Adverse childhood experiences, physiological wear-and-tear and mortality: pathways towards chronic disease

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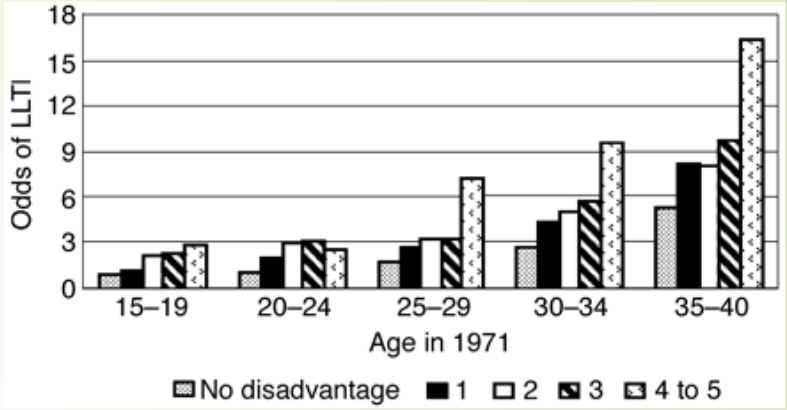
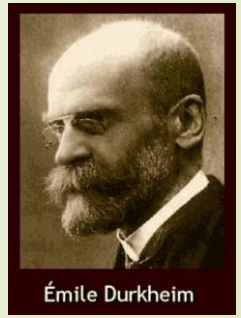
The socioeconomic gradient in health



The gradient is characterised by:

- an omnipresence across countries
- its resurgence on emerging health conditions
- not fully explained by classic risk factors (typically about 20-35%)
- a large array of potential pathological processes
- observed gender/ sex differences
- begins as a developmental gradient in early life



The gradient is a ‘social fact’ (Hertzman 2012)

How and why do socioeconomic gradients in health occur?

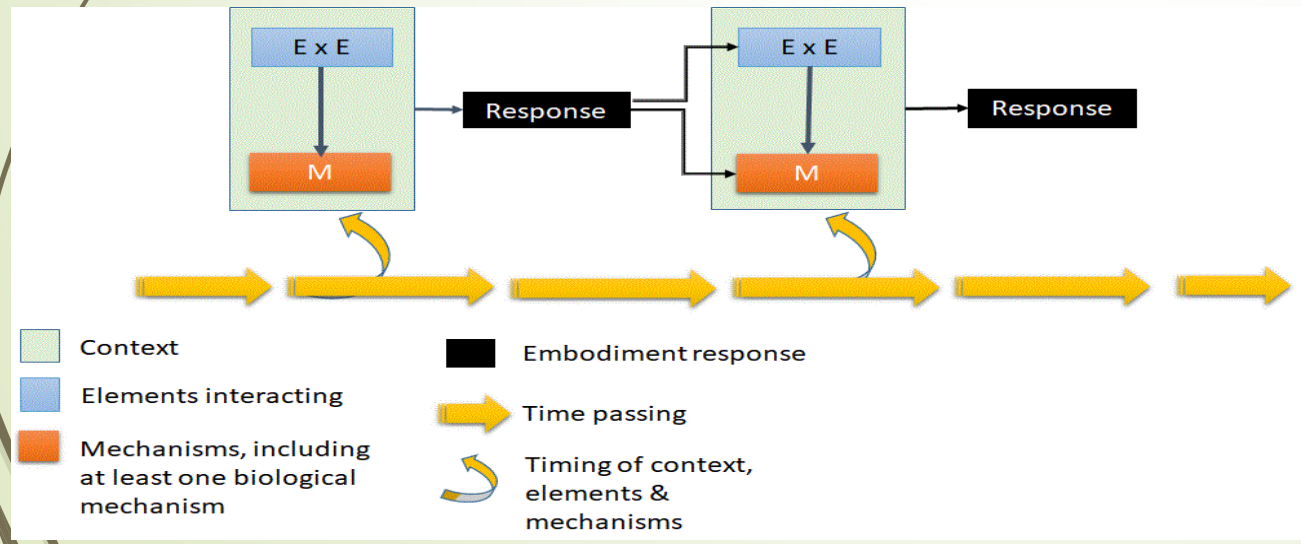
Embodiment as a dynamic

Conceptual developments based on Krieger's work

a) Elements within the environment structured socially

b) Mechanisms –numerous ones, but there is always at least one biological mechanism to identify

