

# **The Coming Epidemic of Late-Life Cognitive Impairment**

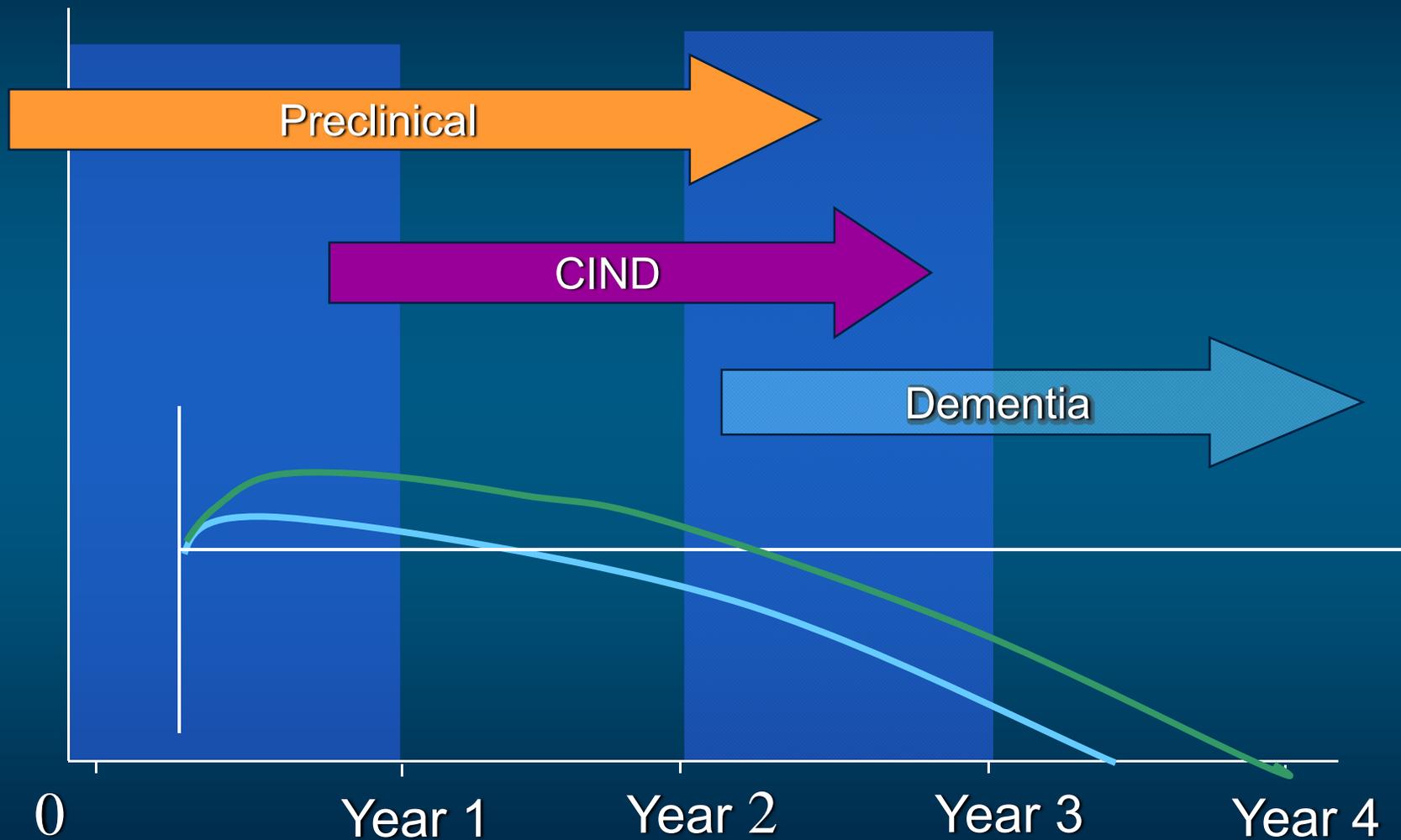
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**McCarron Professor of Neurology  
University of Southern California**

# Late life cognitive impairment

- ◆ **Magnitude**
  - Cognitive impairment (CIND, MCI)
  - Dementia
- ◆ **Diagnosis**
  - Alzheimer disease
  - Cerebrovascular disease
- ◆ **Prevention is the best treatment**

