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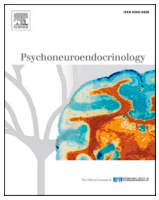

Primary and secondary allostatic processes in the context of high-stress work: A multigroup moderation from the English longitudinal study of ageing

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ABSTRACT

Evidence suggests that chronic cortisol excess may precede the development of an allostatic load, and that this association may be influenced by the level of work stress. This study aims to investigate the associations between hair cortisol concentration and the development of systemic allostatic load cross-sectionally and at a lag of four years, stratified by level of effort-reward imbalance.

The sample consisted of respondents from the English Longitudinal Study of Ageing (ELSA) who were in employment with hair cortisol measurements at baseline (wave 6), and allostatic load markers at baseline and follow-up (wave 8; n=411; 64 % female). Hair cortisol was used as a measure of total cortisol expression over the preceding two months. Allostatic load was modelled as a count-based index using nine markers; three per system, across the immune, metabolic and cardiovascular systems. This model was then grouped by a median-cut effort reward-imbalance scale (0.83) and regression pathways were compared between groups using a series of Chi-Squared tests of difference.

Results provide evidence that higher hair cortisol concentrations predict an increase in immune and cardiovascular allostatic load cross-sectionally, and a metabolic allostatic load at a lag of four years. These pathways were found in the high effort-reward imbalance group, but not in the low effort-reward imbalance group. There were also significant differences found between groups for hair cortisol concentration as a predictor of concurrent immune and cardiovascular allostatic load

Findings may indicate a novel temporality to the accumulation of an allostatic load, and that the "tipping point" between allostasis and allostatic load may lie within the ability of the HPA axis to regulate the cardiovascular system concurrently, with longitudinal consequences for metabolic syndrome indicators.

1. Introduction

Allostatic load (AL) is a composite measure of the physiological impact of chronic stress, which is frequently examined as a mechanism through which the social environment influences differences in health outcomes later in the lifecourse (McEwen, 2000). When presented with a stressful situation (e.g. a workplace with high-demands), the body initiates a cascade of primary physiological adaptations to help cope with the stressor (for example elevating levels of cortisol via the hypothalamic-pituitary-adrenal axis; HPA axis). This heightened response can then return to a resting state when the stressor has passed, through the process of allostasis. The repeated activation of these initially adaptive allostatic systems can lead to a secondary adjustment to the set-points for markers in the immune, metabolic and cardiovascular systems, and this persistent dysregulation of physiological systems is referred to as an allostatic *load* (or "the price of adaptation"; McEwen and Stellar, 1993). An increased allostatic load has shown associations with tertiary disease endpoints (like cardiovascular disease), psychological disorders (such as depression) and all-cause mortality (Juster et al., 2010; Ganster and Rosen, 2013). However, the "tipping point" at

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which the body transitions from adaptive allostasis to the accumulation of an allostatic load remains unclear.

The construct of allostatic load is commonly used in epidemiological studies to measure the effect of stressful social experiences on health, with indicators of a poor workplace environment (primarily effort-reward imbalance; Montano et al., 2016) showing longitudinal associations with an increased allostatic load over the lifecourse (Coronado et al., 2018; Wahrendorf et al., 2021). However, most allostatic load literature sums markers into a single composite index. This approach has high predictive validity of health outcomes and situates allostatic load as a biological mechanism through which the workplace becomes embodied. However, this approach also attributes equal weighting to each biological system and cannot assess the temporal sequence through which an allostatic load accumulates. In other words, previous literature lacks clarity on how allostatic systems feedback and interact with one another. Placing further attention on a systems-based approach to allostatic load, and how allostasis may be inter-related with the body's other homeostatic systems (chiefly the HPA axis) may be key in identifying a critical period or threshold in which an intervention may be the most effective.

It is thought that primary mediators of the stress response (such as cortisol, the hormonal endpoint of the Hypothalamic-Pituitary-Adrenal (HPA axis)) sit earlier on the temporal allostatic pathway and may be differentially associated with dysregulation in the immune, metabolic and cardiovascular systems across timepoints (Ganster and Rosen, 2013). Current approaches towards the use of cortisol focus on the acute reactivity of the HPA axis via salivary or blood-based measurement. These measures have shown repeated association with poor health outcomes, but due to the variable diurnal patterns of cortisol, and methodologically costly data collection, cortisol data is usually not collected over a long enough period to reflect chronic HPA axis dysregulation (Iob and Steptoe, 2019) which is perhaps closer to the concept of an allostatic load (Wright et al., 2015). However, hair derived cortisol concentration is increasingly used as a measure of chronic cortisol excess (i.e. frequent HPA axis activation) reflecting average systemic cortisol expression at a rate of around 1 month per centimetre of hair. As a consequence, hair derived cortisol is less prone to reflecting the 'state' or diurnal differences found in the area under the curve approach used in salivary cortisol analysis, offering a high validity method for measuring long-term, total cortisol expression (Iob and Steptoe, 2019).

Previous literature draws a line around the body's allostatic systems and traditionally presents only a composite measure of total cumulative dysregulation (O'Toole et al., 2024). Placing further attention on a systems-based approach to allostatic load, and how allostasis may be inter-related with the body's other homeostatic systems (chiefly the HPA axis) may be key in identifying a critical period or threshold in which an intervention may be the most effective (Chandola, 2024).

Literature has not yet traced differences in primary and secondary allostatic systems between those in poor quality work and those in good quality work. Previous research has linked a higher effort-reward imbalance (a measure of failed reciprocity between effort and reward at work; Siegrist and Wahrendorf, 2016) with higher levels of total allostatic load (Coronado et al., 2018; Siegrist et al., 2018). However, associations between job quality and cortisol are distinctly more mixed, with literature identifying both hyper and hypocortisolaemic profiles in response to chronic occupational stress (Van der Meij et al., 2018; Penz et al., 2019). Occupational health theory states that those in chronic poor-quality work are more susceptible to HPA axis dysregulation, which is thought to precede the accumulation of an allostatic load (Siegrist et al., 1997). A deeper exploration of the physiological differences between poor and good quality work is needed to determine the role of the workplace in shaping biomarker profiles, having implications for psychoneuroendocrine theory and occupational health intervention.

This analysis seeks to address these gaps by exploring the role of hair derived cortisol as a predictor of allostatic load in the immune, cardiovascular and metabolic systems over time. To offer a greater level of visibility on the role of psychosocial work characteristics in driving the stress response, we moderate the relationships between primary and secondary allostatic processes by level of effort-reward imbalance. We utilise a sample of older workers from the two waves of the English Longitudinal Study of Ageing who are employed with valid cortisol measures at baseline and allostatic markers at both timepoints. This design provides a greater level of clarity on the patterning of HPA axis dysregulation across groups of effort-reward imbalance, and the consequent temporality to the development of an allostatic load.