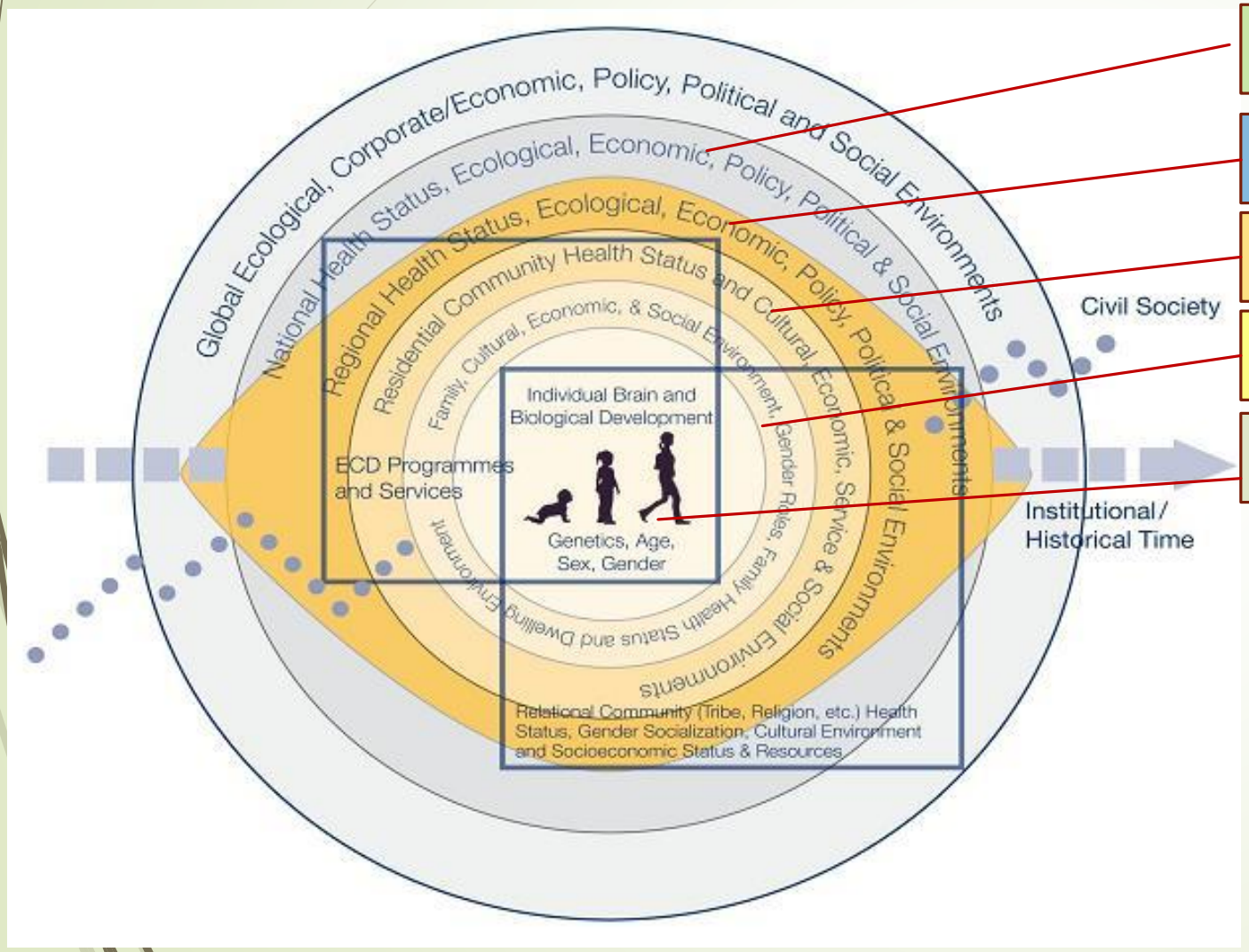
c) Timing – social & biological periods



"Humans come to physically represent their past environments in their present state through a constant process of change"

Kelly-Irving et al 2016 *Advances in lifecourse research;* Kelly-Irving & Delpierre 2018

Embodiment: elements in the environment & mechanisms



- ***Political factors***
- **Health care system**
- ***Social factors***
- ***Cultural & behavioural factors***
- ***Inherited and biological factors***

Elements of the environment structured into layers

Types of biological mechanisms:

- Of exogenous origin
- Of endogenous origin

These interact and involve molecular-level mechanisms (ex: epigenetic)

Endogenous mechanism: Stress response

- **Stress** is a process that entails a stimuli, appraisal of it, and a response [1].

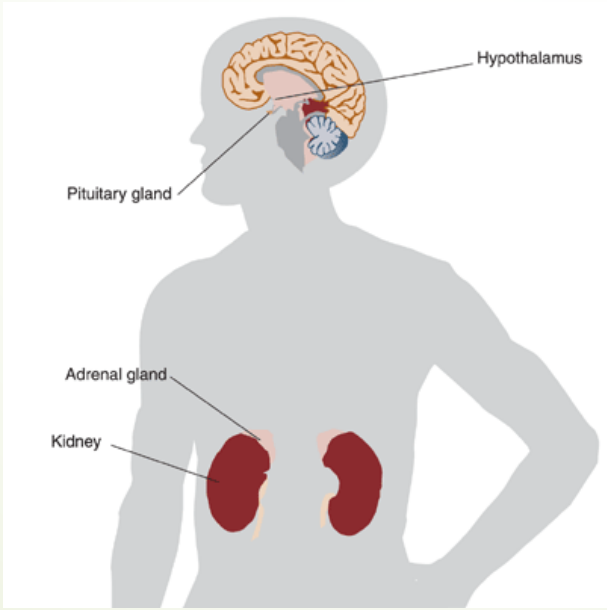
  "*a non-specific response of the body to any demand for change*"[2]

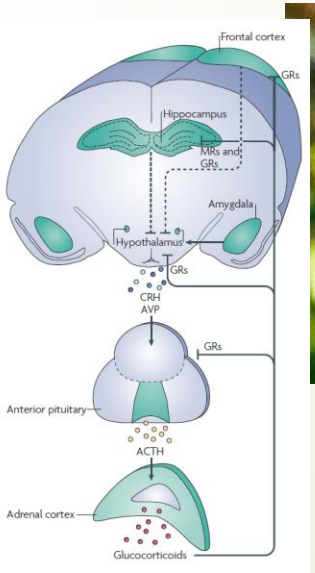
- **Hypothalamo-Pituitary-Adrenal** Axis influences and feedback interactions between:

-hypothalamus

-pituitary gland

-adrenal gland

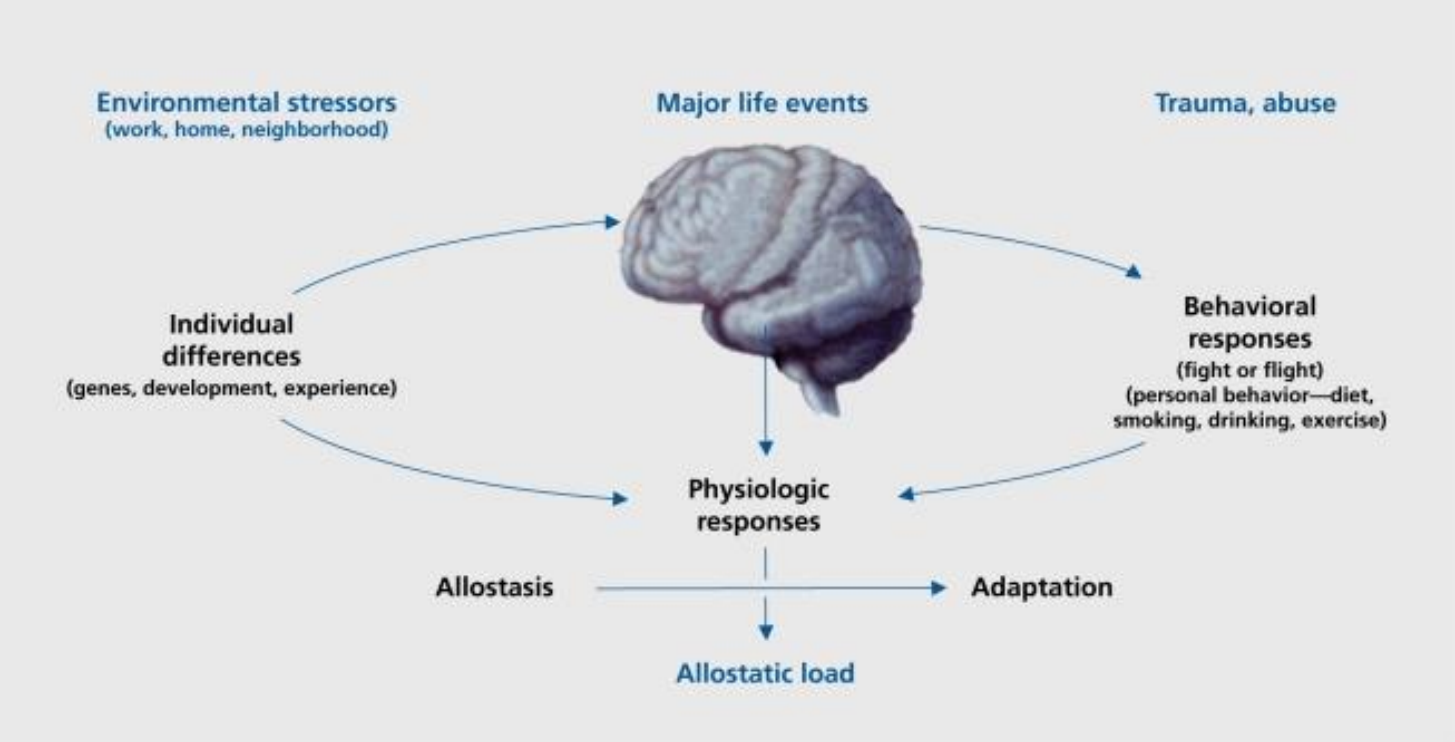




Lupien et al., 2009

1. *Miller et al., 2011*
2. *Seyle, 1936*

Chronic stress & Allostatic load



(McEwen BS. Protective and damaging effects of stress mediators. N Engl J Med. 1998;338:171-179. Copyright © Massachusetts Medical Society 1998)

The strain on the body produced by repeated ups and downs of physiologic response as well as by the elevated activity of physiologic systems under challenge and the changes in metabolism and the impact of wear and tear on a number of organs and tissues, can predispose an organism to disease. We define this state of the organism as allostatic load"

(McEwen & Stellar 1993)

Hypothesis

Chronic exposure to physiological stress (adverse childhood experiences) in early life is associated with the onset of physiological wear and tear

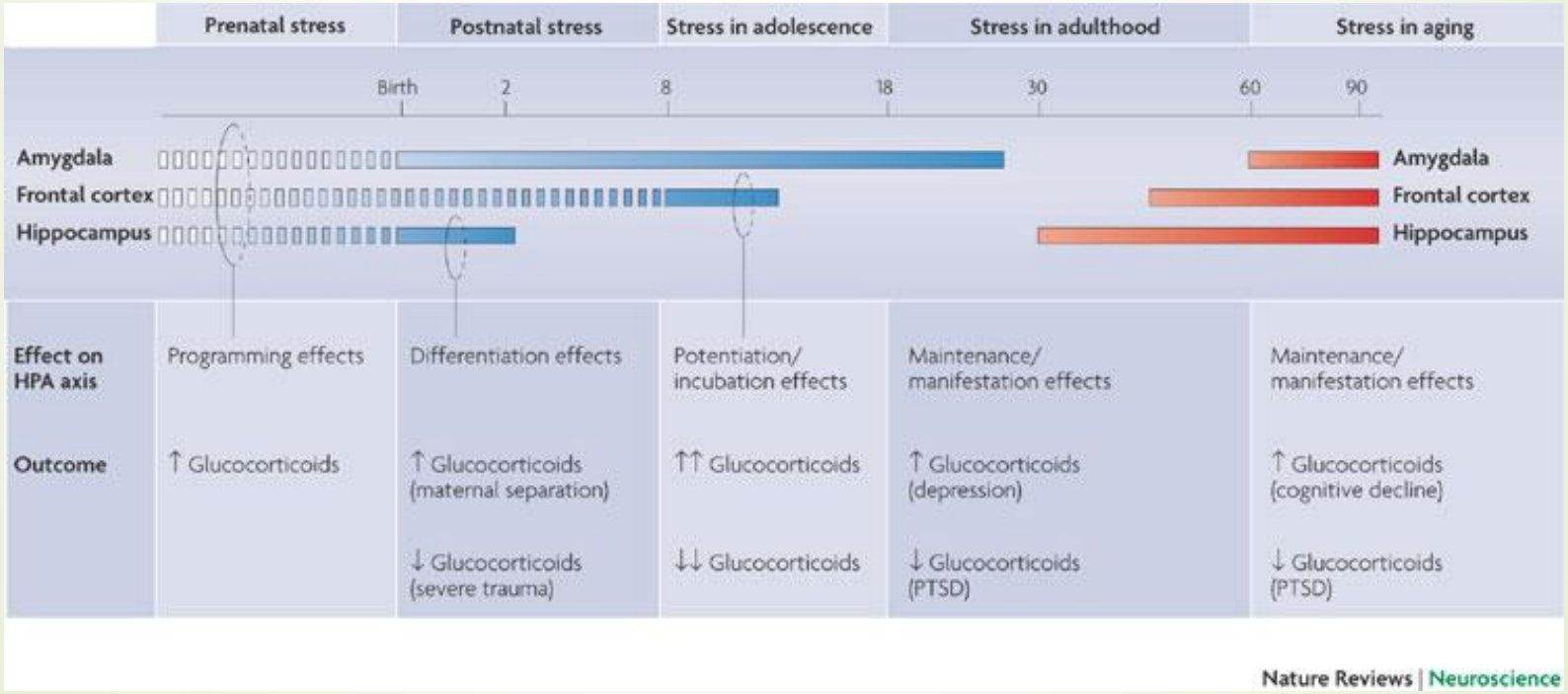
Hypothesised mechanisms:

-Adversity exposes an individual to biological stress responses that may alter physiological processes over time

-Adversity exposes an individual to biological stress responses that may alter health-related behaviours

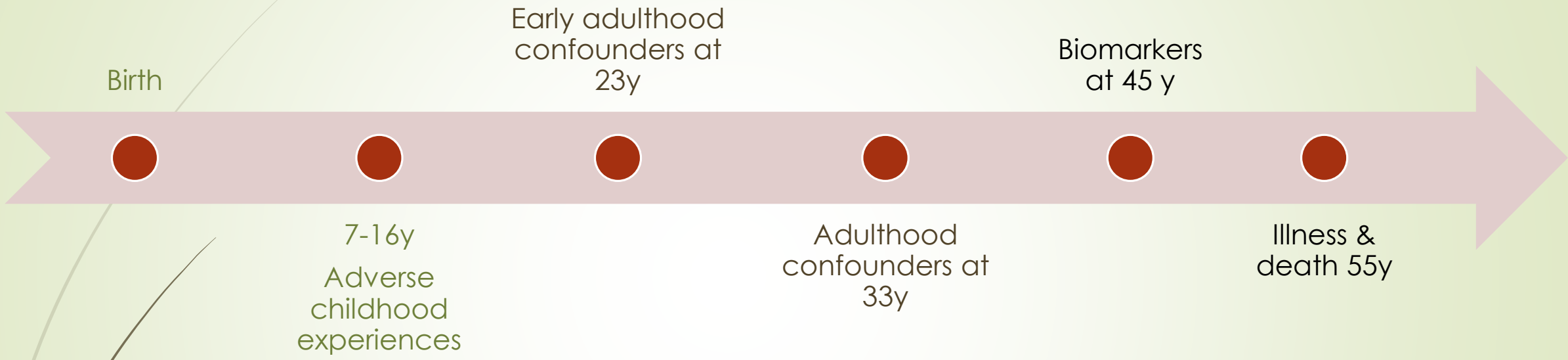
Plausible hypothesis for endogenous embodiment mechanism?

