

# Risk Factors for Dementia and MCI in the Oldest Old The 90+ Study

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# Madame Jeanne-Louis Calmet

Arles, France



**1875 – 1997**

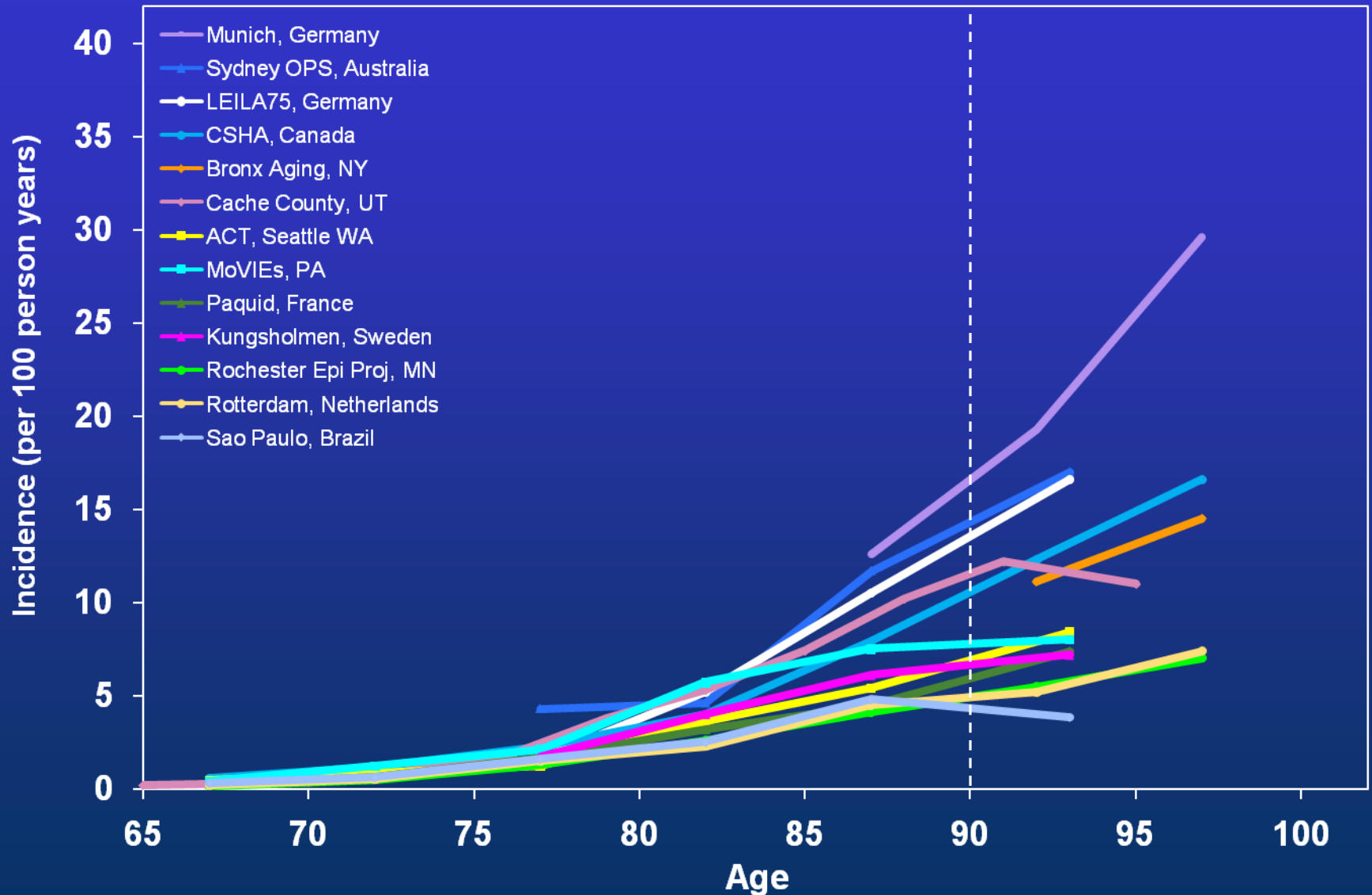
**Age 122**

If increases in life expectancy continue,  
more than half of all children  
born today in developed  
countries can expect to  
celebrate their 100<sup>th</sup> birthdays

# Overview

- I. Background of the Oldest Old and The 90+ Study
- II. MCI and Dementia:  
Incidence and Risk Factors
- III. Clinical Pathological Correlations
- IV. Conclusions

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



# The Relative Frequency of “Dementia of Unknown Etiology” Increases With Age and Is Near 50% in Nonagenarians

- Series of 128 subjects
- Dementia of unknown etiology
  - 5% of all cases dying in their 70's
  - 21% of all cases dying in their 80's
  - 48% of all cases dying in their 90's

# Unknown in 90+ Year Olds

- Prevalence and Incidence of Dementia
- Risk/Protective Factors Related to MCI and Dementia
- Types of Dementia

