RCCN Workshop:
Measuring Biologic Age

Brain Aging: *The 90+ Study*

Jan 18, 2022

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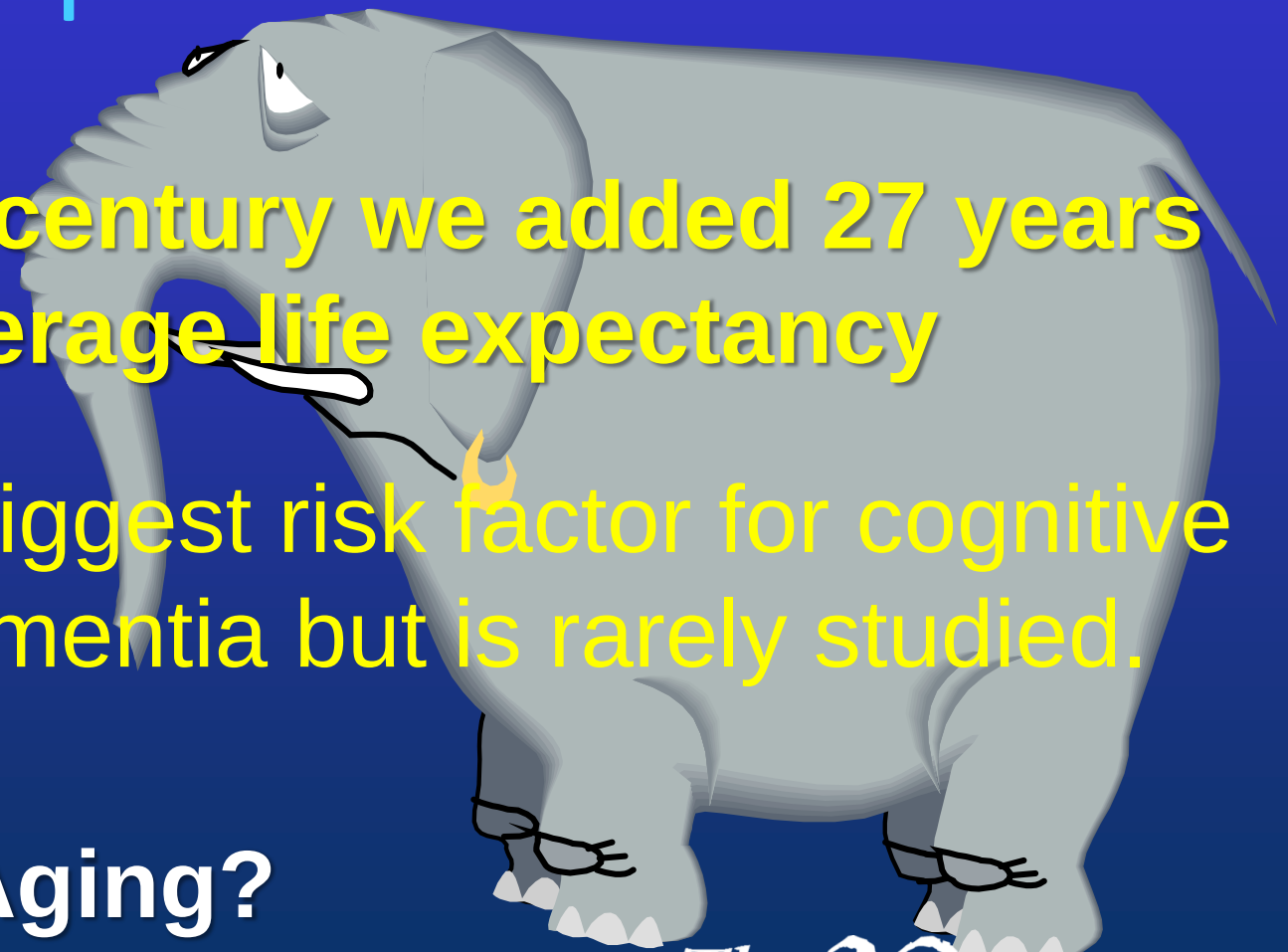
Nothing to Disclose

The 90+ Study

Aging

The Elephant in the Room!



In the past century we added 27 years to average life expectancy

Age is the biggest risk factor for cognitive loss and dementia but is rarely studied.

What is Aging?

The 90+ Study

If increases in life expectancy continue,

more than half of all children born today in developed countries can expect to celebrate their 100th birthdays

Christensen, Ageing Populations: The Challenges Ahead, *Lancet* , 2009

Unknown in 90+ Year Olds

- Risk/Protective Factors Related to Longevity
- Prevalence and Incidence of Dementia, Disability and Frailty
- Risk/Protective Factors Related to Dementia
- Types of Dementia
- Excluded from diagnostic criteria for AD (McKhann, 1984)
- Excluded from most studies including ADNI, Clinical trials

The 90+ Study

The 90+ Study

Population-based study of aging and dementia in persons aged 90 and older

Studies of Factors Associated with Longevity

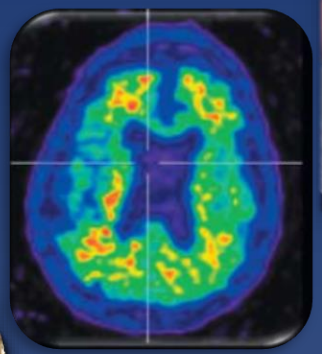
- ~~Vitamin C (diet + supplements)~~
- ~~Vitamin A (diet + supplements)~~
- ~~Vitamin E (supplements)~~
- ~~Calcium (diet)~~
- ~~Soft drinks (cola & other)~~
- ~~Tea (black or green)~~
- Alcohol (wine, beer, other)
- Caffeine
- Body Mass Index
- Activities - Exercise and Leisure
- Positive Attitude

