

# Síndrome de Down y enfermedad de Alzheimer

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# Declaración conflictos de interés

- **Proyectos sobre EA en SD:**
  - Ensayo clínico ACI-24-AD-DS-2102, financiado por AC Immune
  - Ensayo clínico independiente IIBSP-LEV-2024-86, financiado por ISCIII
- **Proyectos no relacionados con EA en SD:**
  - Ensayo clínico AEF0217-102, financiado por AELIS Farma y Comisión Europea (UE.ICOD.899986)

HEALTH

# THE LAST CHILDREN OF DOWN SYNDROME

Prenatal testing is changing who gets born and who doesn't. This is just the beginning.

By Sarah Zhang

DECEMBER 2020 ISSUE

*The Atlantic*

[DC] THE DAILY CITIZEN™

By JULIAN QUINONES, ARIJETA LAJKA / CBS NEWS / August 14, 2017, 4:00 PM

**"What kind of society do you want to live in?": Inside the country where Down syndrome is disappearing**

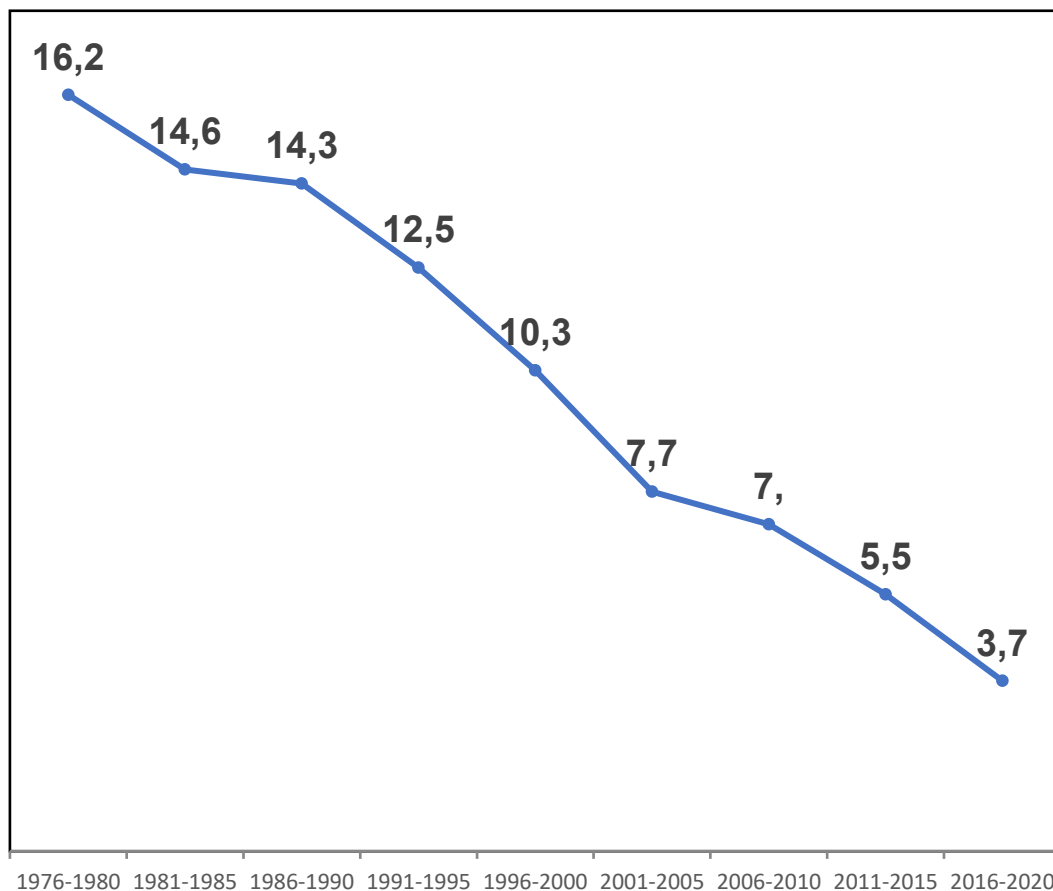
**Why is Down Syndrome Disappearing?**

Posted by Citizen Magazine Staff | Apr 16, 2018 | Classic Citizen

**CBS  
NEWS**

# Incidencia poblacional SD

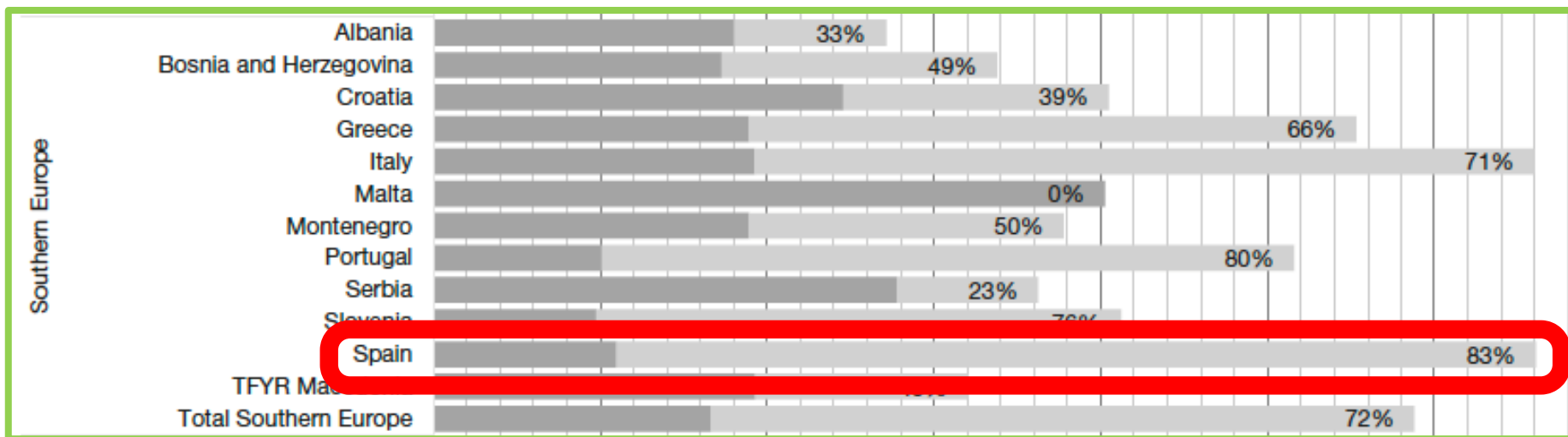
Estudio colaborativo español malformaciones congénitas (1967 - 2020)



## Estimation of the number of people with Down syndrome in Europe

Gert de Graaf<sup>1</sup> • Frank Buckley<sup>2,3</sup> • Brian G. Skotko<sup>4,5</sup>

