Condizioni socio-economiche e salute degli anziani

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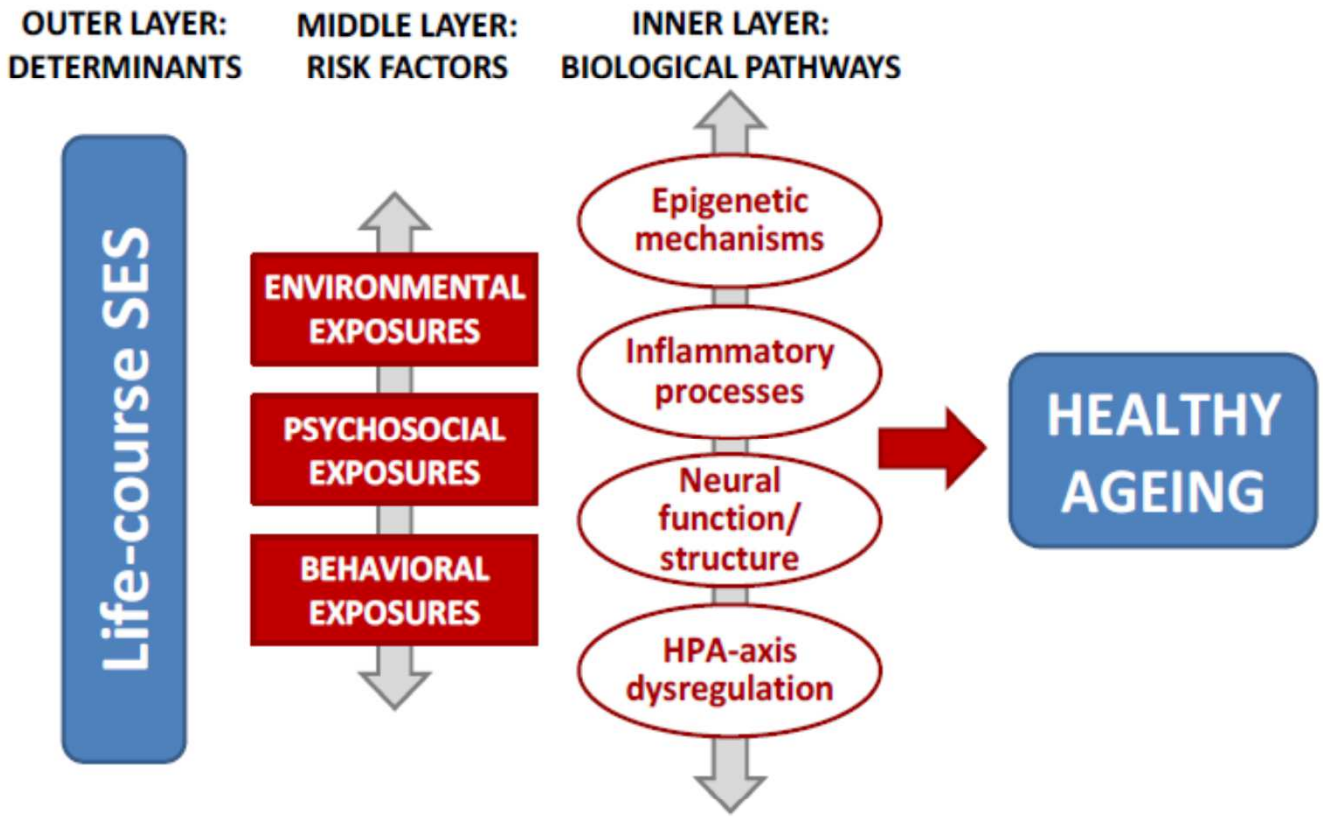
Lifepath

