



Differenze di genere nelle malattie neurodegenerative

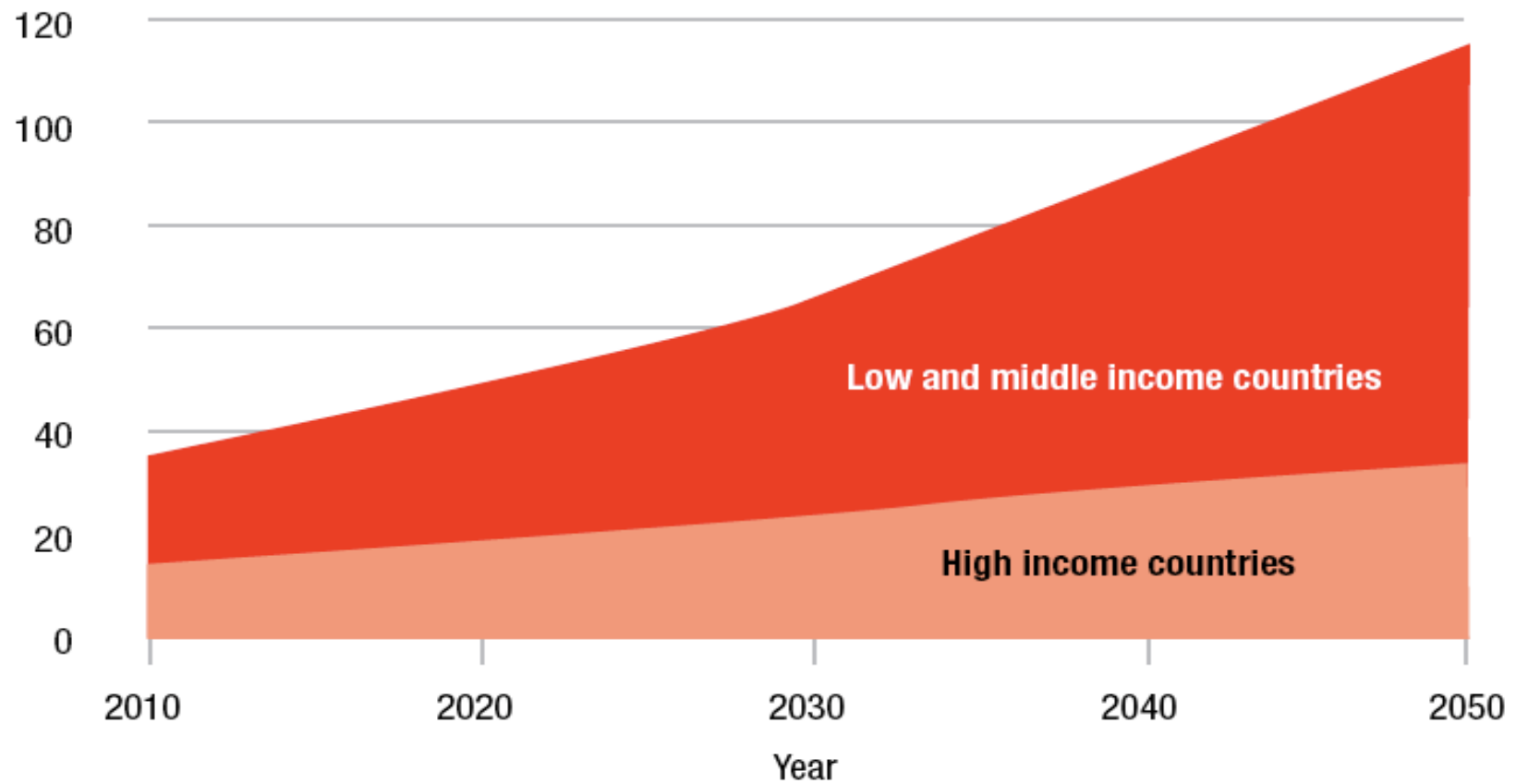
Carlo Gabelli

Università degli studi di Padova
Centro Regionale per lo studio e la cura
dell'Invecchiamento Cerebrale
CRIC



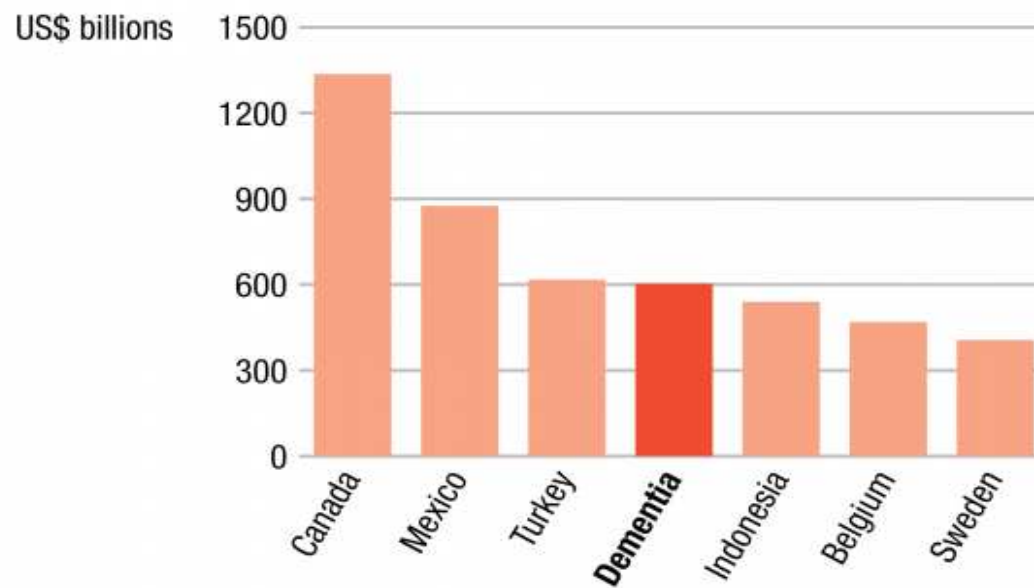
Prevalence of Dementia

Figure 1 The growth in numbers of people with dementia (in millions) in high income countries, and low and middle income countries



Burden of Dementia - Global Cost

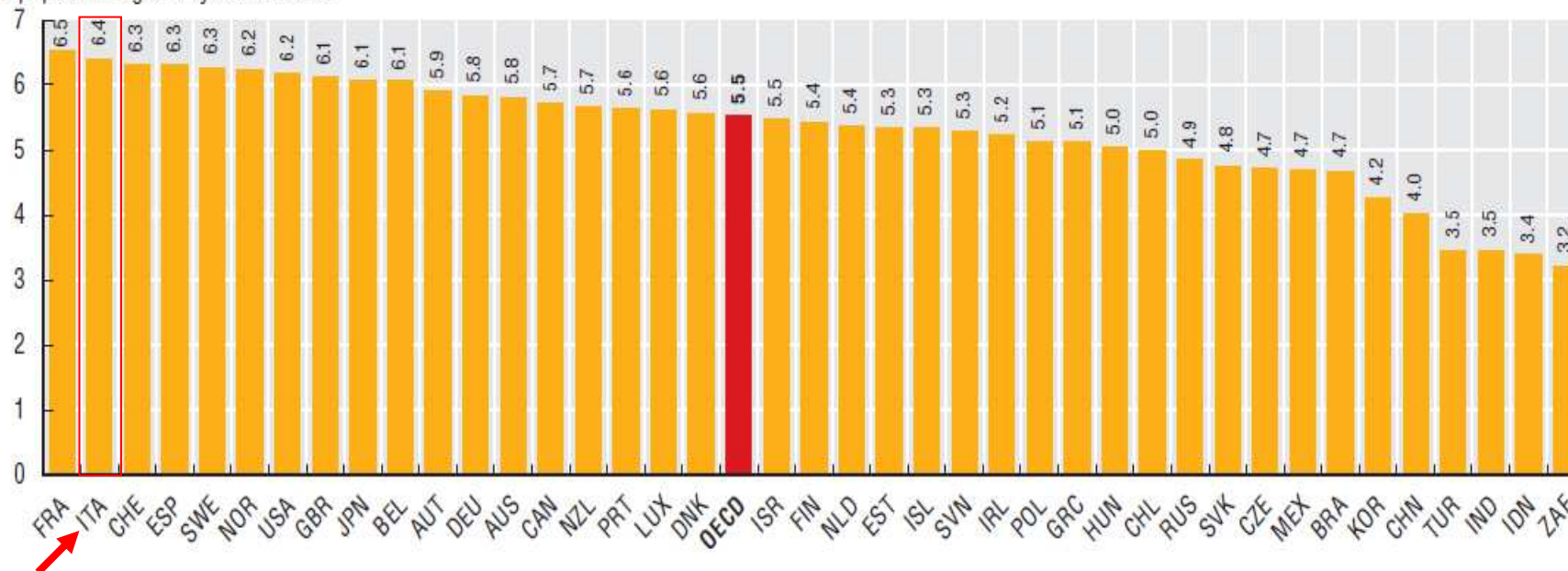
Cost of dementia compared to national economies



Burden of Dementia - Prevalence in different countries

Prevalence of dementia among the population aged 60 years and over, 2009

% of population aged 60 years and over



Source: Wimo et al. (2010).

