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Assessment of multidimensional measures of aging cross-sectionally and longitudinally across the entire adult age span in the United Kingdom

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Abstract

Background: Aging is a complex process, starting early in life, manifesting across a hierarchy of biological bodily domains with heterogeneity by sex and increasing age. Several molecular and organ-level biological aging measurements have been developed. Reported associations of these measurements with aging-related functional health status are typically limited to cross-sectional research and studies in old people only.

Methods: Using data from UK Household Longitudinal Study, we examined associations between composite biological aging measures (Biological Health Score and DNA methylation algorithms) and grip strength, cognitive function, Short Form 12-item Survey scores, self-rated health cross-sectionally (up to 13 231 participants), as well as subsequent 12-year trajectories of Short Form 12-item Survey scores and self-rated health (up to 112 915 observations).

Results: Accelerated biological aging was found to be associated with worse functioning both cross-sectionally and longitudinally. However, associations can be moderated by sex and age group. For example, longitudinally, Biological Health Score was negatively associated with self-rated health (coefficient = −0.06) with a moderating effect of sex (coefficient = −0.02, $p < .05$; male = reference) and some age groups (40-52 years: coefficient = −0.04, $p < .001$; 53-65 years: coefficient = −0.03, $p < .01$; reference = 16-39 years), but not for the oldest group (66+ years: coefficient = −0.01, $p = .34$).

Conclusions: We conclude that measures of biological age are associated with individual functioning trajectories across the entire adult age span, and studies should consider sex differences and examine the entire age range to fully capture distinct facets of aging complexity.

Keywords: Biological age, DNA methylation, Functional status, Longitudinal trajectories

Introduction

Aging is a multisystem process, and can be measured at different bodily domains and levels, including molecular, cellular, organ, and organism. Organ system-level physiological biomarkers can be grouped by the organ systems on which they are based, such as respiratory, renal, bone marrow, neurocognitive, musculoskeletal, integumentary, sensory, digestive and hepatic, cardiovascular, immune, and endocrine. "Biological Age" (BA) has been developed to combine information from multiple organ-system level physiological biomarkers into a single latent variable to quantify a person's biological state.[1,2] Researchers have proposed several algorithms based on theories, such as homeostasis and balance, wear-and-tear, or stress. Biological Health Score (BHS), as one of the algorithms, indicates people's physiological wear-and-tear.[3] Molecular and cellular measures, derived using the hallmarks of aging theory,[4] include biomarkers such as DNA methylation (DNAm). DNAm, the covalent addition of a methyl group to cytosine-guanine (CpG) base pairs on the genome, is a key epigenetic mechanism regulating gene expression. The first-generation DNAm algorithms were tested and trained to predict chronological age using samples from multi-tissue ("Horvath"[5] clock) or whole-blood ("Hannum"[6] clock). These were followed by BA DNAm algorithms built and trained to predict both lifespan and healthspan ("PhenoAge"[7] clock) or "pace of ageing" ("DunedinPACE"[8] DNAm algorithms) using whole-blood samples. There was no apparent overlap between the BA DNAm algorithms' CpG sites and chronological clocks' CpG sites, which might be because biological and chronological DNAm algorithms' CpG sites are largely distinct loci, thus, the chronological and BA DNAm algorithms may reflect different underlying processes.[9,10] Aging-related changes measured at the molecular and organ-system levels have been found across the adults' age span. For example, biological aging was found to fluctuate across life-course from age 40 to 80.[11,12] In addition, sex differences were found in biological aging.[13,14]

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At the individual level, aging can be captured by both subjective and objective healthspan-related characteristics, including measures of functioning such as physical strength, cognitive competence, mental and physical health capacity, and self-assessed general health.[1,15] Functional status is an individual's ability to perform normal daily activities required to meet basic needs, fulfil usual roles, and maintain health and well-being. Both subjective and objective functioning measures encompass the underlying processes that contribute to the development of disease, disability, and frailty. Evidence suggested some dimensions of objective functioning grow over time until old age and then decline, whereas others decline since young adulthood.[16,17] For example, while certain cognitive functions, such as verbal and numerical abilities, show little age-associated decline, others, such as memory, tend to decline from middle age or even earlier.[16,17] A study showed cognitive ability of men outperforms women for younger adults, while men's cognitive performance shows greater decline.[18]

Few studies link the molecular and organ-system level aging measures with longitudinal trajectories of aging-related functional status,[19–21] and no study has used UK cohort. In addition, most studies mainly examine the aging process from mid or later adulthood,[22,23] and few cover the entire age span of adulthood along with sex stratification. We aim to assess the associations between the molecular and organ-system level biological aging measures and aging-related functional status cross-sectionally and longitudinally across the entire adult age span in the United Kingdom, and whether sex and age groups moderate these associations.

Methods

Data

This study used data from the UK Household Longitudinal Study (UKHLS). The main survey of UKHLS began in 2009, collecting data annually with 14 collection waves to date. About 5 months after waves 2 and 3 of the main survey (2010-2012), participants aged 16 years and older in Great Britain received a Nurse Health Assessment in which blood samples and a range of biomedical measures were collected.[24] In total, 13 286 participants provided blood, and due to financial availability, 3654 provided DNAm samples.[25,26] This study used data from Nurse Health Assessment in waves 2 and 3 for cross-sectional analysis, as different people participated in each wave, and waves 3-14 (2012-2024) of the main survey for longitudinal analysis.

Of 13 286 participants recruited at Nurse Health Assessment, 55 participants had missing data in all blood biomarkers and were excluded from analyses. For cross-sectional analysis, we first used the closest main wave (2 or 3) data to impute missing data for variables at Nurse Health Assessment and then did complete case analysis. The participant numbers can be found in Table S1. There were 112 915 observation points available in the subsequent 12 waves (waves 3-14) for longitudinal analysis (Table S2). As there were less than 5% missing in questionnaire-measured variables (Table S1), complete case analysis was conducted for longitudinal analysis.

Aging measurements

In this article, molecular and organ-system level aging measurements referred to as "composite measures of biological ageing" with higher value means biologically older, while individual-level aging measurement referred to as "ageing-related functional status" with higher scores indicate better functioning.

Composite measures of biological aging

BHS measures cumulated biological risk across organ systems. The BHS is a composite measure of physiological wear-and-tear as indicated by adverse (using a "worst quartile" approach) levels of blood-derived biomarkers that reflect liver, kidney, endocrine system, inflammatory, cardiovascular, and metabolic processes. BHS is calculated as the sum across all aging-related biomarkers of binary variables indicating if a person belongs to the "at-risk" quartiles of each biomarker. The "worst quartile" approach follows the previous literature.[3,27,28] The "at-risk" quartiles are calculated for both sexes and each age group (participants' age tertile as cut-off point, and categorized participants to 16-39, 40-52, 53-65, and 66+ years groups) separately. Biomarkers were collected during Nurse Health Assessment and selected based on previous literature,[3,27,28] their availability in the dataset,[25] and statistical significance and strength of their relationship with chronological age (Table S3). Biomarkers used in BHS calculation can be classified into 6 physiological subsystems, and the detailed biomarkers selected are listed in Table S4.