To address the aims, we propose two exploratory research questions:

1. Do elevated hair cortisol levels predict an increased allostatic load across the immune, metabolic and cardiovascular systems both cross-sectionally and at a lag of four years?
2. Will there be a significant difference in the associations between hair cortisol and allostatic load by level of effort-reward imbalance?

2. Methods

2.1. Data and sample

This analysis uses an analytical subsample of 411 participants from waves 6 (2012) and 8/9 (2016/2018) of the English Longitudinal Study of Ageing (ELSA; Banks et al., 2021). The ELSA dataset is a representative panel survey of those aged over 50 in the United Kingdom and was supplemented with a booster sample for under-represented groups at waves 3, 4, 6, 7, and 9 to account for non-response bias and survey attrition. At waves 2, 4, 6, and 8/9 a nurse visit is carried out to collect biomeasures (i.e. blood assaying & anthropometric measurements). At waves 8 and 9, the nurse visit was only carried out with half of the sample at each timepoint, and so waves 8 and 9 have been merged in this analysis; referred to as wave 8 hereafter. The wave 8 nurse assessment is designed to be analysed as a whole, rather than split into its constituent waves (The English Longitudinal Study of Ageing, 2024). Hair analytes were only collected from a small subsample of wave 6 participants with valid hair samples (with the length of the hair sample being the limiting factor).

The final analytical sample was derived from those who took part in the wave 6 and waves 8/9 nurse visits and were in full or part-time employment at wave 6. The sample excludes those who were not present at both waves for the nurse visit, and those who had missing data on blood assay variables, physiological measurements and valid hair cortisol measurements. In addition, those not in full or part-time employment at wave 6 were excluded from this analysis. As employment was the limiting factor for sample inclusion, the level of missing data in the final sample of participants was minimal, and a complete case analysis was conducted. The final sample size consisted of 411 ELSA respondents who were employed at wave 6. In order the retain statistical power and to not introduce further healthy worker bias, respondents not in employment at follow-up were also included and differences were statistically controlled for. The final sample had no missingness on allostatic variables at waves 6 and 8, and no missing hair cortisol measurements at wave 6. See Fig. 1 for a breakdown of how the analytical sample was derived.

When compared to the main ELSA sample at wave 6, this analytical sample in this analysis were disproportionately female (64 % compared to 55 % in the main sample; due to a lack of valid hair samples from the posterior vertex in older males) and showed a similar ratio of white to non-white respondents (97 % compared to 96 % in the main sample. The analytical sample were slightly younger (60 compared to 65) and more likely to be in a managerial or professional job role (41 % compared to 34 %).

2.1.1. Effort-reward imbalance

The present study conceptualises job quality as the degree of reciprocity between the effort and reward at work. This process used the

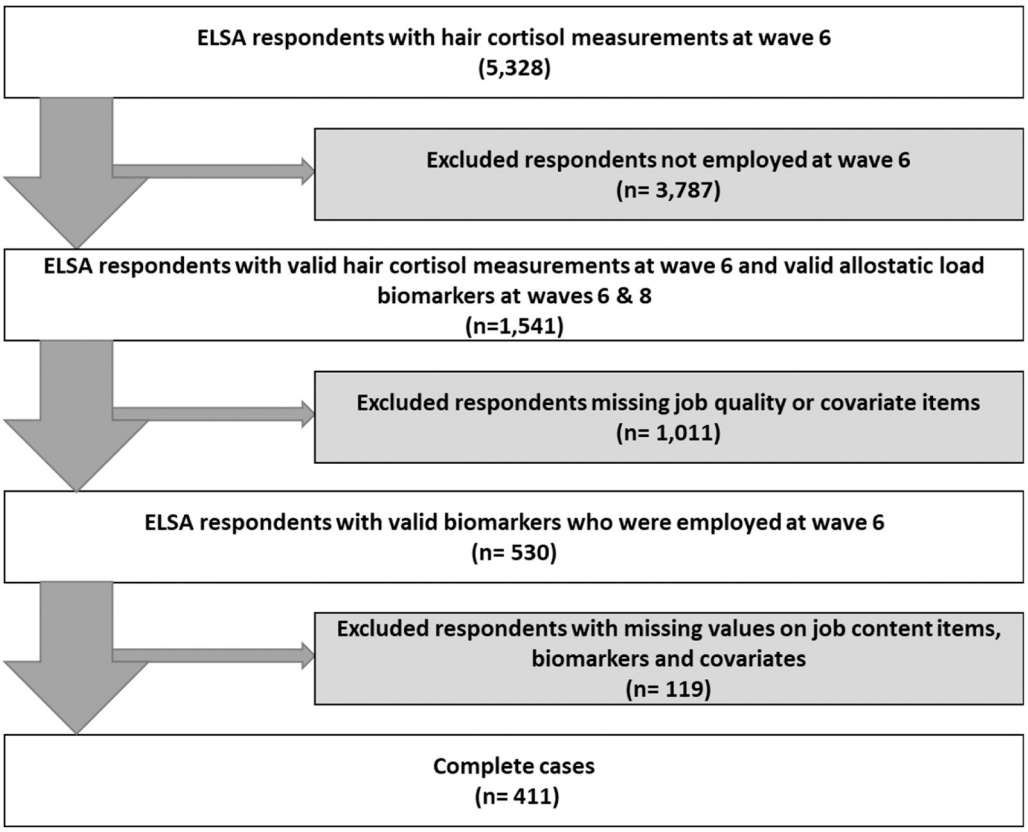

Fig. 1. Analytical sample derivation for individuals employed at wave 6 of ELSA, with a full allostatic load index and hair cortisol at wave 8.

seven individual items from the Job Content Questionnaire (Karasek et al., 1998) available in the ELSA dataset, which asked respondents to rate their agreement with 12 statements on a scale of 1–4 (Strongly Agree – Strongly Disagree).

Two of these items were averaged to represent the effort expended at work ("Feels their job is physically demanding"*; "Feels under constant pressure due to a heavy workload"*) and five of these items were averaged to represent the reward received at work ("Received the recognition they deserved in their work"*; "Feels their salary is accurate*"; "Feels their job prospects are poor"; "Feels their job security is poor"; "Feels they receive adequate support in difficult situations"*). Asterisked items were reverse coded so that higher values of the effort subscale indicated higher levels of effort at work, and higher levels of the reward subscale indicated higher levels of reward (Siegrist and Marmot, 2004; de Araújo et al., 2019).

Effort-reward imbalance was computed as a ratio of mean effort score to mean reward score, with higher values indicating higher levels of imbalance. This method of computing effort-reward imbalance has been previously validated in the ELSA dataset (Coronado et al., 2018). While a threshold of 1 has typically been used to dichotomise an effort-reward imbalance ratio, (Montano et al., 2016) highlight the importance of using values from the sample distribution; the resulting value was cut at the median point (0.83) to account for skewness (DeCoster et al., 2011). Overall, a binary variable was created, representing the psychosocial job quality of the respondent's employment ("Low-Stress"; "High-Stress"). These categorical groups of ERI were computed at wave 6 and used for model stratification and multi-group moderation.