- Insert brief 60 minute segment here



# The 90+ Study

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



# Assessments

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

# 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

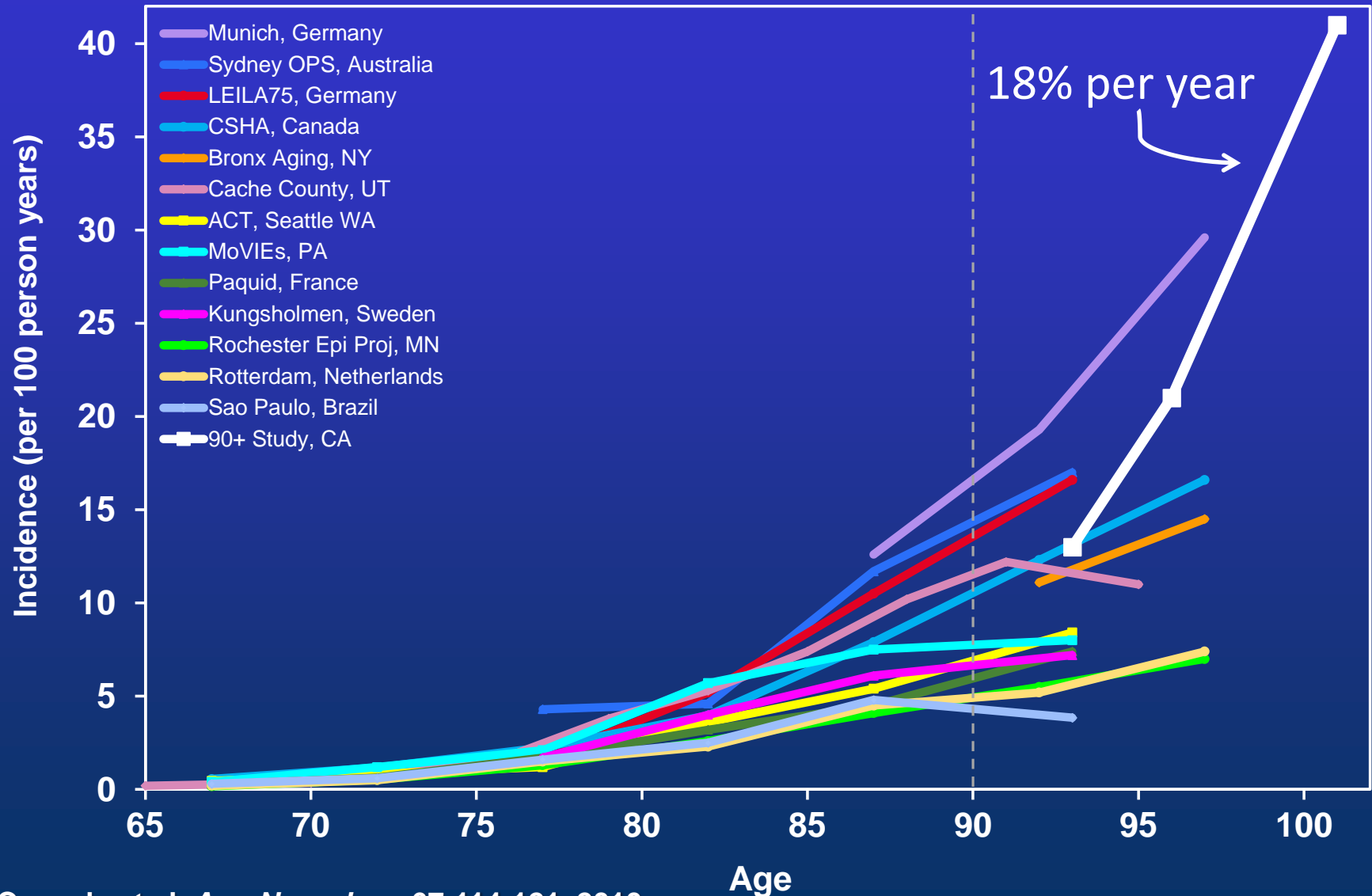
### Type of Residence

Nursing or group home 40%

Home alone 31%

Neurological Exam Cognitive Diagnosis	Women	Men
Normal	33%	43%
Cognitively Impaired, not Demented	26%	33%
Demented	41%	24%

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



# Baseline Cognitive Diagnoses in CIND participants of *the 90+ Study*

25 %      aMCI

25 %      naMCI

50 %      other cognitive impairment

-- functional losses due to cognition

-- MMSE < 24

# Dementia Incidence in The 90+ Study by Baseline Cognitive Diagnosis follow-up 2.5 years

<u>Cognitive Diagnosis</u>	<u>Incidence %</u>	
	<u>AD</u>	<u>VD</u>
Normal	5	2
Amnestic MCI	31	10
Non-amnestic MCI	10	11
Other Cognitive Impairment (MMSE <24, Functional Loss)	42	19

# Investigations of Risk Factors and Dementia

- ~~Vitamin E (supplementation)~~
- ~~Vitamin C (diet and supplementation)~~
- ~~BMI~~
- ~~Alcohol~~
- ~~Caffeine~~
- ~~Activities~~
- ~~Homocysteine levels~~
- ~~Thyroid function~~
- ~~ApoE E4~~