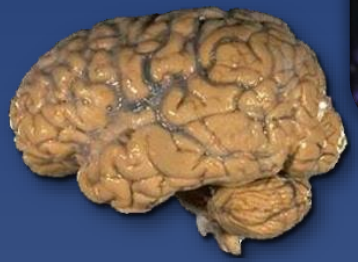
Corrada, et al, AAN 2004

The 90+ Study

90+ Study Assessments

- Demographics & Medical History
- Neuropsychological Tests
  - Memory, language, executive function
- Neurological & Physical Examination
- Informant Questionnaires
- Genetic studies
  - DNA and cell lines
- Brain Imaging
- Brain Donation





The 90+ Study

The 90+ Study Participants
Baseline Results

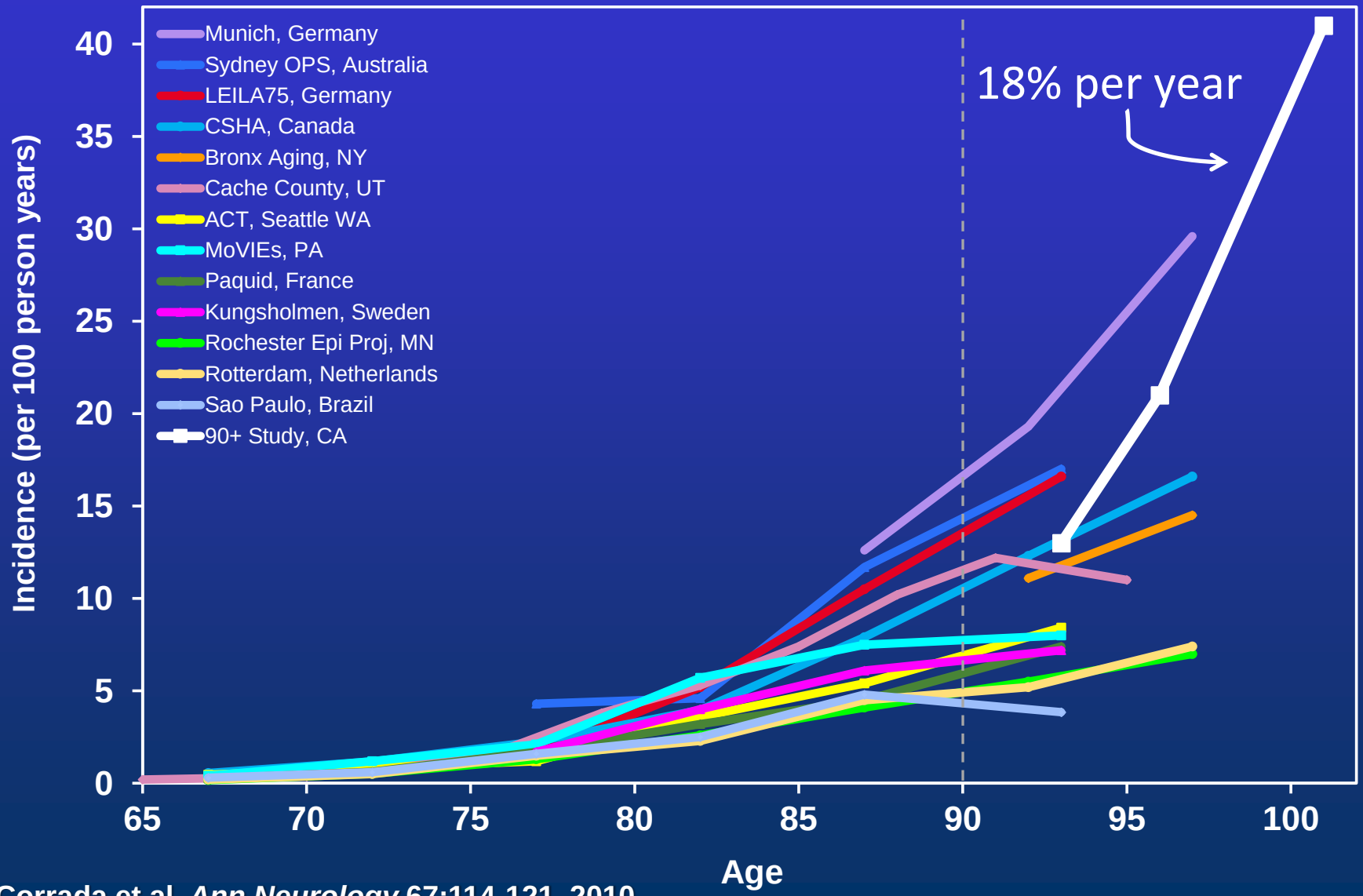
# of Participants	1603
Education	
College grad or more	41%
Marital Status	
Widowed	77%
Married	14%
% of Women	76%
Mean Age	95.8
Type of Residence	
Nursing or group home	40%
Home alone	31%