Eur J Hum Genetics. 2020

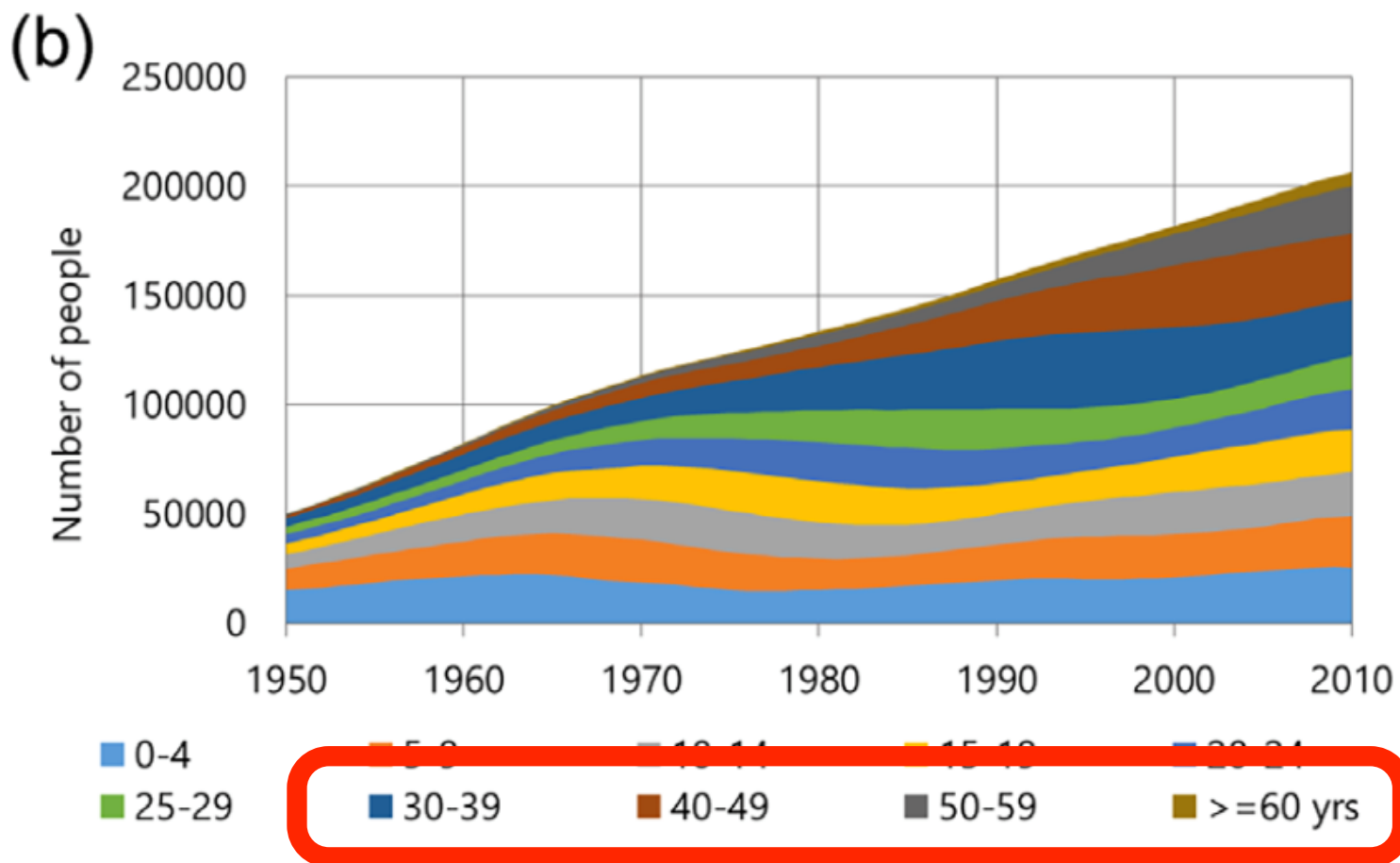


## Countrywide Variables Associated With the Reduction of Fetuses With Down Syndrome

Petrus H. F. M. van Casteren<sup>1</sup> | Gert de Graaf<sup>2</sup> | Frank Buckley<sup>3,4</sup> | Brian G. Skotko<sup>5,6</sup>

Independent variable	Regression coefficient	Robust standard error	p	OR <sup>a</sup>	OR, 95% CI
Only non-serum screening available and not reimbursed	0.15	0.37	0.6925	1.16	0.56–2.40
Only non-serum screening available and reimbursed	0.78	0.33	0.0186	2.18 <sup>b</sup>	1.14–4.19
Serum screening available and not reimbursed	0.83	0.34	0.0145	2.28 <sup>b</sup>	1.18–4.43
Serum screening available and reimbursed	1.17	0.31	0.0001	3.24 <sup>c</sup>	1.77–5.92
Maternal age	0.30	0.04	0.0000		
+1 year				1.36	1.25–1.47
+3 years				2.49 <sup>b</sup>	1.95–3.19
Ln(GNI per capita)	1.18	0.30	0.0001		
GNI per capita +10%				1.12	1.06–1.18
GNI per capita +50%				1.61	1.27–2.05
GNI per capita +100%				2.26 <sup>b</sup>	1.50–3.41
Standard country fixed effect <sup>d</sup>	0.76			2.15 <sup>b</sup>	

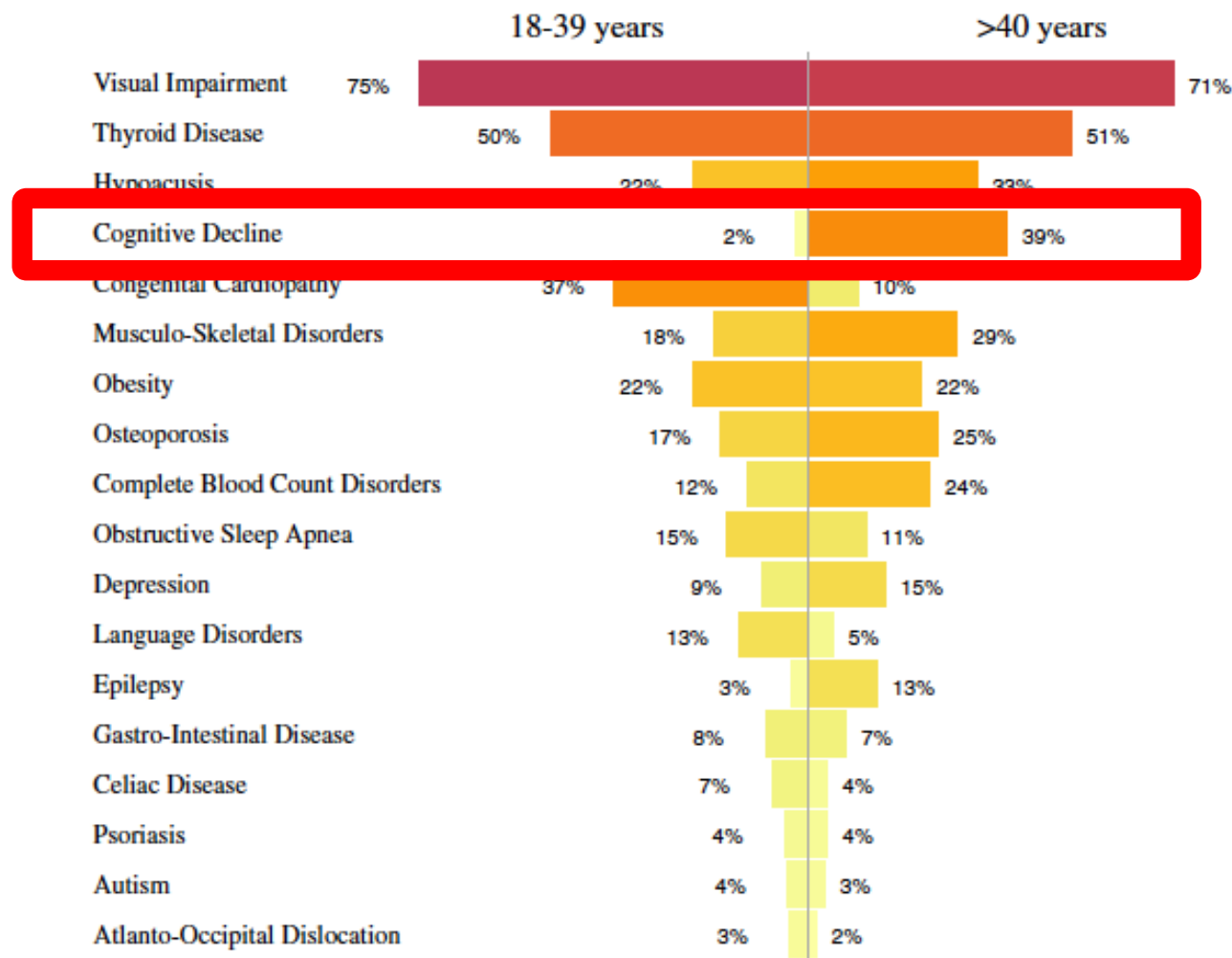
**Am J Med Genet (part A). 2025;0:e64228**