# Vascular Risk Factors and Prevalent Dementia

46% Hypertension

~~12% Coronary Artery Disease~~

~~12% Myocardial Infarction~~

~~17% Congestive Heart Failure~~

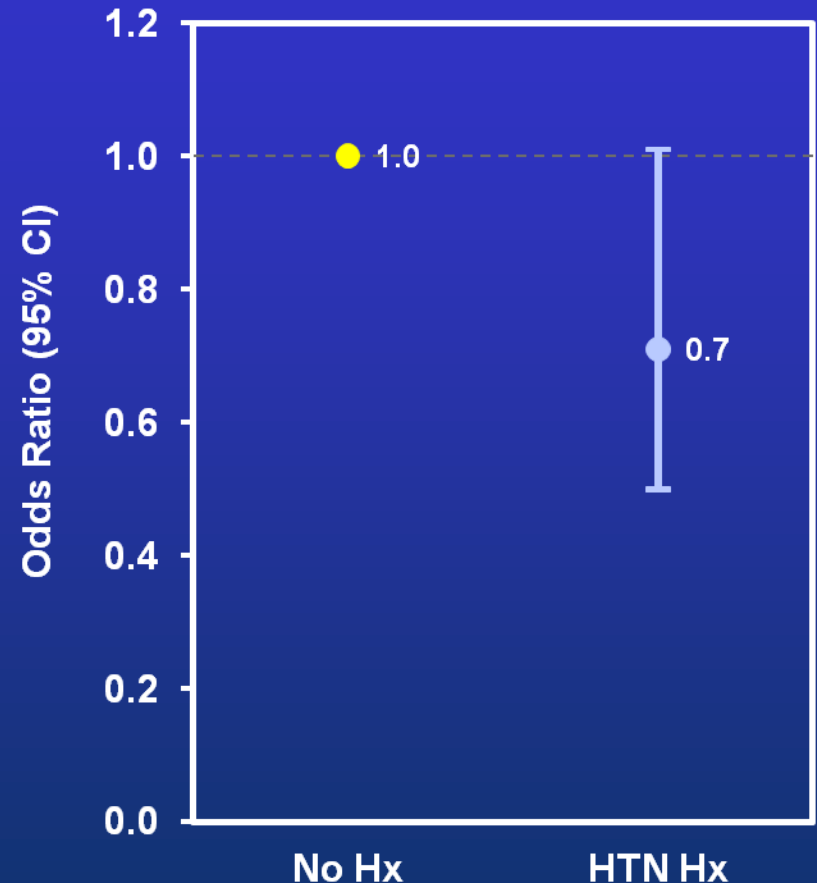
~~22% Atrial Fibrillation~~

Vascular risk factors did not distinguish  
demented and non-demented participants –  
except HTN



# Hypertension and Incident Dementia (History)

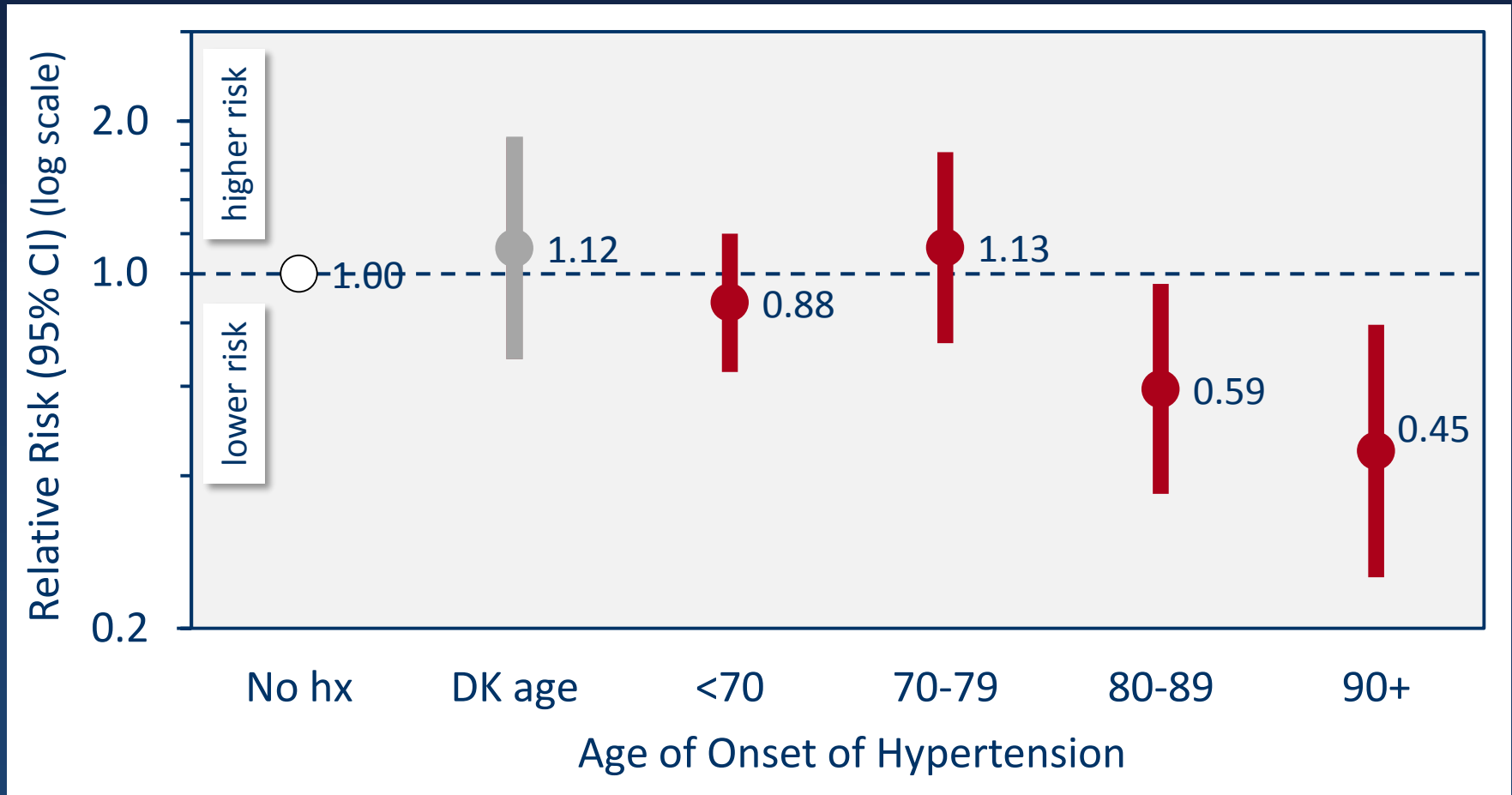
- 325 non-demented participants
  - 70% women
  - Mean age = 94 (90 – 103)
  - 137 incident cases
- History of hypertension at baseline
  - 53% reported a history



