

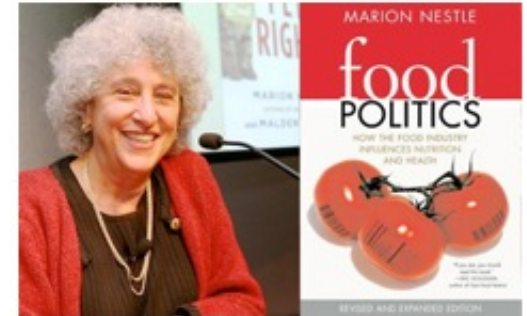
# The dementia impact and scientific conundrum: two challenges in search of a public health solution

Emiliano Albanese

Faculty of Bio-Medicine Università della Svizzera Italiana



LSHTM, London October 27th 2003, a Monday



# WHY ?



LSHTM, London October 27th 2003, a Monday



# WHY ?

**17:15 – 18:15  
WEDNESDAY  
19 FEB TO 27 MAY  
2020**

**ETH ZÜRICH HG  
D16.2**

**19 February** CLEAN AIR  
Nina Künzli, SSPH+ & Swiss TPH

**20 February** LEGAL/TECH IMPACT  
Emilio Albers, USI

**24 March** HEALTH LAW  
Dominique Sornoud, UNINE

**11 March** LAMP ON TOBACCO  
Luciano Ruggeri, UNINE

**18 March** PUBLIC POLICY/IMPACT/IMP  
Caroline Frey, Felix Celi, ETHZ

**20 March** PROSTATIC CANCER  
Sabine Rohrmann, USZ

**22 April** SO PUBLIC HEALTH INTERDISCIPLINARY WORK?  
Simon Wilcox, DHAW

**08 April** PERSONALIZED HEALTH  
Nicole Probst-Herold, Swiss TPH

**21 April** PUBLIC ENGAGEMENT/IMP  
Sara Stieger, UNIL & UNIGE

**29 April** GENETIC INTERVENTIONS  
Marika Kallunki, UNIBAS

**06 May** DATA & DIGITAL  
Deborah Cox, UNIZH/UNIGE

**13 May** MCL-SCHE  
Gerard Stucki, UNINE

**25 May** WORK AND WELLBEING  
Luisa Costa, SSPH+




## LECTURE AND DISCUSSION SERIES ON PRIME TOPICS OF PUBLIC HEALTH

How are new data sources forming public health research?  
How do law and health interact? What challenges does public health face – and what solutions does it offer?

Crisp and interactive talks followed by student led discussion will reflect these and other novel and challenging topics.

This lecture series is designed for students of medicine and health sciences (including those with no background in public health) as well as all interested.

Information, links to reading materials, live streaming and recorded lectures can be found here:  
[ssphplus.ch/19h-lectures](https://ssphplus.ch/19h-lectures)

Moderator: Agnè Uijse



**ETH** zürich



**SSPH+**

SWISS SCHOOL OF  
PUBLIC HEALTH

# Let's start with a definition: PUBLIC HEALTH



Great  
diversity:  
cool!

17:15 - 18:30  
WEDNESDAY  
19 FEB TO 20 FEB  
2020

ETH ZÜRICH HG  
D16.2

19 February CLEAN AIR  
Nina Kolditz, USPH & Swiss TPH

20 February GENETIC IMPACT  
Emiliano Alberici, USI

HEALTH LAW  
24 March  
Dominique Sprent, UNINE

14 March LAW ON TOBACCO  
Luciano Rigotti, UNIDE

18 March PUBLIC POLICY RESPONSES  
Caroline Full, Felix C. Li, ETHZ

PROSTATE CANCER  
25 March  
Sabina Rohrmann, USZL

28 April SO PUBLIC HEALTH INTERVENTIONS WORK?  
Simon Wilcox, ZHAW

08 April PREVENTING HEALTH  
Nicole Probst-Haas, Swiss TPH

21 April SOCIAL INEQUALITIES  
Sara Steingard, UNL & UNICEF

29 April QUANTITATIVE INTERVENTIONS  
Marka Klapack, UNIBAD

06 May DATA & EQUITY  
Deborah Cowling, UNICEF

13 May WELL-BEING  
Gerard Stucki, UNILU

21 May WORK AND WELLBEING  
Luisa Garcia, USPH



THIS IS  
PUBLIC  
HEALTH

The **common ingredient** is a viewpoint, a world view...

Public Health is the **discipline** that addresses health at the **population level**

# WHY am I here ?



**PAST**



**FUTURE**



# Alzheimer

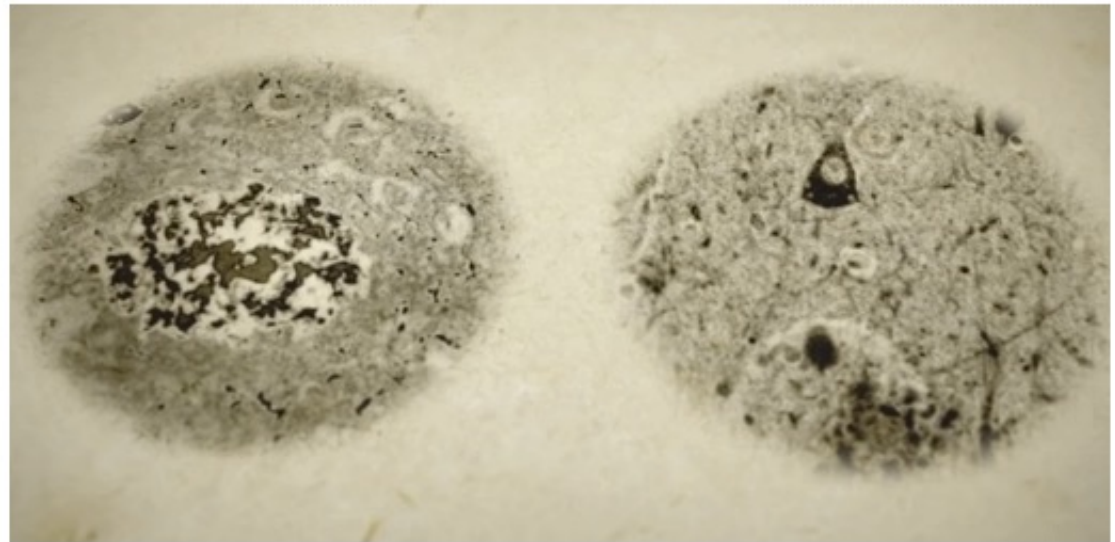


Dr. Alois Alzheimer



Auguste D

Frankfurt, **1901/1906**  
Prof. Alois Alzheimer  
describes a  
**NEW DISEASE** in a 51-  
year-old woman,  
August D.



August D's brain histopathological lesions

Really?

