Centro di Riferimento per l'Epidemiologia
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La biologia delle diseguaglianze sociali legate all'invecchiamento.

Carlotta Sacerdote

XLIII Convegno AIE 2019

AIE CATANIA 2019

Aging

Aging is the progressive decline in physiological ability and loss of function with advancing age:

Chronological aging is a measure of age in years and occurs at a constant rate in all individuals.

Biological ageing is due to the accumulation of damage at cellular level and it is determined by both environmental and genetic factors (*Adams, 2004*).

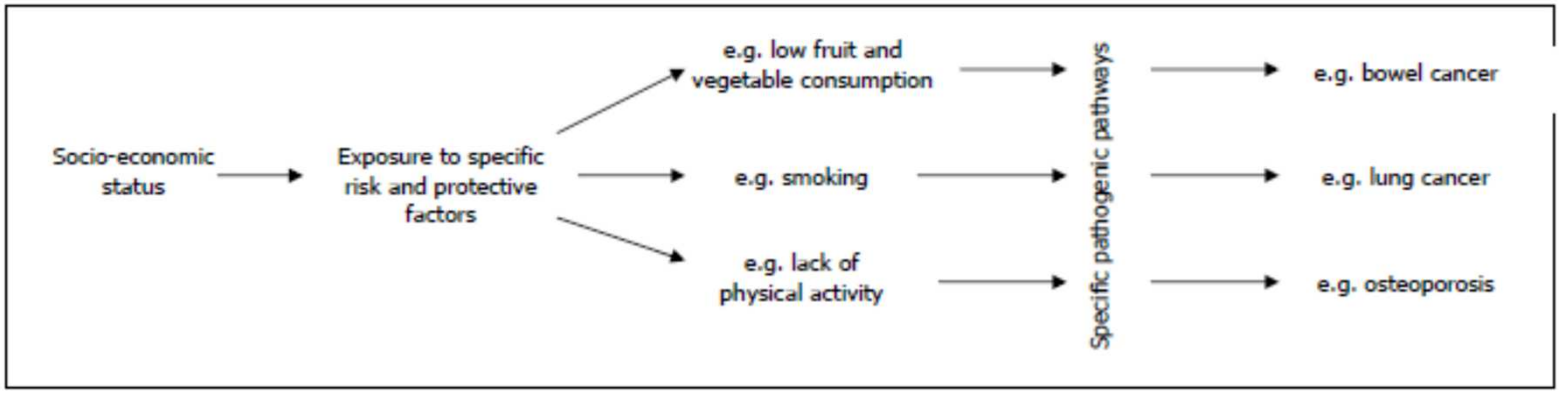
SEP and diseases

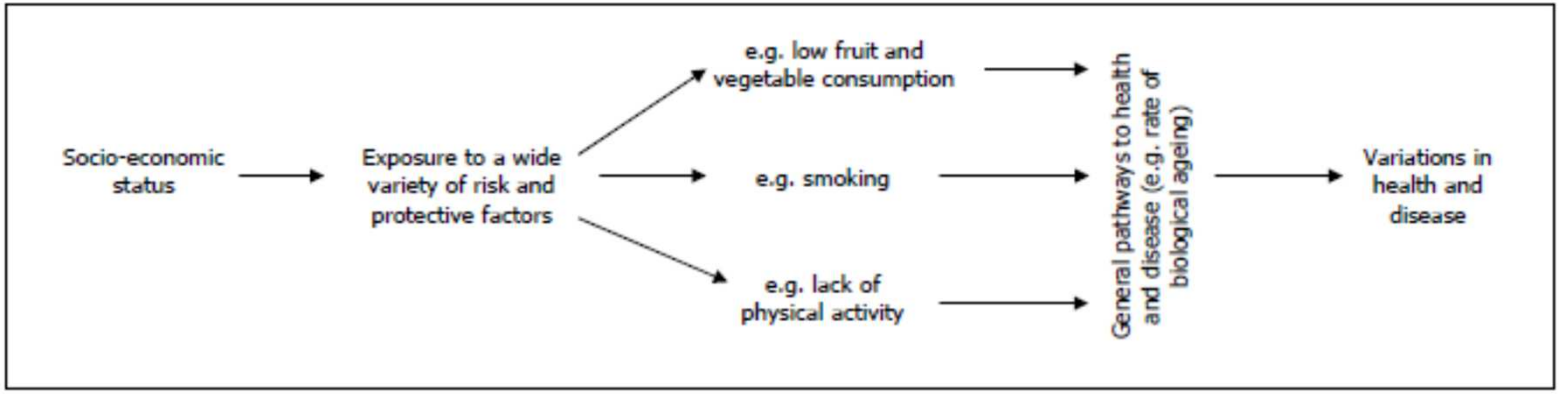
Socioeconomic differences in health could be understood as due to differential exposure:

mediation role of traditional risk factors.

- Relative importance of traditional risk factors is different in different populations
- Differential exposure to traditional risk factors do not explain the increased risk of diseases.