Italia

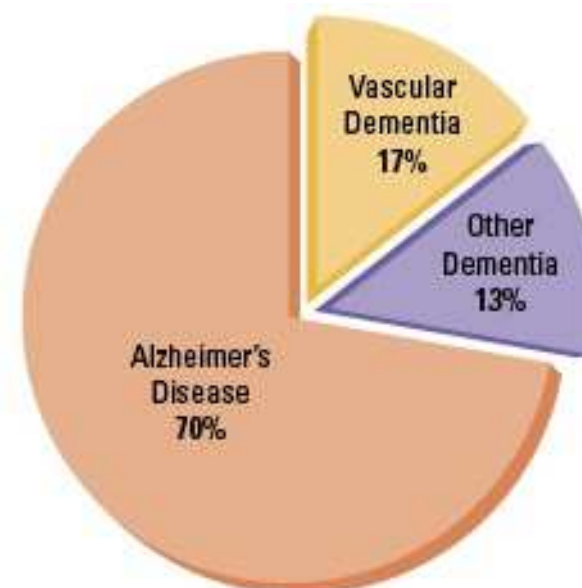
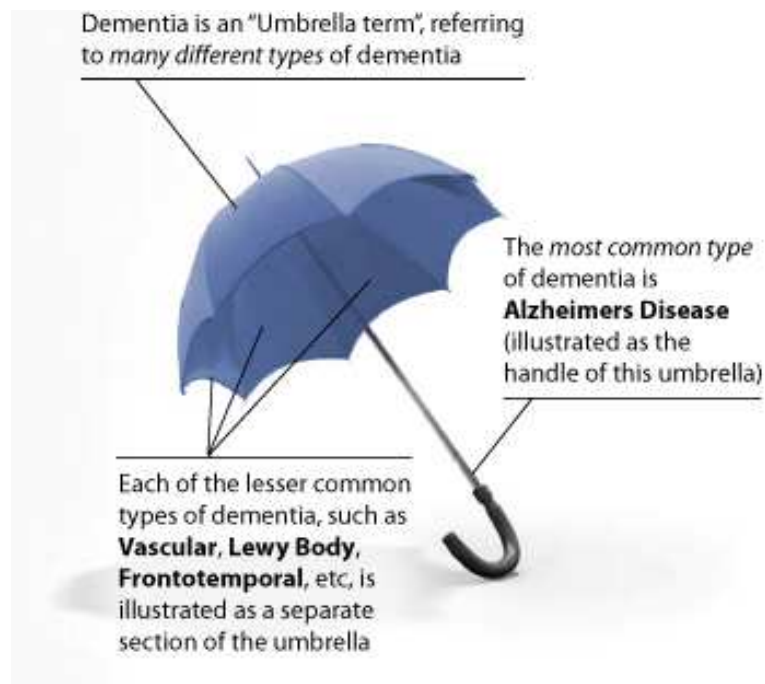
Numero di persone colpite da demenza **1 milione**

affette da demenza di **Alzheimer 600.000**

soggetti con **meno di 65 anni colpiti da Alzheimer 30.000**

Costo globale della patologia in Italia circa **20-30 miliardi di euro/anno (1,5% del PIL)**

Dementia or Major Neurocognitive Disorder (DSM-5)

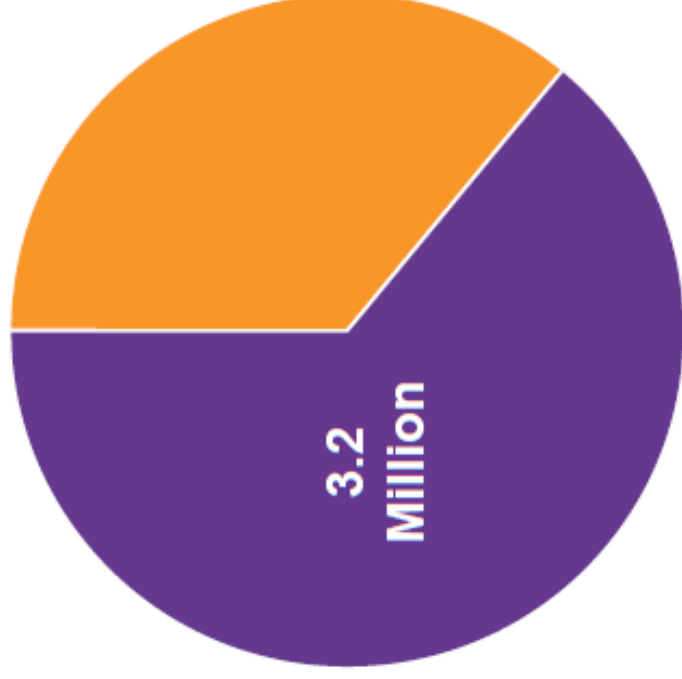


Source: Plassman, BL; Langa, KM; Fisher, GG; Heeringa, SG; Weir, DR; Ofstedal, MB, et al. "Prevalence of Dementia in the United States: The Aging Demographics, and Memory Study. *Neuroepidemiology* 2007; 29:125-132.³¹

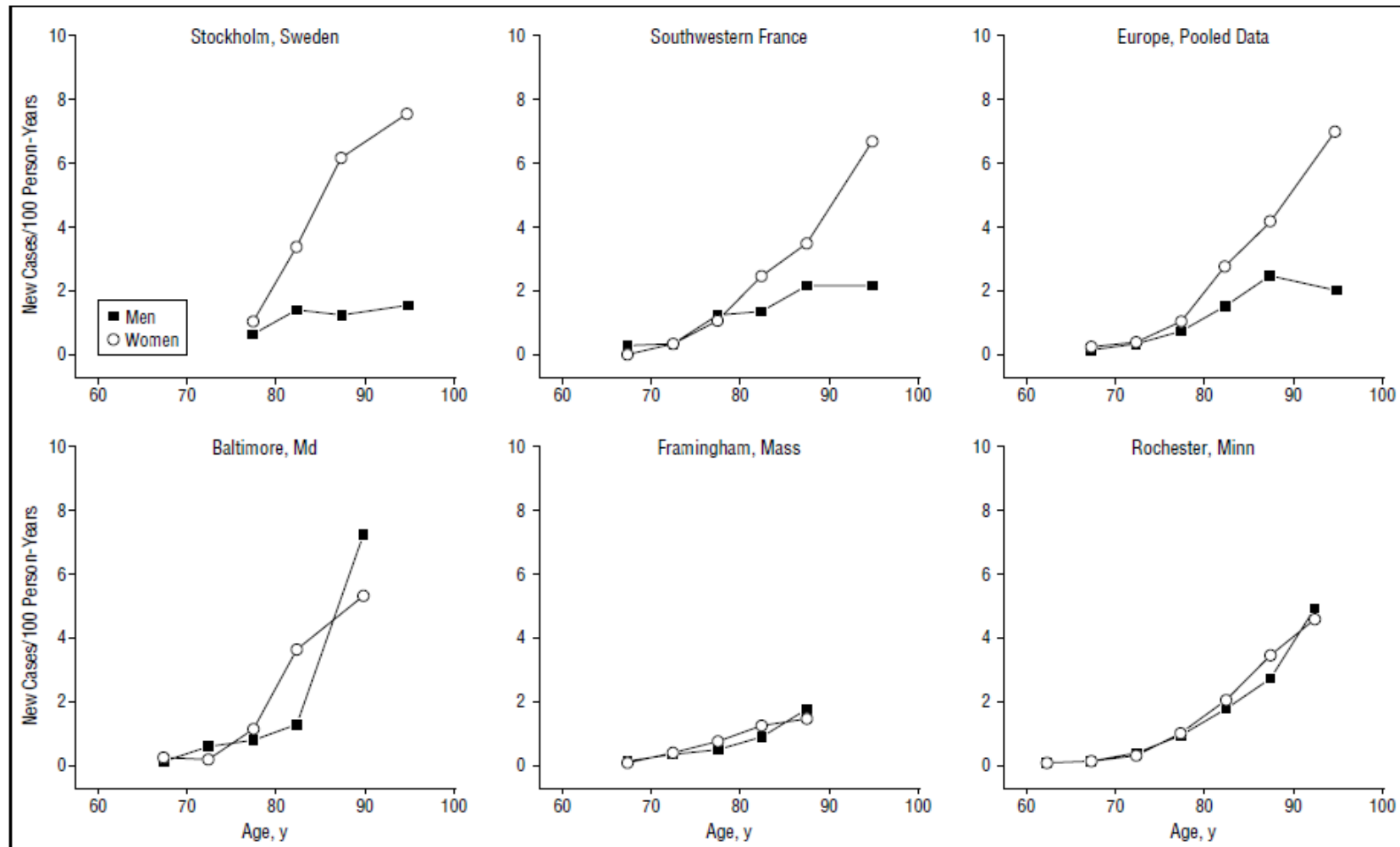
How Alzheimer's Impacts
Men & Women
Differently



