



68° CONGRESSO NAZIONALE SIGG

Ritorno al futuro

FIRENZE, 13-16 DICEMBRE 2023  
PALAZZO DEI CONGRESSI



*Firenze, 15 Dicembre 2023*

# Multimorbilità, cluster di malattie e declino cognitivo

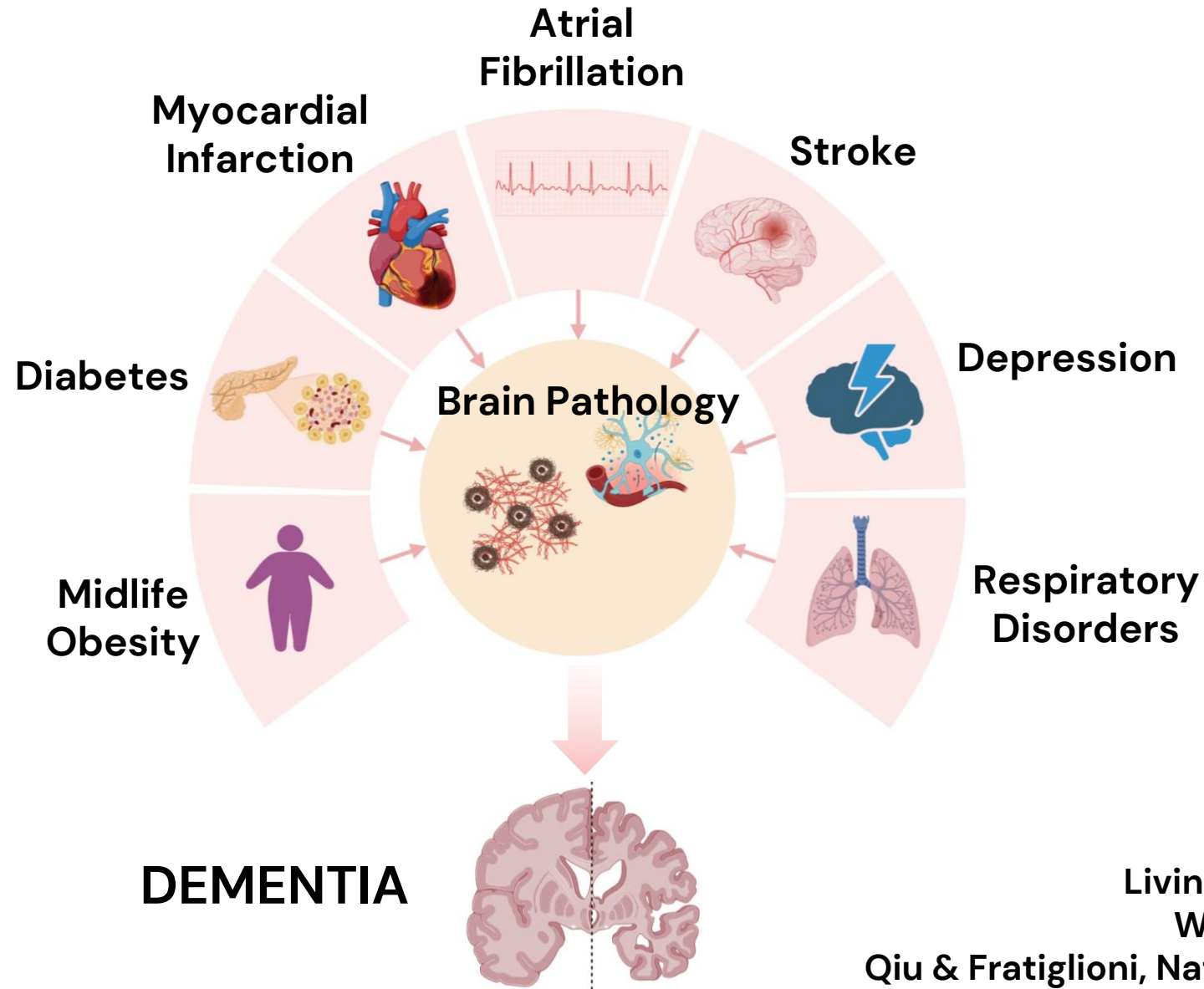
**Giulia Grande, MD, PhD**

*Aging Research Center, NVS  
Karolinska Institutet, Sweden*



**Karolinska  
Institutet**

# Disease burden and dementia

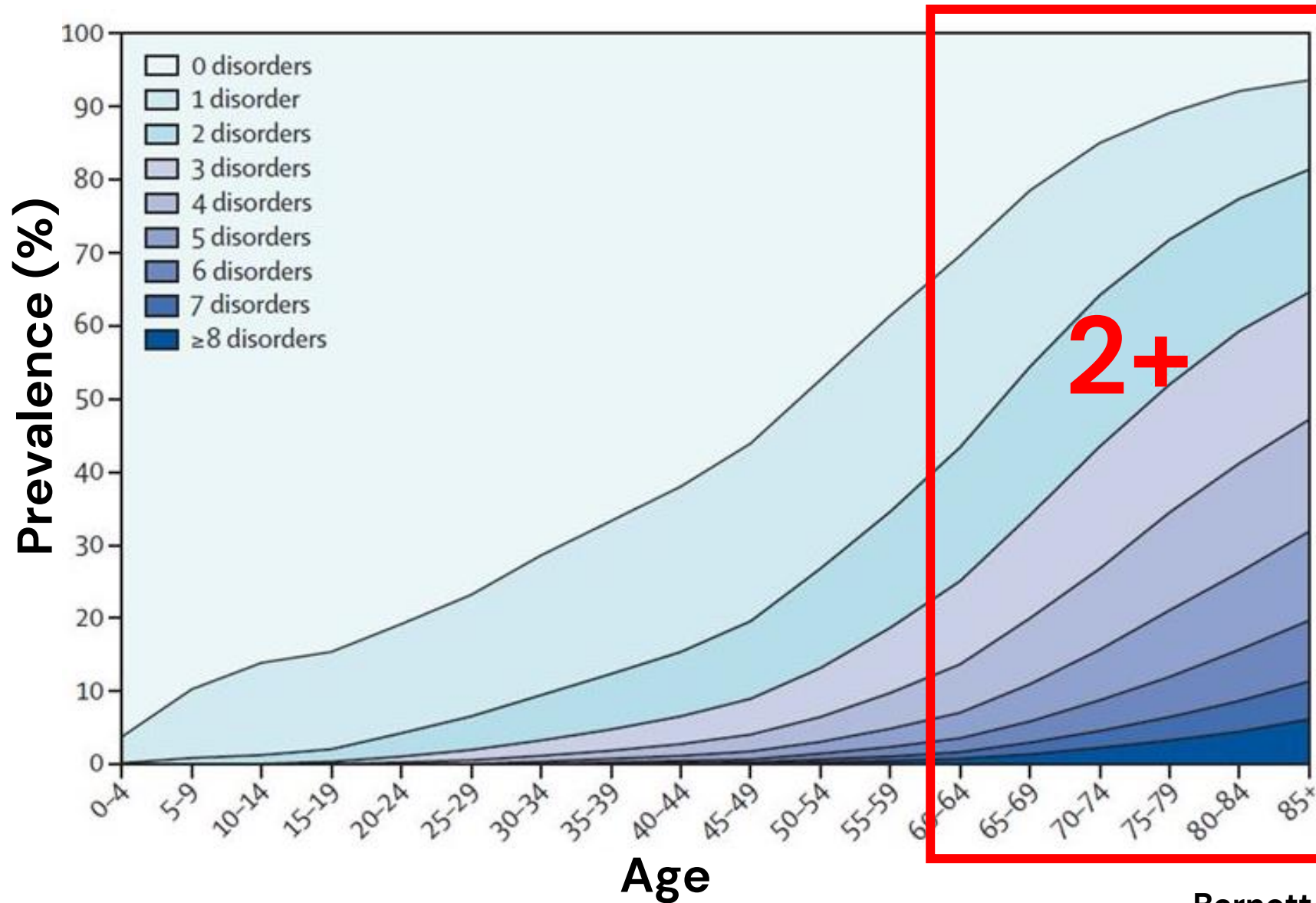


Livingston G, Lancet (2020)

