

ALZHEIMER: I NUOVI ORIZZONTI DELLA CURA  
AFFRONTARLO PRESTO AFFRONTARLO INSIEME



*Biella, 29 settembre 2010*

# La demenza si può predire, prevenire e quindi trattare



Innocenzo Rainero, MD PhD  
Associate Professor of Neurology  
Aging Brain and Memory Clinic  
Department of Neuroscience  
University of Torino, Italy

CALVES' HEADS AND BRAINS OR A PHRENOLOGICAL LECTURE.



What's Alzheimer's disease?

Do we need early diagnosis?

Prevention for Alzheimer?

Ladies and Gentlemen

CONCLUDING ADDRESS

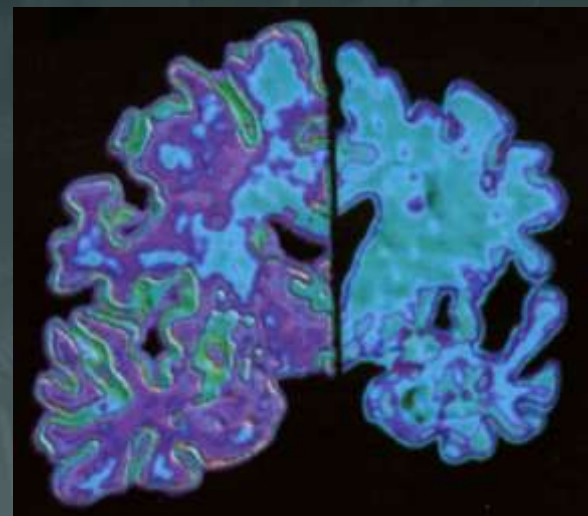
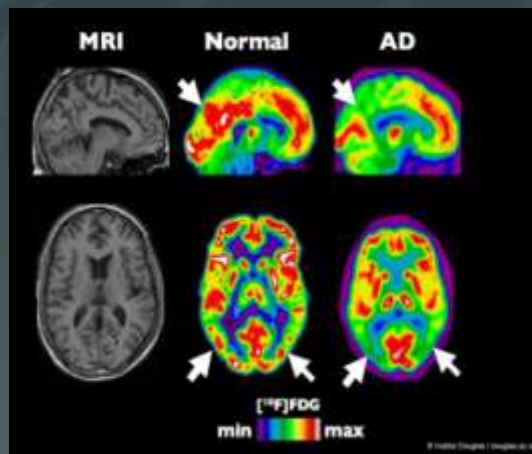
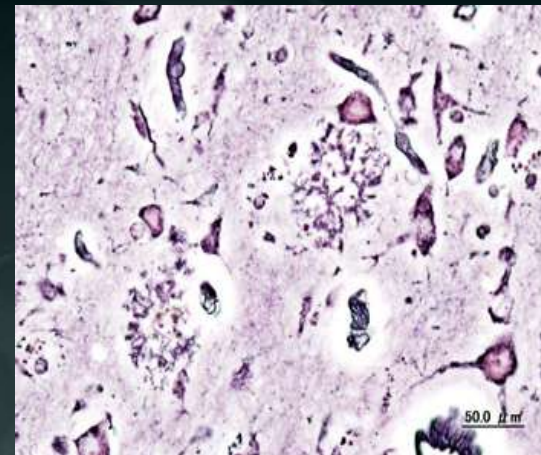
Having thus concluded the hundred and thirty ninth article under the Head or Section of Propensities. I shall bid my leave until the next lecture by clearly elucidating in my own person an instance of Due Proportion of Faculties. Talkativeness with Gall, standing First, and further beg to testify, beyond all doubt, or shadow of contradiction, that on the Cranium of this highly gifted and scientific Audience the Organ of Implicit Faith Under Evident Contradictions, stands beautifully developed to a surprising and prominent degree. Dear Ladies, Worthy Gentlemen, adieu.



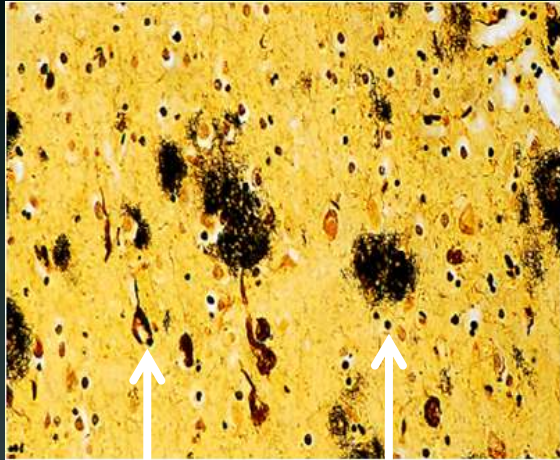
# "Let's Rethink Alzheimer's Disease"



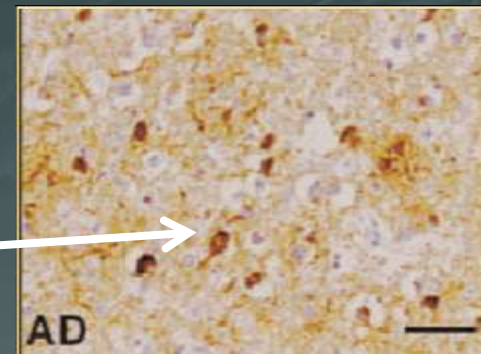
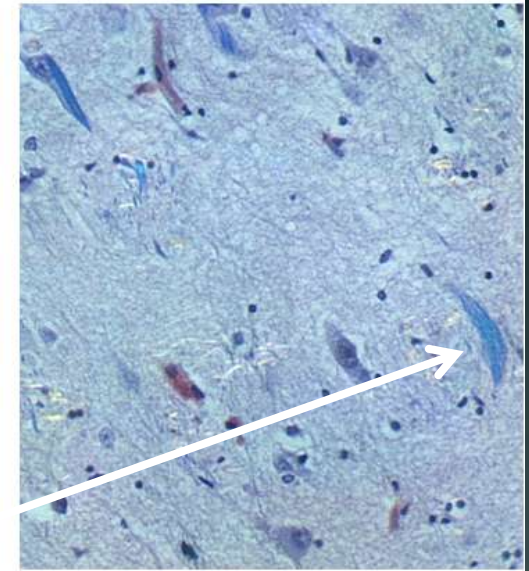
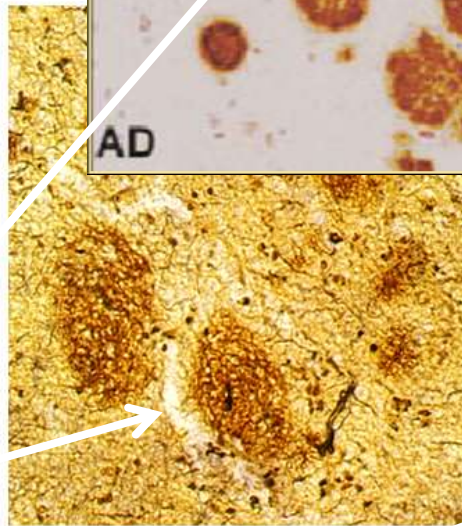
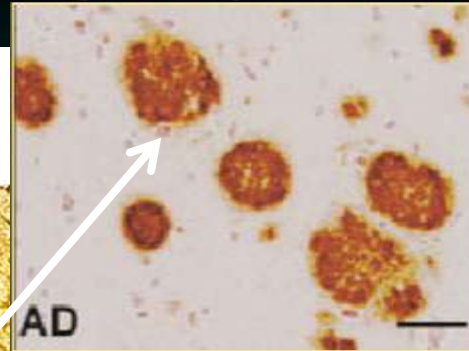
The Huffington Post, October 11, 2013



# AD as “Paradigm” Proteopathy



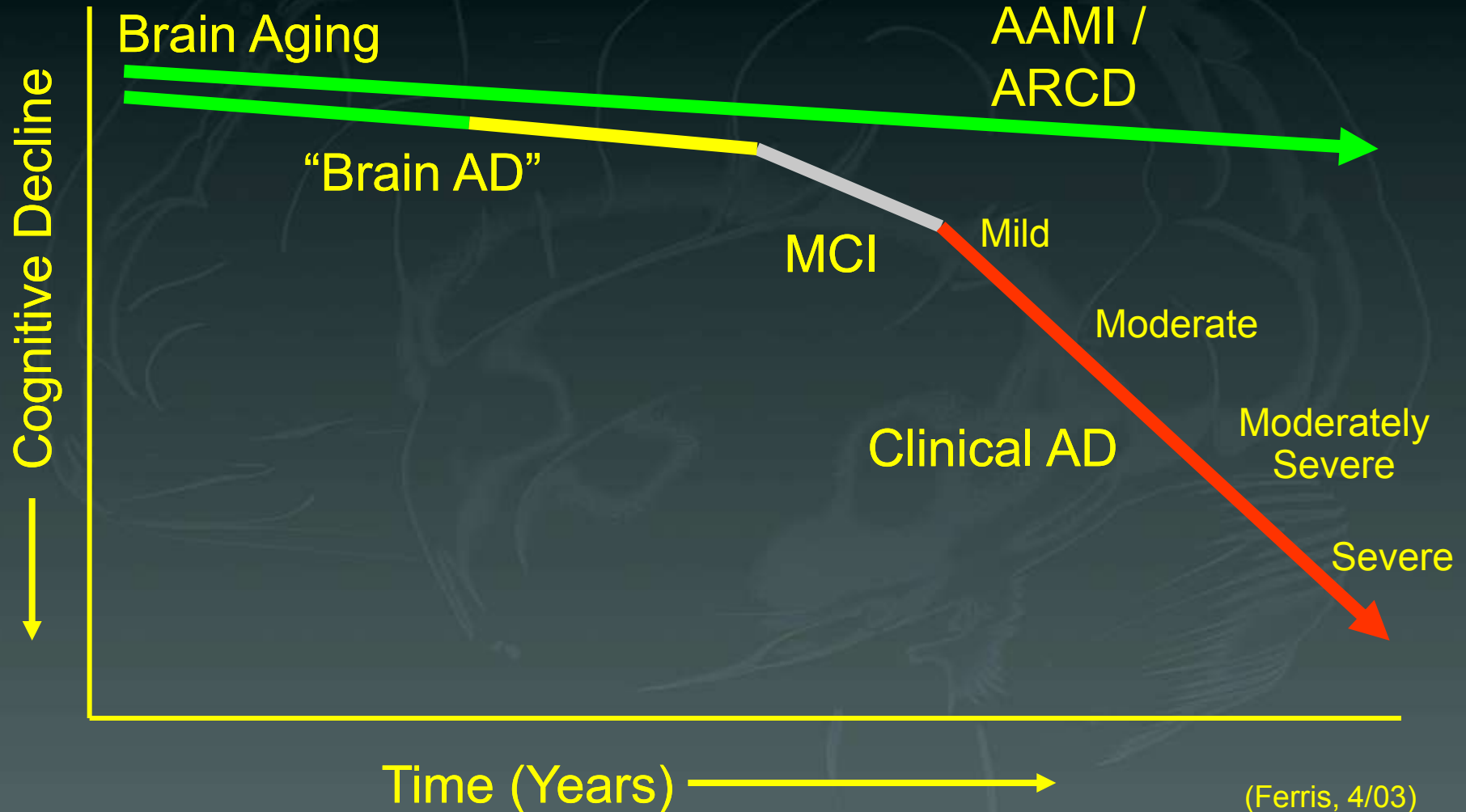
**Plaque**

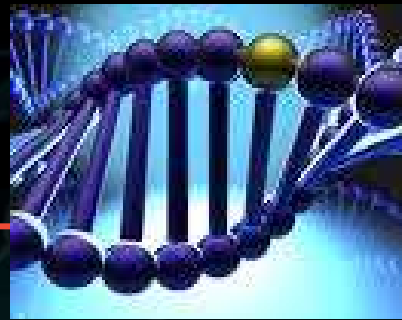
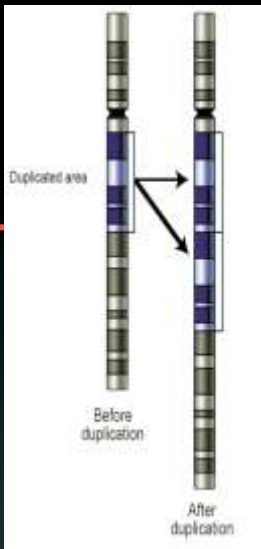