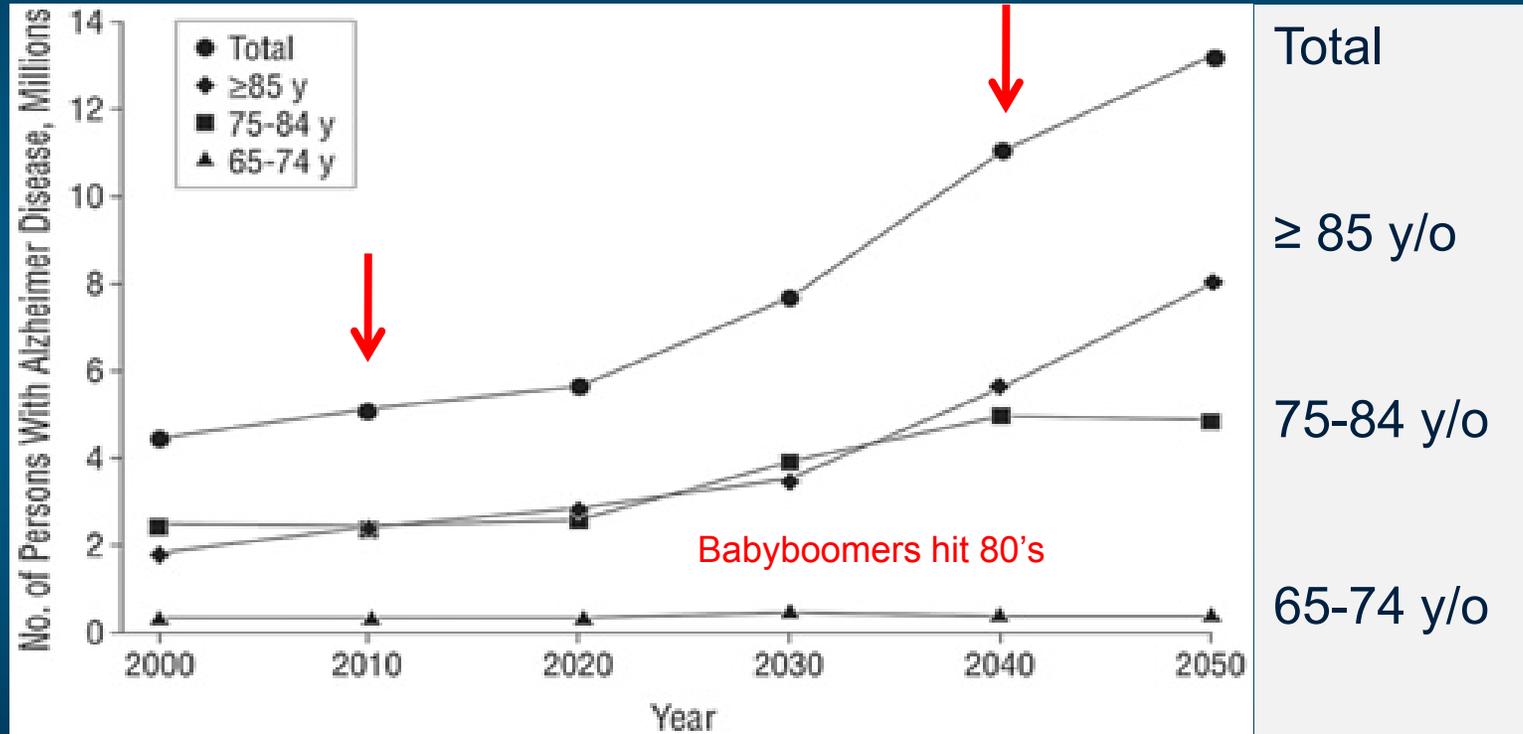
# Three phases of cognitive impairment



Courtesy Lon Schneider, M.D., University of Southern California

# Prevalence of Alzheimer Disease

## 5 million in 2010, 10 million in 2040

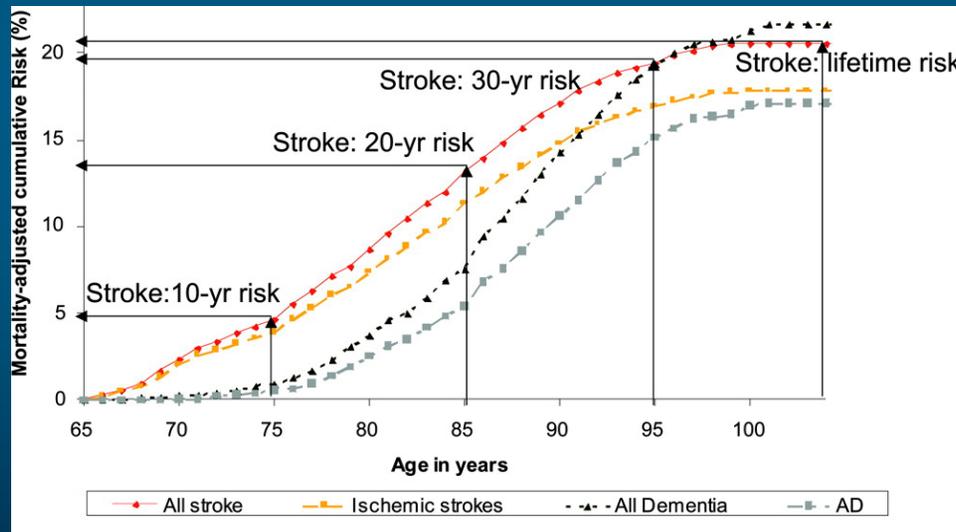


Hebert: Arch Neurol, Volume 60(8).August 2003.1119–1122

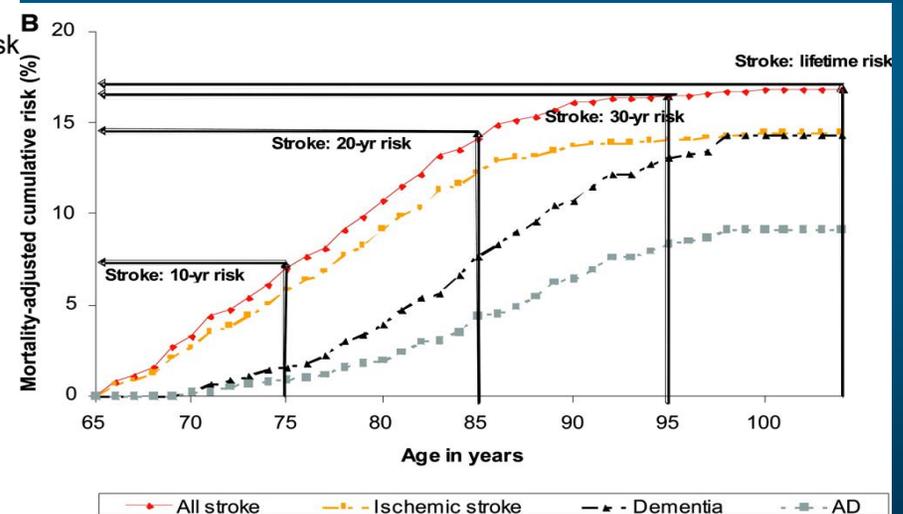
# Women have higher life-time risk of dementia, Alzheimer and stroke.