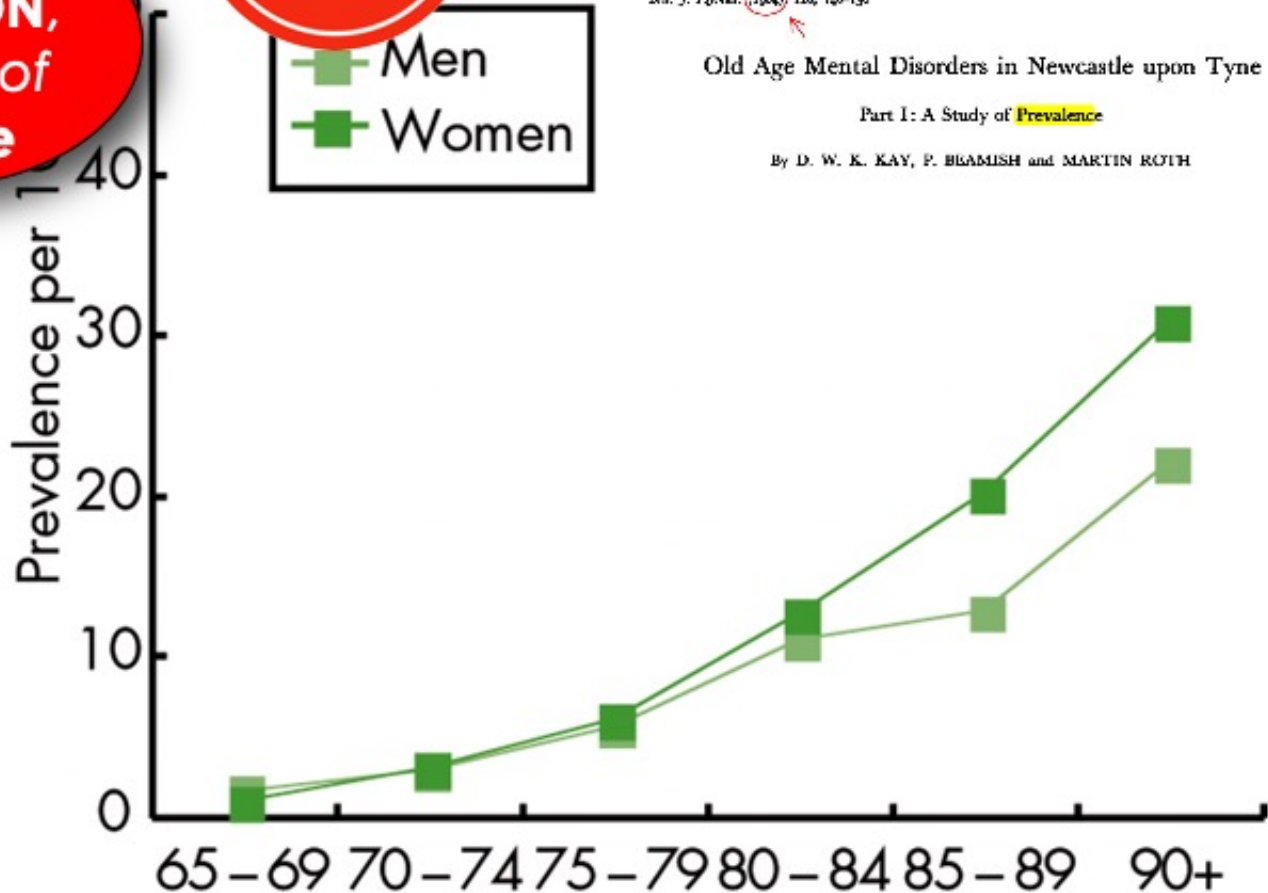


Sir Martin Roth

It's a **COMMON**, disease of **late-life**

**THIS IS PUBLIC HEALTH**

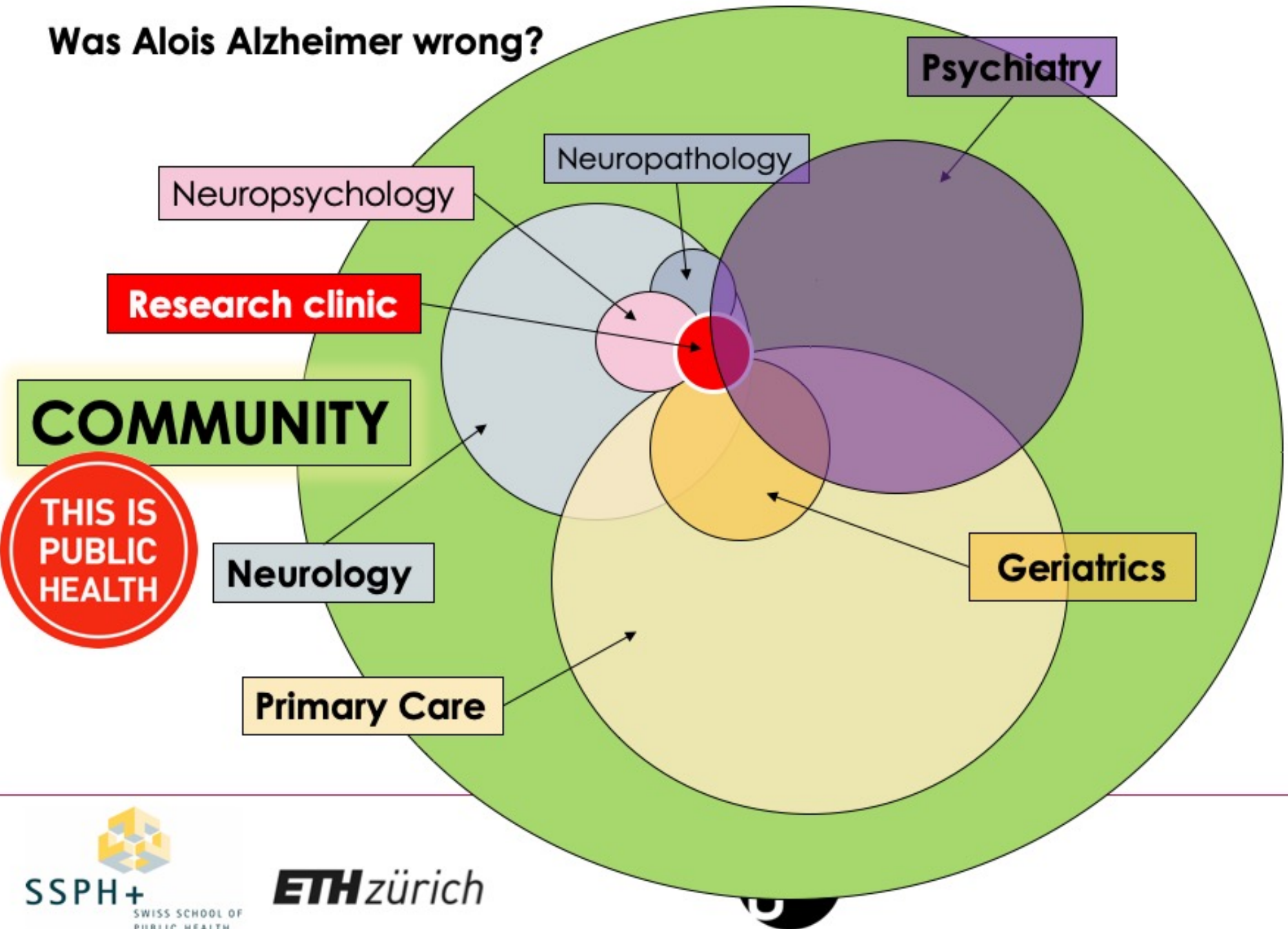
Newcastle, **1965**  
First epidemiological study on dementia



Brit. J. Psychiat. (1964) 110, 146-158  
Old Age Mental Disorders in Newcastle upon Tyne  
Part I: A Study of Prevalence  
By D. W. K. KAY, P. BEAMISH and MARTIN ROTH

