RESEARCH ARTICLE

A Data-driven Framework for Modeling Environmental Exposure Mixtures, Biological Aging Acceleration, and Chronic Disease Risk in U.S. Adults

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Abstract

Environmental exposure biomarkers (EEBs) reflect the internal burden of pollutants, yet the joint effects of multiple exposures on biological aging and chronic disease risk remain insufficiently characterized. We analyzed 8,582 adults from the 2013-2016 National Health and Nutrition Examination Survey (NHANES). Mixed exposure was characterized using 74 EEBs. Phenotypic age acceleration and biological age acceleration were used as aging outcomes. Weighted quantile sum (WQS) regression, Bayesian kernel machine regression (BKMR), and LASSO regression were applied to identify key exposure components associated with aging acceleration. Logistic and Cox regression models were then used to evaluate the associations between aging indicators and chronic disease risks. Higher mixed EEB exposure was significantly associated with accelerated aging, reflected by increases in both phenotypic age and biological age. WQS models identified arsenobetaine, copper, and tin as major contributors to phenotypic age acceleration, whereas selenium, zinc, and MHNCH contributed most strongly to biological age acceleration. Moreover, each one-year increase in phenotypic age was associated with a 30.0% higher risk of dyslipidemia and a 14.3% higher risk of metabolic-associated fatty liver disease, while each one-year increase in biological age was associated with a 59.7% higher risk of chronic obstructive pulmonary disease and a 48.5% higher risk of anemia. This study proposes a unified data-driven analytical framework that integrates exposure mixtures, biological aging, and disease risk modeling. The findings highlight the importance of evaluating mixed exposures rather than single pollutants and may support risk stratification and prevention strategies in environmental health.

Keywords: environmental pollution; aging; phenotypic age; biological age; disease risk.

1 Introduction

Biological aging is a complex process characterized by the progressive decline of multiple physiological systems and an increased susceptibility to chronic diseases [1]. As global population aging accelerates,

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aging-related health burdens are becoming a major challenge for healthcare systems and socioeconomic development worldwide [2]. Age is a fundamental indicator of human development, with broad implications in medicine, psychology, and sociology [3]. However, chronological age alone cannot adequately capture inter-individual heterogeneity in health status and functional decline. Therefore, novel aging metrics, including phenotypic age, biological age, and DNA methylation clocks, have been developed to provide a more precise framework for aging research and personalized health assessment [4].

Although genetic factors contribute to lifespan variation, genome-wide studies suggest that their overall influence on mortality is relatively limited [5]. In contrast, environmental factors are increasingly recognized as major determinants of aging and age-related diseases [6]. These factors include components of the social and natural environment as well as lifestyle-related exposures [7]. Multiple environmental factors may accelerate biological aging. These include chronic psychological stress, low socioeconomic status, social isolation, air pollution, heavy metals, ultraviolet radiation, chemical pollutants, climate extremes, and unhealthy dietary patterns. These exposures may promote aging through mechanisms such as oxidative stress, inflammation, endocrine disruption, and other biological pathways [8].

Despite substantial progress in understanding the health effects of individual pollutants, real-world environmental exposures typically occur as complex mixtures rather than isolated factors [9]. However, the combined effects of mixed environmental exposures and their differential influences on multiple aging phenotypes remain insufficiently understood. To address these limitations, this study proposes a data-driven analytical framework to jointly model environmental exposure mixtures, biological aging acceleration, and chronic disease risk. The main contributions of this study are as follows:

- We characterize real-world environmental exposure mixtures using 74 Environmental exposure biomarkers (EEBs), moving beyond conventional single-pollutant analyses;
- We simultaneously evaluate two complementary aging indicators, phenotypic age and biological age, to capture different dimensions of biological aging;
- We integrate multiple analytical methods, including weighted quantile sum (WQS), Bayesian Kernel Machine Regression (BKMR), and LASSO, to identify key exposure components and quantify mixture effects;
- We further extend the analysis to downstream disease outcomes using logistic and Cox models, thereby establishing an exposure–aging–disease analytical framework.