Early life stress measured by adverse childhood experiences → Physiological imbalance



(*Lupien et al. 2009*)

Methods: 1958 British birth cohort study



Baseline: All births during one week in 1958 in England, Scotland and Wales (n=18558 ~17000 live births)

- Children followed up at ages 7, 11 & 16
- Respondents followed up at ages: 23, 33, 42, 46 and 50

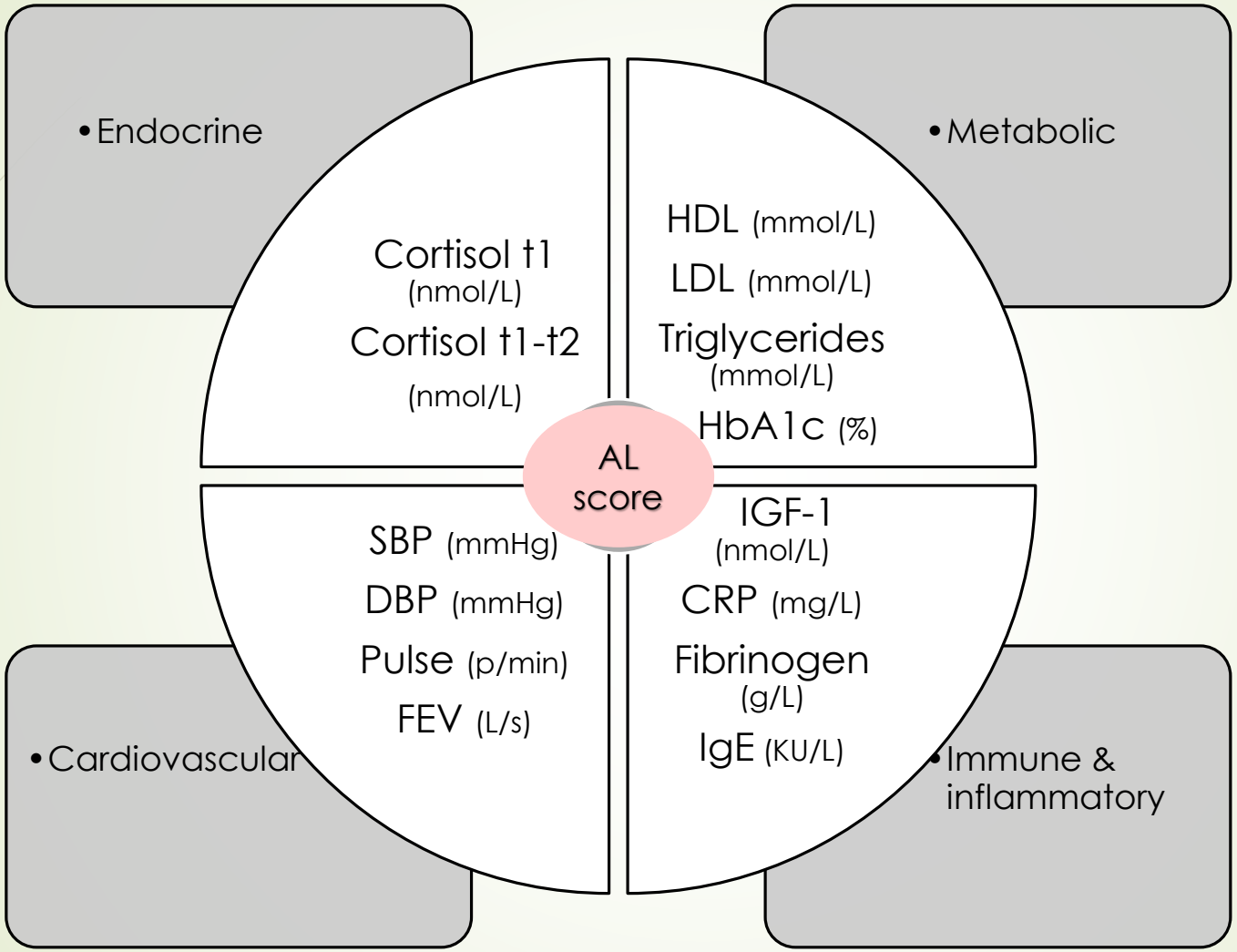
- Prospective data available at 7, 11 and 16 on ACEs
- Biomarkers at 45y & death certificates up to age 55

Methods

- Main exposure: Adverse childhood experiences
  - Felitti et al 1998 and subsequent ACE study papers: "stressful or traumatic childhood experiences that have negative neurodevelopmental impacts that persist over the life span“
  - Surtees et al 2007; Thomas et al 2009; Clark et al 2010
  - WHO working group definition 2009: dimensions of ACE
  - Our working definition: Intra-familial events or conditions in the child’s immediate environment causing chronic stress responses

ACE category	Subcategory	Child’s age
Child in public care		7, 11, 16
Household dysfunction	Household member in prison/ probation	7, 11, 16
	Parental separation	7, 11, 16
	Mental illness	7, 11
	Substance abuse	7
Neglect	Physical	7, 11

