



Segno: "Vedere gli infermi, vederli - Chiesa dell'Immacolata, Pistoia"



Fondazione
Caript

15° CONVEGNO NAZIONALE SUI CENTRI DIURNI ALZHEIMER



GRUPPO ITALIANO
CENTRI DIURNI
ALZHEIMER



Fondazione
Caript

10-11 ottobre 2025

**Diagnosi e terapie biologiche della
Malattia di Alzheimer, tra presente e
futuro: cosa cambia per le persone?**

Marco Canevelli, MD, PhD

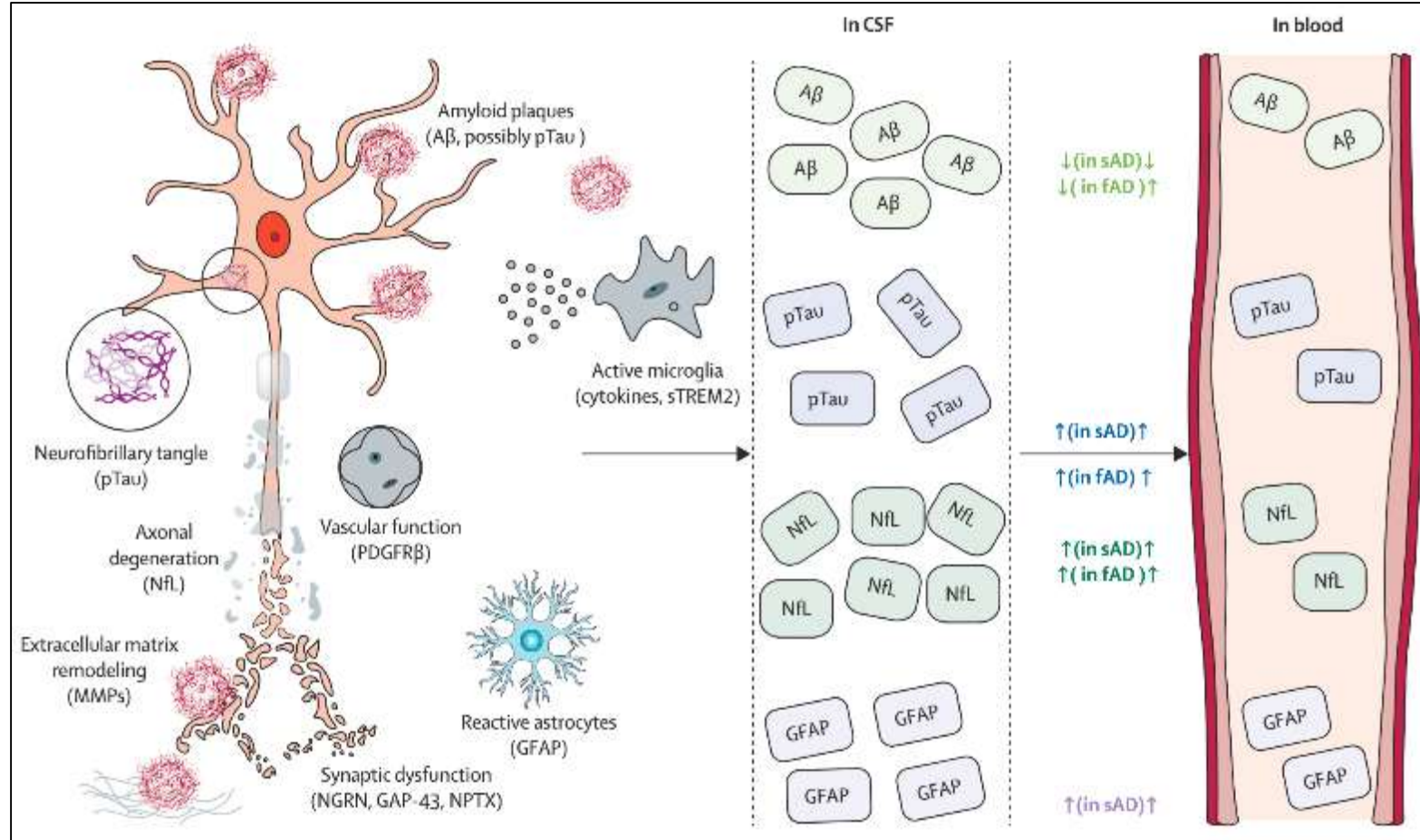
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SAPIENZA
UNIVERSITÀ DI ROMA



Diagnosi biologica di malattia di Alzheimer



Diagnosi biologica di malattia di Alzheimer

Quante persone?

Clinical Review & Education

JAMA Internal Medicine | Special Communication

Guidance for Modifying the Definition of Diseases A Checklist

Jenny Doust, MBBS, PhD; Per O. Vandvik, PhD; Amir Qaseem, MD, PhD; Reem A. Mustafa, MD, PhD; Andrea R. Horvath, MD, PhD; Allen Frances, MD; Lubna Al-Ansary, MBBS, MSc; Patrick Bossuyt, PhD; Robyn L. Ward, MBBS, PhD; Ina Koop, MD; Laragh Golligly, MD, MPH; Holger Schunemann, MD, PhD; Paul Glasziou, MBBS, PhD, for the Guidelines International Network (G-I-N) Preventing Overdiagnosis Working Group

Figure 2. How a New Disease Definition May Impact Disease Prevalence

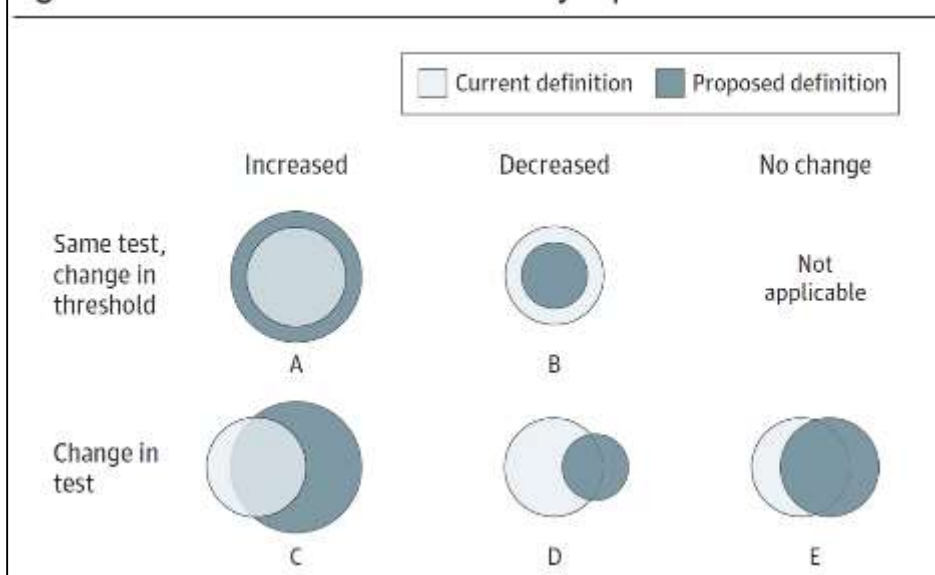



Table 1. Changes in Disease Definitions and Prevalence of a Condition

Condition	Population	Previous Definition	Old Definition Prevalence, %	New Definition	New Definition Prevalence, %
Osteoporosis	Community sample of US women aged >65 years ⁷	Femoral neck BMD T-score of -2.5 or less	21	NOF 2008 guideline	72
Myocardial infarction	Patients presenting to hospital with a troponin level measure ≥ 30 ng/L ⁸	WHO criteria using MB fraction of creatine kinase	18	ESC/ACC 2000 criteria using troponin	29
Polycystic ovary syndrome	Sample of women aged 12-44 years in China ⁹	NIH criteria	7	Rotterdam criteria	11
Prediabetes	Survey of adults aged >18 years in China ¹⁰	Impaired fasting glucose	26	ADA 2010 criteria	50
	NHANES survey of adults ≥ 18 years in the United States ¹¹	Impaired fasting glucose	26	ADA 2010 criteria	31

Diagnosi biologica di malattia di Alzheimer

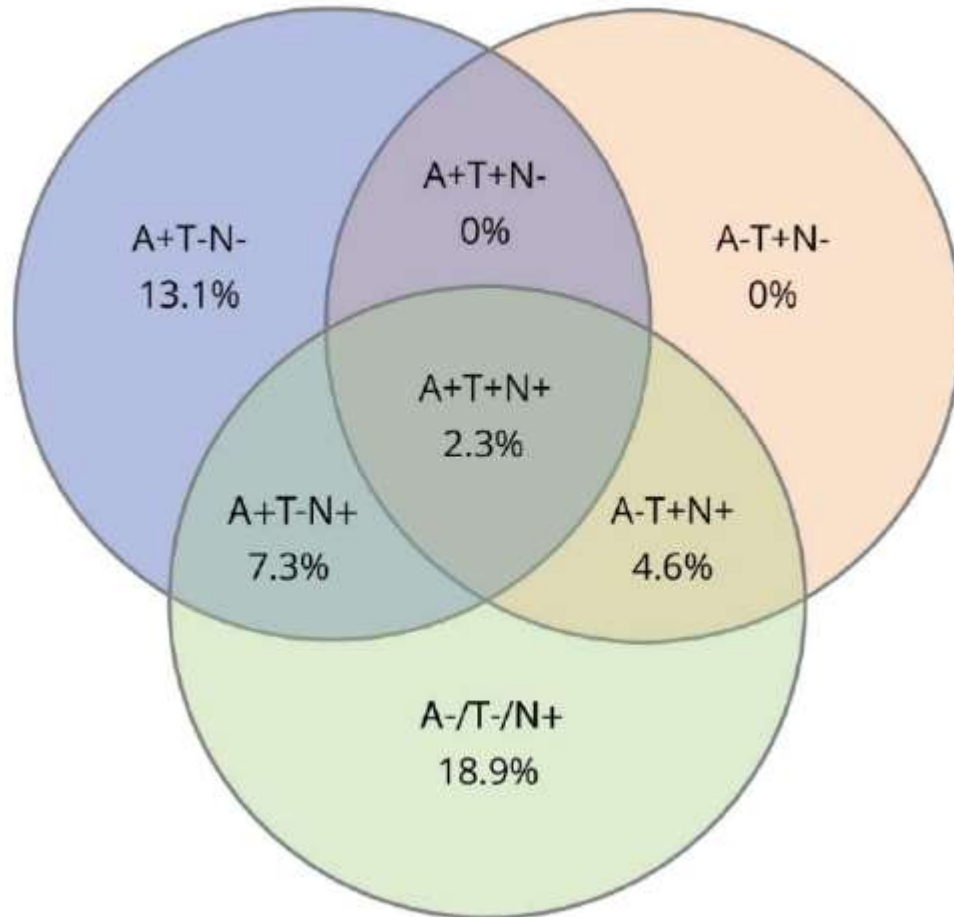
Quante persone?

<h2>Blood Pressure Categories</h2> 			
BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

“...Thirty million Americans became hypertensive overnight with the introduction of a new high blood pressure guideline from the American College of Cardiology (ACC) and American Heart Association (AHA)”

Diagnosi biologica di malattia di Alzheimer

Quante persone?