2.1.2. *Biomarkers*

A total of 11 biomarkers across the neuroendocrine, immune, metabolic and cardiovascular systems were used for analyses (see Table 1).

Cortisol was derived from a hair sample taken at wave 6 of the ELSA dataset. Samples were cut as closely to the scalp as feasible from the posterior vertex, and valid samples measured at least 2 cm long, with a weight of at least 10 mg. Hair samples were washed with isopropanol, after which steroid hormones were extracted using high performance liquid chromatography–mass spectrometry. Further details on the collection and analysis of hair-derived analytes can be found in Jackson et al. (2017).

Immune and metabolic markers were derived from fasting blood samples collected during the nurse assessment of waves 6 and 8. Immune markers were; insulin-like growth factor 1 (nmol/l), c-reactive protein (mg/l),clauss fibrinogen (g/l). Metabolic markers were; glycosylated haemoglobin (mmol/mol), triglycerides (mmol/l), total blood cholesterol (mmol/l) and blood high-density lipoprotein level (mmol/l). Anthropometric and cardiovascular measures were also collected at the nurse assessment; systolic and diastolic blood pressure(mmHg) and pulse (beats per minute). These measures were collected at three times over 1-minute intervals and the mean of the three was reported.

The dataset was then cleaned and corrected along the guidelines of Read and Grundy (2014). C-reactive protein values above 10 mg/l were excluded as these values indicate an acute inflammation reaction, rather than the low-grade systemic inflammation allostatic load captures. Chol/HDL was computed as a ratio of cholesterol to high-density lipoprotein in the blood, and log transformations were used with non-normally distributed measures to reduce skewness (hair cortisol was log 10 transformed to account for nil-values). Following this, each of the biomarkers (excluding cortisol) were cut into binary variables, with the highest quartile being coded as "1" for "at risk" and the rest as "0" for "not at risk". The lowest quartile for insulin-like growth factor 1 was used as lower values indicate a higher risk. This process was carried out for male and female respondents respectively, to compute sex specific-cut points (which can be found in Table 1).

To account for the biochemical changes of medication usage, the

Table 1
Variables, cut points and functions of allostatic load biomarkers at waves 6 and 8 of the ELSA dataset.

System	Variable (Units)	Cut points		Function (Juster et al., 2010)
		Wave 6	Wave 8	
Primary Mediator	Hair-derived Cortisol (pg/ml; trimmed to 2 cm, Log10)			Expression of Glucocorticoid produced by the adrenal glands. Functions as a retrospective measure of cumulative HPA activity over the preceding 2 months.
Immune (0−3)	Insulin-like growth factor 1* (nmol/l; Log)	Male = <2.71 Female = <2.60	Male = <2.65 Female = <2.48	Protein produced in the liver. Functions as a stimulator of cell growth
	C-reactive protein (mg/l; Log)	Male = >0.69 Female = >0.92	Male = >0.83 Female = >1.06	Protein synthesised in the liver. Promotes inflammation due to chronic or acute infection or injury.
	Clauss fibrinogen (g/l; Log)	Male = >1.10 Female = >1.16	Male = >1.22 Female = >1.25	Protein which synthesises fibrin. Functions as a blood clotting factor to promote coagulation.
Metabolic (0−3)	Glycosylated haemoglobin (Hba1c) (mmol/mol; Log)	Male = >3.71 Female = >3.74	Male = >3.71 Female = >3.70	Represents the amount glucose concentration that haemoglobin has been exposed to over multiple days. A marker of undiagnosed or mismanaged diabetes.
	Triglycerides (mmol/l; Log)	Male = >0.69 Female = >0.47	Male = >0.64 Female = >0.47	Glyceride which functions as a transporter of dietary fat in the blood.
	Total cholesterol/HDL ratio	Male = >4.47 Female = >3.82	Male = >4.26 Female = >3.81	Ratio of HDL to total cholesterol. A measure of lipids in the blood.
Cardiovascular (0−3)	Systolic blood pressure (mmHg; Log)	Male = >4.96 Female = >4.91	Male = >4.95 Female = >4.94	Represents the maximal force exerted by blood when the left ventricle is contracting during systole.
	Diastolic blood pressure (mmHg; Log)	Male = >4.42 Female = >4.40	Male = >4.39 Female = >4.38	Represents the minimal force exerted by blood when the left ventricle is contracting during diastole.
	Pulse (beats per minute; Log)	Male = >4.12 Female = >4.05	Male = >4.14 Female = >4.14	A measure of heart rate.
Total	Allostatic Load Index Immune (0−3) Metabolic (0−3) Cardiovascular (0−3)	N/A	N/A	Measure of physiological stress; "wear and tear" on the body by allostatic system.

* Reverse Coded

allostatic load risk markers were corrected for according to the recommendations of Read and Grundy (2014), participants were assigned to the risk category for diastolic and systolic blood pressure if participants used blood pressure lowering medication, fibrinogen if they used anticoagulant medication, triglycerides and HDL cholesterol ratio if participants used lipid lowering medication, and glycosylated haemoglobin if participants used diabetes medication. In addition, the second highest quartile was used for c-reactive protein if blood pressure, cholesterol or diabetes medications were taken. No data was available on steroid medication usage, and so was unable to be controlled for in this analysis.

To create the allostatic load indices, count-based summaries were used per allostatic system (Juster et al., 2010). To compute the immune allostatic load index, risk scores for IGF-1, crp and fibrinogen were summed. Similarly for the metabolic allostatic load variable the risk scores for hba1c, triglycerides and total cholesterol/hdl ratio were summed. Finally for the cardiovascular allostatic load variable risk scores for systolic blood pressure, diastolic blood pressure and pulse were summed. The results of these computations were three variables per wave (6 & 8) representing the allostatic load index across the immune, metabolic and cardiovascular systems, each on a scale of 0–3.

A note for this index is that insulin-like growth factor 1 (IGF-1) is often found to have roles in both the neuroendocrine and inflammatory systems. For index construction in this analysis, IGF-1 was coded as a marker of immune function along the guidelines of Juster et al. (2010). See Table 1 for sex-specific cut-off scores and the function of each marker by corresponding allostatic system.

2.1.3. Covariates

At waves 6 and 8 of ELSA, demographic factors were entered into the structural equation models as dummy coded covariates; sex ("Male", "Female"), age ("Under 59", "60–64", "Over 65"), Ethnicity ("White", "Non-White) and socio-economic classification ("Managerial & Professional", "Intermediate", "Routine & Manual"), in addition to employment at wave 8 ("Yes", "No"), hair treatment status ("Yes", "No") and wave of nurse assessment for the split biomarker collection at waves 8/9 ("Wave 8", "Wave 9". Covariate inclusion was blocked into sociodemographic characteristics and employment characteristics to check the robustness of each model; fully covariate adjusted models are presented.

