

The logo for TILDA (The Irish Longitudinal Study on Ageing) features the word "tilda" in a lowercase, sans-serif font. The letter "i" is stylized with a green dot above it and a green vertical bar below it, resembling a person. A white horizontal line is positioned below the text.

**tilda**

The Irish Longitudinal  
Study on Ageing

# **TILDA Ageing Biomarkers**

Dr. Cathal McCrory

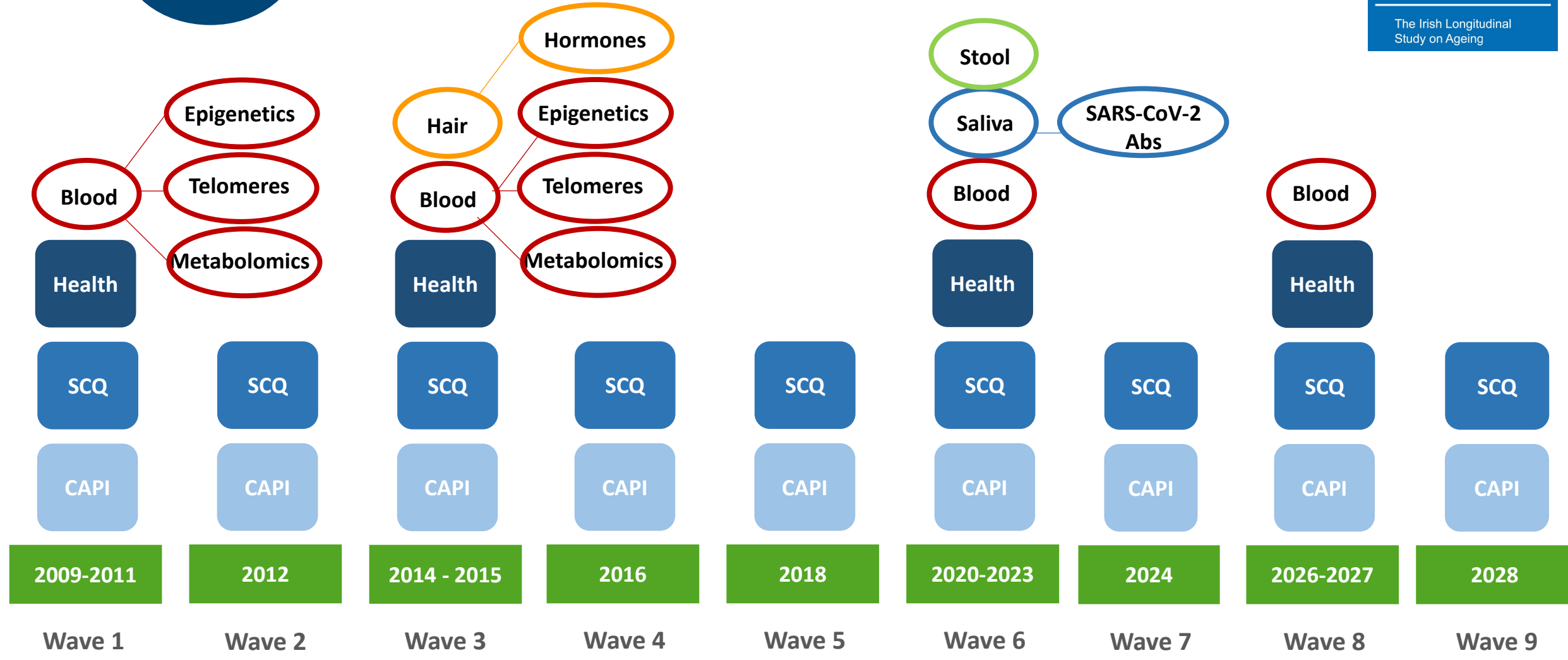
(on behalf of TILDA team)



How does the body know how old it is?

Baseline

8,504  
50+



# TILDA Biomarkers



## Inflammatory

- CRP
- IL1ra, IL2, IL4, IL6, IL8, IL10, IL12p70, IL13, IL17a
- TNFa, TNF – receptor 2
- Interferon gamma

## Neuroendocrine (W3 only)

- Cortisol
- DHEA
- Cortisone
- Melatonin
- Progesterone
- Testosterone

## Kidney Function

- Cystatin C
- Creatinine
- eGFR

## Cardiovascular

- Systolic Blood Pressure,
- Diastolic Blood Pressure
- Resting Heart Rate
- Resting Heart Rate (ECG)
- Pulse Wave Velocity
- Pulse Pressure (SBP-DBP)

