17·20 Dicembre 2025 Napoli

70° CONGRESSO NAZIONALE SIGG

LIBERI E LONGEVI

Università degli Studi di Napoli Federico II Polo Didattico di **SCAMPIA**

SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

17:10-18:10 **SIMPOSIO SIGG-SIN**

IL DELIRIUM E IL SUO IMPATTO SULLA SALUTE DEL CERVELLO

Moderatori: *Dario Leosco (Napoli), Alessandro Padovani (Brescia)*

Delirium e demenza: fattore di rischio e/o segno prodromico?

Maria Cristina Ferrara

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

Medico Specialista in Geriatria
PhD candidate in Sanità Pubblica
Ricercatore presso Università degli Studi di Milano-Bicocca

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Disclosure

No conflicts of interest to disclose.

Outline

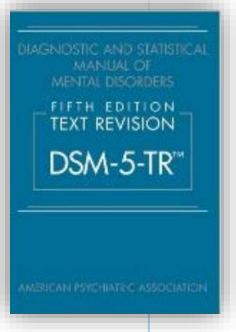
1. Delirium e demenza
2. Una relazione controversa
3. Il ruolo dei biomarcatori
4. Conclusioni e key messages

Outline

1. Delirium e demenza
2. Una relazione controversa
3. Il ruolo dei biomarcatori
4. Conclusioni e key messages

1

Delirium e demenza: cosa?



Delirium = **sindrome neuropsichiatrica acuta**, caratterizzata da:

Ridotta capacità di dirigere, focalizzare, sostenere e spostare **l'attenzione; ridotto orientamento** nell'ambiente

Sviluppo rapido **(ore o pochi giorni),** che rappresenta un **cambiamento rispetto al baseline** e tende a **fluttuare** in gravità nel corso della giornata

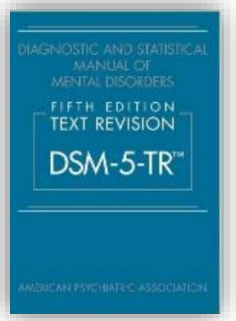
Coesistenza con un altro deficit cognitivo (memoria, linguaggio, abilità visuospaziali o percezione)

Disturbi **non meglio spiegati da un disturbo neurocognitivo preesistente**, nè nel contesto di uno stato di **coma**

Evidenza anamnestica, di esame obiettivo o di laboratorio, che si tratta di **conseguenza fisiologica diretta di un'altra condizione medica o è dovuto a molteplici eziologie**

1

Delirium e demenza: cosa?



Demenza

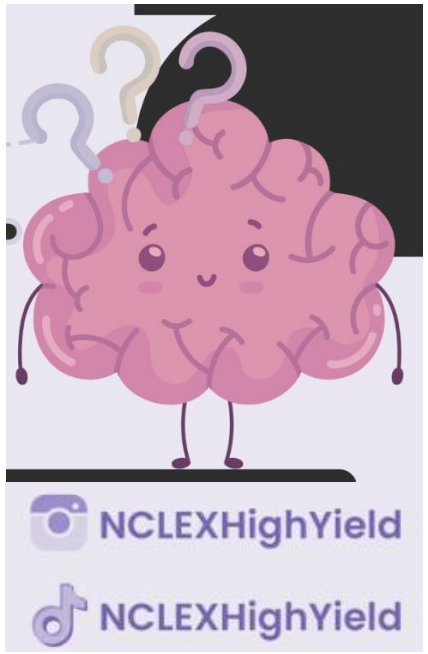
(Disturbo neurocognitivo maggiore)

= **Significativo declino cognitivo** rispetto a un precedente livello di prestazioni **in uno o più domini** cognitivi, che **interferisce con l'indipendenza nelle attività quotidiane dell'individuo.**

Le prestazioni cognitive compromesse sono preferibilmente documentate da test neuropsicologici standardizzati, e **non si verificano solo nel contesto di un delirium.**

1

Delirium e demenza: cosa?

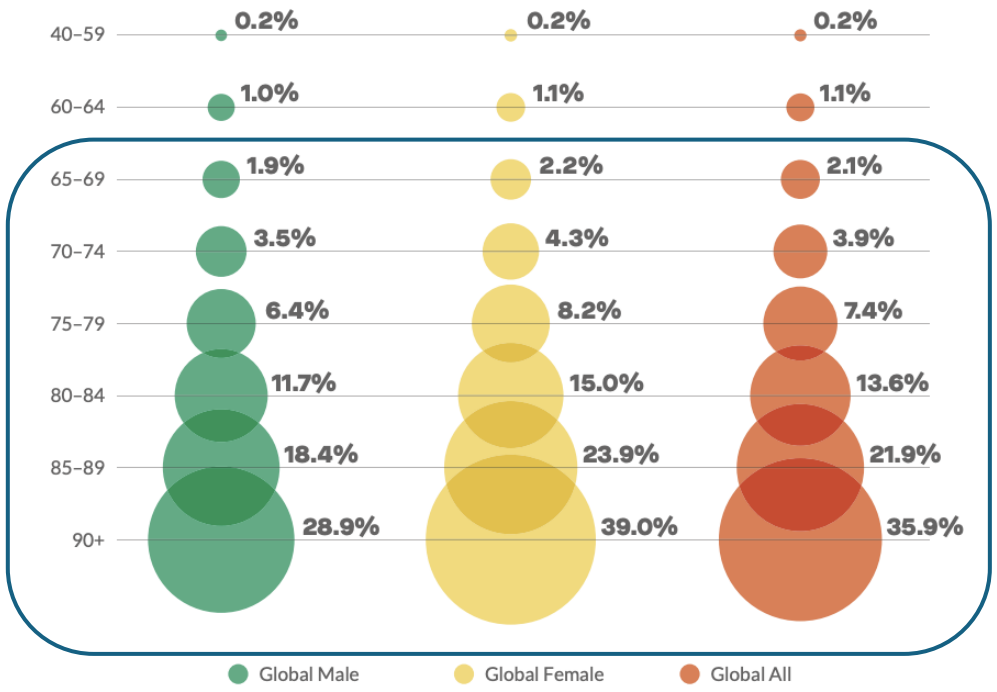


	Delirium	Dementia
ONSET	Sudden	Gradual
REVERSIBLE?	Yes (if treated)	No
AWARENESS	Fluctuates	Clear until late

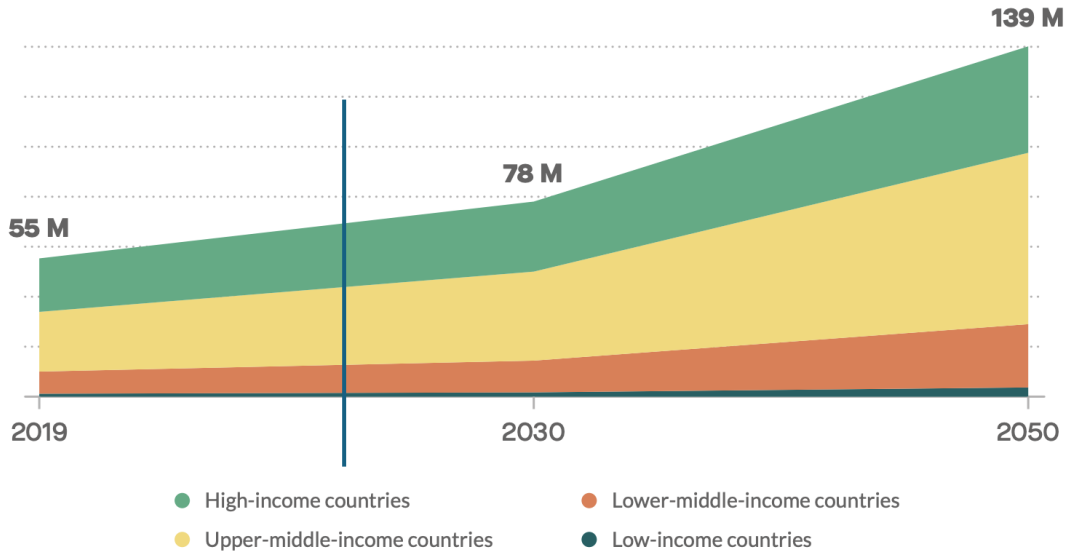
Delirium e demenza: perché?

