Educational inequalities in all-cause mortality: the mediating role of epigenetic aging in a multi-cohort cohort study and meta-analysis

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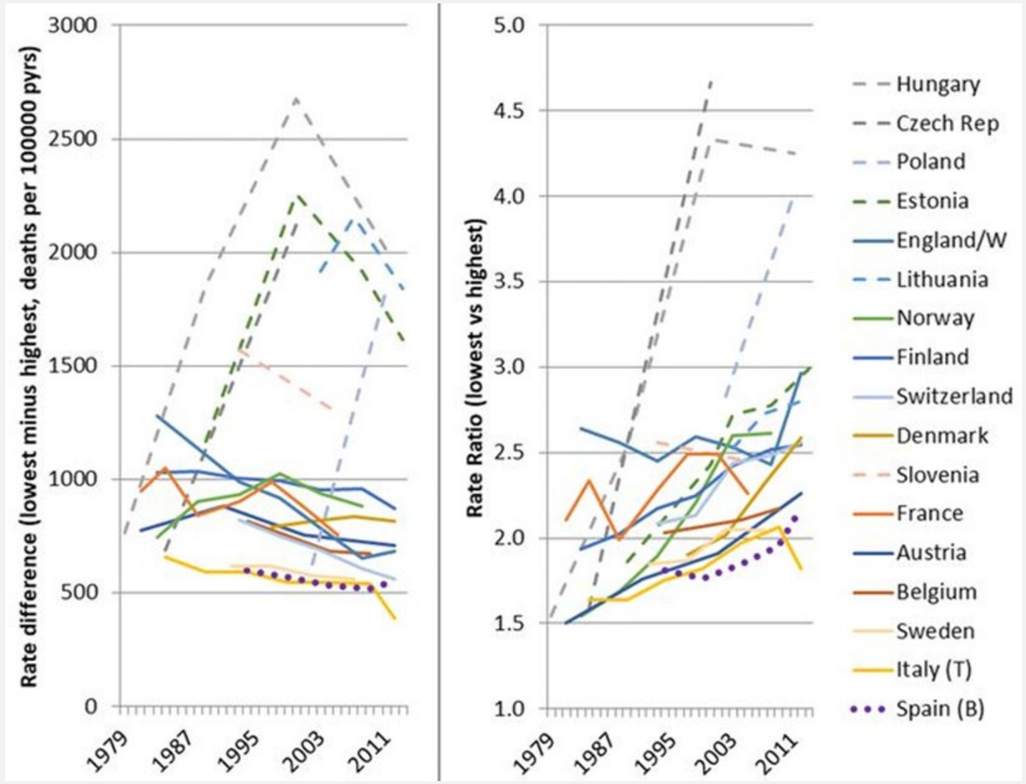
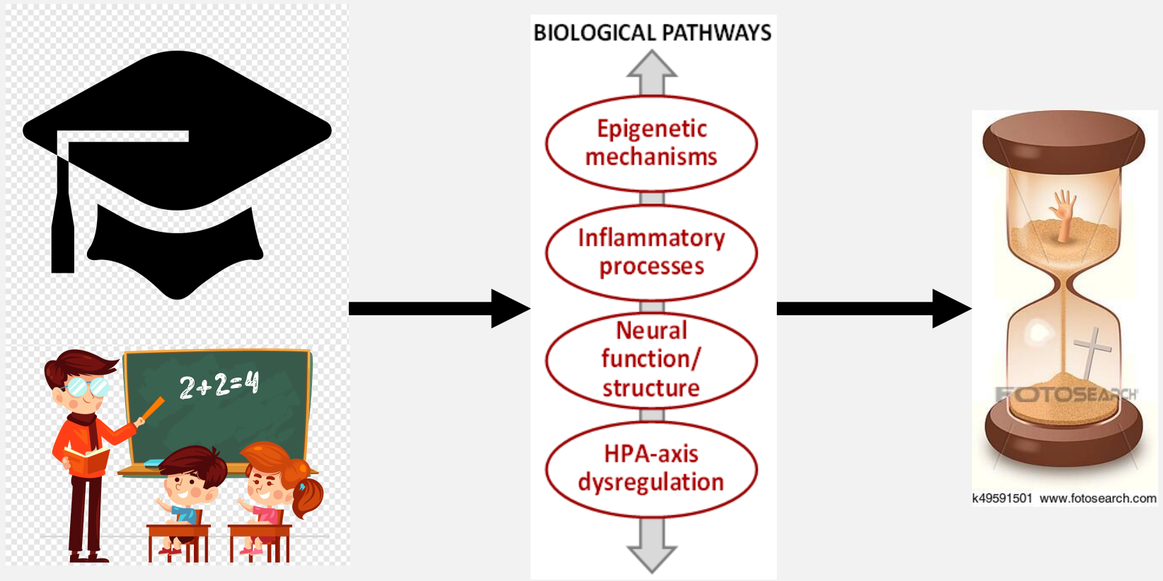
Educational inequalities in mortality persist: how do they get «under the skin»?