## Sympathetic

- LF/HF ratio
- Orthostatic HR recovery

## Parasympathetic

- Low frequency HRV
- High frequency HRV
- SDNN
- RMSSD
- pNN50
- Total power

## Metabolic

- High density lipoprotein
- Low density lipoprotein
- Triglycerides
- Cholesterol
- Adiponectin
- GDF15
- ILGF-1

## Glucose Metabolism

- HBA1c

## Anthropometric

- Waist circumference
- Waist-hip ratio
- BMI

## Eye

- Macular degeneration
- Lutein
- Zeaxanthin

## Summary of 'Omics' and Biomarkers in TILDA

Name	No. of Participants	
	W1	W3
<b>Epigenetics (DNAm) + Epigenetic clocks</b>	490	
850K DNA methylation sites	(820)	(820)
<b>Telomeres</b>	4,956	500
Leukocyte telomere length (LTL)		
<b>Metabolomics</b>	1,400	500
RPC-MS small molecules and lipids ionised in +ve and -ve modes (n~700 molecules)		
<b>Proteins &amp; Lipids</b>	5,000	1000-4000
CV, Inflammatory, Kidney (25 proteins and lipids)		
<b>Vitamins &amp; Antioxidants</b>	5,000	5,000*
D3*, Folate, B12, Lutein, Zeaxanthin		
<b>Hormones</b>	-	2,600
Cortisol, Cortisone, DHEA, Progesterone, Testosterone		