SEP and biological aging





Biological ageing: A fundamental, biological link between socio-economic status and health?

Article in The European Journal of Public Health · October 2004

La biologia delle diseguaglianze sociali legate all'invecchiamento

Lifepath

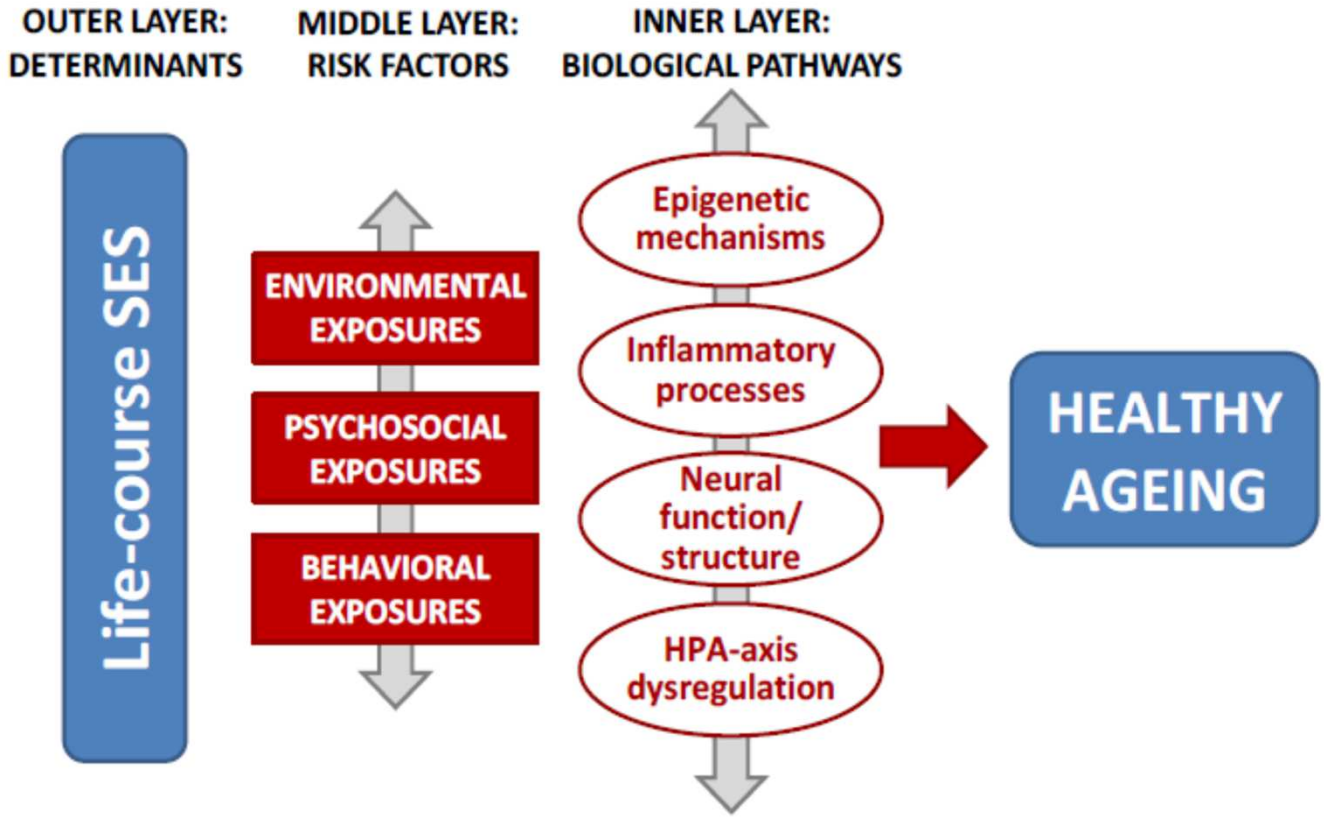
- **Lifepath Funder** – **European Union H2020**

- **Lifepath coordinator – Paolo Vineis, Imperial College, London**

- **Lifepath Collaborators**

Rotterdam University - Johan Mackenbach
Lausanne University - Silvia Stringhini
IIGM (ex HuGeF) - Silvia Polidoro, Giovanni Fiorito
CPO - Carlotta Sacerdote
ICL - Marc Chadeau-Hyam, Paolo Vineis (coordinator)
KCL - Mauricio Avendano
Toulouse University - Michelle Kelly Irving
UCL - Michael Marmot, Mika Kivimaki
SEPI – Giuseppe Costa, Angelo D'Errico, Fulvio Ricceri
Zadig - Luca Carra

Lifepath



The biology of inequalities in health: the LIFEPATH project

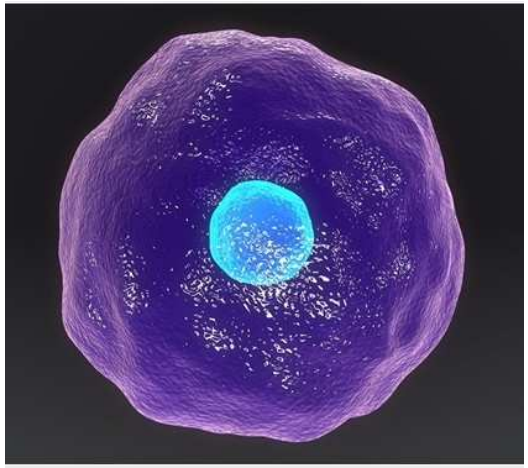
Longitudinal and Life Course Studies 2017 Volume 8 Issue 4 Pp 417 – 439

La biologia delle diseguaglianze sociali legate all'invecchiamento

Biological aging

Imperfect operation of maintenance mechanisms and the resultant accumulation of cellular damage.