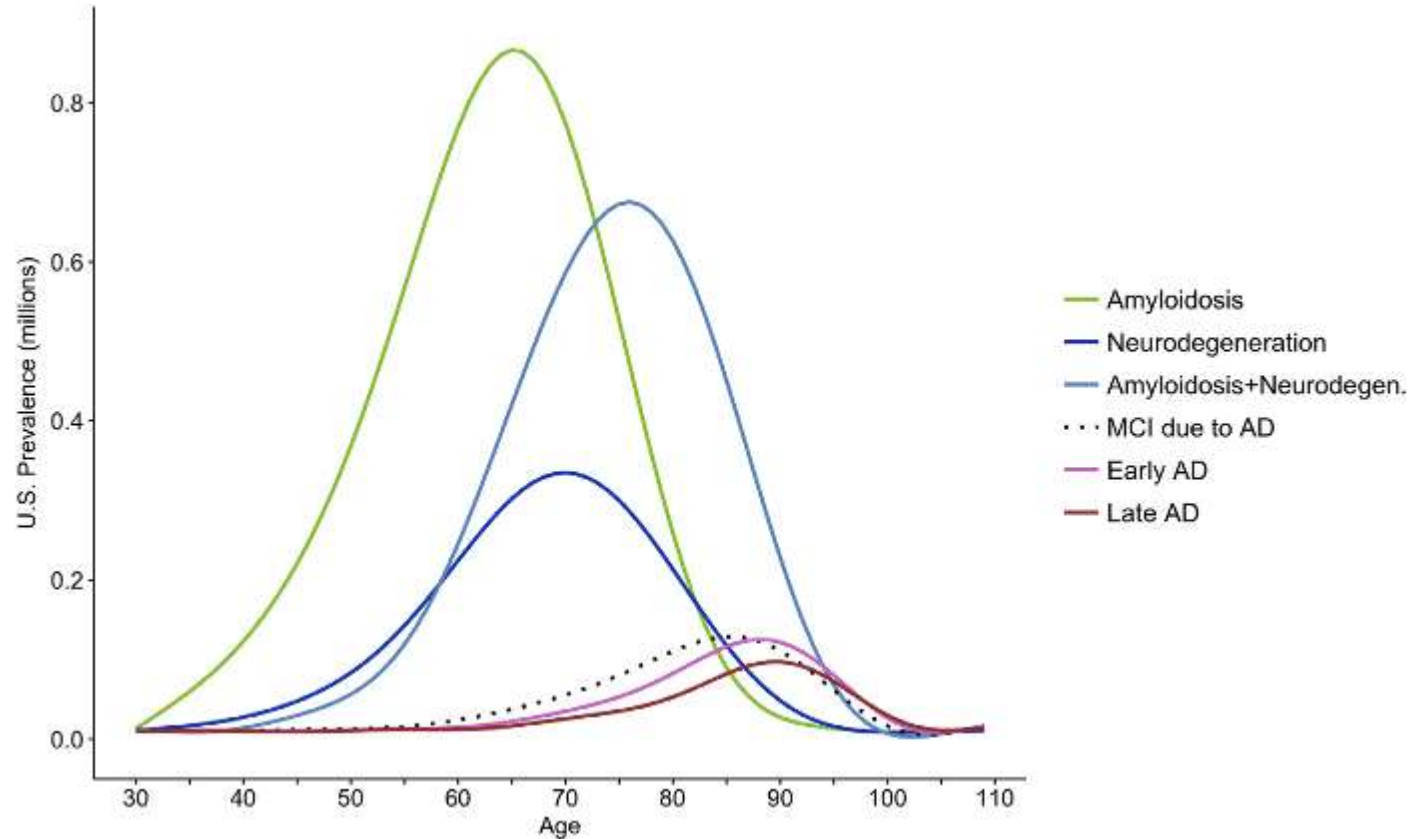
Venn diagram of the ATN distribution of amyloid and tau pathology according to the A/T/N classification scheme in a representative population-based sample of 70-year-olds (n=259) with a Clinical Dementia Rating score of 0.

Conclusion

The prevalence of pathologic AD markers was very common (46%) in a representative population sample of 70-year-olds.

Diagnosi biologica di malattia di Alzheimer

Quante persone?

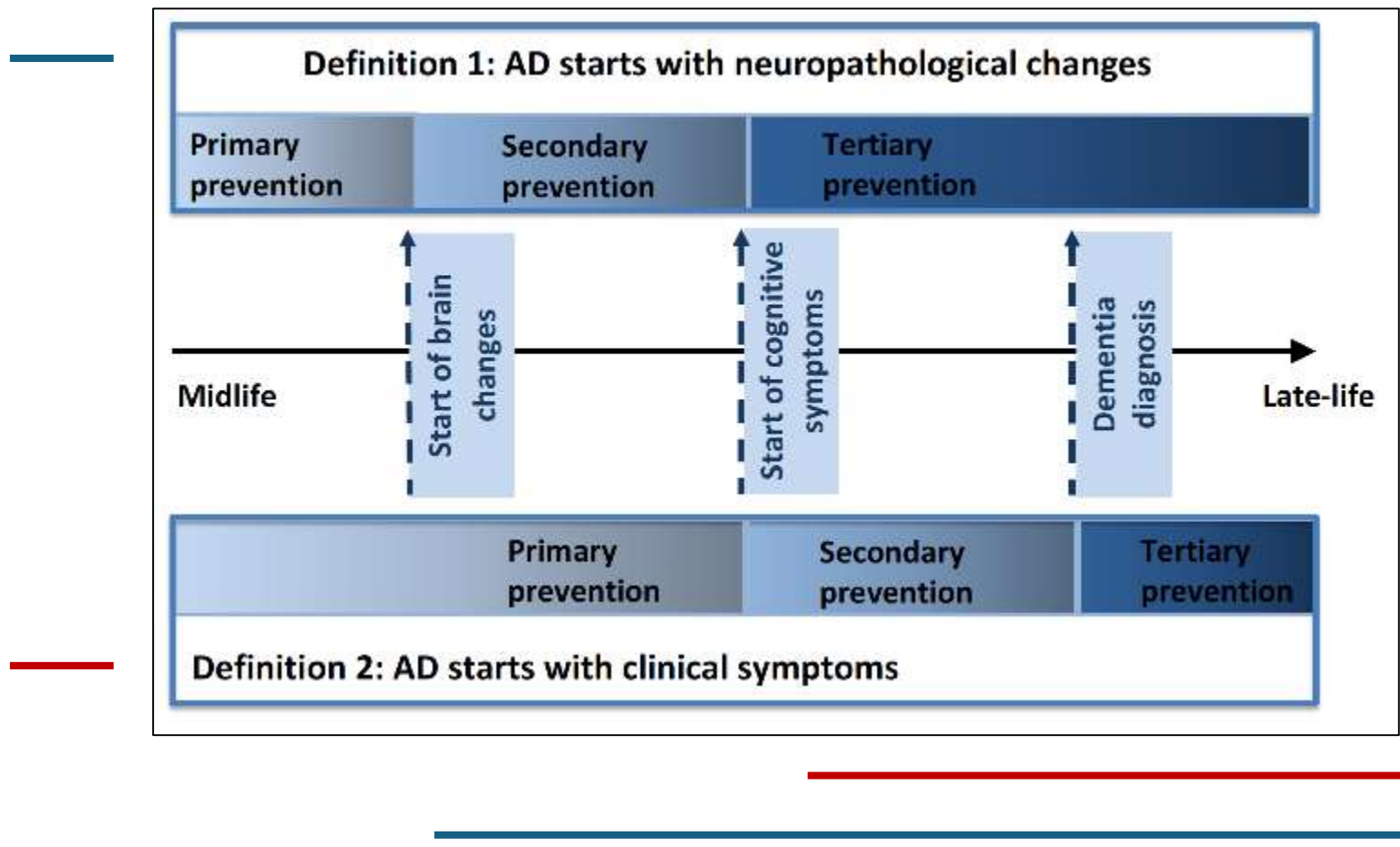


Approximately **6.08 million** Americans had either **clinical AD** or mild cognitive impairment due to AD in 2017 and that will grow to 15.0 million by 2060. In 2017, **46.7 million** Americans had **preclinical AD** (amyloidosis, neurodegeneration, or both), although many may not progress to clinical disease during their lifetimes.

Brookmeyer R et al., Alzheimers Dement. 2018;14:121-

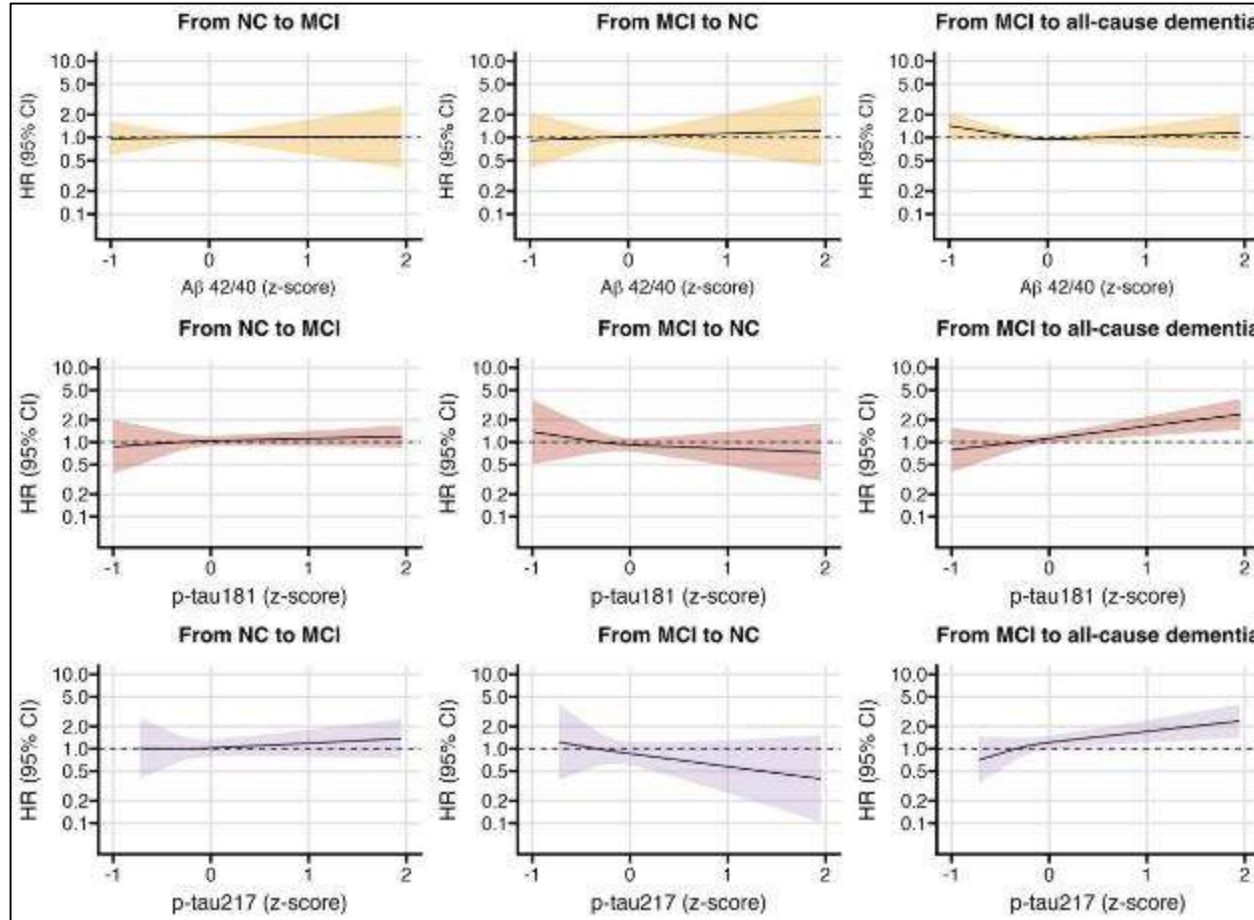
Diagnosi biologica di malattia di Alzheimer

Che impatto sulla durata di malattia?



