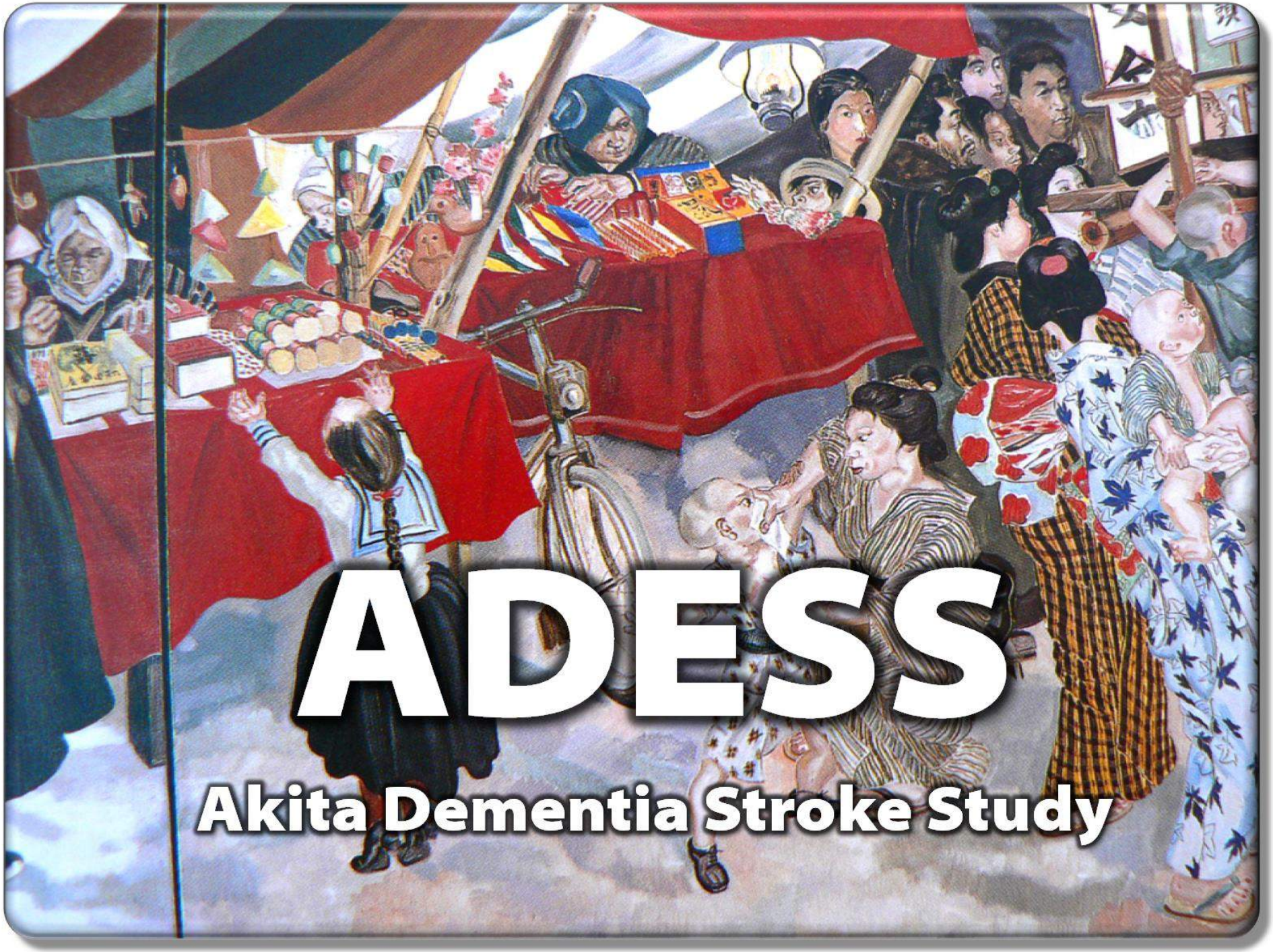
The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Guy M. McKhann[a,b,*], David S. Knopman[c], Howard Chertkow[d,e], Bradley T. Hyman[f], Clifford R. Jack, Jr.[g], Claudia H. Kawas[h,i,j], William E. Klunk[k], Walter J. Koroshetz[l], Jennifer J. Manly[m,n,o], Richard Mayeux[m,n,o], Richard C. Mohs[p], John C. Morris[q], Martin N. Rossor[r], Philip Scheltens[s], Maria C. Carrillo[t], Bill Thies[t], Sandra Weintraub[u,v], Creighton H. Phelps[w]

Hypothetical Model of AD Pathophysiological Cascade



R.A. Sperling et al. / Alzheimer's & Dementia 7 (2011) 280–292


ADESS
Akita Dementia Stroke Study

Vascular Risk Factors in AD

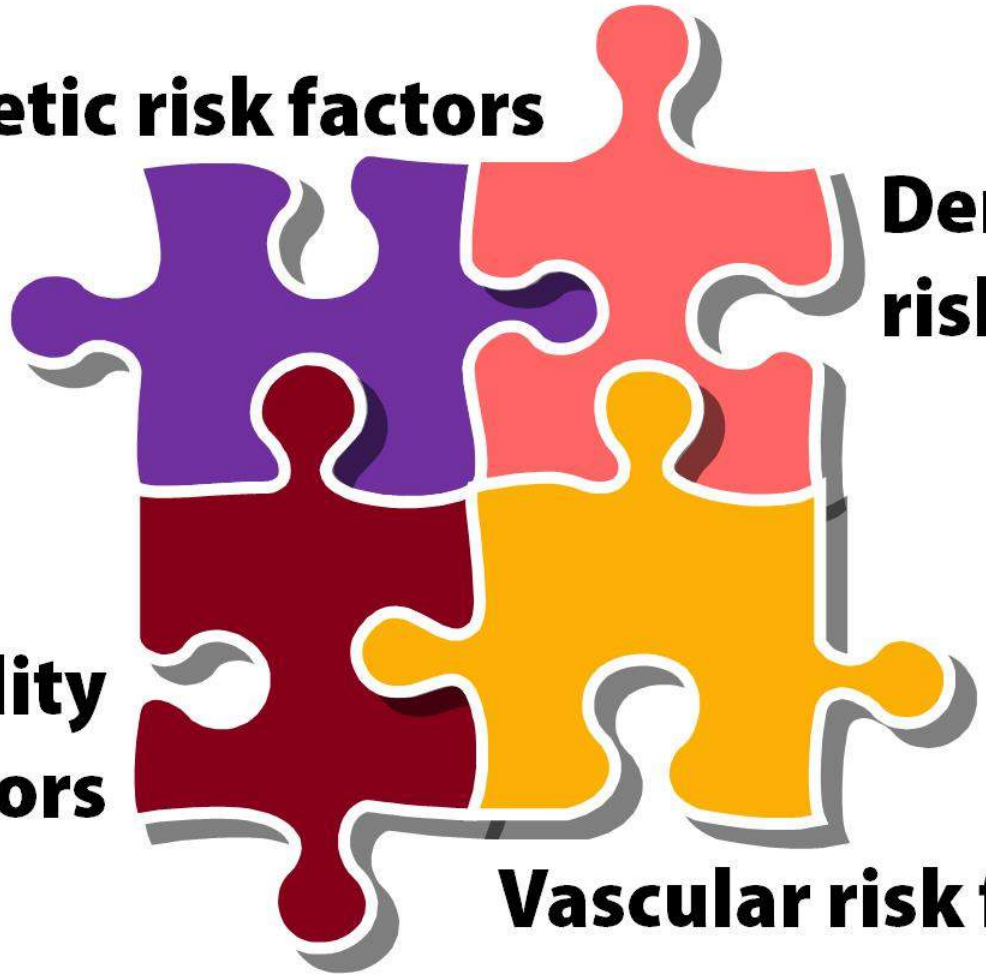
	Overall (n=124)	Men (n=43)	Women (n=81)
Age (yrs)	78.1 ± 7.4	77.9 ± 8.6	77.2 ± 7.3
MMSE	16.0 ± 4.3	15.5 ± 4.4	16.9 ± 4.0
Education (yrs)	9.6 ± 2.8	9.3 ± 2.5	10.3 ± 3.0
BMI	22.4 ± 3.8	22.6 ± 2.6	22.2 ± 4.4
Smoking	24.8%	55.3%	8.5%
Drinking	42.7%	71.8%	26.8%
Hypertension	42.3%	39.5%	43.8%
Diabetes	18.5%	13.6%	27.0%
Hyperlipidemia	30.4%	19.1%	37.2%
CAD	18.7%	23.1%	16.2%

