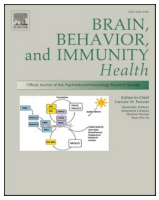
Brain, Behavior, & Immunity - Health 48 (2025) 101096

Contents lists available at ScienceDirect

Brain, Behavior, & Immunity - Health

journal homepage: www.editorialmanager.com/bbih/default.aspx



Cumulative social advantage is associated with slower epigenetic aging and lower systemic inflammation

Anthony D. Ong [a,b,*], Frank D. Mann [c], Laura D. Kubzansky [d]

[a] Department of Psychology, Cornell University, USA
[b] Joan and Sanford I. Weill Department of Medicine, Weill Cornell Medicine, USA
[c] Department of Medicine, Renaissance School of Medicine at Stony Brook University, USA
[d] Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, USA

ARTICLE INFO

Keywords:
Cumulative social advantage
Biological aging
Epigenetic clocks
Systemic inflammation

ABSTRACT

Background: Social relationships are established determinants of health across the lifespan, yet the cumulative and multidimensional effects of sustained social advantage on biological aging remain poorly understood.
Methods: Drawing on data from 2117 adults in the Midlife in the United States (MIDUS) study, we used structural equation modeling to examine whether cumulative social advantage (CSA)—a latent construct encompassing social connection across familial, religious, emotional, and community domains—was associated with epigenetic aging, systemic inflammation, and neuroendocrine activity.
Results: Higher CSA was linked to slower epigenetic aging, particularly as indexed by GrimAge ($\beta = -0.09$ to -0.10, $q < 0.001$) and DunedinPACE ($\beta = -0.12$, $q = 0.010$) clocks. CSA was also associated with lower levels of interleukin-6 (IL-6; $\beta = -0.11$, $q = 0.010$). No significant associations were observed for urinary cortisol, cortisone, or catecholamines.
Conclusion: Sustained social advantage is associated with more favorable biological aging profiles, including slower epigenetic aging and reduced inflammatory signaling. These findings add to growing evidence that social resources are embedded in the physiological pathways that shape aging and health.

1. Introduction

Social relationships are robust determinants of health, functional capacity, and longevity, with strong and supportive networks linked to lower risks of morbidity and mortality, enhanced immune function, and improved cognitive outcomes (Holt-Lunstad et al., 2010; Yang et al., 2016). Yet access to these relational resources is unevenly distributed, and advantages tend to accumulate over time, contributing to widening health disparities across the life course (Crystal et al., 2017; Ferraro and Shippee, 2009). Cumulative advantage theory offers a framework for understanding these disparities, proposing that social resources cluster and compound over time and are associated with increasingly divergent trajectories of health and aging (Dannefer, 2003; DiPrete and Eirich, 2006).

Building on this framework, we conceptualize cumulative social advantage[1] (CSA) as a multidimensional construct reflecting sustained access to social resources across four domains: family relationships, religious involvement, emotional support, and community engagement. Prior research has often examined individual social indicators—such as marital status or network size—in isolation (Holt-Lunstad, 2018; Yang et al., 2016). By contrast, CSA captures the breadth, persistence, and co-occurrence of social connection across multiple contexts. This construct has been empirically validated and linked to lower multimorbidity, better functional health, and reduced mortality risk (Ong and Mann, 2025). Here, we extend this work by testing whether CSA is associated with biological aging, conceptualized as the progressive decline in molecular and physiological systems integrity. Drawing on the concept of biological embedding (Hertzman, 2012), we hypothesize that sustained social advantage becomes reflected in core regulatory systems linked to aging, including epigenetic, inflammatory, and neuroendocrine pathways.

Epigenetic aging, measured by DNA methylation clocks such as

* Corresponding author. Department of Psychology, Cornell University, Ithaca, NY, 14853-4401, USA.
E-mail address: anthony.ong@cornell.edu (A.D. Ong).

[1] Following cumulative advantage theory (Dannefer, 2003) and our recent empirical validation (Ong and Mann, 2025), we use "advantage" to emphasize that social relationships function as stratified resources that accumulate and compound over time, distinct from but parallel to socioeconomic stratification.

https://doi.org/10.1016/j.bbih.2025.101096
Received 29 August 2025; Accepted 30 August 2025
Available online 3 September 2025

GrimAge and DunedinPACE, captures cumulative molecular changes predictive of morbidity and mortality, and is sensitive to social adversity and relationship quality (Belsky et al., 2020; Horvath and Raj, 2018; Raffington and Belsky, 2022; Rentscher et al., 2023). Chronic low-grade inflammation ("inflammaging"), indexed by circulating cytokines and adhesion molecules such as IL-6 and TNF-α, contributes to cardiovascular, metabolic, and neurodegenerative disease and is shaped by social-environmental exposures (Franceschi and Campisi, 2014). Neuroendocrine function, assessed via overnight urinary concentrations of cortisol, cortisone, and catecholamines, reflects integrated hypothalamic–pituitary–adrenal and sympathetic–adrenomedullary activity—systems highly responsive to psychosocial contexts (Hostinar et al., 2014; Oster et al., 2016).

Our conceptual model integrates life course theory (Elder et al., 2003), which emphasizes the cumulative accrual of relational resources; the weathering hypothesis (Forde et al., 2019; Geronimus, 1992), which describes how these accumulated resources are reflected in biological markers through differential wear and tear on stress-responsive systems; and the stress-buffering model (Cohen and Wills, 1985; Hostinar et al., 2014), which posits that social resources attenuate physiological stress responses. Together, these perspectives predict that CSA should relate most strongly to biomarkers reflecting cumulative biological burden—such as DNA methylation–based aging indices and chronic inflammatory markers—rather than short-term activation markers (e.g., urinary catecholamines, cortisol). Using data from the Midlife in the United States (MIDUS) study, a large national cohort with extensive psychosocial and biomarker data, we model CSA as a higher-order latent factor derived from 16 validated indicators, testing its associations with epigenetic aging, systemic inflammation, and neuroendocrine function.

2. Methods

2.1. Transparency and openness

This study used publicly available data from the Midlife in the United States (MIDUS) project. All survey instruments, codebooks, and documentation are accessible via the MIDUS Colectica Portal (https://midus.colectica.org/). Analytic code is available from the corresponding author upon request. This work adheres to Level 2 of the American Psychological Association's Transparency and Openness Promotion (TOP) Guidelines.

2.2. Participants and procedures

Data were drawn from two MIDUS biomarker cohorts: MIDUS-II (2004–2005) and the MIDUS Refresher (2011–2014), which include identical assessments of psychosocial, demographic, and biological characteristics (Love et al., 2010). MIDUS-II participants were recruited during a period of economic stability, while the Refresher cohort was enrolled following the 2008–2009 financial crisis. The analytic sample comprised 2117 adults with biomarker data. Participants were 55 % female, with a mean age of 55.07 years (SD = 12.71), and approximately 75 % identified as White. All participants provided written informed consent, and study protocols were approved by institutional review boards at each participating institution.