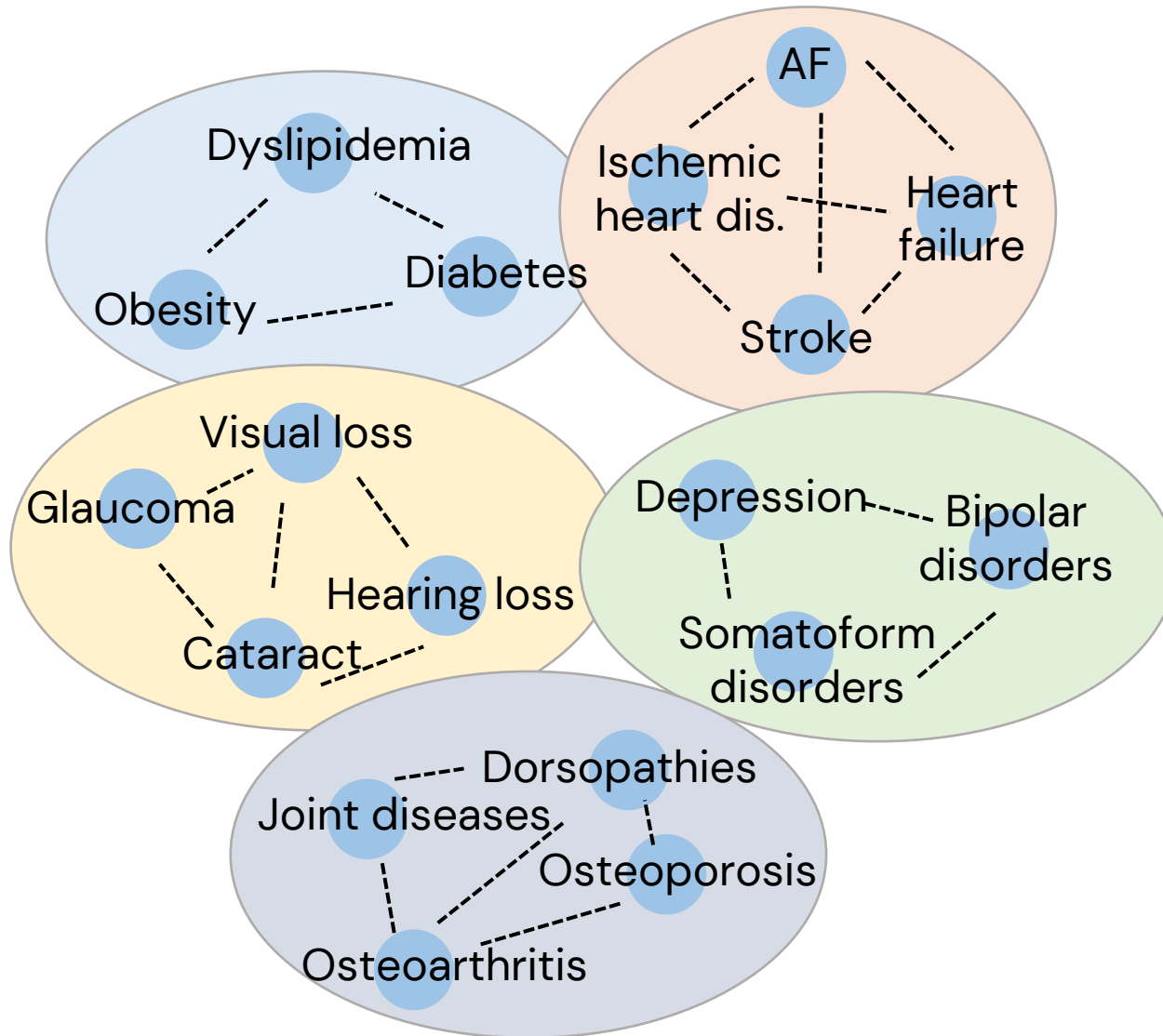
Winblad B, Lancet (2016)

Qiu & Fratiglioni, Nat Rev Cardiology (2015)

# Multimorbidity in old age



# Clusters of diseases



- **Diseases** tend to **cluster** in the same person following specific **patterns**
- **Shared pathophysiological** underlying **mechanisms** and/or **risk and protective factors**
- Differential association with several health-related outcomes

# What is the impact of disease burden and different disease clusters on cognitive and brain aging?

- Disease clusters on dementia risk (**Study I**)
- Disease clusters on transitions across cognitive stages and death (**Study II**)
- Multimorbidity burden on structural brain changes (**Study III**)