FIGURE 2

Global dementia prevalence rates by sex and age

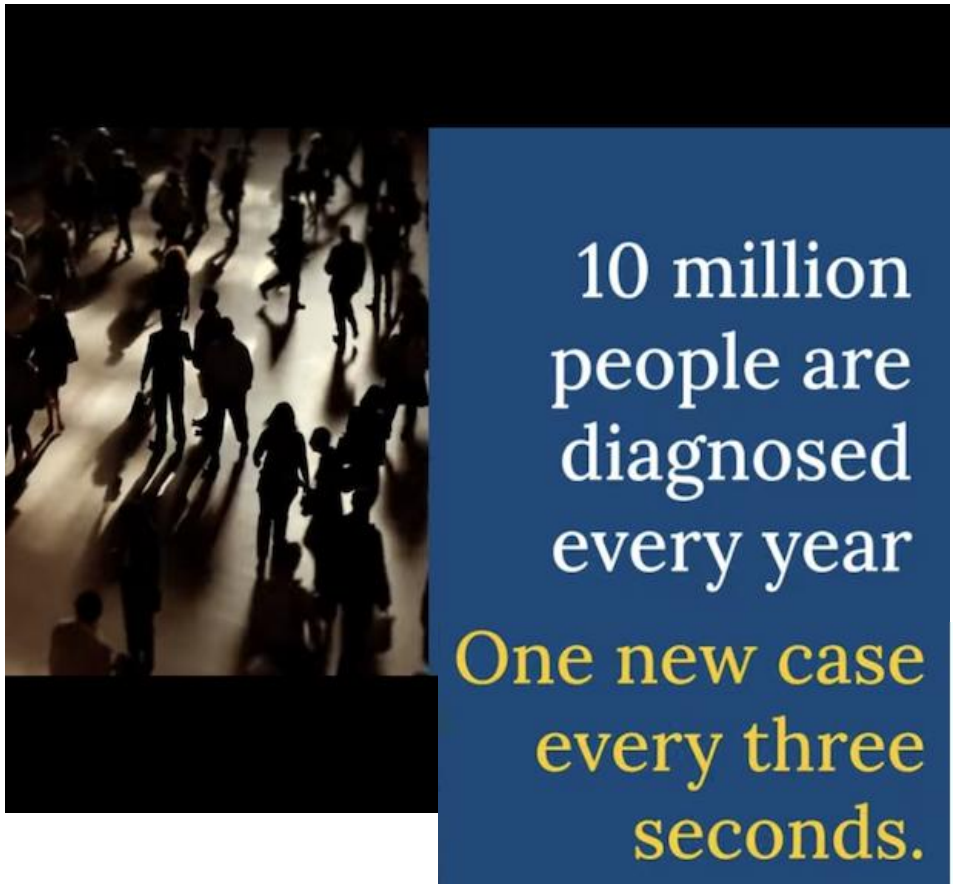


Number of people living with dementia in 2019, 2030 and 2050 (in million) by country income group



Global status report on the public health response to dementia
ISBN 978-92-4-003324-5 (electronic version)
ISBN 978-92-4-003325-2 (print version)

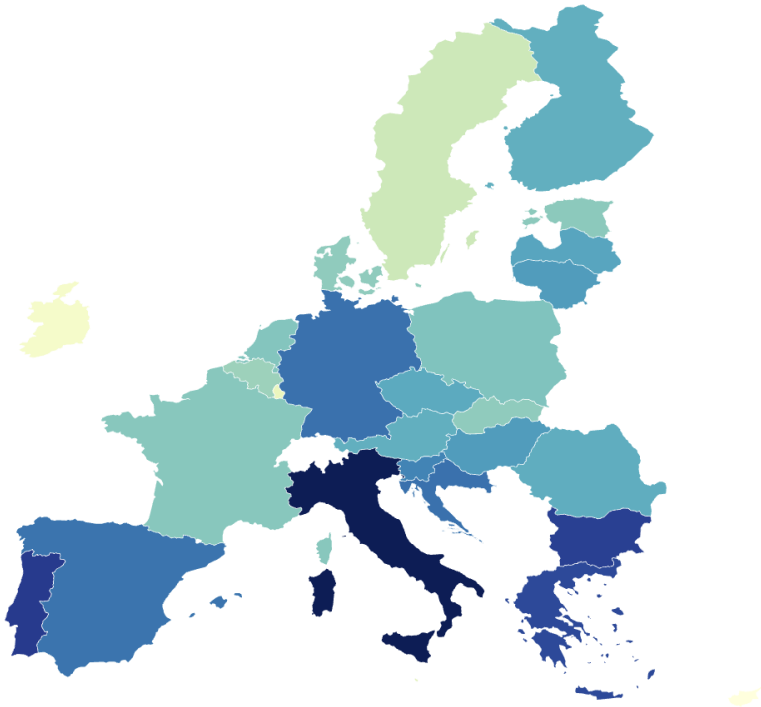
Delirium e demenza: perché?



Quali sono i Paesi Ue più anziani

Età mediana dei 27 Stati membri dell'Unione europea, anno 2023

38.4 anni — 48.4 anni

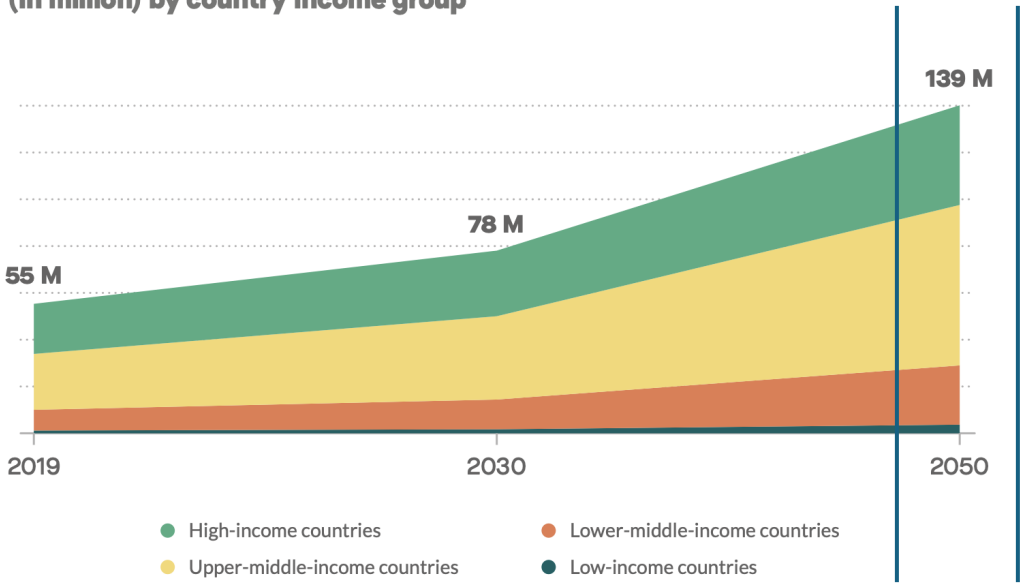


Fonte: Eurostat

1

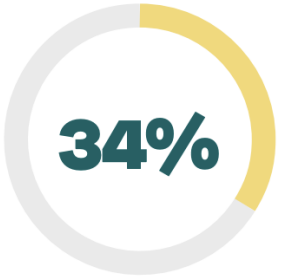
Delirium e demenza: perché?

Number of people living with dementia in 2019, 2030 and 2050 (in million) by country income group



7th
leading cause of death

+



of total dementia costs are attributable to social care costs

Informal care accounts for nearly
50%
of the global cost of dementia

“Do you want our healthcare system and our economy to prosper? Address dementia. The return on investment will be ten-fold.”

Roger Marple,
Canada

Global status report on the public health response to dementia

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1

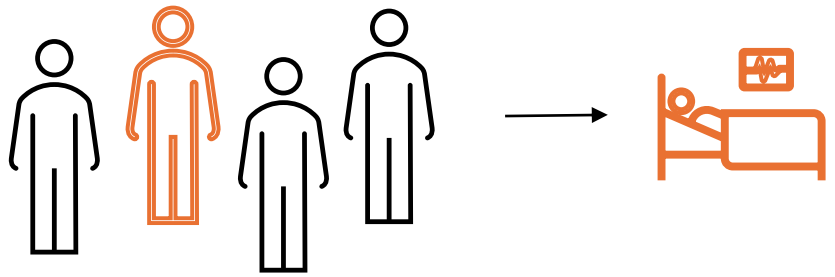
Delirium e demenza: perché?

