

17-20  
Dicembre  
2025  
Napoli

70<sup>o</sup> C O N G R E S S O  
N A Z I O N A L E  
**SIGG**  
LIBERI E LONGEVI

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



# La diagnosi di Malattia di Alzheimer al tempo dei biomarcatori: implicazioni sulla pratica clinica

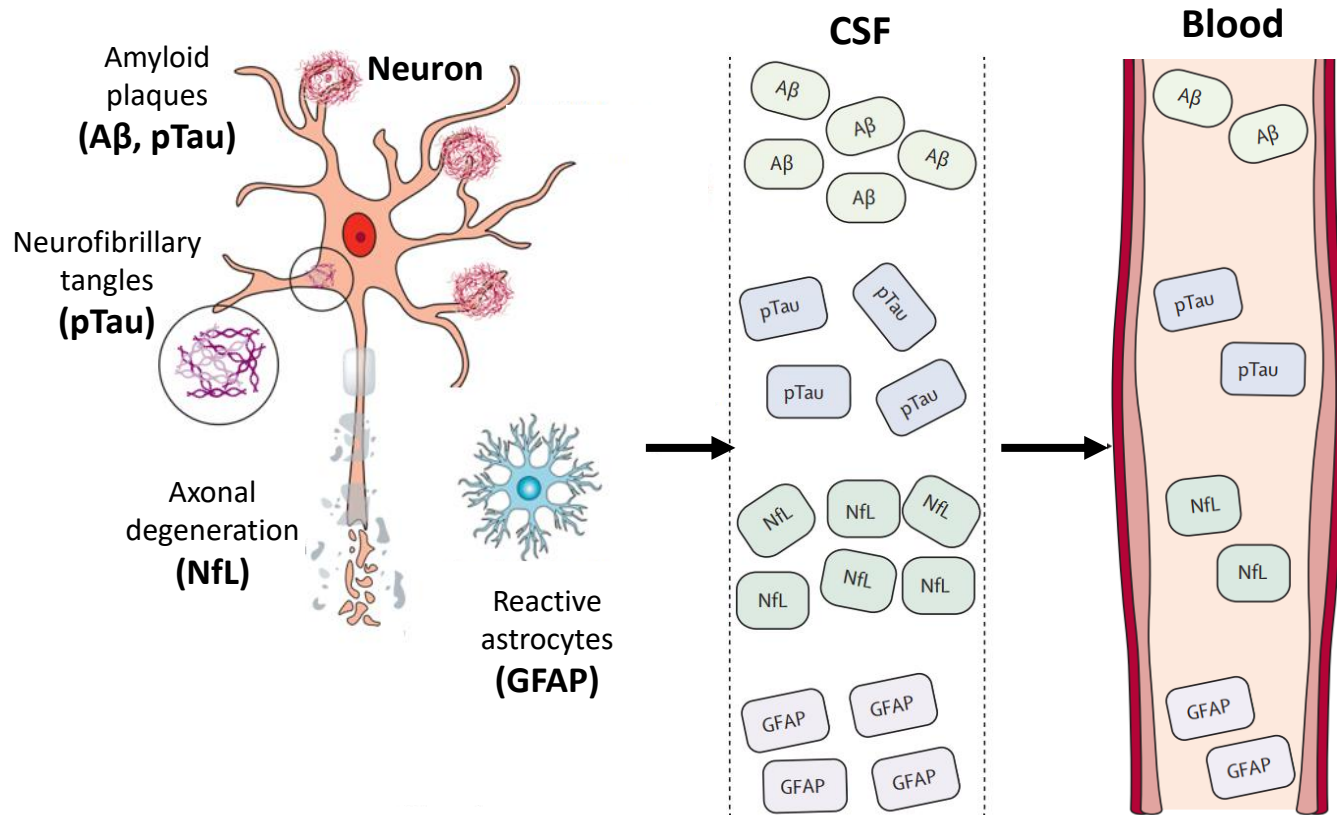
**Giulia Grande, MD, PhD**

*Aging Research Center, NVS  
Karolinska Institutet, Sweden*



**Karolinska  
Institutet**

# Blood biomarkers of Alzheimer's disease



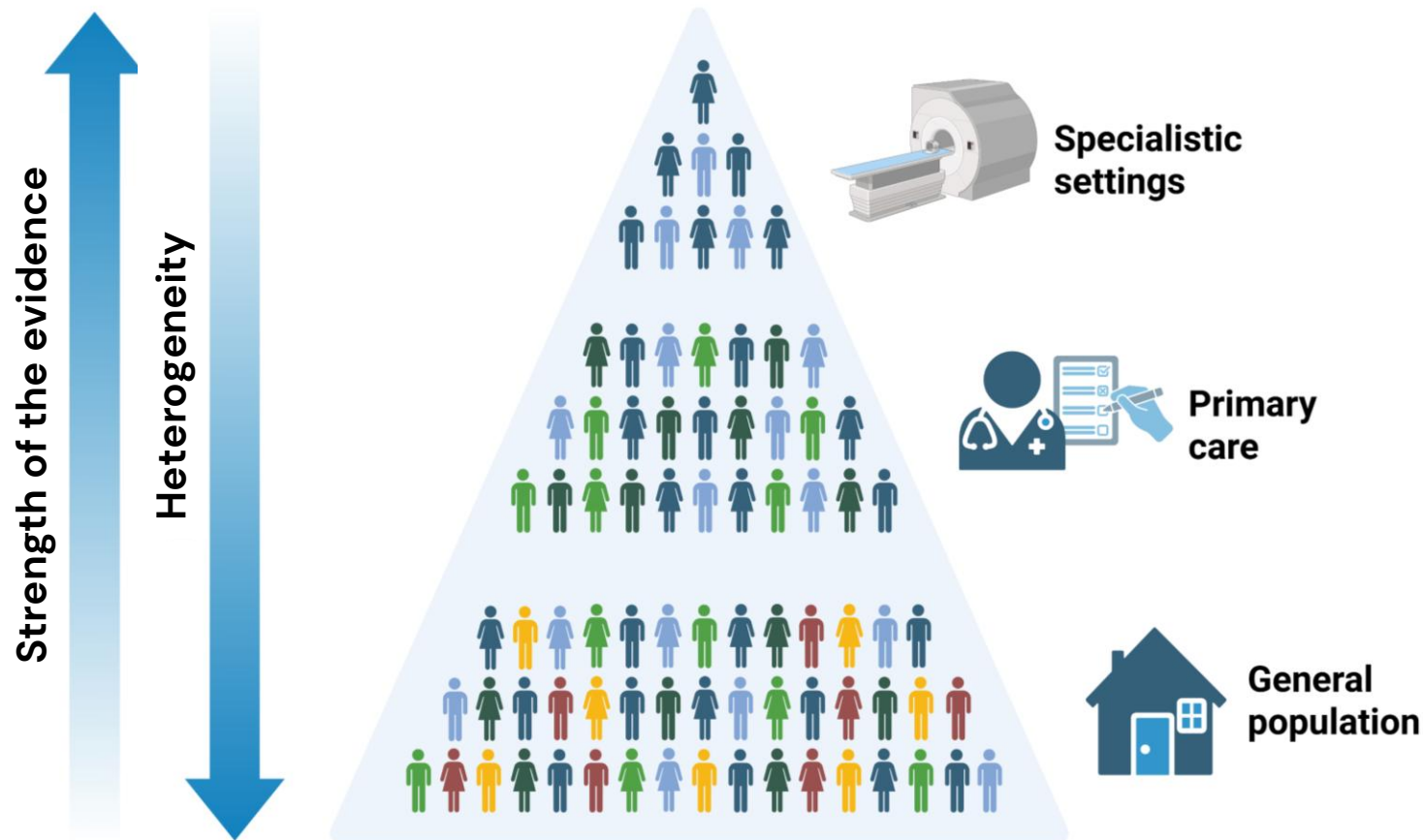
Adapted from Teunissen, *Lancet Neurology*, 2022

- AD blood biomarkers correlate with **AD pathology** and with **CSF** and **PET** imaging markers.
- They also predict **future** cognitive decline and (AD) **dementia onset**.

