L'incorporation biologique des différences socioéconomiques dans la santé

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Outline

- Social inequalities in health
- Mechanisms explaining social inequalities in health
  - ✓Biological mechanisms linking the social environment to health outcomes
- Socioeconomic status and gene regulation of the immune function
  - ✓The Human Social Genomics
- Perspectives
- Conclusions

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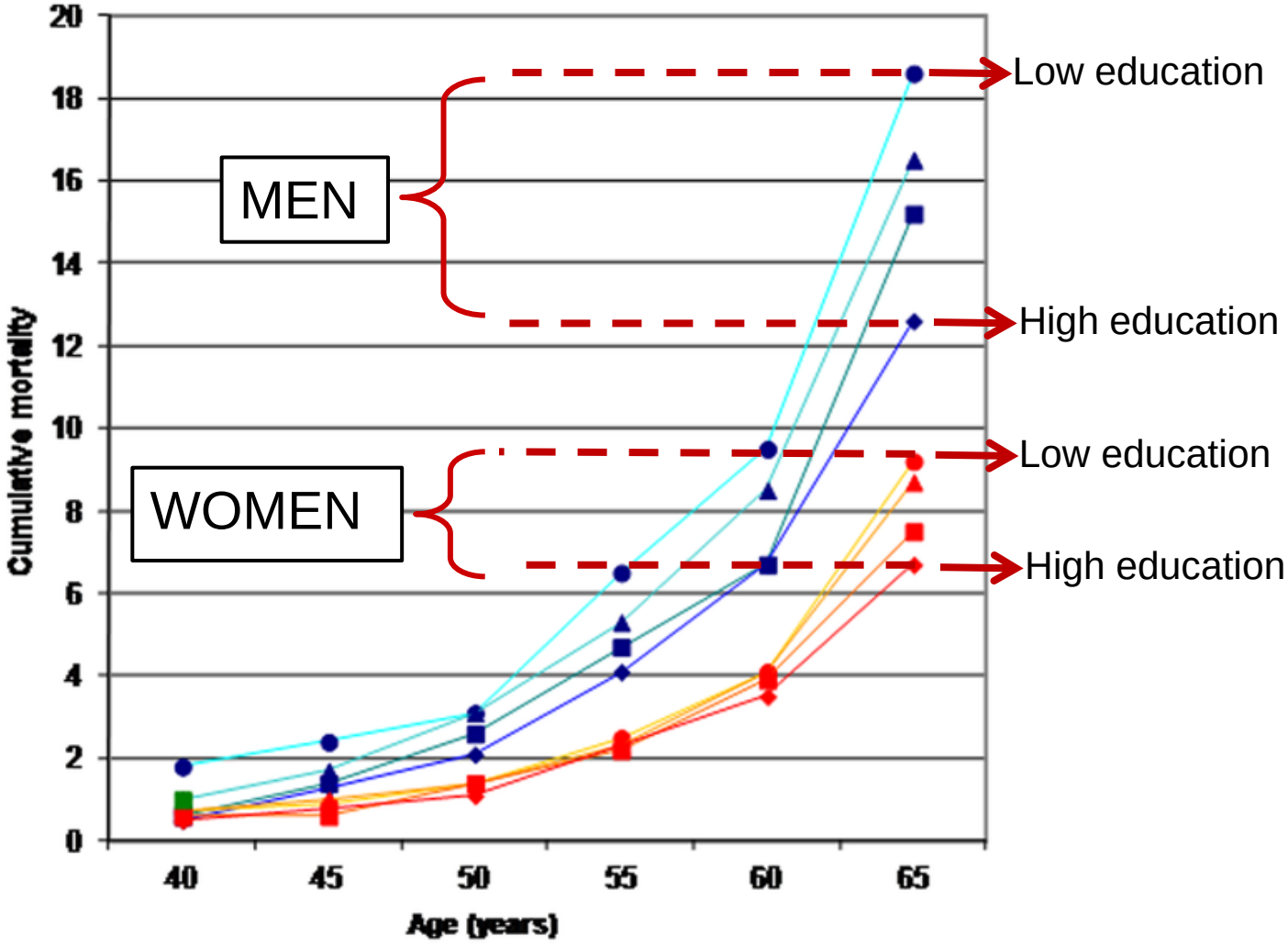
Health inequalities between and within countries: male life expectancy at birth

Country	Male life expectancy
Angola	40
UK, Glasgow (Calton)	54
India	62
US, Washington D.C. (Black)	63
Bolivia	64
Lithuania	65
Mexico	72
United States	75
Cuba	76
Switzerland	79
US, Montgomery County (White)	80
UK, Glasgow (Lenzie N.)	82

Sources: WHO, World Health Statistics 2008; Hanlon, Walsh & Whyte 2006; Murray et al. 2006

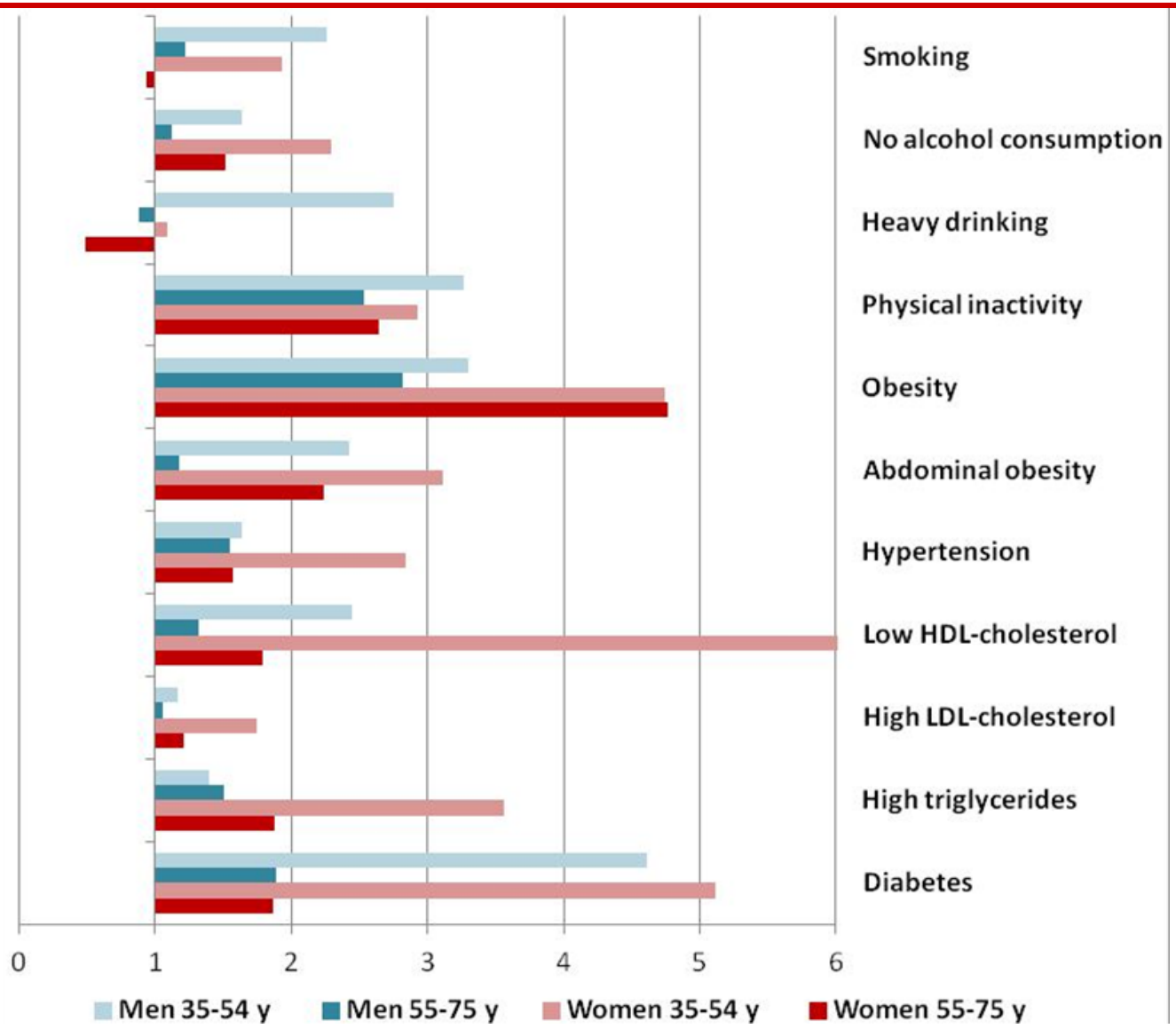
Educational inequalities in mortality

Education and cumulative mortality in Europe (EPIC, 371,295 participants, 9 countries)



Source: Gallo V. et al, PLoS ONE, 2012.