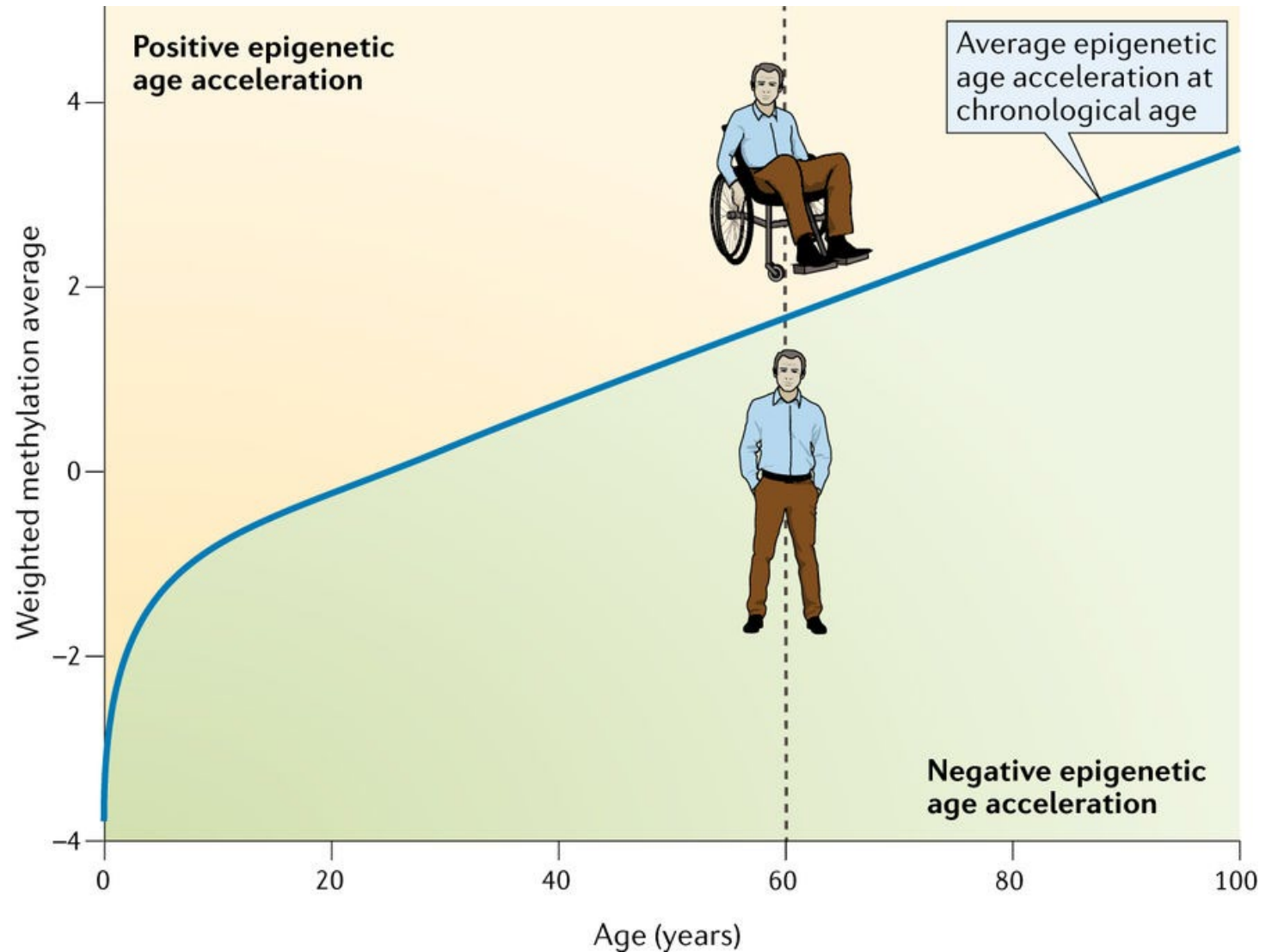


**Dr. Aisling O'Halloran**  
TILDA Biobank Manager

# The epigenetic clock(s)

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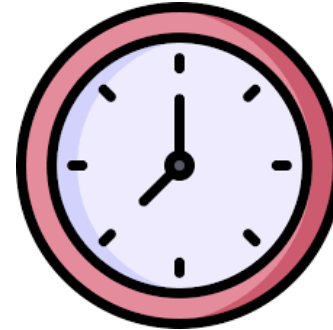
- 28 million CpG sites in the human genome
- 1/3 of them change with age
- 353-1000 CpG sites can be used to build highly accurate measures of ageing.