The consistent burden in published estimates of delirium occurrence in medical inpatients over four decades: a systematic review and meta-analysis study

Kate Gibb[1,2], Anna Seeley[1,3], Terry Quinn[4], Najma Siddiqi[5], Susan Shenkin[6], Kenneth Rockwood[1,7], Daniel Davis[1,2,3]

According to this systematic review and meta-analysis, the published prevalence and incidence of delirium in acute medical adult inpatients have remained broadly stable at about one in four older patients. We quantified this from studies using consistent methods in comparable populations.

is associated with a wide range of adverse outcomes, particularly those relevant to patient safety. These include: mortality, falls, increased length of stay, and risk of institutionalisation [3,4]. In longitudinal studies, dementia is the biggest risk factor for delirium, and reciprocally, delirium is linked with worsening cognitive decline and incident dementia [5,6].



In this updated systematic review and meta-analysis, we found that the epidemiology of delirium among hospitalised patients has not changed substantially between 1980 and 2019. At least in estimates from the published literature, case mix also appears not to have changed much. With this burden of delirium in hospitals, contemporary priorities around disseminating delirium knowledge, increasing the proportion diagnosed and implementing care pathways remain as challenging yet urgent as ever.

Age and Ageing 2020; **49:** 352–360
doi: 10.1093/ageing/afaa040
Published electronically 2 April 2020

Outline

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Una relazione controversa

Una relazione controversa

Delirium

dementia have nothing to do with each other. However, the experienced clinician should remember that the onset of a neurodegenerative process can lower the threshold for delirium occurrence, that delirium can initiate a series of events leading to functional decline,[1] and that recurrent delirium might be the clinical manifestation of prodromal dementia with Lewy bodies, for example.[2] The Article reported in this issue of *The Lancet Healthy Longevity* by Krogseth and colleagues[3] will make me change my message next autumn.

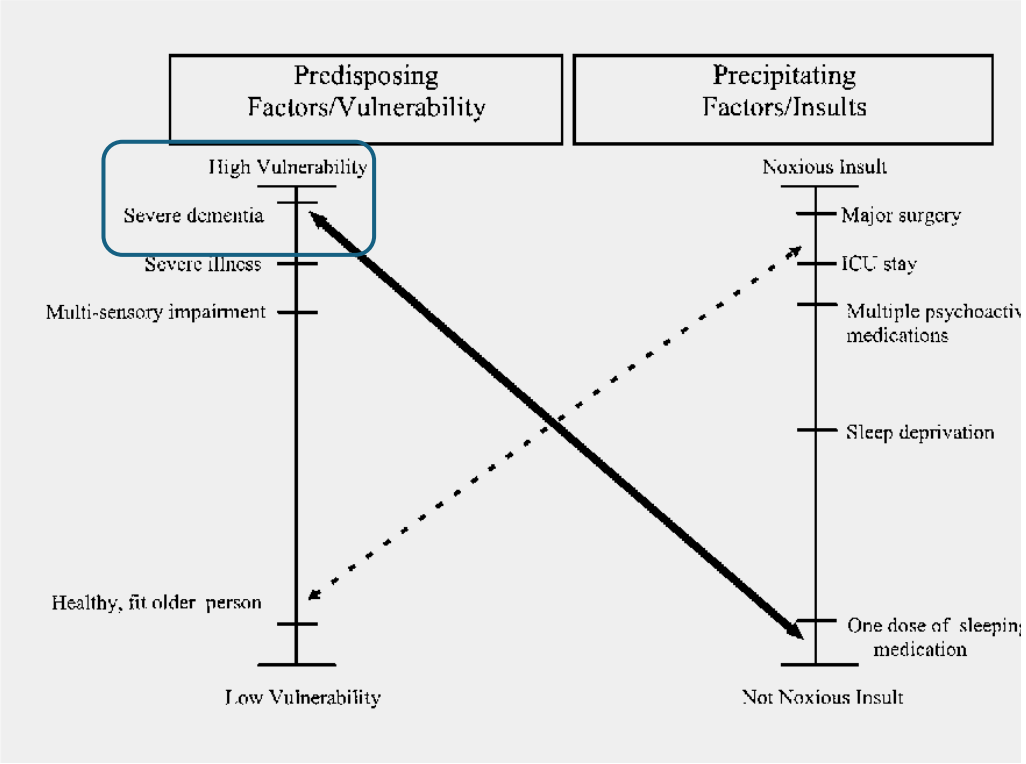
Demenza

Planche V. Delirium, blood biomarkers for neurodegeneration, and dementia, The Lancet Healthy Longevity, July 14, 2023

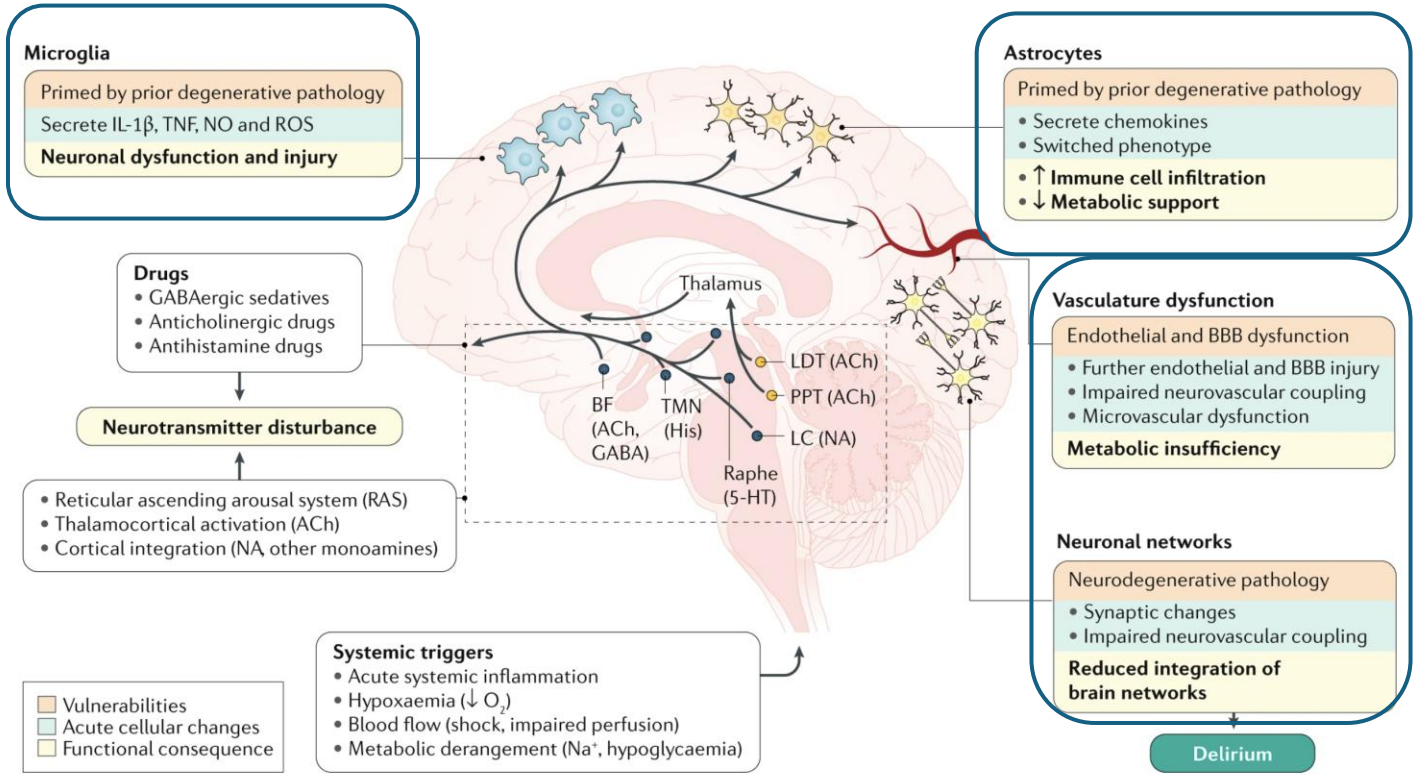
Una relazione controversa

2

Una relazione controversa: chi predispone a cosa?



Inouye SK. Predisposing and precipitating factors for delirium in hospitalized older patients. Dement Geriatr Cogn Disord. 1999 Sep-Oct;10(5):393-400. doi: 10.1159/000017177.



