

WHY IS AN EARLY DIAGNOSIS OF ALZHEIMER'S IMPORTANT AND HOW DO WE ACHIEVE IT?

Frederick A. Schmitt
University of Kentucky

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The Dementia Screening 'Controversy'

- 1996 U.S. Preventive Services Task Force finds insufficient evidence to recommend for or against dementia screening

BUT the evidence is evolving.....

- ⦿ Brief screening tools can detect some persons with early dementia
- ⦿ Screening tests can detect undiagnosed dementia (mild to moderate Alzheimer's).
- ⦿ Among primary care patients 65+ years of age **3.2% to 12% met criteria for dementia** *without dementia documentation or physician knowledge of dementia*

(Boustani et al, Ann Intern Med, 2003)

- ⦿ Note: Freund (*J Am Geriatr Soc*, 2006) estimates that missed diagnoses exceed 25% of the dementia cases (might be as high as 90%).

Benefits and Harms From Early Dementia Recognition

- ⦿ Psychological and social benefits
- ⦿ Medical benefits
- ⦿ Harms from failure to recognize early dementia
- ⦿ Harms that might occur do to:
 - Positive screening result
 - Negative screening test result

(Ashford et al, Alzheimer's & Dementia 2007)

Psychological and Social Benefits

1. Early education of caregivers on patient care
2. Advance planning while patient is competent
 - establishing a will, proxy, power of attorney, advance directives
3. Reduced patient / family anxiety, uncertainty, and stress
 - improve family understanding of dementia symptoms & course
4. Reduce caregiver burden, blame, denial
5. Promote safety in driving, medication compliance, cooking, and other daily activities
6. Patient's and family's right to know (genetic risks)
7. Promote advocacy for research and development of more effective treatment(s)

Medical Benefits of Early Detection

- ◎ Treatments and appropriate interventions may improve overall disease course
 - lessens disease burden on caregivers and society
- ◎ Current symptomatic therapies:
 - Temporarily improve cognitive function
 - Temporarily improve function (ADLs)
 - Decrease development of behavior problems
 - Delay nursing home placement

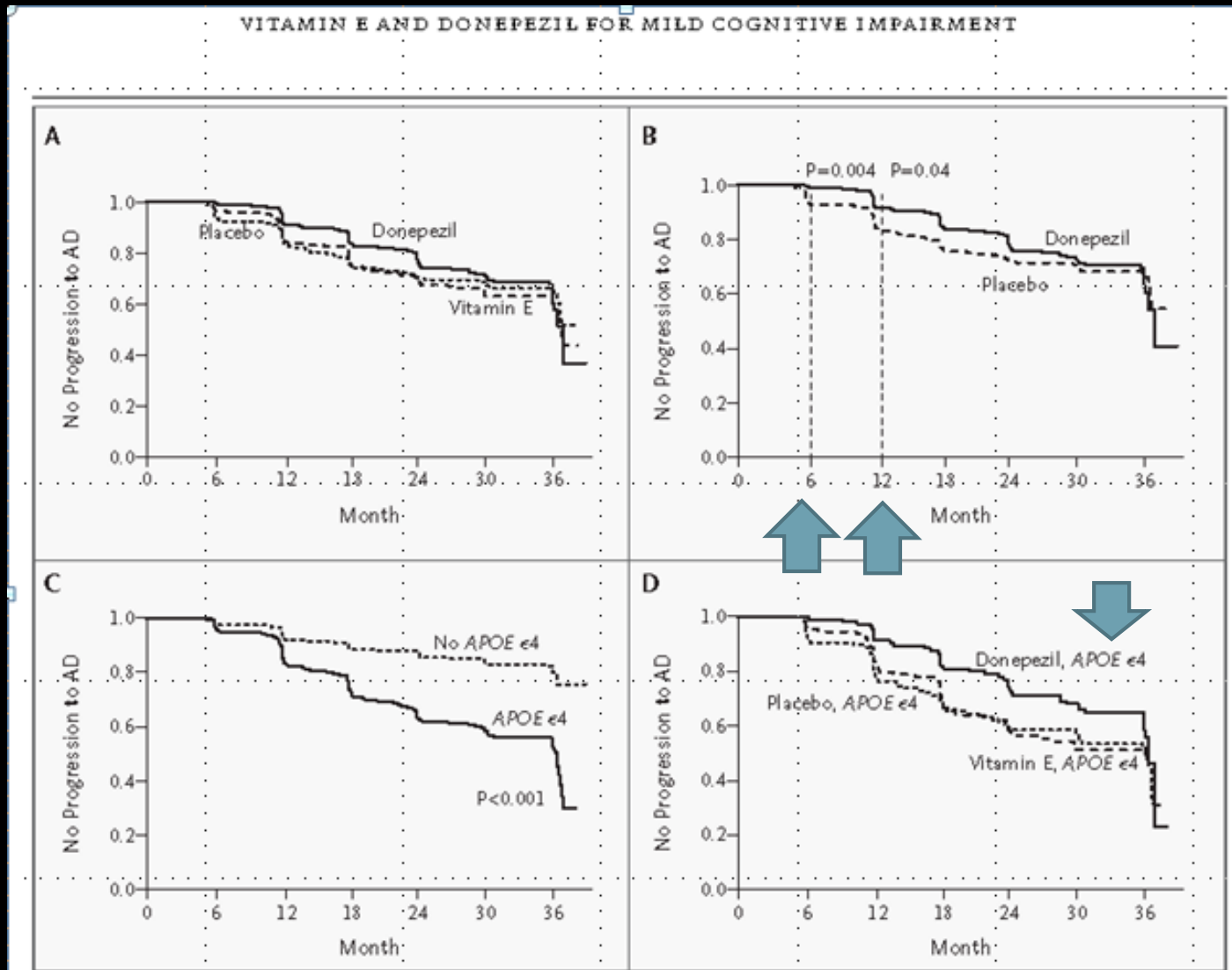
Harms: Failure to Recognize Early Dementia