**Tangles**

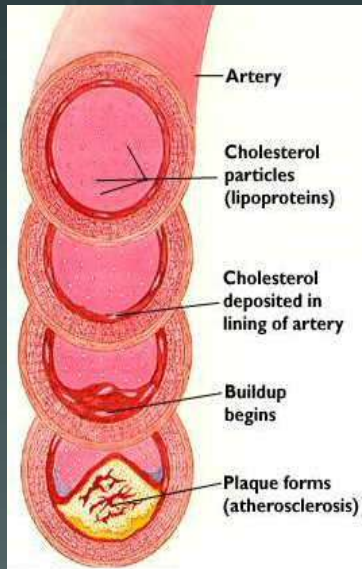


# The long way to Alzheimer





**“Alzheimer’s disease and related dementias are multifactorial diseases, due to an interaction of genetic and environmental risk factors”**



# Risk Factors

## Non-Modifiable

- Age >65
  - 5 yrs = double risk
- Gender
  - Female Survival?
- Family History
- Ethnicity
- Genetics
  - ApoE-4
  - ↑ risk

## Modifiable

- High Blood Pressure
- High Cholesterol
- Obesity
- Diabetes
- Smoking
- Head Trauma
- Exercise
- Nutrition
- Education



# NIA-AA diagnostic guidelines for Alzheimer's disease

*Alzheimer's & Dementia 2011;7:257-292*



- Preclinical stages of Alzheimer's disease
  - Mild cognitive impairment (MCI) due to Alzheimer's disease
  - Dementia due to Alzheimer's disease

National  
Institute  
on Aging



END  
ALZ

alzheimer's  
association™



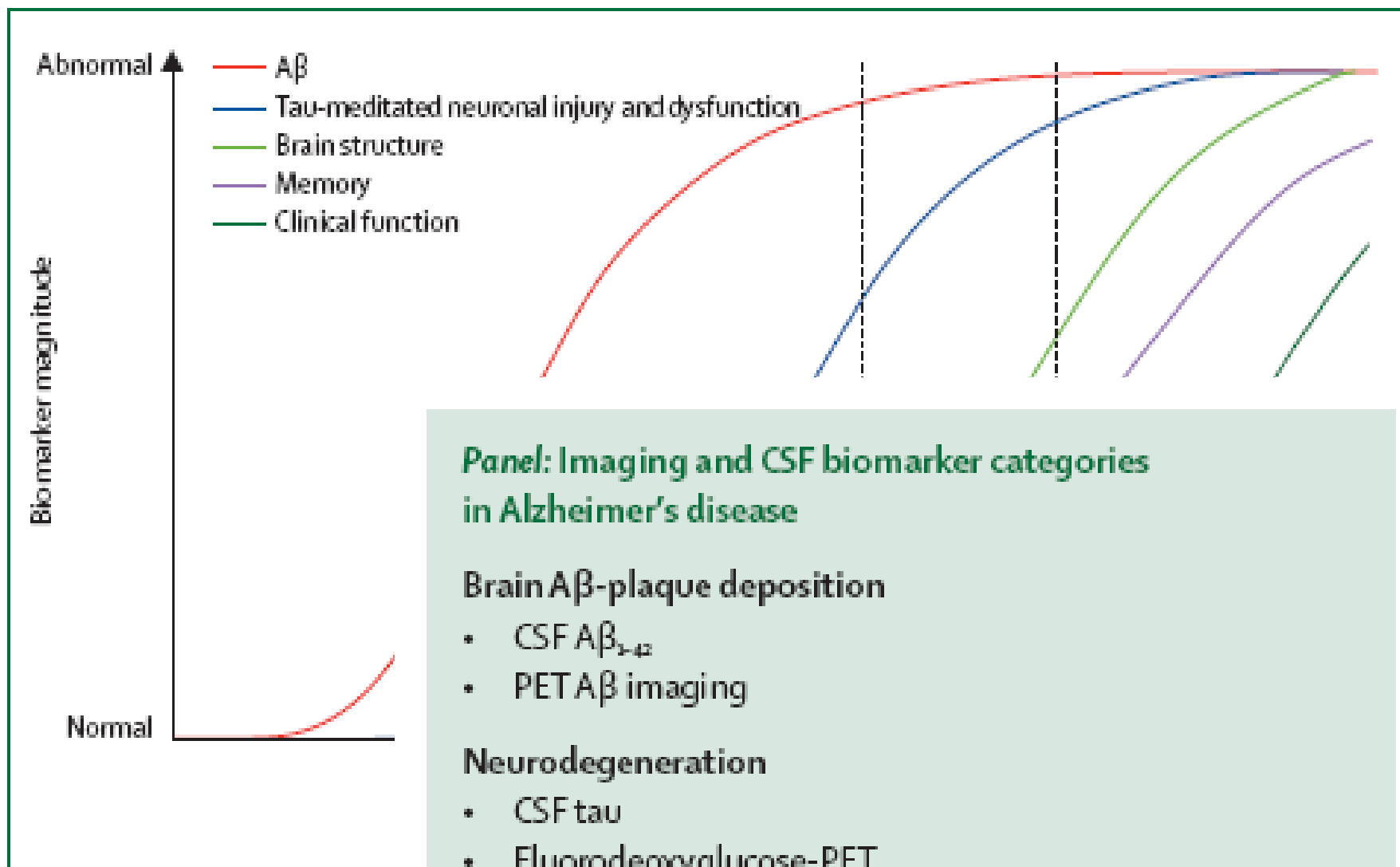
To be discussed:

# Early diagnosis: the biomarkers

---



- CSF examination.
- Hippocampal volumetry.
- FDG-PET.
- Amyloid PET
- Genetic testing
- Neuropsych testing
- National and International guidelines



**Panel: Imaging and CSF biomarker categories in Alzheimer's disease**

**Brain Aβ-plaque deposition**

- CSF Aβ<sub>1-42</sub>
- PET Aβ imaging

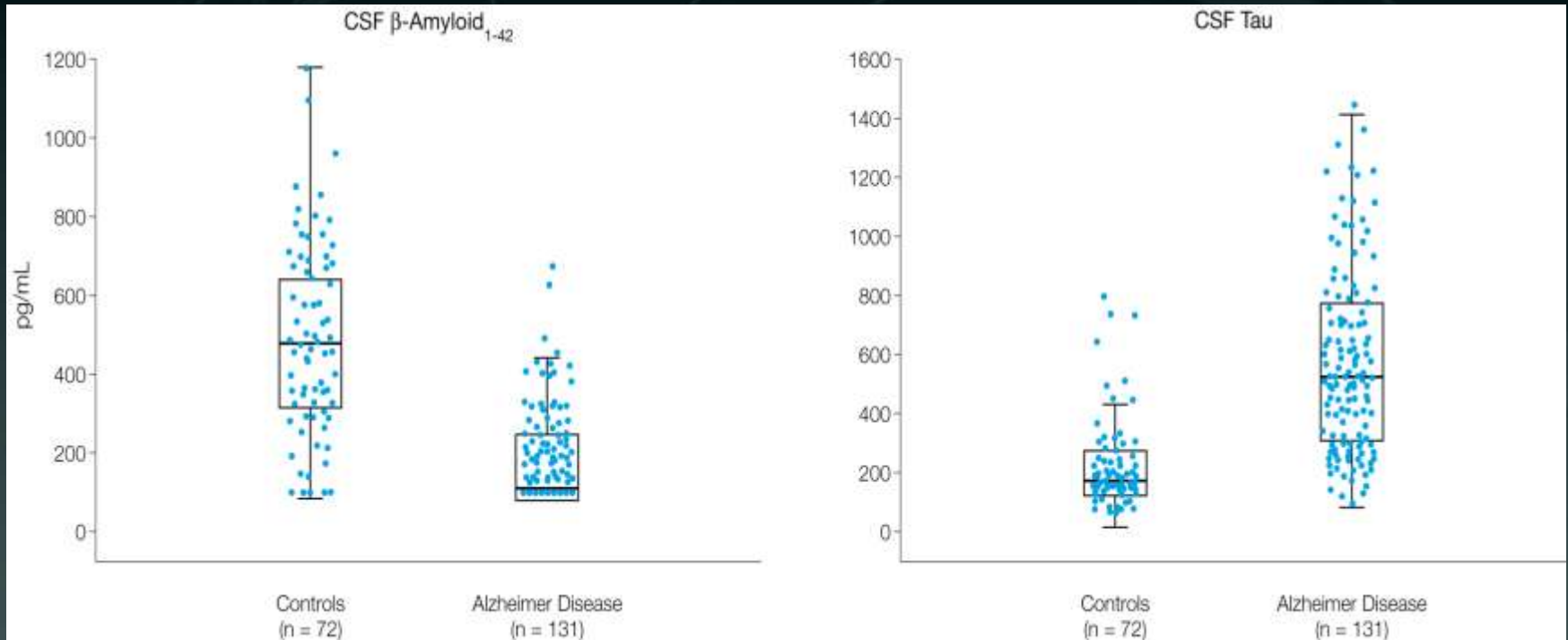
**Neurodegeneration**

- CSF tau
- Fluorodeoxyglucose-PET
- Structural MRI

Aβ= β-amyloid.

**Figure 2: Dynamic biomarkers** | Aβ is identified by CSF Aβ<sub>1-42</sub> or PI CSF tau or fluorodeoxyglucose-<sup>18</sup>F cognitive impairment.

