Hospital Central de la Cruz Roja
San José y Santa Adela

La enfermedad de Alzheimer. Enfoque actual

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Jefe de Servicio H Central de la Cruz Roja.

Madrid 2017

¿Qué vamos a desarrollar?

- SIGLO XXI ENVEJECIMIENTO-DEMENCIA
- **SIGLO XXI: PATOGENIA Y FX DE RIESGO ENF ALZHEIMER**
- TRATAMIENTO Y NUEVAS PERSPECTIVAS
- LINEAS DE FUTURO: PREVENCIÓN

El logro del envejecimiento YA está aquí

Oldest old , very old people

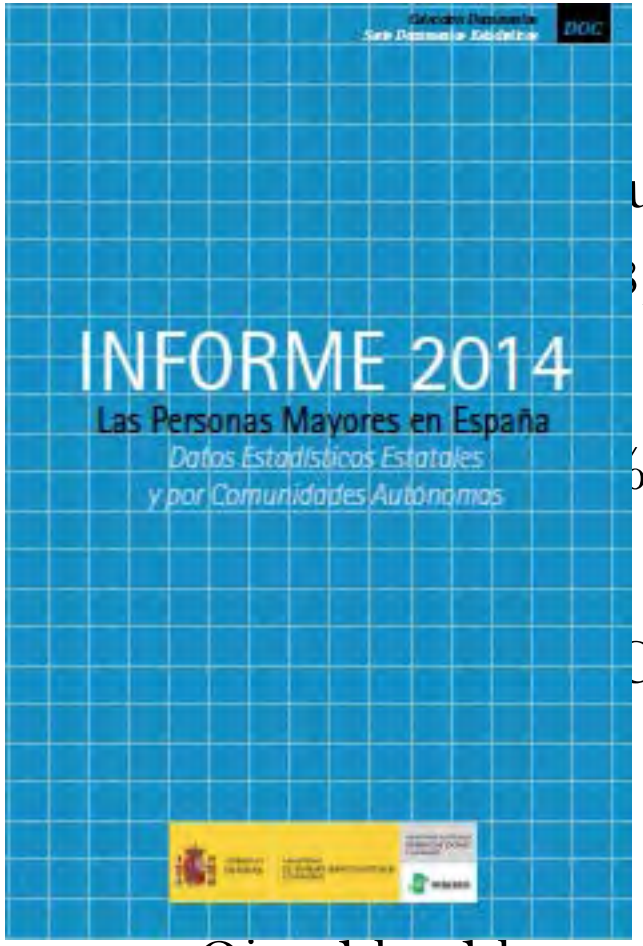
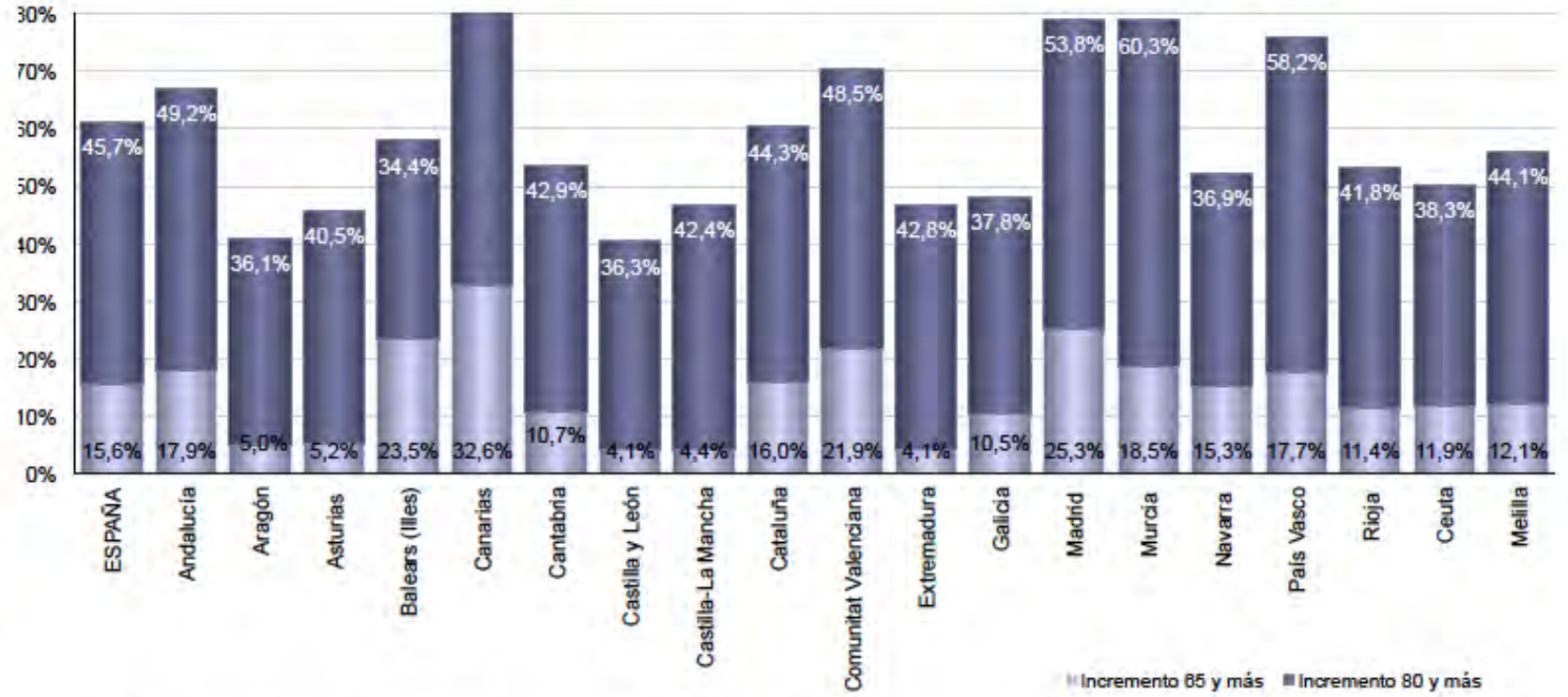


GRÁFICO 1.18

INCREMENTO DE LA POBLACIÓN DE 65 Y MÁS AÑOS, SEGÚN COMUNIDAD AUTÓNOMA, 2003-2013



Fuente: INE. Padrón Municipal de Habitantes a 1 de Enero de 2004 y a 1 de enero de 2014.

5. ¡¡¡Ojo olds old > 90 100 años

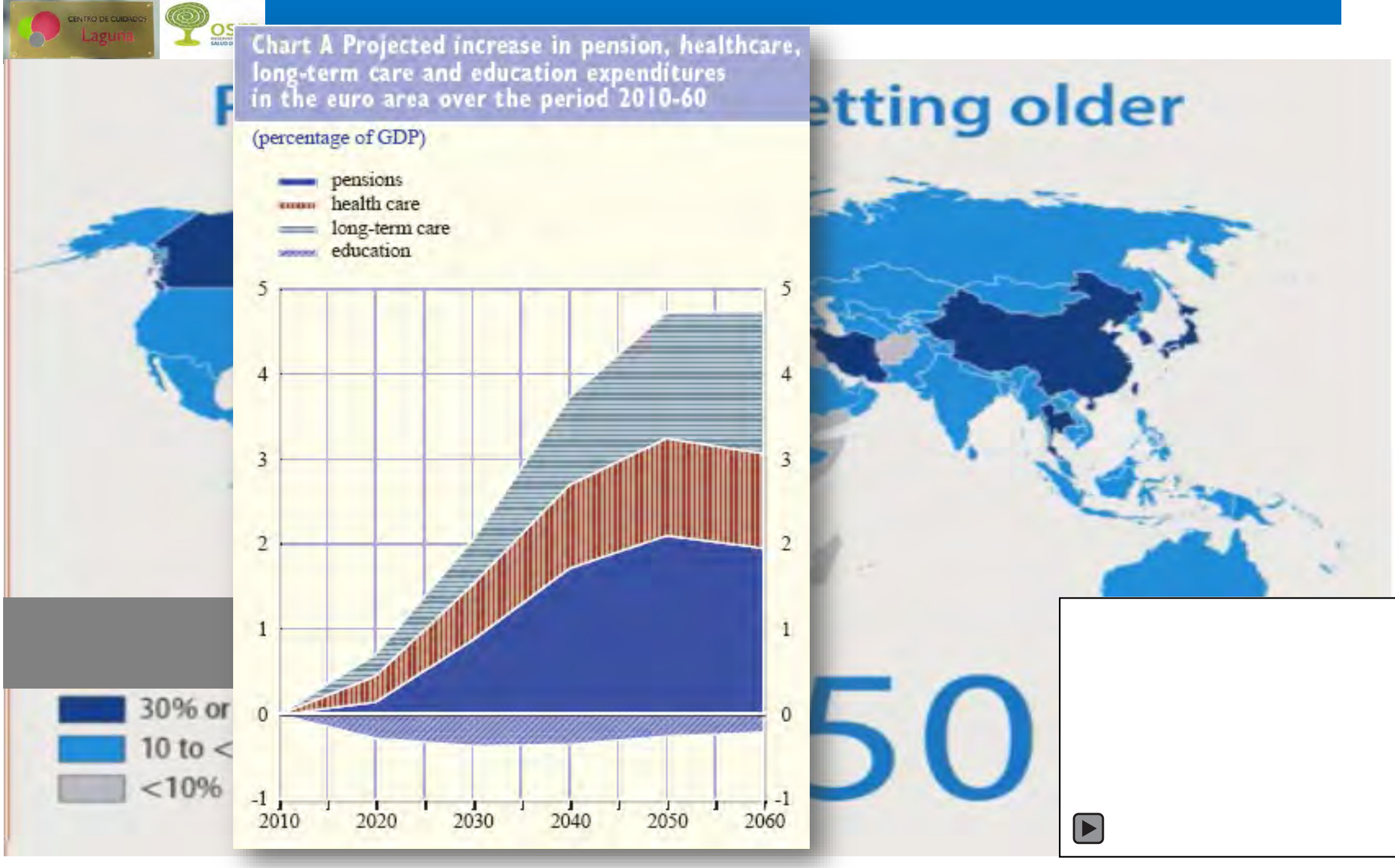
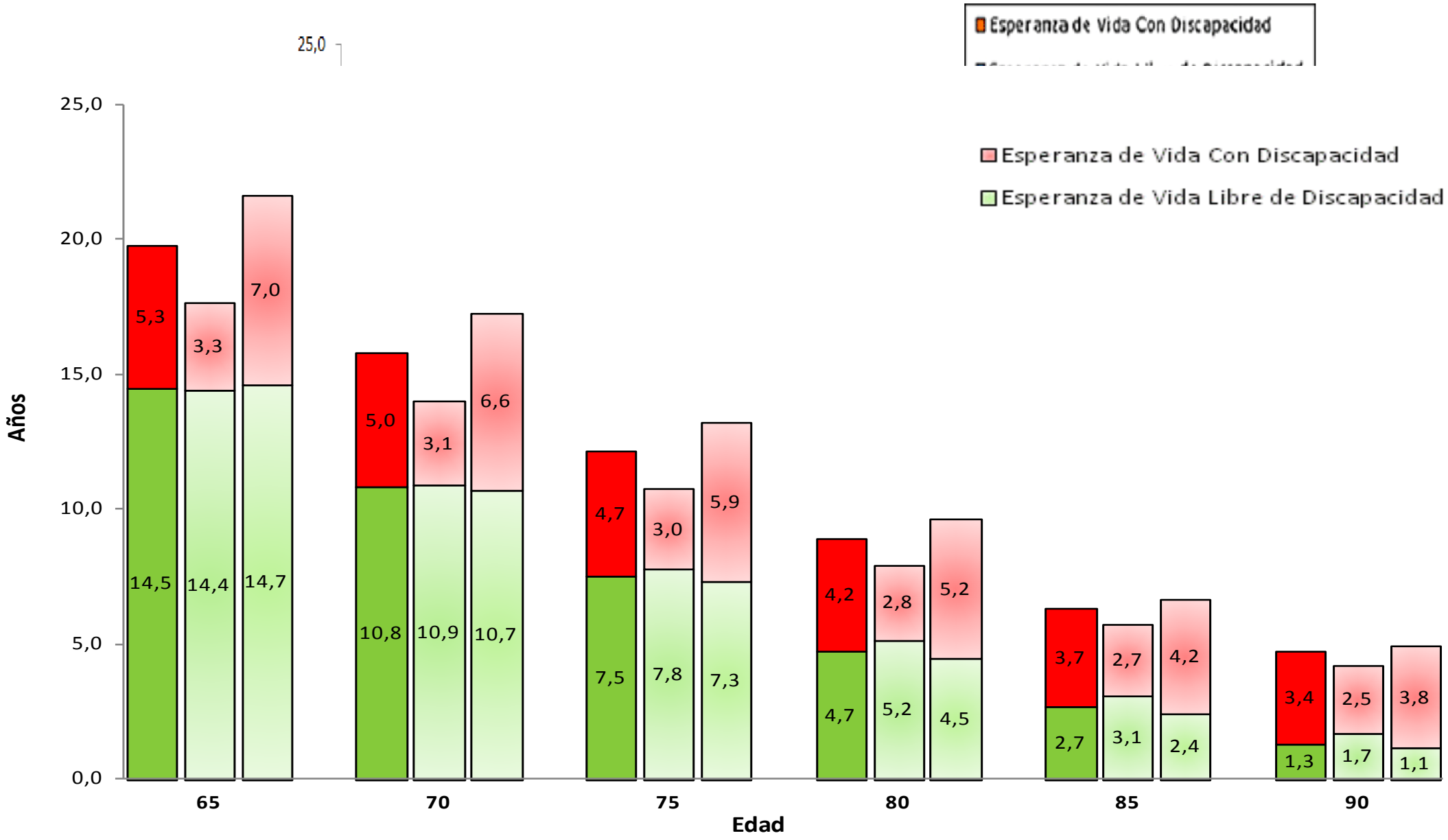


Chart A Projected increase in pension, healthcare, long-term care and education expenditures in the euro area over the period 2010-60
(percentage of GDP)
pensions
health care
long-term care
education
5
4
3
2
1
0
-1
2010
2020
2030
2040
2050
2060
etting older
50
30% or
10 to <
<10%

¿Cuál es el indicadorr de salud en la persona mayor?



tamos comprimiendo la dependencia?

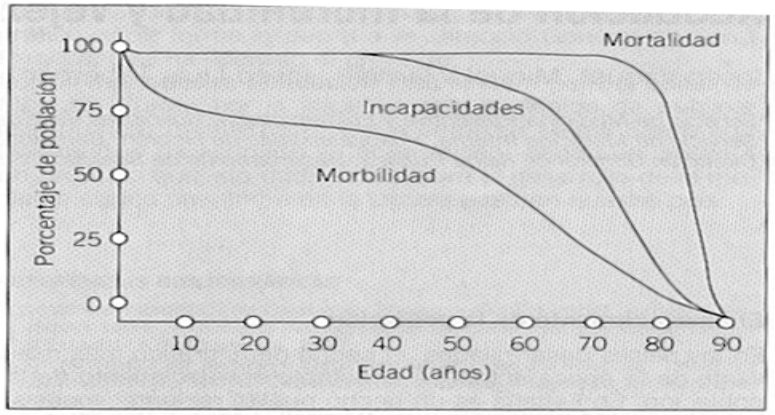
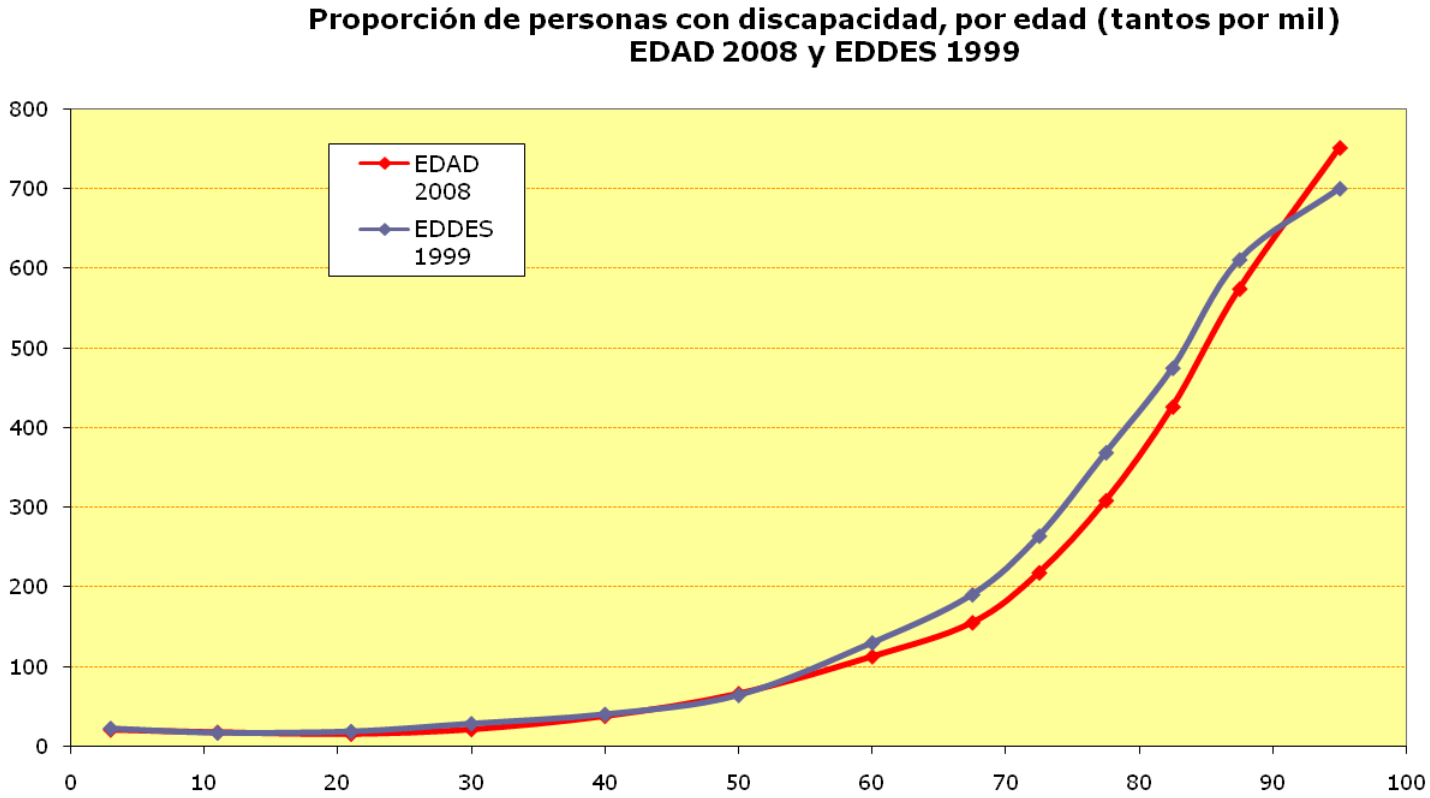


Fig. 2. Compresión de la morbilidad. Curvas de supervivencia de la morbilidad, incapacidades y mortalidad.

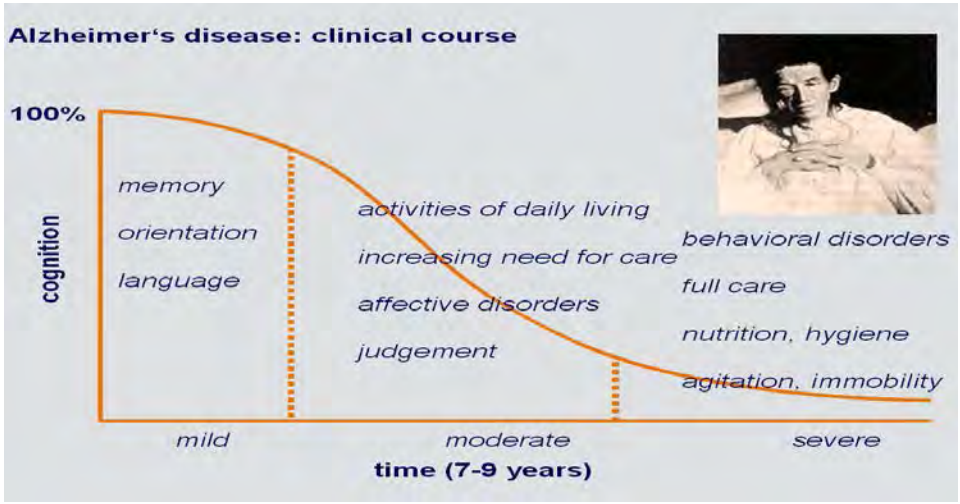


INFORMES PORTAL MAYORES
ISSN: 1885-6780
108
Abril 2011

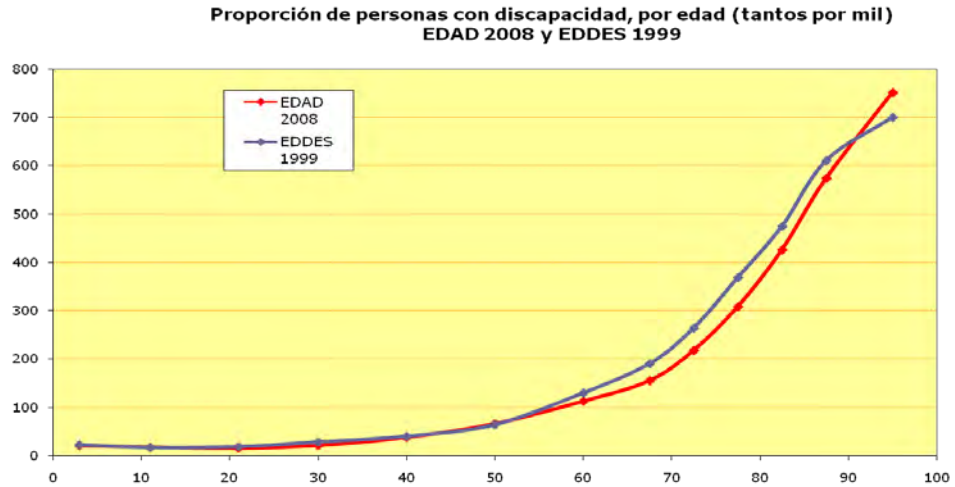
EDAD	TASAS			Distribución
	Varones	Mujeres	TOTAL	
65-69	14,0	17,0	15,6	13,1
70-74	17,6	25,3	21,8	18,2
75-79	26,3	34,3	30,9	22,6
80+	41,9	56,9	51,5	46,1
TOTAL	24,1	34,9	30,3	100

SIGLO XXI
ENVEJECIMIENTO POBLACIONAL

Evolución de la enfermedad crónica



Prevalencia de Enfermedades Crónicas



COMORBILIDAD-PLURIPATOLOGÍA

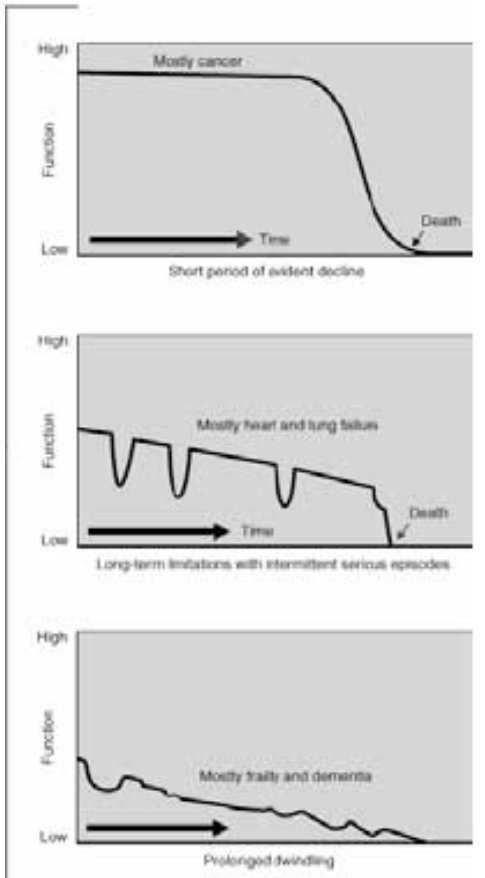
Functional trajectories at the end of life.

Lunney J.R. JAGS 2002;50:1108-1112

Cáncer

Mayoría de enf. Crónicas:
ICC, EPOC, Demencia

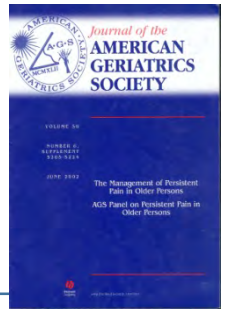
Fragilidad



INCLUSO LA FUNCIÓN ES IMPORTANTE AL

- Estudio cualitativo, de opinión de mayores de 80 años, que viven en la comunidad con pluripatología, comorbilidad, polifarmacia ...:
  - Buena muerte:
    - No ser dependiente, no incapacidad mental
    - No sufrimiento: no dolor, poder dormir, no disnea, ...
    - Rodeados de su familia y amigos
    - Medidas adecuadas, no agresivas, no abandono
    - No ocultar información

Good Deaths, Bad Deaths, anpreferences for the end of life: a quaalitative Study of Geriatric outpatients.EK Vig, NA Davenport and RA Pearlman. J Am Geriatr Soc 50:1541-1548, 2002.