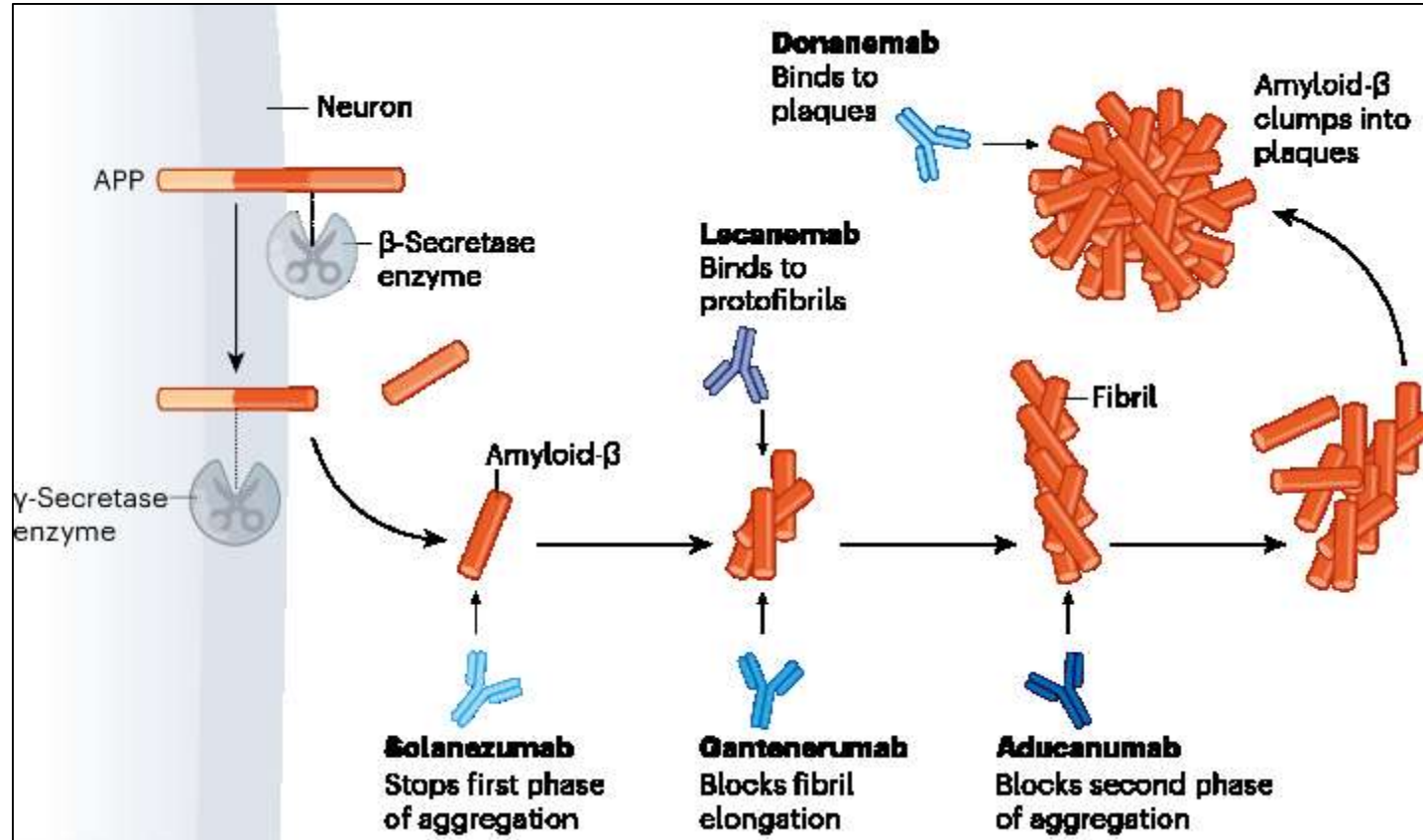
Diagnosi biologica di malattia di Alzheimer

Quali persone?



Valletta M et al., Submitted

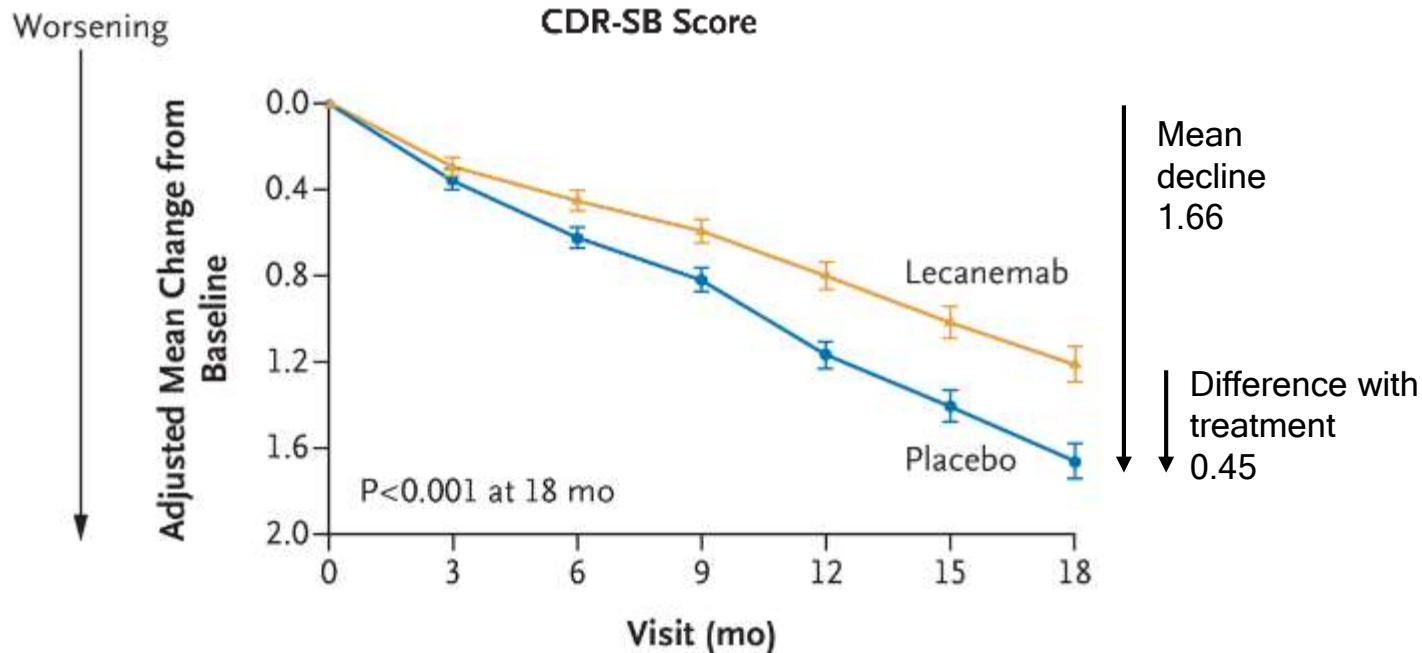
Terapie biologiche per la malattia di Alzheimer



Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

Minimal clinically important difference (MCID)



Lecanemab (CLARITY-AD):

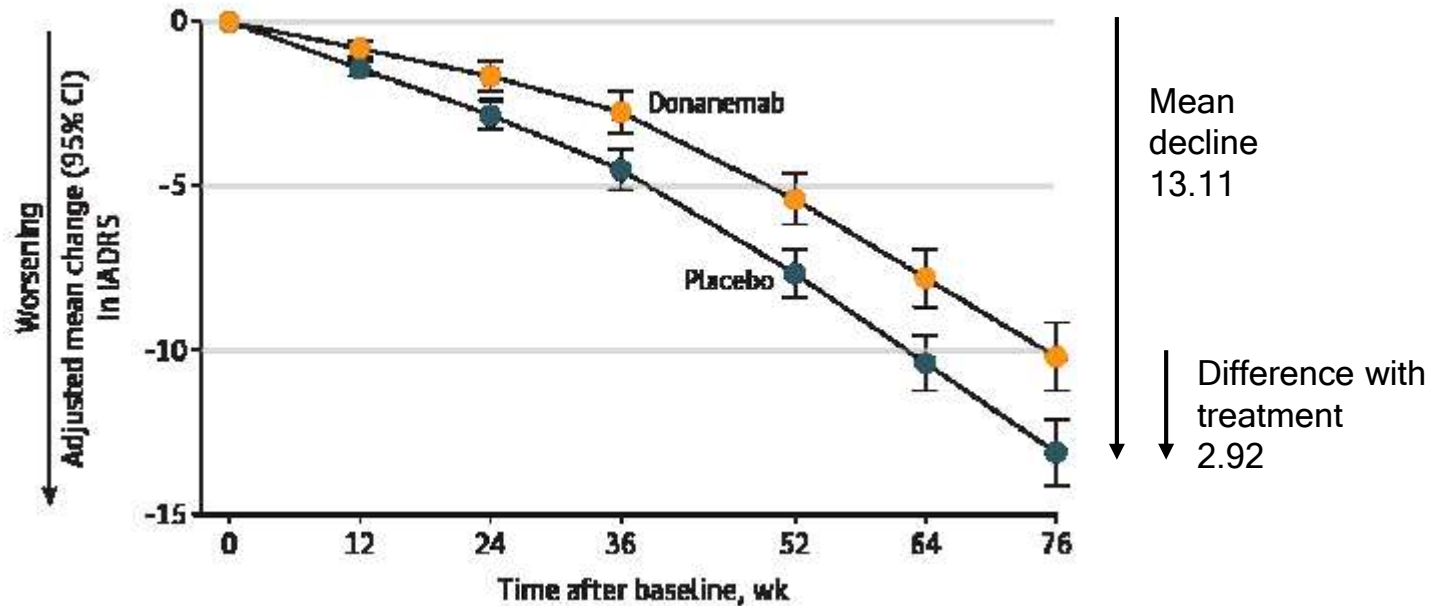
- The mean decline in placebo at 18 months on CDR-SB: +1.66 points, exceeding the MCID for MCI (+1) but not for mild AD (+2)
- The difference with treatment was **-0.45** points (27.1%) → not exceeding the MCID

Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

Minimal clinically important difference (MCID)

B IADRS in combined population



Donanemab (TRAILBLAZER-ALZ2):

- The mean decline in placebo at 18 months on iADRS: -13.11 points, exceeding the MCID for MCI (-5) and mild AD (-9)
- The difference with treatment was -2.92 points (22.3%) → not exceeding the MCID
- In the low/medium tau population, the difference with treatment was -3.25 points (35.1%) → not exceeding the MCID

Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

Minimal clinically important difference (MCID)

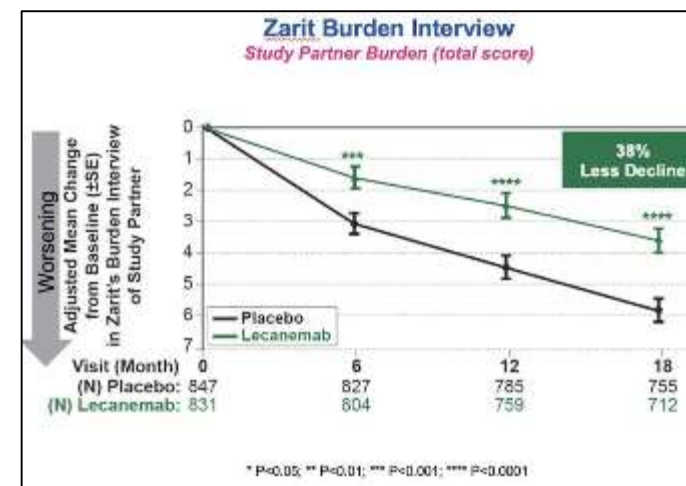
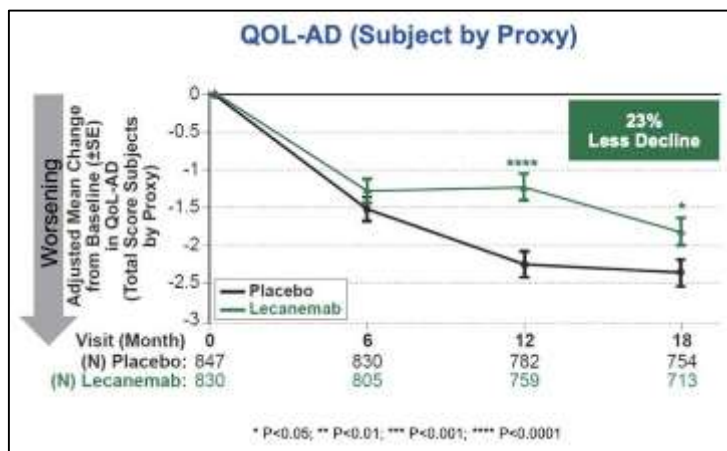
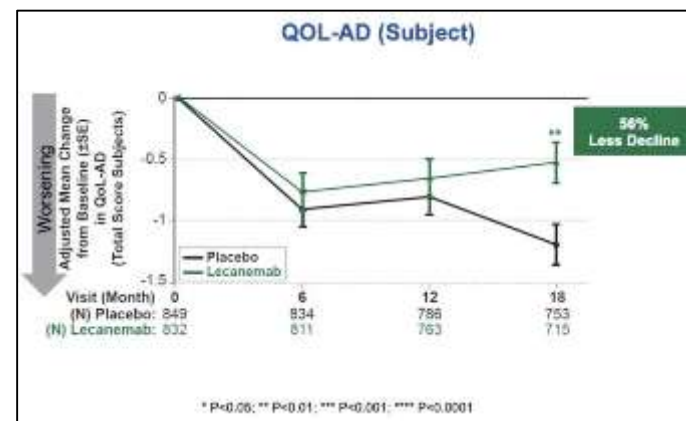
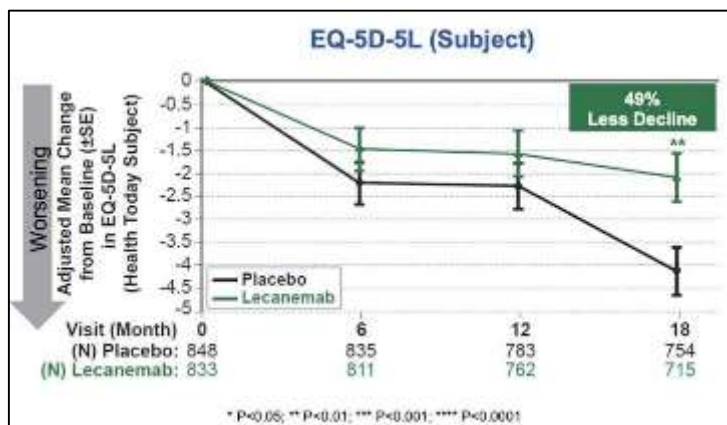
	ADAS-Cog	CDR-SB	iADRS	MMSE
MCI	+2 to +3	+1	-5	-1 to -2
Mild AD	+3	+2	-9	-2
Mod-Severe AD	--	+2	--	-1.4 to -3

The minimal clinically important difference (MCID) has been defined as the **smallest unit of change** in an outcome measure that **would be perceived** as a difference that is **clinically meaningful** for patients, caregivers, or health practitioners, and would constitute the grounds for change in a patient's care.

Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

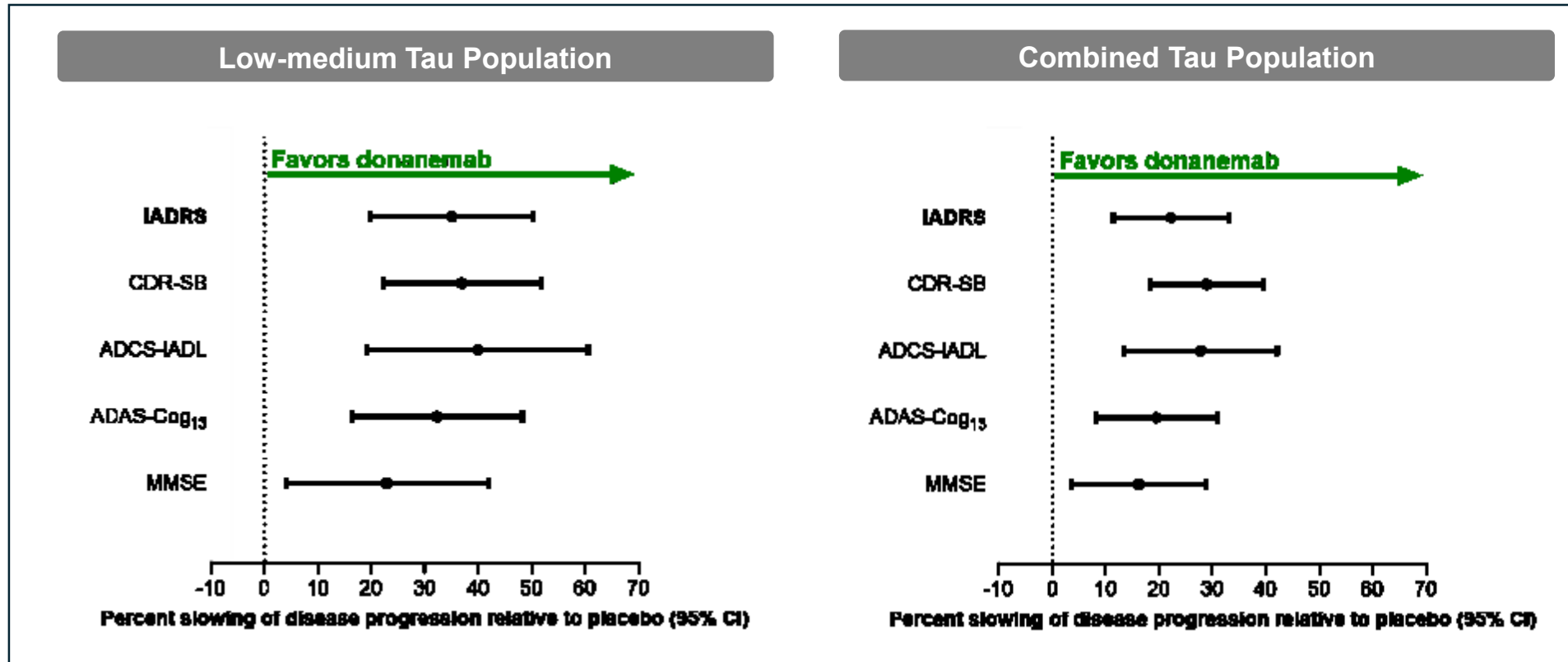
Endpoint secondari



Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

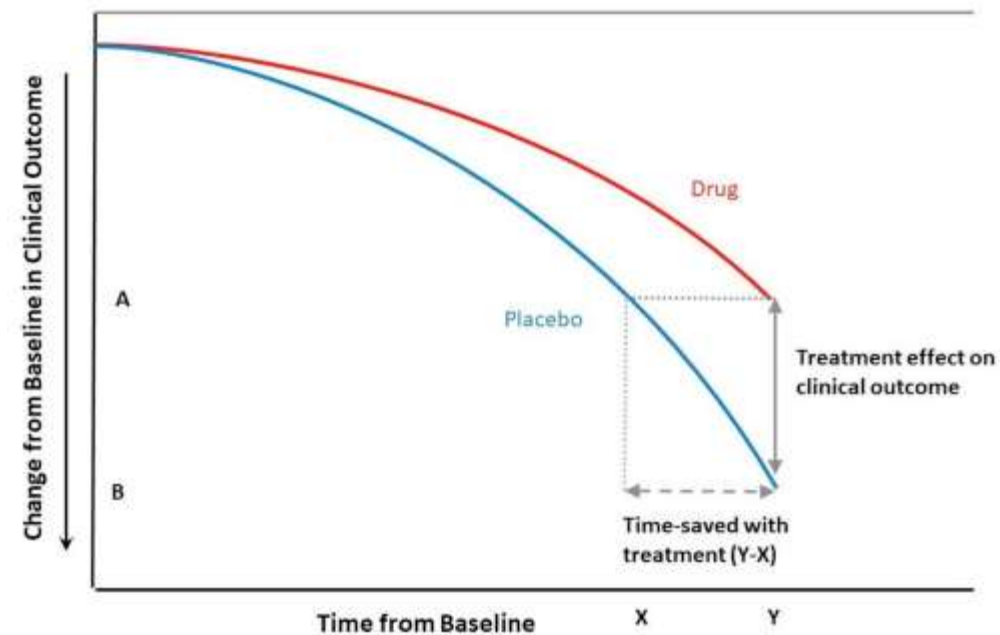
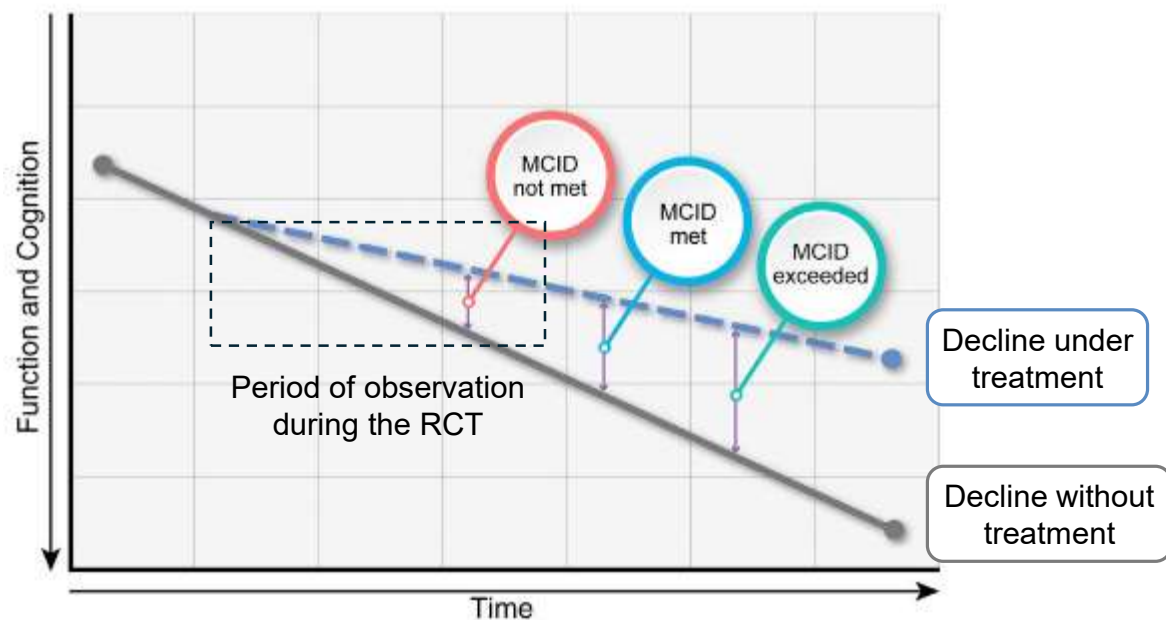
Endpoint secondari



Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

Time saved vs. MCID

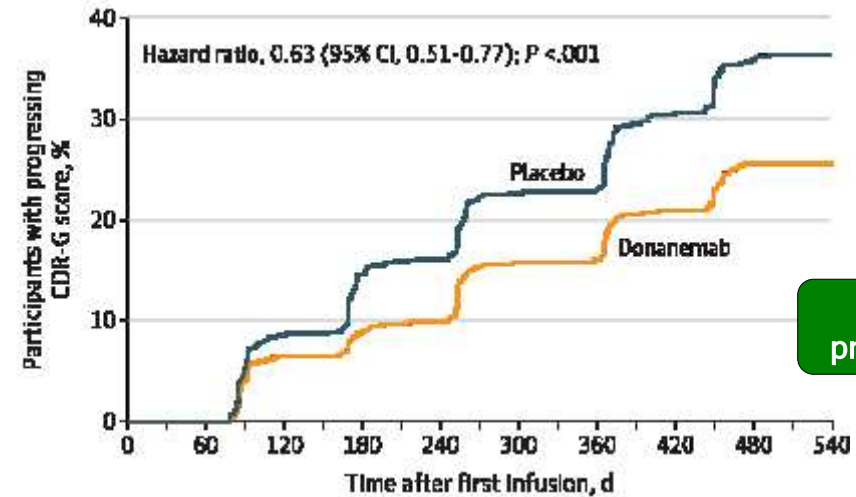
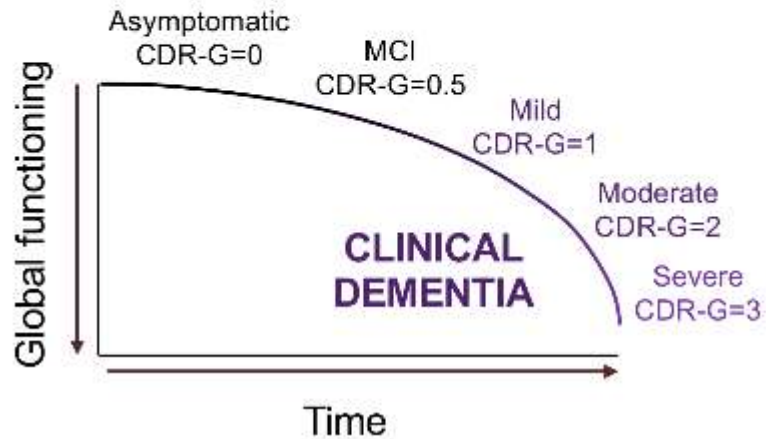


Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

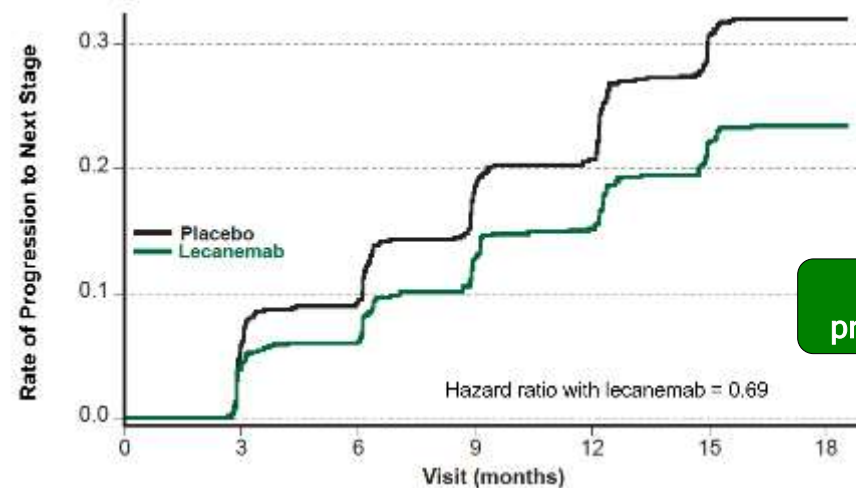
Time saved vs. MCID

Any progression on the CDR-G score means advancement to a more severe stage of AD.