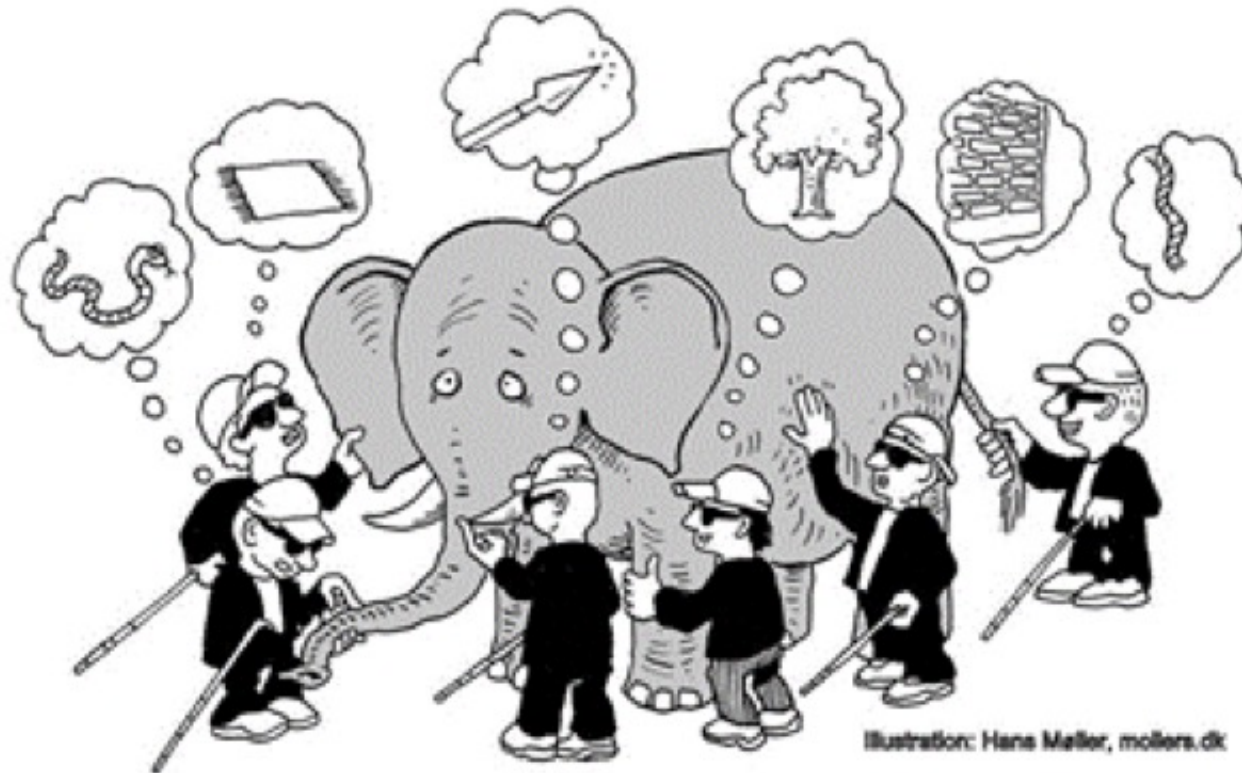


# Was Alois Alzheimer wrong?

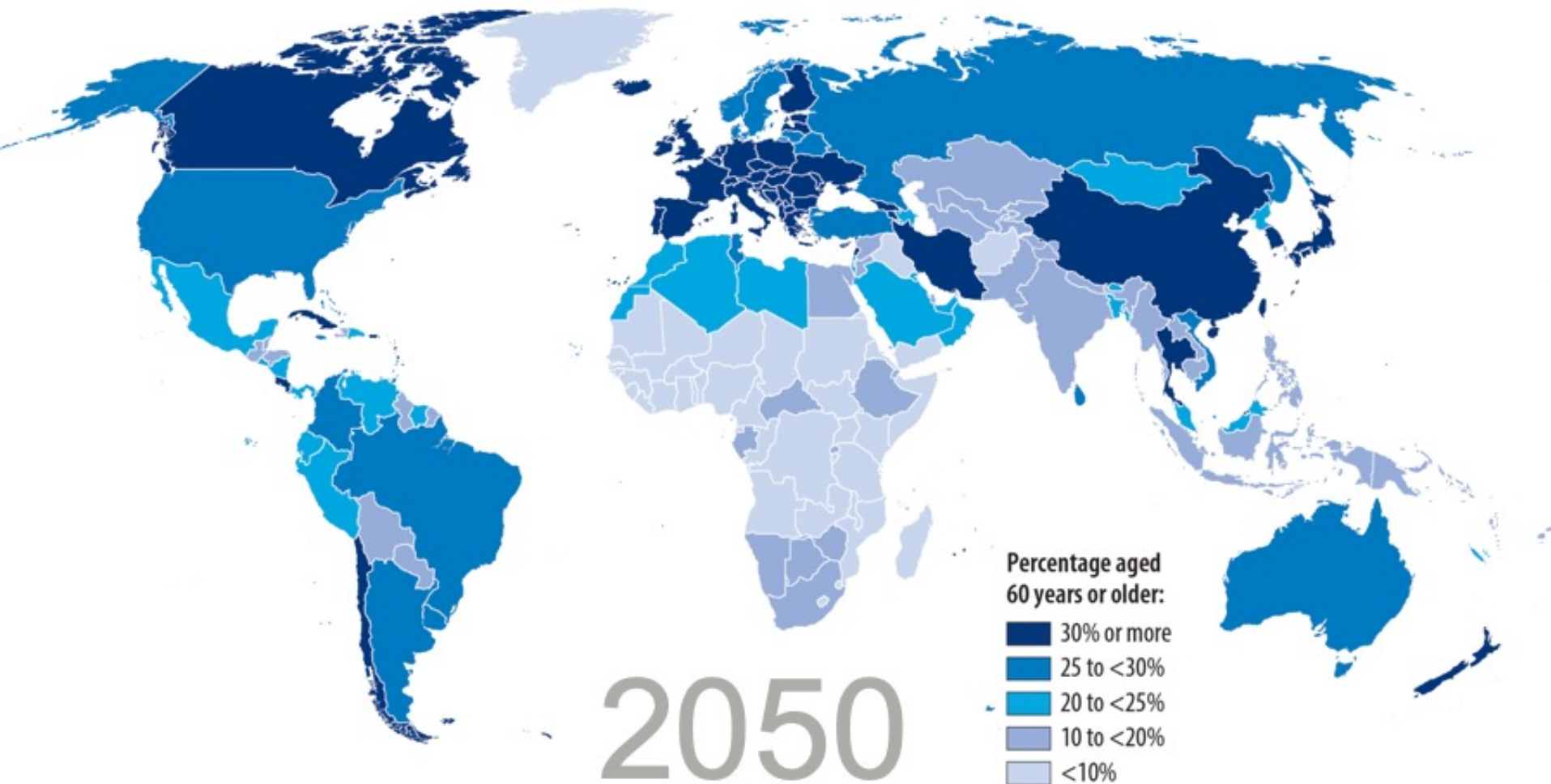


## Viewpoints and world views

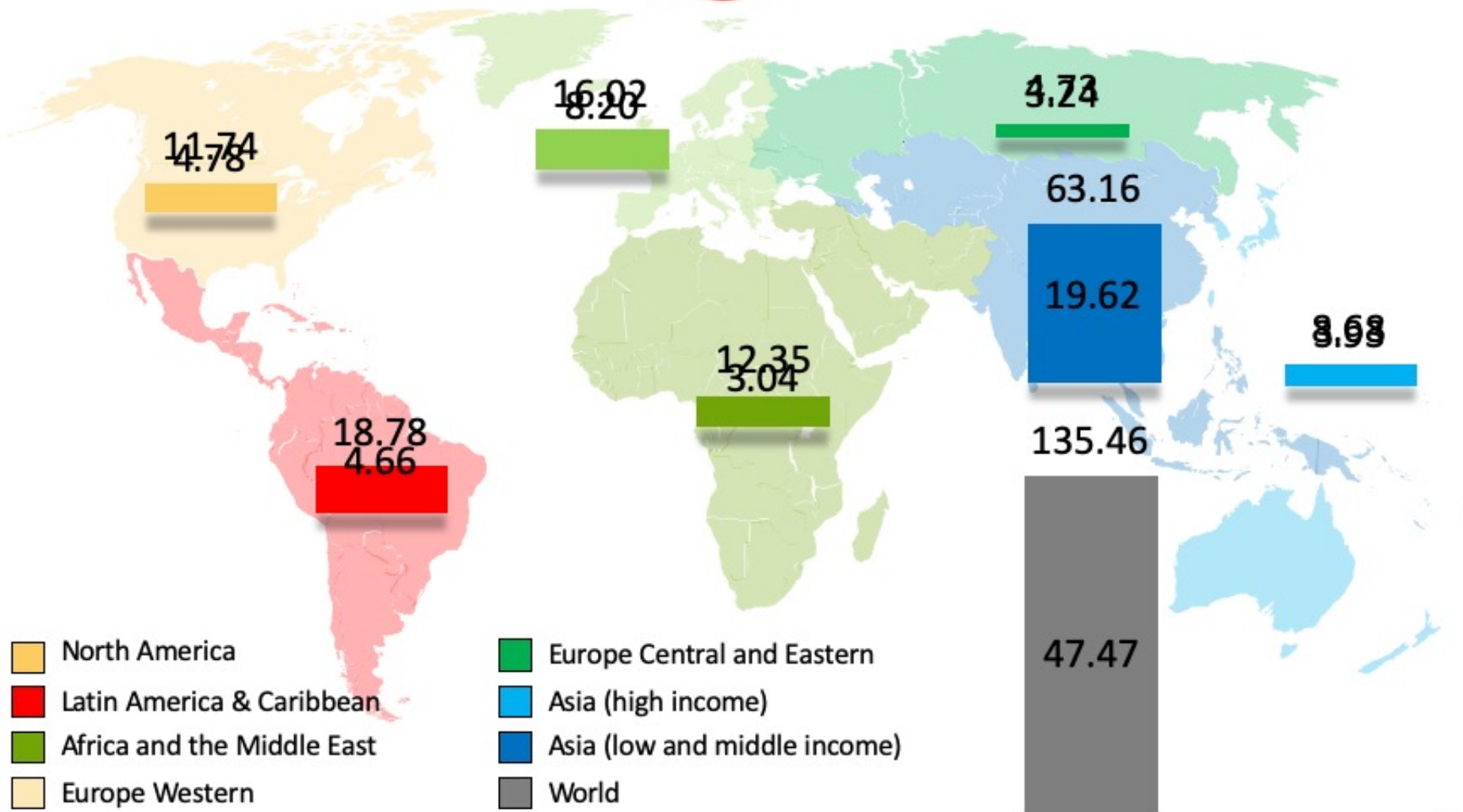
Where are patients with dementia seen?