Horvath,[5] Hannum,[6] PhenoAge,[7] and DundinPACE[8] algorithms calculated from DNA extracted from blood samples collected during Nurse Health Assessment were used as molecular-level aging measures. Detailed information on DNAm algorithms in UKHLS can be found in previous papers.[29,30] Measurement is restricted to samples from White/European participants. Horvath,[5] Hannum,[6] and PhenoAge[7] algorithms were regressed with chronological age to calculate residuals, and named "DNAm age deviation"[22,31]: Horvath age deviation (ΔHorvathDev), Hannum age deviation (ΔHannumDev), and PhenoAge age deviation (ΔPhenoAgeDev). DundinPACE was measured in years of accelerated aging per year of aging. Technical covariates, including barcode and various cell composition estimates, were controlled for all DNAm algorithms.[26]

Aging-related functional status

Grip strength as an objective measurement was assessed using a dynamometer during the Nurse Health Assessment. Both valid maximum readings of grip strength for the dominant hand (in kg) and the nondominant hand (in kg) were collected. Grip strength was averaged if both left and right-hand data available, otherwise only used dominant hand data.

Cognitive function as the other objective measurement was collected at wave 3 of the main survey.[32] Indicators include episodic memory, working memory, fluid reasoning, category fluency, and numeracy ability. Considering different domains of cognitive function decline at different speeds,[16,17,33,34] we combined episodic and working memory as memory domain measurement, and combined fluid reasoning, category fluency, and numeracy ability as non-memory domain measurement. All indicators were min–max normalized considering the difference in measurement range, and then the mean score of memory and non-memory domains was calculated separately.

We used both the physical component score (PCS) and mental component score (MCS) of the Short Form 12-item Survey (SF12) as subjective measurements collected at waves 2 and 3

for cross-sectional analyses and at subsequent waves 3-14 for longitudinal analyses.

Self-rated health was measured at all waves captures a dimension related to overall health and was assessed by the question "In general, would you say your health is excellent, very good, good, fair, or poor?" collected at all waves on a 5-point scale (1 = poor to 5 = excellent).

Covariates

This paper controlled several sociodemographic factors, including sex, age groups (participants' age tertile as cut-off point, and categorized participants to 16-39, 40-52, 53-65, and 66+), income (quintiles of individual monthly disposable income, and higher quintile is lower income), occupation ("management & professional", "intermediate", "routine" based on the 3 class National Statistics Socio-economic classification (NS-SEC), and added "retired", "full-time student", as well as "others" groups), education (highest education attainment, "degree/professional or higher" (higher than A-levels or equivalent), "school level" (up to A-levels or equivalent), and "no qualification"), urbanity (living in "urban" or "rural") and partnership status ("married or living with a partner", "others"). Except for the DNAm subsample, ethnicity ("white" and "others") was included as a covariate.

Statistical analysis

Because some aging measurements were not normally distributed, Spearman's correlations with permutation test were used to examine the correlation between aging measurements and age, as well as between the composite measures of biological aging.

Missingness is patterned sociodemographic factors (Table S5); thus, we controlled for previously mentioned covariates to minimize the influence from the biomarkers' missing on the results.

Linear regressions were used to assess cross-sectional associations between composite measures of biological aging and aging-related functional status.

Growth curve models were specified as multilevel models to estimate longitudinal associations, with participants as level 2 and each time observation as level 1. Sex, baseline age groups, ethnicity (not for DNAm), and technical covariates (only for DNAm) were controlled as fixed covariates; income, occupation, education, urbanity, and partnership status as time-varying factors. This paper used the unstructured variance–covariance structure of random effects.

All tests were two-sided with a significance level of $p < .05$. Statistical analyses were conducted using Stata 18.0.

Results

Descriptive statistics

The mean age of participants included in the cross-sectional analyses was 51.58 years, and 55.43% were female. Table 1 describes baseline characteristics in men and women. As anticipated, the functioning performance of males and females has some differences. For example, the mean grip strength in males (mean: 41.60, SD: 9.81) is greater than the mean grip strength in females (mean: 25.70, SD: 6.59). Those with advancing age achieve lower scores on all aging measurements (Table S6). For example, people aged over 66 were more likely to have lower physical functioning measured by PCS (mean: 43.92 [SD: 11.49] for males and mean 42.45 [SD: 12.38] for females), compared to people aged 16-39 (mean: 54.26 [SD: 7.06] for males and mean 53.75 (SD: 8.45) for females).

Links of aging measurements to chronological age

Table S7 showed that both biological aging and functioning measures correlated with chronological age. The correlation coefficients showed that people of older age were biologically older and had poorer function. However, for MCS, older people had better mental well-being. For sex and age-specific correlation (Table S8), correlation coefficients varied in each sex and age group.

Correlation between composite measures of biological aging

BHS positively correlated with DNAm algorithms (Table S9), while the correlations between BHS with ΔHorvathDev (0.029) and ΔHannumDev (0.048) were very weak. All DNAm algorithms positively correlated with each other, and exhibited low-to-moderate intercorrelations (r value range: 0.029-0.478).

Cross-sectional associations between composite measures of biological aging and aging-related functional status

The associations between composite measures of biological aging and aging-related functional status (Table S10) were mostly negative from crude to fully adjusted models, which means accelerated biological aging was associated with worse functioning. Fully adjusted model between BHS, ΔPhenoAgeDev, and DunedinPACE with PCS, MCS, cognitive functions, and self-rated health largely remain robust.

When fully adjusted models stratified by sex (Figure 1 and Table S11), some sex differences can be found (see the difference in β values [standardized coefficient]), for example, in the associations between DunedinPACE and grip strength. While for most of the associations, β values of male and female groups looked similar.

When we further stratified models by age groups (Table S12), a higher proportion of females were found to have negative associations between BHS and functioning. In addition, most of the previous significant results were only found now in early mid-adulthood and later mid-adulthood.

Longitudinal associations between composite measures of biological aging and aging-related functional status

Table S13 showed that before and after making sex and age groups interaction with composite measures of biological aging, except ΔHorvathDev and ΔHannumDev, most biological aging measures were negatively associated with functioning. In addition, random effects indicated significant variability in intercepts and slopes, suggesting heterogeneity in individual functioning trajectories. For example, the BHS (baseline composite measures of biological aging) was negatively associated with PCS, and the fixed intercept (coefficient = 58.87) random intercept (variance = 90.05) and fixed slope (coefficient = −0.33) random slope (variance = 0.51) varied at the sex and age groups interaction model. The moderation effect of sex and age groups was seen for the association between BHS and functioning, while for DNAm, only the age groups' moderation effect was shown for some DNAm algorithms, including ΔHorvathDev and DunedinPACE.

