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The exposome of healthy and accelerated aging across 40 countries

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Protective and risk factors can drive healthy or accelerated aging, with distinct environments modulating their effects. The impact of the exposome—the combined physical and social exposures experienced throughout life—on accelerated aging remains unknown. We assessed delayed and accelerated aging in 161,981 participants from 40 countries (45.09% female; mean age, 67.06; s.d., 9.85) by measuring biobehavioral age gaps (BBAGs), defined as the difference between estimated age from protective and risk factors and chronological age, in cross-sectional and longitudinal designs. BBAGs predicted chronological age, followed by regional and exposomal factor analyses, linked to accelerated aging. Europe led in healthy aging, while Egypt and South Africa showed the greatest acceleration; Asia and Latin America fell in between (Cliff's delta (δd) = 0.15–0.52; all $P < 0.0001$). Accelerated aging was more evident in eastern and southern Europe; globally, it was also associated with lower income ($\delta d = 0.48–0.56$, $P < 1 \times 10^{-15}$). Exposomal factors of accelerated aging include physical (air quality), social (socioeconomic and gender inequality, migration) and sociopolitical (representation, party freedom, suffrage, elections and democracy) determinants (all Cohen's d (d) > 0.37, $P < 0.0001$). BBAGs predicted future functional (r (Pearson correlation) = −0.33, $P < 1 \times 10^{-15}$, $d = 0.70$) and cognitive declines ($r = -0.22$, $P < 1 \times 10^{-15}$, $d = 0.44$), and larger BBAGs ($P < 0.0001$, $d = 1.55$). Healthy and accelerated aging are influenced by physical, social and sociopolitical exposomes, with considerable disparities across nations.

Aging is defined as the process of biological and health changes that occur over time, influenced by a combination of biological, behavioral and environmental factors[1]. Biological clocks[2–7], clinical risk accumulation[8] and frailty have been identified as proxies for systemic biological aging[9]. While no consensus exists on the exact definition of biological aging[10], evidence shows that protective and risk factors influence aging trajectories[11]. Identifying these predictors is essential to improving health, reducing healthcare burdens and mitigating socioeconomic impacts associated with age-related conditions[12]. Global aging trajectories unfold differently owing to the interplay of protective and risk factors[13–15]. Key protective[16] (cognitive reserve, functional ability) and risk (cardiometabolic conditions, sensory impairments) factors have global effects on aging[13,14,17]. Beyond individual-level factors[17,18], aggregate-level[18] and regional inequalities[19,20] can influence healthy aging and dementia risk[2,13,15,17], with low-income and disadvantaged nations facing disproportionate age-related burdens[21]. Country-level exposomes[22,23]—including physical (for example, pollution)[24,25], social (for example, structural inequalities)[26,27] and sociopolitical (for example, ideological radicalization and threats to democracy)[28,29] factors—have been associated with unhealthy aging. However, the ways in which protective and risk factors relate to accelerated or delayed aging as the exposome are still not well understood.

Healthy aging results from the interaction of biological processes, social behavior and the environment. The biobehavioral[30]

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age gap[2,3] (BBAG)—defined as the difference between an individual's chronological age and their predicted age based on protective and risk factors—serves here as a metric for understanding aging beyond chronological measures by emphasizing modifiable influences. While aligned with biological clocks (for example, epigenetic, proteomic and multi-omic)[2,3,6,31] that estimate biological aging relative to chronological age, BBAGs differ by focusing on biobehavioral factors that are accessible in large-scale, population-based studies. Unlike frailty indices, which reflect late-life physical decline, BBAGs provide a continuous measure of aging clocks (estimated age) applicable across the adult lifespan[32]. This approach also integrates life course epidemiology, allowing for the examination of cumulative exposures and their effects on aging trajectories.

Despite advances in the field of aging, critical gaps remain. While previous research using brain or biological clocks has provided valuable insights into aging mechanisms[2–7], these studies have not examined the role of biobehavioral clocks and combined environmental factors associated with delayed or accelerated aging. Limited research has considered combined biobehavioral protective and risk factors in association with accelerated and delayed aging; geographic diversity in terms of locations and income levels; or physical, social and sociopolitical factors as the exposome. In particular, sociopolitical factors—such as the state of democracy—are increasingly recognized as critical determinants of health[28,29] but remain unexplored in the context of aging.

Here we examined how a broad range of individual- and macro-level factors are associated with delayed and accelerated aging across diverse global regions in healthy individuals. We first generated a model of predicted age based on individual-level protective (preserved cognition, functional ability, education) and risk (cardiometabolic conditions such as hypertension, diabetes and cardiovascular risks; female sex; and visual and hearing impairments) factors. We leveraged additional protective (well-being, physical activity, memory, walking ability) and risk (unhealthy weight, alcohol consumption, sleep problems) factors that were available in a subset of the data. We calculated BBAGs as the difference between predicted and chronological age, measuring accelerated (BBAG > 0) or delayed (BBAG < 0) aging, and identified factors linked to these patterns. We hypothesize that protective and risk biobehavioral factors are associated with delayed and accelerated aging, respectively. Furthermore, we expect that aging trajectories are influenced by socioeconomic disparities and the exposome. Lastly, we anticipate that BBAGs will serve to predict healthy aging trajectories—including functional ability, cognition, well-being and future accelerated aging—in longitudinal analyses.

Results

We analyzed data from 161,981 healthy participants from 40 nations across 4 continents: 6 in Latin American and Caribbean countries (LACs), 27 in Europe, 4 in Asia (China, India, Israel and South Korea) and 2 in Africa (Egypt and South Africa) (Table 1 and Fig. 1a). The cross-sectional dataset included 161,981 individuals, of whom 21,631 also contributed longitudinal data (Extended Data Fig. 1a–c). We analyzed BBAG differences by continent and country income (gross national income (GNI) or gross domestic product (GDP) per capita, as well as low-income countries (LICs) versus high-income countries (HICs)). We explored how environmental (air quality[24]), social (gender inequality[27], migration[33], structural socioeconomic inequality[20,26,34]) and sociopolitical (political representation, party freedom, inclusive suffrage, credible elections, local democracy[20,28,29]) exposomal factors are associated with BBAGs. Using longitudinal datasets, we assessed whether BBAGs predict future decline in healthy aging (preserved cognition, functional ability, well-being) and future long-term BBAG trajectories. Validation analyses included epidemiological measures to assess the strength and consistency of associations and meta-analyses to evaluate findings across different datasets and populations. We performed several sensitivity analyses to further assess the validity of our results. Table 2 provides an overview of the effect size metrics used in this study, along with their interpretation.

Prediction of chronological age and aging trajectories

Chronological age was estimated using biobehavioral predictors (protective and risk factors) from cross-sectional data (R^2 (coefficient of determination) = 0.26, Cohen's f^2 (F^2) = 0.35, r (Pearson correlation) = 0.51, root mean squared error (RMSE) = 8.47, n = 161,981 participants). Key protective predictors were functional ability, education and cognition, while main risks were hearing impairment, heart disease and hypertension (Fig. 2a).

To examine biobehavioral contributions to aging, participants were grouped into delayed or accelerated aging (Methods). Both models showed high predictive accuracy, particularly for accelerated aging. For delayed aging (Fig. 2b; R^2 = 0.57, F^2 = 1.31, r = 0.75, RMSE = 6.51), top protective factors were education, functional ability and cognition, while hypertension, hearing impairment and heart disease were leading risks. For accelerated aging (Fig. 2b; R^2 = 0.69, F^2 = 2.26, r = 0.84, RMSE = 5.44), functional ability, cognition and education remained key protective factors, with heart disease, hearing and visual impairments as the strongest risk factors. Analyses in the subsample with additional predictors (protective factors: well-being, physical activity, memory, walking ability; risk factors: unhealthy weight, alcohol consumption, sleep problems) showed stronger accuracy, identifying education and functional ability as top protectors and hearing impairment as the strongest risk (Extended Data Fig. 2a,b).

Regional and income-level differences in accelerated aging

BBAGs varied substantially across regions and income levels, with the lowest BBAGs observed in European countries followed by Asia (we categorized China, South Korea, Israel and India), LACs and Egypt (Fig. 2c). Participants from Egypt had the oldest biobehavioral ages compared with those from Europe (Cliff's delta (δd) = 0.73, $P < 1 \times 10^{-15}$), Asian countries (δd = 0.56, $P < 1 \times 10^{-15}$) and LACs (δd = 0.42, $P < 1 \times 10^{-15}$). LAC participants showed accelerated aging compared with participants from Europe (δd = 0.52, $P < 1 \times 10^{-15}$) and Asian countries (δd = 0.20, $P < 1 \times 10^{-15}$). Participants from Asia showed accelerated aging relative to European participants (δd = 0.31, $P < 1 \times 10^{-15}$). Within Europe, southern European individuals had older biobehavioral ages than northern (δd = 0.18) and western European individuals (δd = 0.23). Eastern European individuals also showed accelerated aging compared with western Europeans (δd = 0.52) (Fig. 2d).

Participants from LICs showed accelerated aging compared with those from HICs, based on GNI (δd = 0.48, $P < 1 \times 10^{-15}$) and GDP (δd = 0.56, $P < 1 \times 10^{-15}$)(Fig. 2e). In the subsample with additional predictors, large effects of accelerated aging were consistently observed in LACs and Asia (China, South Korea, Israel and India) compared with Europe, and in LICs compared with HICs (Extended Data Fig. 2c–e).

Exposome and accelerated aging

Adverse exposomal factors across combined categories (physical, social and sociopolitical) were associated with accelerated aging (Fig. 2f; $P < 1 \times 10^{-15}$, Cohen's d (d) = 0.53). Similarly, adverse social and physical (gender equality, migration, structural equality, air quality) and sociopolitical (political representation, free political parties, inclusive suffrage, credible elections, local democracy) exposomal factors were associated with larger BBAGs (Fig. 2f; $P < 1 \times 10^{-15}$, d = 0.50 and d = 0.44, respectively). Individual analyses of each exposomal factor showed that adverse indicators were linked to larger BBAGs (Fig. 2g,h; all $P < 1 \times 10^{-15}$, all d > 0.37). Stronger associations were observed in the subsample with additional predictors (well-being, physical activity, unhealthy weight, alcohol consumption, sleep problems), showing large effect sizes for all combined exposomal factors (r = −0.26,

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Table 1 | Demographic information for cross-sectional and longitudinal demographic datasets

Cross-sectional				Longitudinal					
Latin America									
Total (*n*=58,442; 25,520 females, mean age=67.02, s.d.=9.17)				Total, wave 1 (*n*=8,608; 3,536 females, mean age=62.14, s.d.=6.10)			Total, wave 2 (*n*=8,608; 3,536 females, mean age=65.22, s.d.=6.09)		
Countries	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**
Brazil	64.33 (9.49)	(51, 90)	8,710 (3,822)						
Chile	71.01 (7.65)	(60, 90)	1,056 (387)						
Colombia	70.39 (7.65)	(60, 90)	22,879 (9,789)						
Costa Rica				Wave 1: 2012			Wave 2: 2015–2016		
	59.63 (3.18)	(53, 67)	2,557 (1,008)	69.60 (3.18)	(53, 66)	1,963 (719)	62.60 (3.18)	(56, 69)	1,963 (719)
Ecuador	70.01 (7.53)	(60, 90)	3,676 (1,880)						
Mexico				Wave 1: 2015			Wave 1: 2018		
	64.0 (9.76)	(51, 90)	18,202 (8,125)	64.68 (9.02)	(41, 97)	6,645 (2,817)	67.84 (8.99)	(44, 100)	6,645 (2,817)
Europe									
Total (*n*=86,149; 39,034 females, mean age=66.55, s.d.=9.91)				Total, wave 1, 2017 (*n*=4,899; 1,825 females, mean age=72.32, s.d.=7.72)			Total, wave 2, 2019–2020 (*n*=4,899; 1,825 females, mean age=74.32, s.d.=7.77)		
Countries	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**
Austria	67.26 (9.67)	(51, 90)	4,320 (1,873)	74.95 (7.97)	(57, 98)	120 (41)	76.95 (7.97)	(59, 100)	120 (41)
Belgium	63.68 (10.4)	(51, 90)	4,942 (2,309)	71.98 (8.06)	(49, 98)	381 (137)	73.98 (8.05)	(49, 98)	381 (137)
Bulgaria	67.61 (9.48)	(51, 90)	1,953 (834)						
Croatia	65.45 (9.0)	(51, 90)	2,798 (1,270)						
Cyprus	69.87 (10.0)	(51, 90)	1,205 (508)						
Czechia	67.66 (9.37)	(51, 90)	5,575 (2,418)	71.95 (6.93)	(52, 93)	359 (130)	73.55 (6.93)	(54, 95)	359 (130)
Denmark	63.66 (9.96)	(51, 90)	2,609 (1,263)	70.72 (7.78)	(54, 97)	433 (175)	72.72 (7.78)	(56, 99)	433 (175)
Estonia	68.31 (10.48)	(51, 90)	7,522 (3,162)						
Finland	67.21 (9.39)	(51, 90)	1,982 (925)						
France	65.74 (10.6)	(51, 90)	3,640 (1,674)	71.87 (8.50)	(46, 96)	541 (205)	73.87 (7.78)	(48, 98)	541 (205)
Germany	66.42 (9.83)	(51, 90)	4,567 (2,198)	72.19 (7.27)	(53, 93)	356 (141)	74.19 (7.27)	(55, 95)	356 (141)
Greece	64.95 (10.29)	(51, 90)	2,599 (1,179)	73.23 (7.98)	(49,92)	699 (268)	73.30 (7.98)	(51, 93)	699 (268)
Hungary	66.8 (9.13)	(51, 90)	3,010 (1,324)						
Italy	64.97 (9.75)	(51, 90)	4,541 (2,138)	73.30 (7.68)	(51, 98)	487 (167)	75.30 (7.68)	(53, 100)	487 (167)
Latvia	67.84 (10.01)	(51, 90)	1,684 (640)						
Lithuania	67.57 (10.26)	(51, 90)	2,033 (763)						
Luxembourg	66.11 (9.56)	(51, 90)	2,104 (985)						
Malta	68.13 (8.77)	(51, 90)	1,259 (569)						
Netherlands	65.95 (9.72)	(51, 90)	2,546 (1,176)						
Poland	64.74 (9.49)	(51, 90)	3,612 (1,697)	70.24 (7.24)	(53, 96)	387 (152)	72.24 (7.24)	(55, 98)	387 (152)
Portugal	64.72 (9.0)	(51, 90)	1,914 (912)						
Romania	66.66 (9.15)	(51, 90)	2,083 (913)						
Slovak Republic	63.1 (8.02)	(51, 90)	2,022 (954)						
Slovenia	67.82 (9.76)	(51, 90)	5,291 (2,383)						
Spain	67.77 (10.43)	(51, 90)	4,912 (2,374)	73.75 (8.42)	(55, 975	342 (106)	75.75 (8.42)	(57, 97)	342 (106)
Sweden	69.07 (9.22)	(51, 90)	2,792 (1,342)	74.21 (7.40)	(57, 97)	450 (181)	76.21 (7.40)	(57, 99)	450 (181)
Switzerland	67.56 (9.69)	(51, 90)	2,634 (1,251)	71.65 (8.90)	(45, 97)	344 (122)	73.56 (8.90)	(47, 99)	344 (122)
Asia									
Total (*n*=17,119; 8,360 females, mean age=69.87, s.d.=11.19)				Total, wave 1 (*n*=8,124; 3,792 females, mean age=69.51, s.d.=9.54)			Total, wave 2 (*n*=8,124; 3,792 females, mean age=76.36, s.d.=9.54)		
Countries	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**
China				Wave 1: 2011			Wave 2: 2014–2015		
	78.64 (7.28)	(52, 90)	6,672 (3,510)	80.48 (9.78)	(50, 114)	3,534 (1,801)	83.11 (9.78)	(53, 117)	3,534 (1,801)