2 Related Work

EEBs are measurable indicators that reflect an individual's internal burden of environmental pollutants. These biomarkers are commonly derived from biological samples such as blood, urine, saliva, exhaled breath condensate, and hair, and provide a comprehensive assessment of internal exposure levels [10]. Increasing evidence indicates that EEBs are closely associated with aging-related biological changes. For example, exposure to fine particulate matter (PM2.5) has been linked to accelerated DNA methylation age progression, while persistent organic pollutants (POPs) have been associated with increased phenotypic age [11].

Existing studies on environmental exposures and aging can be broadly categorized into single-exposure and mixture-exposure approaches. A large body of research has focused on individual pollutants and their biological effects; however, such approaches may oversimplify real-world exposure scenarios, where individuals are simultaneously exposed to multiple environmental factors [12]. In contrast, emerging studies have begun to examine exposure mixtures, yet these studies remain limited in scope and often fail to fully capture the complex interactions and nonlinear relationships among multiple pollutants.

From a mechanistic perspective, environmental pollutants may accelerate aging through multiple biological pathways. These include excessive production of reactive oxygen species (ROS), which can lead to mitochondrial dysfunction, DNA damage, and cellular senescence [13–16], as well as activation of inflammatory signaling pathways such as NF-kB, contributing to chronic inflammation and inflammaging [17]. In addition, environmental exposures may induce epigenetic alterations, including DNA methylation and histone modifications, thereby reshaping aging-related gene expression profiles [18–20].

Beyond molecular and cellular mechanisms,

Table 1. Structured comparison of representative recent studies.

Study	Exposure type	Analytic focus	Aging metric	Disease outcome	Main limitation
Chen et al. [27]	Single pollutant (ethylene oxide)	Exposure–aging	Biological age acceleration	No	Limited to a single exposure and does not account for mixture effects
Fu et al. [28]	Mixture exposure (PAHs)	Exposure–aging	Biological age	No	Focuses on a single aging metric and does not extend to disease outcomes
Yang et al. [29]	No environmental exposure	Aging–disease	Phenotypic age and KDM-BA	Yes	Does not incorporate environmental exposure variables
This study	74 EEB mixtures	Exposure–aging–disease	Phenotypic age and biological age	Yes	Cross-sectional design limits causal inference

accelerated biological aging has been consistently associated with increased risks of metabolic, cardiovascular, and neurological diseases [21–23]. For instance, environmental pollutants may impair insulin signaling through oxidative stress and inflammatory pathways, contributing to obesity and type 2 diabetes [24]. Similarly, volatile organic compounds (VOCs) have been linked to cardiovascular disease through their effects on blood pressure and atherosclerosis [25], while air pollution has been associated with cognitive decline and neurodegenerative disorders via blood–brain barrier disruption and neuroinflammation [26].

These limitations highlight the need for a more integrated analytical framework to examine the relationships among environmental exposure mixtures, biological aging acceleration, and disease risk (Table 1).

3 Methodology

3.1 Study Population and Data Source

The National Health and Nutrition Examination Survey (NHANES), conducted biennially by the National Center for Health Statistics (NCHS), uses a stratified multistage sampling design to assess the health and nutritional status of U.S. children and adults [1] [30]. This study focused on the 2013-2016 cycles, as these were the only cycles among 11 spanning 1999-2023 containing all necessary variables.

After excluding individuals under 20 years old and those with missing biomarker or EEB data, 8,582 eligible participants remained (Figure 1). Due to the large number of EEBs, participants were clustered into high-exposure (n = 1,472) and low-exposure (n = 7,110) groups using the K-Medoids algorithm, which partitions samples around medoids and determines optimal cluster number via average silhouette width and elbow methods, offering robustness against noise and outliers (Supplementary Table S1; Supplementary Figure S1) [31, 32].