**Am J Med Genet A. 2017;173A:2710**



## Rompiendo fronteras

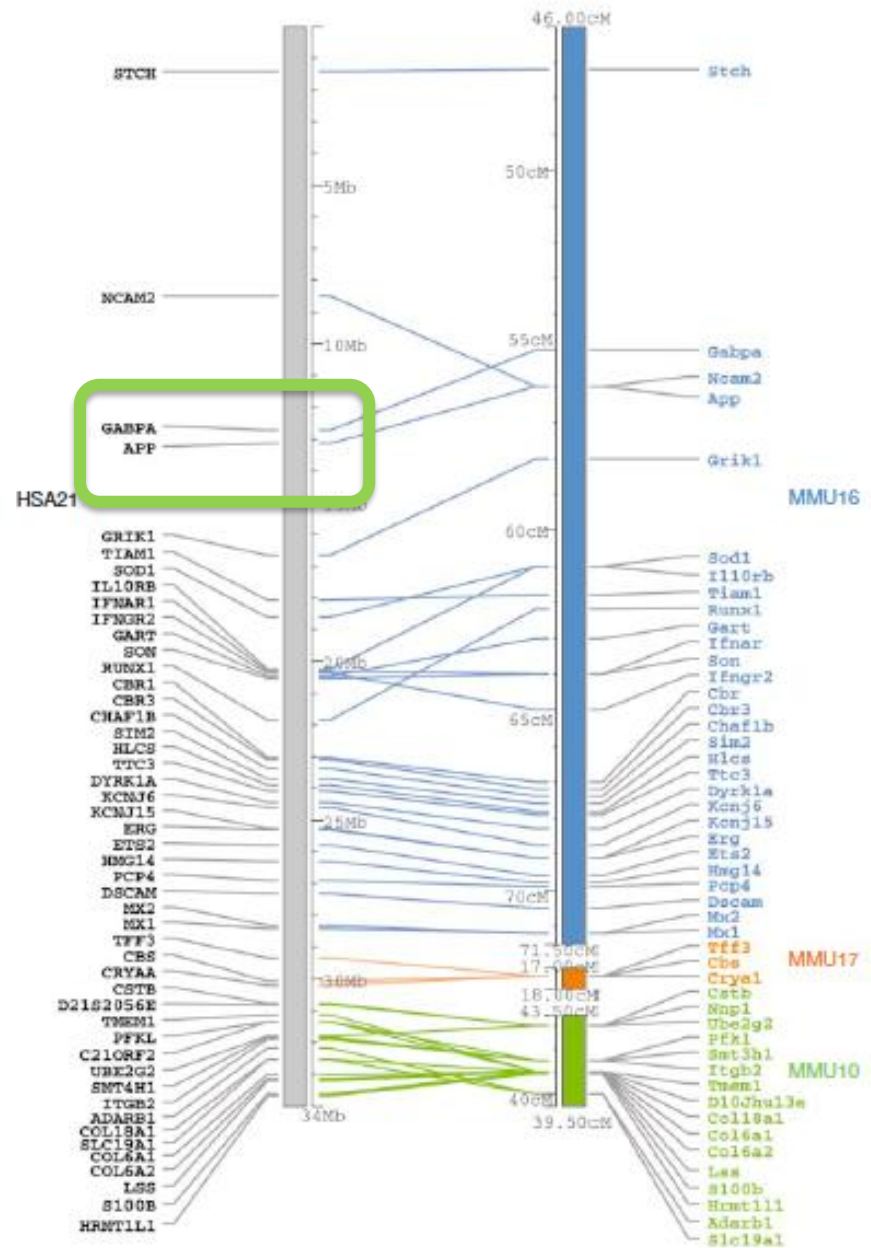


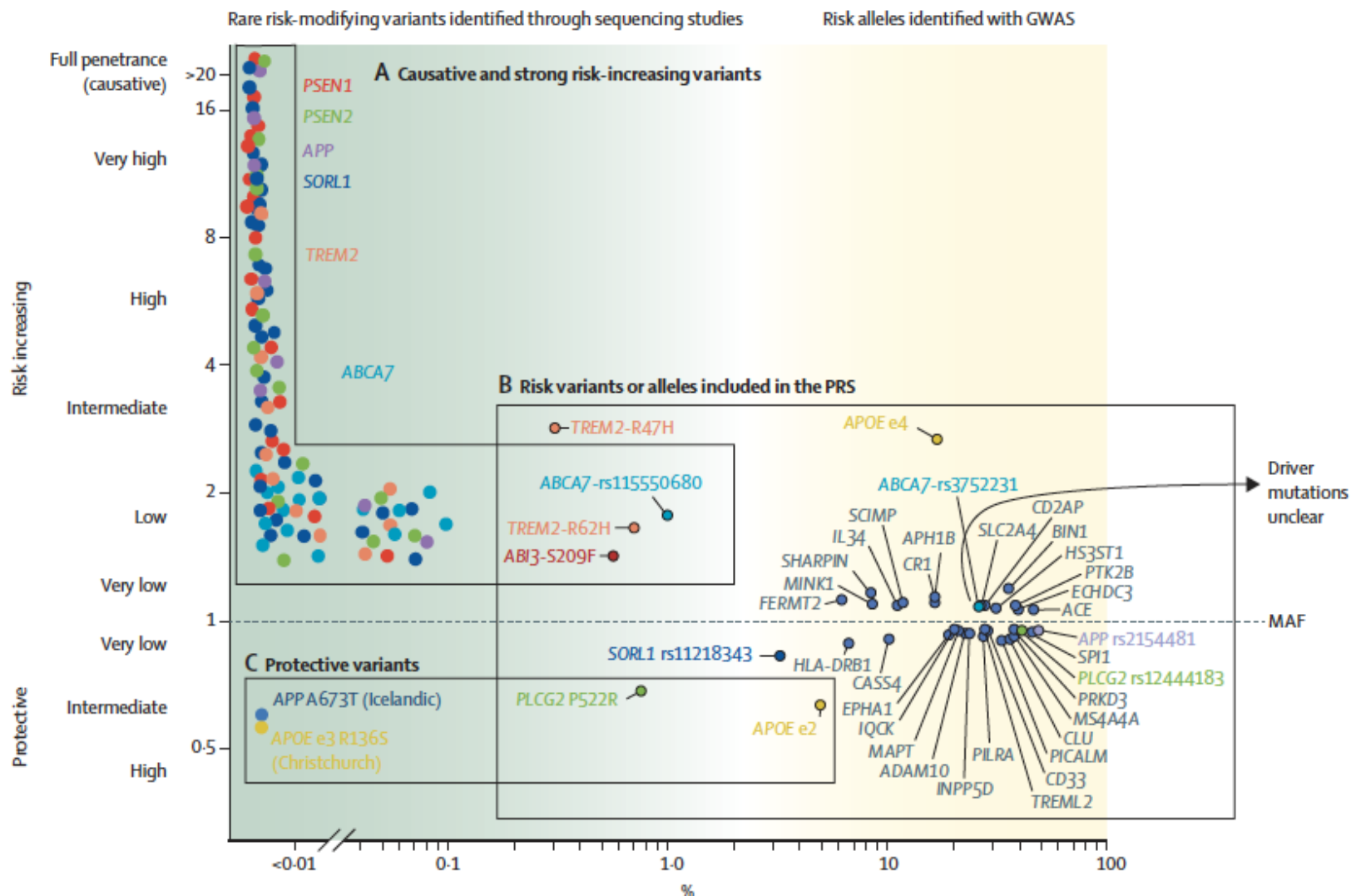
Am J Med Genet A. 2020;182:1735



# The DNA sequence of human chromosome 21

Nature. 2000;405:311

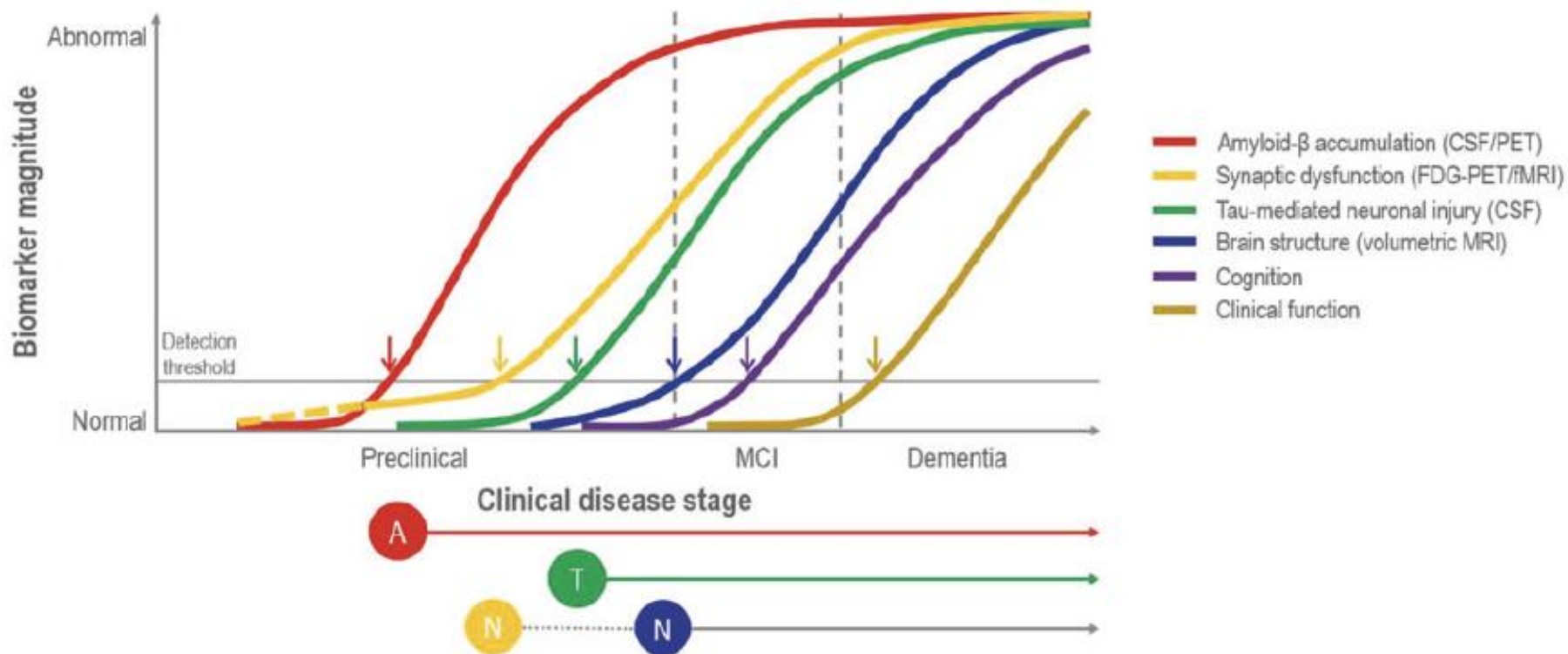




Lancet. 2021;397:1577

# The Amyloid- $\beta$ Pathway in Alzheimer's Disease

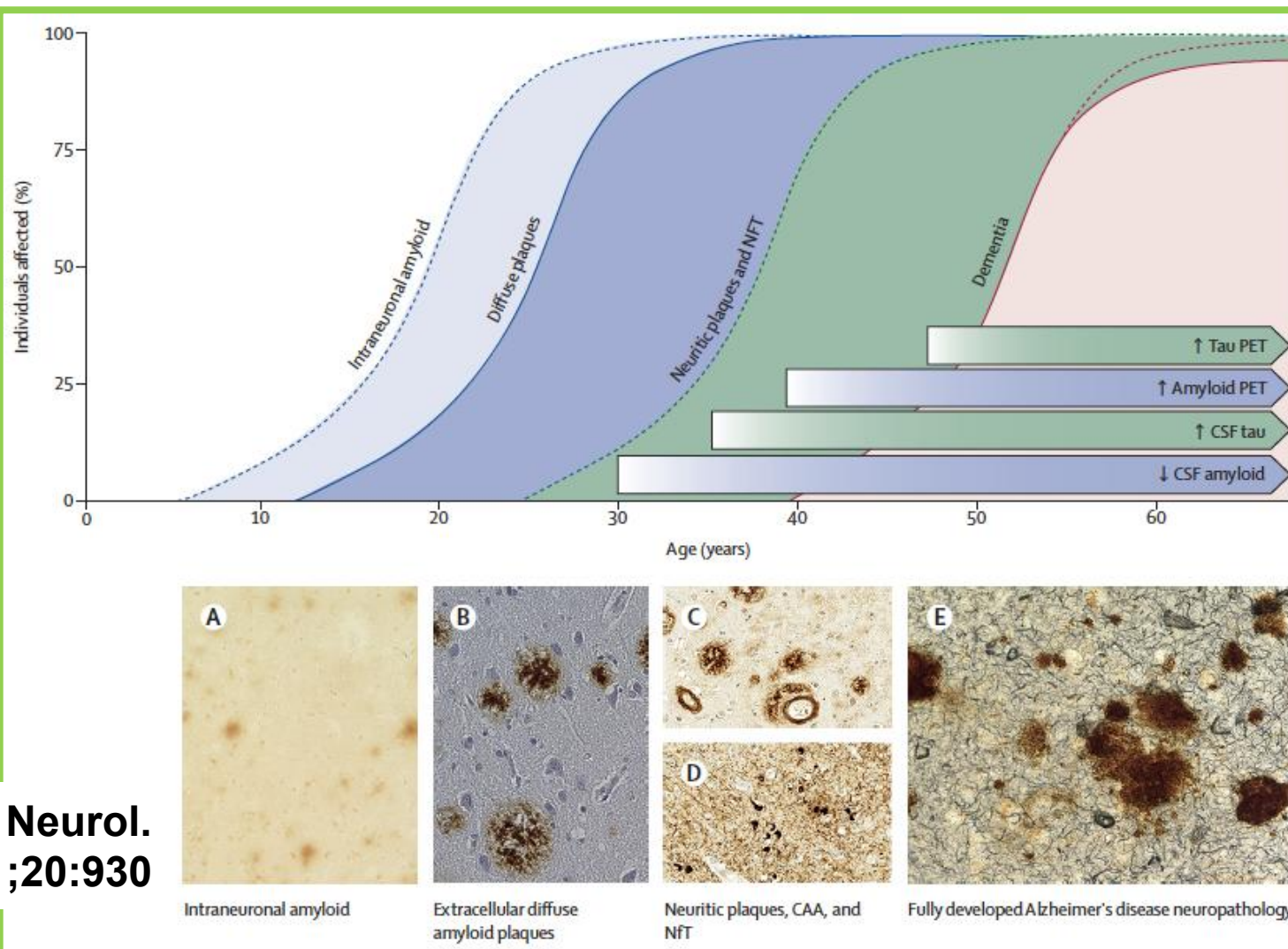
Harald Hampel<sup>1,2,3</sup>, John Hardy<sup>2</sup>, Kaj Blennow<sup>3,4</sup>, Christopher Chen<sup>5</sup>, George Perry<sup>6</sup>, Seung Hyun Kim<sup>7</sup>, Victor