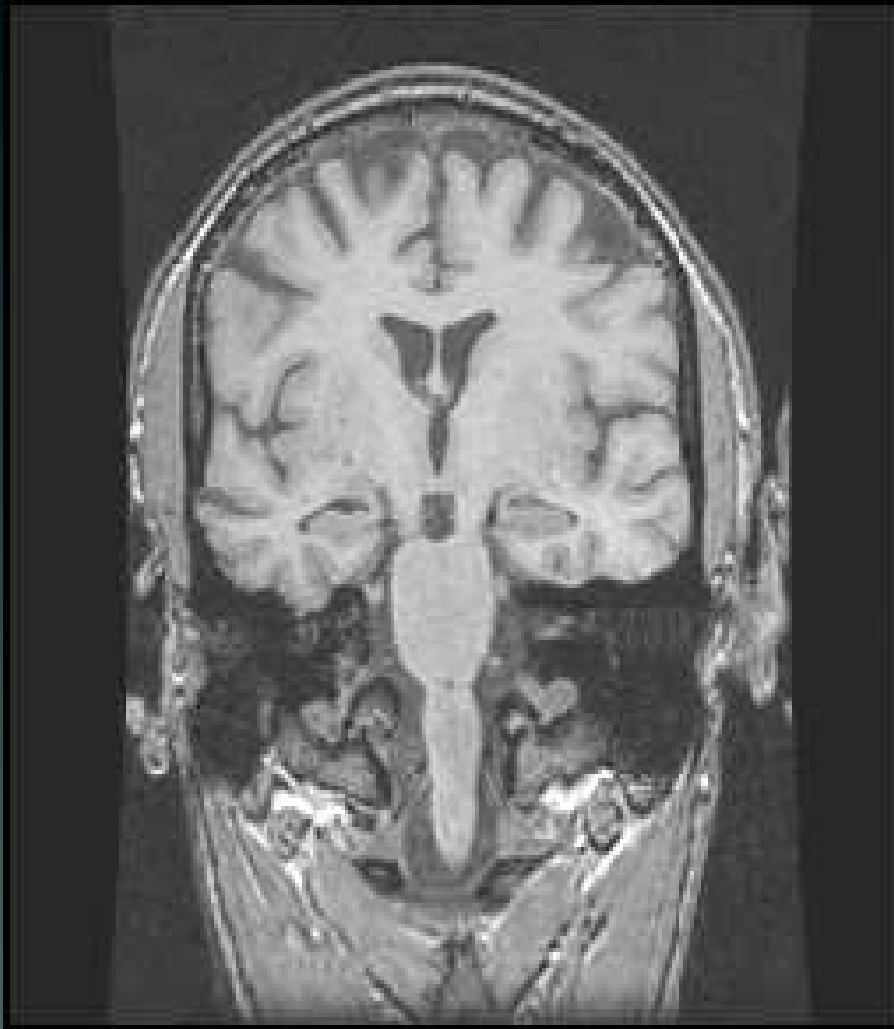
# CSF findings in dementia



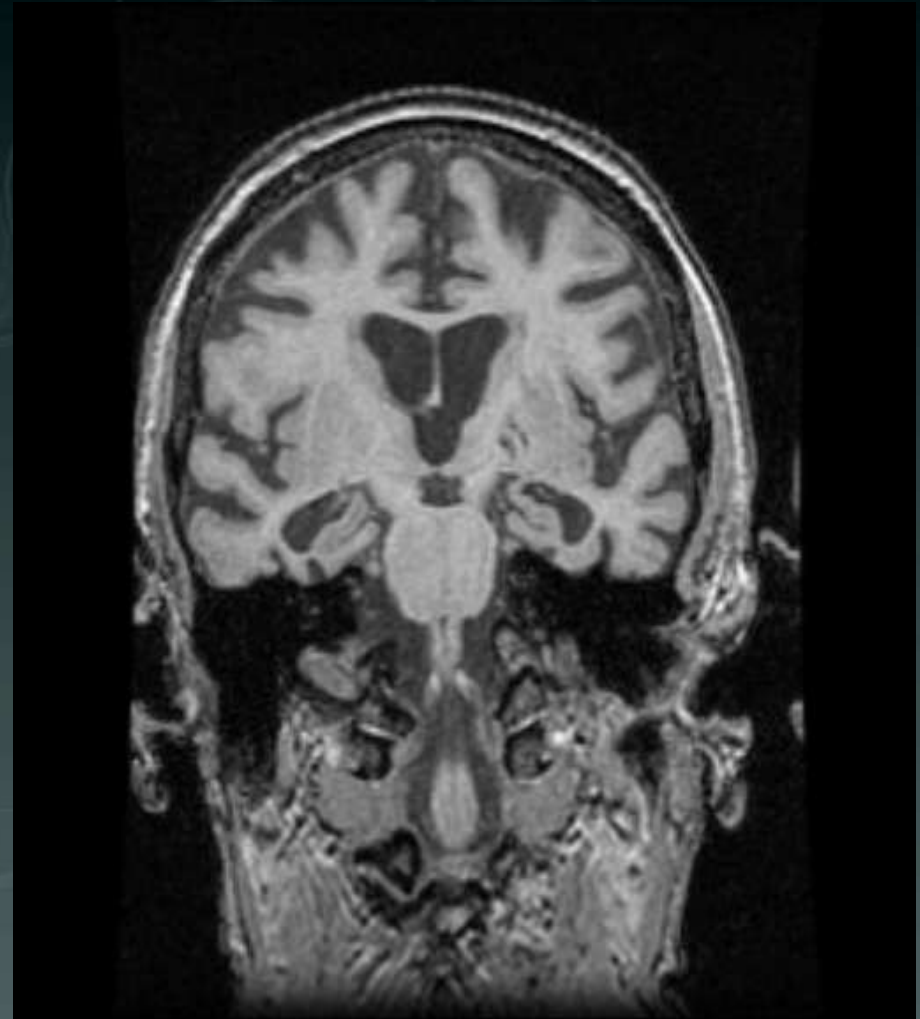
**Decreased  $\beta$ -Amyloid<sub>1-42</sub> and Increased Tau Levels in Cerebrospinal Fluid of Patients With Alzheimer Disease**



# MRI findings in dementia



**Normal**



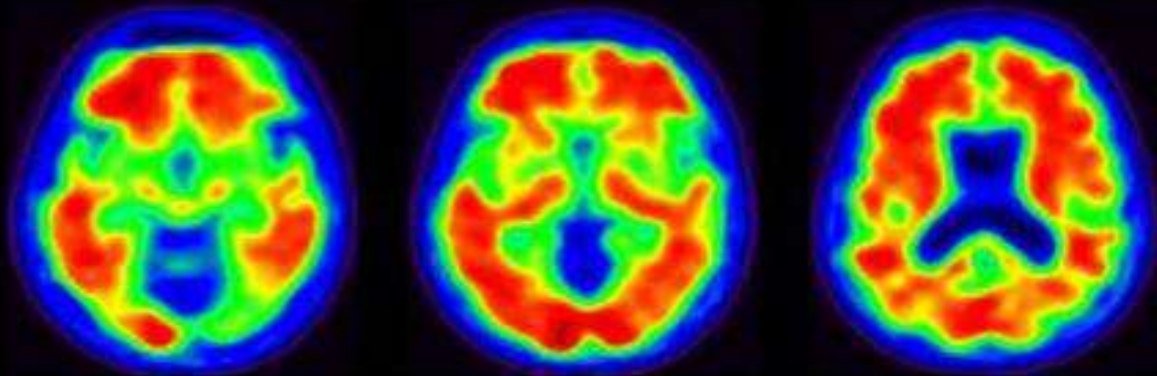
**AD**

# PET in Alzheimer's disease

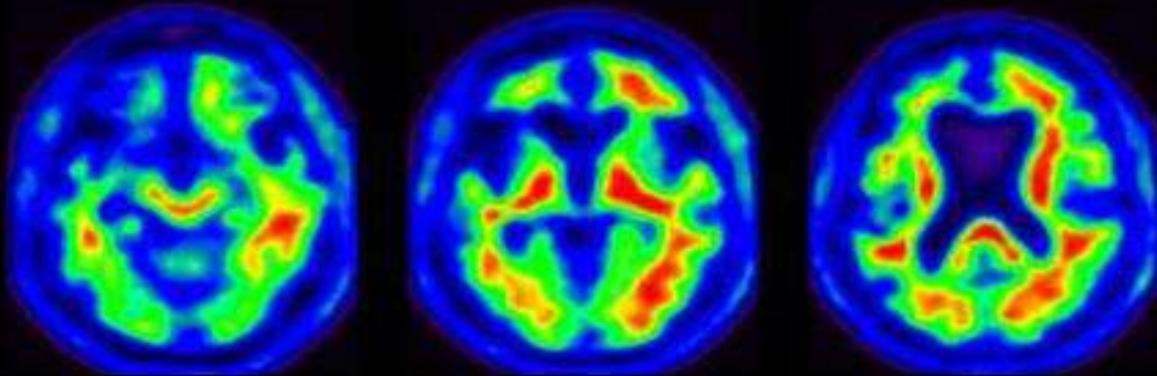


## Amyloid PET Imaging in Alzheimer's Disease and Frontotemporal Dementia

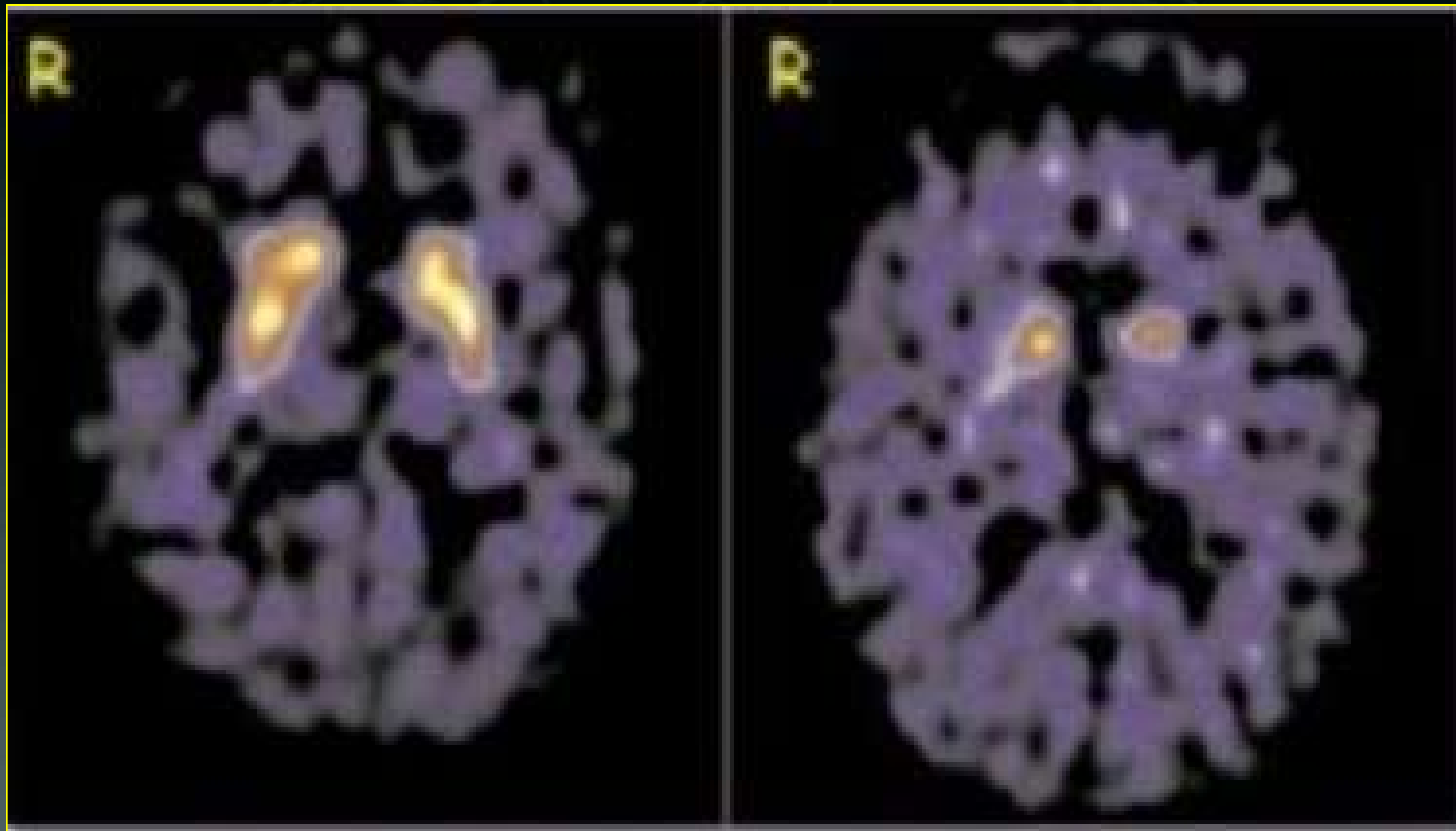
Alzheimer's Disease:  
Amyloid PET positive



Frontotemporal  
Dementia:  
Amyloid PET negative



# DAT scan and Alzheimer's disease



AD

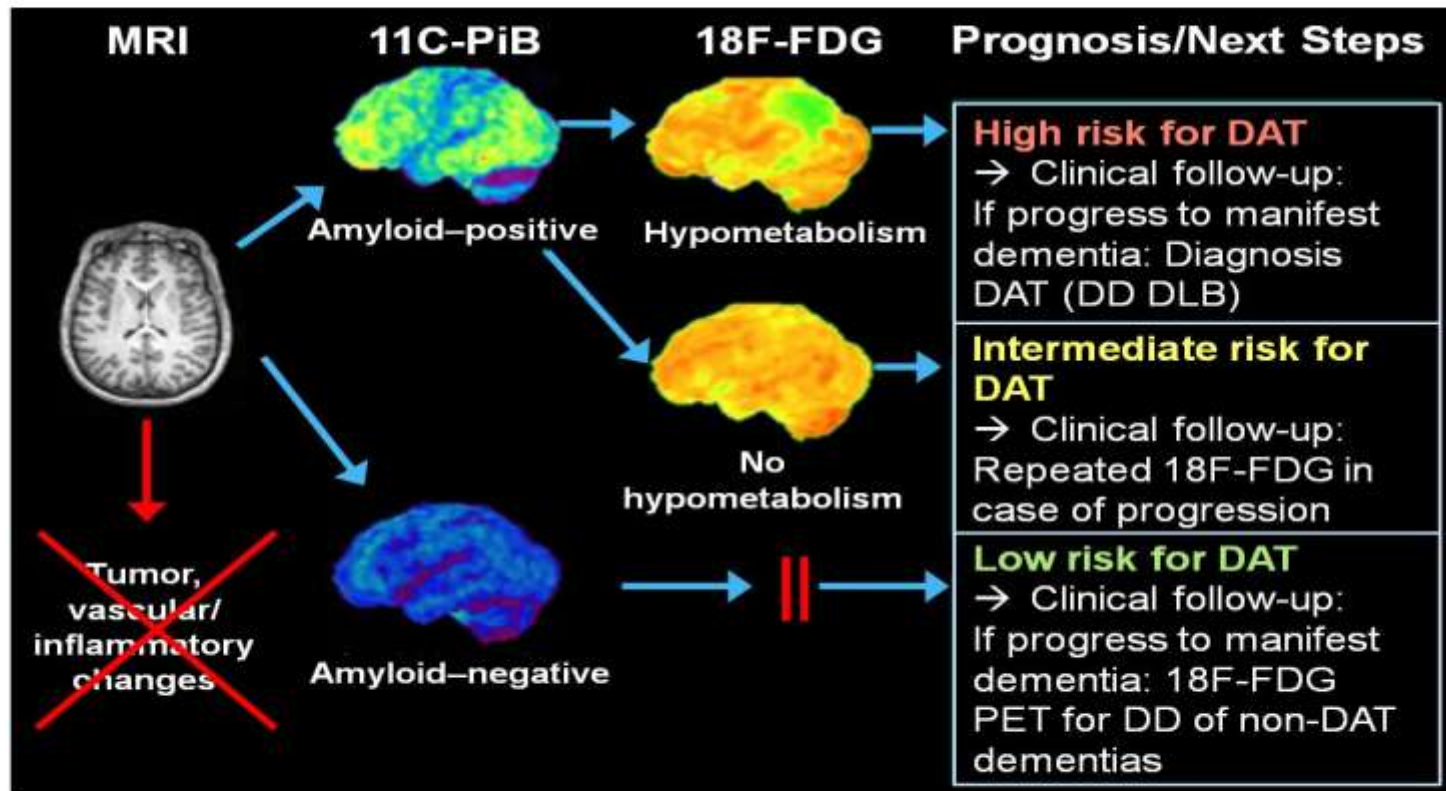
DLB



# Biomarkers: all together or step by step?



## MCI: Appropriate Stage of the Disease for Molecular Imaging



# Guidelines for early diagnosis of AD



**Clinics Review Articles**

MEDICAL CLINICS OF NORTH AMERICA

---

## Early Diagnosis and Intervention in Predementia Alzheimer's Disease

---

**EDITORS**  
José L. Molinuevo  
Jeffrey L. Cummings  
Bruno Dubois  
Philip Scheltens

---

MAY 2013

**Psicogeriatría**  
ANNO 2 - SUPPLEMENTO - NUMERO 1 - GIUGNO-APRILE 2013

**Raccomandazioni dell'Associazione Italiana di Psicogeriatría (AIP) e della Società Italiana Neurologia delle Demenze (SINDEM) sulla diagnosi precoce della Malattia di Alzheimer**

