



Differenze di genere nelle malattie neurodegenerative

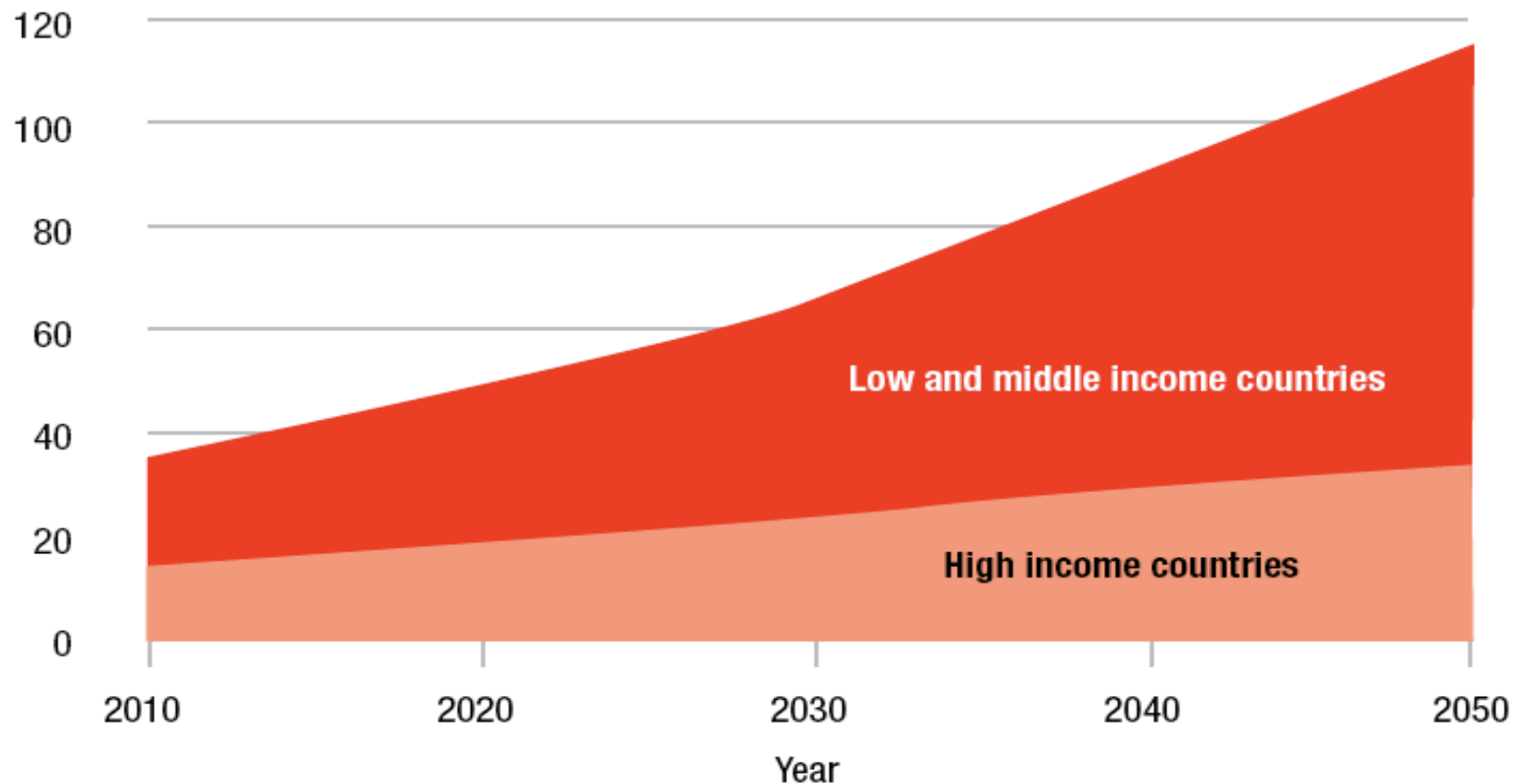
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dell'Invecchiamento Cerebrale
CRIC



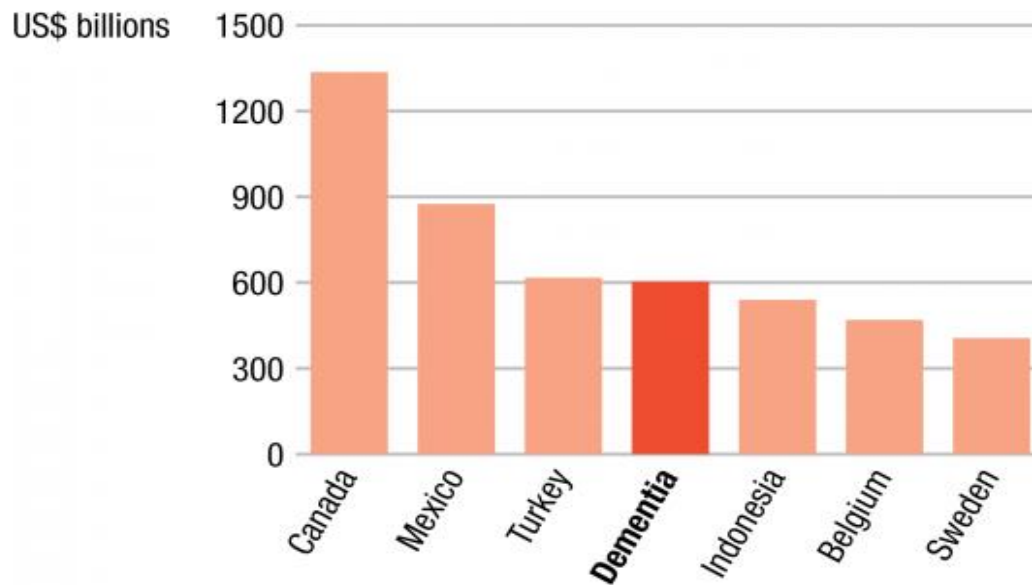
Prevalence of Dementia

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

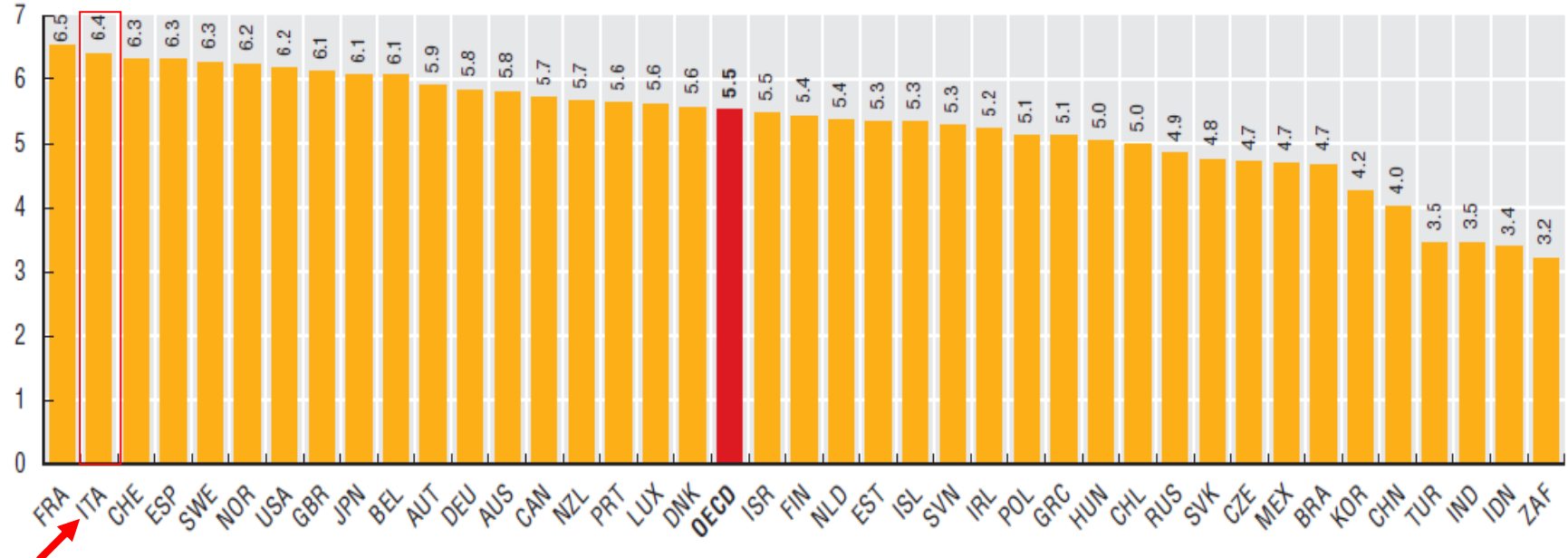
Cost of dementia compared to national economies