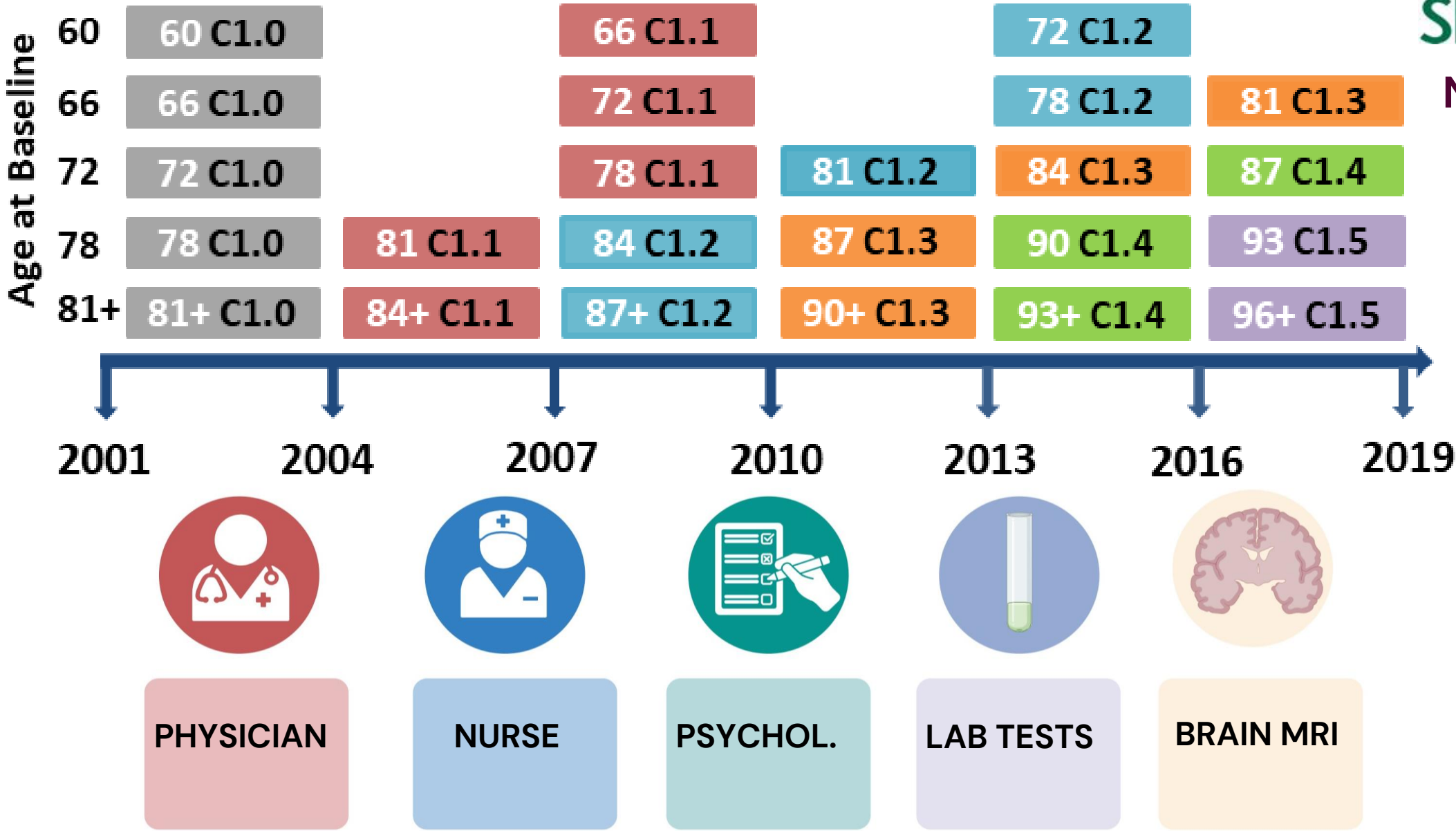


# Swedish National Study on Aging and Care in Kungsholmen



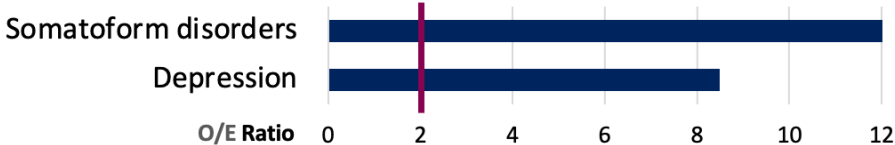
# SNAC-K

  
**SNAC-K**  
**N=3363**

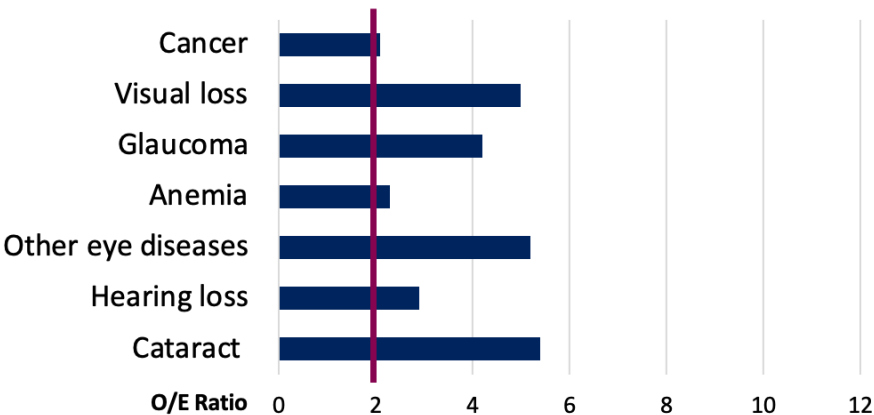


# MM patterns (Study I & II)

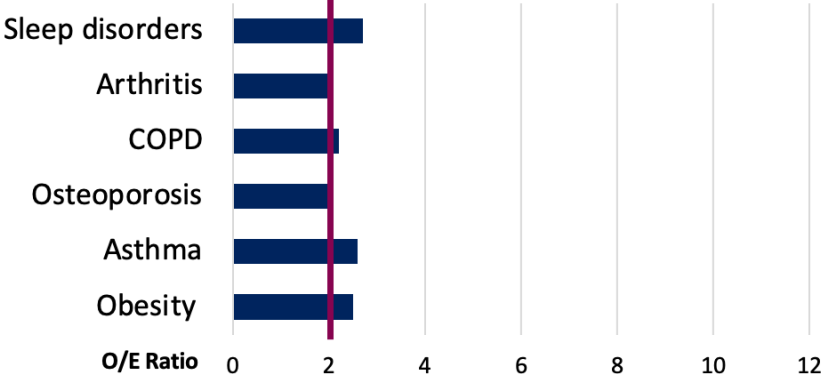
## Neuropsychiatric



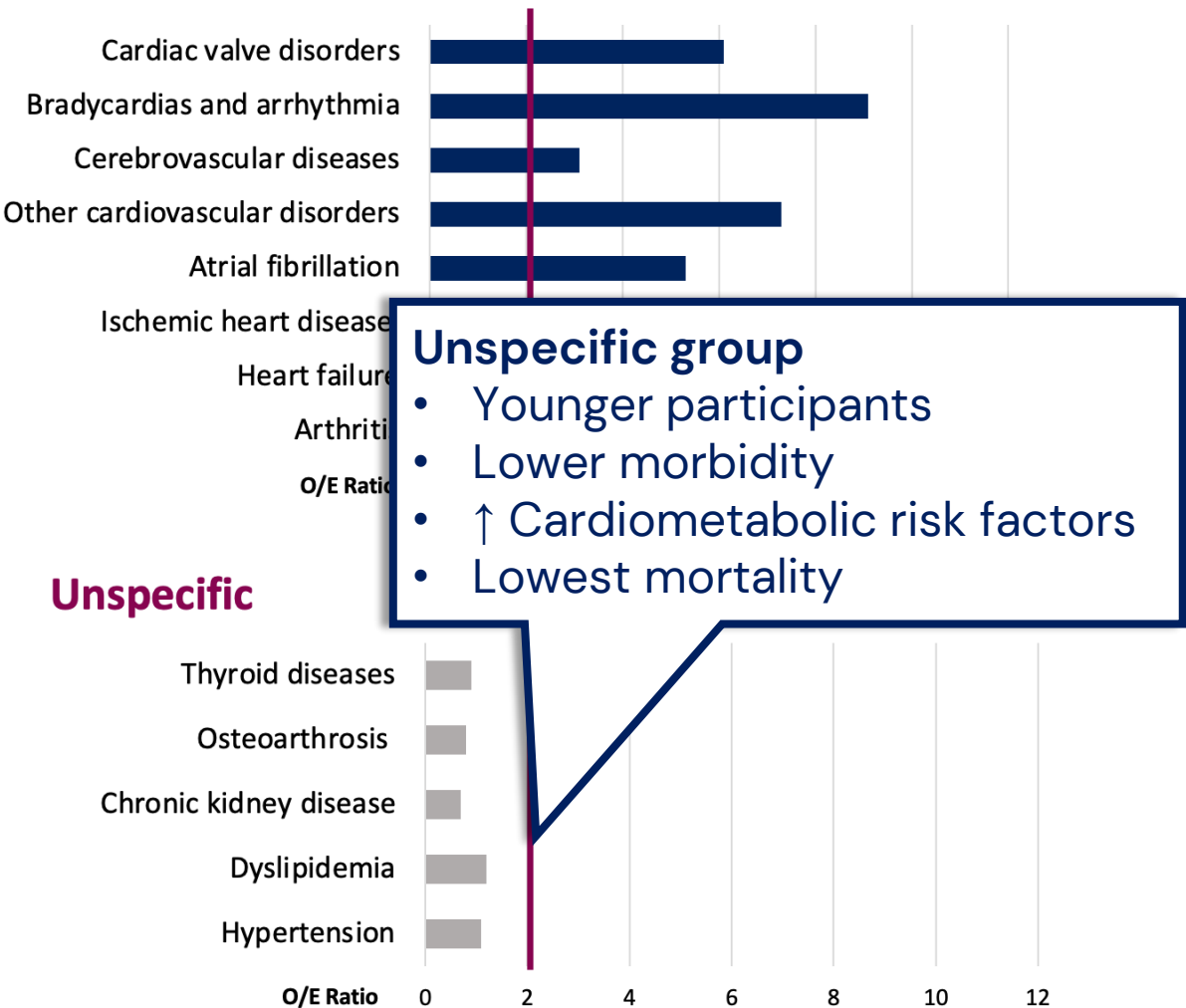
## Sensory impairment-Cancer



## Respiratory-Metabolic-Musculoskeletal



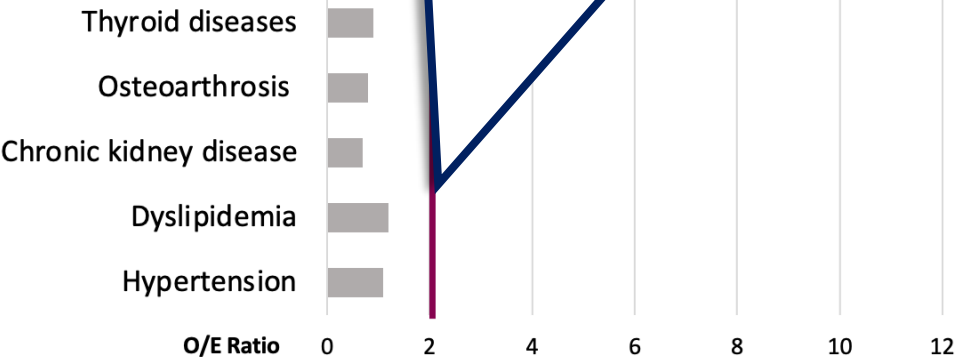