Mackenbach et al., PNAS 2018



- Lack of studies assessing biological embedding of educational inequalities with data encompassing: *education* (exposure), *biological pathways* (mediator), and *all-cause mortality* (outcome)
- In this study we assessed the mediating role of *epigenetic aging of immune functioning*, measured via altered patterns of *DNA methylation* in immune cells

Data and methods

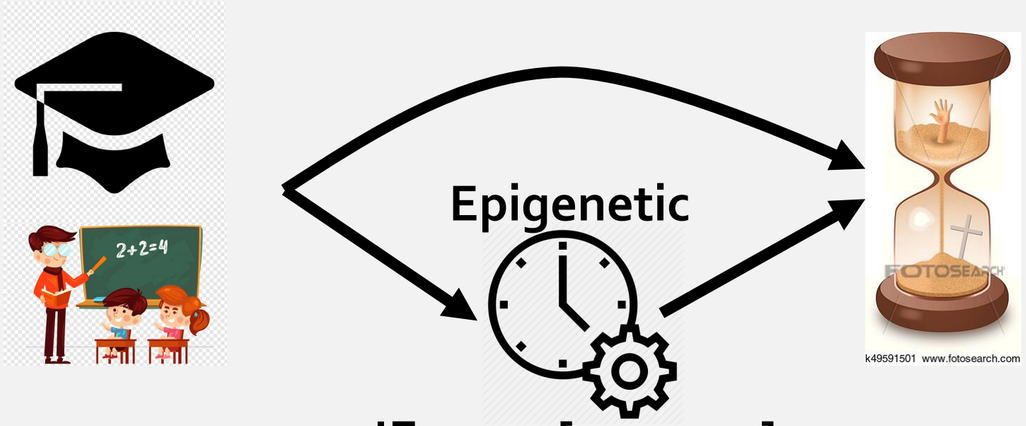
- 13,021 participants – 50% women; 8 prospective population-based cohorts – 6 EU, 1 USA, 1 Australia
- 2,640 deaths; Follow-up: 5y to 15y; Age at baseline: 53y to 70y
- Exposure – educational attainment (low if high school not attained, high otherwise)
- Mediator – epigenetic aging – was derived via GrimAge estimator (Lu et al., Aging 2019)
- Mediation method based on counterfactuals (IORW – Tchetgen Tchetgen, Stat Med 2013)
  - Decomposed educational inequalities in all-cause mortality (total effect TE) into:
    1. Portion through epigenetic aging – indirect effect IE
    2. Portion through other (unmeasured) biological pathways
  - Aalen and Cox survival models to estimate:
    1. Absolute inequalities – excess deaths
    2. Relative inequalities – hazard ratios

Results – low vs high education

Excess deaths per 100,000 person-years [95% CI]

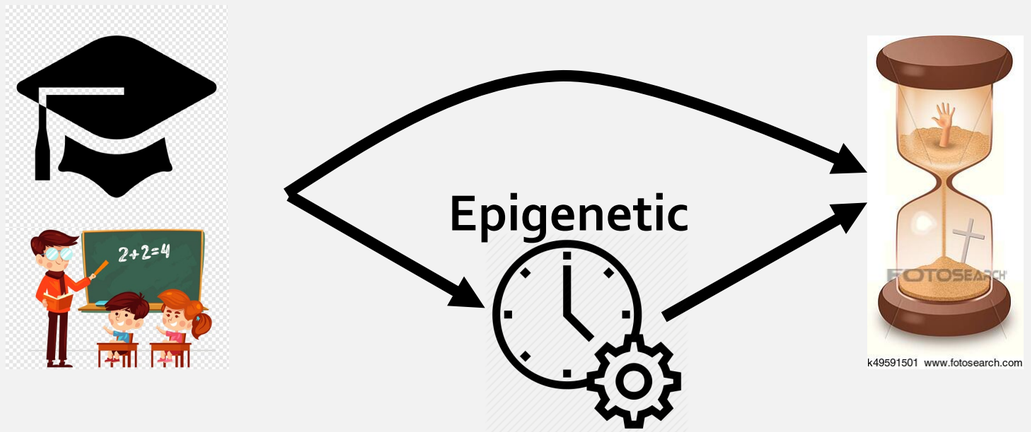
Hazard ratios [95% CI]