Calidad de Vida

Organización Mundial de la Salud

ESPACIO VITAL

Salud= Función

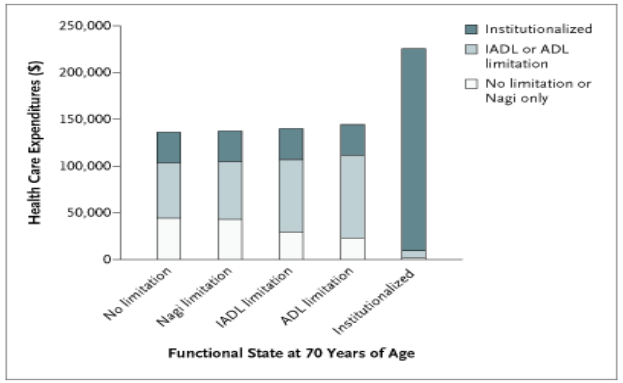
Pérdida funcional=Mayor gasto sanitario y social

ncia

COSTE SANITARIO Y SOCIAL

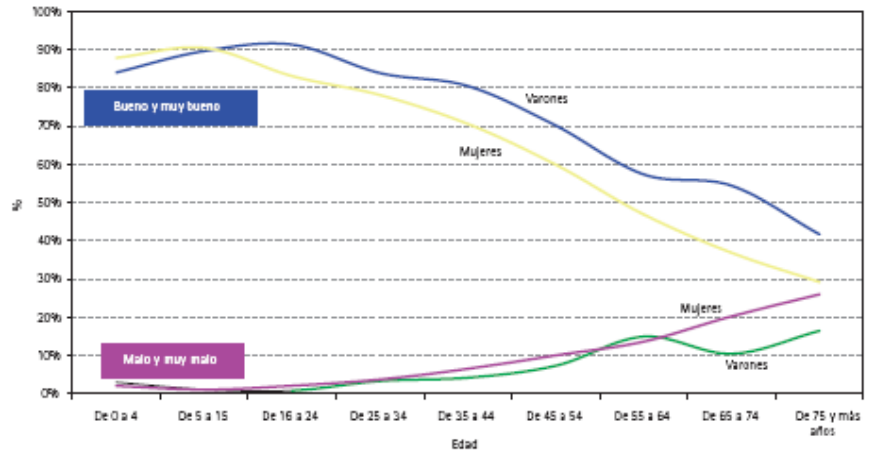
Mor

Consumo de Recursos



- Sufrimiento (ttnos. Afectivos psicofamiliares)
- Baja calidad de vida

Percepción del estado de salud según sexo y edad, 2006



Nota: Estado de salud general percibido en los últimos 12 meses. No está representado «regular».
Fuente: INE: INEBASE: *Encuesta Nacional de Salud. Tablas nacionales, 2006. Estado de salud.* INE, consulta en junio de 2008.

DEPENDENCIA

Se han ganado años a la vida a costa de discapacidad y

Riesgo atribuible de dependencia

- 37% enfermedades osteomusculares (artrosis, artritis, osteoporosis).
- 20% enf. y dolencias del corazón y enf. circulatorias (ictus).
- 13% fracturas y traumatismos.
- 4% problemas psíquicos (demencia, depresión)

Riesgo Relativo de dependencia

“Carga de la dependencia”

“The Global Burden of Diseases”: % años vividos con discapacidad en > 60 años corresponde:

- Demencia: 11,2%
- Ictus: 9,5%
- Enf. Musculoesquelética: 8,9%
- Enf. Cardiovascular: 5%
- Cáncer: 2,4%

Cantidad de personas con demencia en el mundo

América
- 29.9m 2050
- 15.8m 2030
- 9.4m 2015

África
- 15.8m 2050
- 7.0m 2030
- 4.0m 2015

Europa
- 18.6m 2050
- 13.4m 2030
- 10.5m 2015

Asia
- 67.2m 2050
- 38.5m 2030
- 22.9m 2015

Mundo
- 131.5m 2050
- 74.7m 2030
- 46.8m 2015

www.thelancet.com Published online July 16, 2013

Good news on dementia prevalence—we can make a difference

A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II

Published Online
July 16, 2013

Fiona E Matthews, Antony Arthur, Linda E Barnes, John Bond, Carol Jagger, Louise Robinson, Carol Brayne, on behalf of the Medical Research Council Cognitive Function and Ageing Collaboration

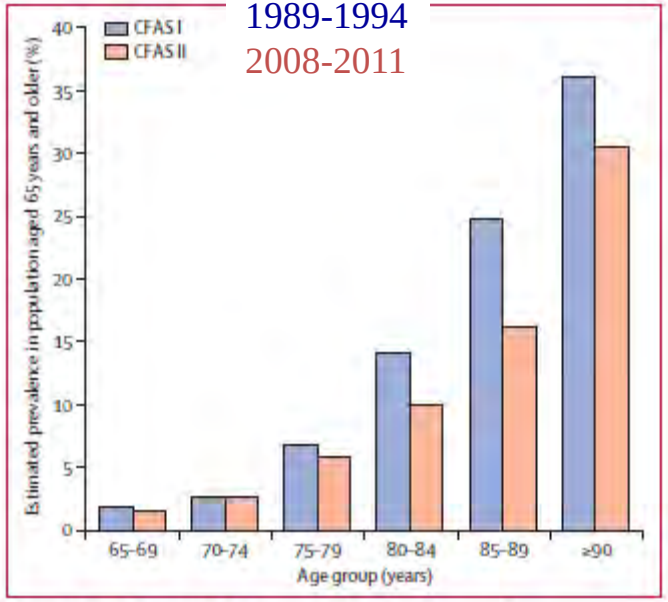


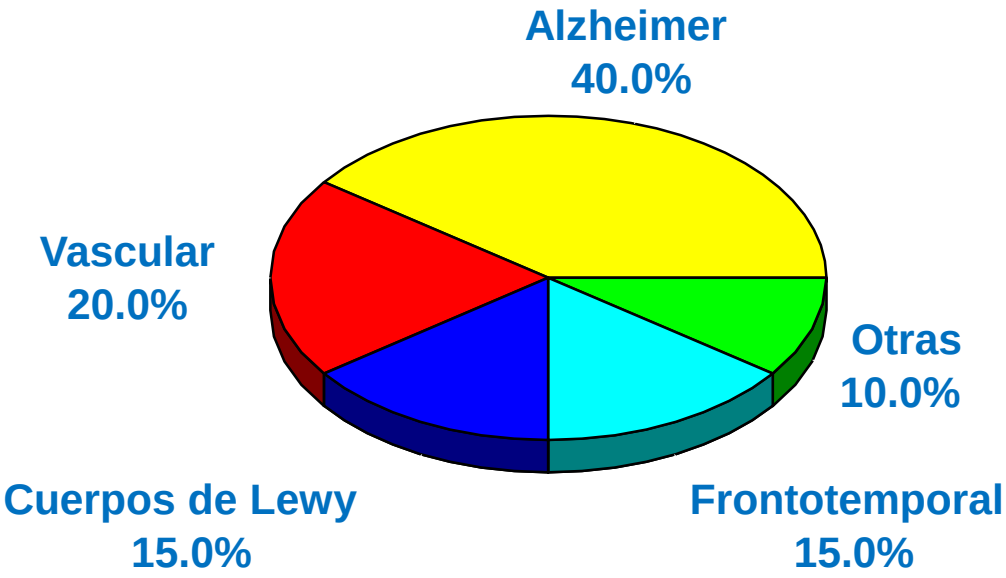
Figure 1: CFAS I and CFAS II age-specific dementia prevalence
CFAS=Cognitive Function and Ageing Study.

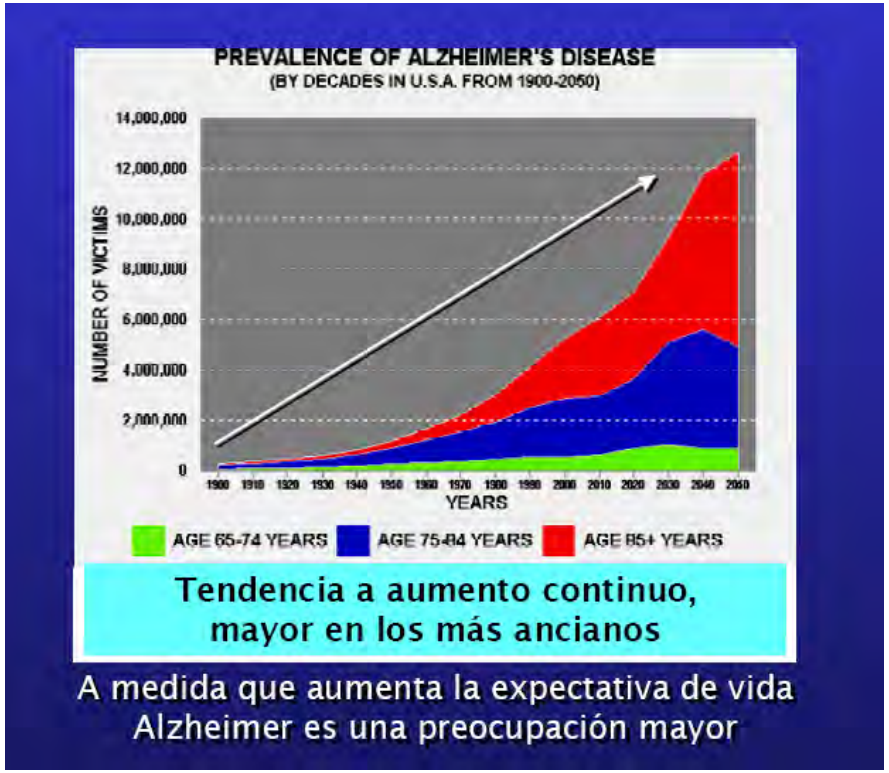
1989-1994
2008-2011

Prevalencia demencia > 65 años
1989-1994= 8,3%
2008-2011= 6,5%

➢ **↓demencia por ↓ componente vascular:**
Mejor control cardiovascular (HTA, diabetes, …)
Mejor supervivencia al ictus
Mayor nivel educativo y social

TIPOS DE DEMENCIA MÁS FRECUENTES





Cummings JL, Vinters HV, Cole GM, Khachaturian Zs. Alzheimer's disease: Etiologies, pathophysiology, cognitive reserve, and treatment opportunities. Neurology 1998;51 (suppl 1): 2-17

Demencia-Anciano

Hechos probados: Aumento demencia

Maturitas 70 (2011) 164–168

Review

Diagnosing dementia in the oldest-old

Carrie Brumback-Peltz [a,*], Archana B. Balasubramanian [a], María M. Corrada [a,b], Claudia H. Kawas [a,b,c]

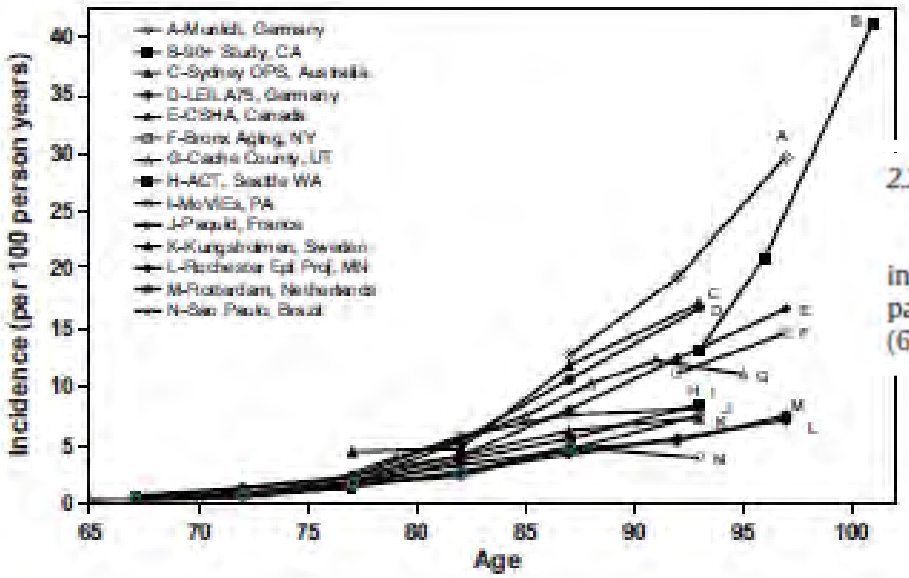


Fig. 1. Age-specific incidence of dementia in studies with subjects aged 90+. Note: Munich, Germany [44], 90+ Study, CA [6], Sydney OPS, Australia [45], LEILA75, Germany [46], CSHA, Canada [47], Bronx Aging, NY [48], Cache County, UT [49], ACT, Seattle, WA [50], MoVIEs, PA [51], Paquid, France [52], Kungsholmen, Sweden [53], Rochester Epi Proj, MN [54], Rotterdam, Netherlands [55], Sao Paulo, Brazil [56].

2.2. The 90+ Study

The 90+ Study is a population-based sample of more than 1600 individuals, aged 90–108 years. Initiated in 2003, 90+ participants are predominantly white, female (76%) and well educated (63% >high school).

ELSEVIER

Alzheimer's & Dementia 12 (2016) 459-509

Alzheimer's & Dementia

Alzheimer's Association Report

2016 Alzheimer's disease facts and figures

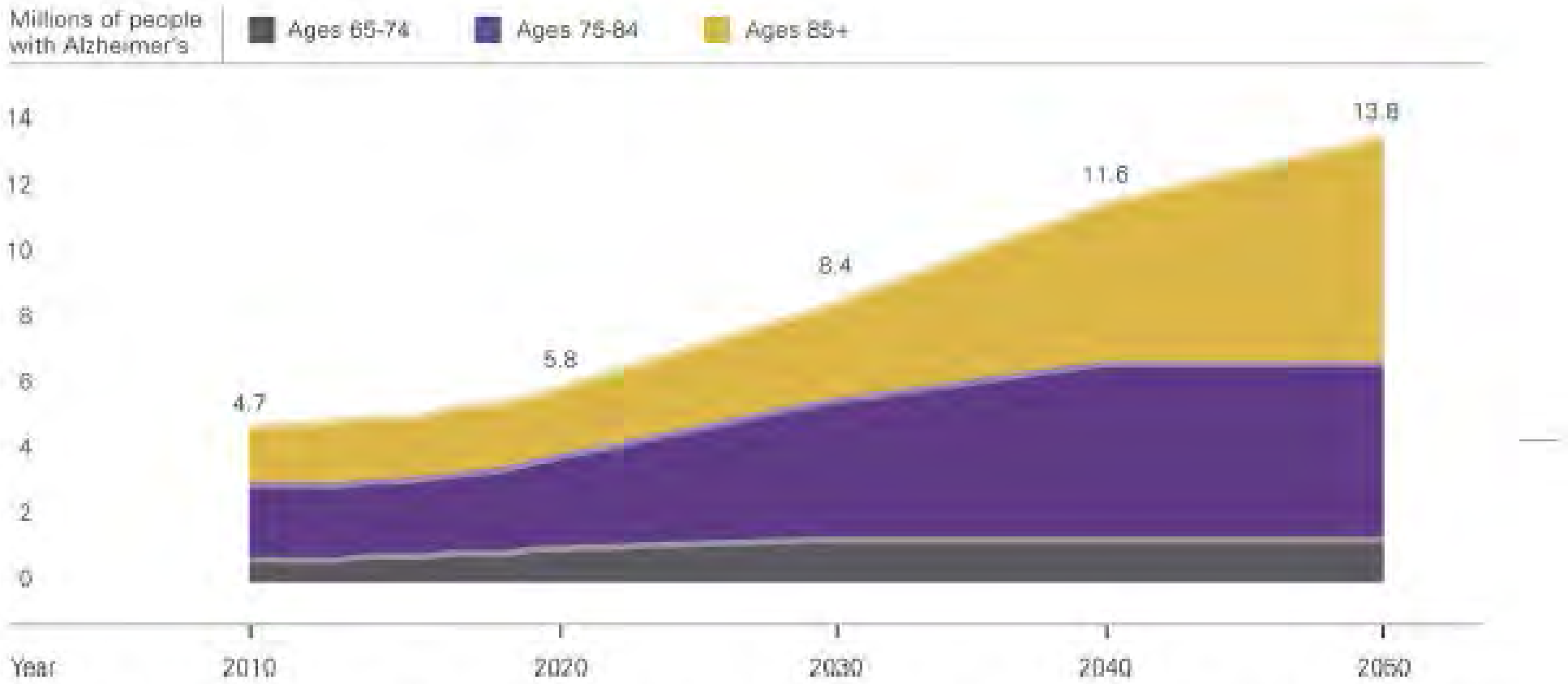


Fig. 5. The projected number of people aged 65 years or older (total and by age group) in the United States population with AD, 2010 to 2050. Created from data from Hebert et al. [114].[A1.1]

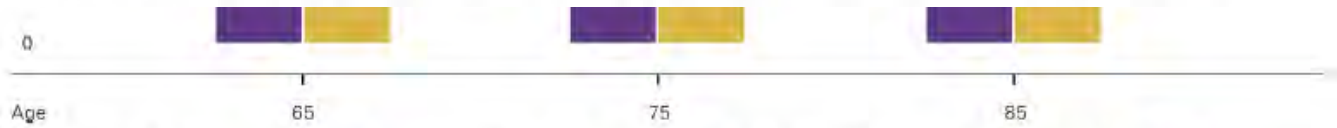


Fig. 3. Estimated lifetime risks for AD, by age and sex, from the Framingham Study. Created from data from Seshadri et al. [142].

ELSEVIER

Alzheimer's & Dementia 10 (2014) e47–e92

Alzheimer's Association Report

2014 Alzheimer's disease facts and figures

Alzheimer's Association*

Alzheimer's & Dementia

Demencia-Anciano

Hechos probados: Aumento demencia

Causa de muerte

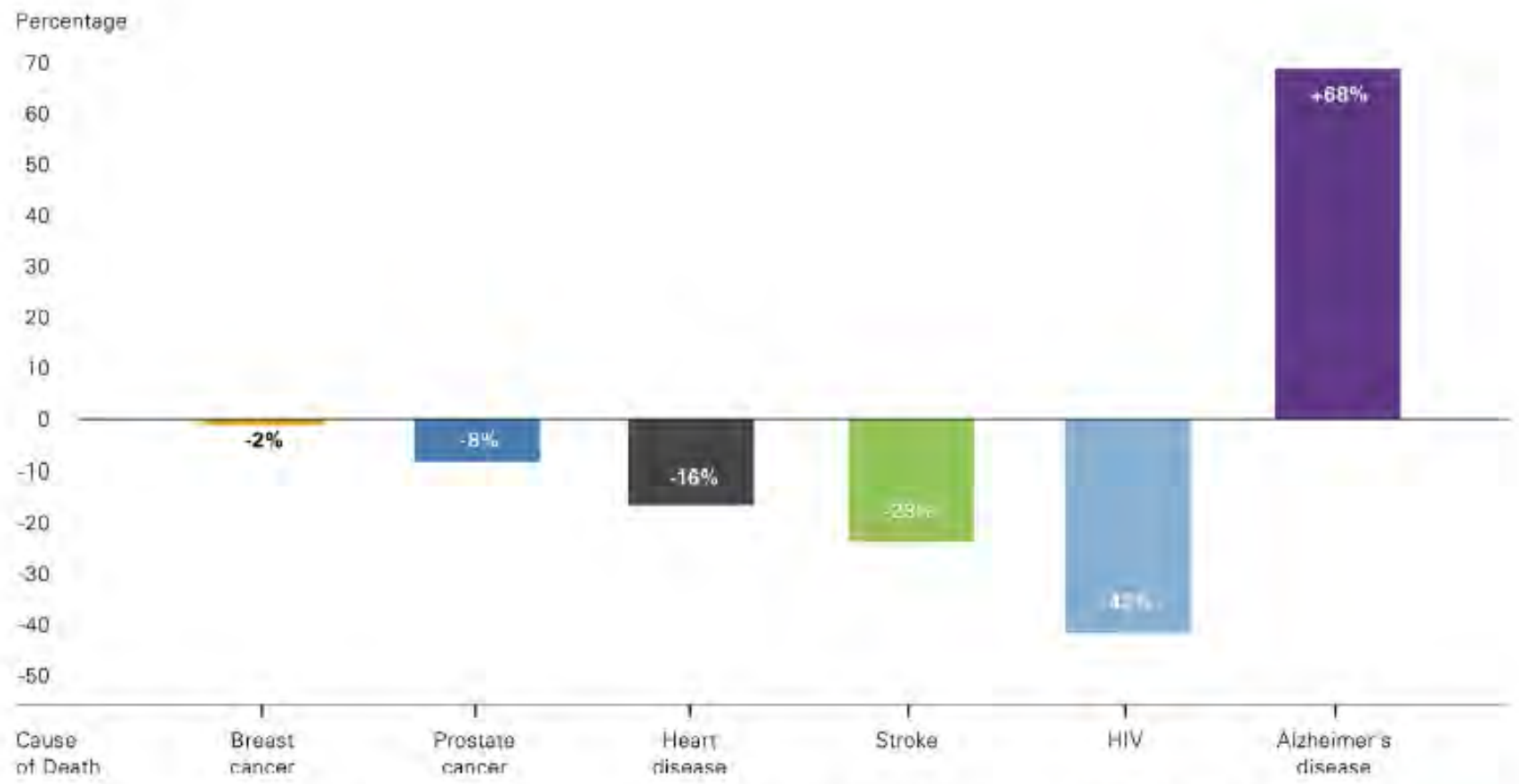


Fig. 6. Percentage changes in selected causes of death (all ages) between 2000 and 2010. Created from data from the National Center for Health Statistics [145,158].

COSTE DE LA DEMENCIA

RESEARCH ARTICLE

International Journal of Geriatric Psychiatry

The economic impact of dementia in Europe in 2008—cost estimates from the Eurocode project

Int J Geriatr Psychiatry 2011; **26**: 825–832.