# The Epigenetic Clocks

**1<sup>st</sup> gen - built to measure the passage of chronological time**

- Horvath
- Hannum



**2<sup>nd</sup> gen - built to predict clinical outcomes and mortality**

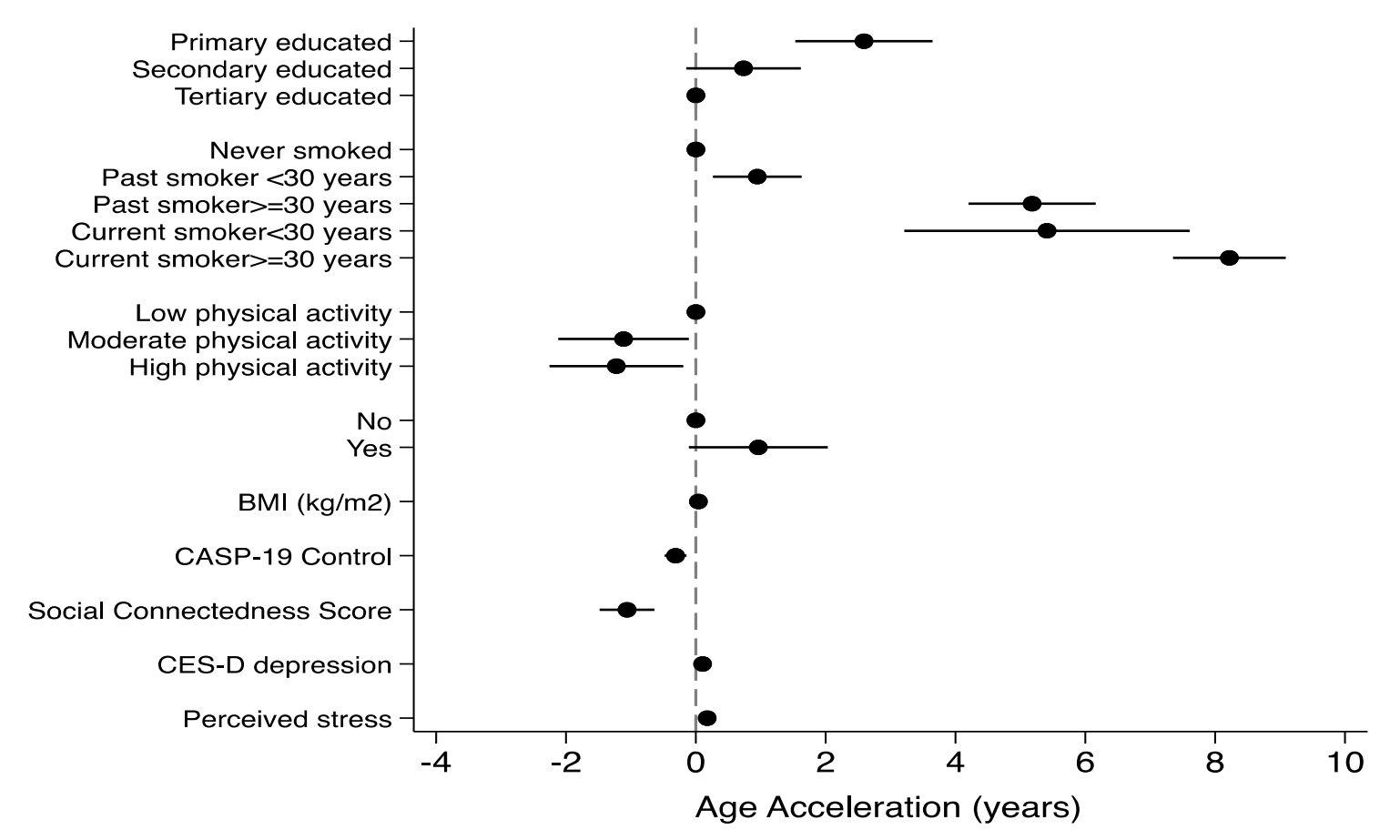
- PhenoAge
- GrimAge



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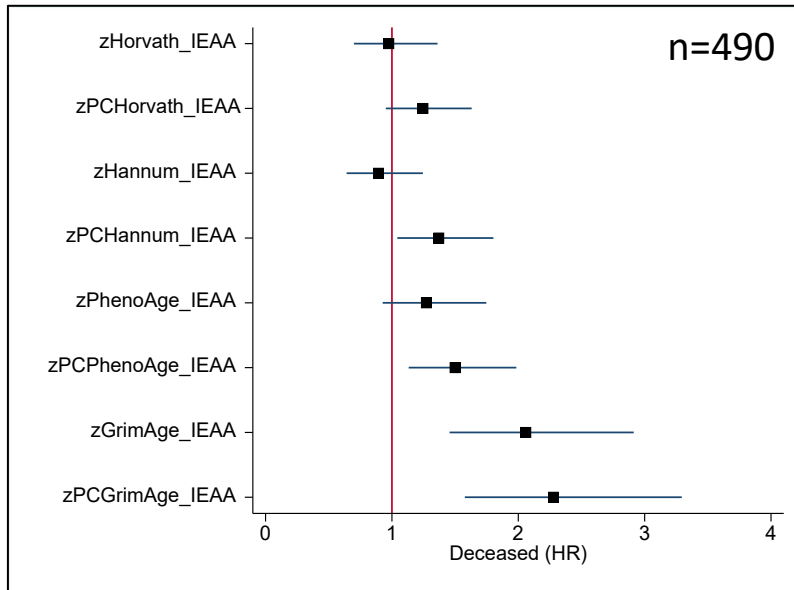