Table 1 (continued) | Demographic information for cross-sectional and longitudinal demographic datasets

Cross-sectional				Longitudinal					
India	71.16 (6.96)	(60, 90)	677 (479)						
Israel	63.55 (9.38)	(51, 90)	956 (455)						
South Korea				Wave 1: 2012	Wave 2: 2015–2016				
	63.82 (9.53)	(51, 90)	8,814 (3,916)	58.54 (9.29)	(45, 91)	4,590 (1,991)	69.54 (9.29)	(56, 10)	4,590 (1,991)
Africa									
Total (*n*=271; 117 females, mean age=61.69, s.d.=8.05)									
Countries	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**	**Age (years) (s.d.)**	**Age range (years)**	**Total *n* (female)**
Egypt	61.69 (8.05)	(51, 89)	271 (117)						
South Africa				Wave 1: 2020			Wave 2: 2021		
				45.69 (14.15)	(25, 90)	5,431 (2,285)	46.69 (14.1)	(26, 91)	5,431 (2,285)

$P < 1 \times 10^{-15}$, $d = 0.53$) and moderate effect sizes for physical and social ($r = -0.24$, $P < 1 \times 10^{-15}$, $d = 0.50$) and sociopolitical ($r = -0.22$, $P < 1 \times 10^{-15}$, $d = 0.44$) categories (Extended Data Fig. 2f–h). We conducted additional analyses adjusting for combined effects of other exposome categories and excluding low-density data owing to sparse intermediate values and potential outliers. Both analyses confirmed the results (Extended Data Fig. 3).

Longitudinal assessment of health outcomes

In longitudinal analyses, BBAG effects were adjusted to control for varying time gaps between waves (Methods). Regression models examined whether BBAGs in wave 1 predicted cognition, functional ability, well-being and BBAGs in wave 2. These outcomes were selected for their relevance to healthy aging[17]. Accelerated aging (larger BBAGs) in wave 1 predicted declines in healthy aging factors in wave 2, with a large effect on functional ability ($r = -0.33$, $P < 1 \times 10^{-15}$, $d = 0.70$, $n = 21{,}631$ participants) and a moderate effect on cognition ($r = -0.22$, $P < 1 \times 10^{-15}$, $d = 0.44$; Fig. 3a). Effects on well-being were negligible (Fig. 3a). Accelerated aging in wave 1 also predicted accelerated aging in wave 2 ($r = 0.61$, $P < 1 \times 10^{-15}$, $d = 1.55$; Fig. 3b), showing that BBAGs have long-lasting effects. To prevent circularity (using a related measure as both predictor and outcome), BBAGs were recalculated excluding the specific outcome variable for each model. Extended Data Fig. 4 shows these associations, yielding similar results with slightly smaller effects. In the South African cohort, accelerated aging in wave 1 significantly predicted declines in memory ($r = -0.17$, $P < 1 \times 10^{-15}$, $d = 0.35$) and walking abilities ($r = -0.25$, $P < 1 \times 10^{-15}$, $d = 0.55$) in wave 2 (Extended Data Fig. 5a). Larger BBAGs in wave 1 predicted larger BBAGs in wave 2 ($r = -0.90$, $P < 1 \times 10^{-15}$, $d = 4.21$; Extended Data Fig. 5b).

Epidemiological analysis of accelerated aging

In the cross-sectional analysis, odds ratios (Fig. 4a, top panel) showed that participants with accelerated aging were ~8 times more likely to have reduced functional ability (odds ratio = 7.64, 95% confidence interval (CI): 7.13–8.19) and ~4 times more likely to experience poorer cognition (odds ratio = 4.41, 95% CI: 4.11–4.74). The attributable risk (Fig. 4a, bottom panel) to accelerated aging was 27.18% (95% CI: 27.15–27.22) for reduced functional ability and 14.83% (95% CI: 14.77–14.89) for poorer cognition. In the subsample, the strongest association was with reduced functional ability (odds ratio = 9.31, attributable risk = 28.45), followed by decreased well-being (odds ratio = 4.94, attributable risk = 16.91) and poorer cognition (odds ratio = 2.29, attributable risk = 6.74; Extended Data Fig. 6a).

In the longitudinal analysis, the relative risk (Fig. 4b, top panel) showed that participants with accelerated aging were ~1.4 times (95% CI: 1.36–1.44) more likely to experience functional declines, ~1.25 times (95% CI: 1.22–1.29) more likely to have poorer cognition and ~1.16 times (95% CI: 1.12–1.19) more likely to experience reduced well-being. The attributable risk (Fig. 4b, bottom panel) to accelerated aging was 28.42% (95% CI: 28.34–28.50) for functional decline, 20.07% (95% CI: 19.95–20.19) for poorer cognition and 13.46% (95% CI: 13.27–13.65) for reduced well-being. Similar relative risks were found for walking (relative risk = 17.29) and memory (relative risk = 3.75), although the confidence interval for memory was less stable, and attributable risks were higher (Extended Data Fig. 6b).

Meta-analyses of aging and unhealthy aging outcomes

In the cross-sectional meta-analysis (Fig. 4c), common-effects and random-effects models confirmed significant associations between accelerated aging and poorer healthy aging outcomes. Participants with accelerated aging had substantially increased odds of experiencing cognitive decline (common effects: odds ratio = 2.18, 95% CI: 2.10–2.25; random effects: odds ratio = 2.12, 95% CI: 1.88–2.37) compared with those with delayed aging. The association was even stronger for declines in functional ability (common effects: odds ratio = 2.39, 95% CI: 2.28–2.51; random effects: odds ratio = 2.56, 95% CI: 2.23–2.94). In the subsample, participants with accelerated aging had about twice the odds of reduced cognitive functioning and functional ability, while well-being showed a weaker association (odds ratio ≈ 1.5) (Extended Data Fig. 6c). Despite high heterogeneity across countries, associations between accelerated aging and poorer healthy aging outcomes were observed in most nations (Supplementary Tables 1 and 2).

In the longitudinal meta-analysis (Fig. 4d), accelerated aging significantly increased the risk of declines in functional ability and cognition. Risk of cognitive decline were nearly double (common effects: relative risk = 1.99, 95% CI: 1.89–2.11; random effects: relative risk = 2.03, 95% CI: 1.75–2.36), while the risks for functional decline were even higher, exceeding twofold (common effects: relative risk = 2.37, 95% CI: 2.21–2.54; random effects: relative risk = 3.57, 95% CI: 2.74–4.67). For well-being, the common effects model showed no significant increase (common effects: relative risk = 0.97, 95% CI: 0.94–1.00), while the random-effects model indicated a moderate increase (random-effects: relative risk = 1.47, 95% CI: 1.29–1.68). Cross-country variability was high, but most countries showed significant associations between accelerated aging and declines in healthy aging outcomes (Supplementary Table 3).

Figure 4e summarizes cross-sectional and longitudinal model averages by income level (GNI and GDP classifications). Accelerated aging was more strongly associated with poorer healthy aging outcomes—cognition, functional ability and well-being—in LICs compared with HICs, based on GNI ($P = 5.28 \times 10^{-5}$, $r = 0.57$) and GDP ($P = 2.41 \times 10^{-9}$,

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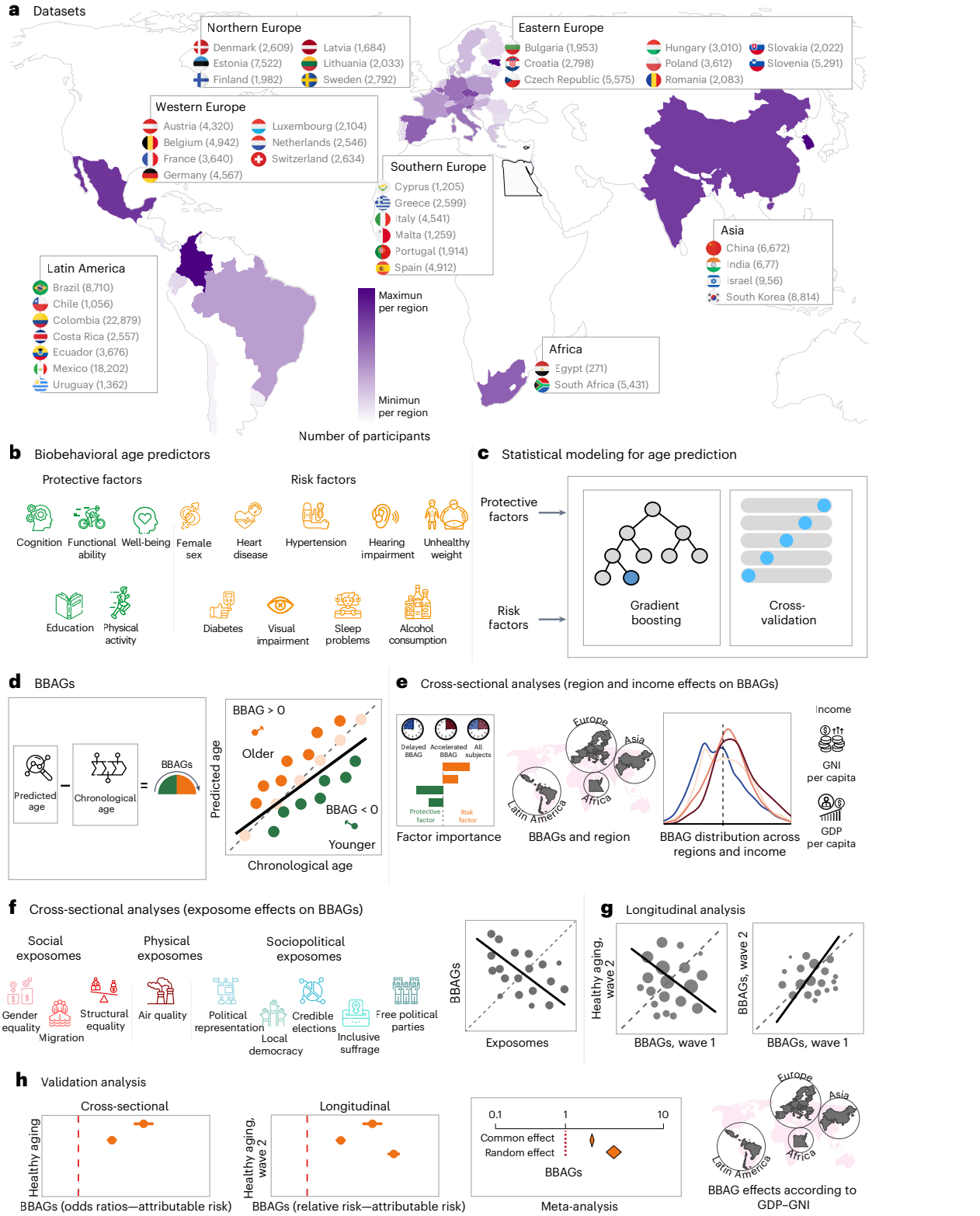

Fig. 1 | Study design and analysis pipeline. a, The dataset includes 161,981 participants from aging, health and well-being surveys across LACs, Europe, Asia (China, South Korea, Israel and India) and Africa (Egypt and South Africa) (sample sizes by country are in parentheses). **b**, Chronological age was predicted using harmonized risk and protective factors. **c**, A gradient boosting regression model, trained on 90% of the dataset with 10-fold cross-validation, estimated chronological age based on these factors. **d**, BBAGs were computed as the difference between predicted and chronological age (BBAG > 0: accelerated aging; BBAG < 0: delayed aging), adjusted for regression-to-the-mean bias. **e**, Feature importance was assessed via MDI, and BBAG distributions were compared across continents and income groups. **f**, BBAGs were tested cross-sectionally by different exposomal factors including macro-level social (gender equality, migration, structural inequality), physical (air quality) and sociopolitical (democracy indicators) variables. **g**, Longitudinal analyses evaluated BBAGs as predictors of future aging trajectories, examining their association with changes in cognition, functional ability and well-being over time. **h**, Validation analyses included epidemiological metrics (odds ratios and risk ratios) and meta-analyses to assess the validity of associations by income level (low versus high, based on GNI and GDP classifications). Supplementary Table 7 details subsample datasets. The maps were created in Python using the Plotly library (https://plotly.com/python/maps/). All other illustrations and icons were designed using GIMP (https://www.gimp.org).