**ASSOCIAZIONE ITALIANA DI PSICOGERIATRÍA**

**Direttore Editoriale**  
Marco Toloschi

**Comitato Editoriale**  
Carlo Caffarelli  
Riccardo Marchisani  
Flavio Pilo  
Umberto Sisti

**Consulente**  
Comitato Scientifico  
Luigi Ferrante

**Segreteria di Redazione**  
Angela Bianchi  
Vincenzo Calamia

**Comitato Scientifico**  
Giorgio Anzani  
Pierluigi Antonelli Invernizzi  
Fabrizio Aiani  
Giovanna Barbagallo  
Lidia Barozzi  
Giovanna Bellini  
Carlo Adriano Baggio  
Enrico Bricoli  
Anna Maria Cacioppo  
Fabio Carlini  
Alberto Cejudo  
Enrico Conzani  
Antonio Ciarrocca  
Luis Pastor De Vries  
Fabio Di Lorenzo  
Anita Falbo  
Antonio Falco  
Giovanna Ferrante  
Nicola Ferrara  
Giuseppe Fichera  
Maurizio Formica  
Ludovico Fratini  
Piero Galea  
Giuseppe Galli  
Maurizio Gasparini  
Guido Gatti  
Antonio Giarola  
Maurizio Invernizzi  
Christian Ianni  
Daniela Ianni  
Giovanna Ippolito  
Marta Los Luberski  
Alberto Marchi  
Pierluigi Marchisani  
Franzetta Marzocchi  
Enrico Muzio  
Claudia Nardi  
Maurizio Nanni  
Luis Nanni  
Giovanna Nanni  
Pierluigi Odier  
Alessandro Padelloni  
Luigi Pampaloni  
Nicola Ranata Pini  
Alfonso Piro  
Piero Francesco Piro  
Renzo Rocchi  
Michele Santoro  
Francesco Scapellato  
Domenico Scarpino  
Luca Scarpino  
Carlo Serrati  
Sandro Terzi  
Gianfranco Tardito  
Anna Laura Tassinari  
Gabriele Tassi  
Claudio Vignati  
Tiziana Vignati  
Oreste Zaveri  
Giovanni Zuffanti

**Documenti dell'Associazione Italiana di Psicogeriatría**

# THE IMPORTANCE OF EARLY-DIAGNOSIS

---



- Early diagnosis allows people with dementia and their families to receive timely practical information, advice and support.
- Early therapeutic interventions can be effective in improving cognitive function, treating depression, improving caregiver mood, and delaying institutionalization.
- Early detection of dementia provides an opportunity for the individual to adjust to the diagnosis and to participate actively in planning for the future.
- Undetected dementia places older adults at risk for delirium, motor vehicle accidents, medication errors, and financial difficulties.



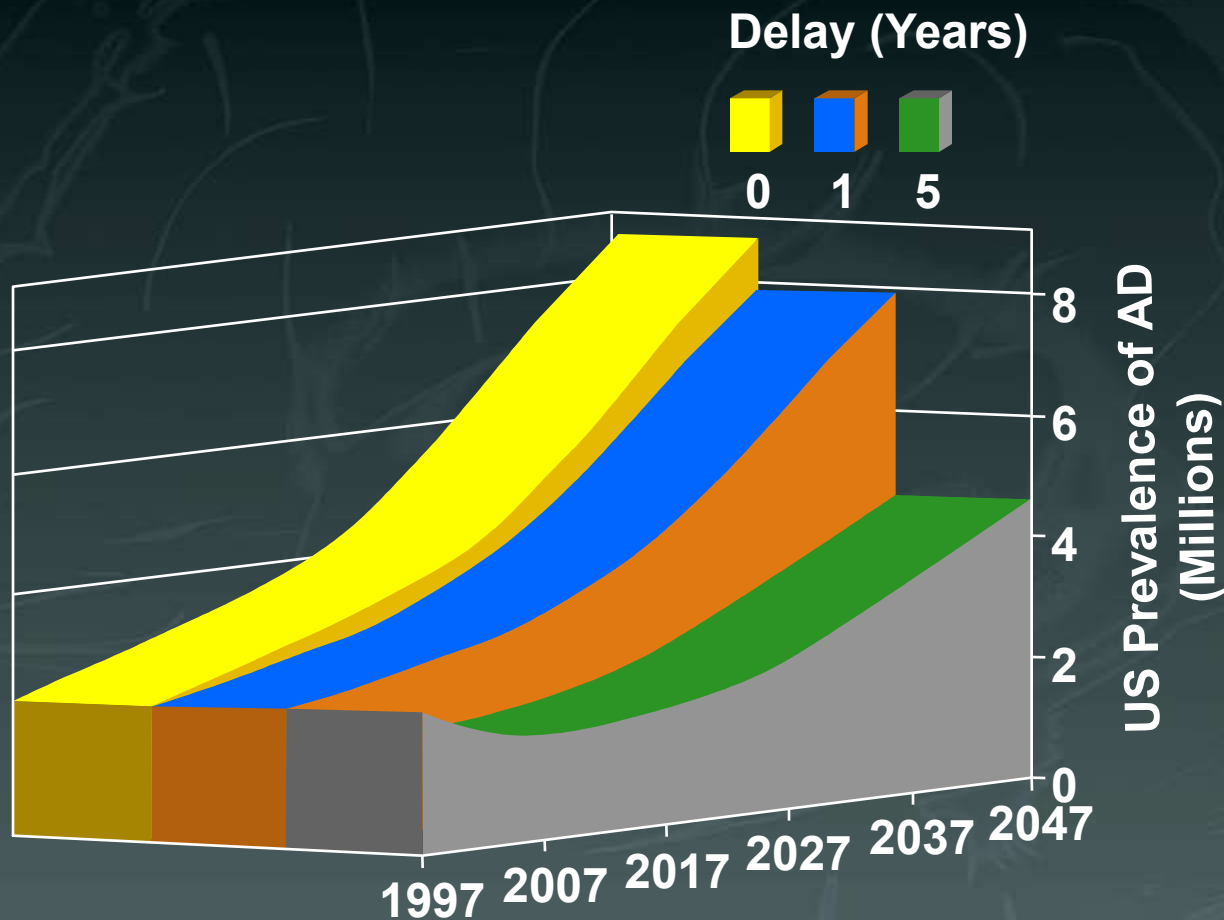
# To be discussed:

# Prevention



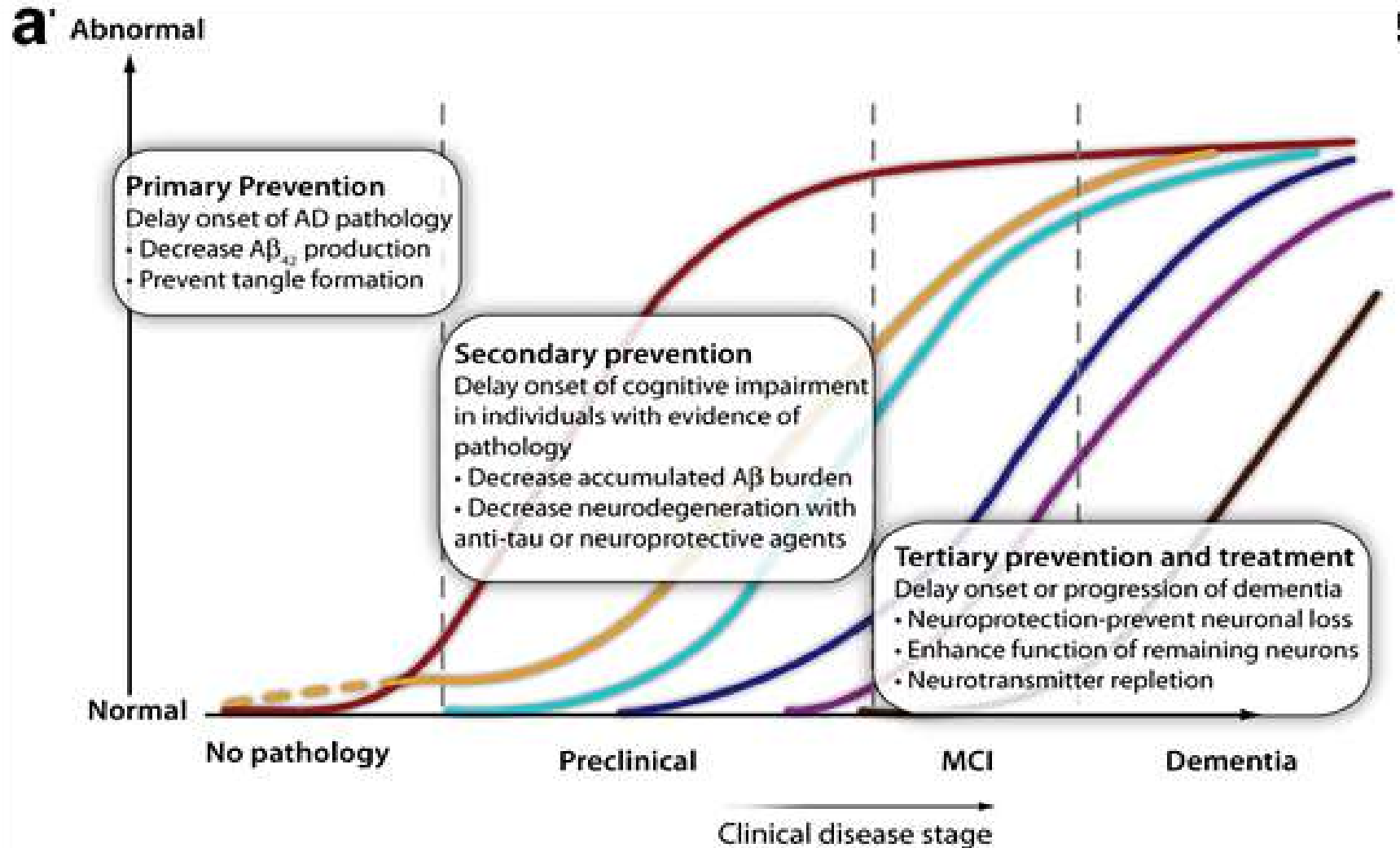
- Potential impact of interventions.
- Primary, secondary and tertiary prevention of AD.
- The timing of interventions.
- Physical interventions.
- Cognitive interventions.
- Psychological and social interventions.
- The FINGER and the my-AHA studies.