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)**

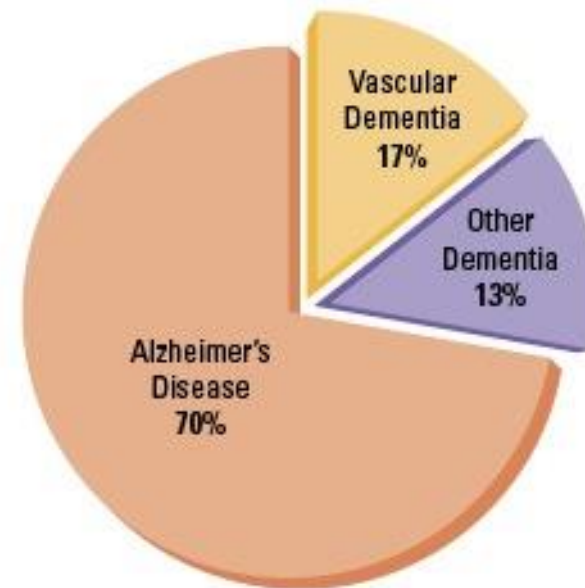
Dementia or Major Neurocognitive Disorder (DSM-5)

Dementia is an "Umbrella term", referring to *many different types* of dementia



The *most common* type of dementia is **Alzheimer's Disease** (illustrated as the handle of this umbrella)

Each of the lesser common types of dementia, such as **Vascular, Lewy Body, Frontotemporal**, etc, is illustrated as a separate section of the umbrella

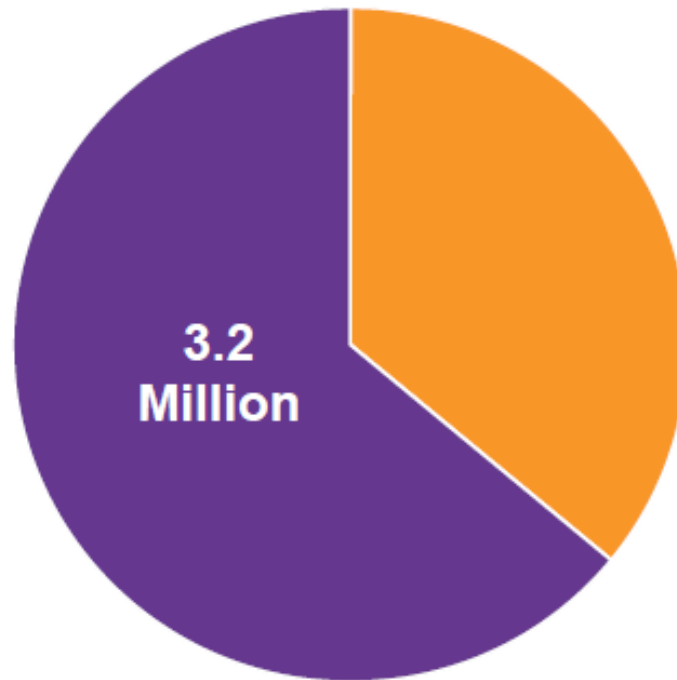


Source: Plassman, BL; Langa, KM; Fisher, GG; Heeringa, SG; Weir, DR; Ofstedal, MB, et al. "Prevalence of Dementia in the United States: The Aging Demographics, and Memory Study. *Neuroepidemiology* 2007; 29:125-132.³¹

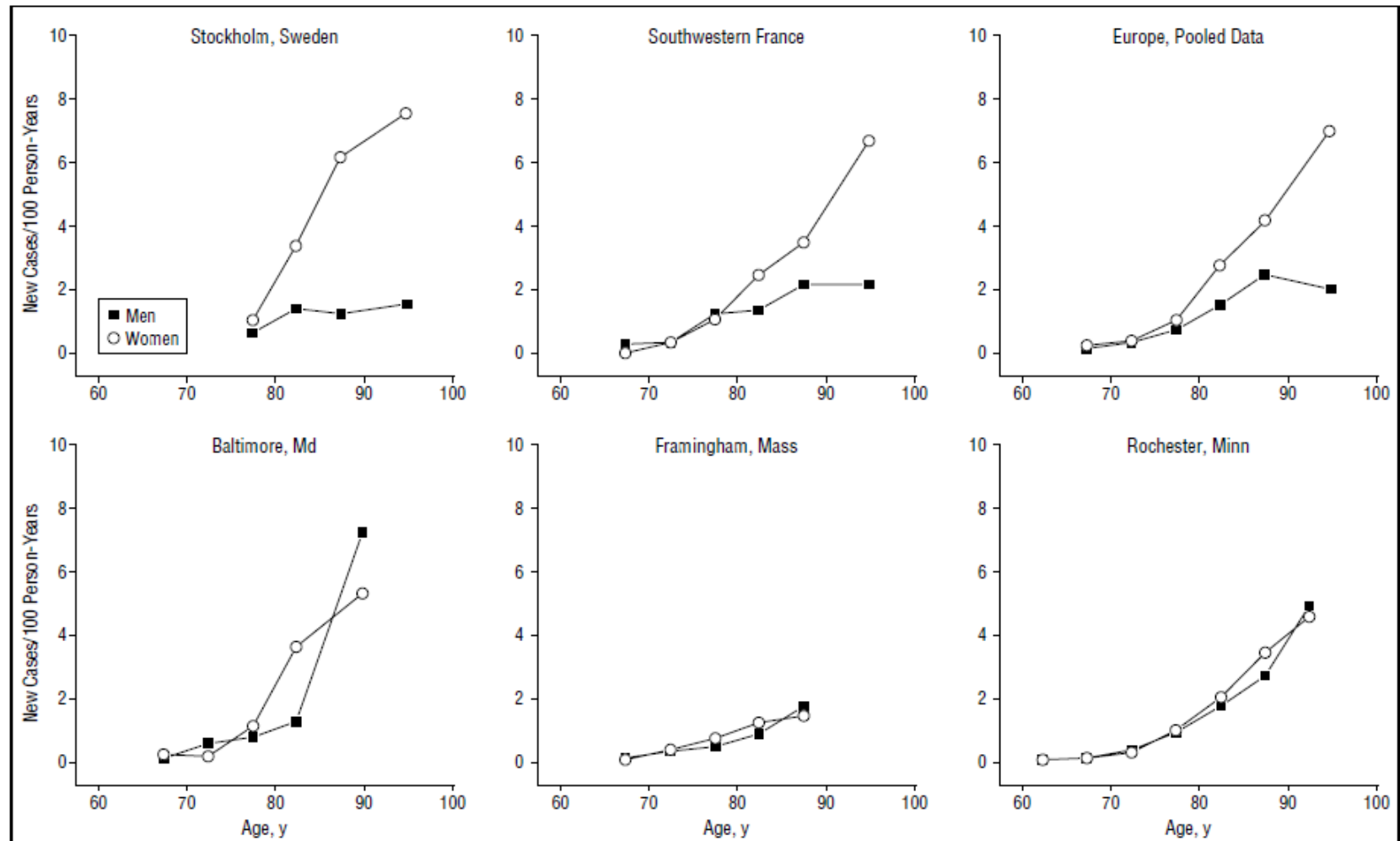
How Alzheimer's Impacts
Men & Women
Differently