Table 1. Characteristics of participants (2010-2012).

Characteristics	Male *n* = 5897	Female *n* = 7334	Maximum *n* = 13 231
ΔHorvathDev, mean (SD)	0.58 (4.53)	−0.47 (4.34)	1.68e-9 (4.46)
ΔHannumDev, mean (SD)	1.29 (3.76)	−1.03 (3.43)	8.50e-10 (3.76)
ΔPhenoAgeDev, mean (SD)	−0.02 (5.43)	0.01 (5.43)	3.27e-10 (5.43)
DunedinPACE, mean (SD)	1.07 (0.14)	1.05 (0.13)	1.06 (0.14)
BHS (0-16), mean (SD)	3.65 (2.33)	3.61 (2.27)	3.63 (2.30)
Grip strength (kg), mean (SD)	41.60 (9.81)	25.70 (6.59)	32.84 (11.39)
Cognitive function (memory domains), mean (SD)	0.74 (0.13)	0.73 (0.15)	0.74 (0.14)
Cognitive function (non-memory domains), mean (SD)	0.58 (0.12)	0.54 (0.12)	0.56 (0.12)
PCS, mean (SD)	49.82 (10.44)	49.14 (11.61)	49.44 (11.11)
MCS, mean (SD)	51.42 (8.80)	49.19 (9.91)	50.18 (9.49)
Self-rated health, *N* (%)			
Poor	306 (5.19)	405 (5.52)	711 (5.37)
Fair	878 (14.89)	1159 (15.80)	2037 (15.39)
Good	1707 (28.95)	2043 (27.86)	3750 (28.34)
Very good	2110 (35.78)	2545 (34.70)	4655 (35.19)
Excellent	896 (15.19)	1182 (16.12)	2078 (15.70)
Highest qualification, *N* (%)			
Degree/professional or higher (higher than A-levels or equivalent)	2011 (34.26)	2559 (35.01)	4570 (34.67)
School level (up to A-levels or equivalent)	3143 (53.54)	3583 (49.02)	6726 (51.04)
No qualification	716 (12.20)	1168 (15.98)	1884 (14.29)
Occupation, *N* (%)			
Management and professional	1533 (26.00)	1641 (22.38)	3174 (23.99)
Intermediate	799 (13.55)	991 (13.51)	1790 (13.53)
Routine	1216 (20.62)	1293 (17.63)	2509 (18.96)
Retired	1657 (28.10)	2096 (28.58)	3753 (28.36)
Full-time student	162 (2.75)	167 (2.28)	329 (2.49)
Others	530 (8.99)	1146 (15.63)	1676 (12.67)
Quintiles of individual monthly disposable income, *N* (%)			
1 (high)	1277 (21.66)	1374 (18.73)	2651 (20.04)
2	1230 (20.86)	1420 (19.36)	2650 (20.03)
3	1176 (19.94)	1467 (20.00)	2643 (19.98)
4	1139 (19.31)	1500 (20.45)	2639 (19.95)
5 (Low)	1075 (18.23)	1573 (21.45)	2648 (20.01)
Ethnicity, *N* (%)			
White	5627 (95.42)	6997 (95.42)	12 624 (95.41)
Others	270 (4.58)	336 (4.58)	606 (4.59)
Urbanity, *N* (%)			
Urban	4360 (73.95)	5443 (74.22)	9803 (74.10)
Rural	1536 (26.05)	1,891 (25.78)	3427 (25.90)
Partnership status, *N* (%)			
Married or cohabitation	4287 (72.70)	4754 (64.82)	9041 (68.33)
Others	1610 (27.30)	2580 (35.18)	4190 (31.67)

Numbers may not sum to the total due to missing values. These are the maximum numbers available in the dataset rather than the actual numbers for later regression models. Abbreviations: BHS, Biological Health Score; DunedinPACE, DunedinPACE DNAm algorithm; HannumDev, Hannum age deviation DNAm algorithm; HorvathDev, Horvath age deviation DNAm algorithm; MCS, Mental Component Score; PCS, Physical Component Score; PhenoAgeDev, PhenoAge age deviation DNAm algorithm.

When we additionally introduce interaction of composite measures of biological aging with data collection wave to the previous models (Table S14), the coefficients of the most wave and composite measures of biological aging interaction term were negative, although only for measuring aging-related functional status by PCS, interaction terms were statistically significant. Thus, for people with accelerated biological aging at baseline, their physical functioning declined faster. The predicted trajectories (Figure 2A-C) showed that health functioning declined with time. People with baseline accelerated biological aging (higher than mean BHS, DNAm age deviation > 0, and DunedinPACE > 1) have worsened functioning. The aging-related functional status decreased in all sexes and age groups. Older people had worse functional status compared to younger people for PCS and self-rated health. However, for MCS, people in higher age groups had better mental well-being. Females had lower MCS in almost all age groups compared to males at the baseline.

Discussion

This study extends the existing body of literature demonstrating associations between biological aging and aging-related functional status, which is largely in older age groups and reports that these associations are apparent across the entire age range.