# Potential Impact of Interventions to Delay Onset of Alzheimer's Disease

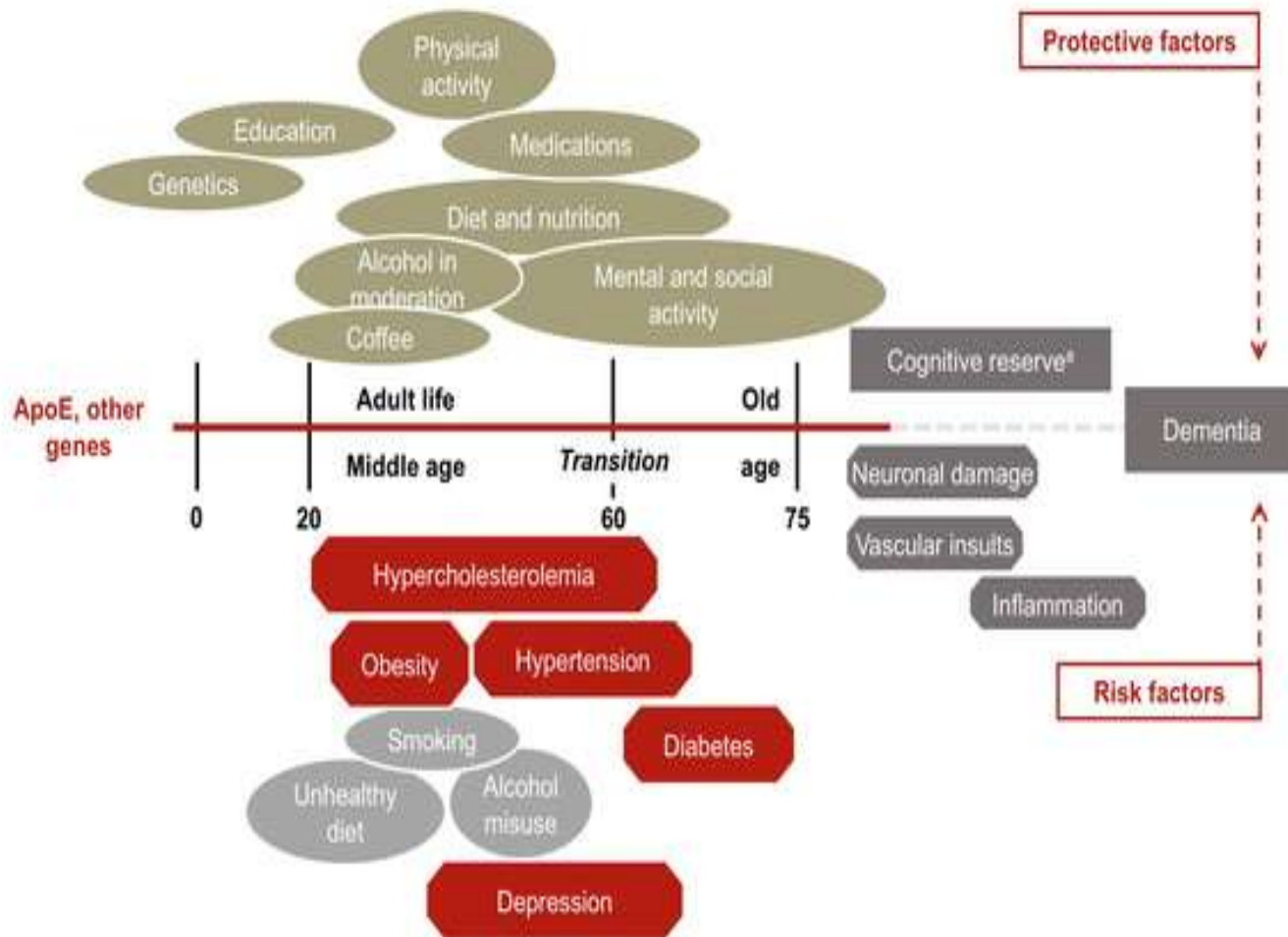


Adapted from Brookmeyer et al, 1998.

# Primary, secondary, and tertiary prevention of Alzheimer's disease



# Accumulation of Alzheimer's disease risk factors over time

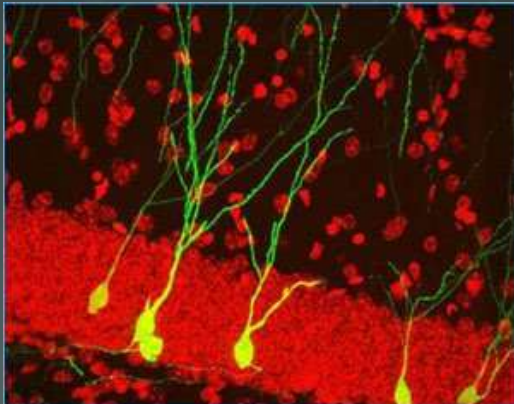


<sup>a</sup>Resilience to neuropathological damage

Jiang et al. *Curr Alzheimer Res* 2013;10(8):852-867; Bendlin et al. *Maturitas* 2010;65(2):131-137; Winblad et al. *Lancet Neurol* 2016;15:455-532



# Physical activity and dementia



**JAMA**<sup>®</sup>

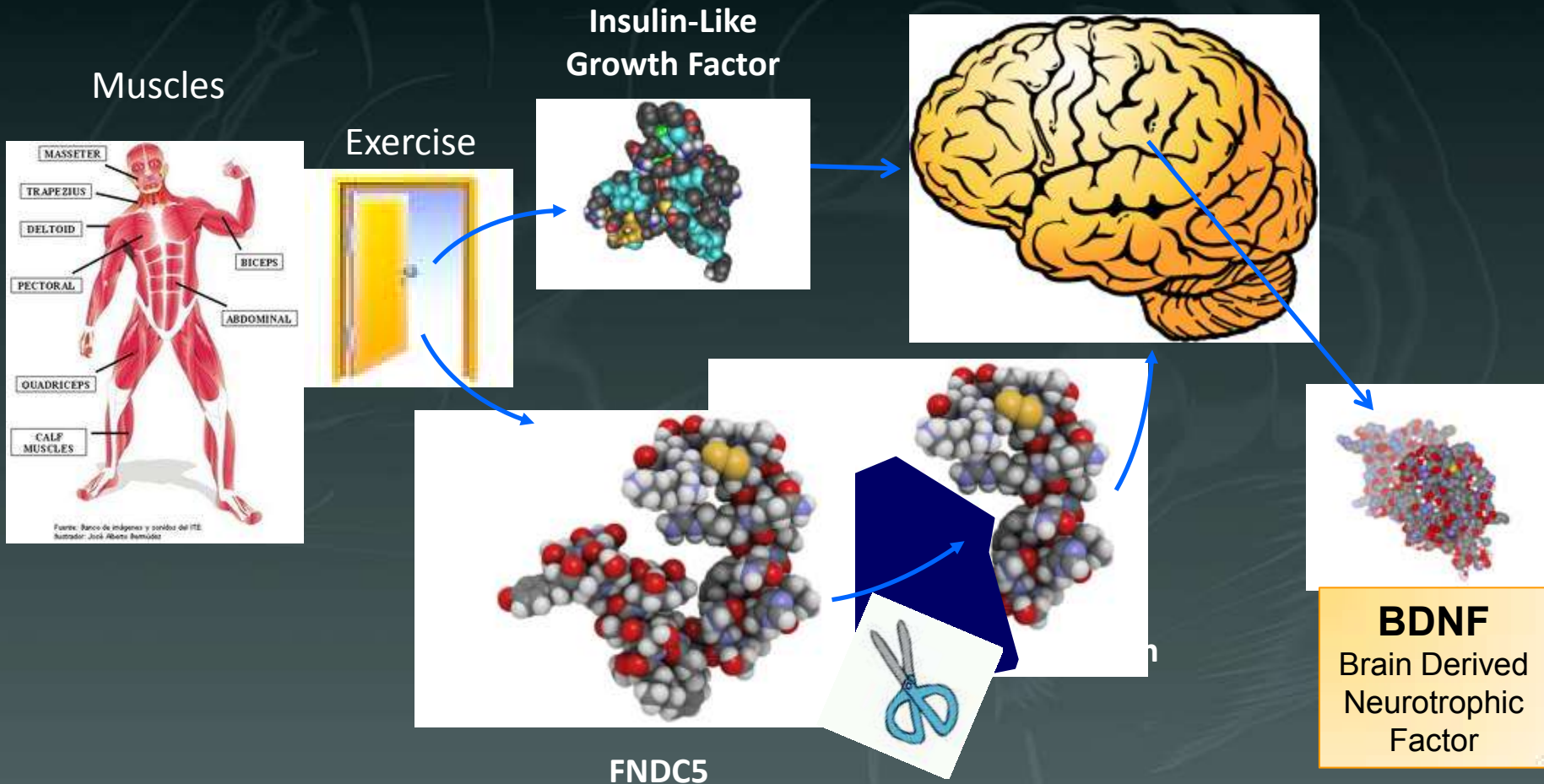
Online article and related content  
current as of September 2, 2008.

**Effect of Physical Activity on Cognitive Function in  
Older Adults at Risk for Alzheimer Disease: A  
Randomized Trial**

Nicola T. Lautenschlager; Kay L. Cox; Leon Flicker; et al.

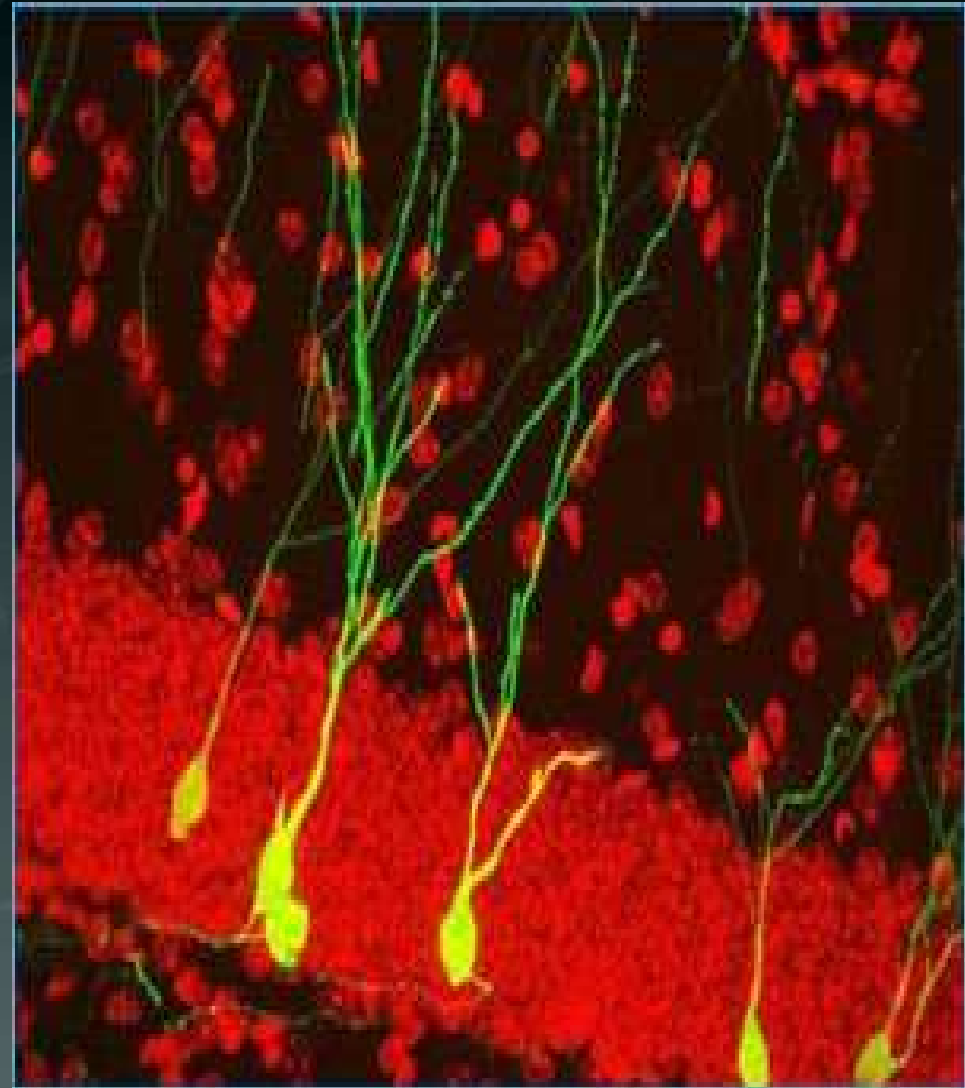
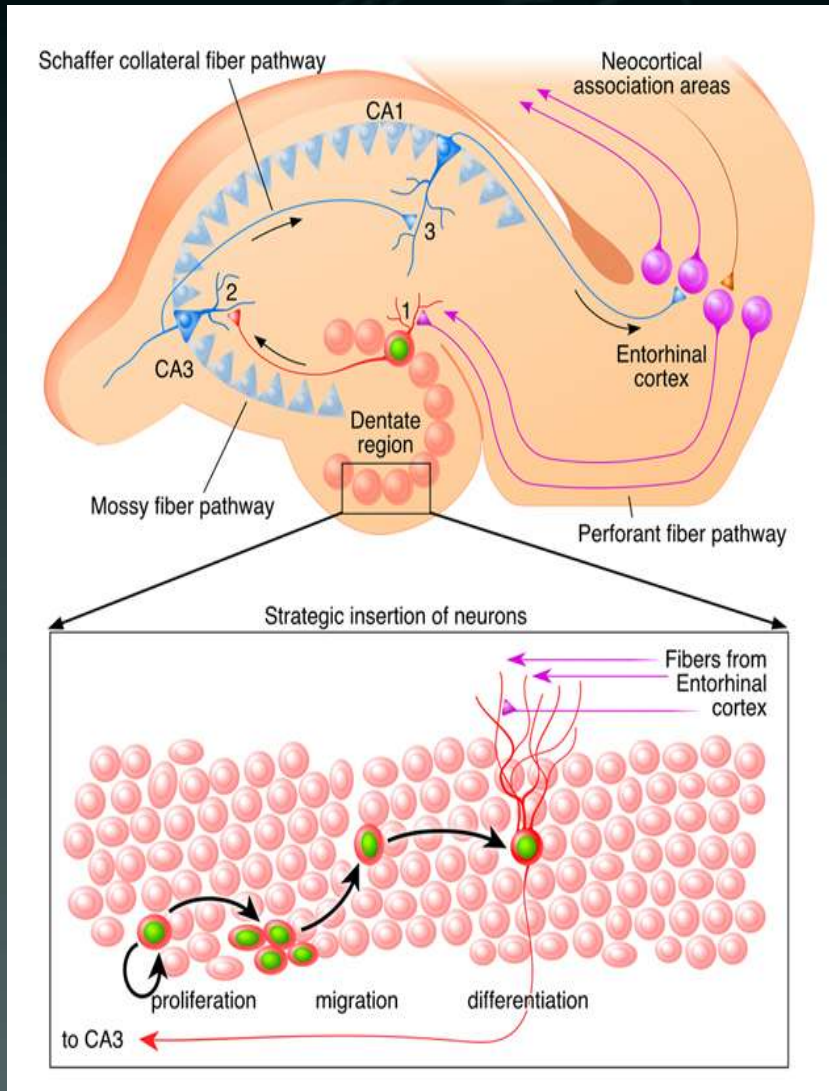
*JAMA*. 2008;300(9):1027-1037 (doi:10.1001/jama.300.9.1027)