## How common is it?



# How common is it?

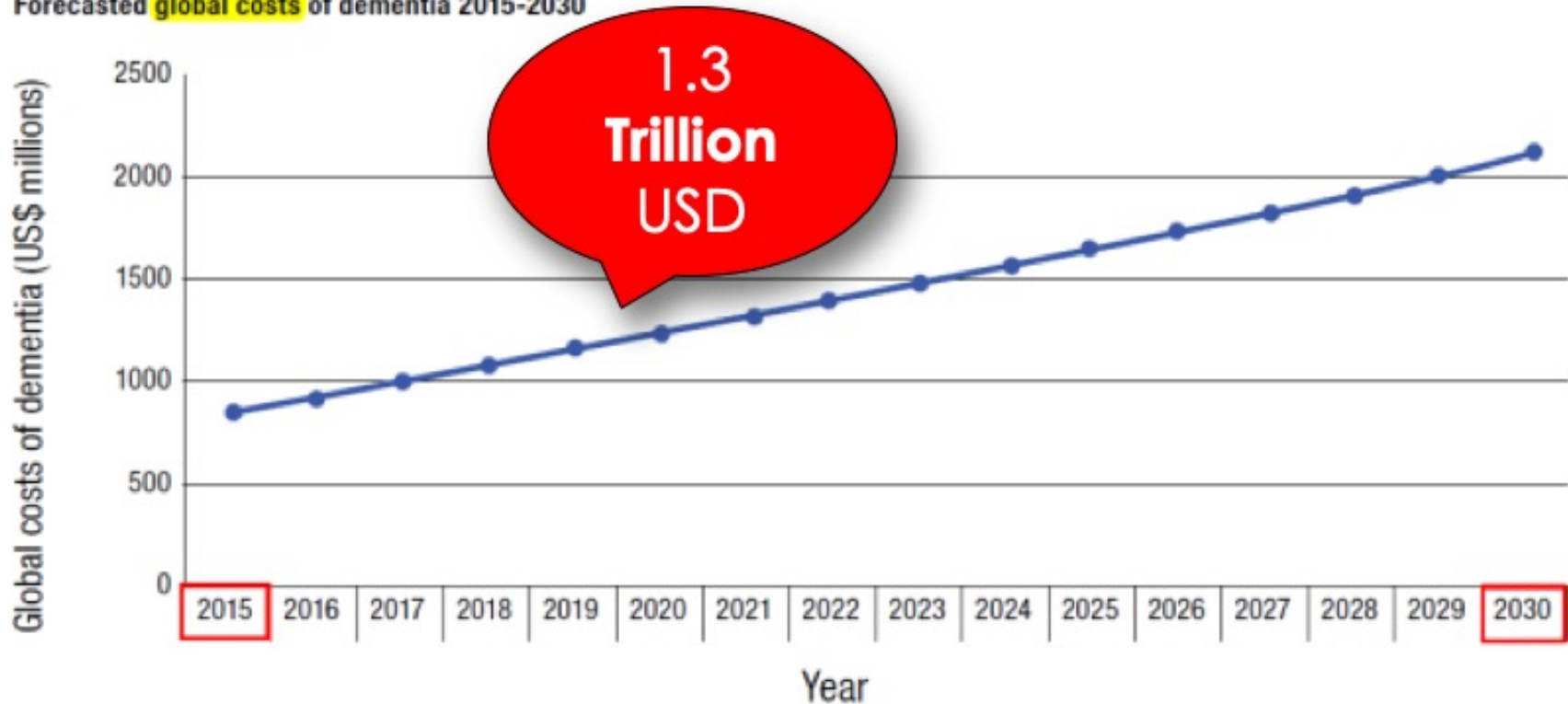


## How much does it COST?

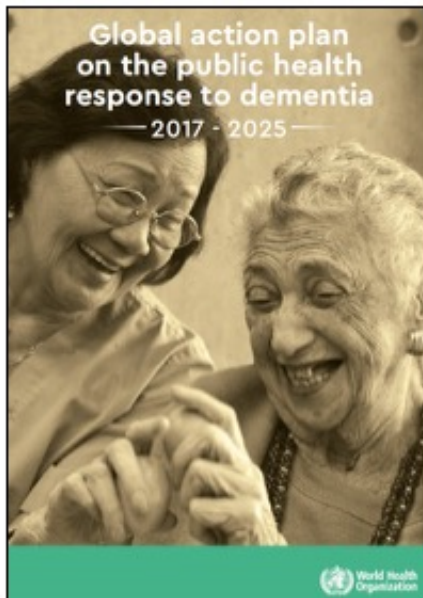
- 1.3 trillion USD in 2019
- = Apple market value



Forecasted global costs of dementia 2015-2030



Are we doomed?



## The Global Action Plan on the Public Health Response to Dementia 2017 - 2025

### Vision

A world in which dementia is prevented and people with dementia and their carers live well and receive the care and support they need to fulfil their potential with dignity, respect, autonomy and equality.

### Goal

To improve the lives of people with dementia, their carers and families, while decreasing the impact of dementia on them as well as on communities and countries.

Geneva, in **2017**

The **WHO** launched the dementia global action plan

# What's the plan?



## 7 action areas A public health approach



Risk reduction

Research

## The problem

What are the **causes** of dementia?

**WE DO NOT KNOW**



## Problem: **we do not know the causes**

1. Primary prevention is **impossible**
2. Secondary prevention is **difficult**



Risk  
reduction

A 2 year **multidomain intervention** of **diet**, **exercise**, **cognitive training**, and **vascular risk monitoring** versus control to prevent cognitive decline in at-risk elderly people (**FINGER**): a randomised controlled trial

Tilo Ngandu, Jenni Lehtisalo, Aino Solomon, Esko Levälahti, Satu Ahtiluoto, Riitta Antikainen, Lars Backman, Tuomo Hänninen, Antti Jula, Tiina Laatikainen, Joana Lindström, Francesca Mangialasche, Teemu Paajanen, Satu Pajala, Meri Peltanen, Rainer Rauramaa, Anna Stålskov et al., Timo Strandberg, Jaakko Tuomi, Heikki Soininen, **Mika Kivipelto**