- **P-tau217**: Amyloid pathology
- **NfL**: Neurodegeneration
- **GFAP**: Glial activation

*Hansson 2021; Karikari et al. 2020; Janelidze et al. 2020; Teunissen et al 2022; Therriault et al. 2023; Ashton et al. 2024*

# From specialist settings to the community: where evidence stands for AD blood biomarkers



- **Most evidence** comes from **specialist settings** with selected participants, often already symptomatic
- **Limited evidence** on their accuracy and performance in real-world, **non-specialist populations**

# AD blood biomarkers in the community → facing complexity

## Predicting clinical outcomes

- Most research has been conducted in specialized settings, with **limited evidence on their clinical validity in community-based settings.**

## How systemic health influences AD biomarkers

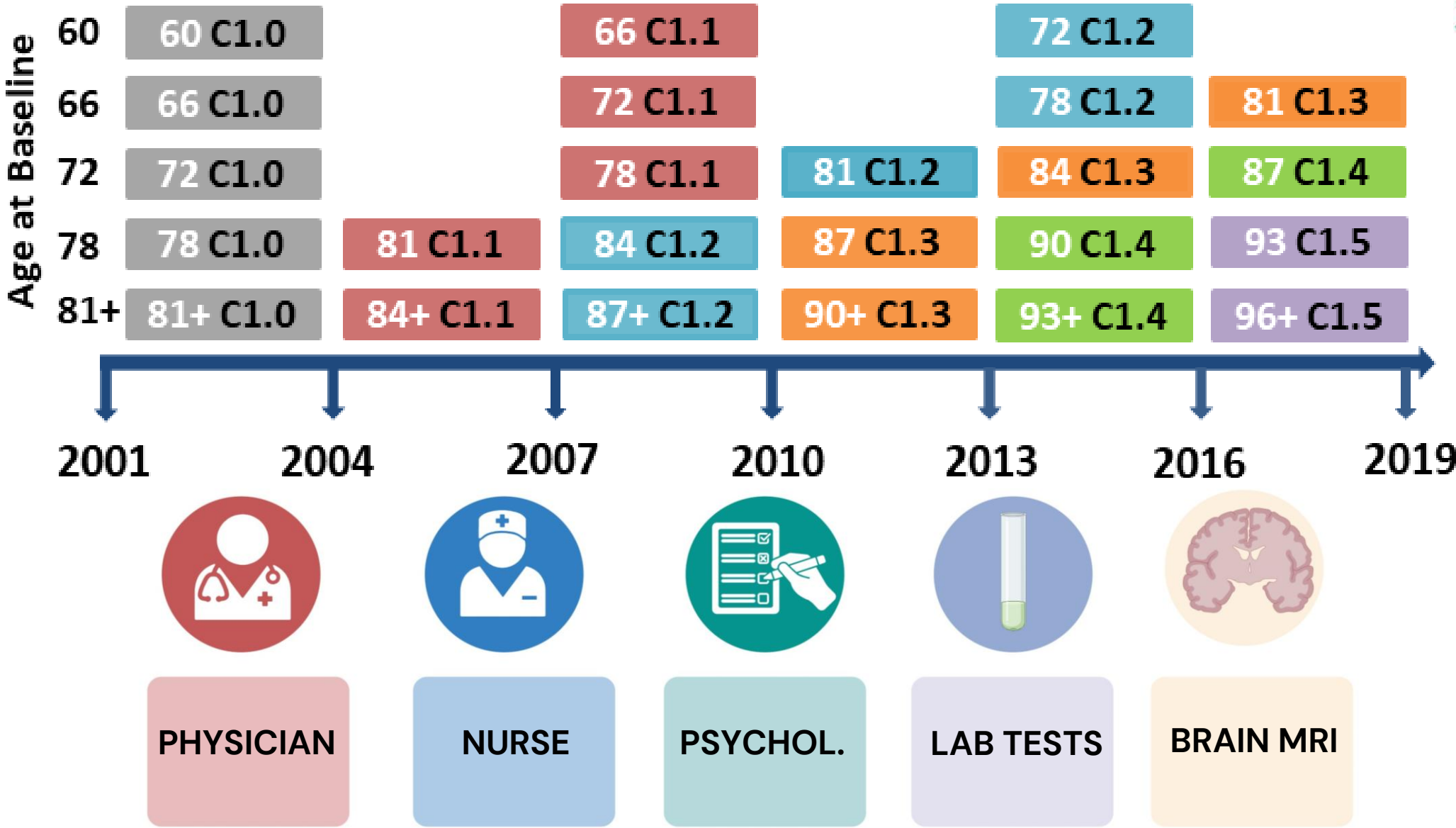
- **Population** studies often include a more diverse and **heterogeneous group of individuals** compared to clinical settings.
- Peripheral conditions can **influence the circulating level** of these biomarkers.

**Understanding the clinical validity of blood biomarkers in the community and the factors that influence their levels is crucial for maximizing their use.**

# Swedish National Study on Aging and Care in Kungsholmen



# SNAC-K



# SNAC-K data collection



## Physician's examination

- Medical history. General and neurological examination
- Cognitive assessment including MMSE, CDT
- Three-step procedure of dementia diagnosis (DSM-IV)
- Somatic chronic conditions: Clinical examination (incl. EKG), clinical charts, lab tests, administrative data, medications (ICD-10)



## Nurse's examination

- Functional tests (grip strength, gait speed) and independence, PEF, calf circumferences, nutritional status, lifestyle



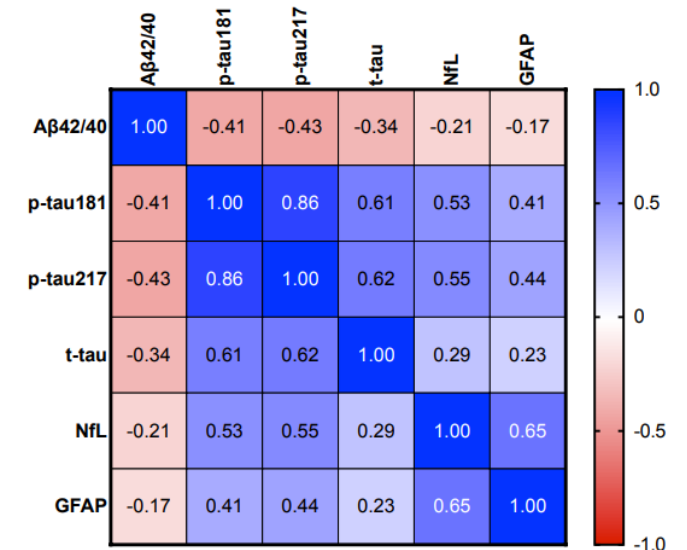
## Neuropsychological battery

- Executive function, episodic memory, visuospatial abilities, language, and perceptual speed