2.2. Analysis

To address the aims of this analysis, a multivariate regression was conducted with cortisol as an independent variable and immune, metabolic and cardiovascular allostatic load at waves 6 and 8 as dependant variables. In this model, we pool variables collected at waves 8 and 9 of the nurse assessment as described in the user guide, and control for any temporal effects using a wave marker (The English Longitudinal Study of Ageing, 2024). The effects of hair treatments were also statistically controlled for using binary flags, as were the effects of wave 6 allostatic load on wave 8 allostatic load measures. This analysis was then grouped by "no imbalance" and "imbalance" on the effort-reward imbalance measure to compare the biological processes of those who are in high-stress work to low-stress work. To compare statistical differences between groups, a Chi Square test of difference was used to compare the covariate adjusted "free" model to a model in which the intercepts and regressions were constrained to equality. To further explore which regression pathways were significantly different between groups the coefficients of the "free" model were sequentially constrained to equality between groups. This series of constrained models were compared to the "free" model via Chi Squared tests of difference.

As the allostatic load variables were ordinal, and cortisol was used as a continuous variable, Weighted Least Squares with Mean and Variance

adjustments (WLSMV) was determined to be the most appropriate estimator in the structural equation models generated. WLSMV is a variation of Diagonally Weighted Least Squares (DWLS) which accounts for non-normality by applying weights to observations based on the mean and variance of the data distribution.

This sub-sample is primarily contingent on those present in the nurse assessment of wave 6 with blood assay data available, as such the wave 6 blood sample weights were applied to the structural equation model. Data cleaning and descriptive statistics were generated in R RStudio 2022.07.02 (R Core Team, 2022). The Lavaan package was used for structural equation modelling (Rosseel, 2022). A statistical power analysis was performed with the semPower package in r (Moshagen and Erdfelder, 2016). The fully adjusted model has 63 degrees of freedom. Results from an a-priori power analysis show that a sample size of 84 is needed to obtain an 80 % power for detecting a model misspecification, for RMSEA of at least.08 with 63 degrees of freedom. Both the full sample analysis and sub-group analyses meet these power requirements.

3. Results

Table 2 shows means and standard deviations for hair cortisol and systemic allostatic load (at baseline and follow-up), in addition to the demographic covariates of sex, ethnicity, age and socio-economic classification, employment and follow-up and hair treatment status stratified by level of ERI, and total.

3.1. RQ1: Do elevated hair cortisol levels predict an increased allostatic load across the immune, metabolic and cardiovascular systems, both cross-sectionally and at a lag of four years?

To address the first research question, a multivariate regression analysis was carried out, using log10 transformed hair cortisol at wave 6 as a predictor of immune, metabolic and cardiovascular allostatic load at waves 6 and 6 (cross-sectionally and at a follow-up of four years). In this model, the time varying sociodemographic covariates of age group and socio-economic classification were entered into the model. Sex and ethnicity showed no variation across waves in this sample and were treated as time-invariant.

Results of the multivariate regression analysis showed that higher hair cortisol concentrations predict an increased level of immune allostatic load and cardiovascular allostatic load cross sectionally. Higher hair cortisol concentrations also predicted a higher metabolic allostatic load at a lag of 4 years. This structural equation model showed good model fit (Comparative fit index; CFI = 1.00, Tucker-Lewis Index; TLI = 1.00, Root Mean Square Error of Approximation; RMSEA = 0.00, Standardized Root Mean Square Residual; SRMR = 0.03). See Fig. 2 for a path diagram for hair cortisol as a predictor of systemic allostatic load cross-sectionally at and a lag of four years. Please see appendix item A for the key total group model parameters.

3.2. RQ2: Will there be a significant difference in the associations between hair cortisol and allostatic load by level of effort-reward imbalance?

To address the second research question, a multi-group moderation analysis was carried out by level of ERI (using the median value of 0.83 as a sample-specific cut-point). In the high-stress group, an increase in hair cortisol concentration was found to cross-sectionally predict an increase in immune allostatic load (est.std 0.18, (0.05, 0.30), $p < 0.05$) and cardiovascular allostatic load (est.std 0.27, (0.14, 0.40), $p < 0.001$). An increase in hair cortisol concentration at wave 6 was also found to predict an increased metabolic allostatic load at wave 8, across a gap of four years (est.std 0.16, (0.05, 0.26), $p < 0.05$). For the low-stress groups, none of the regression pathways between cortisol and systemic allostatic load were statistically significant. The multi-group model also showed good model fit (CFI = 1.00, TLI = 1.08, RMSEA = 0.00, SRMR = 0.03). See Table 3 for a comparison of parameters

Table 2
The distribution of allostatic load by system and demographic covariates at waves 6 and 8 in the ELSA dataset by level of effort-reward imbalance.

Variable	Dimension/ Category	Low ERI (<0.83)	High ERI (>0.83)	Total
Total n		*(n = 184)*	*(n = 227)*	*(n = 411)*
Hair-derived Cortisol	Wave 6			
Mean (SD)	Trimmed to <660 pg/ml	25 (72)	21 (70)	23 (71)
	Trimmed to <660 pg/ml, Log 10	0.86 (0.55)	0.78 (0.53)	0.82 (0.54)
Allostatic Load	Wave 6			
Mean (SD)	Immune	0.80 (0.89)	0.91 (0.91)	0.86 (0.90)
	Metabolic	0.99 (1.06)	1.02 (0.98)	1.01 (1.02)
	Cardiovascular	0.87 (1.00)	0.88 (1.00)	0.87 (1.04)
	Wave 8			
	Immune	0.83 (0.90)	0.84 (0.90)	0.84 (0.90)
	Metabolic	1.10 (1.10)	1.10 (1.10)	1.06 (1.05)
	Cardiovascular	0.97 (1.03)	0.89 (0.99)	0.93 (1.00)
Sex	Male	75 (41 %)	73 (32 %)	148 (36 %)
Freq (%)	Female	109 (59 %)	154 (68 %)	263 (64 %)
Ethnicity	White	177 (96 %)	220 (97 %)	397 (97 %)
Freq (%)	Non-White	7 (4 %)	7 (3 %)	14 (3 %)
Age Group	Wave 6			
Freq (%)	59 & Under	53 (29 %)	109 (48 %)	162 (39 %)
	60–64	93 (51 %)	93 (41 %)	144 (35 %)
	65 & Over	38 (21 %)	25 (11 %)	105 (26 %)
	Mean (SD)	61 (5.10)	60 (5.00)	60 (5.09)
	Wave 8			
	59 & Under	13 (7 %)	26 (11 %)	39 (10 %)
	60–64	84 (46 %)	134 (59 %)	160 (39 %)
	65 & Over	87 (47 %)	67 (30 %)	212 (52 %)
	Mean (SD)	65 (5.10)	64 (5.00)	64 (5.13)
Socio-Economic Classification	Wave 6			
Freq (%)	Managerial & Professional	84 (46 %)	85 (37 %)	169 (41 %)
	Intermediate	55 (30 %)	55 (24 %)	110 (27 %)
	Routine & Manual	45 (24 %)	87 (38 %)	132 (32 %)
	Wave 8			
	Managerial & Professional	78 (42 %)	77 (34 %)	155 (38 %)
	Intermediate	61 (33 %)	56 (25 %)	117 (28 %)
	Routine & Manual	45 (24 %)	94 (41 %)	139 (34 %)
Employment Status	Wave 8			
Freq (%)	Yes	97 (53 %)	133 (59 %)	230 (56 %)
	No	87 (47 %)	94 (41 %)	181 (44 %)
Hair Treatment	Wave 6			
Freq (%)	Yes	4 (2 %)	8 (3 %)	12 (3 %)
	No	180 (98 %)	219 (97 %)	399 (97 %)

* Reverse Coded

between high and low ERI groups. Please see appendix item B for the key multi-group model parameters.