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Table 2 | Effect size metrics and interpretation. References for the effect sizes and their corresponding cutoffs are available in Supplementary Note 6

Effect size	Small	Moderate	Large
Cohen's f^2 (F^2)	0.02	0.15	0.35
Cliff's delta (δd)	0.15	0.33	0.47
Cohen's *d* (*d*)	0.20	0.41	0.63
Correlation (*r*)	0.10	0.20	0.30
Rank-biserial correlation (*r*)	0.10	0.30	0.50

$r = 0.84$). Analysis in the subsample with additional predictors showed comparable results (Extended Data Fig. 6d).

Sensitivity analyses

To assess the impact of missing data imputation, we conducted the BBAG calculation and main analyses with and without imputed data. Without imputation, model performance remained consistent for predictor-based age estimation ($R^2 = 0.26$, $F^2 = 0.35$, $r = 0.51$, RMSE = 8.44, $n = 148{,}188$ participants) and classification into delayed-aging ($R^2 = 0.56$, $F^2 = 1.28$, $r = 0.75$, RMSE = 6.57) or accelerated-aging groups ($R^2 = 0.69$, $F^2 = 2.24$, $r = 0.84$, RMSE = 4.34) (Extended Data Fig. 7).

We tested whether different domains of physical activity—work-related versus leisure-time activities—had distinct effects on BBAGs in a subsample. BBAGs were estimated by including each measure as an independent predictor ($R^2 = 0.48$, $F^2 = 0.92$, $r = 0.69$, RMSE = 8.05). Leisure- and work-related physical activity yielded delayed BBAGs, with the former having stronger effects (Supplementary Table 4).

Sex-stratified analyses revealed distinct patterns for females and males. In both groups, the top protective factors were education, functional ability and cognition, while hearing impairment, hypertension and heart disease were the top risk factors. However, education was a stronger protective factor in females, whereas hearing impairment was a stronger risk factor in males (Extended Data Fig. 8a–d). Although adverse exposomal factors were linked to accelerated aging in both sexes, these effects were stronger in females than in males (Extended Data Fig. 8e–g).

We assessed individual-level socioeconomic status on BBAGs in a subsample. Lower socioeconomic status was significantly associated with increased BBAGs, when socioeconomic status was calculated both by excluding years of education ($r = -0.17$, $d = 0.34$, $P < 1 \times 10^{-15}$) and by including education ($r = -0.36$, $d = 0.76$, $P < 1 \times 10^{-15}$). Adjusting for socioeconomic status as a covariate did not suppress the associations between macro-level exposomal factors and BBAGs (Supplementary Tables 5 and 6). As expected, larger effect sizes of socioeconomic status were observed when calculated using education, as this variable is used in BBAG estimation. Comparisons among individuals classified as high and low socioeconomic status and living in HICs and LICs (based on GDP and GNI classifications) showed the biggest effect sizes when comparing individuals from LICs with low socioeconomic status with HIC individuals with low socioeconomic status (excluding education—GDP (δd = 0.90), GNI (δd = 0.92); including education—GDP (δd = 0.87), GNI (δd = 0.92)). When comparing LIC individuals with high socioeconomic status with HIC individuals with low socioeconomic status, effect sizes were small (excluding education—GDP (δd = 0.21), GNI (δd = 0.02); including education—GDP (δd = 0.22), GNI (δd = 0.13)) (Supplementary Tables 7 and 8). Thus, individual socioeconomic status modulated the accelerated aging, but the effects of country income and exposomal factors were partially independent of these individual disparities (Supplementary Tables 5–8). Finally, model calibration tests confirmed the stability of estimated odds ratios (Supplementary Table 9).

Discussion

We investigated the impact of individual protective and risk factors, along with macro-level regional income and exposome influences, on accelerated aging across global populations. BBAGs predicted healthy aging outcomes, with protective factors associated with delayed aging and risk factors associated with accelerated aging. Global disparities revealed more accelerated aging in participants from African countries (Egypt, South Africa) and LACs than in participants from Europe and Asia (China, South Korea, Israel and India). Individuals from lower-income countries showed larger BBAGs than those from high-income countries, suggesting the adverse health effect of socioeconomic inequalities. Adverse physical, social and sociopolitical exposomal factors were associated with accelerated aging. Larger baseline BBAGs predicted declines in cognition and, in particular, functional ability over time. Larger baseline BBAGs also predicted long-term BBAGs in aging trajectories, confirming lasting effects. Validation through odds ratios, attributable and relative risks, and meta-analyses consistently associated larger BBAGs with unhealthy aging across regions and incomes. BBAGs capture aging trajectories by incorporating protective and risk factors, rather than relying on biological markers or chronological age. The identification of functional ability, cognition, education and cardiometabolic conditions as key predictors that remain consistent across regions confirms the relevance of these metrics in aging research[15–17,35–37]. Moreover, accelerated aging metrics have the potential to enhance inclusion criteria in clinical and epidemiological research by refining risk stratification models that integrate exposomal factors[22,23] alongside biological aging measures. These findings highlight how individual and macro-level exposomal factors contribute to global and regional disparities in aging, shaping life course trajectories. They also offer synergetic[38,39], cumulative exposure-based metrics that can inform future research and guide targeted preventive interventions across diverse populations.

Protective and risk factors vary across populations, shaping aging quality and dementia risk[13–15,17]. Combined protective and risk factors in the prediction of chronological age suggest aging as a multidimensional process shaped by health, lifestyle, psychosocial, cognitive and biological factors[40,41]. Inspired by studies relying on brain or organ clocks[2,3], we estimated accelerated aging using noninvasive, easily accessible measures suitable for diverse populations, including low-resource settings. By identifying which factors have the greatest associations with accelerating or delaying aging, interventions can be tailored to optimize healthy aging outcomes. While brain and biological clocks[3–5] provide valuable insights into aging mechanisms, they require more costly biological measures (that is, plasma or brain imaging). The aging metric presented here facilitates cross-regional and cross-country comparisons by leveraging available national survey data. Longitudinal analyses, epidemiological measures and meta-analyses validate BBAGs as predictive markers of unhealthy aging, supporting their use in identifying at-risk populations and guiding targeted interventions. This metric may enable cross-country comparisons of other healthy aging outcomes, encouraging nations to prioritize integrative[42] investments in healthy aging[22].

Inequalities and multimodal exposomal factors were associated with accelerated aging, shedding light on previous individual reports of brain health[2,26,27] and aging trajectories[24,25]. Regional inequalities among low-income populations in Egypt, South Africa, LACs and Asia[43–45], combined with the higher prevalence of cardiometabolic conditions[13] and hearing impairment[46], exacerbate dementia risk. Classical exposomal factors, including physical (air pollution) and social (structural socioeconomic inequality[20,26,34], gender inequalities[27] and migration[33]) factors are known to impact brain health and aging, which we show to also be associated with accelerated aging. A biological embedding of socioeconomic inequality[47] and adverse exposomal factors may drive accelerated aging particularly in LACs and African countries such as Egypt and South Africa and, to a lesser

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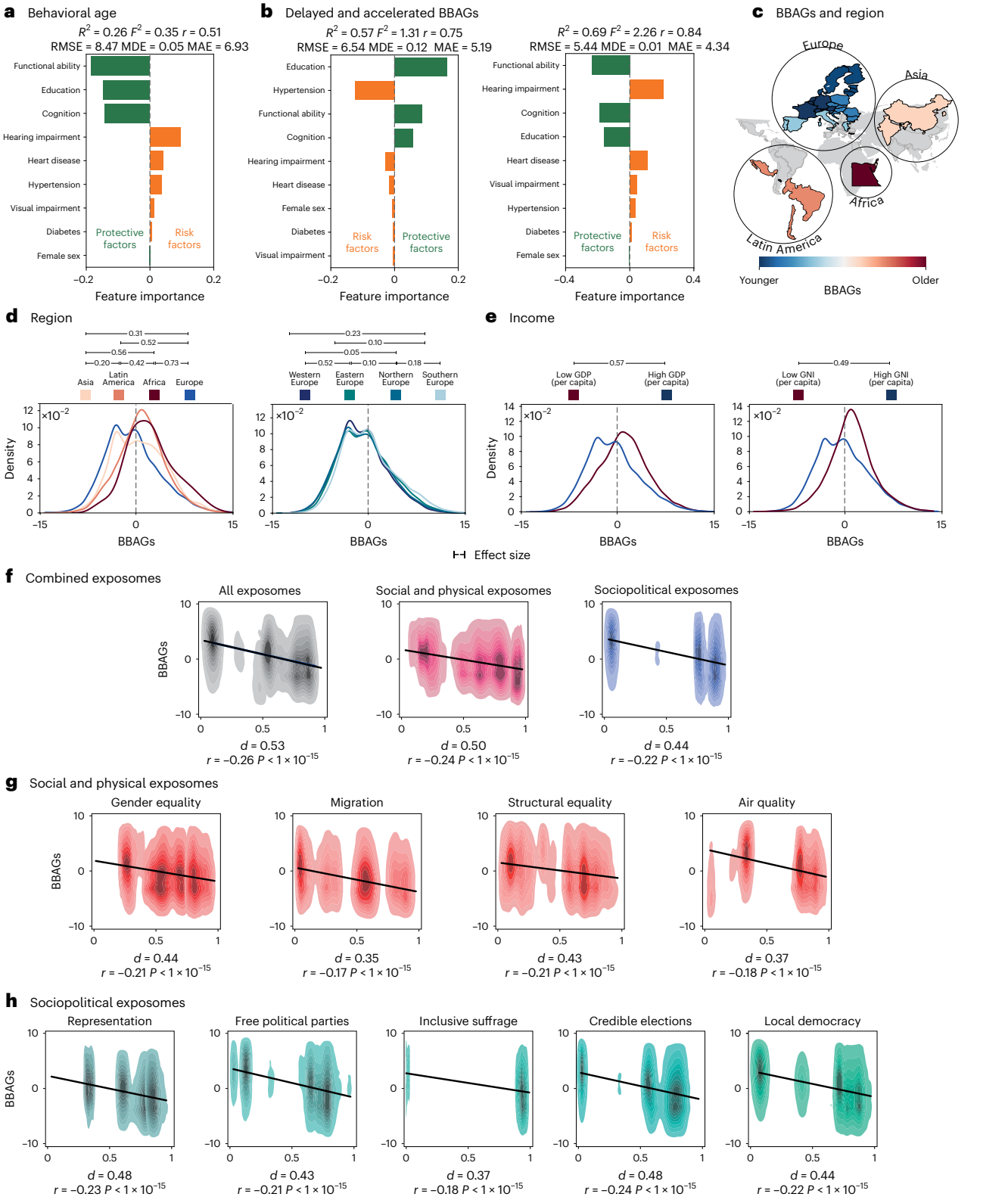

Fig. 2 | Cross-sectional results on BBAGs and multiple associations. a, Feature importance, assessed via MDI, enabled the prediction of chronological age using biobehavioral factors. The sample size for the analyses reported in this figure included 161,981 individuals. Goodness-of-fit and feature importance metrics are provided. **b**, MDI facilitated the characterization of groups with more delayed (left panel) and more accelerated (right panel) aging. Goodness-of-fit and feature importance metrics are provided. **c**, Average BBAG distribution by continent. The color bar indicates younger and older BBAGs. **d**, BBAG comparisons by continent and by European regions. **e**, BBAG comparisons between low- and high-income countries, based on GNI and GDP indicators. **f**, Linear regression models were used to assess the interaction between BBAGs and all exposomal factors, as well as the combined effects of social, physical and sociopolitical exposomes. **g**, Linear regression models were applied to examine the associations between BBAGs and individual social (gender equality, migration and structural equality) and physical (air quality) exposomal factors. **h**, Linear regression models were used to assess the relationship between BBAGs and individual sociopolitical exposomal factors (democracy indicators). Extended Data Figs. 2 and 3 present additional results.

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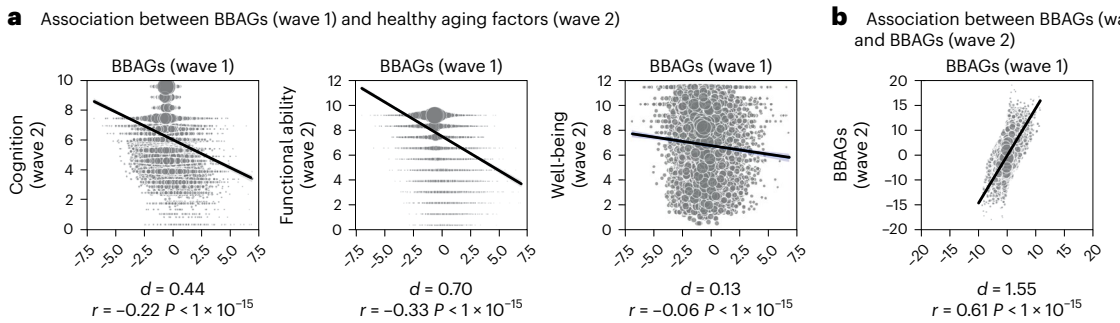

Fig. 3 | Longitudinal results on healthy aging outcomes. a, Linear regression models tracking the relationships between BBAGs in wave 1 and healthy aging factors (cognition, functional ability, well-being) in wave 2. The sample size for the analyses reported in this figure included 21,631 individuals. BBAGs in wave 1 significantly predicted adverse outcomes in cognition, functional ability and well-being in wave 2. **b**, Linear regression models assessing BBAGs in wave 1 as significant predictors of BBAGs in wave 2. Results excluding the healthy aging factor assessed for association and those from the South African dataset are shown in Extended Data Figs. 4 and 5, respectively. All *P* values reported in **a** and **b** were $<1 \times 10^{-15}$.

extent, in Asian countries, where physical, social and sociopolitical factors have substantial roles. Variability in effect sizes may reflect regional differences in how exposomal factors influence aging, with larger effects observed in countries experiencing greater disparities. This pattern suggests that the combination of aggregate-level metrics and BBAGs captures the disproportionate burden of accelerated aging in disadvantaged populations. Macro-level exposomal effects persist even after adjusting for individual socioeconomic status differences, suggesting that structural and environmental determinants have a substantial influence on aging beyond individual conditions[20,34]. When multiple disparity-related measures are included as predictors, smaller sex differences are observed[20,34]. Sex-stratified analyses confirmed that education is more protective for women[48], probably owing to historical disparities in access[49], whereas hearing loss is a stronger risk factor[50] and associated with cognitive decline in men[51]. Sex-specific factors are intertwined with environmental factors and gender inequalities[52]. Despite advances in gender equality, women still face disproportionate disadvantages owing to caregiving roles, economic inequalities and healthcare access, potentially exacerbating accelerated aging[2,53]. These differences highlight the importance of incorporating sex-specific frameworks in aging research and intervention design[52].