A. Wimo[1], L Jönsson[2], A. Gustavsson[1,2], D. McDaid[3], K. Ersek[4], J. Georges[5], L. Gulácsi[4], K. Karpati[4], P. Kenigsberg[6] and H. Valtonen[7]

- **Coste de la demencia en Europa en 2008 fue de 160 billones €**
  - ✓22.000€ anuales por paciente.
- **Coste de la demencia en España:**
  - ✓Entre 27.000€ y 37.000€ anuales por paciente:

77-81% • Gasto cuidador informal

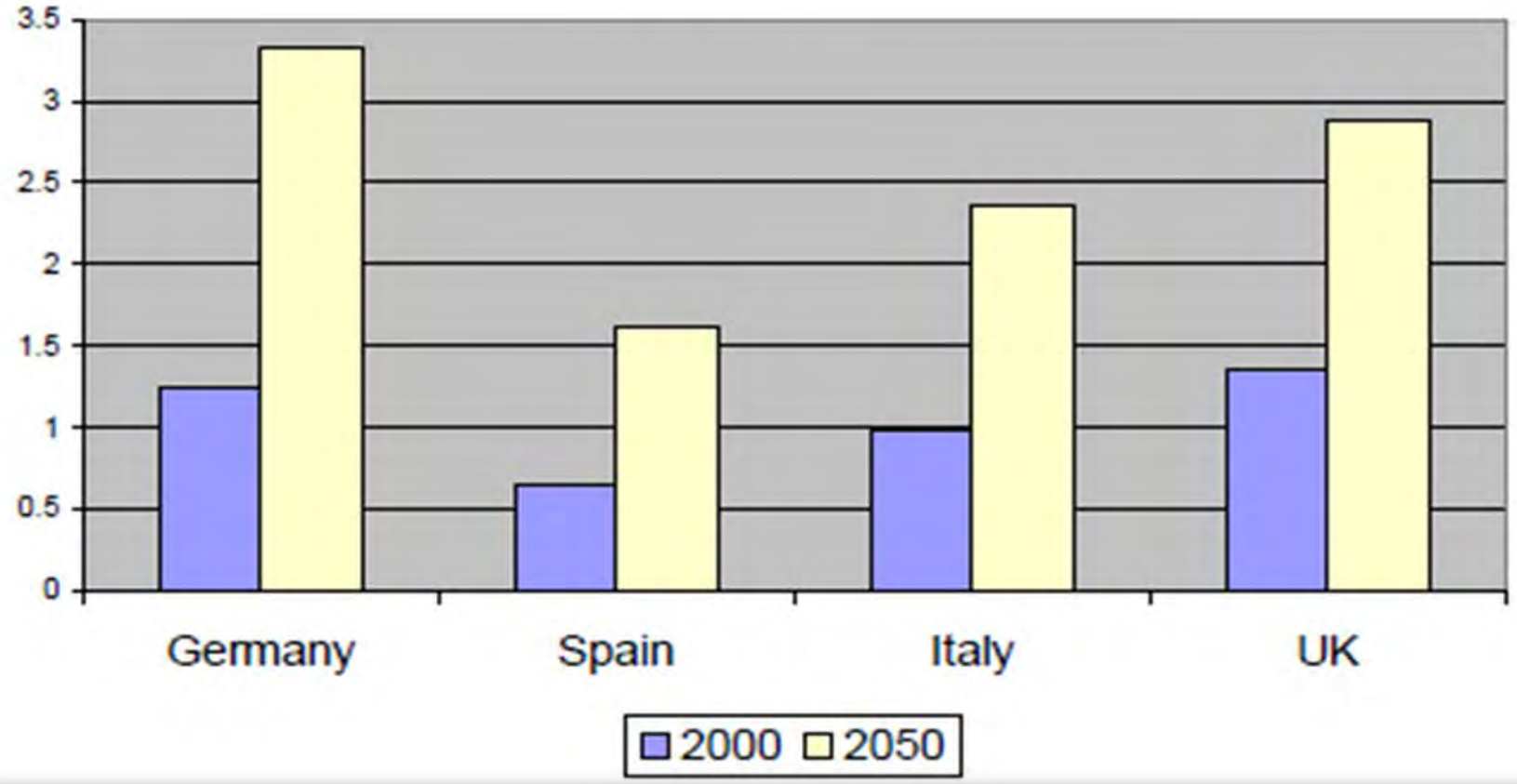
10-13% • Gasto sanitario

6-12% • Gasto cuidado formal (social)

GASTO SANITARIO
Países de nuestro entorno
21-56%

AUMENTA EN FUNCIÓN DEL ESTADIO

Figure 1
Projected long-term care expenditure as a proportion of GDP in Germany, Spain, Italy and the United Kingdom, under central base case assumptions, 2000-2050

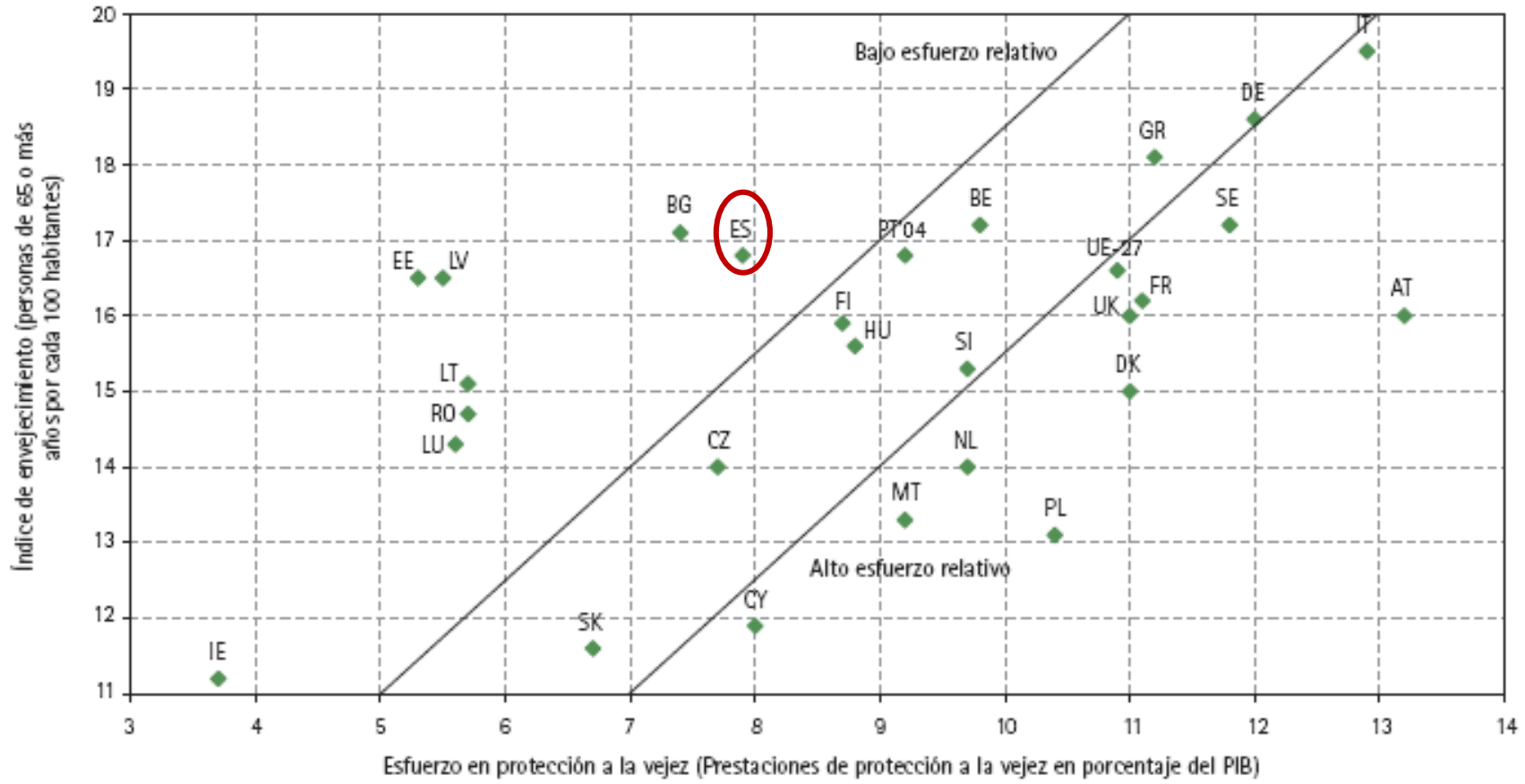


Pickard L, et al: Modelling an entitlement to longterm care services for older people in Europe: projections for long-term care expenditure to 2050. Journal of European Social Policy 2007.

Gráfico 4.4.- Persona que cuida según el sexo de la persona mayor que necesita ayuda, 2008

Fuente: INE: Encuesta sobre Discapacidad, Autonomía personal y Situaciones de Dependencia (EDAD), 2008. Elaboración propia a partir de los microdatos

Relación entre el esfuerzo de protección a la vejez y el índice de envejecimiento en los países de la Unión Europea, 2005



Fuente: EUROSTAT (http://epp.eurostat.ec.europa.eu/), consulta en junio de 2008.

ELSEVIER
Alzheimer's & Dementia 10 (2014) e47–e92
Alzheimer's Association Report
2014 Alzheimer's disease facts and figures
Alzheimer's Association*
Alzheimer's & Dementia

Demencia-Anciano

Hechos probados: Aumento demencia
Sobrecarga cuidadores

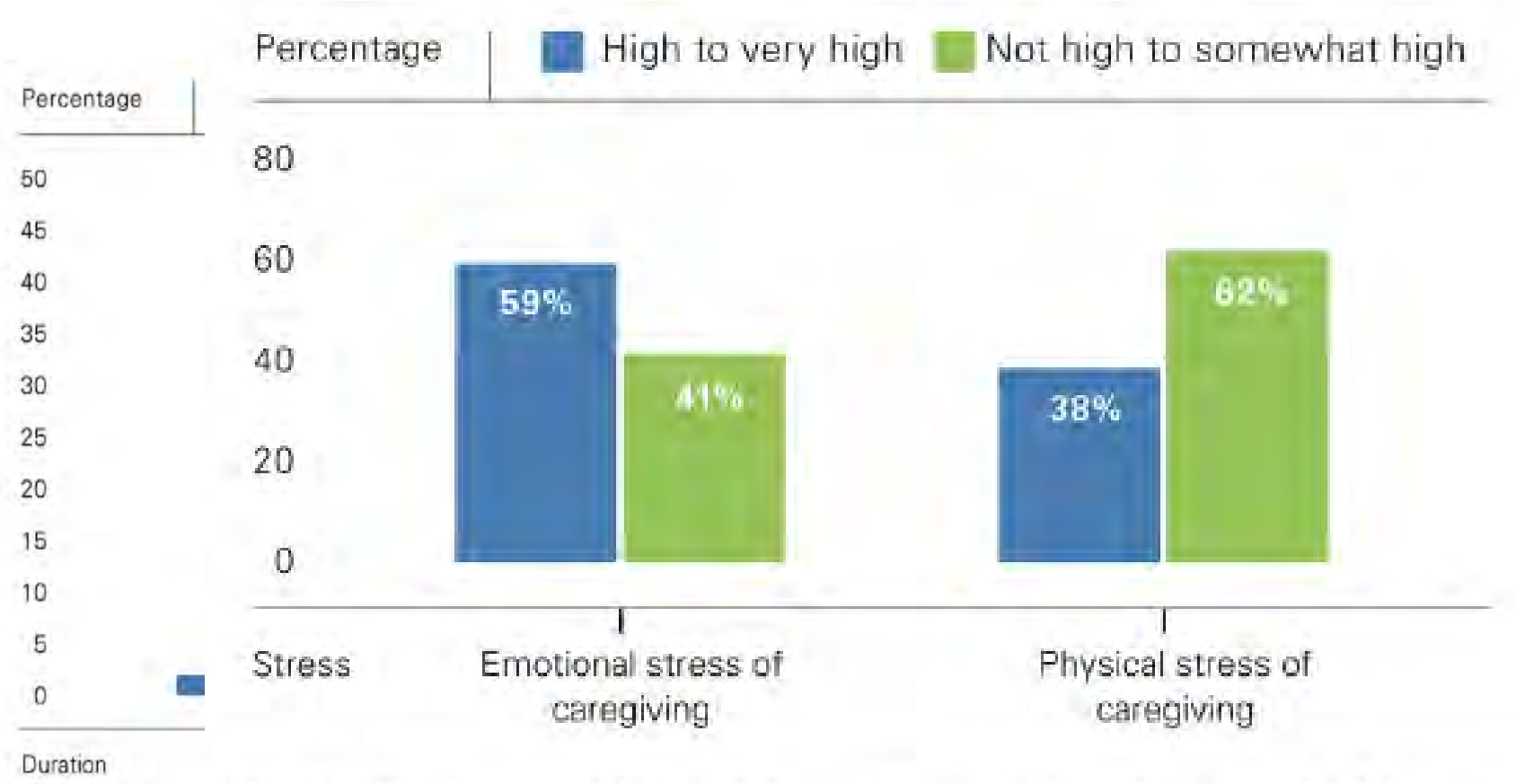
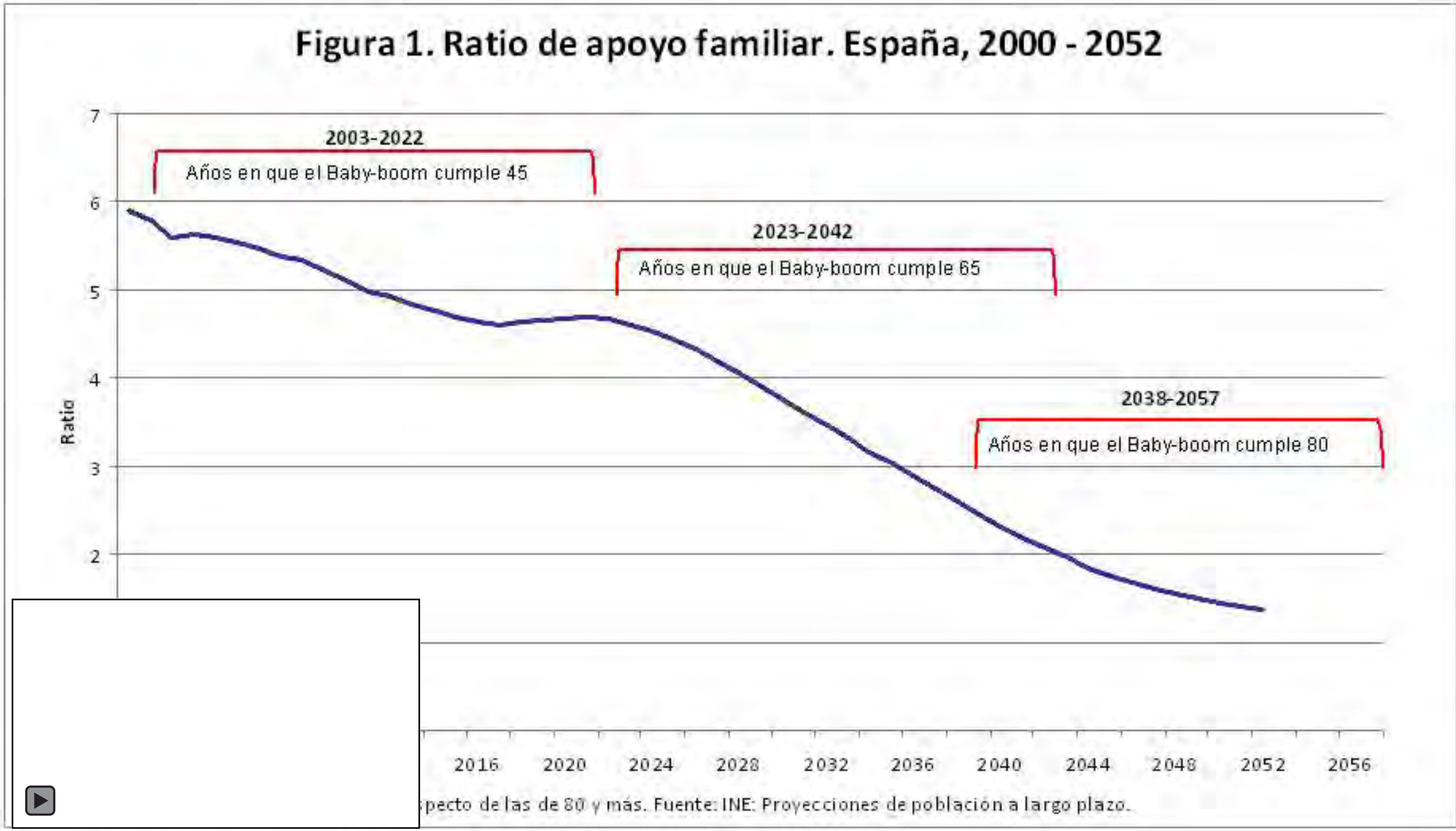


Fig. 8. Proportion
the National Allian

Fig. 9. Proportion of AD and dementia caregivers who report high or very high emotional and physical stress due to caregiving. Created from data from the Alzheimer's Association.[A17]

data from

Figura 1. Ratio de apoyo familiar. España, 2000 - 2052



pecto de las de 80 y más. Fuente: INE: Proyecciones de población a largo plazo.

RECURSOS ASISTENCIALES PERSONA DEPENDIENTE

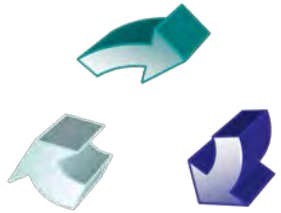
www.segg.es

Guía práctica
de la ley de la dependencia

Ley de Promoción de la Autonomía Personal y atención a las personas en situación de dependencia
LAAD

Persona con demencia

Cuidado informal



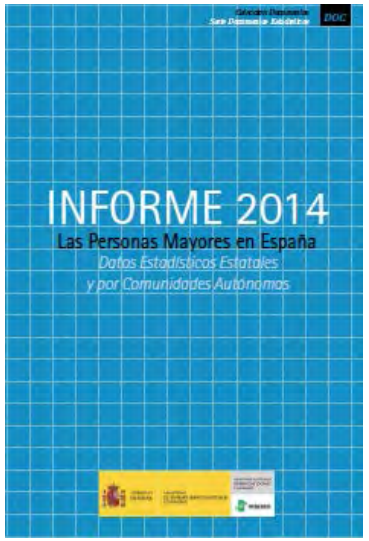
SERVICIOS SOCIALES

Comunitarios
Hogares, clubes
Ayuda a domicilio
Teleasistencia
Adaptación viviendas

Intermedios
Estancia diurnas (centros de día)
Estancias temporales
Alojamientos alternativos

Institucionales
Residencias

Residencias

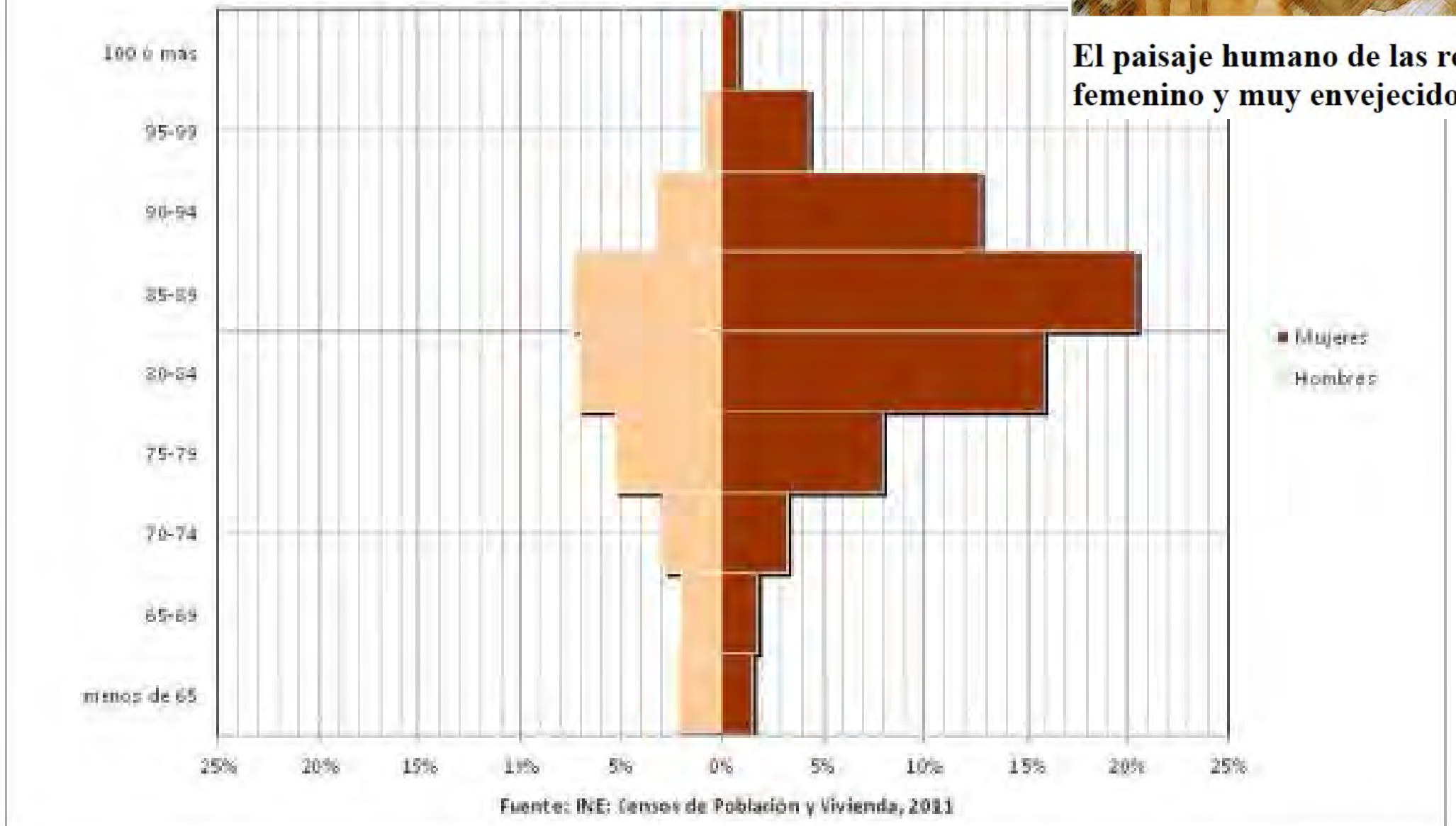


Centros de convivencia y alojamiento alternativo

- Hostelería-alojamiento
- Restauración
- Animación sociocultural

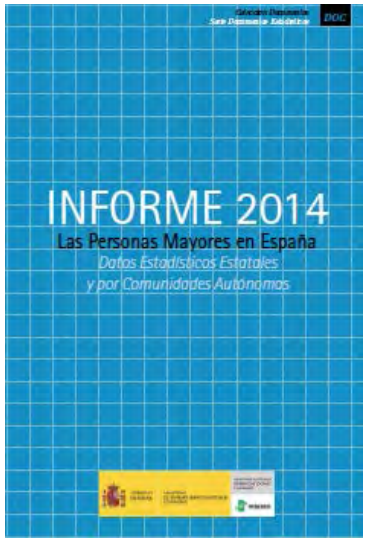
Figura 1.- Población que vive en residencias de personas mayores, por sexo y edad. España, 2011

El paisaje humano de las residencias es femenino y muy envejecido



Fuente: INE: Censos de Población y Vivienda, 2011

Residencias



Centros de convivencia y alojamiento alternativo

- Hostelería-alojamiento
- Restauración
- Animación sociocultural

- Cuidados Sanitarios
  - Larga duración
  - Subagudos

Pero ... ¿Qué es la enfermedad de Alzheimer?

DE FORMA DIRECTA O INDIRECTA NOS AFECTA A TODOS

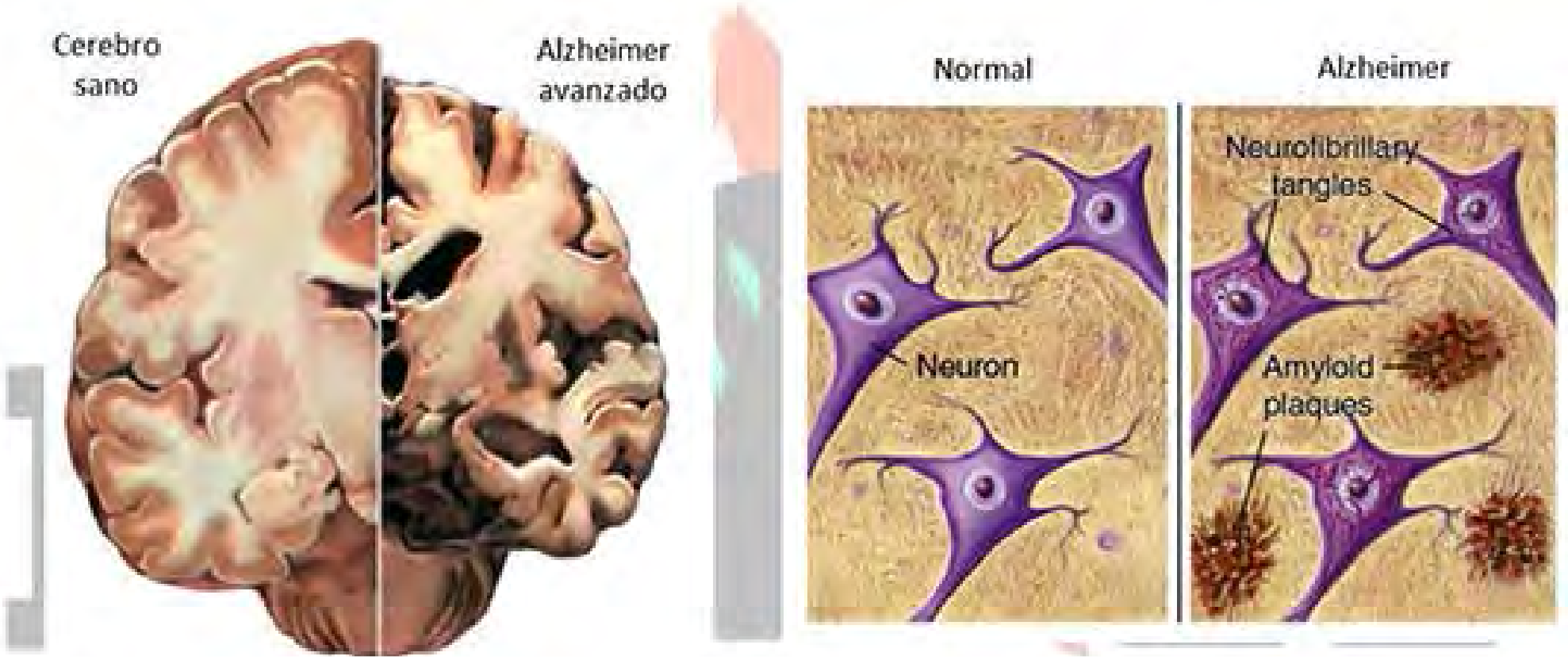
Quien era “Alzheimer”

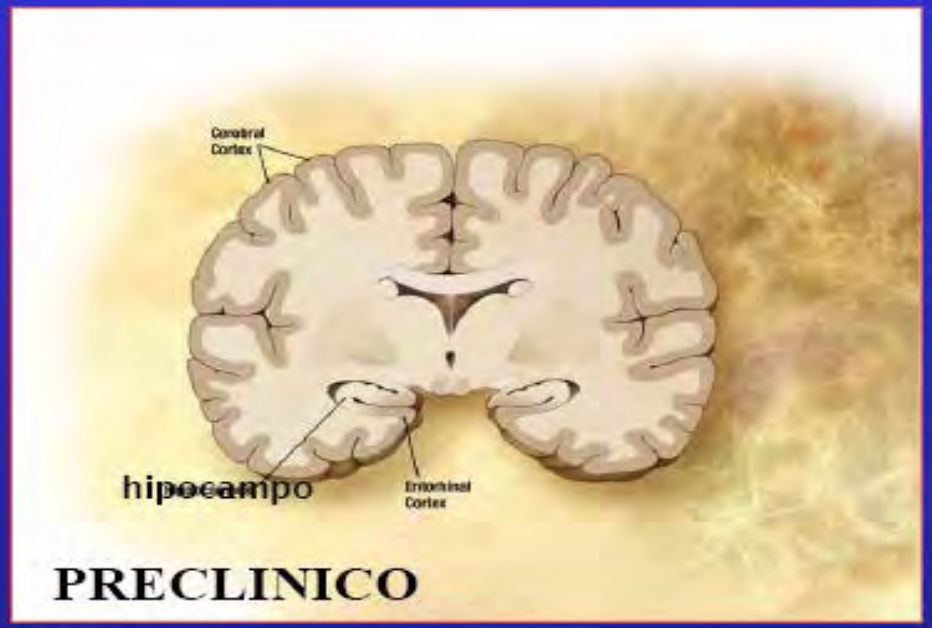
- Alois Alzheimer (1864-1915)
- Hospital Psiquiátrico Frankfurt.
- “El psiquiatra del microscopio”
- 1906 da a conocer las lesiones características.
- 1910 Psiquiatra Kraepelin la denomina Enfermedad de Alzheimer.