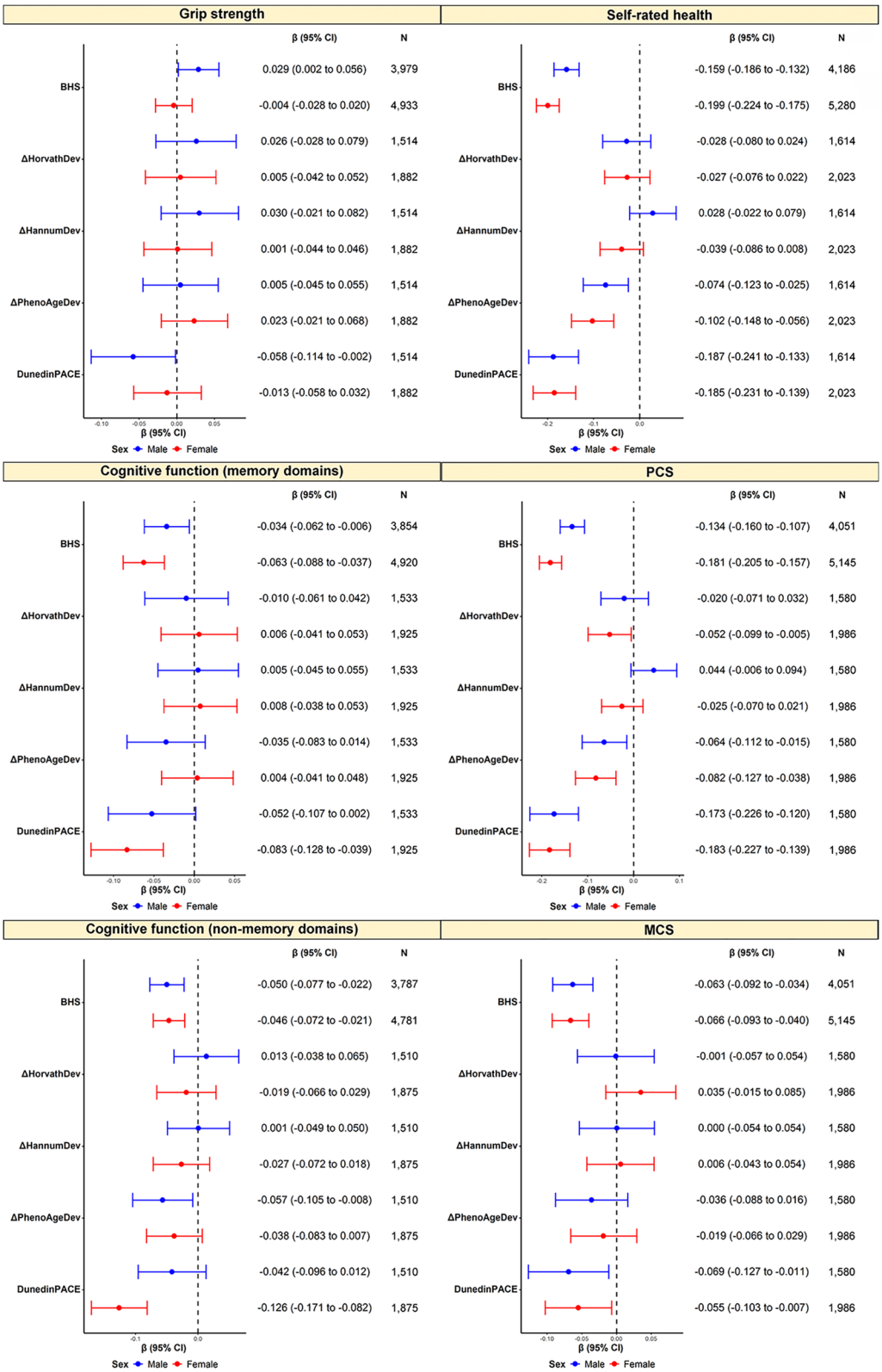

Figure 1. Sex stratified cross-sectional associations. BHS, Biological Health Score; DunedinPACE, DunedinPACE DNAm algorithm; HannumDev, Hannum age deviation DNAm algorithm; HorvathDev, Horvath age deviation DNAm algorithm; MCS, Mental Component Score; PhenoDevAge, PhenoAge age deviation DNAm algorithm; PCS, Physical Component Score.

This study reveals that no matter which aging measurements are used, accelerated biological aging is associated with worse functioning both cross-sectionally and longitudinally. This research advocates for a life-course or life span approach for aging studies, incorporating diverse measures and longitudinal analyses to fully capture the complexities of aging dynamics.

As anticipated,[13,35–37] all biological aging measures correlated with chronological age, though less strongly in some sex and

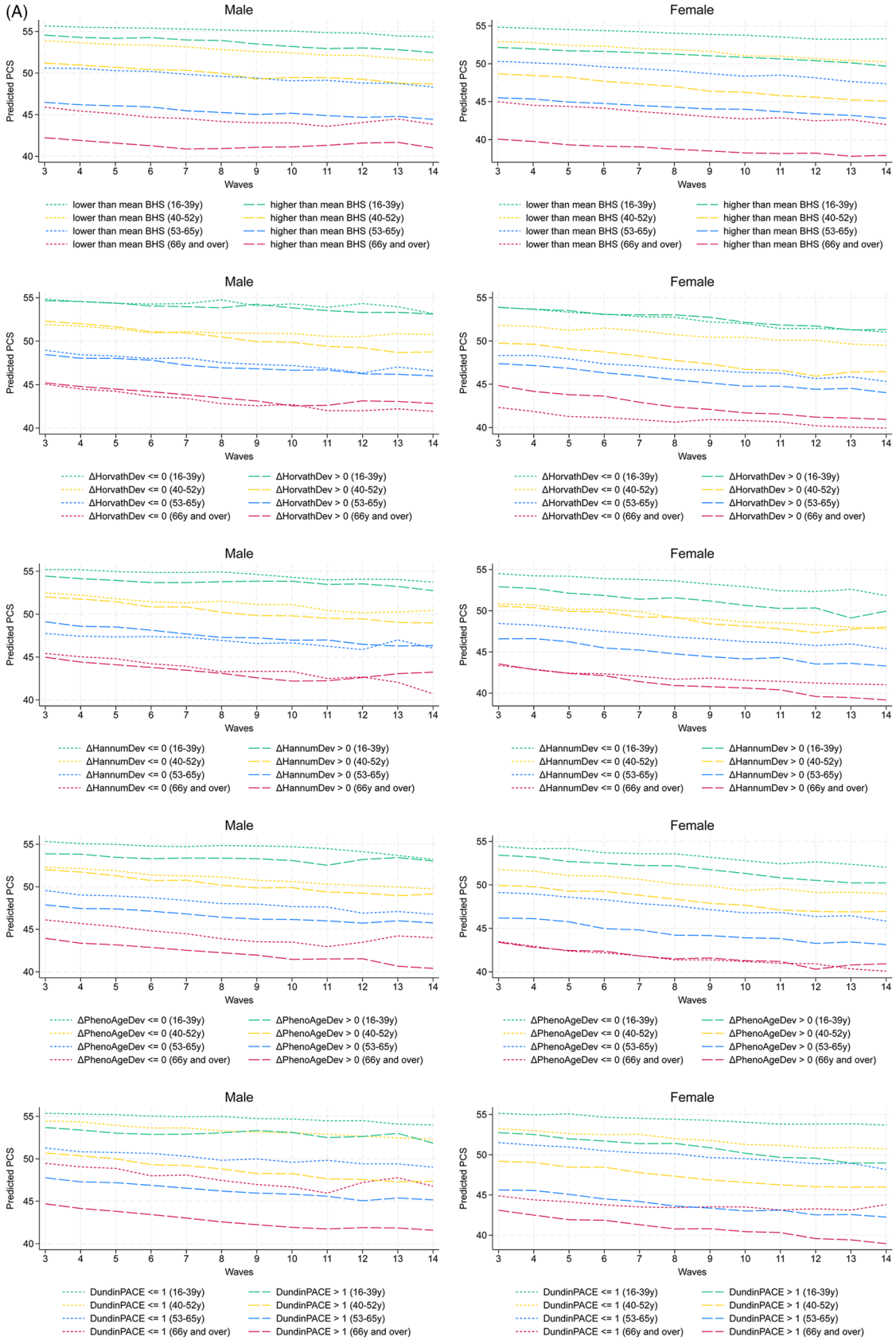

Figure 2. Predicted trajectories of aging-related functional status (A) Predicted trajectories of PCS. (B) Predicted trajectories of MCS. (C) Predicted trajectories of self-rated health. BHS, Biological Health Score; DunedinPACE, DunedinPACE DNAm algorithm; HannumDev, Hannum age deviation DNAm algorithm; HorvathDev, Horvath age deviation DNAm algorithm; PCS, Physical Component Score; PhenoAgeDev, PhenoAge age deviation DNAm algorithm; MCS, Mental Component Score.