NHANES data collection was approved by the NCHS Research Ethics Review Board (Protocol ♯2011-17 and its continuation), with all participants providing written informed consent. This study complied fully with the Declaration of Helsinki, using only anonymized data without direct human interventions [33].

3.2 Measurement of EEBs

The NHANES database provides extensive environmental pollutant data, from which 74 commonly encountered EEBs were selected for analysis (Supplementary Table S2). Concentrations below the limit of detection (LLOD) were imputed as LLOD divided by the square root of 2 [34]. The analyzed EEBs included a range of mercapturic acids (e.g., AAMA, AMCC, BPMA, CYMA), various metals (e.g., Barium, Cadmium, Copper, Lead, Selenium, Zinc), polycyclic aromatic hydrocarbon metabolites (e.g., 1-Hydroxynaphthalene, 1-Hydroxypyrene), phthalate metabolites (e.g., MEHP, MEP, MiBP), and other environmental chemicals such as arsenic species, nitrate, perchlorate, acrylamide, and insecticide metabolites (e.g., 3-PBA, TCPy).

3.3 Assessment of Adverse Health Outcomes

This study selected 15 diseases associated with environmental pollutant exposure (Supplementary Table S3). The selected diseases include: Hypertension [35], Heart disease [36], Dyslipidemia [37–39], Asthma [40], Chronic obstructive pulmonary disease (COPD) [41], Chronic bronchitis [42], Diabetes [43], Obesity [44], Gout [45], Depression [46, 47], Metabolic-associated fatty liver disease (MAFLD) [48–50], Arthritis [51], Oral problems [52], Anemia [53], Cancer [54].

