Dementia Review
HELIAD and ALBION studies

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Medical School

National and Kapodistrian University of Athens

Aiginitio Hospital

www.comfortage.eu

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Funded by
the European Union

ATHENS DIGITAL HEALTH WEEK 27-31th January 2025 I Royal Olympic Hotel

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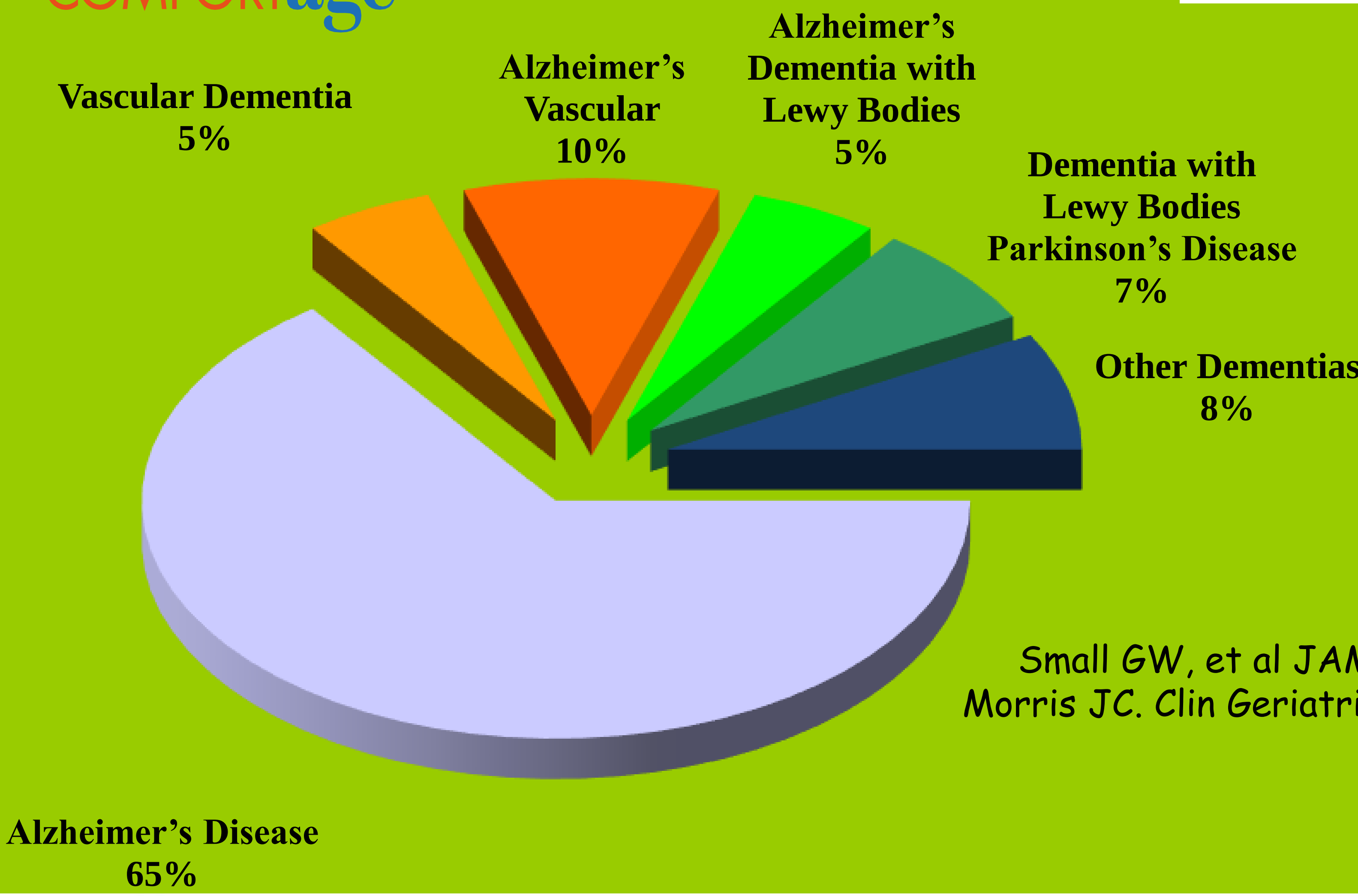
HL7

Dementia

- Loss of cognitive abilities including
  - Learning and memory
  - Language
  - Attention
  - Executive function
  - Abstract thinking and reasoning
  - Perception
  - Judgment
  - Social cognition - Personality change
- Impairment in social or occupational functioning (decline from a previous level)
- No delirium

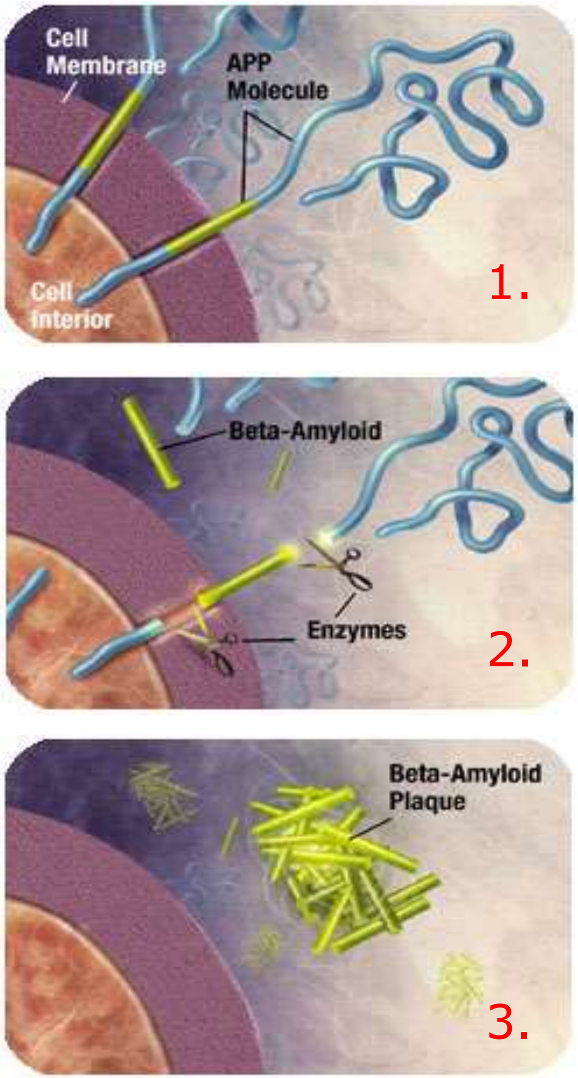


Small GW, et al JAMA 1997
Morris JC. Clin Geriatri Med 1994

Alois Alzheimer

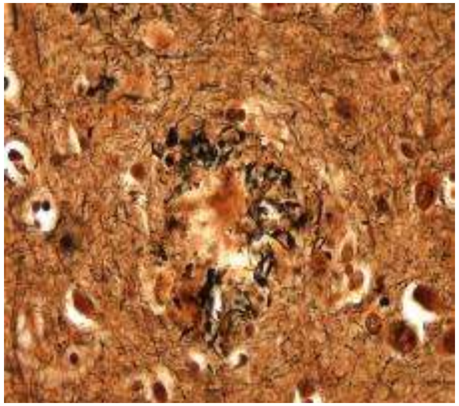
- 1864 (Bavaria Germany) -1915
- Psychiatrist in Frankfurt
- Since 1901 for 5 years extensive study of the patient rs. Auguste Deter (51 years old).
- After her death in 1906,
    - Senile plaques and neurofibrillary tangles with silver staining,
    - Published in Tubigen in a conference of German psychiatrists (presenile dementia).
- Kraepelin (Alzheimer’s mentor) named the disease in 1910 in his famous book

Beta-amyloid Plaques



Amyloid precursor protein (APP) is the precursor to amyloid plaque.

1. APP sticks through the neuron membrane.
2. Enzymes cut the APP into fragments of protein, including beta-amyloid.
3. Beta-amyloid fragments come together in clumps to form plaques.



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Neurofibrillary Tangles

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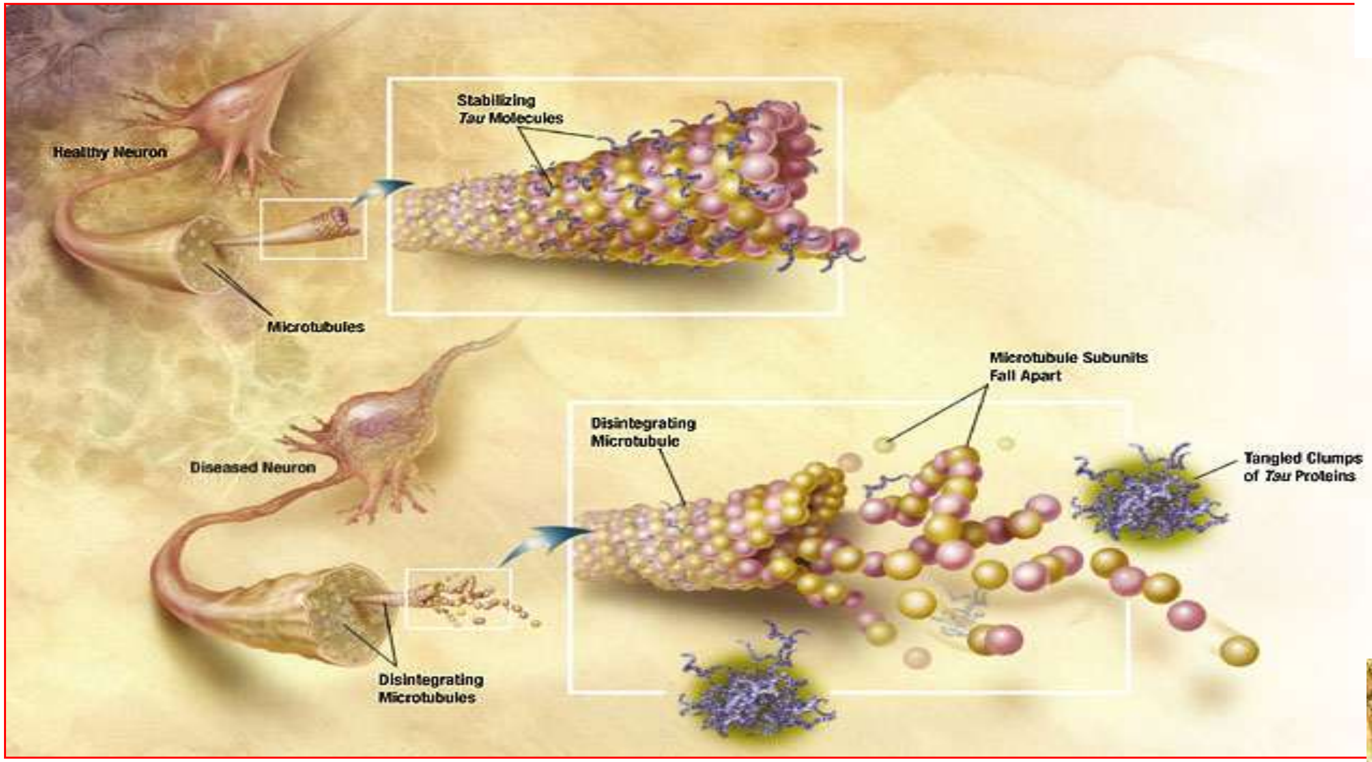
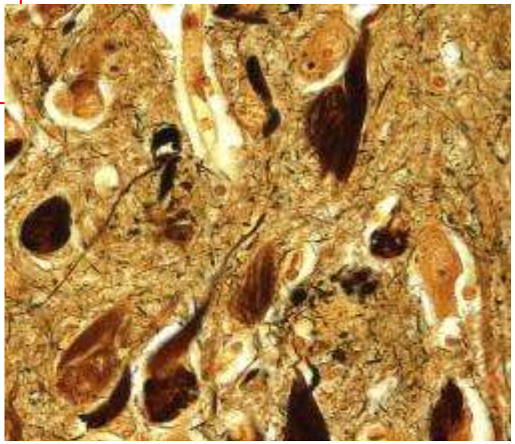
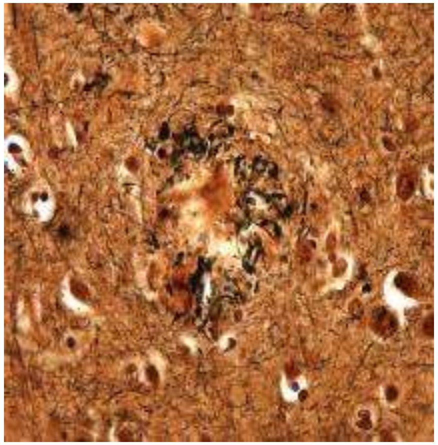