Neurological Exam Cognitive Diagnosis

Normal	32%
Cognitively Impaired, No Dementia	34%
Dementia	34%

The 90+ Study

Age-Specific Incidence of Dementia in Studies with Subjects Aged 90+

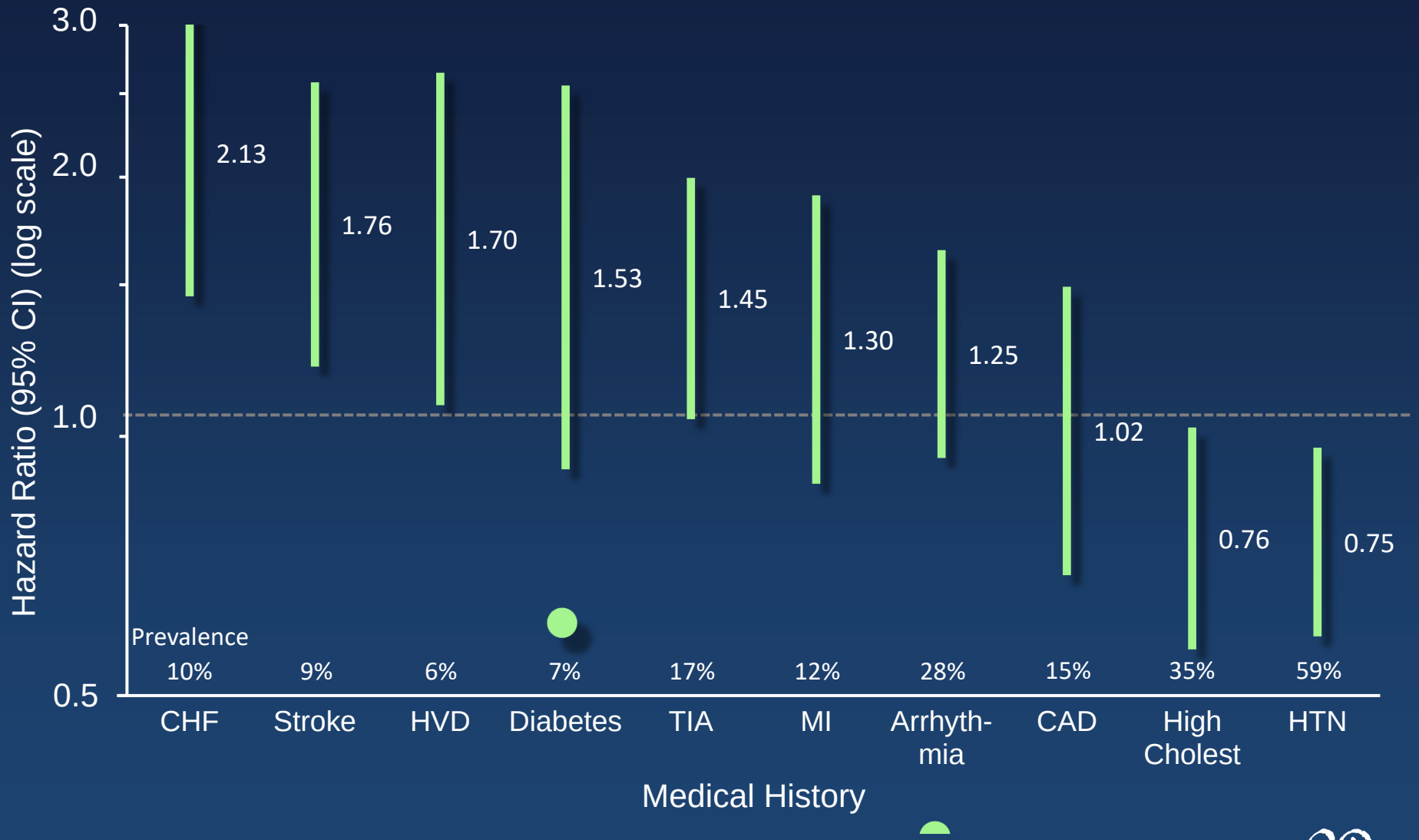


Corrada et al. *Ann Neurology* 67:114-121, 2010

Many putative risk factors for dementia do not appear to be risk factors for dementia at this age

- ~~Vitamin E (supplementation)~~
- ~~Vitamin C (diet and supplementation)~~
- ~~BMI~~
- ~~Alcohol~~
- ~~Caffeine~~
- ~~Apolipo~~protein E ϵ4
- ~~Homocysteine levels~~
- ~~Thyroid function~~
- Education and physical performance