# Hypotension and Increased Risk of Dementia

- Gothenburg H-70 & Rotterdam
  - Ruitenberg et al, *Ann Neurol*, 2001
- East Boston Study
  - Morris et al., *Arch Neurol*, 2001
- Bronx Aging Study
  - Verghese et al, *Neurology*, 2003
- OCTO-Twin Study
  - Nilsson et al., *Aging Clin Exp Res*, 2007

# Risk of Dementia in Relation to Age of Onset of Hypertension



# Blood Pressure & Dementia

## Potential Interpretations

1. “Normal” blood pressure may be different for 90+ year olds
2. Elderly torturous cerebral vessels may require increased pressure for adequate perfusion
3. Low blood pressure may be a marker for other diseases
4. Medication effects – ACE-inhibitors, Ca-channel blockers, others
5. Differential medical care

# What is Related to Dementia in Oldest-Old?



O<sub>2</sub> Saturation <93%

OR

2.3



Performance Based  
Physical Function

Walk Speed

11.8

Hand Grip

5.3



History of HTN

0.7

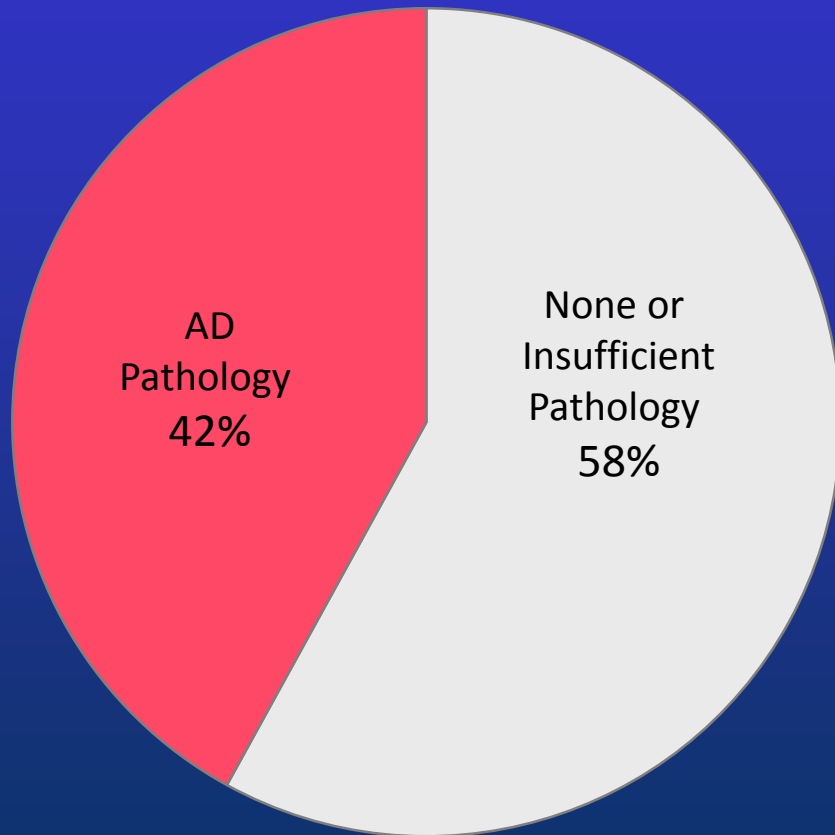
# The 90+ Autopsy Study



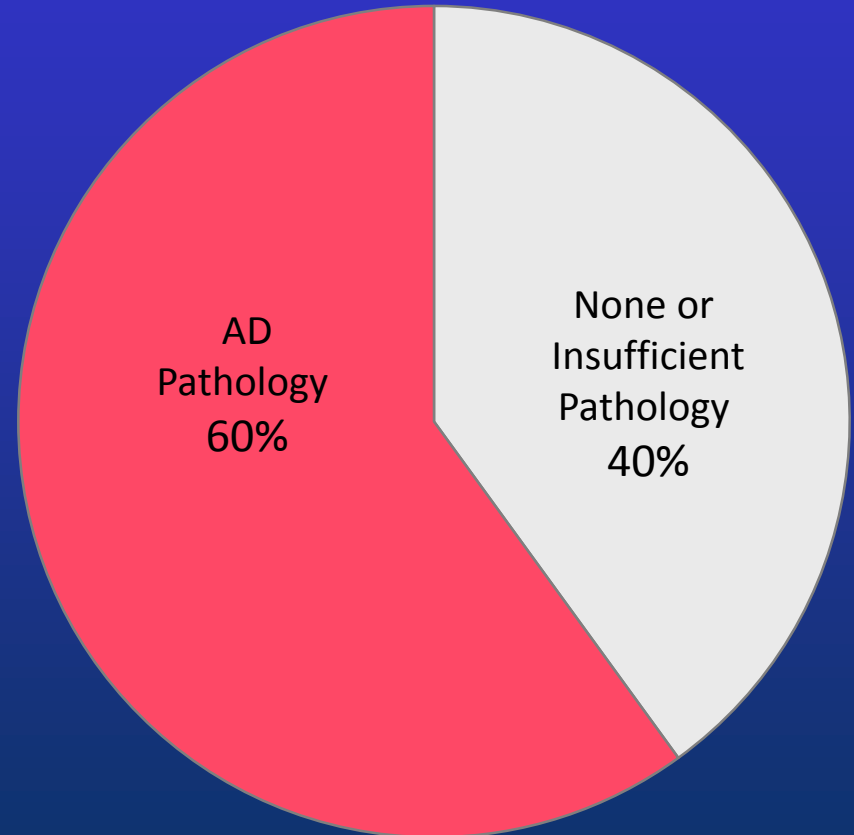
- 342 people enrolled
- 233 have come to autopsy
- Brain sections are both fixed and frozen
- Mean Post-Mortem Interval 4.9 hours