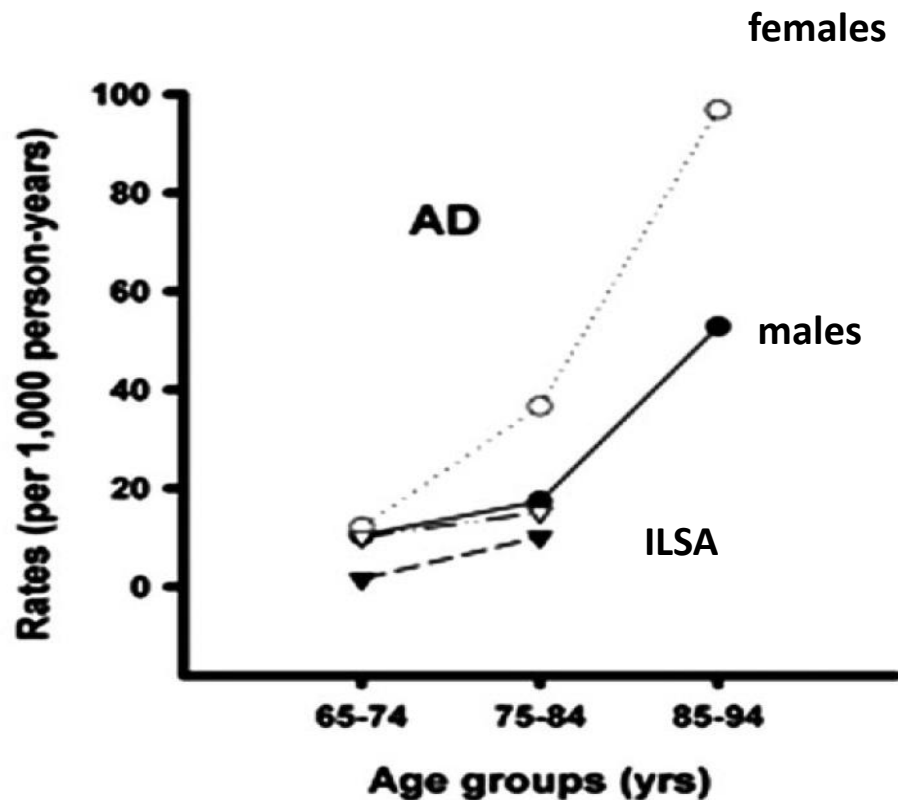
**Two-thirds of the 5 Million Seniors with
Alzheimer's Disease Are Women**



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

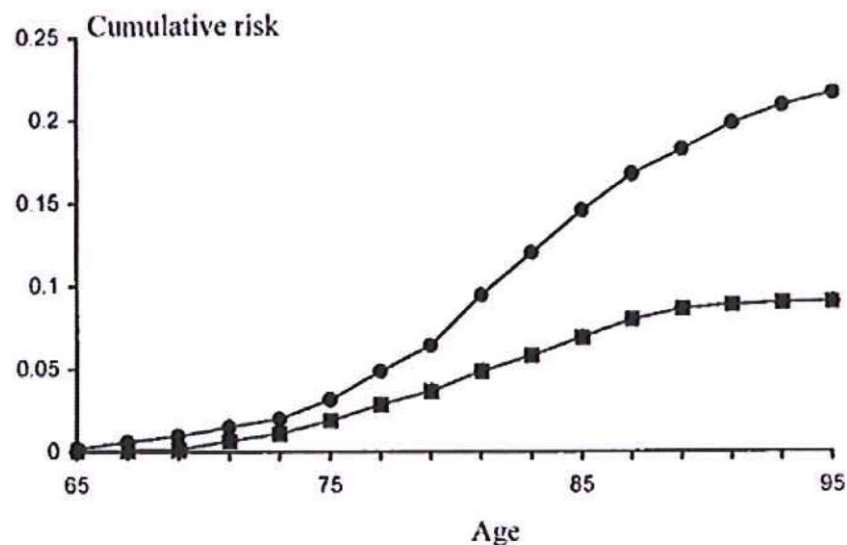


Figure 1. Sex-specific cumulative risk for a 65-year-old to develop AD by 95 years of age. Squares = men; circles = women.

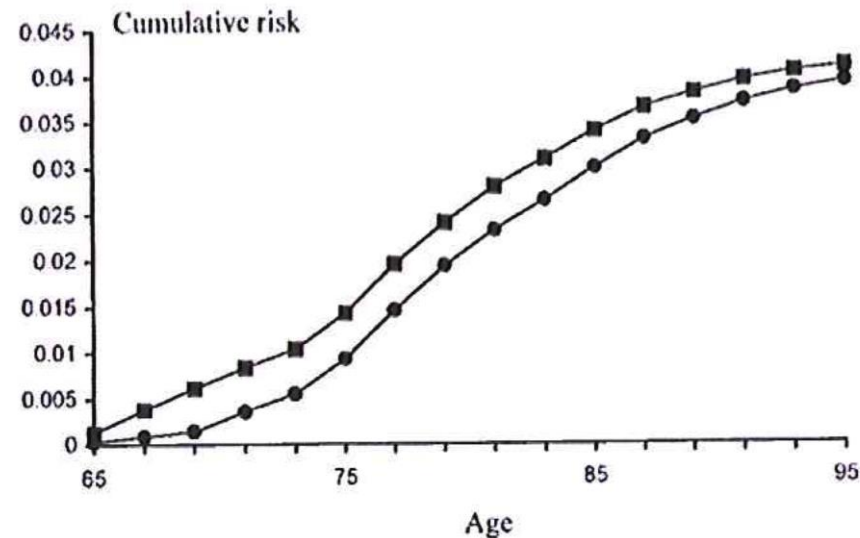
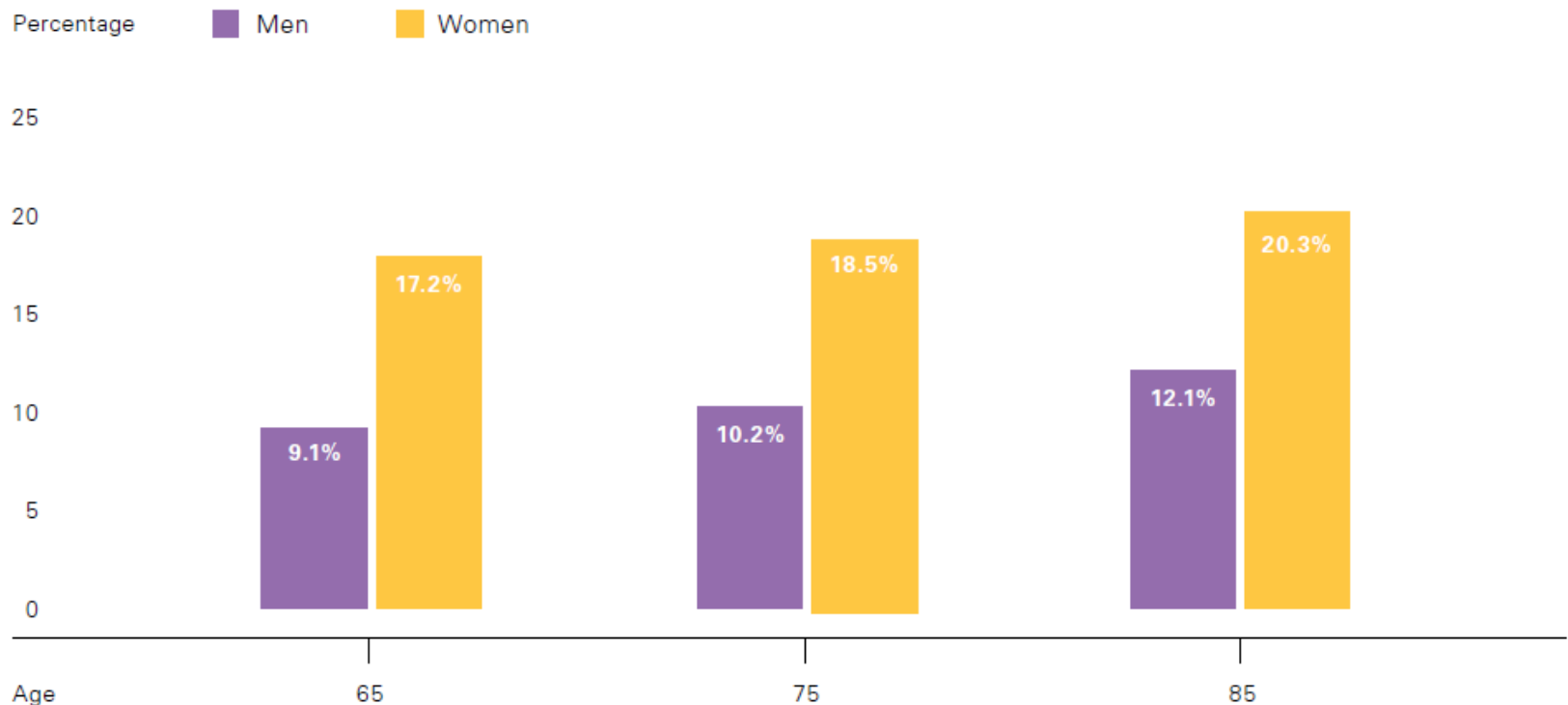


Figure 2. Sex-specific cumulative risk for a 65-year old to develop vascular dementia by 95 years of age. Squares = men; circles = women.