The link between sociopolitical instability and accelerated aging underscores the role of political, institutional and governance factors in shaping health outcomes[28,29,54,55]. Political polarization, governance failures and institutional instability impact health through policy-driven resource allocation, social cohesion and healthcare system stability[54], increasing aging disparities. Polarization discourages health-seeking behaviors and deepens disparities in care access[29]. Affective and ideological polarization are emerging key health determinants, with trust in government linked to better health, while distrust and political polarization increase mortality and weaken public health responses[56]. Countries with corrupt, weakly democratic and opaque governments experience more severe health inequalities[55]. These factors may collectively accelerate aging at the population level. Aging research has largely overlooked sociopolitical instability as a key driver of health outcomes. Sociopolitical factors can impact health through chronic stress pathways[29]. Chronic exposure to unstable governance may induce prolonged activation of stress, leading to allostatic interoceptive overload[57,58] and accelerating cardiovascular and cognitive decline[29,55]. Future studies should expand cross-national analyses of brain health by incorporating political governance and polarization measures, and investigating causal links between sociopolitical instability and accelerated aging. Our findings are intended to support inclusive and equitable policy responses that mitigate structural vulnerabilities—not to label or penalize countries or communities. Our results provide specific tools to advance global health equity and inform more precise risk-prediction models for aging.

While our findings suggest that accelerated aging predicts cognitive and functional decline, aging can have bidirectional effects. Risk and protective factors influence aging trajectories but can also change over time owing to aging trajectories. For instance, individuals with higher BBAGs may experience increased frailty, reduced resilience and diminished access to protective resources, further reinforcing the risk factors contributing to aging disparities. Longitudinal analyses support the role of BBAGs as early markers of aging-related decline, as they predict future cognitive and functional declines. While reverse causation may apply to individual-level variables, it is unlikely that accelerated aging directly influences macro-level exposomal factors, such as air pollution, democracy or socioeconomic inequality. These structural conditions shape population-wide aging disparities rather than being direct consequences of individual trajectories.

Accelerated aging influenced by the exposomal factors could be partially mitigated through targeted interventions. Cognition, functional ability, education, well-being, physical activity, sensory impairments and cardiometabolic conditions can be addressed through lifestyle changes, multicomponent interventions and public health policies. Accelerated aging measures may support the early identification of at-risk individuals, particularly in resource-limited settings lacking access to more expensive biomarkers. Less modifiable factors—such as air quality and sociopolitical conditions including inequality and political representation—require addressing systemic disparities. Incorporating country-level exposome data into global surveillance could help identify structural drivers of accelerated aging and guide equitable resource allocation. Differentiating between immediate intervention targets and broader systemic barriers enhances the practical relevance of BBAGs for both clinical and policy decision-making. The stronger effect sizes in the accelerated aging model suggest that risk factors have greater associations with accelerated aging trajectories than protective factors do in delaying aging, underscoring the importance of early intervention for modifiable risks. The findings also highlight the synergetic nature[38] of risk exposure, in which multiple vulnerabilities may exponentially drive aging acceleration. Affordable global markers of personalized aging trajectories represent a critical priority to guide public decision-making processes. Universal strategies such as improving education, enhancing air quality and reducing inequalities benefit all populations, but prioritizing at-risk populations maximizes their impact on reducing disparities. Addressing these challenges requires policies that enhance access to protective resources, mitigate modifiable risks and reduce global inequalities.

Our study strengths include its use of a large, diverse dataset spanning four continents and multiple income levels, enabling

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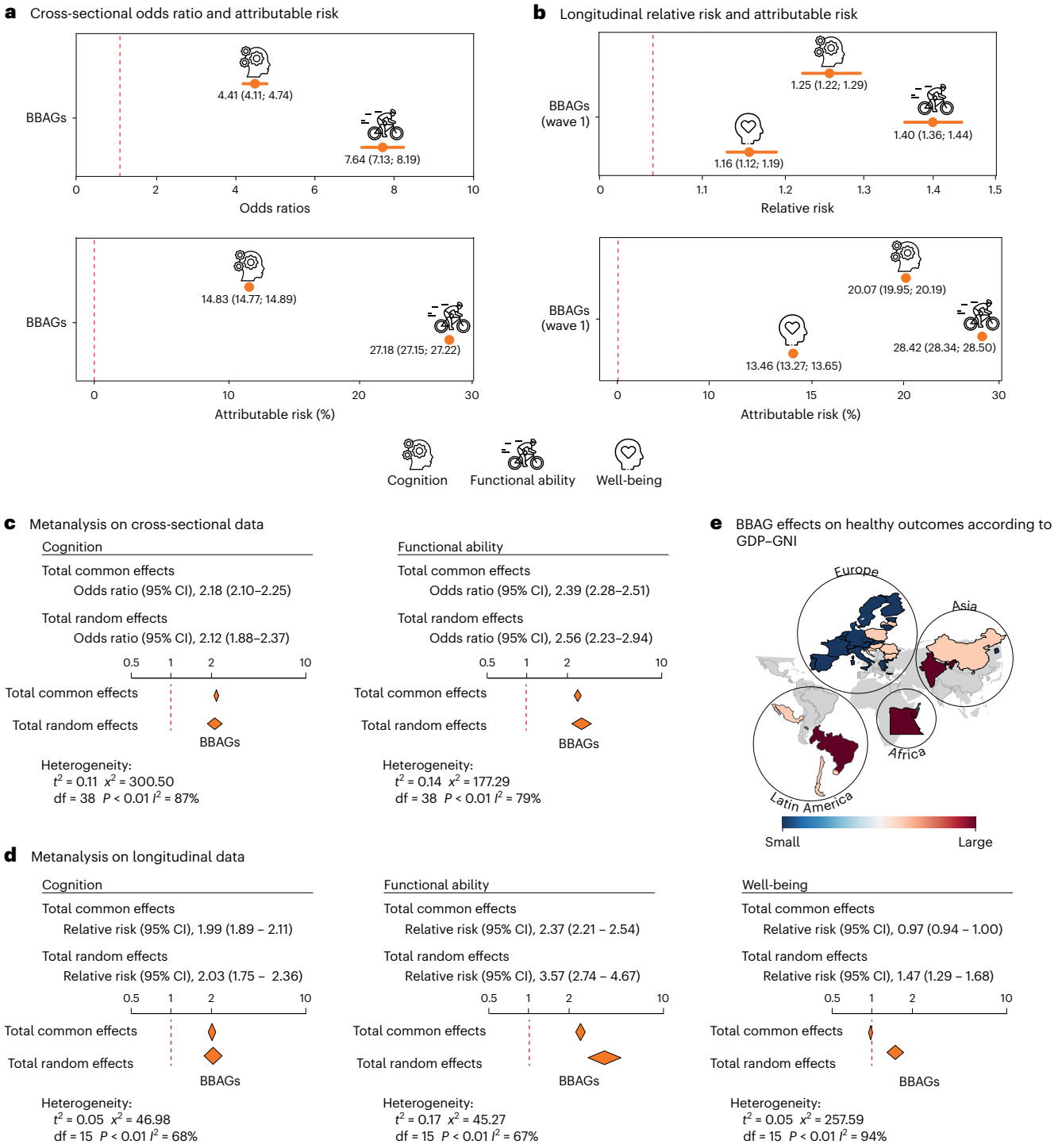

Fig. 4 | Validation via epidemiological metrics and meta-analysis. a, Odds ratios and attributable risk for the cross-sectional analysis. Results show that BBAGs are significantly associated with poorer functional ability and cognition. Cognition results were based on 161,564 participants, and functional ability results, on 157,825 participants. **b**, Relative risk and attributable risk for the longitudinal analysis. BBAGs in wave 1 were significantly associated with declines in functional ability, cognition and well-being. Cognition, functional ability and well-being results were based on 20,597 participants. **c**, Meta-analysis of cross-sectional data for cognition and functional ability using common-effects and random-effects models. Larger BBAGs were associated with poorer outcomes in both domains, with high heterogeneity across countries. All *P* values reported in the meta-analysis of cross-sectional data were <0.01. **d**, Meta-analysis of longitudinal data for cognition, functional ability and well-being using common-effects and random-effects models. Increased BBAGs predicted declines across all outcomes, particularly for functional ability, with high heterogeneity. All *P* values reported in the meta-analysis of longitudinal data were <0.01. In **c** and **d**, we used Cochran's *Q* test to assess heterogeneity across studies, reporting the associated *P* value, degrees of freedom and I^2 statistic. **e**, Summary of cross-sectional and longitudinal results showing the average effect sizes from common- and random-effects models by income level (low or high), based on GNI and GDP classifications. The color bar represents effect sizes. Accelerated aging was more strongly associated with worse healthy aging outcomes—cognition, functional ability and well-being—in low-income countries across LACs, Asia (China, South Korea and India) and Egypt. Extended Data Fig. 6 and Supplementary Tables 1–3 provide complementary results. The maps were created in Python using the Plotly library (https://plotly.com/python/maps/). All other illustrations and icons were designed using GIMP (https://www.gimp.org).

cross-sectional and longitudinal analyses. Our findings highlight the value of integrating protective and risk factors and the exposome when studying aging trajectories beyond chronological age. These results were obtained using cost-effective, harmonized measures suitable for broad application in global populations.

This study has multiple limitations. While various (1) health factors, such as smoking, grip strength and comorbidities (including cancer, pulmonary diseases and renal diseases); (2) social factors such as isolation, social interaction and healthcare access; and (3) biomarkers (including blood cholesterol and glycemia measures) have a key role in aging, inconsistencies in reporting and measurement across countries prevented their inclusion here. Future research on aging trajectories should incorporate a broader range of health, biological and social factors in aging models. Studies can track mortality rates and disability-adjusted life years (DALYs) to better understand the long-term impact of accelerated aging. The limited representation of certain high-risk populations, particularly from Africa, reduces the generalizability of the findings. Longitudinal data were not available for all countries, increasing the risk of reverse causality for some exposomal factors. Available longitudinal data included only two waves, limiting the assessment of long-term trajectories. Lag-time effects—in which the consequences of exposures take years or decades to manifest—could be mitigated by incorporating ongoing metrics and wearable technologies in future research. Changes in exposures across the life course or transitions between poor and enriched environments warrant further investigation. Future studies should map spatial and temporal patterns more precisely using wearables and innovative indexes. Incorporating additional contributors, such as regional genetic–environmental interactions[59] and biological metrics, into predictive models is also recommended.

Our findings reflect associations rather than definitive causal relationships. While our longitudinal analyses offer evidence of temporal precedence, they do not necessarily establish causality. Proper causal inference would require experimental, quasi-experimental or intervention-based designs that manipulate risk or protective factors and assess their direct effects on BBAGs and aging-related outcomes. In addition, while exposome-level factors (for example, environmental and socioeconomic conditions) may shape aging clocks, the individual-level causal mechanisms driving these relationships have yet to be fully explored. Future research should incorporate causal inference approaches, such as Mendelian randomization, instrumental variable analyses or randomized controlled trials, to disentangle the complex interplay between risk and protective factors in aging trajectories. As in other studies[2,20], aggregate-level metrics are not without bias from data sources, especially those of national relevance. Although sociopolitical indicators are derived from widely used international databases (for example, the Global State of Democracy Indices), these sources are subject to measurement biases owing to data collection methodologies, country-level reporting inconsistencies and potential ideological influences. The consistent directional and systematic effects across countries and democracy indexes mitigate these concerns. In addition, potential inconsistencies are diminished by analyzing multiple sociopolitical indicators rather than relying on a single measure. While these indicators provide valuable insights, they should be interpreted with caution in the context of accelerated aging. Future studies should provide additional external validation of these aggregate-level sources.

In conclusion, our findings underscore the relevance of how protective and risk factors—embedded within macro-level influences, regional variation and the exposome—are associated with delayed and accelerated aging across a global context. The results highlight the need for tailored precision risk-prediction models, targeted interventions and policy actions to address health disparities. As the increasing trends in dementia and accelerated aging make it a global public health priority, reducing modifiable risks, strengthening protective factors and addressing inequalities are crucial at the population level. Promoting healthy aging requires integrated environmental, social and policy-driven solutions.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-025-03808-2.

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Methods

Cross-sectional study

We included 161,981 healthy participants (45.09% female, mean age = 67.06, s.d. = 9.85, age range = 51–90) from national surveys on health and aging in LACs, Europe, Asia (China, South Korea, Israel and India) and Egypt (Table 1, Fig. 1a and Extended Data Fig. 1a). Sex information was determined by self-report. No information regarding gender was available. A subset of data (excluding India and Egypt, n = 102,725; 46,765 female, mean age = 67.96, s.d. = 9.56, age range = 51–90) was used to analyze additional predictors (Supplementary Table 10 and Extended Data Fig. 1b). To handle missing data, we used mean imputation, assuming few outliers and improving interpretability[60]. This approach increased the sample size while maintaining a consistent set of variables across countries for model comparisons. Data collection followed standardized procedures, face-to-face interviews and a probabilistic, clustered, stratified, multistage design. Only participants without a dementia diagnosis were included. The databases of national surveys from all countries are open and were obtained according to the established procedures for each country (Supplementary Table 11). All methods adhered to the Declaration of Helsinki, with informed consent and ethics approvals (Supplementary Table 11; Institutional Review Board (IRB): Pontificia Universidad Javeriana FM-773-2021).