Note: Before age 75 men have higher risk of stroke,

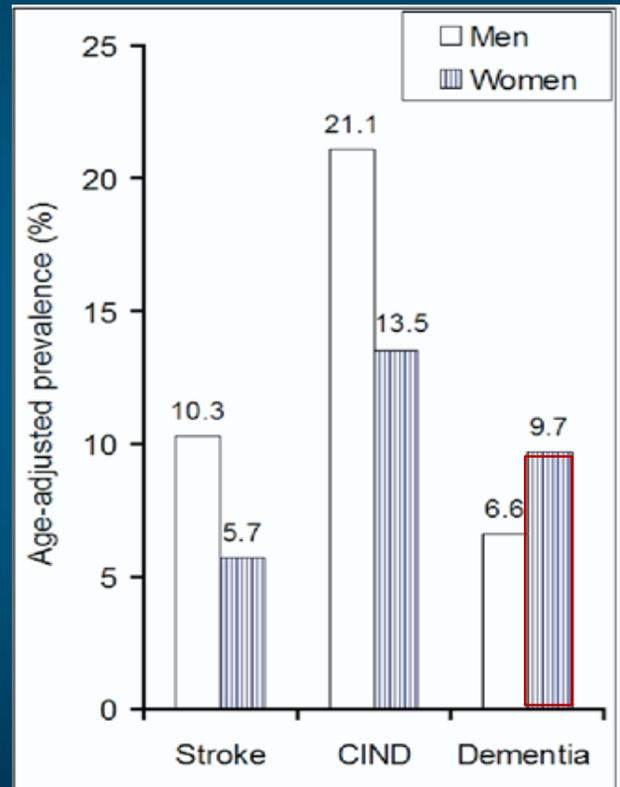
## Women



## Men



# For each person with Stroke or Dementia, there is another with CIND (Canadian Study of Health and Aging)

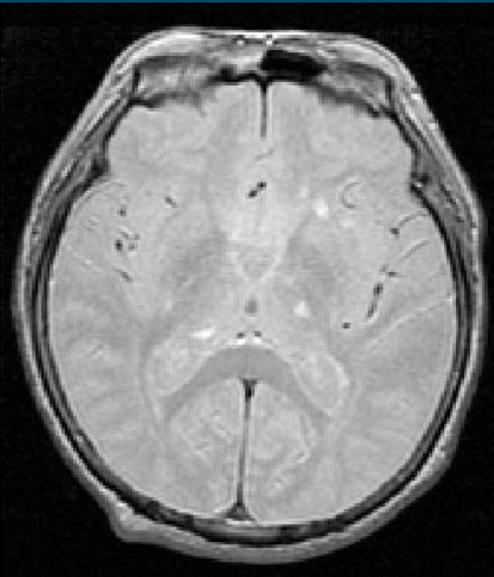


Women at  
higher risk  
of dementia

# Vascular Brain Injury seen by T-2 weighted MRI: Infarcts, white matter changes, and hemorrhage



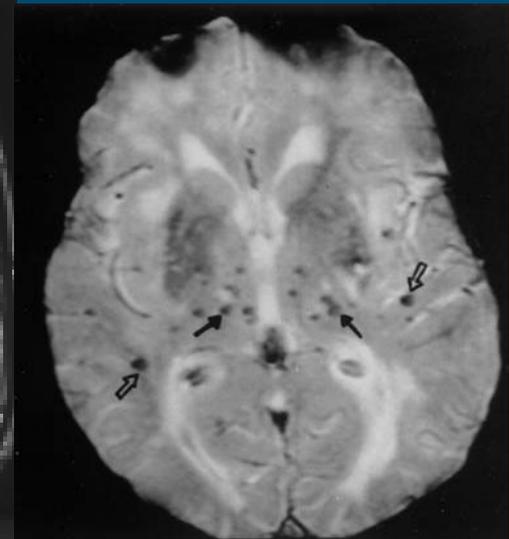
**Major artery  
infarcts**



**Small artery infarcts  
Lacunar infarcts  
Silent vs. symptomatic**



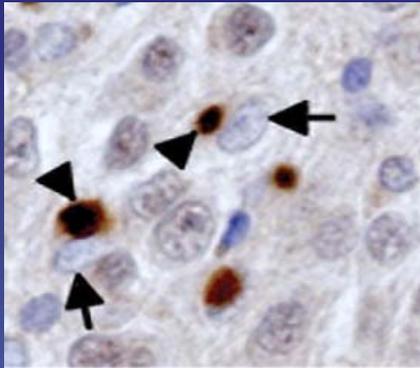
**White matter  
hyperintensities**



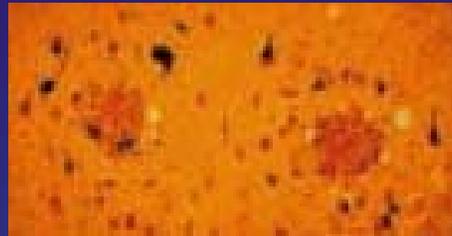
**Microbleeds  
T2\*-weighted gradient  
echo planar**

# Misfolded Proteins and Amyloid Fibrils in Neurodegenerative Disorders

Fronto Temporal  
Dementia (FTLD)  
(tau or TDP-43)



Alzheimer Disease (AD)  
(Amyloid  $\beta$ ; tau)



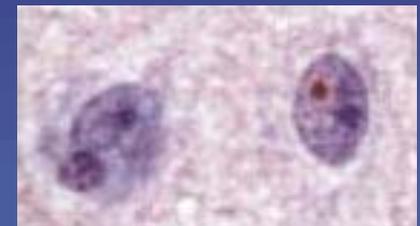
Parkinson Disease (PD, DLB)  
( $\alpha$ -synuclein Lewy  
bodies)