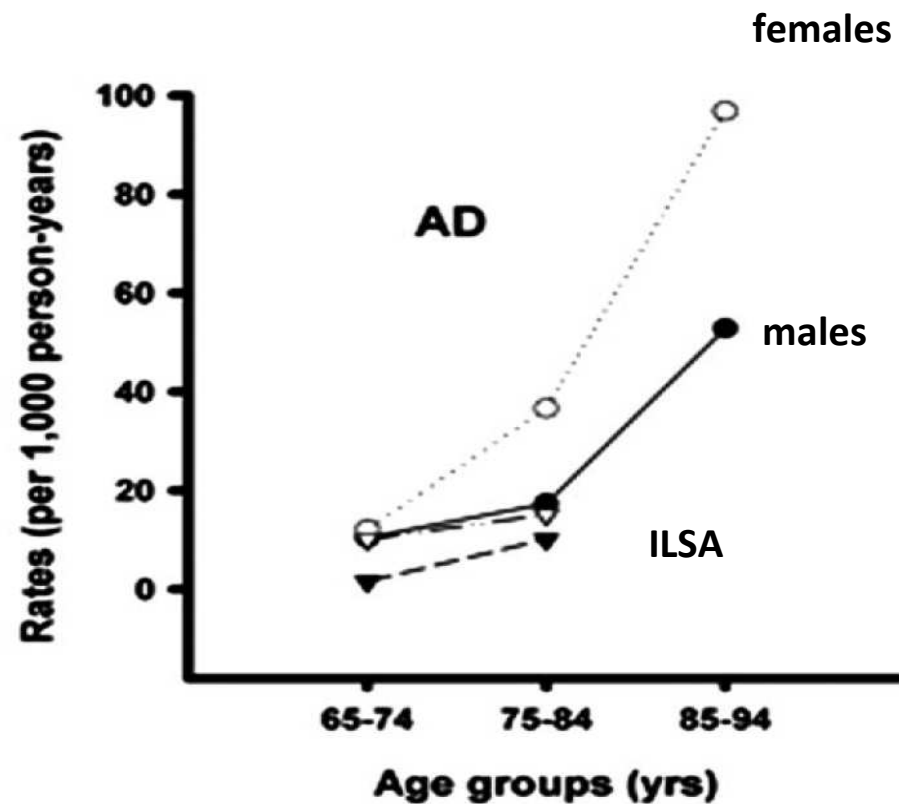
Two-thirds of the 5 Million Seniors with
Alzheimer's Disease Are Women



AD and gender - Incidence rates in different countries



AD incidence rates and gender in Italy – Conselice Study

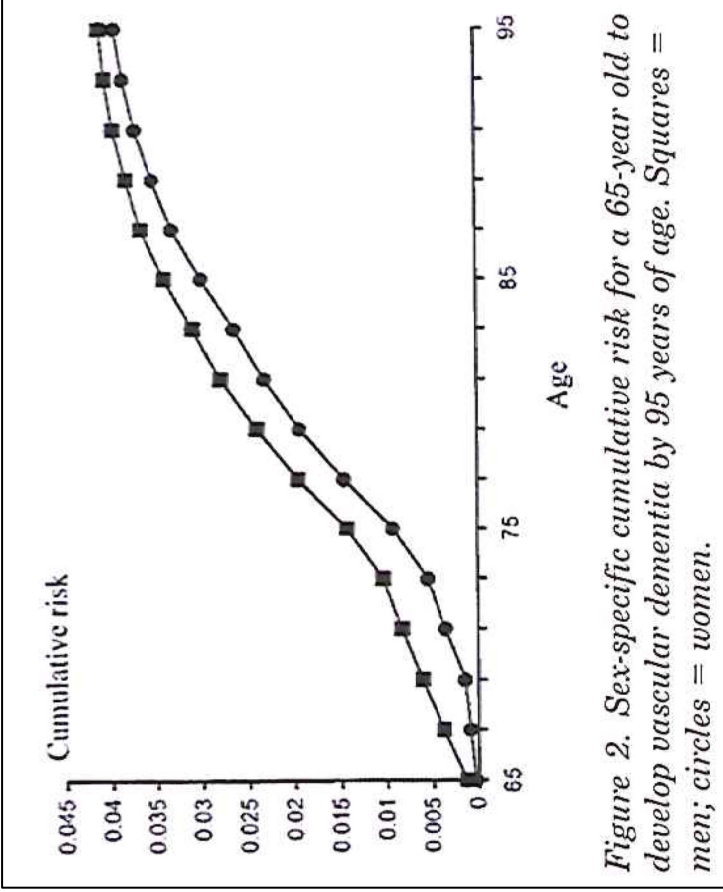
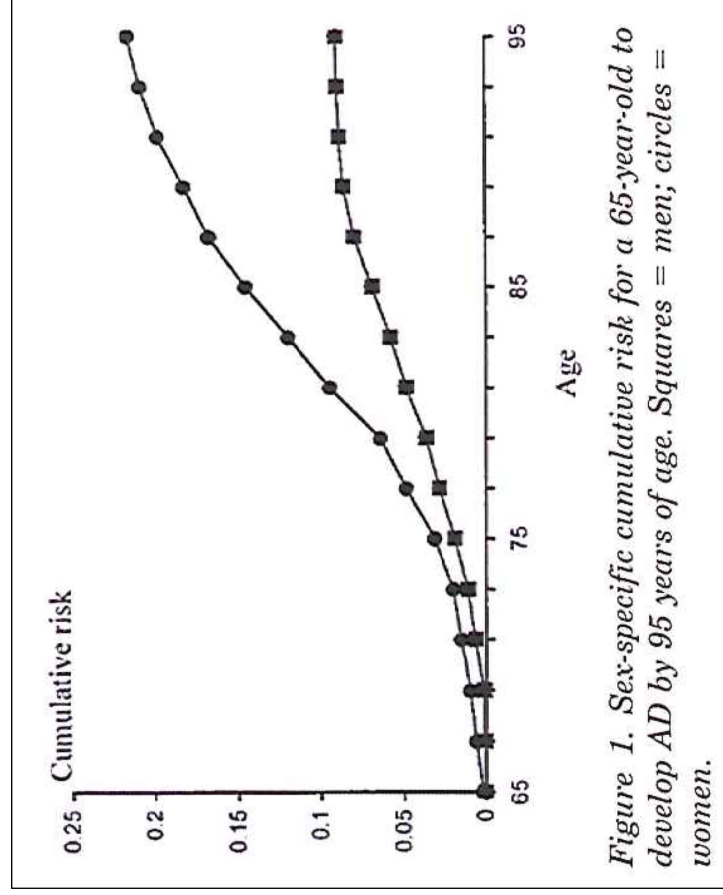


Age groups, y	Alzheimer disease	
	No. of cases	Rate per 1,000 person-years
Men		
65-74	8	10.4 (5.2-20.7)
75-84	9	17.4 (9.1-33.5)
85-94	7	52.8 (25.2-110.1)
All ages	24	15.6 (10.5-22.9)*
Women		
65-74	10	12.1 (6.5-22.6)
75-84	24	36.6 (24.5-54.6)
85-94	14	96.8 (57.3-163.5)
All ages	48	31.8 (25.1-40.3)*
Total sample		
65-74	18	11.3 (7.1-17.9)
75-84	33	28.1 (20.0-39.6)
85-94	21	75.8 (49.4-116.2)
All ages	72	23.8 (17.3-31.7)*

* Standardized to the 2003 Italian population.