Allostatic load score



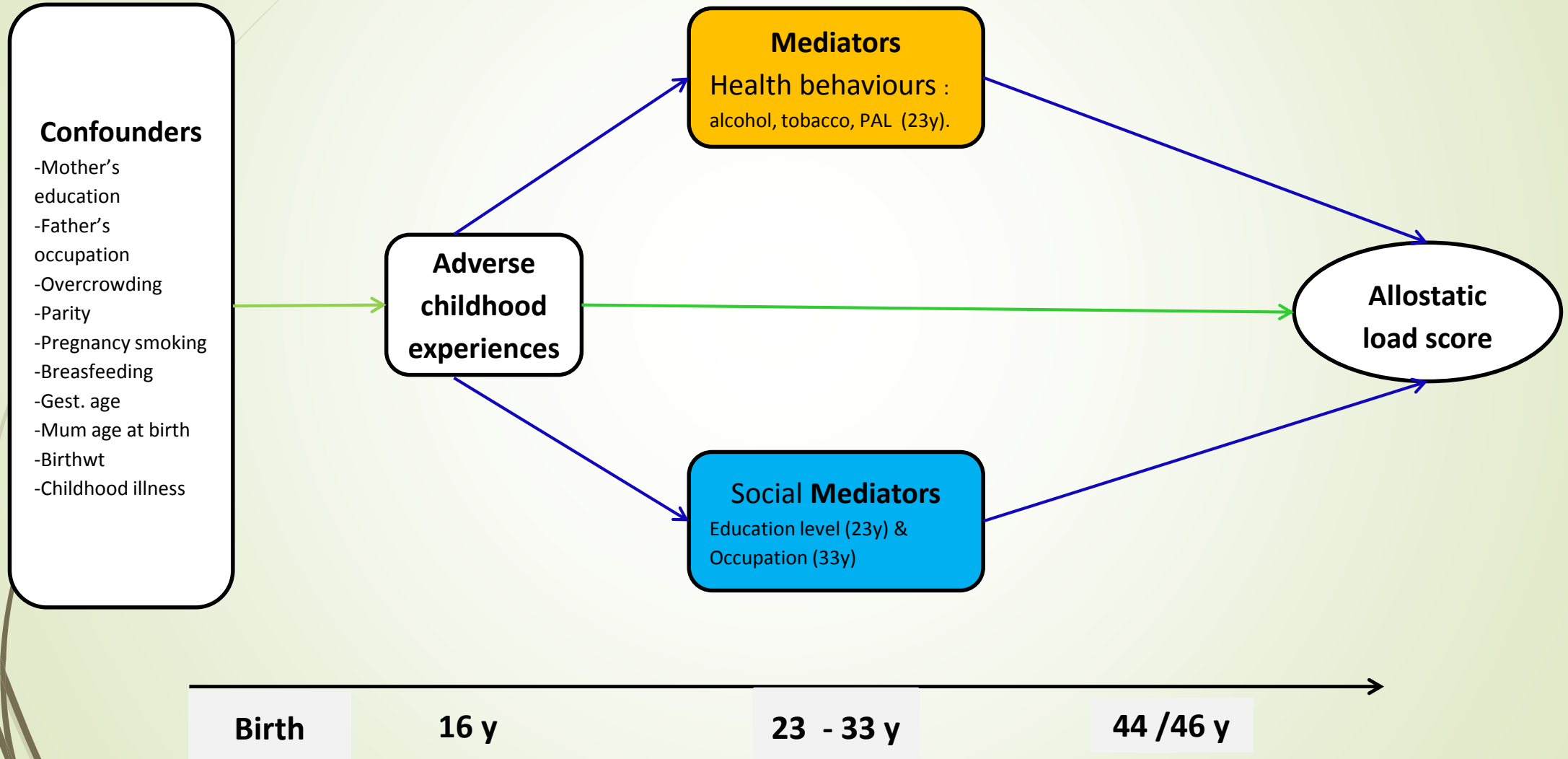
"*Health sciences should not wait until these become clinically significant but identify subclinical states before pathology*"[1]

-75th or 25th percentile cut-offs applied for relevant biomarkers

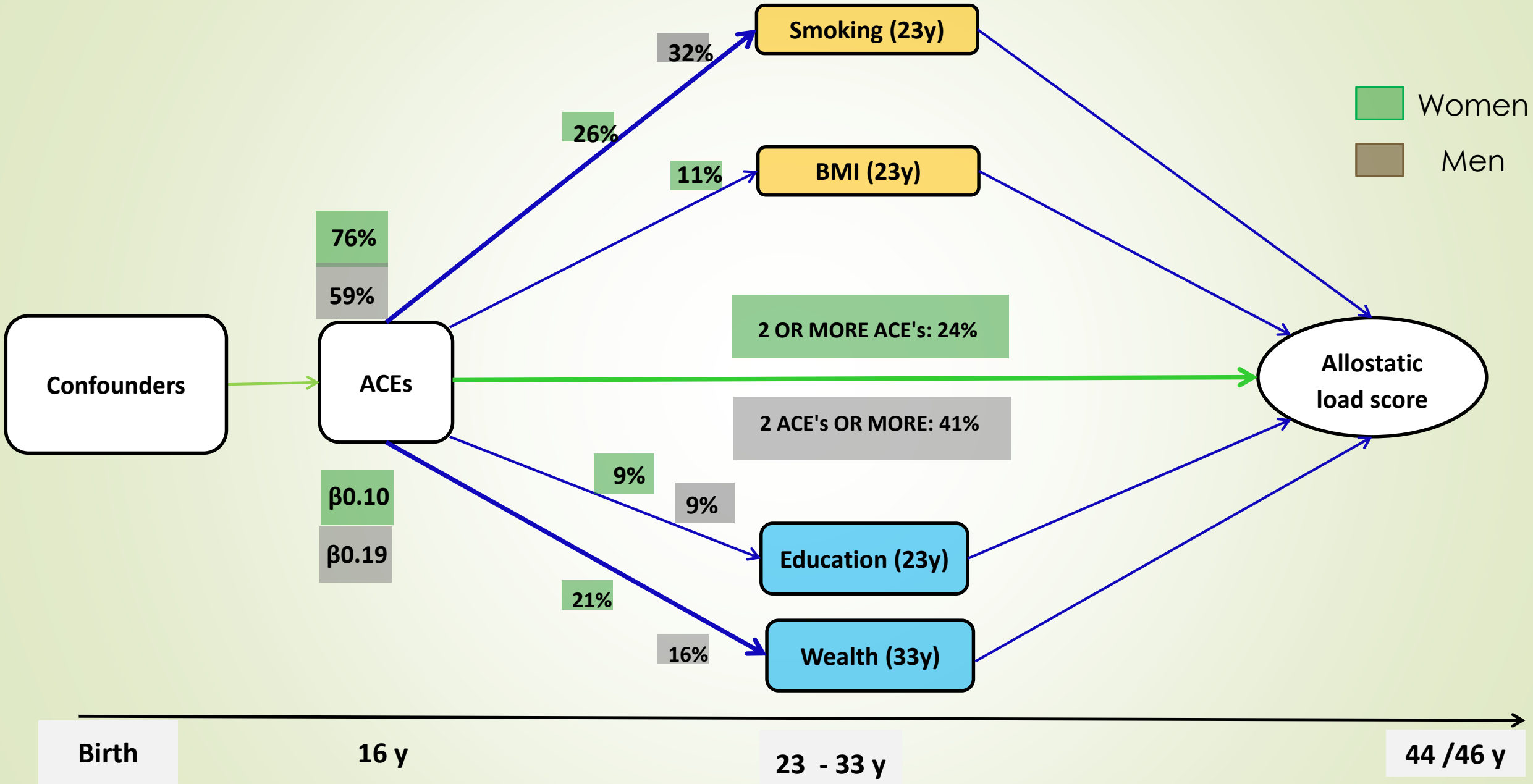
-Sex specific

1. *McEwen & Steller, 1993*
2. AL operationalisation inspired from *Seeman et al., 1997*