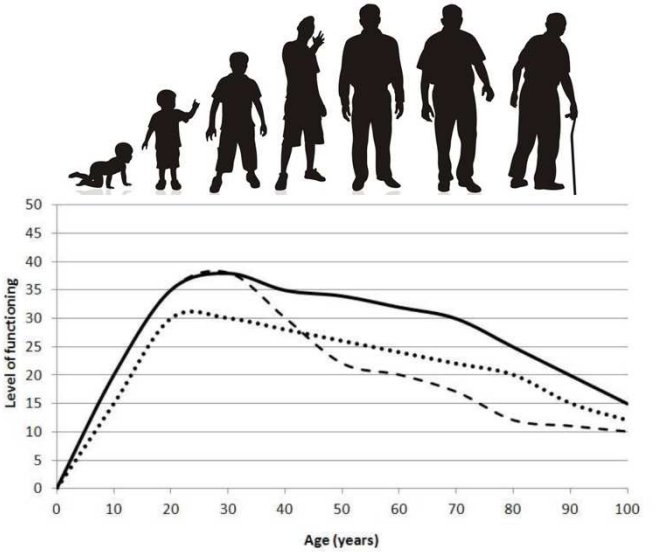


The biology of inequalities in health: the LIFEPATH project

Longitudinal and Life Course Studies 2017 Volume 8 Issue 4 Pp 417 – 439

Biological aging

- Ageing has been defined as the **“time-dependent decline of functional capacity and stress resistance, associated with increased risk of morbidity and mortality”**
- Lifestyle and environment can affect ageing rates at both the ‘build-up’ and ‘decline phase’
- Recently, molecular clocks have been developed to assess *biological age,* based on epigenetic and other ‘omic’ data



(Source: Strachan & Sheikh 2004)

Biomarkers of biological aging

Several biomarkers of biological aging have been proposed:

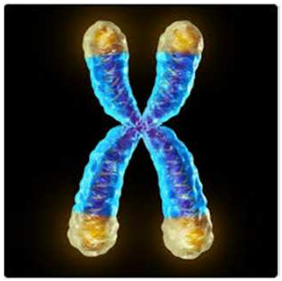
- Telomere length
- DNA methylation (epigenetic clock, epigenetic drift)
- Allostatic load
- Metabolomic clock
- …

Telomere length

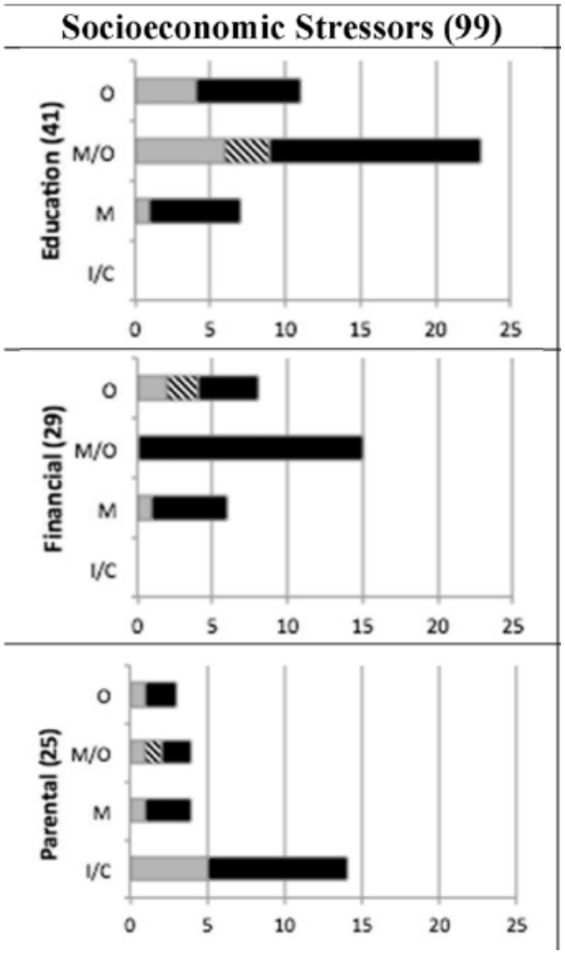
Telomeres are the protective nucleoprotein structures capping the ends of eukaryotic chromosomes.