The rate at which cellular damage accumulates is determined by the balance between damage and repair mechanisms.



Biomarkers of biological aging

Several biomarkers of biological aging have been proposed:

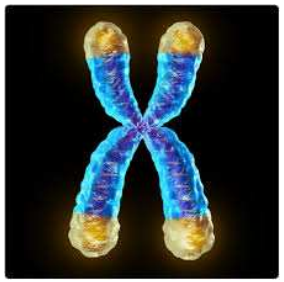
- Telomere length
- DNA methylation (epigenetic clock, epigenetic drift)
- Allostatic load
- …

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

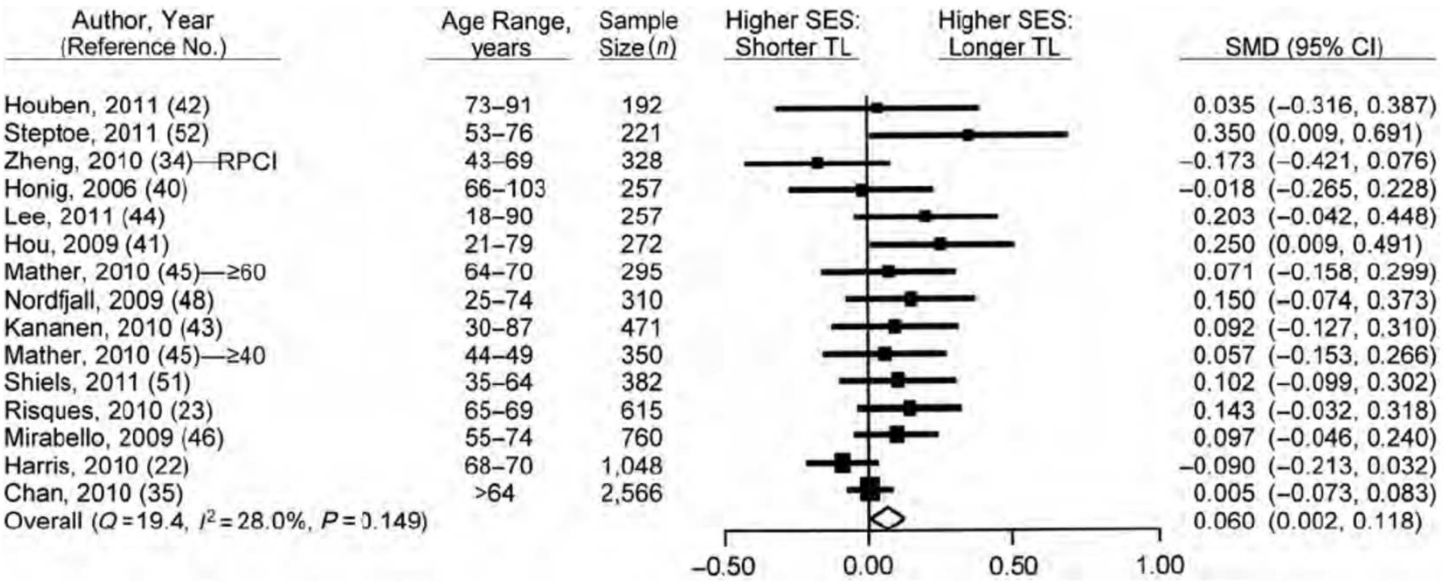


Figure 3. Results from random-effects meta-analysis for the standardized mean difference (SMD) (i.e., effect size) between low and high education categories in the relation of socioeconomic status (SES) with telomere length (TL), ranked by weights applied in the analysis. Squares, SMDs for individual studies; diamond, overall SMD. Bars, 95% confidence interval (CI). (RPCI, Roswell Park Cancer Institute).

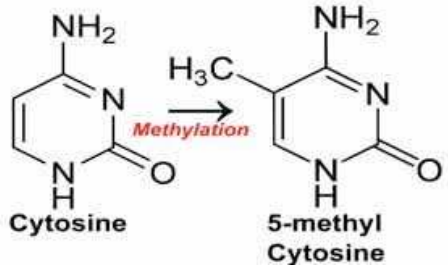
Epidemiol Rev 2013;35:98–111

Epigenetic clock

Epigenetic clock refers to specific CpG sites identified in specific DNA regions at which DNAm levels constantly increase (or decrease) during aging can be used to predict chronological age with high accuracy.