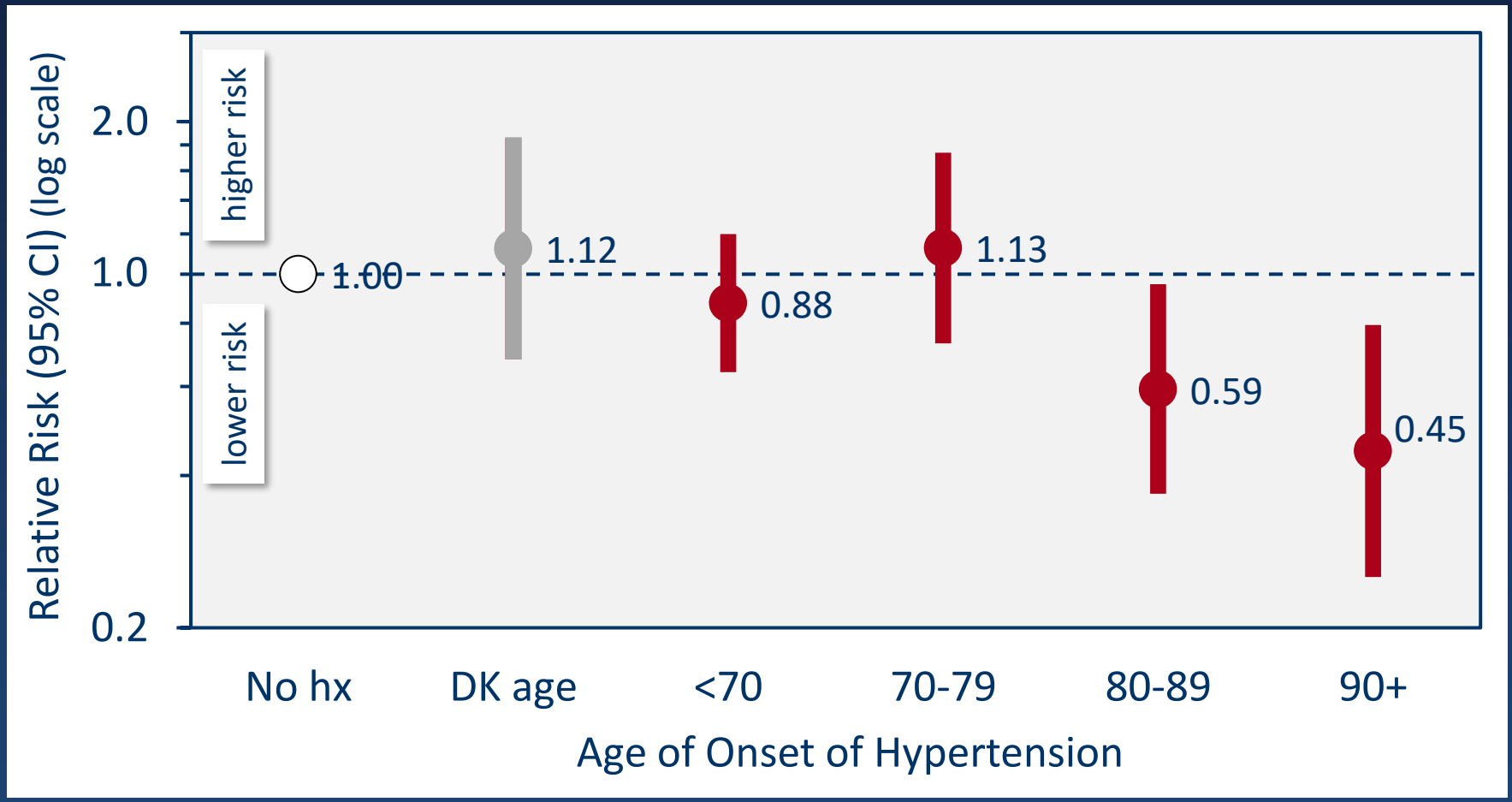
Cardio- and Cerebrovascular Disease & Risk of Dementia (N=625)



Cox regression adjusting for age, gender, & education

The 90+ Study

Risk of Dementia in Relation to Age of Onset of Hypertension



Adjusted for age & education

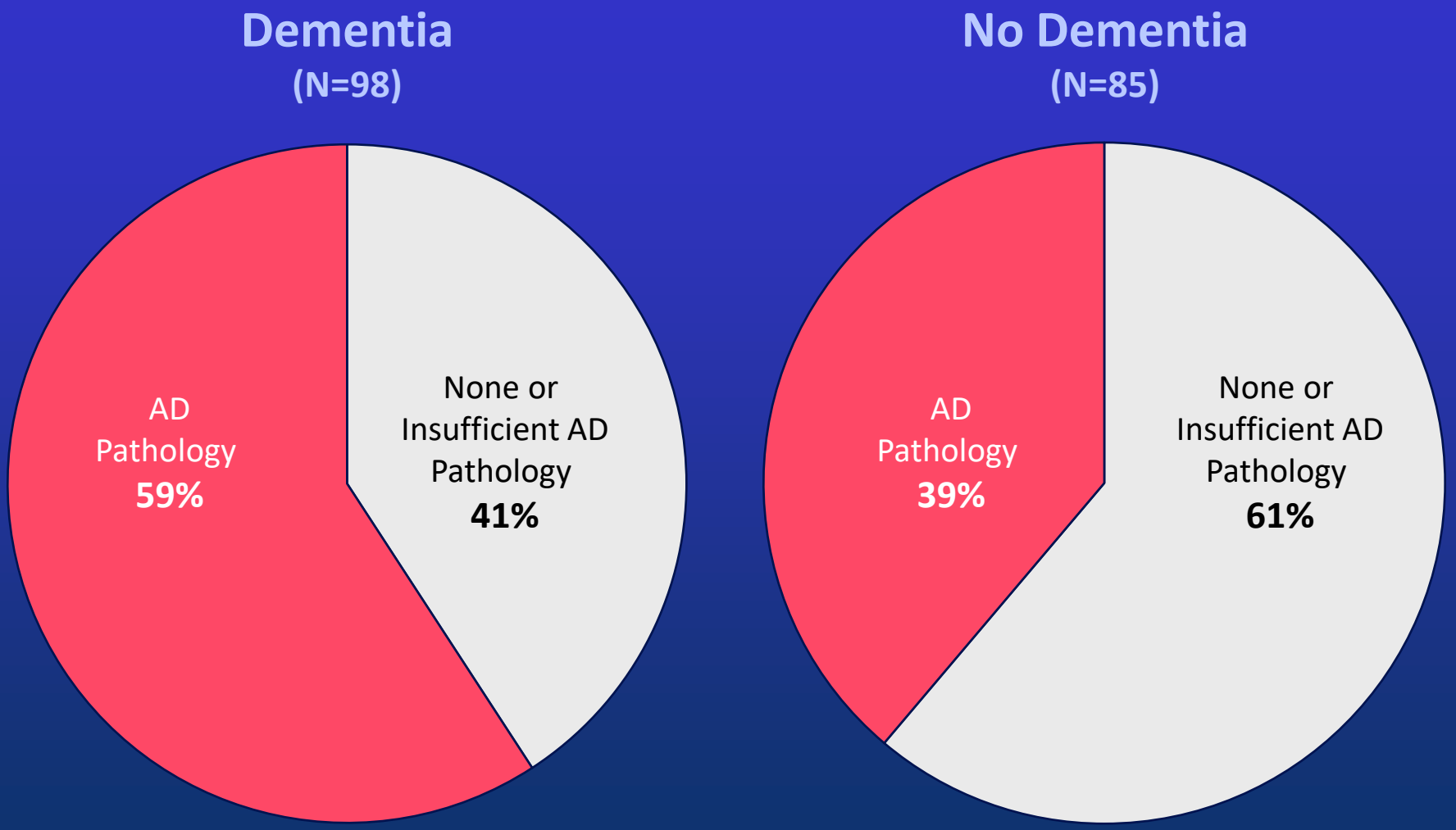
Corrada, et al. 2017

What are the causes of dementia in 90+ year olds?

