# IHI Call Days | CALL 9

## Disentangling complexity of multimorbidity in aging

**Cluster of Excellence in Ageing Research CECAD, Cologne**

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# Challenges and objectives

o Topic 1: Boosting innovation for a better understanding of the determinants of health

o Enabling new technologies and treatments with **deep** understanding and prognosis of aging processes

o Unmet public health need addressed: the high burden of multimorbidity in late lifecourse due to number of patients affected and economic impact



Death rates among people aged 65 and over, by selected leading causes of death, 2000-2018.
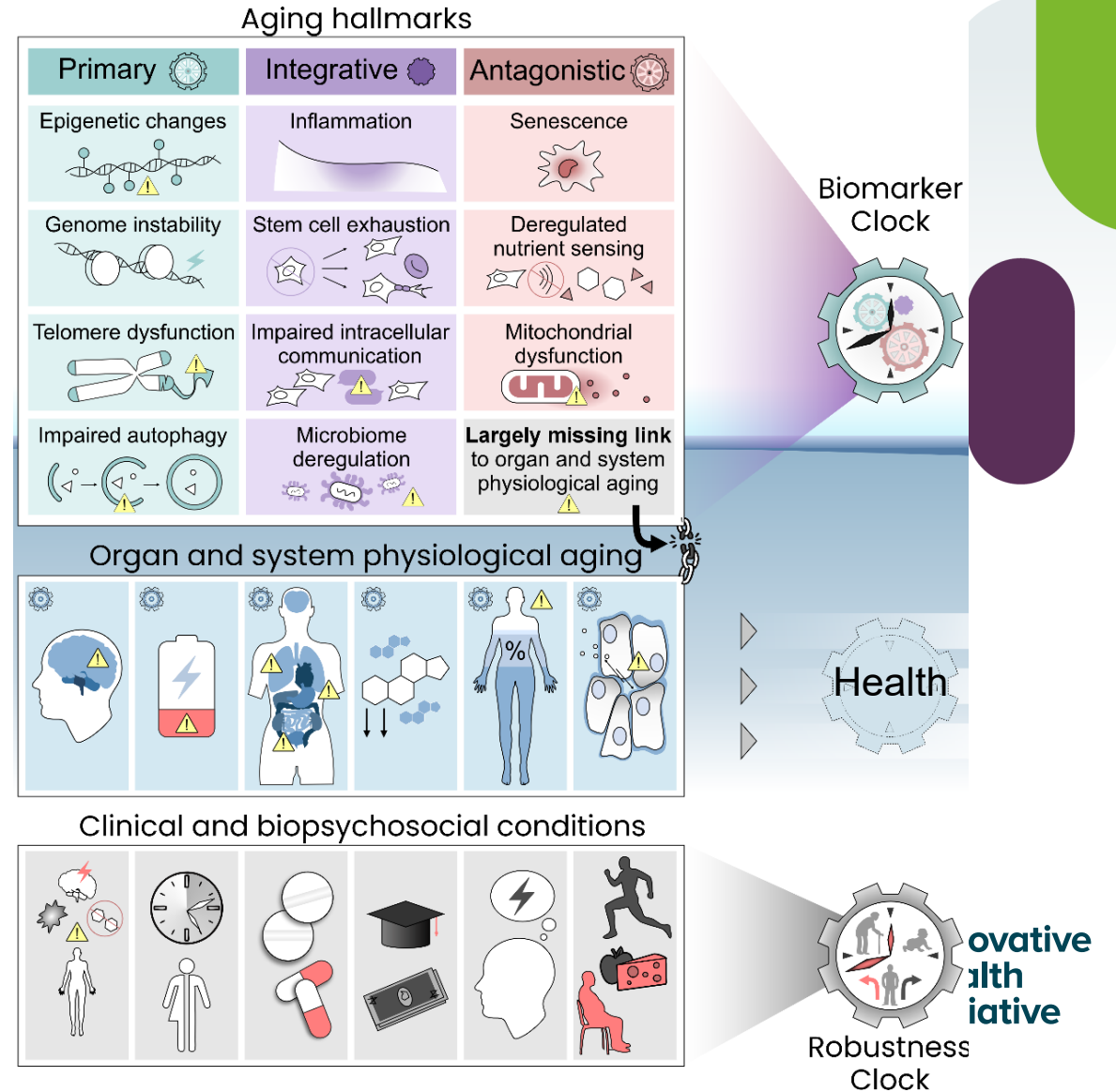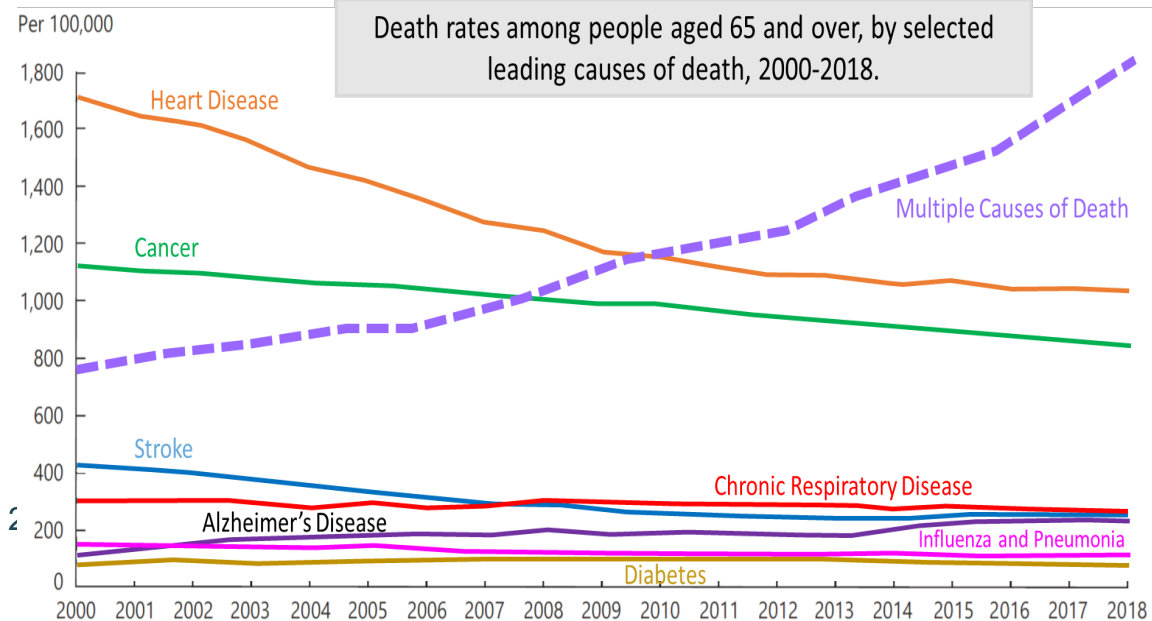
# Approach