MEN



IE = 320 [250, 390]

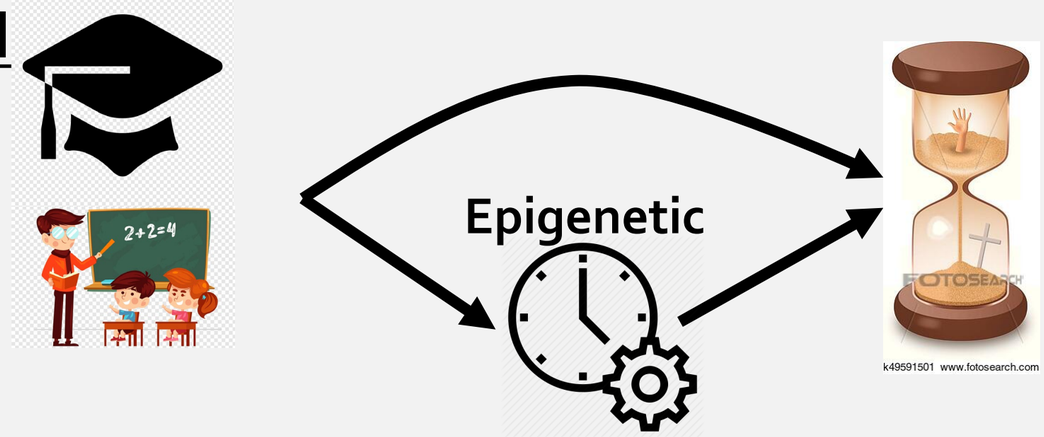
TE = 550 [380, 720]



IE = 1.13 [1.07, 1.18]

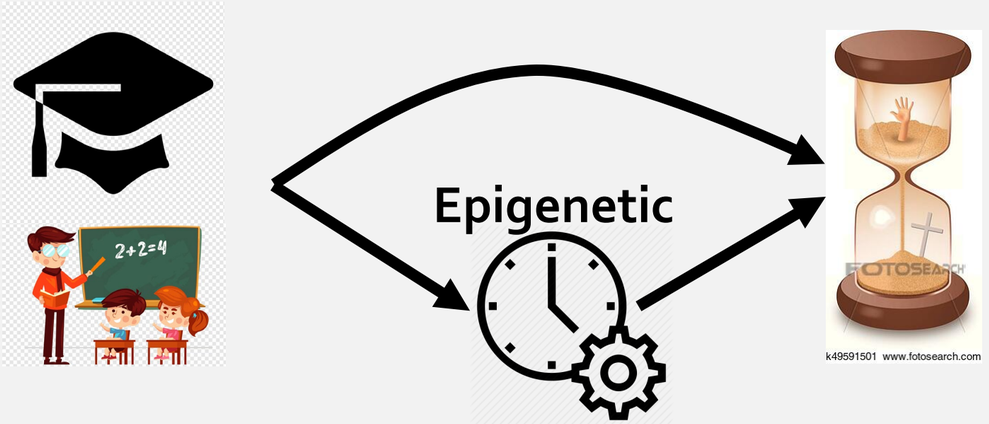
TE = 1.27 [1.11, 1.44]

WOMEN



IE = -30 [-80, 20]

TE = 70 [-50, 200]



IE = 1.02 [0.97, 1.08]

TE = 1.18 [1.01, 1.37]

Results summary

- Epigenetic aging of immune cells explained about 50% of educational inequalities in mortality in men
- These results support DNA methylation-based epigenetic aging as a signature of educational inequalities in life expectancy
- More results including role of unhealthy lifestyle behaviours, sensitivity analyses, and discussion of limitations are reported in a preprint available here
  https://www.medrxiv.org/content/10.1101/2021.07.01.21259023v1

Any questions? Join zoom meeting on Wed 25 1pm-1.30pm:
https://us04web.zoom.us/j/71289567609?pwd=UGwyU1FWajRSdmFqSod1RWV5bGxsUT09

Meeting ID: 712 8956 7609
Passcode: CW33ja

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