## Cardiovascular



**Unspecific group**

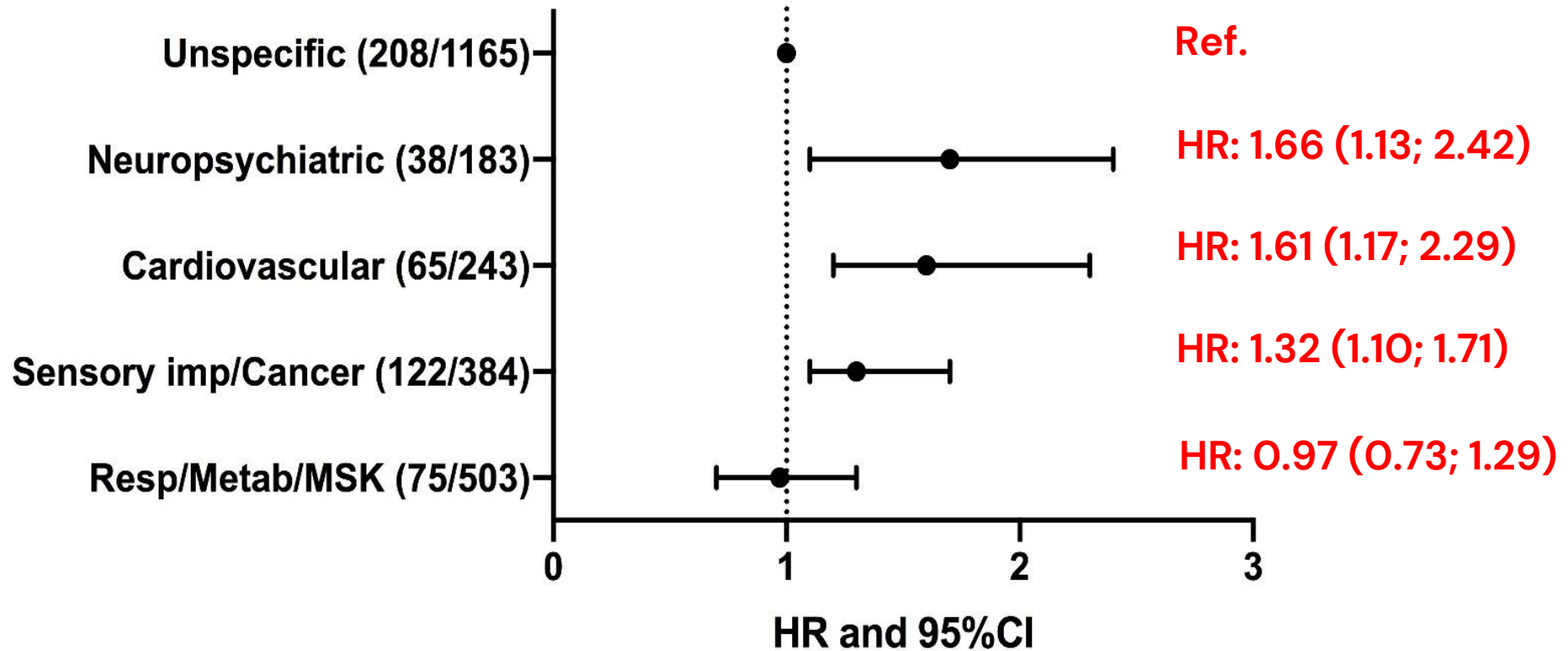
- Younger participants
- Lower morbidity
- ↑ Cardiometabolic risk factors
- Lowest mortality

## Unspecific



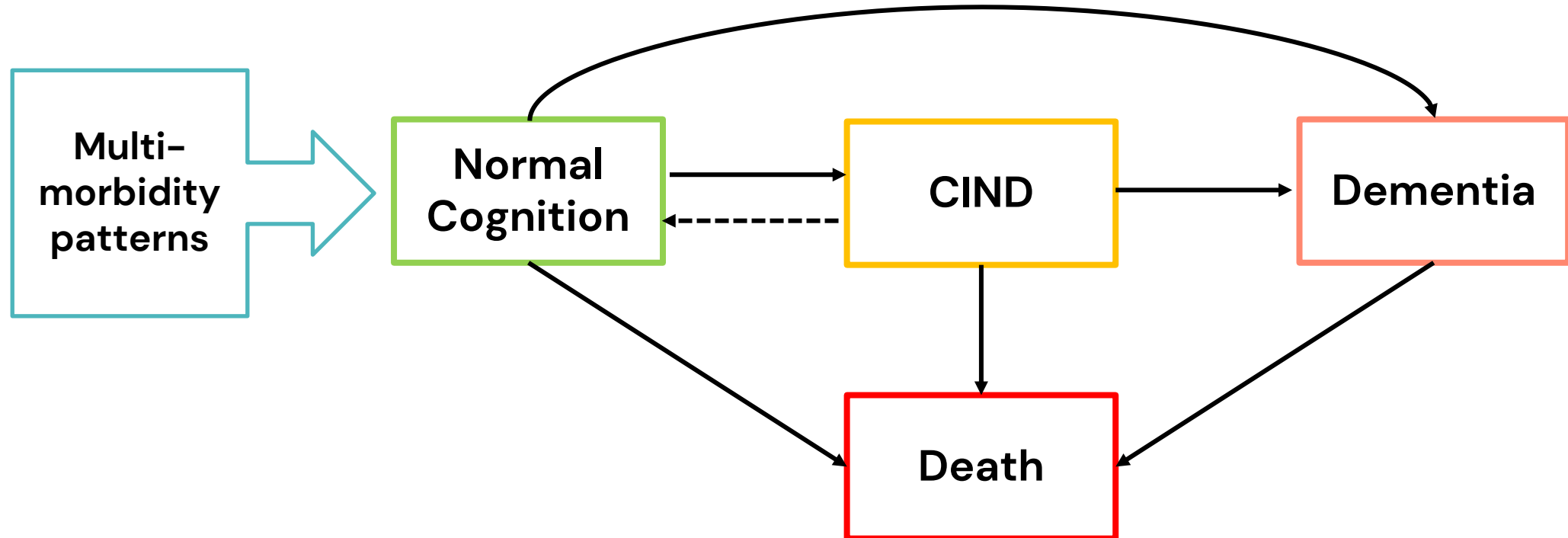


# MM patterns and dementia (Study I)

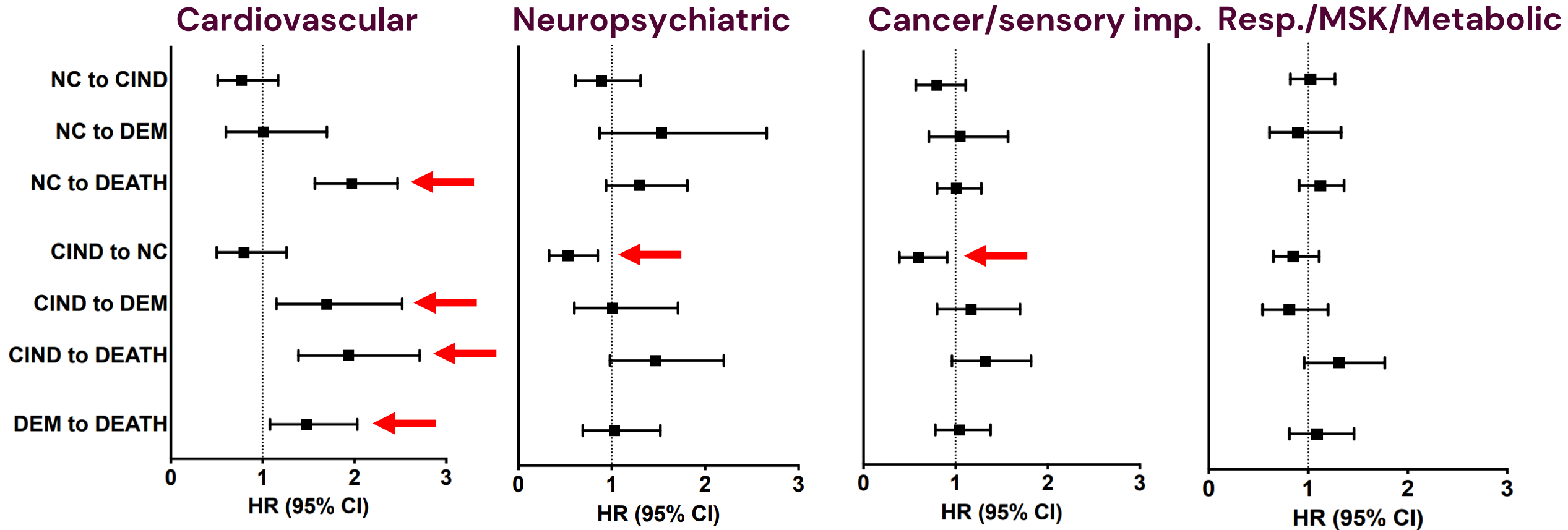


HR and 95% CI from multi-adjusted Cox models.