Longitudinal study

Longitudinal datasets (wave 1: n = 21,631, 42.31% females, mean age = 67.18, s.d. = 11.47, range = 41–114; wave 2: n = 21,631, 42.31% females, mean age = 71.64, s.d. = 10.47, range = 41–117) included LACs (Mexico, Costa Rica), Europe (Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Italy, Poland, Spain, Sweden, Switzerland) and Asia (China, South Korea) (Table 1 and Extended Data Fig. 1c). In a subset, we leveraged additional protective (well-being, physical activity) and risk (unhealthy weight, alcohol consumption, sleep problems) factors. As these predictors were unavailable for India and Egypt, these countries were excluded from this specific analysis. A South African dataset (wave 1: n = 5,431, 42.07% females, mean age = 45.69, s.d. = 14.15, range = 25–90; wave 2: n = 5,431, 42.07% females, mean age = 46.69, s.d. = 14.10, range = 26–91) was analyzed independently owing to distinct measures of cognition and functional ability not harmonizable with other datasets (Supplementary Note 2). To handle missing data, we also used mean imputation[60].

Predictors of age

A model predicting chronological age (Fig. 1b) used biobehavioral data of protective (cognition, functional ability, education) and risk factors (cardiometabolic conditions: hypertension, diabetes, heart disease; female sex; sensory impairments: visual and hearing impairments). Predictors were selected based on their established relevance to healthy aging and dementia risk, as well as their availability across datasets to ensure consistency. Cardiometabolic factors (hypertension, diabetes, obesity and dyslipidemia) were prioritized as they are strongly associated with aging and represent key modifiable risk factors. The included predictors were harmonized across datasets as they were systematically available. In a subset, we leveraged additional protective (well-being, physical activity) and risk (unhealthy weight, alcohol consumption, sleep problems) factors. The South African dataset included memory and walking abilities as predictors (Supplementary Note 2 and Supplementary Table 10). Measurements and harmonization details are in Supplementary Notes 1 and 2.

Statistical analyses

We reported P values and effect sizes, considering only small or larger effects while excluding negligible ones. Table 2 lists the cutoff values used in each analysis (Supplementary Note 6).

Predictor-based age estimation

Gradient boosting regression models[61] predicted participants' chronological age (Fig. 1c) based on biobehavioral risk and protective factors. The model was trained on 90% of the dataset and tested on an independent 10% subset with 10-fold cross-validation[62]. Performance was assessed with R^2, mean directional error (MDE) and RMSE[63]. F^2 measured effects sizes[63] (Table 2). Mean decrease in impurity (MDI)[64] evaluated feature importance. Bayesian optimization[65] tuned hyperparameters, identifying optimal settings.

We used several validation techniques to mitigate overfitting and increase robustness, including 10-fold cross-validation[62], feature importance analysis[64] and Bayesian optimization[65]. Machine learning offers key advantages over conventional regression by capturing non-hypothesis-driven patterns, minimizing bias and handling complex, high-dimensional data[66]. Unlike traditional models, it allows for data partitioning into training and testing sets, ensuring validation of identified patterns[67]. In addition, it controls for overfitting, multicollinearity and interdependencies across variables, making it well suited for analyzing aging-related factors[68].

BBAG estimation

We calculated BBAGs as the difference between participants' chronological age and predictor-based estimates (Fig. 1d), in which positive values (BBAG > 0) indicate accelerated aging, while negative values (BBAG < 0) suggest delayed aging[69]. The chronological age was regressed from the estimated BAGs to correct for regression-to-the-mean bias. Residuals were used to adjust BBAGs, with regression coefficients derived from the training data and applied to the test data. We also grouped participants with more accelerated or delayed aging based on extreme BBAGs (top and bottom 25% quartiles) and evaluated model goodness-of-fit and feature importance.

Cross-sectional diversity modulation (region and income)

We analyzed BBAG differences across continents and European regions (western, eastern, northern, southern; Fig. 1e and Supplementary Note 4) and compared them between HICs and LICs using two standard indicators: GNI per capita (high and upper-middle versus low and lower-middle) and GDP per capita (high or low), via median split. Data were sourced from the World Bank (https://databank.worldbank.org)[70]. Permutation tests with 100,000 iterations ensured robustness to non-normality. Bonferroni correction addressed multiple comparisons. Effect sizes were calculated using δd (ref. 71; Table 2).

Cross-sectional exposome modulation of accelerated aging

Linear regressions (Supplementary Note 5.1) examined the relationship between macro-level exposomal factors and BBAGs. Predictors encompassed social (gender inequality—gender inequality index (GII), migration—international migrant volumes as a percentage of the population, structural inequality—Gini index), physical (air quality—PM2.5 exposure) and sociopolitical (political representation, party freedom, inclusive suffrage, credible elections, local democracy) exposomal factors (Fig. 1e,f). Data sources included the World Health Organization (GII: https://www.who.int/data/), the World Bank (Gini, migration, air quality: https://databank.worldbank.org) and the Global State of Democracy Indices (sociopolitical exposomal factors: https://www.idea.int/democracytracker/dataset-resources). As in previous reports, exposomes were based on participants' year and country of residence at the time of the interview. Effect sizes were calculated using d (Table 2 and Supplementary Table 6)[72]. First, associations between all exposomal factors and BBAGs were analyzed by normalizing each measure (0 to 1) and calculating a global score as the average of normalized values, with higher scores indicating better conditions. Next, the impact of social and physical, and sociopolitical, exposomes on BBAGs was assessed using separate linear regressions, each with the corresponding exposomal factor score as a predictor. Finally, linear

models were used to evaluate the individual contributions of each exposome, controlling for the effects of other categories and excluding low-density data.

Longitudinal analyses of healthy aging outcomes

Longitudinal analyses (Fig. 1g) incorporated BBAGs to predict healthy aging outcomes, including preserved cognition, functional ability, well-being and future BBAG decline. These outcomes were selected owing to their established relevance as key indicators of healthy aging[73]. Regression models assessed whether (1) BBAGs in wave 1 predicted cognition, functional ability and well-being in wave 2, and (2) BBAGs in wave 1 predicted BBAGs in wave 2. This approach evaluates the impact of accelerated aging without attributing outcomes to specific risk or protective variables that have already been reported[2,3]. The calculation of BBAGs followed the same methodology in both cross-sectional and longitudinal analyses. However, to ensure comparability across countries in longitudinal analyses, wave 1 BBAGs were adjusted for time differences between waves. This adjustment ensures that differences in follow-up intervals across countries do not bias the results. To account for time differences between waves across countries, we adjusted wave 1 BBAGs by normalizing them relative to the time interval between assessments. First, we calculated the time difference (delta time) between wave 1 and wave 2 for each country. Then, we adjusted wave 1 BBAGs by dividing each value by the corresponding delta time.

In addition, to avoid circularity in our models, we conducted supplementary analyses in which BBAGs in wave 1 were recalculated excluding the specific factor used as the outcome. For instance, when cognition, functional ability or well-being was the outcome, the corresponding factor was independently removed from the BBAG calculation before running the regression models. This ensures that the predictive associations between BBAGs and healthy aging outcomes are not driven by self-correlations. Effect sizes were measured using *d* (Table 2 and Supplementary Table 6).

Validation analyses

Epidemiological metrics in cross-sectional and longitudinal studies. BBAGs were dichotomized, with values above zero indicating accelerated aging. Cross-sectional and longitudinal analyses were conducted using odds ratio, attributable risk and relative risk[74].

The odds ratios were obtained by calculating the exponent of the logistic models:

$$\text{Odds ratio}_n = e^{B_n}$$

where B_n is the estimated coefficient for predictor n.

Relative risk is expressed as:

$$\text{Relative risk} = \frac{\text{Probability of event in exposed group}}{\text{Probability of event in unexposed group}}$$

Attributable risk is expressed as:

$$\text{Attributable risk} = \text{Risk}_{\text{exposed}} - \text{Risk}_{\text{unexposed}}$$

In cross-sectional analyses, odds ratios and attributable risks were calculated using cognition and functional ability as outcomes. For longitudinal analyses, well-being, cognition and functional ability were included as outcomes, with relative risk and attributable risk quantifying the predictive value of BBAGs for changes over time. All measures were calculated after excluding outliers (Supplementary Note 4).

Meta-analysis in cross-sectional and longitudinal studies. Meta-analyses (Fig. 1h) were used to confirm the associations between BBAGs and healthy aging outcomes across countries and incomes. Odds ratios (cross-sectional) and relative risks (longitudinal) were calculated for each country. Meta-analyses used both random-effects and common-effects models to estimate pooled effect sizes. Higgins' I^2 values (which indicate the percentage of total variation across studies due to heterogeneity) exceeding 50% indicated substantial heterogeneity. The restricted maximum likelihood (REML) estimator calculated between-country variance. Results were summarized by averaging random effects and common effects from cross-sectional and longitudinal analyses, grouped by income level (GNI and GDP). Mann–Whitney tests compared these effects, with *r* measuring effect sizes (Table 2).

Sensitivity analyses

We performed multiple tests to further assess the robustness of the results. The main analyses were repeated using complete cases (no missing data). The predictor-based age estimation, BBAG calculation and analyses of participants with more accelerated or delayed aging based on extreme BBAGs (top and bottom 25% quartiles) were conducted both with and without imputation. To evaluate the effects of different types of physical activity on BBAGs, we analyzed work-related and leisure-time activities separately where available. BBAGs were recalculated, including each measure as an independent predictor. Data were available in datasets from Brazil and China (n = 15,258 (7,992 women), mean age = 70.51 (s.d. = 11.15), range = 51–90).

In addition, we performed sex-stratified analyses. First, we conducted predictor-based age estimation, calculated BBAGs and assessed whether the impact of protective and risk factors differed between female and male individuals. Second, linear regressions examined the relationship between social, physical and sociopolitical exposomes and BBAGs separately for each sex. Then, we tested whether the regression slopes differed between sexes by performing 10 iterations, splitting the data 90/10 in each iteration, and compared the slopes using *t*-tests.

To assess the impact of individual socioeconomic status differences, we conducted a sensitivity analysis using a subset of datasets with available individual data. Socioeconomic status was calculated based on three variables: individual or household income, occupation or profession, and years of formal education. The available values for each subject were averaged. If only one value was available, this variable defined their socioeconomic status. If two values were available, the socioeconomic status was the average of those two variables. If all three values were present, the final socioeconomic status was the mean of the three variables. As education was already included in the BBAG calculation, we reported the results by computing socioeconomic status both with (n = 142,052) and without education (n = 67,871). First, we conducted regression analyses to examine whether socioeconomic status, as a predictor, influenced BBAGs. Second, we reran the main models, incorporating socioeconomic status as a covariate, to determine whether the associations between macro-level exposomes and BBAGs remained significant after adjusting for individual differences. Finally, we conducted permutation tests to compare individuals classified as high and low socioeconomic status (based on the median) and living in HICs and LICs (according to GDP and GNI classifications).

To evaluate potential overfitting of odds ratios, we conducted model calibration tests, including the Hosmer–Lemeshow goodness-of-fit test[75] and bootstrapped confidence intervals, testing the reliability and robustness of the results. We applied 10 iterations, using 1,000 subjects per iteration and varying the number of groups, following recommendations[75]. The Hosmer–Lemeshow metric was calculated using both 10 (default value) and 50 groups to assess parameter sensitivity. In each iteration, we computed the odds ratio and its confidence interval. Finally, we reported the combined *P* value for both groupings, the range of confidence intervals across iterations and the 99% global confidence interval for the odds ratios. A good model fit is indicated by a *P* value > 0.05 (ref. 75).

Ethics approval

All methods adhered to the Declaration of Helsinki, with informed consent and ethics approvals (Supplementary Table 11). The National surveys on health, well-being and aging (SABE surveys) in Chile and Uruguay were approved by the IRB of the Institute of Nutrition and Food Technology, University of Chile, and the Ethics Committee of the Chilean National Council for Science and Technology Research. In Colombia, SABE received approval from the Human Ethics Committee of the Faculty of Health at Universidad del Valle (Acts numbers 09-014 and 011-015) and the Bioethics Committee of Universidad de Caldas (Code CBCS-021-14). In Ecuador, ethical approval was granted by Universidad San Francisco de Quito and the Instituto de Investigación en Salud y Nutrición. In Brazil, the Brazilian Longitudinal Study of Ageing (ELSI-Brazil) study was approved by the ethics committee of Fundação Oswaldo Cruz, Minas Gerais (Protocol Number 34649814.3.0000.5091). In Costa Rica, the Costa Rican Study on Longevity and Healthy Aging (CRELES) study received approval from the Ethics Committee of the University of Costa Rica (VI-763-CEC-23-04). In Mexico, the Encuesta Nacional sobre Salud y Envejecimiento (ENASEM) study was approved by the IRB or Ethics Committee of the University of Texas Medical Branch, Instituto Nacional de Estadística y Geografía (INEGI) and the Instituto Nacional de Salud Pública. In China, the Chinese Longitudinal Healthy Longevity Survey Series (CLHLS) study was approved by the Research Ethics Committees of Peking University (IRB00001052-13074). The Korean Longitudinal Study of Aging (KLoSA) followed strict anonymization protocols and was approved under the national public data infrastructure. The Survey of Health, Ageing and Retirement in Europe (SHARE) study in multiple European countries was approved by the Ethics Council of the Max Planck Society. In Egypt, the Longitudinal Study of Egyptian Healthy Aging (AL-SEHA) study received approval from the American University in Cairo's IRB (Case Number 2021-2022-029). In India, the Longitudinal Aging Study in India (LASI) study was approved by the Institute Ethics Committee of the All India Institute of Medical Sciences, New Delhi (ref. IEC-667/06.09.2019). Finally, the General Household Survey (GHS) in South Africa was conducted under ethical guidelines set by the Department of Statistics South Africa, following international standards for identity protection (QCC-GHS-2020 and QCC-GHS-2021). The IRB of Pontificia Universidad Javeriana (FM-773-2021) approved the study protocols.