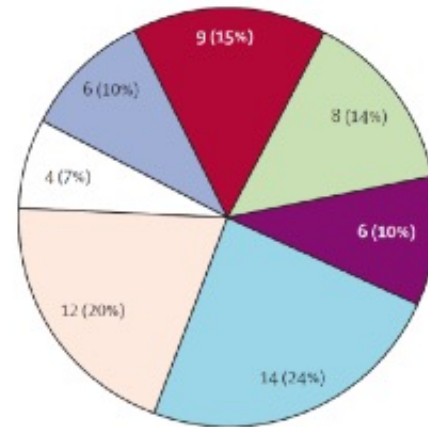


## Problem: **we do not know the causes**

1. Primary prevention is **impossible**
2. Secondary prevention is **difficult**
3. Research is crucial!



Research



- Prevention, identification, and reduction of risk (ie, genetic, lifestyle, or environmental)
- Diagnosis, biomarker development, and disease monitoring
- Pharmacological and non-pharmacological clinical-translational research
- Quality of care for people with dementia and their carers
- Delivery of care and services for people with dementia and their carers
- Physiology and progression of normal ageing and disease pathogenesis
- Public awareness and understanding

## Research priorities to reduce the global burden of dementia by 2025

Hiral Shah\*, Emiliano Albanese\*, Cynthia Duggan, Igor Rudan, Kenneth M Langa, Maria C Carrillo, Kit Yee Chan, Yves Joanette, Martin Prince, Martin Rossor, Shekhar Saxena, Heather M Snyder, Reisa Sperling, Mathew Varghese, Huili Wang, Marc Wortmann, Tarun Dua

Lancet Neurol 2016; 15: 1285-94

**Problem: we do not know the causes**

1. Primary prevention is **impossible**
2. Secondary prevention is **difficult**
3. Research is crucial!
4. Treatment is... "a prescription to **failure**"



## The problem

What are the **causes** of dementia?

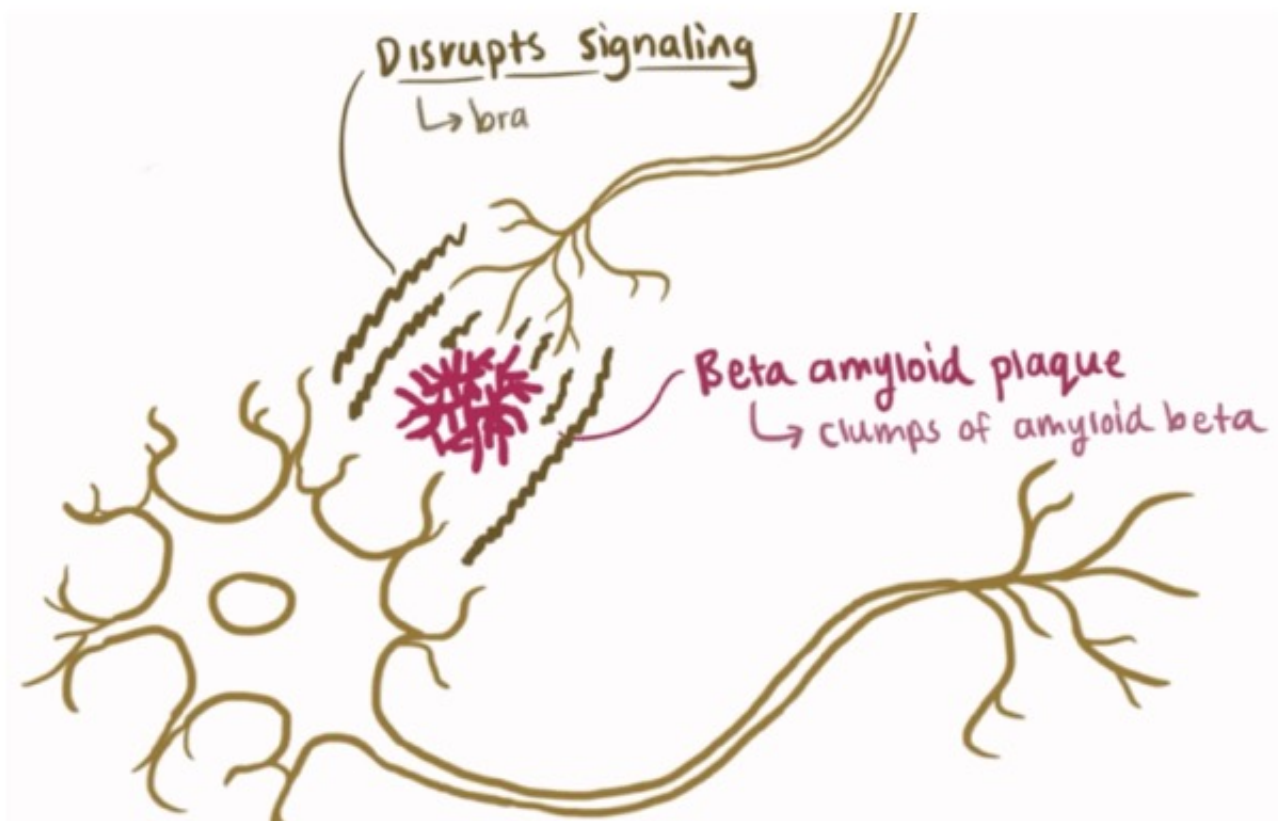
**...we do have some clues**

# Neuropathological hallmarks



## Disease pathways

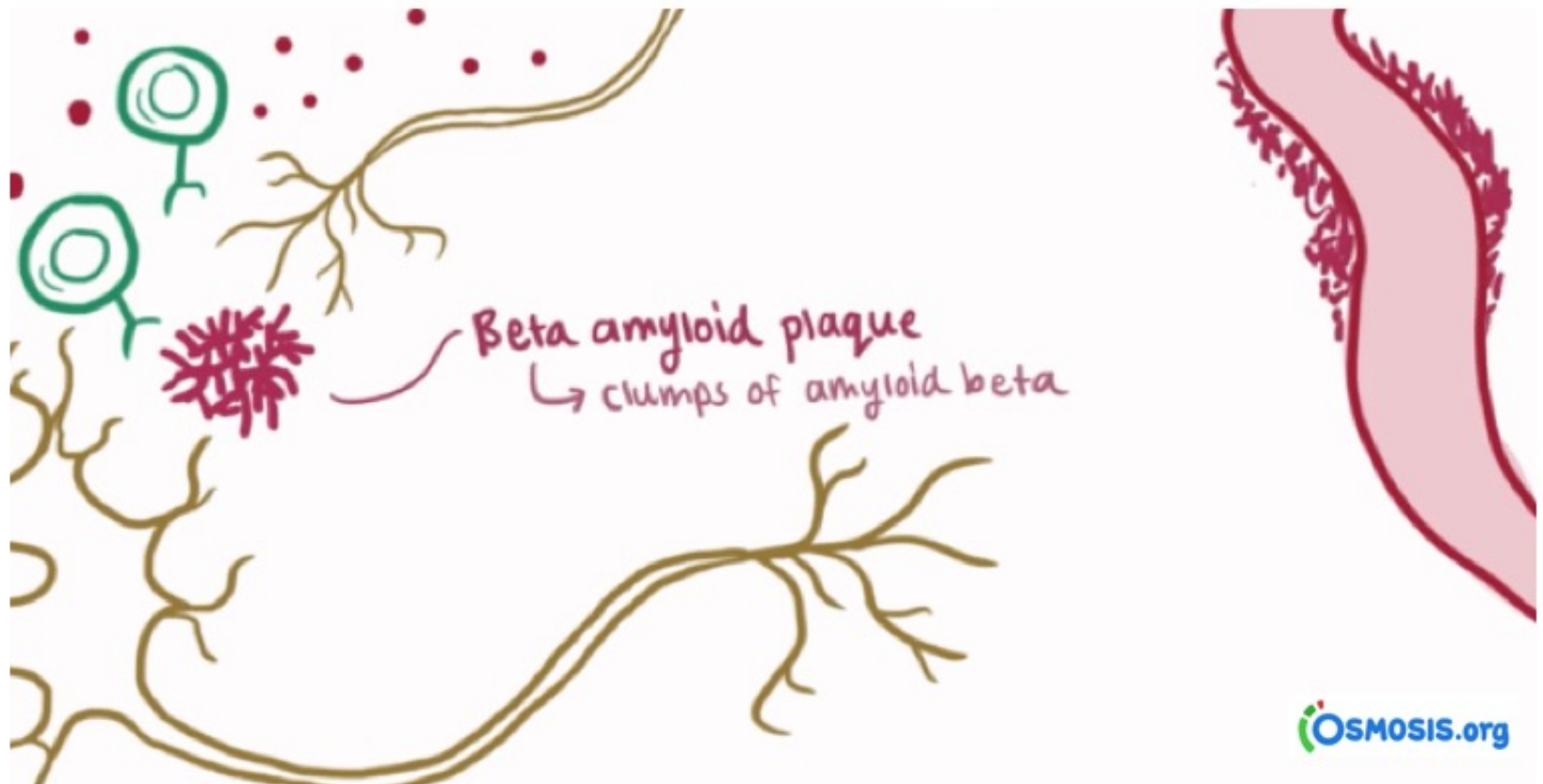
1. Synaptic disruption
2. Immune response