To assess the level of overall difference between groups, a scaled Chi-Square difference test was conducted to compare the free model to a nested constrained model in which the intercept and regression pathways were equal between groups using the Satorra-Bentler method (Satorra, 2000).

Results showed a significant difference between the free model ($\chi^2 = 91.2$, df = 126) and the constrained model ($\chi^2 = 196.8$, df = 186). In other words, a scaled χ^2 difference of 97.4 on a degrees of freedom difference of 60 was statistically significant ($p < 0.05$). Results indicate that model coefficients vary significantly between groups, and so further multi-group comparisons can be carried out.

To explore the extent to which regression coefficients differ between those in high and low-stress work, we computed a series of six structural equation models, in each of which the regression pathways between hair cortisol and the six allostatic load outcomes (three per timepoint) were sequentially constrained and the models were re-fitted. Each of these models were compared to the baseline free model in order to determine which regression pathways were significantly different between groups.

Between groups comparison revealed that the paths between cortisol and immune allostatic load, and cortisol and cardiovascular allostatic load differed significantly between groups. Please see Table 4 for multi-group model comparisons.

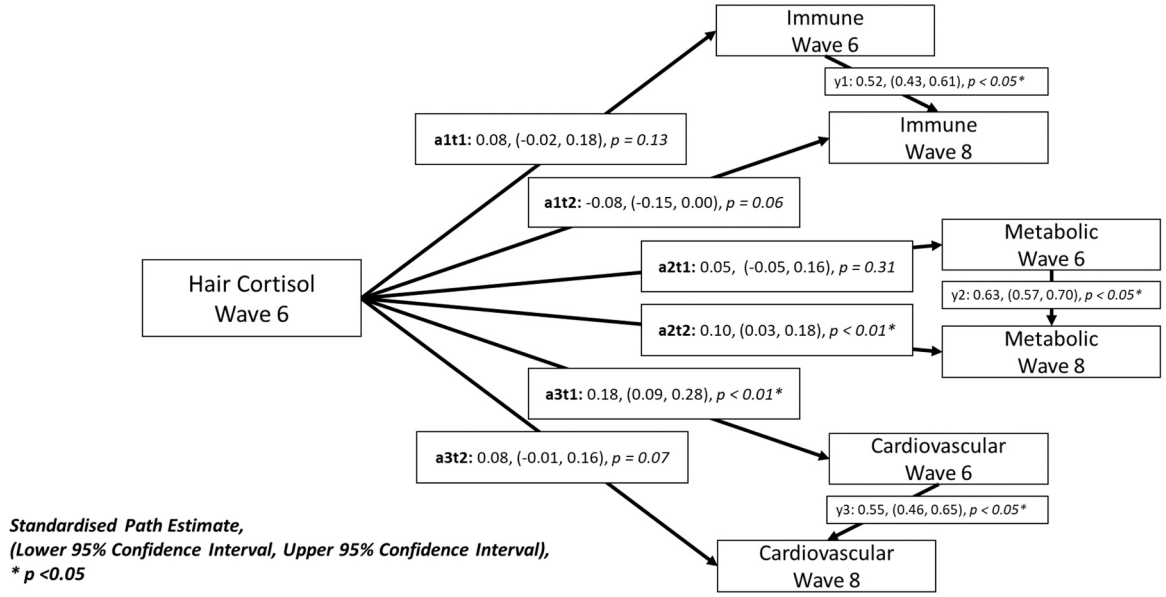

Fig. 2. Path diagram for hair cortisol and immune, metabolic and cardiovascular dysregulation. Standardised path estimates and 95 % confidence intervals (in parentheses) are shown.

Table 3
Standardised coefficients for cortisol and allostatic load.

			Total Sample					High Effort-Reward Imbalance					Low Effort-Reward Imbalance				
Outcome	Predictor	label	est. std	*p*	*	95 % CI		est. std	*p*	*	95 % CI		est. std	*p*	*	95 % CI	
						lower	upper				lower	upper				lower	upper
Immune (Wave 6)	**Hair Cortisol (Wave 6)**	a1t1	0.08	0.13		−0.02	0.18	0.18	0.00	***	0.05	0.30	−0.09	0.22		−0.24	0.06
Metab (Wave 6)	**Hair Cortisol (Wave 6)**	a2t1	0.05	0.31	.	−0.05	0.16	0.10	0.15		−0.04	0.25	−0.06	0.45		−0.20	0.09
Cardio (Wave 6)	**Hair Cortisol (Wave 6)**	a3t1	0.18	0.00	***	0.09	0.28	0.27	0.00	***	0.14	0.40	0.04	0.61		−0.11	0.18
Immune (Wave 8)	**Hair Cortisol (Wave 6)**	a1t2	−0.08	0.06	.	−0.15	0.00	−0.08	0.16		−0.20	0.03	−0.07	0.28		−0.17	0.04
Metab (Wave 8)	**Hair Cortisol (Wave 6)**	a2t2	0.10	0.01	**	0.03	0.18	0.16	0.00	***	0.05	0.26	0.07	0.23		−0.04	0.18
Cardio (Wave 8)	**Hair Cortisol (Wave 6)**	a3t2	0.08	0.07		−0.01	0.16	0.09	0.08		−0.01	0.19	0.02	0.81		−0.12	0.15

Note: est.std = standardised path estimate (variables are standardised to have a variance of 1), se = standard error, *p* = p value,. p < 0.10,* p < 0.05; ** p < 0.01; *** p < 0.001, ci = 95 % confidence intervals; Immune = Immune allostatic load; Metab = Metabolic allostatic load; Cardio = Cardiovascular allostatic load.
Covariates: sex (Male; Reference group=Female), age (Under 59; 60–64; Reference group=Over 65), ethnicity (White; Reference group="Non-White), socio-economic classification (Managerial & Professional; Intermediate; Reference group="Routine & Manual"), employment at wave 8 (Yes; Reference group="No") and hair treatment status (Reference group=Yes; No).