Donanemab

37.4% lower risk of progression over 76 weeks



Lecanemab

32.4% lower risk of progression over 78 weeks

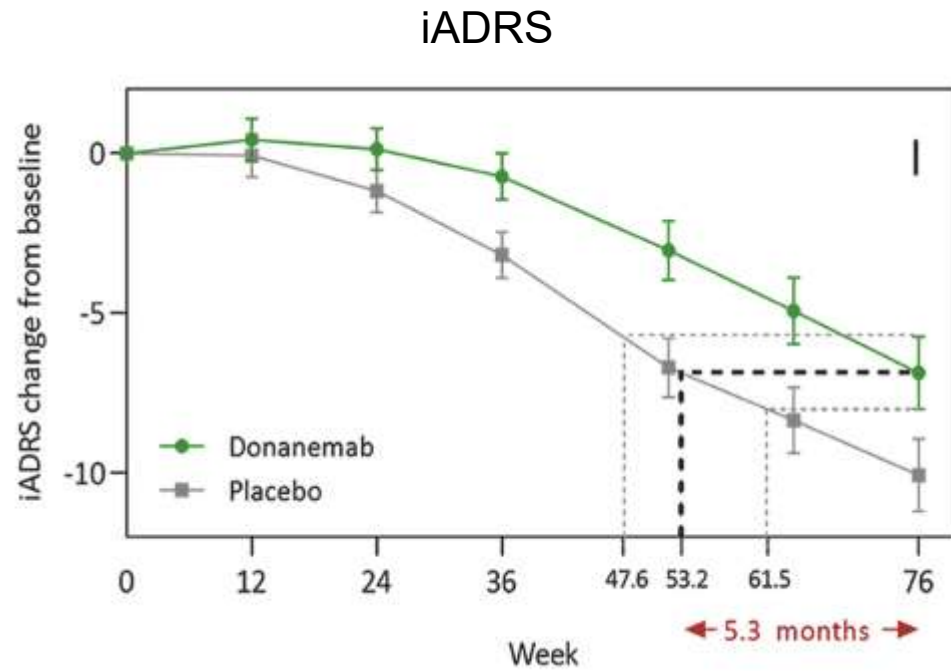
Sims JR et al., JAMA. 2023;330(6):512-527

van Dyck CH et al., N Engl J Med. 2023;388(1):9-

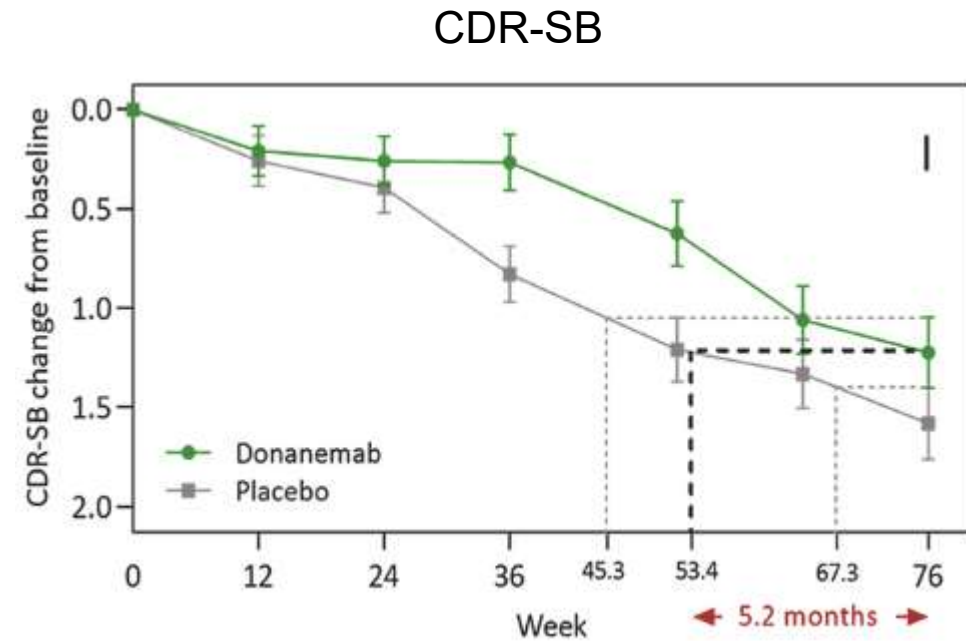
Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

Time saved vs. MCID



30% slowing

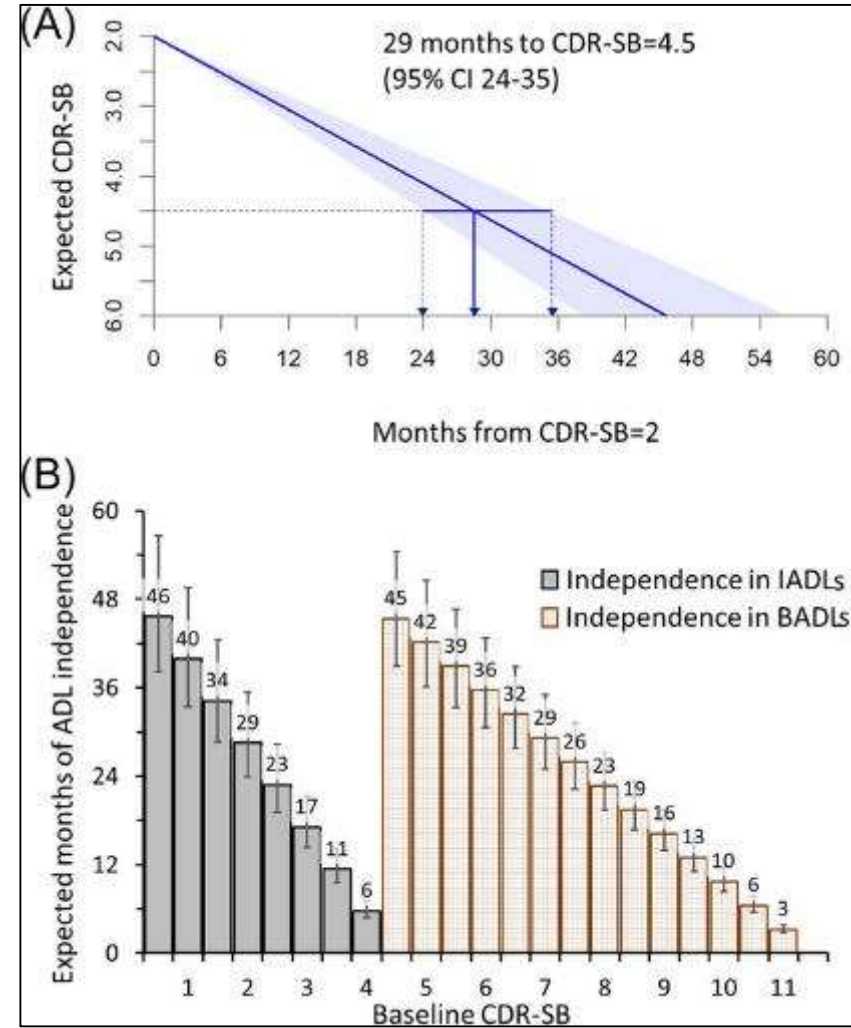
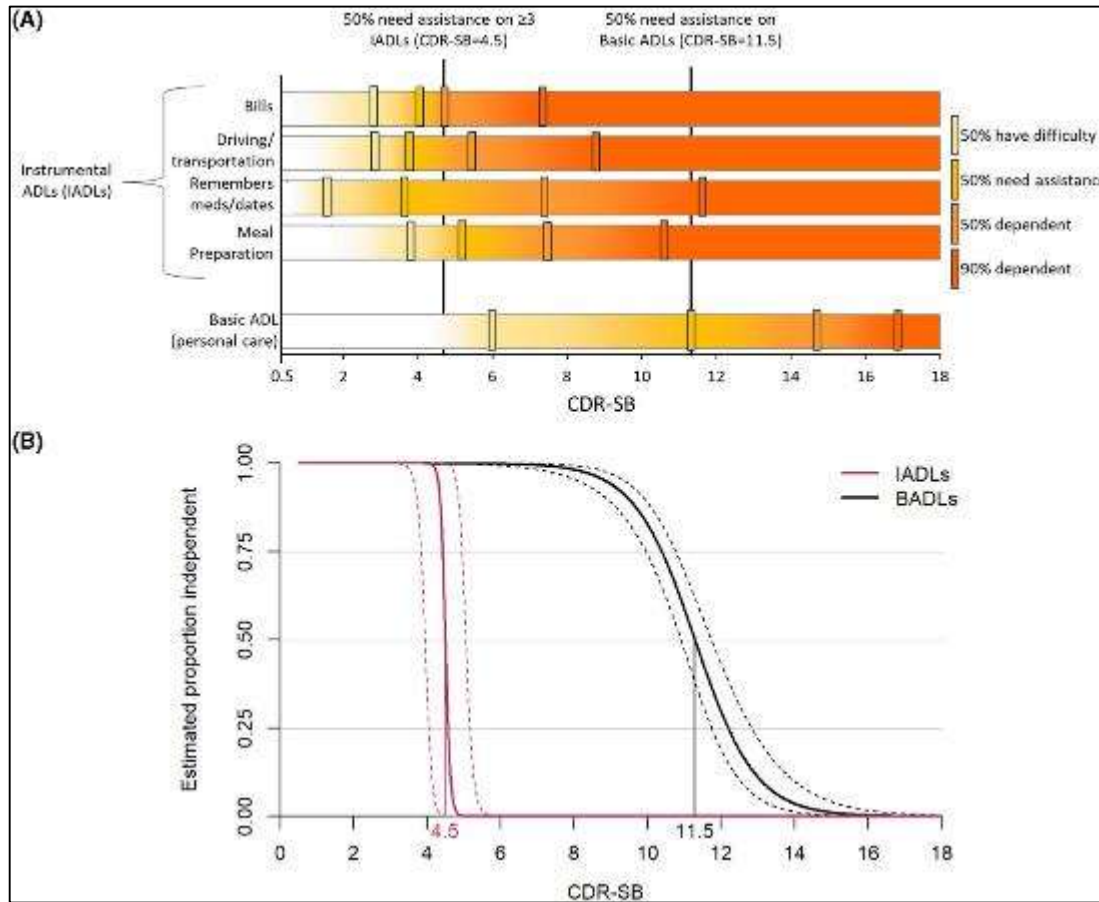