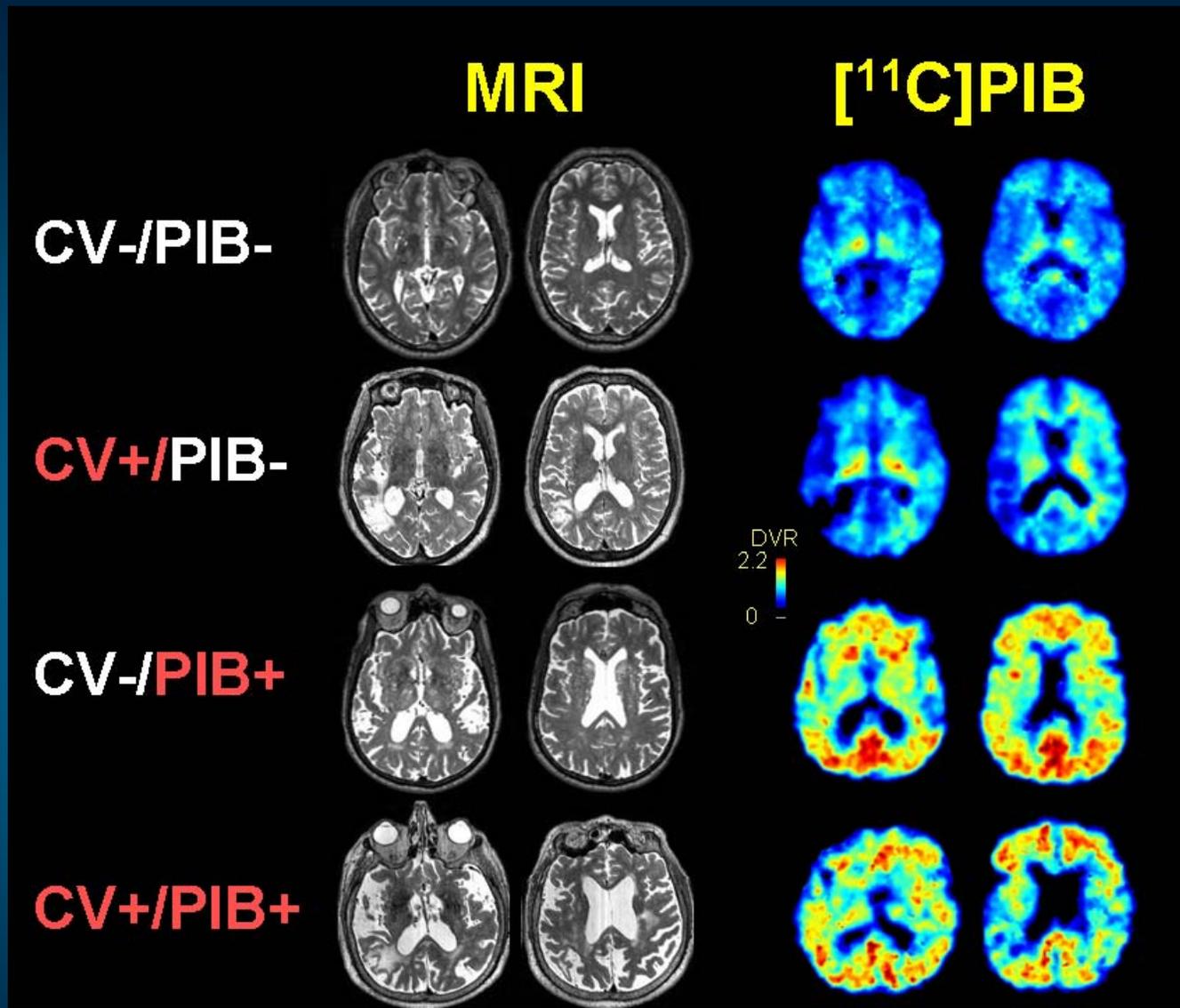


Prion Disease (CJD)  
(Prion deposits)



Huntington Disease (HD)  
(Huntingtin deposits)