Three epigenetic clocks: Horvat, Hannum and Levine.

Epigenetic aging acceleration differences DNAm age and chronological age.

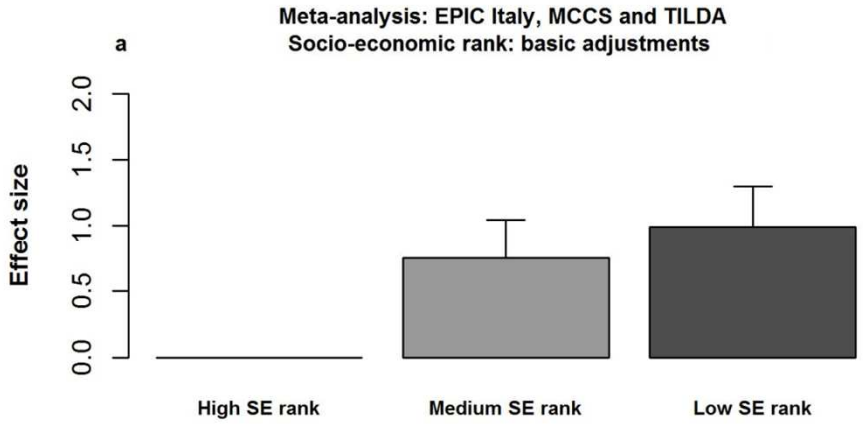


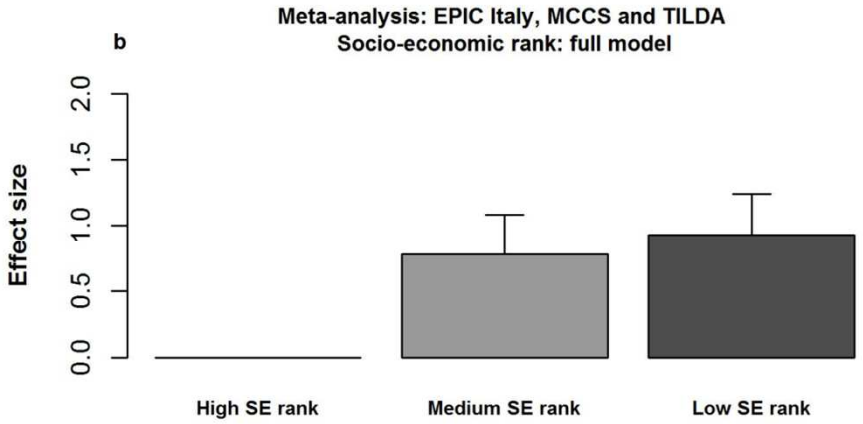
Epigenetic clock

Epigenetic aging acceleration has been associated with:

- Risk factors: obesity, poor physical activity, unhealthy diet, cumulative lifetime stress, infections.
- All causes mortality
- Diseases: cancer incidence, neurodegenerative disorders.

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

SCIENTIFIC REPORTS

Lifepath
HEALTHY AGEING FOR ALL

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Epigenetic drift

Epigenetic drift represents the trend of increasing DNAm variability over time across the whole genome.

Age related genomic instability and chromatin deterioration lead to increased variability of genome-wide DNAm levels at older ages.