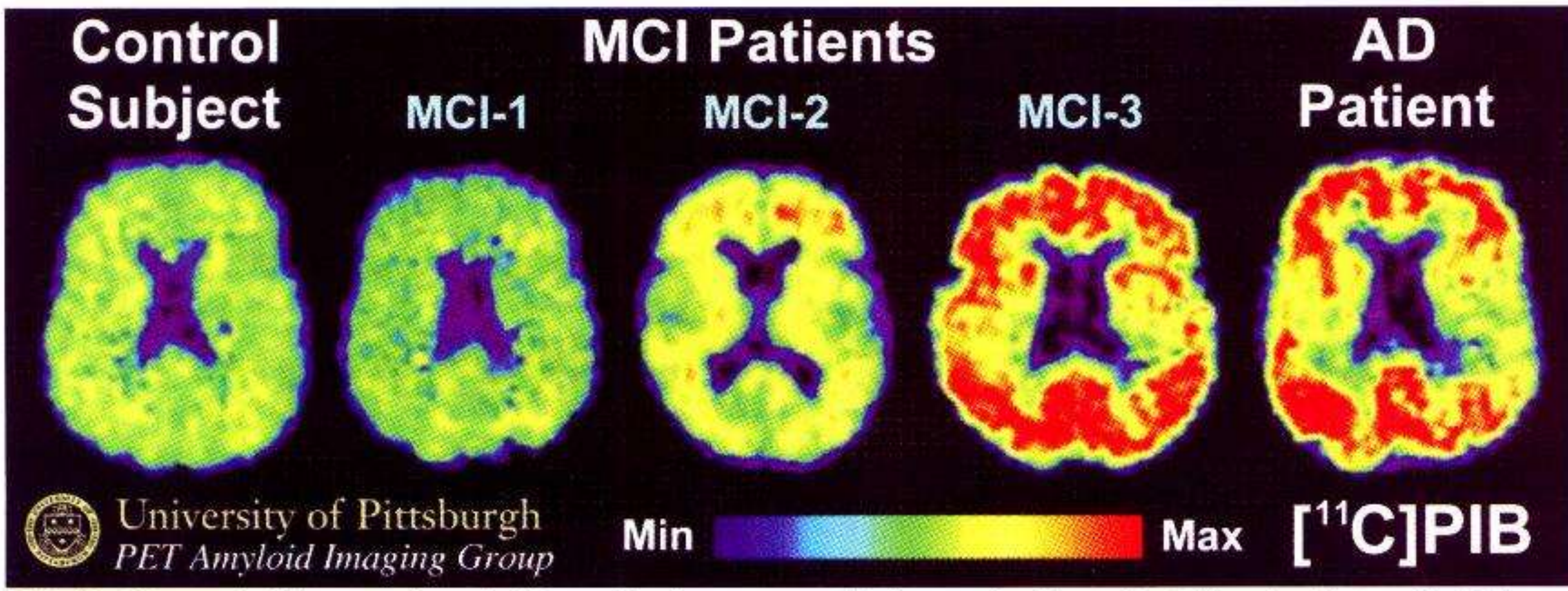
Neurons have an internal support structure partly made up of microtubules. A protein called *tau* helps stabilize microtubules. In AD, *tau* changes, causing microtubules to collapse, and *tau* proteins clump together to form neurofibrillary tangles.



PET: AMYLOID IMAGING

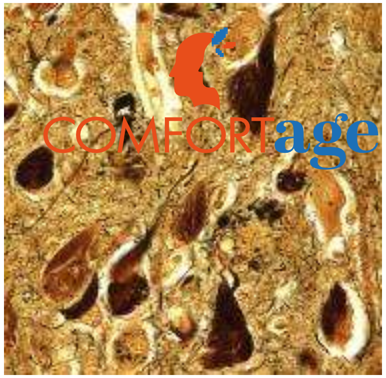
"Pittsburgh Compound B" (PIB)

N-methyl-[11C]2-(4'-methylaminophenyl)-6-hydroxybenzothiazole



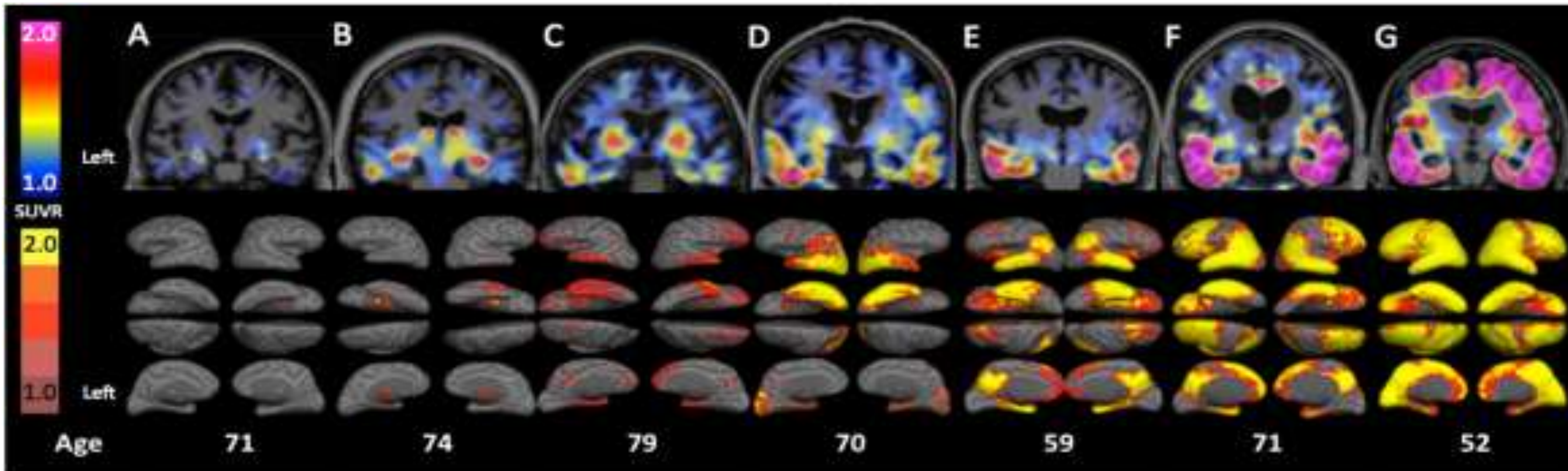
COURTESY DR. WILLIAM E. KLUNK, PH.D. AND CHESTER MATHIS, PH.D./UNIVERSITY OF PITTSBURGH

PET with PIB reveals differences in amyloid deposition between cognitively normal subjects (far left) and subjects with AD (far right). PET with PIB also reveals the range of amyloid accumulation in subjects with clinically mild cognitive impairment (center).



Tau PET imaging in aging and early Alzheimer disease

Annals of Neurology
[Volume 79, Issue 1,](#) pages 110-119, 15 DEC 2015
DOI: 10.1002/ana.24546;
http://onlinelibrary.wiley.com/doi/10.1002/ana.24546/full#ana24546-fig-0001



MMSE	30	30	29	27	26	23	11
PiB (DVR)	Low (1.0)	High (1.2)	High (1.8)	High (1.5)	High (1.7)	High (1.5)	High (1.5)
Dx	CN	CN	CN	MCI	MCI	AD	AD
PET	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

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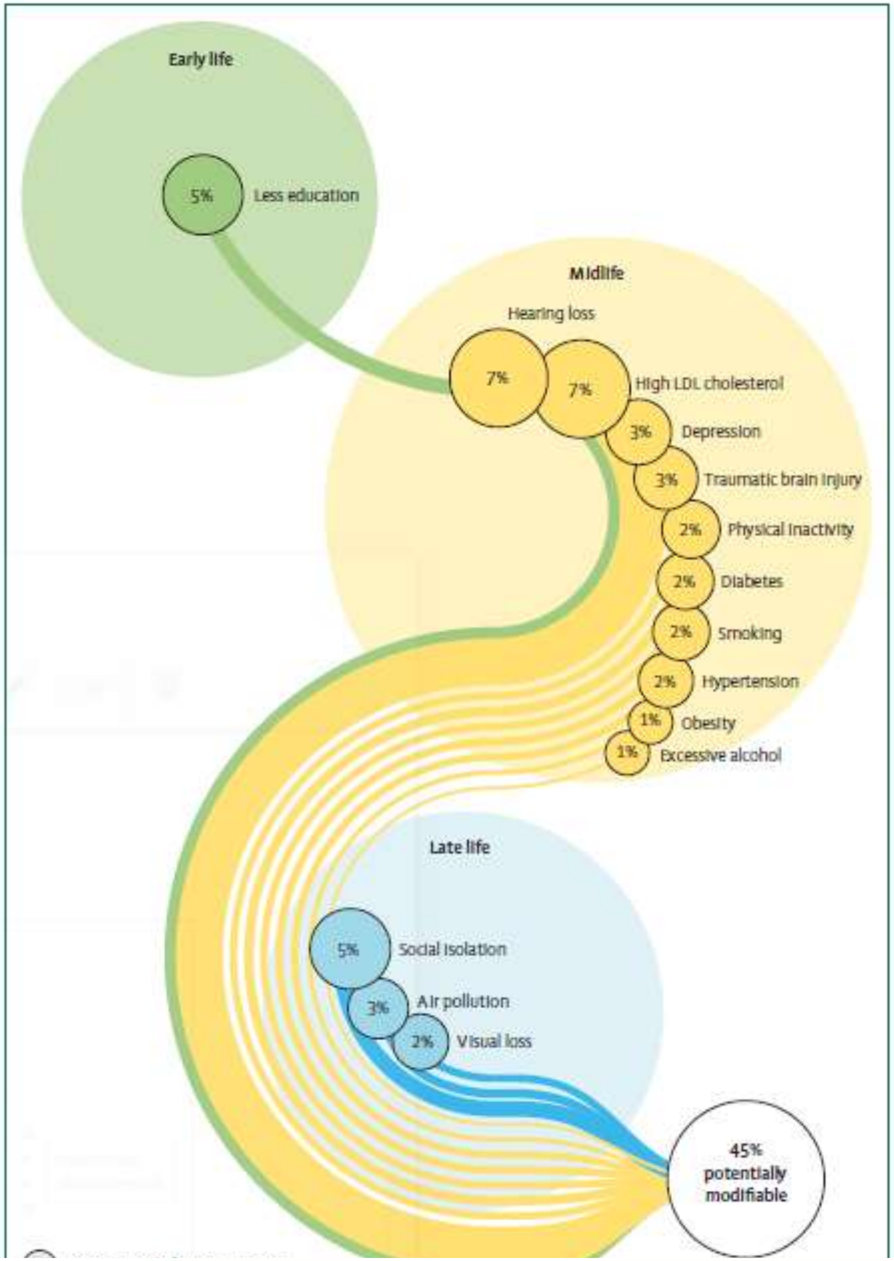
Risk – Protective Factors