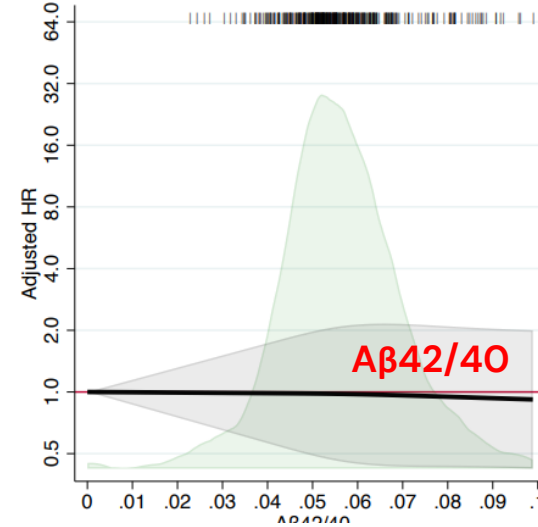
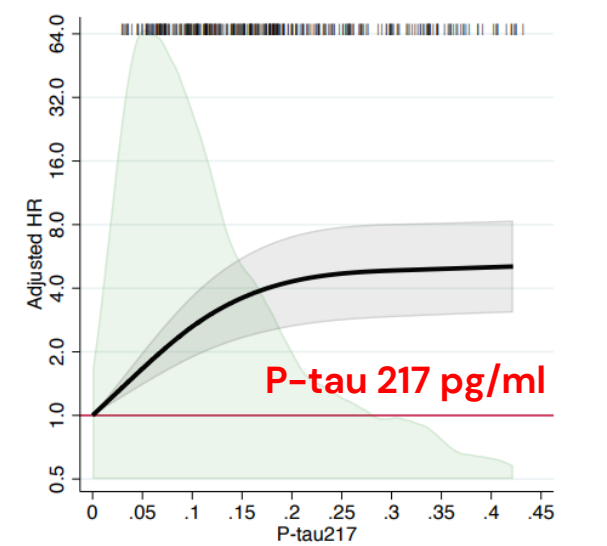
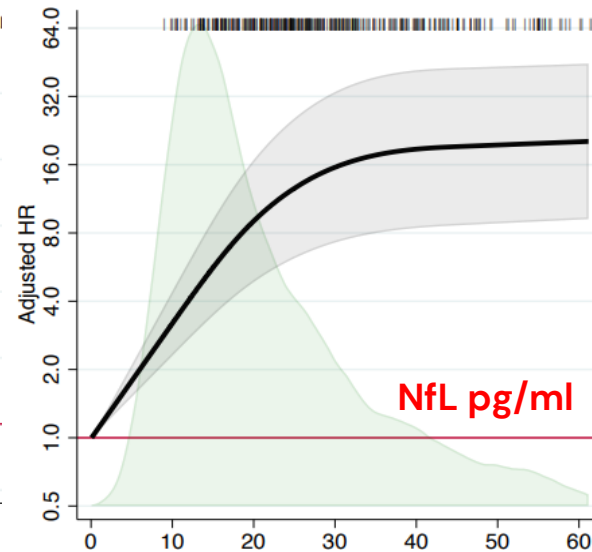
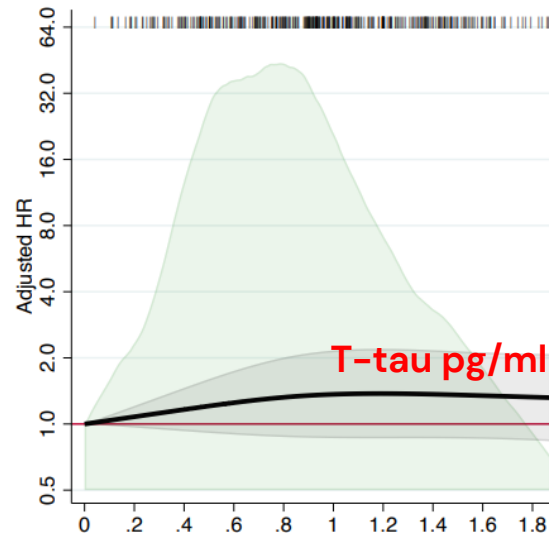
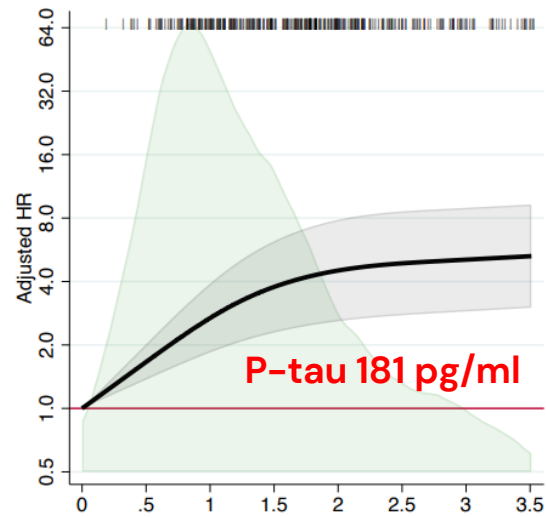
## Laboratory tests and biomarkers

- 55 biomarkers measured at baseline in serum in 2290 participants
- Quanterix and Luminex assays



# Blood-based biomarkers of Alzheimer's disease and incident dementia in the community

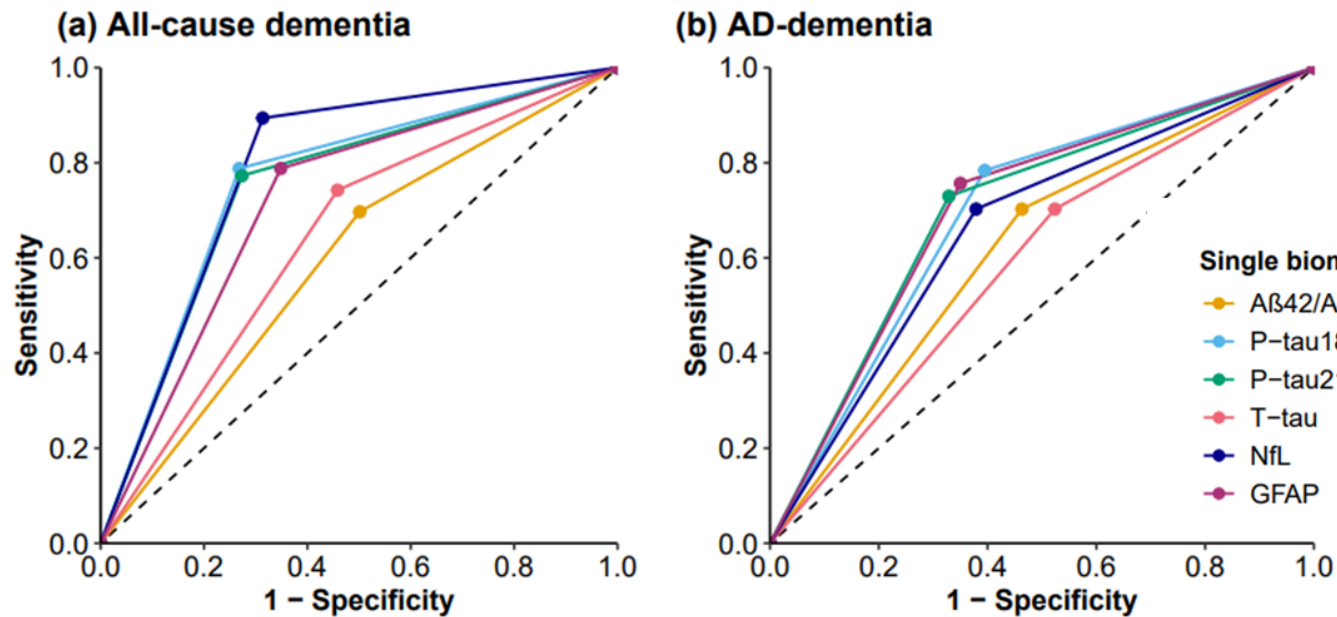
Giulia Grande <sup>1,2</sup>✉, Martina Valletta <sup>1</sup>, Debora Rizzuto<sup>1,2</sup>, Xin Xia<sup>3</sup>, Chengxuan Qiu <sup>1</sup>, Nicola Orsini<sup>4</sup>, Matilda Dale <sup>5</sup>, Sarah Andersson<sup>5</sup>, Claudia Fredolini <sup>5</sup>, Bengt Winblad <sup>3,6</sup>, Erika J. Laukka<sup>1,2</sup>, Laura Fratiglioni<sup>1,2</sup> & Davide L. Vetrano <sup>1,2</sup>



Hazard ratios derived from multi-adjusted Cox regression survival models.