Quien era “Alzheimer”

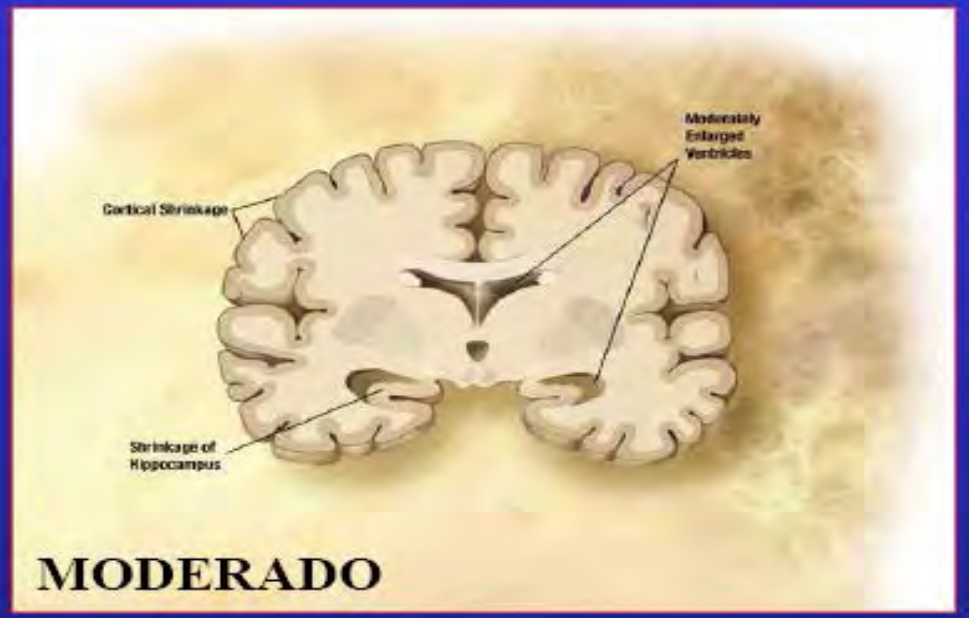
- Auguste D. 1901 ingresa a la clínica
- Fallece 8 Abril, 1906
- Resultado de la autopsia.

ESTRUCTURA DEL CEREBRO CON ALZHEIMER





PRECLINICO



MODERADO

SEVERO

*Reducción de corteza e hipocampo

*Agrandamiento de ventrículos

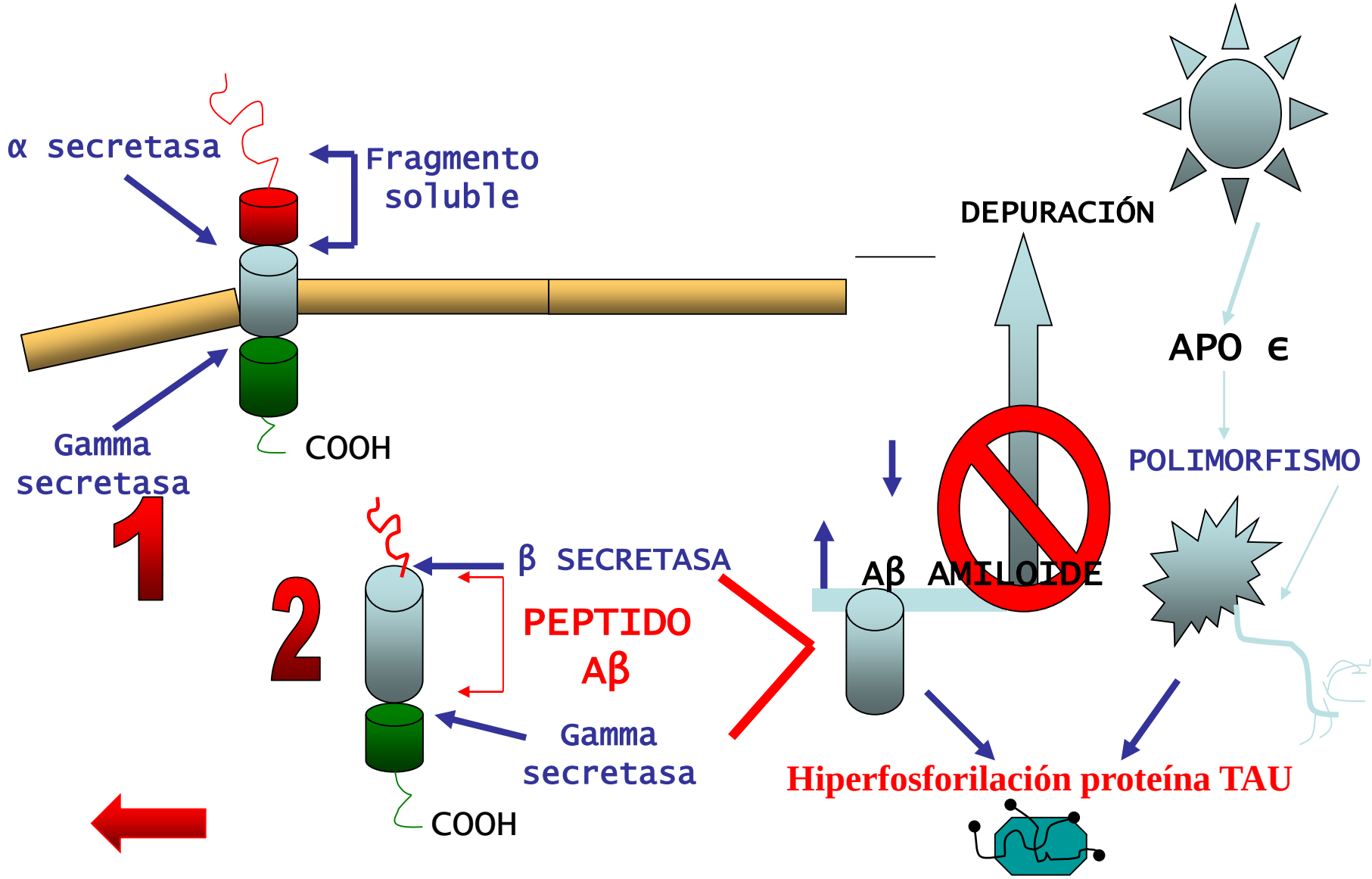
MICROSCÓPICAMENTE

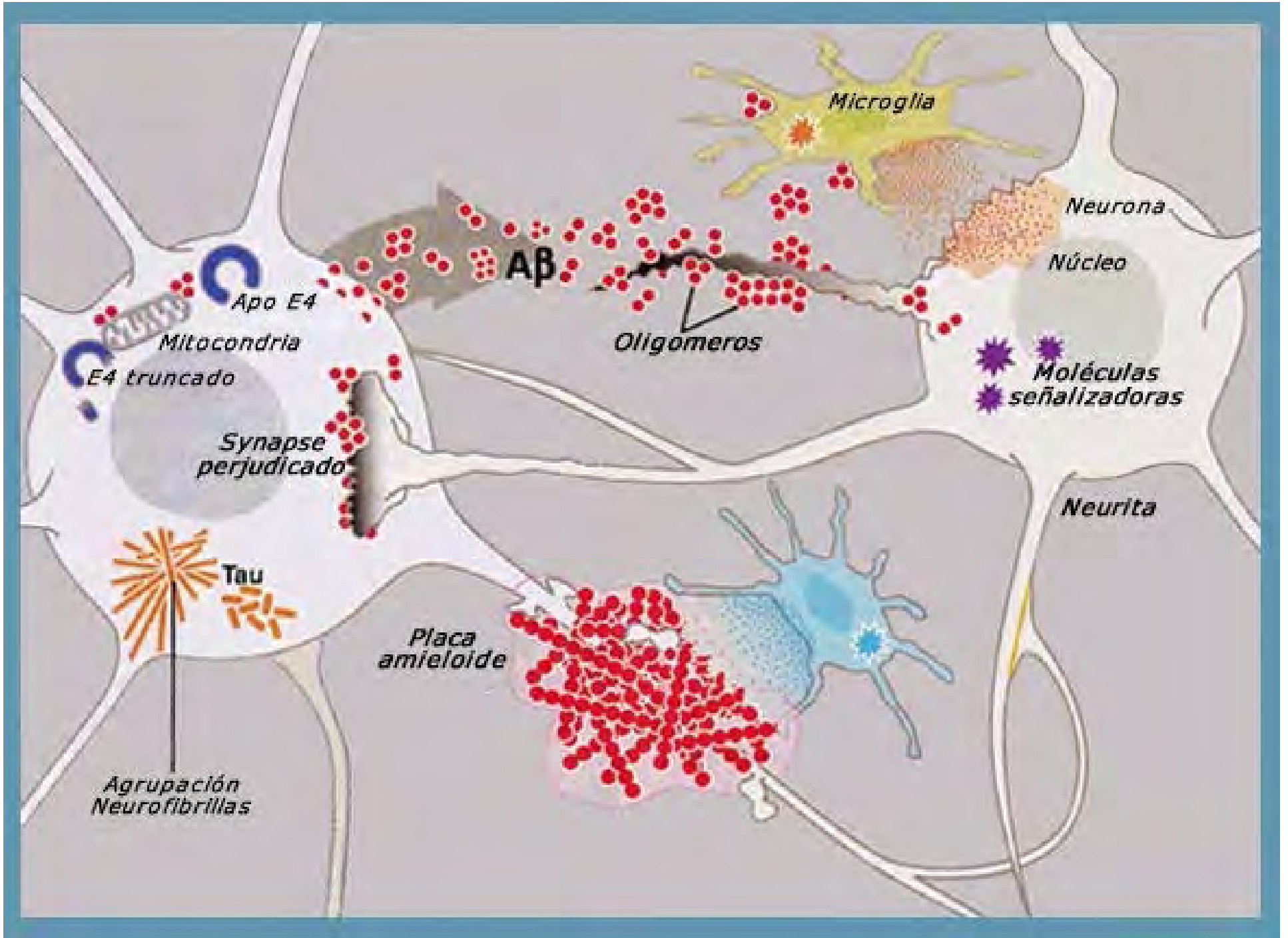
Hay un 70% de la genética no resuelta en Alzheimer

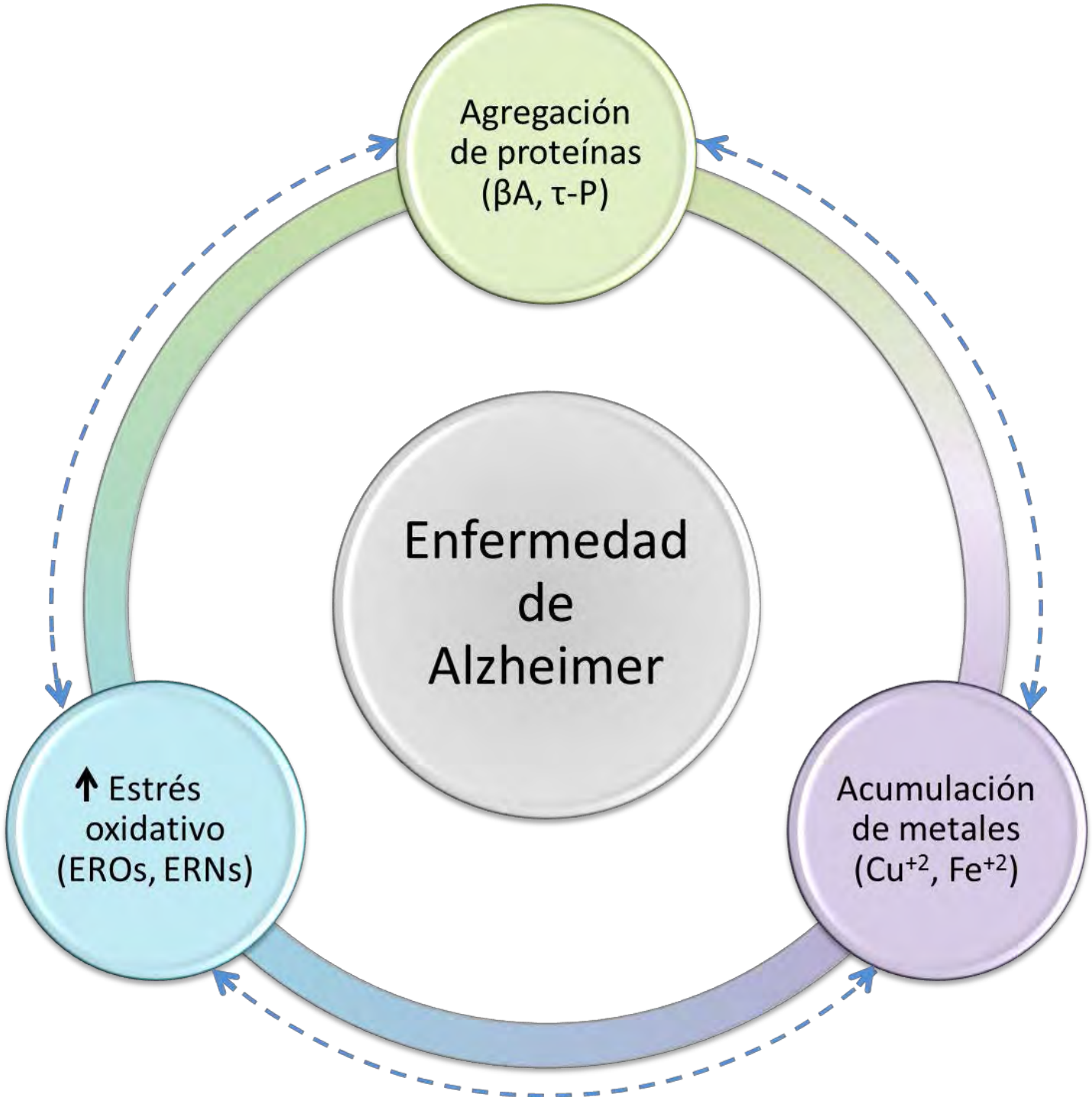
"I found one! I found one!"

(Weiss & Terwilliger, Nature Genetics, 2000)

PATOLOGÍA


α secretasa
Fragmento soluble
Gamma secretasa
COOH
1
2
β SECRETASA
PEPTIDO Aβ
Gamma secretasa
COOH
DEPURACIÓN
APO ϵ
POLIMORFISMO
Aβ AMILOIDE
Hiperfosforilación proteína TAU


Microglia
Neurona
Núcleo
Aβ
Apo E4
Mitocondria
E4 truncado
Oligomeros
Moléculas
señalizadoras
Synapse
perjudicado
Neurita
Tau
Placa
amieloide
Agrupación
Neurofibrillas

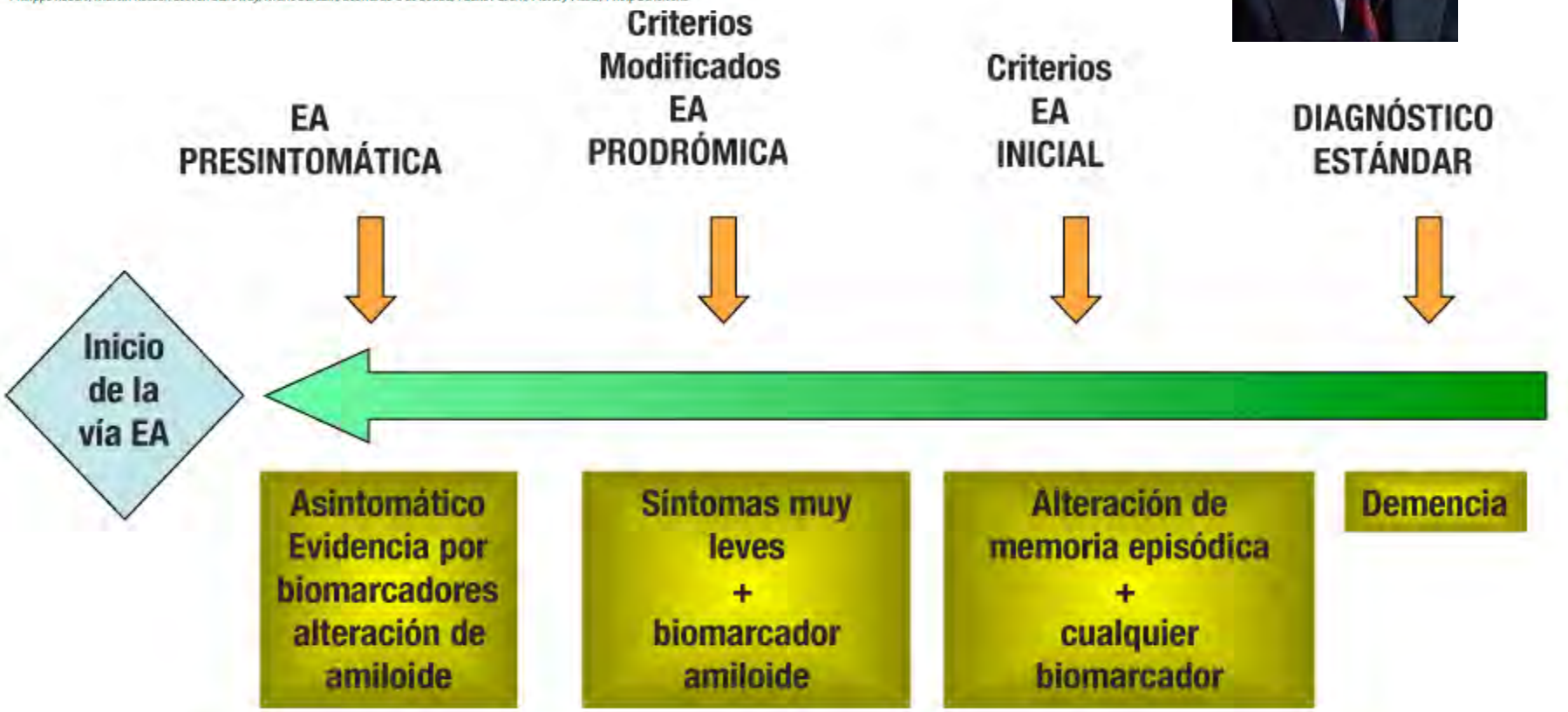

Agregación de proteínas (βA, τ-P)
Enfermedad de Alzheimer
↑ Estrés oxidativo (EROs, ERNs)
Acumulación de metales (Cu^{+2}, Fe^{+2})

Diagnóstico de EA: "giro a la izquierda"

Position Paper

Revising the definition of Alzheimer's disease: a new lexicon

Bruno Dubois, Howard H Feldman, Claudia Jacova, Jeffrey L Cummings, Steven T DeKosky, Pascale Barberger-Gateau, André Delacourte, Giovanni Frisoni, Nick C Fox, Douglas Galasko, Serge Gauthier, Harald Hampel, Gregory A Jicha, Kenichi Meguro, John O'Brien, Florence Pasquier, Philippe Robert, Martin Rossor, Steven Salloway, Marie Sarazin, Leonardo C de Souza, Yaakov Stern, Pieter J Visser, Philip Scheltens



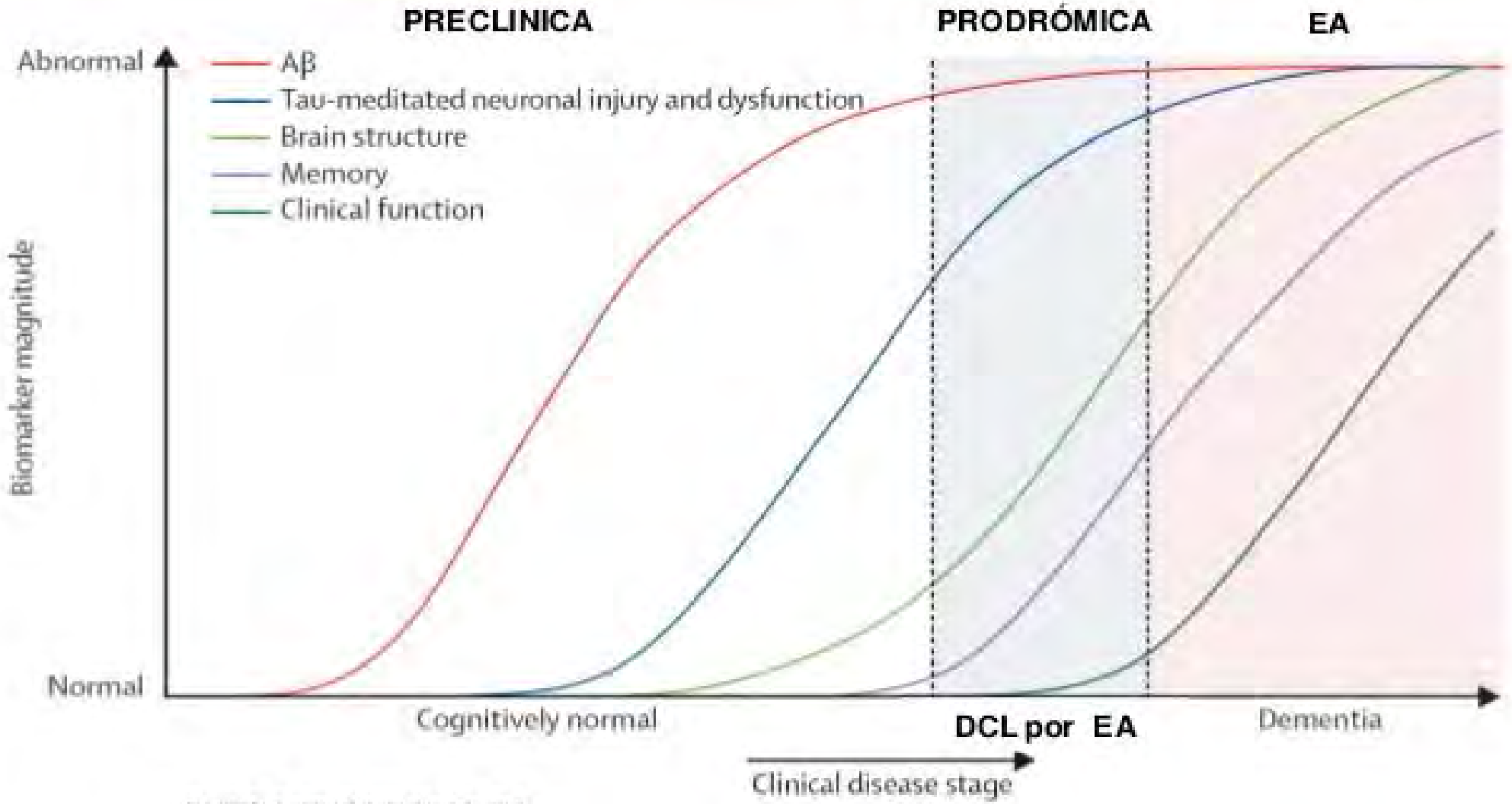
Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria

Lancet Neurol 2014; 13: 614–29

Bruno Dubois, Howard H Feldman, Claudia Jacova, Harald Hampel, José Luis Molinuevo, Kaj Blennow, Steven T DeKosky, Serge Gauthier, Dennis Selkoe, Randall Bateman, Stefano Cappa, Sebastian Crutch, Sebastiaan Engelborghs, Giovanni B Frisoni, Nick C Fox, Douglas Galasko, Marie-Odile Habert, Gregory A Jicha, Agneta Nordberg, Florence Pasquier, Gil Rabinovici, Philippe Robert, Christopher Rowe, Stephen Salloway, Marie Sarazin, Stéphane Epelbaum, Leonardo C de Souza, Bruno Vellas, Pieter J Visser, Lon Schneider, Yaakov Stern, Philip Scheltens, Jeffrey L Cummings

Nueva teoría fisiopatológica de la EA

Lancet Neurol 2010; 9: 119–28



CURSO EVOLUTIVO EA

NIA-AA
IWG: In

Focalidad en la década mediana de la vida (50 años)

Preclinical Alzheimer's disease and its outcome: a longitudinal cohort study

Lancet Neurol 2013; 12: 957–65

Stephanie J B Vos, Chengjie Xiong, Pieter Jelle Visser, Mateusz S Jasielec, Jason Hassenstab, Elizabeth A Grant, Nigel J Cairns, John C Morris, David M Holtzman, Anne M Fagan

Panel 1: Preclinical AD stages and symptomatic AD

Normal group
CDR 0 (no dementia), no amyloid, no neuronal injury, no subtle cognitive decline

Preclinical AD stage 1
CDR 0 (no dementia), amyloid, no neuronal injury, no subtle cognitive decline

Preclinical AD stage 2
CDR 0 (no dementia), amyloid, neuronal injury, no subtle cognitive decline

Preclinical AD stage 3
CDR 0 (no dementia), amyloid, neuronal injury, subtle cognitive decline

SNAP group
CDR 0 (no dementia), no amyloid, neuronal injury, with or without subtle cognitive decline

Unclassified group
CDR 0 (no dementia), with or without amyloid, no neuronal injury, subtle cognitive decline

Symptomatic AD
CDR>0, memory and at least one other domain received a score of ≥0·5 and the clinician felt the cognitive impairments to be due to AD (probable AD according to NINDS-ADRDA criteria), no reference to biomarkers

AD=Alzheimer's disease. No amyloid=CSF amyloid-β_{1-42} ($A\beta_{1-42}$) ≥459 pg/mL. Amyloid=CSF $A\beta_{1-42}$ <459 pg/mL. CDR 0=clinical dementia rating score of 0, no dementia. CDR 0·5=very mild impairment or very mild dementia. CDR 1=mild dementia. CDR 2=moderate dementia. CDR 3=severe dementia. No neuronal injury=CSF total tau (t-tau) ≤339 pg/mL and phosphorylated tau_{181} (p-tau_{181}) ≤67 pg/mL. Neuronal injury=CSF t-tau >339 pg/mL or p-tau_{181} >67 pg/mL. SNAP=suspected non-Alzheimer pathophysiology. Subtle cognitive decline=episodic memory composite score in the lowest 10th percentile. No subtle cognitive decline=episodic memory composite score in the highest 90th percentile.