Yamazaki T, 2008

Risk Factors for Dementia

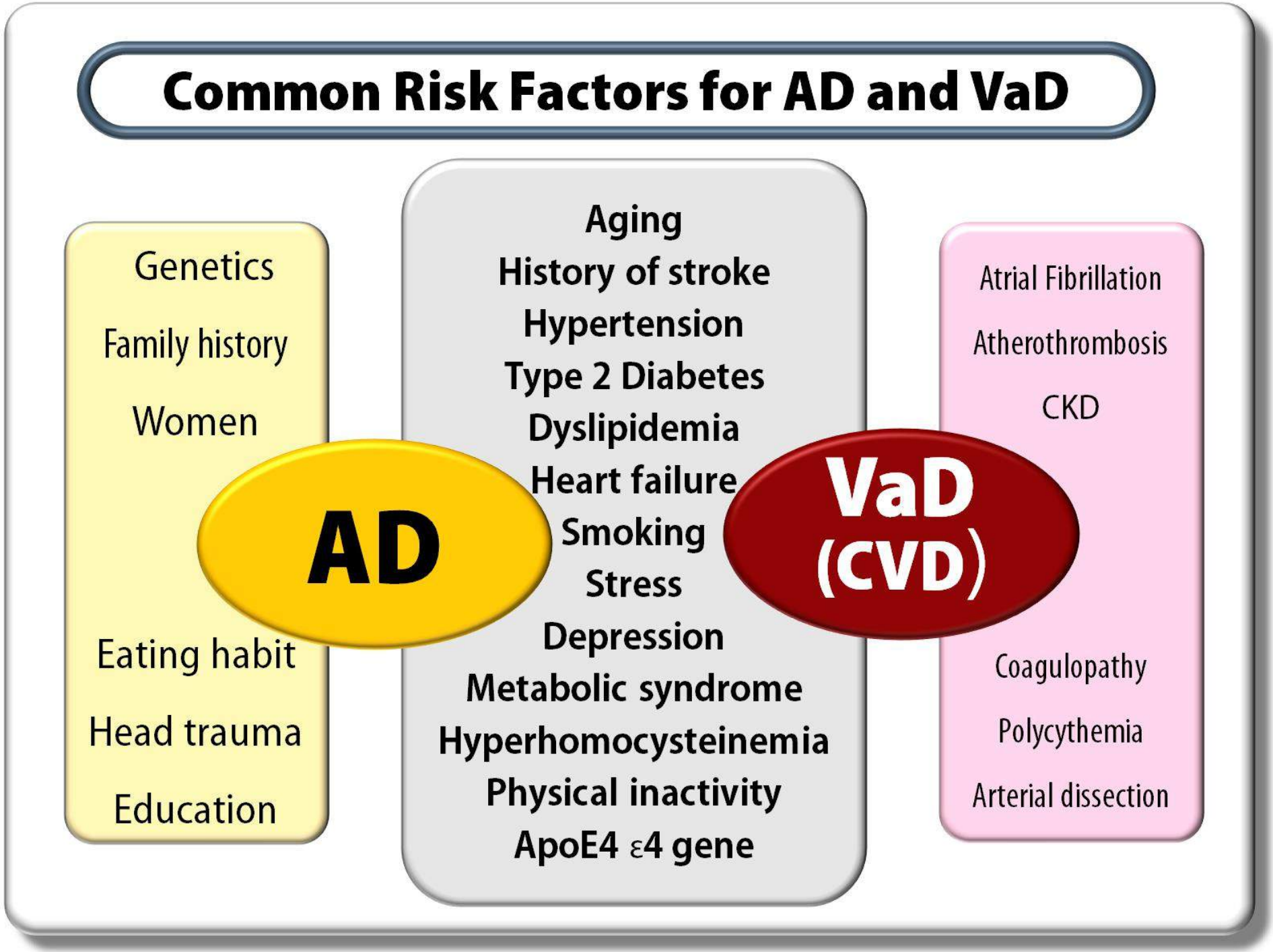


Risk Factors for AD



Vascular Risk Factors

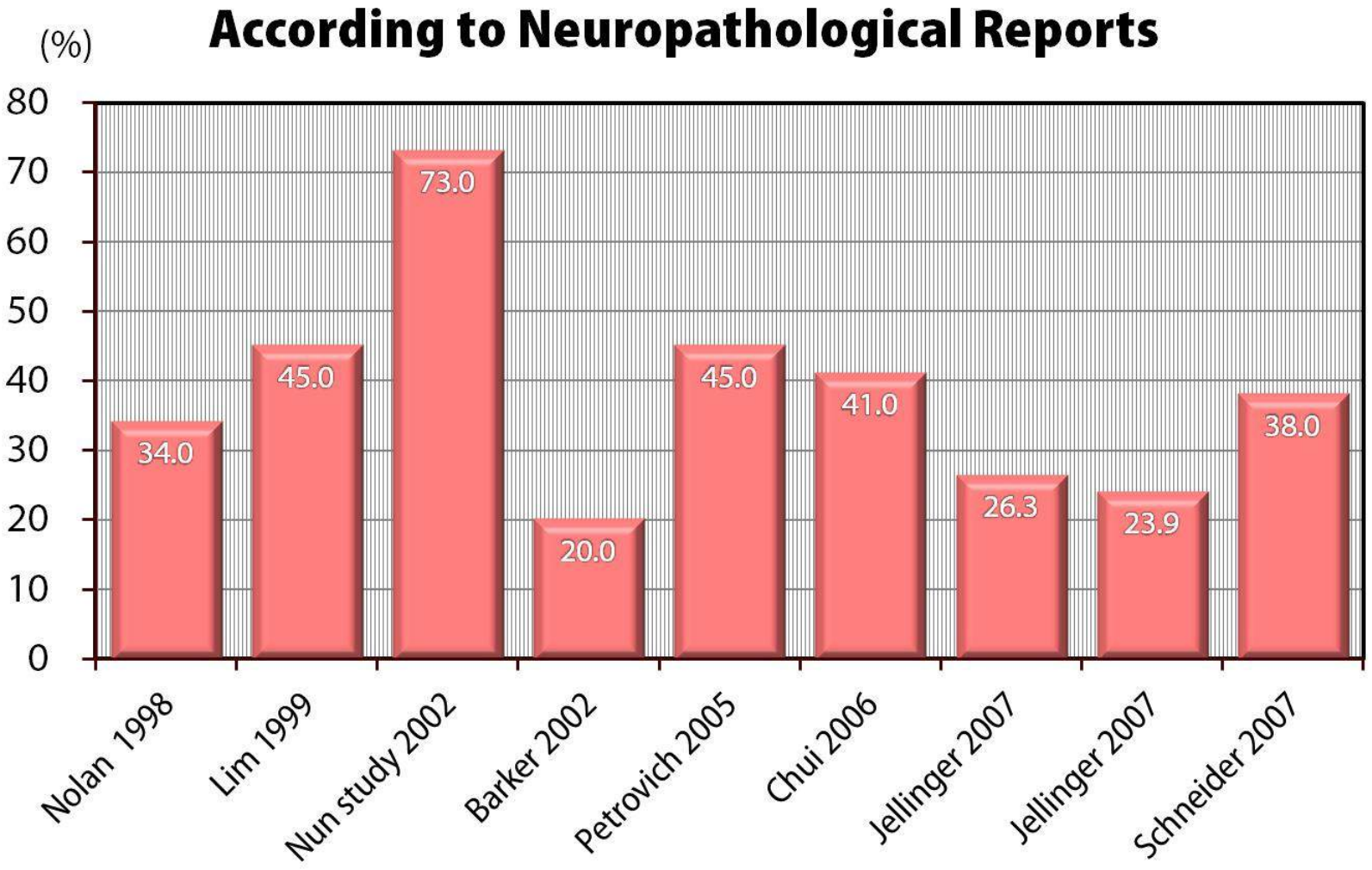


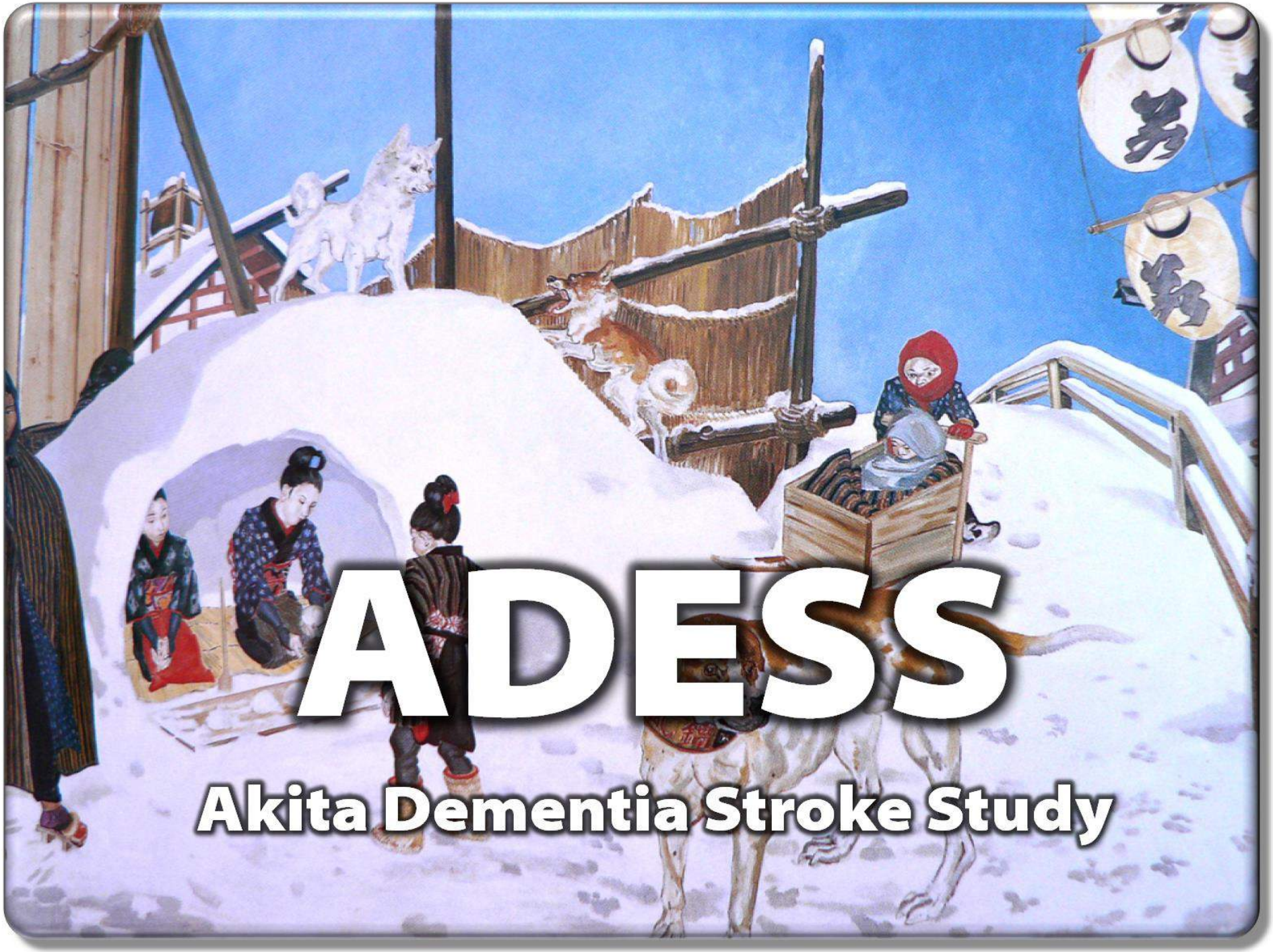

Common Risk Factors for AD and VaD
Genetics
Family history
Women
Eating habit
Head trauma
Education
AD
Aging
History of stroke
Hypertension
Type 2 Diabetes
Dyslipidemia
Heart failure
Smoking
Stress
Depression
Metabolic syndrome
Hyperhomocysteinemia
Physical inactivity
ApoE4 ε4 gene
VaD (CVD)
Atrial Fibrillation
Atherothrombosis
CKD
Coagulopathy
Polycythemia
Arterial dissection