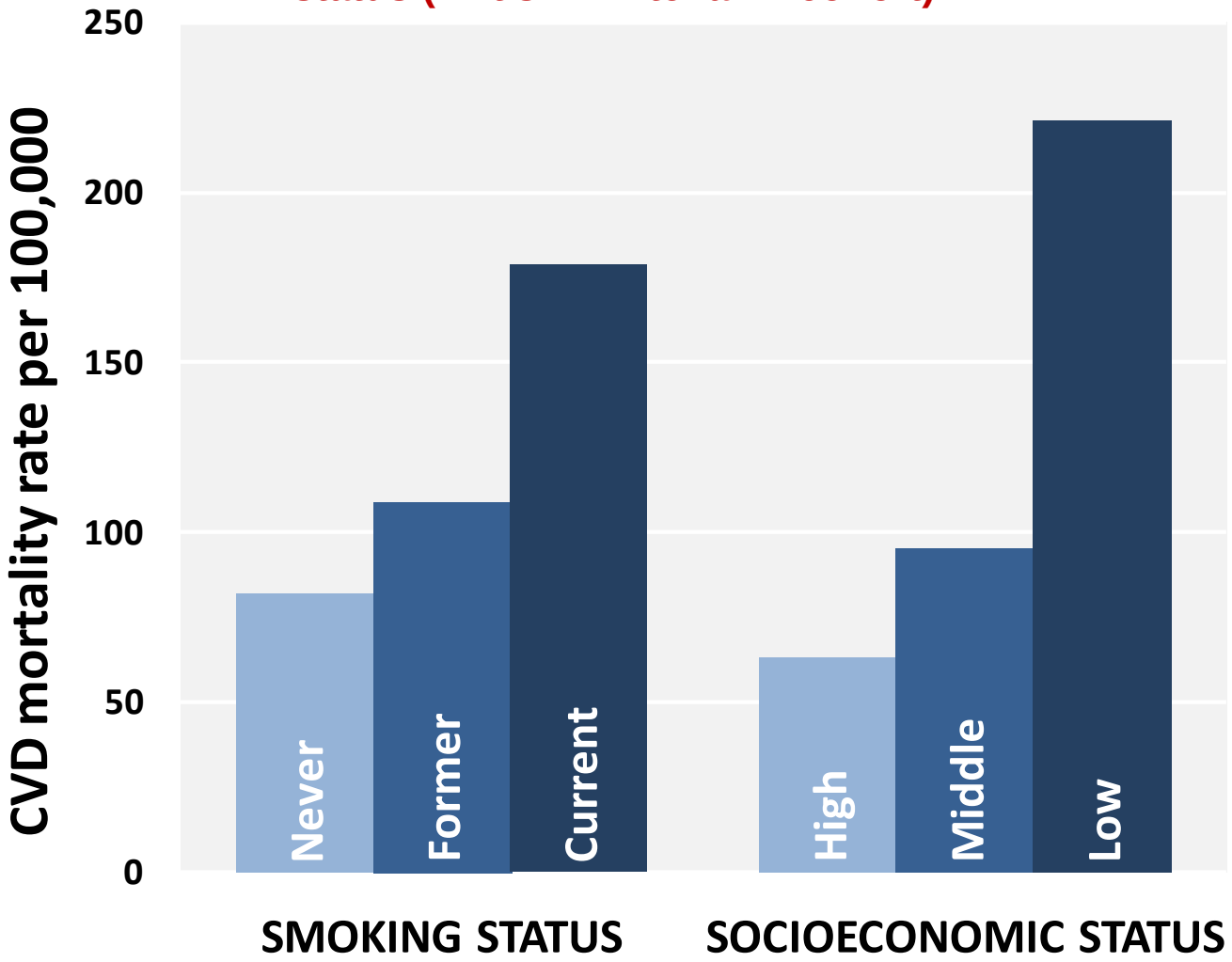
Educational inequalities in cardiovascular risk factors



Stringhini et al. PLOS ONE 2012 (COLAUS Study – lausanne)

Social inequalities in health

Cardiovascular disease mortality by smoking status and socioeconomic status (British Whitehall II cohort)



Source: Stringhini S et al. JAMA, 2010.

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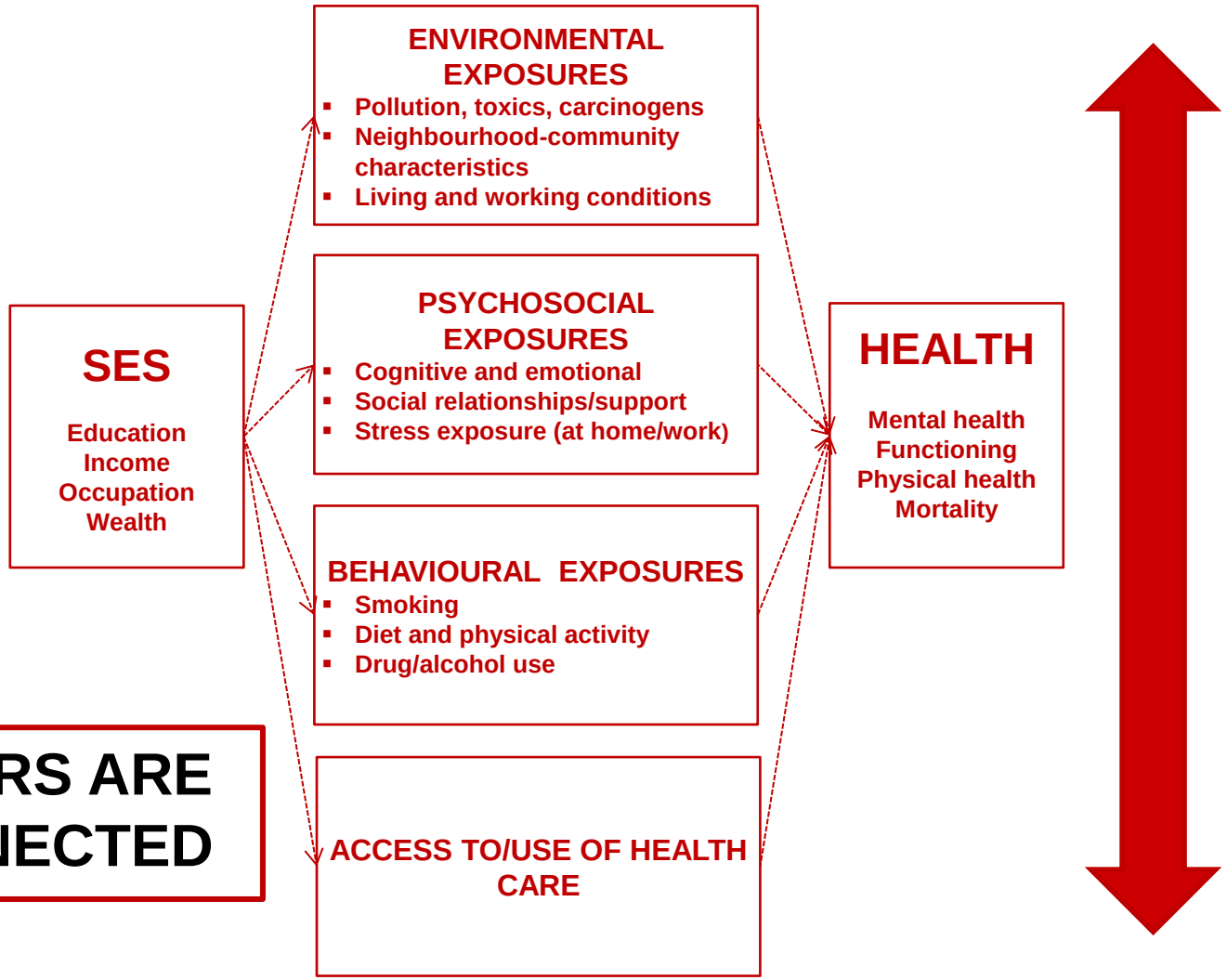
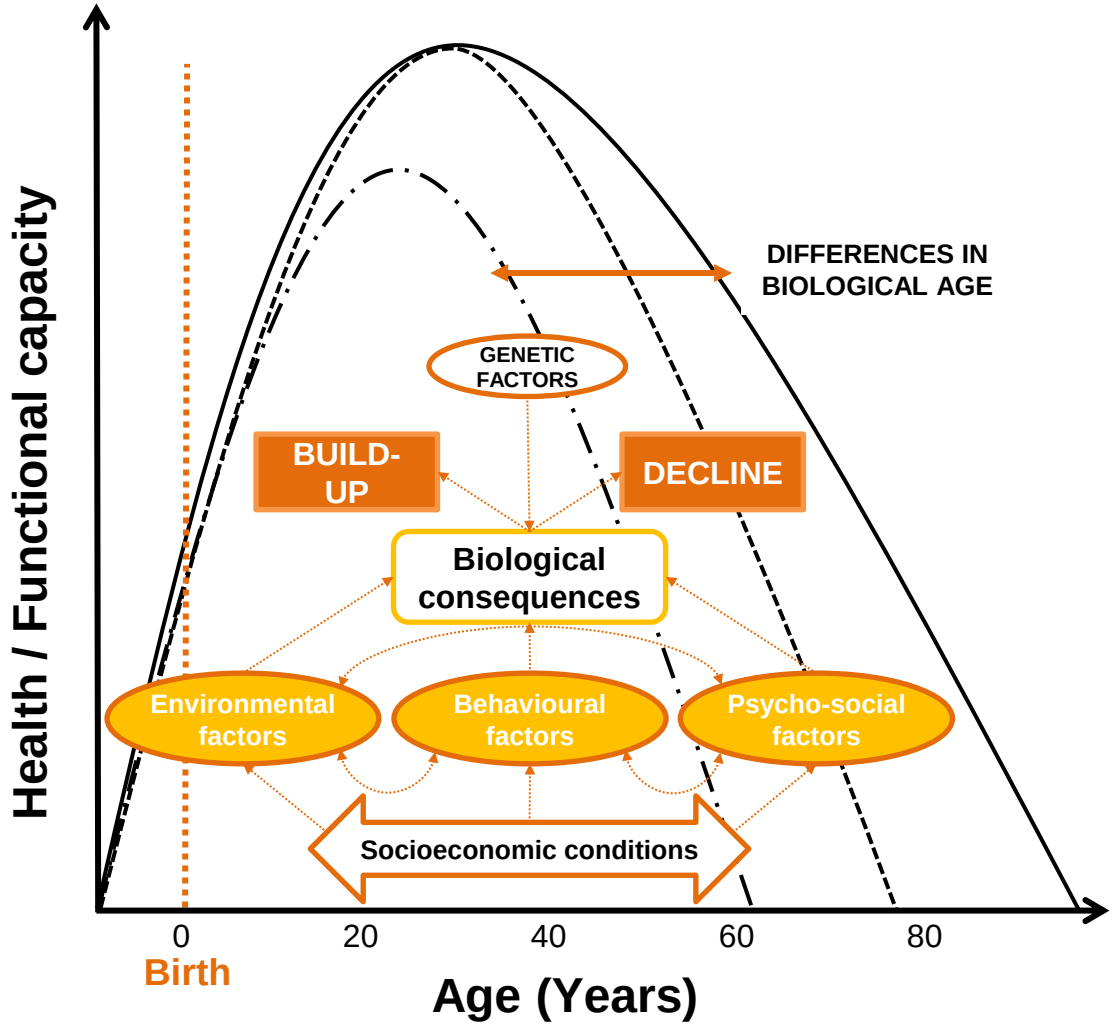
Causal explanations for social inequalities in health