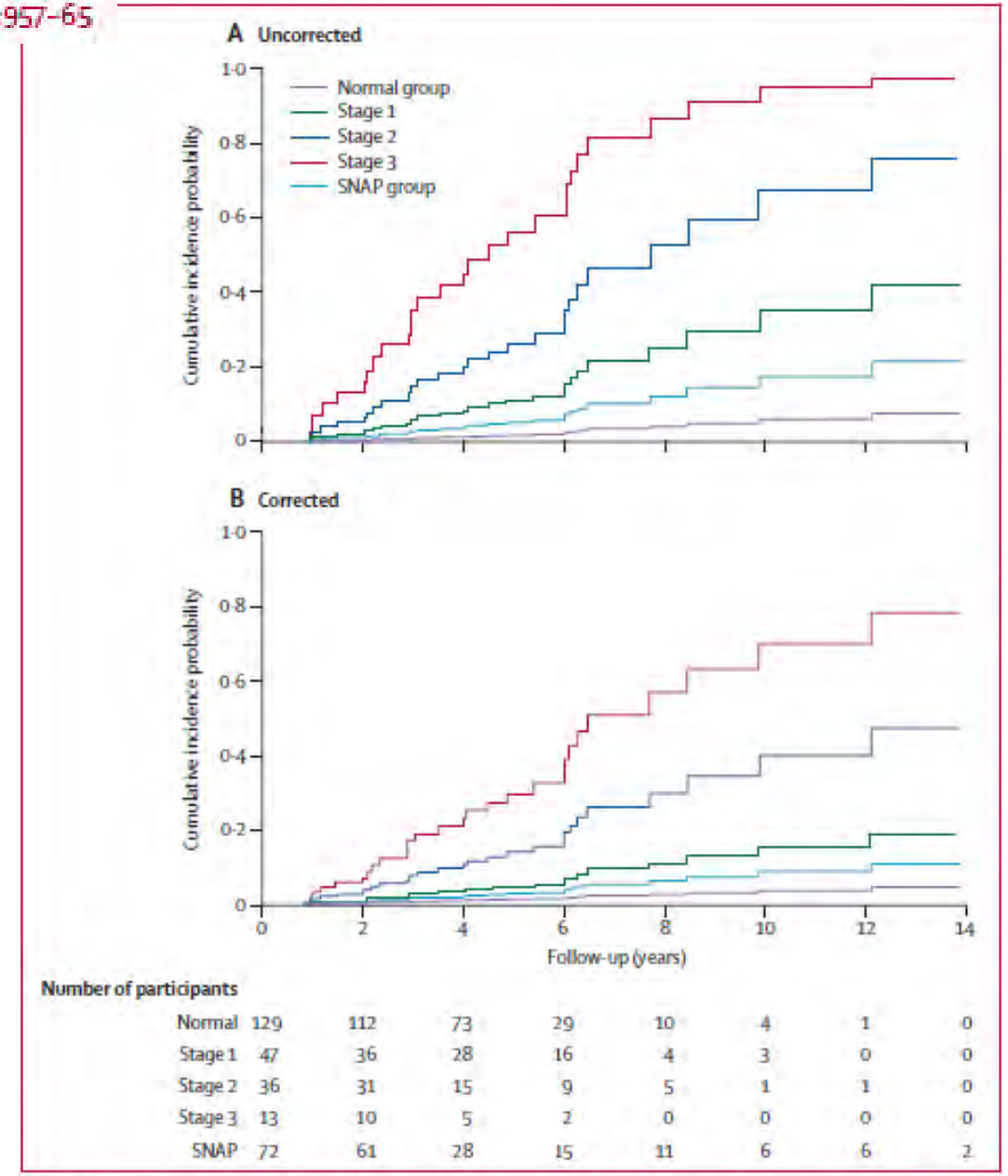


Figure: Progression to clinical dementia rating scale at least 0·5, symptomatic Alzheimer's disease by preclinical Alzheimer's disease stage

Predicting the risk of mild cognitive impairment in the Mayo Clinic Study of Aging

V. Shane Pankratz, PhD

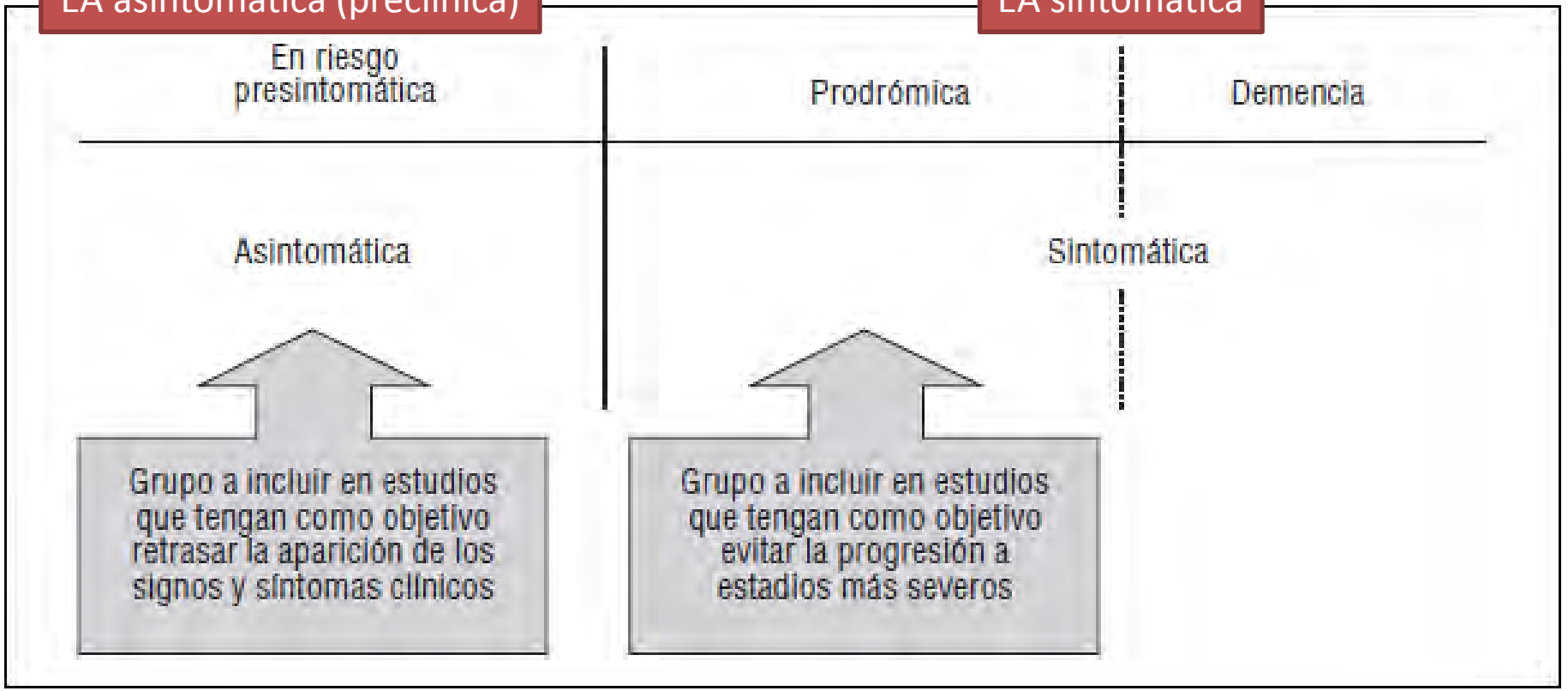
Neurology® 2015;84:1433-1442

Table 2 Predictors of MCI in the clinical risk model based on basic demographic and medical history features[a]

Variable	HR (95% CI)[b]	Risk score contribution
Men and women		
Education ≤12 y	1.50 (1.24-1.83)	2
Self-reported memory concerns	1.41 (1.15-1.73)	2
Ever diagnosed with alcohol problem	1.70 (1.09-2.65)	3
History of stroke	1.26 (0.94-1.70)	1
Diabetes and age at assessment <75 y	2.21 (1.27-3.84)	5
Diabetes and age at assessment 75-84 y	1.35 (0.97-1.87)	2
History of atrial fibrillation	1.20 (0.93-1.53)	1
Predictors for women only		
Current smoker	1.83 (0.93-3.60)	3
Midlife dyslipidemia	1.34 (0.96-1.87)	2
Definite or probable diabetes in midlife	1.34 (0.67-2.69)	2
Midlife hypertension	1.27 (0.94-1.72)	1
Predictors for men only		
Maximum adult BMI ≥30 kg/m^2	1.41 (1.03-1.92)	2
Never married or widowed	1.56 (1.12-2.18)	3

EA asintomática (preclínica)

EA sintomática



Revista Española de Geriatría y Gerontología
www.elsevier.es/regg

Factores de riesgo

La mitad de los casos de Alzheimer en el mundo están asociados a siete factores de riesgo que podrían prevenirse. Según una revisión de estudios publicada en 'Lancet Neurology', reducir esta lista en torno a un 25% podría evitar unos tres millones de afectados.

- Tabaco
- Sedentarismo
- Escasa actividad mental
- Hipertensión
- Diabetes
- Obesidad
- Depresión

El fac
para
avanz
perso
años
un te
de
enfer

do

Alzheimer's disease: clinical course

100%

cognition

memory

orientation

language

activities of daily living

increasing need for care

affective disorders

judgement

behavioral disorders

full care

nutrition, hygiene

agitation, immobility

mild

moderate

severe

time (7-9 years)

Los **10** Signos de Alarma

1. Cambios de memoria que afectan a la vida cotidiana: olvidar información recién aprendia, depender de ayudas para hacer cosas que antes hacía solo.
2. Dificultad para planificar o resolver problemas.
3. Dificultad para desempeñar tareas habituales en la casa, en el trabajo o en su tiempo libre.
4. Desorientación en tiempo y lugar
5. Dificultad para comprender imágenes visuales y relacionar objetos en el entorno.
6. Problemas nuevos en el lenguaje oral y escrito
7. Colocar objetos fuera de su lugar habitual y ser incapaces de recuperarlos.
8. Disminución o falta de juicio para tomar decisiones.
9. Pérdida de iniciativa a la hora de tomar parte en el trabajo o en las actividades sociales.
10. Cambios en el humor o en la personalidad.

1. **ORIENTACIÓN**
   - Dígame el día — Fecha — Mes
   - Dígame el lugar — Planta — Ciudad
2. **FIJACIÓN**
   - Repita estas t
3. **CONCENTRAC**
   - Si tiene 30 pe
   - Repita: 5-9-2
   - Ahora hacia a
4. **MEMORIA**
   - ¿Recuerda la
5. **LENGUAJE Y**
   - Mostrar un bo
   - Repita esta fr
   - Una manzana
   - Coja este pap
   - Lea esto y ha
   - Escriba una fr
   - Copie este dit

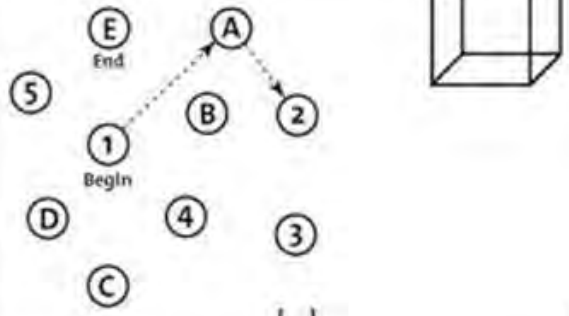
Puntuación:
>= 30: Normal
29-24: Discreto
<24: Deterior
Punto de corte: 2
19-23: deterioro c
14-18: moderado
<14:grave

Figura 22. *Miniexamen cognoscitivo o MEC de*

MONTREAL COGNITIVE ASSESSMENT (MOCA)

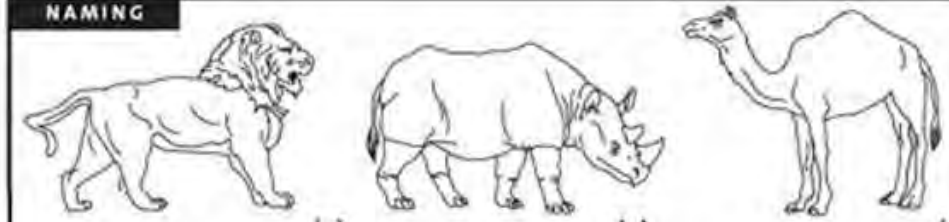
NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE — Copy cube — Draw CLOCK (Ten past eleven) (3 points) — POINTS



[ ] [ ] [ ] Contour [ ] Numbers [ ] Hands /5

NAMING



[ ] [ ] [ ] /3

MEMORY — Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION — Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4. Subject has to repeat them in the backward order [ ] 7 4 2 /2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B /1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** /3

LANGUAGE — Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ] /2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words) /1

ABSTRACTION — Similarity between e.g. banana - orange = fruit [ ] train - bicycle [ ] watch - ruler /2

DELAYED RECALL

	Has to recall words	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
	WITH NO CUE	[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

/5

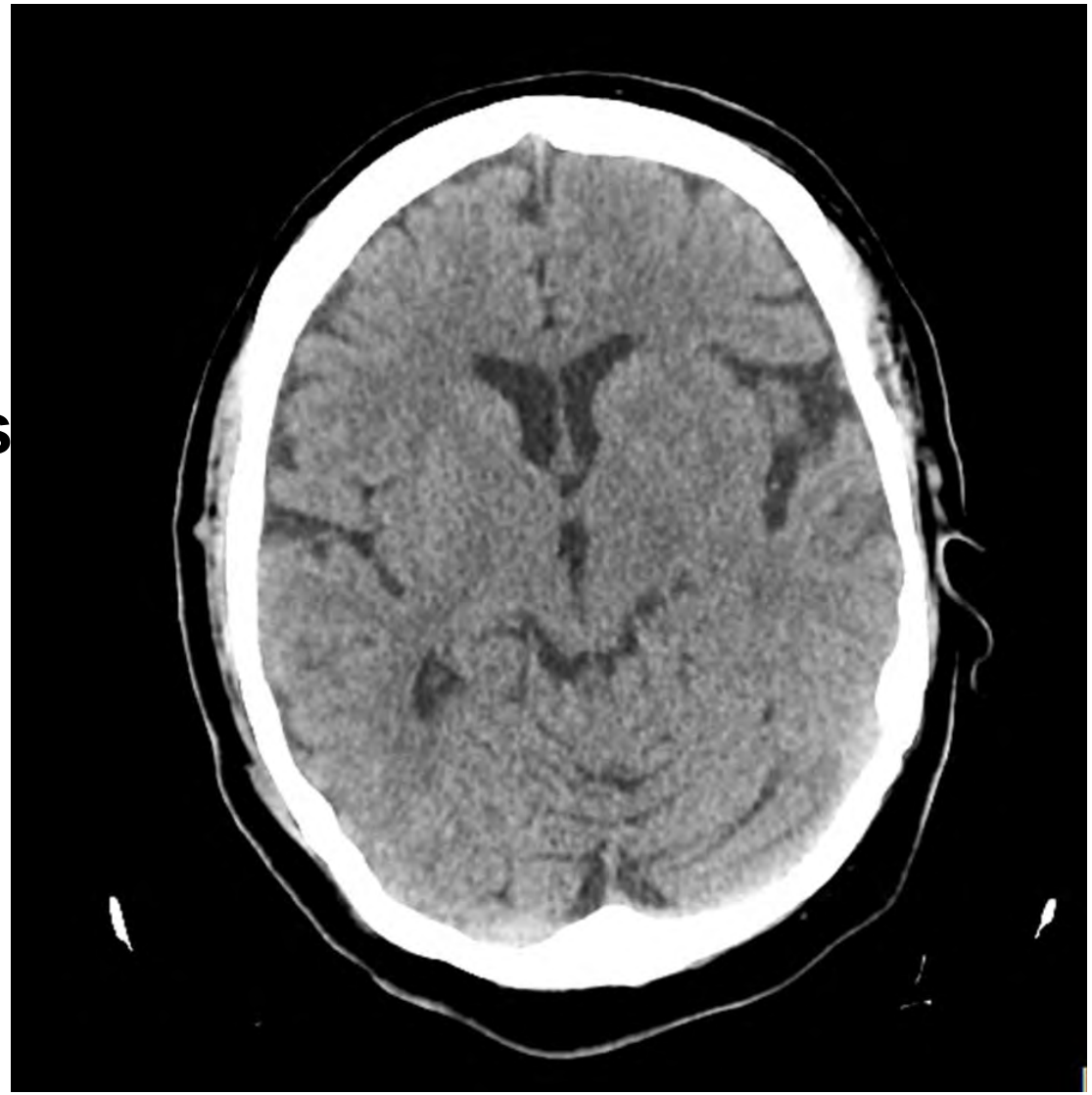
ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City /6

© Z.Nasreddine MD Version November 7, 2004
Normal ≥ 26 / 30
TOTAL /30
Add 1 point if ≤ 12 yr edu

www.mocatest.org

DIAGNÓSTICO

- **Historia Clínica**
- **Exploraciones complementarias**
  - ✓ **Examen neuropsicológico**
  - ✓ **Estudios de neuroimagen**



N

- A
- P
- P

n

- P
- IR
- IR

te

a

fr

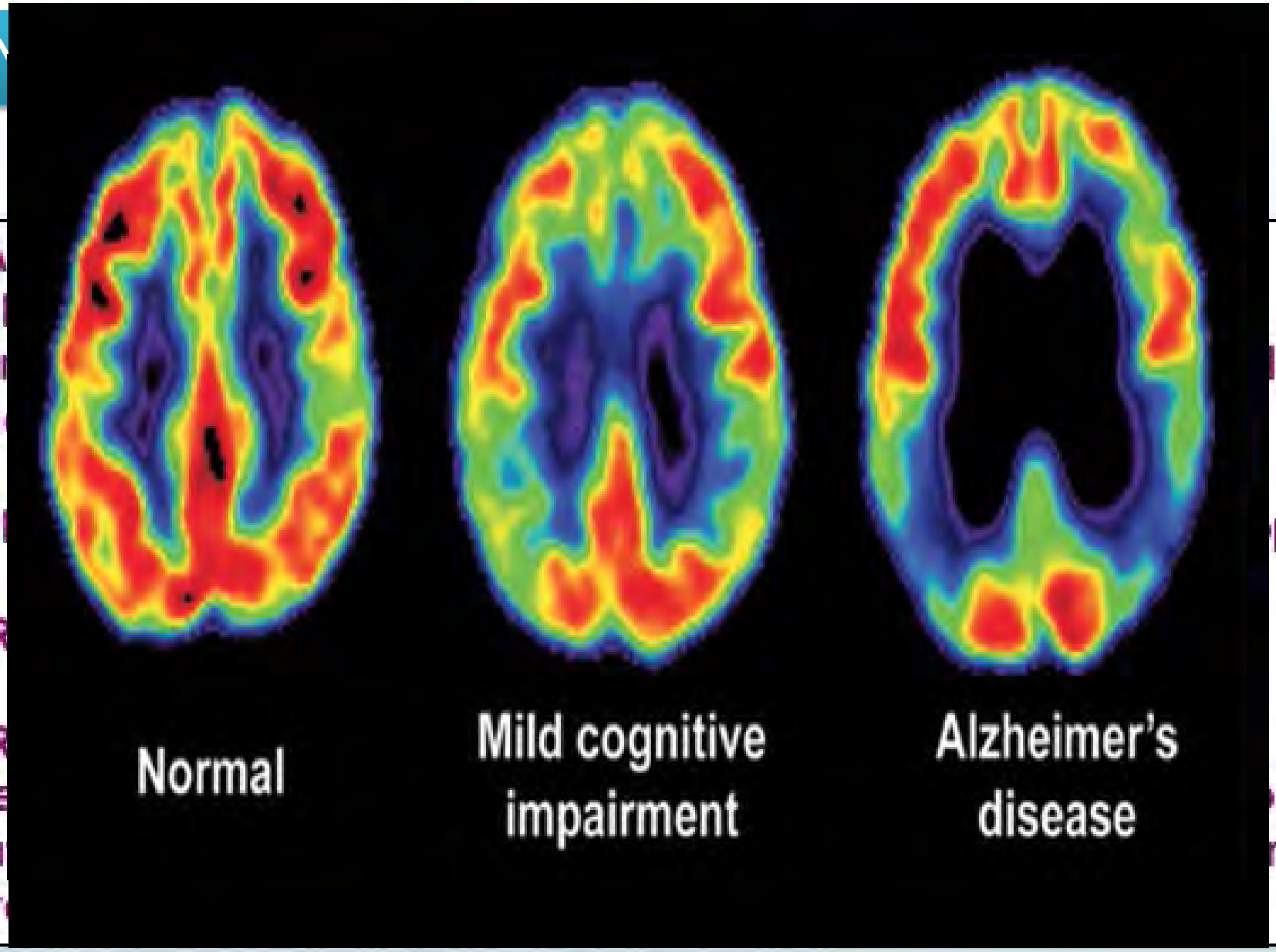
le lesión

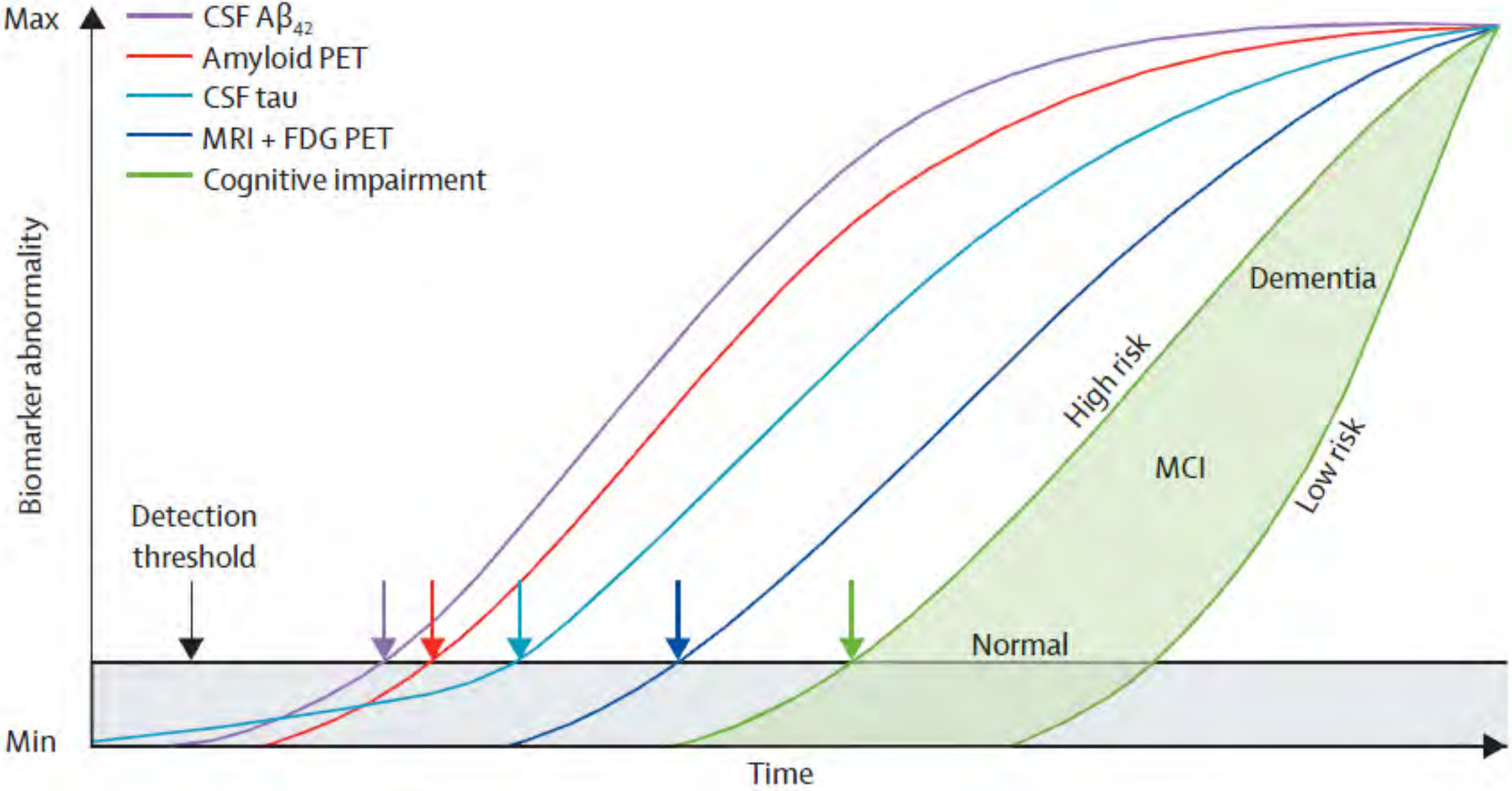
parietal

lóbulos

rrinal) y

regiones




Max
CSF Aβ42
Amyloid PET
CSF tau
MRI + FDG PET
Cognitive impairment
Biomarker abnormality
Detection threshold
Min
Time
Normal
High risk
MCI
Low risk
Dementia