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:

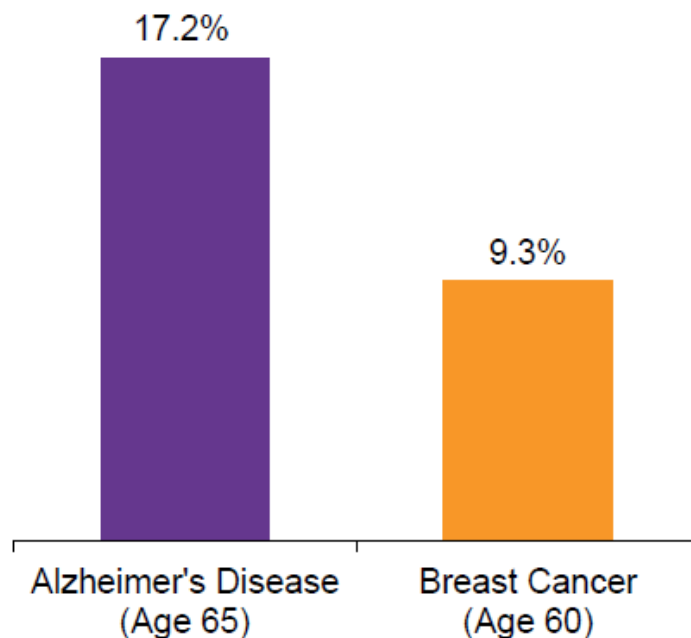
Framingham Estimated Lifetime Risks for Alzheimer's by Age and Sex



2014 Alzheimer's Disease Facts and Figures

Includes a Special Report on
Women and Alzheimer's Disease

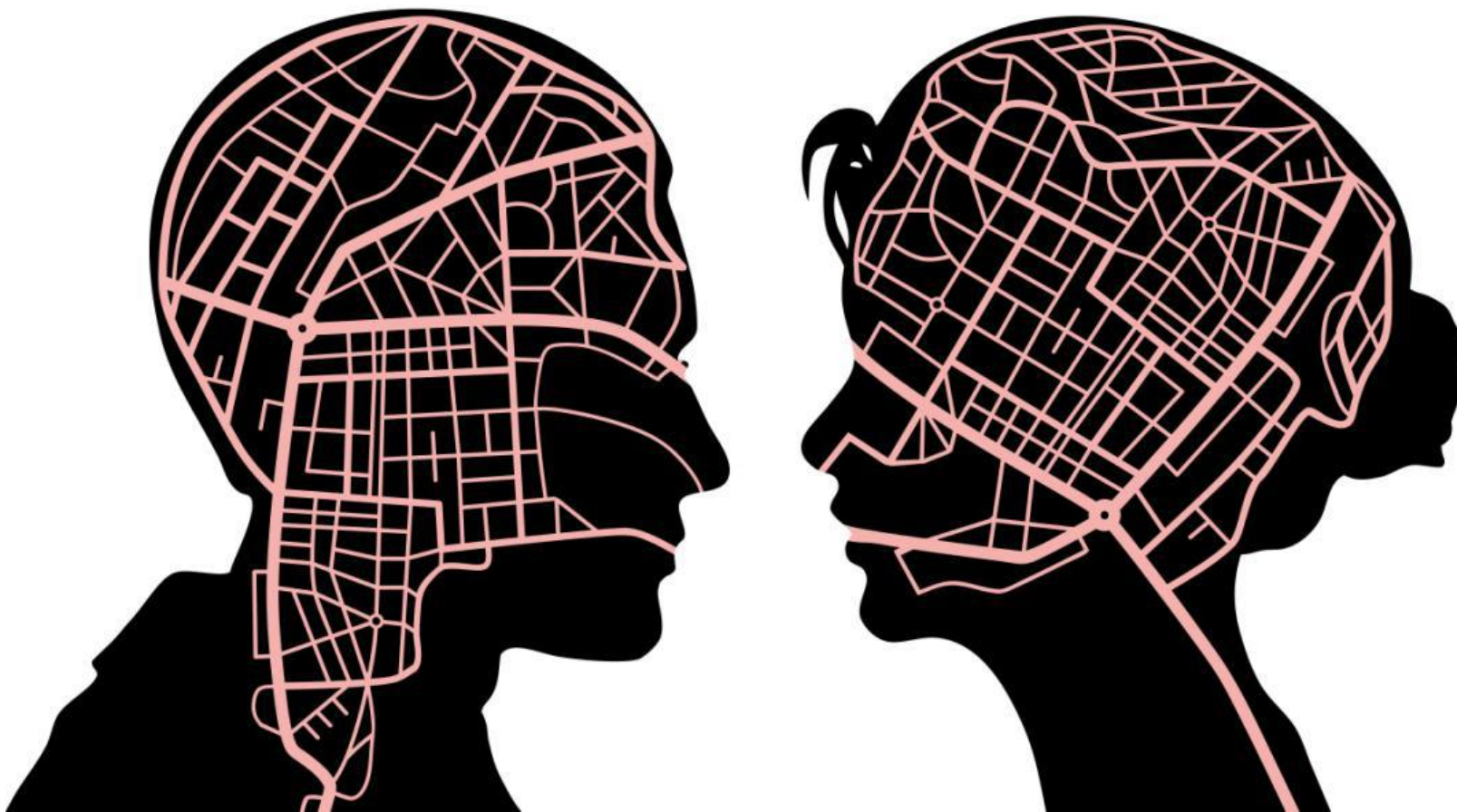
Remaining Lifetime Risk of Women
Developing Alzheimer's Disease and
Breast Cancer