Gender differences in the incidence of AD and vascular dementia

The EURODEM Studies

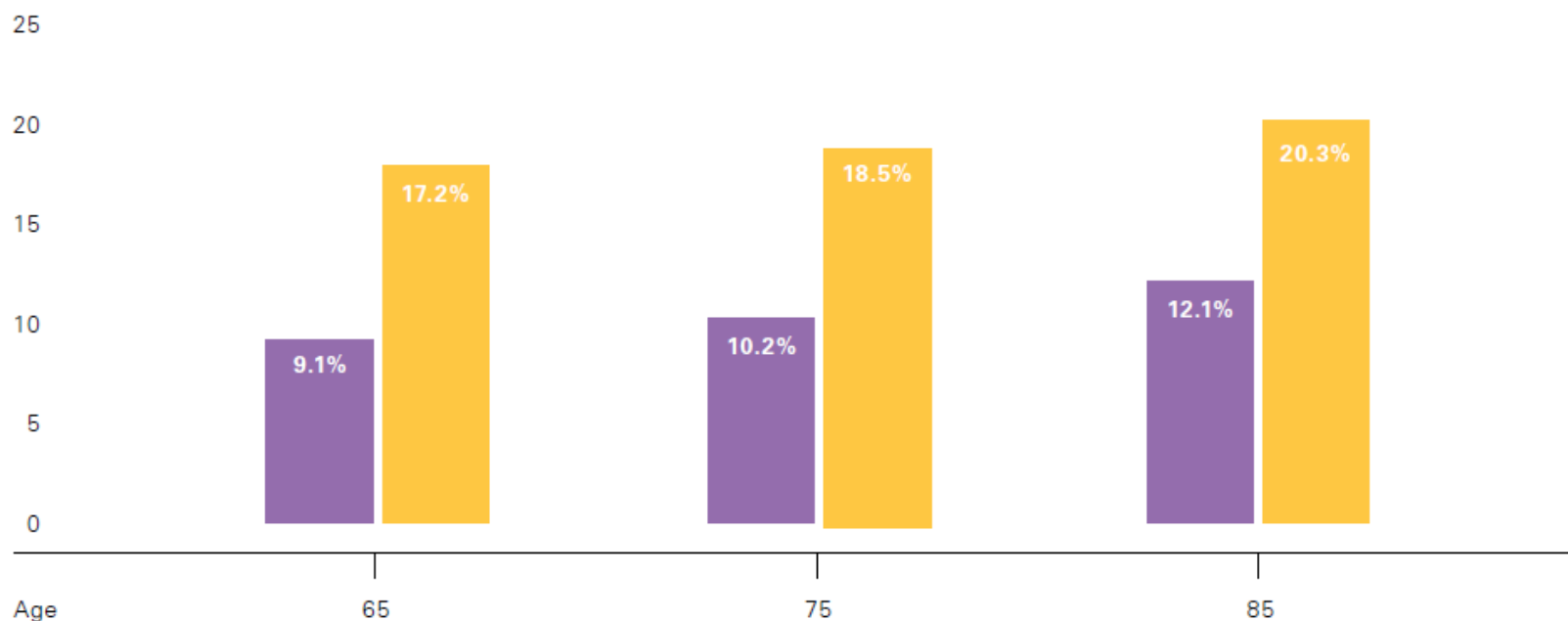


Secondo i dati prospettici ricavati dallo studio Framingham il *lifetime risk* per una donna di ammalarsi di Alzheimer è quasi doppio rispetto al maschio; all'età di 65 anni è pari a 1/6 verso 1/11 nel maschio

figure 2:

Framingham Estimated Lifetime Risks for Alzheimer's by Age and Sex

Percentage ■ Men ■ Women

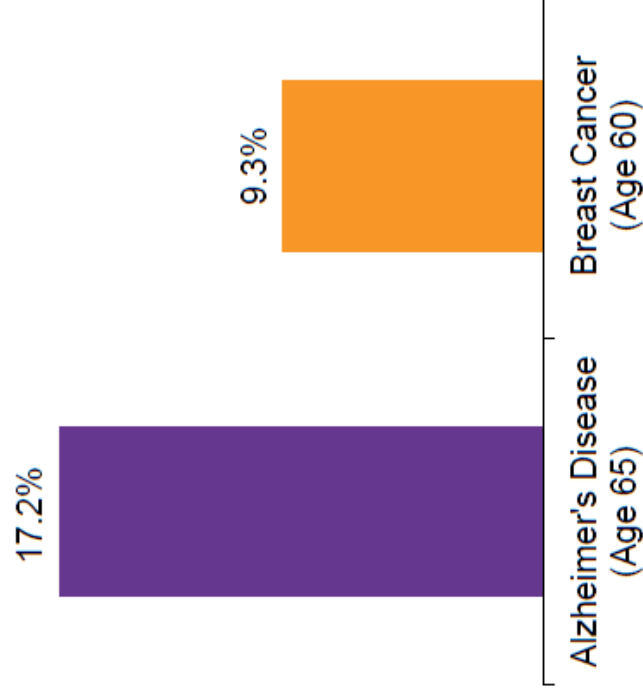


Created from data from Seshadri et al. ⁽⁷⁸⁾

2014 Alzheimer's Disease Facts and Figures

Includes a Special Report on
Women and Alzheimer's Disease

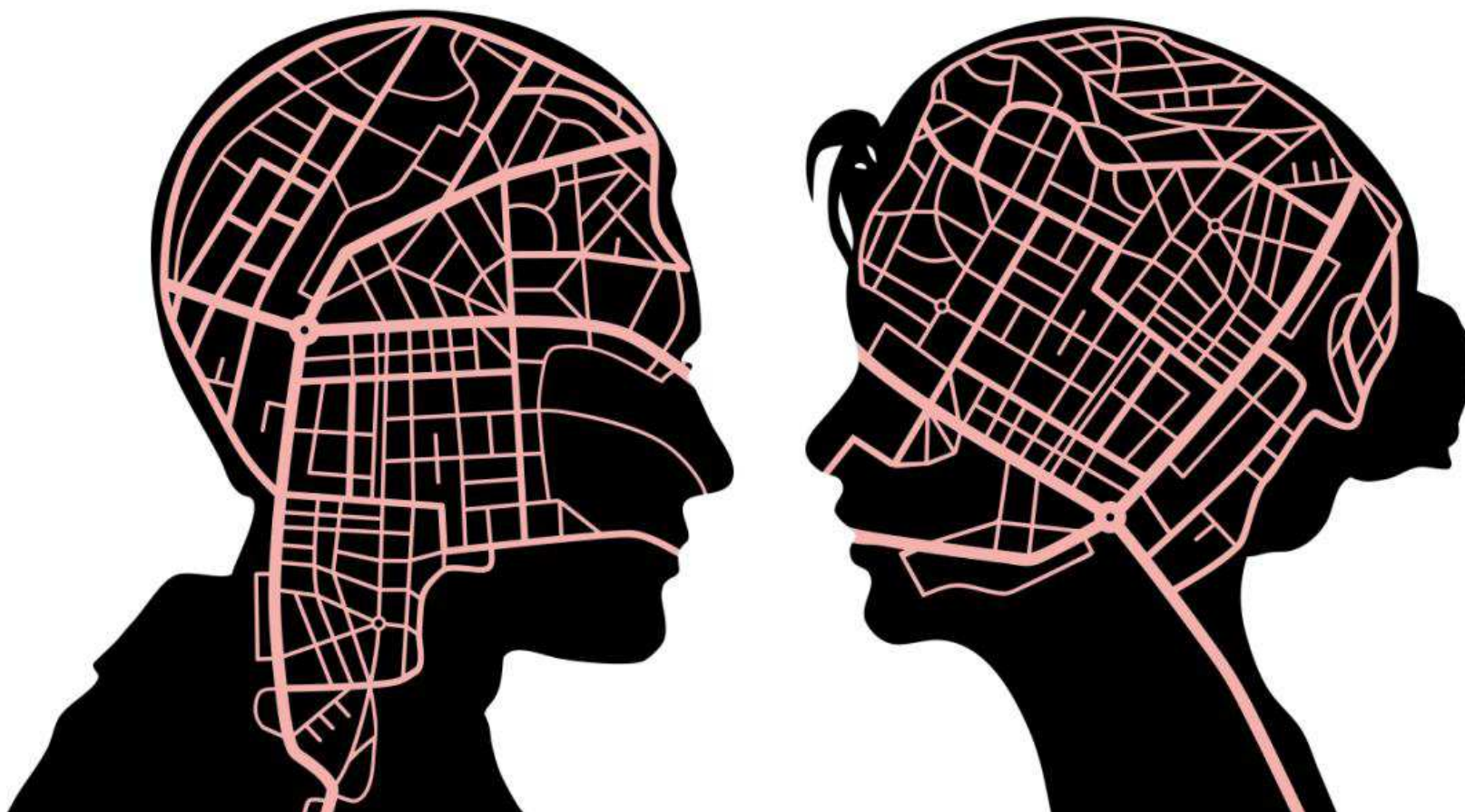
Remaining Lifetime Risk of Women
Developing Alzheimer's Disease and
Breast Cancer