Telomeres length can be decreased by aging for the increasing rounds of cell division, but also by biochemical environment.

The telomere shortening has important functional consequences: short telomeres lead to genomic instability and cellular senescence (i.e. short telomeres in leucocytes lead to the secretion of pro-inflammatory cytokines)



Telomere length



Legend:

O=Older

M/O= Mid-age and Older

M=Mid-age

I/C=Infants/Children

Significant, as expected

Significant, contrary to expectation

Not significant

Ageing Research Reviews 47 (2018) 89–104

Telomere length

Table 2
Structural life-course models, with goodness of fit statistics (n = 5754).

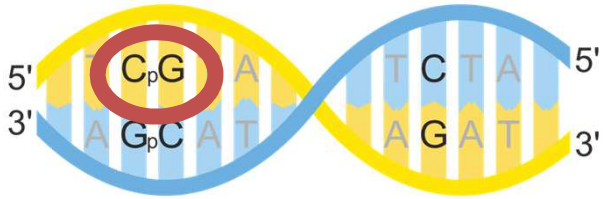
Model[1]	***BIC***[2]	***LR***[3]	***Modification Indices, p<.05***
Social Trajectory (full mediation) **.14(.02) p<.001** **-.01(.004) p=.001** Child Stress → Adult Stress → Telomere Length	196765	p=.576	N/A
Early Critical Period (no mediation) **.14(.02) p<.001** Child Stress → Adult Stress Telomere Length -.006(.004) p=.156	196773	p=.010	Adult stress → TL
Cumulative Risk (partial mediation) **.14(.02) p<.001** **-.01(.004) p=.002** Child Stress → Adult Stress → Telomere Length -.005(.004) p=.312	196772	p=.776	N/A

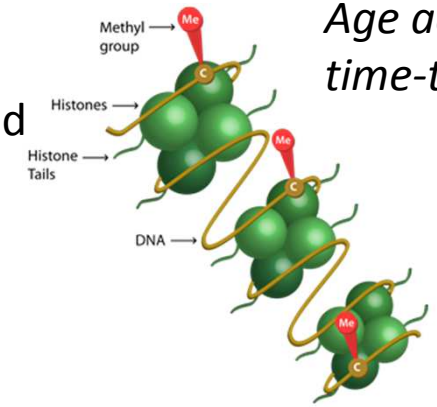
Epigenetic Clocks

Multiple epigenetic clocks have been developed:

- Horvath's original epigenetic clock (353 CpG loci, not-tissue specific)
- Hannum's epigenetic clock (71 CpG loci, blood specific)
- Levine's epigenetic clock (513 CpG loci, trained on "phenotype age" derived using 8 clinical markers)
- "Grimage" (>1000 CpG Loci, derived from blood levels of proteins and smoking years)

CpG dinucleotides + Regression model = EPIGENETIC CLOCK





Age acceleration biomarkers and time-to-death prediction

Age Acceleration Biomarker	Hazard Ratio	Meta P-value
Horvath	1.02	8.9E-5
Hannum	1.04	6.8E-16
Levine	1.05	3.5E-36
Grimage	1.10	2.0E-75