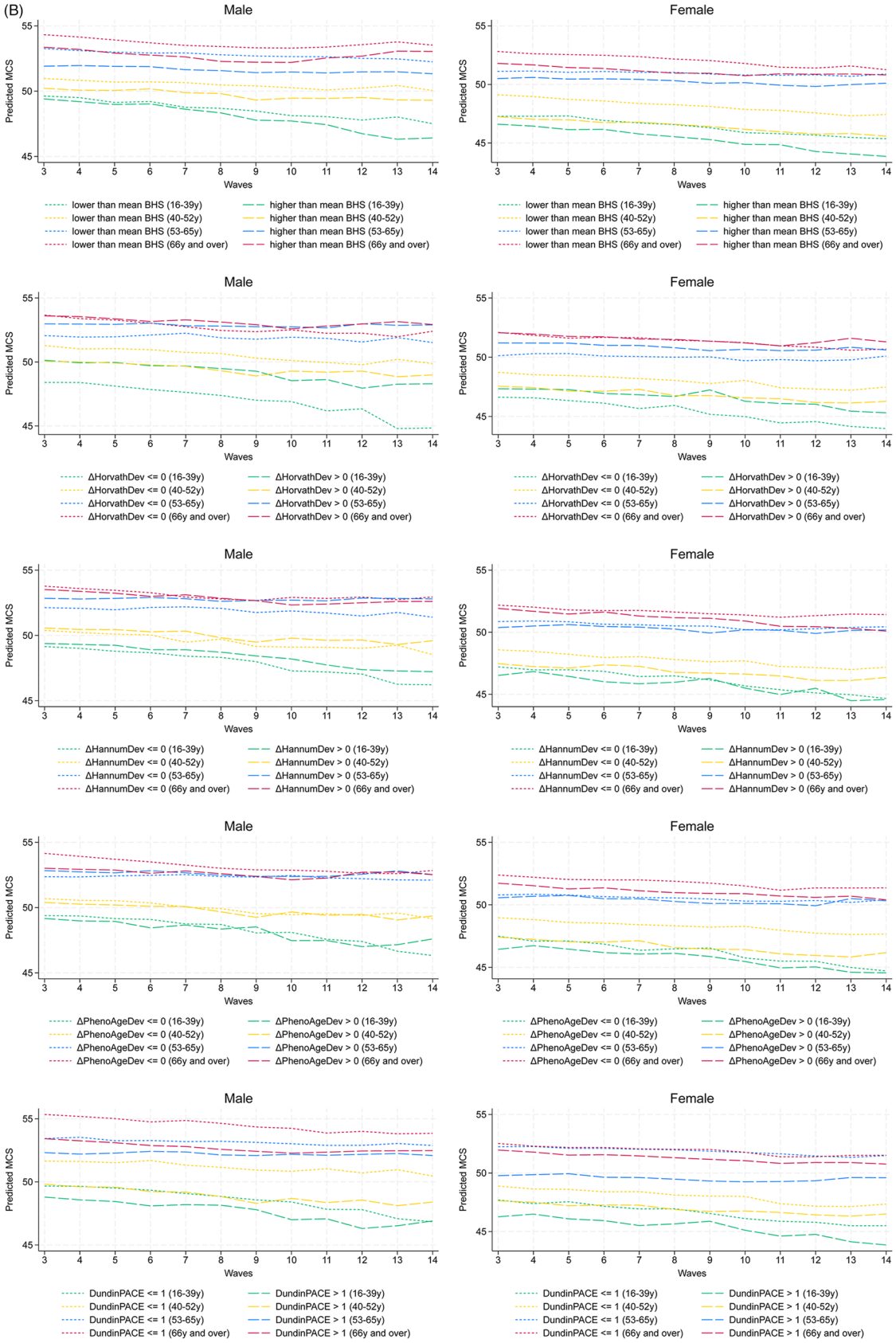

Figure 2. Continued.