- Measuring and projecting ageing processes

- Profiling individual resources and establishing prognostic signatures

- Predicting quality of life for clinical decision making

- Use of established links with molecular ageing hallmarks and organ and physiological markers

**Multidimensional Prognostic Index**

# Biomolecular mechanisms of the intrinsic pace of aging

A transcriptomic analysis reveals a fasting-like transcriptional program (FLTP) associated with reduced expression of an $AMPK_{\gamma1}$ regulatory subunit (positively regulated by refeeding in young but not in old animals). Killifish with sustained $AMPK_{\gamma1}$ have no sign of FLTP and exhibit metabolic health and longevity.

**In humans, expression is associated with the MPI but not with chronological age**
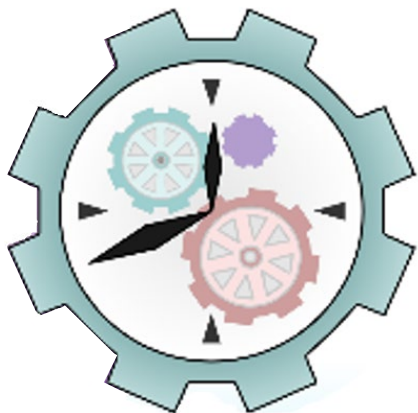
BiT age: A transcriptome-based aging clock near the theoretical limit of accuracy.