ALL FACTORS ARE INTERCONNECTED

The lifecourse perspective



Models of lifecourse perspective

- **Latency model:**
  - Exposure to adverse SES in critical/sensitive periods alters biological parameters permanently (fetal programming; traumatic events during first year etc.)
- **Cumulation model:**
  - Cumulative effect of exposure to low SES (and its associated factors) across the lifecourse
- **Pathway model:**
  - Low SES in early life influence social mobility pathways and behaviours

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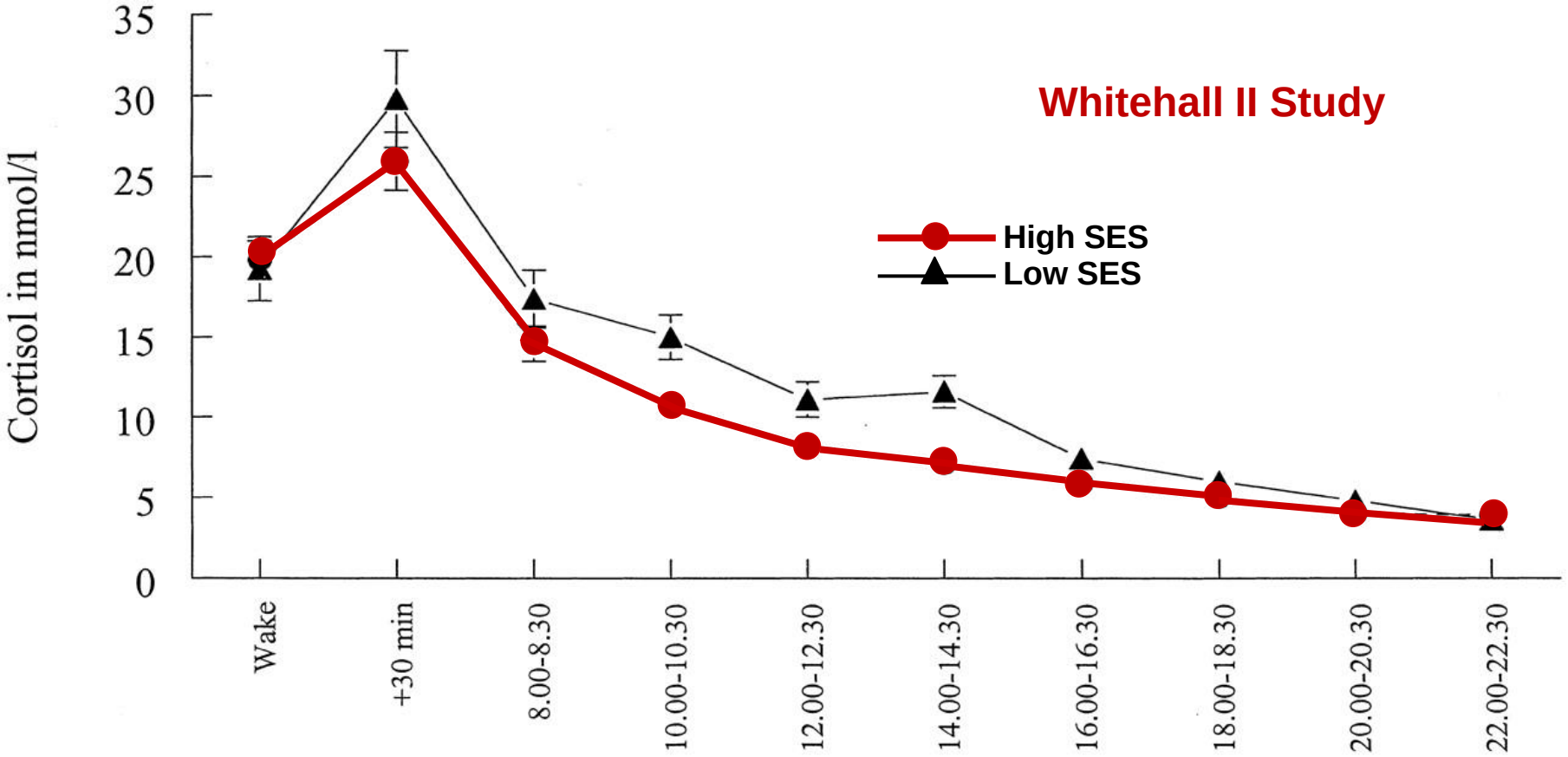
SES and biomarkers

Hypothalamic-pituitary-adrenal axis	***Cortisol*** - Saliva, urine
	Dehydroepiandrosterone sulfate - Blood
Sympathetic neuro-hormonal system	***Norepinephrine/Epinephrine*** - Urine
	Alpha-amylase - Saliva
Parasympathetic neuro-hormonal system	***Heart rate variability*** - Pulse rate recording
Inflammatory/Immune system	***C-reactive protein***- Blood
	Erythrocyte sedimentation rate- Blood
	Interleukins- Blood
	Lymphocyte number and function- Blood
	Circulating serum albumin - Blood, saliva
Cardiovascular	***Diastolic/systolic blood pressure***
	Resting heart rate
Glucose metabolism	***Fasting glucose***- Blood
	Glycosylated hemoglobin- Blood
	Fasting insulin- Blood
Lipid metabolism	***Cholesterol and lipoprotein fractions*** - Blood
	BMI, waist to hip ratio
	Total body fat - DXA scan
Hematological	***Serum hemoglobin***- Blood
	Clotting factors and clotting time - Blood
Renal	***Creatinine*** - Serum or 24h urine
	Urine albumin leakage - Urine
	Cystatin C - Serum or dried blood spot
Hepatic	***Circulating serum albumin*** - Blood, saliva
Reproductive	***Serum testosterone/estradiol***- Blood
	Follicle-stimulating hormone - Blood
Pulmonary	***Arterial oxygen saturation*** - Pulse oximeter
	Peak expiratory flow - Spirometer
Bone	***Bone density*** - DXA scan
	Bone turnover markers - Blood, fasting urine
Muscle	***Skeletal muscle mass*** - DXA scan, body impedance
	Grip strength - Dynamometer
DNA	***Epigenetic markers***

Source: Wolfe B, Evans W, Seeman T. The biological consequences of health inequalities (2012).

SES and HPA-axis dysregulation

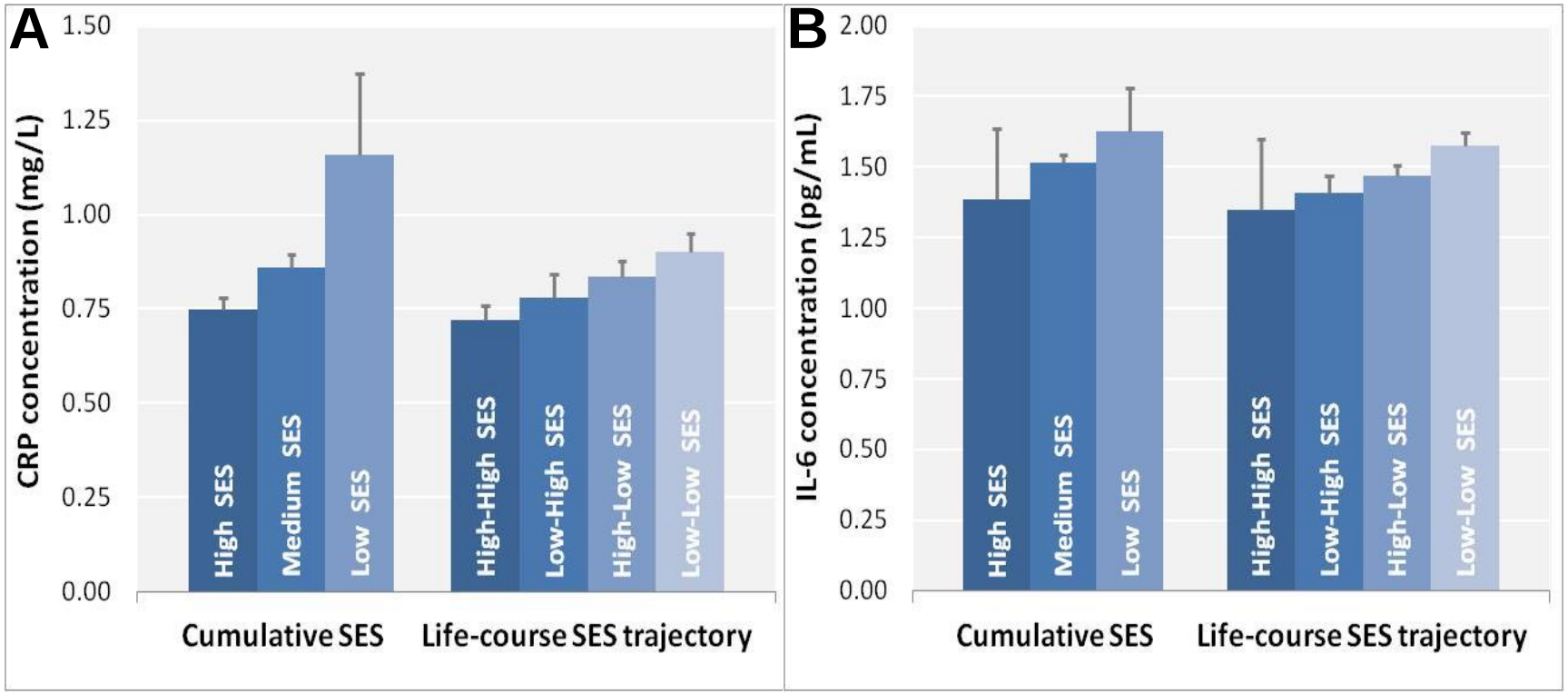
Mean saliva-free cortisol sampled on waking up, 30 minutes later, and then at 2-hour intervals