- Age
- Gender
- Down syndrome
- Genetic contributions
  - Hereditary AD (1-2%)
  - Sporadic AD (98%)

- **Cardiovascular disease**
- **Traumatic brain injury**
- **Smoking**
- **Estrogen**
- **Medications**
- **Depression - Stress**
- **Cognitive reserve**
  - **Intellectual / Social / Physical**
- **Diet**
- **Sensory (vision – hearing) deficits**
- **Pollution**



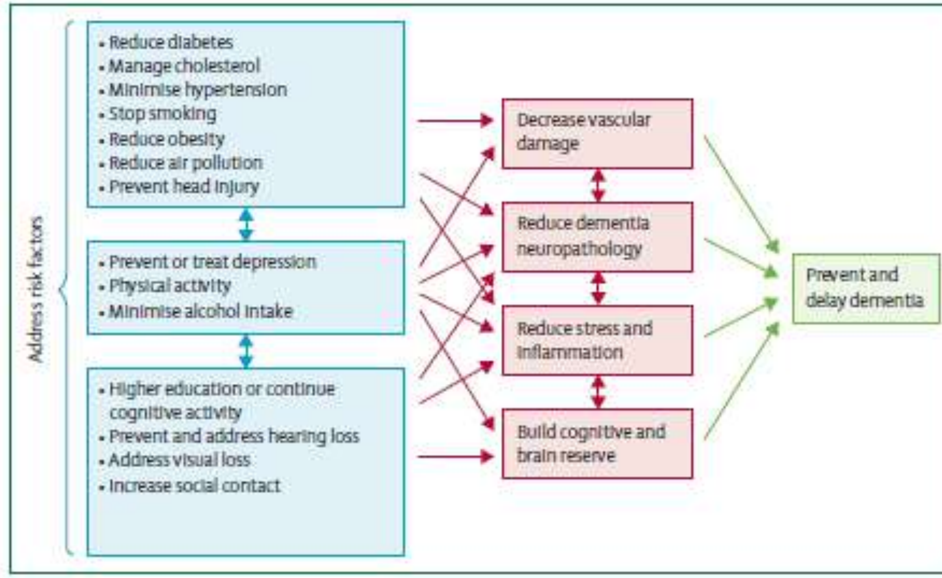
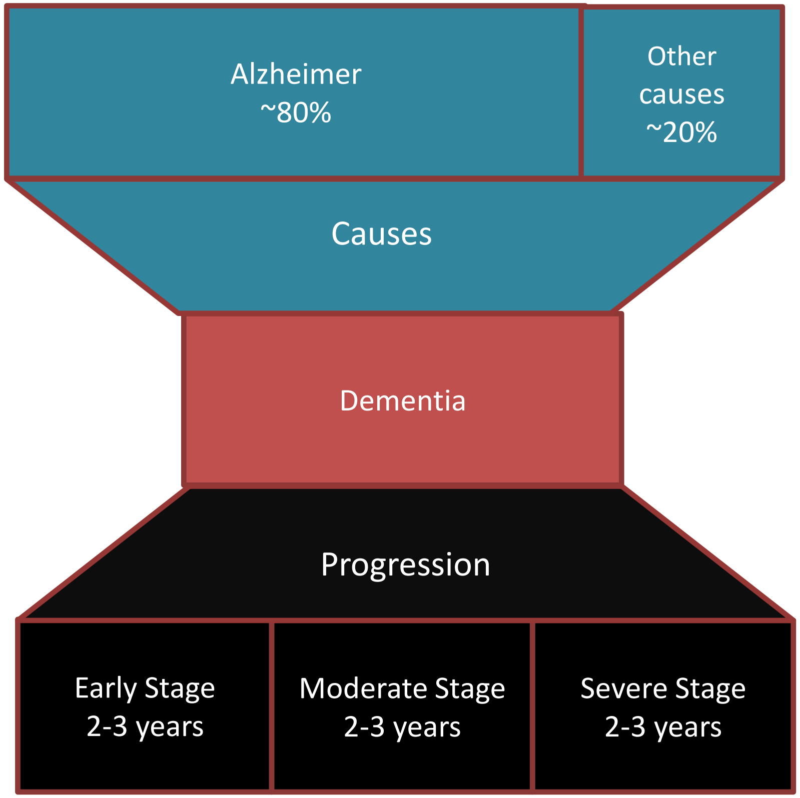


Figure 2: Possible brain mechanisms for enhancing or maintaining cognitive reserve and risk reduction of potentially modifiable risk factors in dementia

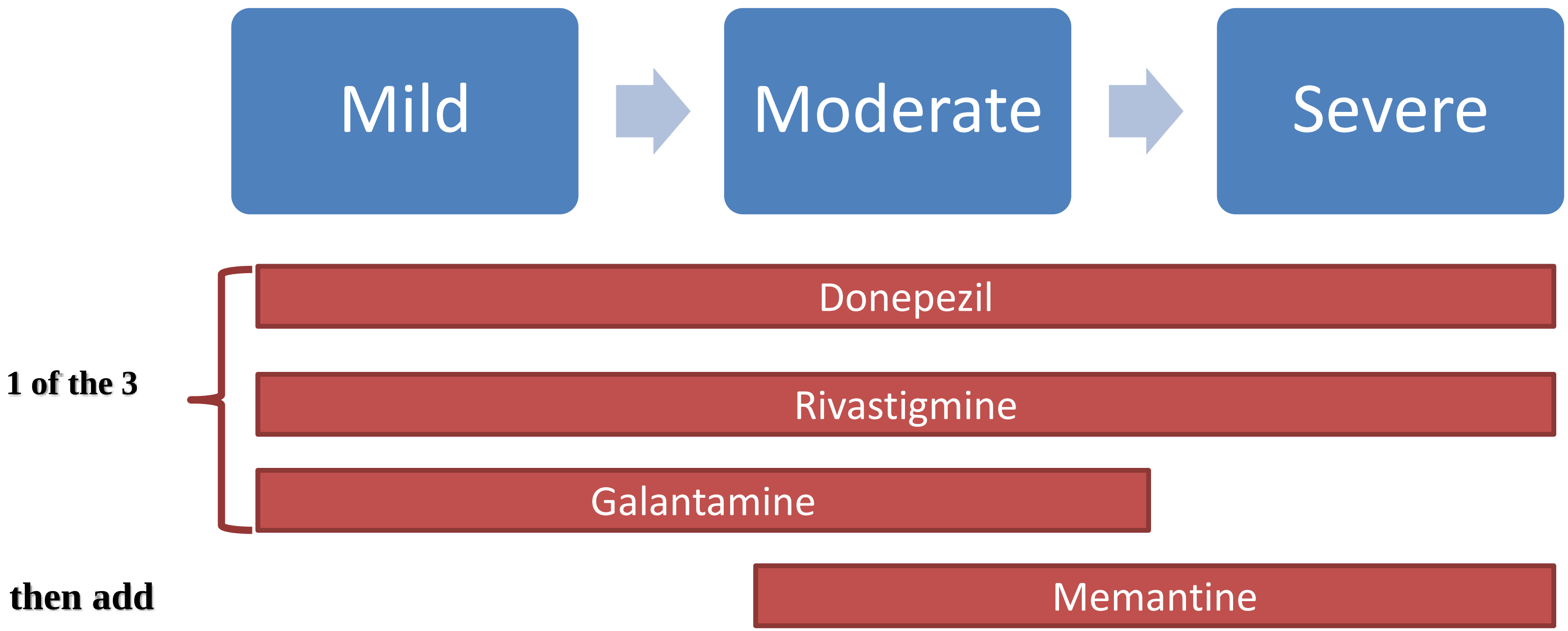
Dementia prevention, intervention, and care: 2024 report of the *Lancet* standing Commission

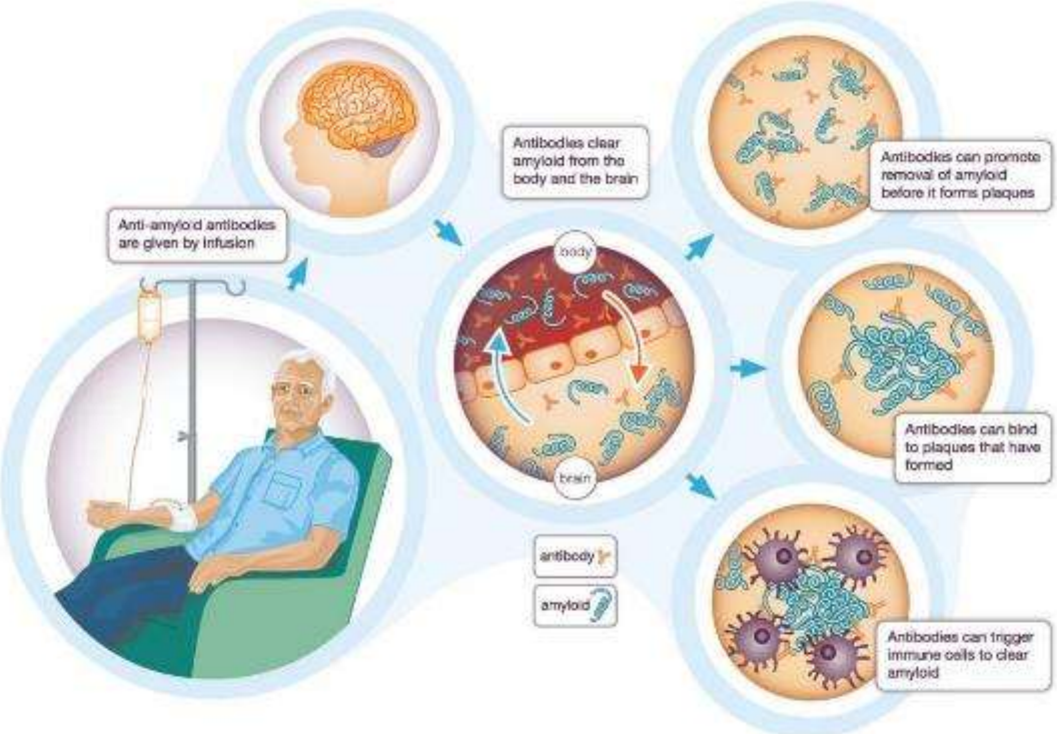
Prognosis

- Expected survival
  - 6-9 years [4-20]
- Disease Stages
  - Early [2-3]
  - Moderate [2-3]
  - Severe [2-3]
- Causes of death
  - Infections
  - Cardiovascular