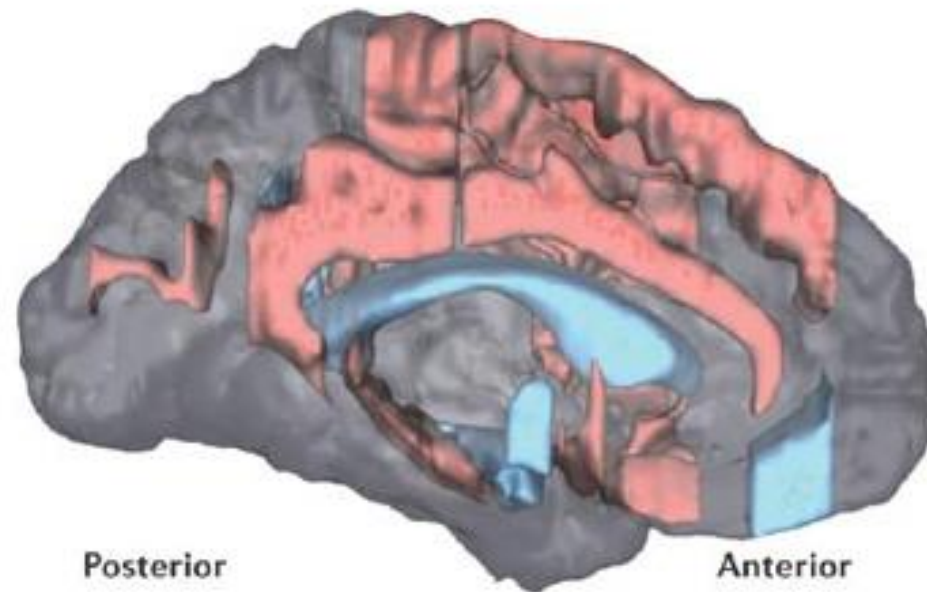


**Quali sono le ragioni perché le donne
presentano una maggiore
prevalenza di malattia di Alzheimer?**

Parità \neq Eguaglianza



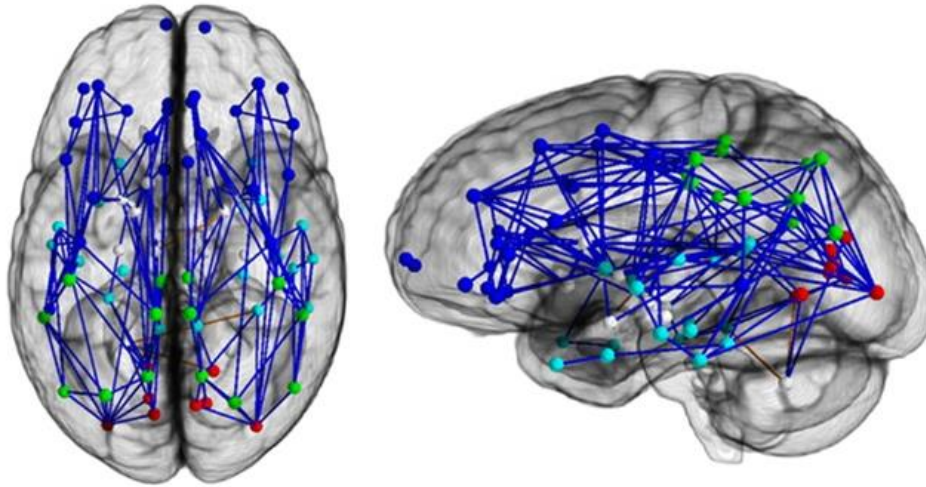
Brain structure and sex



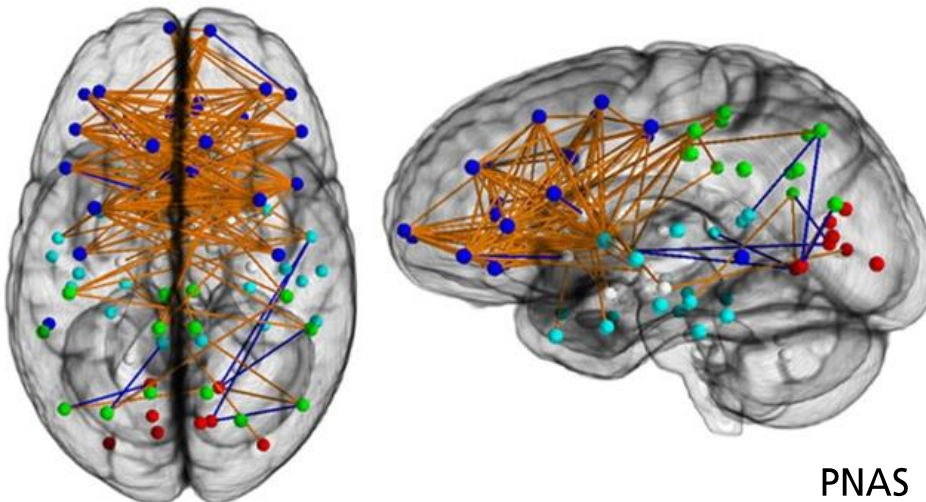
- Structures that are larger in the healthy female brain, relative to cerebrum size
- Structures that are larger in the healthy male brain, relative to cerebrum size

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

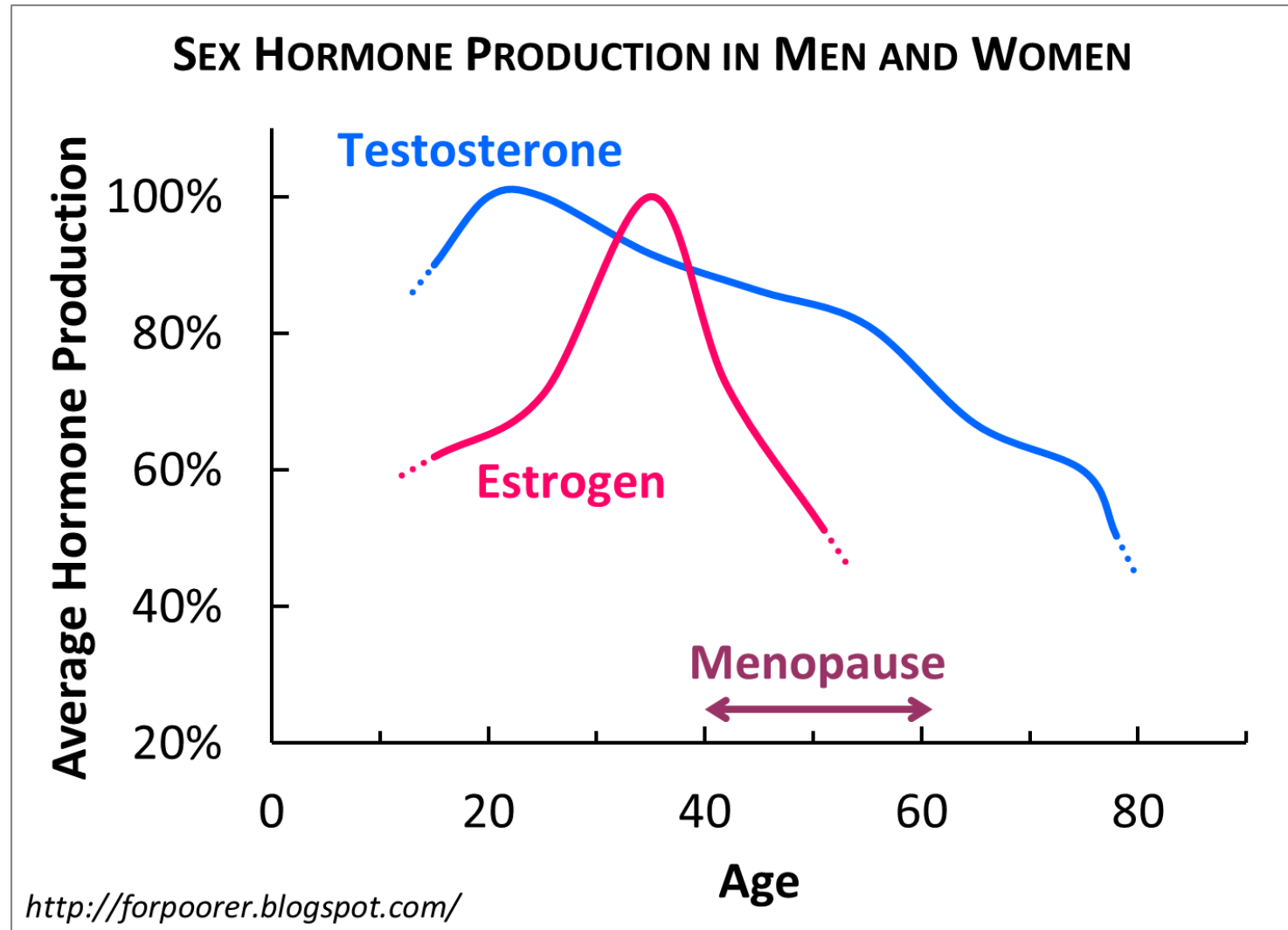
IRVINE 2012

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.