Source: Steptoe A et al. Psychosom Med (2003).

SES and immune system biomarkers

Lifecourse SES and CRP and IL-6 concentation

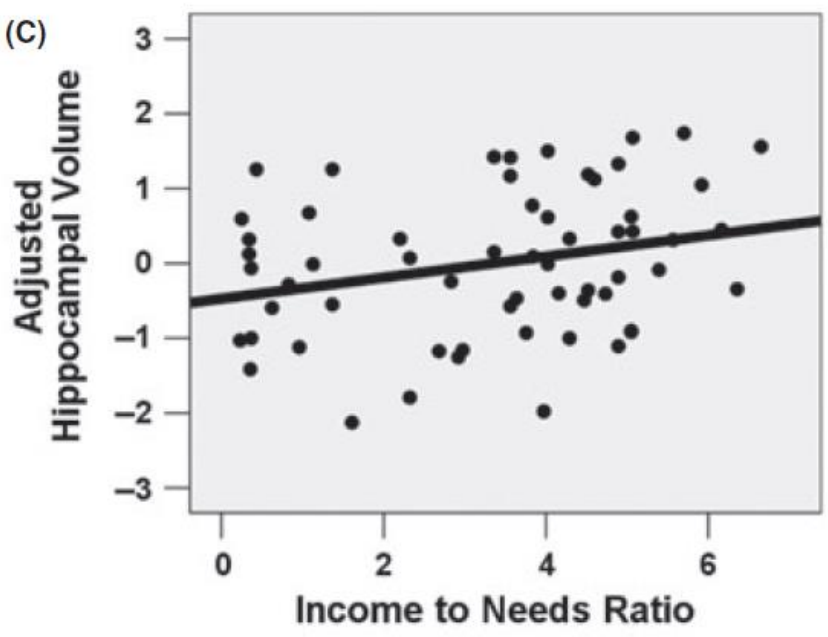


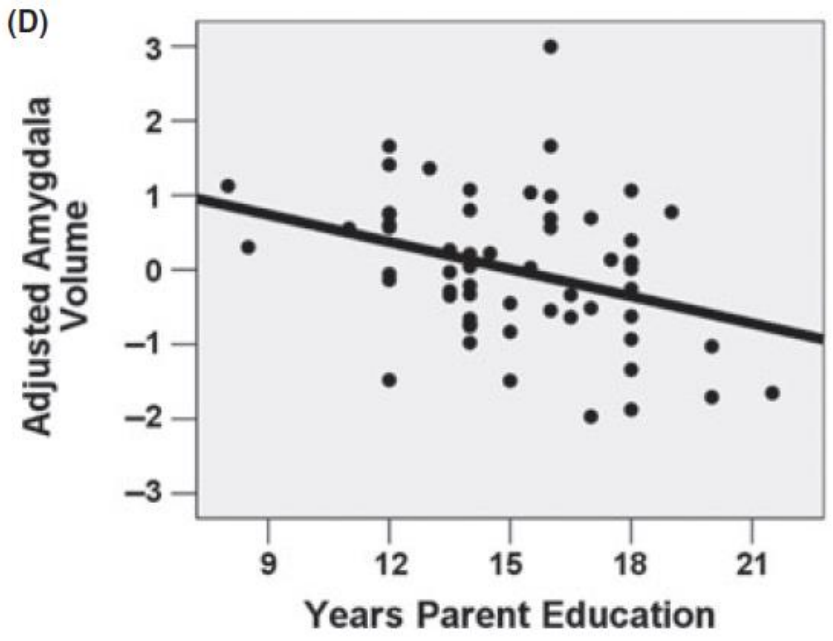
Whitehall II Study

Source: Stringhini S et al. PLoS Medicine (2013).

SES and neural structure

60 typically developing , native English speaking children (US)

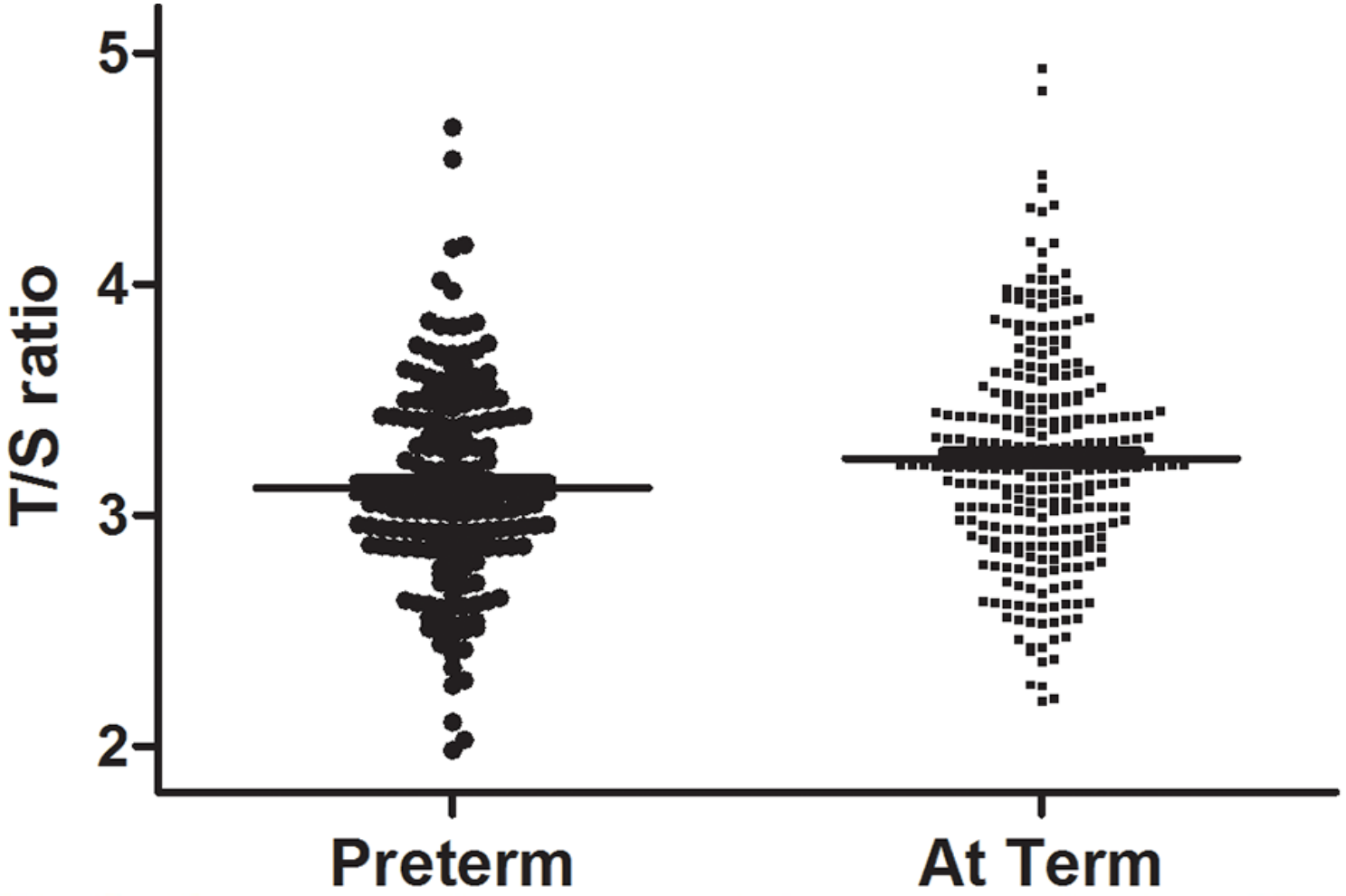




Stressful events in early life generally related to lower hippocampal and higher amygdala volume

Source: Noble et al. Developmental Science (2012).