The 90+ Autopsy Study

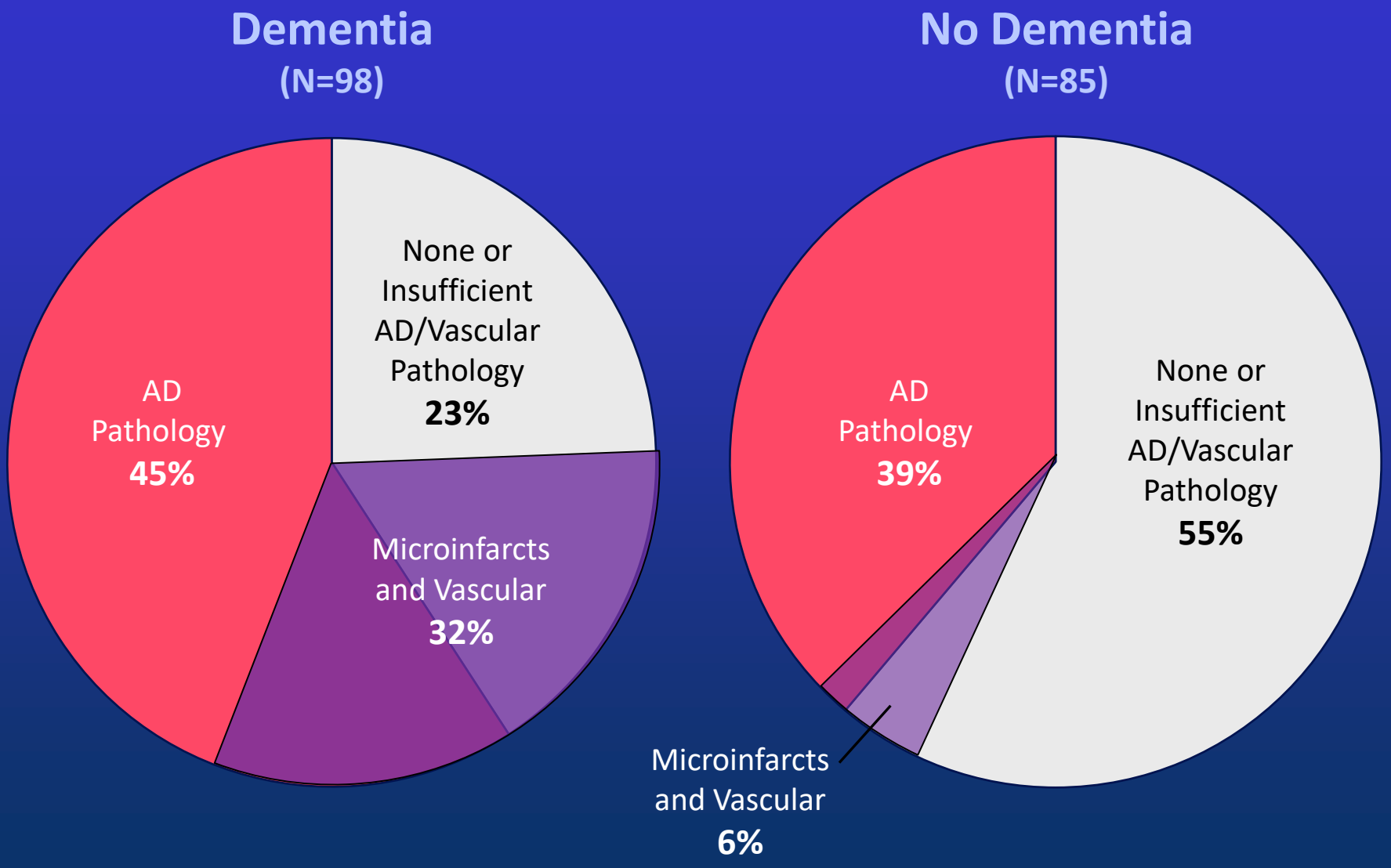
- 587 people enrolled
- 432 have come to autopsy