 OSMOSIS.org

## Disease pathways

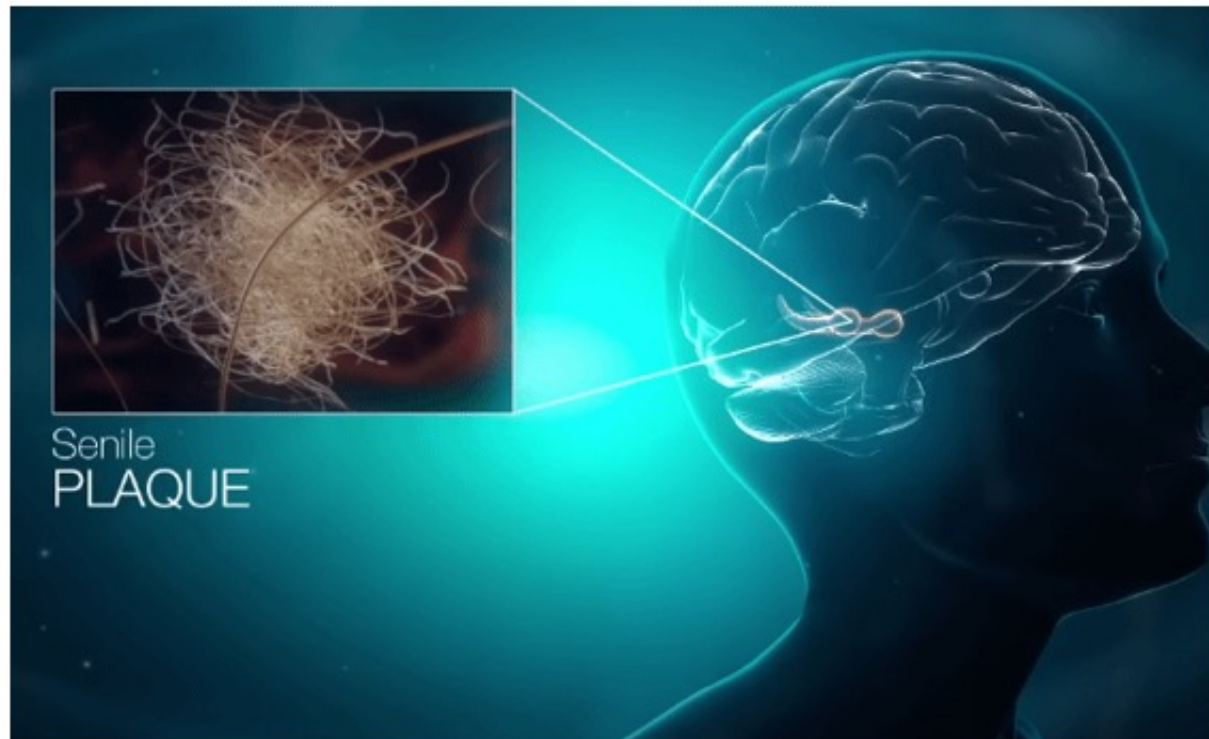
1. Amyloid angiopathy
2. (cerebral) Micro-bleeds