Lu et al., 2019

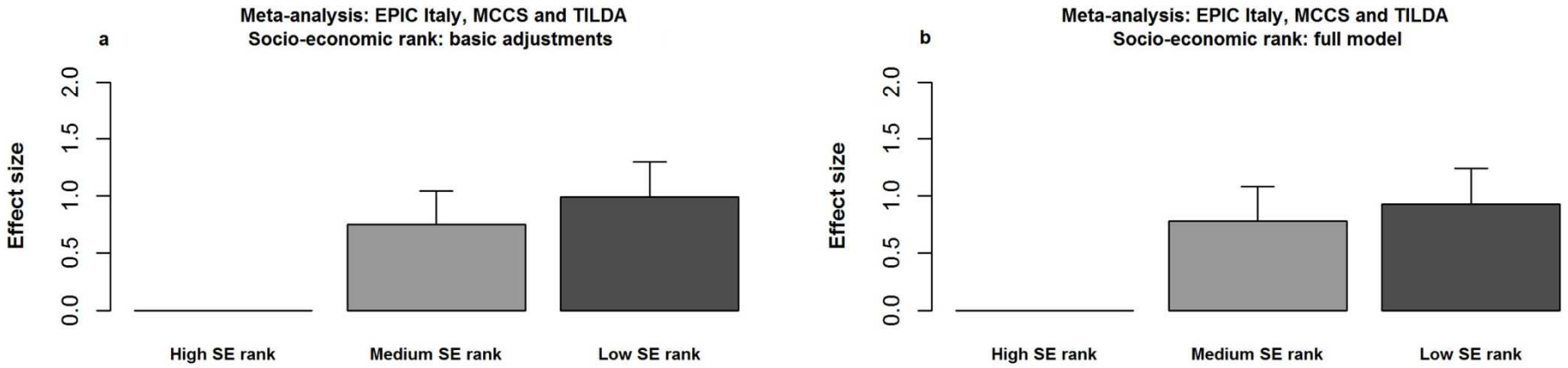
Stochastic epimutations

The number of stochastic epimutations (SEMs) increases exponentially with age although there is high variability within individuals of the same age.

Higher number of SEMs is associated with:

- risk factors such as cigarette smoking, alcohol intake and exposure to toxicants
- Hepatocellular carcinoma tumor staging

Age acceleration based on DNAm



Social adversity and epigenetic aging: a multi-cohort study on socioeconomic differences in peripheral blood DNA methylation

Giovanni Fiorito[1,2], Silvia Polidoro[1], Pierre-Antoine Dugué[3,4], Mika Kivimaki[5], Erica Ponzi[6], Giuseppe Matullo[1,2], Simonetta Guarrera[1,2], Manuela B. Assumma[1,2], Panagiotis Georgiadis[7], Soterios A. Kyrtopoulos[7], Vittorio Krogh[8], Domenico Palli[9], Salvatore Panico[10], Carlotta Sacerdote[11], Rosario Tumino[12], Marc Chadeau-Hyam[13], Silvia Stringhini[14], Gianluca

SCIENTIFIC REPORTS

Lifepath

SCIENTIFIC REPORTS | 7: 16266 | DOI:10.1038/s41598-017-16391-5

Risk factors of epigenetic age acceleration

- Meta-analysis of 16,000 people across 18 cohorts)
- Comparison of effects of leading NCD risk factors on epigenetic ageing
- Horvath, Hannum and Levine measures of epigenetic age acceleration and stochastic epigenetic mutations (SEMs) assessed
- SEMs are sites with extreme methylation levels, randomly distributed throughout genome, which accumulate with age ("epigenetic drift")