Lifecourse model & pathways



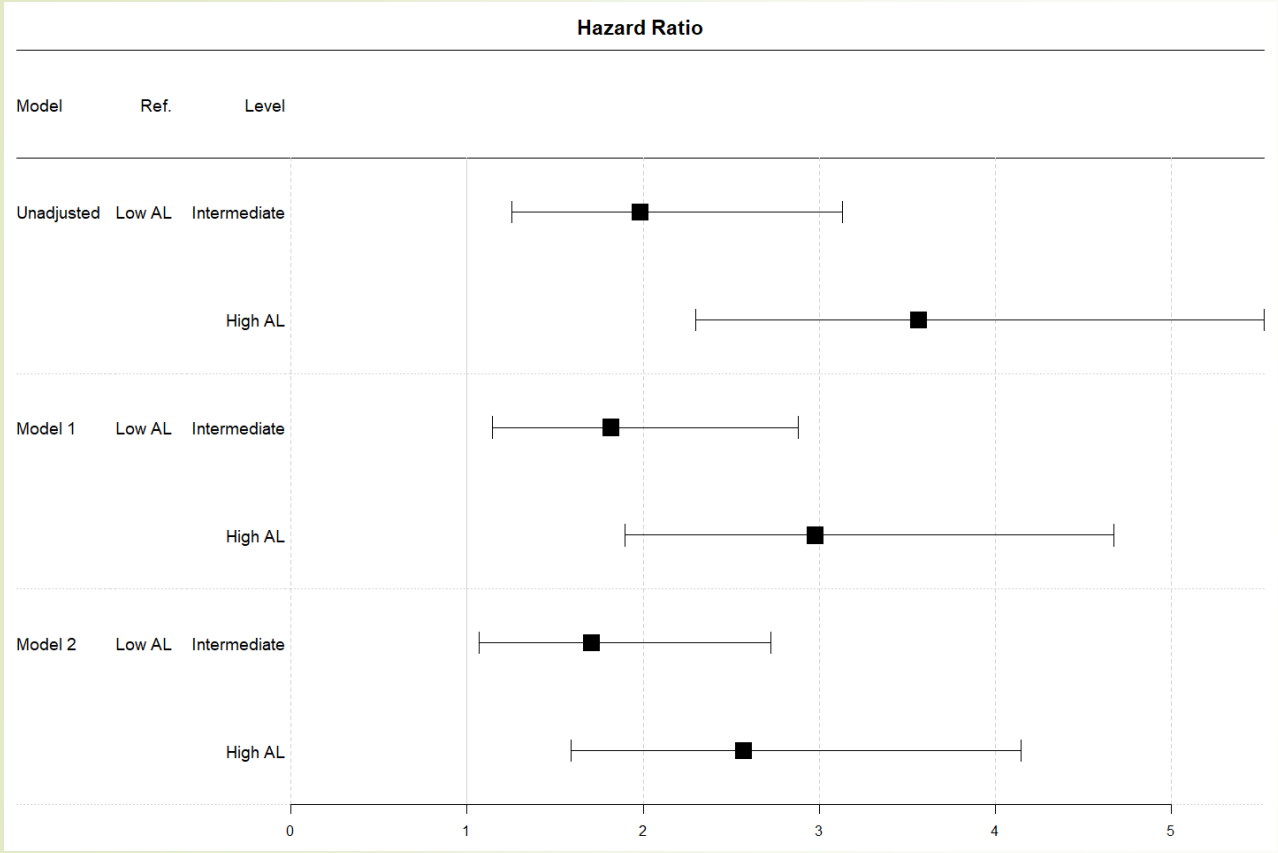
Pathways: Adverse childhood experiences & allostatic load



Barboza Solis et al 2015 *PNAS*

Low AL: [0:2]
Mid AL:[3:4]
High AL:[5:12]