# Association of GrimAge with economic, lifestyle and psychosocial factors



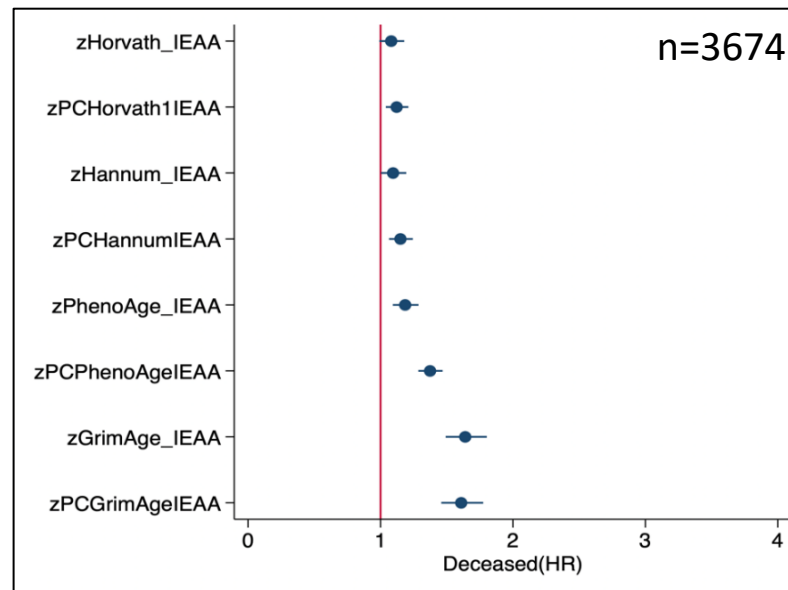


# Epiclocks and mortality in 3 countries



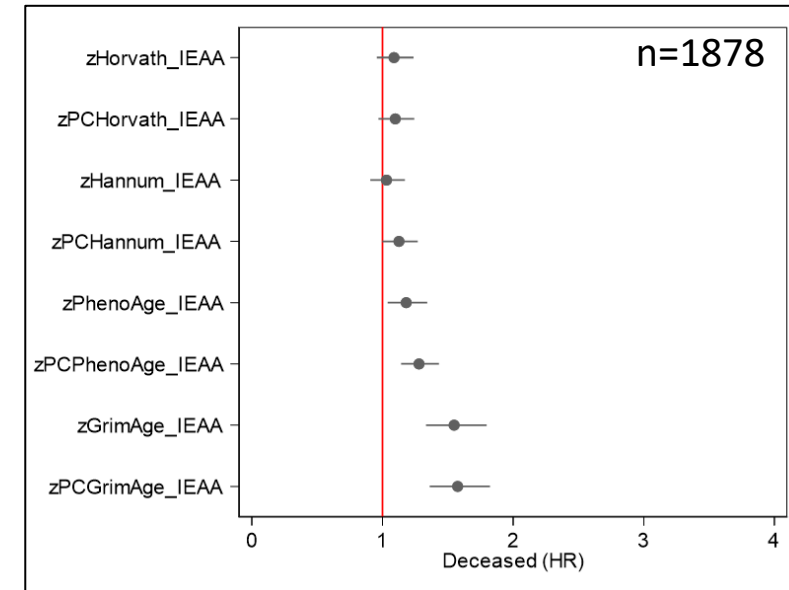
**TILDA**

Harmonisation



**HRS**

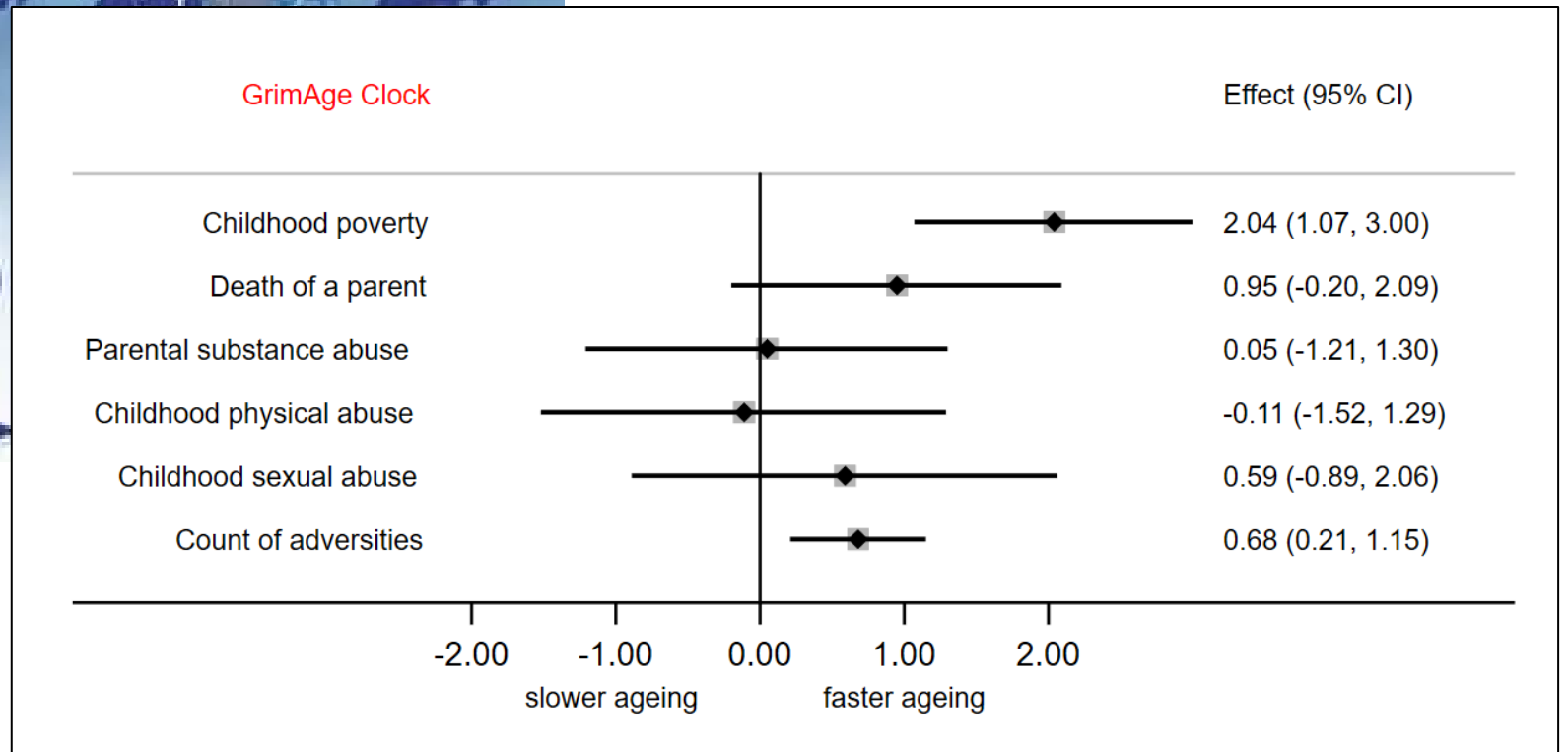
Harmonisation



**NICOLA**

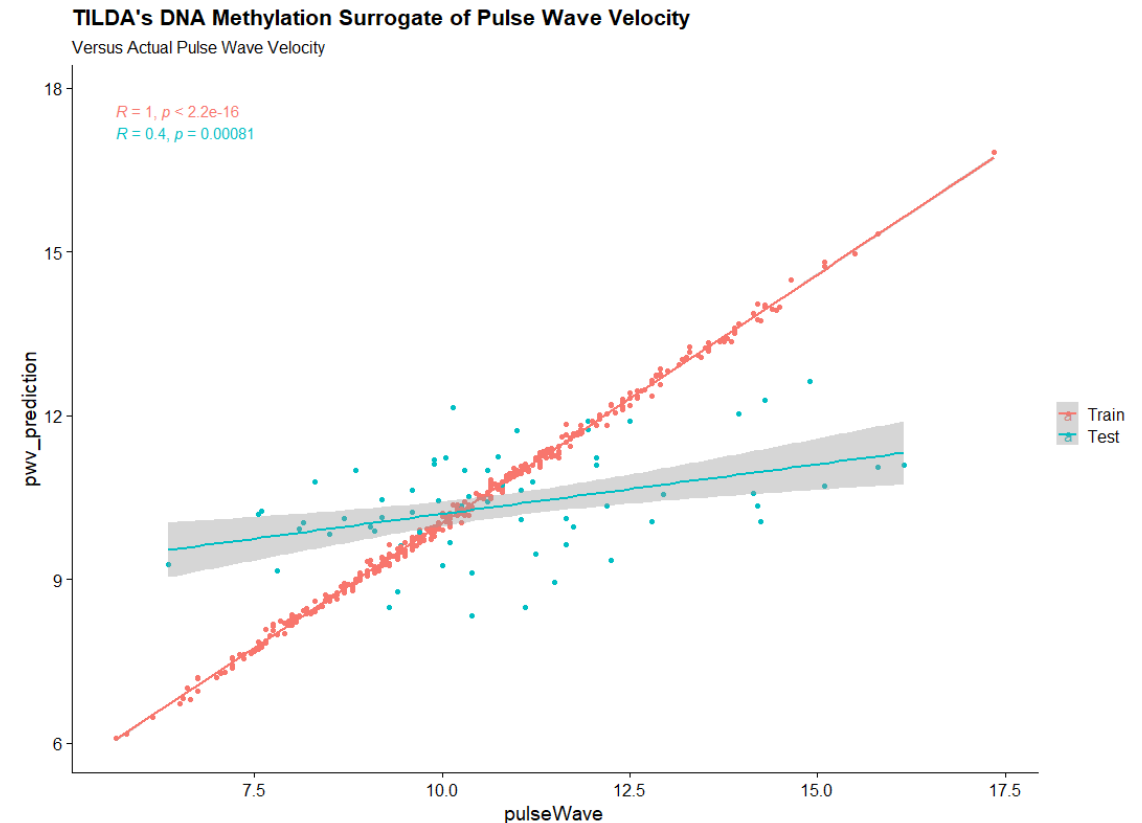
Harmonisation

# Life-time smoking history explained 50-60% of the effect of childhood poverty on biological ageing



# DNA methylation surrogate biomarkers

- Allow for investigation of exposure-outcome relationships even if the specific exposure was not measured, but DNAm data is available
- DNAm surrogate may predict outcomes more strongly than measured levels.
- Have utility when a biomarker is expensive or challenging to measure  
(e.g. cortisol, telomere length, NFL)



# Development of Methylation Risk Scores

- A new DNAm cardiovascular risk score derived from DNAm surrogate markers
- Predicts short-term CVD risk better than the Framingham risk score

Cappozzo et al. *Clinical Epigenetics* (2022) 14:121  
<https://doi.org/10.1186/s13148-022-01341-4>