Cerebrovascular Lesions



Cerebrovascular Lesions in AD




ADESS
Akita Dementia Stroke Study

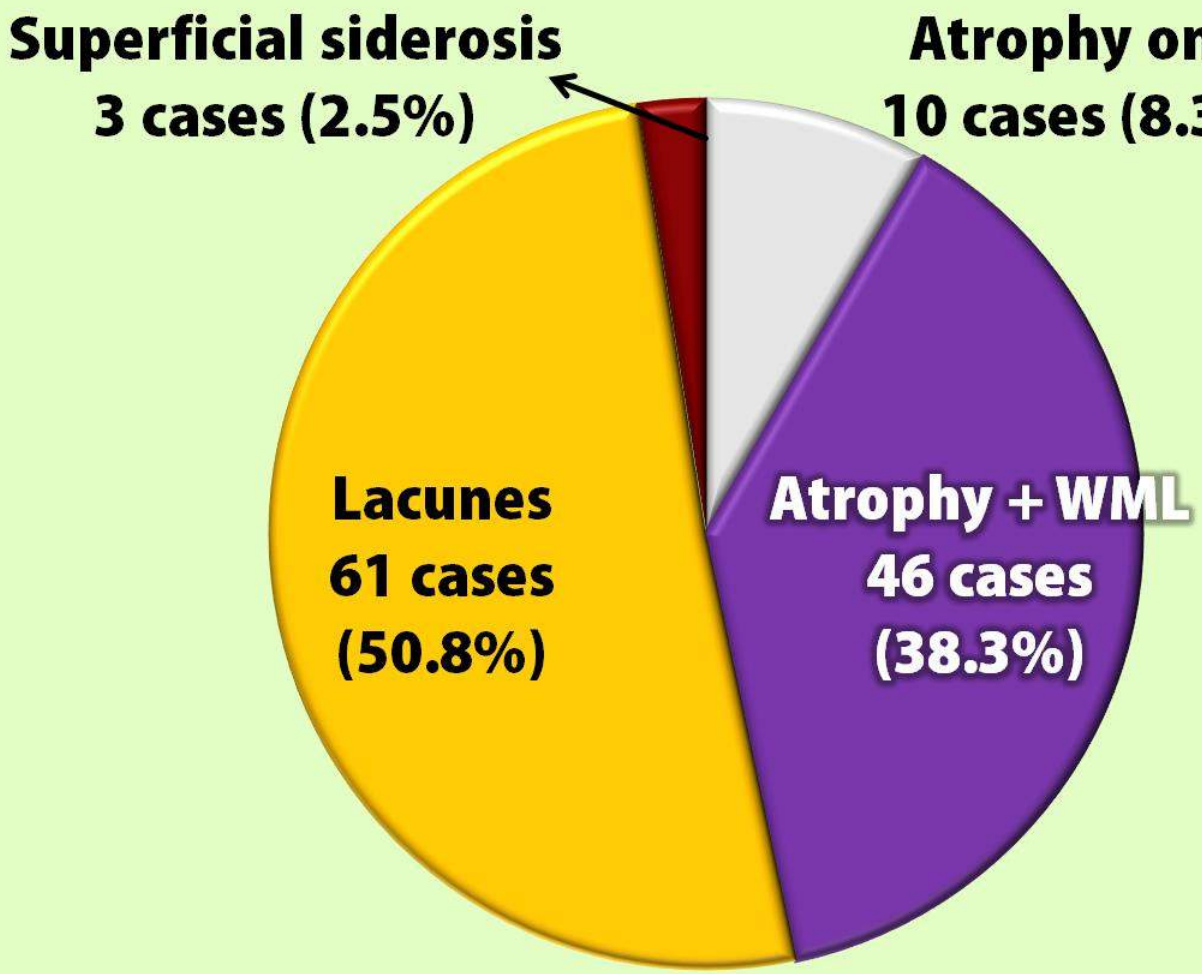
Subjects

- Total 120 cases with Probable AD

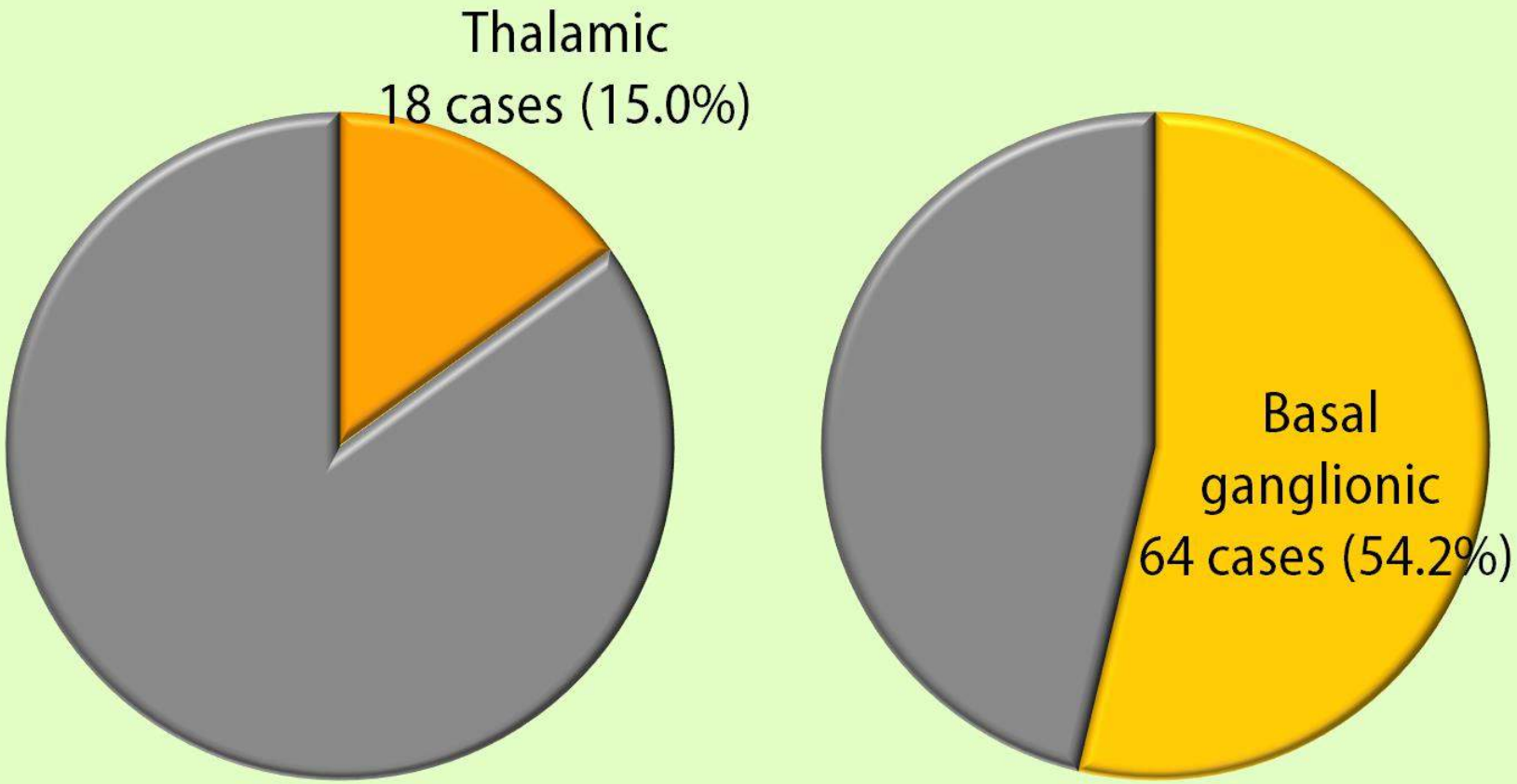
  According to the NINCDS-ADRDA criteria

- Age range: 56-89 years
- Mean age: 75.6 + 6.1 years
- Men : Women = 41 : 79
- 1.5Tesla MRI: T1WI, T2WI, T2*WI, FLAIR + MRA

MR Findings


Superficial siderosis
3 cases (2.5%)
Atrophy only
10 cases (8.3%)
Lacunes
61 cases
(50.8%)
Atrophy + WML
46 cases
(38.3%)