Allostatic load and mortality risk



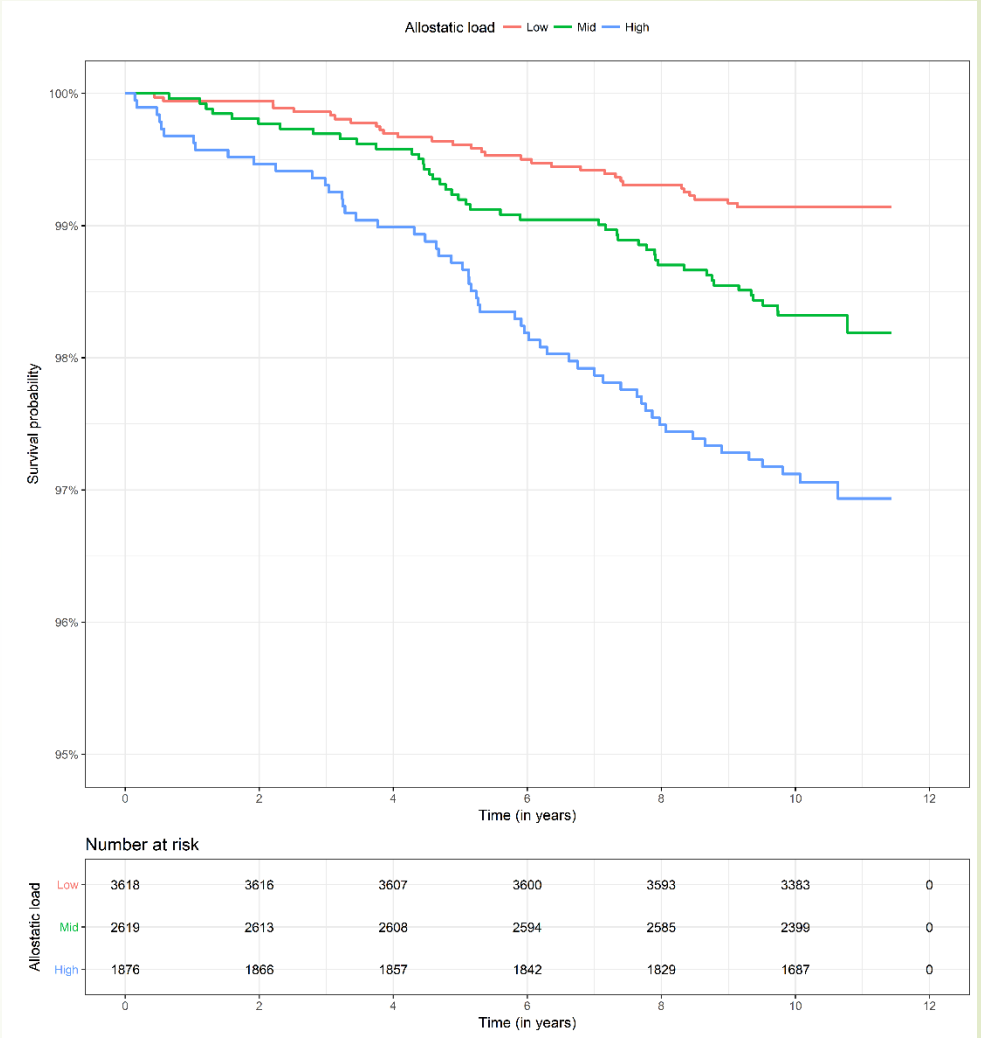
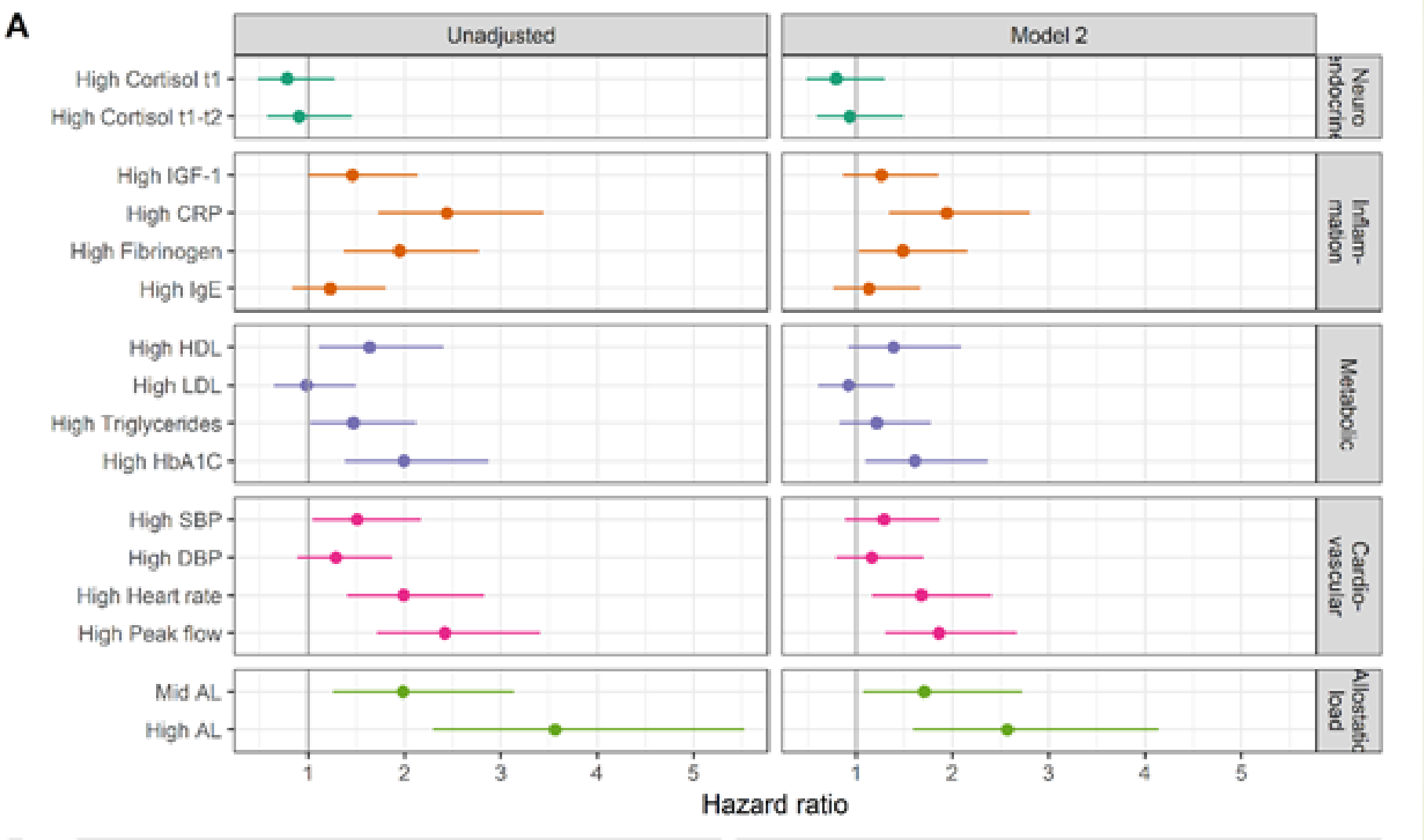


Figure: Hazard ratio for all-cause mortality in a life-course multivariate Cox model

⇒ Risk of death is three times higher in the High AL group (3.56 [2.3 -5.53])

⇒ Adjusting for lifecourse factors slightly affects strength and effect size of the association

Individual biomarkers and future risk of death in the NCDS (I)