# Blood-based biomarkers of Alzheimer's disease and incident dementia in the community

Giulia Grande <sup>1,2</sup>✉, Martina Valletta <sup>1</sup>, Debora Rizzuto<sup>1,2</sup>, Xin Xia<sup>3</sup>, Chengxuan Qiu <sup>1</sup>, Nicola Orsini<sup>4</sup>, Matilda Dale <sup>5</sup>, Sarah Andersson<sup>5</sup>, Claudia Fredolini <sup>5</sup>, Bengt Winblad <sup>3,6</sup>, Erika J. Laukka<sup>1,2</sup>, Laura Fratiglioni<sup>1,2</sup> & Davide L. Vetrano <sup>1,2</sup>



	PPV (95%CI)	NPV (95%CI)
<b>P-tau 217</b>	<b>33.3</b> (26.1-41.0)	<b>94.8</b> (92.1-97.2)
<b>NfL</b>	<b>33.5</b> (26.6-40.8)	<b>97.3</b> (95.2-99.2)
<b>GFAP</b>	<b>28.6</b> (22.2-35.4)	<b>94.6</b> (91.6-97.2)

### Area under the curve

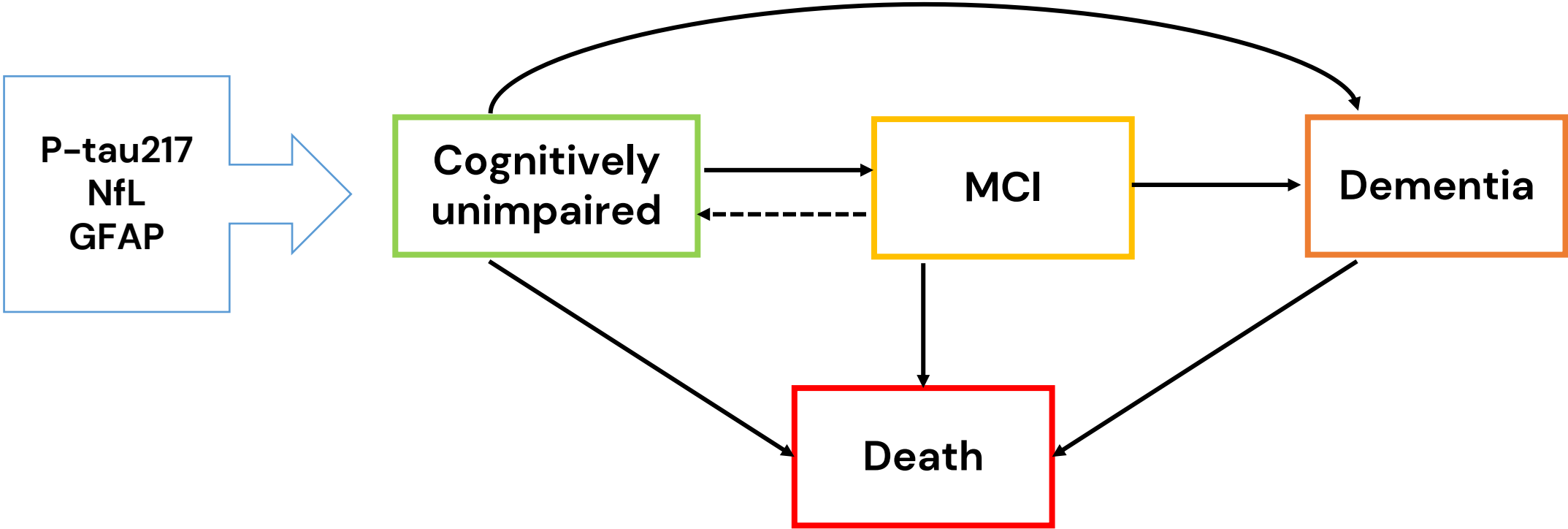
	Panel a	Panel b
Aβ42/Aβ40 ratio	64.0%	63.0%
P-tau181	81.5%	73.6%
P-tau217	81.0%	76.8%
T-tau	68.6%	55.3%
NfL	82.6%	70.9%
GFAP	77.5%	72.0%

AD blood biomarkers have the potential to rule out impending dementia in community settings, but they might need to be used in **at-risk subgroups** or **combined with other biological or clinical markers** to be used as screening tools.