Clinical Epigenetics

RESEARCH

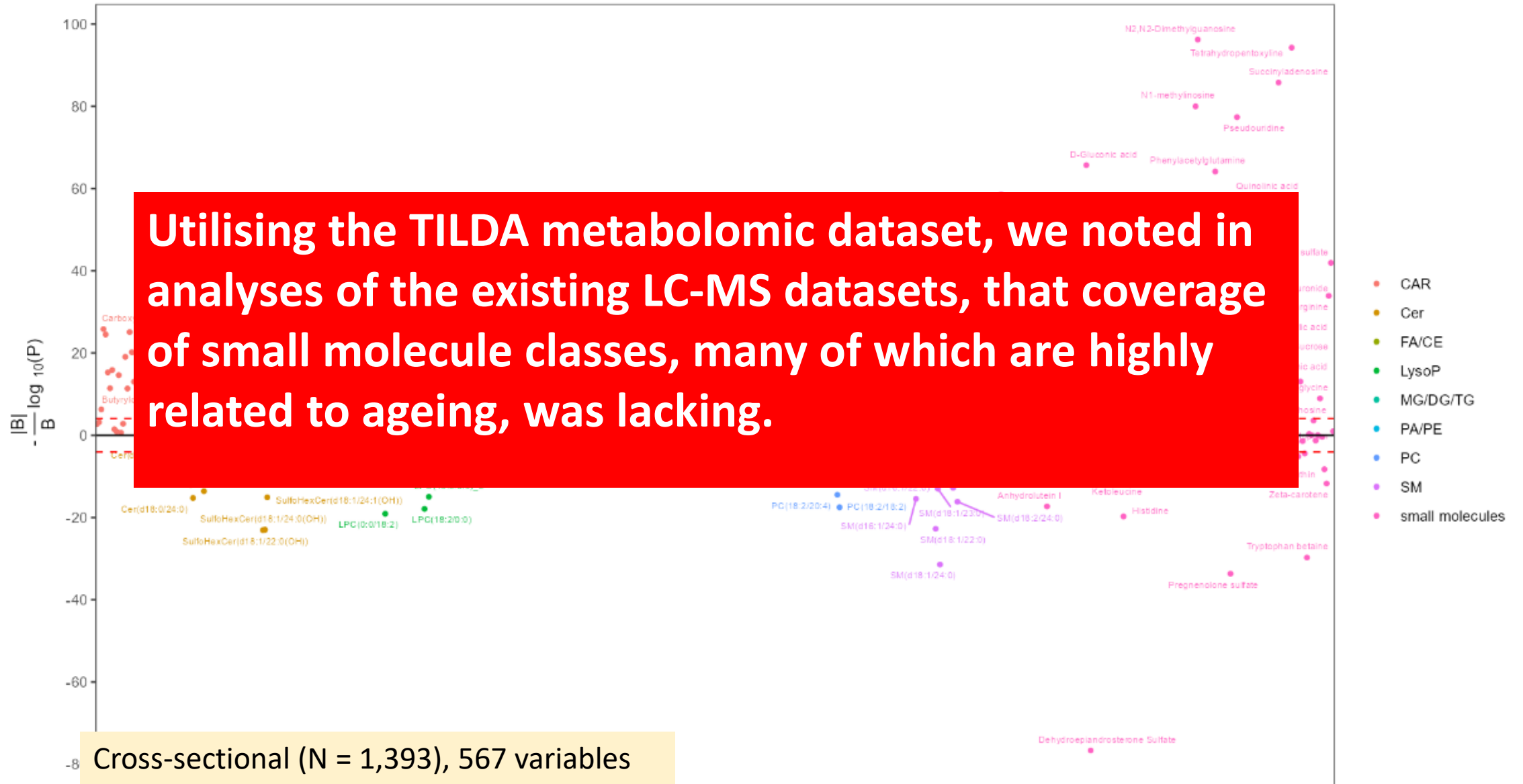
Open Access



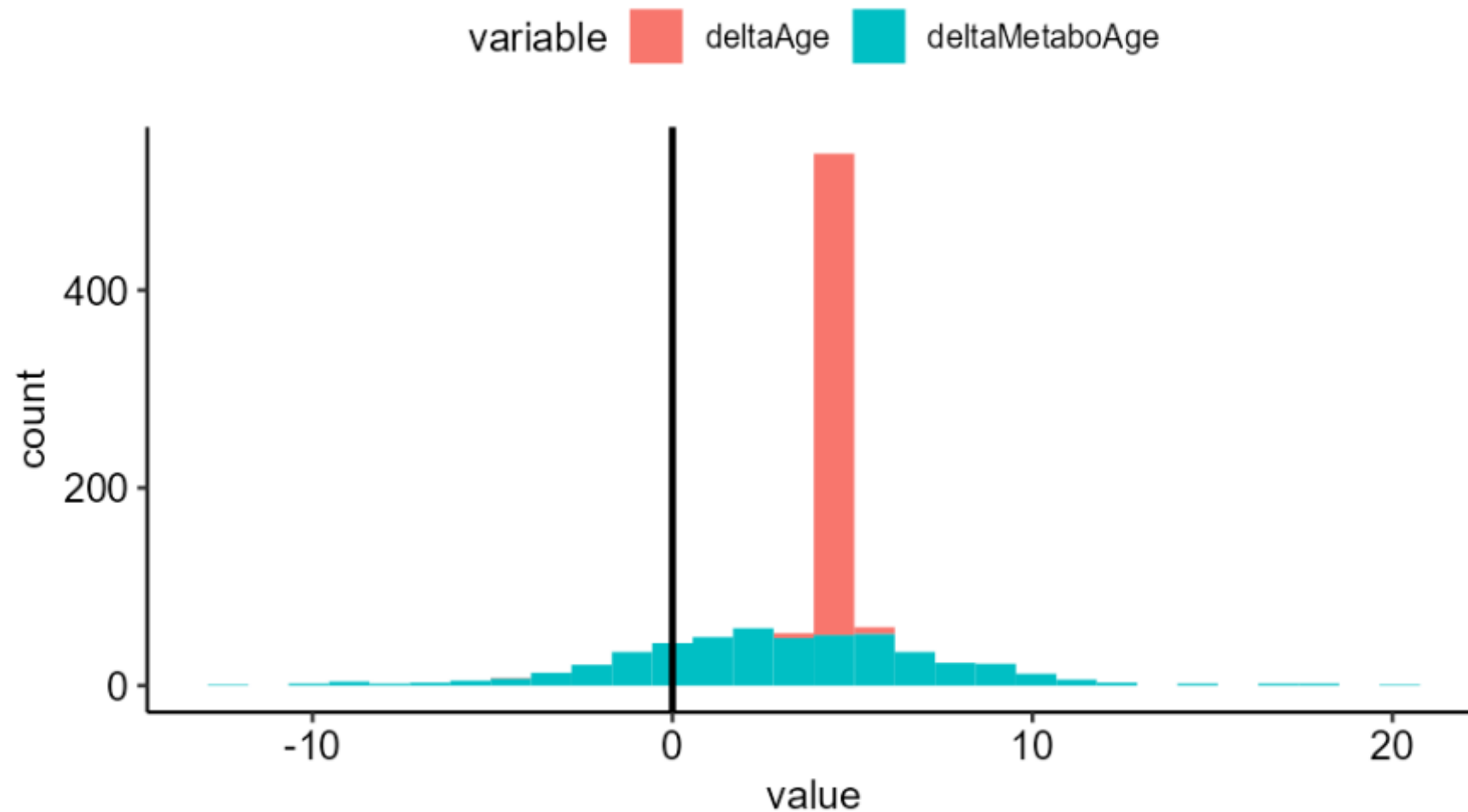
## A blood DNA methylation biomarker for predicting short-term risk of cardiovascular events

Andrea Cappozzo<sup>1</sup>, Cathal McCrory<sup>2</sup>, Oliver Robinson<sup>3</sup>, Anna Freni Sterrantino<sup>3,4</sup>, Carlotta Sacerdote<sup>5</sup>, Vittorio Krogh<sup>6</sup>, Salvatore Panico<sup>7</sup>, Rosario Tumino<sup>8</sup>, Licia Iacoviello<sup>9,10</sup>, Fulvio Ricceri<sup>11,12</sup>, Sabina Sieri<sup>6</sup>, Paolo Chiodini<sup>13</sup>, Gareth J. McKay<sup>14</sup>, Amy Jayne McKnight<sup>14</sup>, Frank Kee<sup>14</sup>, Ian S. Young<sup>14</sup>, Bernadette McGuinness<sup>14</sup>, Eileen M. Crimmins<sup>15</sup>, Thalida Em Arpawong<sup>15</sup>, Rose Anne Kenny<sup>2</sup>, Aisling O'Halloran<sup>2</sup>, Silvia Polidoro<sup>16</sup>, Giuliana Solinas<sup>17</sup>, Paolo Vineis<sup>3</sup>, Francesca Ieva<sup>1,18</sup> and Giovanni Fiorito<sup>2,3,17\*</sup>

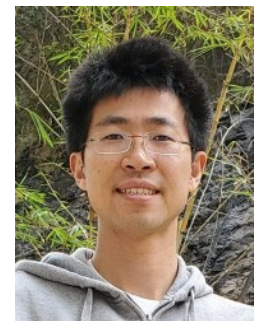
## Associations with Age in TILDA Wave 1 - adjusted for sex



# Delta difference in metabolomic age over 4 years



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Imperial College London



Dr. Chungho Lau  
Imperial College London

# The future?

- 3<sup>rd</sup> generation epigenetic clocks trained on changes in clinical phenotypes and changes in the biomarkers
- A multi-omics clock
- A harmonised biological ageing protocol (HBAP)?



With thanks to  
the TILDA team