Wilson JE, Mart MF, Cunningham C, Shehabi Y, Girard TD, MacLullich AMJ, Slooter AJC, Ely EW. Delirium. Nat Rev Dis Primers. 2020 Nov 12;6(1):90. doi: 10.1038/s41572-020-00223-4. Erratum in: Nat Rev Dis Primers. 2020 Dec 1;6(1):94. doi: 10.1038/s41572-020-00236-z.

2

Una relazione controversa: chi predispone a cosa?

REVIEW ARTICLE

Delirium in older adults is associated with development of new dementia: a systematic review and meta-analysis

Jarett Vanz-Brian Pereira, May Zin Aung Thein, Anita Nitchingham, Gideon A. Caplan

First published: 09 February 2021 | https://doi.org/10.1002/gps.5508 | VIEW METRICS

Older adult inpatients who developed delirium **had almost 12 times the odds of subsequently developing new dementia compared to non-delirious patients** (OR = 11.9 [95% CI: 7.29–19.6]; $p < 0.001$).

JOURNAL ARTICLE

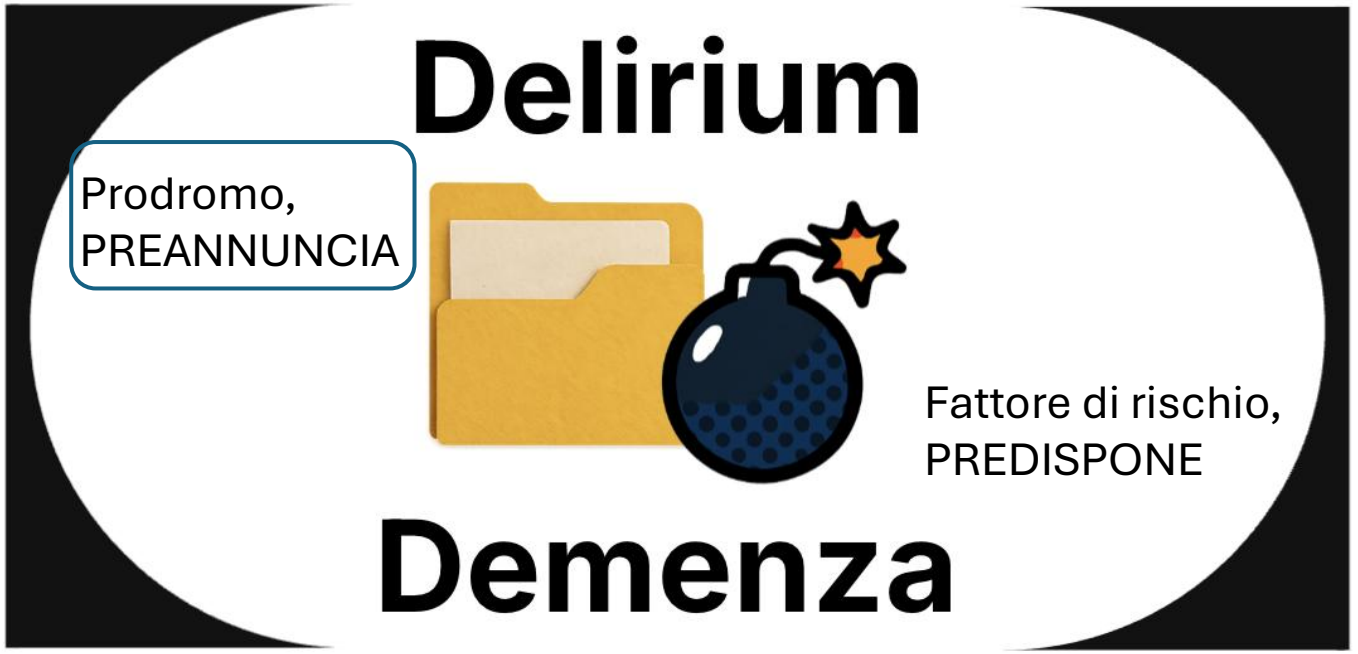
Long-term clinical outcomes of delirium after hospital discharge: a systematic review and meta-analysis

Yonas Tesfaye, Courtney R Davis, Melissa J Hull, Danielle Greaves, James du Preez, Sally Johns, Alice Bourke, Hannah A D Keage

Age and Ageing, Volume 54, Issue 7, July 2025, afaf188,
https://doi.org/10.1093/ageing/afaf188
Published: 08 July 2025 **Article history**

Those who experienced delirium had **higher odds of incident dementia than those who did not at ≤6 months** (**OR = 5.60**, $P < .001$), **>6–12 months** (**OR = 4.09**, $P < .001$), **>12 months** (**OR = 5.19**, $P < .001$) follow-up.

Una relazione controversa



2

Una relazione controversa: delirium come prodromo?

Table 7. Population characteristics (overall and by delirium status)

	Overall (N=639)	Delirium° (N=301)	No Delirium (N=338)	p-value
Age	87 (84-90)	87 (84–91)	87 (84–90)	0.068
Sex (female)	340 (53.2%)	151 (50.2%)	189 (55.9%)	0.146
ADL	3 (1-6)	2 (1–5)	5 (2–6)	<0.001
IADL (female)	1 (0-4)	0 (0–2)	2 (1–5)	<0.001
IADL (male)	1 (0-4)	0 (0–2)	2 (1–5)	<0.001
Charlson Comorbidity Index	3 (2-4)	3 (2–4)	3 (2–4)	0.357
N° of drugs at admission	7 (5-10)	7 (5–10)	7 (5–10)	0.083
Anamnestic dementia	266 (41.6%)	187 (62.1%)	79 (23.4%)	< 0.001
Possible dementia (AD8 ≥ 2)	192 (30%)	79 (26.2%)	113 (33.4%)	< 0.001
Global Deterioration Scale				< 0.001
1 (No cognitive decline)	193 (30.2%)	41 (13.6%)	152 (45.0%)	
2 (Age associated memory impairment)	73 (11.4%)	27 (9.0%)	46 (13.6%)	
3 (MCI)	70 (11.0%)	26 (8.6%)	44 (13.0%)	
4 (Mild dementia)	105 (16.4%)	54 (17.9%)	51 (15.1%)	
5 (Moderate dementia)	115 (18.0%)	81 (26.9%)	34 (10.1%)	
6 (Moderately severe)	54 (8.5%)	45 (15.0%)	9 (2.7%)	
7 (Severe dementia)	29 (4.5%)	27 (9.0%)	2 (0.6%)	
Clinical Frailty Scale	6 (5-7)	7 (6–7)	6 (5–7)	<0.001
Primary Care - Frailty Index	0.2 (0.12-0.28)	0.2 (0.16–0.28)	0.2 (0.12–0.24)	<0.001

Notes Values are expressed as median (Q1-Q3) for continuous variables, and n(%) for categorical variables; ° At least one day during hospitalisation (4AT positive and confirmed diagnosis). *Abbreviations*: Activities of Daily Living; Instrumental Activities of Daily Living; AD8: Ascertain Dementia 8; MCI: Mild Cognitive Impairment.