2.3. Measures

Cumulative Social Advantage (CSA). Cumulative Social Advantage (CSA) was modeled as a second-order latent construct reflecting concurrent access to social resources across four theoretically grounded domains: (1) religious and faith-based support (Ellison and George, 1994). (2) parent-child relationship quality (Eisenberg et al., 2015), (3) community engagement (Berkman et al., 2000), and (4) extended emotional support (Cohen and Wills, 1985). Sixteen self-report indicators were selected based on prior evidence of measurement invariance and structural validity across sociodemographic groups (Ong and Mann, 2025).

Religious and faith-based support was measured using three scales: religious identification (e.g., "How important is religion in your life?"), religious practice (e.g., "How often do you read the Bible or other religious literature"), and religious coping (e.g., "When you have problems or difficulties in your family, work, or personal life, how often do you seek comfort through religious or spiritual means such as praying, meditating, attending a religious or spiritual service, or talking to a religious or spiritual advisor?"). Parent-child relationship quality included four retrospective assessments: maternal warmth (e.g., "How much affection did she give you?"), maternal generosity (e.g., "How generous and helpful was she to people outside the family?"), paternal warmth (e.g., "How much time and attention did he give you when you needed it?"), and paternal generosity (e.g., "How sociable and friendly was he to people outside the family?").

Community engagement was assessed using six scales reflecting both attitudinal and relational dimensions: social integration (e.g., "I feel close to other people in my community"), social actualization (e.g., "The world is becoming a better place for everyone"), social contribution (e.g., "I have something valuable to give to the world"), social acceptance (e.g., "I believe that people are kind"), friendship support (e.g., "How much can you open up to them if you need to talk about your worries?"), and positive relations with others (e.g., "I enjoy personal and mutual conversations with family members and friends"). Finally, extended emotional support was indexed by the number of hours per month participants reported receiving emotional support from parents, children, and other kin or friends. These responses were categorized into eight ordinal bins to minimize the potential leverage of large values and help normalize distributional skew.

In prior work, the CSA construct was conceptualized as a higher-order latent factor capturing the life-course accumulation of social connection and relational resources, indicated by two temporally anchored domains: (a) retrospective indicators of early parental relationship quality that shape social competencies and internal working models, and (b) contemporary indicators of adult relational embeddedness and resources (Ong and Mann, 2025). . This specification is theoretically grounded in cumulative advantage (Dannefer, 2003) and life-course perspectives on linked lives and developmental scaffolding (Elder et al., 2003) and aligns with attachment-based evidence that early caregiving organizes the acquisition and maintenance of adult relationships (Fraley et al., 2013; Ong and Mann, 2025). Modeling childhood and adult indicators within a single latent construct, thus, permits estimation of the combined influence of past and present embeddedness on profiles of biological aging.

Epigenetic Aging Clocks. Biological aging was assessed using whole-blood DNA methylation data processed through a panel of seven validated epigenetic clocks. These algorithms estimate either chronological age or the rate of physiological aging by modeling methylation levels at specific cytosine–phosphate–guanine (CpG) sites.

The Horvath clock (Horvath, 2013) is a widely used cross-tissue predictor based on 353 CpGs and was trained to estimate chronological age across multiple cell types. Horvath2 (Horvath and Raj, 2018) updates this model using 391 CpGs optimized for blood and skin-derived samples, improving precision in those tissues. The Hannum clock (Hannum et al., 2013) is specific to whole-blood methylation and includes 71 CpGs selected from adult cohorts.

To evaluate aging phenotypes more directly linked to morbidity risk, we included three health-optimized clocks. PhenoAge (Levine et al., 2018) is derived from 513 CpGs weighted against a composite of clinical biomarkers (e.g., glucose, albumin, C-reactive protein) predictive of mortality and chronic disease. GrimAge (Lu et al., 2019, 2022) incorporates DNA methylation-based surrogates for plasma proteins and cumulative smoking exposure to estimate time-to-death. Three versions were used: the original GrimAge, a re-implementation using the GrimAge2 framework, and an extended variant incorporating

methylation-based proxies for C-reactive protein and glycated hemoglobin. These clocks have demonstrated high prognostic value and are increasingly employed to investigate the biological embedding of social and environmental conditions. Finally, DunedinPACE (Belsky et al., 2020) was included as a dynamic measure of biological aging rate. Unlike the other clocks, DunedinPACE estimates the *pace* of physiological decline by leveraging longitudinal methylation change, providing a temporal index of aging trajectory rather than a static age estimate.

Serum-Based Markers of Inflammation. Systemic inflammation was assessed using eight serum biomarkers indexing key components of immune activation, including cytokine signaling, endothelial function, and acute-phase response. All biomarkers were assayed in duplicate, with intra- and inter-assay coefficients of variation maintained below 10 %. To address non-normal distributions, values were natural log-transformed prior to analysis.

Soluble E-Selectin and intercellular adhesion molecule-1 (ICAM-1) were measured as indicators of vascular inflammation (Shapiro et al., 2010; Wayne Smith, 1997). C-reactive protein (CRP), a prototypic acute-phase reactant, was assayed using a particle-enhanced immunonephelometric method (BN II platform), enabling high-sensitivity detection of low-grade systemic inflammation (Sin et al., 2015). Interleukin-6 (IL-6), a central pro-inflammatory cytokine, was quantified via two analytic platforms: high-sensitivity ELISA and electrochemiluminescent multiplex assay (Meso Scale Discovery). Additional cytokines measured on the MSD platform included interleukin-8 (IL-8), a neutrophil chemoattractant involved in acute immune response; interleukin-10 (IL-10), an anti-inflammatory regulatory cytokine with immunoregulatory properties; and tumor necrosis factor-alpha (TNF-α), a key upstream activator of NF-κB–mediated inflammatory signaling (Hartanto et al., 2021). This biomarker panel provides a comprehensive profile of inflammatory activity relevant to aging and social-environmental exposures.

Urinalysis of Neuroendocrine Function. Neuroendocrine function was evaluated using overnight urine collection (~19:00 to 07:00), providing a cumulative hormonal output index over the sleep interval. This sampling window minimizes diurnal fluctuation and yields a stable index of HPA and SAM system activation. Cortisol and its metabolite cortisone were quantified via competitive radioimmunoassay following organic solvent extraction. Elevated concentrations reflect greater HPA axis activation. Catecholamines—norepinephrine, epinephrine, and dopamine—were measured using high-performance liquid chromatography with electrochemical detection, indexing SAM system activity over a 12-h interval. To account for variability in urine volume, catecholamine concentrations were normalized to total 12-h excretion mass. All hormone values were natural log–transformed prior to analysis to correct for right-skewed distributions.

Covariates. All models adjusted for demographic and socioeconomic variables selected *a priori* for their potential to confound associations between CSA and biological aging indicators. Covariates included age (in years), sex (male vs. female), race/ethnicity (White, Black, Other), educational attainment (12-point ordinal scale), and log-transformed current household income (USD). These variables were treated as exogenous predictors—assumed to temporally precede both CSA and biological outcomes—and were included to block potential backdoor paths and minimize bias.