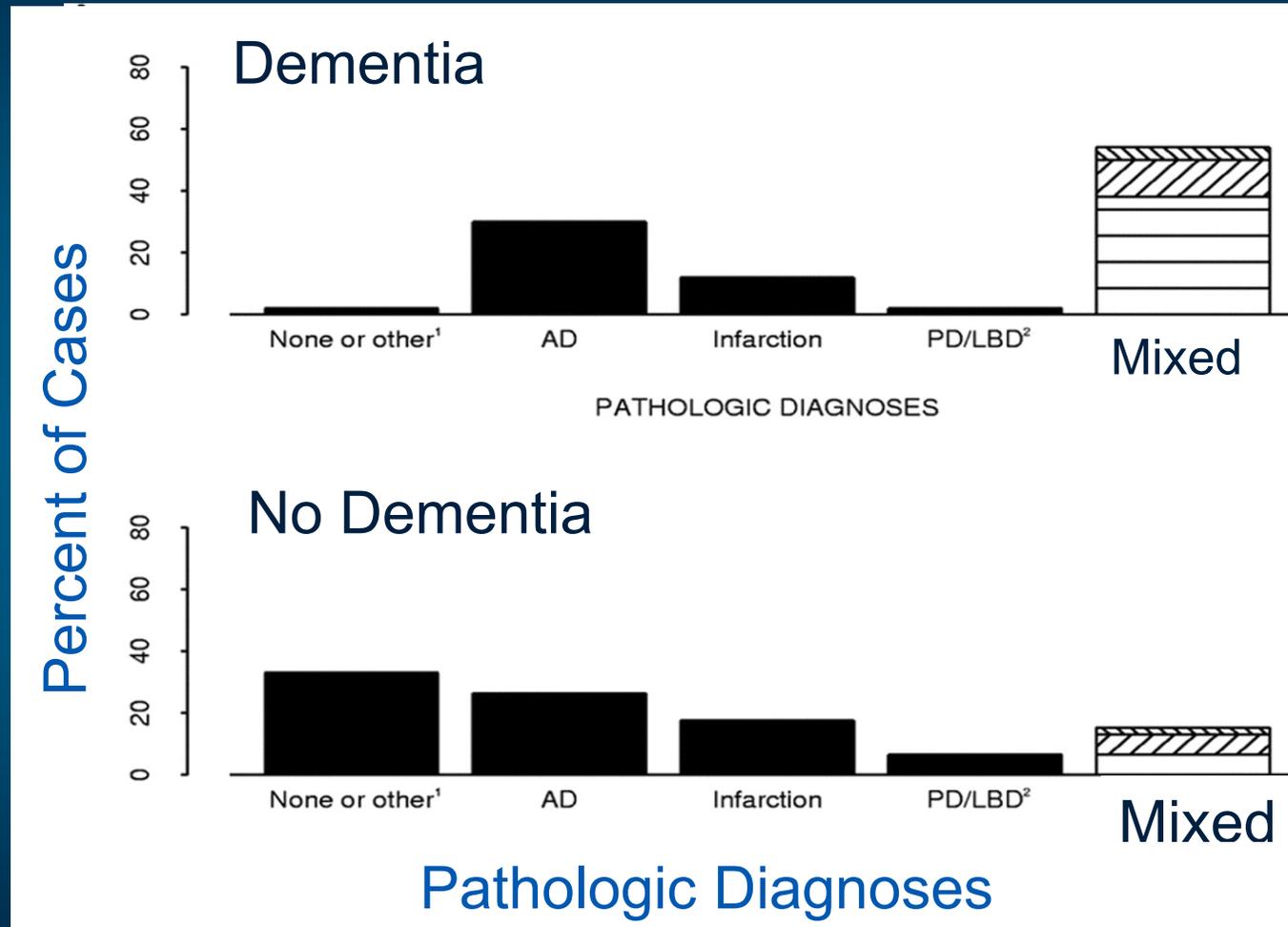


**Future:**  
**Infarcts on**  
**MRI for**  
**VCI**

**Amyloid**  
**PET**  
**Retention**  
**for AD**

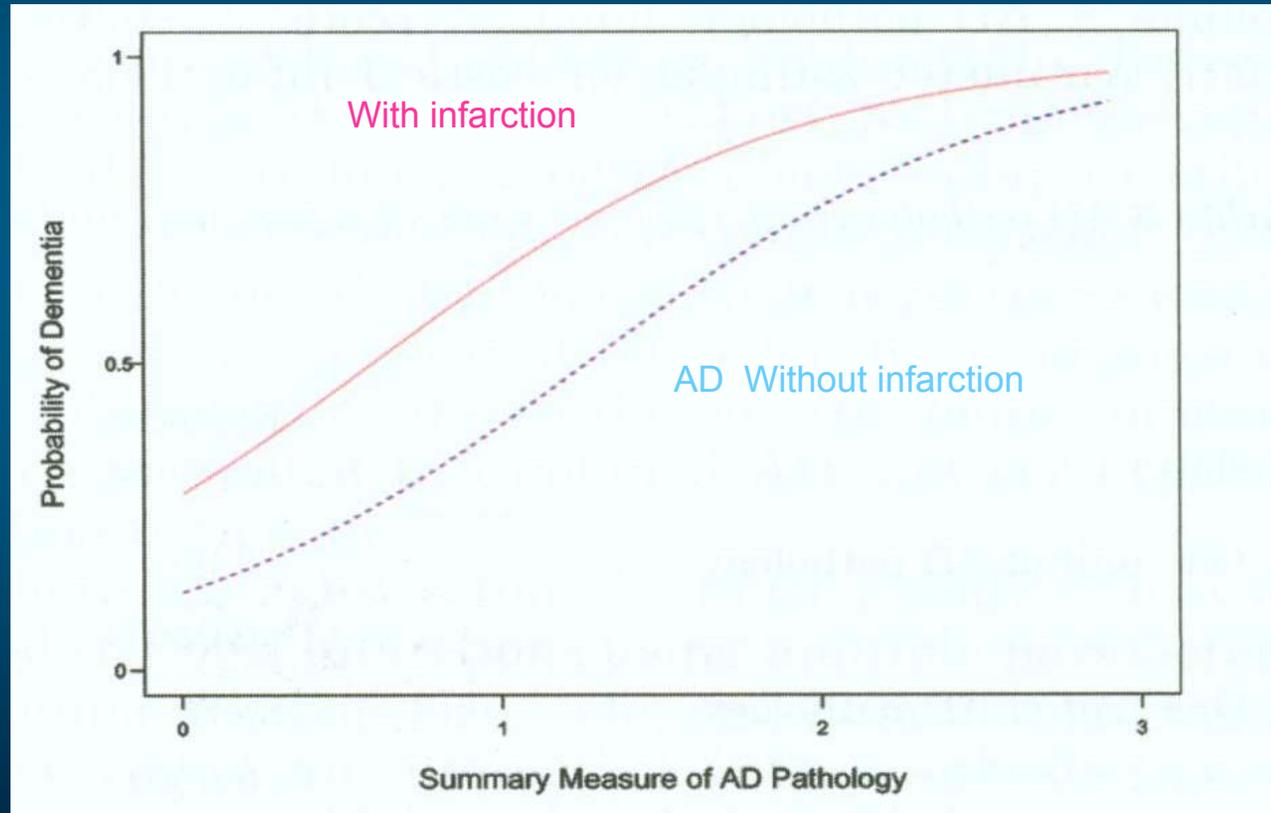
*Rabinovici GC. Presented at Human Amyloid Meeting, Toronto, 2010  
 Aging Brain Program Project*

50% of Older Adults with Dementia have  
**Mixed Pathology**  
(i.e., Multiple Neuropathologic Diagnoses)