Location of Lacunes



Subcortical Infarcts



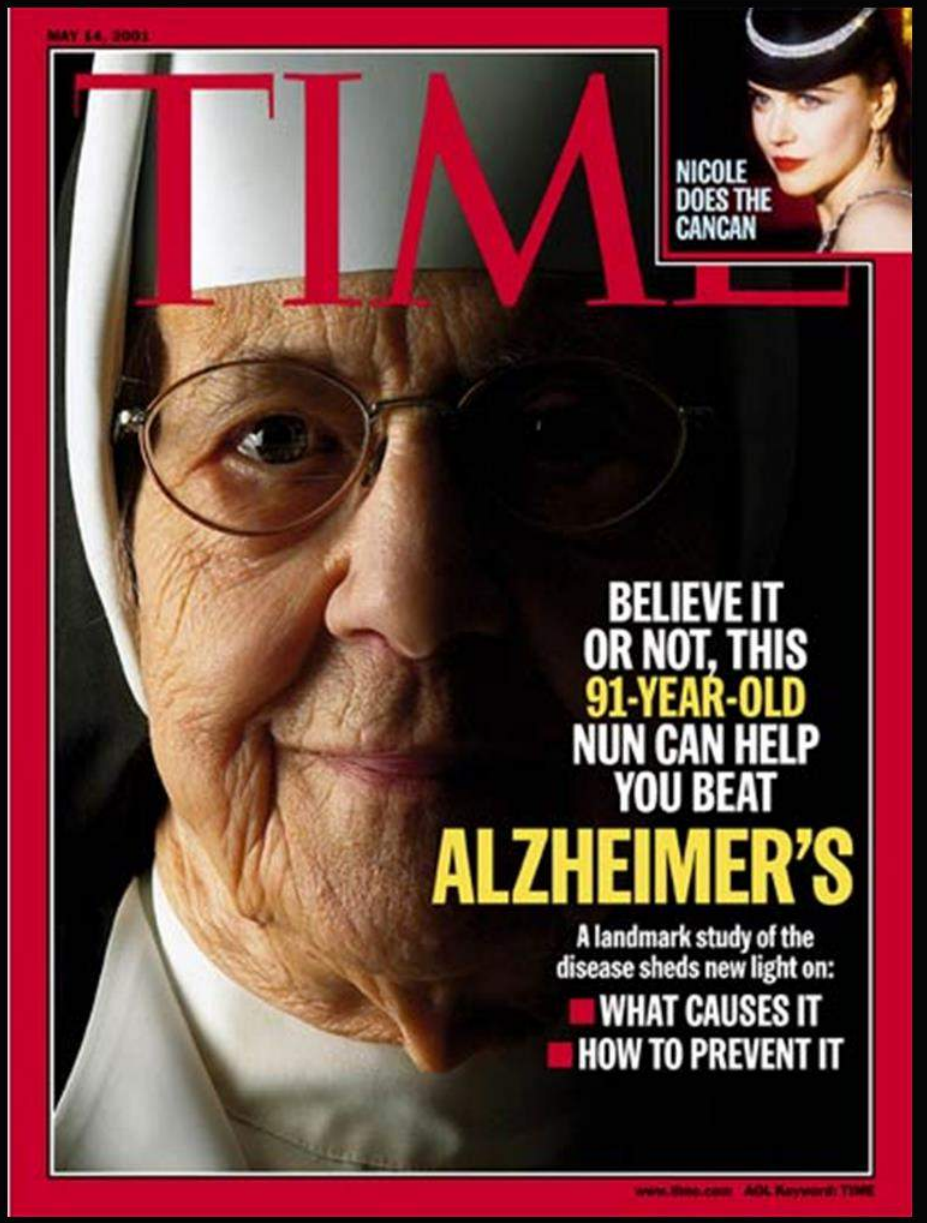

The Nun Study
Aging with Grace

Aging with GRACE

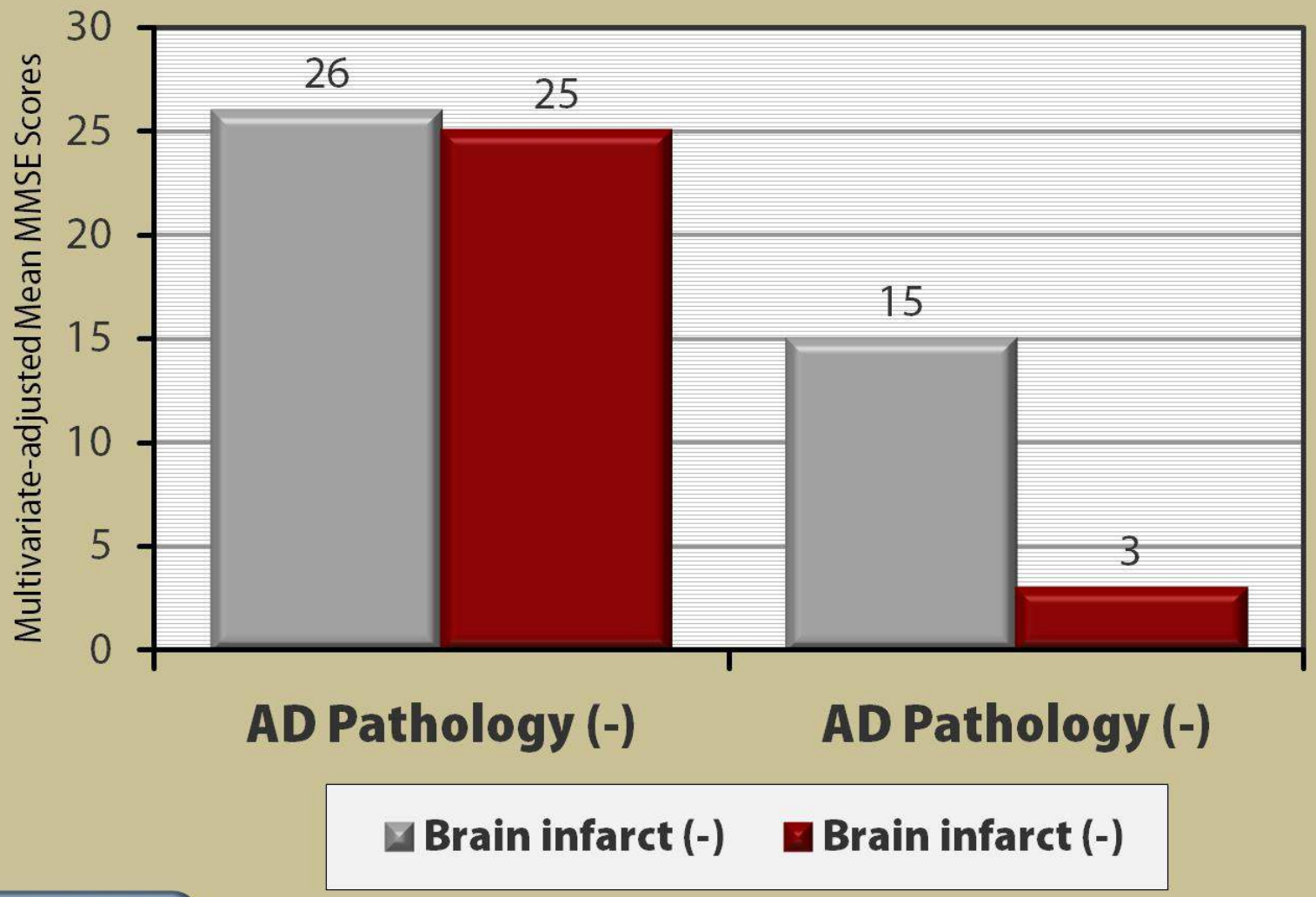
What the Nun Study Teaches Us About Leading Longer, Healthier, and More Meaningful Lives



DAVID SNOWDON, PH.D.