- ⦿ Dangerous behaviors: cooking, operating machinery, driving problems
- ⦿ Missed opportunities for:
 - application of available treatments
 - participation in research
 - advance care planning
 - support of caregivers
- ⦿ Impact of Positive and Negative screening results

Screening Outcomes

- ⦿ False negative result might wrongly diminish concern and motivation to participate in future evaluation
- ⦿ Clinical error of equating positive screen with diagnosis
- ⦿ Anxiety resulting from screening (also by further workup and treatment)
- ⦿ Costs and inconvenience incurred during additional diagnostic workup

ADCS MCI Treatment Trial



Real-World Diagnosis of AD

Table 1. Steps in the diagnosis and assessment of a patient with suspected AD in primary care.⁴⁶

Step	Purpose	Tools/information required
Step 1: Prediagnostic tests	Identify risks for neurocognitive disorders	<ul style="list-style-type: none"> • Risk factor assessment • Medical history • Laboratory tests to identify risk factors and define comorbidities and early warning signs of preclinical dementia
Step 2: Assess performance	Cognitive assessment	<ul style="list-style-type: none"> • Cognitive tests e.g., MMSE,¹²⁶ Mini cog,¹²⁷ MoCA,¹²⁸ SIB 8¹²⁹ • Informant rated tools e.g., AD8¹³⁰
Step 3: Assess daily functioning	Determine level of independence and degree of disability	<ul style="list-style-type: none"> • Daily function assessment tool e.g., ADCS ADL¹³¹
Step 4: Assess behavioral symptoms	Determine presence and degree of behavioral symptoms	<ul style="list-style-type: none"> • Behavioral assessment tool e.g., NPI Q¹³² • Assess for other potential causes of behaviors (e.g., drug toxicity, medical or psychiatric comorbidity)
Step 5: Identify caregiver and assess needs	Identify primary caregiver and assess adequacy of family and other support systems	<ul style="list-style-type: none"> • Identify caregiver(s) and establish collaboration • Assess health of primary caregiver • Refer to psychologist, social worker, or other healthcare resources as needed

Galvin & Sadowsky, J Am Board Fam Med, 2012
Cummings, et al, Ann Clin Transl Neurol, 2015

A practical algorithm for managing Alzheimer's disease: what, when, and why?