Each covariate is theoretically and empirically linked to both social and biological processes. Age is a primary determinant of both social network dynamics and physiological aging, influencing immunosenescence and inflammatory profiles (Franceschi and Campisi, 2014). Sex shapes patterns of social interaction and is associated with baseline differences in glucocorticoid and cytokine levels, likely mediated by hormonal and genetic mechanisms (Klein and Flanagan, 2016). Race and ethnicity capture exposure to cumulative structural disadvantage—such as systemic discrimination and unequal access to healthcare—which influence both social opportunity and stress physiology (Geronimus, 1992). Educational attainment and income reflect stratified access to material and psychosocial resources that affect both health behavior and biological risk processes (Adler and Newman, 2002). Treating these covariates as exogenous minimizes bias due to confounding while avoiding over-adjustment for potential mediators or introducing collider bias (Schisterman et al., 2009).

2.4. Statistical analysis

Hypotheses were tested using structural equation modeling (SEM) implemented in the R package lavaan (Rosseel, 2012), which allows for simultaneous estimation of latent constructs and their associations with multiple observed outcomes. This approach is well-suited to modeling CSA as a second-order construct and testing its multivariate associations with biomarkers.

Measurement Model. First, a higher-order confirmatory factor analysis (CFA) was conducted to validate the hypothesized structure of CSA. Four first-order latent domains—religious and faith-based support, community engagement, parent-child relationship quality, and extended emotional support—were each estimated from their respective observed indicators. These domain-specific factors were then modeled to load onto a second-order latent construct representing CSA. Cross-loadings and inter-factor covariances were constrained to zero to impose a strictly hierarchical model, while residual covariances among theoretically related indicators were freely estimated (cf., Ong and Mann, 2025).

Structural Model. In the structural phase, each biological outcome variable was regressed on the second-order CSA construct, adjusting for a set of eight exogenous covariates: centered linear and quadratic age terms, sex (0 = female, 1 = male), race/ethnicity (dummy-coded for Black and Other; White as reference), educational attainment (12-point scale), log-transformed household income (USD), and cohort (0 = MIDUS-II, 1 = MIDUS Refresher). Models were clustered at the family level to accommodate non-independence due to shared family IDs, and a robust sandwich estimator was used for the sampling covariance matrix. Estimation was performed using the robust maximum likelihood (MLR) estimator, which yields standard errors and fit indices robust to non-normality and unbalanced cluster sizes. Missing data were addressed using Full Information Maximum Likelihood (FIML), and all exogenous covariates were freely intercorrelated to fully specify their joint distribution.

Multiple Comparison Correction. To address multiple testing, we controlled the false discovery rate (FDR) across all 24 tests using the Benjamini–Hochberg (BH) procedure and report BH-adjusted p-values (q-values) (Benjamini and Hochberg, 1995). Coefficients with $q < 0.05$ were deemed statistically significant, and for these we report false coverage rate (FCR)-adjusted, BH-selected confidence intervals (Benjamini and Yekutieli, 2005). For coefficients with $q > 0.05$, we display BH-ordered confidence intervals $\left(\beta_k \pm z_{[1-\alpha_k/2]} \times SE_k\right)$ by ranking p-values across all tests and setting $\alpha_k = \left(\frac{k}{m}\right) \times 0.05$, where $m = 24$ (the total number of tests) and k is the rank of the p-value.

3. Results

3.1. Descriptive statistics and Measurement Model

Descriptive statistics for sample characteristics, CSA indicators, and biomarker outcomes are presented in Tables 1 and 2. Bartlett's test ($\chi 2$ (190) = 12062.75, $p < 0.001$) and the Kaiser-Meyer-Olkin (KMO) test (0.77) revealed that the CSA indicators were suitable for factor analysis. Internal consistency across the 16 items was acceptable ($\alpha = 0.75$; $\omega = 0.82$), and confirmatory factor analysis (CFA) supported the proposed hierarchical structure. Model fit indices indicated strong global fit ($\chi^2(90) = 363.31$, *CFI* = 0.97, *TLI* = 0.96, *RMSEA* = 0.038 [90 % *CI* = 0.034, 0.042], *SRMR* = 0.040).

Table 1
Sample characteristics.

Characteristic	$n = 2117$
Age (years)	55.07 (12.71)
Sex	
Female	1162 (55 %)
Male	954 (45 %)
Missing	1(<0.1 %)
Race	
White	1591 (75 %)
Black	375 (18 %)
Native American	39 (1.9 %)
Asian	15 (0.7 %)
Pacific Islander	2 (<0.1 %)
Other	86 (4.1 %)
Missing	9 (<0.1 %)
Level of Education	
Grades 1-6	2 (<0.1 %)
Junior High School	17 (0.8 %)
Some High School	88 (4.2 %)
GED	31 (1.5 %)
High School Diploma	360 (17 %)
1–2 Years College	354 (17 %)
3–4 Years College	98 (4.6 %)
Associate's Degree	186 (8.8 %)
Bachelor's Degree	465 (22 %)
Some Graduate School	79 (3.7 %)
Master's Degree	336 (16 %)
Doctoral Degree	97 (4.6 %)
Missing	4 (<0.1 %)
Annual Household Income (USD)	75,671 (61,964)
Missing	49 (2.31 %)

Notes. Means and standard deviations or frequencies and percentages are reported.

Table 3 displays standardized loadings for the second-order structure, including both: (1) the loadings of the higher-order CSA factor onto its four first-order domains, and (2) the loadings of those domains onto their constituent indicators. All direct and indirect loadings were significant after FDR correction ($q < 0.001$). Fig. 1 presents the proportion of variance each observed indicator contributed to the CSA construct. Indicators related to communal integration emerged as the most empirically salient, including social integration (18.5 %), positive relations with others (10.5 %), and social contribution (9.7 %). Additional contributors included social acceptance (7.7 %), paternal generosity (7.2 %), religious coping (6.9 %), and religious practice (6.8 %). Together, these findings validate the multidimensional structure of CSA while underscoring that communal, relational, and religious forms of engagement play a central role in defining the construct.

3.2. Socioeconomic covariates and biomarker outcomes

Covariate associations with biomarker outcomes are presented in Fig. 2, which depicts a heat map of standardized regression coefficients across the full biological panel. Age was the most robust and consistent correlate, showing significant positive associations with nearly all measures of epigenetic aging and inflammation ($q < 0.001$), including DunedinPACE, both GrimAge clocks, IL-6 (both assays), IL-8, and TNF-α. Quadratic age terms captured modest curvilinear effects, suggesting potential deceleration of epigenetic aging in later midlife.

Clear socioeconomic gradients also emerged. Higher educational attainment was associated with lower systemic inflammation and slower epigenetic aging, with multiple associations surviving FDR correction ($q < 0.01$ or $q < 0.001$). Fewer associations were observed for household income, which showed smaller and less consistent effects. Racial disparities were pronounced: Black participants exhibited accelerated epigenetic aging and elevated inflammatory activity, particularly for IL-6, TNF-α, and GrimAge, relative to White participants. Participants categorized as "Other race" showed smaller, more heterogeneous effects. Sex differences generally favored women in epigenetic and neuroendocrine measures, although CRP levels were higher among women. Cohort differences between MIDUS-II and the Refresher sample were minimal after covariate adjustment.