Teschendorff: differential DNAm variability

Gentilini: stochastic epimutations

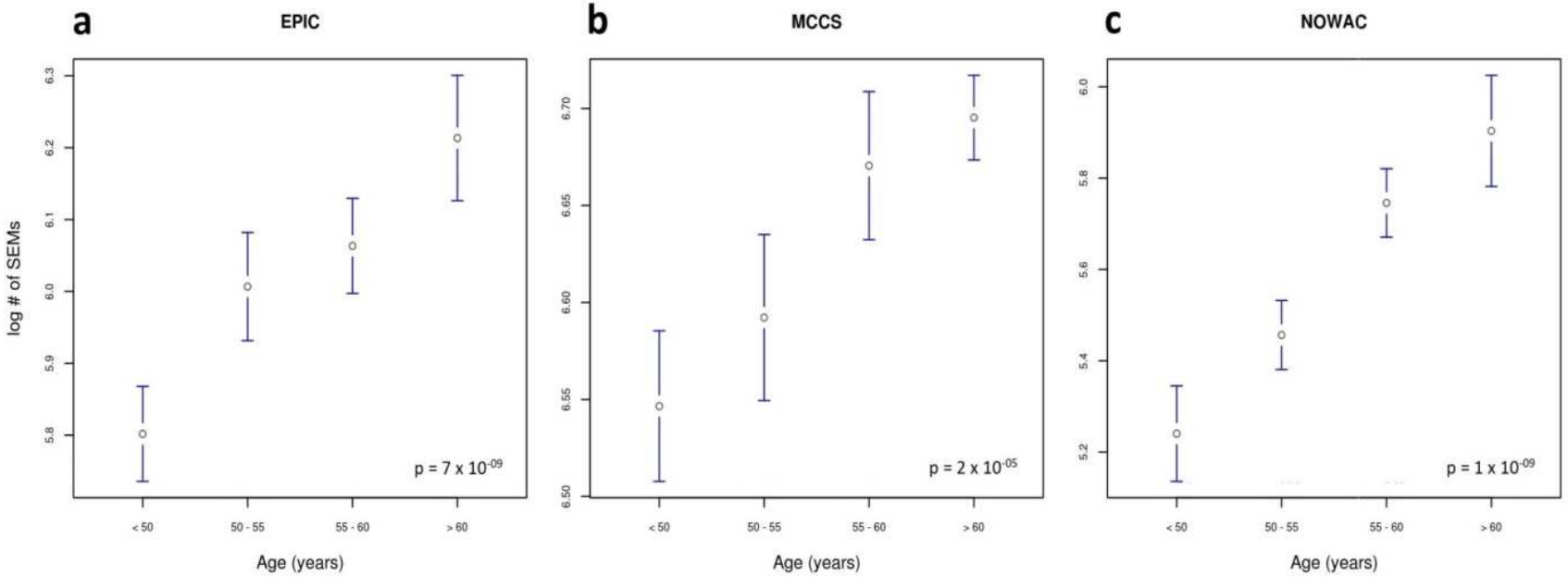
Stochastic epimutations

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

Stochastic epigenetic mutations



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

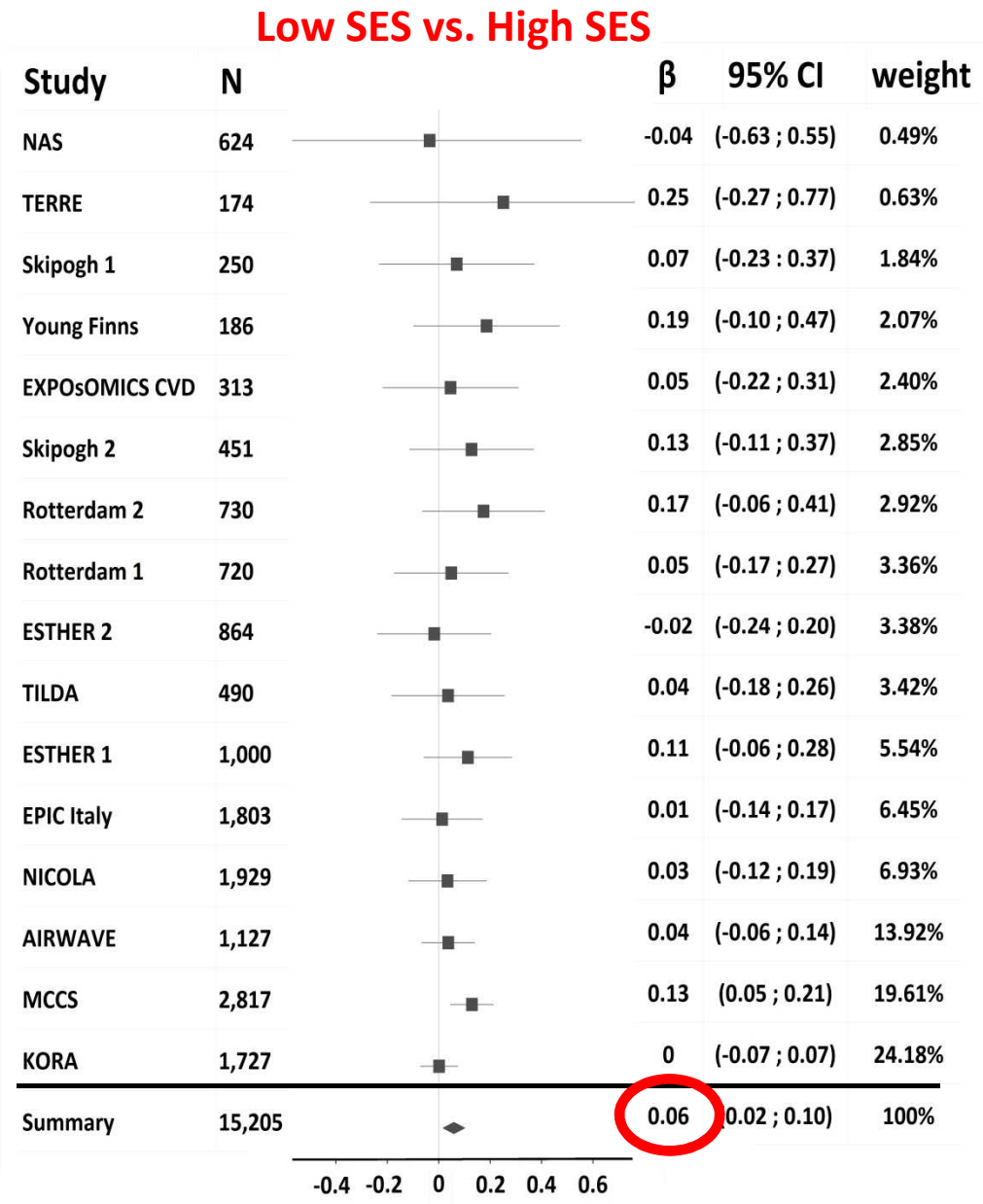
Giovanni Fiorito[1,40], Cathal McCrory[2,40], Oliver Robinson[3,40], Cristian Carmeli[4,40], Carolina Ochoa Rosales[5,6,40], Yan Zhang[7,40], Elena Colicino[8,40], Pierre-Antoine Dugué[9,10,11,40], Fanny Artaud[12,40], Gareth J McKay[13,40], Ayoung Jeong[14,15,40], Pashupati P Mishra[16,40], Therese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