Pathological Diagnoses by Dementia Status



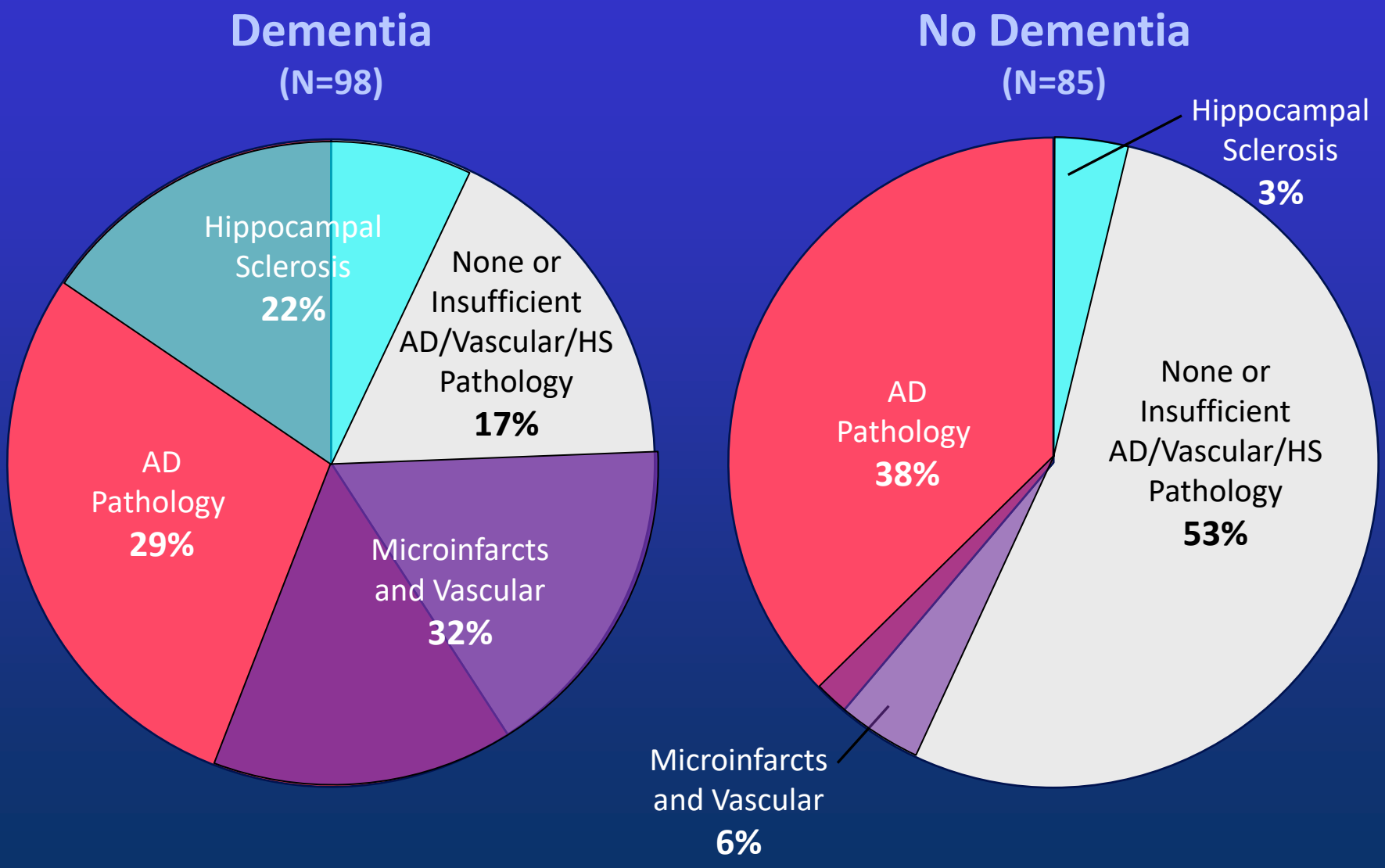
AD=Intermediate/High NIA Reagan Criteria

Pathological Diagnoses by Dementia Status



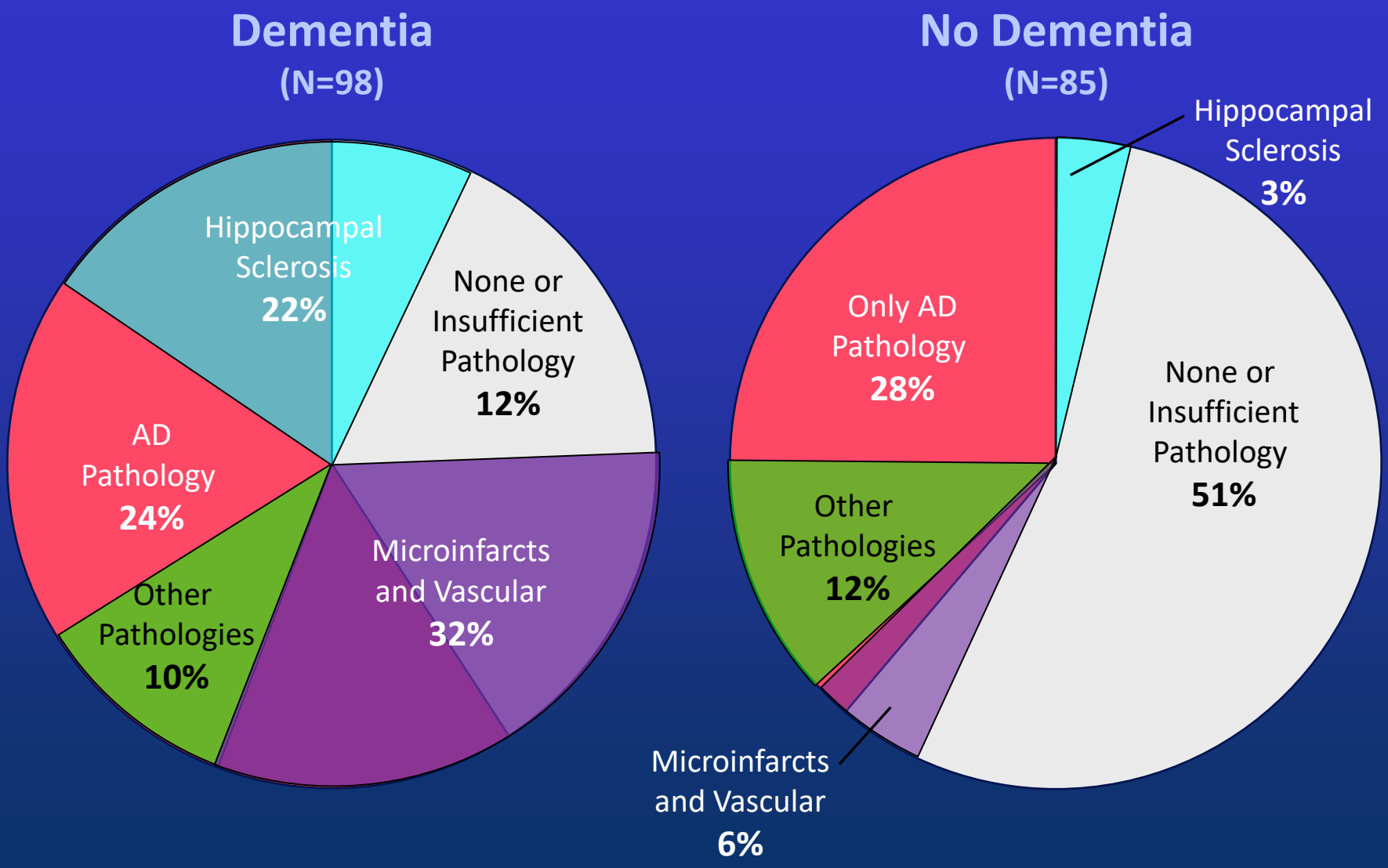
AD=Intermediate/High NIA Reagan Criteria; Vascular = lacunes, large infarcts, WM gliosis