3.3. Associations between CSA and biomarkers

Fig. 3 summarizes associations between CSA and 24 biomarkers spanning three domains: epigenetic aging, systemic inflammation, and neuroendocrine function. Higher CSA was consistently associated with more favorable biological profiles, though effect sizes varied. In the epigenetic domain, all seven DNA methylation clocks showed negative associations with CSA (β range ≈ −0.01 to −0.12), indicating slower molecular aging among more socially advantaged individuals. GrimAge (both generations) and DunedinPACE demonstrated the strongest and most consistent effects, remaining significant after FDR correction ($q < 0.001$ and $q = 0.010$, respectively).

A similar pattern emerged for systemic inflammation, with CSA showing negative associations across all cytokines and vascular adhesion markers (β ≈ −0.01 to −0.11). IL-6, assayed via two platforms, showed the most robust association with CSA and remained significant after FDR correction ($q < 0.05$). IL-10 and E-Selectin yielded non-significant associations, with confidence intervals overlapping zero and FDR-adjusted q-values >0.10.

In the neuroendocrine domain, CSA was unrelated to all five overnight urinary markers—cortisol, cortisone, norepinephrine, epinephrine, and dopamine. Effect sizes were small, and FDR-adjusted 95 % confidence intervals encompassed the null for each marker. These findings suggest that CSA showed no significant associations with neuroendocrine function as indexed by overnight urinary markers, in contrast to its more robust associations with inflammatory and epigenetic markers of longer-term physiological regulation.

4. Discussion

This study provides evidence that cumulative social advantage (CSA)—operationalized as a multidimensional latent construct—is associated with slower biological aging and reduced systemic inflammation. Drawing on a large, population-based cohort and a comprehensive panel of molecular, immunological, and neuroendocrine biomarkers, the findings extend the literature on the biological embedding of social conditions (Hertzman, 2012) by demonstrating consistent links between sustained social resources and physiological systems central to aging. Viewed through the lenses of life course (Elder et al., 2003), weathering (Geronimus, 1992), and stress buffering perspectives (Cohen and Wills, 1985), the results suggest that accumulated social resources may be associated with sustained health benefits, potentially reflected in biological processes that evolve over years or decades. This integrative framework provides a foundation for interpreting the domain-specific patterns observed in the present analyses and for refining mechanistic hypotheses about how social advantage becomes embedded in the body.

4.1. CSA and epigenetic aging

The strongest and most consistent associations were observed in the epigenetic domain. Higher CSA was significantly linked to slower biological aging as indexed by both generations of GrimAge and by DunedinPACE—epigenetic clocks designed to capture mortality risk and the pace of biological aging (Belsky et al., 2020; Lu et al., 2019). These findings build on prior work suggesting that relationship quality and social support predict DNA methylation-based aging acceleration (Raffington and Belsky, 2022; Rentscher et al., 2023). Notably, the DunedinPACE results suggest that CSA may be associated with differences in the accumulated biological burden and the tempo at which molecular aging unfolds. The pattern is consistent with models positing that social environments regulate the methylome through sustained

Table 2
Descriptive statistics for focal study variables.

Variable	*n*	*M*	*Median*	*SD*	*Min*	*Max*	*Skew*
Indicators of CSA							
Religious Identification	2103	19.37	20.00	6.04	7.00	28	−0.44
Religious Practice	2099	9.78	10.00	4.47	3.00	18	0.13
Religious Coping	2092	5.60	6.00	2.17	2.00	8	−0.45
Social Integration	2100	14.57	15.00	4.10	3.00	21	−0.49
Social Actualization	2099	12.53	13.00	4.07	3.00	21	−0.13
Social Contribution	2100	16.22	17.00	3.53	3.00	21	−0.61
Social Acceptance	2099	13.71	14.00	3.48	3.00	21	−0.30
Friendship Support	2097	3.28	3.50	0.68	1.00	4	−0.94
Positive Relations	2108	39.99	42.00	7.28	7.00	49	−0.77
Maternal Affection	1854	3.08	3.29	0.72	0.86	4	−0.81
Paternal Affection	1718	2.70	2.75	0.80	0.75	4	−0.28
Maternal Generosity	1853	3.36	3.50	0.72	1.00	4	−1.05
Parental Generosity	1714	3.23	3.50	0.81	1.00	4	−0.83
Emotional Support - Child	2048	1.04	1.00	1.49	0.00	7	2.34
Emotional Support - Other	2057	1.01	1.00	1.11	0.00	7	2.70
Emotional Support - Parent	2053	0.63	0.00	1.13	0.00	7	3.24
Plasma Assays							
IL6	2094	0.77	0.74	0.77	−2.15	3.14	0.10
IL6 (MSD)	2092	−0.16	−0.22	0.69	−2.81	4.98	0.99
IL8	2092	2.47	2.46	0.46	0.97	5.85	0.97
IL10	2092	−1.40	−1.47	0.64	−3.91	4.72	2.17
CRP	2083	0.38	0.31	1.20	−3.94	4.37	0.09
TNF-a	2092	0.72	0.70	0.35	−1.17	3.67	0.69
E-Selectin	2093	3.63	3.65	0.51	−2.41	5.18	−1.08
ICAM-1	2093	5.55	5.57	0.42	1.03	8.11	−1.03
DNA Methylation Clocks							
Horvath	1309	55.46	55.60	11.12	25.34	107.27	0.06
Horvath2	1309	51.90	52.34	12.44	18.82	98.38	−0.10
Hannum	1309	42.43	42.35	11.46	14.01	110.44	0.28
PhenoAge	1309	43.63	43.61	13.00	10.27	85.01	0.00
GrimAge (1st gen)	1309	52.64	52.79	11.13	22.50	104.59	0.07
GrimAge (2nd gen)	1308	62.67	62.39	10.74	33.01	94.14	0.04
GrimAge (1st gen v2)	1308	57.09	57.07	10.94	29.74	90.01	0.06
DunedinPACE	1309	0.99	0.98	0.14	0.53	1.45	0.30
Urine Assays							
Cortisol	2101	0.05	0.23	0.90	−3.96	3.66	−1.11
Cortisone	2107	1.05	1.09	0.64	−2.30	3.78	−0.53
Norepinephrine	2116	0.54	0.53	0.84	−3.51	4.90	0.48
Epinephrine	2070	−1.85	−1.93	1.05	−6.21	3.18	0.48
Dopamine	2101	2.10	2.14	0.84	−2.81	5.20	−0.69
Norepinephrine (12 h)	2041	2.78	2.79	0.67	−1.16	6.10	−0.34
Epinephrine (12 h)	2077	0.64	0.42	1.15	−2.30	5.32	1.53
Dopamine (12 h)	2027	4.37	4.45	0.74	−0.98	9.19	−0.52

Notes. *n* = number of observations. *M* = mean. *SD* = standard deviation. *Min* = minimum observed value. *Max* = Maximum observed value. Serum and urine assay values were log transformed to correct positive skew.

modulation of stress and immune-related pathways (Epel and Prather, 2018; Horvath and Raj, 2018).