# Methods (Study II)

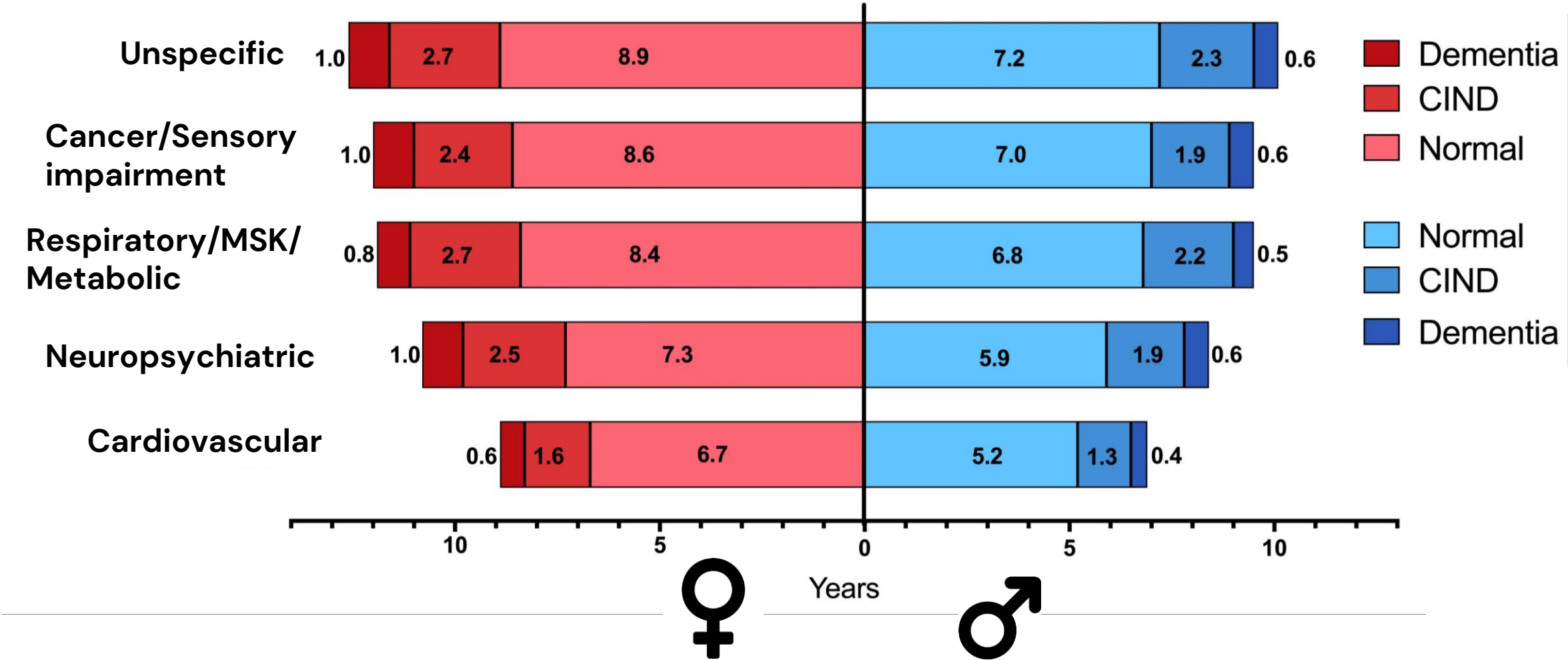


# MM patterns across cognitive stages and death (Study II)



HR and 95%CI from multi-adjusted Markov models.  
Unspecific cluster as reference.

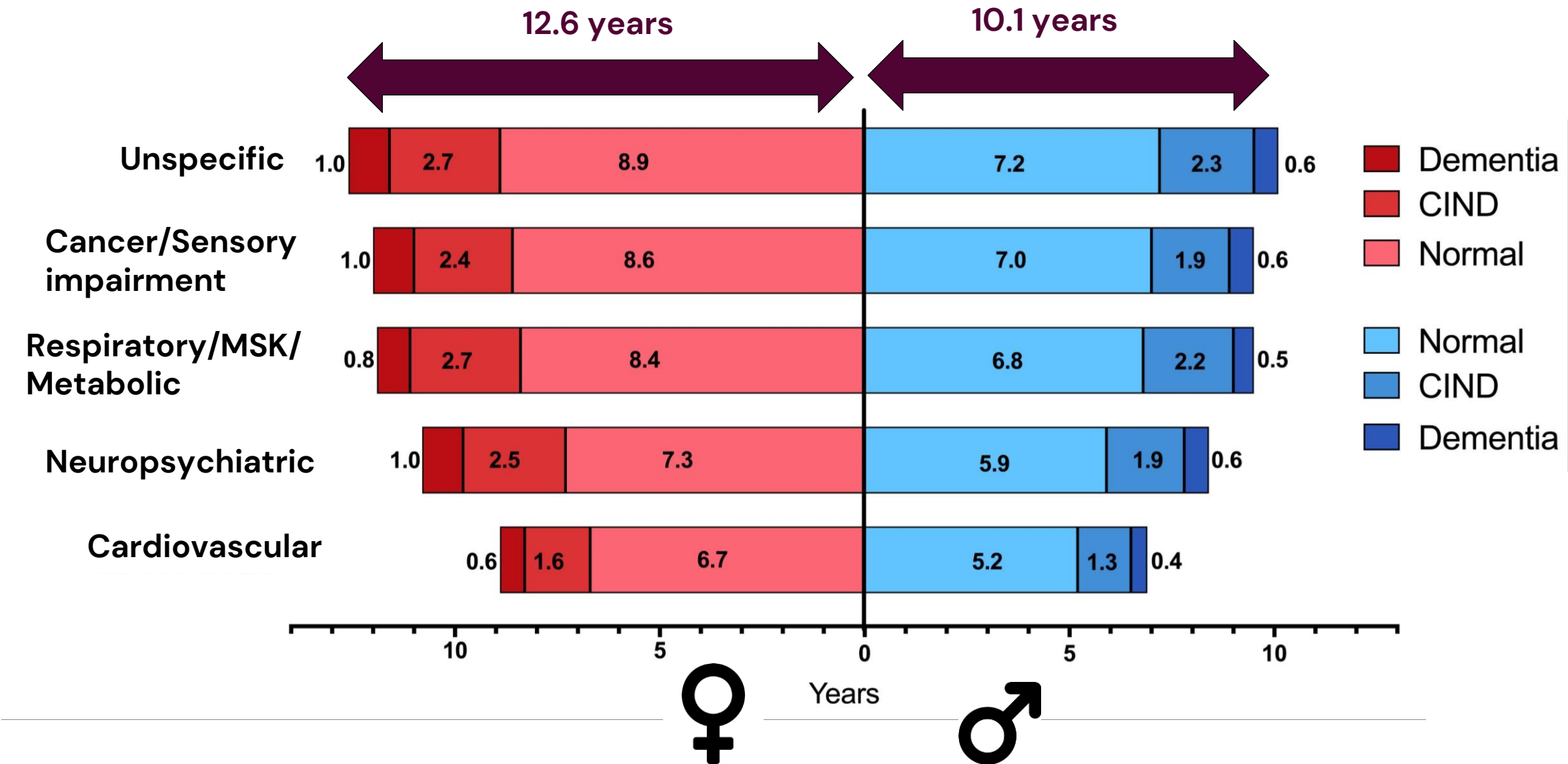
# Estimated life expectancies (Study II)



For individuals free from dementia at age 75

Valletta M, [...] Grande G. JIM (2022)