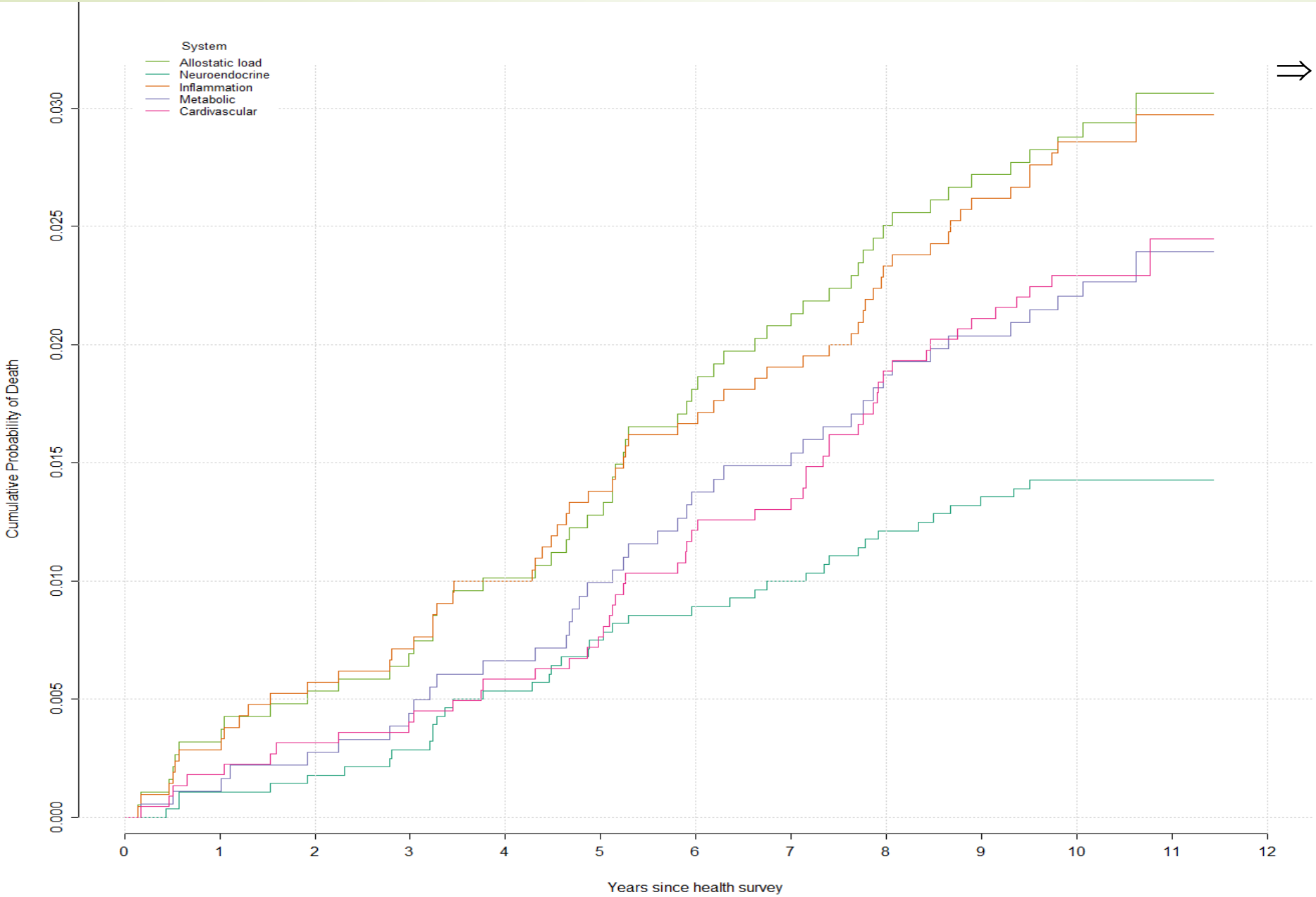


⇒ AL is a strong predictor of mortality

⇒ Strong contribution of inflammatory/ immune & cardio systems to the AL effect

Castagné et al 2018, Europ J Epi

Biological systems and future risk of death in the NCDS (II)



⇒ People with high AL had a greater risk of death compared to other sub-scales followed by the inflammatory and immune system

Discussion: Adverse Childhood Experiences

When you observe the the literature

- ACEs have been associated with:
  - ischaemic heart disease (Dong et al. 2004)
  - obesity (Thomas et al. 2008)
  - perceived health (Dube et al. 2010)
  - psychopathology (Clark et al. 2010)
  - inflammation (Danese 2009)
  - mortality (Felitti 1998)
  - health behaviours (Dube 2003; Anda 2002)

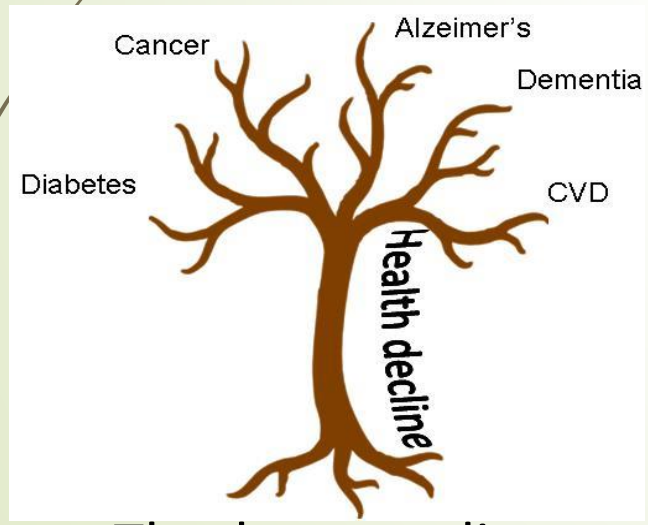
Hughes et al 2017 Meta-analysis

Discussion: ACEs and embodiment

Is there a common stem to these chronic diseases?

Evidence for disease interrelatedness:

- Obesity, Diabetes, CVD
- CVD, Diabetes & cognitive decline/ dementia (Vagelatos 2013, Fatke 2013)
- Diabetes & Alzeimer's disease (Tolppanen 2013)
- Diabetes & Cancer (Giovannucci 2012)



Biological plausibility:

- Endocrine physiology (IGF/ insulin)
- Inflammatory processes (cytokines)
- Hyperglyceamia
- Behavioural/ environmental factors (diet, physical activity, smoking, alcohol)

The human disease network: the molecular relationships between phenotypes (Goh et al 2007; Barabasi et al 2011)

Discussion

Adverse childhood experiences:

-Probably underestimated here (prospective design)

-Do not include maltreatment & abuse

-Each one may have a different effect/ meaning

-Exogenous & endogenous mechanisms

Allostatic Load: a heuristic

-Criticised methodologically & conceptually (Delpierre et al LLCS 2015; Gruenwald PNAS 2006, Johnson Soc Sci Med 2017)

-Appears to capture some form of physiological buffering

-Association with mortality here mainly driven through inflammation

« Unexplained » direct effect

-Residual confounding/ mediation; measurement error…

Discussion: beyond research

Adverse childhood experiences in policy:

-Should these measures be transferred directly into policy use?

-Social-to-biological research may ‘convince’ policy makers, but is it stigmatising?

A solution? Capabilities approach

-Sen & Nussbaum’s capabilities framework based on Rawls’ theory of social justice

-Promotes a positive and non-stimatising method of conceptualising areas of invervention to reduce adversities (ex: parenting)

-Gupta et al 2016, British journal of social work

Conclusions

Evidence of ACEs as being a set of factors involved in endogenous biological mechanisms at the root of **multiple chronic health outcomes**

- Need to be taken seriously as a major public health concern (British Crime Survey 2015/16): primary & secondary prevention

- Research & policy into how to limit the consequences of having experienced ACEs (12000 unaccompanied migrant children entered the EU in 2015 – Unicef)

-Questions raised:

Types of stressors? Timing of stressors?

Thank you!

Acknowledgements:

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