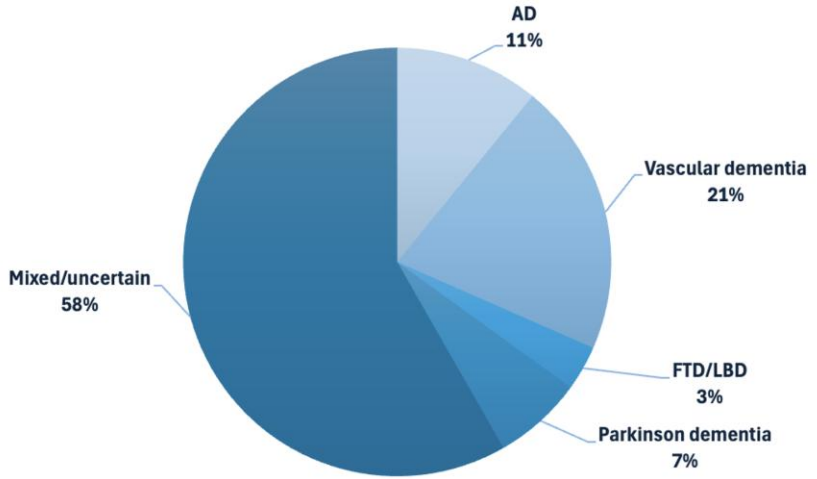
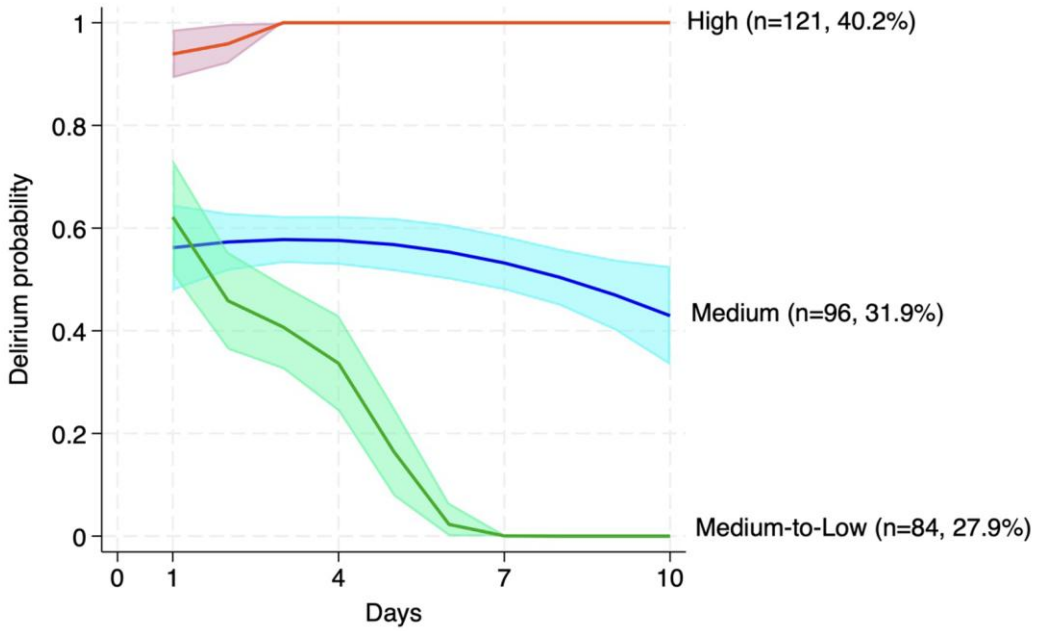


Figure 24. Etiologic subtypes of anamnestic dementia. *Notes*. AD: Alzheimer's disease; VaD: Vascular dementia; FTD/LBD: Frontotemporal/Lewy body dementia.

Unpublished data

2

Una relazione controversa: delirium come prodromo?



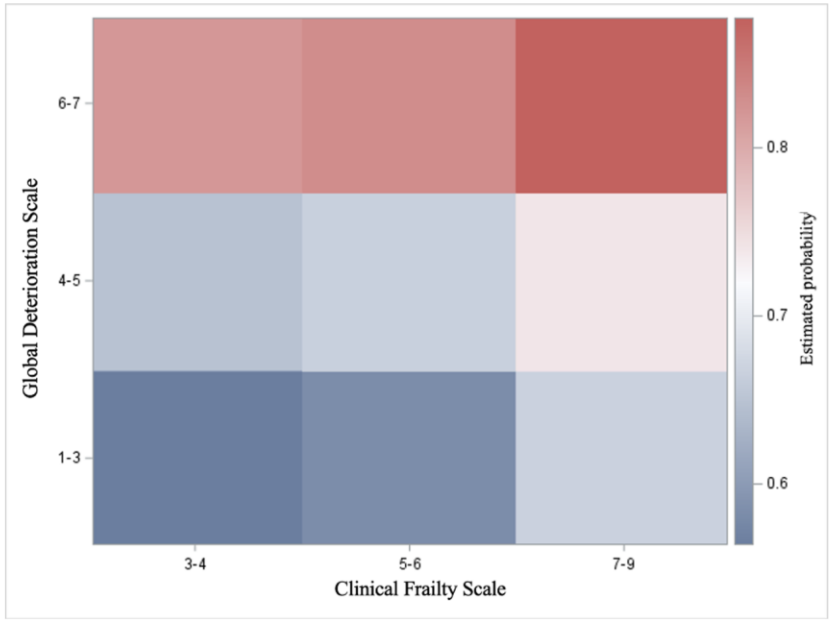


Figure 26. Heatmap of the estimated probability of following unfavourable trajectories (Medium or High) among patients with delirium. Rows show Global Deterioration Scale strata (1–3, 4–5, 6–7); columns show Clinical Frailty Scale strata (3–4, 5–6, 7–9). Colour scale: blue = lower probability; red = higher probability (legend at right). Probabilities are derived from a logistic model with trajectory class as outcome and predictors GDS and CFS.
Note: because the analysis is conditional on having delirium, and Medium/High classes were common in the cohort (≈72% overall), even the most favourable cell exceeds 0.50.

Unpublished data

2

Una relazione controversa: delirium come prodromo?

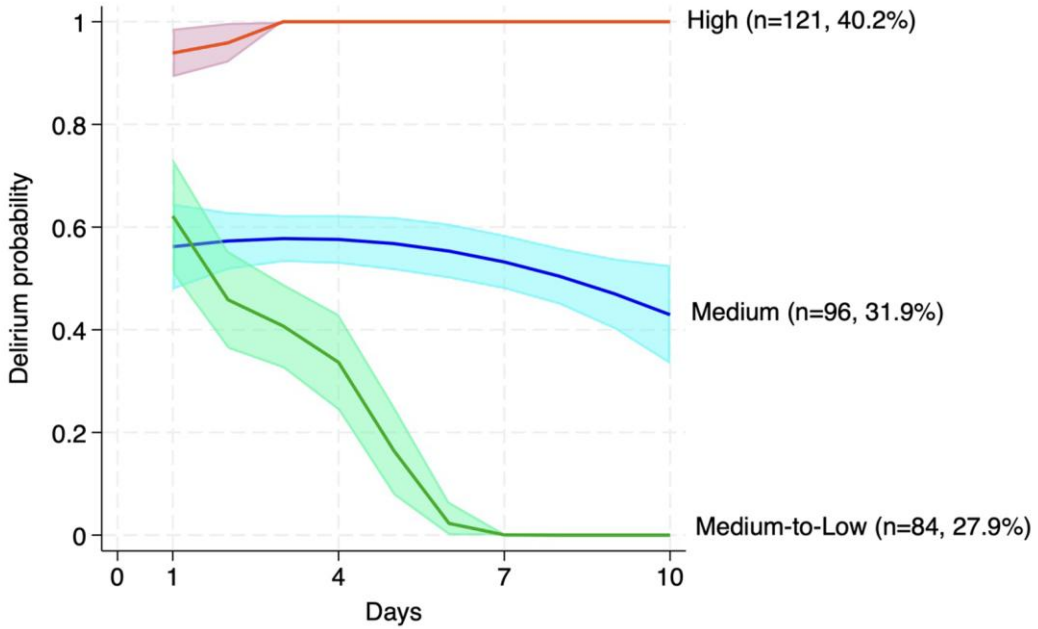


Table 14. Association between delirium trajectories and 3-month all-causes mortality

	RR	IC 95%	p-value
Delirium trajectory			
Medium°	1.56	1.02 – 2.36	0.038
High°	2.07	1.41 – 3.05	<0.001
Clinical Frailty Scale *(per one-level increase)*	1.23	1.06 – 1.43	0.008
Albumin *(per one decimal increase)*	0.70	0.57-0.86	0.001
Age	1.02	1.00 – 1.04	0.112
Female sex (vs male)	0.93	0.75 – 1.15	0.505

Note. ° Reference: Medium-to-Low.
Abbreviations. RR: Relative Risk; 95%CI: 95% Confidence Interval