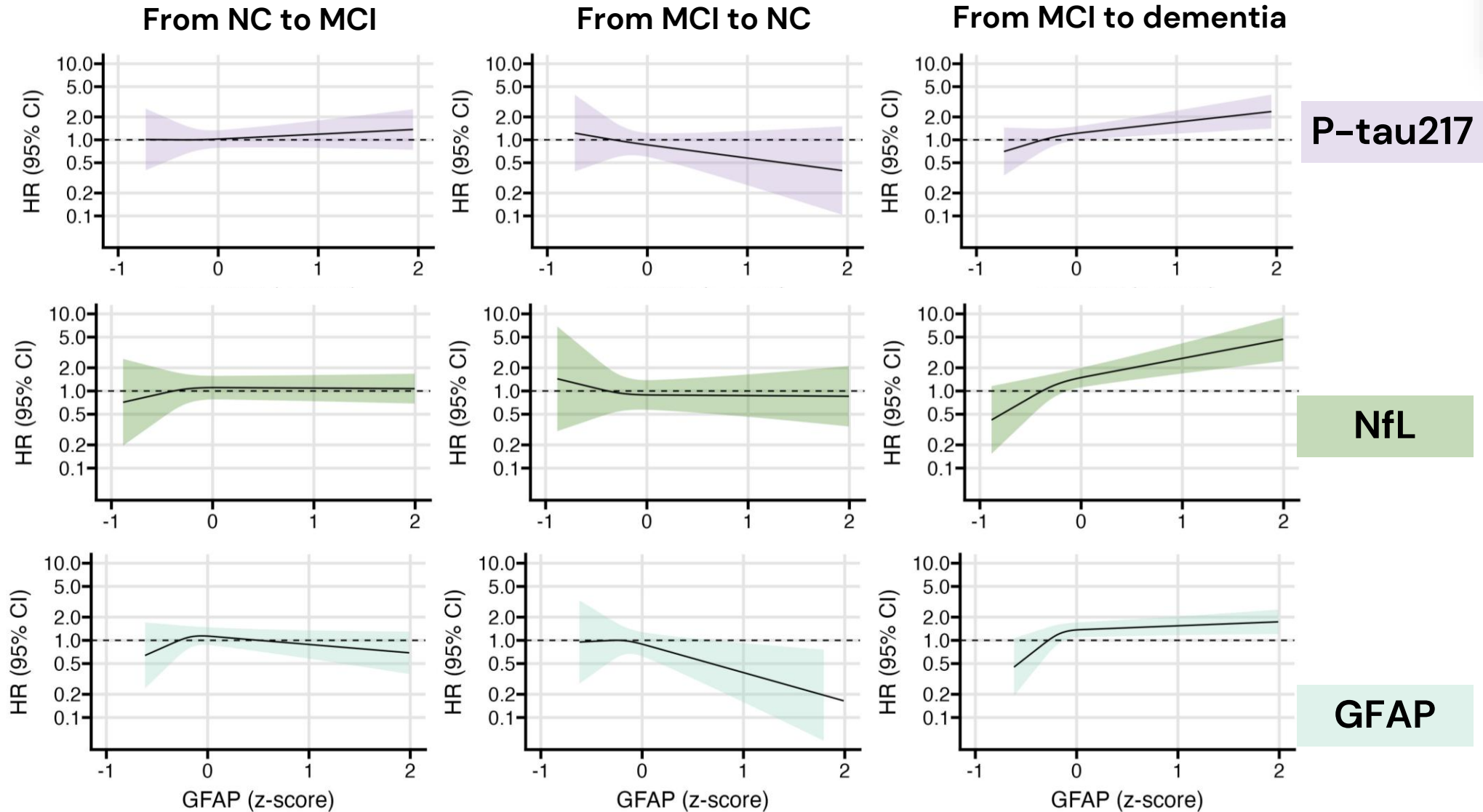


# Blood biomarkers of Alzheimer’s disease and progression across different stages of cognitive decline in the community

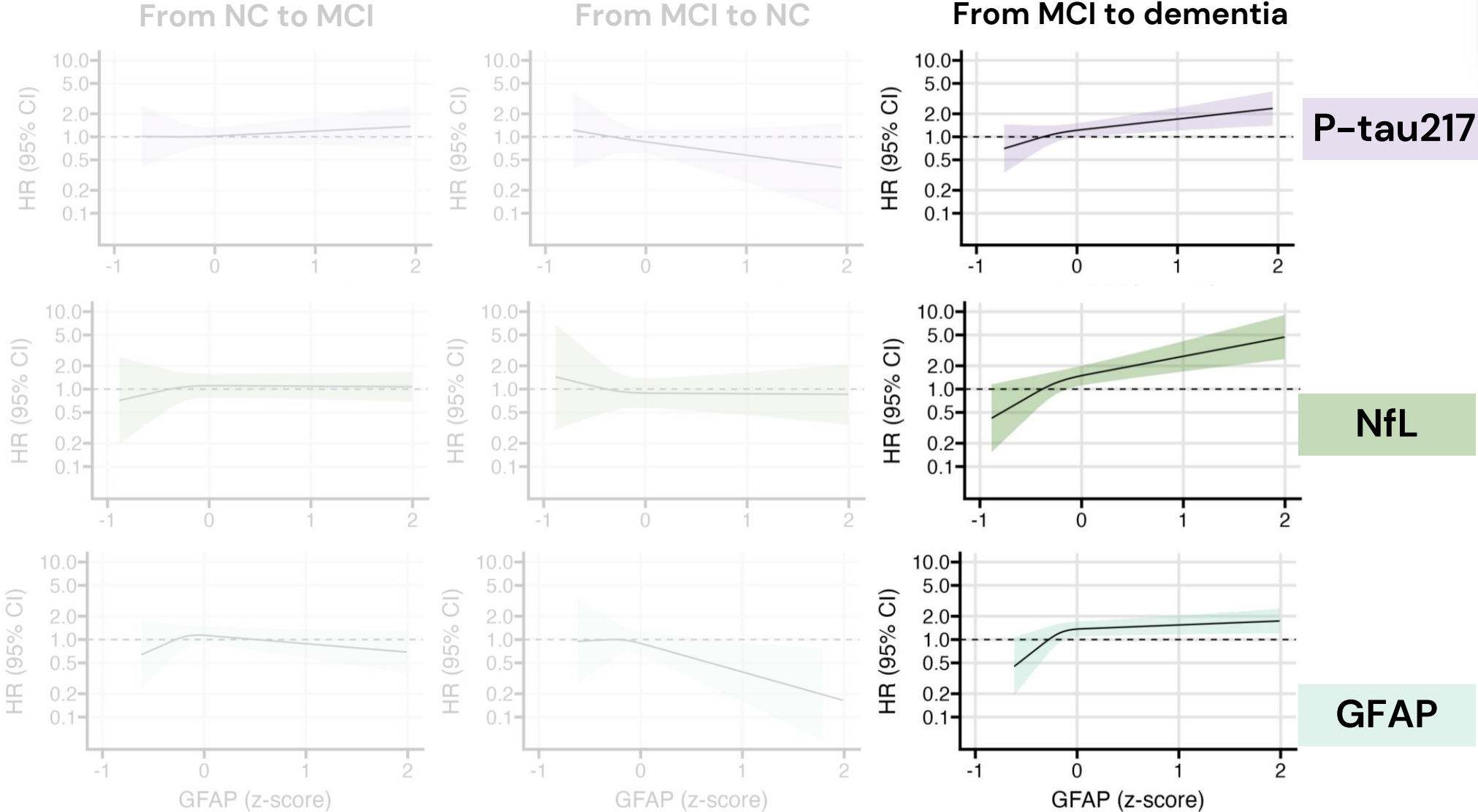
Martina Valletta <sup>1</sup>✉, Davide Liborio Vetrano <sup>1,2</sup>, Caterina Gregorio <sup>1</sup>,  
Debora Rizzuto <sup>1,2</sup>, Bengt Winblad <sup>3,4</sup>, Marco Canevelli <sup>1,5,6</sup>, Sarah Andersson <sup>7</sup>,  
Matilda Dale <sup>7</sup>, Claudia Fredolini <sup>7</sup>, Erika J. Laukka <sup>1,2</sup>, Laura Fratiglioni <sup>1</sup> &  
Giulia Grande <sup>1,2</sup>



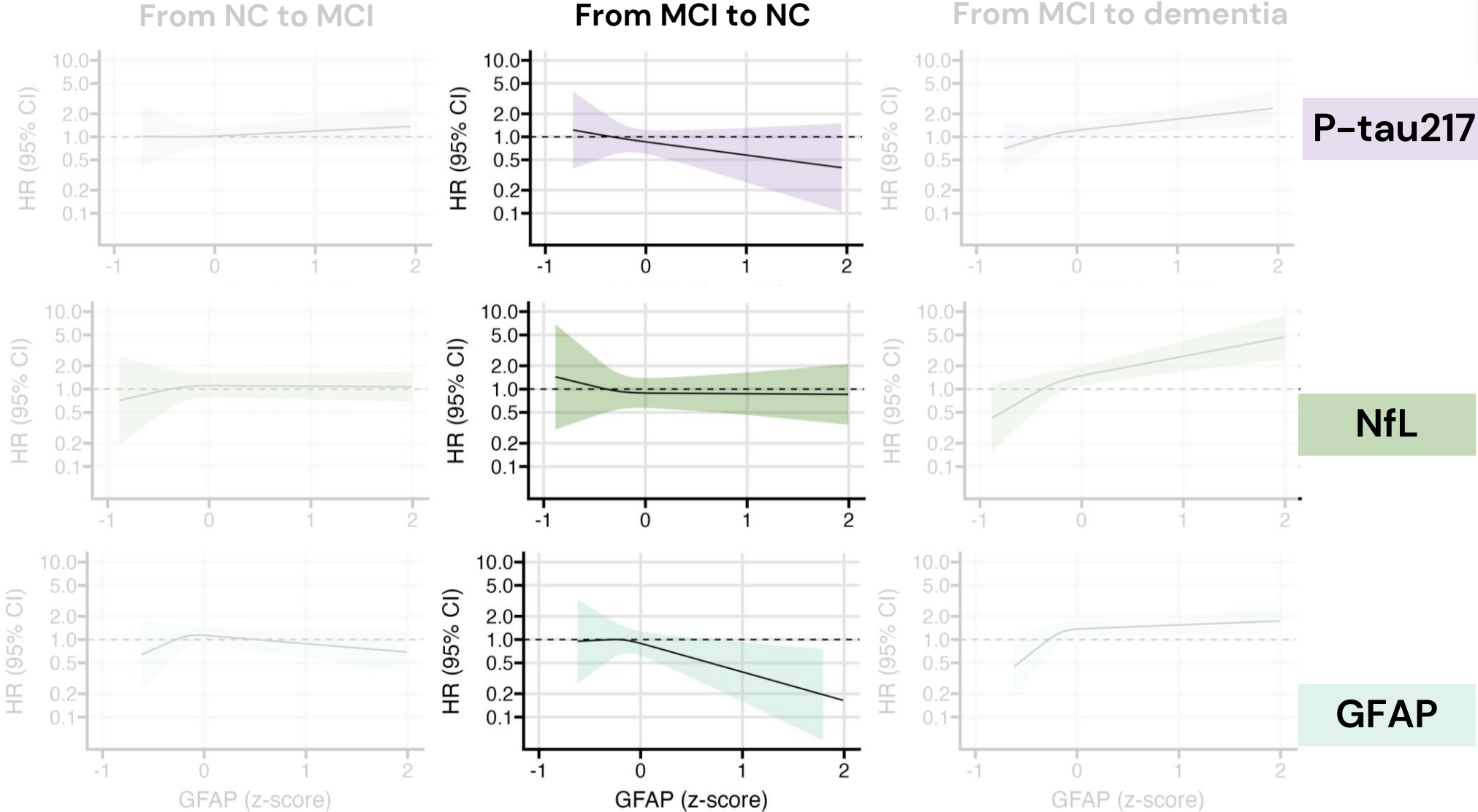
# AD biomarkers and transitions across cognitive stages