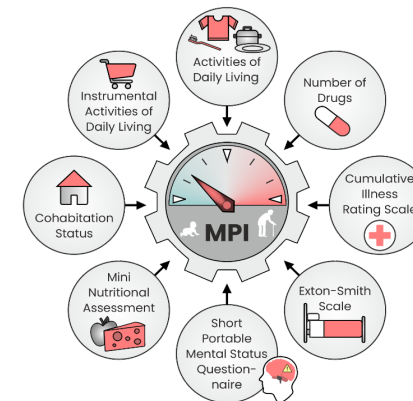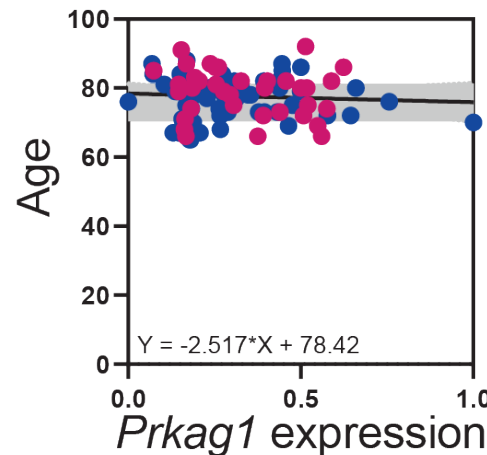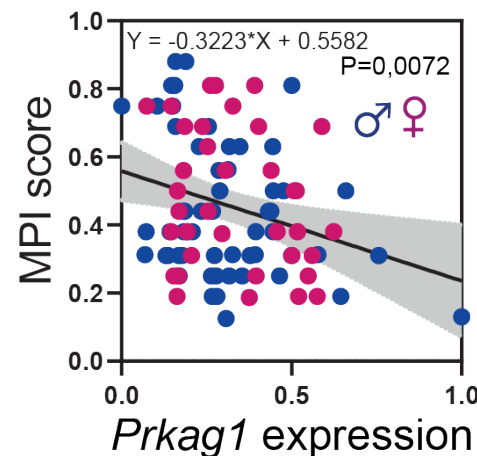*Meyer and Schumacher, 2021*