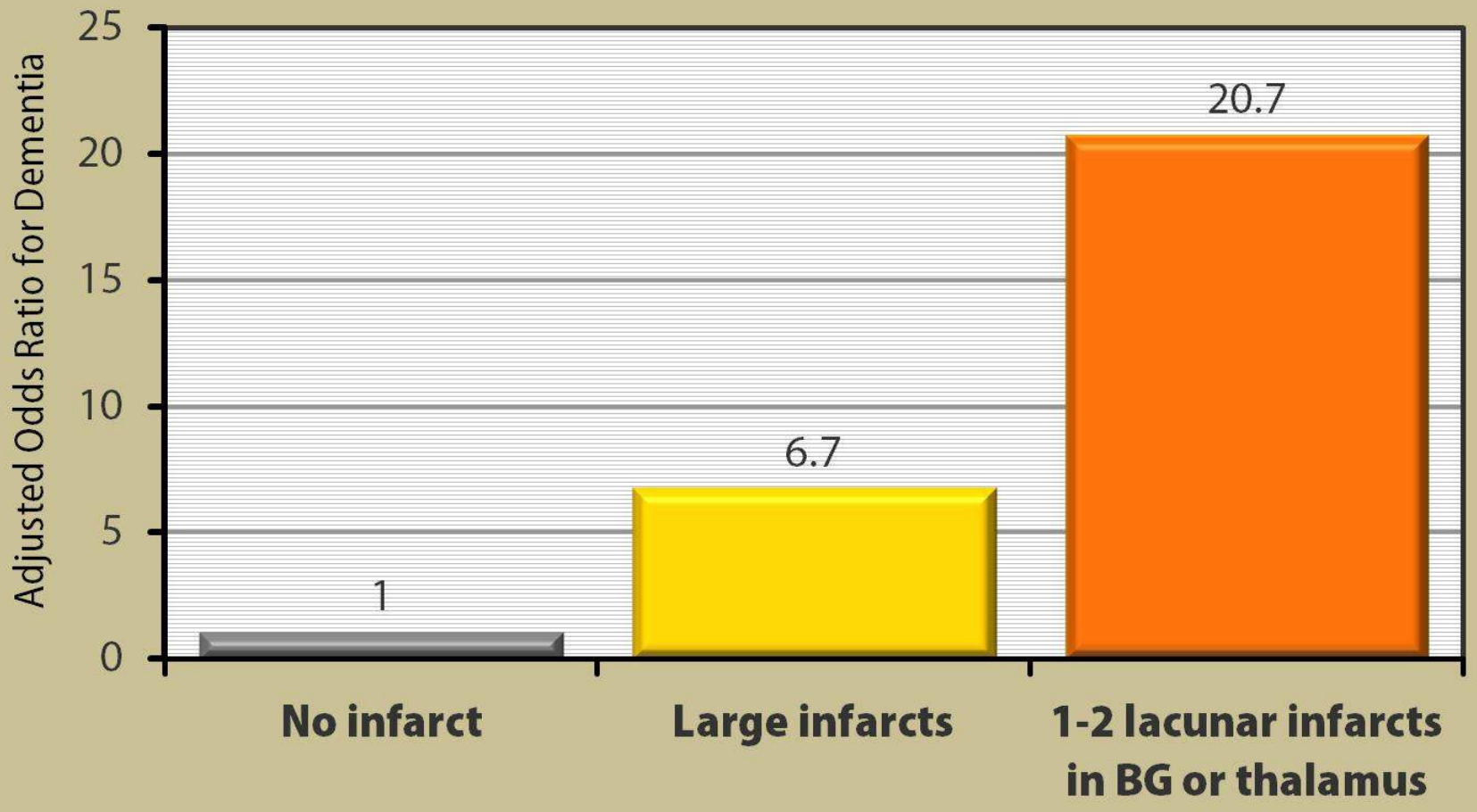
MMSE, AD Pathology and Infarcts



The Nun Study

Nun Study Snowdon, et al. JAMA 1997

Prevalence of AD for Those with and without Infarcts



The Nun Study

Nun Study Snowdon, et al. JAMA 1997

The NEW ENGLAND JOURNAL of MEDICINE

Small Vessels, Big Problems

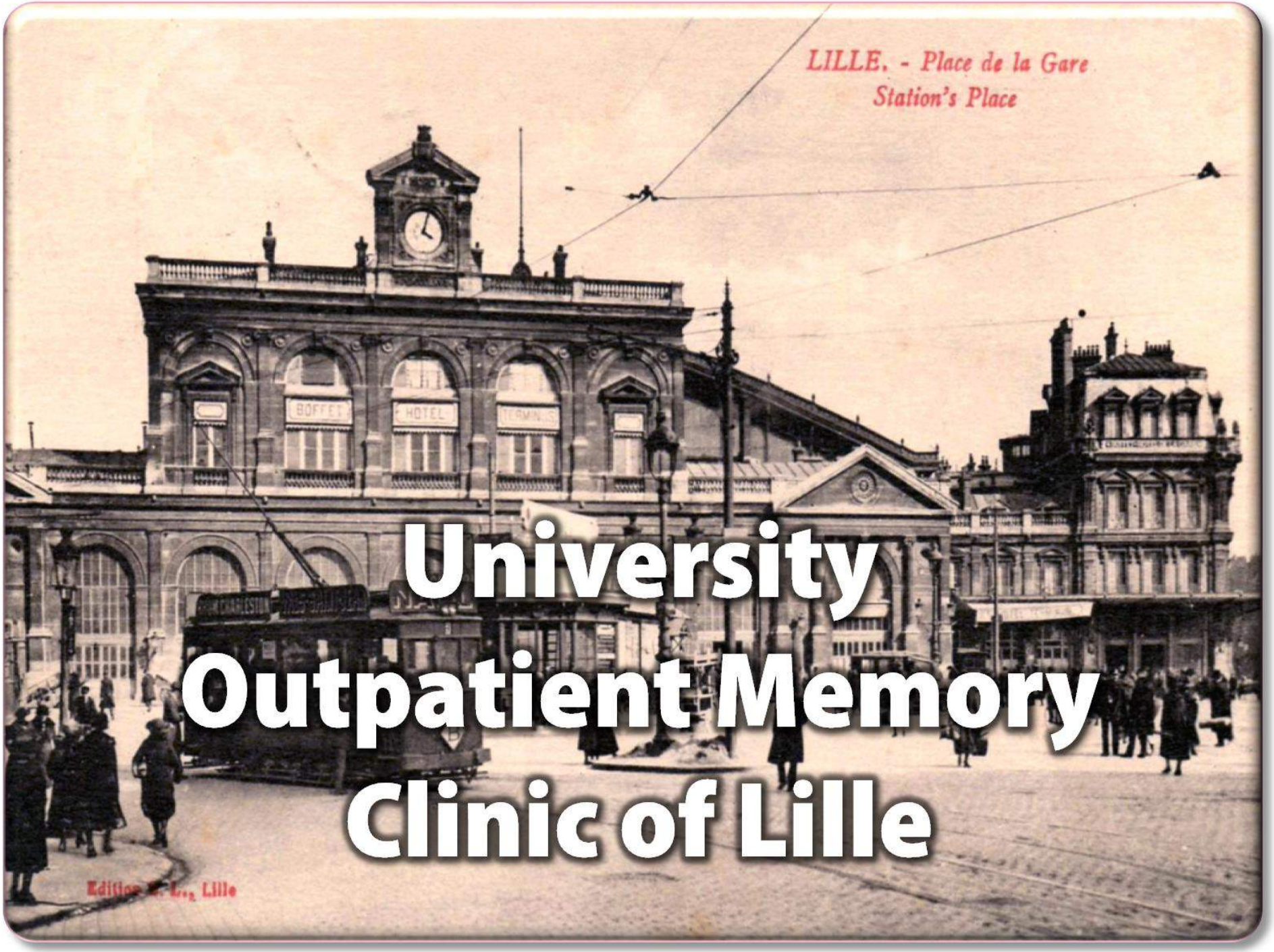
Steven M. Greenberg, M.D., Ph.D.

N Engl J Med 2006; 354:1451-1453 | April 6, 2006 | DOI: 10.1056/NEJMp068043

The impressive gains in stroke prevention and treatment seen over the past decade have not been evenly distributed across all types of stroke. Most advances have pertained to the approximately two thirds of symptomatic strokes that are caused by disease of the large arteries (those more than 0.1 mm in diameter) that run from the neck into the skull, the circle of Willis, and the surface of the brain. These large-vessel subtypes of stroke include atherosclerotic narrowing and occlusion of the large neck vessels, aneurysmal rupture and subarachnoid hemorrhage over the brain surface, and thromboembolic occlusion of the major vessel . . .

Management of VRFs



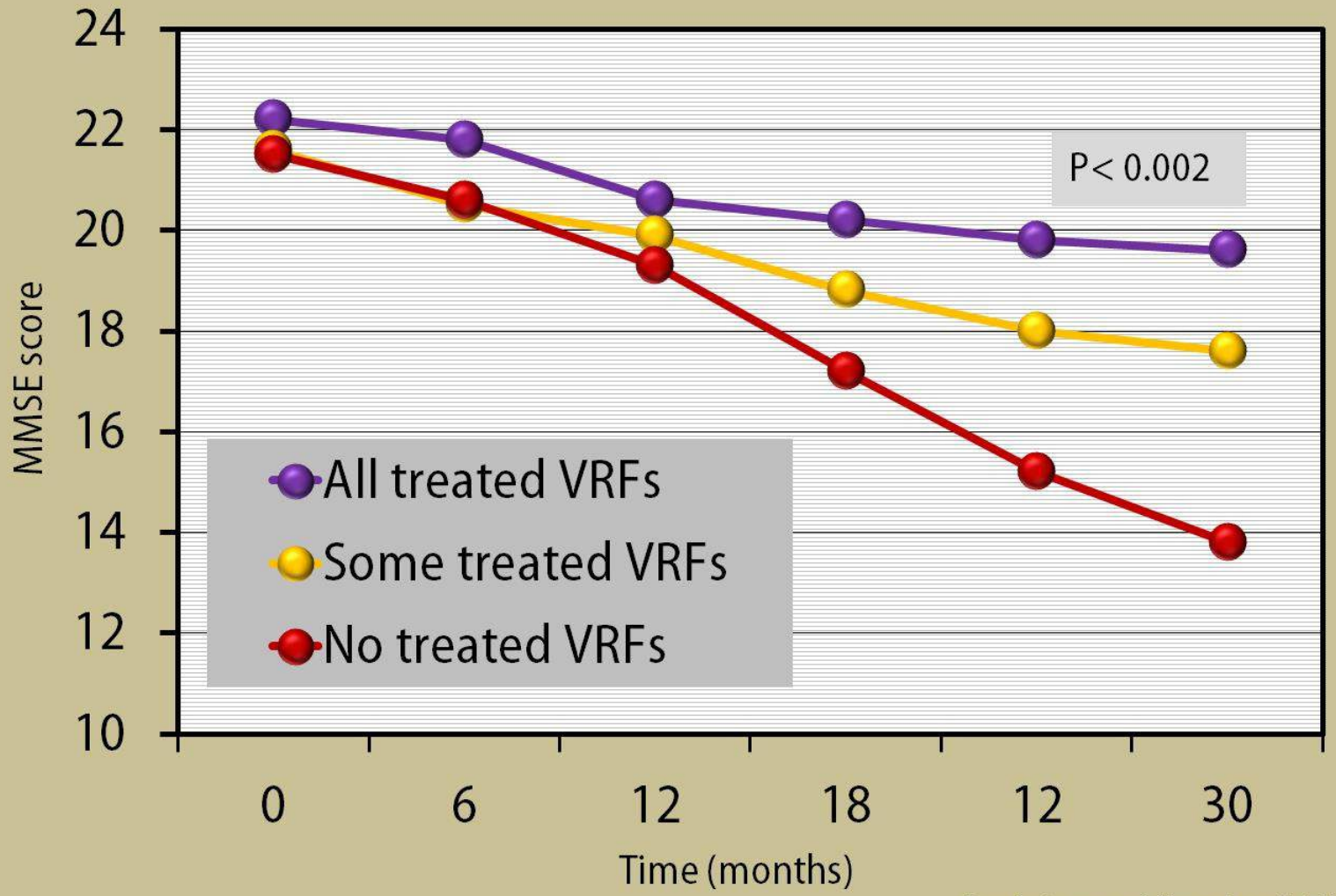

LILLE. - Place de la Gare
Station's Place
BUFFET
HOTEL
University
Outpatient Memory
Clinic of Lille