29% slowing

Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

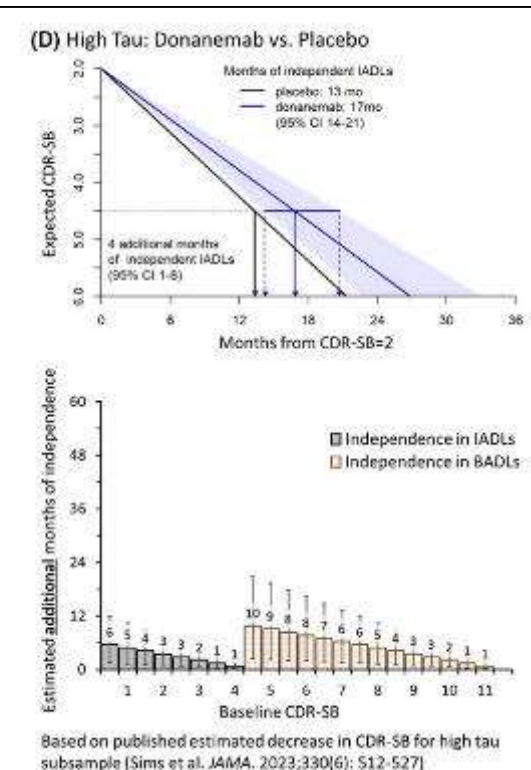
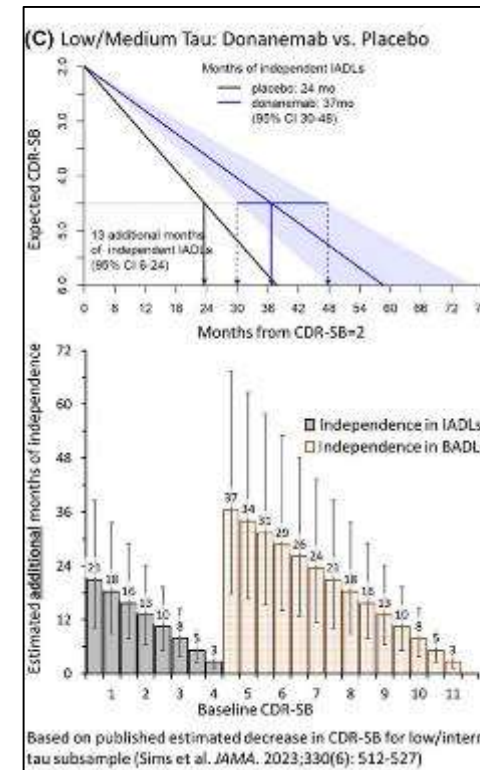
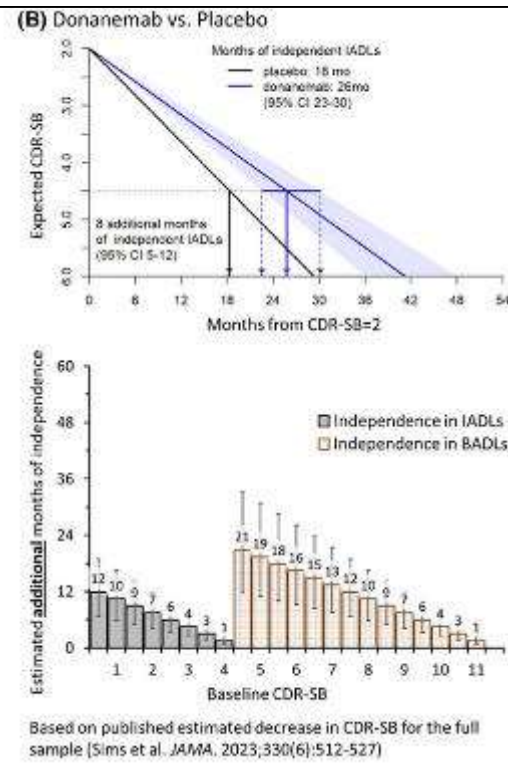
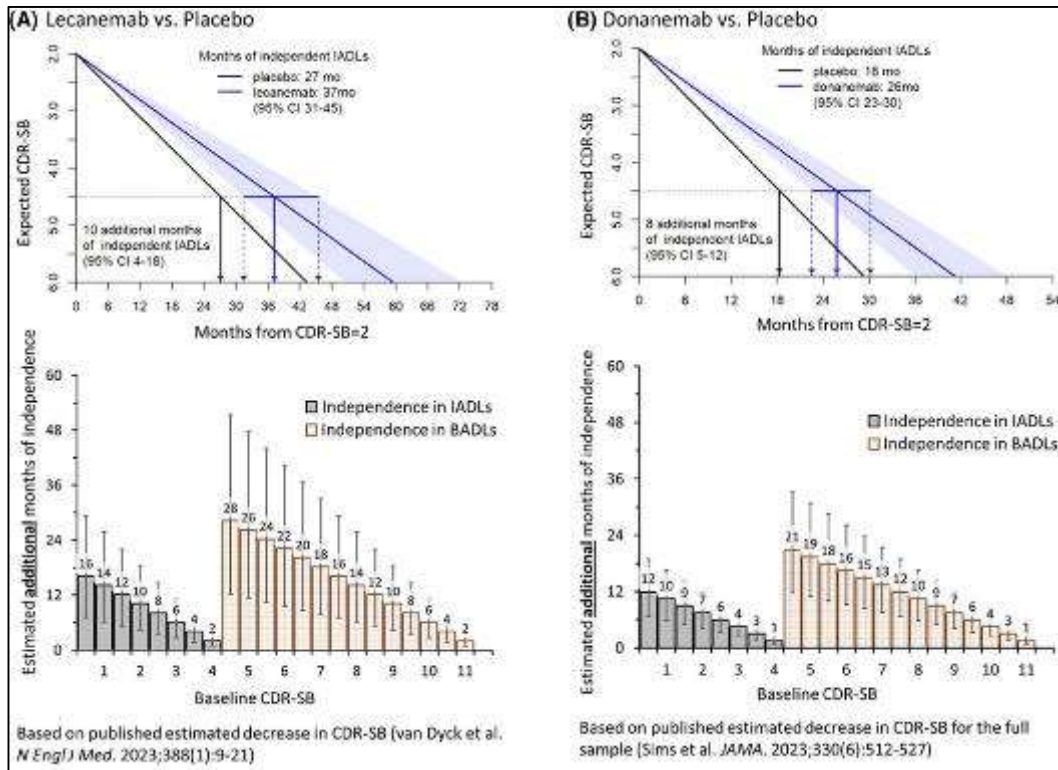
Time saved vs. MCID



Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

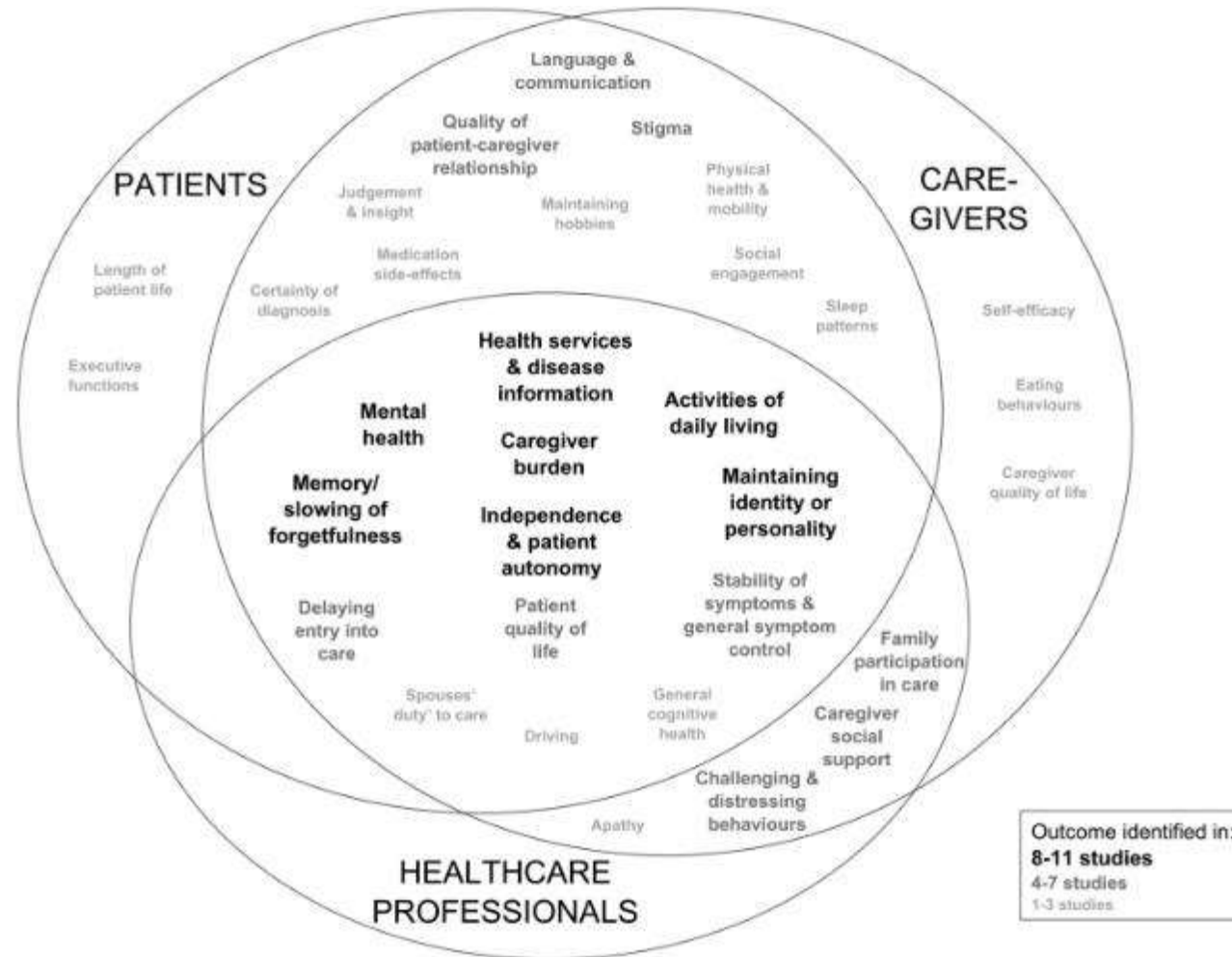
Time saved vs. MCID



Terapie biologiche per la malattia di Alzheimer

Come valutare l'efficacia?

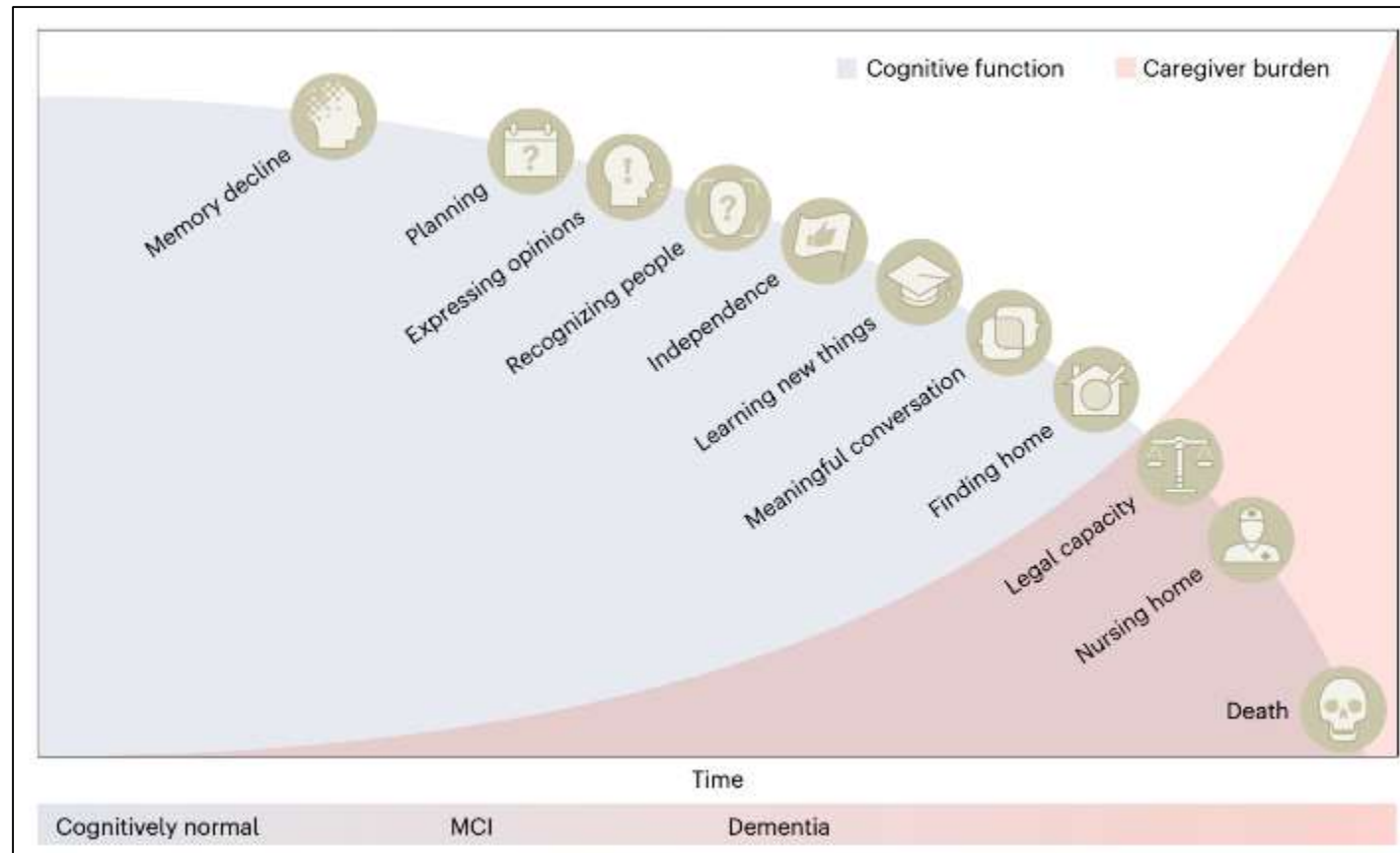
Patient Reported Outcome Measures (PROMs)