4. Discussion

Results of modelling provide some evidence that the "tipping point" between an adaptive and a maladaptive stress response is tied to the ability of the HPA axis to modulate the cardiovascular system. This analysis provides two main contributions to the field. Firstly, we establish elevated hair-derived cortisol as a predictor of a higher immune and cardiovascular allostatic load cross-sectionally, and an elevated metabolic allostatic load at lag of four years. Secondly, we provide evidence that these allostatic temporal mechanisms are moderated by level of job quality: high vs low effort reward imbalance. We found that for individuals in low-quality, high-stress jobs, hair cortisol concentration predicted immune and cardiovascular allostatic load cross-sectionally, and metabolic allostatic load at a gap of four years. However, for those in high-quality, low-stress employment, cortisol was not associated with systemic allostatic load at any time-point. Further, while we identified significant differences between the high and low-stress groups for elevated levels of cortisol as a predictor of immune and cardiovascular allostatic load cross-sectionally.

4.1. Glucocorticoids & The Cardiovascular System

Elevated levels of cortisol showed the strongest association with higher levels of cardiovascular allostatic load cross sectionally. Recent review has found that cortisol production has shown repeated association with cardiovascular measures (Iob and Steptoe, 2019); this relationship may be explained when considering that glucocorticoids are directly implicated in the maintenance of vascular tone, blood pressure and pulse rate through the sympathetic and parasympathetic pathways (adaptation to a stressor and return to resting respectively; McEwen, 2005). It is the set-point adjustment of these pathways that can lead to the persistence of metabolic strain (via the extended production of glucocorticoids) and consequently, cardiovascular disease (i.e. elevated blood pressure and consequent hypertension; Iob and Steptoe, 2019; Burford et al., 2017). Cardiovascular dysregulation is not seen longitudinally, which may be explained by the inherent state-variability of cardiovascular measures; heart rate and blood pressure are more closely related to the external environment and perhaps become less "embedded" than immune and metabolic markers (Thielmann et al., 2021). In sum, cardiovascular allostatic may act as strong, early indicator of subsequent poor health.

4.2. The Accumulation of the Metabolic Syndrome

The significant association found between higher cortisol concentrations and metabolic dysregulation falls in line with key literature, which has found a longitudinal dose-response relationship between exposure to chronic stress and risk of metabolic syndrome (a grouping of metabolic risk factors which has been found to precede an increased risk of heart disease and type 2 diabetes; Chandola et al., 2006). This analysis corroborates previous literature by finding an association between cortisol and metabolic dysregulation over a lag of four years. Findings suggest that the metabolic syndrome persists and significantly increases over time as a result of elevated cortisol levels (Jackson et al., 2017). Higher cortisol levels can lead to the dysregulation of glucose metabolism, resulting in an increase of HbA1c levels (Joseph et al., 2015; Sapolsky, 2004). Additionally, an elevated level of cortisol in the blood as stimulate the release of fatty acids from adipose tissue, resulting in a raised level of triglycerides and the suppression the production of HDL cholesterol, increasing the ratio of HDL to total cholesterol in the blood over time (McEwen, 2007; Iob and Steptoe, 2019). We do not find evidence of an association between cortisol and metabolic markers cross-sectionally, which dovetails with previous research to suggest that it takes time to see the effects of chronic stress in the dysregulation of metabolic markers (Chandola et al., 2006). These findings provide evidence of a longitudinal, cumulative association between hair cortisol and markers of the metabolic syndrome, with a dysregulated HPA axis being implicated in the persistence and later dysregulation of metabolic systems over time.

Table 4
Aggregated Results for Sequential, Nested, Scaled Chi-Squared Tests of Difference.

Model	Constraint	df	χ^2	χ^2 Diff	*P* - value	
1	Free Model	126	91.2			
	Immune Wave 6	127	98	6.60	0.01	**
2	Free Model	126	91.2			
	Metabolic Wave 6	127	93.5	2.15	0.14	
3	Free Model	126	91.2			
	Cardiovascular Wave 6	127	95.7	4.96	0.03	*
4	Free Model	126	91.2			
	Immune Wave 8	127	91.2	0.04	0.89	
5	Free Model	126	91.2			
	Metabolic Wave 8	127	91.7	1.35	0.25	
6	Free Model	126	91.2			
	Cardiovascular Wave 8	127	91.5	0.64	0.42	

= p = <0.10; * = p = 0.05; ** = p < 0.01

4.3. The HPA Axis & Immunomodulation

In the high-stress group, elevated hair cortisol concentrations showed significant direct association with a higher level of immune allostatic load cross sectionally. While the coefficients for this association at a lag of four years did not meet the threshold for statistical significance, results may still warrant interpretation. Explanation of these findings can be found in immunomodulatory effects of cortisol, as elevated cortisol levels have been found to stimulate the production of pro-inflammatory cytokines (Glaser and Kiecolt-Glaser, 2005). However, when examining immune dysregulation at follow-up (four years later), the association between cortisol levels and immune dysregulation was negative. This temporal switch from an elevated immune allostatic load to a lower immune allostatic load may be explained when considering that the adaptive elevation of immune function will slowly return to normal operating ranges, and in the presence of a chronic stressor can overshoot and fall to 40–60 % of baseline (Sapolsky, 2004). Over time, repeated exposure to stressors can lead to a less responsive HPA axis, a consequence of which is a desensitisation of the immune system to stress signals, leading to an inhibited production of IGF1, CRP and fibrinogen and a blunted immune response (Iob and Steptoe, 2019). Future research might focus on potential differences between pro and anti-inflammatory cytokines for a greater visibility on the temporality of immune dysregulation.

4.4. The Physiological Difference Between High and Low-Quality Work

The second arm of this analysis focussed on a comparison of between-group differences for those in high-stress and low-stress work; poor and good quality employment. When comparing high and low-stress groups, we find similar patterns of cardio-metabolic dysregulation in the high-stress group, but for the low stress group cortisol was not associated with any form of allostatic load. We find evidence that the only pathways which may differ between those in high and low-stress employment are those of the cardiovascular and immune systems cross-sectionally. These findings may be explained by previous literature, which identified that more recent experiences of effort reward imbalance are associated with a higher allostatic load index (Coronado et al., 2018). Taken together, these findings reveal that allostatic load may be more variable, more tied to recent exposures to (work) stressors and potentially more open to amelioration via intervention than is supposed by the standard epidemiological model of accumulation (Ben-Shlomo and Kuh, 2002). The accumulation of an allostatic load may be a slower drift towards cardiovascular and metabolic risk which accumulates in an adaptive temporal sequence. These findings

emphasise the importance of early, tailored occupational health intervention which should be implemented before markers of primary dysregulation (i.e. cortisol and cardiovascular markers) become embodied within the metabolic system, at which point intervention may be more difficult.