Treatment of cognitive changes





https://www.alzheimersresearchuk.org/blog/behind-the-headlines-is-a-new-alzheimers-treatment-in-sight/

Treatment of Neuropsychiatric symptoms

- Non-pharmacologic
  - Behavioral – environmental changes (if possible)

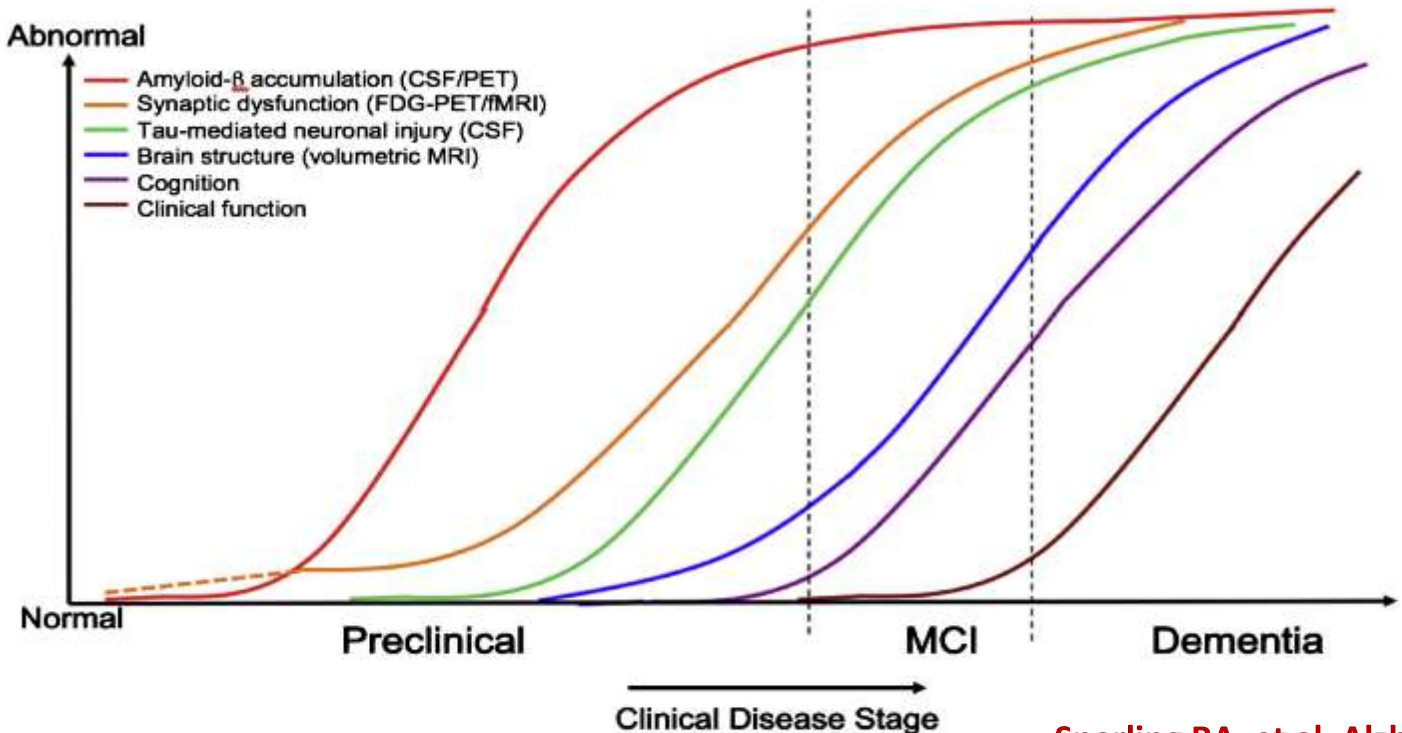
- Pharmacological
  - Depression
    - SSRIs
  - Agitation – Aggression – Irritability
    - Atypical Neuroleptics
      - Quetiapine , Olanzapine, Risperidone, Aripiprazole, Ziprasidone
  - Paranoia – Hallucinations
    - Atypical neuroleptics
  - Sleep problems
    - Atypical neuroleptics
    - SSRIs (paroxetine) or other antidepressents (mirtazapine, trazodone)
    - Other hypnagogics

Interest for earlier stages

Age related cognitive decline	Mild Cognitive Impairment	Dementia

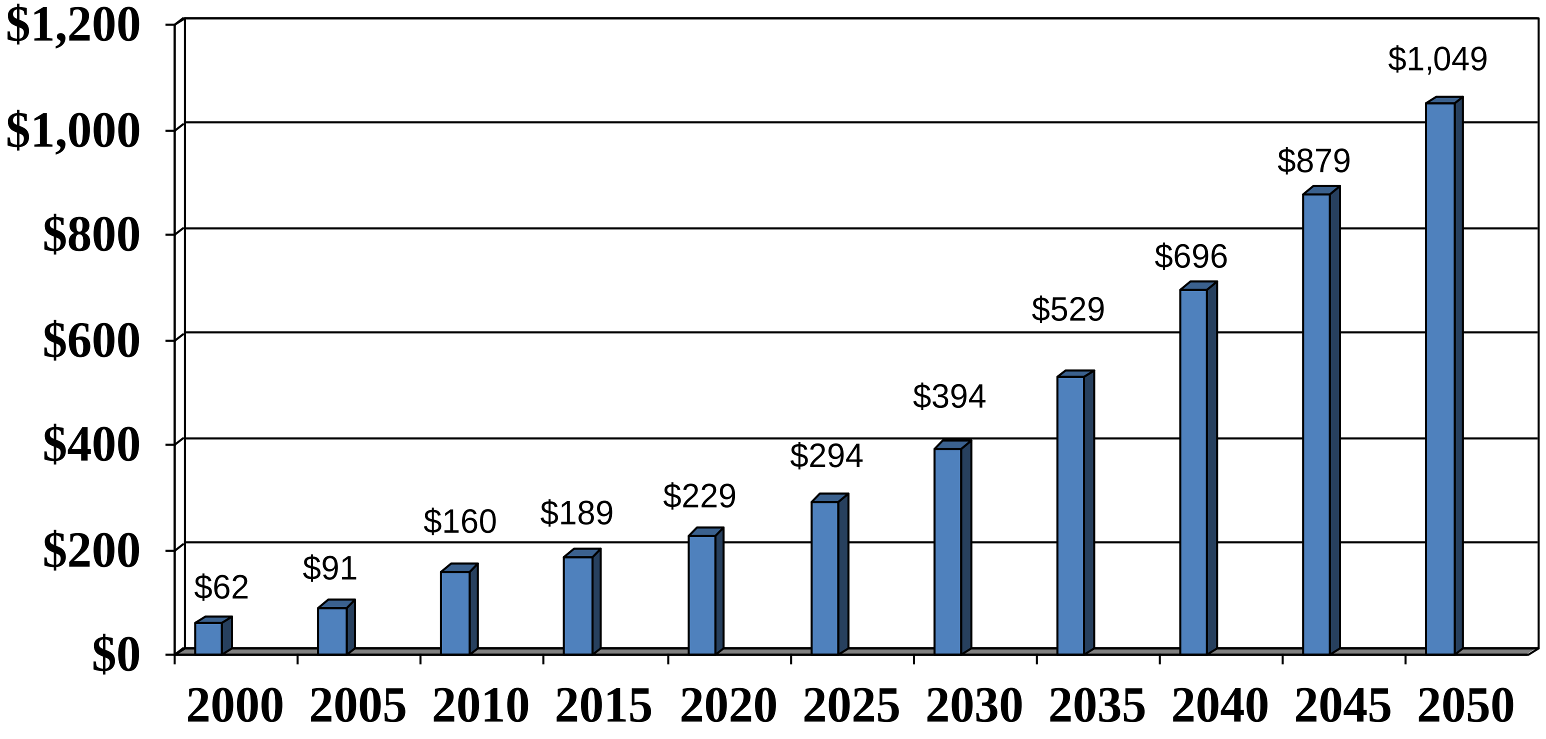
Progression - Stages

Mild	Moderate	Severe
2-3 years	2-3 years	2-3 years

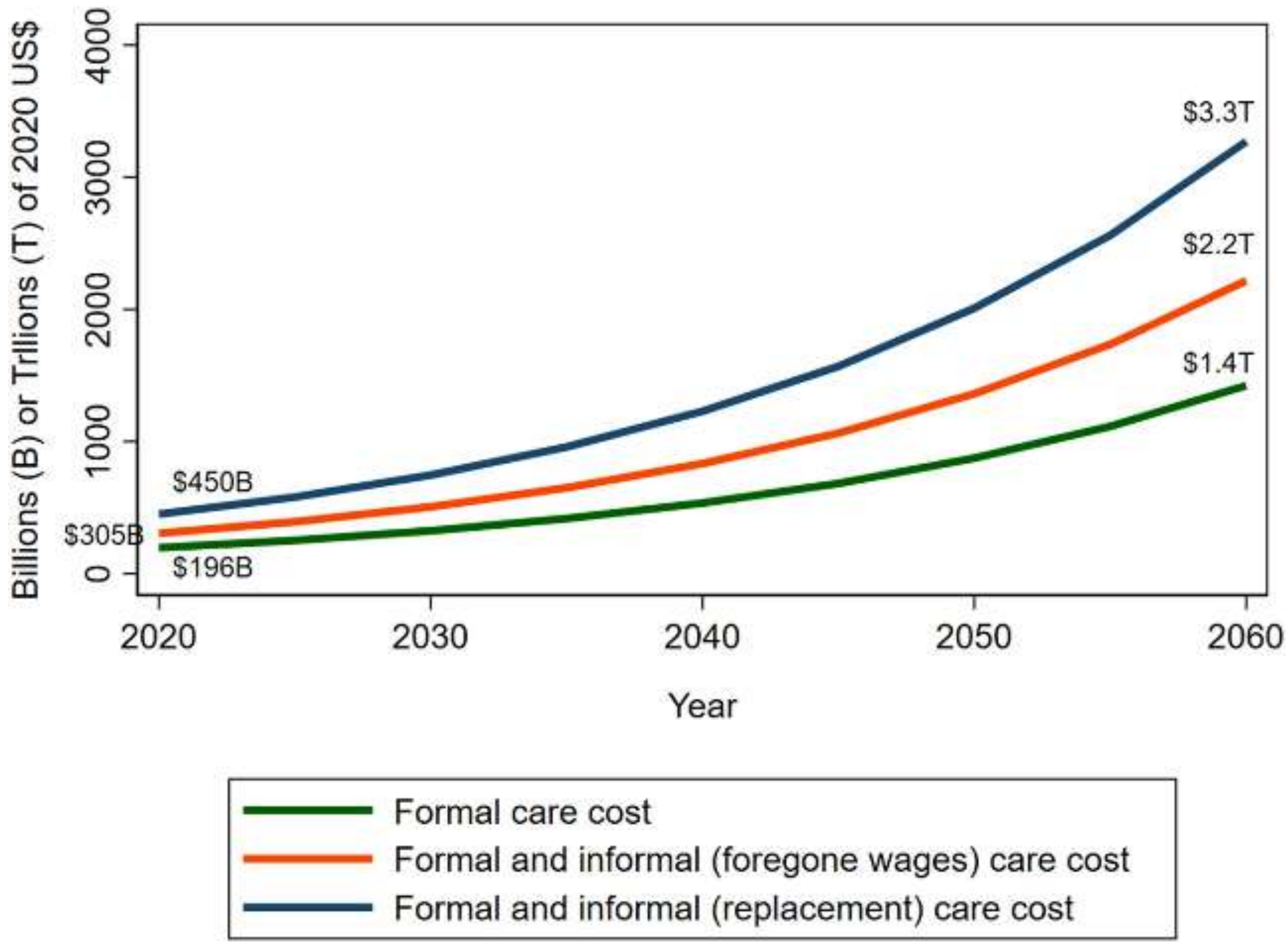


Sperling RA, et al. Alzheimers Dement 2011

Medicare Alzheimer Cost (billion $)



Source: “Saving Lives, Saving Money: Dividends for Americans Investing in Alzheimer’s Research”, The Lewin Group & the Alzheimer’s Association, June 2004.