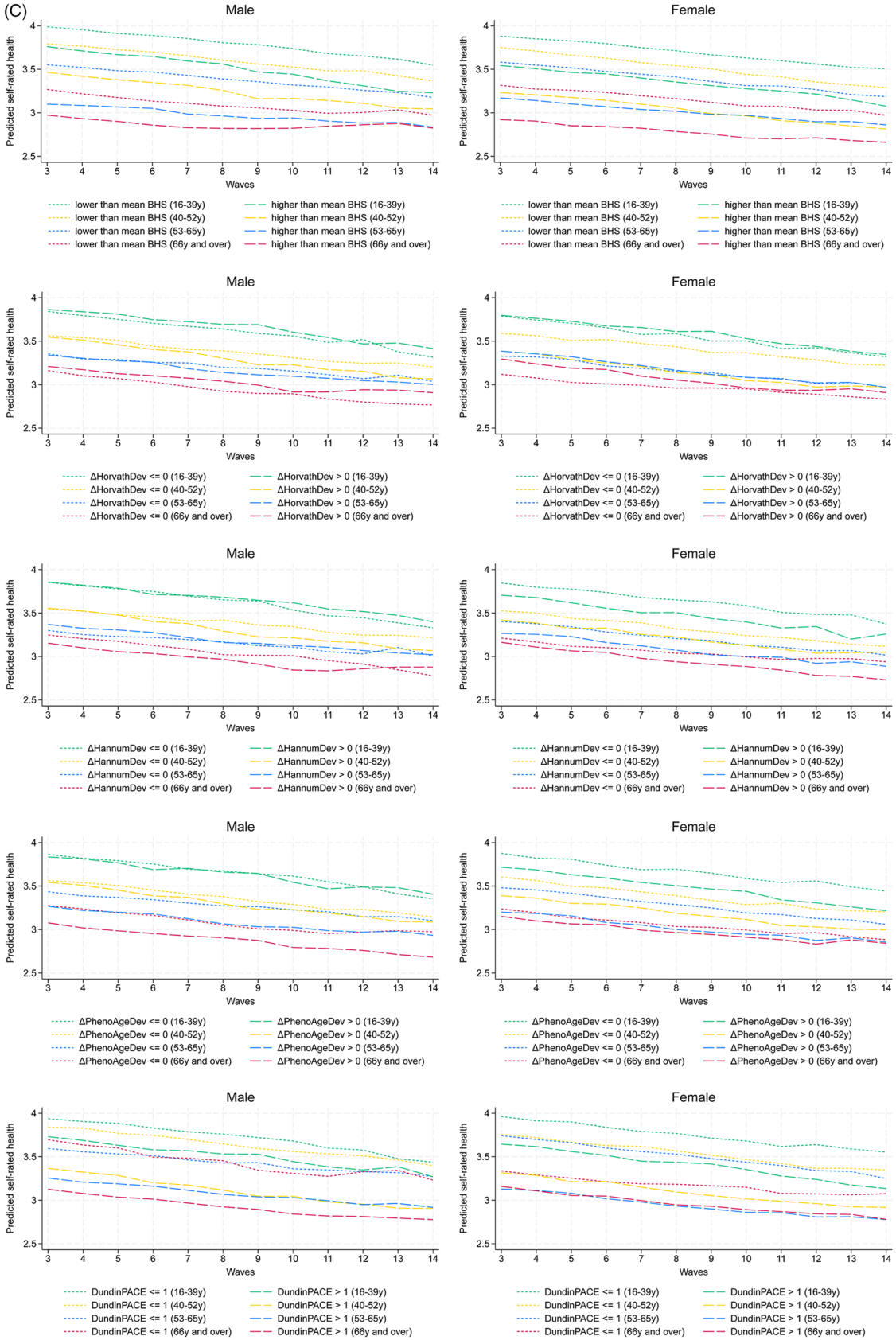

Figure 2. Continued.

age groups. Low-to-moderate intercorrelations among molecular and organ-system level measures suggest they capture distinct aspects of biological aging, consistent with prior studies.[13,19,20,38]

Except ΔHorvathDev and ΔHannumDev, most composite measures of biological aging were significantly negatively associated with functioning both cross-sectionally and longitudinally, which may be because Horvath and Hannum DNAm algorithms have near-perfect predictive accuracy of chronological age. This accords with previous research that Horvath and Hannum DNAm algorithms do not correlate with people's aging-related functioning.[39,40] Horvath and Hannum DNAm algorithms were trained to predict chronological age,[5,6,41,42] while the other BA algorithms additionally reflected different healthspan characteristics.

BHS and DunedinPACE performed similarly, strongly associated with most functional status, particularly with cognitive function and PCS. Besides, longitudinally, accelerated biological aging predicted faster functional decline over 12 years, in line with previous research.[23] The cross-sectional and longitudinal associations between epigenetic and blood-based measures of biological aging and deficits in physical functioning, identified here are consistent with previous studies on US and Irish cohorts.[8,23,43] Theoretically, aging is driven by several interconnected biological processes known as the hallmarks of aging, and aging hallmarks are interdependent among each other as well as among the hallmarks of health.[4,44,45] Our findings align with these theories and previous evidence on associations between BA and physical/cognitive function.[20,21,23,39,46] Whilst there is still a lack of consensus surrounding whether organ-system or DNA based algorithms are most effective,[20,43,47] our results, much like previous studies in the United Kingdom, United States, and Ireland showed that BHS, and PhenoAge/DunedinPACE DNAm algorithms were associated with objectively and subjectively measured functioning.[23,43,47] The subjectively assessed functional status, although using different scales in different studies, all have good performance in aging research,[20,21] like our finding, which highlighted the advantages of using them to identify the healthy aging process as a complement to objective measures.

We find no single aging measure is consistently strongly associated with all others across sex and age groups, aligning with prior research that different measures capture distinct aspe cts.[19,37,39,46] Aging measures may vary in sensitivity and specificity across sexes and life stages. While our findings, which are consistent with evidence that men's functioning outperformed women,[18] past cross-sectional studies reported faster biological aging in men.[14] We found that more pronounced cross-sectional associations appeared in females and mid-adulthood, consistent with prior findings.[11,37,48] Longitudinally, some DNAm measures showed age moderation, while BHS exhibited both sex and age moderation. Unlike our findings, previous longitudinal study showed men presented lower functional status,[20] possibly due to differences in measurement, social and cultural variation and population characteristics compared to our study.[49,50] Subjective measures like SF12 and self-rated health effectively tracked functional aging across adult ages, not just in old populations. Given that aging-related decline in different bodily domains and levels may begin since young adulthood until old age,[11,12,16,17,20,33] it is recommended to include participants from a young age to ensure healthy or general populations included to avoid selection bias in aging-related research.

Blood biomarkers and functional trajectories may help identify high-risk populations before disability or disease onset, making them promising for clinical translation.[31] Aging measures in our study, including minimally or noninvasive assessments, like BHS, cognitive function, and subjective health status, showed interrelationships, supporting their combined use. Subjective functioning measures, which are linked to quality of life, effectively tracked aging across whole adulthood. Besides, our findings supported that there was potential for clinical use of both biochemical and physiological biomarkers to identify aging-associated dysfunction from a young age. Young adulthood offers a key window for early intervention, yet is often overlooked.[51] Aging begins before old age, so research and interventions should span the full adult lifespan to address early physiological decline and promote healthier aging outcomes in later life.

This study captured aging dynamics across molecular, physiological systems, and included both objective and subjective measures. Unlike most previous studies focused on old people only, we included adults from a young age, thus moving closer toward a life span approach. Limitations include incomplete understanding of biological aging mechanisms, because of lack consensus on which molecular, cellular, or physiological changes are causal to aging.[22,52] We didn't disentangle disease, disability, and biological aging processes fully, and further studies need to distinguish physiological from pathological processes.[53] BHS was constructed using cohort-specific worst quartile thresholds, which may limit direct comparability with epigenetic aging measures derived from externally validated algorithms and suggests that the observed associations could partly reflect sample-specific variability. DNAm was only collected in white people, limiting generalizability to other ethnicities. The biological aging metrics and objective functioning were available only at baseline, and thus, temporal changes in those were not investigated. While analyses were limited to aging measures available in UKHLS, our findings and others' suggest that similar trends are apparent whichever measure of aging is used.[23] In addition, as with most longitudinal studies, there was attrition over the follow-up period. Although less than 5% missing on sociodemographic variables, there was a large amount of missing blood biomarkers. Despite controlling for some covariates, unmeasured and residual confounders may bias findings.

Supplementary material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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writing of this study, or the decision to submit the paper for publication.

Conflict of interest

None declared.

Author contributions

Wen Wang and Meena Kumari conceptualized the study. Wen Wang performed all analyses and wrote the manuscript. Yanchun Bao advised on statistical methods and Steven Haworth aided in analyses. Steven Haworth, Yanchun Bao, and Meena Kumari edited the manuscript and supervised the study. All authors read and approved the final version of the manuscript.