Preterm birth and telomere lenght

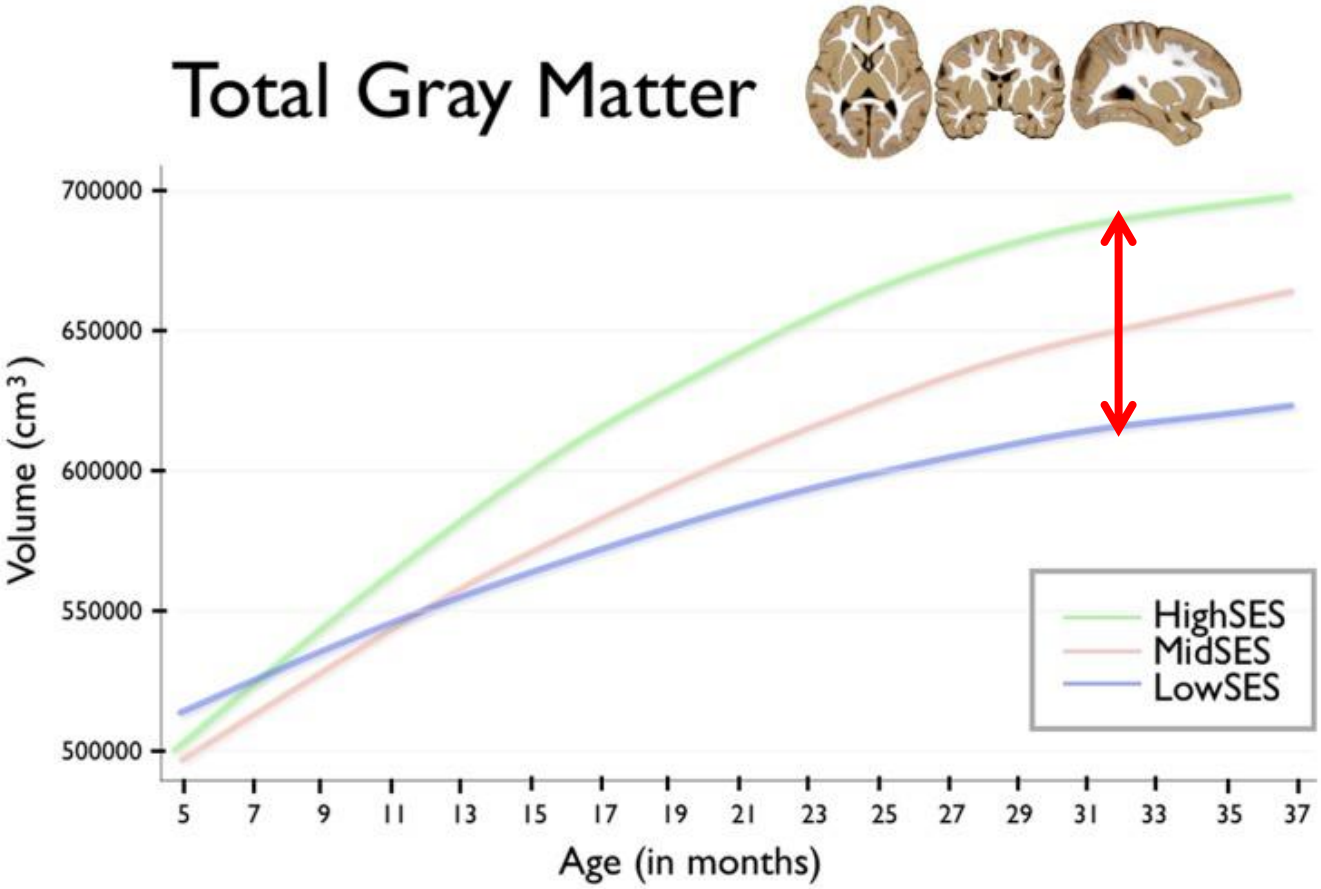


T/S ratio = Telomere to single-gene copy ratio. Preterm = gestational age <37 weeks.
The horizontal bars represent the mean values.

Source: Smeets et al. PLOS ONE 2014.

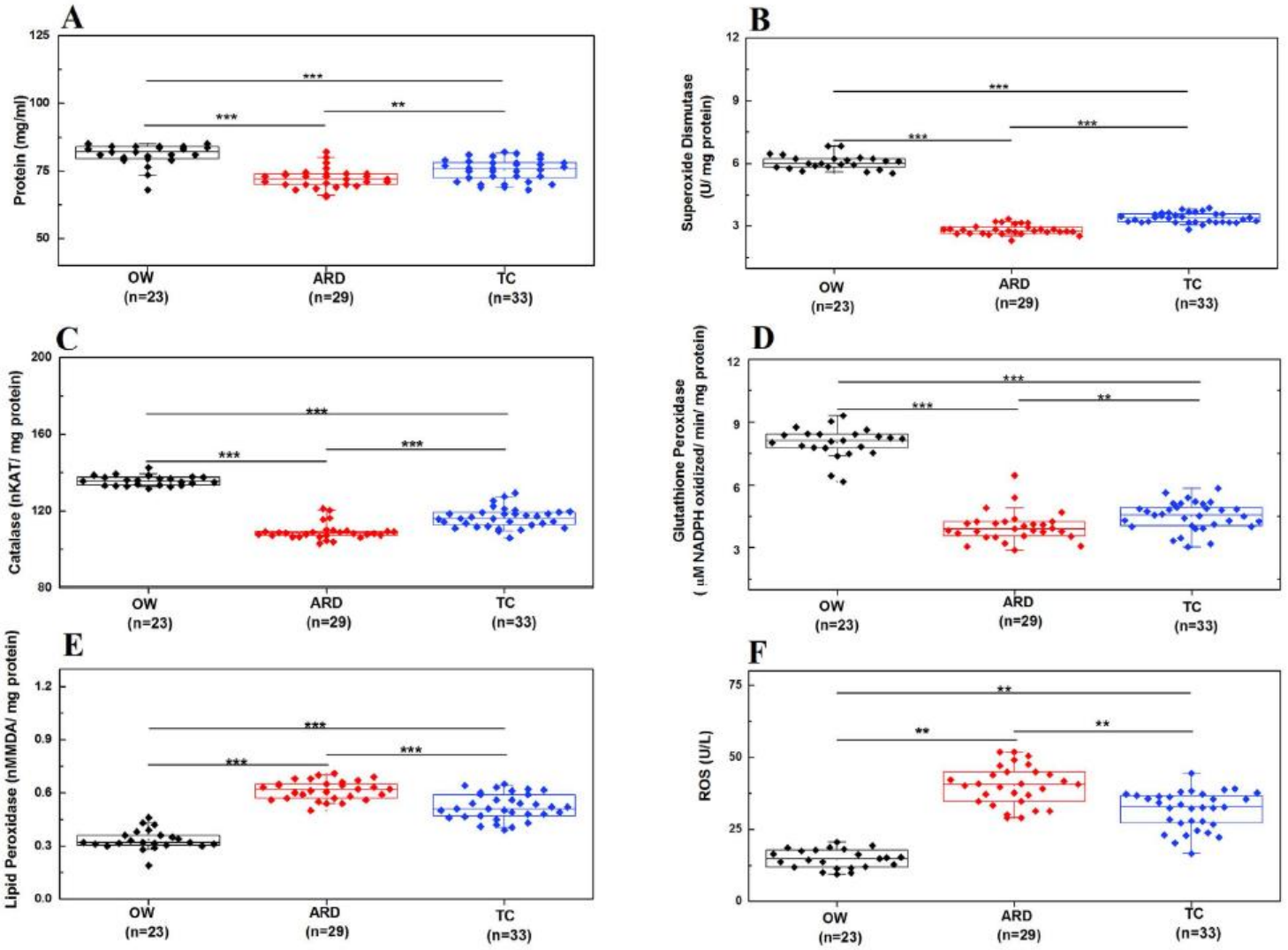
Social factors and brain development

US NIH MRI Study of Normal Brain Development, N=55 healthy children



Source: Wolfe et al. PLoS ONE 2013

Occupational exposures and oxidative stress



Source: Pradhan et al. Scientific Reports 2016.

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SES and gene regulation

Low early-life social class leaves a biological residue manifested by decreased glucocorticoid and increased proinflammatory signaling

Social environment is associated with gene regulatory variation in the rhesus macaque immune system

Int. J. Epidemiol. Advance Access published October 20, 2011

Published by Oxford University Press on behalf of the International Epidemiological Association

International Journal of Epidemiology 2011;1–13
doi:10.1093/ije/dyr147

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Published by Oxford University Press on behalf of the International Epidemiological Association