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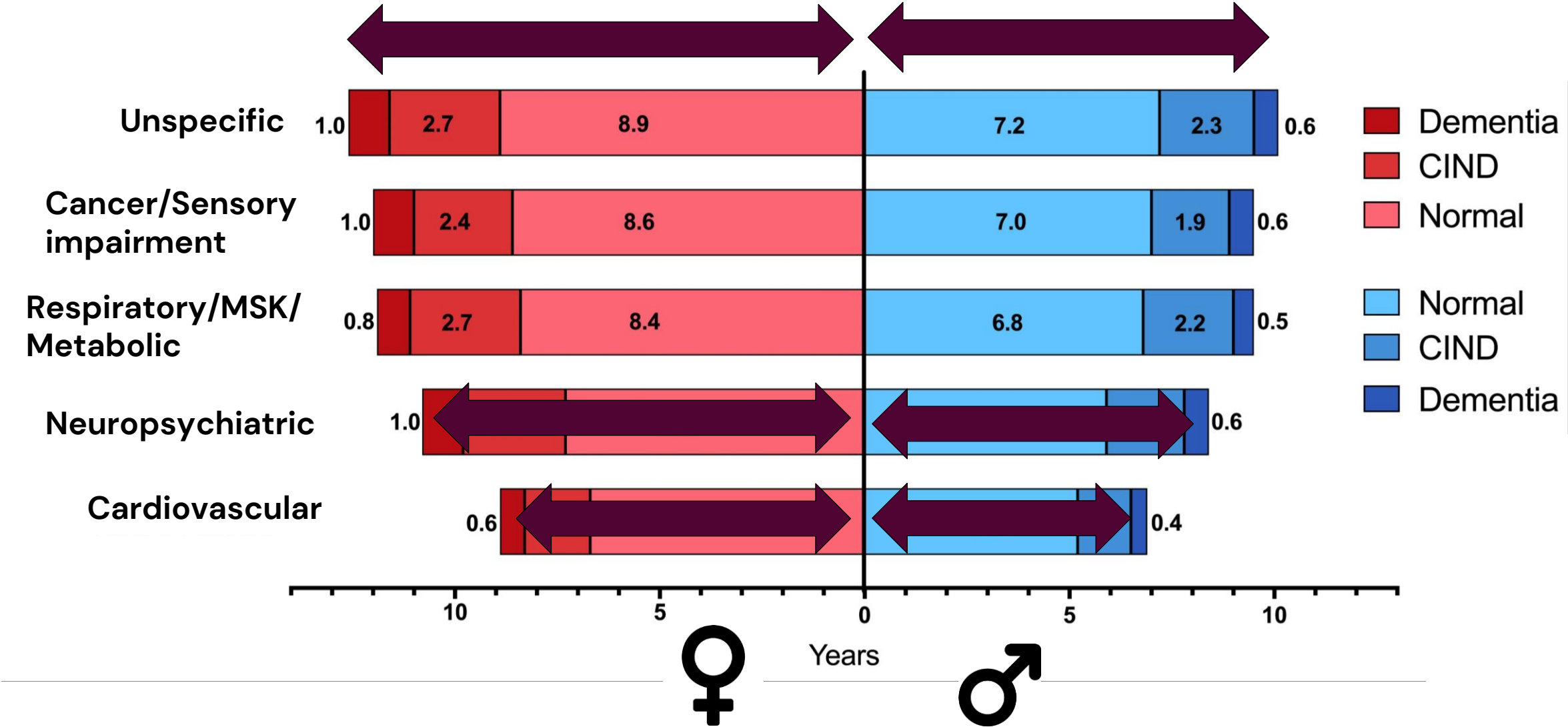


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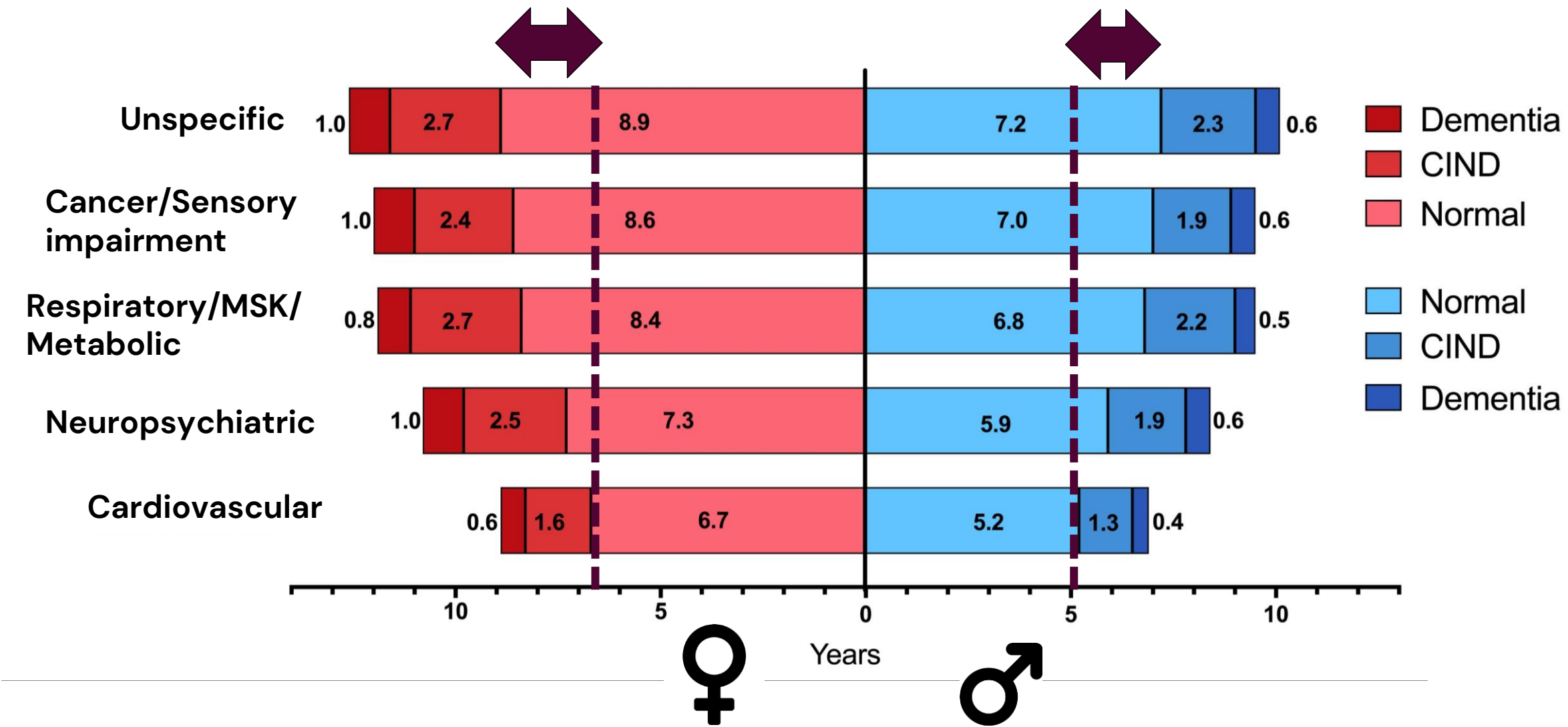
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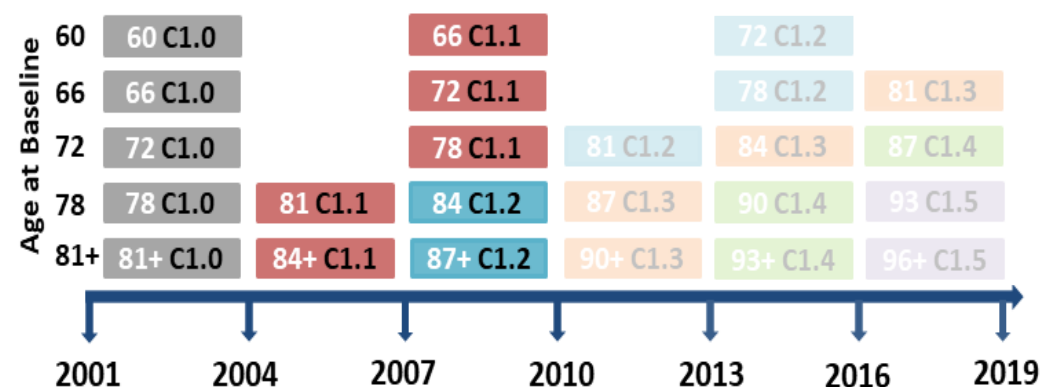
# SNAC-K MRI

**390 dementia free participants**  
from SNAC-K who underwent brain MRI

## Multimorbidity

60 chronic diseases diagnosed at baseline and grouped into 14 body systems

- **Mild multimorbidity:** 2+ chronic diseases affecting one or two body systems
- **Complex multimorbidity:** 3+ chronic diseases affecting three or more body systems



## Neuroimaging

1.5T MRI at baseline and after 3 and 6 years

# Mild and complex MM (Study III)

## Multimorbidity

60 chronic diseases  
diagnosed at baseline and  
grouped into 14 body systems

- **Mild multimorbidity:** 2+ chronic diseases affecting one or two body systems
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Diseases of cardiocirculatory system

Diseases of digestive system

Diseases of ear, nose and throat

Diseases of the endocrine/metabol. system

Diseases of the eye

Diseases of the genitourinary system

Diseases of the respiratory system

Cancers

Hematological/immunological conditions

Infectious diseases

Musculoskeletal conditions

Skin conditions

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# Mild and complex MM (Study III)