Unpublished data

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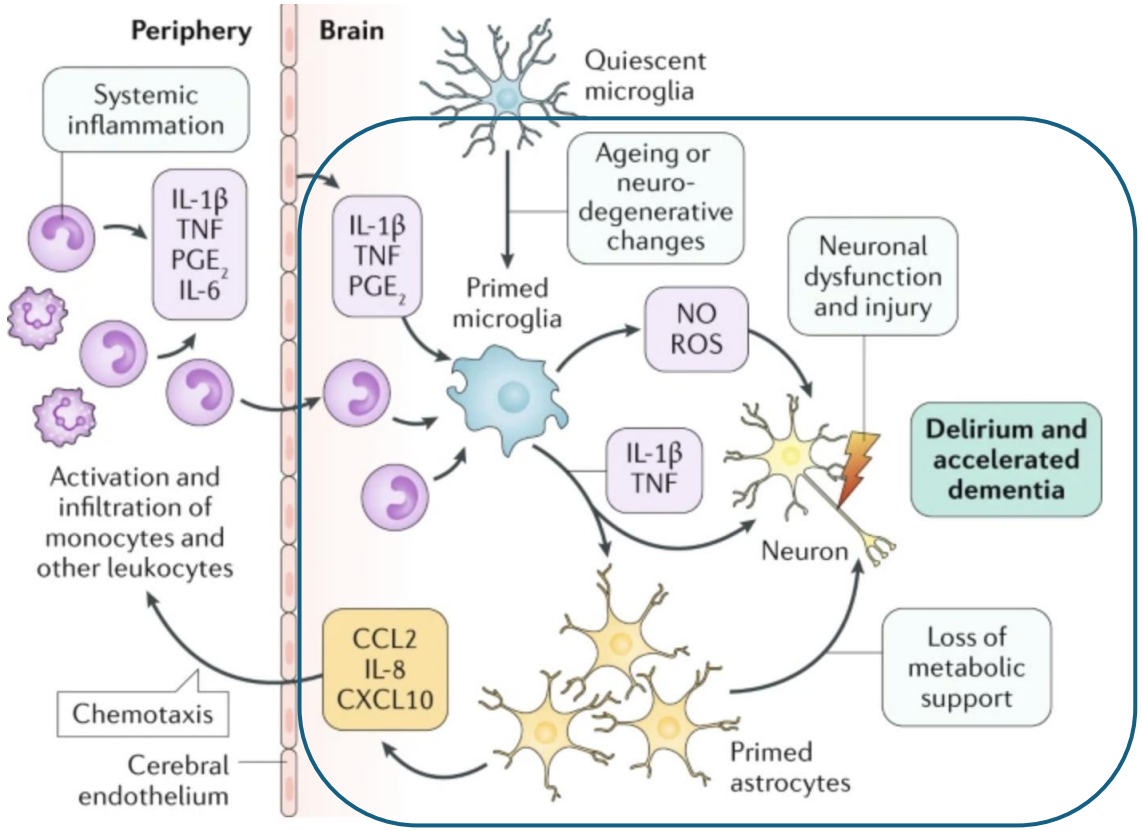
3

Il ruolo dei biomarcatori: unmasking



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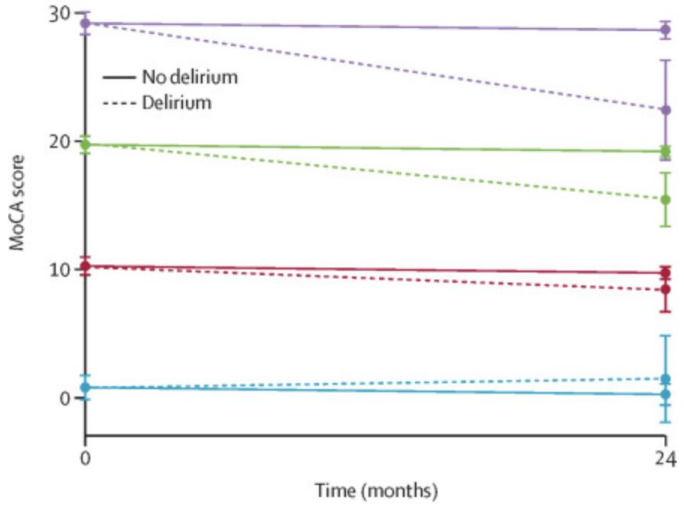
Delirium, neurofilament light chain, and progressive cognitive impairment: analysis of a prospective Norwegian population-based cohort

Maria Krogseth, PhD [a,b,e] · Prof Daniel Davis, MRCP [f] · Thomas Andrew Jackson, PhD [i] · Prof Henrik Zetterberg, MD [g,h,j,k,l,m] · Prof Leiv Otto Watne, MD [a,n,o] · Morten Lindberg, PhD [c] · et al. Show more



3

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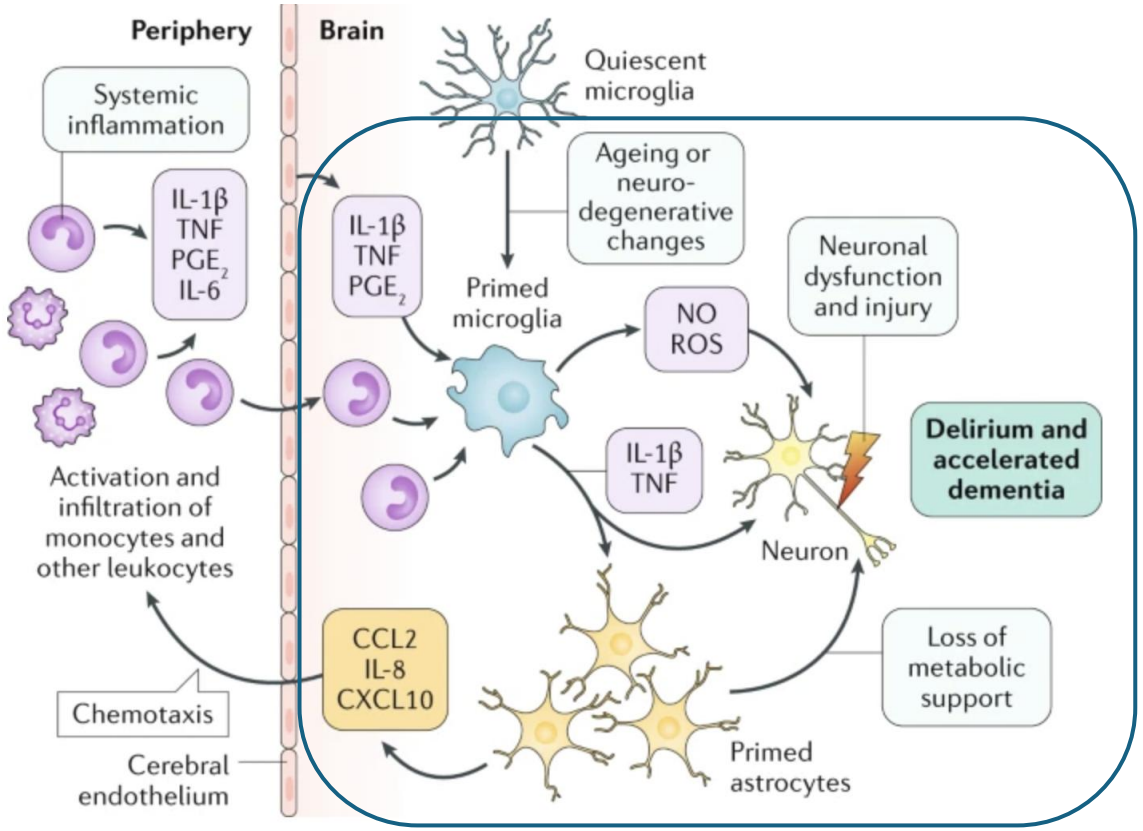

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Increased NfL as a marker of neuronal injury implicates delirium as harmful for the brain.