EL MUNDO

SOCIEDAD

Prueban el primer diagnóstico
detectar el Alzheimer

Es un radiofármaco que percibe la presencia

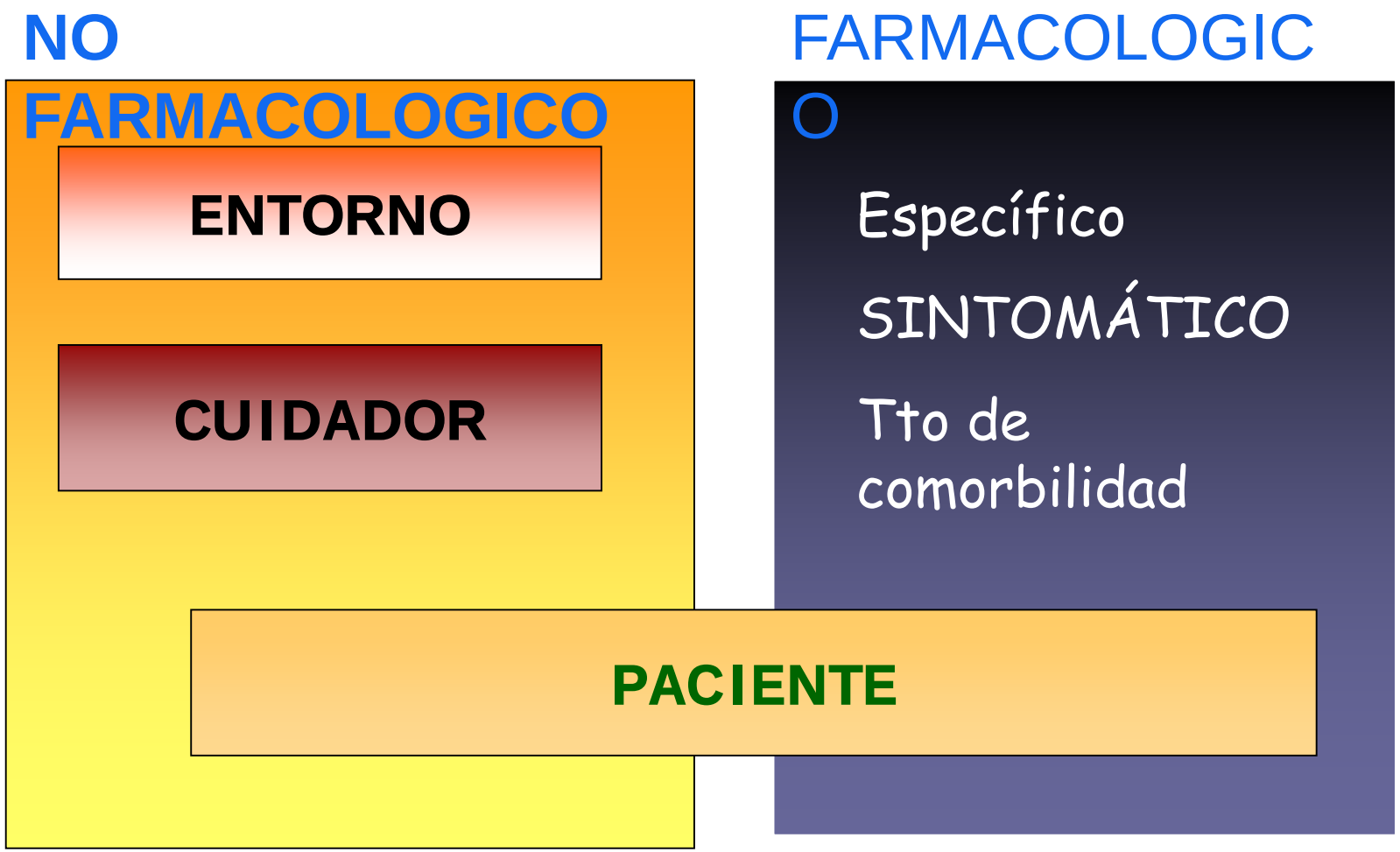
Evita diagnósticos incorrectos que llegaban a ser uno de cada cinco

SOLO EN INVESTIGACIÓN PARA NUEVOS TRATAMIENTOS
ALZHEIMER PRECOZ O CON DUDAS DIAGNÓSTICAS

¿Qué vamos a desarrollar?

- SIGLO XXI ENVEJECIMIENTO-DEMENCIA
- **SIGLO XXI: PATOGENIA Y FX DE RIESGO ENF ALZHEIMER**
- TRATAMIENTO Y NUEVAS PERSPECTIVAS
- LINEAS DE FUTURO: PREVENCIÓN

RECOMENDACIONES TRATAMIENTO



Tratamiento actual sintomático

1. Inhibidores de AChE para aumentar T. ACh
   - Donepezil
   - Rivagstigmine
   - Galantamina

2. Bloqueadores de R. NMDA
   - Memantine NAMENDA

3. Combinación de Memantine + Donepezil

4. Psicotrópicos

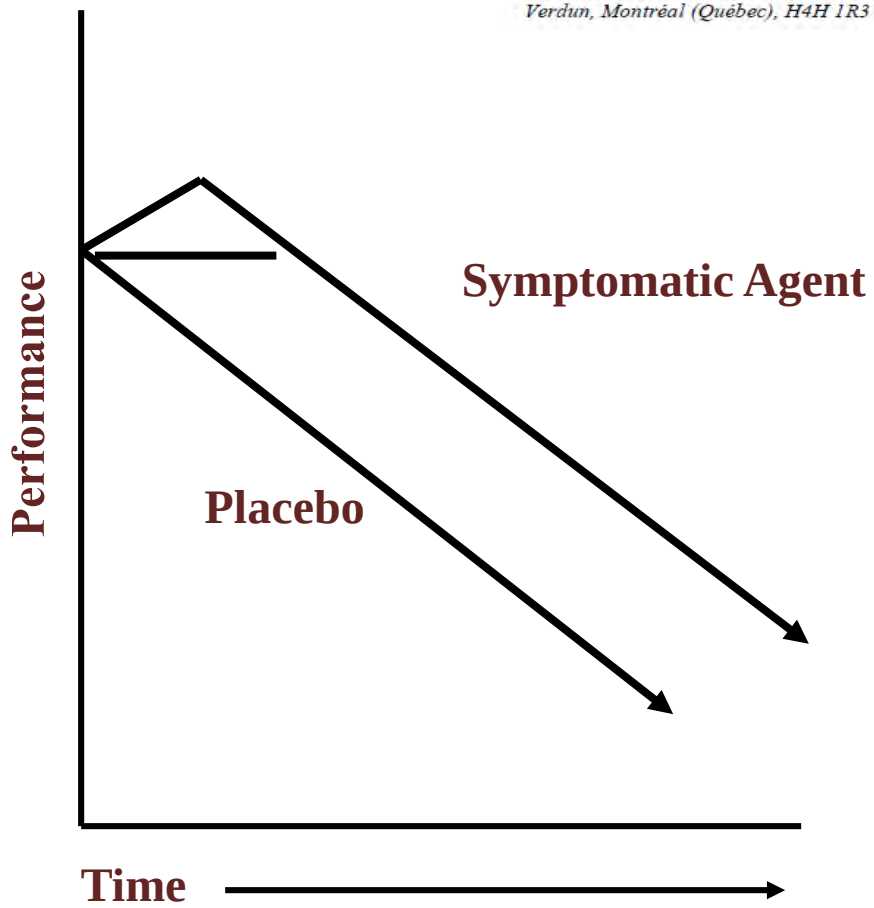
Current Neuropharmacology, 2010, *8*, 69-80

Update on the Pharmacological Treatment of Alzheimer's Disease

Fadi Massoud[1,*] and Serge Gauthier[2]

[1]*Department of Medicine, University of Montreal, Centre Hospitalier de l'Université de Montréal (CHUM), Hôpital Notre-Dame, Service de Gériatrie, 1560 Sherbrooke Est, Montreal, Quebec, H2L 4M1*

[2]*Departments of Neurology & Neurosurgery, Psychiatry, Medicine, McGill University, Alzheimer Disease and Related Disorders Unit, McGill Center for Studies in Aging, Douglas Mental Health University Institute, 6825, boul. LaSalle, Verdun, Montréal (Québec), H4H 1R3*



¿QUÉ FÁRMACOS?

PROMETAX EBIXA

ARICEPT REMINYL EXELON AXURA

	DONEPEZILO	GALANTAMINA	RIVASTIGMINA	MEMANTINA
MODO ACCIÓN	IAChE	IAChE M.R.Nic.	IAChE IBuChE	Antag. NMDA
Metab. CYP450	SI	SI	NO	NO
Vida media	70 h	7-8 h	1 h	60-100h
Dosis/día	1	2	2	2
Dosis/inicial	5 mgr/día	8 mgr/día	3 mgr/día	5 mgr/día
Dosis/escalada	4-6 semana	4 semana	2 semana	1 semana
Dosis recomendada	10 mgr/día	16-24 mgr/día	6-12 mgr/día	20 mgr/día

TABLA 1. Tratamiento sintomático de la Enfermedad de Alzheimer

***IAChE**: inhibidor de acetil-colinesterasa. **IbuChE**: inhibidor de butiril-colinesterasa. **M.R.Nic**: modulador alostérico del receptor nicotínico **Antag. NMDA**: antagonista no competitivo del receptor NMDA*


Pfizer
Aricept®
10mg DONEPEZILHYDROKLORID
28 tabletter


Reminyl 12 mg
Each tablet contains 15,380 mg galantamine hydrobromide (equivalent to 12 mg galantamine). Each tablet contains orange yellow S aluminium lake.
56 comprimés pelliculés - film-coated tablets
JANSSEN-CILAG


NOVARTIS
PRESCRIPTION MEDICINE
Exelon®
Rivastigmin.
3 mg


UNA VEZ AL DIA
AXURA 20mg
comprimidos recubiertos con película
Clorhidrato de memantina
56 comprimidos recubiertos con película


PROMETAX® 3 mg
Rivastigmina
Cápsulas
Vía oral


56 potahovaných tablet
Ebixa® 10 mg
Potahované tablety
Memantini hydrochloridum
Ebixa® 10 mg/g
50 g
Ebixa®
10 mg/g
Memantini hydrochloridum
H. Lundbeck A/S
Ottiliavej 9
DK-2500 Valby
Dánsko

ARTÍCULO ESPECIAL

Tratamiento farmacológico de la demencia: cuándo, cómo y hasta cuándo. Recomendaciones del Grupo de Trabajo de Demencias de la Sociedad Catalana de Geriatría y Gerontología

Daniel Rodríguez[a,*,1], Francesc Formiga[b,1], Isabel Fort[c,1], María José Robles[d,1], Elena Barranco[e,1] y Dolors Cubí[f,1], en representación del grupo de Trabajo de Demencias de la Sociedad Catalana de Geriatría y Gerontología

Rev Esp Geriatr Gerontol. 2012;47(5):228–233

GDS 3-4	GDS 5-6	GDS 7
Alzh. leve	Alzh. Mod-grave	Alzh. grave
IACE	**IACE- MEMANTINA**	

Review Article

Dementia and Geriatric Cognitive Disorders

Dement Geriatr Cogn Disord 2010;30:161–178
DOI: 10.1159/000316119

Accepted: May 26, 2010
Published online: September 10, 2010

Nonpharmacological Therapies in Alzheimer's Disease: A Systematic Review of Efficacy

Javier Olazarán[a] Barry Reisberg[i] Linda Clare[e] Isabel Cruz[a] Jordi Peña-Casanova[a, d] Teodoro del Ser[a, b] Bob Woods[e] Cornelia Beck[j] Stefanie Auer[m] Claudia Lai[n] Aimee Spector[f] Sam Fazio[k] John Bond[g] Miia Kivipelto[o] Henry Brodaty[p] José Manuel Rojo[c] Helen Collins[h] Linda Teri[l] Mary Mittelman[i] Martin Orrell[f] Howard H. Feldman[q, r] Ruben Muñiz[a]

Neurosciences 2012; 66: 1–7 doi:10.1111/j.1440-1819.2011.02304.x

acological intervention for dementia patients

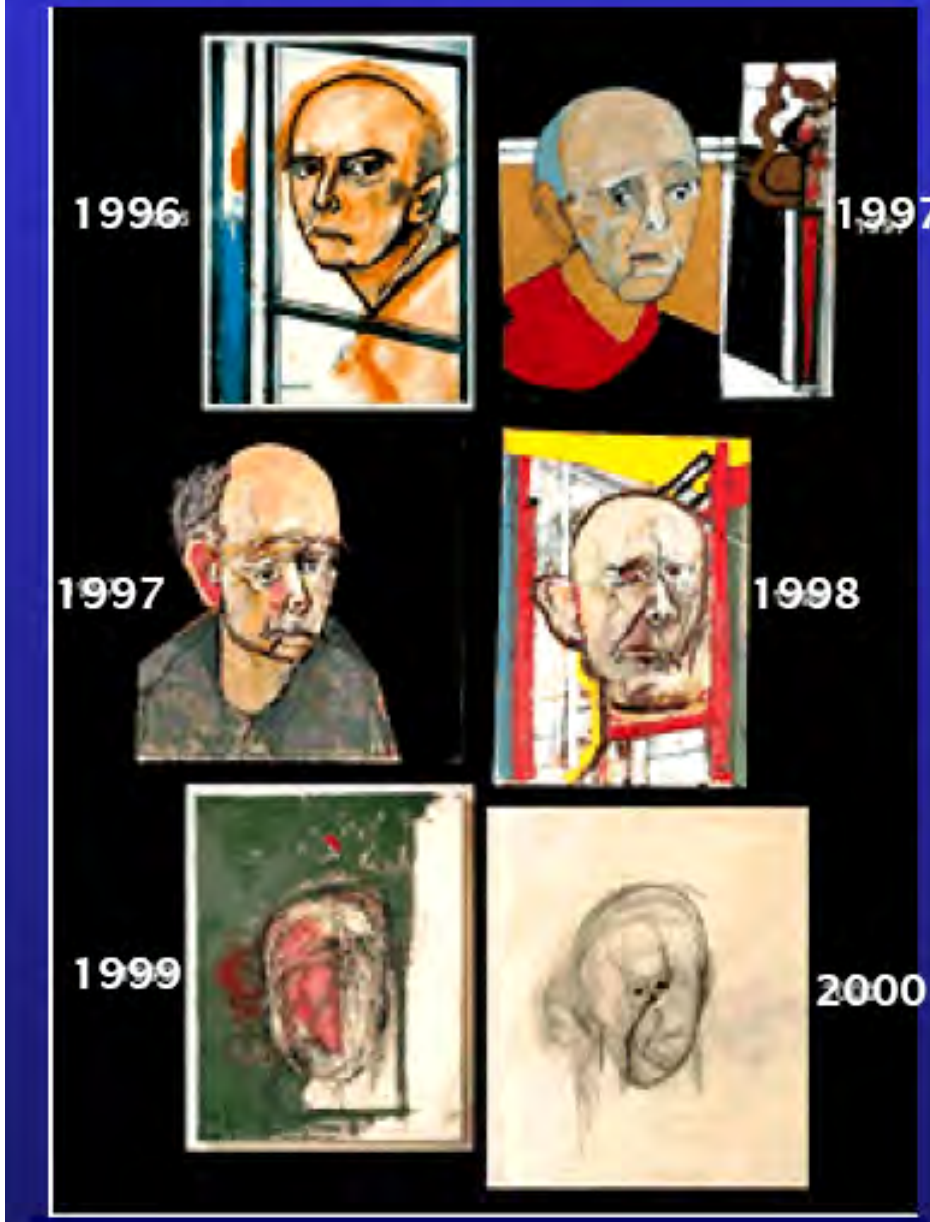
Table 1. Non-pharmacological intervention to Alzheimer patients

Therapy	Cognitive	ADL	BPSD
Cognitive training	+	+	+
Cognitive rehabilitation	+	+	+
Cognitive stimulation therapy	+	+	+
Snoezelen/multisensory stimulation	+	+	+
Reality orientation	+	+	+
Reminiscence therapy	+	–	+
Validation therapy	+	–	+
Physical activity	+	+	+
Light therapy	+	–	+
Music therapy	+	–	+
Aromatherapy	–	–	+
Animal-assisted therapy	–	–	+

ADL, activities of daily living; BPSD, behavioral and psychological symptoms of dementia.

Conducta disruptiva ¡¡¡qué hacer!!!

"Las cosas no son como son sino como uno las vive"



W. Utermohlen

Autoretratos muestran la progresión de la enfermedad en 4 años!!

AROMATERAPIA Y AGITACIÓN: ¿ES EFICAZ?

Management of agitation and aggression associated with Alzheimer disease

Clive G. Ballard, Serge Gauthier, Jeffrey L. Cummings, Henry Brodaty, George T. Grossberg,
Philippa Robert and Constantine G. Lyketsos

NATURE REVIEWS NEUROLOGY VOLUME 5 | MAY 2009 | 245

article reviews the increasing evidence in support of psychological interventions or alternative therapies (such as aromatherapy) as a first-line management strategy for agitation, as well as the potential pharmacological alternatives to atypical antipsychotics—preliminary evidence for memantine, carbamazepine, and citalopram is encouraging.

“Las cosas no son como son sino como uno las vive”

APROXIMACIÓN FARMACOLÓGICA

Psicosis	Quetiapina, risperidona	pregabalina
Agitación	ISRS / IRNS o NL atípicos	Pregabalina, Memantina
Agresividad	Quetiapina, risperidona	Otros NL, Memantina, pregabalina, carbamacepina, valproato.
Depresión	ISRS	IRNS, IACE
Depresión psicótica	Quetiapina, risperidona+ISRS	Otros NL+ISRS o IRNS
Ansiedad	ISRS/IRNS, pregaba	
Apatía	IACE	Bupropión
Insomnio	Trazodona	Mirtazapina

Evidencia PEG-SNG demencias avanzadas

Sondas de alimentación en las demencias avanzadas: ¿mejoran algo?

V. Ruiz García

Unidad de Hospitalización a Domicilio. Hospital Universitario La Fe. Valencia.

Gastrostomies in dementia: bad practice or bad evidence?

Age and Ageing 2010; **39:** 282–284

CLAUD REGNARD[1,4,*], PAULA LESLIE[2], HANNAH CRAWFORD[3], DOROTHY MATTHEWS[5], LYNN GIBSON[5]

Evidencia PEG-SNG demencias avanzadas

Palliative care in dementia

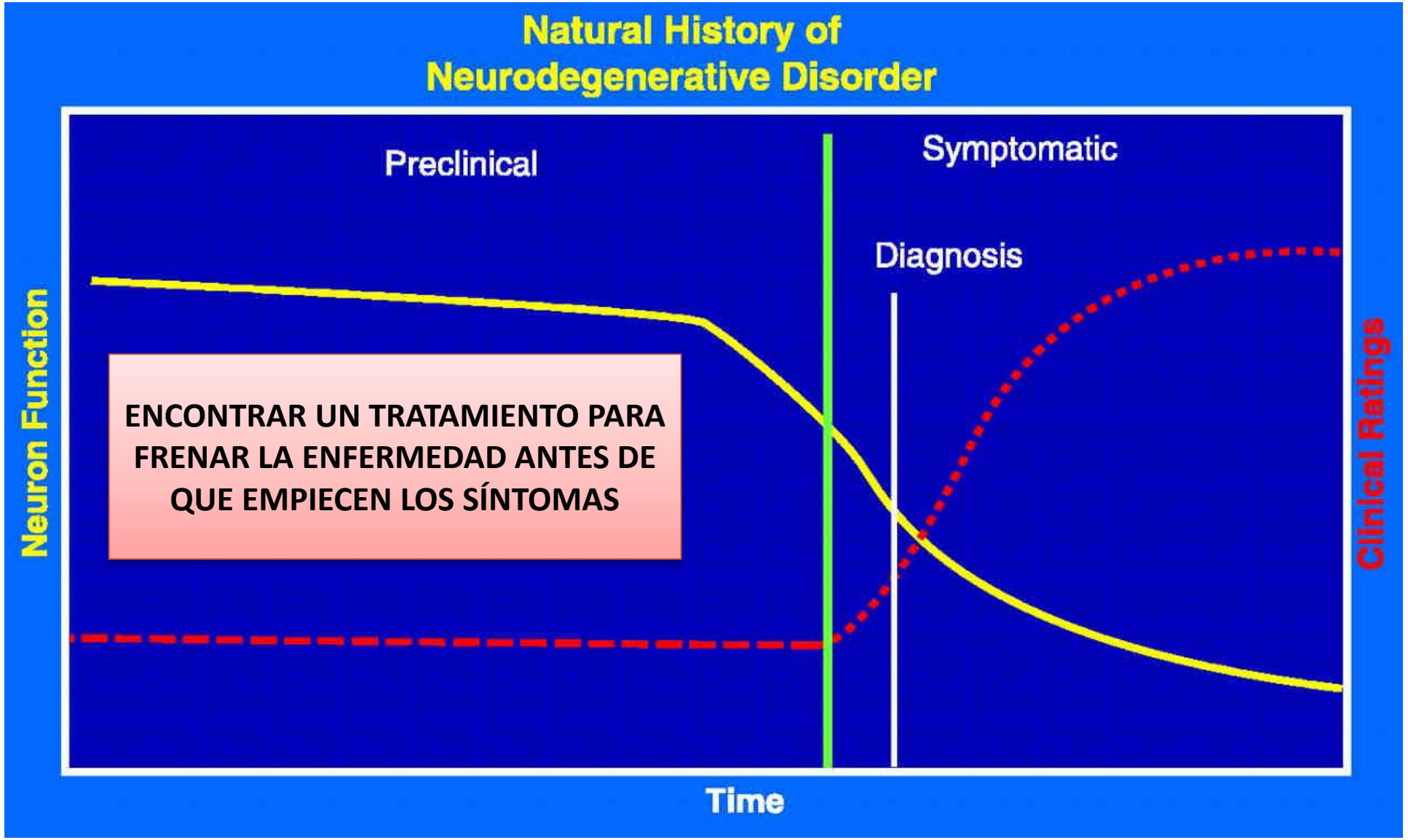
L. Rexach

Unidad de Cuidados Paliativos, Hospital Universitario Ramón y Cajal, Ctra. Colmenar Km 9100, 28034 Madrid, Spain

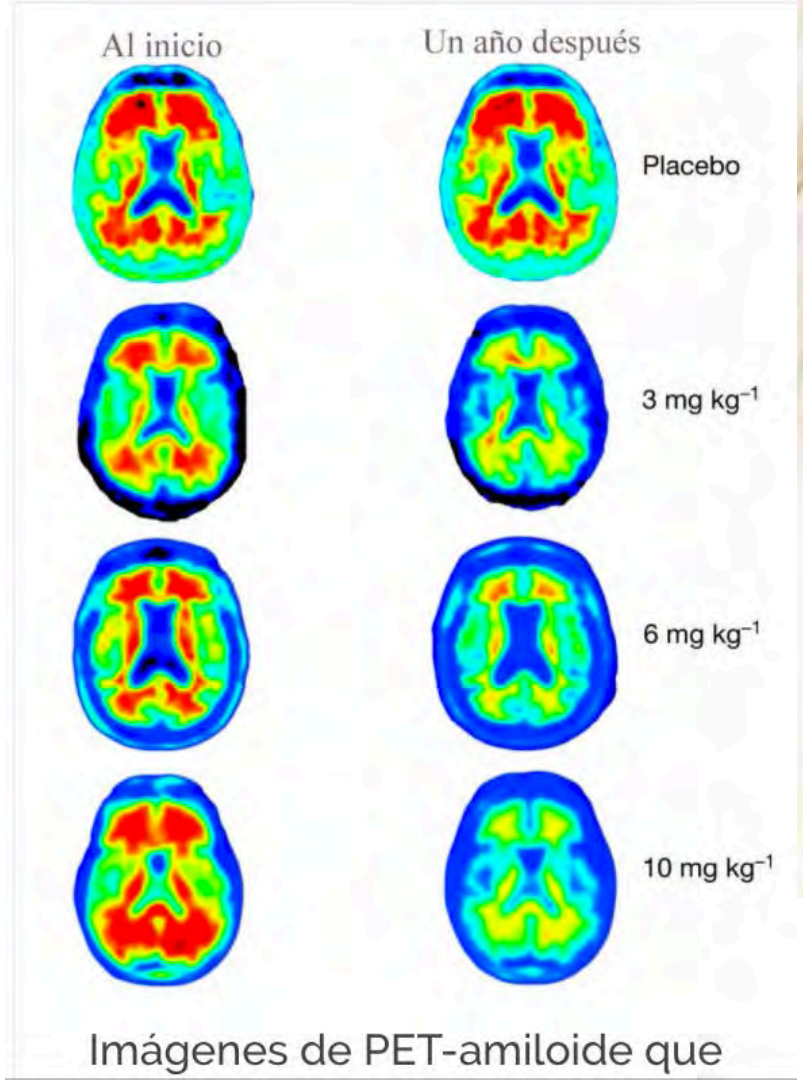
Table 1
Objectives argued to initiate enteral nutrition in advanced dementia.