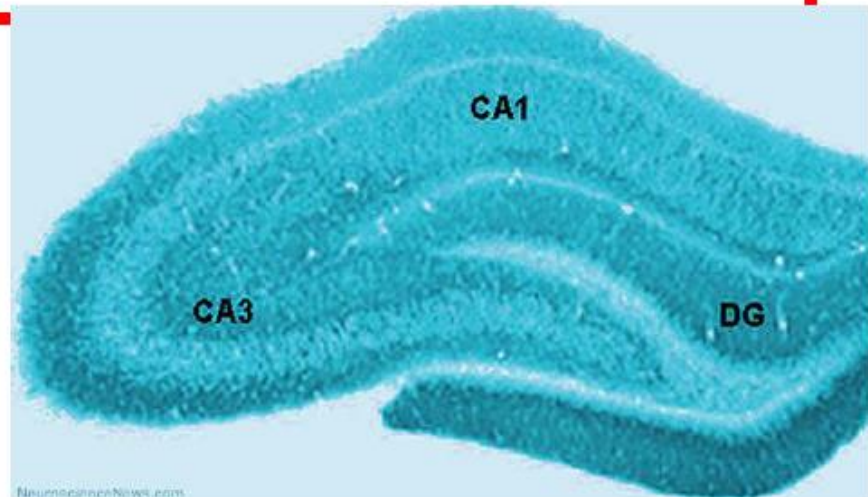
Sex hormones



Oestrogen deprivation

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

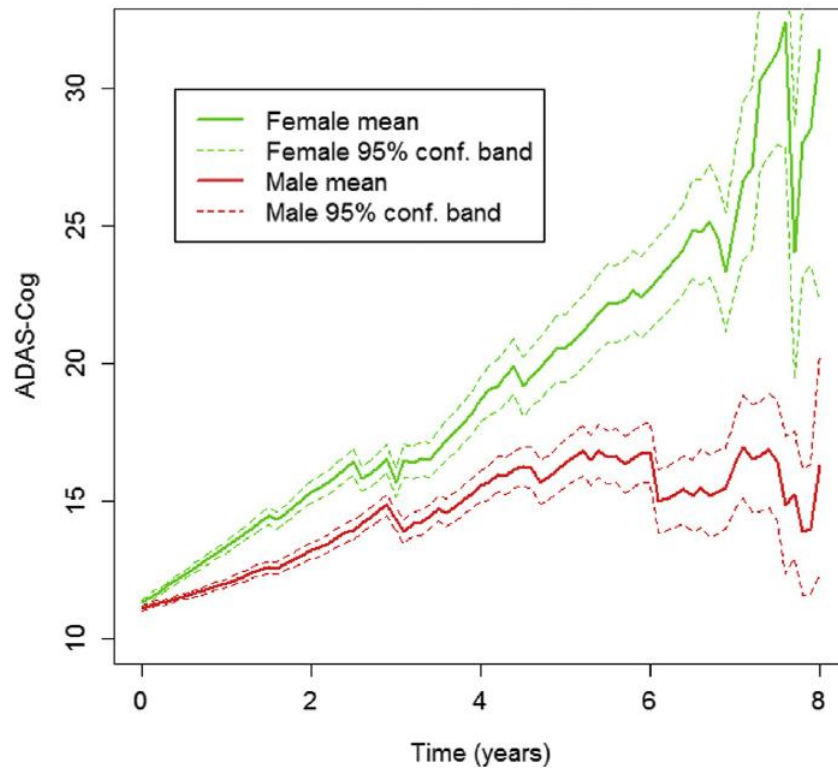
On animal model long-term oestrogen deprivation dramatically increases sensitivity of the normally resistant hippocampal CA3 region to ischaemic stress, an effect that was gender-specific



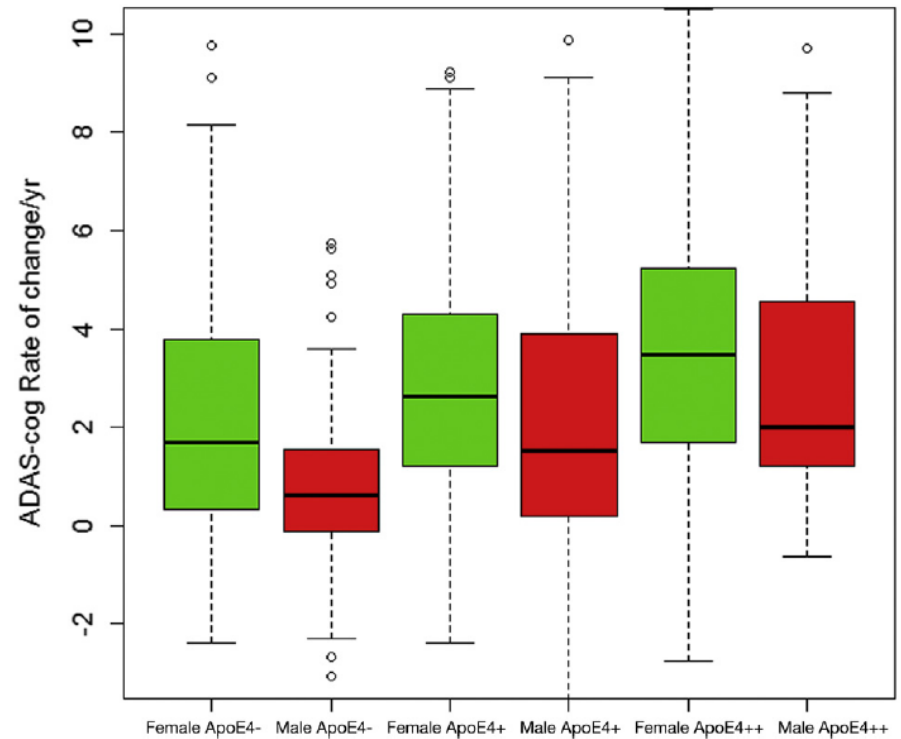
Featured Article

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

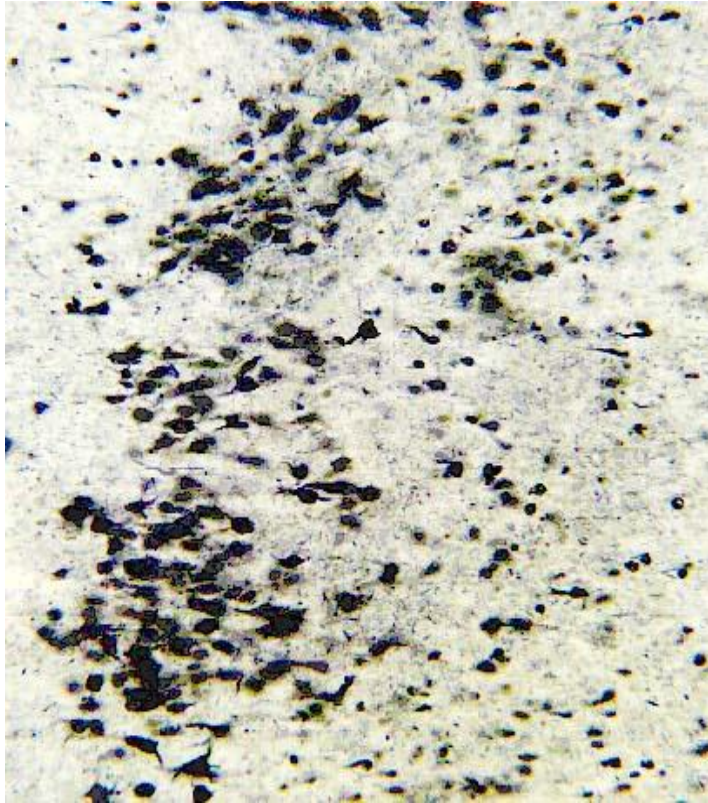
Mean trajectories



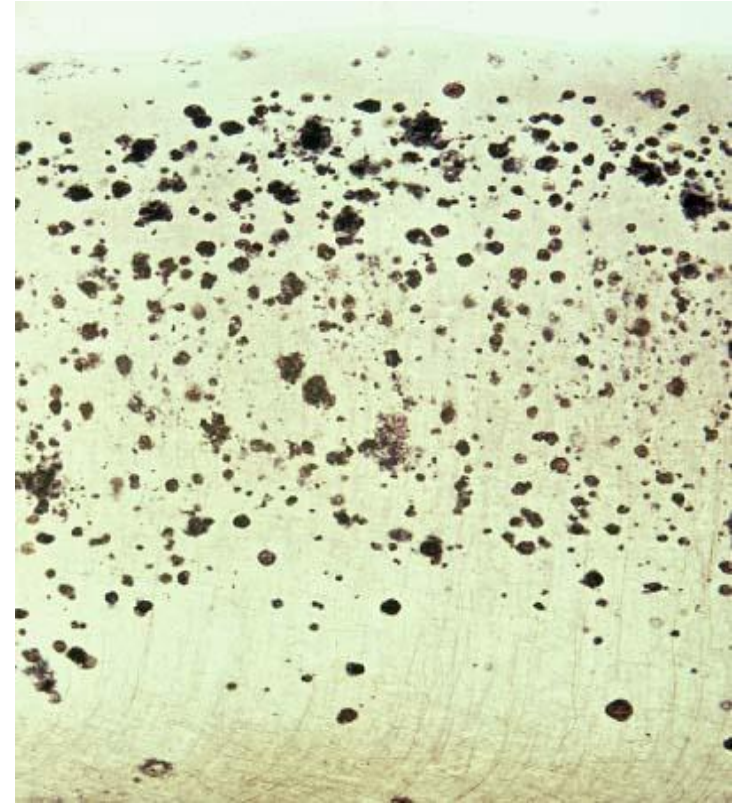
Median ADAS-Cog rate of change/yr by gender and apoE4 status