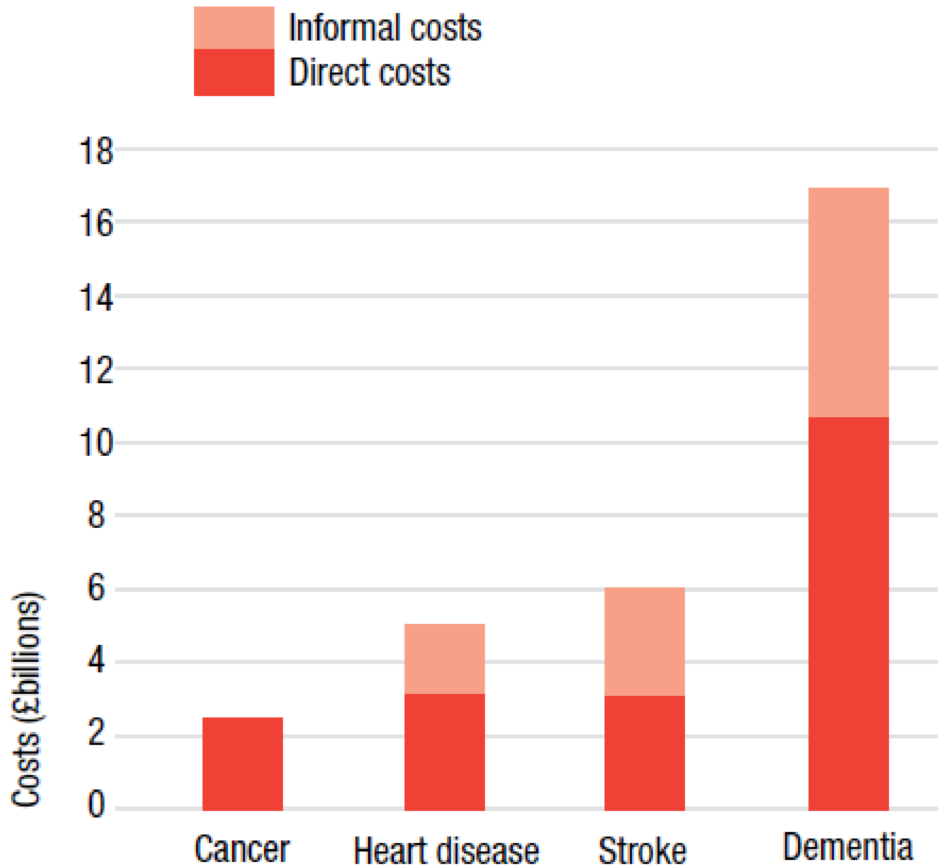
Cost of care for Alzheimer's disease and related dementias in the United States: 2016 to 2060

Arindam Nandi, Nathaniel Counts, Janina Bröker, Sabrina Malik, Simiao Chen, Rachael Han, Jessica Klusty, Benjamin Seligman, Daniel Tortorice, Daniel Vigo & David E. Bloom

npj Aging 10, Article number: 13 (2024) | Cite this article

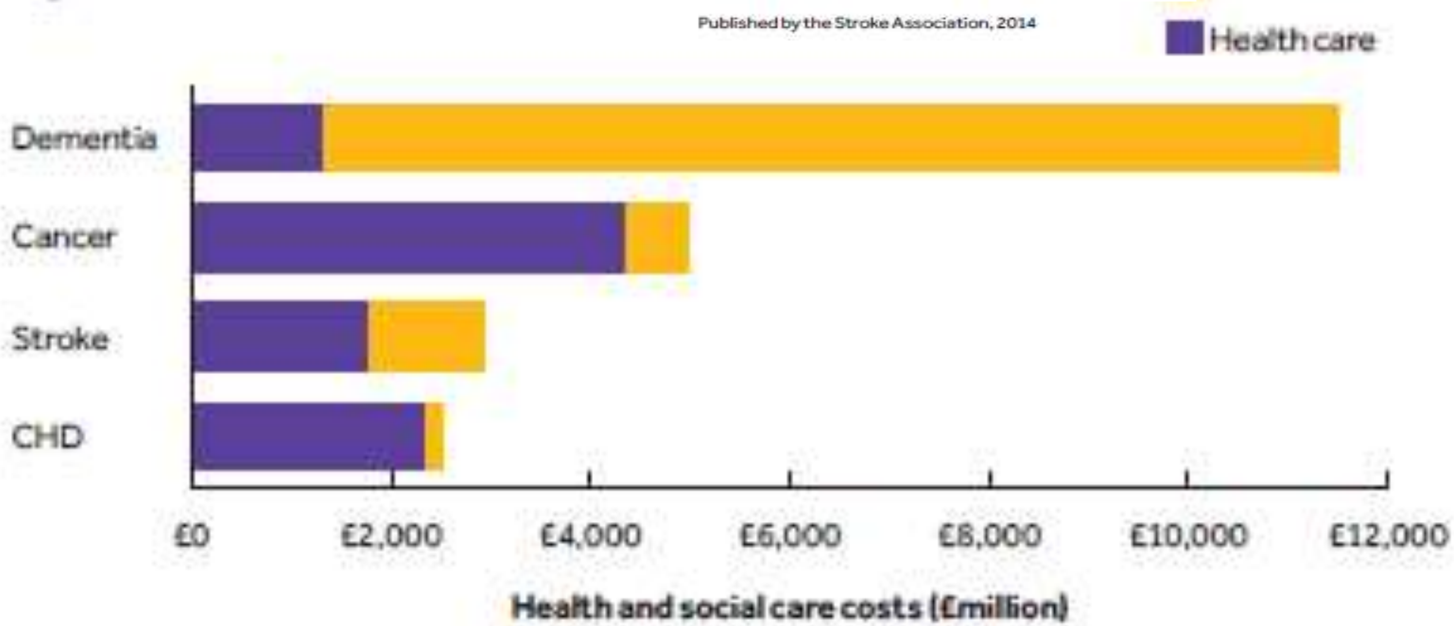
Figure 2.7

The comparative societal costs of cancer, ischaemic heart disease, stroke and dementia in the United Kingdom



Alzheimer Disease International 2009 annual report

Figure 1. Economic burden of disease



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H.E.L.I.A.D

HELLENIC EPIDEMIOLOGICAL LONGITUDINAL INVESTIGATION OF AGING AND DIET

- Random population sample, ≥65
- Areas of Larisa and Athens
- Baseline evaluation N = 2000
- Follow-up evaluations every ~3 years.

HELIAD Evaluation

- Demographics
- Early life events (parental education, occupation, birth order etc)
- Socio economics

- Comorbidities - drugs
- Smoking, Alcohol etc
- Anthropometrics

- Family history of neuropsychiatric diseases
- Family ages of death (for longevity analyses)

HELIAD evaluation

- Social activities (currently and when <50)
- Intellectual activities (currently and when <50)
- Physical activities (currently and when <50)
  - Exercise questionnaire (METS)
  - Subjective motoric complaints
  - Gait speed
  - Grip strength – dynamometer
- Activities of daily living
  - (basic + instrumental)
- Subjective cognitive complaints

HELIAD evaluation

- Sleep questionnaire

- Food Frequency Questionnaire (FFQ)
- Nutritional risk questionnaire

- Pesticides questionnaire

- Collection of blood (serum, plasma, DNA, - centrifugion, aliquoting, deep freezing -80)

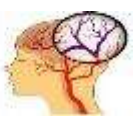
HELIAD Evaluation

- Examination by Neurologists
- Consensus diagnosis
- Full neuropsychological battery
- CDR

Dementias

- UPDRS / Spirals
- Clinical Fluctuating Cognition Rating Scale
- Prodromal Parkinsonism questions
- Essential Tremor questions
- Subjective motoric complaints
- Restless Leg Syndrome questions

Movement Disorders



- Stroke symptomatology questionnaire
- Hachinski Ischaemic Scale

Strokes

- Depression / Anxiety / Psychosis questionnaires

Psychiatric

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Ελληνική Πρωτοβουλία Ενάντια στην Αλτσχάιμερ

Μια συνεργασία Ελλήνων επιστημόνων του Πανεπιστημίου Johns Hopkins (ΗΠΑ) και επιστημόνων του Εργαστηρίου Βιοπληροφορικής και Ανθρώπινης Ηλεκτροφυσιολογίας Bi.HE.Lab του Ιονίου Πανεπιστημίου.