**A Q0 clock with a higher variance and error correlates less with chronological age and better with the MPI**

*Meyer, Janning et al., work in progress*

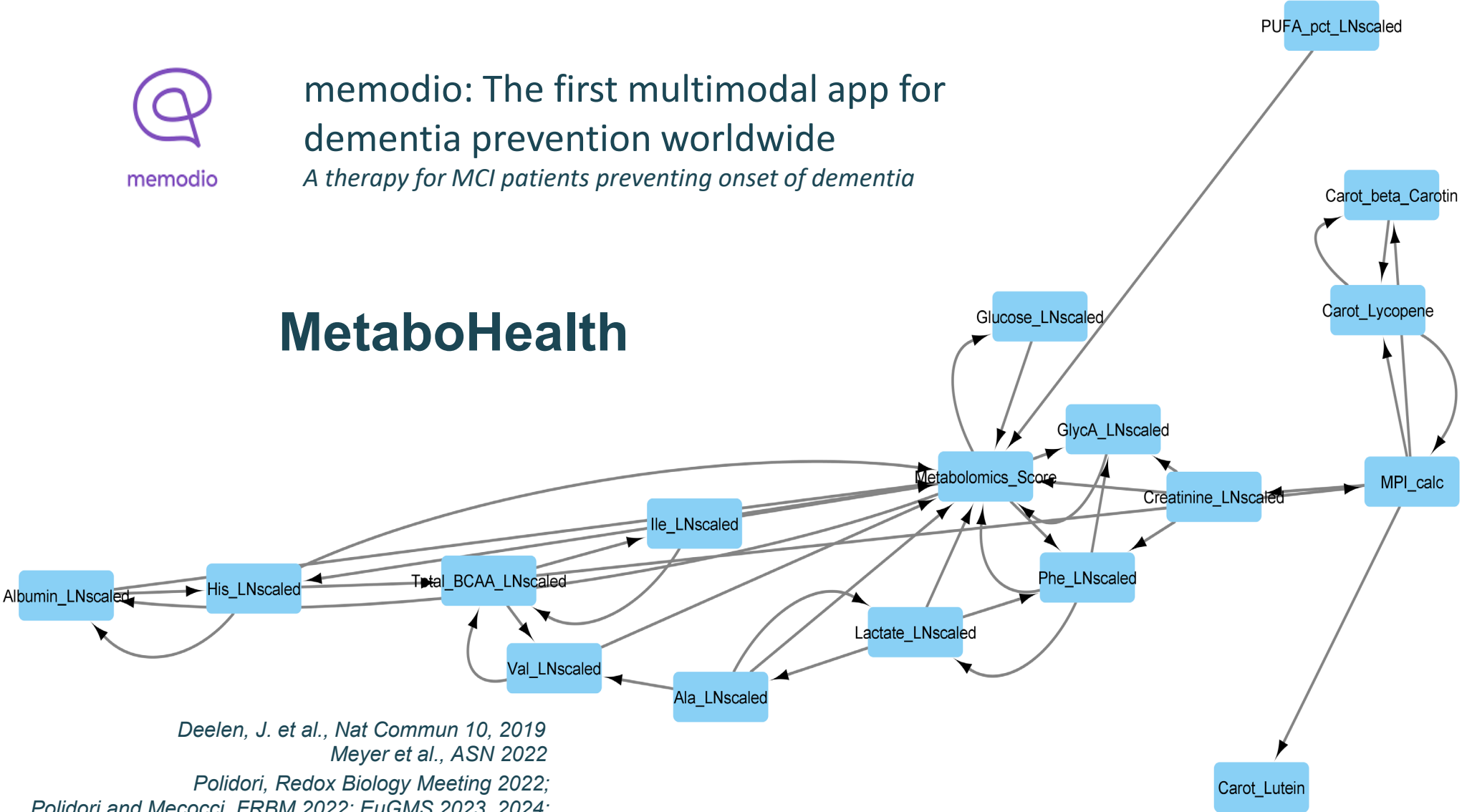*Ripa et al., Nature Aging, 2023*



Biomarker Clock



$Y = -0.3223*X + 0.5582$

$P=0{,}0072$

♂ ♀

MPI score

*Prkag1* expression



Age

$Y = -2.517*X + 78.42$

*Prkag1* expression



Robustness Clock

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# Enabling Technology: Data accesibility

memodio: The first multimodal app for dementia prevention worldwide

*A therapy for MCI patients preventing onset of dementia*

**MetaboHealth**



*Deelen, J. et al., Nat Commun 10, 2019*
*Meyer et al., ASN 2022*
*Polidori, Redox Biology Meeting 2022;*
*Polidori and Mecocci, FRBM 2022; EuGMS 2023, 2024;*
*Deelen, Müller, Polidori, Schumacher, et al., work in progress*

# Suitability for IHI

- We bring clinically validated measurements and prognostic tool for ageing citizens in practice

- We enable industry to change perspective towards cost models for maintaining robustness in health

- We support Pharma and IT Industry and can connect between them

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# Outcomes and Impact

- Bigger Picture: Change of paradigm from predicting disease trajectories to health trajectories focusing on existing resources of ageing citizens

- Based on the plural approach of MPI, data from system-physiology and molecular level, we possess measurements and biomarkers for innovations ranging from clinical practice guidelines on surveillance of health trajectories up to clinical decision-making and self-management

- Patients will benefit
  - from preventive interventions before onset of symptoms
  - from early prediction of diseases combined with better understanding of the mechanisms involved, leading to the development of more cost-effective strategies
  - from improved healthcare through regular monitoring of critical parameters using validated tools;

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# Expertise and resources

- We have Expertise in:
  - Geriatric Medicine
  - Long. studies e.g. Leiden Longevity Study (LLS)
  - Molecular profiling of ageing processes

- We are looking for:
  - Tech,
  - Nutrition
  - or pharma companies applying the approach

- We can contribute with IKOP and IKAA (in-kind contributions to operational activities and to additional activities