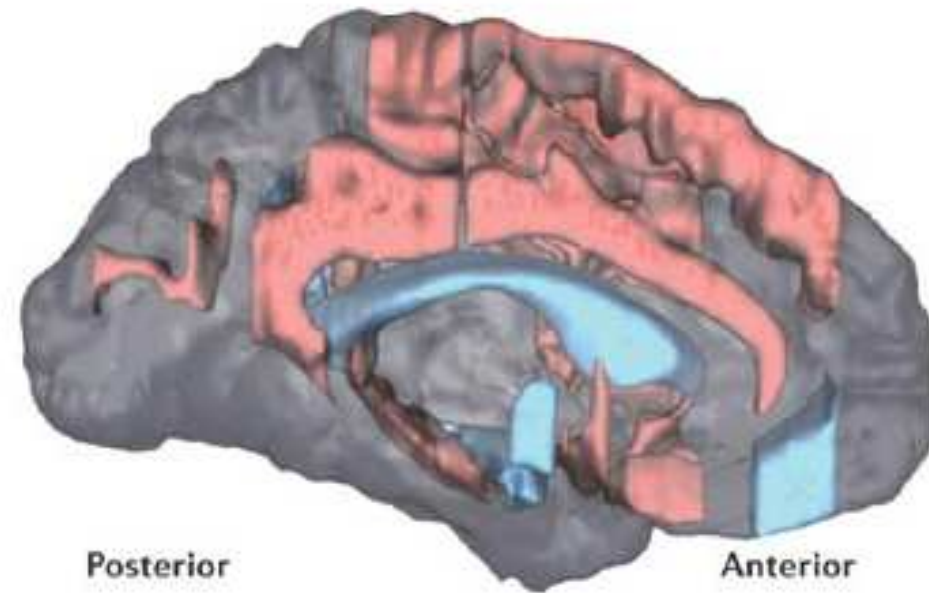


**Quali sono le ragioni perché le donne
presentano una maggiore
prevalenza di malattia di Alzheimer?**

Parità $\neq$ Eguaglianza



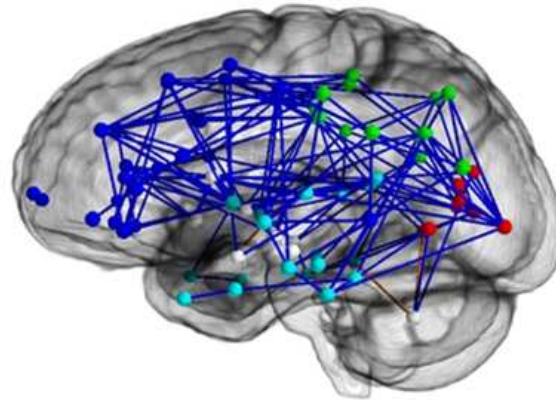
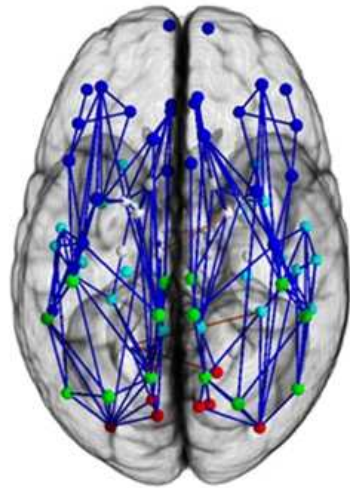
Brain structure and sex



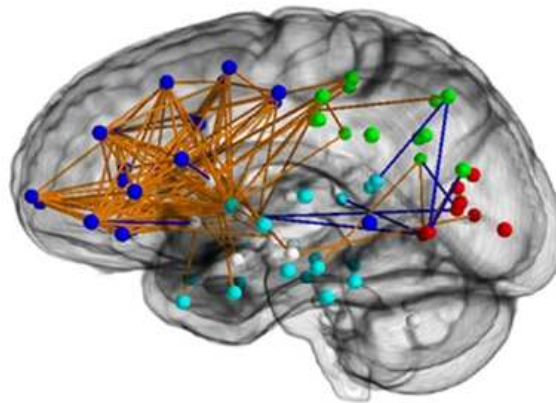
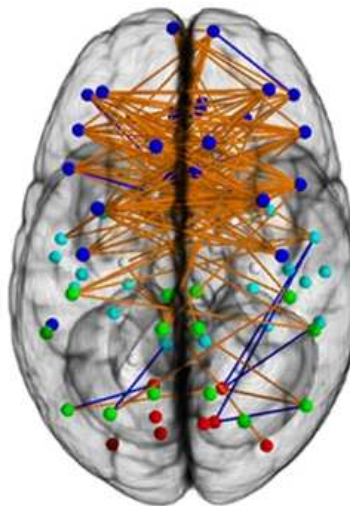
- Structures that are larger in the healthy female brain, relative to cerebrum size
- Structures that are larger in the healthy male brain, relative to cerebrum size

Sex differences in the structural connectome of the human brain

Ingalhalikar et al.



Males



Females

GREATER COGNITIVE DETERIORATION IN WOMEN THAN MEN WITH ALZHEIMER'S DISEASE: A META ANALYSIS

IRVINE 2012

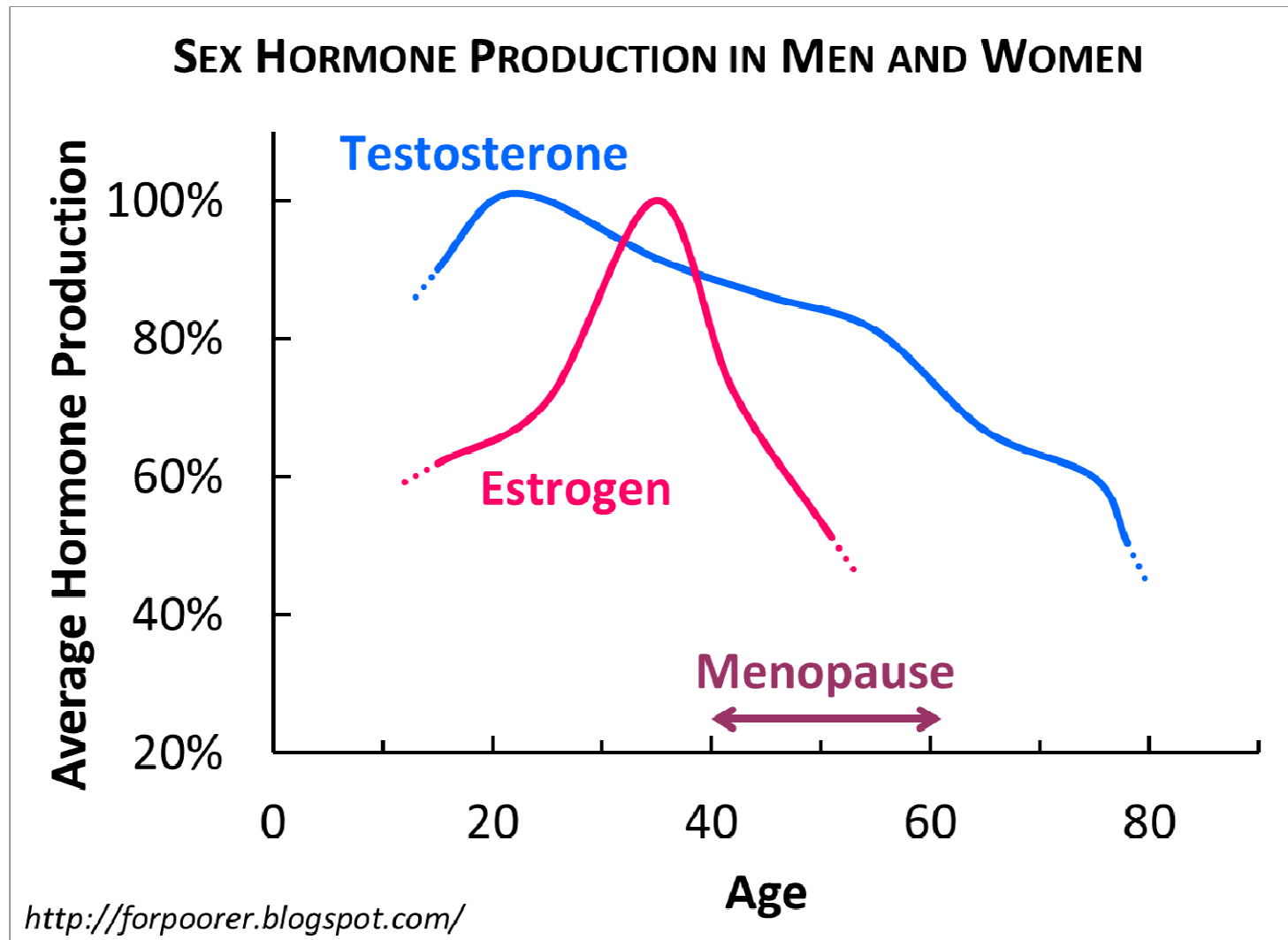
Studies reporting on the cognitive abilities of men and women with Alzheimer's disease (AD) are surprisingly rare.

We carried out a meta-analysis of neurocognitive data from 15 studies ($n = 828$ men; 1,238 women), which revealed **a consistent male advantage on verbal and visuospatial tasks and tests of episodic and semantic memory.**

Moderator regression analyses showed that age, education level, and dementia severity did not significantly predict the male advantage.

Reasons posited for this advantage include a reduction of estrogen in postmenopausal women, sex differences in AD pathology, and greater cognitive reserve in men.

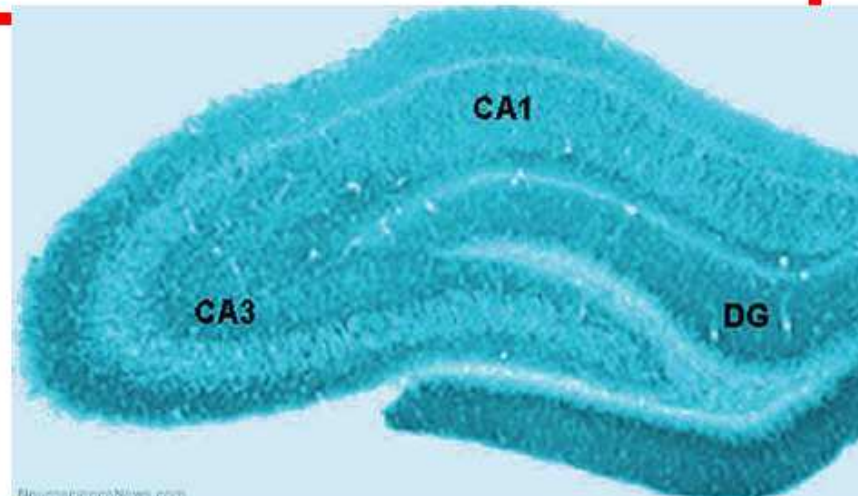
Sex hormones



Oestrogen deprivation

Females who enter menopause prematurely via bilateral ovariectomy (surgical menopause) have a significantly increased risk for cognitive decline and dementia