International Journal of Epidemiology 2012;**41**:151–160
doi:10.1093/ije/dyr215

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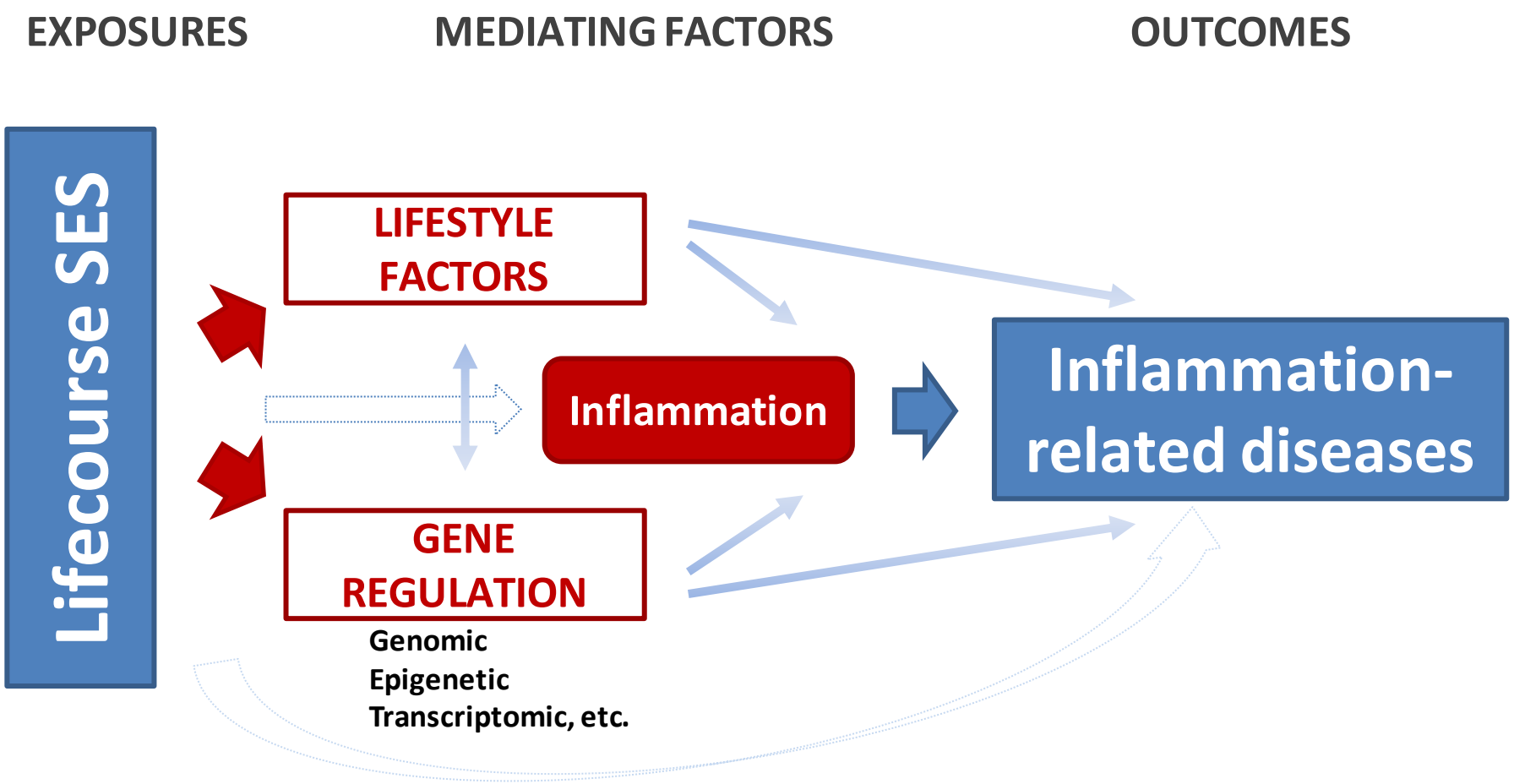
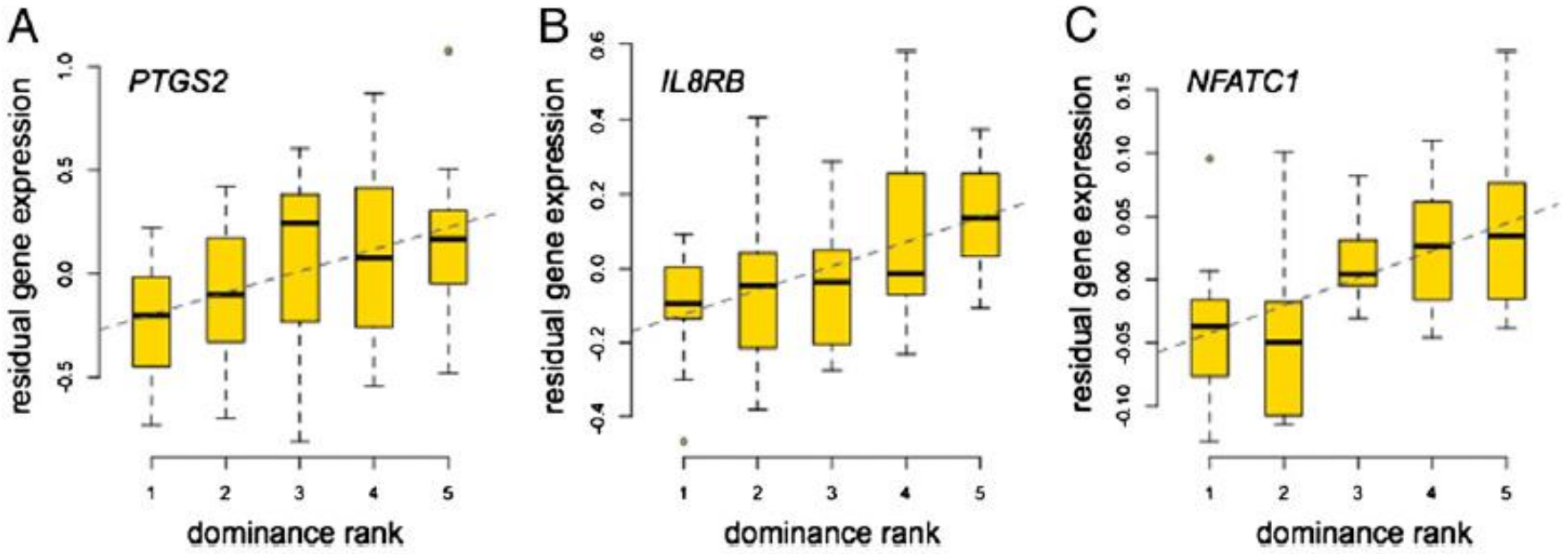
Socio-economic status is associated with epigenetic differences in the pSoBid cohort

Dagmara McGuinness,[1] Liane M McGlynn,[1] Paul CD Johnson,[2] Alan MacIntyre,[1] G David Batty,[3] Harry Burns,[4] Jonathan Cavanagh,[5] Kevin A Deans,[6] Ian Ford,[2] Alex McConnachie,[2] Agnes McGinty,[7] Jennifer S McLean,[8] Keith Millar,[5] Chris J Packard,[7] Naveed A Sattar,[9] Carol Tannahill,[8,10] Yoga N Velupillai[8,11] and Paul G Shiels[1]*

SES and gene regulation



Dominance rank and proinflammatory genes expression (macaques)

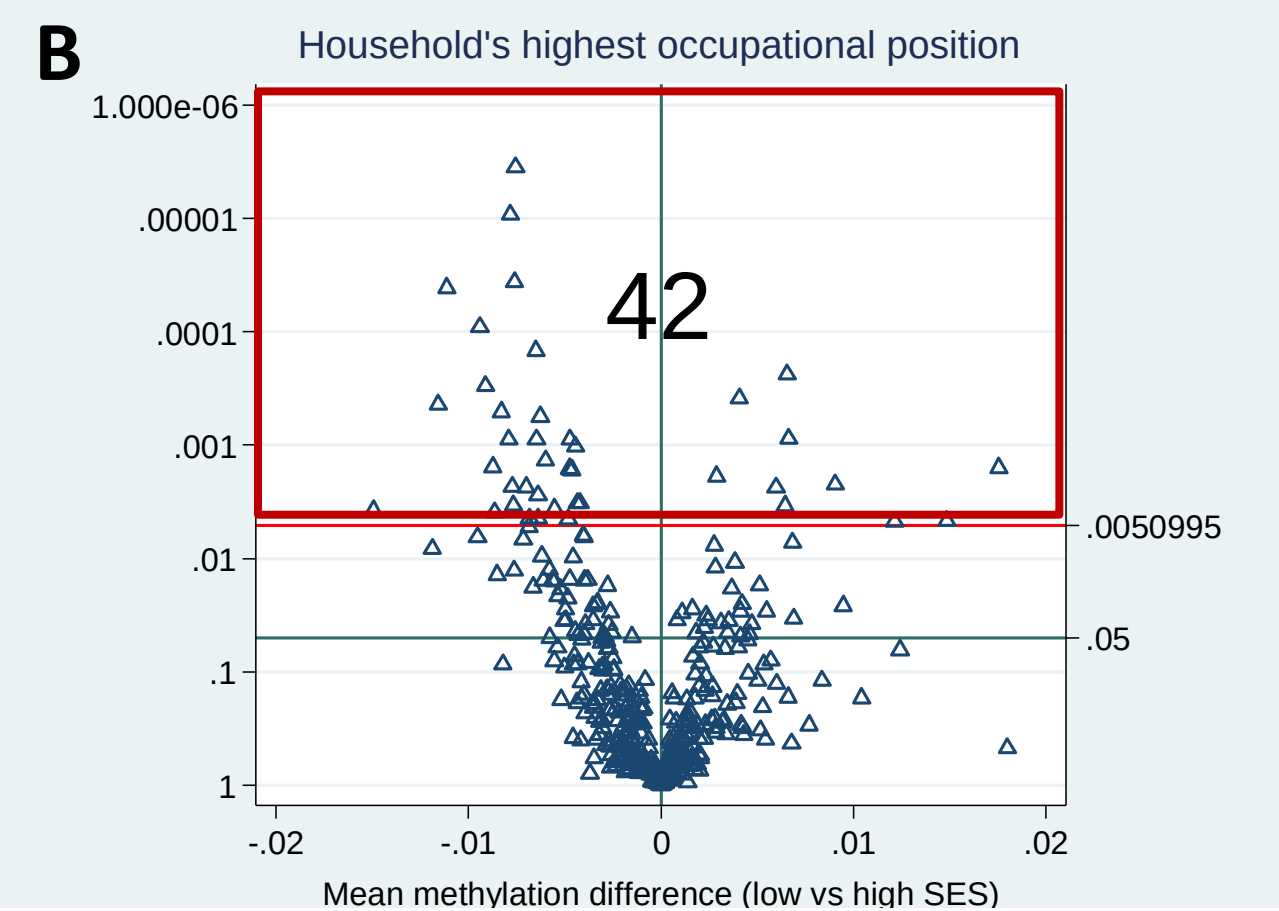


Source: Tung et al. Proc Natl Acad Sci U S A. 2012 Apr 24;109(17):6490-5.