L. Villemagne<sup>8,9</sup>, Paul Aisen<sup>10</sup>, Michele Vendruscolo<sup>11</sup>, Takeshi Iwatsubo<sup>12</sup>, Colin L. Masters<sup>13</sup>, Min Cho<sup>1</sup>, Lars Lannfelt<sup>14,15</sup>, Jeffrey L. Cummings<sup>16</sup> and Andrea Vergallo<sup>1,2,3</sup>



Molecular Psychiatry. 2021;26:5481

# Alzheimer's disease associated with Down syndrome: a genetic form of dementia

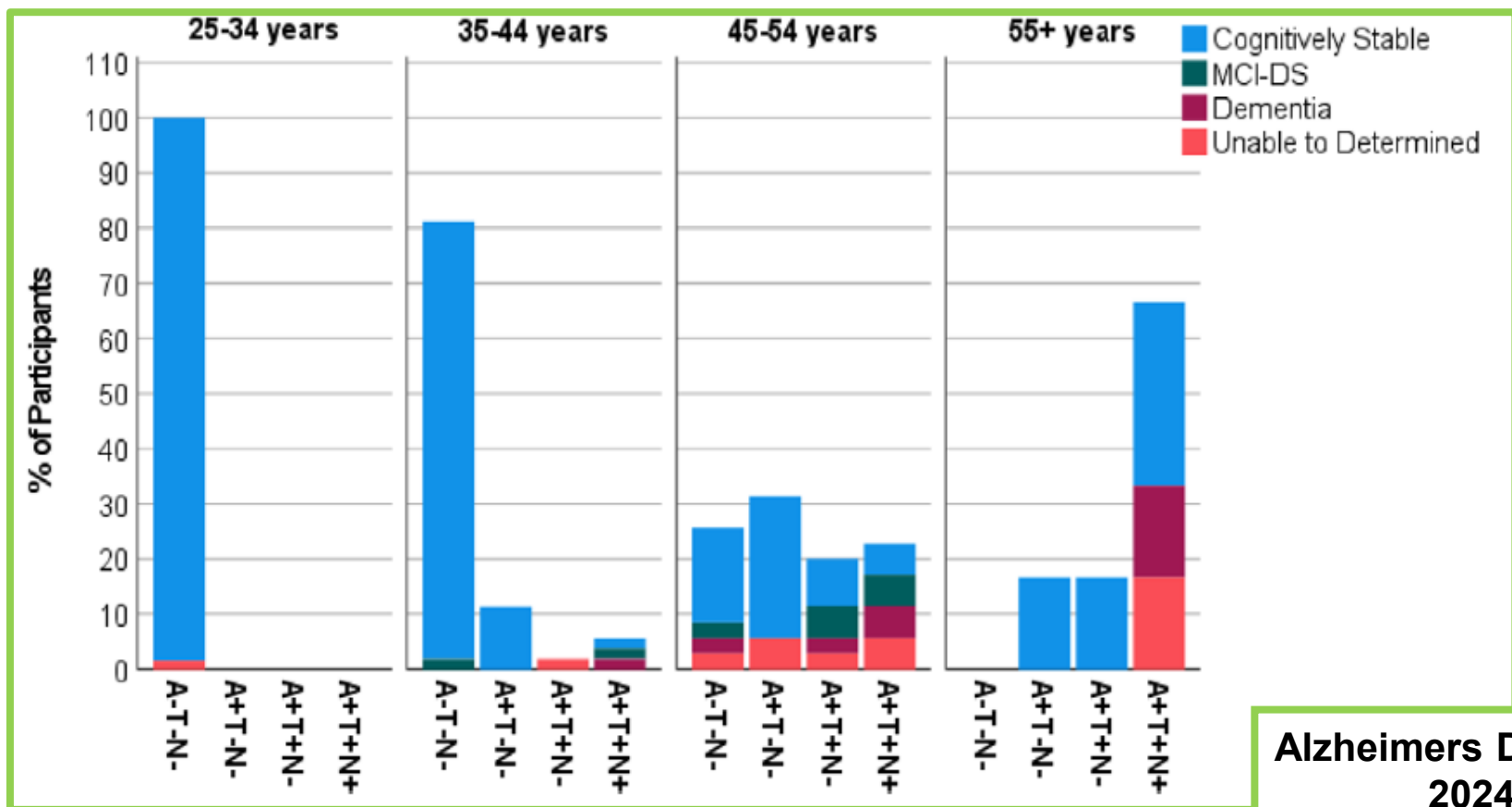
Juan Fortea, Shahid H Zaman, Sigan Hartley, Michael S Rafi, Elizabeth Head, Maria Carmona-Iragui



**Lancet Neurol.**  
**2021;20:930**

## AT(N) biomarker profiles and Alzheimer's disease symptomology in Down syndrome

Sigan L. Hartley<sup>1,2</sup> | Benjamin Handen<sup>3</sup> | Dana Tudorascu<sup>3</sup> | Laisze Lee<sup>3</sup> |  
Annie Cohen<sup>3</sup> | Emily K. Schworer<sup>1</sup> | Jamie C. Peven<sup>3</sup> | Matthew Zammit<sup>1,4</sup> |  
William Klunk<sup>3</sup> | Charles Laymon<sup>5,6</sup> | Davneet Minhas<sup>5</sup> | Weiquan Luo<sup>5</sup> |  
Shahid Zaman<sup>7</sup> | Beau Ances<sup>8</sup> | Gregory Preboske<sup>9</sup> | Bradley T. Christian<sup>1,4</sup> |  
the Alzheimer Biomarker Consortium – Down Syndrome