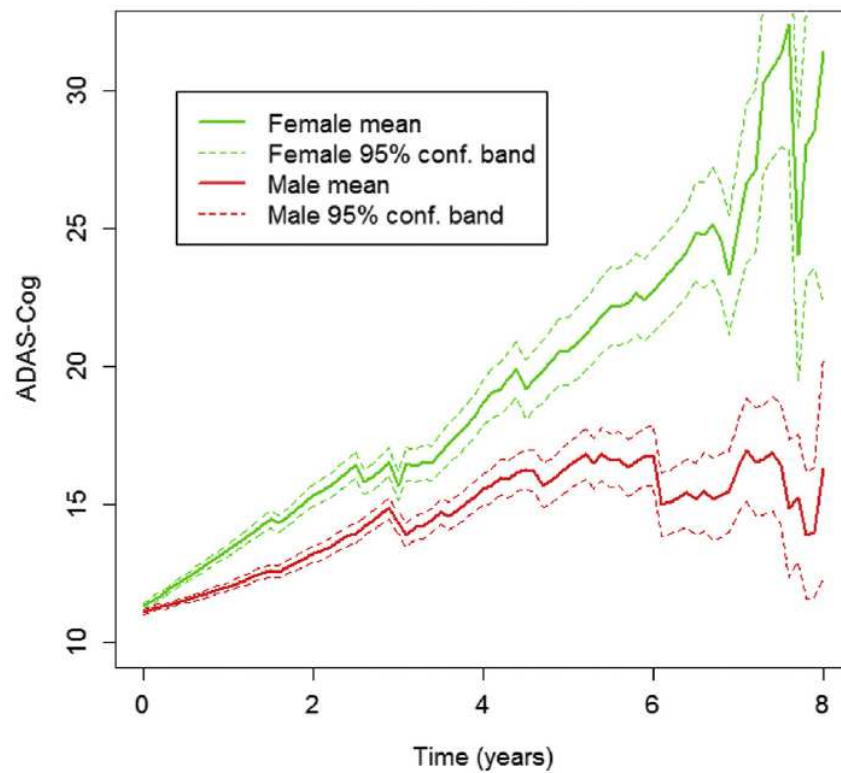
On animal model long-term oestrogen deprivation dramatically increases sensitivity of the normally resistant hippocampal CA3 region to ischaemic stress, an effect that was gender-specific



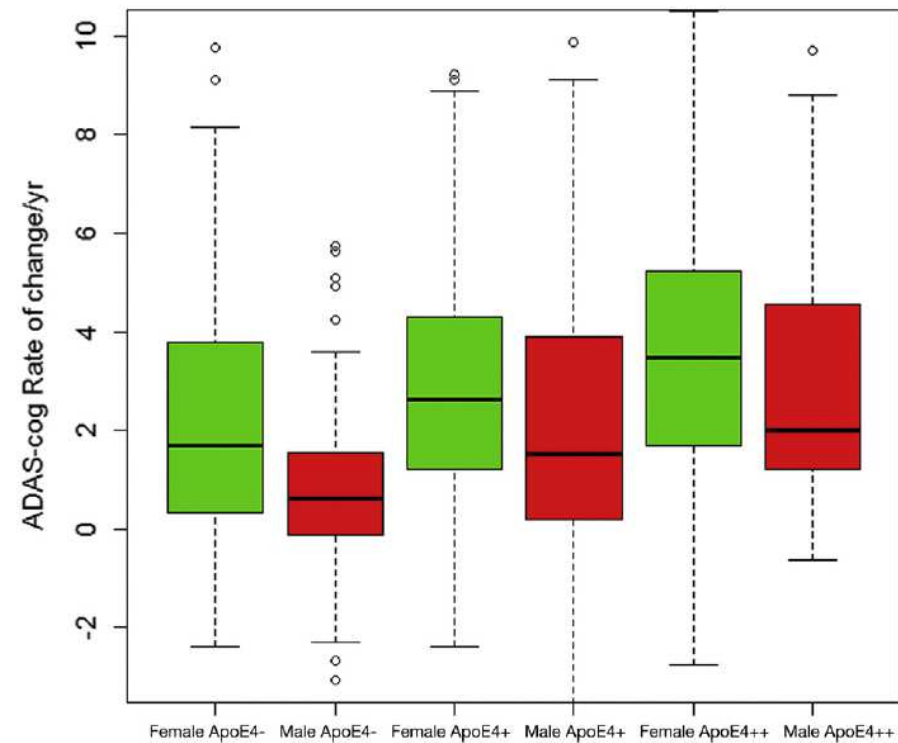
Featured Article

Marked gender differences in progression of mild cognitive impairment over 8 years

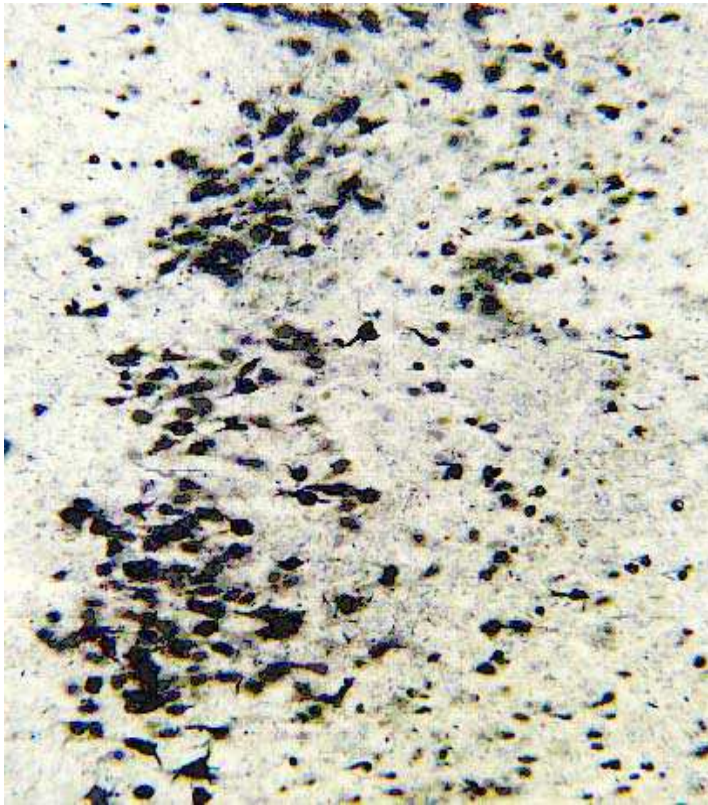
Mean trajectories



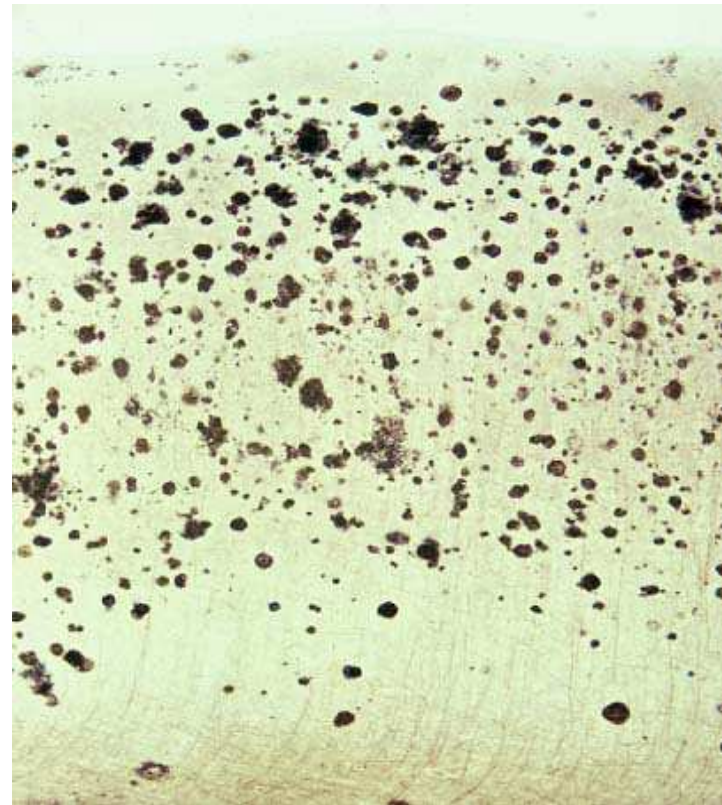
Median ADAS-Cog rate of change/yr by gender and apoE4 status