# $\beta$ -Amyloid plaques

## SPREADING

1. Cortex
2. Hippocampus
3. Whole brain **centripetal**





# TAU-Neurofibrillary tangles

## SPREADING

1. Hippocampus
2. Whole brain **centrifugal**
3. Brain atrophy

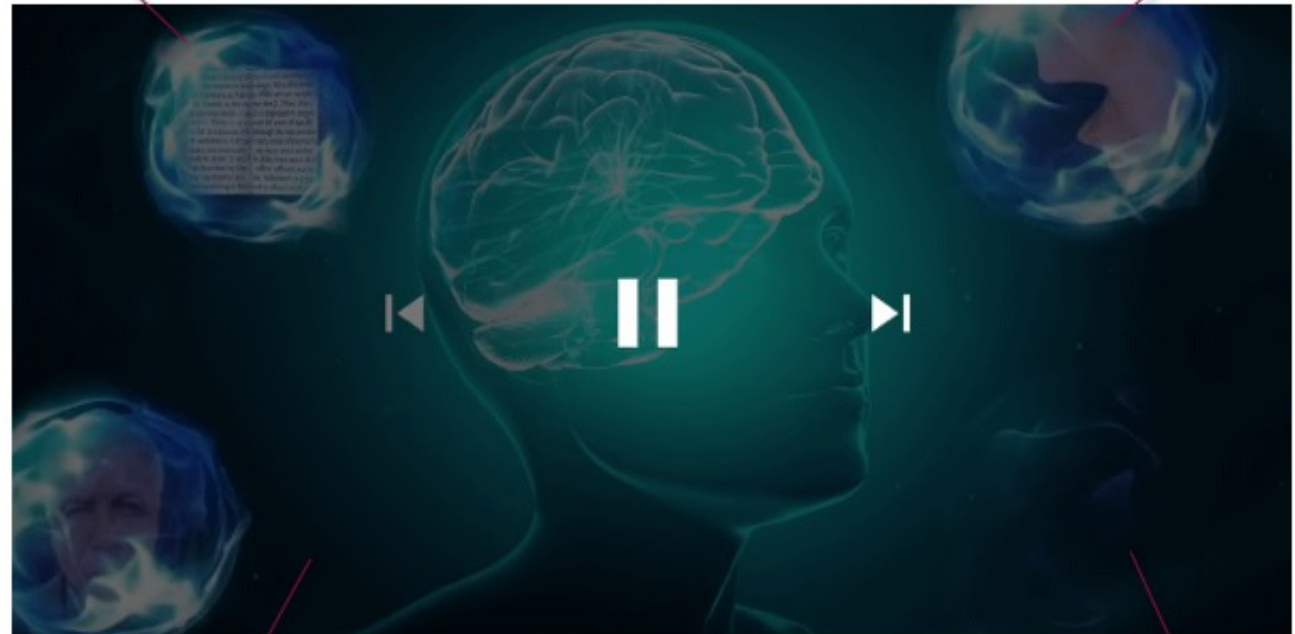


# Cognitive impairment

Only TAU diffusion correlates with cognitive deficits

Memory

Language

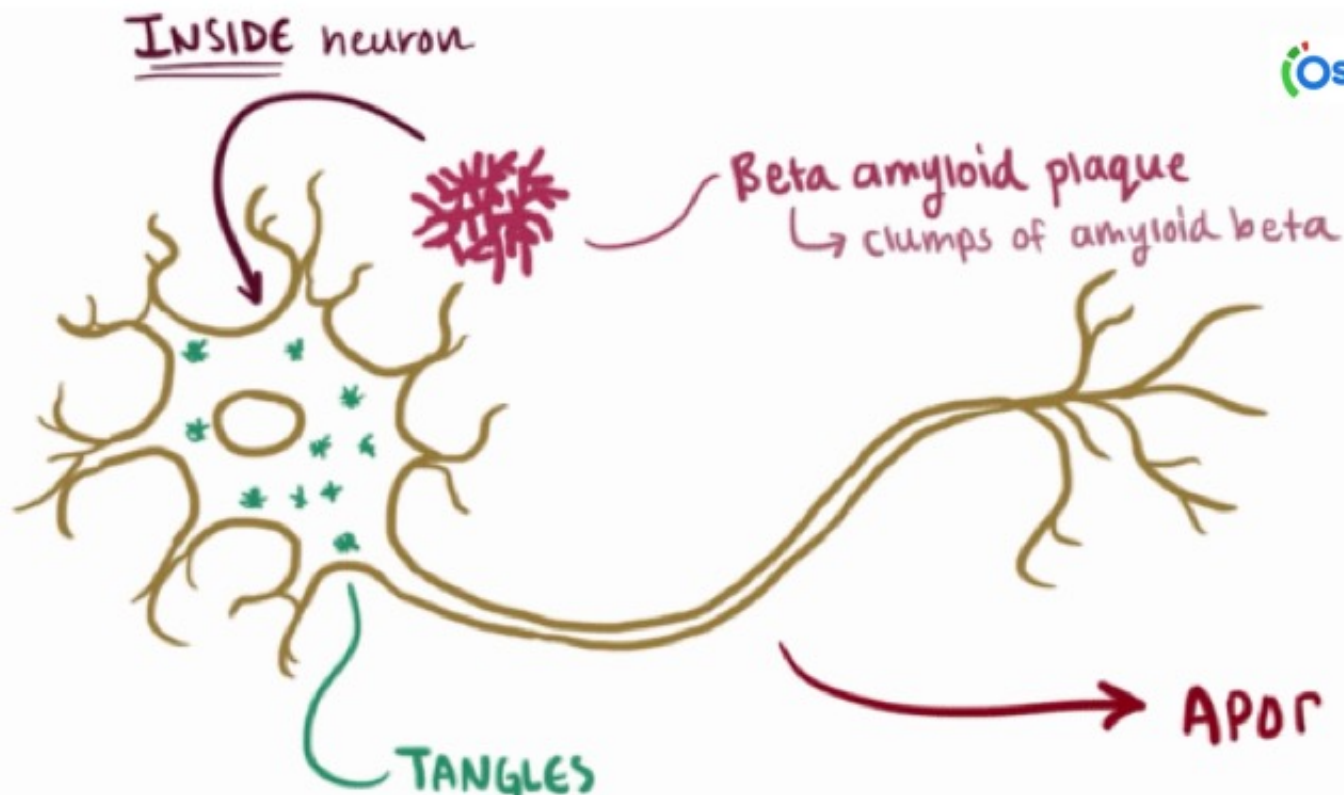


Agnosia

Apraxya

## Amyloid cascade hypothesis

1. **Amyloid triggers** tau phosphorylation (*kinase*)
2. Neurofibrillary **tangles** form
3. Neuronal death (**apoptosis**) > **brain atrophy**



# Amyloid cascade hypothesis

John Hardy posited this HP to explain AD



John Hardy, **1992**  
The amyloid cascade HP

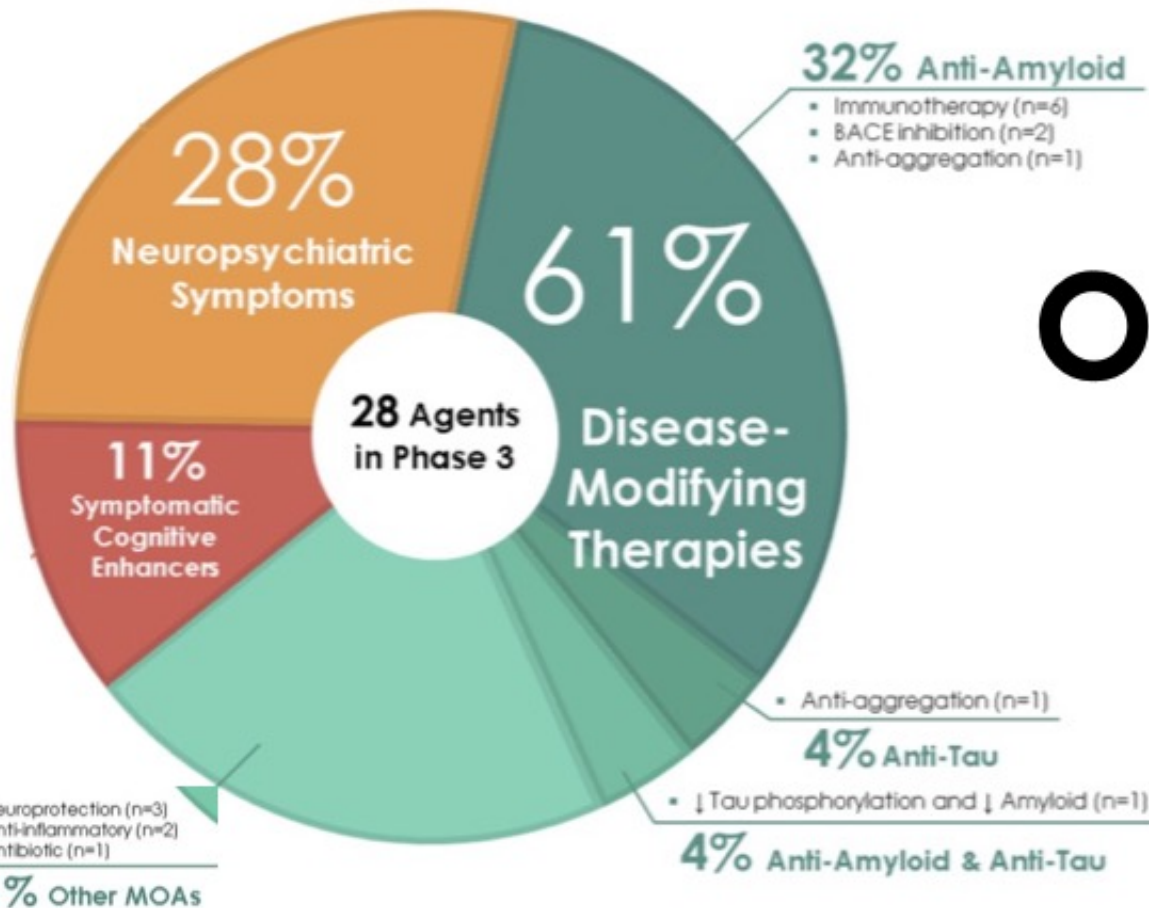
## ■ PERSPECTIVE

### Alzheimer's Disease: The Amyloid Cascade Hypothesis

John A. Hardy and Gerald A. Higgins

Hardy, J.A.; Higgins, G.A. Alzheimer's disease: the amyloid cascade hypothesis. *Science*, **1992**, *256*, 184-185. [<http://dx.doi.org/>]

# Drug development pipeline



# One main idea\*

\*Hypothesis

Agents in phase 3.