4.2. CSA and immune aging

CSA was also associated with lower concentrations of interleukin-6 (IL-6), a pro-inflammatory cytokine centrally implicated in chronic disease risk and mortality (Franceschi and Campisi, 2014). Although other inflammatory markers showed similar trends, IL-6 yielded the most consistent and statistically robust association after FDR correction. These findings align with evidence linking higher levels of social integration to attenuated inflammatory activity (Holt-Lunstad, 2018; Yang et al., 2016). Given that chronic low-grade inflammation—or "inflammaging"—is a key mechanism linking psychosocial adversity to aging-related disease (Franceschi and Campisi, 2014), the results suggest that CSA may be associated with more favorable long-term immunoregulatory profiles.

4.3. CSA and neuroendocrine function

By contrast, CSA showed no significant associations with neuroendocrine function as indexed by overnight urinary cortisol, cortisone, or catecholamines. These null findings may reflect limitations in measurement sensitivity. HPA and SAM axis outputs are characterized by high intraindividual variability and marked circadian dynamics—features that are only partially captured through integrated overnight sampling (Oster et al., 2016). It is also plausible that CSA may be related to stress-related biology primarily through slower-acting regulatory systems—such as epigenetic and inflammatory processes—rather than transient endocrine fluctuations. To resolve these dynamics, future research should leverage high-frequency designs (e.g., diurnal cortisol profiling, ecological momentary assessment) capable of capturing within-day hormonal variability in response to social exposure.

5. Limitations and future directions

Several limitations merit consideration. First, the cross-sectional design limits causal inference. Although both CSA and biomarker data were drawn from MIDUS Wave 2, CSA measures were collected during the initial survey phase, and biomarker assessments occurred later during separate clinic visits, providing modest temporal separation between predictor and outcome. This sequencing offers some protection against simultaneity bias, yet reverse causality remains possible—for example, individuals in poorer health may withdraw from social

Table 3
Standardized estimates from the higher-order factor model of cumulative social advantage.

Factor	Indicator	λ (*CI*)	Indirect λ on GF (*CI*)
GF	F1	0.38 (0.27, 0.49)	
	F2	0.66 (0.52, 0.80)	
	F3	0.45 (0.36, 0.55)	
	F4	0.24 (0.15, 0.34)	
F1	Religious Identification	0.79 (0.76, 0.82)	0.30 (0.23, 0.37)
	Religious Practice	0.87 (0.85, 0.89)	0.33 (0.26, 0.41)
	Religious Coping	0.88 (0.86, 0.89)	0.33 (0.26, 0.41)
F2	Social Actualization	0.36 (0.29, 0.44)	0.24 (0.18, 0.30)
	Friendship Support	0.46 (0.41, 0.50)	0.30 (0.24, 0.37)
	Social Acceptance	0.54 (0.49, 0.58)	0.35 (0.28, 0.42)
	Social Contribution	0.60 (0.56, 0.65)	0.40 (0.32, 0.48)
	Positive Relations	0.62 (0.59, 0.66)	0.41 (0.33, 0.50)
	Social Integration	0.83 (0.78, 0.87)	0.55 (0.45, 0.65)
F3	Maternal Generosity	0.41 (0.35, 0.47)	0.19 (0.14, 0.23)
	Maternal Affection	0.66 (0.57, 0.75)	0.30 (0.24, 0.36)
	Paternal Affection	0.70 (0.64, 0.76)	0.32 (0.25, 0.39)
	Paternal Generosity	0.75 (0.69, 0.80)	0.34 (0.28, 0.40)
F4	Emotional Support - Parent	0.33 (0.24, 0.43)	0.08 (0.04, 0.12)
	Emotional Support - Child	0.56 (0.43, 0.69)	0.14 (0.08, 0.19)
	Emotional Support - Other	0.78 (0.65, 0.91)	0.19 (0.12, 0.26)

Notes. λ = standardized factor loading. *CI* = confidence intervals. All direct and indirect loadings are statistically significant after adjustment for FDR (*q*-values <0.001).

relationships. Longitudinal analyses with repeated biomarker assessments, such as those available in future MIDUS Refresher waves, will be essential for establishing temporal precedence and testing mediation pathways.

In addition, even with extensive covariate adjustment, residual confounding is a concern. Unmeasured variables—such as early-life adversity, environmental exposures, or genetic predispositions—could shape both social conditions and biological aging (Adler and Newman, 2002; Shonkoff et al., 2009). Richer contextual measures in prospective designs will help address these sources of bias and clarify the mechanisms linking CSA to biological outcomes.

A separate limitation concerns the measurement structure of CSA. Although the second-order model demonstrated good fit, variance decomposition indicated that communal and relational indicators—particularly social integration, social contribution, and positive relations with others—accounted for most of the variance, whereas dyadic emotional support from parents and children contributed comparatively little. This asymmetry suggests that CSA, as operationalized here, disproportionately reflects individual differences in communal embeddedness rather than interpersonal intimacy. Disaggregating CSA into its constituent domains in future work could reveal domain-specific associations with biological aging (Rentscher et al., 2023; Uchino, 2009).

Measurement constraints also extend to the neuroendocrine outcomes. The use of overnight urine collection, while practical for large-scale field studies, lacks the temporal resolution to capture dynamic hormonal patterns. More intensive protocols, such as serial saliva sampling or ambulatory hormone monitoring, may yield a clearer picture of how social advantage shapes endocrine regulation (Oster et al., 2016; Hostinar et al., 2014). Likewise, although the observed pattern of associations is consistent with stress-buffering mechanisms operating over longer timescales, the absence of direct measures of stress exposure and reactivity limits our ability to assess these processes explicitly. Incorporating such measures into longitudinal designs will be important for identifying the specific contexts in which CSA is most strongly associated with indicators of physiological protection.

6. Conclusion

Cumulative social advantage emerges as a consistent and multidimensional predictor of more favorable biological aging profiles, including reduced systemic inflammation and decelerated epigenetic aging. These findings support the hypothesis that sustained access to