Fiorito et al 2019

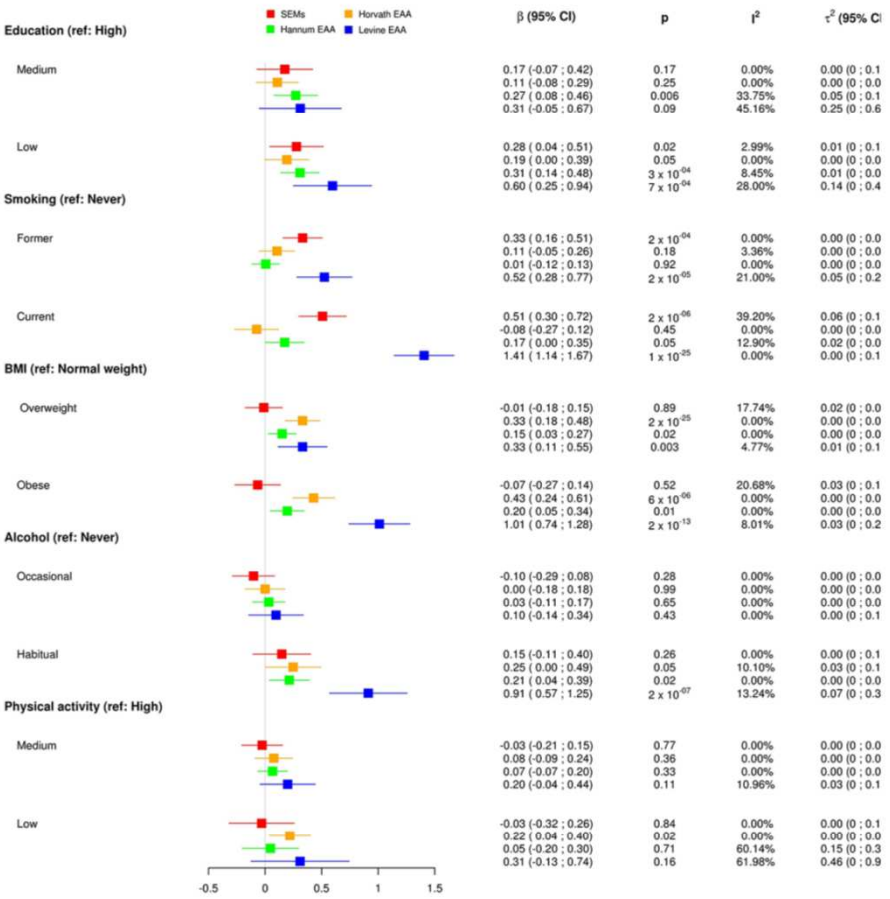
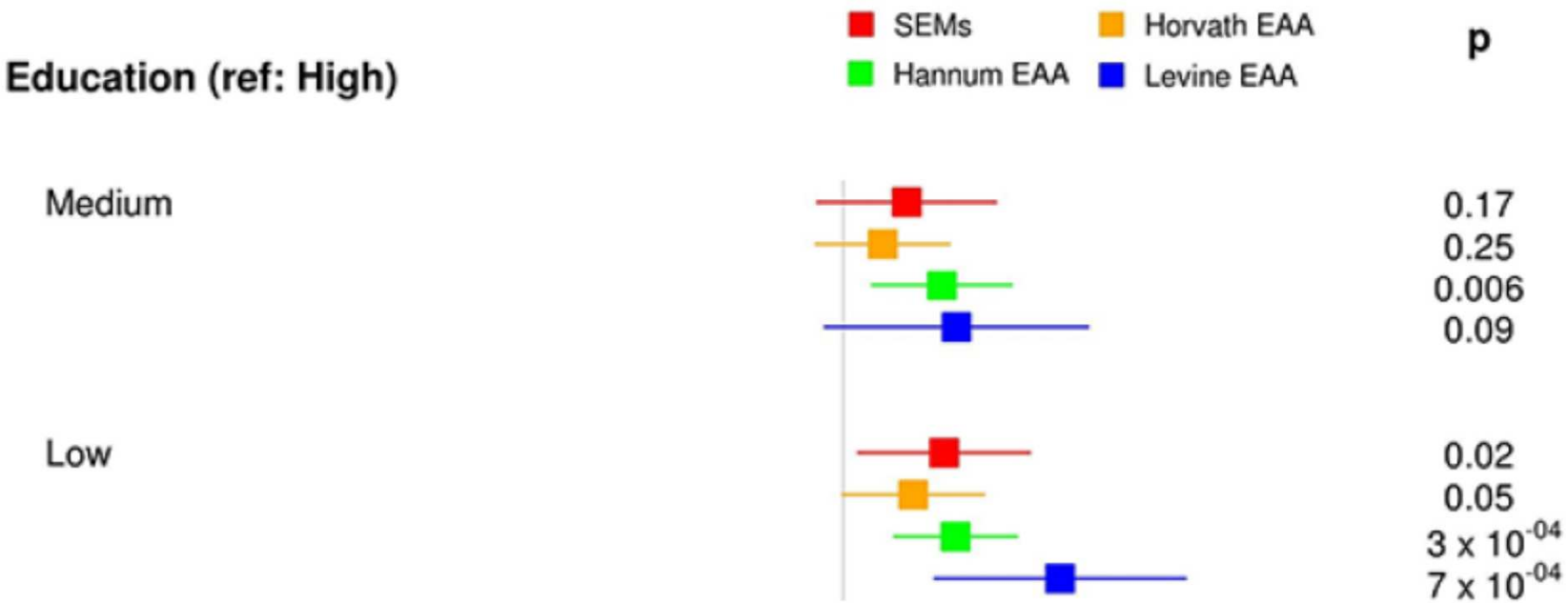