## Multimorbidity

60 chronic diseases diagnosed at baseline and grouped into 14 body systems

- **Mild multimorbidity:** 2+ chronic diseases affecting one or two body systems
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Mild	
Diseases of cardiocirculatory system	Atrial fibrillation
Diseases of digestive system	
Diseases of ear, nose and throat	
Diseases of the endocrine/metabol. system	Diabetes
Diseases of the eye	
Diseases of the genitourinary system	
Diseases of the respiratory system	
Cancers	
Hematological/immunological conditions	
Infectious diseases	
Musculoskeletal conditions	
Skin conditions	



# Mild and complex MM (Study III)

## Multimorbidity

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	Mild	Complex
Diseases of cardiocirculatory system	Atrial fibrillation	Atrial fibrillation
Diseases of digestive system		
Diseases of ear, nose and throat		
Diseases of the endocrine/metabol. system	Diabetes	Diabetes
Diseases of the eye		
Diseases of the genitourinary system		Kidney disease
Diseases of the respiratory system		
Cancers		
Hematological/immunological conditions		
Infectious diseases		
Musculoskeletal conditions		
Skin conditions		

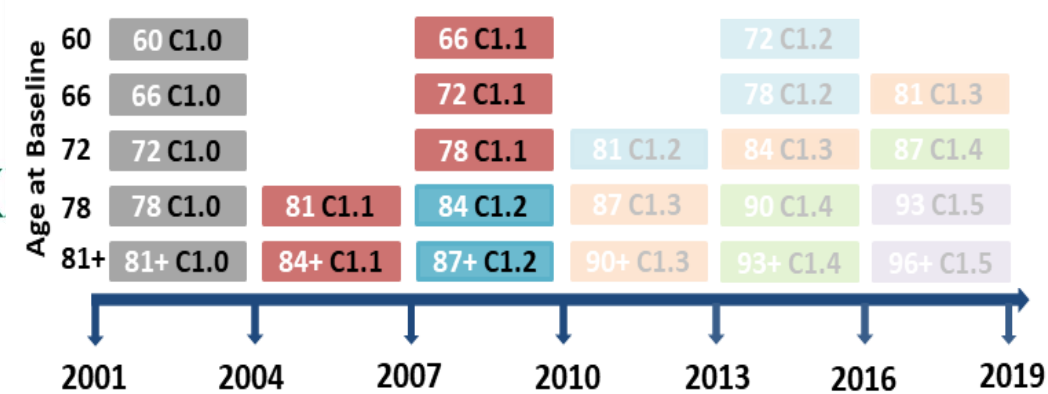
# SNAC-K MRI

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## Neuroimaging

1.5T MRI at baseline and after 3 and 6 years

**Total brain  
tissue volume**

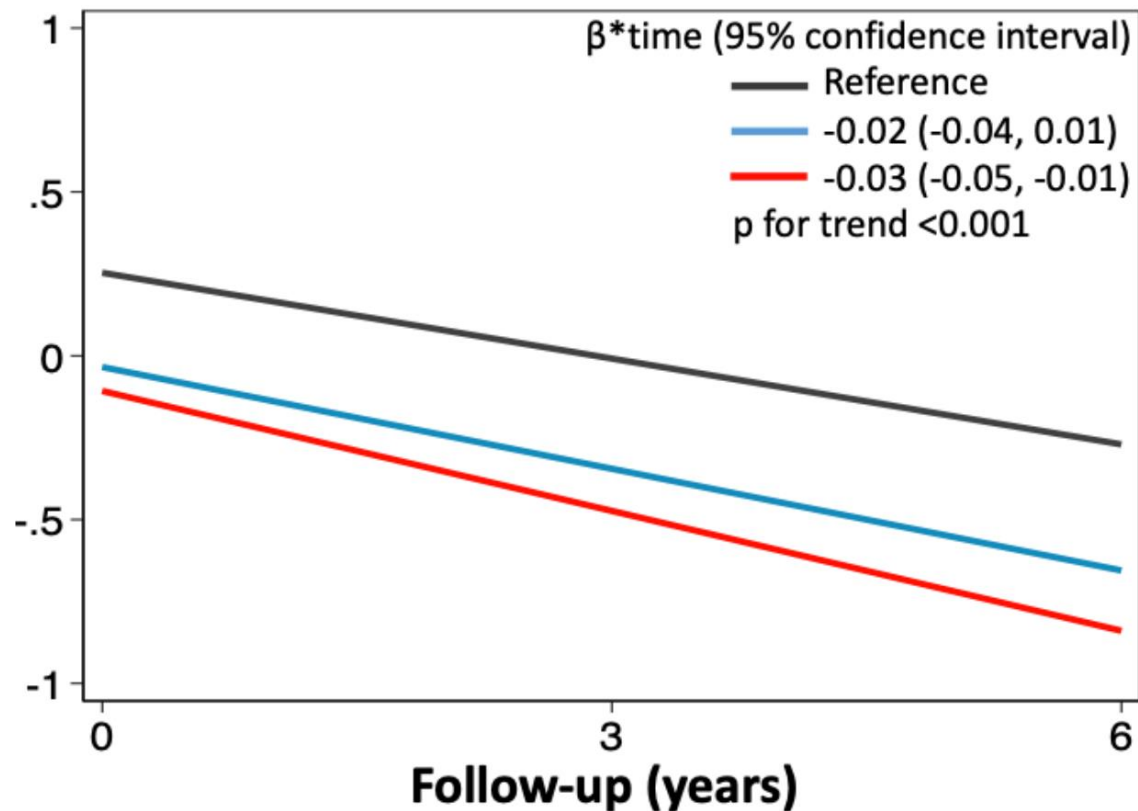
**Ventricular  
volume**

**Hippocampal  
volume**

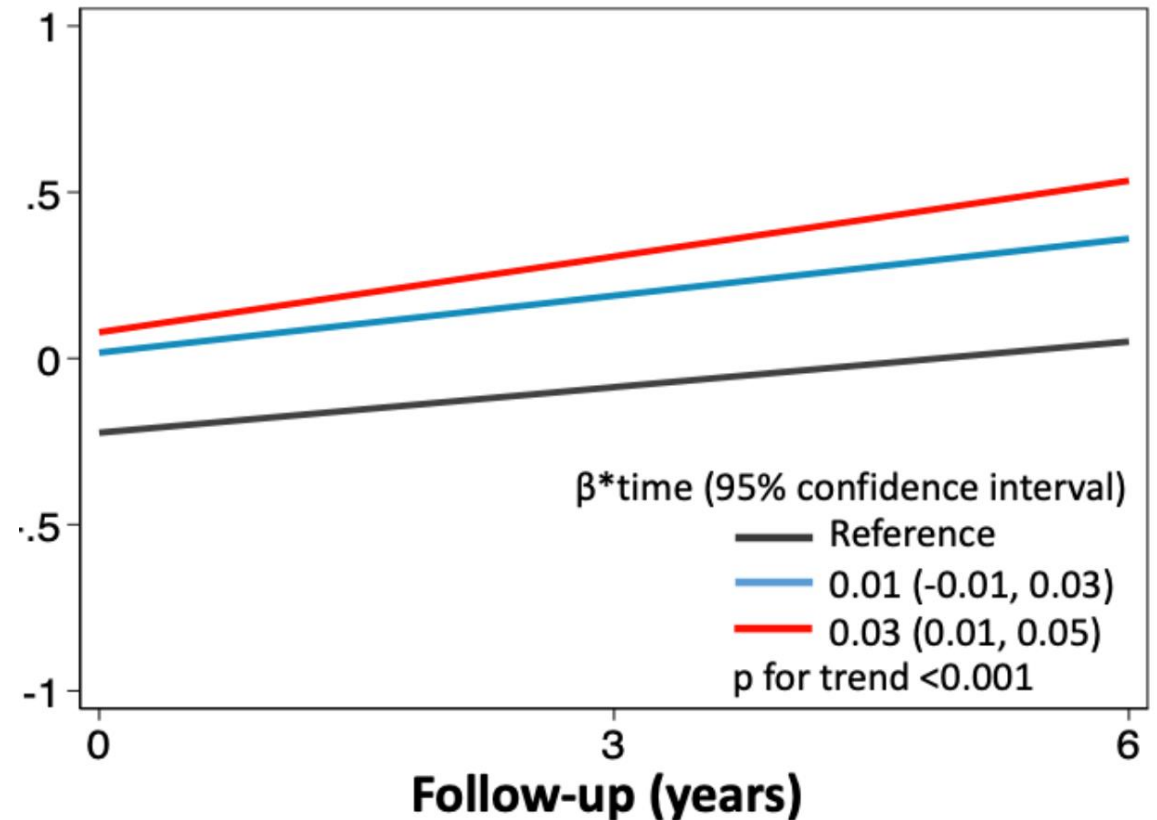
**White matter  
hyperintensities  
volume**