# Pathological Diagnoses by Dementia Status

No Dementia  
(N=76)



Dementia  
(N=90)



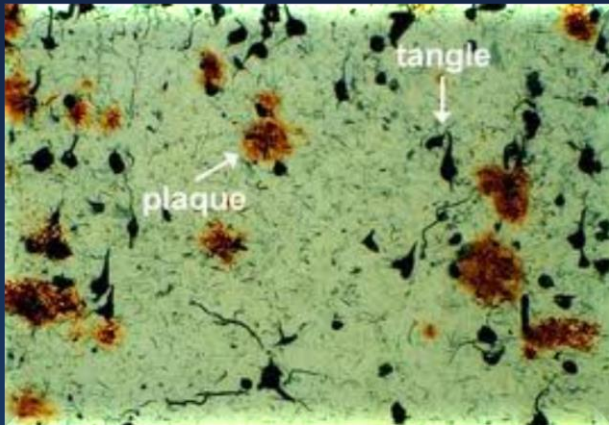
AD = Intermediate/High NIA Reagan Criteria

# The Effect of Multiple Pathologies

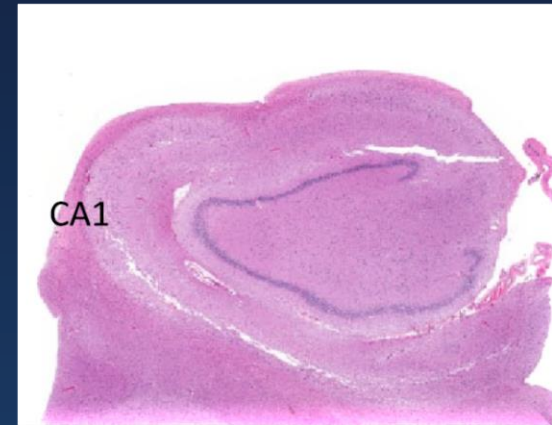


# Brain Pathologies

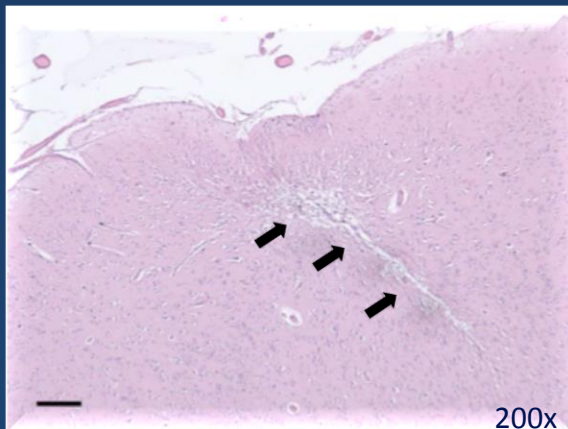
Alzheimer's  
Plaques & Tangles



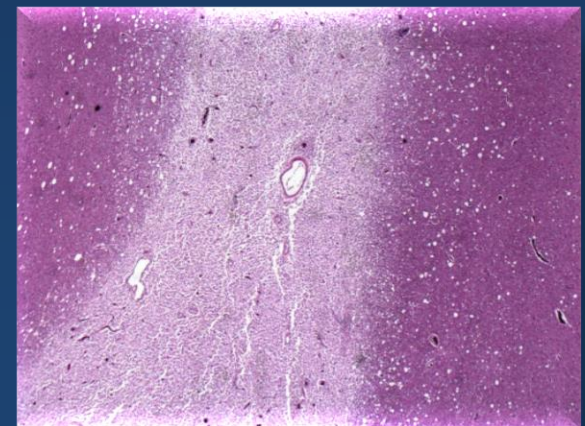
Hippocampal  
Sclerosis



Microinfarct



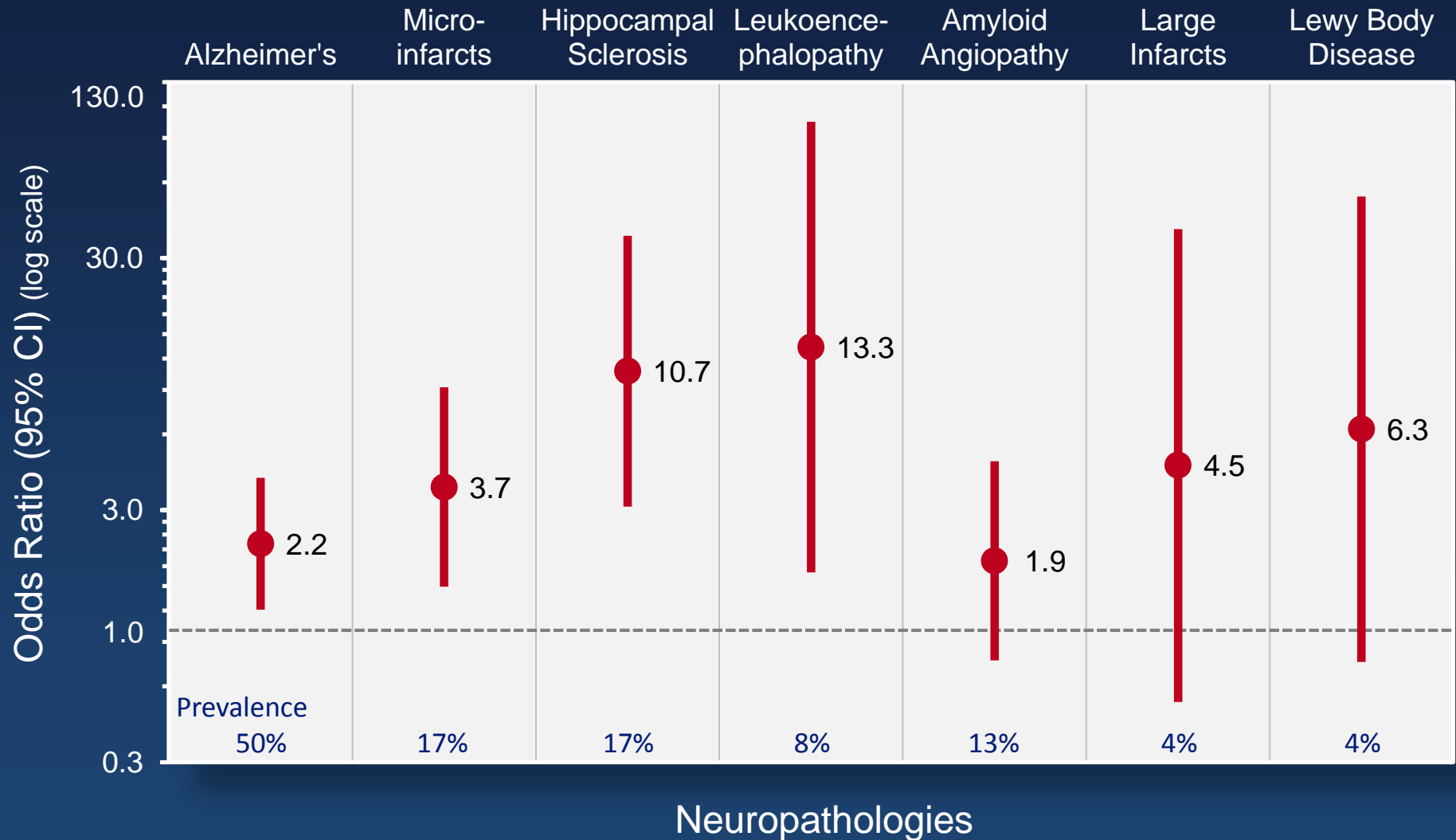