Figure 1. Effect sizes (interpretable as years of increasing/decreasing epigenetic age) of the association between different risk factors and four epigenetic aging biomarkers: total number of stochastic epigenetic mutations (SEMs, red), Horvath epigenetic age acceleration (orange), Hannum epigenetic age acceleration (green) and Levine epigenetic age acceleration next-generation clock (blue).

SEMs and Clocks



www.aging-us.com AGING 2019, Vol. 11, No. 7

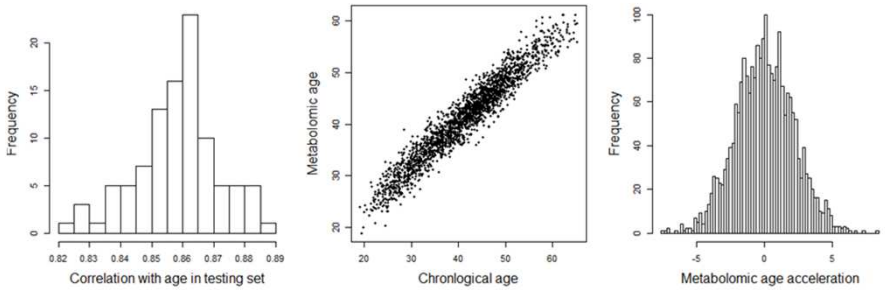
Research Paper

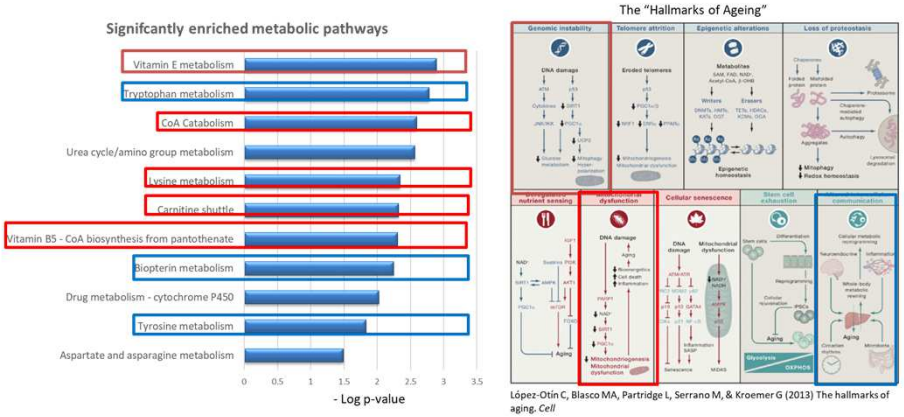
Socioeconomic position, lifestyle habits and biomarkers of epigenetic aging: a multi-cohort analysis