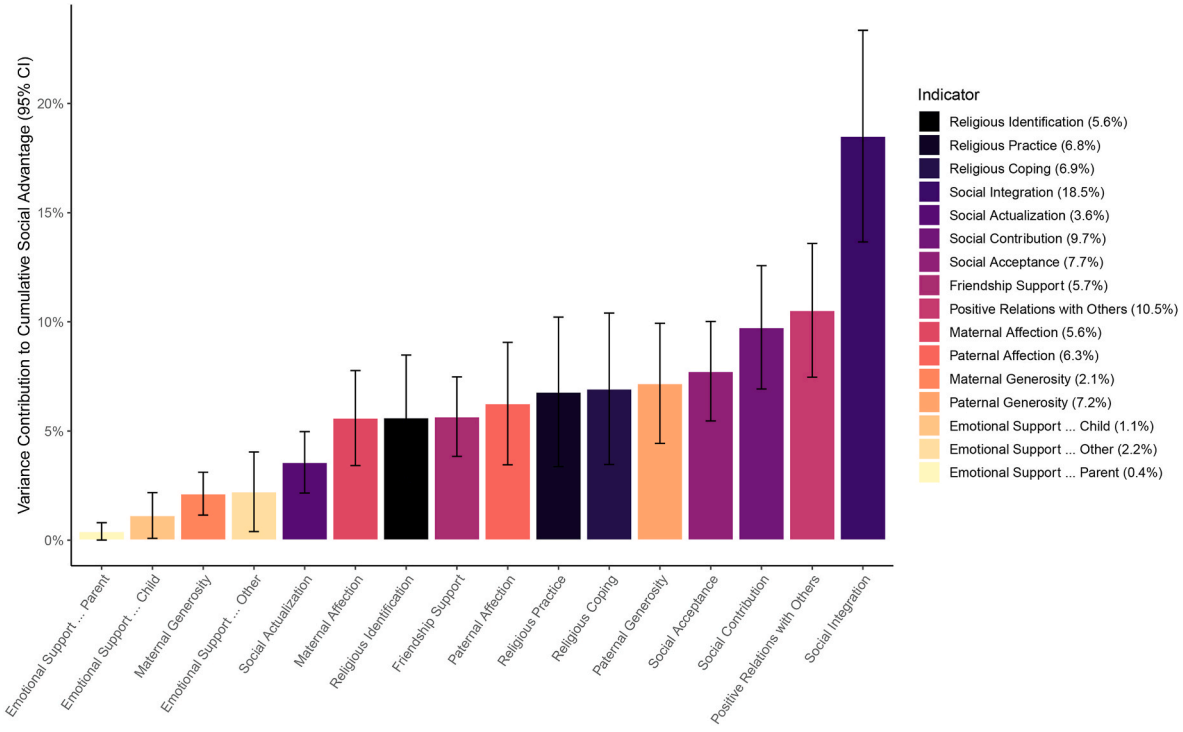


Fig. 1. Variance Contributions to Cumulative Social Advantage.
Notes. Each bar denotes the variance contribution (y-axis) of the observed indicator (x-axis) to the latent CSA factor variance. Vertical bars denote confidence intervals.

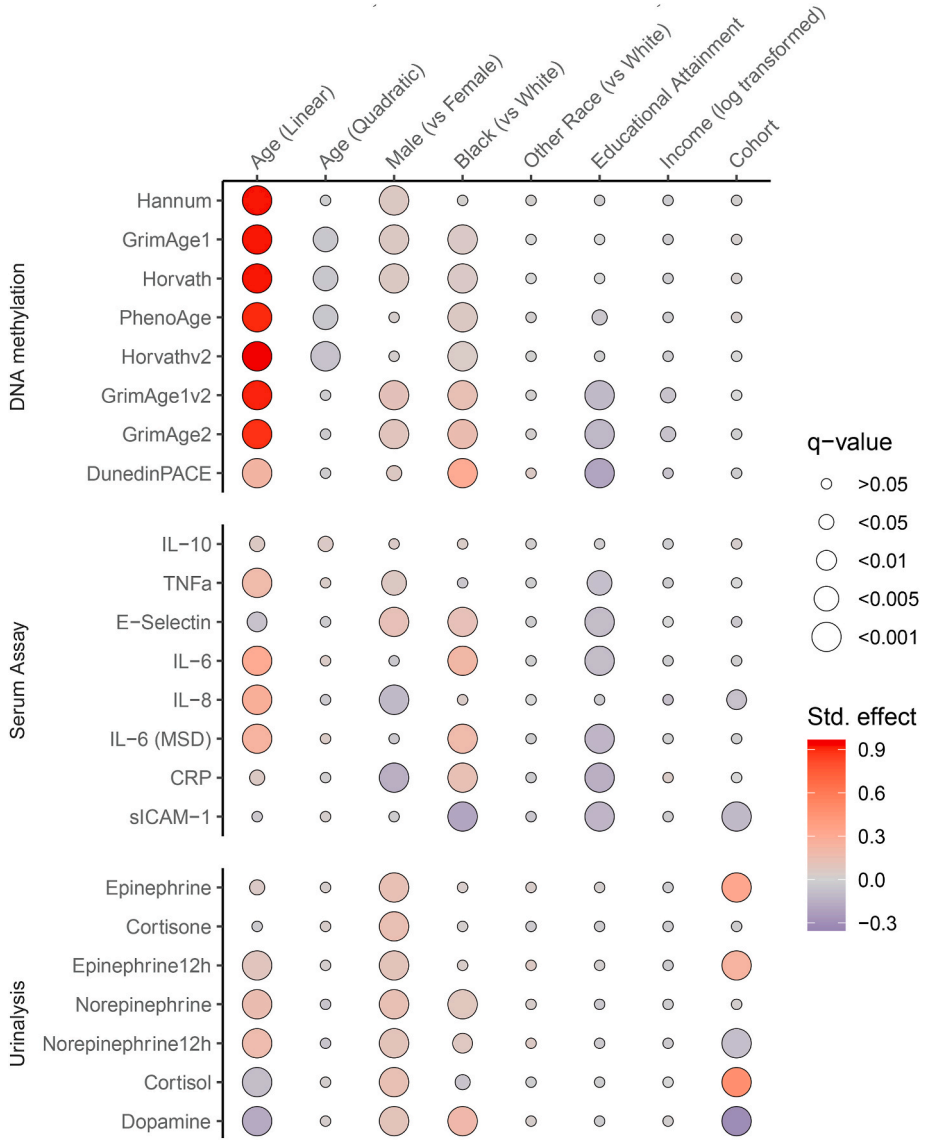


Fig. 2. Heat Map of Demographics, Socioeconomic Variables, and Biomarkers

Notes. Standardized associations between sociodemographic characteristics and biomarkers of systemic inflammation, stress physiology, and biological aging. Each circle reflects a regression coefficient from multivariate models predicting biomarker levels (rows) from sociodemographic predictors (columns), adjusted for covariates. Color hue indicates direction (blue = negative; red = positive) and color saturation reflects strength of the association (darker = stronger). Circle size denotes FDR-adjusted significance thresholds. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

diverse social resources is embedded in physiological systems that govern the pace of biological aging. By integrating theoretically grounded measures of social conditions with robust molecular and immunological biomarkers, this study advances understanding of how social advantage is associated with biological resilience. Future research should prioritize longitudinal and mechanistic designs to clarify how distinct dimensions of social integration influence the molecular architecture of aging and identify pathways amenable to intervention.

CRediT authorship contribution statement

Anthony D. Ong: Conceptualization, Writing – original draft, Writing – review & editing. **Frank D. Mann:** Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Laura D. Kubzansky:** Writing – review & editing.

Author note

This research was supported, in part, by Grant P01-AG020166 from the National Institute on Aging to conduct a longitudinal follow-up of the MIDUS (Midlife in the United States) investigation. The original study was supported by the John D. and Catherine T. MacArthur Foundation Research Network on Successful Midlife Development.

Funding

The Midlife in the United States (MIDUS I) Study was supported by the John D. and Catherine T. MacArthur Foundation Research Network on Successful Midlife Development. The MIDUS II research was supported by a grant from the National Institute on Aging (P01-AG020166) to conduct a longitudinal follow-up of the MIDUS I investigation.