Ethics and inclusion statement

This study was conducted in collaboration with researchers from multiple countries, with contributors from different sites listed as coauthors based on their specific contributions. Researchers from Low- and Middle-Income Countries (LMICs) actively participated in the study design, implementation, methodological procedures and reviewing processes. The study holds substantial local relevance, particularly given the pronounced disparities observed in Africa, LACs and other regions. Roles and responsibilities were clearly defined and agreed upon among collaborators before the research commenced. Ethical approval was obtained for all studies involving participants, as detailed in Supplementary Table 11. To safeguard privacy and prevent any potential stigmatization, all identifying information has been removed. We fully support the Nature Portfolio journals' guidelines on LMIC authorship and inclusion. Authorship was determined based on intellectual contributions, commitment and active involvement in the study, ensuring the inclusion of researchers born in LMICs and other underrepresented regions.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

Preprocessed data are freely available via GitHub (https://github.com/euroladbrainlat/Biobehavioral-age-gaps). Additional details can be found in Supplementary Table 11. The datasets come from sources that are either publicly available for direct download after registration or accessible upon request. For Chile and Uruguay, SABE data are available at https://pubmed.ncbi.nlm.nih.gov/16053641/; for Colombia, at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6774577/; for Ecuador, at https://www.ecuadorencifras.gob.ec/encuesta-de-salud-bienestar-del-adulto-mayor/; for Brazil, ELSI-Brazil: https://elsi.cpqrr.fiocruz.br; for Costa Rica, CRELES: http://www.creles.berkeley.edu/index.html; for Mexico, ENASEM: https://enasem.org/Home/index_esp.aspx; for China, CLHLS: https://charls.pku.edu.cn/en/; for South Korea, KLoSA: https://survey.keis.or.kr/eng/klosa/klosa01.jsp; for Europe, SHARE: https://www.share-eric.eu; and for Egypt (AL-SEHA), requests should be sent to M. Salama (mohamed-salama@aucegypt.edu). Data may be shared upon approval of a brief research proposal and signing of a data use agreement. The estimated response time is 3–4 weeks. For India (LASI), requests can be directed to S. Bajpai (swati.bajpai@gbhi.org). Access is granted based on a research purpose review and data sharing agreement. Timelines for access may vary depending on the review process, typically within 3–4 weeks. For South Africa (GHS), data requests should be addressed to C. Mostert (cyprian.mostert@aku.edu). Data may be shared upon approval of a brief research proposal and the signing of a data use agreement. The estimated response time is typically 3–4 weeks. Country-level indicators of GNI, GDP, air quality, socioeconomic inequality (Gini index) and migration were obtained from the World Bank (https://databank.worldbank.org/). GII data are available from the WHO (https://www.who.int/data/nutrition/nlis/info/gender-inequality-index-(gii)). Sociopolitical indicators were sourced from the Global State of Democracy Indices (https://www.idea.int/democracytracker/dataset-resources).

Code availability

Analysis codes are freely available via GitHub (https://github.com/euroladbrainlat/Biobehavioral-age-gaps).

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Author contributions

A.I., H.H., H.S.-G. and S.B. were responsible for conceptualization and formal analysis, and wrote the original draft. All authors contributed to the review and editing. H.H., H.S.-G., L.U.D.R., W.V.B., E.R.Z., S.B., C. Mostert, M.S. and S.M. had access to the raw data. All authors had access to all data in the study, and the corresponding authors had final responsibility for the decision to submit for publication.

Competing interests

E.R.Z. has served on scientific advisory boards for Nintx, Novo Nordisk and Masima. He is also a cofounder and a minority shareholder at Masima. The other authors declare no competing interests.

Additional information

Extended data is available for this paper at https://doi.org/10.1038/s41591-025-03808-2.

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Correspondence and requests for materials should be addressed to Sandra Baez or Agustin Ibanez.

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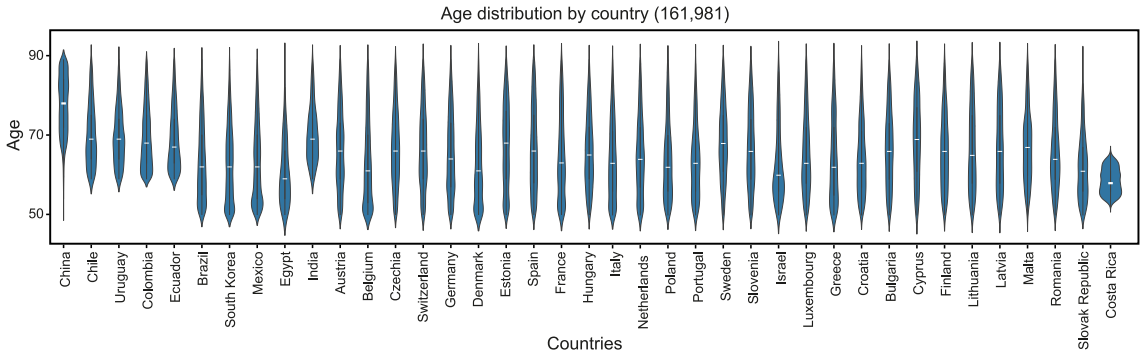
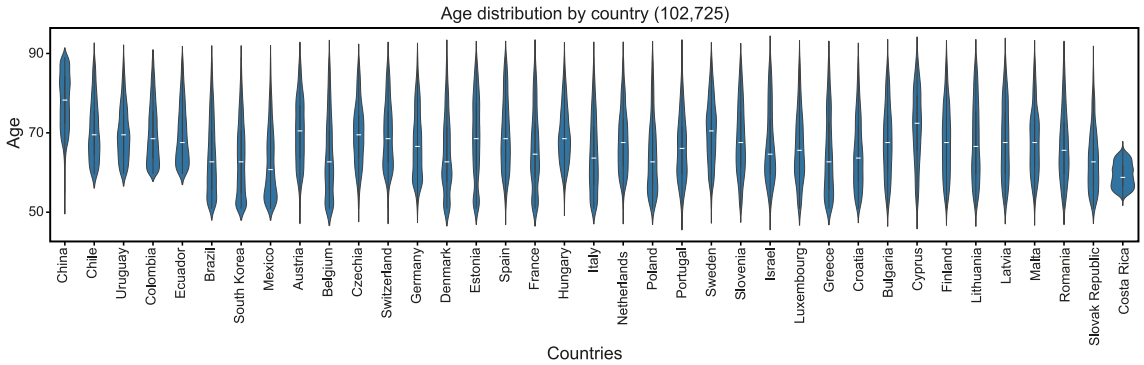
https://doi.org/10.1038/s41591-025-03808-2

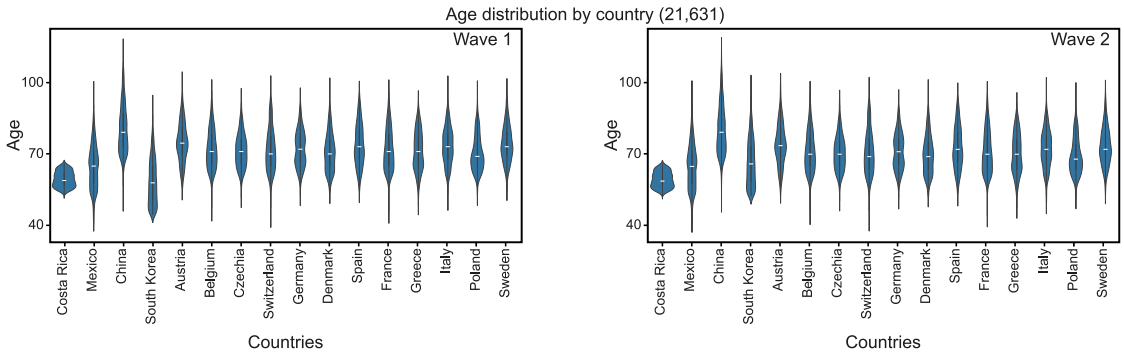
a. Cross-sectional dataset



b. Cross-sectional subsample

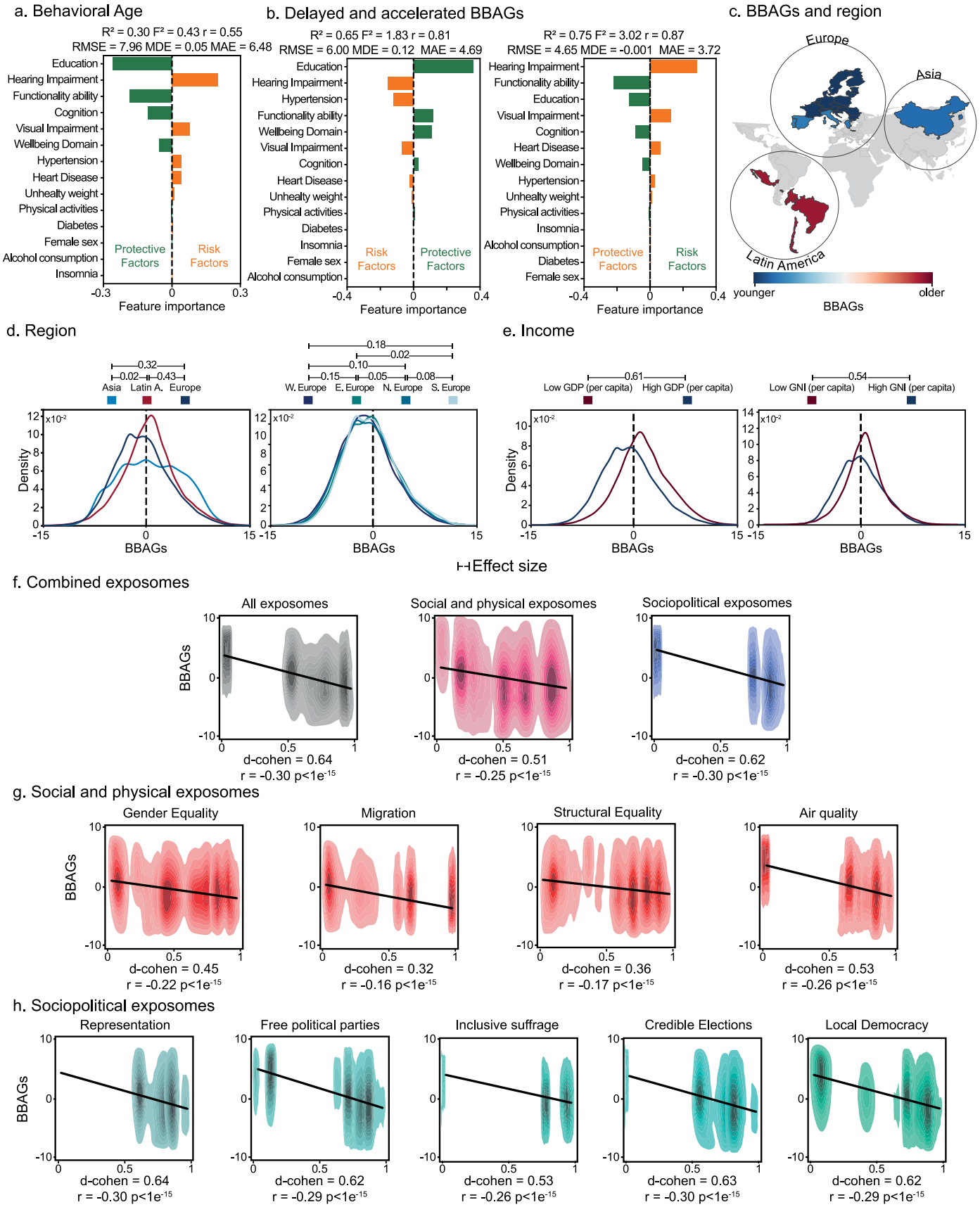


c. Longitudinal dataset



Extended Data Fig. 1 | Age distribution by countries. The figure illustrates the age distribution across countries for three different datasets. **a**) Age distribution for the cross-sectional dataset, which includes a total of 161,981 participants. **b**) Age distribution for the cross-sectional subsample consisting of 102,725 participants, with additional predictors available for analysis. **c**) Age distribution for the longitudinal dataset, where the same group of 21,631 participants is observed across two waves (Wave 1 and Wave 2), highlighting the distribution of age by country in each wave.

https://doi.org/10.1038/s41591-025-03808-2



Extended Data Fig. 2 | See next page for caption.

https://doi.org/10.1038/s41591-025-03808-2

Extended Data Fig. 2 | Supplementary analysis on the cross-sectional subsample. (**a**) Feature importance, assessed via mean decrease in impurity (MDI), enabled the prediction of chronological age using biobehavioral factors. The sample size for the analyses reported in this figure included 102,725 individuals. Goodness-of-fit and feature importance metrics are provided. (**b**) MDI facilitated the characterization of groups with more delayed (left panel) and more accelerated (right panel) aging. Goodness-of-fit and feature importance metrics are provided. (**c**) Average BBAGs distribution by continent. The color bar indicates younger (blue) and older (red) BBAGs. (**d**) BBAGs comparisons by continent (left panel) and by European regions (right panel). (**e**) BBAGs comparisons between low- and high-income countries, based on gross national income (GNI) and gross domestic product (GDP) indicators. (**f**) Linear regression models were used to assess the relationship between BBAGs and all exposomes, as well as combined social, physical, and sociopolitical exposomes. (**g**) Linear regression models were also used to assess the associations between BBAGs and individual social (gender equality, migration, and structural equality) and physical exposomes (air quality). (**h**) Linear regression models were used to examine the association between BBAGs and individual sociopolitical exposomes (democracy indicators). All P-values reported in Panels **f**, **g**, and **h** were < 1e-15. The maps were created in Python using the Plotly library (https://plotly.com/python/maps/). All other illustrations and icons were designed using GIMP (https://www.gimp.org).