Epimutations, SES and unhealthy lifestyle habits: meta-analysis within Lifepath cohorts.

Methods

logSEMs ~ f(age, sex, SES, lifestyle variables, technical covariates, cohort specific variables*).

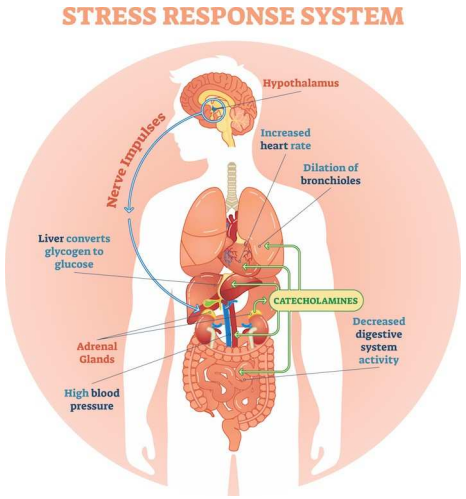
Random effect meta-analysis.



Allostatic Load

McEwen and Stellar (1993): “wear and tear” on the body as a result of exposure to chronic stress.

Indexes constructed from biomarkers to assess the physiological deregulation of nervous, metabolic, immune, cardiovascular and endocrine system.



Allostatic Load

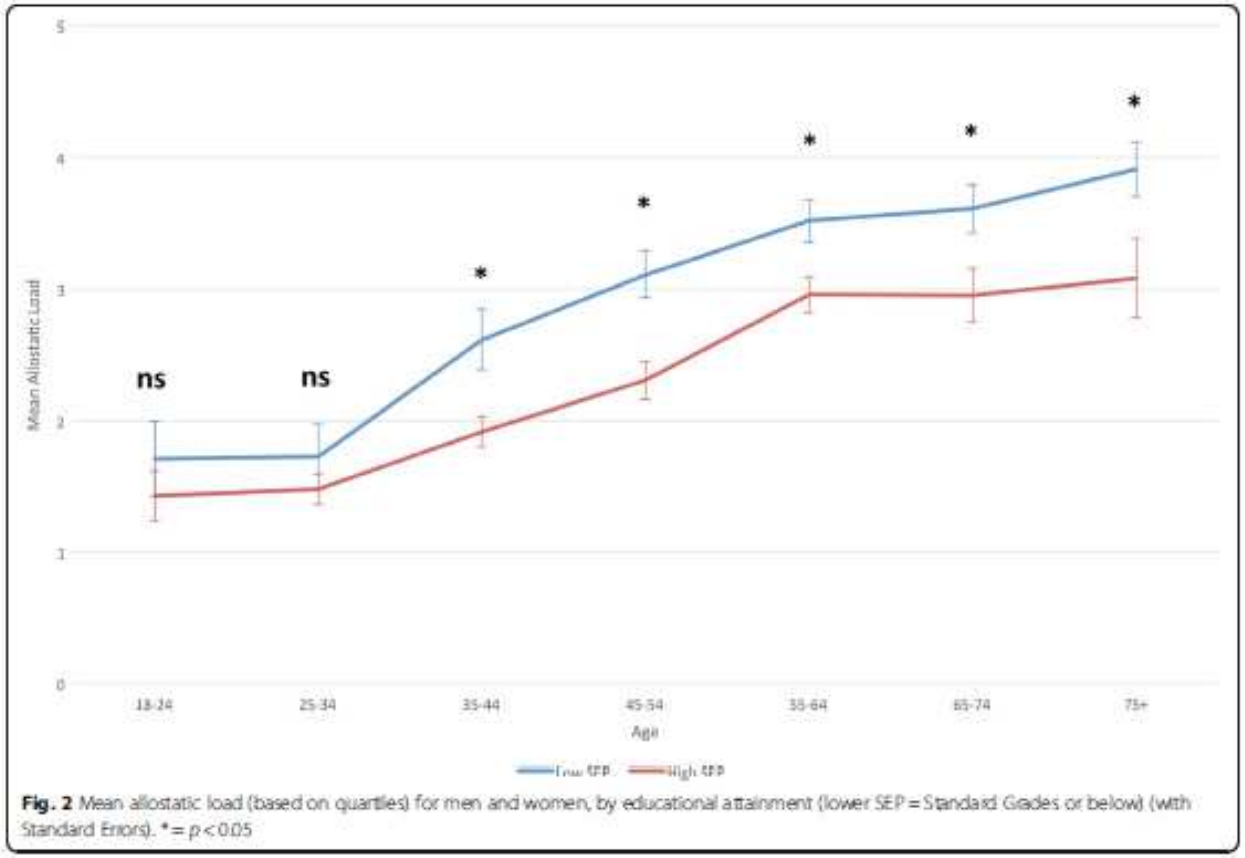
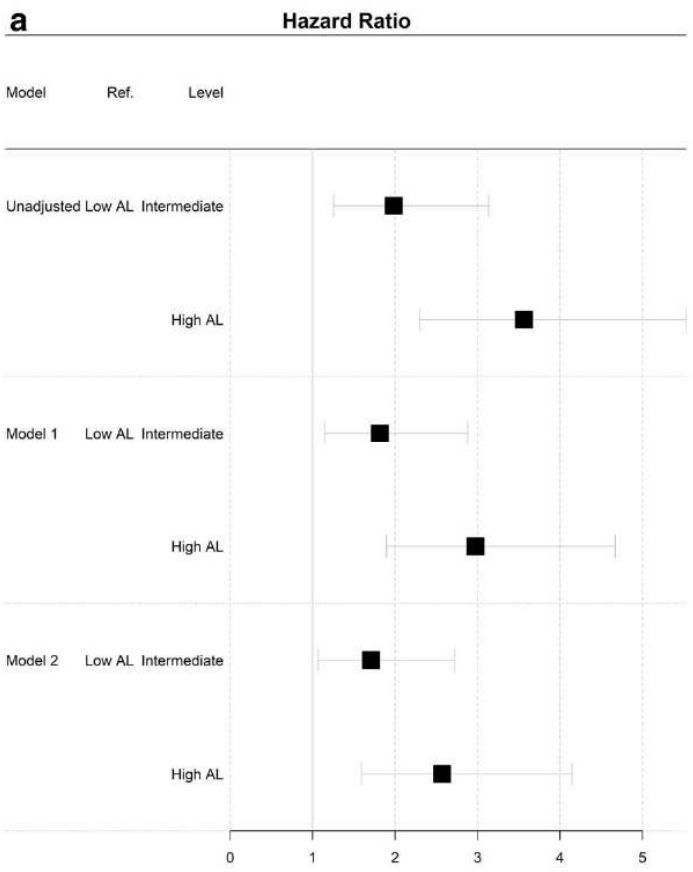
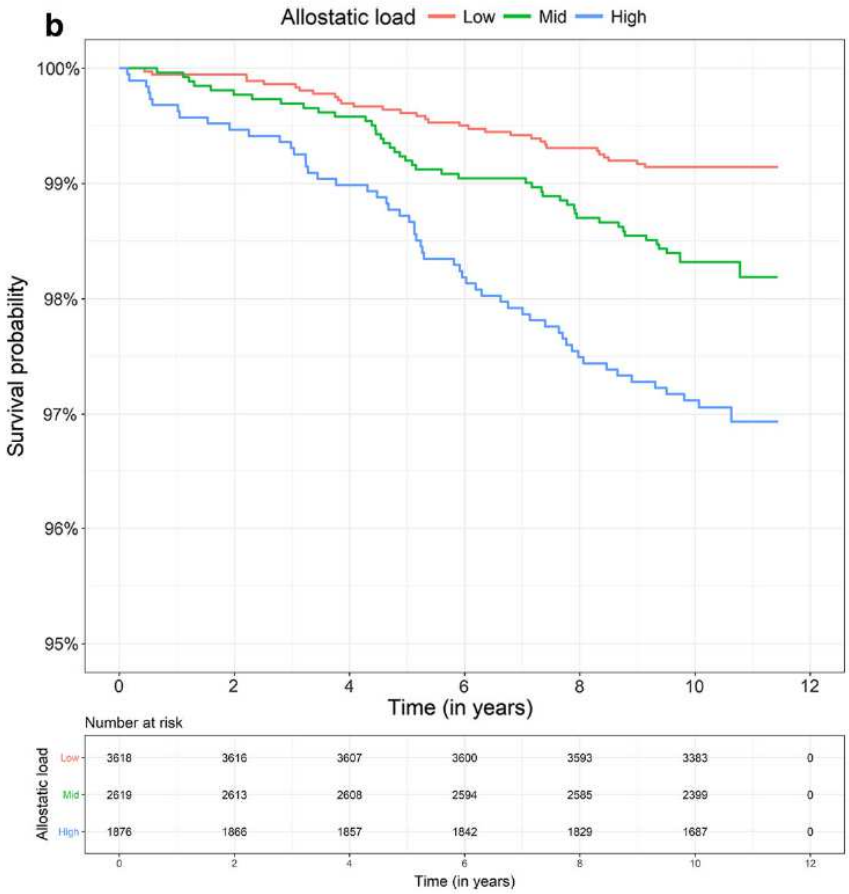


Fig. 2 Mean allostatic load (based on quartiles) for men and women, by educational attainment (lower SEP = Standard Grades or below) (with Standard Errors). * = $p < 0.05$

Robertson and Watts *BMC Public Health* (2016) 16:126

Allostatic Load





European Journal of Epidemiology (2018) 33:441–458

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Conclusions

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]

Grazie dell'attenzione!