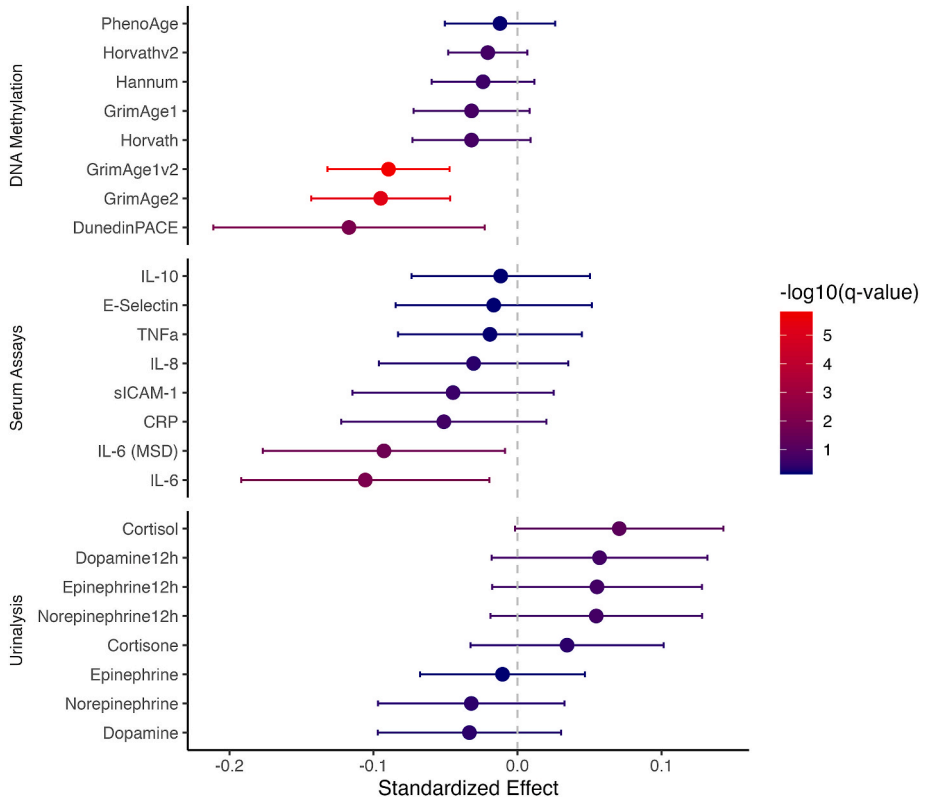


Fig. 3. Forest Plot of Biomarkers for Cumulative Social Advantage

Notes. Circles denote standardized regression coefficients; horizontal lines indicate confidence intervals. Circle color reflects the strength of statistical evidence, with shading scaled to the $\log_{10}$-transformed FDR-adjusted *p*-values (*q*-values). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Declaration of competing interest

The authors declare that they have no conflict of interest.

References

Adler, N.E., Newman, K., 2002. Socioeconomic disparities in health: pathways and policies. Health Aff. 21 (2), 60–76. https://doi.org/10.1377/hlthaff.21.2.60.

Belsky, D.W., Caspi, A., Arseneault, L., Baccarelli, A., Corcoran, D.L., Gao, X., Hannon, E., Harrington, H.L., Rasmussen, L.J., Houts, R., Huffman, K., Kraus, W.E., Kwon, D., Mill, J., Pieper, C.F., Prinz, J.A., Poulton, R., Schwartz, J., Sugden, K., et al., 2020. Quantification of the pace of biological aging in humans through a blood test, the DunedinPoAm DNA methylation algorithm. eLife 9, e54870. https://doi.org/10.7554/eLife.54870.

Benjamini, Y., Yekutieli, D., 2005. False discovery rate–adjusted multiple confidence intervals for selected parameters. J. Am. Stat. Assoc. 100 (469), 71–81. https://doi.org/10.1198/016214504000001907.

Berkman, L.F., Glass, T., Brissette, I., Seeman, T.E., 2000. From social integration to health: Durkheim in the new millennium. Soc. Sci. Med. 51 (6), 843–857. https://doi.org/10.1016/s0277-9536(00)00065-4.

Cohen, S., Wills, T.A., 1985. Stress, social support, and the buffering hypothesis. Psychol. Bull. 98 (2), 310–357. https://doi.org/10.1037/0033-2909.98.2.310.

Crystal, S., Shea, D.G., Reyes, A.M., 2017. Cumulative advantage, cumulative disadvantage, and evolving patterns of late-life inequality | the gerontologist | oxford academic. Gerontol. 57 (5), 910–920.

Dannefer, D., 2003. Cumulative advantage/disadvantage and the life course: cross-fertilizing age and social science theory. J. Gerontol.: Series B 58 (6), S327–S337. https://doi.org/10.1093/geronb/58.6.S327.

DiPrete, T.A., Eirich, G.M., 2006. Cumulative advantage as a mechanism for inequality: a review of theoretical and empirical developments. Annu. Rev. Sociol. 32 (1), 271–297. https://doi.org/10.1146/annurev.soc.32.061604.123127.

Eisenberg, N., Spinrad, T.L., Knafo-Noam, A., 2015. Prosocial development. In: Handbook of Child Psychology and Developmental Science: Socioemotional Processes, seventh ed., vol. 3. John Wiley & Sons, Inc, pp. 610–656. https://doi.org/10.1002/9781118963418.childpsy315.

Elder, G.H., Johnson, M., Crosnoe, R., 2003. The emergence and development of life course theory. In: Handbook of the Life Course, pp. 3–19. https://doi.org/10.1007/978-0-306-48247-2_1.

Ellison, C.G., George, L.K., 1994. Religious involvement, social ties, and social support in a southeastern community. J. Sci. Stud. Relig. 33 (1), 46–61. https://doi.org/10.2307/1386636.

Epel, E.S., Prather, A.A., 2018. Stress, telomeres, and psychopathology: toward a deeper understanding of a triad of early aging. Annu. Rev. Clin. Psychol. 14, 371–397. https://doi.org/10.1146/annurev-clinpsy-032816-045054.

Ferraro, K.F., Shippee, T.P., 2009. Aging and cumulative inequality: how does inequality get under the skin? Gerontol. 49 (3), 333–343. https://doi.org/10.1093/geront/gnp034.

Forde, A.T., Crookes, D.M., Suglia, S.F., Demmer, R.T., 2019. The weathering hypothesis as an explanation for racial disparities in health: a systematic review. Ann. Epidemiol. 33, 1–18. https://doi.org/10.1016/j.annepidem.2019.02.011.

Fraley, R.C., Roisman, G.I., Booth-LaForce, C., Owen, M.T., Holland, A.S., 2013. Interpersonal and genetic origins of adult attachment styles: a longitudinal study from infancy to early adulthood. J. Personality Soc. Psychol. 104 (5), 817–838. https://doi.org/10.1037/a0031435.