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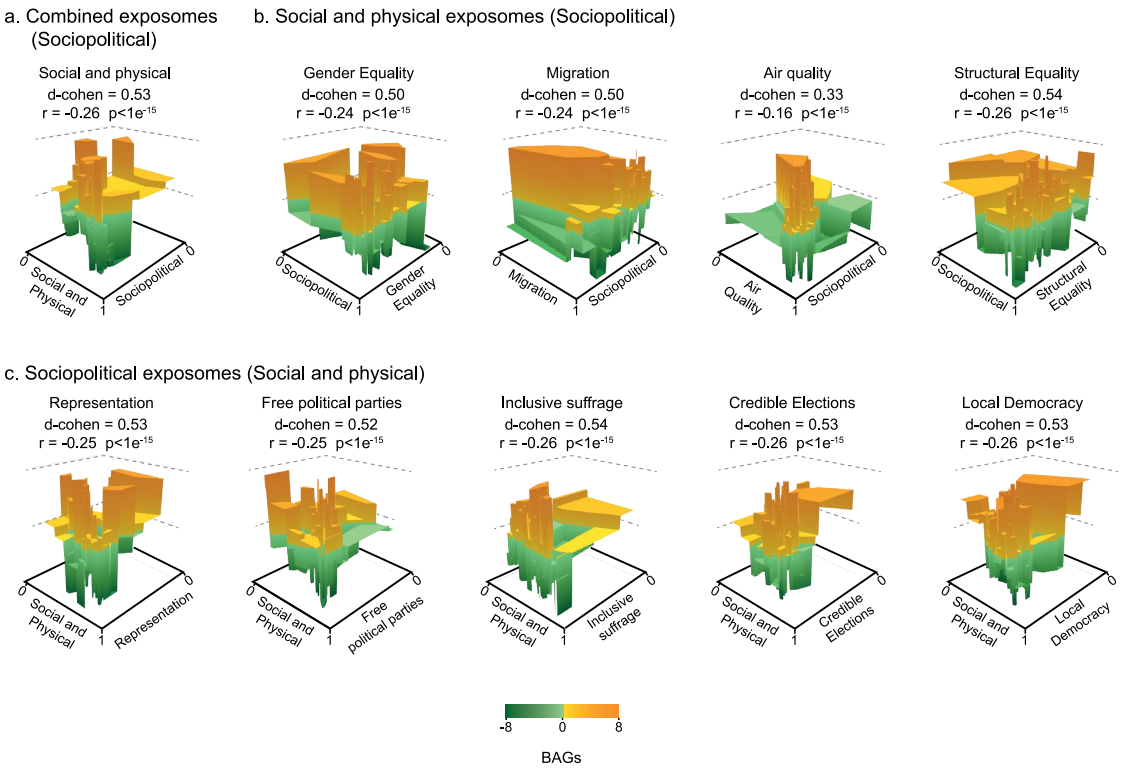

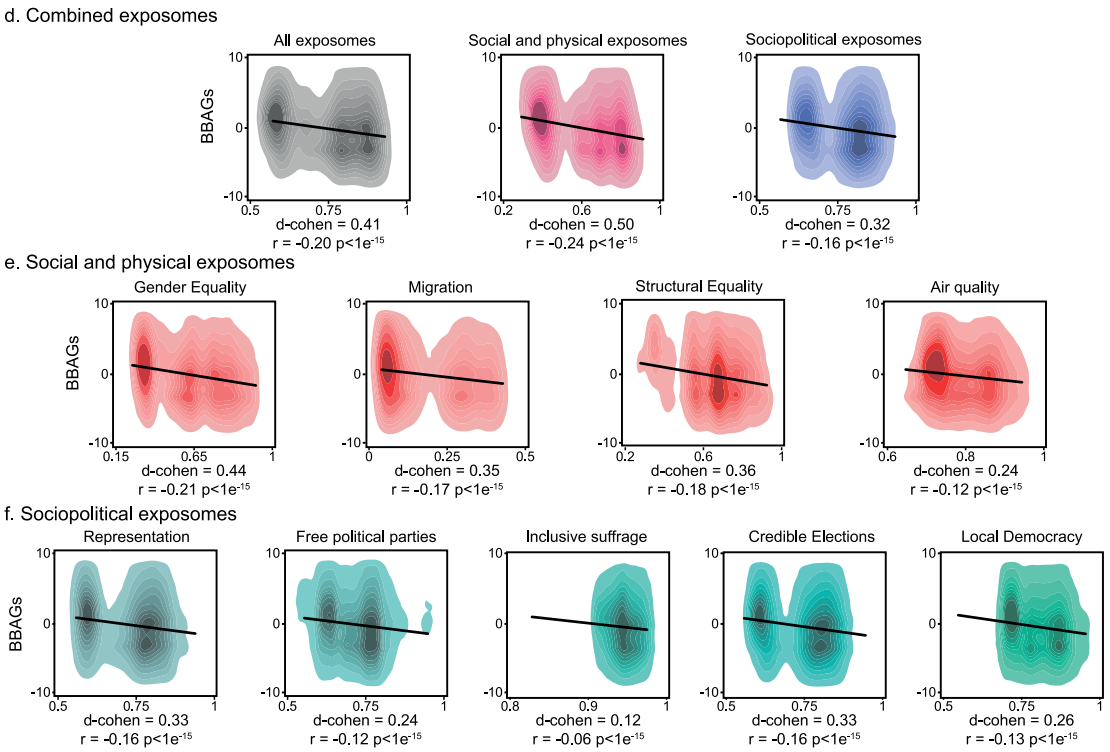

Extended Data Fig. 3 | Sensitivity analyses of exposome effects. The 3D plots display the density of exposomes and BBAGs. The sample size for the analyses reported in this figure included 161,981 individuals. (**a**) Linear regression models tracked the relationship between BBAGs and combined social exposomes, controlling for physical and sociopolitical exposomes. (**b**) Linear regression models assessed the role of individual social exposomes (gender equality, migration, and structural equality) and physical exposomes (air quality) on BBAGs, controlling for sociopolitical exposomes. (**c**) Linear regression models examined the association between BBAGs and individual sociopolitical exposomes (democracy indicators), controlling for social and physical exposomes. We used a one-sided F-test to evaluate the statistical significance of the linear regression model, testing whether the model explains a substantially greater proportion of variance than expected by chance. (**d**) Linear fit between BBAGs and all exposomes, excluding zones with sparse exposome density, and combined social, physical, and sociopolitical exposomes. (**e**) Linear regression models assessing the relationship between BAGs and individual social (gender equality, migration, and structural equality) and physical exposomes (air quality), excluding zones with sparse exposome density. (**f**) Linear regression models examining the association between BBAGs and individual sociopolitical exposomes (democracy indicators), excluding zones with sparse exposome density. All P-values reported in Panels (**a**) to (**f**) were < 1e-15.

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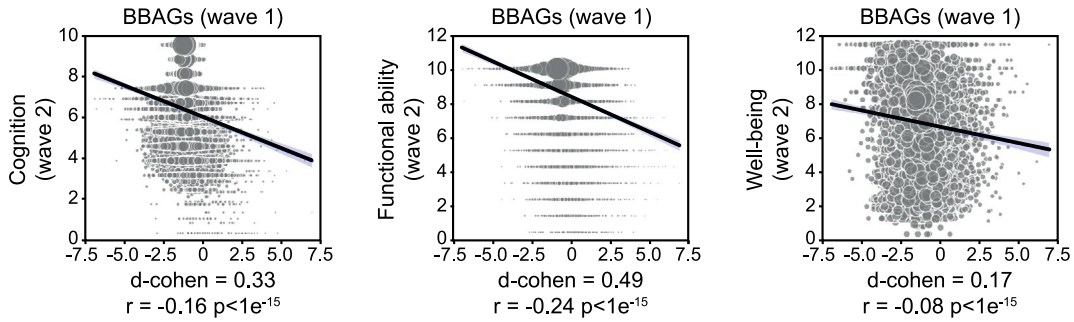
a. Association between BBAGs (wave 1) and healthy aging factors (wave 2)



Extended Data Fig. 4 | Longitudinal analysis excluding the healthy aging factor assessed for association. The sample size for the analyses reported in this figure included 21,631 individuals. (**a**) Linear regression models tracked the relationships between recalculated BBAGs in wave 1 (excluding the specific healthy aging factor used as the outcome) and healthy aging factors (cognition, functional ability, and well-being) in wave 2. Recalculated BBAGs in wave 1 significantly predicted poorer cognition, functional ability, and well-being in wave 2. All P-values reported were < 1e-15.

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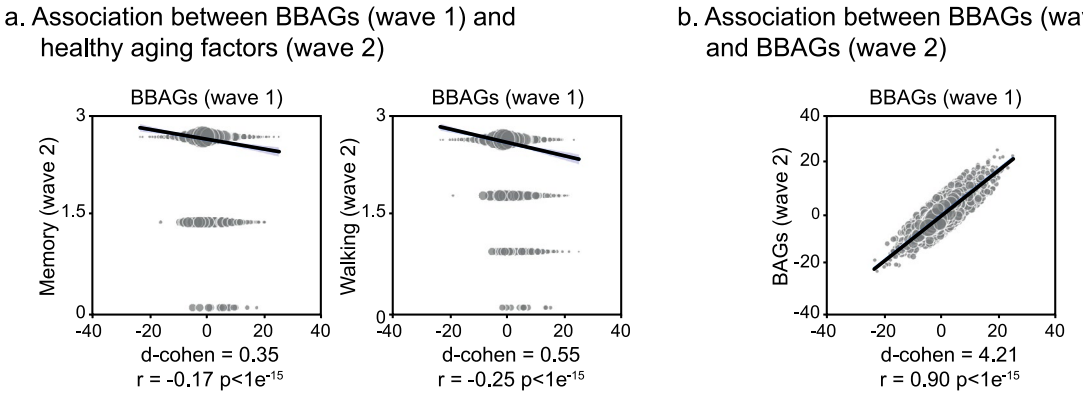

Extended Data Fig. 5 | Longitudinal analysis on the South African dataset. The sample size for the analyses reported in this figure included 5,431 individuals. (**a**) Linear regression models were used to assess the relationships between BBAGs in wave 1 and healthy aging factors (walking and memory) in wave 2. BBAGs in wave 1 significantly predicted poorer cognition, functional ability, and well-being in wave 2. (**b**) Linear regression models tracked the relationships between BBAGs in wave 1 as significant predictors of BBAGs in wave 2. All P-values reported were < 1e-15.

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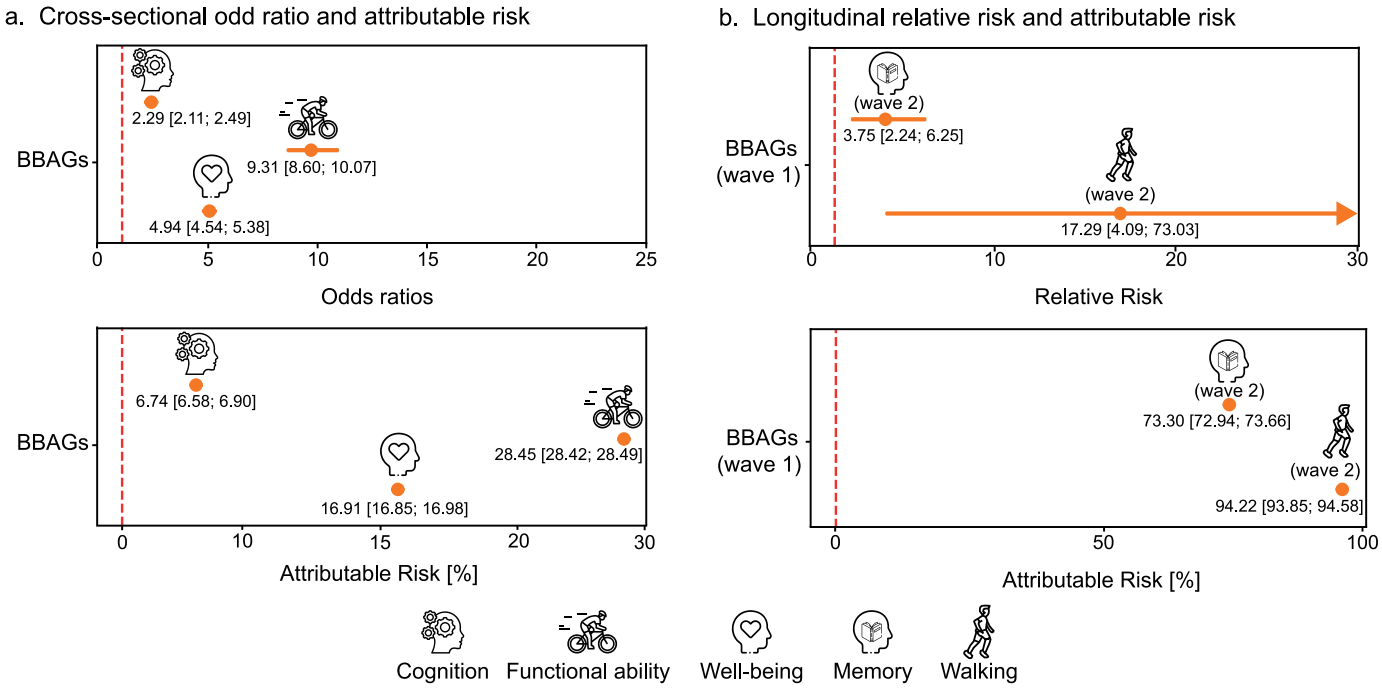
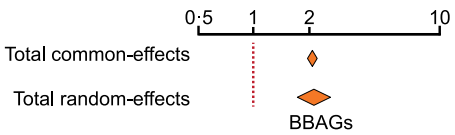


c. Metanalysis on cross-sectional data

Cognition

Total common-effects
Odds ratio [95% CI] 2.05 [1.96 - 2.15]

Total random-effects
Odds ratio [95% CI] 2.07 [1.71 - 2.50]

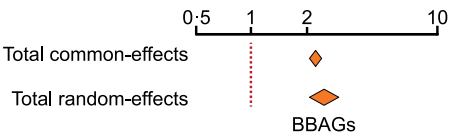


Heterogeneity:
$t^2 = 0.29$ $\chi^2 = 475.87$
df = 35 $p < 0.01$ $I^2 = 93\%$

Functional ability

Total common-effects
Odds ratio [95% CI] 2.21 [2.07 - 2.36]

