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# Physiological wear-and-tear and later subjective health in mid-life: Findings from the 1958 British birth cohort

Cristina Barboza Solís[a,b,*], Romain Fantin[a], Michelle Kelly-Irving[a], Cyrille Delpierre[a]

[a] LEASP – UMR 1027 Inserm-Université Toulouse III Paul Sabatier, France
[b] Universidad de Costa Rica, 2060 San José, Costa Rica

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ABSTRACT

*Objective:* Our body adapts continuously to environmental challenges and stressful conditions. Allostatic load (AL) is a concept that aims to capture the overall physiological wear-and-tear of the body triggered by the repeated activation of compensatory physiological mechanisms as a response to chronic stress. Growing evidence has shown a link between AL and later health decline, morbidity and mortality. However, due to the global physiological effect captured by the AL concept, it is particularly pertinent to examine its association with subsequent health by taking a broad definition of the latter. We examined the association between AL at 44 years and general health as measured by a latent multidimensional measure of subjective health at 50 years integrating sleep patterns, physical and mental health.
*Methods:* AL was constructed using 14 biomarkers representing four physiological systems on 7573 members of the 1958 British birth cohort. Health status was captured using self-reported information about subjective health and summarized using a principal component analysis including: seven dimensions of the SF-36 questionnaire of health-related quality of life, the sleep subscale of the Medical Outcomes Study characterizing quality of sleep patterns, and a malaise inventory score detecting depressive symptoms.
*Results:* Higher AL score was gradually associated with worse subjective health, after taking into account classic confounders.
*Conclusions:* Using a physiological index to grasp how the environment can "get under the skin" leading to poor health is of great interest, permitting a better understanding of life course origins of disease and social gradients in health.


## 1. Introduction

Krieger et al. defined the concept of embodiment as "how we, like any living organism, literally incorporate, biologically, the world in which we live, including our societal and ecological circumstances" (Krieger, 2005). Growing evidence supports the idea that exposure to chronic stress over the life course contributes to physiological dysregulation, subsequently translated into disease (McEwen and Seeman, 1999; McEwen and Stellar, 1993; Seeman et al., 2001). Allostasis is the active process of adaptation where our body tries to maintain physiological stability in response to environmental challenges (Sterling, 2004, 2012). The repeated activation of compensatory physiological mechanisms as a result of chronic exposure to stress can lead to a physiological wear-and-tear, known as allostatic load (AL) (Juster et al., 2010; McEwen and Stellar, 1993; McEwen and Wingfield, 2003). AL may be a useful conceptual tool in measuring the biological effect of embodiment.

Based on prospective data, used to capture the history of prior environmental insults (Seeman et al., 2010) researchers have studied the life course origins of AL development. They highlighted the role of social adversity (Gustafsson et al., 2012), and socioeconomic position (SEP) (Gustafsson et al., 2011) as predictors of AL, also identifying the mediating role of material, behavioural and psychosocial factors between SEP and later AL (Barboza Solis et al., 2015; Robertson et al., 2015, 2014). These findings suggest that (a) AL is socially patterned (Dowd et al., 2009; Robertson et al., 2014; Seeman et al., 2010; Szanton et al., 2005), determined by socioeconomic position, material, psychosocial and behavioural factors all over the life span (Robertson et al., 2015), (b) AL conceptual framework may contribute to clarify the biological component of the socioeconomic gradient observed in morbidity and mortality (Carlson and Chamberlain, 2005; Gruenewald et al., 2012).

* Corresponding author at: UMR 1027 Inserm-Université Paul Sabatier, Faculté de médecine, 37 allées Jules Guesde, 31000 Toulouse, France.
*E-mail address:* cristina.barboza-solis@inserm.fr (C. Barboza Solís).

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Empirical research has investigated the link between AL and later health outcomes (Beckie, 2012; Karlamangla et al., 2006). However, the conceptual framework of AL is constructed on the basis of a global effect of stress on health, via multiple physiological mechanisms and by impacting several systems and brain structures. Therefore, AL is not designed to be specific, but rather to show an overall effect on health. Several studies have shown links between AL and, diverse health outcomes (Juster et al., 2010; Karlamangla et al., 2002, 2006). However, testing the link between AL and one specific aspect of health, for instance, cardiovascular disease, fragments the notion of overall physiological wear-and-tear. Therefore, due to the global physiological effect captured by the AL concept, it is particularly pertinent to examine its association with subsequent health by taking a broad definition of the latter, not only measured by the absence or presence of diseases.

Health status is indeed a multidimensional and integrative attribute, a latent concept, capturing subjective (e.g. self-rated health, well-being, quality of life, health related quality of life, happiness, life satisfaction), clinical (e.g. morbidity, functional decline) and biological (e.g. biomarkers) dimensions (Hyland et al., 2014). Self-rated health and health-related quality of life (HRQoL) – defined as the perception of the impact of health problems on different spheres of life, including physical, mental, and social aspects (Testa and Simonson, 1996)- have been used as measures of health status since they correlate to morbidity and mortality (Power et al., 1998). Subjective health measures are then frequently used as surrogate endpoints of morbidity and mortality, where their main advantage is to define health through its various dimensions. In this paper we investigate the link between AL and a holistic/integrative latent measure of health using a subjective health variable integrating sleep patterns, physical and mental health at 50 years. We aimed to address this question studying the impact of AL measured at 44 years of age on a latent variable of subsequent subjective health measured at 50. We hypothesised that AL could influence health status in the long term, independently of social determinants and health behaviours.