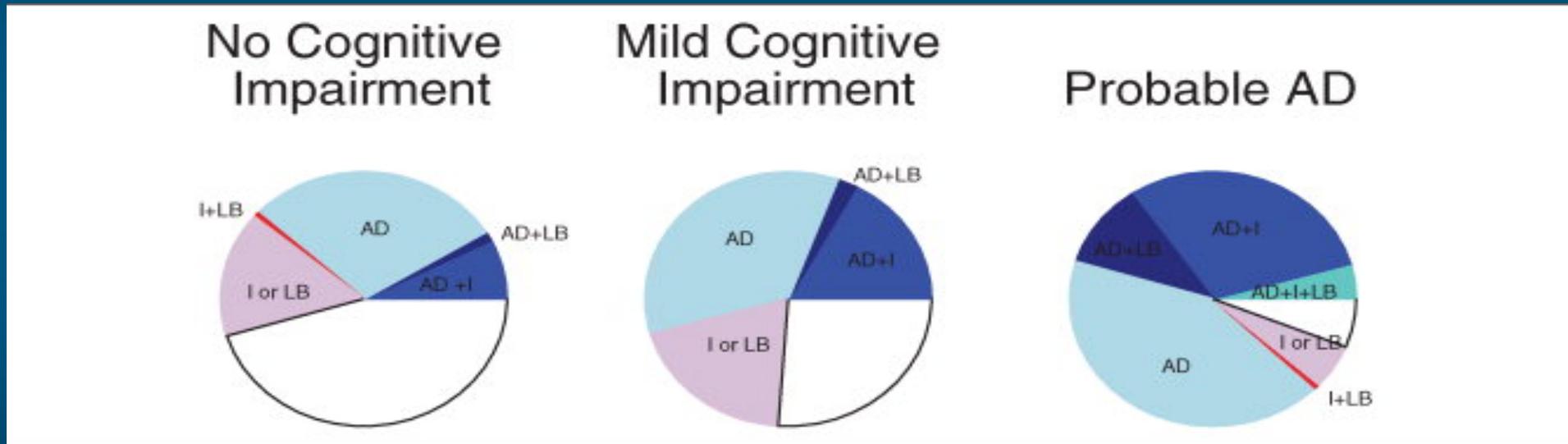


# Additive effects of cerebral infarction and AD pathology on risk for dementia

(Religious Orders Study n=153)

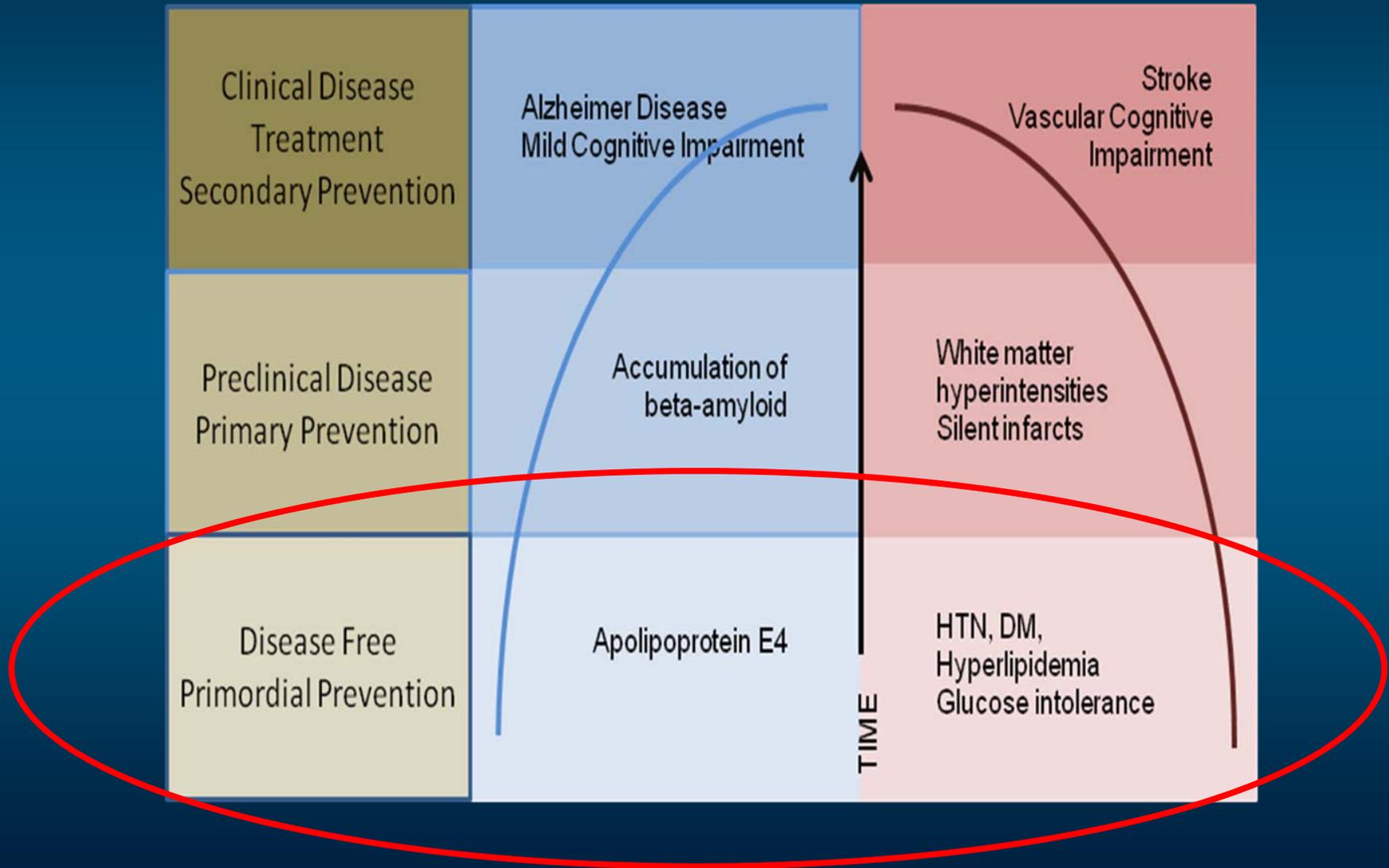


# Growing AD portfolio with increasing severity of cognitive impairment



Schneider et al., Ann Neurology 2009; 66:200–208.

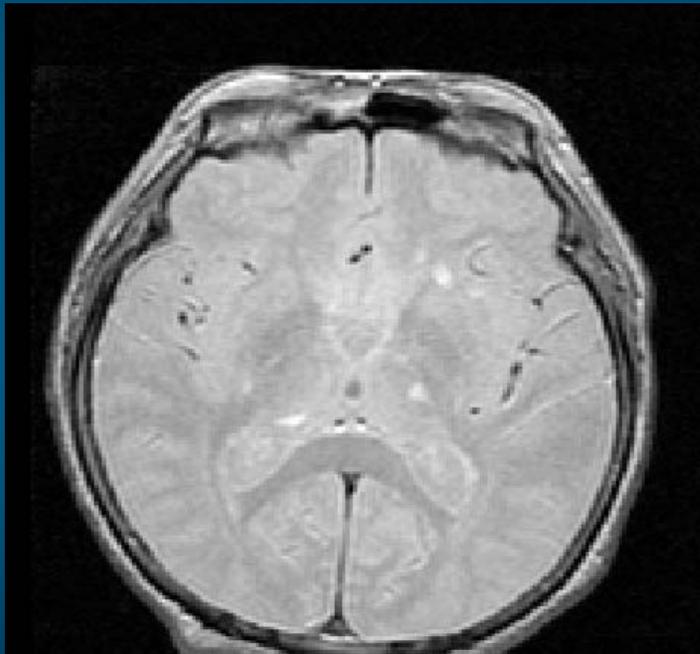
# Prevention is best treatment



# Subcortical Ischemic Vascular Disease (SIVD, S-CVD)

Silent infarcts in 24% of population –

Vermeer et al. Rotterdam Scan Study, Stroke 2002; 33:21-5.