White Matter Disease



# Pathological Diagnoses

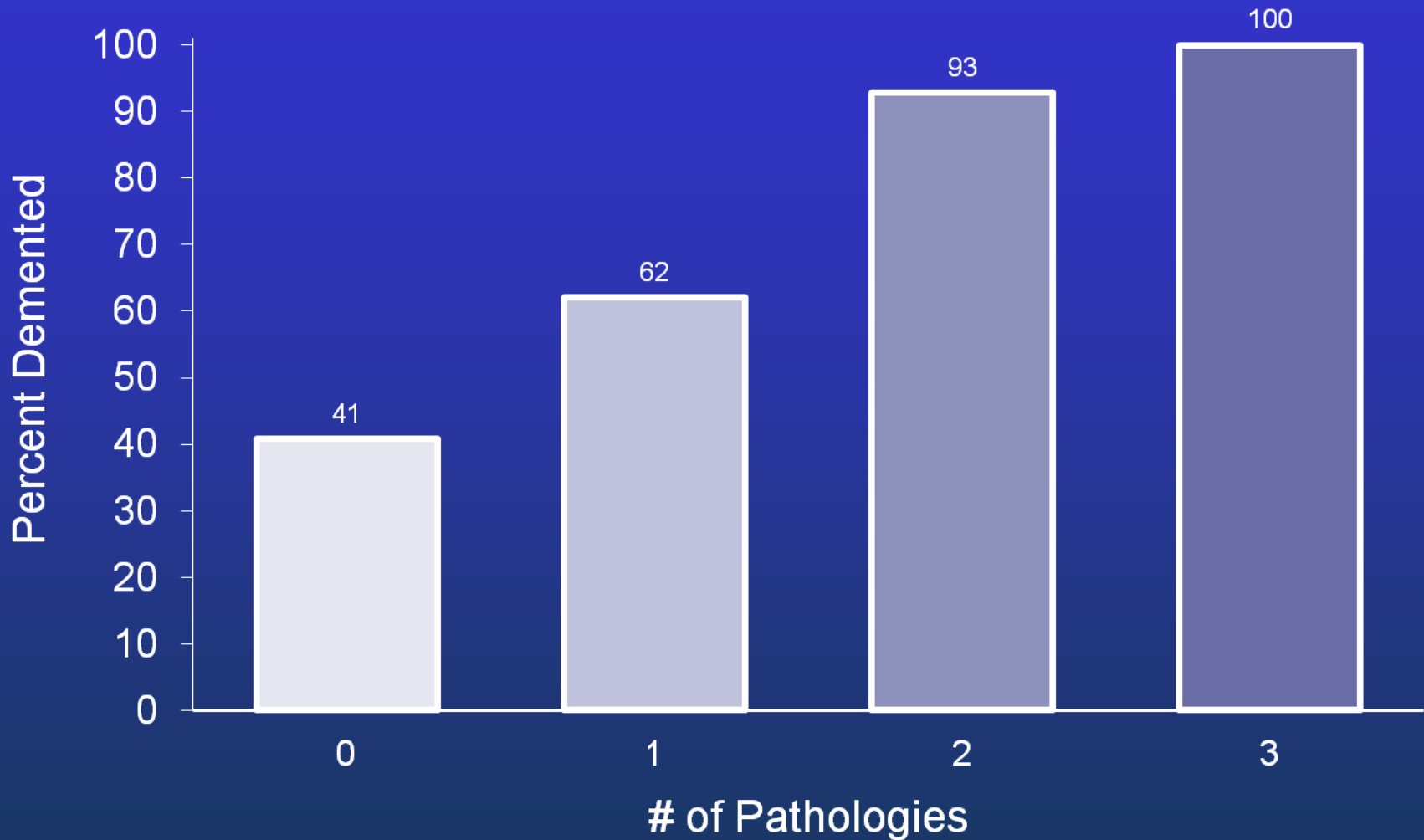
- Alzheimer's (NIA Reagan No-Low vs Interm-High)
- Microinfarcts (0-2 vs 3+)
- Hippocampal Sclerosis (No vs Yes)
- Amyloid Angiopathy (no-mild vs mod-severe)
- Subcortical Arteriosclerotic Leukoencephalopathy (No vs Yes)
- Lewy Bodies (No-brainstem vs limbic-neocortical)
- Macroinfarcts-large & lacunes (0-1 vs 2+)
- Other pathologies (CBD & glioblastoma)