Total random-effects 2.46 [2.06 - 2.93]
Odds ratio [95% CI] 2.46 [2.06 - 2.93]

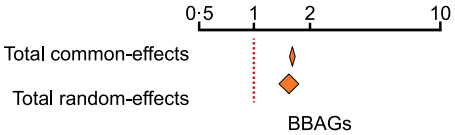


Heterogeneity:
$t^2 = 0.21$ $\chi^2 = 202.38$
df = 38 $p < 0.01$ $I^2 = 83\%$

Well-being

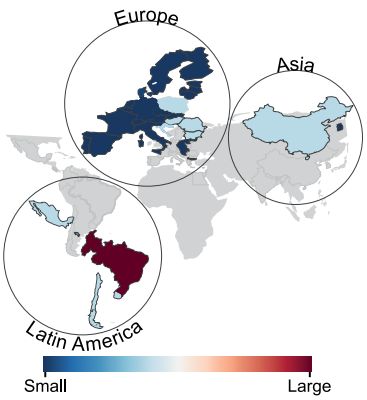
Total common-effects
Odds ratio [95% CI] 1.59 [1.54 - 1.65]

Total random-effects
Odds ratio [95% CI] 1.53 [1.36 - 1.70]



Heterogeneity:
$t^2 = 0.10$ $\chi^2 = 628.75$
df = 34 $p < 0.01$ $I^2 = 95\%$

d. BBAG effects on healthy outcomes according to GDP-GNI



Extended Data Fig. 6 | See next page for caption.

https://doi.org/10.1038/s41591-025-03808-2

Extended Data Fig. 6 | Validation using epidemiological metrics and meta-analysis on the cross-sectional subsample and the South African dataset. (**a**) Odds ratios and attributable risk for the cross-sectional subsample. Results showed that BBAGs are significantly associated with poorer functional ability and cognition. Analyses reported in this panel included 101,870 individuals for cognition, 99,588 for functional ability, and 101,618 individuals for well-being. (**b**) Relative risk and Attributable risk for the South African dataset. BBAGs in wave 1 were significantly associated with declines in walking and memory, despite the effects on walking ability showing an uncertain confidence interval. Analyses reported in this panel included 3,868 individuals. (**c**) Meta-analysis on cross-sectional subsample for cognition, functional ability, and wellbeing using common-effects and random-effects models. Larger BBAGs are linked to poorer outcomes in all domains, with high heterogeneity across countries. All P-values reported in this panel were < 0.01. We used Cochran's Q test to assess heterogeneity across studies, reporting the associated p-value, degrees of freedom, and I^2 statistic. (**d**) Summary of cross-sectional results, showing the average of common- and random-effects models by income level (low or high) based on gross national income (GNI) and gross domestic product (GDP) classifications. Color bar indicates effect sizes (small: blue and large: red). Accelerated aging is more strongly linked to poorer healthy aging outcomes—cognition, functional ability, and well-being—in low-income countries compared to high-income countries for both classifications (GNI: p = 4.05e-9, r = 0.82 and GDP: p = 8.35e-4, r = 0.47). The maps were created in Python using the Plotly library (https://plotly.com/python/maps/). All other illustrations and icons were designed using GIMP (https://www.gimp.org).

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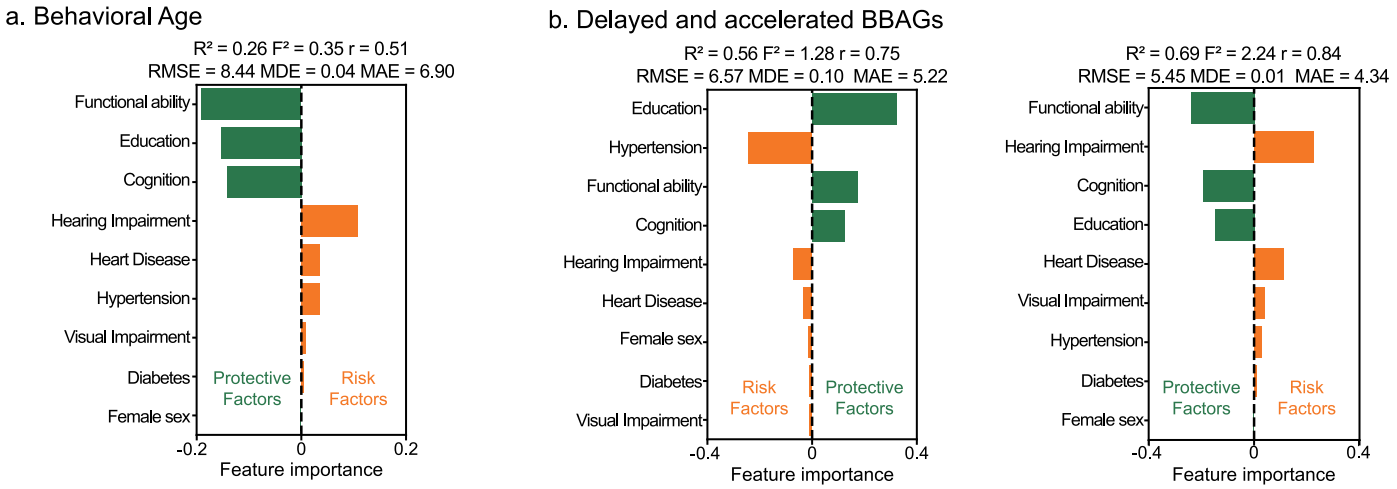

Extended Data Fig. 7 | Behavioral age and BBAGs calculation without imputation. (**a**) Feature importance analyses enabled the prediction of chronological age using biobehavioral factors. The sample size for the analyses reported in this figure included 148,188 individuals. Goodness-of-fit and feature importance metrics are provided. (**b**) Mean decrease in impurity (MDI) facilitated the characterization of groups with more delayed (left panel) and more accelerated (right panel) aging. Goodness-of-fit and feature importance metrics are provided.

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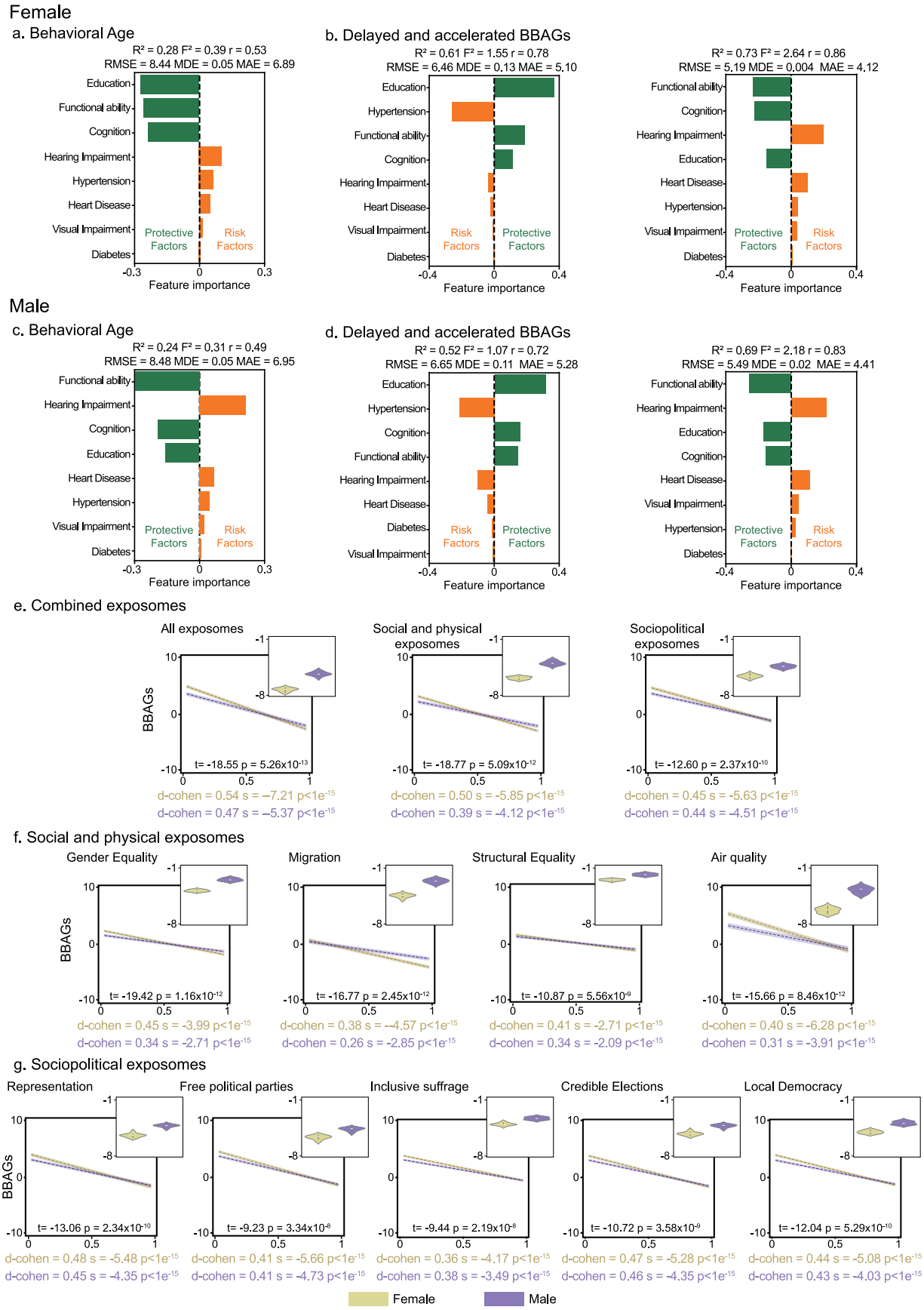

Extended Data Fig. 8 | See next page for caption.

https://doi.org/10.1038/s41591-025-03808-2

Extended Data Fig. 8 | Behavioral age and BBAGs modulation by sex. The sample size for the analyses reported in this figure was 148,188 individuals. Panels (**a**) and (**c**): Feature importance analyses enabled the prediction of chronological age using biobehavioral factors in females and males, respectively. Goodness-of-fit and feature importance metrics are provided. Panels (**b**) and (**d**): Feature importance analyses characterized groups with more delayed (left panel) and more accelerated (right panel) aging in females and males, respectively. Goodness-of-fit and feature importance metrics are provided. Panels (**e**), (**f**), and (**g**): Linear regression models tracked the relationship between BBAGs and various social exposomes across sex: Panel (**e**): Combined social exposomes. Panel (f): Social and physical exposomes. Panel (**g**): Sociopolitical exposomes. All P-values reported were < 1e-15.

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Corresponding author(s): Agustin Ibanez and Sandra Baez

Last updated by author(s): May 8, 2025

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☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
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☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
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Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	We included 161,981 participants from LA, Europe, Asia, and Africa. Data collection followed standardized procedures, face-to-face interviews and a probabilistic, clustered, stratified, multistage design. Only participants without a dementia diagnosis were included.
Data analysis	Python (3.8.18); numpy (1.24.4); pandas (2.0.3); pingouin (0.5.5); scikit-learn (1.3.2); scikit-optimize (0.9.0); scipy (1.10.1); statsmodels (0.14.1); R version (4.4.2); G*Power (3.1.9.7)

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- A description of any restrictions on data availability
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Preprocessed data and analyses codes are available on GitHub (https://github.com/euroladbrainlat/Biobehavioral-age-gaps). More details about the data are available on Supplementary Table 2. Datasets comprise sources currently publicly available for direct download after registration and access application or available

after contacting the researcher. Indicators of GNI, GDP, air quality, socioeconomic inequality (the Gini index), and migration were sourced from the updated country-specific data provided on the World Bank's platform (https://databank.worldbank.org/). Country-level gender inequality indexes (GII) are available on the World Health Organization's website (https://www.who.int/data/nutrition/nlis/info/gender-inequality-index-(gii). Sociopolitical exposomes indicators are available on the Global State of Democracy Indices (sociopolitical exposomes: https://www.idea.int/democracytracker/dataset-resources).

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	We considered female sex as a risk factor for accelerated aging. The surveys utilized did not contain questions regarding gender. All methods adhered to the Declaration of Helsinki, with informed consent and ethics approvals. We included 161,981 participants (45.09% females)
Reporting on race, ethnicity, or other socially relevant groupings	We did not use any socially relevant or socially constructed categorization
Population characteristics	We analyzed biobehavioral data consisting of protective factors (cognition, functional ability, education) and risk factors (cardiometabolic conditions: hypertension, diabetes, heart disease; female sex; sensory impairments: visual and hearing impairments) relevant to healthy aging and dementia risk. In a subset, additional protective factors (well-being, physical activity) and risk factors (unhealthy weight, alcohol intake, sleep problems) were considered. The South African dataset specifically included memory and walking abilities as predictors.
Recruitment	Data collection followed standardized procedures, face-to-face interviews and a probabilistic, clustered, stratified, multistage design.
Ethics oversight	All methods adhered to the Declaration of Helsinki, with informed consent and ethics approvals.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

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Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	We conducted Power calculations with G*Power 3.1.9.7 to confirm that the data size was adequate. All datasets were population-based and met or exceeded the minimum sample size needed.
Data exclusions	Only participants without a dementia diagnosis were included.
Replication	We reported R^2, Mean Directional Error (MDE), and Root Mean Squared Error (RMSE) for Gradient Boosting. Cohen's f^2 measured effect sizes, and Mean Decrease in Impurity (MDI) was used to evaluate feature importance. For statistical analyses, we reported the corresponding statistic, p-values, and effect sizes, considering only small or larger effects and excluding negligible ones. For epidemiological metrics, we reported Odds ratios, Attributable risk, and Relative Risk. For the meta-analysis, I^2 values exceeding 50% indicated substantial heterogeneity, and the Restricted Maximum Likelihood (REML) estimator calculated between-country variance.
Randomization	Data collection followed standardized procedures, face-to-face interviews and a probabilistic, clustered, stratified, multistage design.
Blinding	The investigators of this work were blinded to allocation during experiments and outcome assesment

Reporting for specific materials, systems and methods

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☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a