Neuropathological features of AD



**Neurofibrillary tangles
(NFT)**



**Amyloid- β deposition
(A β)**

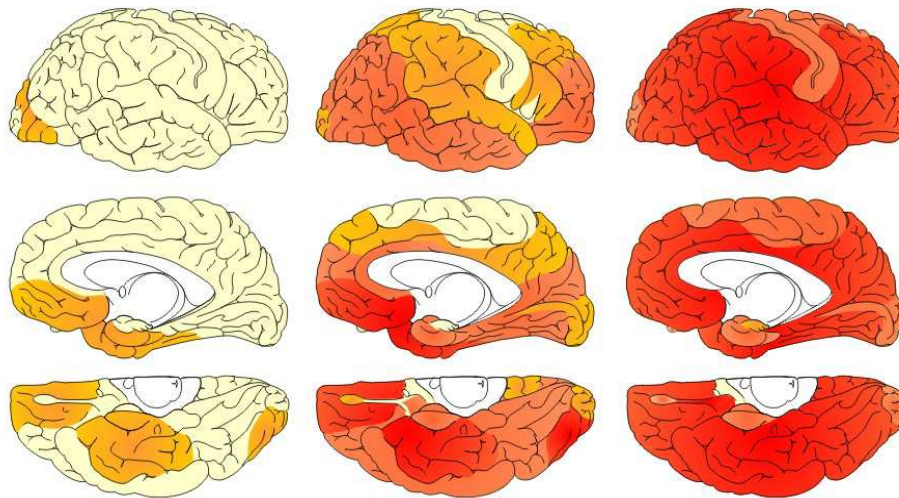
Neuropathological staging of AD

Amyloid β

**Stage
A**

**Stage
B**

**Stage
C**



Neurofibrillary tangles = NFT

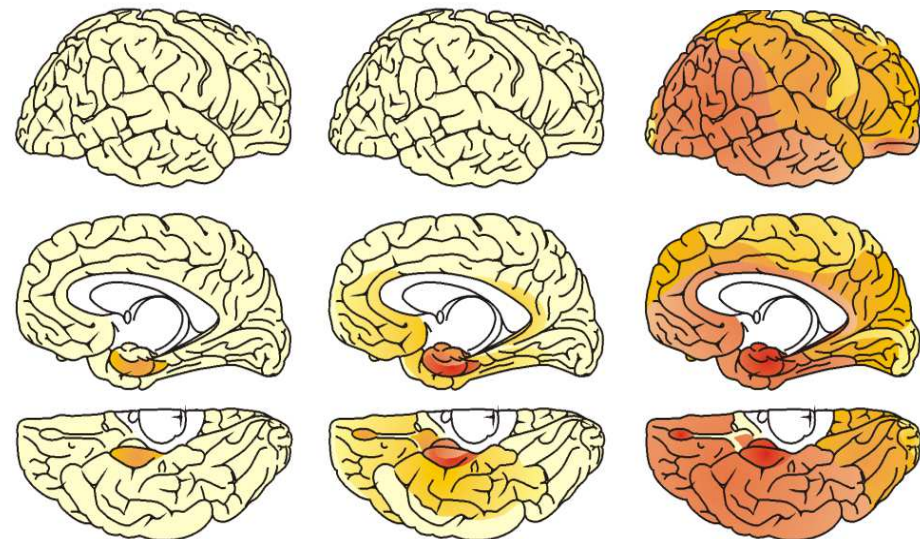
**NFT I-II
(Entorhinal
stages)**

**NFT III-IV
(Limbic
stages)**

**NFT V-VI
(Neocortical
stages)**

Entorhinale Stadien
I-II

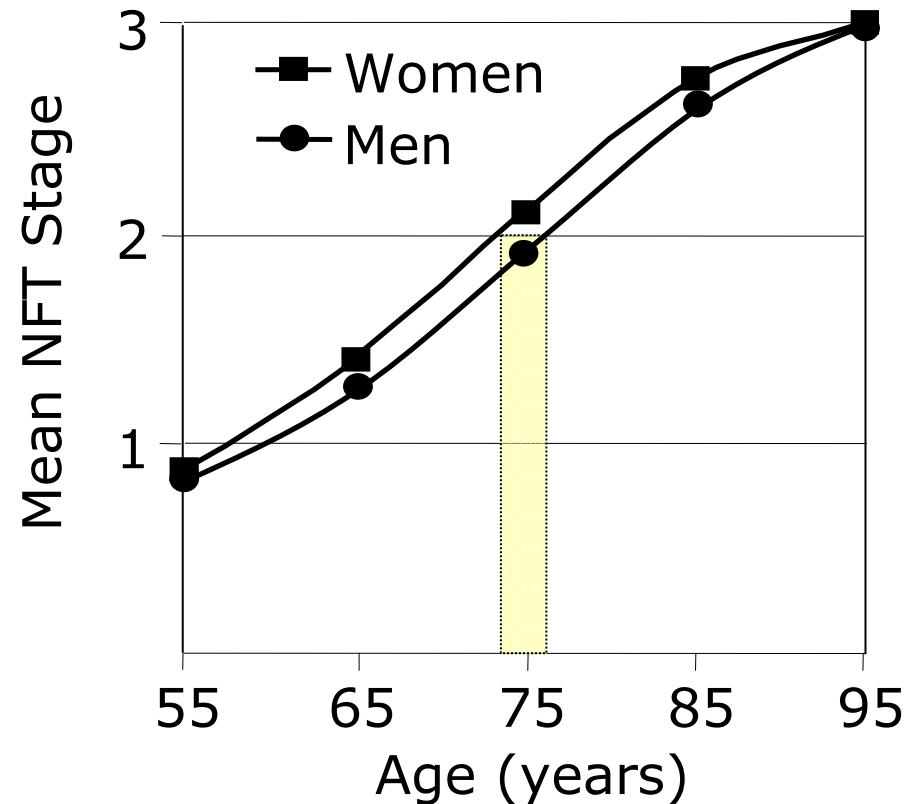
Limbische Stadien
III-IV



Braak and Braak 1991

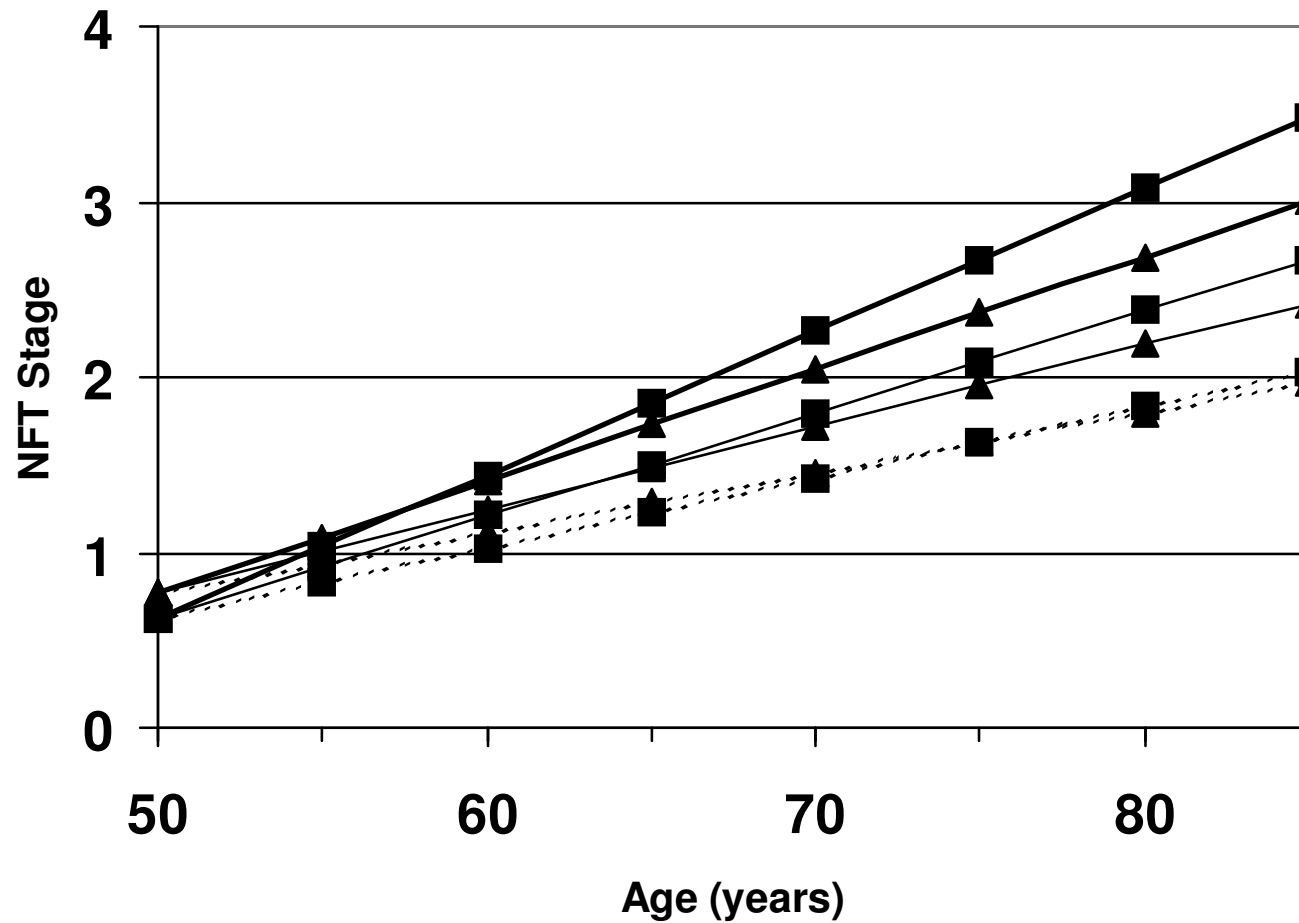
NFT Stage for Men & Women

- 5615 (3165 men and 2450 women) consecutive autopsy cases aged 20–105 years
- All brains were assessed for NFT- and A β - pathology
- Linear regression analysis was used to predict stage by age and gender