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Research ethics

The University of Essex Ethics Committee has approved all data collection on Understanding Society main study. Approval for the collection of biosocial data by trained nurses in Waves 2 and 3 of the main survey was obtained from the National Research Ethics Service (Understanding Society—UK Household Longitudinal Study: A Biosocial Component, Oxfordshire A REC, Reference: 10/H0604/2).

Data availability information

UK Household Longitudinal Study is available for download from the UK Data Service (https://ukdataservice.ac.uk/).

References

1. Chen RY, Wang YY, Zhang SR, et al. Biomarkers of ageing: current state-of-art, challenges, and opportunities. *Medcomm—Future Med*. 2023;2:e50. https://doi.org/10.1002/mef2.50
2. Khan SS, Singer BD, Vaughan DE. Molecular and physiological manifestations and measurement of aging in humans. *Aging Cell*. 2017;16:624-633. https://doi.org/10.1111/acel.12601
3. Karimi M, Castagné R, Delpierre C, et al. Early-life inequalities and biological ageing: a multisystem biological health score approach in understanding society. *J Epidemiol Community Health*. 2019;73:693-702. https://doi.org/10.1136/jech-2018-212010
4. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. Hallmarks of aging: an expanding universe. *Cell*. 2023;186:243-278. https://doi.org/10.1016/j.cell.2022.11.001
5. Horvath S. DNA methylation age of human tissues and cell types. *Genome Biol*. 2013;14:R115. https://doi.org/10.1186/gb-2013-14-10-r115
6. Hannum G, Guinney J, Zhao L, et al. Genome-wide methylation profiles reveal quantitative views of human aging rates. *Mol Cell*. 2013;49:359-367. https://doi.org/10.1016/j.molcel.2012.10.016
7. Levine ME, Lu AT, Quach A, et al. An epigenetic biomarker of aging for lifespan and healthspan. *Aging (Albany NY)*. 2018;10:573-591. https://doi.org/10.18632/aging.101414
8. Belsky DW, Caspi A, Corcoran DL, et al. DunedinPACE, a DNA methylation biomarker of the pace of aging. *eLife*. 2022;11:e73420. https://doi.org/10.7554/eLife.73420
9. Field AE, Robertson NA, Wang T, Havas A, Ideker T, Adams PD. DNA methylation clocks in aging: categories, causes, and consequences. *Mol Cell*. 2018;71:882-895. https://doi.org/10.1016/j.molcel.2018.08.008
10. Duan R, Fu QY, Sun Y, Li QF. Epigenetic clock: a promising biomarker and practical tool in aging. *Ageing Res Rev*. 2022;81:101743. https://doi.org/10.1016/j.arr.2022.101743
11. Shen X, Wang C, Zhou X, et al. Nonlinear dynamics of multi-omics profiles during human aging. *Nat Aging*. 2024;4:1619-1634. https://doi.org/10.1038/s43587-024-00692-2
12. Lehallier B, Gate D, Schaum N, et al. Undulating changes in human plasma proteome profiles across the lifespan. *Nat Med*. 2019;25:1843-1850. https://doi.org/10.1038/s41591-019-0673-2
13. McCrory C, Fiorito G, McLoughlin S, et al. Epigenetic clocks and allostatic load reveal potential sex-specific drivers of biological aging. *J Gerontol A Biol Sci Med Sci*. 2020;75:495-503. https://doi.org/10.1093/gerona/glz241
14. Oblak L, van der Zaag J, Higgins-Chen AT, Levine ME, Boks MP. A systematic review of biological, social and environmental factors associated with epigenetic clock acceleration. *Ageing Res Rev*. 2021;69:101348. https://doi.org/10.1016/j.arr.2021.101348
15. Guo J, Huang X, Dou L, et al. Aging and aging-related diseases: from molecular mechanisms to interventions and treatments. *Signal Transduct Target Ther*. 2022;7:391. https://doi.org/10.1038/s41392-022-01251-0
16. Salthouse TA. When does age-related cognitive decline begin? *Neurobiol Aging*. 2009;30:507-514. https://doi.org/10.1016/j.neurobiolaging.2008.09.023
17. Deary IJ, Corley J, Gow AJ, et al. Age-associated cognitive decline. *Br Med Bull*. 2009;92:135-152. https://doi.org/10.1093/bmb/ldp033
18. Congdon EL, Liu S, Upton EM. A cross-sectional exploration of cognitive ability across age via stacked ensembles. *Psychol Aging*. 2025;40:159-177. https://doi.org/10.1037/pag0000868
19. Belsky DW, Moffitt TE, Cohen AA, et al. Eleven telomere, epigenetic clock, and biomarker-composite quantifications of biological aging: do they measure the same thing? *Am J Epidemiol*. 2018;187:1220-1230. https://doi.org/10.1093/aje/kwx346
20. Li X, Ploner A, Wang Y, et al. Longitudinal trajectories, correlations and mortality associations of nine biological ages across 20-years follow-up. *eLife*. 2020; 9: e51507. https://doi.org/10.7554/eLife.51507
21. Elliott ML, Caspi A, Houts RM, et al. Disparities in the pace of biological aging among midlife adults of the same chronological age have implications for future frailty risk and policy. *Nat Aging*. 2021;1:295-308. https://doi.org/10.1038/s43587-021-00044-4
22. Moqri M, Herzog C, Poganik JR, et al. Biomarkers of aging for the identification and evaluation of longevity interventions. *Cell*. 2023;186:3758-3775. https://doi.org/10.1016/j.cell.2023.08.003
23. Crimmins EM, Hernandez B, Potter C, et al. Epigenetic clocks relate to four age-related health outcomes similarly across three countries. *J Gerontol A Biol Sci Med Sci*. 2025;80:glaf036. https://doi.org/10.1093/gerona/glaf036
24. Institute for Social and Economic Research. Understanding Society: Waves 2 and 3 Nurse Health Assessment, 2010-2012, User Guide, Version 3. Colchester, UK: University of Essex; September 2022. Accessed 01/07/2025. https://doc.ukdataservice.ac.uk/doc/7251/mrdoc/pdf/7251_nurse_health_assessment_user_guide.pdf.
25. Institute for Social and Economic Research. Understanding Society: Biomarker User Guide and Glossary, Version 2. Colchester, UK: University of Essex; September 2022. Accessed 01/07/2025. https://www.understandingsociety.ac.uk/wp-content/uploads/documentation/user-guides/7251-user-guide-health-biomarker.pdf.
26. Institute for Social and Economic Research. Understanding Society: Waves 2-3 Nurse Health, 'Epigenetic Clocks' derived from DNA methylation, 2010-2012, User Guide, Version 1. Colchester, UK:

University of Essex; September 2022. Accessed 01/07/2025. https://doc.ukdataservice.ac.uk/doc/7251/mrdoc/pdf/7251_epigenetic_clocks_user_guide.pdf
27. Chadeau-Hyam M, Bodinier B, Vermeulen R, et al. Education, biological ageing, all-cause and cause-specific mortality and morbidity: UK biobank cohort study. *EClinicalMedicine*. 2020;29-30:100658. https://doi.org/10.1016/j.eclinm.2020.100658
28. Whitley E, Benzeval M, Kelly-Irving M, Kumari M. When in the lifecourse? Socioeconomic position across the lifecourse and biological health score. *Ann Epidemiol*. 2024;96:73-79. https://doi.org/10.1016/j.annepidem.2024.06.006
29. Wang W, Dearman A, Bao Y, Kumari M. Partnership status and positive DNA methylation age acceleration across the adult lifespan in the UK. *SSM Popul Health*. 2023;24:101551. https://doi.org/10.1016/j.ssmph.2023.101551
30. Bao Y, Gorrie-Stone T, Hannon E, et al. Social mobility across the lifecourse and DNA methylation age acceleration in adults in the UK. *Sci Rep*. 2022;12:22284. https://doi.org/10.1038/s41598-022-26433-2
31. Moqri M, Herzog C, Poganik JR, et al. Validation of biomarkers of aging. *Nat Med*. 2024;30:360-372. https://doi.org/10.1038/s41591-023-02784-9
32. Institute for Social and Economic Research. (2013), Understanding Society: UK Household Longitudinal Study: Cognitive Ability Measures, Version 1.1, October, 2013, Colchester: University of Essex. https://www.understandingsociety.ac.uk/wp-content/uploads/documentation/user-guides/6614-user-guide-cognitive-ability-measures.pdf
33. Glorioso C, Sibille E. Between destiny and disease: genetics and molecular pathways of human central nervous system aging. *Prog Neurobiol*. 2011;93:165-181. https://doi.org/10.1016/j.pneurobio.2010.11.006
34. Whitley E, Deary IJ, Ritchie SJ, Batty GD, Kumari M, Benzeval M. Variations in cognitive abilities across the life course: cross-sectional evidence from understanding society: the UK household longitudinal study. *Intelligence*. 2016;59:39-50. https://doi.org/10.1016/j.intell.2016.07.001
35. Belsky DW, Caspi A, Houts R, et al. Quantification of biological aging in young adults. *Proc Natl Acad Sci U S A*.. 2015;112:E4104-E4110. https://doi.org/10.1073/pnas.1506264112
36. Herzog CMS, Goeminne LJE, Poganik JR, et al. Challenges and recommendations for the translation of biomarkers of aging. *Nat Aging*. 2024;1-12. https://doi.org/10.1038/s43587-024-00683-3
37. Han J-DJ. The ticking of aging clocks. *Trends Endocrinol Metab*. 2024;35:11-22. https://doi.org/10.1016/j.tem.2023.09.007
38. Jansen R, Han LK, Verhoeven JE, et al. An integrative study of five biological clocks in somatic and mental health. *eLife*. 2021; 10: e59479. https://doi.org/10.7554/eLife.59479
39. Maddock J, Castillo-Fernandez J, Wong A, et al. DNA methylation age and physical and cognitive aging. *J Gerontol A Biol Sci Med Sci*. 2020;75:504-511. https://doi.org/10.1093/gerona/glz246
40. Starnawska A, Tan Q, Lenart A, et al. Blood DNA methylation age is not associated with cognitive functioning in middle-aged monozygotic twins. *Neurobiol Aging*. 2017;50:60-63. https://doi.org/10.1016/j.neurobiolaging.2016.10.025
41. Kusters CDJ, Horvath S. Quantification of epigenetic aging in public health. *Annu Rev Public Health*. 2025;46:91-110. https://doi.org/10.1146/annurev-publhealth-060222-015657
42. Zhang Q, Vallerga CL, Walker RM, et al. Improved precision of epigenetic clock estimates across tissues and its implication for biological ageing. *Genome Med*. 2019;11:54. https://doi.org/10.1186/s13073-019-0667-1
43. Graf GH, Crowe CL, Kothari M, et al. Testing black-white disparities in biological aging among older adults in the United States: analysis of DNA-methylation and blood-chemistry methods. *Am J Epidemiol*. 2022;191:613-625. https://doi.org/10.1093/aje/kwab281
44. López-Otín C, Kroemer G. Hallmarks of health. *Cell*. 2021;184:33-63. https://doi.org/10.1016/j.cell.2020.11.034
45. Kroemer G, Maier AB, Cuervo AM, et al. From geroscience to precision geromedicine: understanding and managing aging. *Cell*. 2025;188:2043-2062. https://doi.org/10.1016/j.cell.2025.03.011
46. Crimmins EM, Thyagarajan B, Kim JK, Weir D, Faul J. Quest for a summary measure of biological age: the health and retirement study. *Geroscience*. 2021;43:395-408. https://doi.org/10.1007/s11357-021-00325-1
47. Balachandran A, Pei H, Shi Y, et al. Pace of aging analysis of healthspan and lifespan in older adults in the US and UK. *Nat Aging*. 2025;5:1132-1142. https://doi.org/10.1038/s43587-025-00866-6
48. Reicher L, Bar N, Godneva A, et al. Phenome-wide associations of human aging uncover sex-specific dynamics. *Nat Aging*. 2024;4:1643-1655. https://doi.org/10.1038/s43587-024-00734-9
49. Mauvais-Jarvis F, Merz NB, Barnes PJ, et al. Sex and gender: modifiers of health, disease, and medicine. *Lancet*. 2020;396:565-582. https://doi.org/10.1016/S0140-6736(20)31561-0
50. Henstra M, Rhebergen D, van der Velde N, et al. Patterns of discordance of physical functioning in older persons: different associations for apathy and depression? Results from the NESDO-study. *Aging Ment Health*. 2022;26:1580-1588. https://doi.org/10.1080/13607863.2021.1932738
51. Farina FR, Bridgeman K, Gregory S, et al. Next generation brain health: transforming global research and public health to promote prevention of dementia and reduce its risk in young adult populations. *Lancet Healthy Longev*. 2024;5:100665. https://doi.org/10.1016/j.lanhl.2024.100665
52. Gladyshev VN, Anderson B, Barlit H, et al. Disagreement on foundational principles of biological aging. *PNAS Nexus*. 2024;3:pgae499. https://doi.org/10.1093/pnasnexus/pgae499
53. de Magalhães JP. Cellular senescence in normal physiology. *Science*. 2024;384:1300-1301. https://doi.org/10.1126/science.adj7050