Vascular Risk Factors

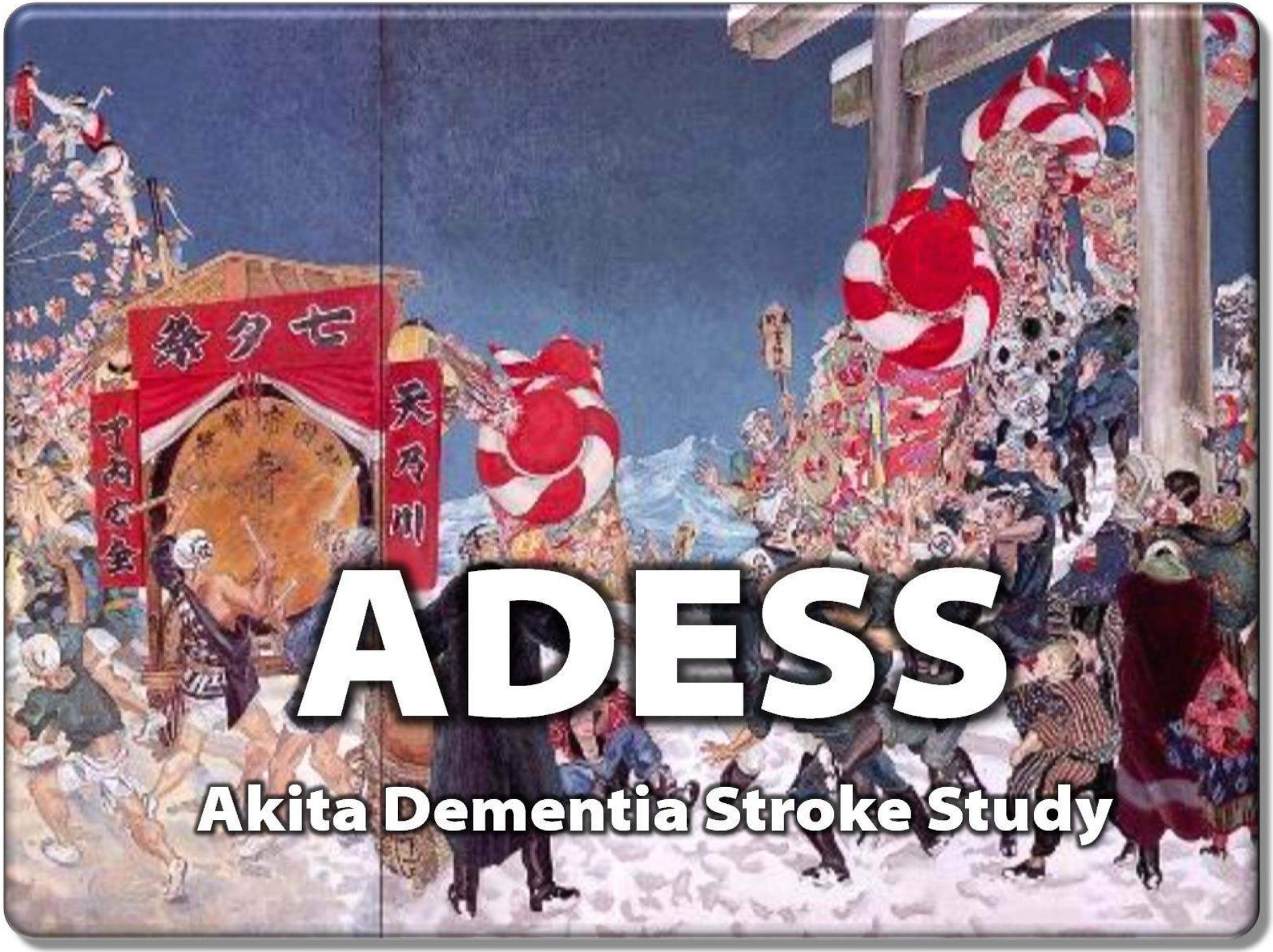
- High blood pressure
- Dyslipidemia
- Diabetes mellitus (type I or II)
- Tobacco smoking
- Atherosclerotic disease