Cummings J 2019

# Amyloid-centric viewpoint (world view)

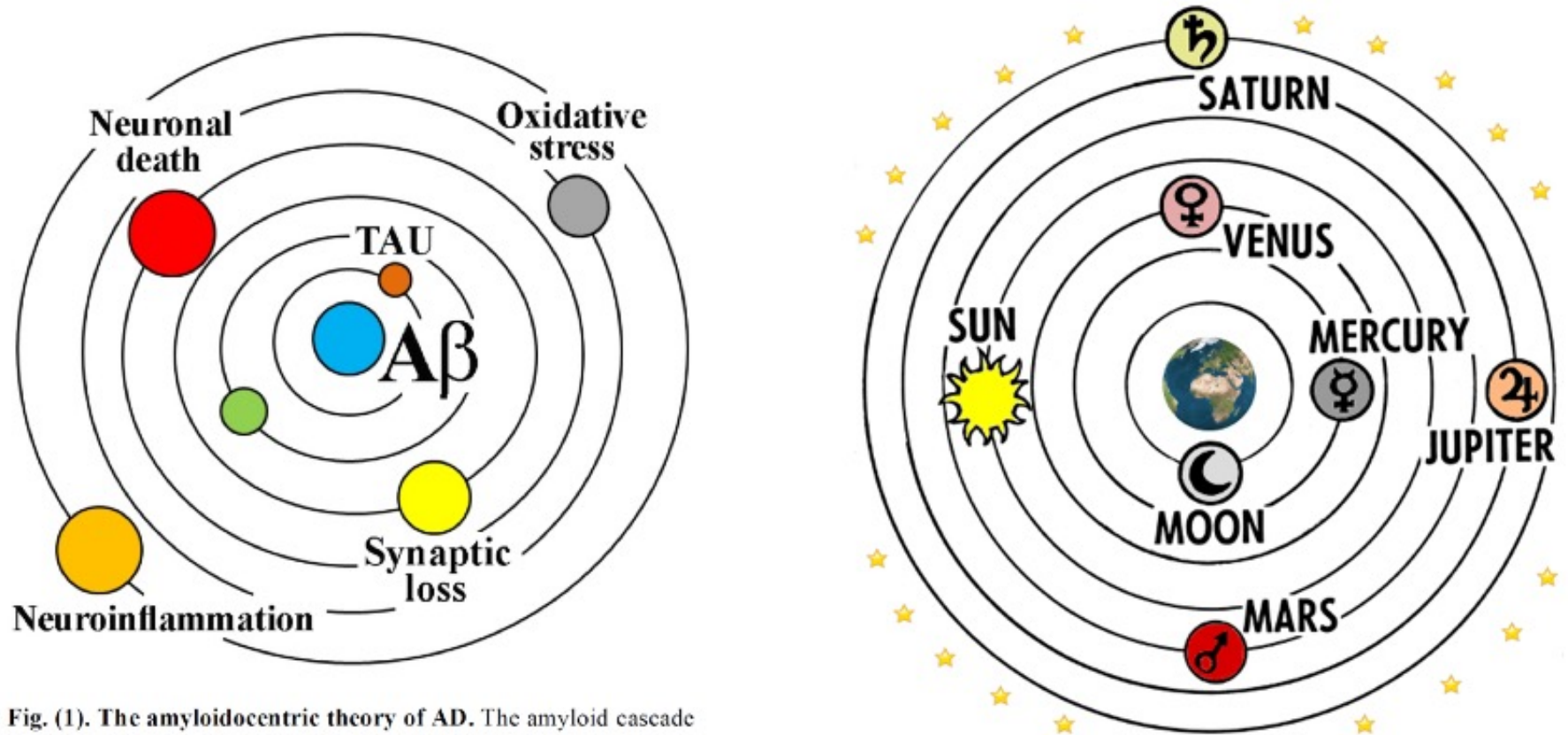


Fig. (1). The amyloid-centric theory of AD. The amyloid cascade hypothesis represented as the geocentric Ptolemy's theory of the solar system, which placed the Earth at the center and was accepted for many centuries.

Roberta Ricciarelli<sup>1,\*</sup> and Ernesto Fedele<sup>2,3,\*</sup>



Ptolemy, 100 a.d.

# Public health approach (viewpoint)

A NEW discipline is born: Population Neuroscience



T. Paus



M Ganguli



E Albanese



## Population Neuroscience

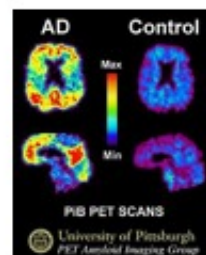
*Dementia Epidemiology Serving Precision Medicine  
and Population Health*

*Mary Ganguli, MD, MPH,\* Emiliano Albanese, MD,† Sudha Seshadri, MD,‡  
David A. Bennett, MD,§ Constantine Lyketsos, MD, MHS,||  
Walter A. Kukull, PhD,¶ Ingmar Skoog, MD, PhD,#  
and Hugh C. Hendrie, MB, ChB, DSc\*\**

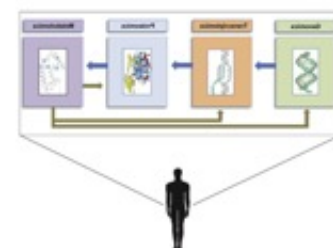
Epidemiology



Neuroscience



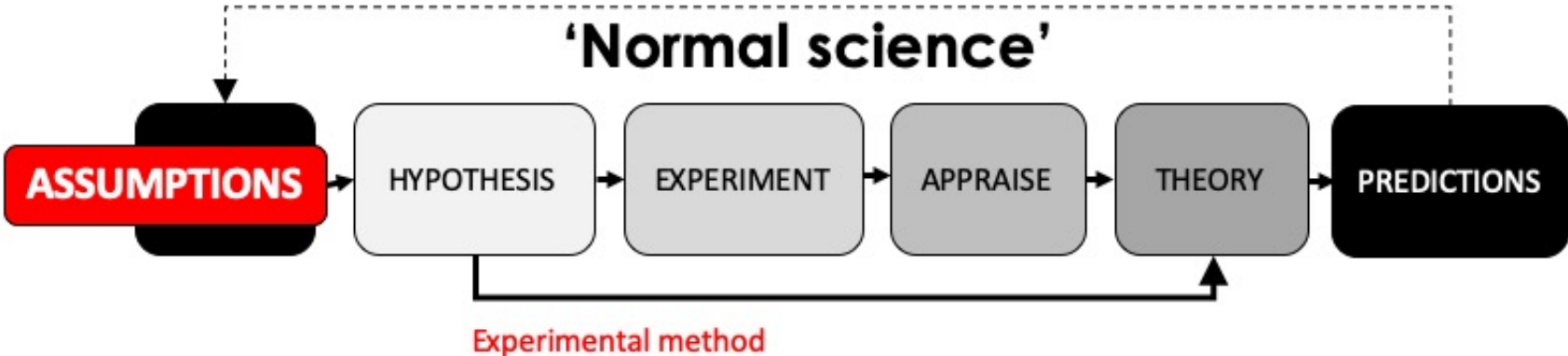
'Omics'



# The challenge

Population Neuroscience *blends*:

- 1. METHODOLOGIES rationale for choosing methods
- 2. METHODS techniques to conduct research



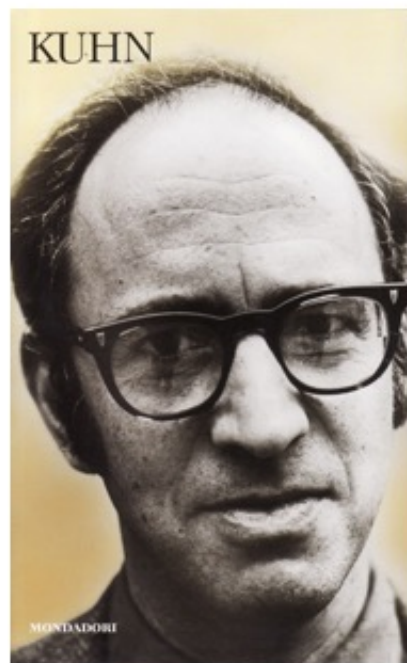
Population Neuroscience should shake the assumptions



The solution

# A scientific revolution

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- Scientific **progress** is NOT about '*development by accumulation*'.
- **Assumptions** must change, not the HP:
- A **paradigm shift** is a mix of enthusiasm and promise, not a logically determined procedure
- **Inspiration** is crucial...

Thoma Kuhn, **1962**  
*The structures of  
Scientific Revolutions*

## Back to the past

Seeking inspiration from literature



Homer,  
VIII century BC



**Odyssey, Book XI**  
Odysseus meets the  
dead and his  
mother Anticleia,  
who does not  
recognize him...

**The dead in classical mythology are forgetful**

## Take home message

The SSPH+ is our 'School of Athens', where several disciplines concur  
Pop Neuroscience aspires to cause a paradigm shift in dementia research

# WHY am I here ?



*The school of Athens, Raphael 1510, symbolizes the marriage of art, philosophy, and science*

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The  
combination of  
Plato's gesture  
towards the sky  
with Aristotle's  
empiricist 'hand'

# SSPH+ Lugano Summer School in Public Health Policy, Economics, and Management

Course 1, Aug 24 – 26, 2020:

Policy Options on Mental Health in the SDGs era

Course 2: Aug 27 – 29, 2020:

The digital epidemiology of mental health: Leveraging geo-referenced social media to improve well-being



**Emiliano Albanese**

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