Pathological Diagnoses by Dementia Status



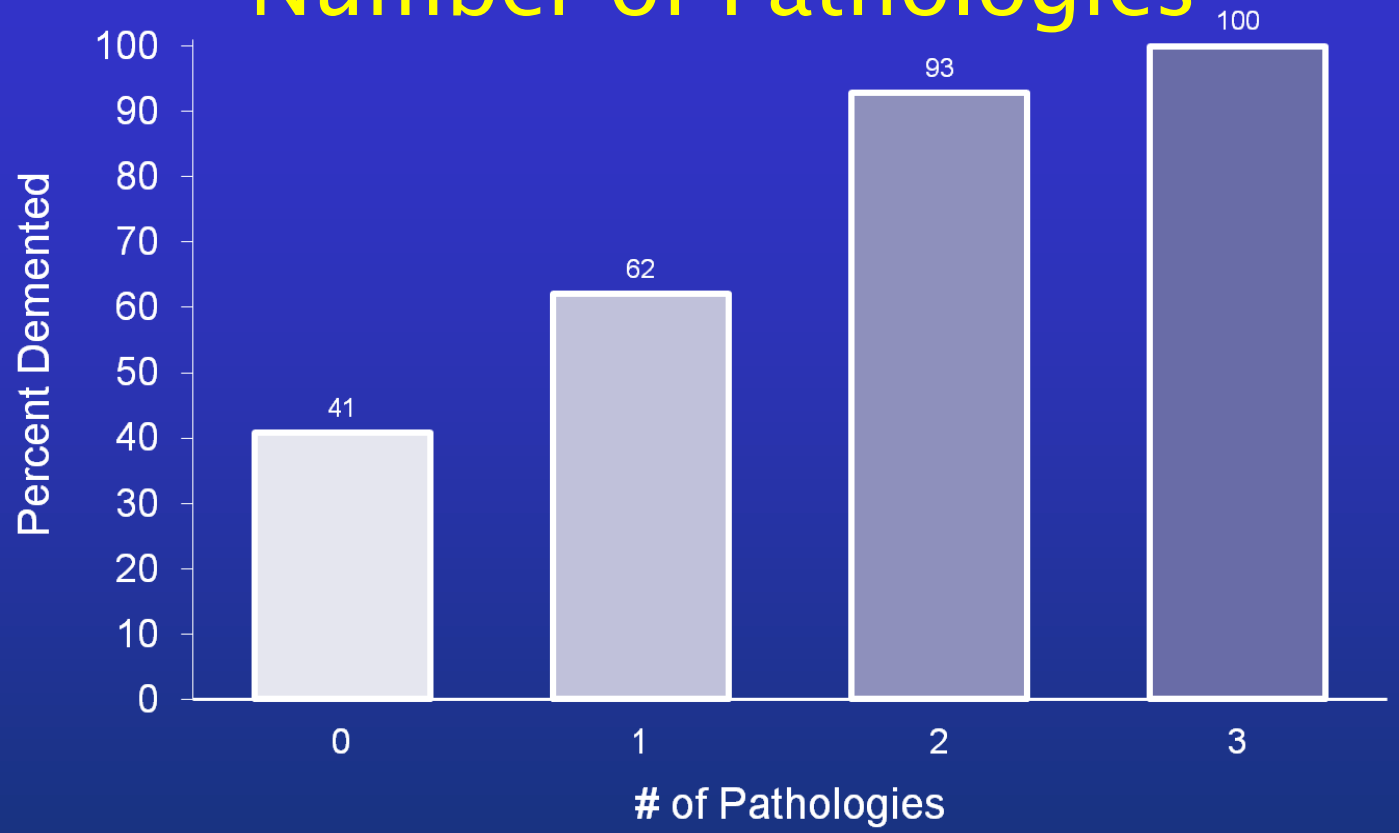
AD=Intermediate/High NIA Reagan Criteria; Vascular = lacunes, large infarcts, WM gliosis ; HS = Hippocampal Sclerosis

Pathological Diagnoses by Dementia Status



AD=Intermediate/High NIA Reagan Criteria; Vascular = lacunes, large infarcts, WM gliosis ; Other = LBD, CAA, glioblastoma, cortical basal degeneration