# Odds of Dementia For Different Pathologies (vs not having that pathology)

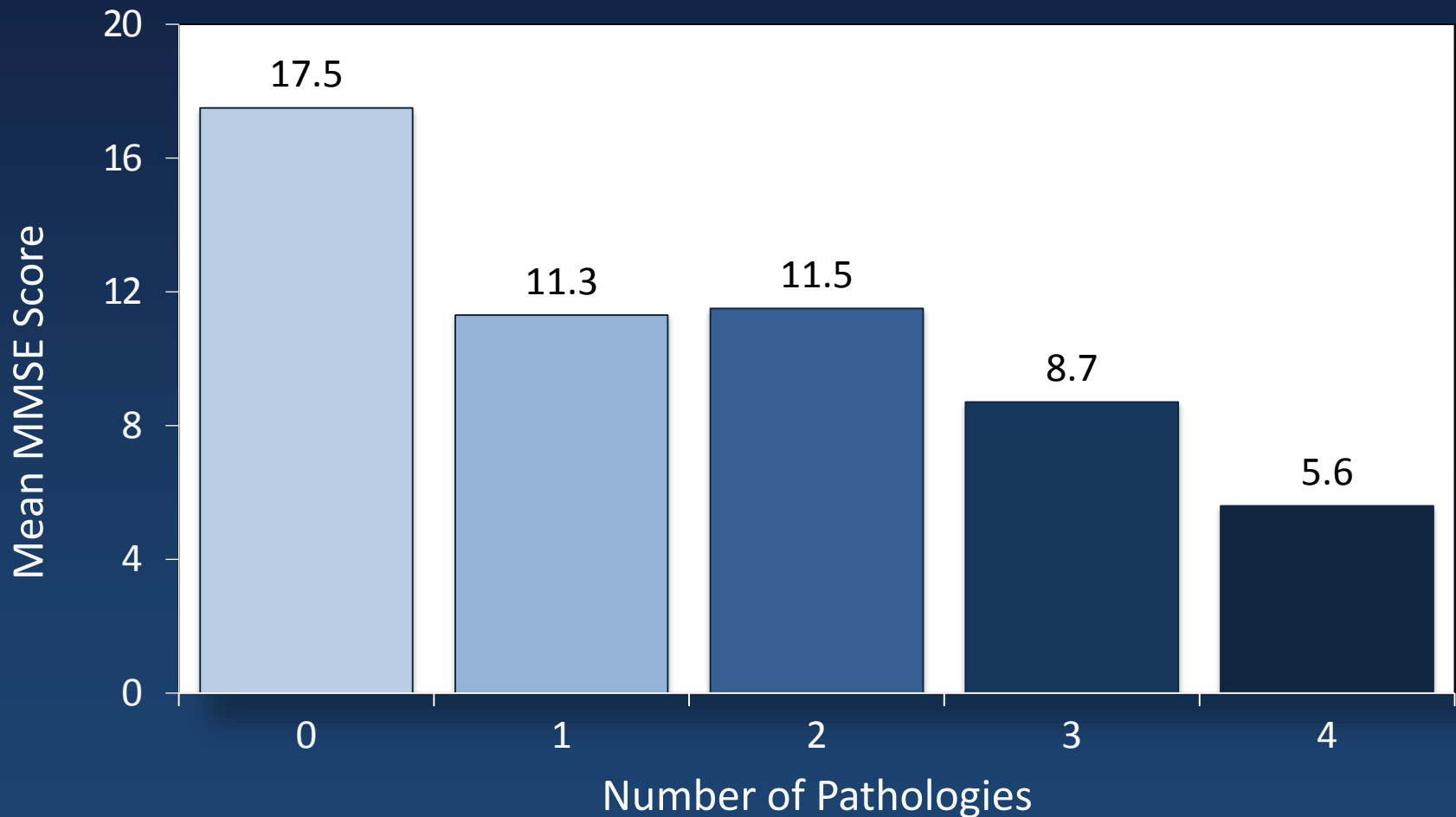


N=183 From logistic regression adjusting for age at death and sex

# Frequency of Dementia by Number of Pathologies (N=183)



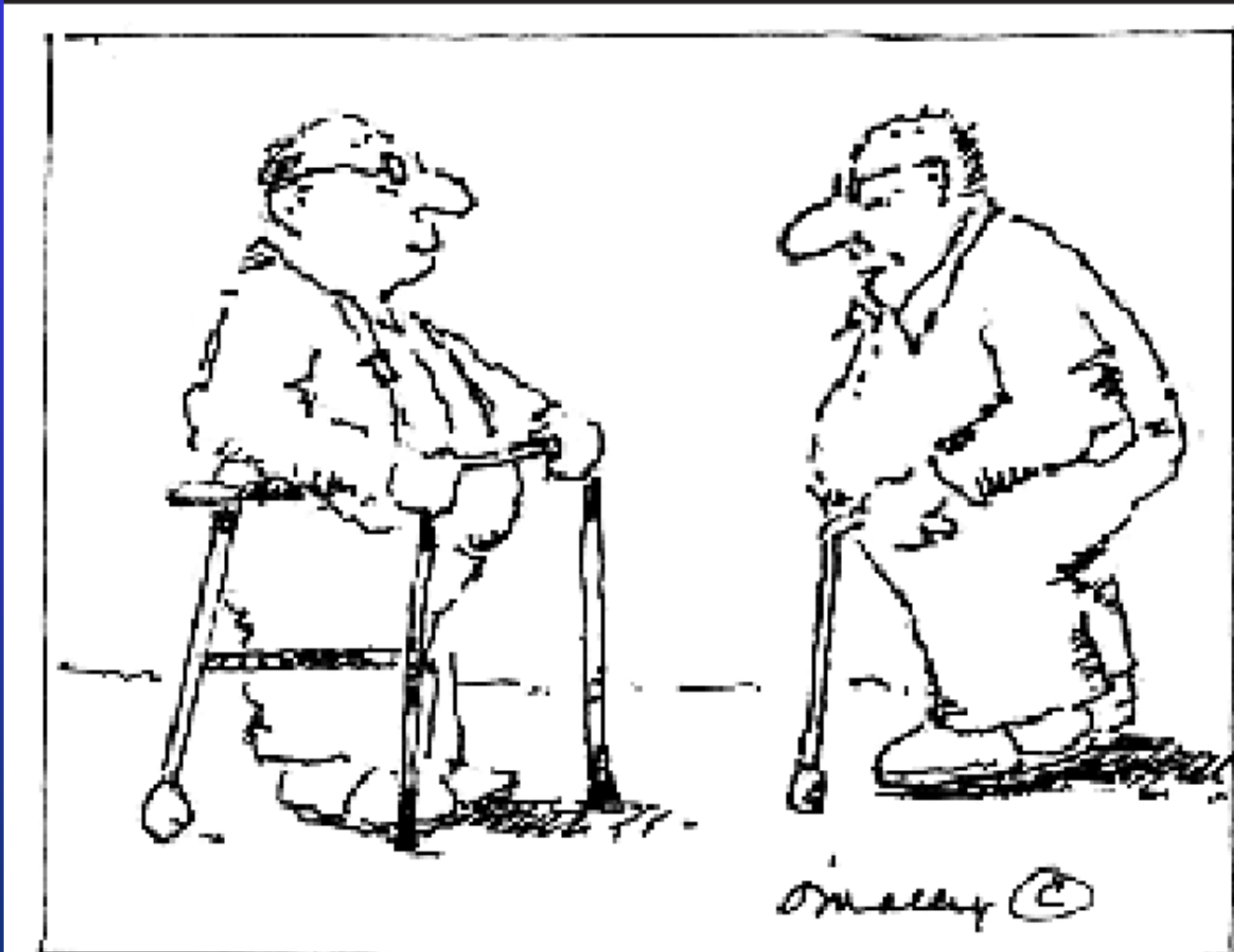
# MMSE Score by Number of Pathologies in people with Dementia



N=94 From multiple linear regression adjusting for age at death, sex, and duration of dementia

# Summary

- Remarkable increase in longevity and numbers of oldest-old world-wide
- Risk of MCI and dementia is exceptionally high in these individuals, most likely due to multiple pathologies
- We know little about other pathologies or their risk and protective factors
- Old people are not bad versions of younger people
- More research is needed!



**Did you hear? 95 is the new 65!**

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