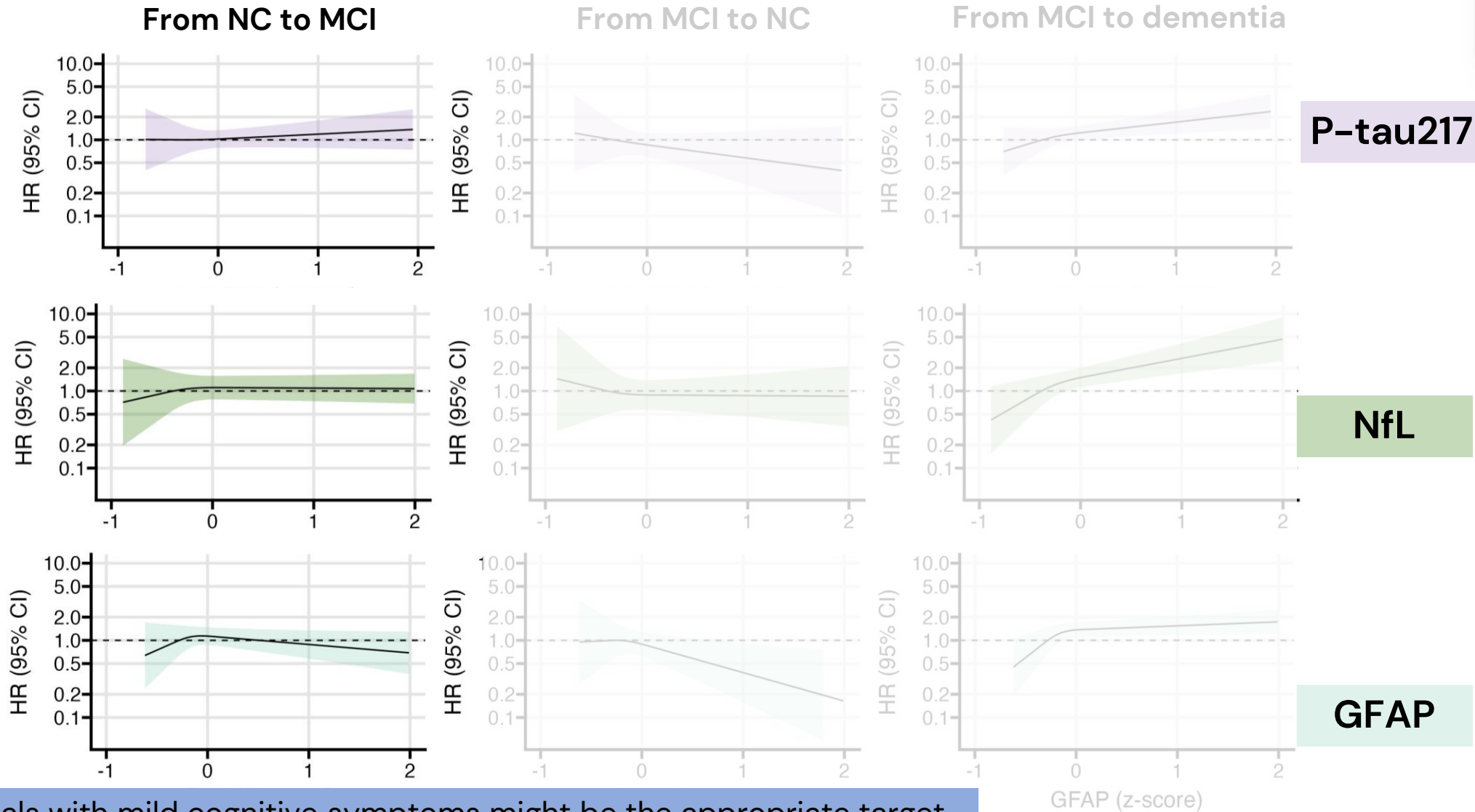
# AD biomarkers and transitions across cognitive stages



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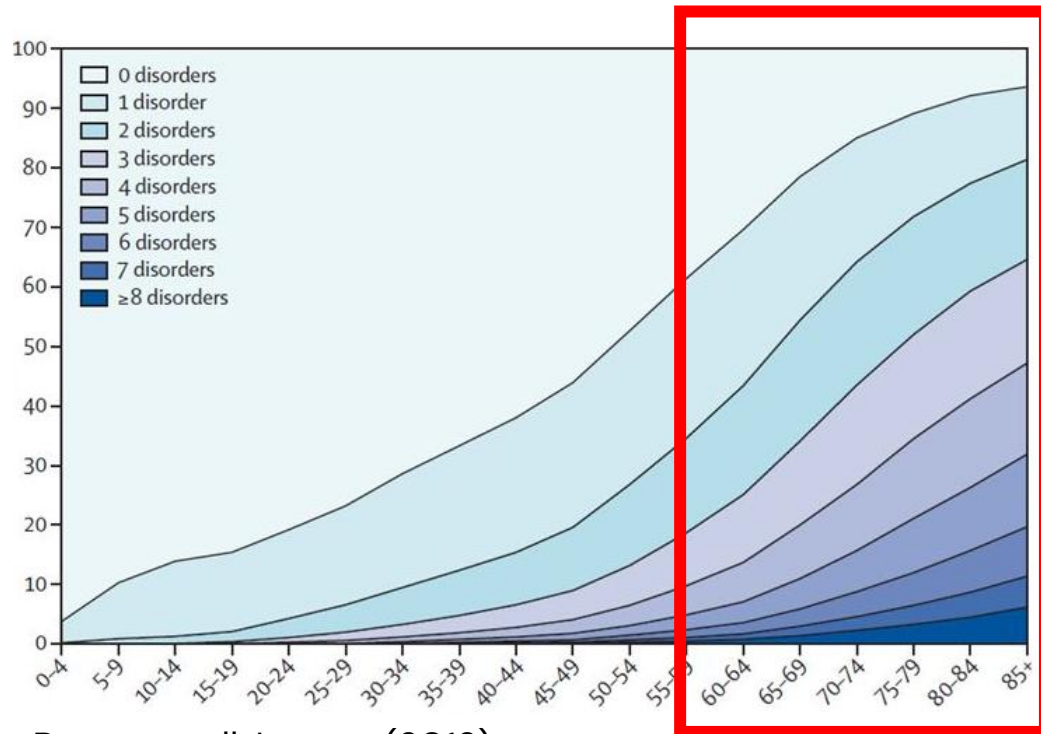


# AD biomarkers and transitions across cognitive stages

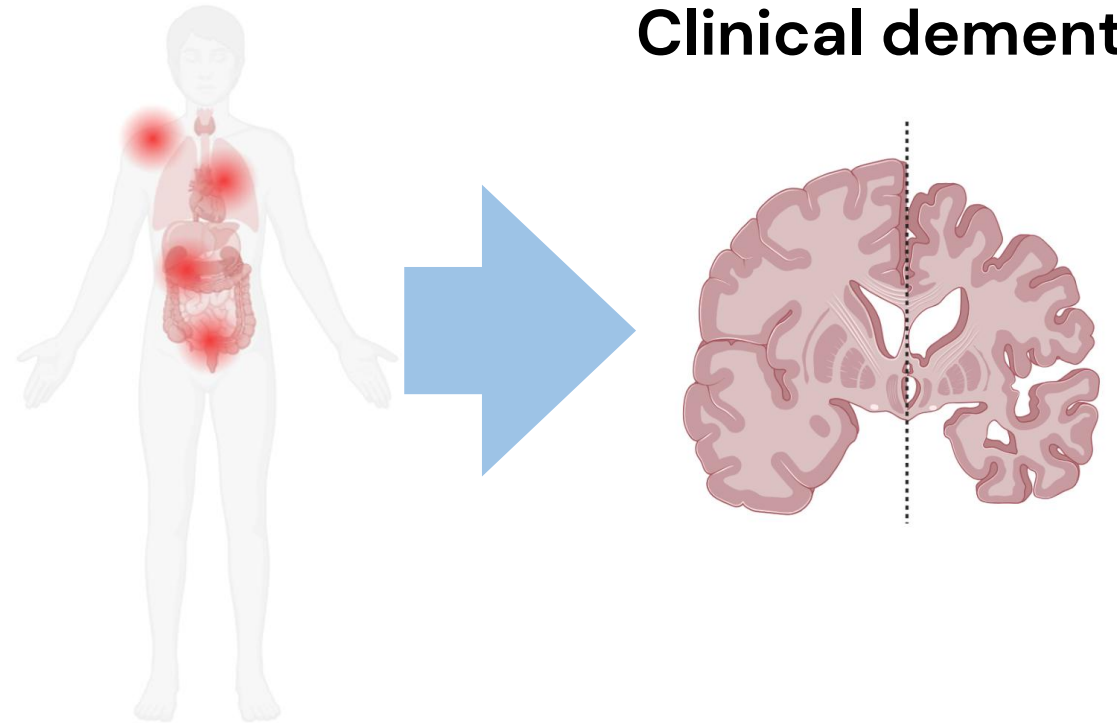


Individuals with mild cognitive symptoms might be the appropriate target for biomarker testing in the community

# Systemic health as a determinant of brain health



Barnet et al, Lancet (2012)