Socioeconomic status and DNA methylation

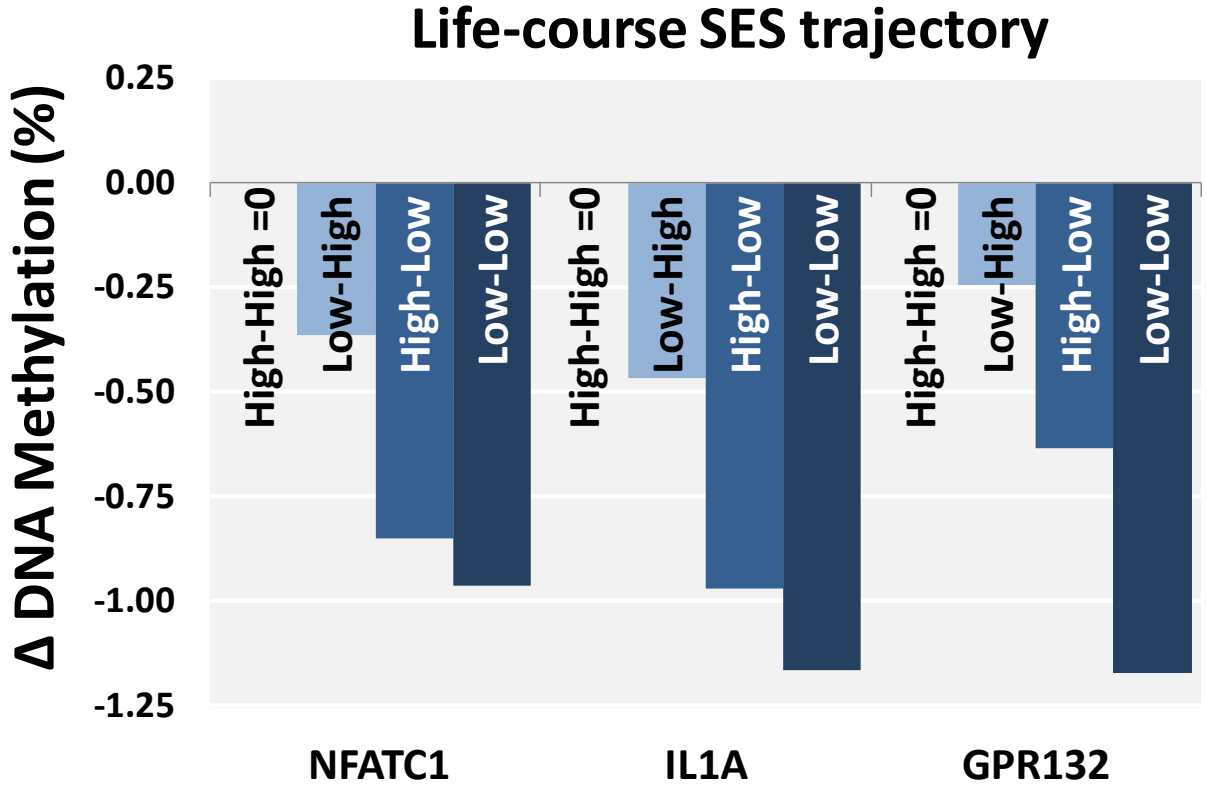
- **Population**: prospective cohort study of 857 individuals, sampled from the 47'749 participants of the EPIC-Italy study
- DNA extracted from white blood cells
- SES in early and adult life + lifecourse SES trajectories
- Genome wide methylation data available (450K)
- 17 genes (403 CpG sites) chosen on the basis of their involvement in SES-related inflammation in previous studies

Main results: household's occupation and DNA methylation



SES trajectory e DNA methylation of proinflammatory genes

EPIC ITALY



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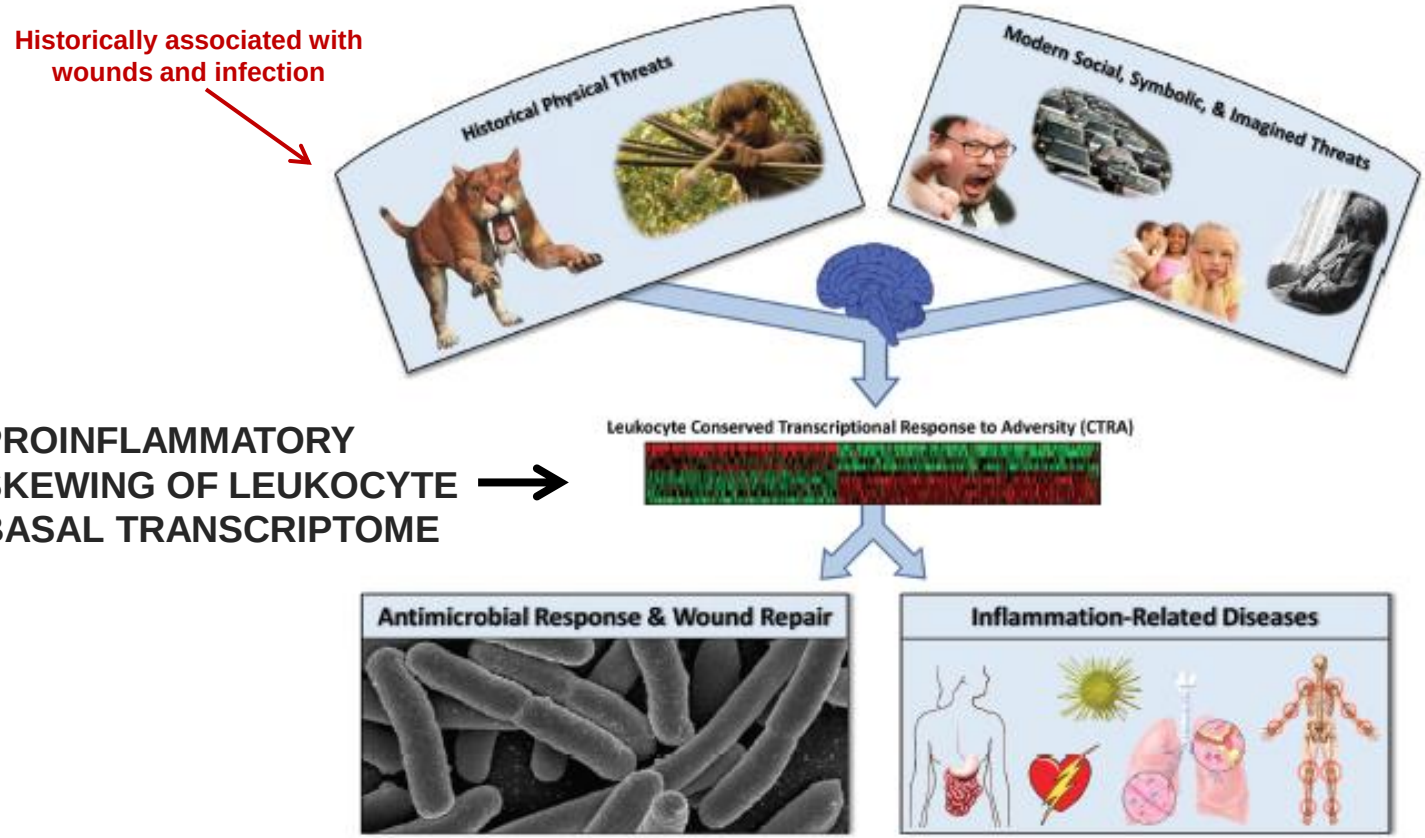
Conserved transcriptional response to adversity (CTRA)

Neurobiological activation of leukocyte inflammatory genes and inhibition of innate antiviral genes in response to subjectively experienced physical or social threat