EH Corder

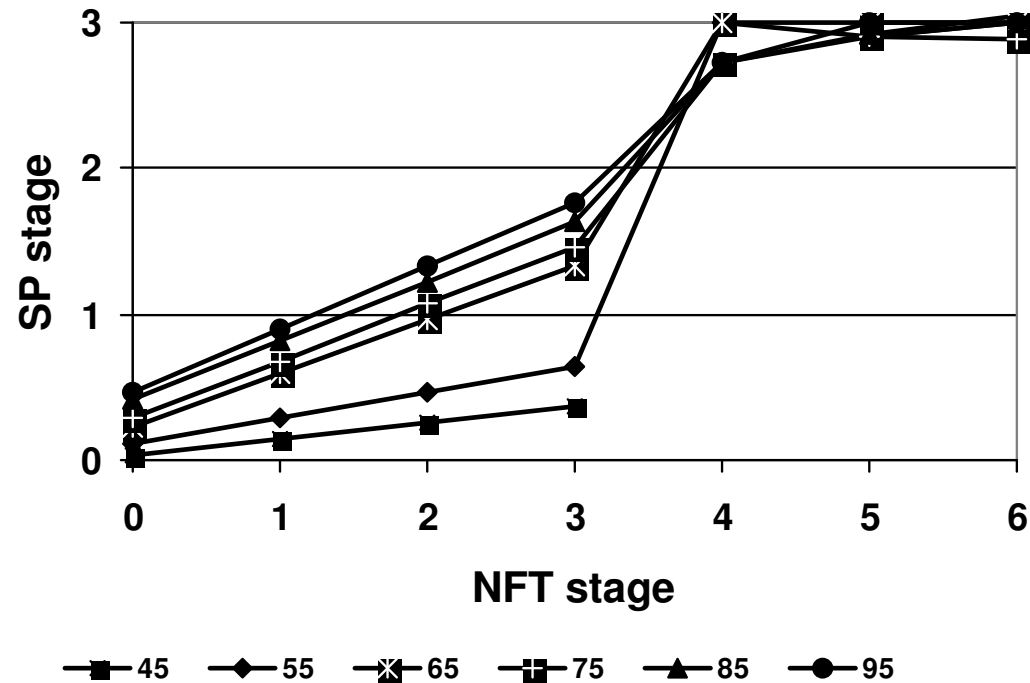
APOE genotype and NFT stage



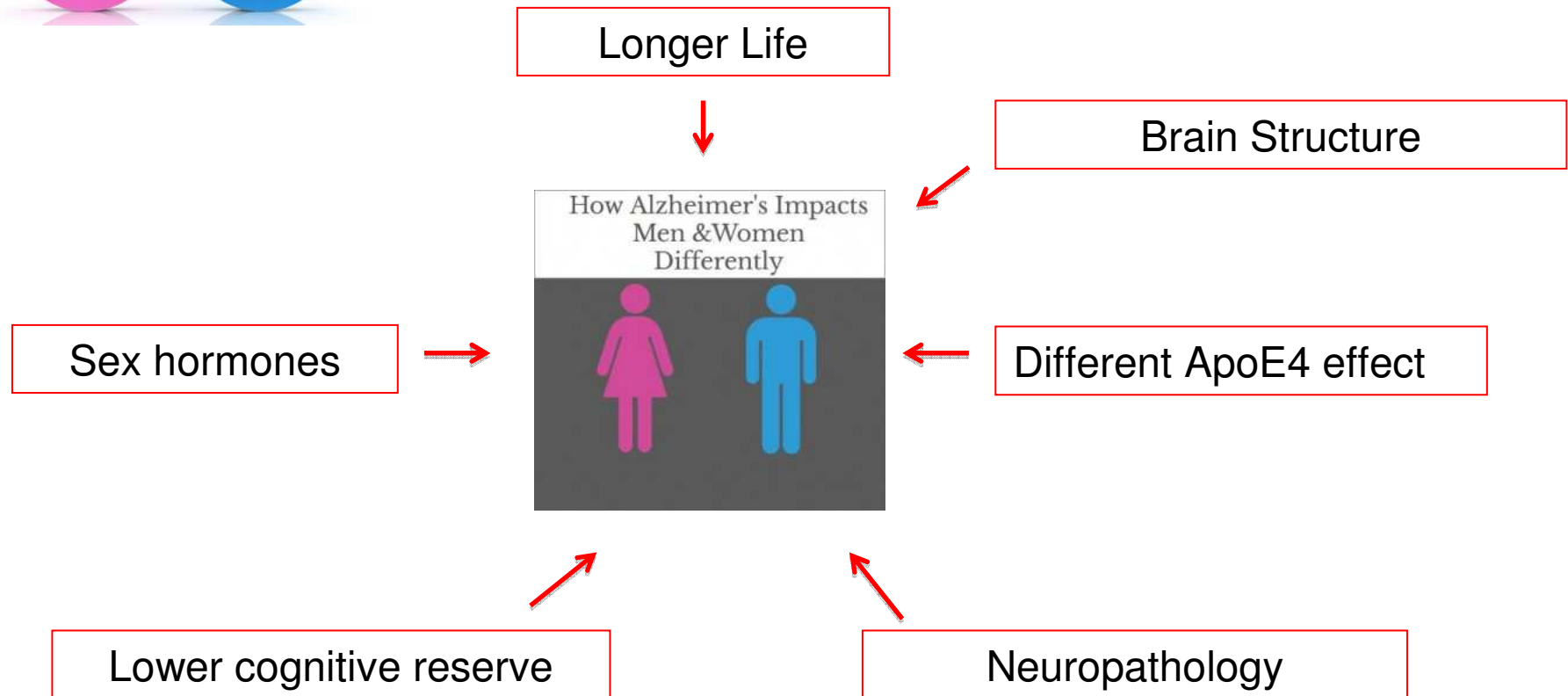
---■--- 2/3 w —■— 3/3 w —■— 3/4 w
---▲--- 2/3 m —▲— 3/3 m —▲— 3/4 m

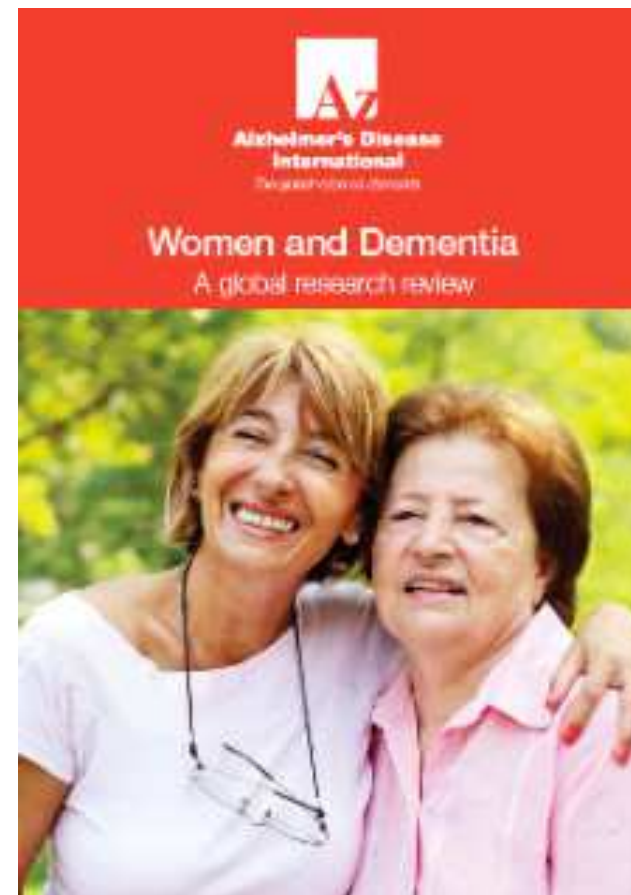
EH Corder

SP and NFT stage for women



- Women have a 3-year acceleration in tangle neuropathology associated with APOE4
- APOE4+ women have a large jump in senile plaque distribution in late middle age





Conclusioni

- La questione della medicina di genere diventa fondamentale quando si affronta il problema del declino cognitivo correlato all'età e alla malattia di Alzheimer
- Particolare attenzione deve essere data alla prevenzione di queste patologie nelle donne

GENDER DIFFERENCES IN CLINICAL MANIFESTATIONS AND OUTCOMES AMONG HOSPITALIZED PATIENTS WITH BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA

Symptoms	Men 122	Women 170	p
aggressiveness	78 %	52 %	<.001
Diurnal rhythm disturbances	89%	79%	<.05
Paranoid delusional ideation	12%	41%	<.001
Hallucination	7%	29%	<.001
Anxiety phobias	15%	44%	<.001
Favorable discharge	58%	77%	<.001

ME

THE
LONGEVITY
ISSUE

The Alzheimer's Pill

A radical new drug could change old age

By Alice Park

Plus

How to be wealthy at 100 [p92](#)

Three daily habits to change now [p80](#)

Long-life secrets from a clam [p74](#)