Hellenic Initiative Against Alzheimer's Disease

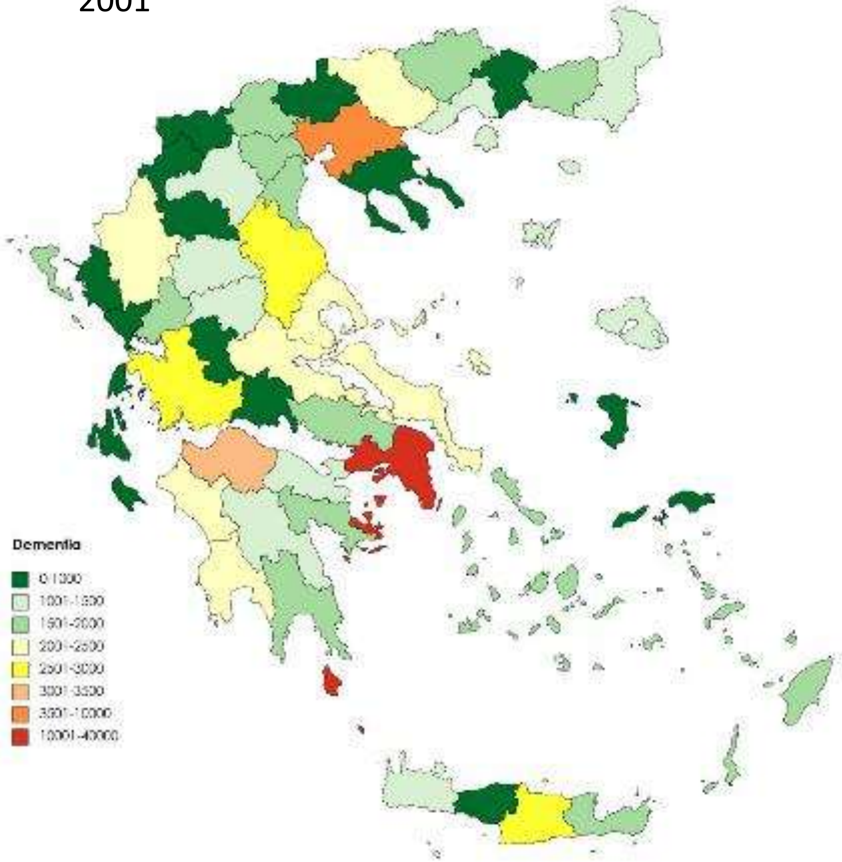
HIAAD

H.E.L.I.A.D

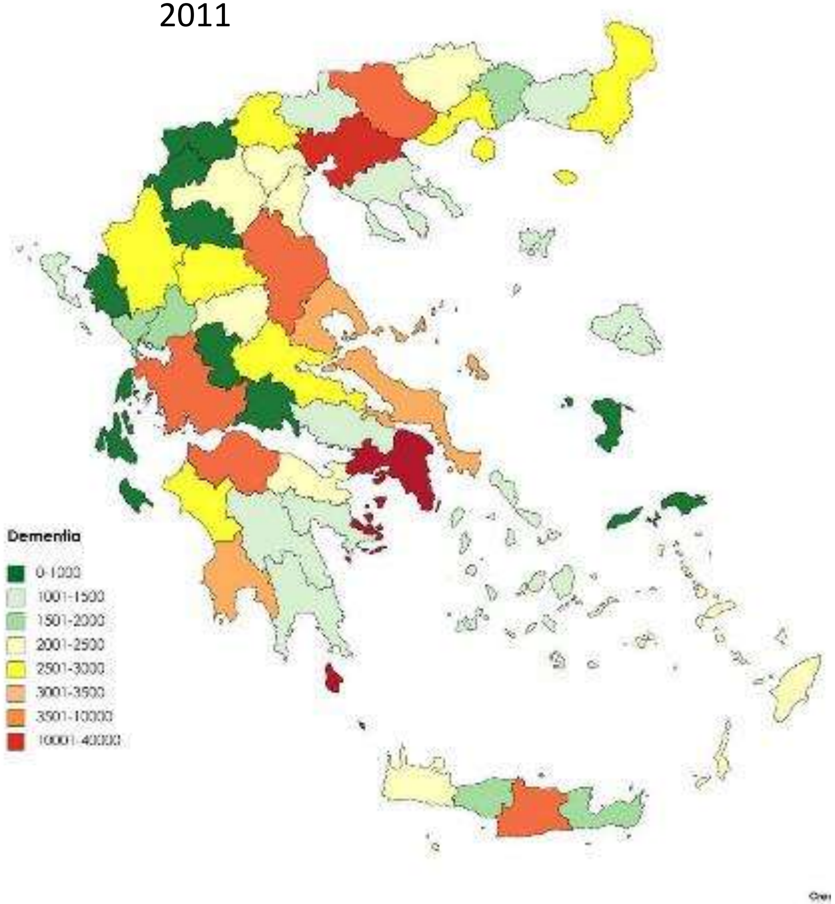
HELLENIC EPIDEMIOLOGICAL LONGITUDINAL INVESTIGATION OF AGING AND DIET

47%	250.000	1.5εκ
αύξηση στον αριθμό των ατόμων που πάσχουν από άνοια και συναφείς παθήσεις στην Ελλάδα μεταξύ 2001 και 2011.	άτομα πάσχουν από άνοια και επιπλέον 350.000 άτομα με ήπια γνωστική εξασθένηση στην Ελλάδα το 2022.	άνθρωποι θα επηρεάζονται καθημερινά από άνοια συμπεριλαμβανομένων και των οικογενειών / φροντιστών μέχρι το 2030.

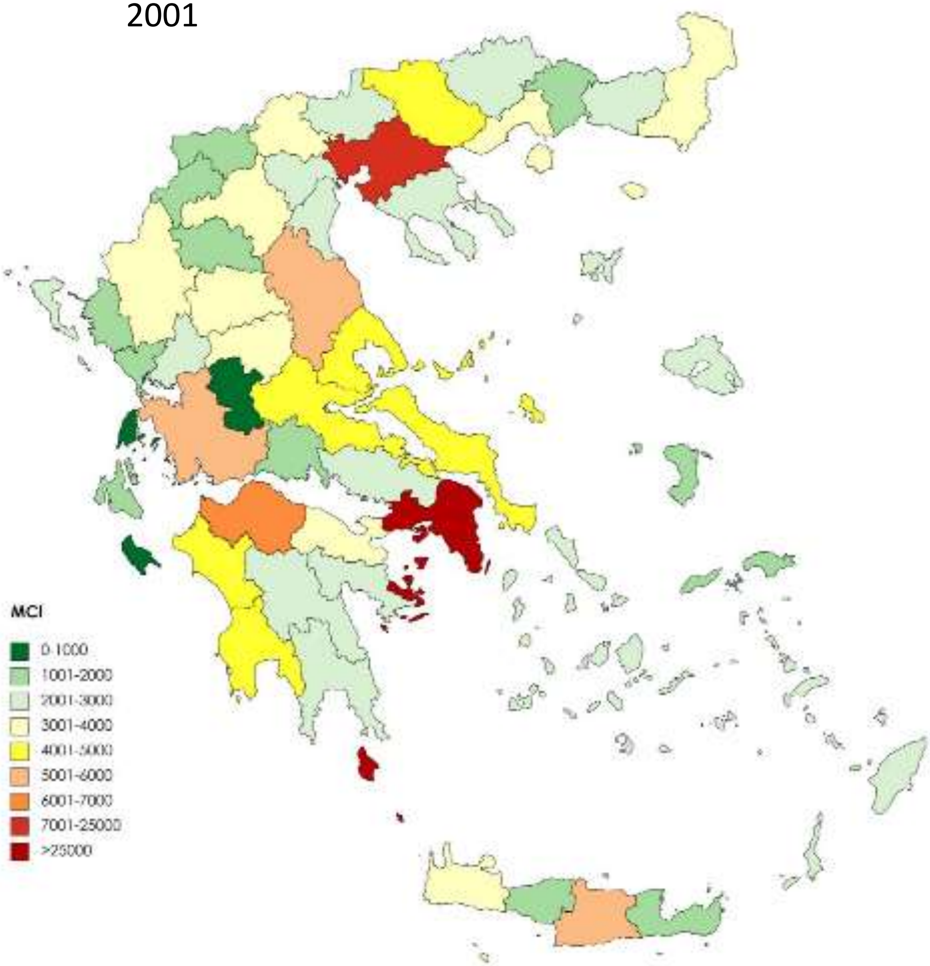
2001


Dementia
0-1000
1001-1500
1501-2000
2001-2500
2501-3000
3001-3500
3501-10000
10001-40000

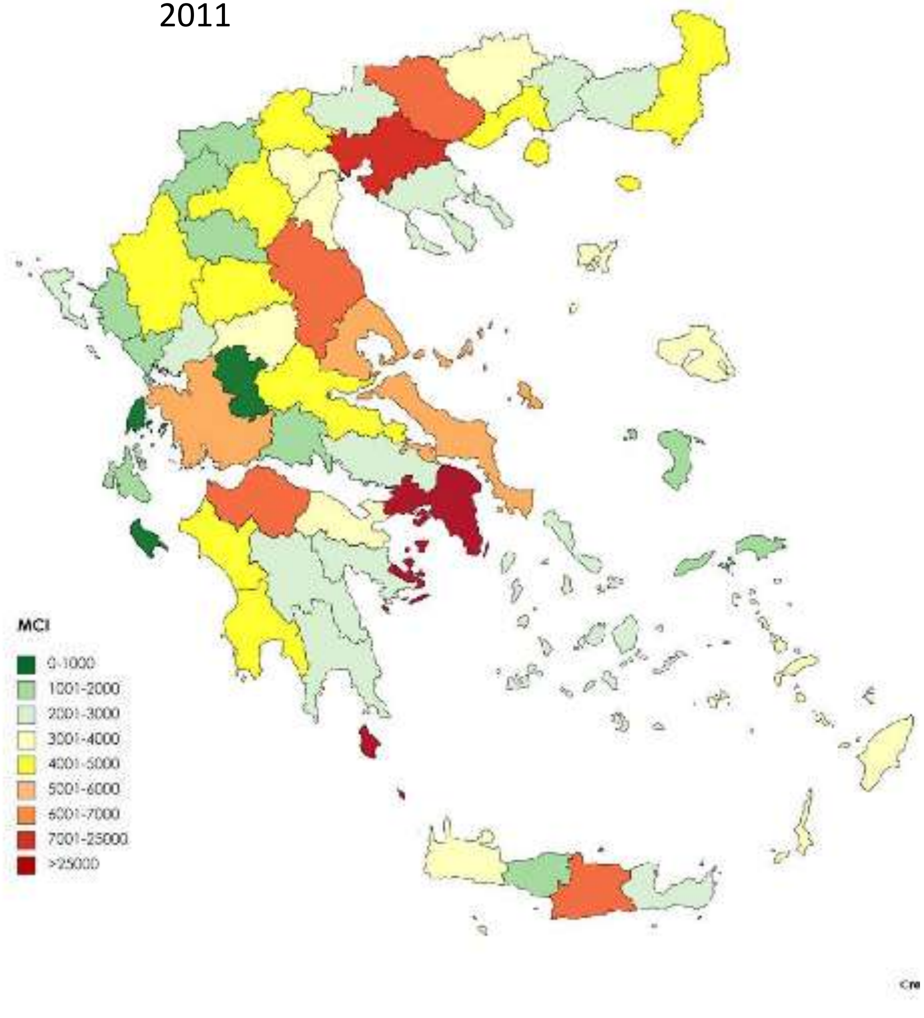
2011


Dementia
0-1000
1001-1500
1501-2000
2001-2500
2501-3000
3001-3500
3501-10000
10001-40000