Terapie biologiche per la malattia di Alzheimer

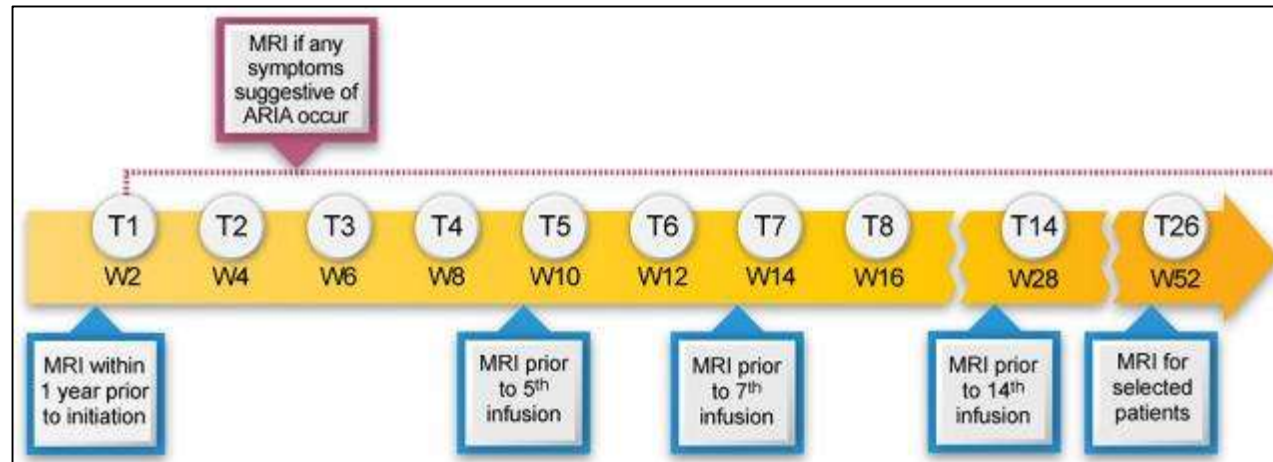
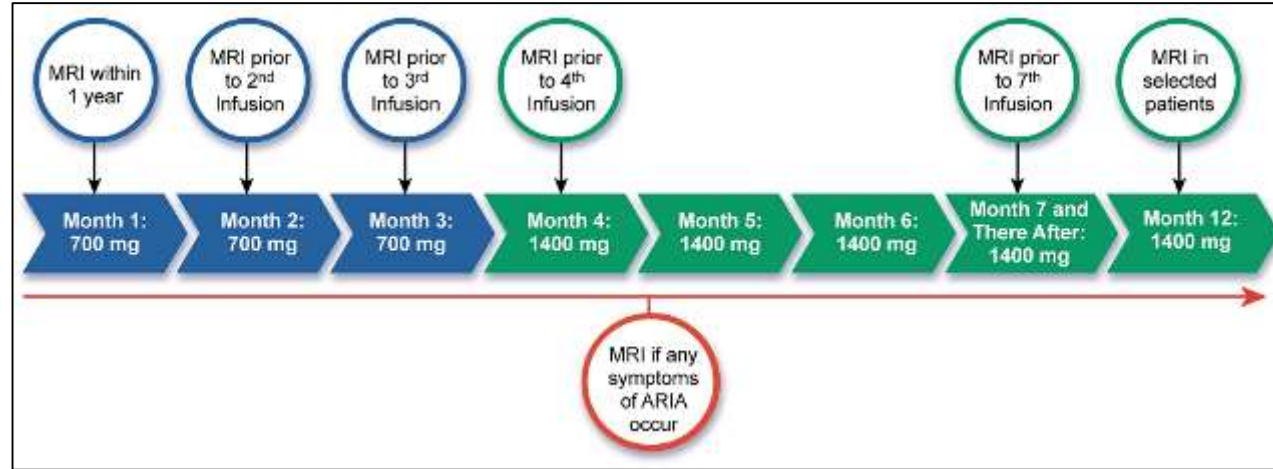
Come valutare l'efficacia?

Patient Reported Outcome Measures (PROMs)



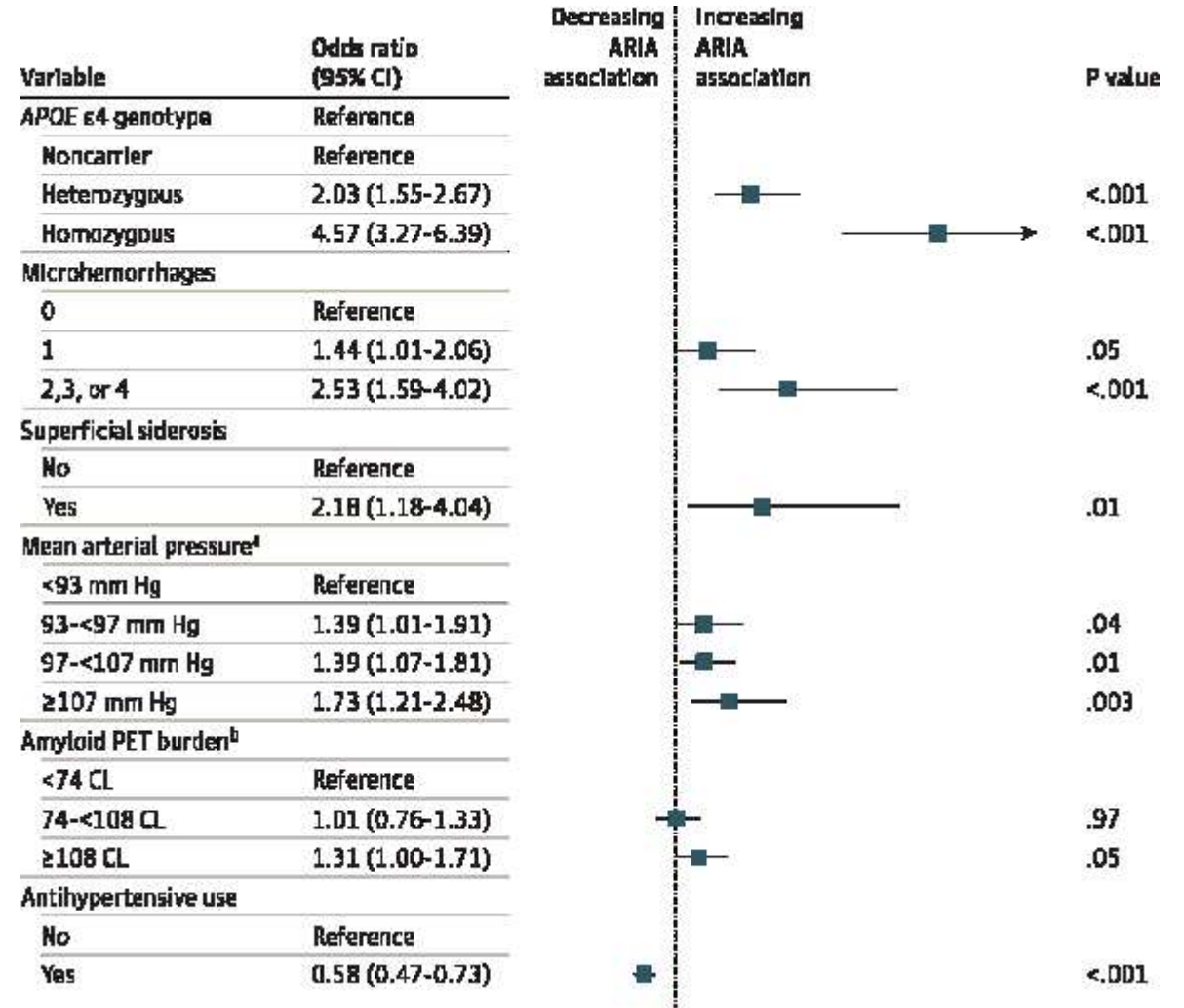
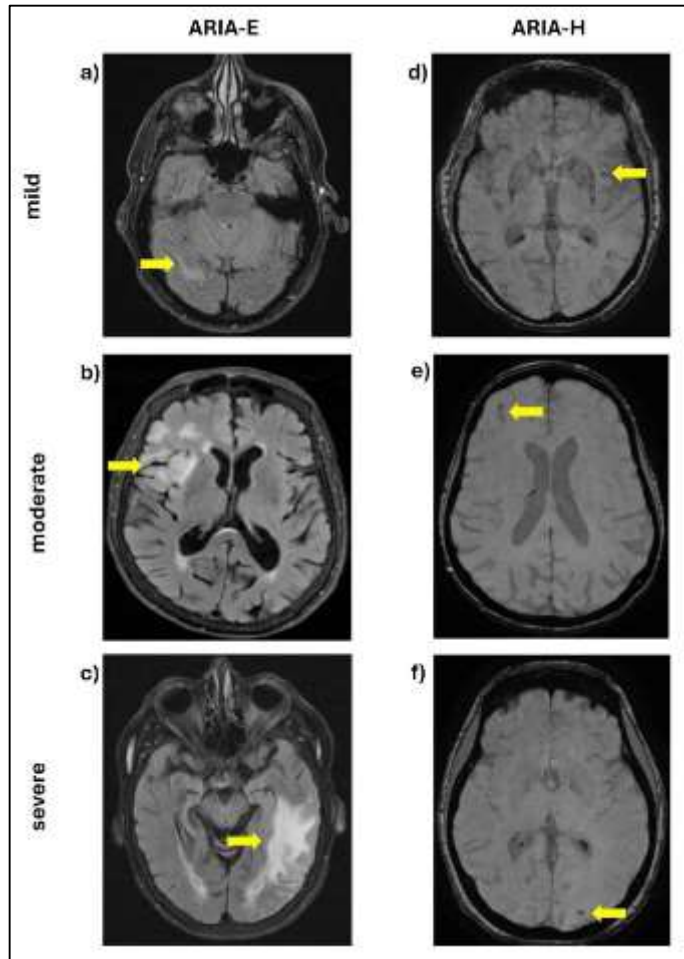
Terapie biologiche per la malattia di Alzheimer

Che impatto sul patient's journey?