## 2. Materials and methods

### 2.1. Participants

The National Child Development Study (NCDS) includes all children born during one week in 1958 (N = 18558) in Great Britain. Data collection was carried out on cohort members between birth and 50y. At age 44–45y a biomedical survey was conducted including a self-reported questionnaire, physical measurements, blood and saliva samples (Power and Elliott, 2006). The sample used for this study is described in Fig. S1.

### 2.2. Ethics & data

Written informed consent was obtained from parents for childhood measurements and ethical approval for the adult data collection was obtained from the National Research Ethics Advisory Panel. NCDS data are open access datasets available to non-profit research organizations. Ethical approval for the age 45 year survey (Gruenewald et al., 2012; Gustafsson et al., 2011) was given by the South East Multicentre Research Ethics Committee.

### 2.3. Measurements

#### 2.3.1. Allostatic load at 44y

Among available biomarkers, we selected fourteen parameters representing four physiological systems: the neuroendocrine system (salivary cortisol t1 (nmol/L), salivary cortisol t1-t2 (nmol/L)); the immune & inflammatory system (C-reactive protein (CRP mg/L), fibrinogen (g/L), immunoglobulin E (IgE KU/L), insulin-like growth factor-1 (IGF-1 nmol/L),); the metabolic system (high density lipoprotein (HDL mmol/L), low density lipoprotein (LDL mmol/L), triglycerides (mmol/L), glycosylated hemoglobin (%)); the cardiovascular & respiratory systems: (systolic blood pressure (SBP mmHg), diastolic blood pressure (DBP mmHg), heart rate/pulse (p/min), peak expiratory flow (L/min)). These biomarkers were chosen based on previous measures of AL (Barboza Solis et al., 2015; Karlamangla et al., 2002, 2006; Seeman et al., 1997) and according to evidence of their relationship to stressful conditions over life (Butland et al., 2008; Kumari et al., 2013, 2011, 2008). In accordance with the most classical AL operationalization proposed by Seeman et al. (1997), our score was the sum of the fourteen parameters for which the subject was rated in the highest-risk quartile ('1' vs low risk '0') according to gender specific quartiles. A full description of each parameter is given in Table S1. Individuals with missing data were considered as not at risk for the missing biomarker adopting a conservative approach (maximum bias). Exclusion criteria for the analysis is shown in the flow chart (Fig. S1). We additionally run the multivariate analysis using a different operationalization of AL score, by calculating a 0–1 risk score within each system and the results did not vary.

#### 2.3.2. Subjective health index at 50y

We conceptualize health status following an integrative approach incorporating three different dimensions of health from subjective health measures collected at the 8th sweep of the NCDS 1958 British birth cohort. The *SF-36* is a general questionnaire measuring Health Related Quality of Life (HRQoL) (Ware, 2000) through its physical and mental components (Taft et al., 2001) that captures, for instance, the interference with work or other daily activities due to physical health, emotional problems, interference with normal social activities, symptoms associated with anxiety/depression and measures of positive affect (Supplementary material). Each of the eight dimensions is ranged from 0 to 100 with higher scores related to better HRQoL. The SF-36 has been shown to be predictive of subsequent morbidity and mortality (Kaplan et al., 2007; Otero-Rodriguez et al., 2010; Rodriguez-Artalejo et al., 2005; Tsai et al., 2007).

A subscale of four items from twelve original *Sleep Scale of the Medical Outcomes Study* (MOS) was used in NCDS to collect information about sleep patterns in the last four weeks measuring quality of sleep (Hays and Stewart, 1992). Previous studies have provided evidence on the validity and reliability of the MOS sleep measures (Hays et al., 2005; Viala-Danten et al., 2008) (Supplementary material). The self-completion sleep scale included: usual time taken to fall asleep, average number of hours sleep per night, waking-up during night frequency and trouble falling back to sleep, and whether the respondents had slept enough, based on whether they felt rested upon waking. These four items capture three different dimensions of sleep problems, relating to quantity of sleep/optimal sleep duration, perceived sleep adequacy, and sleep disturbance (Chatzitheochari, 2013). Sleep patterns are known to be related to chronic diseases (diabetes, hypertension, cardiovascular), poor health-related quality of life and self-rated poor health (Chatzitheochari, 2013). In terms of physiological balance, sleep disturbances have an impact on metabolic and endocrine functioning (Spiegel et al., 1999).

Finally, the *malaise Inventory* which measures psychological distress, comprising a nine-item score from the original twenty four (Rutter et al., 1970), was included as a continuous variable, with higher scores relating to worst mental health (Supplementary material). The malaise inventory score has been found to have acceptable internal validity in different socio-economic groups in the NCDS sample (Rodgers et al., 1999). Mental health has been