Jeffrey L. Cummings¹, Richard S. Isaacson², Frederick A. Schmitt³ & Drew M. Velting⁴

¹Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, Nevada and Cleveland, Ohio

²Weill Cornell Medical College, New York, New York

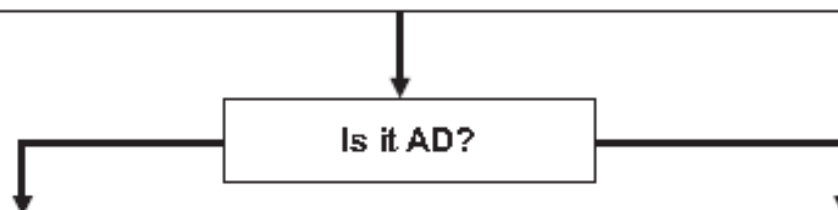
³Sanders Brown Center on Aging, University of Kentucky Medical Center, Lexington, Kentucky

⁴Novartis Pharmaceuticals Corporation, East Hanover, New Jersey

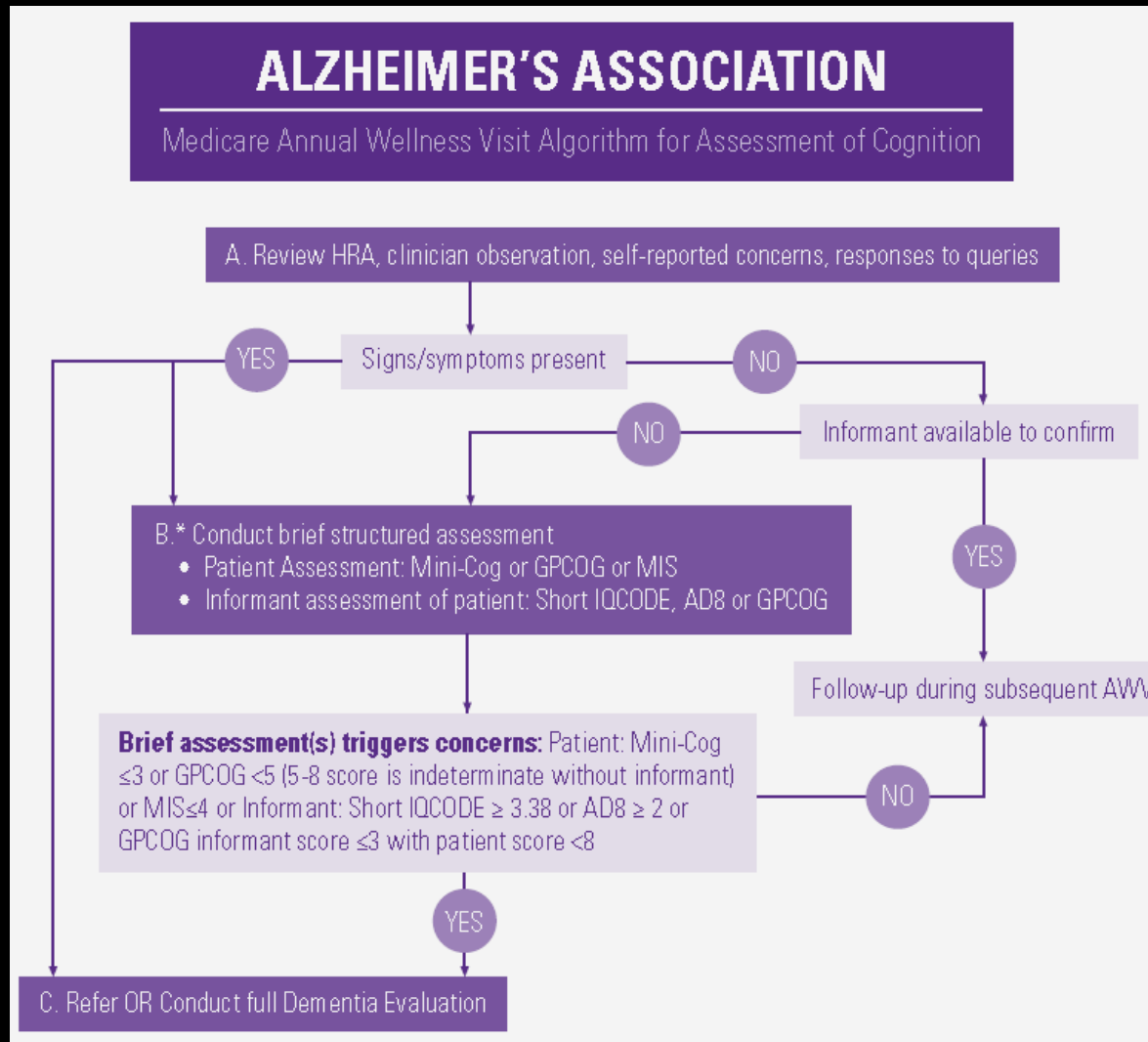
Is dementia present? i.e. cognitive and behavioral (neuropsychiatric) symptoms that

1. Interfere with the ability to function at work or at usual activities; and
2. Represent a decline from previous levels of functioning and performing; and
3. Are not explained by delirium or major psychiatric disorder.