2001


MCI
0-1000
1001-2000
2001-3000
3001-4000
4001-5000
5001-6000
6001-7000
7001-25000
>25000

2011


MCI
0-1000
1001-2000
2001-3000
3001-4000
4001-5000
5001-6000
6001-7000
7001-25000
>25000

Albion

AIGINITIO
LONGITUDINAL BIOMARKERS
INVESTIGATION
OF NEURODEGENERATION

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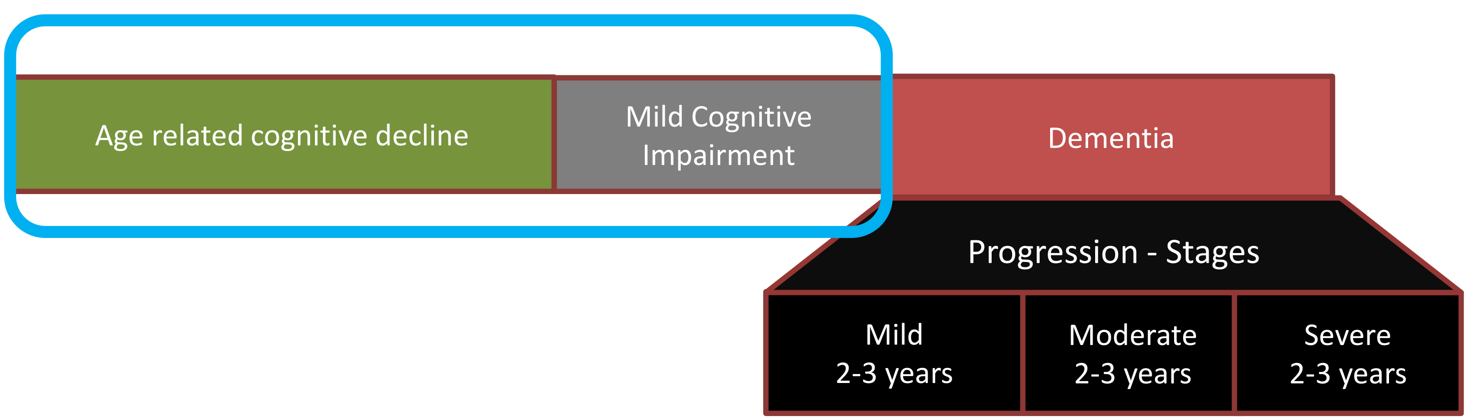
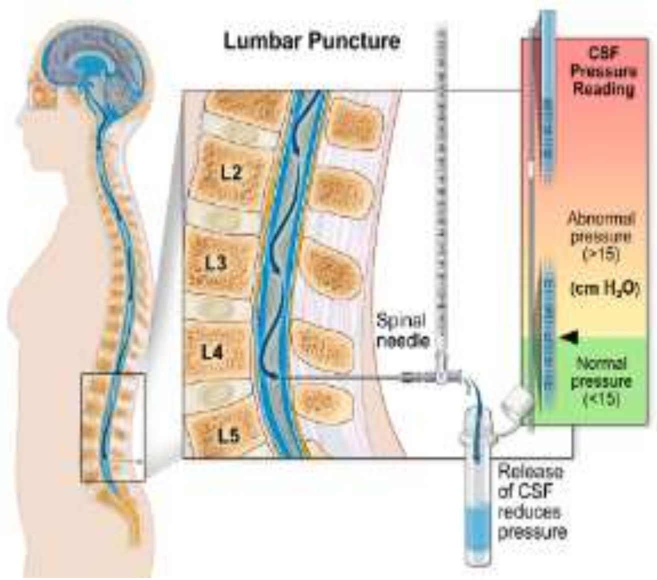
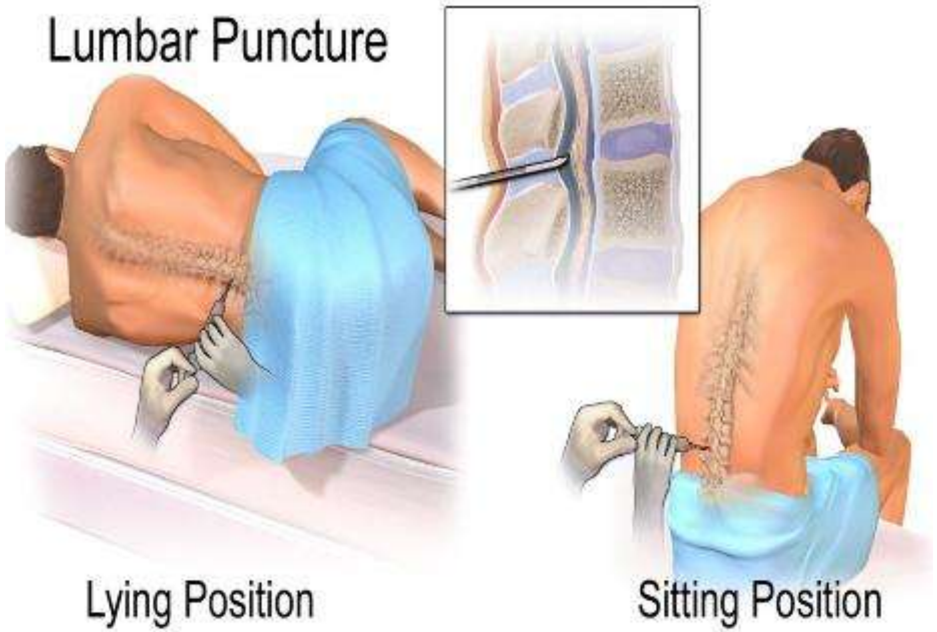
- Cognitive Disorders Clinic - Aiginitio
- Prospective
- Initiation 2018
- Investigation of preclinical and prodromal stage of dementia
- Emphasis on lifestyle
- Population
  - > 45 ετών
  - (+/-) Subjective cognitive decline
  - Normal or MCI (preferably preMCI or earlyMCI)



CSF biomarkers





Blood

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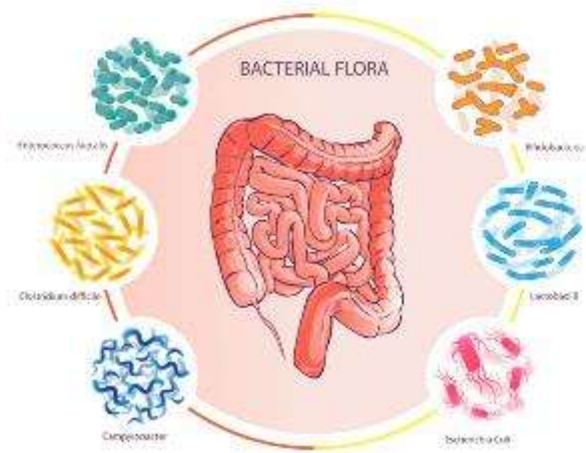
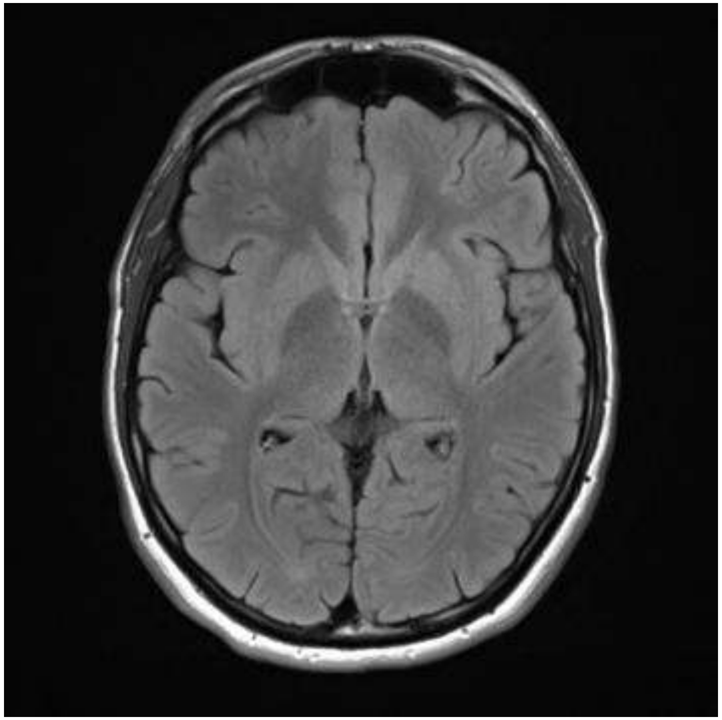
Microbiome



- Sinha R, Chen J, Amir A, et al. Collecting fecal samples for microbiome analyses in Epidemiology studies. Cancer Epidemiol Biomarkers Prev. 2016 Feb;25(2):407–416.
- Vogtmann E, Chen J, Amir A, et al. Comparison of collection methods for fecal samples in Microbiome studies. Am J Epidemiol. 2017 Jan 15;185(2):115–123.
- Riegler G, Esposito I. Bristol scale stool form. A still valid help in medical practice and clinical research. Tech Coloproctol. 2001 Dec;5(3):163–164.

MRI



AIGINITIO LONGITUDINAL BIOMARKERS INVESTIGATION OF NEURODEGENERATION

Sleep - Actigraphy

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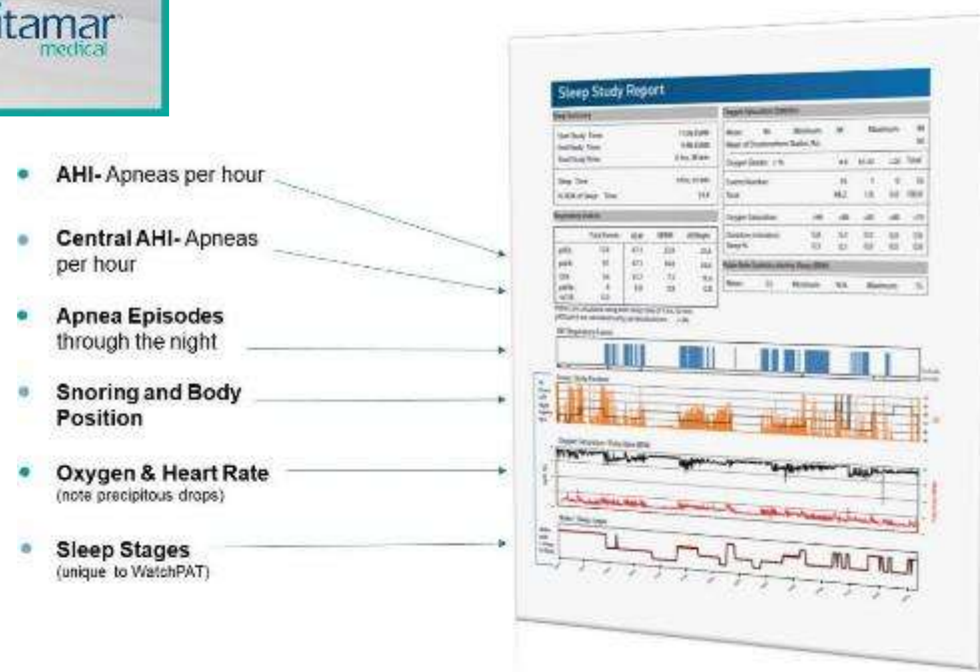
Sleep - WatchPAT

Choi JH, Lee B, Lee JY, et al. Validating the watch-PAT for diagnosing bstructive sleep apnea in adolescents. J Clin Sleep Med. 2018 Oct 15;14(10):1741–1747.