Franceschi, C., Campisi, J., 2014. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 69 (Suppl. 1), S4–S9. https://doi.org/10.1093/gerona/glu057.

Geronimus, A.T., 1992. The weathering hypothesis and the health of African-American women and infants: evidence and speculations. Ethn. Dis. 2 (3), 207–221.

Hartanto, A., Majeed, N.M., Ng, W.Q., Chai, C.K.N., Lua, V.Y.Q., 2021. Subjective age and inflammation risk in midlife adults: findings from the midlife in the united states (MIDUS) studies. Comprehensive Psychoneuroendocrinology 7, 100072. https://doi.org/10.1016/j.cpnec.2021.100072.

Hertzman, C., 2012. Putting the concept of biological embedding in historical perspective. Proc. Natl. Acad. Sci. 109, 17160–17167.

Holt-Lunstad, J., 2018. Why social relationships are important for physical health: a systems approach to understanding and modifying risk and protection. Annu. Rev. Psychol. 69 (1), 437–458. https://doi.org/10.1146/annurev-psych-122216-011902.

Holt-Lunstad, J., Smith, T.B., Layton, J.B., 2010. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 7 (7), e1000316. https://doi.org/10.1371/journal.pmed.1000316.

Horvath, S., 2013. DNA methylation age of human tissues and cell types. Genome Biol. 14 (10), 3156. https://doi.org/10.1186/gb-2013-14-10-r115.

Horvath, S., Raj, K., 2018. DNA methylation-based biomarkers and the epigenetic clock theory of ageing. Nat. Rev. Genet. 19, 371–384. https://doi.org/10.1038/s41576-018-0004-3.

Hostinar, C.E., Sullivan, R.M., Gunnar, M.R., 2014. Psychobiological mechanisms underlying the social buffering of the hypothalamic–pituitary–adrenocortical axis: a

review of animal models and human studies across development. Psychol. Bull. 140 (1), 256–282. https://doi.org/10.1037/a0032671.

Klein, S.L., Flanagan, K.L., 2016. Sex differences in immune responses. Nat. Rev. Immunol. 16 (10), 626–638. https://doi.org/10.1038/nri.2016.90.

Levine, M.E., Lu, A.T., Quach, A., Chen, B.H., Assimes, T.L., Bandinelli, S., Hou, L., Baccarelli, A.A., Stewart, J.D., Li, Y., Whitsel, E.A., Wilson, J.G., Reiner, A.P., Aviv, A., Lohman, K., Liu, Y., Ferrucci, L., Horvath, S., 2018. An epigenetic biomarker of aging for lifespan and healthspan. Aging (Albany NY) 10 (4), 573–591. https://doi.org/10.18632/aging.101414.

Love, G.D., Seeman, T.E., Weinstein, M., Ryff, C.D., 2010. Bioindicators in the MIDUS national study: Protocol, measures, sample, and comparative context. Journal of Aging and Health 22 (8), 1059–1080. https://doi.org/10.1177/0898264310374355.

Lu, A.T., Binder, A.M., Zhang, J., Yan, Q., Reiner, A.P., Cox, S.R., Corley, J., Harris, S.E., Kuo, P.-L., Moore, A.Z., Bandinelli, S., Stewart, J.D., Wang, C., Hamlat, E.J., Epel, E. S., Schwartz, J.D., Whitsel, E.A., Correa, A., Ferrucci, L., et al., 2022. DNA methylation GrimAge version 2. Aging (Albany NY) 14 (23), 9484–9549. https://doi.org/10.18632/aging.204434.

Lu, A.T., Quach, A., Wilson, J.G., Reiner, A.P., Aviv, A., Raj, K., Hou, L., Baccarelli, A.A., Li, Y., Stewart, J.D., Whitsel, E.A., Assimes, T.L., Ferrucci, L., Horvath, S., 2019. DNA methylation GrimAge strongly predicts lifespan and healthspan. Aging 11 (2), 303–327. https://doi.org/10.18632/aging.101684.

Ong, A.D., Mann, F.D., 2025. Cumulative social advantage across the lifespan: examining the validity of a multidimensional hierarchical construct for health and longevity. Am. Psychol.doi/10.1037/amp0001513.

Oster, H., Challet, E., Ott, V., Arvat, E., de Kloet, E.R., Dijk, D.-J., Lightman, S., Vgontzas, A., Van Cauter, E., 2016. The functional and clinical significance of the 24-hour rhythm of circulating glucocorticoids. Endocr. Rev. 38 (1), 3–45. https://doi.org/10.1210/er.2015-1080.

Raffington, L., Belsky, D.W., 2022. Integrating dna methylation measures of biological aging into social determinants of health research. Curr. Environ. Health Rep. 9 (2). https://doi.org/10.1007/s40572-022-00338-8. Article 2.

Rentscher, K.E., Klopack, E.T., Crimmins, E.M., Seeman, T.E., Cole, S.W., Carroll, J.E., 2023. Social relationships and epigenetic aging in older adulthood: results from the health and retirement study. Brain Behav. Immun. 114, 349–359. https://doi.org/10.1016/j.bbi.2023.09.001.

Rosseel, Y., 2012. Lavaan: an R package for structural equation modeling. J. Stat. Software 48 (2), 1–36. https://doi.org/10.18637/jss.v048.i02.

Schisterman, E.F., Cole, S.R., Platt, R.W., 2009. Overadjustment bias and unnecessary adjustment in epidemiologic studies. Epidemiology 20 (4), 488–495. https://doi.org/10.1097/EDE.0b013e3181a819a1.

Shapiro, N.I., Schuetz, P., Yano, K., Sorasaki, M., Parikh, S.M., Jones, A.E., Trzeciak, S., Ngo, L., Aird, W.C., 2010. The association of endothelial cell signaling, severity of illness, and organ dysfunction in sepsis. Crit. Care 14 (5), R182. https://doi.org/10.1186/cc9290.

Shonkoff, J.P., Boyce, W.T., McEwen, B.S., 2009. Neuroscience, molecular biology, and the childhood roots of health disparities: building a new framework for health promotion and disease prevention. JAMA 301 (21), 2252–2259. https://doi.org/10.1001/jama.2009.754.

Sin, N.L., Graham-Engeland, J.E., Ong, A.D., Almeida, D.M., 2015. Affective reactivity to daily stressors is associated with elevated inflammation. Health Psychol.: Official Journal of the Division of Health Psychology, American Psychological Association 34 (12), 1154–1165. https://doi.org/10.1037/hea0000240.

Uchino, B., 2009. Understanding the links between social support and physical health: a life-span perspective with emphasis on the separability of perceived and received support. Perspect. Psychol. Sci. 4, 236–255.

Wayne Smith, C., 1997. Potential significance of circulating e-selectin. Circulation 95 (8), 1986–1988. https://doi.org/10.1161/01.CIR.95.8.1986.

Yang, Y.C., Boen, C., Gerken, K., Li, T., Schorpp, K., Harris, K.M., 2016. Social relationships and physiological determinants of longevity across the human life span. Proc. Natl. Acad. Sci. 113 (3), 578–583. https://doi.org/10.1073/pnas.1511085112.