Giovanni Fiorito[1,40], Cathal McCrory[2,40], Oliver Robinson[3,40], Cristian Carmeli[4,40], Carolina Ochoa Rosales[5,6,40], Yan Zhang[7,40], Elena Colicino[8,40], Pierre-Antoine Dugué[9,10,11,40], Fanny Artaud[12,40], Gareth J McKay[13,40], Ayoung Jeong[14,15,40], Pashupati P Mishra[16,40], Therese H Nøst[17,18,40], Vittorio Krogh[19], Salvatore Panico[20], Carlotta Sacerdote[21], Rosario Tumino[22], Domenico Palli[23], Giuseppe

Stochastic epigenetic mutations appear randomly in the genome

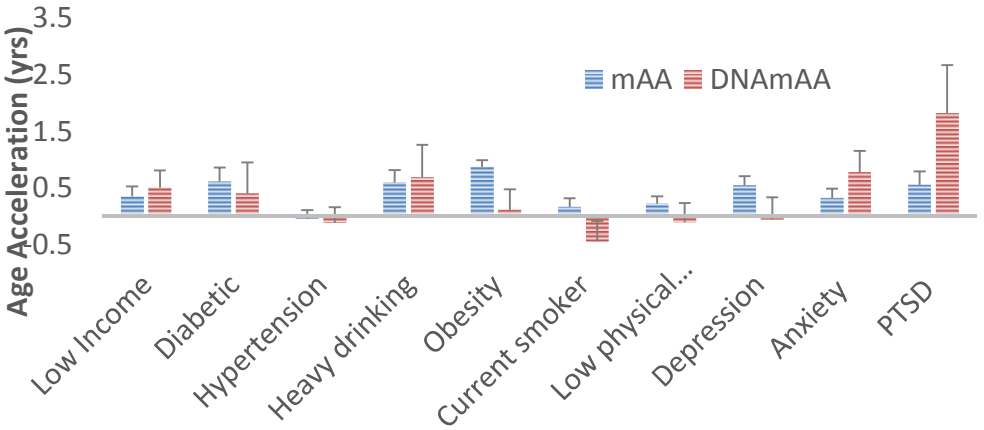
The Metabolomic clock





Robinson et al, *under review*

- ~500 metabolites selected into model from four platforms. Excellent prediction of chronological age (mean *r* = 0.85 in validation sets)
- Model predictors enriched in pathways related to the 'Hallmarks of Ageing'
- Metabolomic age acceleration (mAA) associated with low income, diabetes, overweight/obesity, heavy drinking and depression
- Complementary to DNA methylation age acceleration (DNAmAA), which has stronger association with anxiety related disorders



European Journal of Epidemiology
https://doi.org/10.1007/s10654-019-00539-w

CORRESPONDENCE

Biography and biological capital

Paolo Vineis[1,2] · Michelle Kelly-Irving[3]

The French sociologist Pierre Bourdieu has explained the role of **economic, social and cultural capital** in the functioning of societies and in social inequality. Like “the social world is accumulated history” , so is the individual life at any particular time/age: it is the accumulated history of all economic, social, cultural and eventually biological experiences that had an impact on the body.

Biology (Zoe) and biography (Bios) meet for example through health status, depending on social position at a given age.

This connects to biology is not explained by Bourdieu, and biological capital is the missing concept. However, the ability to access the three other forms of individual capital and therefore position in life depends on **inherited biological health/skills, epigenetic imprinting and the accumulation of embodied biological changes that make an individual more or less successful in life.**

Lifepath

- **Lifepath Funder** – **European Union H2020**
- **Lifepath coordinator – Paolo Vineis, Imperial College, London**
- **Lifepath Collaborators**

Rotterdam University - Johan Mackenbach
Lausanne University - Silvia Stringhini
IIGM (ex HuGeF) - Silvia Polidoro, Giovanni Fiorito
ICL - Marc Chadeau-Hyam, Paolo Vineis (coordinator)
KCL - Mauricio Avendano
Toulouse University - Michelle Kelly Irving
UCL - Michael Marmot, Mika Kivimaki
Zadig - Luca Carra