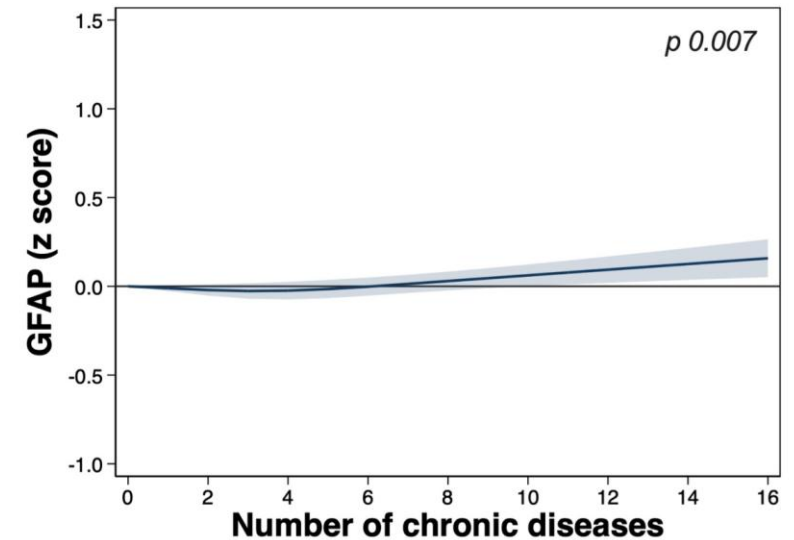
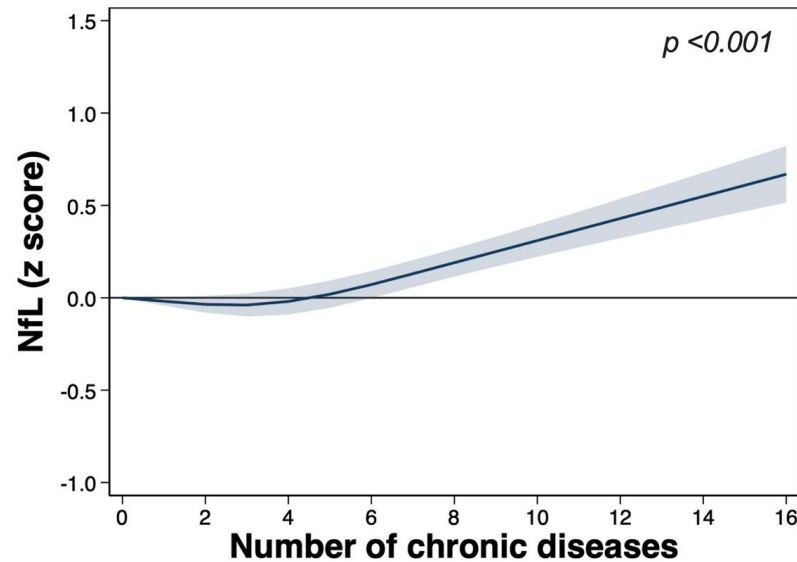
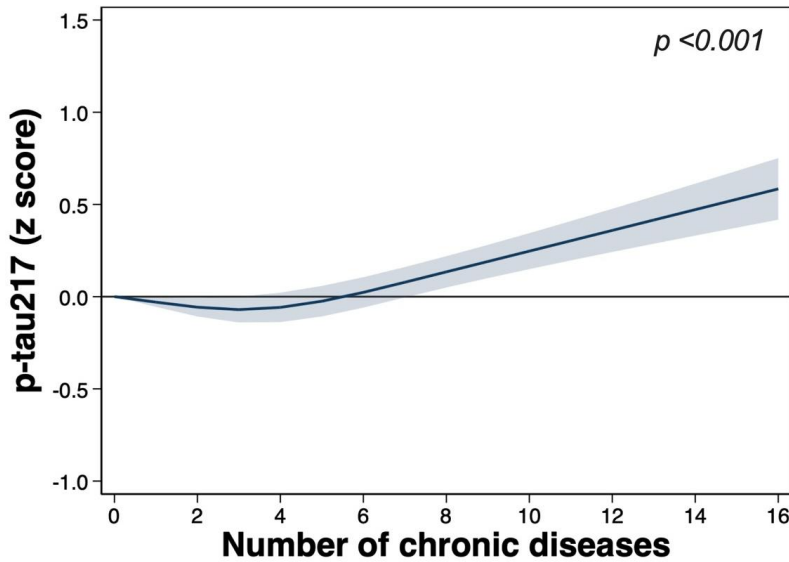


Smith E et al, Nature Review Neurology 2024  
Livingston et al, Lancet 2024  
Grande et al, Ageing Res Rev. 2020  
Winblad B et al, Lancet Neurology 2016  
Barnet et al, Lancet (2012)

RESEARCH ARTICLE

# Multimorbidity patterns and blood biomarkers of Alzheimer's disease in community-dwelling cognitively unimpaired older adults

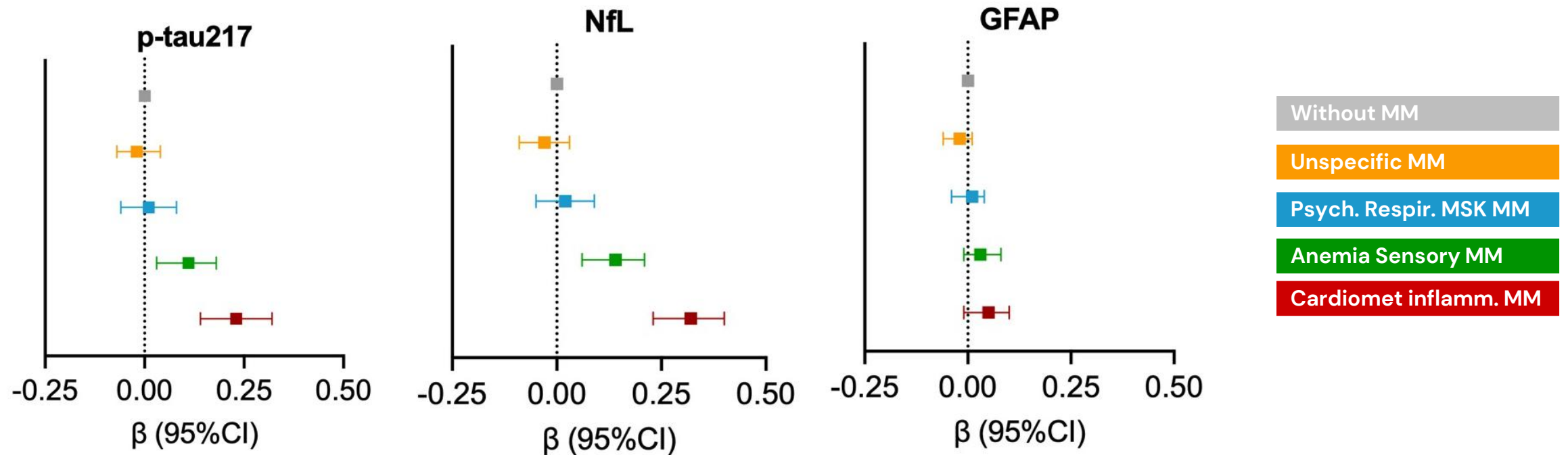
Alessandra Marengoni<sup>1,2</sup> | Giulia Grande<sup>1,3</sup> | Martina Valletta<sup>1</sup> | Caterina Gregorio<sup>1</sup> |  
Amaia Calderón-Larrañaga<sup>1,3</sup> | Matilda Dale<sup>4</sup> | Claudia Fredolini<sup>4</sup> |  
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RESEARCH ARTICLE