Objectives	Evidence they may be achieved
Prevent aspiration pneumonia	None
Prevent malnutrition and its consequences, including death by starvation	None
Increase survival	None
Prevent or treat pressure ulcers	None
Reduce infections	None
Improve performance status	None
Provide comfort (prevent hunger and thirst) and thus improve quality of life	None

FUTURO


Natural History of
Neurodegenerative Disorder
Preclinical
Symptomatic
Diagnosis
Neuron Function
Clinical Ratings
Time
ENCONTRAR UN TRATAMIENTO PARA FRENAR LA ENFERMEDAD ANTES DE QUE EMPIECEN LOS SÍNTOMAS

¿Podrá el Aducanumab contra el alzhéimer? Este anticuerpo planta cara a la enfermedad.

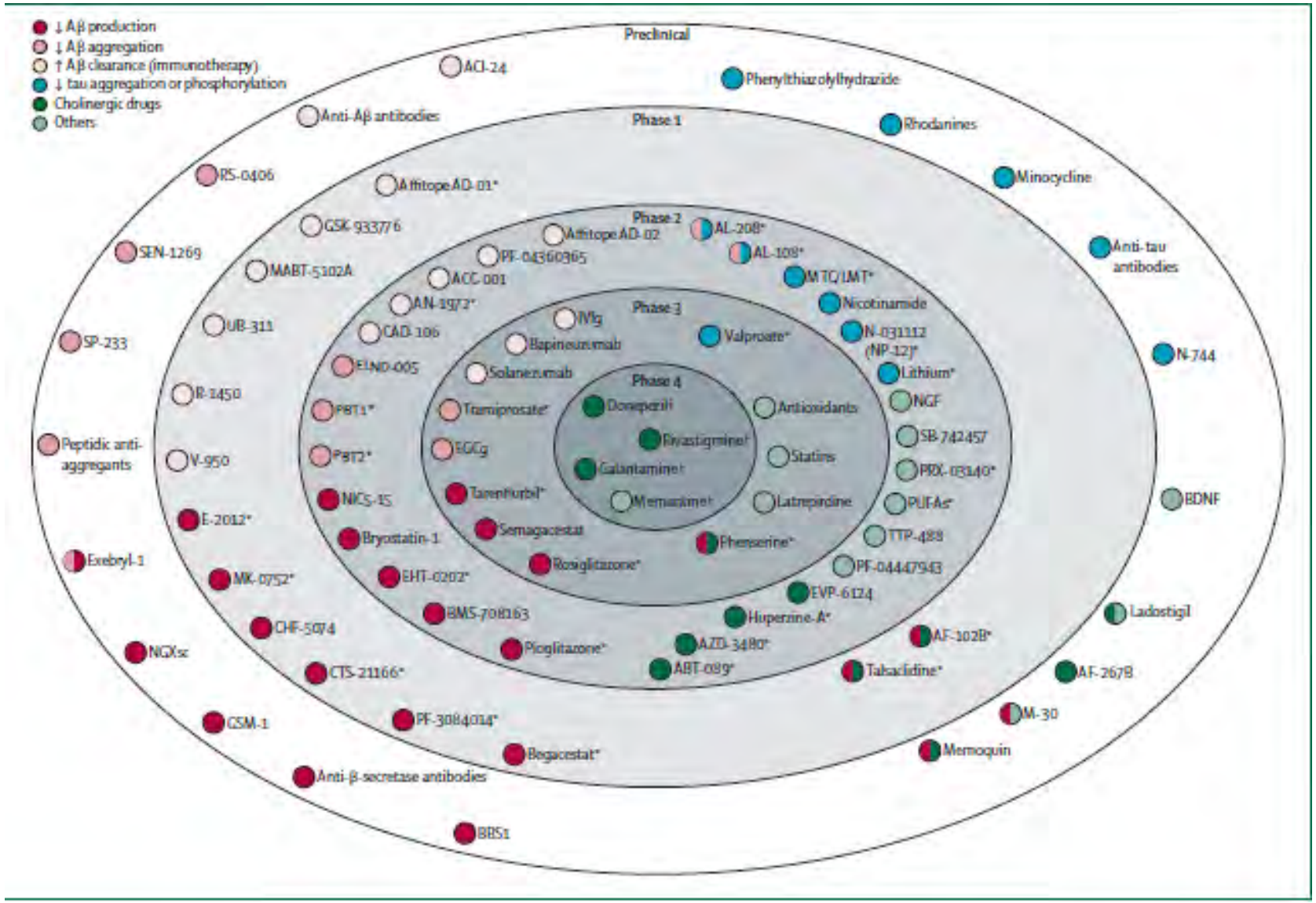


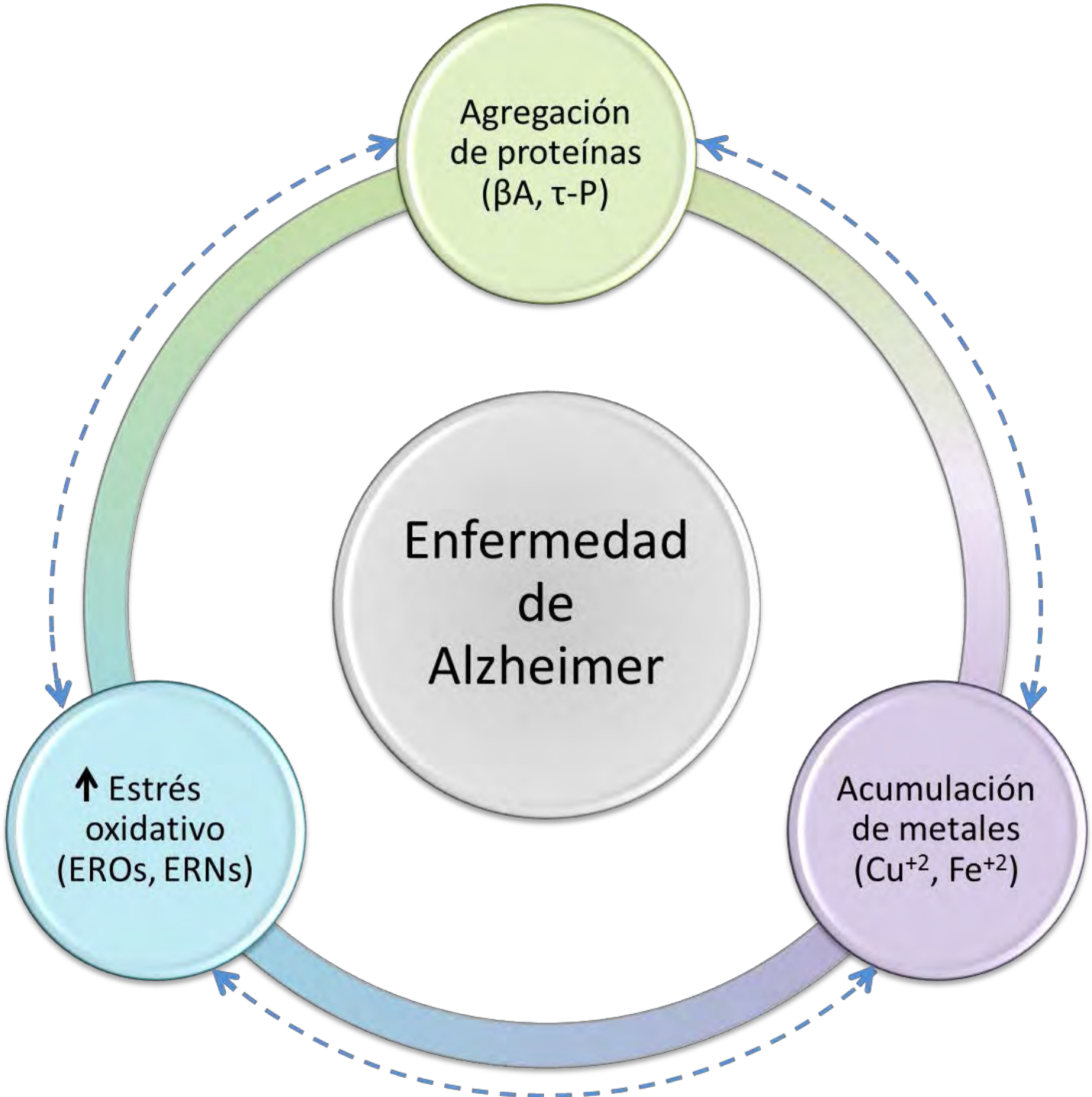
Imágenes de PET-amiloide que

Lancet Neurol 2010; 9:702–16

Alzheimer's disease: clinical trials and drug development

Francesca Mangialasche, Alina Solomon, Bengt Winblad, Patrizia Mecocci, Miia Kivipelto




Agregación de proteínas (βA, τ-P)
Enfermedad de Alzheimer
↑ Estrés oxidativo (EROs, ERNs)
Acumulación de metales (Cu^{+2}, Fe^{+2})

ES POSIBLE PREVENIR EL ALZHEIMER

Potential for primary prevention of Alzheimer's disease: an analysis of population-based data

Sam Norton, Fiona E Matthews, Deborah E Barnes, Kristine Yaffe, Carol Brayne

Lancet Neurol 2014

	Relative risk (95% CI)*	Communality (%)†
Diabetes mellitus	1·46 (1·20–1·77)	50·9%
Midlife hypertension	1·61 (1·16–2·24)	65·0%
Midlife obesity	1·60 (1·34–1·92)	43·7%
Physical inactivity	1·82 (1·19–2·78)	49·0%
Depression	1·65 (1·42–1·92)	37·4%
Smoking	1·59 (1·15–2·20)	58·1%
Low educational attainment	1·59 (1·35–1·86)	45·6%

*Sources are provided in the appendix. †The proportion of the variance in each risk factor shared with the other risk factors, estimated using the Health Survey for England 2006.[7]

Table 1: Relative risks for Alzheimer's disease and shared variance between risk factors

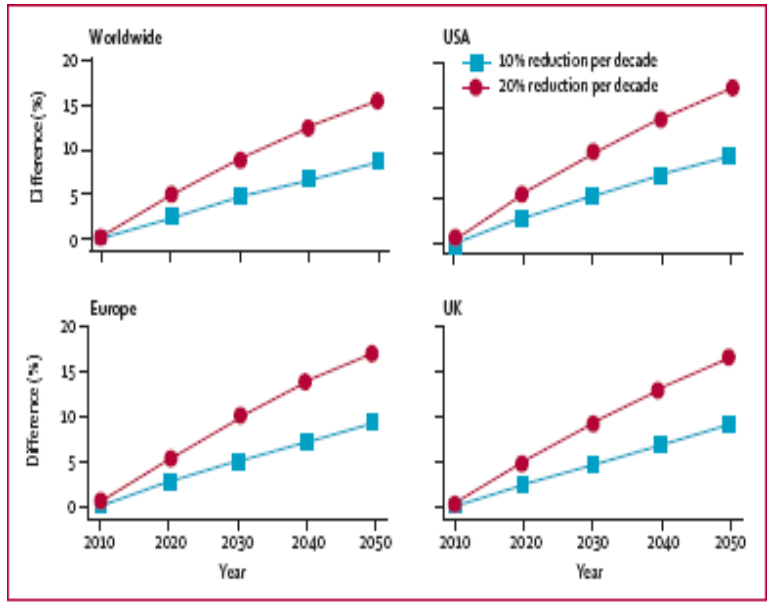
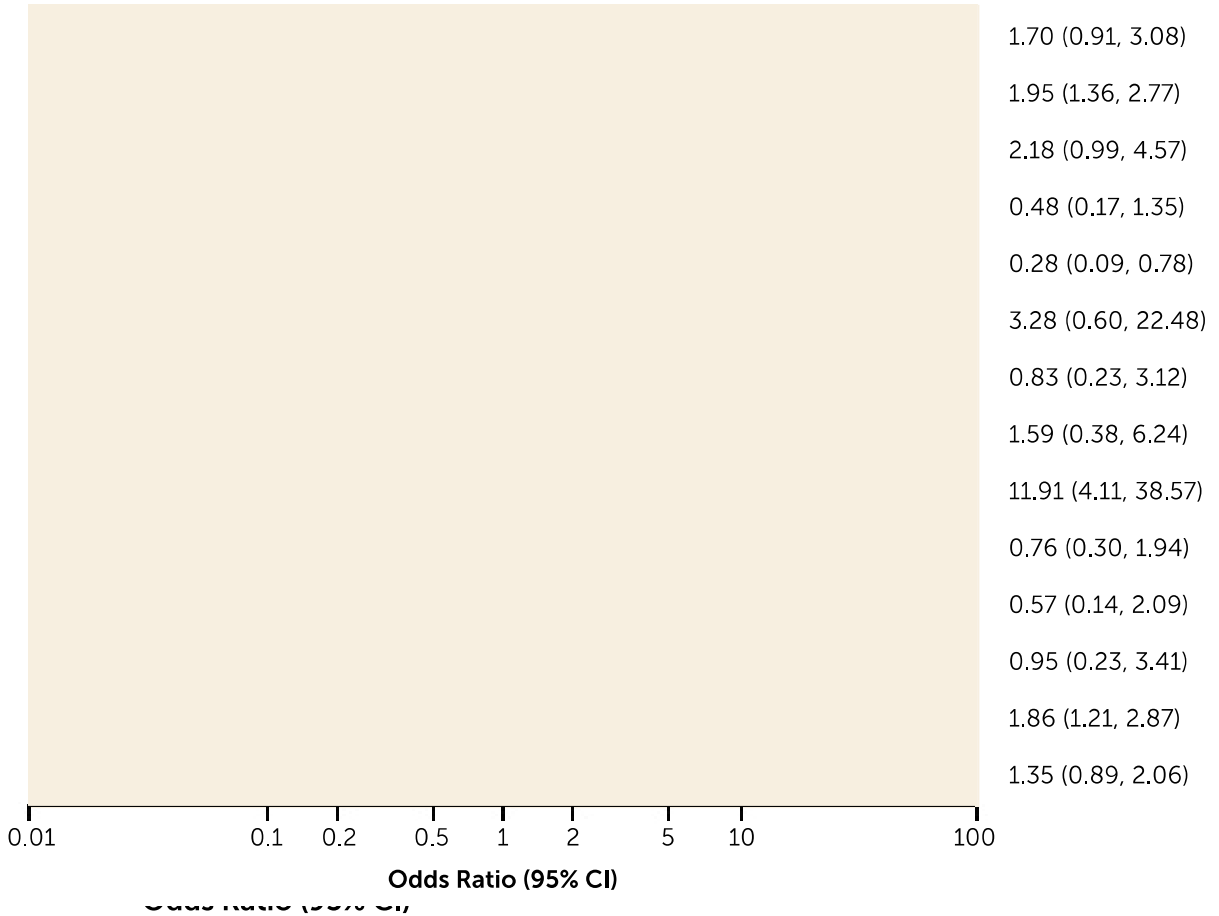


Figure: Projected percentages of Alzheimer's disease cases that could be prevented, with 10% or 20% reductions per decade in each risk factor

Interpretation After accounting for non-independence between risk factors, around a third of Alzheimer's diseases cases worldwide might be attributable to potentially modifiable risk factors. Alzheimer's disease incidence might be reduced through improved access to education and use of effective methods targeted at reducing the prevalence of vascular risk factors (eg, physical inactivity, smoking, midlife hypertension, midlife obesity, and diabetes) and depression.

PREDICTORES

FIGURE 5. Meta-Analysis Plot With Odds Ratios for Presence of Depressive Symptoms as Predictor of MCI Conversion to Dementia[a]

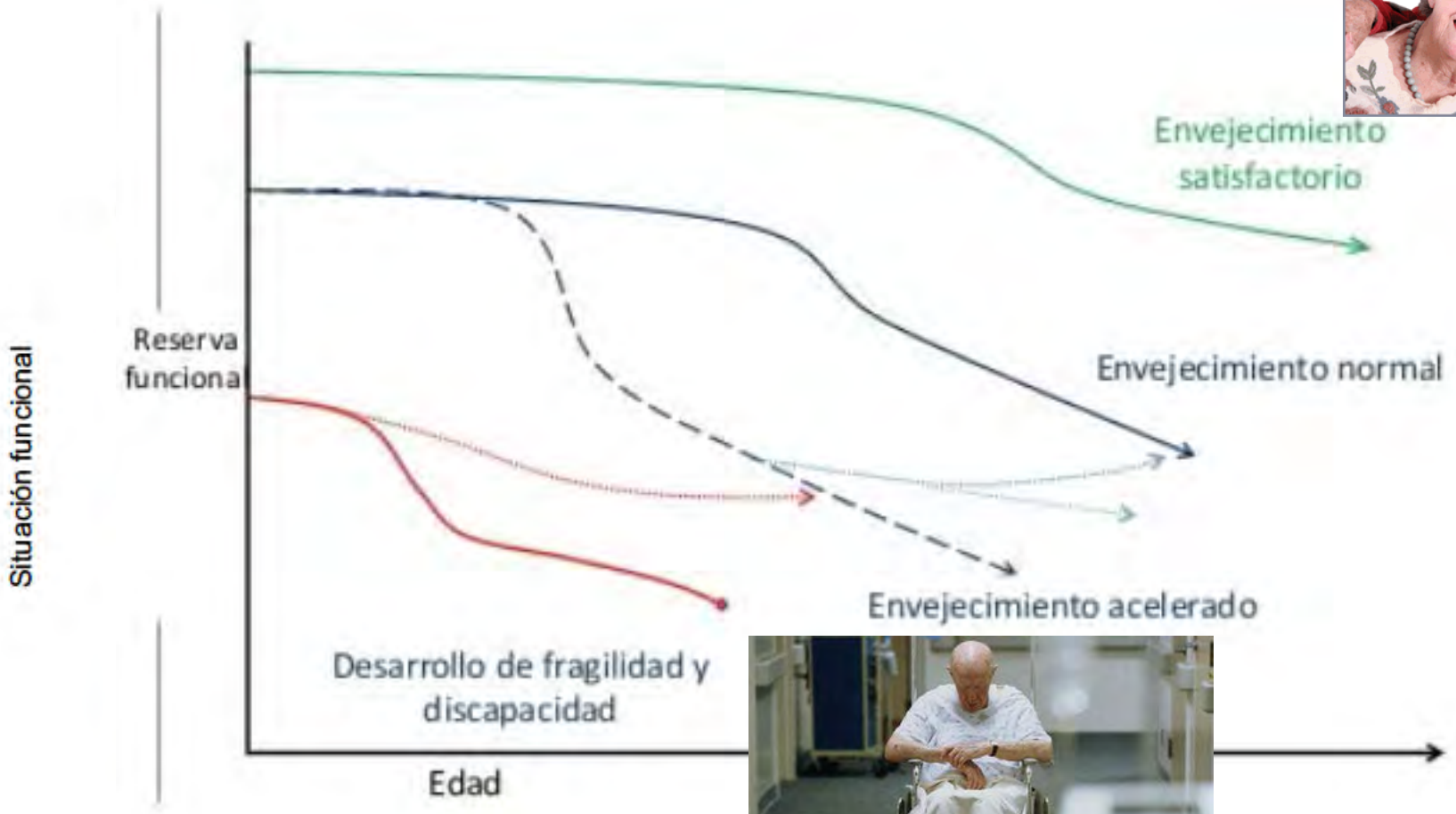


Mod
Impa

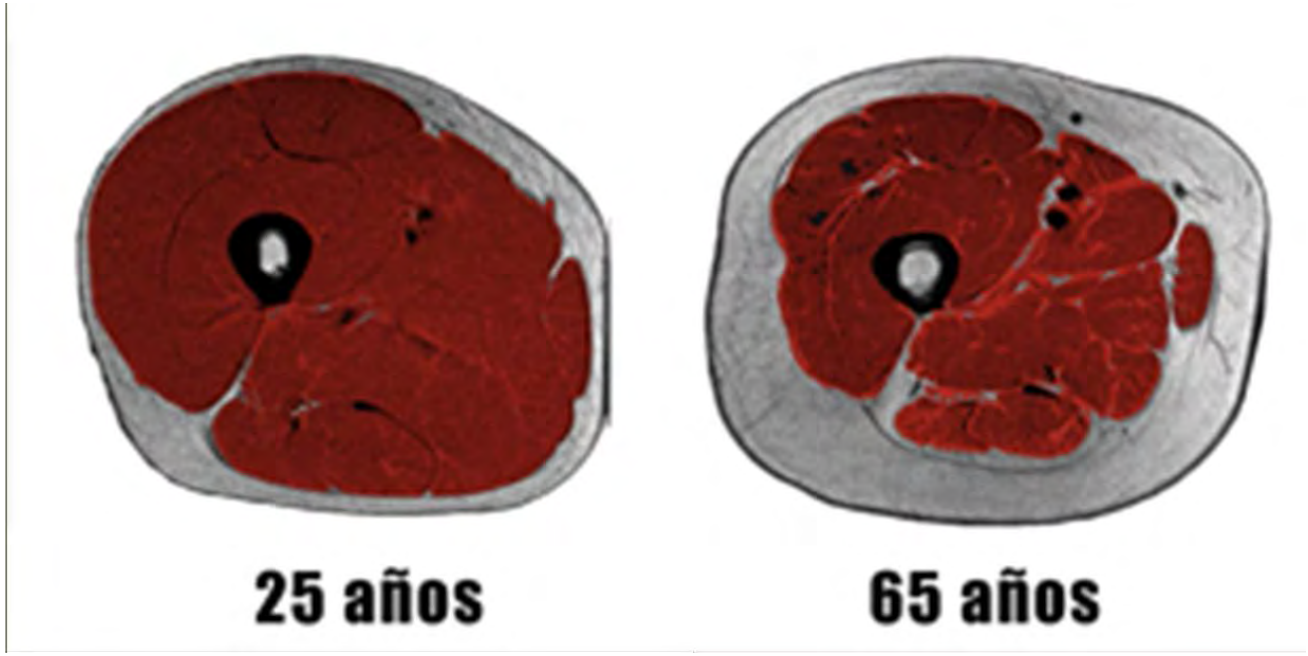
Claudia C
Gill Living

- DE

¿Qué es la fragilidad?



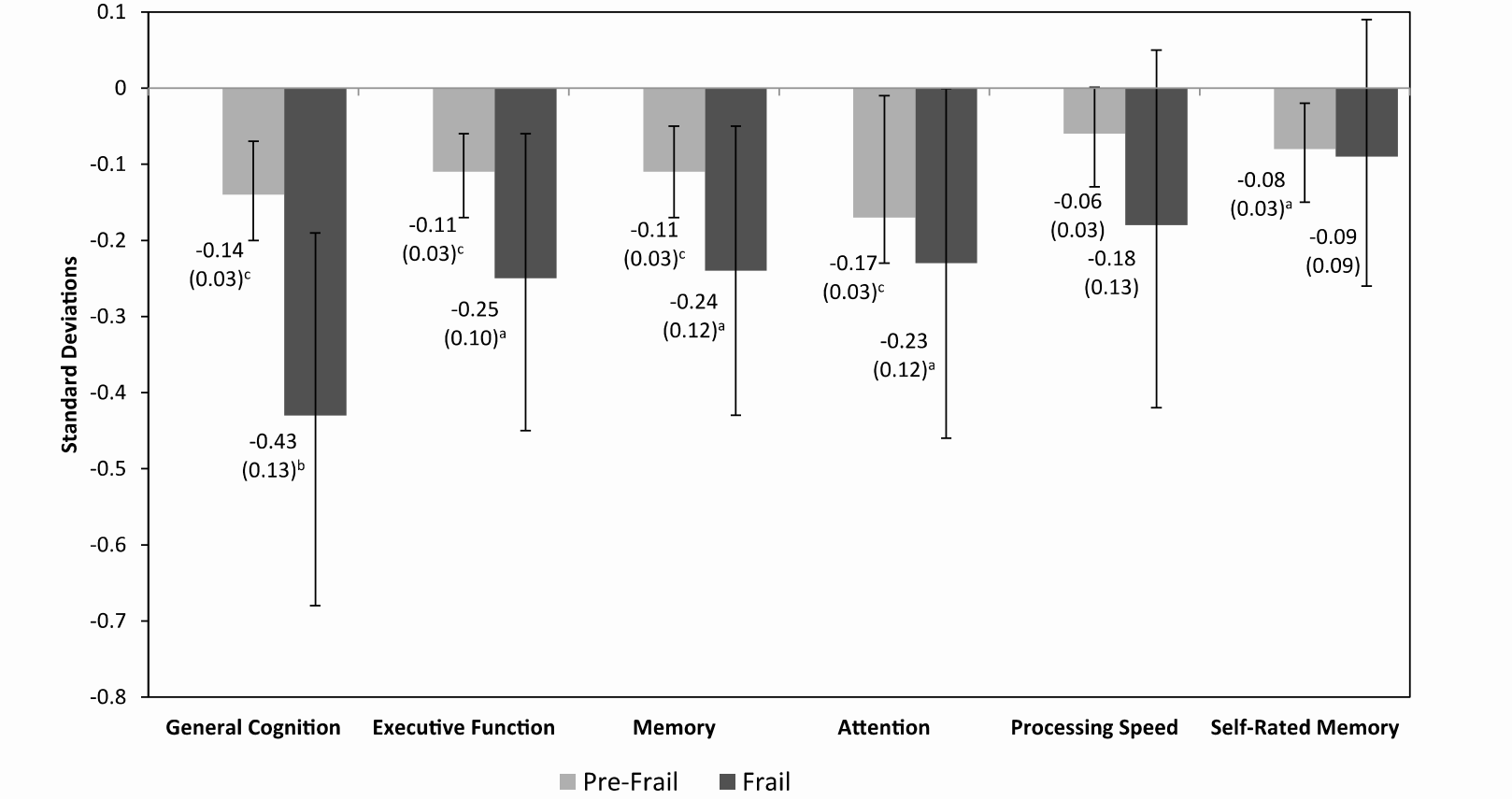
SARCOPENIA: pérdida de masa magra y aumento de masa grasa



Cognitive Function in the Prefrailty and Frailty Syndrome

Deirdre A. Robertson, MSc, George M. Savva, PhD,† Robert F. Coen, PhD,‡ and Rose-Anne Kenny, MD*§*

J Am Geriatr Soc 62:2118–2124, 2014.