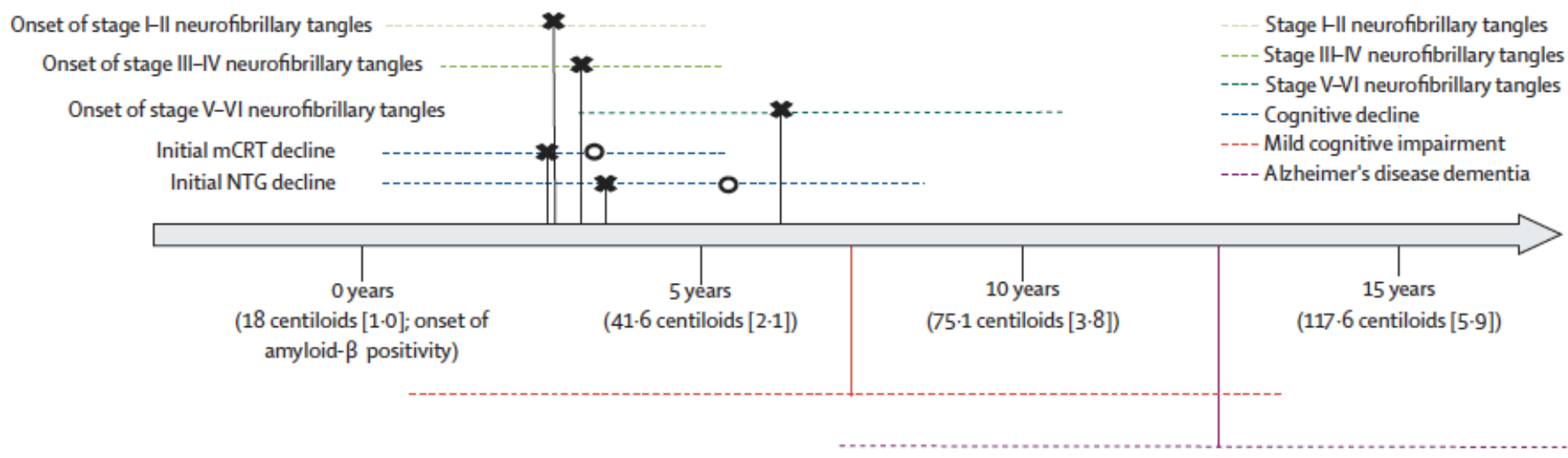
Alzheimers Dement.  
2024;20:366



## Timeline to symptomatic Alzheimer's disease in people with Down syndrome as assessed by amyloid-PET and tau-PET: a longitudinal cohort study

Emily K Schworer\*†, Matthew D Zammit\*†, Jiebiao Wang, Benjamin L Handen, Tobey Betthausen, Charles M Laymon, Dana L Tudorascu, Annie D Cohen, Shahid H Zaman, Beau M Ances, Mark Mapstone, Elizabeth Head, Bradley T Christian, Sigan L Hartley, for the Alzheimer's Biomarker Consortium-Down Syndrome (ABC-DS)

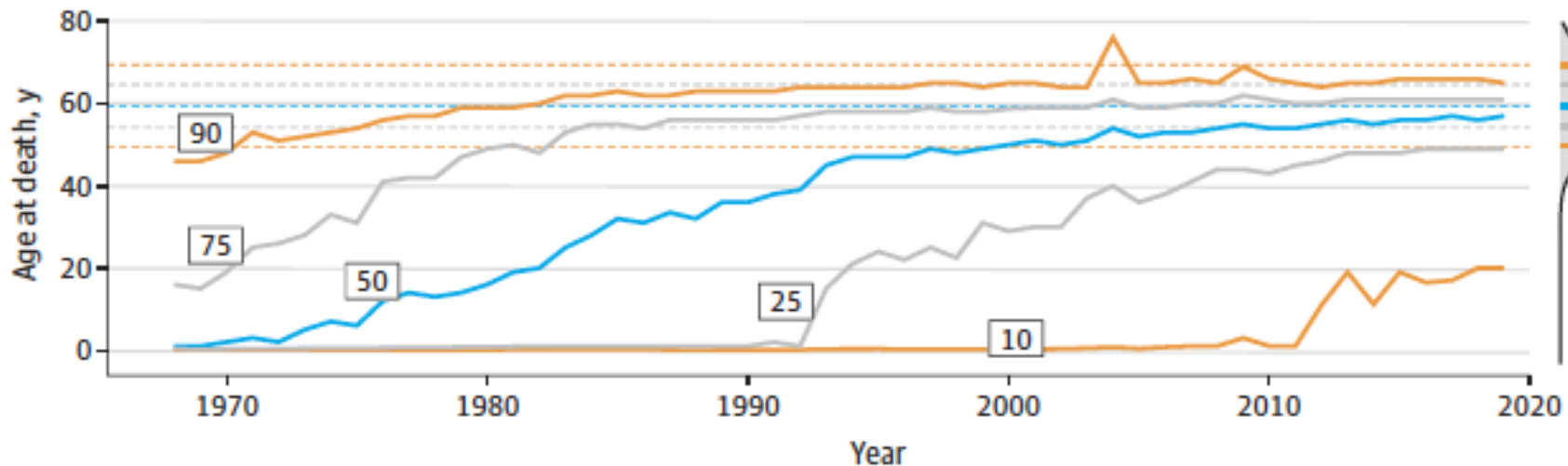
**Lancet Neurol 2024; 23:1214**



## Association of Alzheimer Disease With Life Expectancy in People With Down Syndrome

Maria Florencia Iulita, PhD; Diana Garzón Chavez, RN; Maria Klitgaard Christensen, PhD; Natalia Valle Tamayo, MSc; Oleguer Plana-Ripoll, PhD; Sonja A. Rasmussen, MD; Marta Roqué Figuls, PhD; Daniel Alcolea, MD; Laura Videla, MSc; Isabel Barroeta, MD; Bessy Benejam, MSc; Miren Altuna, MD; Concepción Padilla, PhD; Jordi Pegueroles, MSc; Susana Fernandez, MD; Olivia Belbin, PhD; María Carmona-Iragui, MD; Rafael Blesa, MD; Alberto Lleó, MD; Alexandre Bejanin, PhD; Juan Fortea, MD