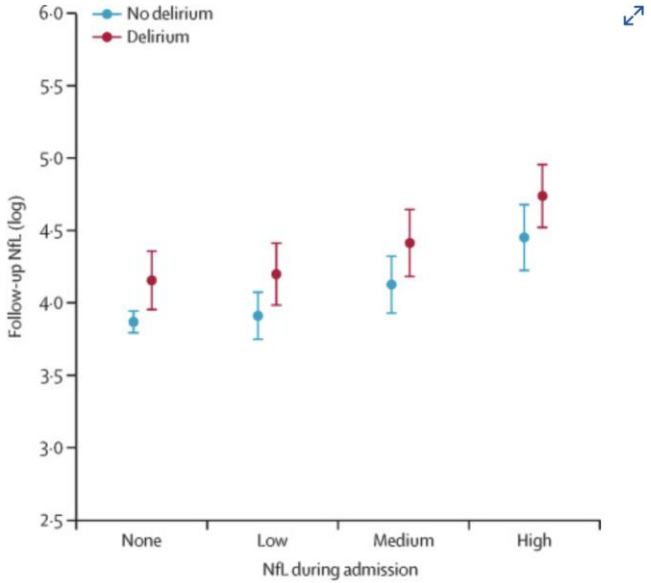

Figure 3 Follow-up NfL (log) by peak concentration of NfL during hospitalisation and delirium

3

Il ruolo dei biomarcatori: unmasking

Aging and disease ›› DOI: 10.14336/AD.2025.0107

Original Article

Neurofilament-Light Chain and Glial Fibrillary Acidic Protein as Blood-Based Delirium Risk Markers: A Multicohort Study

Maria Cristina Ferrara[1#, *], Lucía Lozano-Vicario[2#], Beatrice Arosio[3], Cristina D'Orlando[1], Lara De Luca[4], Alice Margherita Ornago[1], Elena Pinardi[1], Paolo Mazzola[1, 5], Chukwuma Okoye[1, 5], Riccardo Gamberale[1], Francesca Remelli[6], Massimiliano Castellazzi[7], Giovanni Zatti[1, 8], Giuseppe Foti[1, 9], Ángel Javier Muñoz-Vázquez[10], Nicolás Martínez-Velilla[2, 11, 12], Stefano Volpato[6], Giuseppe Bellelli[1, 5], on behalf of the ORTODEL group

Questo studio ha indagato il ruolo di NfL e GFAP come marcatori ematici di rischio per POD nei pazienti anziani sottoposti a chirurgia per frattura di femore.

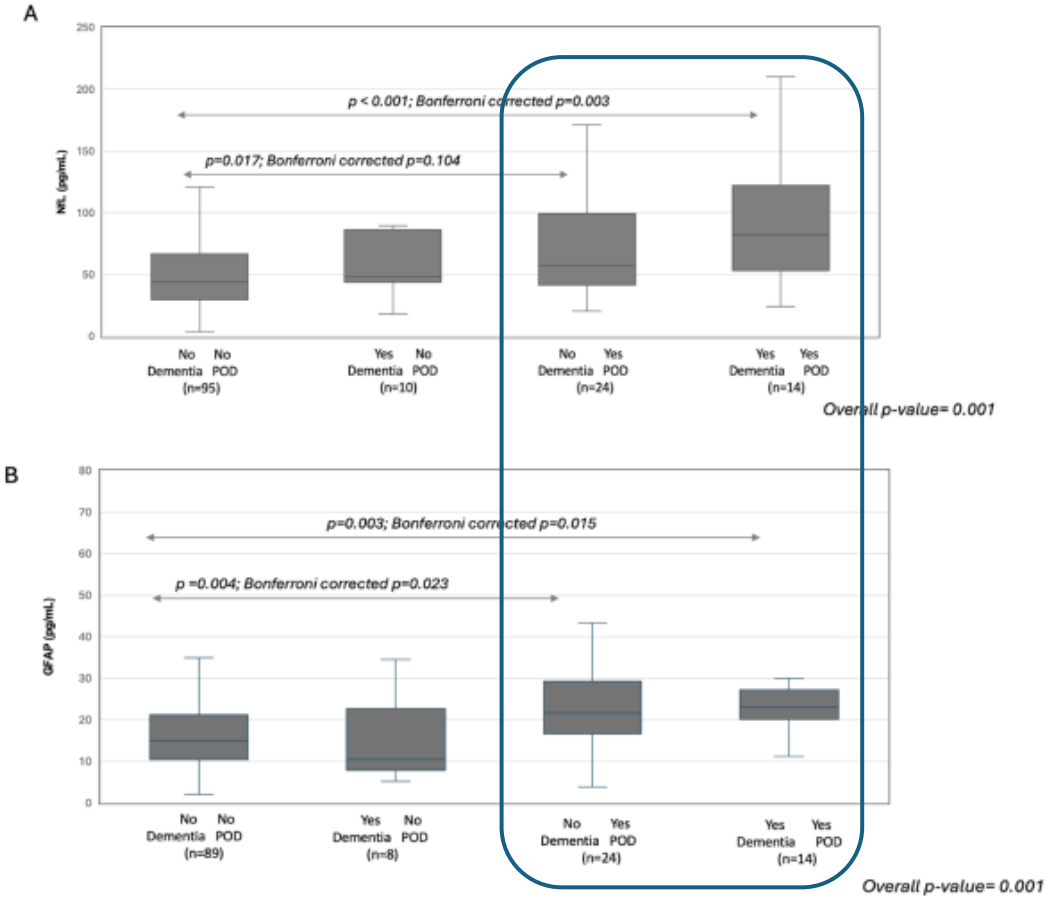

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Table 2. Association of NfL (Model A) and GFAP (Model B) with postoperative delirium.

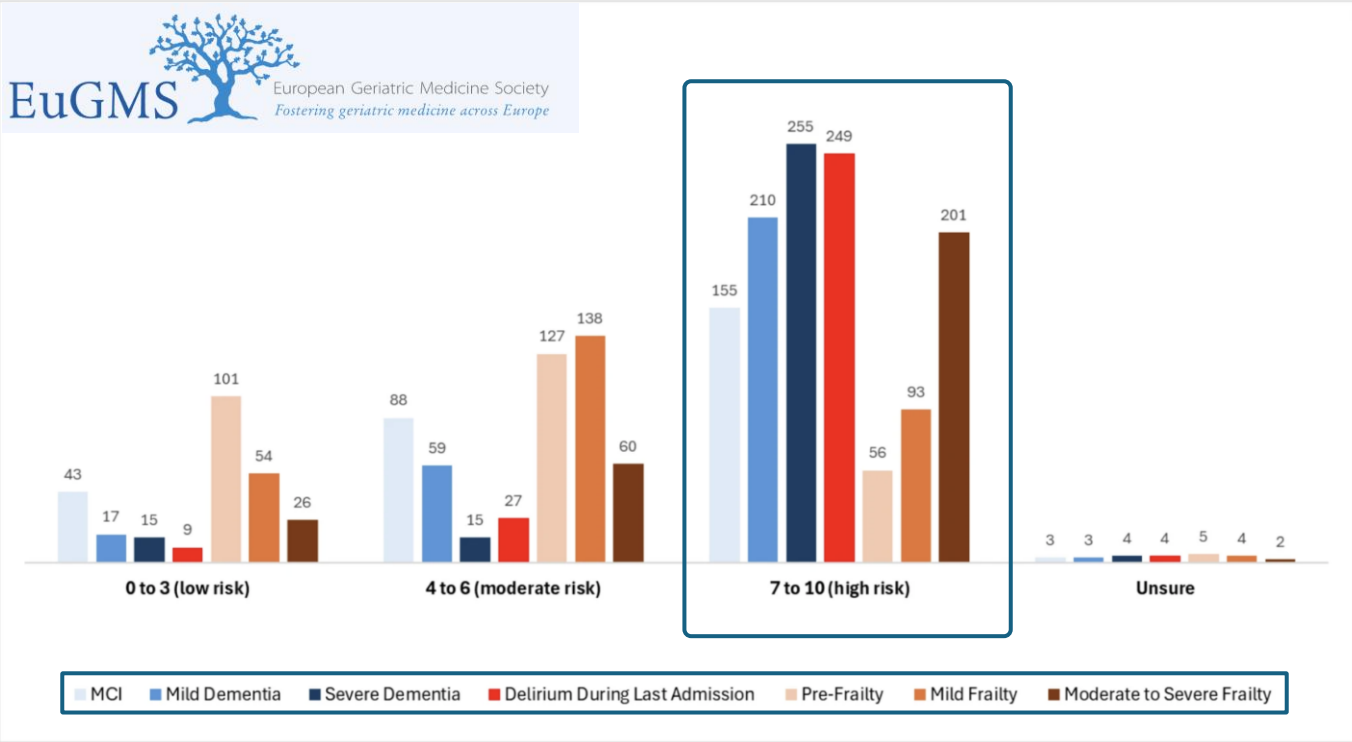
Model A	**OR[a]**	**95% C.I.[b]**		**p-value**
Preoperative blood NfL[c] (> median)	3.21	1.26	8.21	0.015
Age	1.09	1.02	1.17	0.017
Sex (female)	2.41	0.76	7.71	0.137
Dementia	4.88	1.58	15.04	0.006
Clinical Frailty Scale	0.93	0.69	1.26	0.641
Preoperative blood IL-6[d] (> median)	0.91	0.38	2.22	0.844
Model B	**OR[a]**	**95% C.I.[b]**		**p-value**
Preoperative blood GFAP[e] (> median)	3.66	1.38	9.68	0.009
Age	1.06	0.98	1.14	0.120
Sex (female)	2.07	0.64	6.67	0.224
Dementia	6.03	1.91	19.01	0.002
Clinical Frailty Scale	0.98	0.73	1.33	0.921
Preoperative blood IL-6[d] (> median)	1.01	0.42	2.44	0.985