# Mild and complex MM and brain changes (Study III)

## Total brain tissue volume\*



## Ventricular volume\*

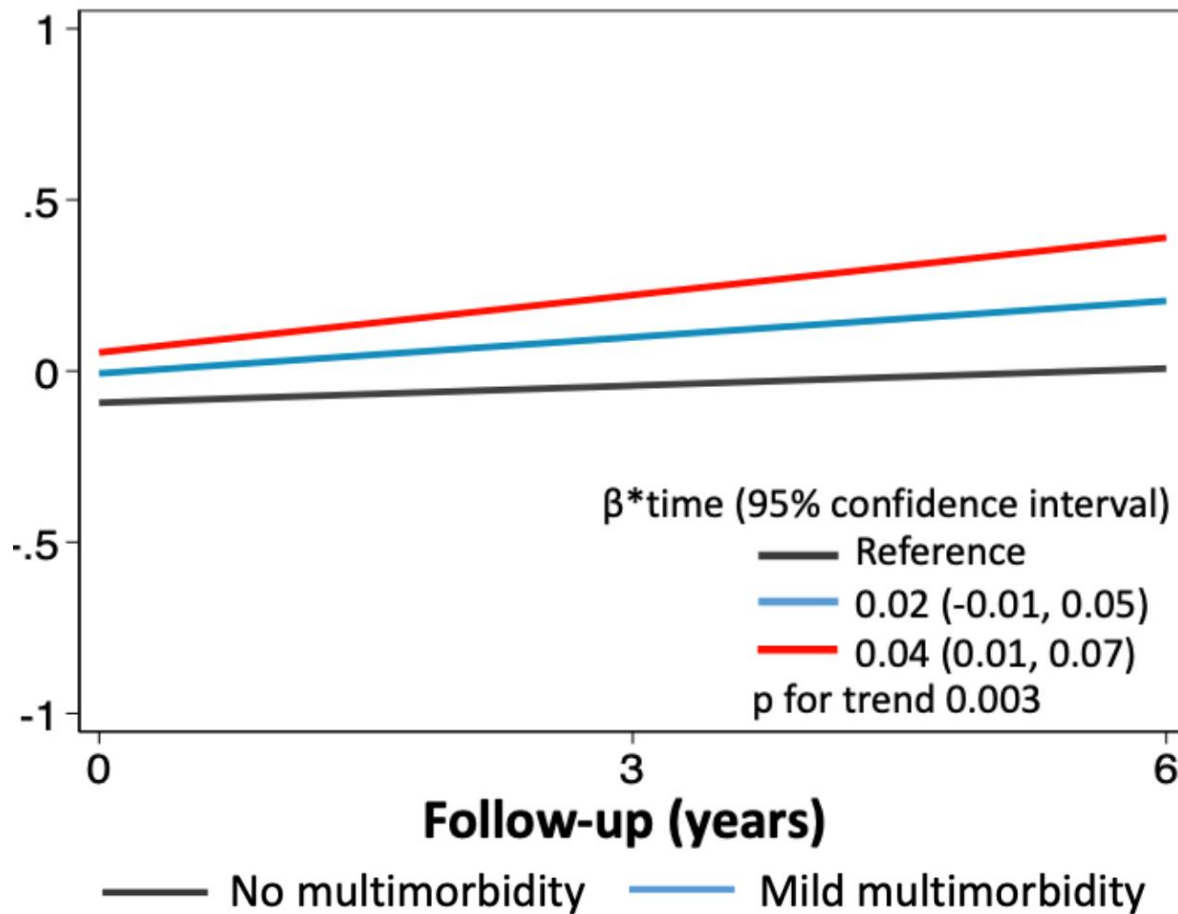


— No multimorbidity — Mild multimorbidity — Complex multimorbidity

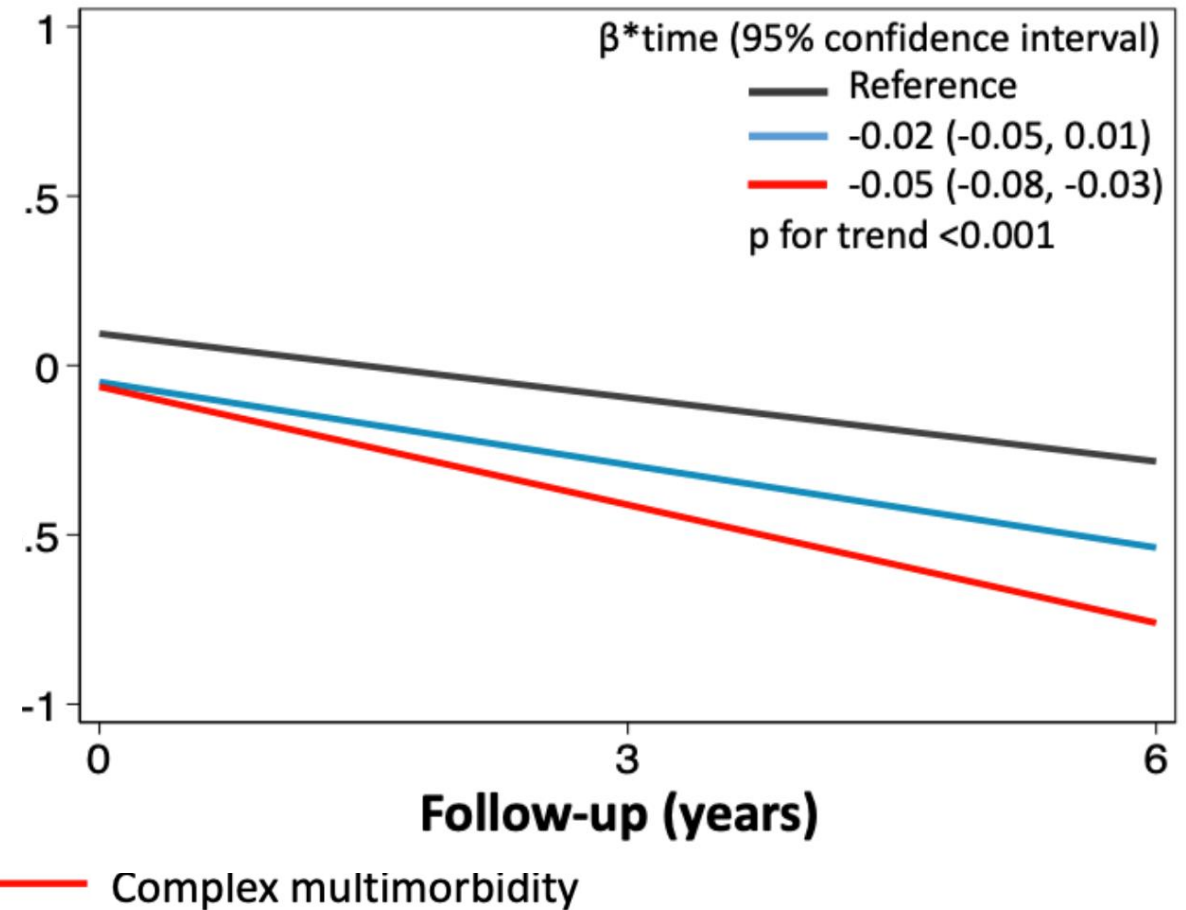
\*Volumes are z-scored

# Mild and complex MM and brain changes (Study III)

## WMHs\*



## Hippocampal volume\*



\*Volumes are z-scored

WMH: white matter hyperintensities

# Summary of results

- Worst cognitive outcomes are observed in *neuropsychiatric, sensory impairment/cancer* and *cardiovascular patterns*
- *Cardiovascular* and *neuropsychiatric* multimorbidity significantly reduces life expectancy and anticipates CIND and dementia onset
- Multimorbidity, especially when involving multiple body systems, is associated with accelerated brain aging, involving both neurodegeneration and vascular pathology



# Conclusions and future directions

- These results reinforce the idea that a connection between somatic conditions and cognitive aging exists
- A deeper understanding of the biological underpinnings that link somatic conditions with dementia is crucial to complement our clinical and epidemiological knowledge