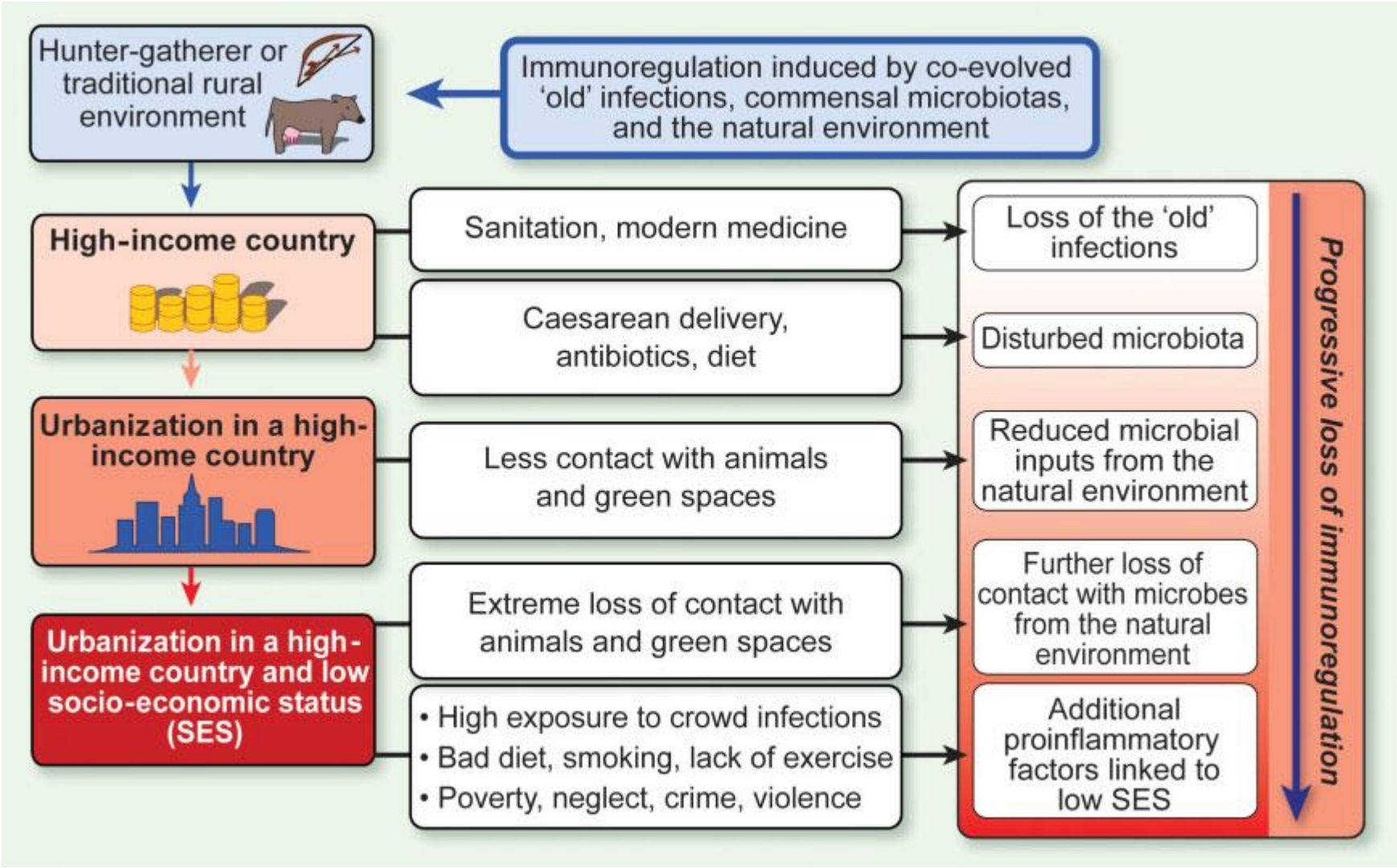


Source:Slavich & Cole. Clinical Psychological Science. 2013

Human Social Genomics

- Socio-environmental conditions associated with hundreds of «socially-sensitive» genes
  - ✓urbanity
  - ✓low socioeconomic status
  - ✓social isolation
  - ✓social threat
  - ✓low or unstable social status
- Majority of studies examined leukocytes or diseases tissues

Other examples of biological embedding



Source: Rook et al. Clinical and Experimental Immunology 2014

Other examples of biological embedding

- High socioeconomic-status related to alpha-diversity of both the colonic sigmoid mucosa and fecal microbiota (possibly through diet) (Miller et al. 2016)
- C-section related to « less healthy » microbiome, C-section related to SES
- Other examples: exposure to environmental toxics during life in utero

Challenges

- Few studies with biomarkers, fewer with repeated measures of biomarkers, very very few with epigenetics and/or transcriptomics measures with good exposure data
- When data exist, sample is small and not always exposure data is good enough (ie: SES indicators poorly collected)
- Concerning SES-epigenetics:
  - ✓ Need to replicate results on larger studies
  - ✓ Test whether SES differences in methylation translate into differences in gene expression and circulating molecules
  - ✓ Test whether this can partly explain social differences in health
  - ✓ Explore link between SES and gene-regulation in other tissues
- At this stage, no clear policy implications of this research if not for identyfication of exposures and of critical time windows

Conclusions

- Social factors are integrated biologically from birth (or earlier)
  - ✓Various pathways of integration
  - ✓ Various windows of integration→ of intervention?
  - ✓ Exposures from conception to old age
- Need better data and more interdisciplinary research
- Public health impact as well as phylosophycal/ethical implications not clear

Thank you for your attention!

Box 2|The ecology of socioeconomic status

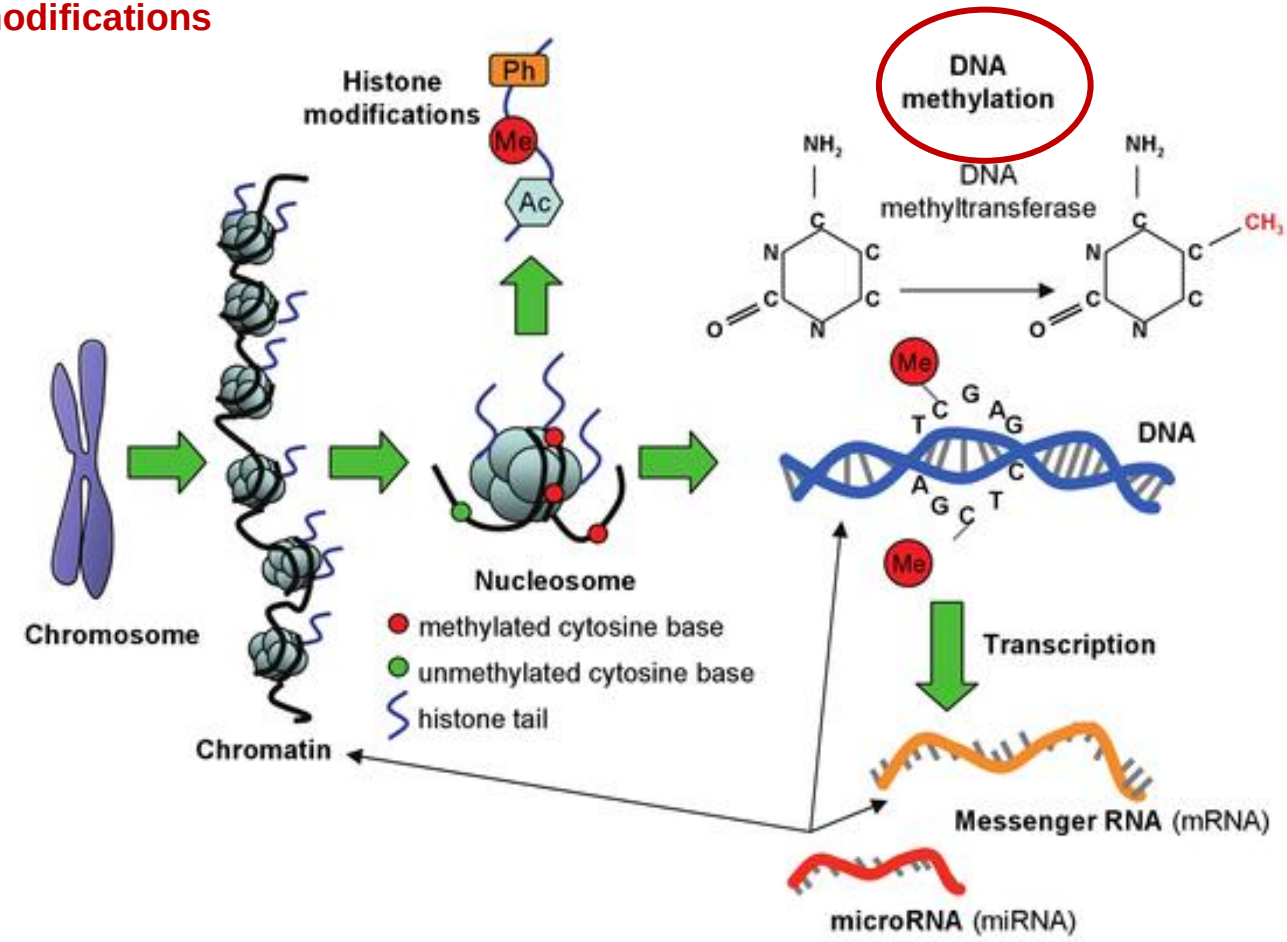
In addition to parenting quality and the *in utero* and home environments, there are other factors that may mediate the effects of socioeconomic status (SES) on neural development. These factors include:

- Toxin exposure: low-SES children show increased levels of lead in the blood5. Lead is a neurotoxin that affects IQ143 and school achievement, particularly affecting reading ability144.
- Nutrition: nutrients and caloric intake influence the neural mechanisms that subserve cognition and emotion145. Lower-SES families have less access to healthy foods and are more likely to experience food insufficiency and nutritional deficiency5.
- Prenatal drug exposure: there is little evidence that prenatal drug exposure is a major contributor to the SES disparities noted in this article. Although alcohol and drug use during pregnancy is related to SES, the direction of the relationship varies by substance, and alcohol use in particular is less common in pregnant women of low SES146,147. Furthermore, the effects of prenatal cocaine exposure seem to be relatively small when the effects of other factors, such as the home environment, are controlled for148.
- Stress: stress affects family relationships, including relationships with children. Low-SES families experience increased stress related to social rank, difficulties in providing for the family's needs, living in dangerous neighbourhoods and other factors. This can lead to chronic stress and thereby affect child development5,95,149,150. There is some evidence from research in animals and humans that stress specifically impairs attentional control151,152, and that indicators of chronic stress exposure mediate the relationship between childhood SES and working memory41.

Source: Hackman et al. Nat Rev Neurosci. 2010

Epigenetics – DNA methylation

Epigenetic modifications



Relton CL, Davey Smith G (2010) Epigenetic Epidemiology of Common Complex Disease: Prospects for Prediction, Prevention, and Treatment. PLoS Med 7(10): e1000356. doi:10.1371/journal.pmed.1000356