**Lacunae:**  
**Silent and  
symptomatic**

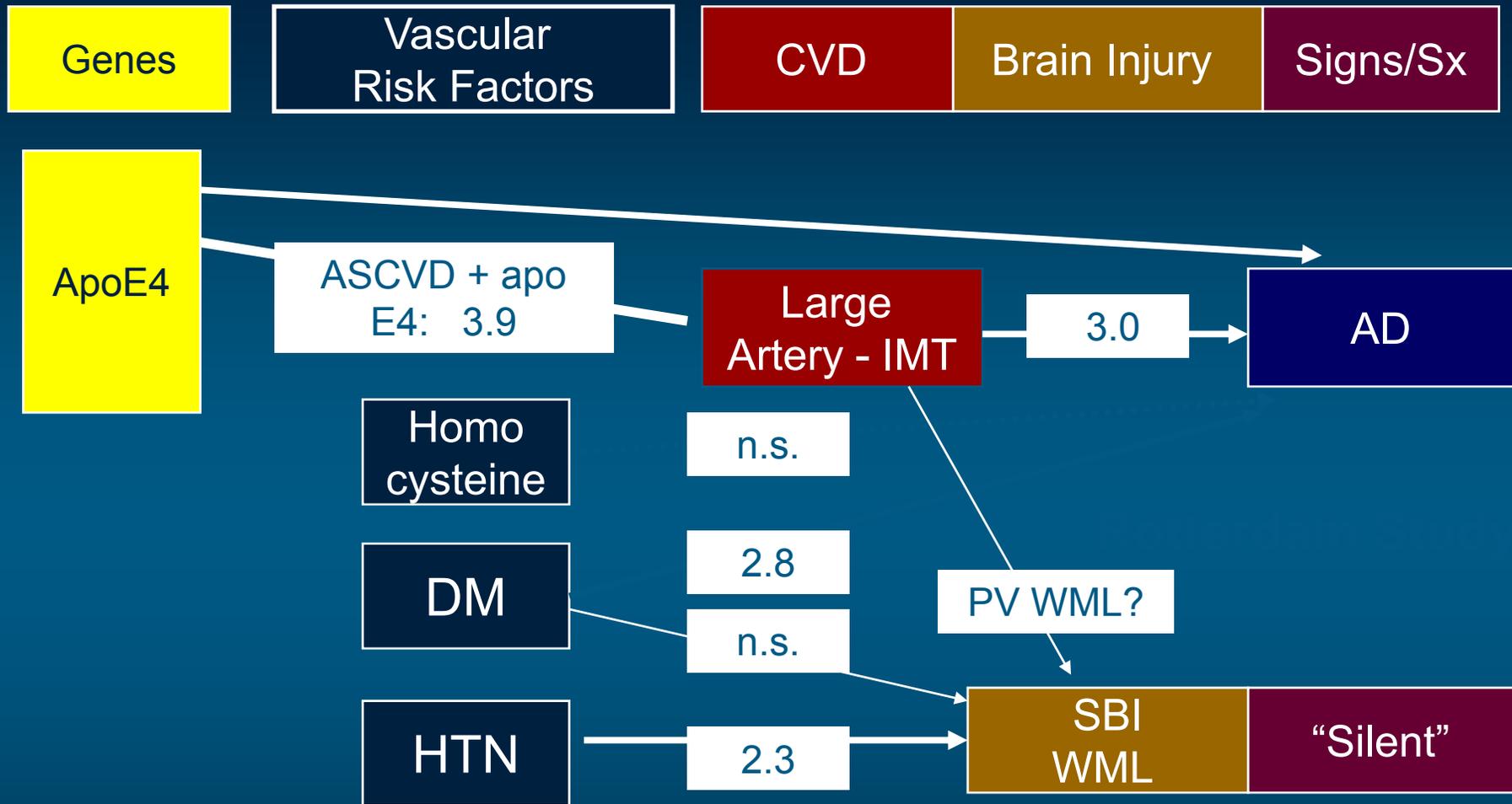


**White matter  
hyperintensities**

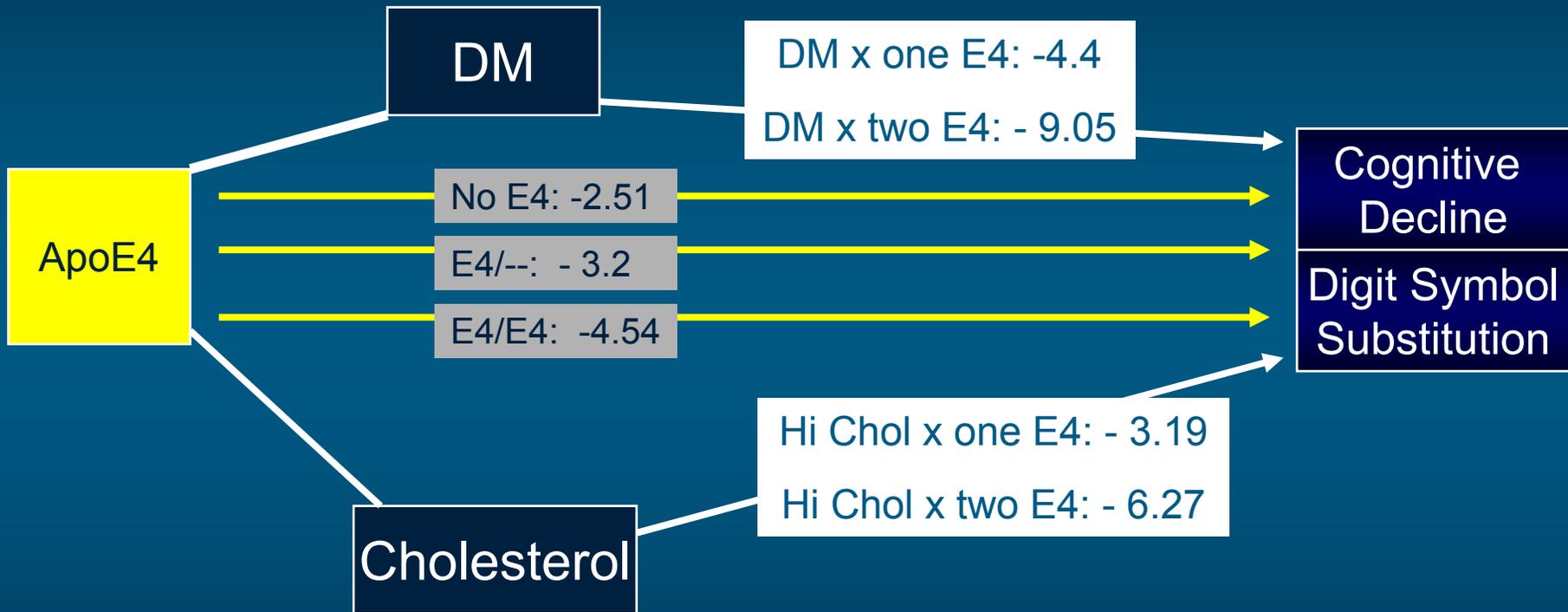
# Primary Prevention

- ◆ Brain at risk
- ◆ Prevent infarction
- ◆ What to do about Apo E4 genotype?
- ◆ Manage vascular risk factors
  - HTN\*
  - Diabetes
  - Hyperlipidemia
  - Heart disease

\*Risk of stroke double for every 20/10 mm increase in BP over 115/75



## Rotterdam Scan Study



Multiple regression analysis

**Atherosclerosis Risk  
in Communities  
(ARIC)**

Blair et al. Neurology 2005; 64: 268-276.

# Evidence favors effectiveness of treatment for hypertension in prevention of cognitive impairment

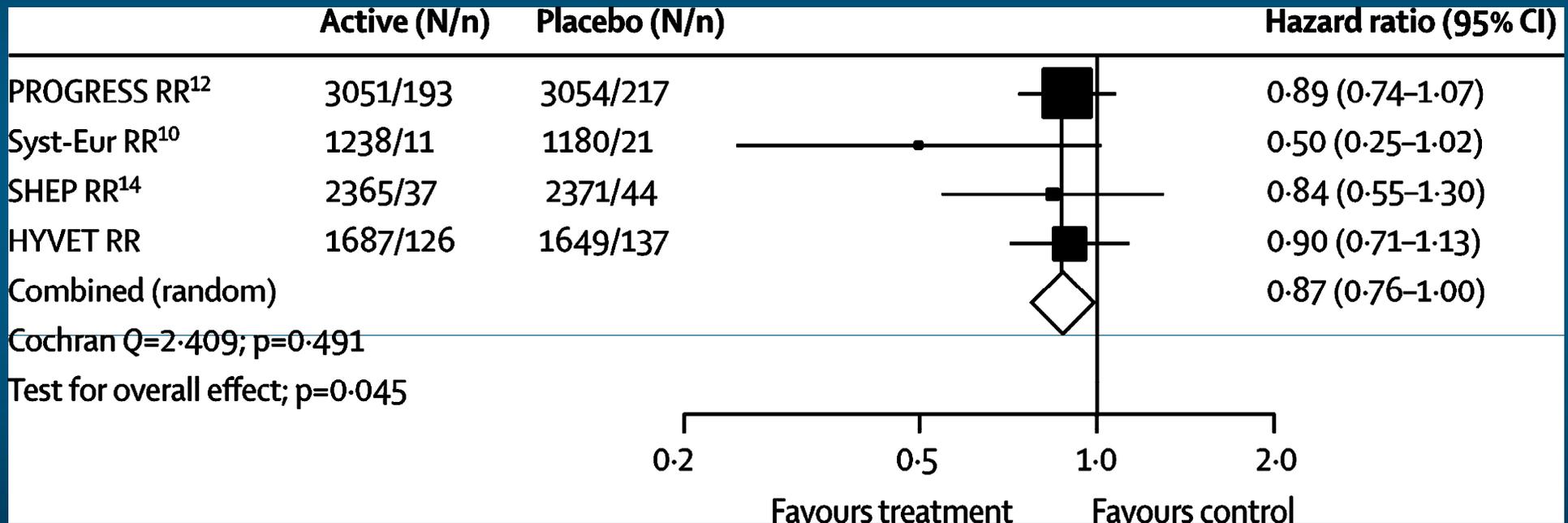


Table 410"&gt;

## Physical activity decreases risk of VaD

	Cases, n (%) <sup>*</sup>	Model 1	Model 2	Model 3
<b>Walking, Kcal/wk</b>				
>417 (n = 239)	0			
209-417 (n = 304)	10 (1.8)	0.27 (0.12-0.63)	0.37 (0.16-0.87)	0.36 (0.15-0.87)
<209 (n = 206)	17 (18.2)	1.00	1.00	1.00

Values are hazard ratio (95% CI). Model 1 is adjusted for age, gender, education, and APOE genotype. Model 2 is adjusted as Model 1 + cardiovascular disease, hypertension, and hyperhomocysteinemia. Model 3 is adjusted as Model 1 + comorbidity and basic activities of daily living motor disability.

<sup>\*</sup>Except when otherwise indicated, HRs for vascular dementia refer to the highest and middle tertiles pooled together compared to the lowest tertile.

# What must we do?

- ◆ **Research to crack the AD code.**
- ◆ **Healthy lifestyle:  
Prevent vascular contributions  
to cognitive impairment.**