- Cognitive impairment is detected and diagnosed through a combination of (1) history-taking from patient and a knowledgeable informant and (2) an objective cognitive assessment
- The cognitive or behavioral impairment involves ≥ 2 of the following domains:
 - Impaired ability to acquire and remember new information
 - Impaired reasoning and handling of complex tasks, poor judgement
 - Impaired visuospatial abilities
 - Impaired language functions
 - Changes in personality, behavior, or comportment



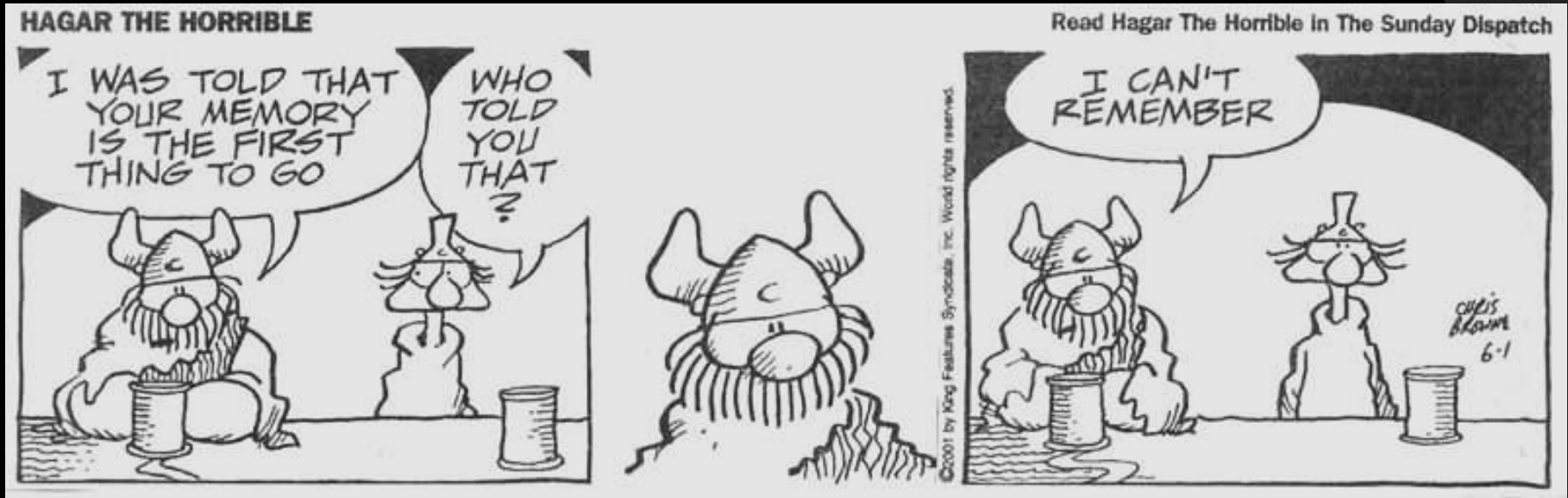
Medicare Annual Wellness Visit





**"This means something
but I can't remember what!"**

Subjective memory complaints (SMC) are self-identified deficits in memory



SMC are common among adults aged 60+

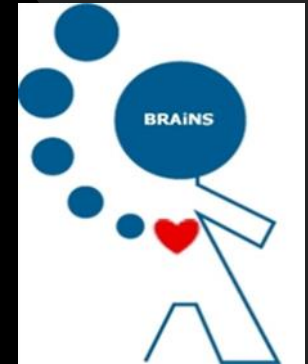
Nurses Health Study: 56%