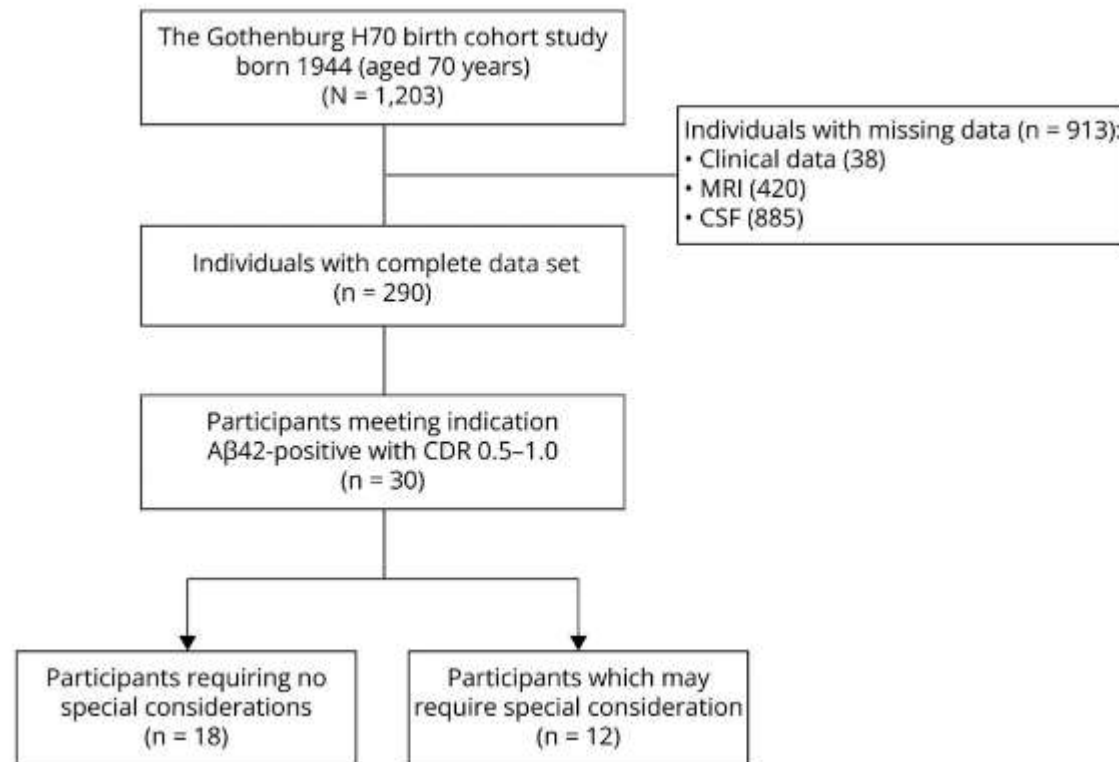
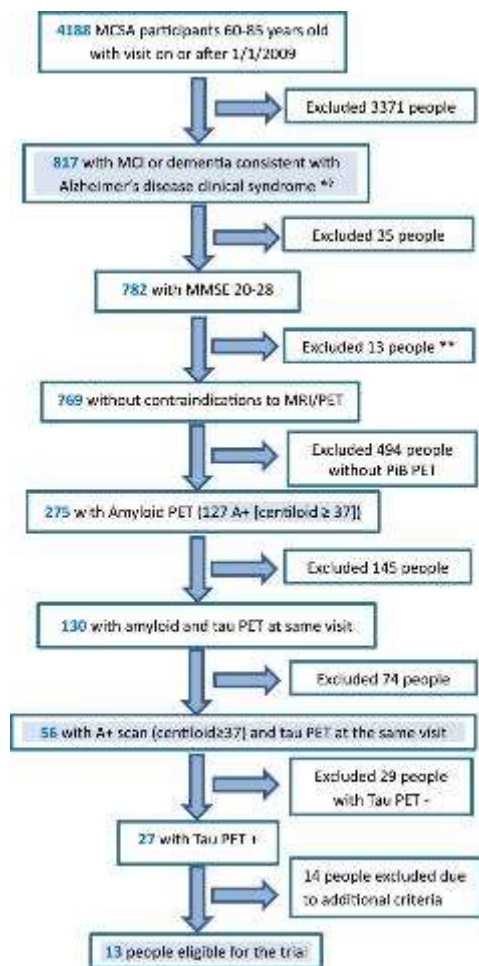
Terapie biologiche per la malattia di Alzheimer

Quali rischi?



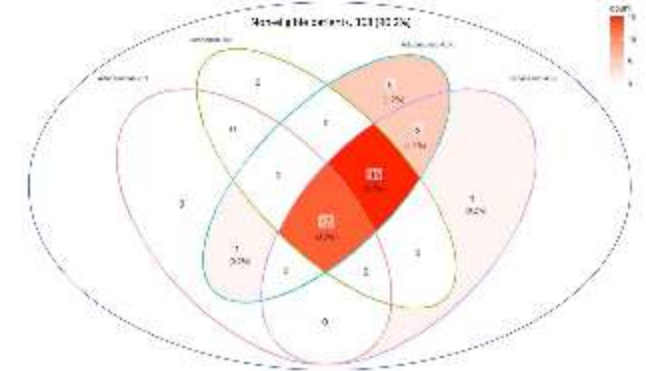
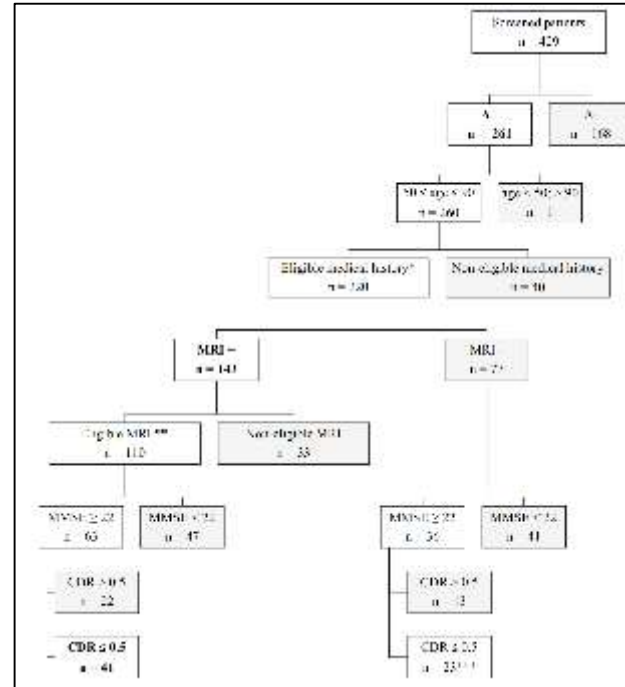
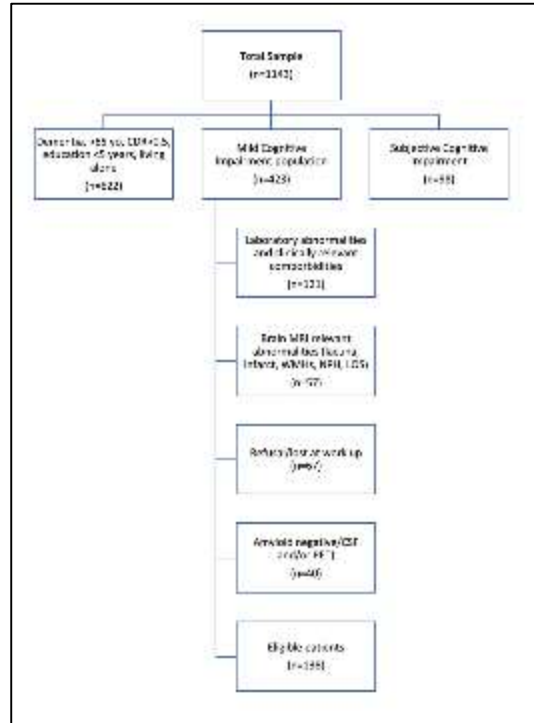
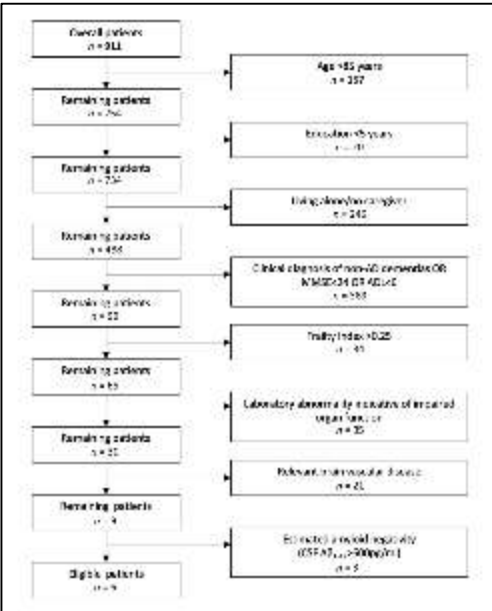
Terapie biologiche per la malattia di Alzheimer

Quante persone?



Terapie biologiche per la malattia di Alzheimer

Quante persone?



Canevelli M. et al., *J Am Geriatr Soc.* 2021;69(10):2995-2998

Padovani A. et al., *J Am Geriatr Soc.* 2022;70(2):626-628

Canu E et al., *J Neurol.* 2024;271(5):2716-2729

Logroscino G et al., *Eur J Neurol.* 2025;32(1):e16534

Terapie biologiche per la malattia di Alzheimer

Quali persone?

Indications

- Adults with mild cognitive impairment or mild AD dementia
- Confirmed amyloid pathology (A β positive)
- Patients who are non-carriers or heterozygotes for ApoE ϵ 4

Exclusion criteria - Medical History

- Patients with two copies of ApoE ϵ 4
- Non-AD neurologic or psychiatric conditions
- Concomitant use of anticoagulants
- Bleeding disorder that is not under adequate control
- Stroke or TIA within the past 12 months or any history of seizures
- Major immunologic disease

Exclusion criteria - Medical History

- Patients unable to undergo MRI due to claustrophobia, pacemaker, defibrillator, or metal implants
- Baseline MRI findings:
 - More than 4 microhemorrhages (≤ 10 mm at the greatest diameter) - 20% ARIA risk
 - A single macrohemorrhage > 10 mm at the greatest diameter
 - An area of superficial siderosis - 18% ARIA risk
 - Evidence of vasogenic edema
 - More than 2 lacunar infarcts or stroke involving a major vascular territory
 - Severe subcortical hyperintensities consistent with a Fazekas score of 3
 - Evidence of amyloid beta-related angiitis
 - CAA-ri
 - Other major intracranial pathology that may cause cognitive impairment

Cummings J et al., J Prev Alzheimers Dis. 2023;10(3):362-377

Rabinovici et al., J Prev Alzheimers Dis. 2025;12(5):100150

Terapie biologiche per la malattia di Alzheimer

Quali persone?



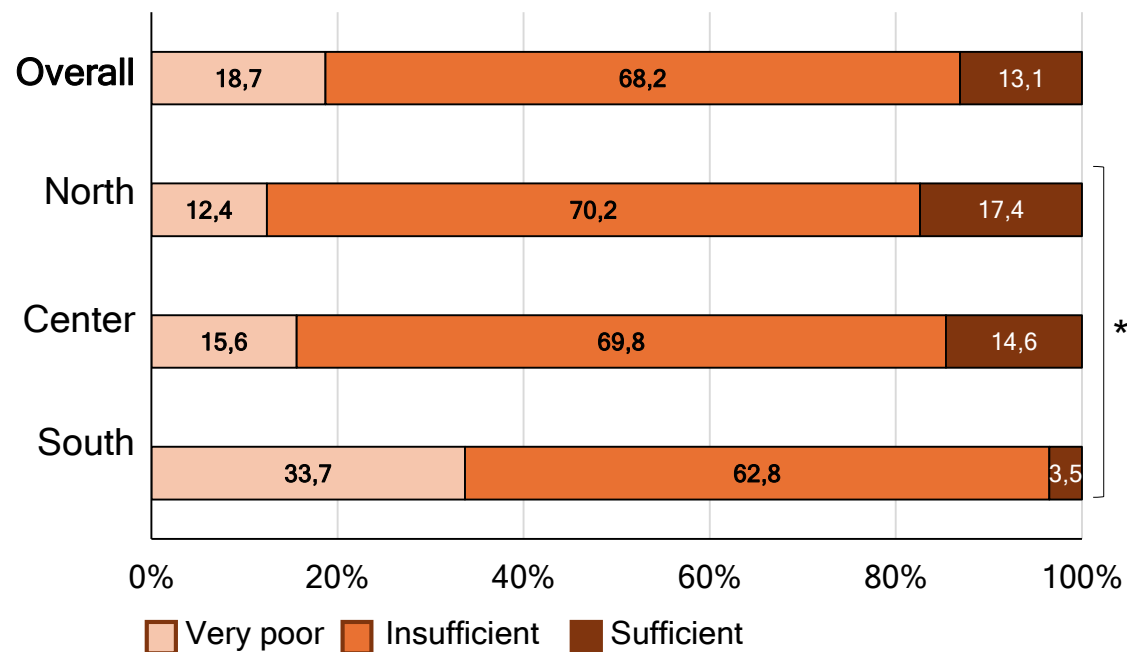
Fig. 1. Distribution of Italian CCDDs encountering requirements for effective disease-modifying therapies prescription. The figure displays the distribution of the 47 CCDDs that meet the specified requirements for effective prescription of disease-modifying therapies. These requirements include a multidisciplinary team, a minimum core test for neuropsychological assessment, amyloid PET, CSF, and Brain MRI assessment. Legend: – Red: Indicates regions with no CCDDs meeting the elective requirements. – Pink: Represents regions with 1 CCDD meeting the elective requirements (first and second quartile of the distribution, excluding regions without elective CCDDs). – Yellow: Denotes regions with 2 CCDDs meeting the elective requirements (third quartile of the distribution, excluding regions without elective CCDDs). – Green: Signifies regions with more than 2 CCDDs meeting the elective requirements (fourth quartile of the distribution, excluding regions without elective CCDDs).

Terapie biologiche per la malattia di Alzheimer

Quali persone?



Overall quality of the cognitive assessment of migrants



Thank you

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