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Allostatic load and epigenetic clocks

Pearson correlations between age, epigenetic clocks and allostatic load

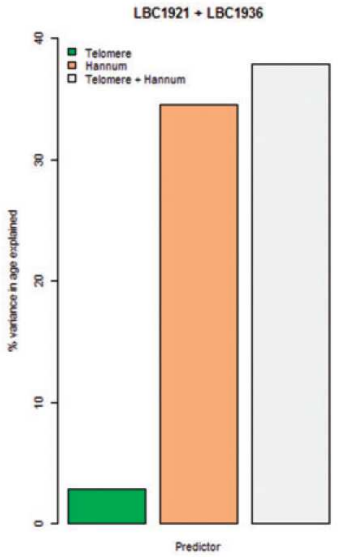
	Age	Horvath's clock	Hannum's clock	Levine's clock
Horvath's clock	0,74***			
Hannum's clock	0,74***	0,92***		
Levine's clock	0,85***	0,66***	0,65***	
Allostatic load	0,32***	0,26***	0,25***	0,38***

Mc Crory, 2019

*** p<0,001

Telomere length and epigenetic clocks

Telomere length and epigenetic clocks measures correlate close to zero → Are they measuring different age related processes?

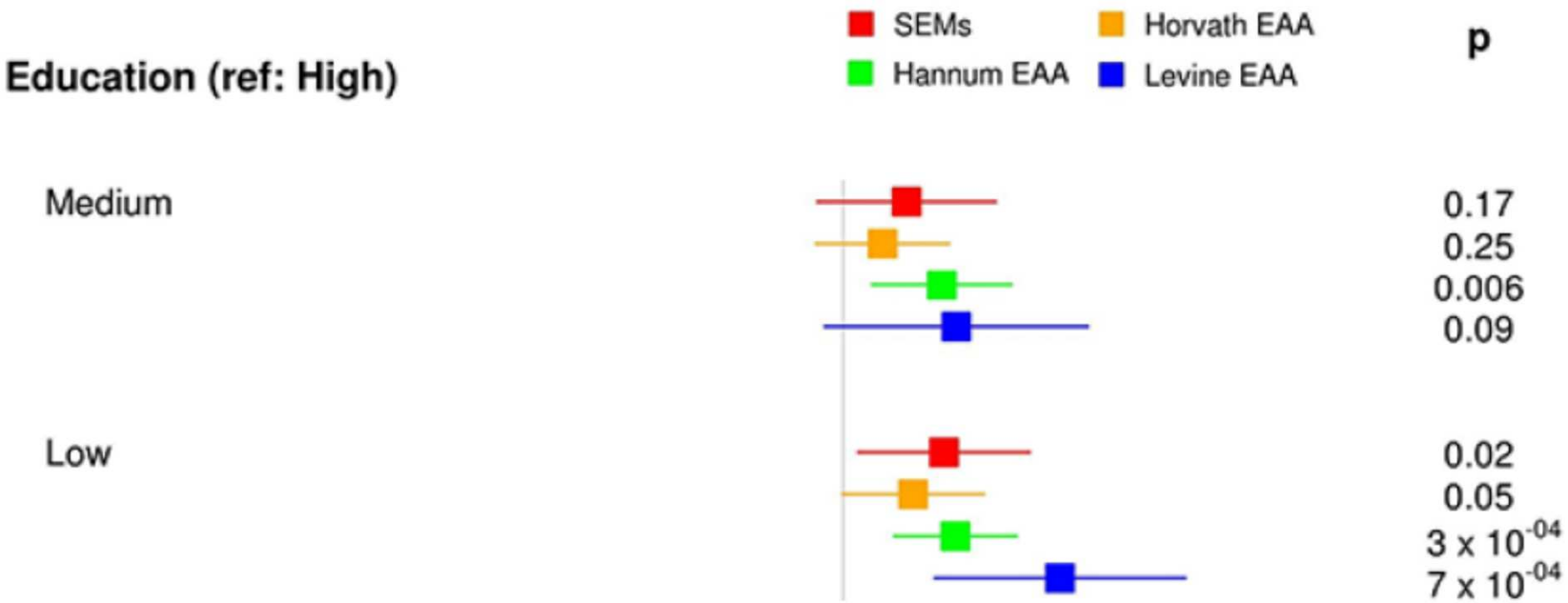


Pearson correlations between Hannum epigenetic clock and telomere lenght

Cohort	N	r (SE)	P-value
Wave 1	920	0.063 (0.03)	0.05
Wave 2	290	0.006 (0.06)	0.92
Wave 3	273	- 0.076 (0.03)	0.21

Marioni R, et al *International Journal of Epidemiology*, 2016, 424–432

SEMs and Clocks



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