  CAD, PAD, CVD, TIA

Evolution of MMSE in AD Patients without CVD



Deschaintre et al. Neurology 7:674-680, 2009

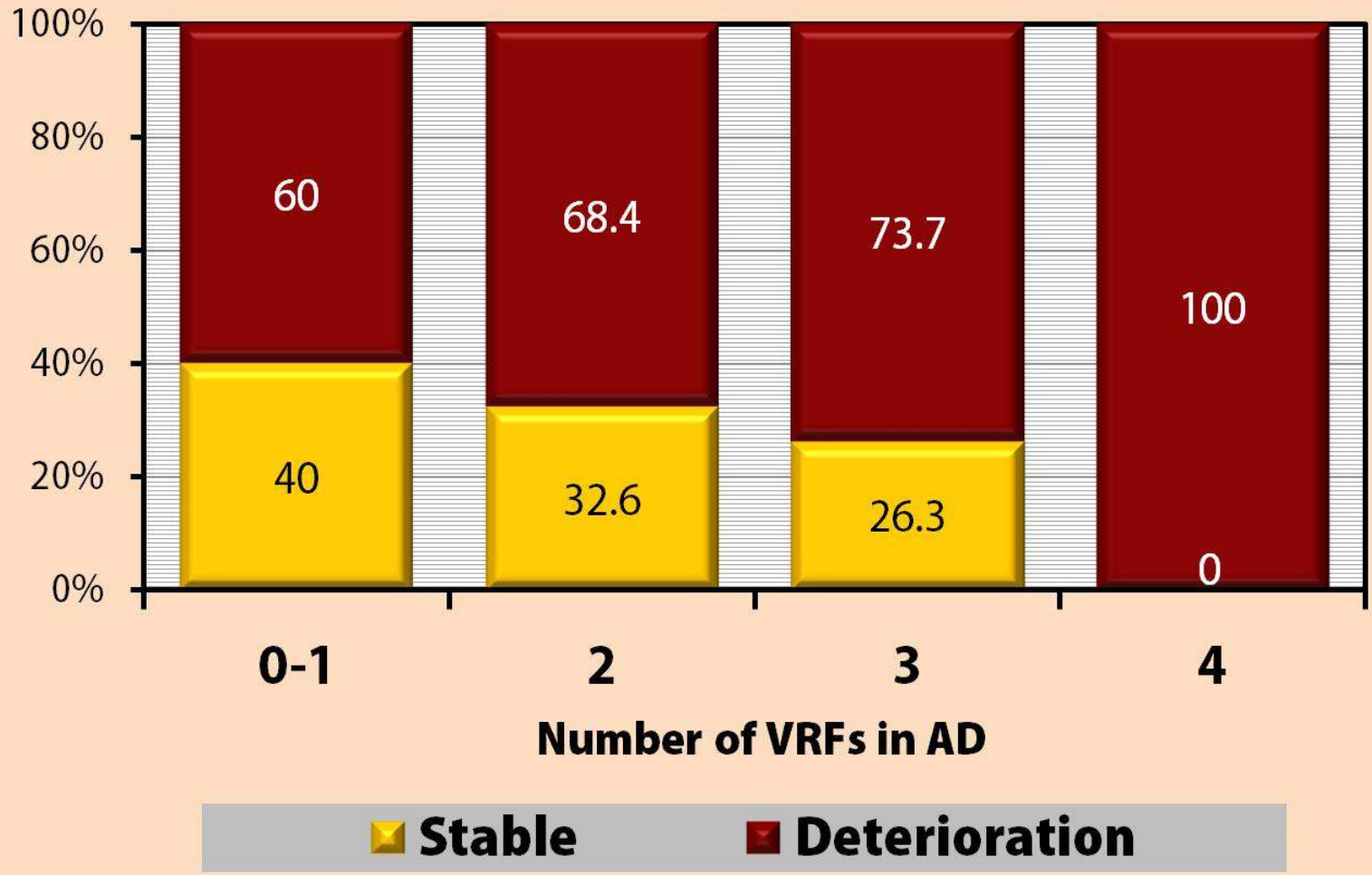


ADESS

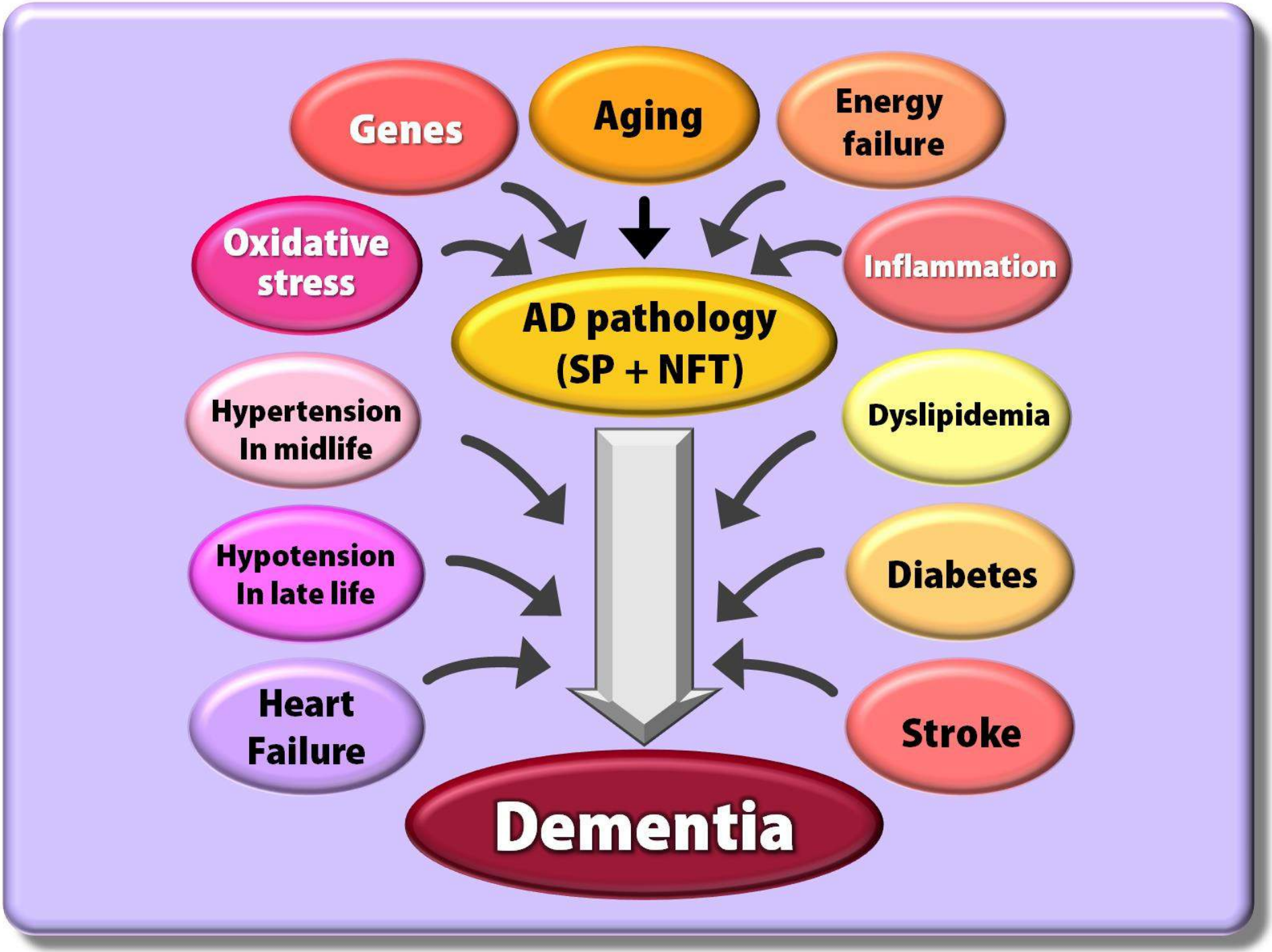
Akita Dementia Stroke Study

Effects of VRF on Evolution of Cognition

The more VRFs, less effective ChEI treatment on AD

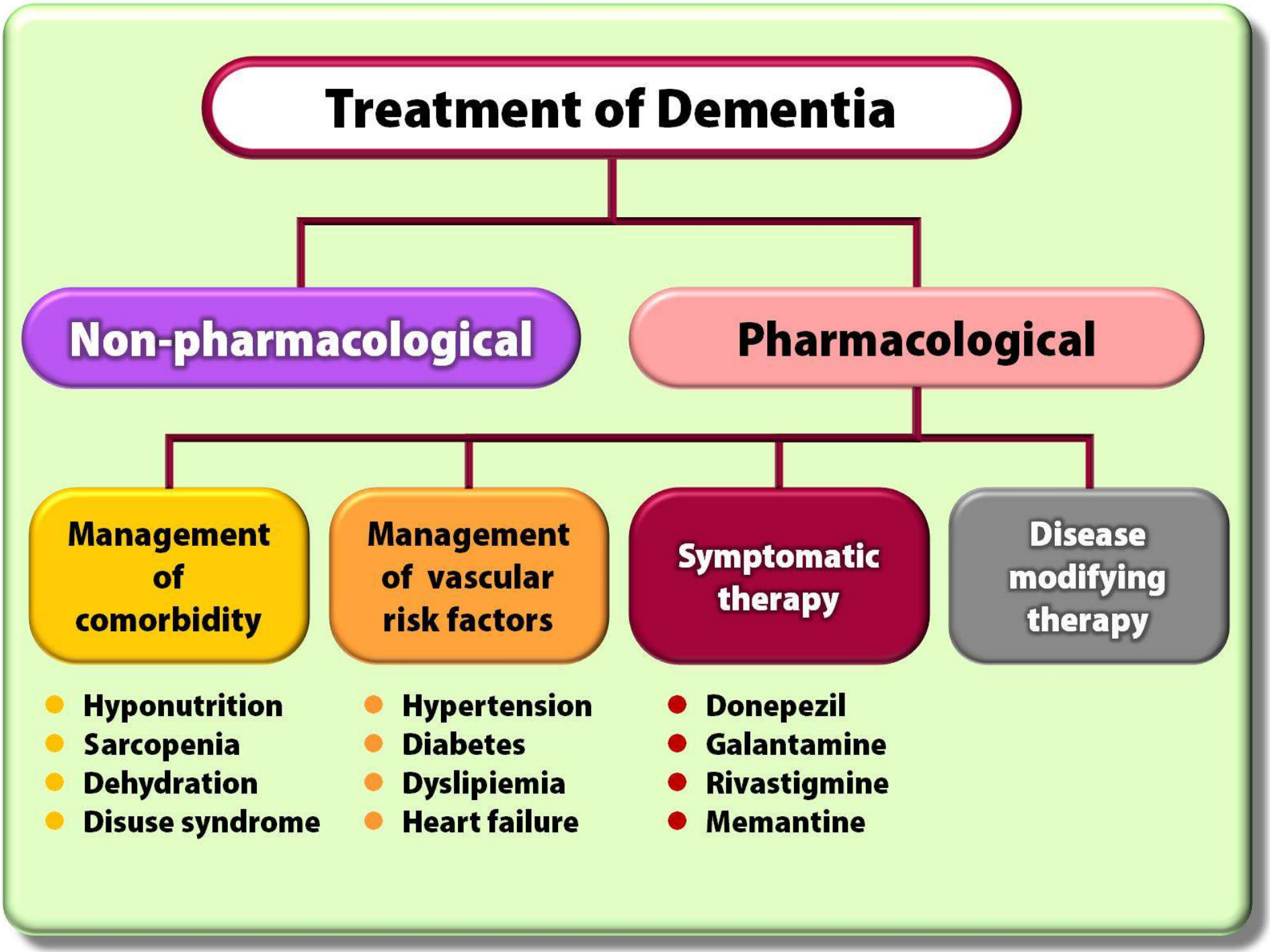


Yamazaki T, et al. submitted for publication


Genes
Aging
Energy failure
Oxidative stress
Inflammation
AD pathology (SP + NFT)
Hypertension In midlife
Dyslipidemia
Hypotension In late life
Diabetes
Heart Failure
Stroke
Dementia

Treatment Strategy



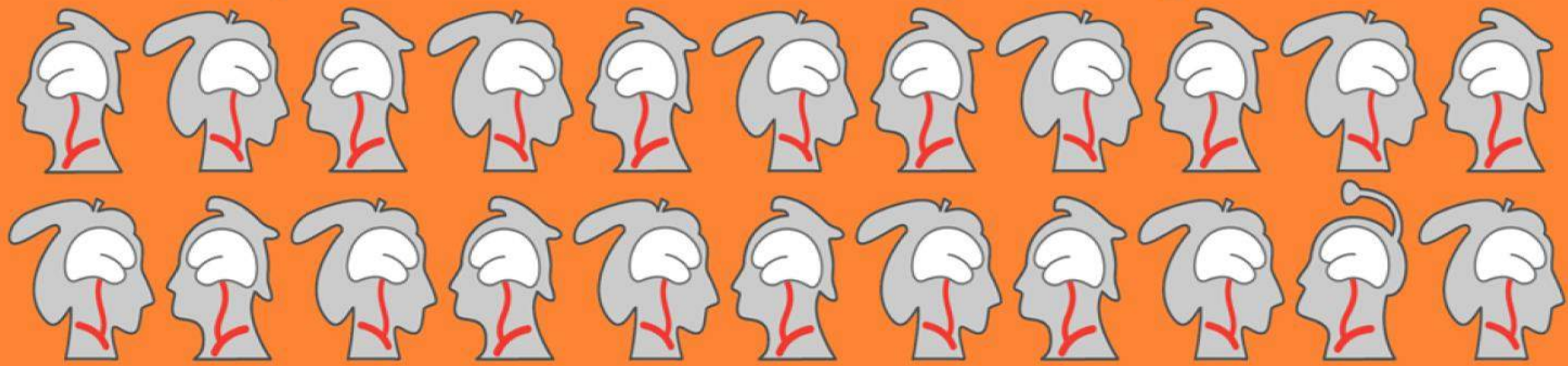

Treatment of Dementia
Non-pharmacological
Pharmacological
Management of comorbidity
Management of vascular risk factors
Symptomatic therapy
Disease modifying therapy
Hyponutrition
Sarcopenia
Dehydration
Disuse syndrome
Hypertension
Diabetes
Dyslipiemia
Heart failure
Donepezil
Galantamine
Rivastigmine
Memantine

7th World Congress of the International Society for Vascular Behavioural and Cognitive Disorders
6th Annual Meeting of the Japanese Society for Vascular Cognitive Impairment

VAS-COG 2015 TOKYO

September 16-19, 2015
Tokyo Fashion Town,
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URL: http://www2.convention.co.jp/vas-cog-world2015/



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VAS-COG Japan 2015

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Thank You

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