For participants in low-stress work, cortisol was not significantly associated with systemic allostatic load measures at either timepoint. This lack of association may indicate that, for those in low-stress work, the HPA axis is not dysregulated, and so does not drive the accumulation of systemic allostatic load as seen in the high-stress group. It may also be important to consider that descriptively, both the high and low ERI groups showed similar levels of hair cortisol, indicating that it may not necessarily be the total level of cortisol expressed which is associated with a higher allostatic load, but how cortisol as a marker of HPA axis activity is associated with function across other bodily systems.

Further context might be added to these findings when considering wider employment patterns. For example, recent findings from Chandola and Zhang (2018) establish that those who transition into poor quality work from unemployment have higher levels of allostatic load than those who remain unemployed, but also that those who transition into good quality employment have lower levels of allostatic load than those who remain unemployed. The prevailing theme across recent literature is that good quality employment (i.e. employment with a favourable effort-reward balance) can be associated with positive health; just as poor-quality work is associated with poor health, so too is good quality work associated with good health.

4.5. Implications and limitations

The findings of the present analysis highlight the role of prolonged activation of the HPA axis as a predictor of later allostatic load. We highlight the theoretical role of the cardiovascular system, which potentially acts as a strong early indicator of allostatic dysregulation and disease. These findings might help to direct future intervention; the integration of low burden cardiovascular measures, coupled with robust psychometric scales of work stress may help to identify those who are not only experiencing low psychosocial quality work, but those who may have the highest risk for poor health outcomes as a consequence. However, it is of note that the state variability of cardiovascular measures may be confounded by concurrent stressors (such as a nurse assessment). As such, a further investigation into measures of both cardiovascular and autonomic nervous system activity is warranted, with current research indicating that heart-rate variability may be an important marker of an individual's (in)ability to return to a resting state following exposure to a stressor (Thielmann et al., 2021).

There are a number of limitations to this analysis, chief among them the restricted sample. The analytical sample in this study is comprised of older, majority white participants; this limitation is compounded by the selective attrition seen in nurse visit waves of survey data collection. Survey weighting was applied to account for these issues, but the generalisability of these results to other demographic groups remains limited. A limitation noted in Jackson et al. (2017) is that it is not possible to account for the pharmacological effects of (predominantly steroid) medications which may influence levels of cortisol expression. We chose to log transform hair derived cortisol for the simplicity of the model and power limitations; however, recent findings highlight that a quantile regression approach has been beneficial for cortisol analysis to increase visibility on how different cortisolemic profiles are associated with psychosocial job quality and allostatic load (Chandola et al., 2023). We do not compare the significance of paths for demographic and control variables; as we do not detect a significant difference between groups for the main effects of cortisol on allostatic load, there may be socio-demographic differences present which we do not test for. We do not account for the impact of major life events; further research is needed to understand the impact of life events on cortisol expression and subsequent health outcomes. We also do not account for behavioural pathways such as diet and exercise which have both shown repeated ameliorating effects between stressful exposures and health outcomes. It is also important to note the small number of respondents who had a hair treatment which may affect cortisol measurement. Sensitivity analyses without these respondents revealed no differences and so these participants were retained for analysis and hair treatment was statistically controlled for.

5. Conclusion

In summary, the present study provides evidence that chronically elevated hair cortisol concentration is positively associated with immune and cardiovascular dysregulation cross-sectionally, and an elevated metabolic dysregulation at a lag of four years. Multi-group comparisons revealed an overall difference in the relationships between HPA axis activity and the accumulation of an allostatic load for those in high versus low-stress employment. We highlight the differences seen between cortisol and both immune and cardiovascular dysregulation cross-sectionally, which may indicate that work stress and allostatic load are more closely, temporally related than previously thought.

CRediT authorship contribution statement

Thomas O'Toole: Writing – original draft, Visualization, Software, Methodology, Formal analysis, Conceptualization. **Christopher J. Armitage:** Writing – review & editing, Supervision. **Martie van Tongeren:** Writing – review & editing, Supervision. **Kimberly A. Dienes:** Writing – review & editing, Supervision, Conceptualization.

Declaration of Competing Interest

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Data Availability

The English Longitudinal Study of Ageing can be accessed through the UK Data Service (SN 5050): https://discover.ukdataservice.ac.uk or via the Gateway to Global Aging data: https://g2aging.org/.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2024.107193.

References

Banks, J., Batty, G. David, Breedvelt, J., Coughlin, K., Crawford, R., Marmot, M., Nazroo, J., Oldfield, Z., Steel, N., Steptoe, A., Wood, M., Zaninotto, P. (2021). English Longitudinal Study of Ageing: Waves 0-9, 1998-2019. [data collection]. 37th Edition. UK Data Service. SN: 5050, doi: ⟨10.5255/UKDA-SN-5050-24⟩.

Ben-Shlomo, Y., Kuh, D., 2002. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. Int. J. Epidemiol. 31 (2), 285–293.

Burford, N.G., Webster, N.A., Cruz-Topete, D., 2017. Hypothalamic-Pituitary-Adrenal Axis Modulation of Glucocorticoids in the Cardiovascular System. Int. J. Mol. Sci. 18 (10), 2150. https://doi.org/10.3390/ijms18102150.

Chandola, T., 2024. A reply to 'Social-to-biological transitions research: review of progress and development' by Thomas O'Toole et al. published online ahead of print 2024). Retrieved Jul 9, 2024, from Longitud. Life Course Stud.. https://doi.org/10.1332/17579597Y2024D000000018.

Chandola, T., Cahill, S., Kumari, M., 2023. Hair Cortisol as a Biomarker of Resilience to Pain Among Adults Living in the UK [Conference presentation]. Society for Longitudinal and Lifecourse Studies International Conference. Ludwig Maximillian University, Munich, Germany.

Chandola, T., Zhang, N., 2018. Re-employment, job quality, health and allostatic load biomarkers: prospective evidence from the UK Household Longitudinal Study. Int. J. Epidemiol. 47 (1), 47–57. https://doi.org/10.1093/ije/dyx150.

Chandola, T., Brunner, E., Marmot, M., 2006. Chronic stress at work and the metabolic syndrome: prospective study. BMJ (Clin. Res. Ed.) 332 (7540), 521–525. https://doi.org/10.1136/bmj.38693.435301.80.

Coronado, J., Chandola, T., Steptoe, A., 2018. Allostatic Load and Effort-Reward Imbalance: Associations over the Working-Career. In: International Journal of Environmental Research and Public Health, 15. MDPI AG, p. 191. https://doi.org/10.3390/ijerph15020191.

de Araújo, T.M., Siegrist, J., Moreno, A.B., de Jesus Mendes da Fonseca, M., Barreto, S. M., Chor, D., Griep, R.H., 2019. Effort-Reward Imbalance, Over-Commitment and Depressive Episodes at Work: Evidence from the ELSA-Brasil Cohort Study. Int. J. Environ. Res. Public Health 16 (17), 3025. https://doi.org/10.3390/ijerph16173025.