Rotterdam: 19%

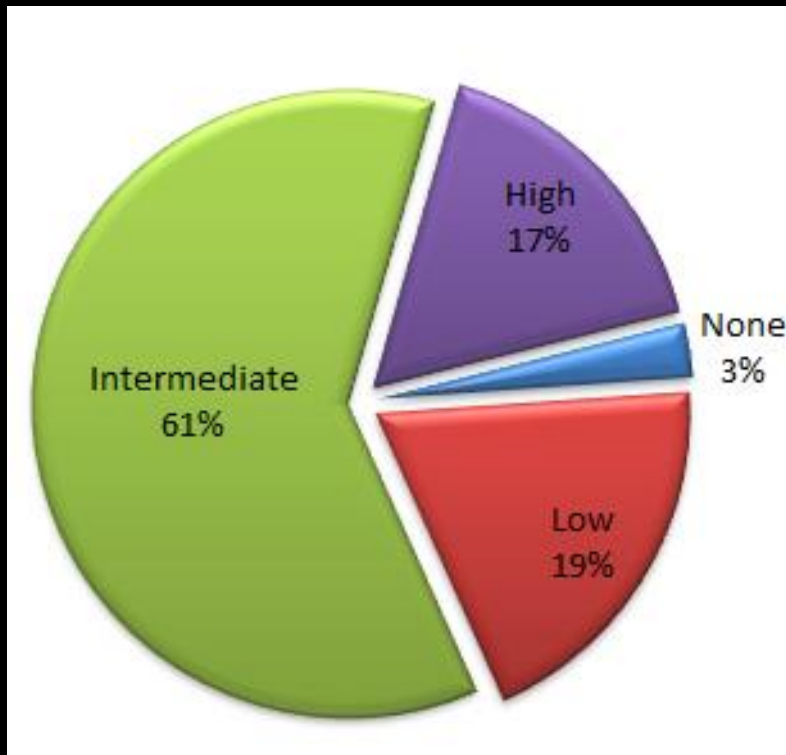
PREADViSE: 22%

BRAiNS: 56%

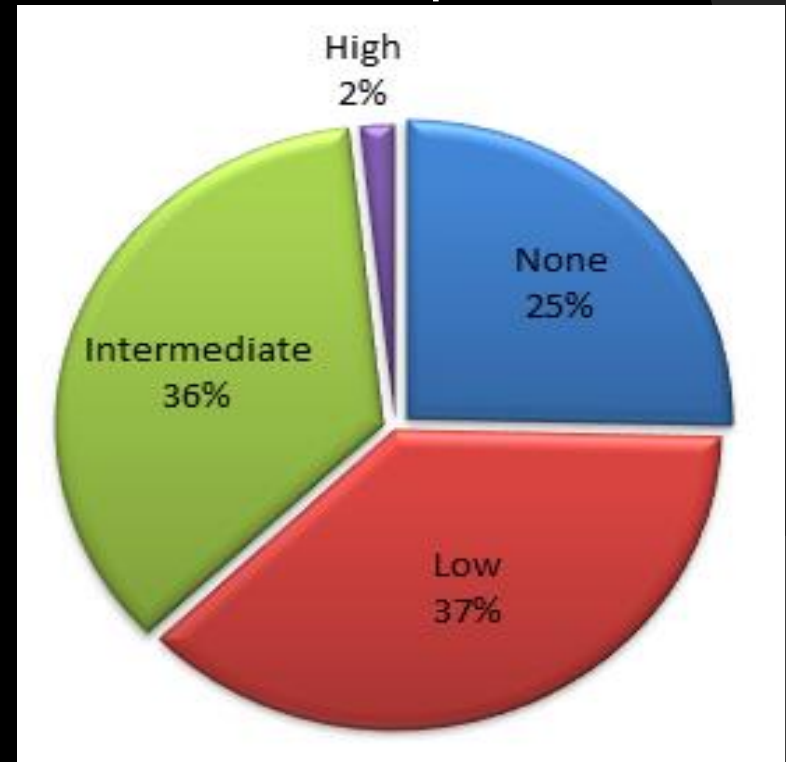
AD Pathologies in SMC



SMC with Impairment

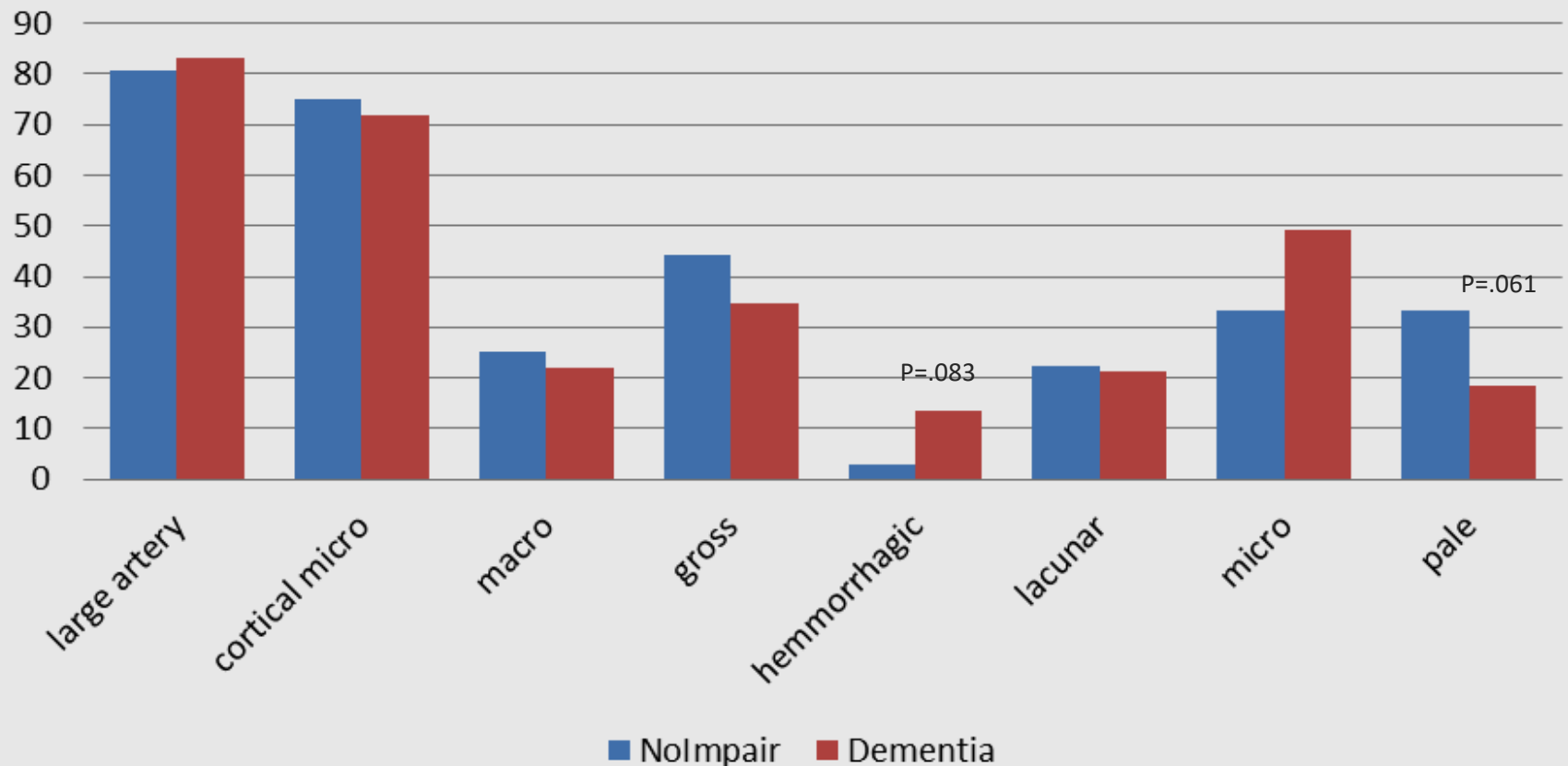


SMC NO Impairment

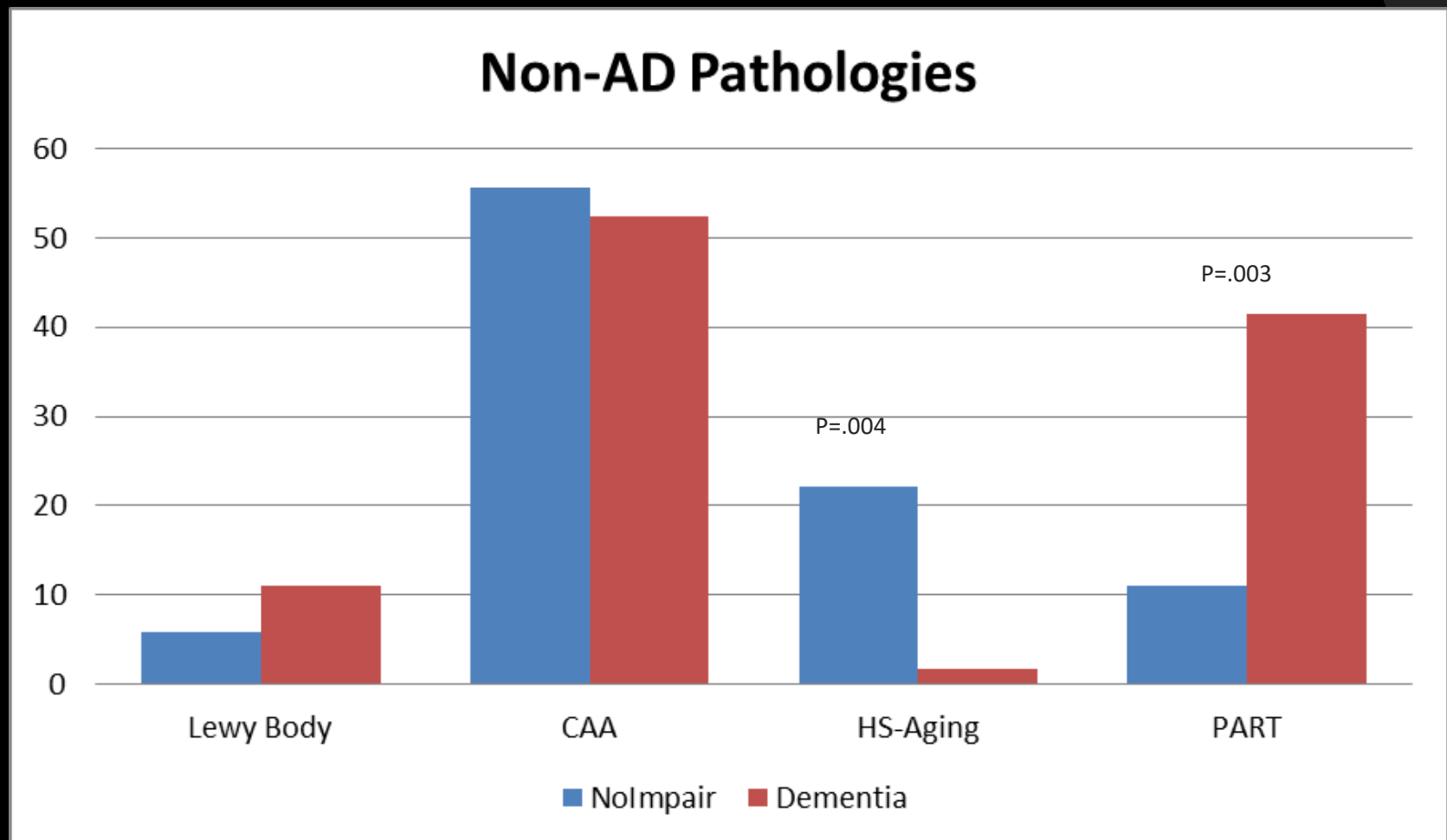


SMC & Cerebrovascular Disease ¹

Infarcts



SMC & Other Brain Disorders ₂

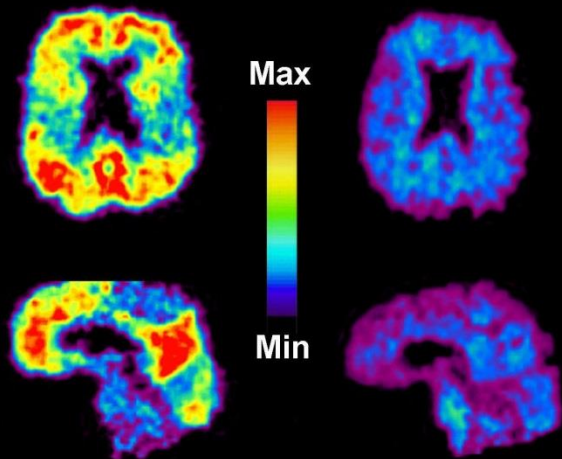


Implications of SMC

- Over half of volunteers have Subjective Memory Complaints during follow-up
- SMC accounts for most MCI/dementia transitions (OR = 2.8)
- **SMC is no guarantee** MCI/dementia will occur
- Identified risks affect the time and probability for transitions to occur
- Autopsy results indicate a subset of individuals (but not all) have AD type pathology
- Can inform the design of future prevention trials