Neuropathological features of AD



**Neurofibrillary tangles
(NFT)**



**Amyloid- β deposition
(A β)**

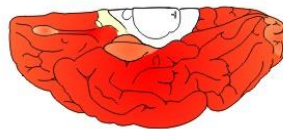
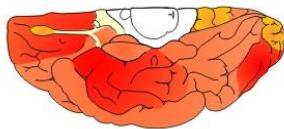
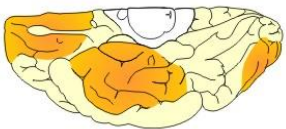
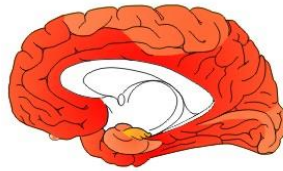
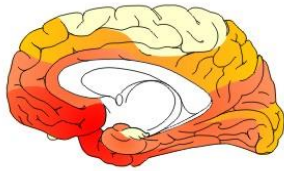
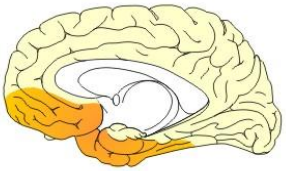
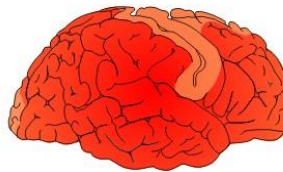
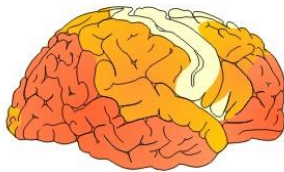
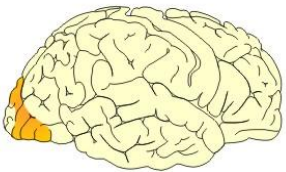
Neuropathological staging of AD

Amyloid β

**Stage
A**

**Stage
B**

**Stage
C**



Neurofibrillary tangles = NFT

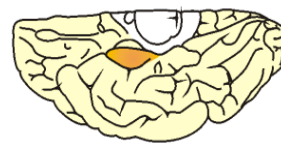
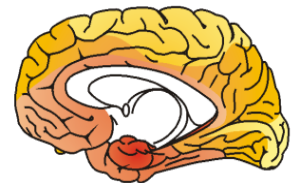
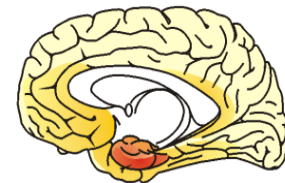
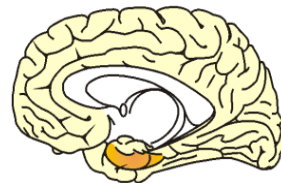
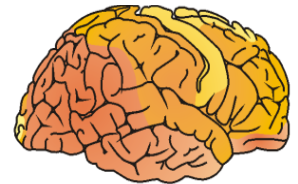
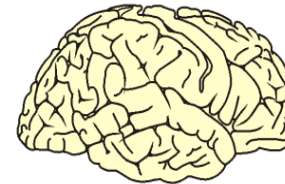
**NFT I-II
(Entorhinal
stages)**