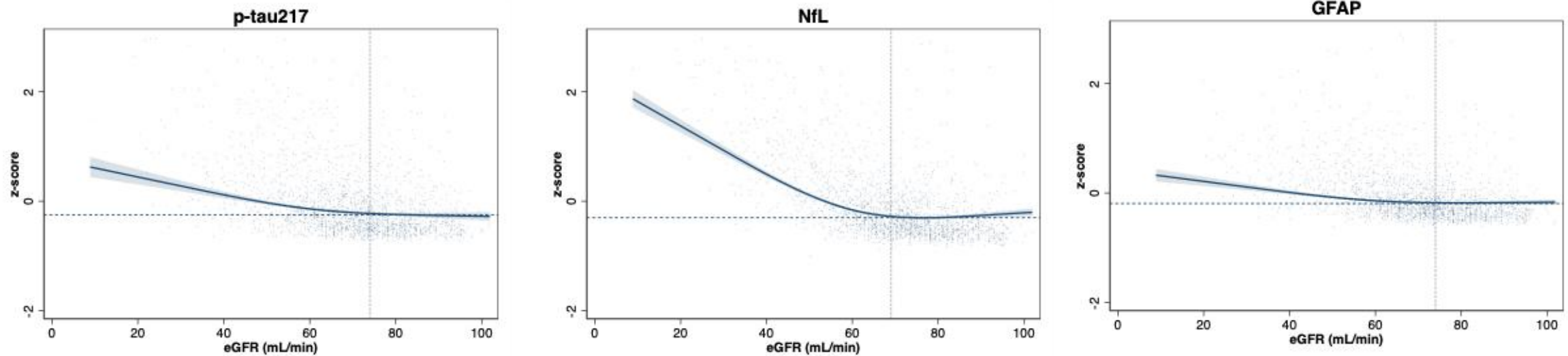
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# Kidney Function, Alzheimer Disease Blood Biomarkers, and Dementia Risk in Community-Dwelling Older Adults

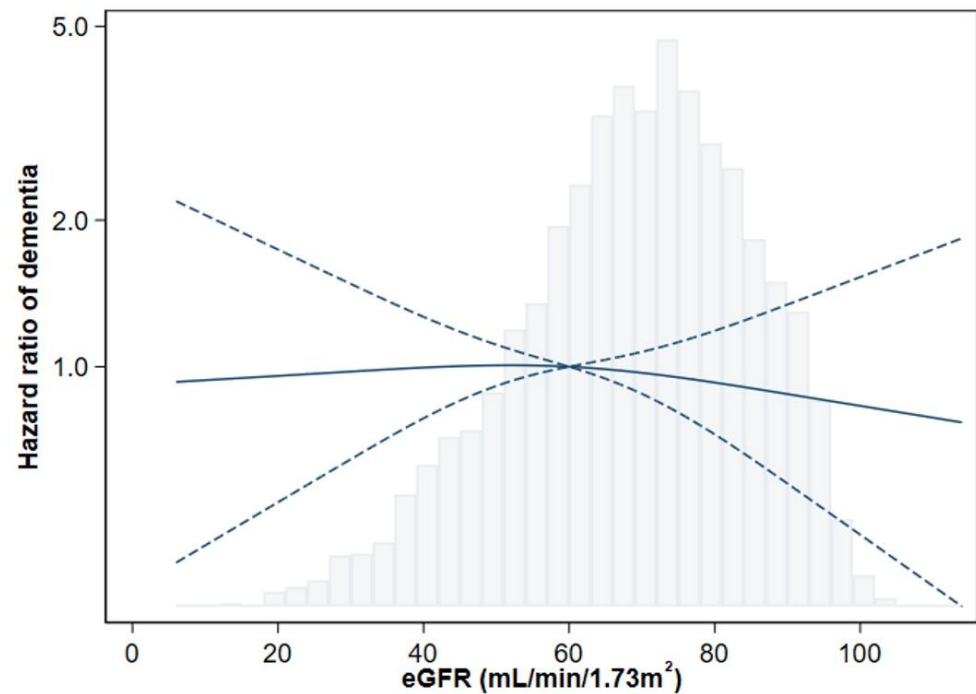
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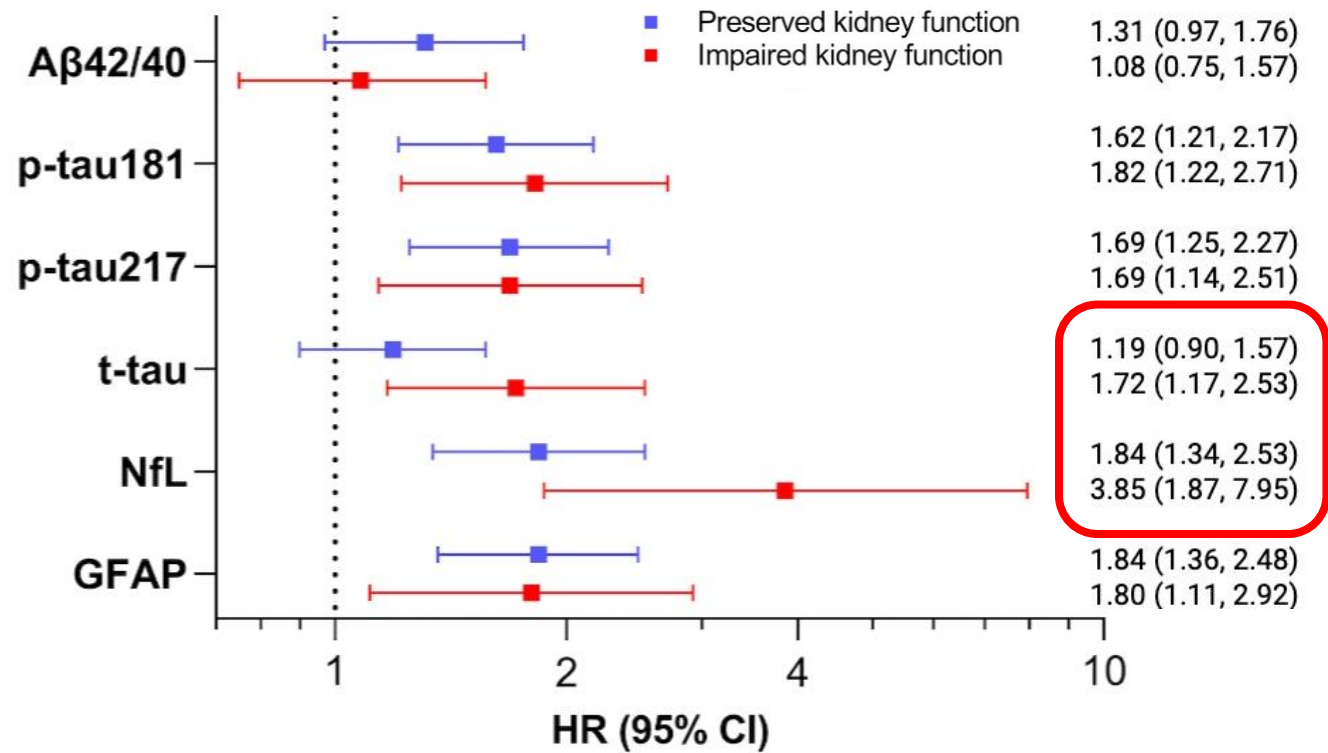
**Estimated glomerular filtration rate and AD blood biomarkers.** Estimates are derived from quantile regression models on the median adjusted for age, sex, education, APOE e4 carrier status, anemia, any CVD and BMI

# Kidney Function, Alzheimer Disease Blood Biomarkers, and Dementia Risk in Community-Dwelling Older Adults

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Multi-adjusted Cox regression models (age, sex, education, APOE, and any cardio- or cerebro-vascular disease, BMI)



Impaired kidney function did not independently increase the risk of dementia but rather appeared to accelerate the clinical expression of underlying neurodegenerative pathology.

# Conclusions

- AD blood biomarkers perform well also in community settings, predicting dementia with good accuracy.
- However, they are not suitable as screening tools in population settings.
- Individual diseases and disease combinations alter biomarkers concentrations (targeted cut-offs?)

# Future directions

- Improve prediction even outside specialist settings, integrate biomarkers with other clinical/biological markers & focus on at-risk subgroups
- Consider somatic co-pathology in the clinical-biological framework of (AD) dementia in older adults

**Davide L Vetrano**  
**Martina Valletta**  
**Bengt Winblad**  
**Francesca Gasparini**  
**Laura Fratiglioni**  
**Amaia Calderón-Larrañaga**  
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**Erika J Laukka**  
**Caterina Gregorio**



**Karolinska  
Institutet**



**SNAC-K**

**Data collection team &  
participants**

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**Claudia Fredolini**  
**Matilda Dale**  
**Sarah Andersson**



## KI Biobank



**Alessandra Marengoni**  
**Alessandro Padovani**  
**Andrea Pilotto**



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