[a] OR= Odds Ratio; [b] 95% C.I.=95% Confidence Interval; [c] NfL= Neurofilament-Light chain; [d] IL-6= Interleukin-6; [e] GFAP= Glial Fibrillary Acidic Protein

3

Il ruolo dei biomarcatori: delirium, demenza… e fragilità

From: The perceptions of European geriatricians on the co-occurrence and links between dementia, delirium and frailty



Respondents' assessment of the strength of selected risk factors for developing incident delirium

Review | Open Access

Delirium and frailty in older adults: Clinical overlap and biological underpinnings

This article relates to:

Giuseppe Bellelli, Federico Triolo, Maria Cristina Ferrara, Stacie G. Deiner, Alessandro Morandi, Matteo Cesari, Daniel Davis, Alessandra Marengoni, Marco Inzitari, Leiv Otto Watne ... See all authors

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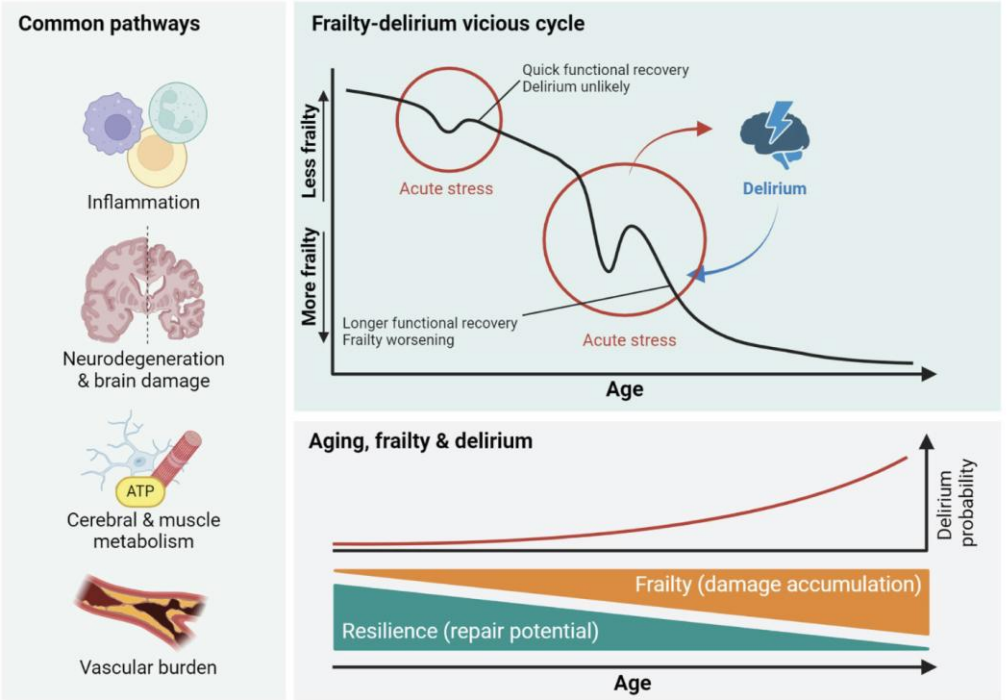

3

Il ruolo dei biomarcatori: delirium, demenza... e fragilità

Prevalence and interconnectedness of delirium, dementia, and frailty pathways in clinical settings: a survey of geriatricians across Europe

Research Paper | Open access | Published: 13 December 2025

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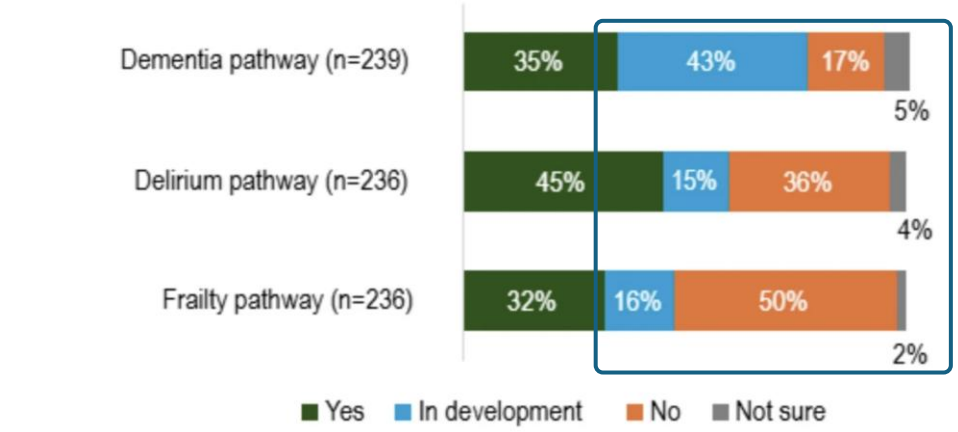
From: Prevalence and interconnectedness of delirium, dementia, and frailty pathways in clinical settings: a survey of geriatricians across Europe



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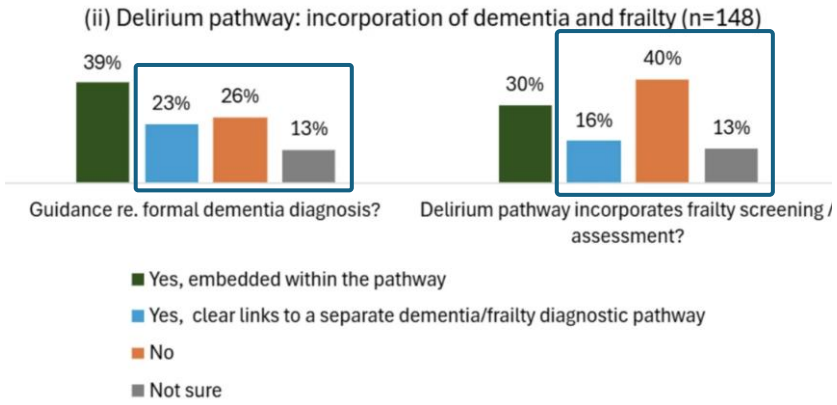

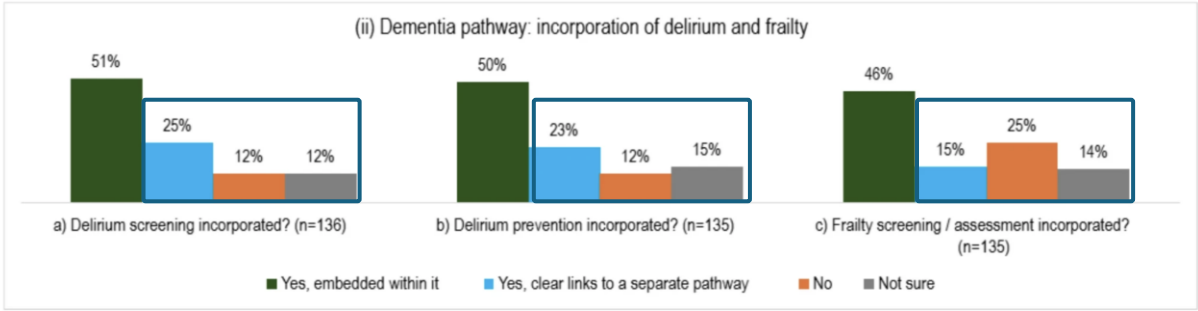

Dementia pathways: **i** prevalence within different clinical areas; **ii** incorporation of delirium (screening/assessment and prevention) and frailty screening/assessment

Conclusioni e key messages

Evidenze recenti suggeriscono che il **delirium non è solo fattore di rischio per demenza** ma anche **segno prodromico**

Unmasking

il delirium può rendere visibile un deficit cognitivo preesistente, che potrebbe essere misurato mediante biomarcatori di *neuroinflammation* e *injury*

Traccia biologica

il delirium non è solo rivelatore, ma può spostare la traiettoria cognitiva e prognostica dei pazienti, e pertanto va adeguatamente riconosciuto e trattato

17·20 Dicembre 2025 Napoli

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UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

Ridurre
"delirium burden"
per ridurre
"dementia burden"

mariacristina.ferrara@unimib.it