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

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

Entorhinale Stadien
I-II

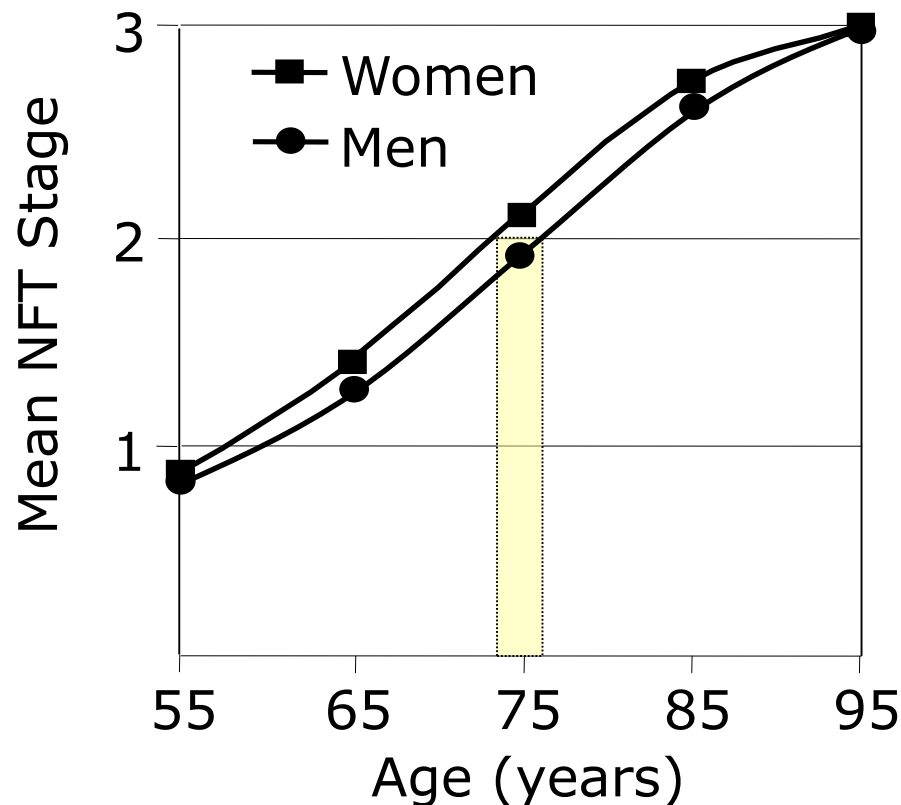
Limbische Stadien
III-IV



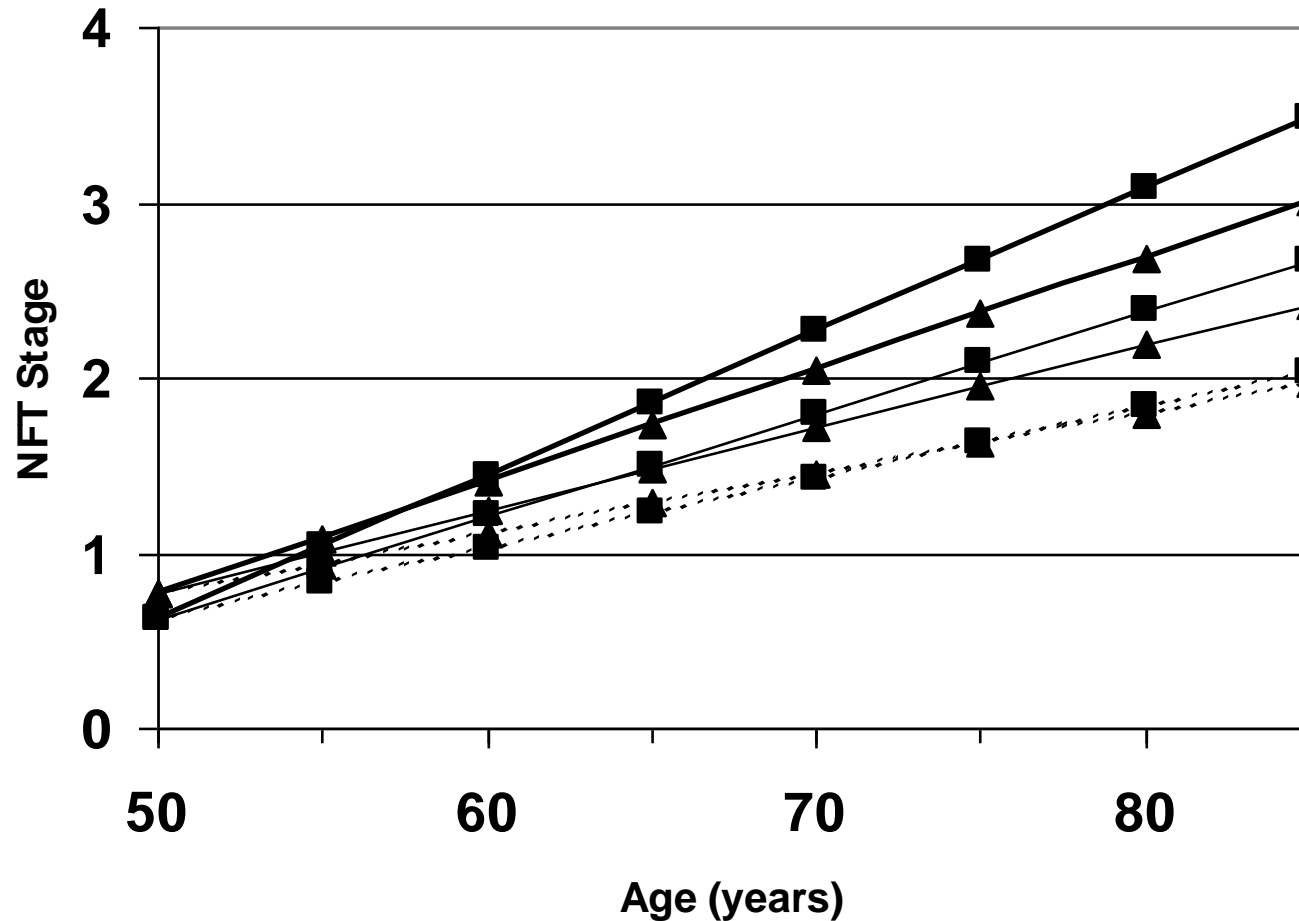
Braak and Braak 1991

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



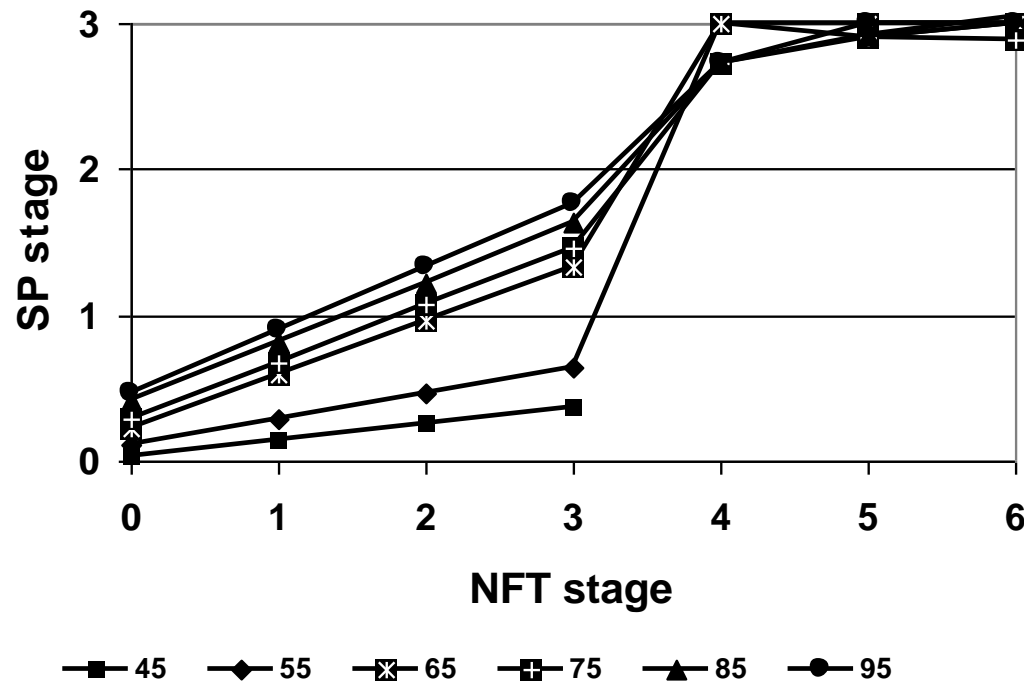
APOE genotype and NFT stage



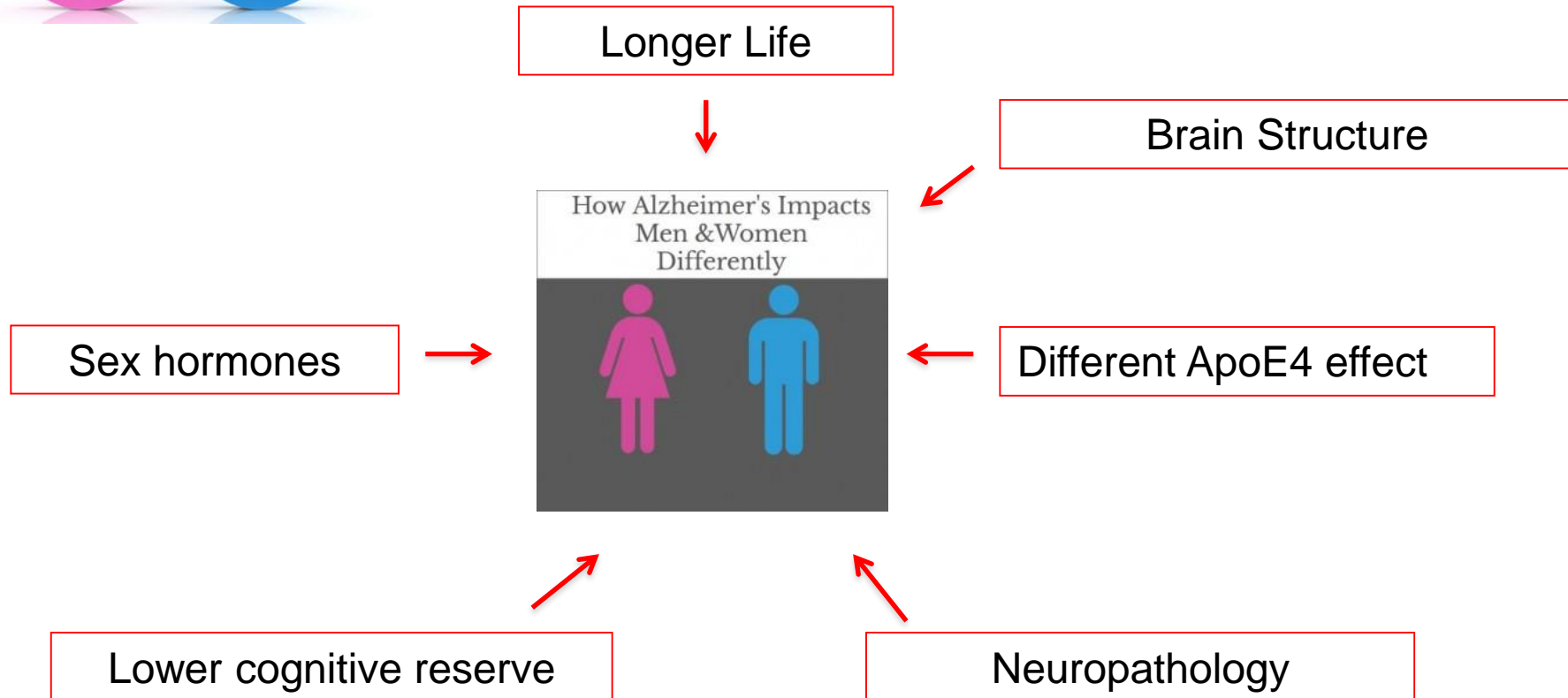
---■--- 2/3 w —■— 3/3 w —■— 3/4 w
---▲--- 2/3 m —▲— 3/3 m —▲— 3/4 m

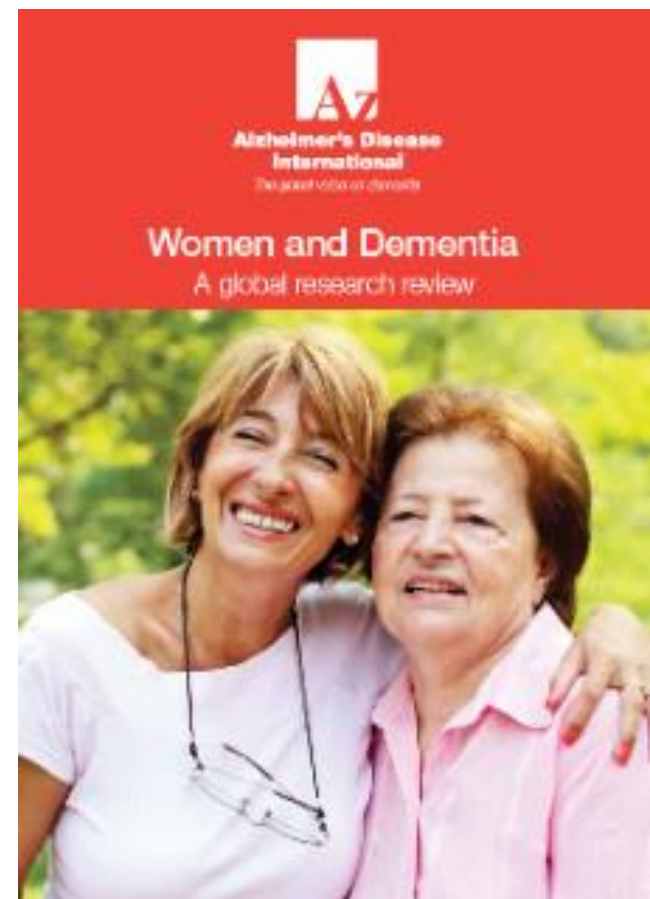
EH Corder

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

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ISSUE

The Alzheimer's Pill

A radical new drug
could change old age

By Alice Park

Plus

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