AD

Control

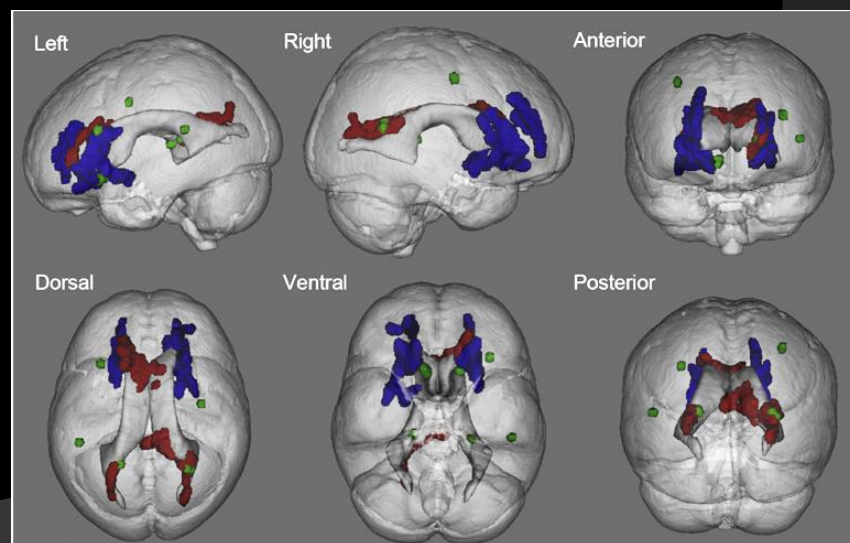
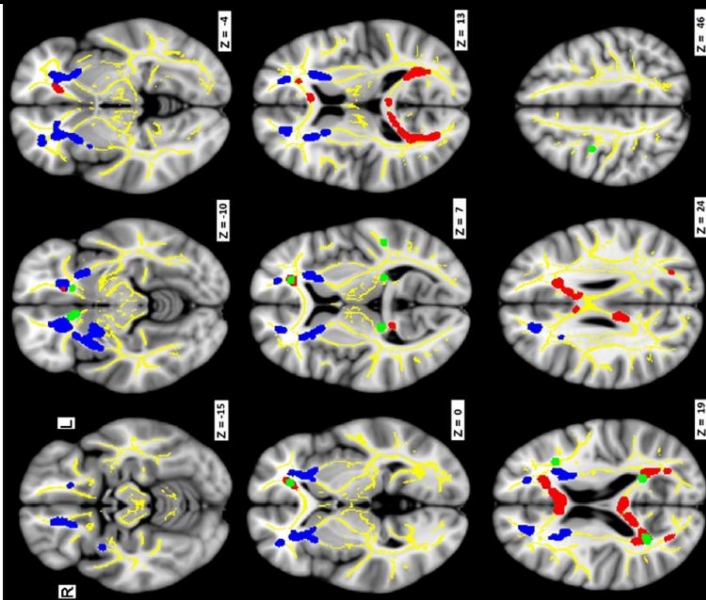
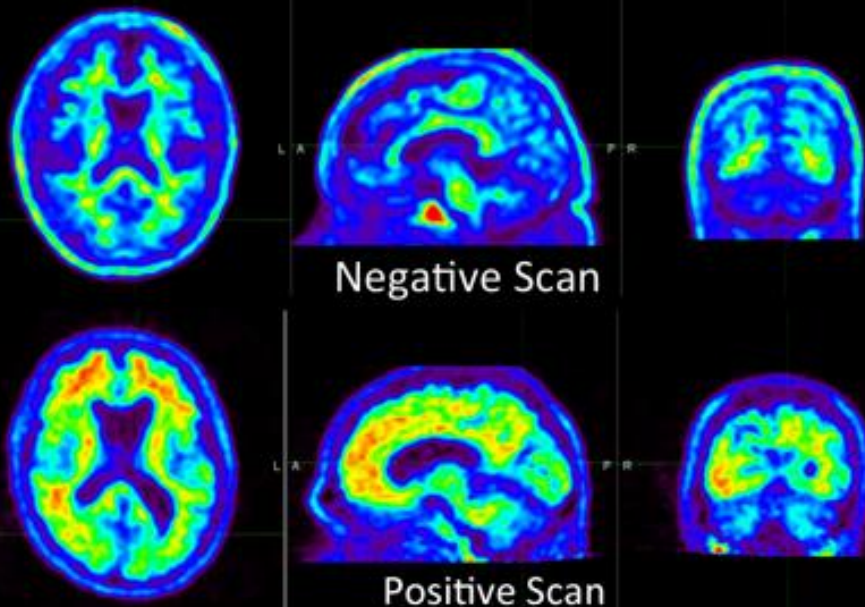


PiB PET SCANS



University of Pittsburgh
PET Amyloid Imaging Group

ADNI Scans



Are More Effective AD Therapies On The Horizon?



www.alz.org (Alzheimer's Association)
www.nia.nih.gov/alzheimers (ADEAR)

Research Team:

Richard J. Kryscio & Frederick A. Schmitt (PI s)
Erin Abner, David Fardo, Peter Nelson, Gregory Jicha