**B** CDC mortality data




JAMA Network Open 2022;5(5):e2212910



**TABLE 4** Multivariate analysis of predictors of mortality in adults with Down syndrome.

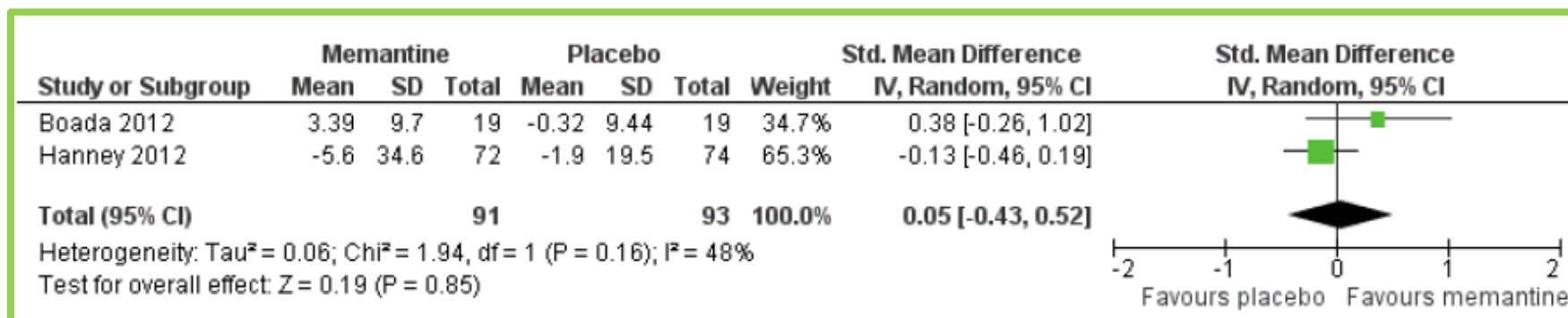
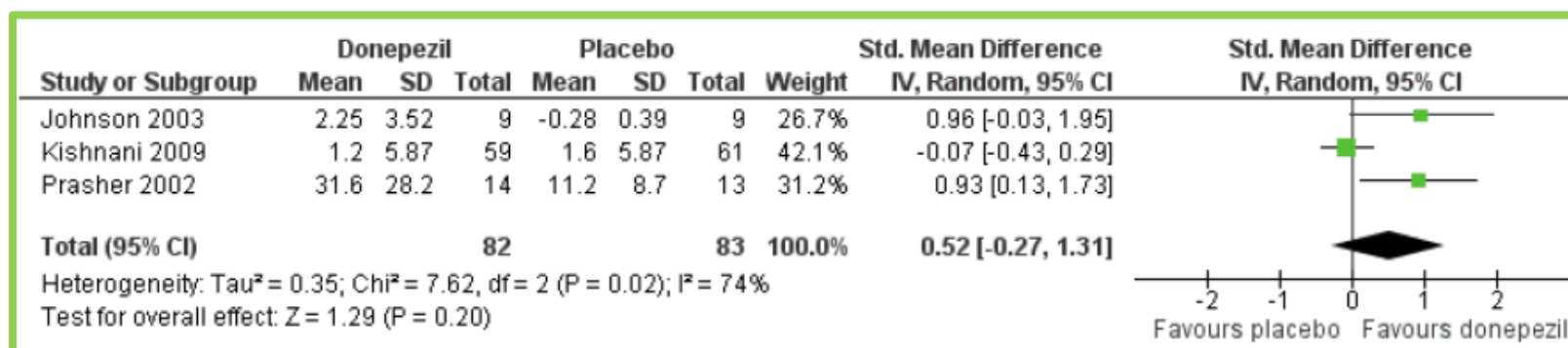
Variable	OR	CI	p
Age	1.03	1.02-1.03	<.001
Charlson comorbidity index	1.20	1.13-1.27	<.001
Dementia	0.91	0.72-1.13	.40
Epilepsy	1.52	1.32-1.74	<.001
Congenital heart disease	2.01	1.68-2.39	<.001
Bed-confined	2.31	1.46-3.62	<.001
Gross aspiration	2.59	2.20-3.04	<.001
Dysphagia	0.71	0.48-1.04	.09
Gastrostomy	2.26	1.39-3.64	<.001
Cancer	2.79	2.07-3.75	<.001
Heart failure	1.95	1.53-2.46	<.001
Acute myocardial infarction	2.04	1.27-3.22	.01
Cerebrovascular disease	2.95	2.30-3.77	<.001
Anaemia	1.30	1.08-1.57	.001
Readmission <30 days	2.43	2.06-2.86	<.001
Readmission in 30-60 days	1.66	1.27-2.16	<.001
Readmission in 60-90 days	1.37	0.96-1.91	.07
Readmission in 90-180 days	1.78	1.38-2.27	<.001
Readmission in 180-365 days	1.20	0.94-1.53	.12
Readmission >1 year	1.19	1.01-1.41	.04

## Analysis of the circumstances associated with death and predictors of mortality in Spanish adults with Down syndrome, 1997-2014

Paloma Aparicio<sup>1</sup> | Alberto Alonso-Babarro<sup>2</sup> | Raquel Barba<sup>3</sup> |  
Fernando Moldenhauer<sup>4</sup> | Carmen Suárez<sup>4</sup> | Diego Real de Asúa<sup>4,5</sup> 

**J Appl Res Intellect Disabil.**  
**2024;37:e13187**

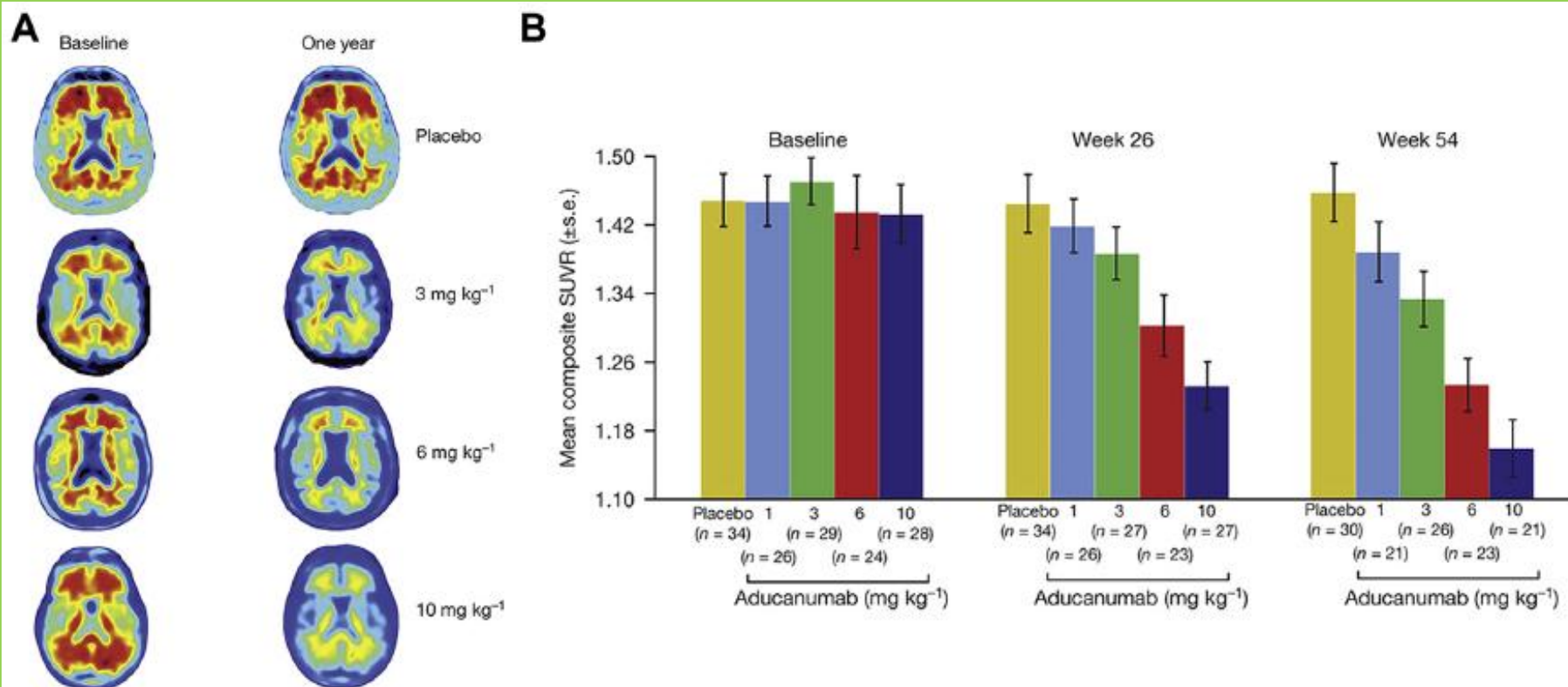
# ¿Sirven los tratamientos habituales?