# How might exercise protect the brain?

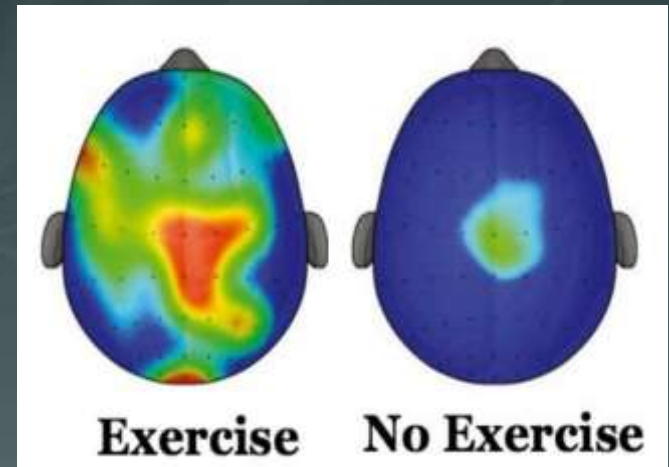
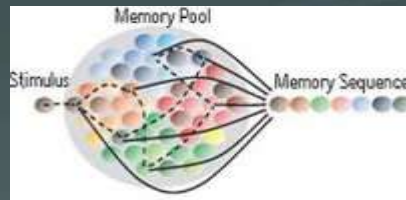




# Neurogenesis in the adult brain: death of a dogma



# Cognition and dementia



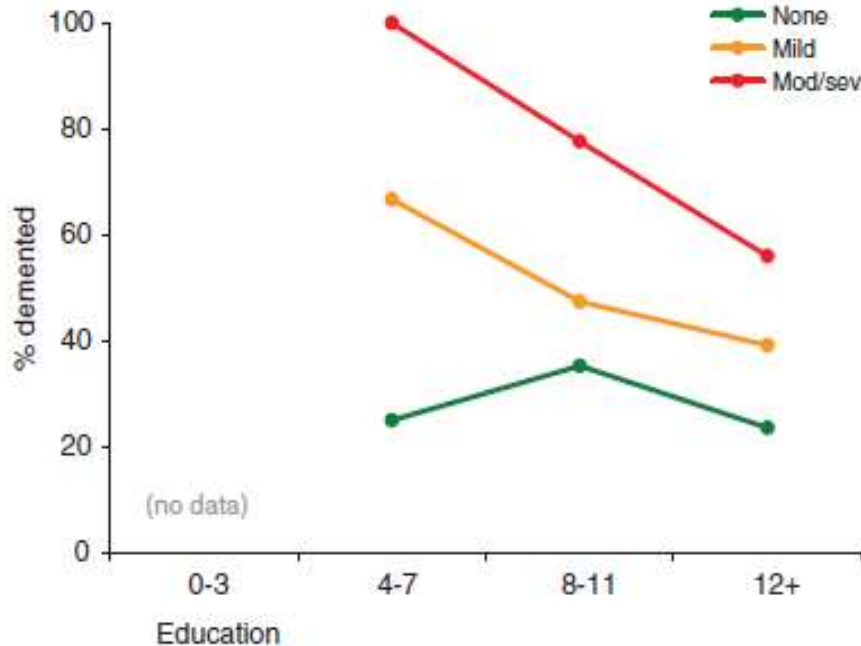


# More education reduce dementia risk (*Brain*, 2010)



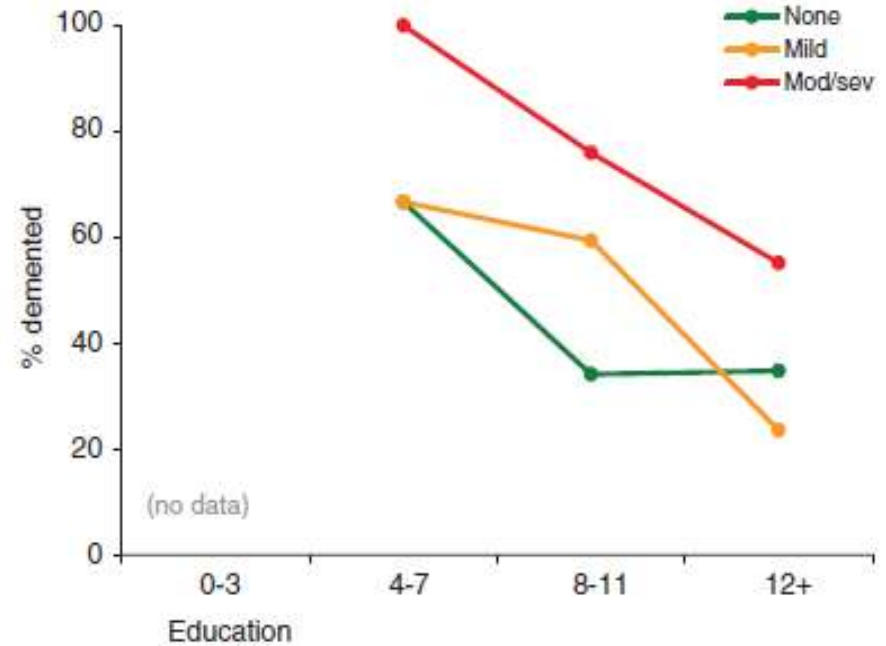
1. Cortical atrophy

(a) 0.02 (b) 0.85



2. Hippocampal neuritic plaques

(a) <0.01, (b) 0.63



**Higher Education Protect Against Alzheimer's Disease**

# Depression and social isolation are risk factors for Alzheimer's disease



Rush University Med  
Cent. 1995 - 2008

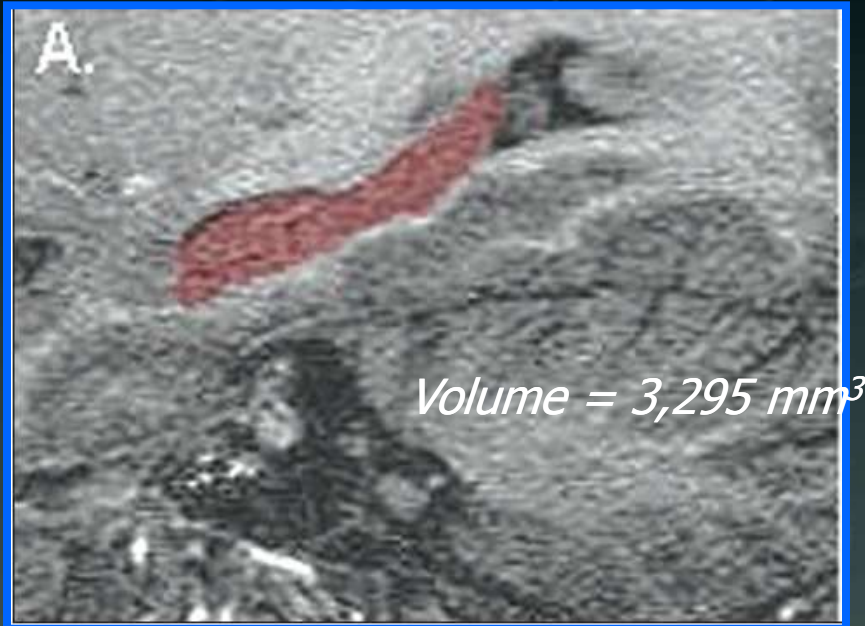


The Mirage study,  
2003

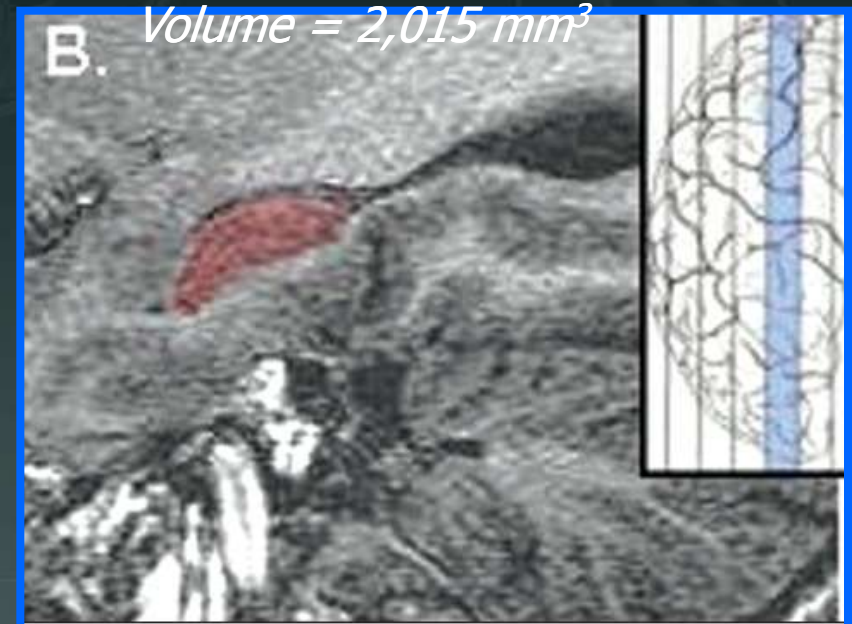


The ESPRIT study,  
2003

# Hippocampal volume in depressed patients



*Controls*



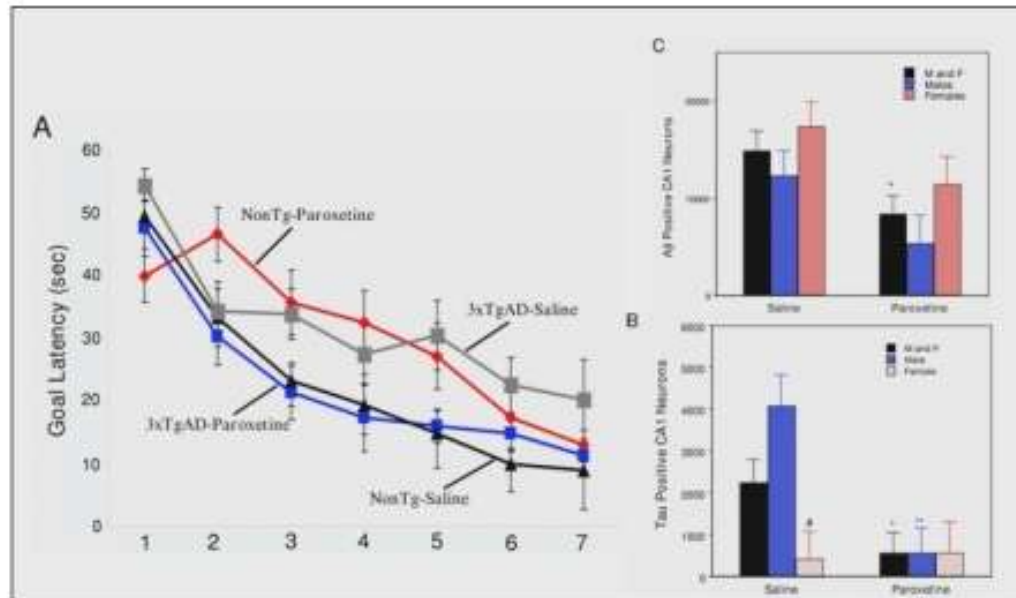


# SSRI antidepressants and AD



In transgenic mice:

## PAROXETINE TREATMENT AMELIORATES COGNITIVE DEFICITS AND AMYLOID/TAU PATHOLOGY IN A MOUSE MODEL OF AD (3xTgAD MICE)



Nelson RL et al, Exp Neurol 205: 166-176 (2007)

- Randomized, controlled trials evaluated the efficacy of fluoxetine, citalopram, fluvoxamine, paroxetine, and sertraline for treatment of AD



# Diet and dementia



THE FUTURE OF BUSINESS  
18 LEADERS AND LUMINARIES TELL YOU WHAT'S NEXT PAGE 48

# FORTUNE



**DRINK WINE AND LIVE LONGER\***

The exclusive story of the biotech startup searching for anti-aging miracle drugs PAGE 68

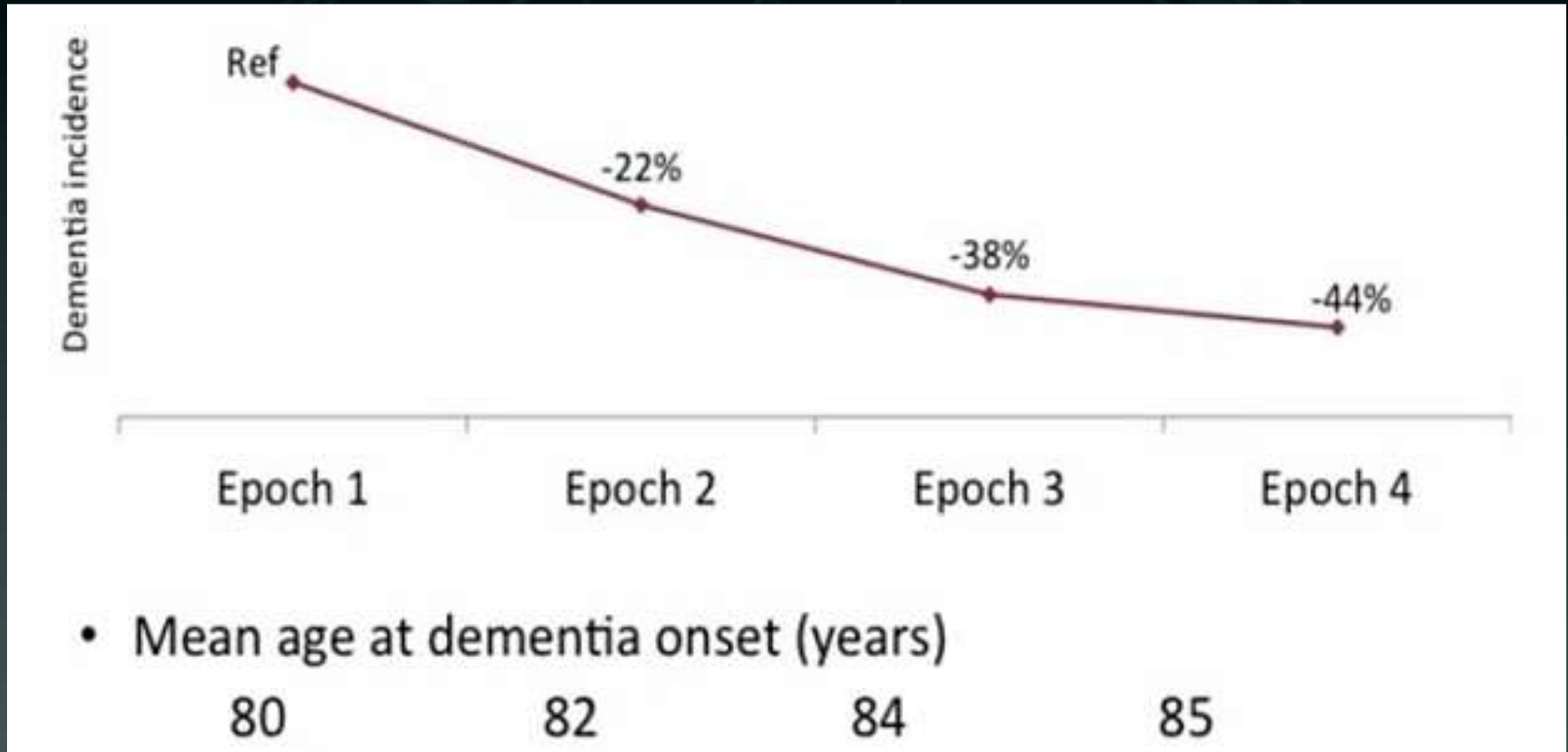
\*The Associated Press and other news organizations have reported on the study of the effects of red wine on the health of the elderly.

WINE & HEALTH: THE NEW FRONTIER IN ANTI-AGING



www.fortune.com

# Prevention: it is already happening!



In the Framingham Heart study a person age 60 today has a 44% lower chance of developing dementia than a similar-aged person 30 years ago

# Clinical Trials

## FINGER

Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)



UNIVERSITY OF  
EASTERN FINLAND



NATIONAL INSTITUTE  
FOR HEALTH AND WELFARE  
FINLAND



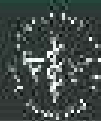
Karolinska  
Institutet



UNIVERSITY OF JYVÄSKYLÄ  
JYVÄSKYLÄ UNIVERSITY



Turun yliopisto  
University of Turku



Karolinska  
Institutet

Miia Kivipelto, MD, PhD, Professor





**FINLAND**  
BY  
VIRTUAL FINLAND

**Oulu cohort**  
T. Strandberg

**Kuopio cohort**  
H.Soininen

**Seinäjoki cohort**  
J. Tuomilehto

**Turku cohort**  
A. Jula

**Helsinki cohort**  
M. Kivipelto

**Vantaa cohort**  
T. Laatikainen

**Safety Committee**  
**Monitoring Committee**

**FINGER Study**  
PI: M. Kivipelto

**Coordination Group/THL:**

**Heads:** T. Laatikainen, J.Lindström,  
**Coordinators:** T. Ngandu, S.  
Ahtiluoto

**Field coordinator:** J. Lehtisalo  
**Data manager, Statistician, Administrator**

**Supervision:**

**Nutrition:** J. Lindström  
**Exercise:** R. Rauramaa, S.Pajala  
**Cognitive&social activation:** T.Hänninen,  
T.Ngandu  
**Vascular factors:** J. Tuomilehto, T.Strandberg,  
R. Antikainen

**Volunteer organizations**  
**Practices in the community**



Recruitment (Dementia risk score)

Screening (Nurse: CERAD; Physician)

Baseline visit (NTB)

RANDOMIZATION

MINI-INTERVENTION

# INTENSIVE INTERVENTION

**NUTRITIONAL COUNSELING:**  
7 group & 3 individual sessions

**PHYSICAL ACTIVITY:**  
1-2x/wk muscle strength &  
1-4x/wk aerobic training

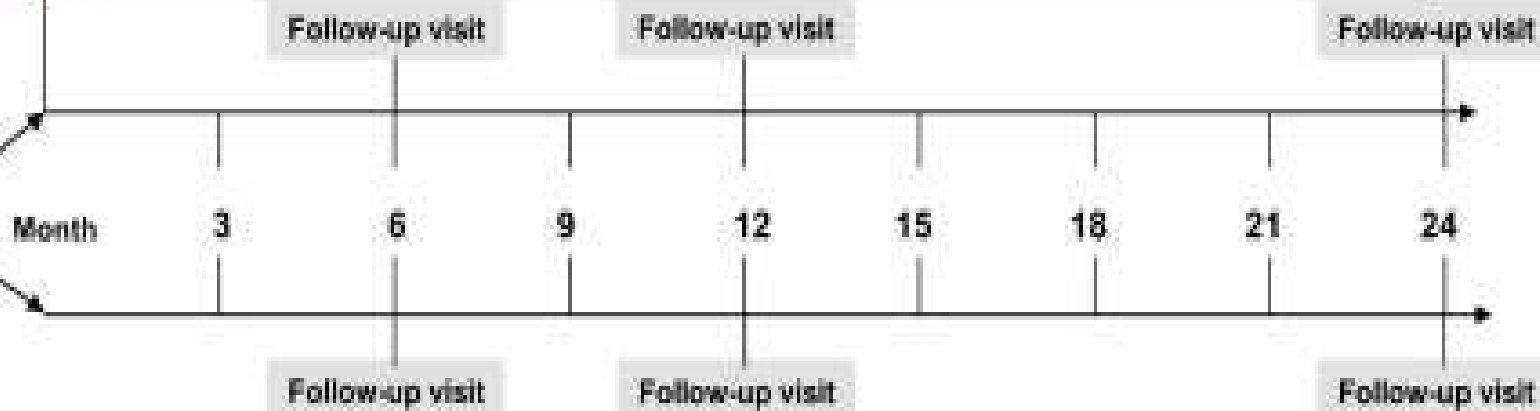
**PHYSICAL ACTIVITY:**  
2-3x/wk muscle strength &  
5-6x/wk aerobic training

**COGNITIVE TRAINING:**  
9 group sessions,  
Independent training 3x/wk 6mo

**COGNITIVE TRAINING:**  
2 group sessions,  
Independent training 3x/wk 6mo

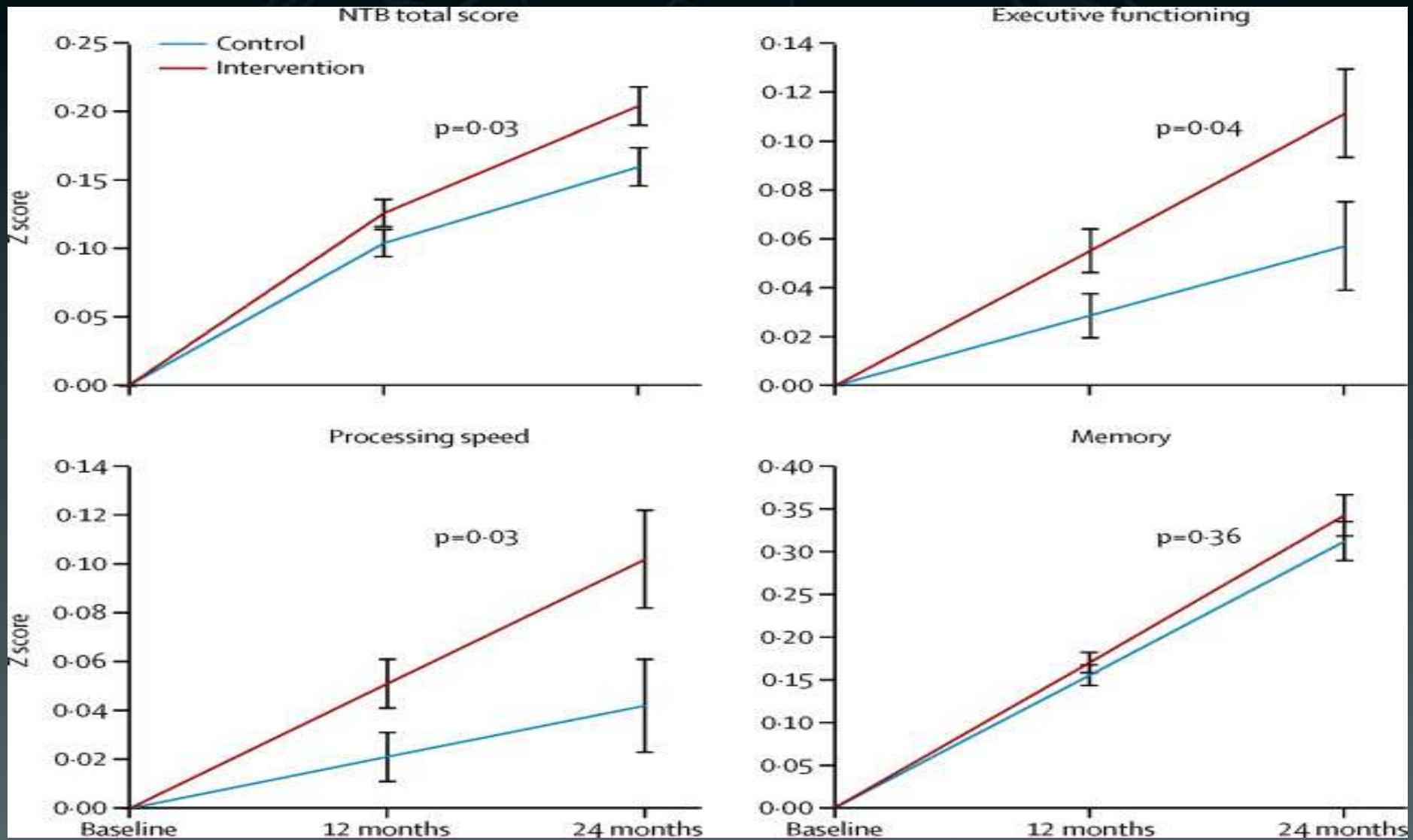
**MANAGEMENT OF METABOLIC AND VASCULAR RISK FACTORS**  
6 nurse visits, 4 physician visits