Frequency of Dementia by Number of Pathologies

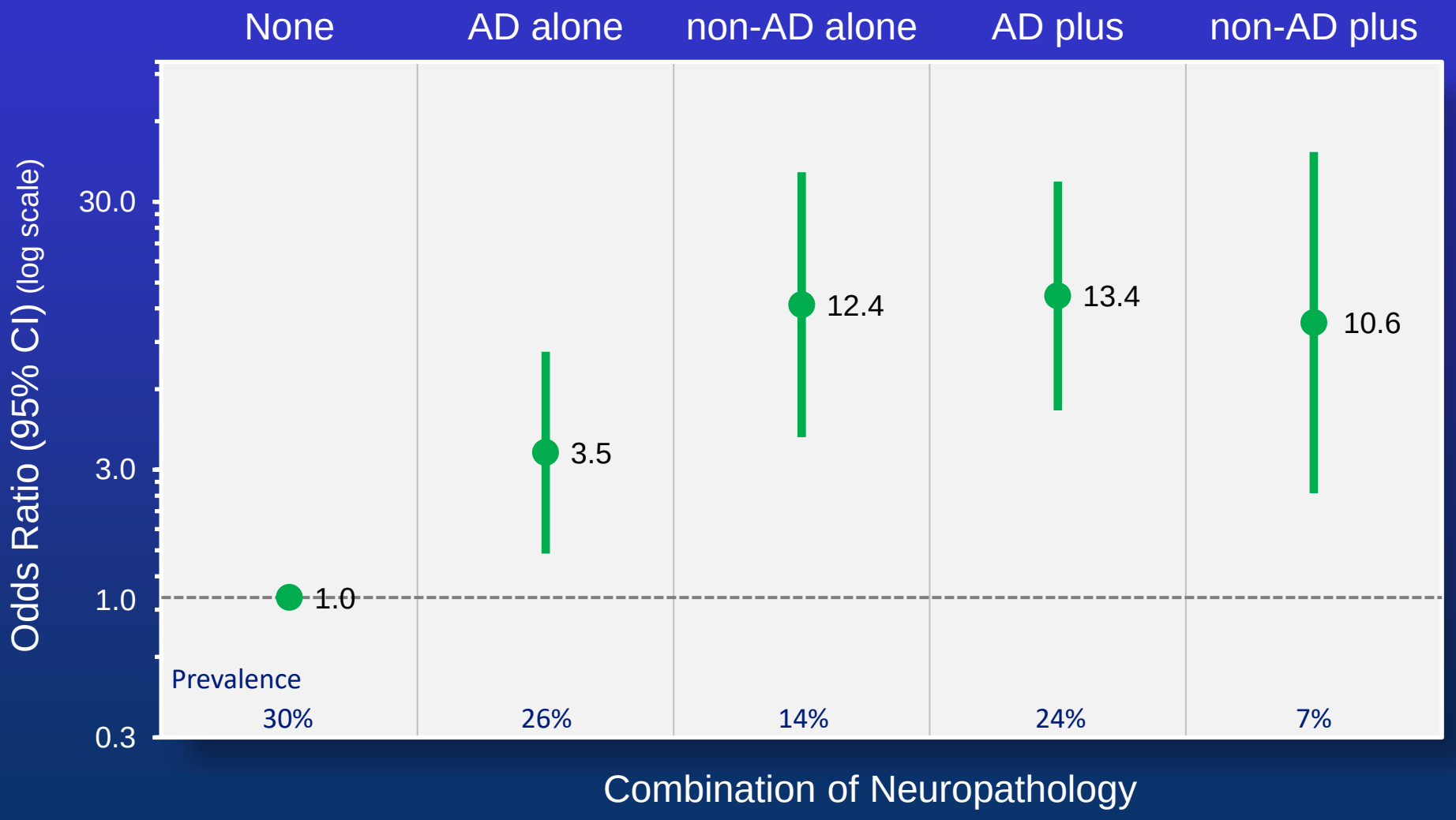


Pathologies: AD (Interm/High), LBD, Hippocampal sclerosis, vascular dementia, CBD

Kawas, et al. Neurology (2015)

Only ~ 2/3 of dementia cases attributable to neurodegenerative pathologies

Odds of Dementia by Combination of Neuropathology



N=183 From logistic regression adjusting for age at death and sex

Some questions relevant to brain aging

- Is amyloid deposition (and other pathologies) in non-demented nonagenerians ***Resilience or Preclinical disease***?
- Is apparent *resilience to AD,* in part, merely the absence of other pathologies?
- What does age have to do with it and how do we measure it?
- In the absence of neurodegenerative disease, what are the biological underpinnings of age-related cognitive declines?

Thank you!
90+ Study participants and families

90+ Investigators & Staff

Maria Corrada – co-Principal Investigator
Annlia Paganini-Hill
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Supported by:
NIH: R01AG21055, R01AG042444, P50AG016573, T32AG000096
Alzheimer's Association: NIRG-10-173916

NIH National Institute on Aging

The 90+ Study

90+ Study Sharable Resources

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Longitudinal Clinical Data

- Demographics
- Neuropsych scores
- Cognitive diagnosis
- Medical hx, medications
- Physical performance
- etc, etc, etc.

The 90+ Study Data and Tissue Resources

NeuroImaging – UC Davis

- MRI antemortem N=239
- MRI postmortem N=55
- Amyloid PET N=317
- Tau PET N=86

Neuropathology Data

- NACC form - UCI, Stanford
- Digital pathology images
- Microinfarcts - Sonnen
- Aβ area, synaptic markers, etc. – UPenn (Trojanowski)

Genetics

DNA storage, ApoE genotype Lymphoblastic cell lines NCRAD

Post-Mortem Tissue Samples

- Frozen / fixed brain tissue
- Plasma /serum
- CSF
- Extracted DNA

The 90+ Study: R01AG021055, MPIs: C. Kawas, M. Corrada