Cochrane Database Syst Rev. 2015;2015(10):CD011546

# The antibody aducanumab reduces A $\beta$ plaques in Alzheimer's disease

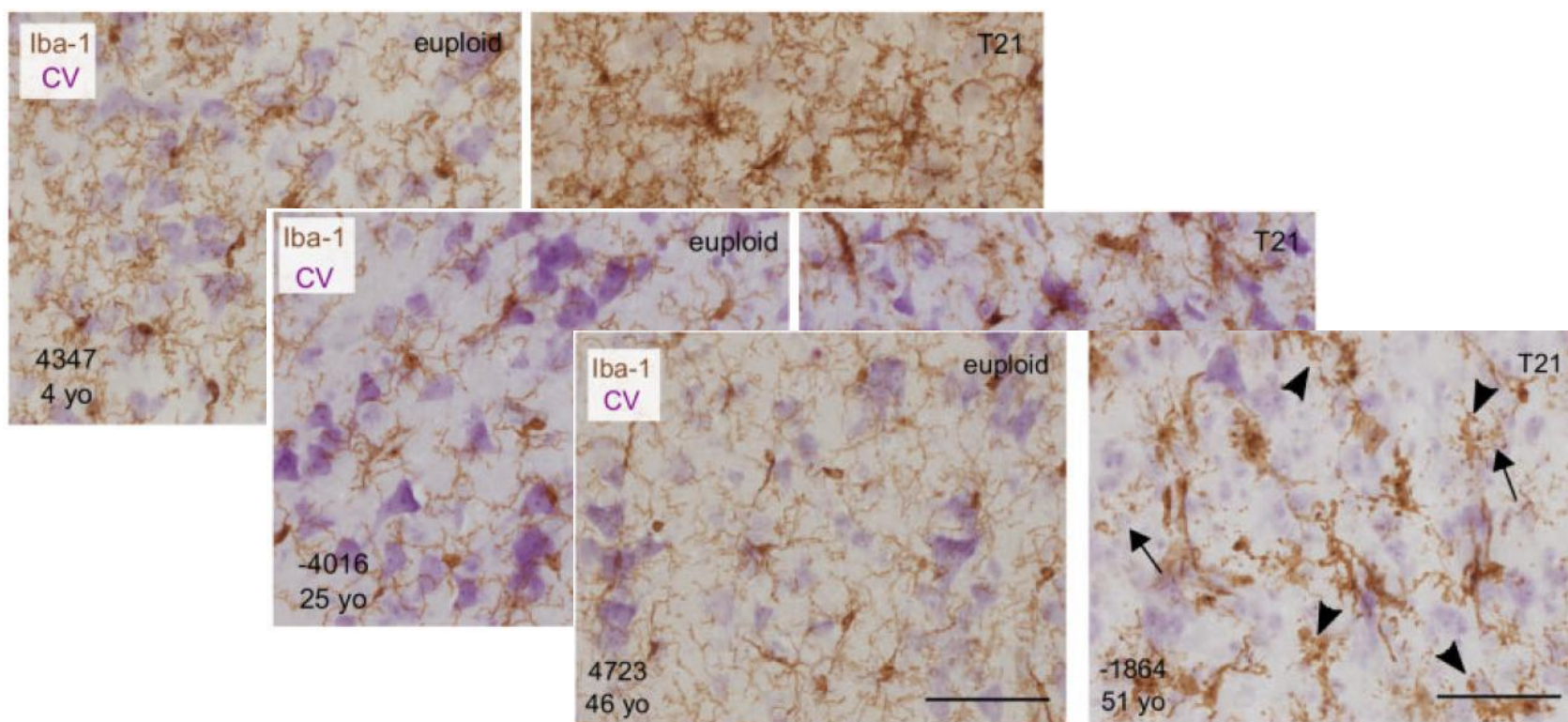
Jeff Sevigny<sup>1\*</sup>, Ping Chiao<sup>1\*</sup>, Thierry Bussière<sup>1\*</sup>, Paul H. Weinreb<sup>1\*</sup>, Leslie Williams<sup>1</sup>, Marcel Maier<sup>2</sup>, Robert Dunstan<sup>1</sup>, Stephen Salloway<sup>3</sup>, Tianle Chen<sup>1</sup>, Yan Ling<sup>1</sup>, John O'Gorman<sup>1</sup>, Fang Qian<sup>1</sup>, Mahin Arastu<sup>1</sup>, Mingwei Li<sup>1</sup>, Sowmya Chollate<sup>1</sup>, Melanie S. Brennan<sup>1</sup>, Omar Quintero-Monzon<sup>1</sup>, Robert H. Scannevin<sup>1</sup>, H. Moore Arnold<sup>1</sup>, Thomas Engber<sup>1</sup>, Kenneth Rhodes<sup>1</sup>, James Ferrero<sup>1</sup>, Yaming Hang<sup>1</sup>, Alvydas Mikulskis<sup>1</sup>, Jan Grimm<sup>2</sup>, Christoph Hock<sup>2,4</sup>, Roger M. Nitsch<sup>2,4</sup>§ & Alfred Sandrock<sup>1</sup>§



**Nature. 2016;537:50**

Lisi Flores-Aguilar,<sup>1</sup> M. Florencia Iulita,<sup>2,3,4</sup> Olivia Kovacs,<sup>2</sup> Maria D. Torres,<sup>5</sup>  
Sarah M. Levi,<sup>2</sup> Yian Zhang,<sup>6</sup> Manor Askenazi,<sup>7</sup> Thomas Wisniewski,<sup>8</sup>  
Jorge Busciglio<sup>5</sup> and A. Claudio Cuello<sup>1,2,9,10</sup>

## ¿Todo es culpa del amiloide?



Brain. 2020;143:3653

# Desafíos en investigación con personas con SD



**Lancet. 2024;403:1830**



# Conclusiones

- Los adultos con SD son una población creciente con necesidades específicas de salud
- La EA es uno de los grandes retos de esta población (frecuencia, precocidad, dificultad diagnóstico y consecuencias)
- Actualmente no disponemos de tratamientos efectivos, pero intenso trabajo en este campo
- La participación de pacientes, familiares y asociaciones en investigación será crucial para superar barreras



**¡Muchas gracias!**  
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