INTERVENTION KICK-OFF



REGULAR HEALTH ADVICE

# Finger Study: the results



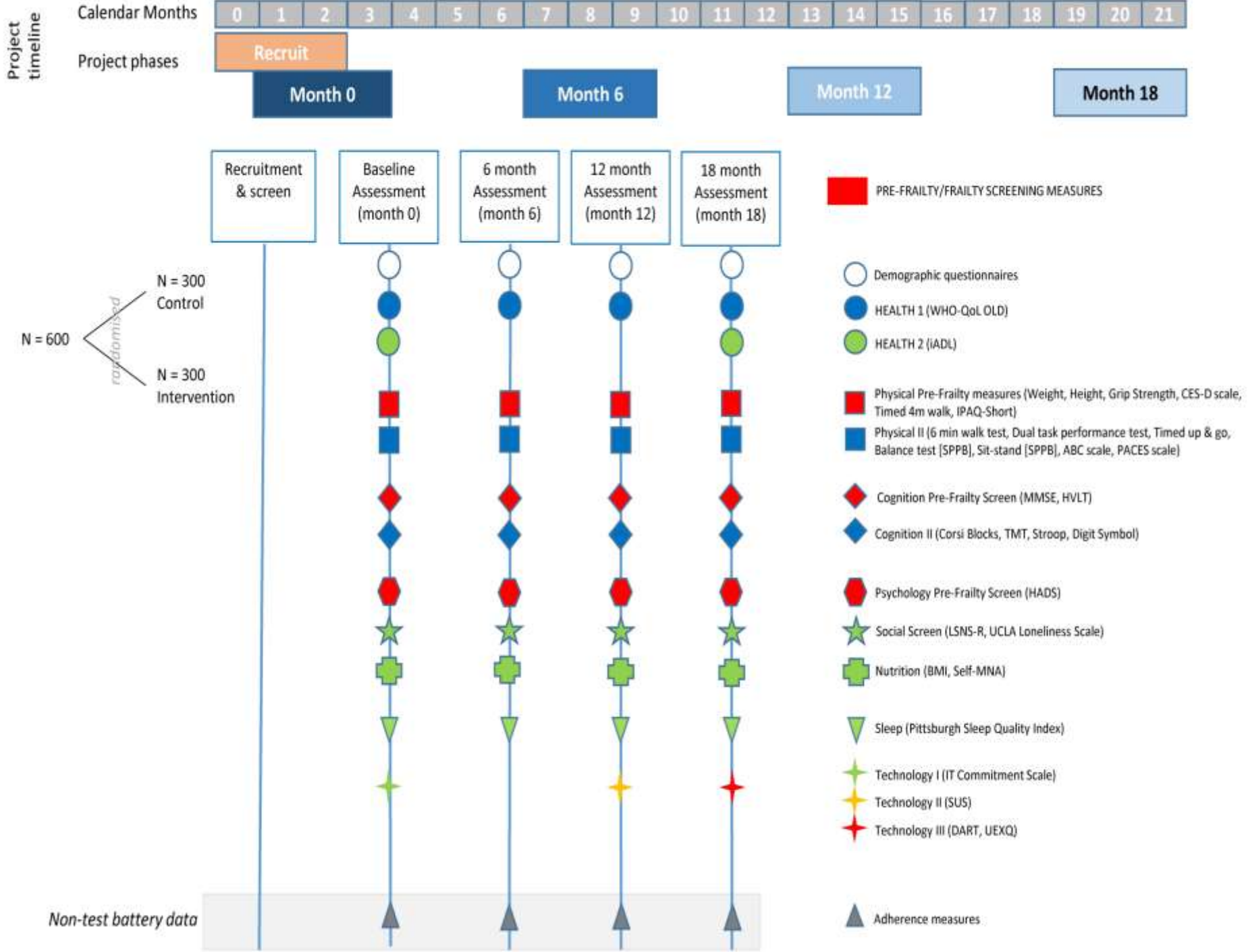
# The my-AHA study



## *My Active and Healthy Ageing*

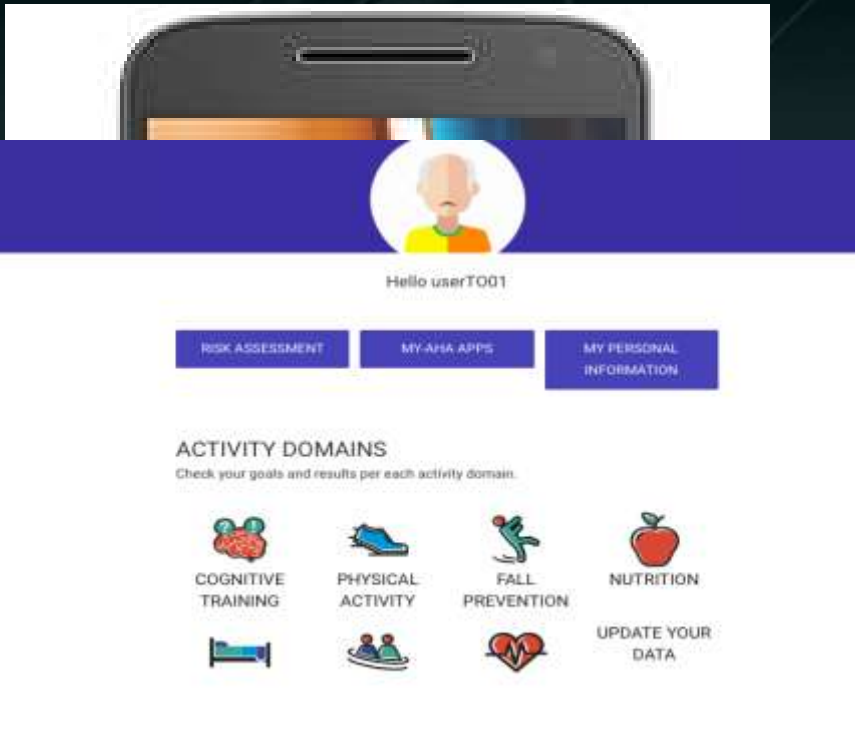
PHC-21-2015: Advancing active and healthy ageing with ICT:  
Early risk detection and intervention  
Contract # 689592







# The my-AHA Study

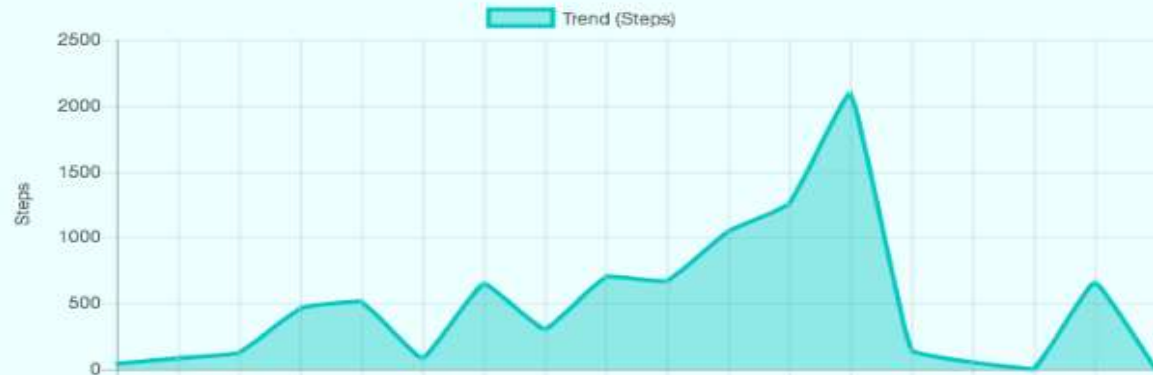


# The my-AHA study



## STEPS

### TREND



## N BACK TRAINING TPR

### TREND



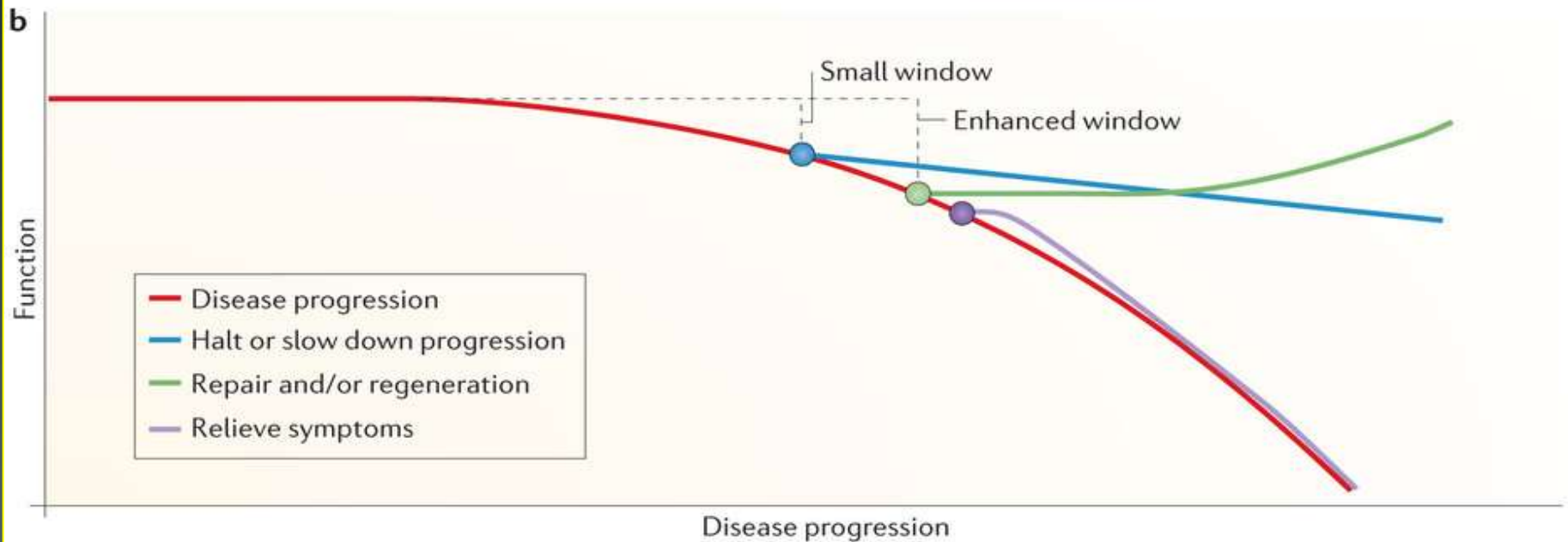
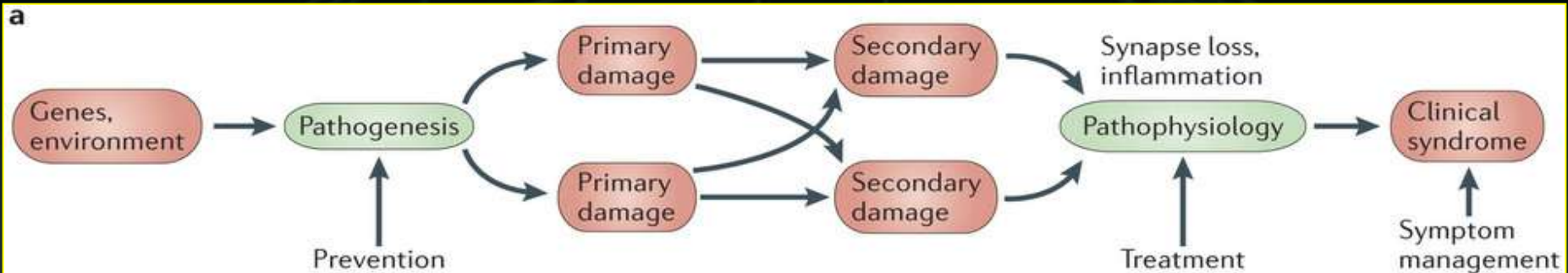
# Multi-Modal and Personalized Interventions



**Two or more of the following treatments:**

- ✓ Exercise (aerobic, endurance, strength training, balance, flexibility training)
- ✓ Caregiver training in behavior management
  - ✓ Cognitive exercises
  - ✓ Cognitive-behavioral therapies
    - ✓ Reality orientation
    - ✓ Nutritional intervention
- ✓ Recreational and social therapies

# Early therapy in Alzheimer's disease





A night-time photograph of the Colorado State Capitol building in Denver, Colorado. The building's iconic dome is illuminated with a warm, golden light, and a tall, slender tower rises from its peak. The surrounding cityscape is visible in the background, with various buildings and streetlights glowing against the dark sky. The sky is a mix of deep blue and purple, suggesting a sunset or twilight. Overlaid on the image is the text "Thank you for your attention" in a bold, yellow, sans-serif font.

**Thank you for your  
attention**