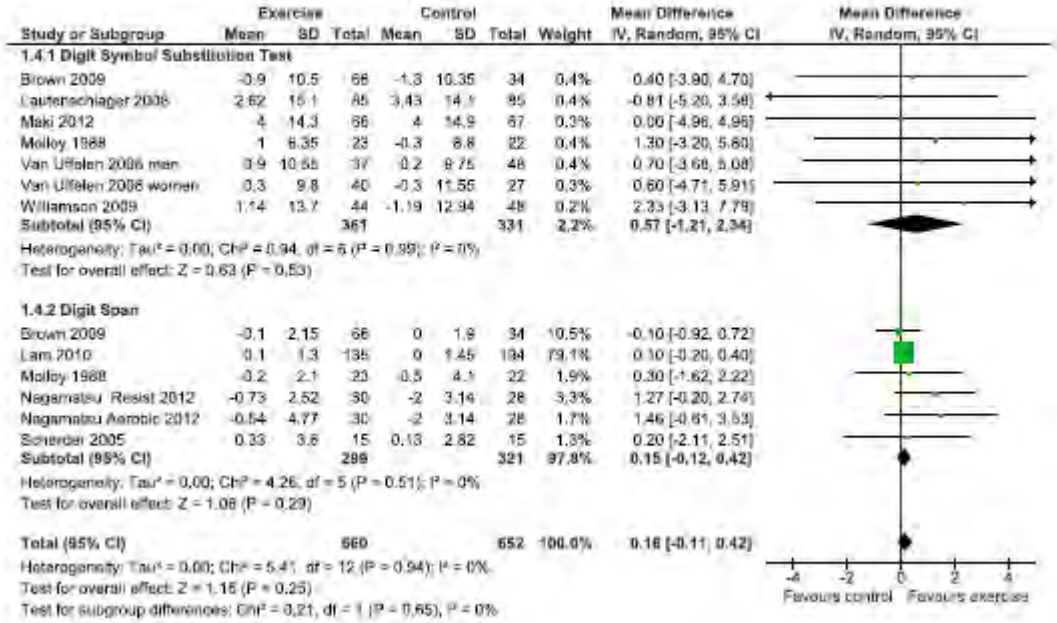
Am J Geriatr Psychiatry 21:11, November 2013

The Effect of Exercise Training on Cognitive Function in Older Adults with Mild Cognitive Impairment: A Meta-analysis of Randomized Controlled Trials

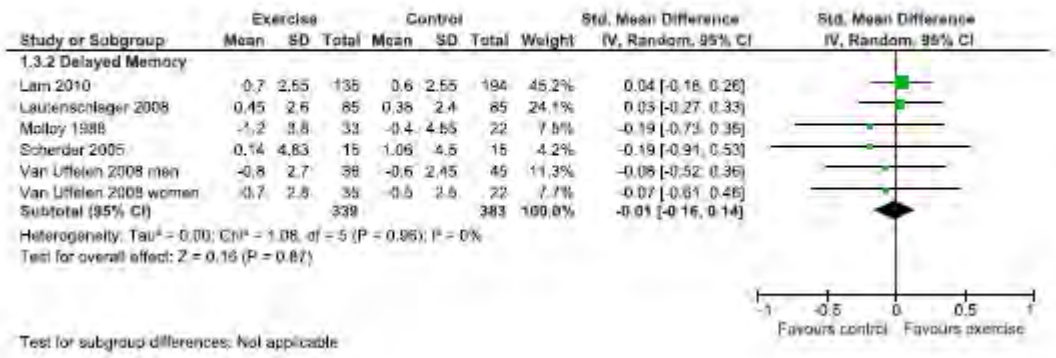
Nicola Gates, M.A., Maria A. Fiatarone Singh, M.D., Perminder S. Sachdev, M.D., Michael Valenzuela, Ph.D.

cognitive domains. **Conclusions:** *There is very limited evidence that exercise improves cognitive function in individuals with MCI, although published research is of moderate quality and inconclusive due to low statistical power. Questions remain regarding the magnitude, generalization, persistence, and mechanisms of benefits. Large-scale, high-quality RCTs are required to determine if exercise improves cognition or reduces dementia incidence in those with MCI.* (Am J Geriatr Psychiatry 2013; 21:1086–1097)

Meta-analysis of exercise on information processing in MCI.



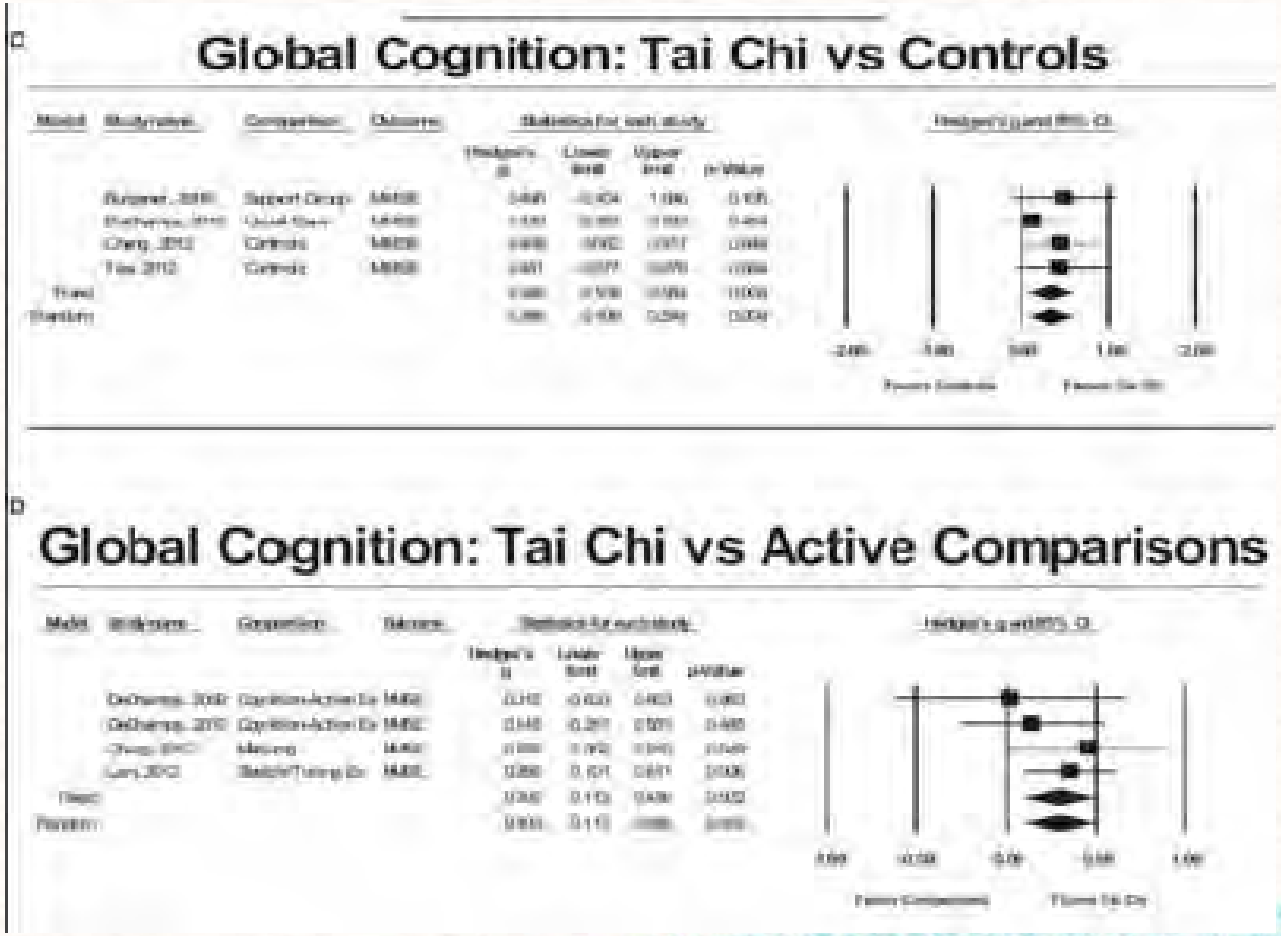
Meta-analysis of exercise on delayed memory in MCI.



Effect of Tai Chi on Cognitive Performance in Older Adults: Systematic Review and Meta-Analysis

JAGS 2014; 62: 25-29.

Peter M. Wayne, PhD,† Jacquelyn N. Walsh, BS,*† Ruth E. Taylor-Piliae, PhD, RN,‡*

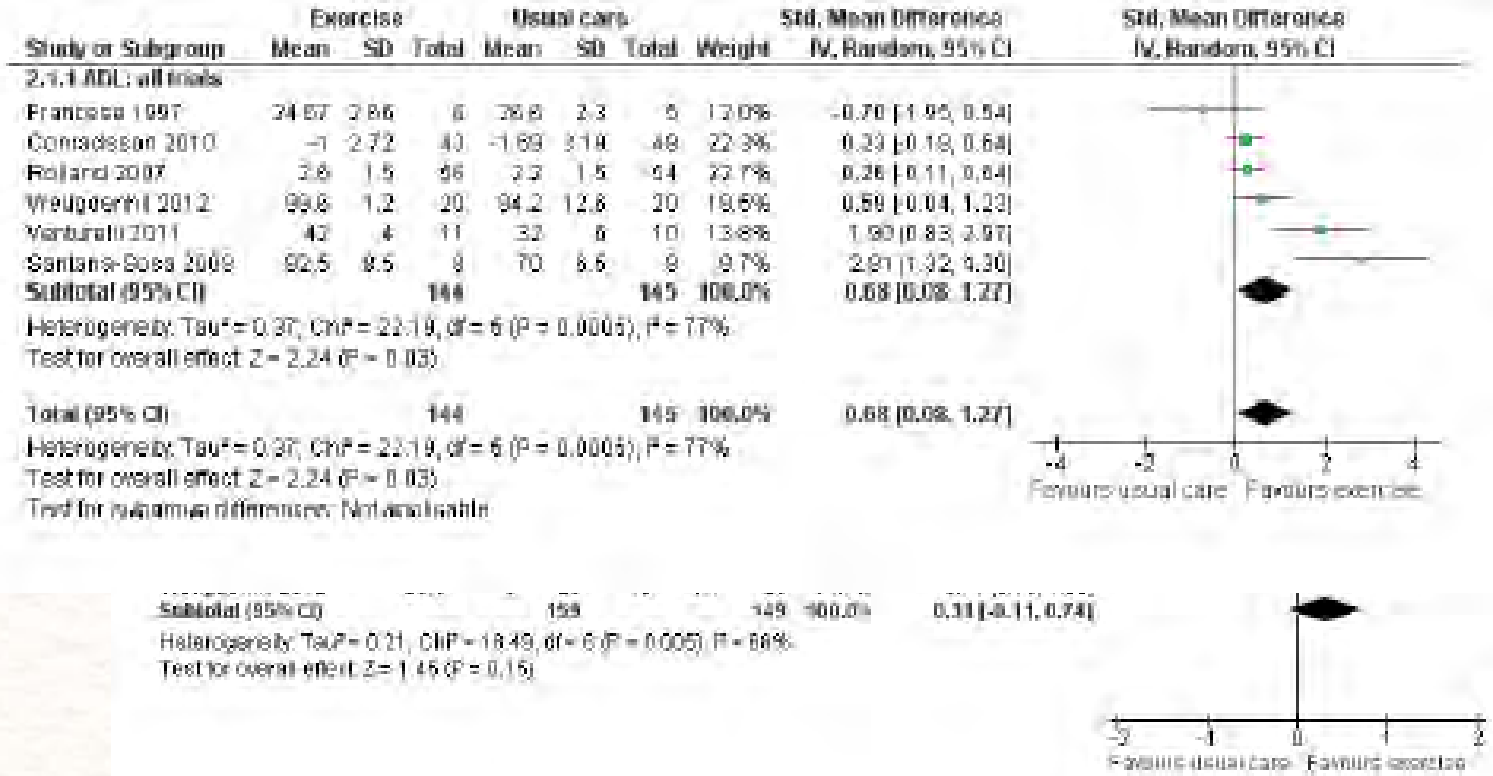


Exercise programs for people with dementia (Review)

Forbes D, Thiessen EJ, Blake CM, Forbes SC, Forbes S

THE COCHRANE COLLABORATION®

Figure 5. Forest plot of comparison 2: Physical activity vs usual care: Activities of daily living (ADLs)



Citation: Forbes D, Thiessen EJ, Blake CM, Forbes SC, Forbes S. Exercise programs for people with dementia. *Cochrane Database of Systematic Reviews* 2013, Issue 12. Art. No.: CD006489. DOI: 10.1002/14651858.CD006489.pub3.

BJCP British Journal of Clinical Pharmacology

Nutrition and neurodegeneration: epidemiological evidence and challenges for future research

Sophie Gillette-Guyonnet,[1,2,3] Marion Secher[1] & Bruno Vellas[1,2,3]

Nutrición-Alzheimer

MACRONUTRIENTES

Review Article

Nutrition and the Risk of Alzheimer's Disease

- ***Efectos de las comidas y bebidas en el riesgo de AD***

BioMed Research International

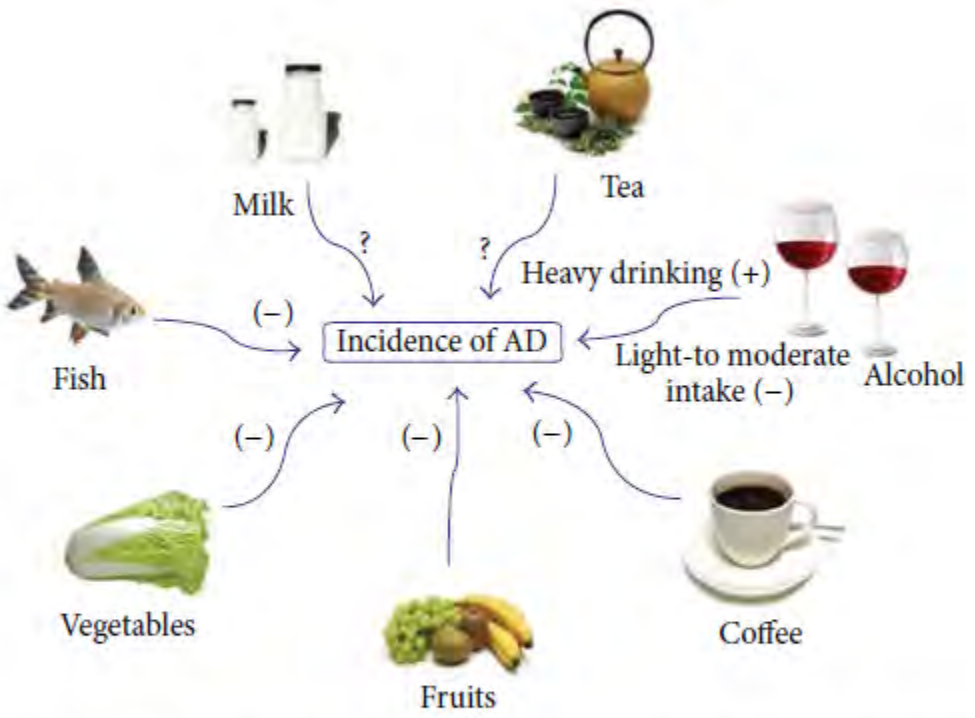


FIGURE 1: Foods and beverages that influence the incidence of AD. Fish, vegetables, fruits, coffee, and light-to-moderate alcohol intake are reported to reduce AD incidence. Milk and tea are reported to influence cognition, but their influence on AD is not clear.

BJCP British Journal of Clinical Pharmacology

Nutrition and neurodegeneration: epidemiological evidence and challenges for future research

Sophie Gillette-Guyonnet,[1,2,3] Marion Secher[1] & Bruno Vellas[1,2,3]

Nutrición-Alzheimer

Datos epidemiológicos evidencian relación

Review Article

Nutrition and the Risk of Alzheimer's Disease

➢ ***Efectos de patrones de dietas y el riesgo de AD***

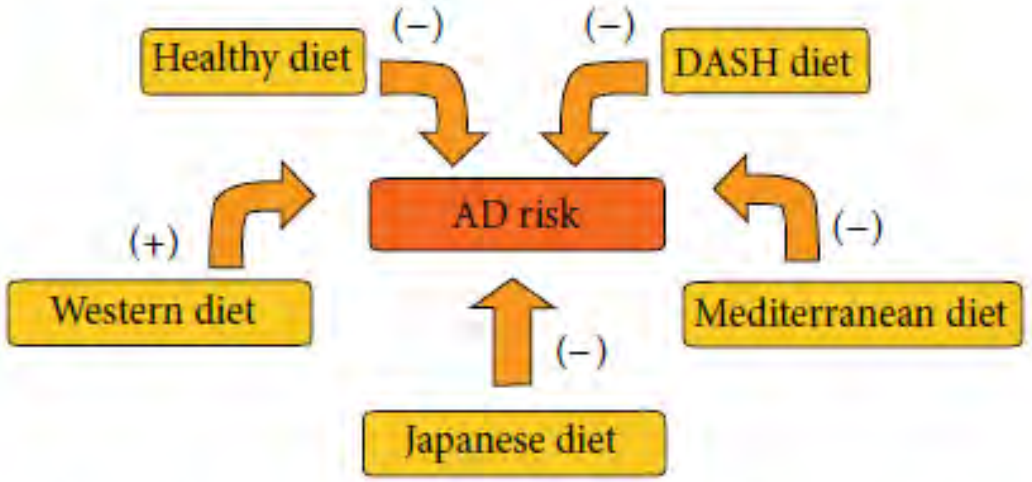


FIGURE 2: Dietary patterns that influence the risk of AD. Healthy diet, DASH-diet, Mediterranean diet, and Japanese diet might decrease the risk of AD. Western diet might increase the risk of AD. DASH diet: the Dietary Approaches to Stop Hypertension.

Mediterranean Diet, C
A S

Ilianna Lourida,[a] *Maya Soni,*[b] *Joa*
Obioha C. U

Epidemiology • V

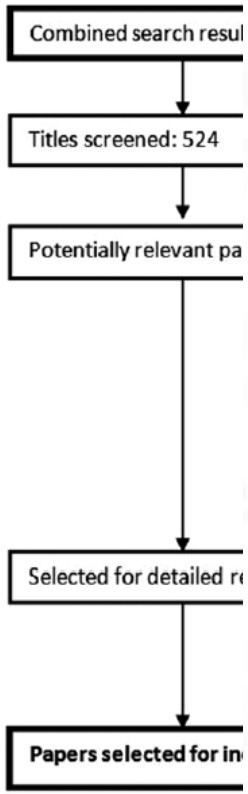


TABLE 3. Results of Included Studies for the Association Between Adherence to Mediterranean Diet and Cognitive Decline or Cognitive Performance

Study	Cognitive Assessment[a]	Methods	Results
Longitudinal (cognitive decline)			
Feart et al[16]	Individual scores on: MMSE, Isaacs Set Test, Benton Visual Retention Test, Free and Cued Selective Reminding Test	Mixed effects models[c,g] 0-9–point MeDi score	Each unit increase in the MeDi score corresponds to 0.006 (95% CI = 0.0003–0.01; $P = 0.04$) less cognitive decline per year on the MMSE
Psaltopoulou et al[17]	MMSE	Linear regression[b,h] 0-9–point MeDi score	Each unit increase in the MeDi score at baseline corresponds to 0.05 (95% CI = −0.09 to 0.19; $P = 0.49$) higher cognitive function on MMSE at follow-up
Cherbuin and Anstey[11] (Wave 2)	Average Z score of: MMSE, California Verbal Learning Test, Symbol Digit Modalities Test, Purdue Pegboard test for investigation of cognitive change	Analysis of covariance[b,i] 0-9–point MeDi score	Each unit increase in the MeDi score corresponds to 0.02 (95% CI = −0.02 to 0.06; $P = 0.37$) less cognitive decline on the cognitive Z score over 4 years
Cherbuin et al[12] (Wave 3)	Average Z score of: MMSE, California Verbal Learning Test, Symbol Digit Modalities Test, Purdue Pegboard test for investigation of cognitive change	Analysis of covariance[b,i] 0-9–point MeDi score	Each unit increase in the MeDi score corresponds to 0.01 (95% CI = −0.04 to 0.06; $P = 0.71$) greater cognitive decline on the cognitive Z score over 8 years
Scarmeas et al[20]	Average Z score of: 12 neuropsychological tests to assess memory, orientation, abstract reasoning, language, construction	Marginal models using Generalised Estimating Equations[d,j] 0-9–point MeDi score	Each unit increase in the MeDi score corresponds to 0.003 (95% CI = 0–0.006; $P = 0.05$) less cognitive decline per year on the composite cognitive Z score
Tangney et al[19]	Average Z score of: MMSE, East Boston tests of immediate and delayed recall, Symbol Digit Modalities Test for global cognitive function measure	Mixed effects models[b,g] 0-45–point MedDiet score	Each unit increase in the MedDiet score corresponds to 0.0014 (95% CI = 0.0006–0.0022; $P < 0.001$) less cognitive decline per year on the global cognitive Z score
Cross-sectional (cognitive function)			
Gu et al[23]	Average Z score of: 15 neuropsychological tests to assess memory, language, processing speed, visual-spatial ability to summarize cognitive performance	Linear regression[a,b] 0-9–point MeDi score	Each unit increase in the MeDi score corresponds to 0.013 (95% CI = 0–0.026; $P = 0.05$) increase on the composite cognitive Z score
Tangney et al[19]	Average Z score of: MMSE, East Boston tests of immediate and delayed recall, Symbol Digit Modalities Test for global cognitive function measure	Linear regression[f,h] 0-45–point MedDiet score	Each unit increase in the MedDiet score corresponds to 0.007 (95% CI = 0.003–0.011; $P < 0.001$) increase on the global cognitive Z score at baseline
Randomized controlled trial			
McMillan et al[18]	Individual scores on: 21 items of the COMPASS battery with tasks to assess change in attention, working memory, long-term memory, executive function	Repeated measures analysis of variance[k] Food diary	The Mediterranean Diet group performed faster on the Corsi Block Task ($P < 0.001$) but was slower on the Numeric Working Memory and Word Recognition tasks (both, $P = 0.04$) than the control group

La Dieta Mediterránea y el Riesgo de desarrollar la EA

- Elevado consumo de vegetales, legumbres, frutas y cereales
- Elevada ingesta de ácidos grasos insaturados
- Baja ingesta de ácidos grasos saturados
- Consumo moderadamente alto de pescado
- Consumo bajo a moderado de productos lácteos
- Bajo consumo de carne de res y carne de ave
- Consumo habitual pero moderado de etanol, principalmente en forma de vino y por lo general acompañando a las comidas

Scarmeas *et al.*, 2006:
Sujetos sanos de la tercera edad evaluados cada 18 meses;

clasificados en función de su adhesión a la dieta mediterránea

Una mayor adhesión a la dieta mediterránea se asocia
con menor riesgo de desarrollo de la enfermedad de Alzheimer

El mejor tratamiento es la pevención

SOLO VIVIMOS UNA VEZ

torno a un 25% podría evitar unos tres millones de afectados.

Tabaco

Sedentarismo

Escasa actividad mental

Hipertensión

Diabetes

Obesidad

Depresión

edicine, Dublin

John Nash
“Una mente maravillosa”

Nobel de Economía y Premio Abel 1994

MUCHAS GRACIAS