DeCoster, J., Gallucci, M., Iselin, A.-M.R., 2011. Best practices for using median splits, artificial categorization, and their continuous alternatives. J. Exp. Psychopathol. 2 (2), 197–209. https://doi.org/10.5127/jep.008310.

Ganster, D.C., Rosen, C.C., 2013. Work stress and employee health: A multidisciplinary review. J. Manag. 39 (5), 1085–1122. https://doi.org/10.1177/0149206313475815.

Glaser, R., Kiecolt-Glaser, J.K., 2005. Stress-induced immune dysfunction: implications for health. Nat. Rev. Immunol. 5 (3), 243–251. https://doi.org/10.1038/nri1571.

Iob, E., Steptoe, A., 2019. Cardiovascular Disease and Hair Cortisol: a Novel Biomarker of Chronic Stress. Curr. Cardiol. Rep. 21 (10), 116. https://doi.org/10.1007/s11886-019-1208-7.

Jackson, S.E., Kirschbaum, C., Steptoe, A., 2017. Hair cortisol and adiposity in a population-based sample of 2,527 men and women aged 54 to 87 years. Obes. (Silver Spring, Md.) 25 (3), 539–544. https://doi.org/10.1002/oby.21733.

Joseph, J.J., Wang, X., Spanakis, E., Seeman, T., Wand, G., Needham, B., Golden, S.H., 2015. Diurnal salivary cortisol, glycemia and insulin resistance: The multi-ethnic study of atherosclerosis. Psychoneuroendocrinology 62, 327–335. https://doi.org/10.1016/j.psyneuen.2015.08.021.

Juster, R.P., McEwen, B.S., Lupien, S.J., 2010. Allostatic load biomarkers of chronic stress and impact on health and cognition. Neurosci. Biobehav. Rev. 35 (1), 2–16. https://doi.org/10.1016/j.neubiorev.2009.10.002.

Karasek, R., Brisson, C., Kawakami, N., Houtman, I., Bongers, P., Amick, B., 1998. The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. J. Occup. Health Psychol. 3 (4), 322–355. https://doi.org/10.1037//1076-8998.3.4.322.

McEwen, B., 2000. Allostasis and Allostatic Load: Implications for Neuropsychopharmacology. Neuropsychopharmacol 22, 108–124. https://doi.org/10.1016/S0893-133X(99)00129-3.

McEwen, B.S., 2007. Physiology and neurobiology of stress and adaptation: central role of the brain. Physiol. Rev. 87 (3), 873–904. https://doi.org/10.1152/physrev.00041.2006.

Montano, D., Li, J., Siegrist, J., 2016. The measurement of effort-reward imbalance (ERI) at work. In: Siegrist, In.J., Wahrendorf, M. (Eds.), Work stress and health in a globalized economy: The model of effort-reward imbalance. Springer International Publishing/Springer Nature, pp. 21–42. https://doi.org/10.1007/978-3-319-32937-6_2.

Moshagen, M., Erdfelder, E., 2016. A new strategy for testing structural equation models. Struct. Equ. Model. 23 (1), 54–60. https://doi.org/10.1080/10705511.2014.950896.

O'Toole, T., Kumari, M., Kelly-Irving, M., Blane, D., 2024. Social-to-biological transitions research: review of progress and development. Longitud. Life Course Stud. https://doi.org/10.1332/17579597Y2024D000000015.

Penz, M., Siegrist, J., Wekenborg, M.K., Rothe, N., Walther, A., Kirschbaum, C., 2019. Effort-reward imbalance at work is associated with hair cortisol concentrations: Prospective evidence from the Dresden Burnout Study. Psychoneuroendocrinology 109, 104399.

R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL ⟨https://www.R-project.org/⟩.

Read, S., Grundy, E., 2014. Allostatic load and health in the older population of England: a crossed-lagged analysis. Psychosom. Med. 76 (7), 490–496. https://doi.org/10.1097/PSY.0000000000000083.

Rosseel, Y., 2022. lavaan: An R Package for Structural Equation Modelling. J. Stat. Softw. 48 (2), 1–36. https://doi.org/10.18637/jss.v048.i02.

Satorra, A., 2000. Scaled and adjusted restricted tests in multi-sample analysis of moment structures. Innovations in multivariate statistical analysis: A Festschrift for Heinz Neudecker. Springer US, Boston, MA, pp. 233–247.

Sapolsky, R.M., 2004. Why Zebras Don't Get Ulcers: The Acclaimed Guide to Stress, Stress-Related Diseases, and Coping, Third Edition. Henry Holt.

Siegrist, J., Wahrendorf, M., 2016. Failed social reciprocity beyond the work role. In: Siegrist, In.J., Wahrendorf, M. (Eds.), Work stress and health in a globalized economy: The model of effort-reward imbalance. Springer International Publishing/Springer Nature, pp. 275–291. https://doi.org/10.1007/978-3-319-32937-6_12.

Siegrist, J., Klein, D., Voigt, K.H., 1997. Linking sociological with physiological data: the model of effort-reward imbalance at work. Acta Physiol. Scand. Suppl. 640, 112–116.

Siegrist, J., Marmot, M., 2004. Health inequalities and the psychosocial environment-two scientific challenges. Soc. Sci. Med. (1982) 58 (8), 1463–1473. https://doi.org/10.1016/S0277-9536(03)00349-6.

Siegrist, J., Wahrendorf, M., Goldberg, M., Zins, M., Hoven, H., 2018. Is effort-reward imbalance at work associated with different domains of health functioning? Baseline results from the French CONSTANCES study. Int. Arch. Occup. Environ. Health 92 (4), 467–480. https://doi.org/10.1007/s00420-018-1374-8.

The English Longitudinal Study of Ageing, (2024). User Guide to the Nurse Visit Datasets Waves 2,4,6,8,9. ⟨https://www.elsa-project.ac.uk/study-documentation⟩.

Thielmann, B., Schierholz, R.S., Böckelmann, I., 2021. Subjective and Objective Consequences of Stress in Subjects with Subjectively Different Sleep Quality-A Cross-Sectional Study. Int. J. Environ. Res. Public Health 18 (19), 9990. https://doi.org/10.3390/ijerph18199990.

Van der Meij, L., Gubbels, N., Schaveling, J., Almela, M., van Vugt, M., 2018. Hair cortisol and work stress: importance of workload and stress model (JDCS or ERI). Psychoneuroendocrinology 89, 78–85.

Wahrendorf, M., Chandola, T., Goldberg, M., Zins, M., Hoven, H., Siegrist, J., 2021. Adverse employment histories and allostatic load: associations over the working life. J. Epidemiol. Community Health 76 (4), 374–381.

Wright, K.D., Hickman, R., Laudenslager, M.L., 2015. Hair Cortisol Analysis: A Promising Biomarker of HPA Activation in Older Adults. Gerontologist 55 (Suppl 1), S140–S145. https://doi.org/10.1093/geront/gnu174.