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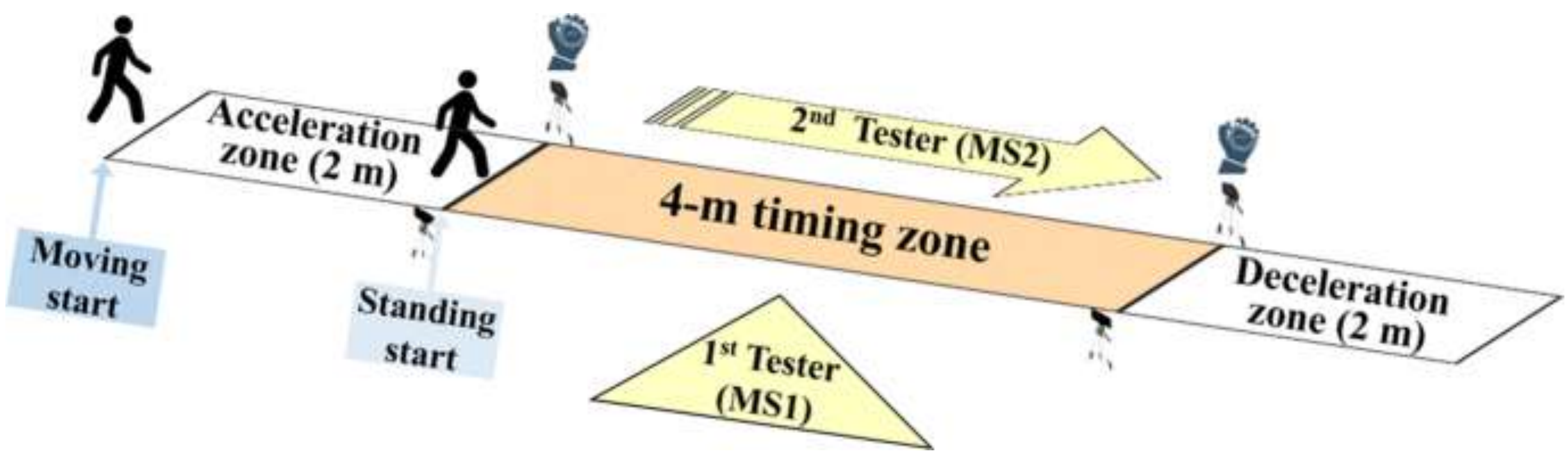
Gait Speed

Dynamic start



Grip Strength - Dynamometer

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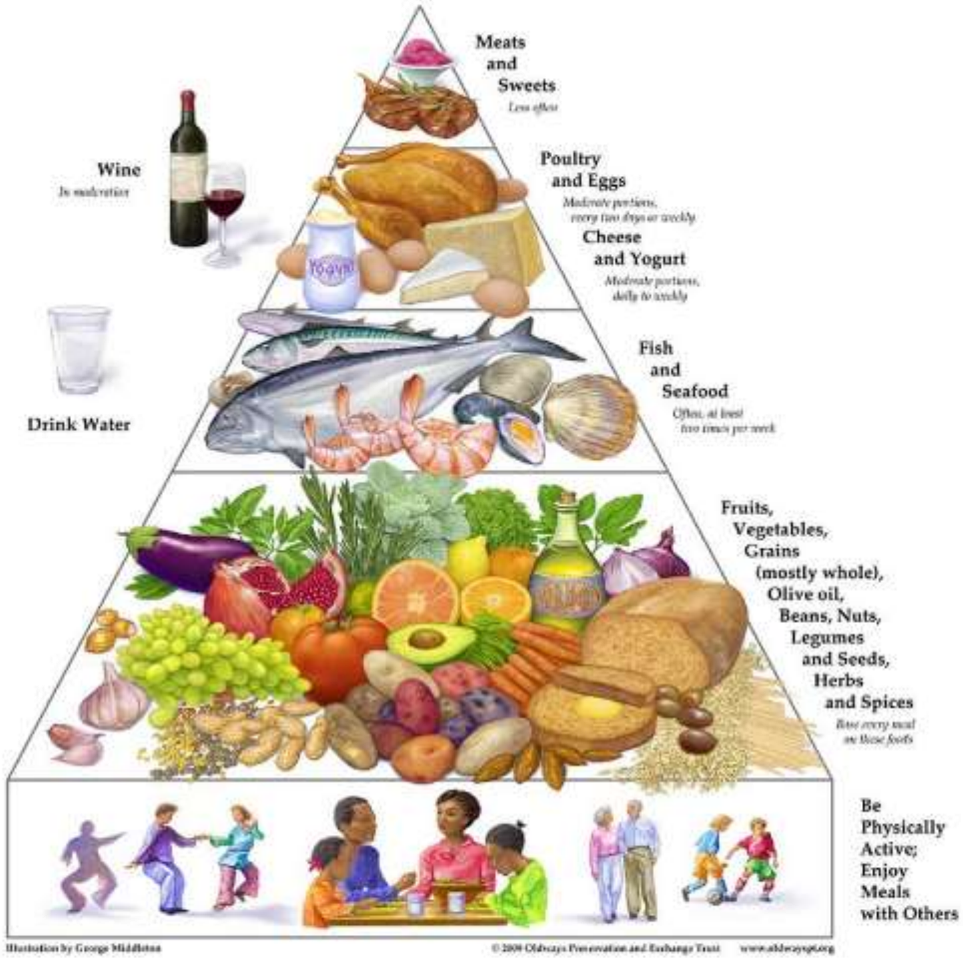
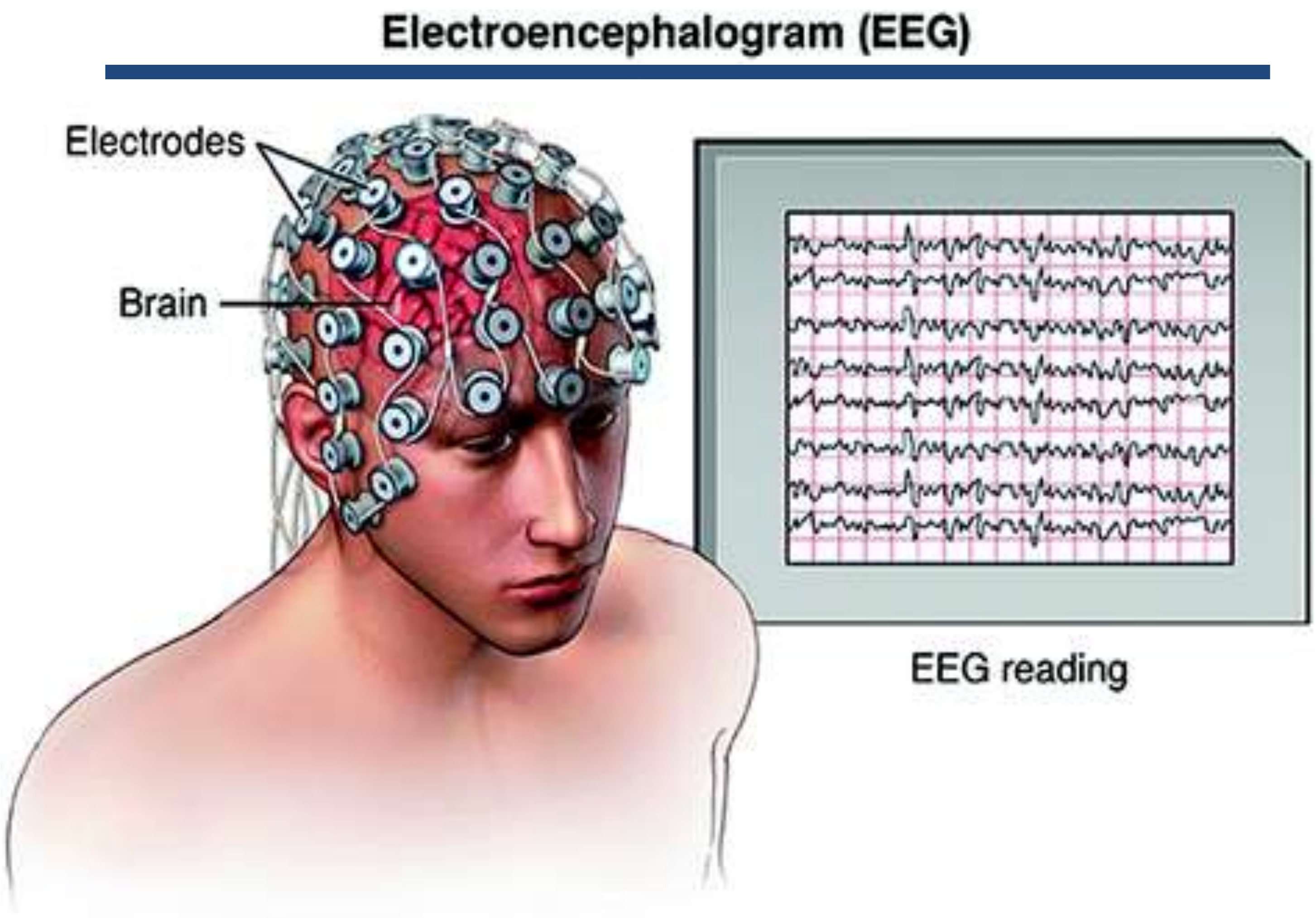
Nutrition





Blackburn DJ, Zhao Y, De Marco M, et al. A pilot study investigating a novel non-linear measure of eyes open versus eyes closed EEG synchronization in people with Alzheimer's disease and healthy controls. Brain Sci. 2018 Jul 17;8(7):134.

Albion
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Table 1. Procedures included in ALBION study organized per visit

	1st visit	2nd visit[a]	3rd visit	4th visit[a]	5th visit	6th visit[a]	7th visit[c]
Neurological examination (+ CDR, NPI, IADL, HACHINSKI, UPDRS)	X	X	X	X	X	X	X
Neuropsychological assessment	X	X	X	X	X	X	X
HADS questionnaire	X	X[b]	X		X[c]		X
Sleep quality and quantity questionnaire	X	X[b]	X		X[c]		X
Leisure Activities questionnaire	X	X[b]	X		X[c]		X
Subjective Cognitive Complaint Questionnaire (SCC questionnaire)	X	X[b]	X		X[c]		X
Athens Physical Activity questionnaire	X	X[b]	X		X[c]		X
Dynamometer (3 trials)	X	X[b]	X		X[c]		X
24h dietary recall	X	X[b]	X		X[c]		X
Anthropometrics (weight/height)	X	X[b]	X		X[c]		X
Gait speed (2 trials)	X	X[b]	X		X[c]		X
Magnetic resonance imaging (MRI)	X						X
Electroencephalogram (EEG)	X		X		X[c, d]		X
Lumbar Puncture	X						X[e]
Blood sample	X		X		X[c, d]		X
Stool sample (microbiome analysis)	X		X		X[c, d]		X
Wrist actigraphy	X		X		X[c, d]		X
WatchPat	X		X		X[c, d]		X

[a] Update 4/2023: These visits will be performed only if a participant is diagnosed with Mild Cognitive Impairment, dementia or if a participant asks it in the contact performed annually by phone

[b] These procedures were performed till August 2021. After that, visit 2 will include only neurological and neuropsychological assessment.

[c] Update 2023

[d] These assessments will be performed only to those participants that did not perform the respective assessment to the previous visit

[e] Excluded from second lumbar puncture are those 1) who have been diagnosed with dementia in a previous visit and b) those who had a lumbar puncture after participating in other department's study (EVOKE…)

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THANKS

For your attention

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