[1] (https://wwwn.cdc.gov/nchs/nhanes/Default.aspx

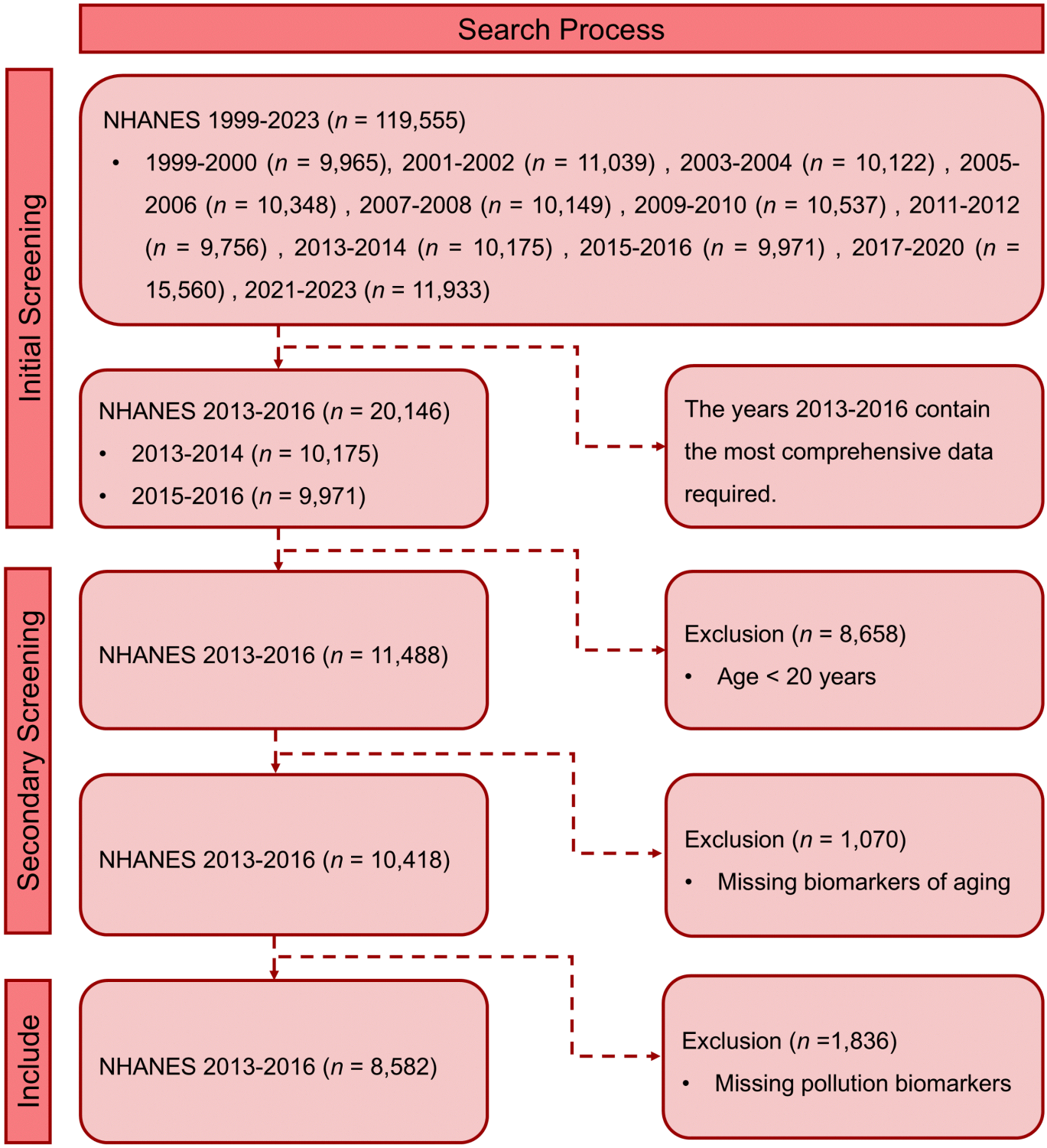


Figure 1. Flowchart of participant selection process.

Mortality information was obtained from the National Center for Health Statistics (NCHS) by linking each participant's unique identifier to the NCHS database and NHANES data [2] [55]. Survival time was measured in months from the survey start date until April 16, 2022, or the date of death, whichever occurred first.

[2] https://www.cdc.gov/nchs/data-linkage/mortality.htm

3.4 Construction of Biological Aging Indicators

3.4.1 Phenotypic Age

Biological aging rate was assessed using two metrics: phenotypic age and biological age. Aging acceleration was calculated by subtracting chronological age from these indicators; a positive value indicates accelerated aging, while a negative value suggests deceleration or

delay. Using the BioAge R package, biomarkers for these calculations were extracted from the NHANES dataset (Supplementary Table S4) [56].

Phenotypic age is based on eight biomarkers strongly linked to aging and inflammation [57]: albumin (g/L), creatinine (μmol/L), glucose (mmol/L), lymphocyte percentage (%), mean corpuscular volume (fL), red cell distribution width (%), alkaline phosphatase (U/L), and white blood cell count (10^9 cells/L). This measure was developed from NHANES III data using an elastic net Gompertz mortality regression model on 42 candidate biomarkers.

$$\text{Phenotypic age} = 141.50225 + \frac{\log\left[-0.0055305 \times \log\left(1 - \text{Mortality score}\right)\right]}{0.090165} \quad (1)$$

$$\text{Mortality score} = 1 - \exp\left(-\frac{1.51714 \times \exp(x_b)}{0.007692696}\right) \quad (2)$$

$$\begin{aligned} x_b = &-19.907 - 0.03359355 \times \text{Albumin} \\ &+ 0.009506491 \times \text{Creatinine} \\ &+ 0.1953192 \times \text{Glucose} \\ &- 0.01199984 \times \text{Lymphocyte percent} \\ &+ 0.02676401 \times \text{Mean cell volume} \\ &+ 0.3306156 \times \text{Red cell distribution width} \\ &+ 0.001868778 \times \text{Alkaline phosphatase} \\ &+ 0.05542406 \times \text{White blood cell count} \\ &+ 0.08035356 \times \text{Chronological age} \end{aligned} \quad (3)$$

3.4.2 Biological Age

Biological age was calculated based on ten biomarkers associated with aging and inflammation [58]: systolic blood pressure (mmHg), albumin (g/dL), alkaline phosphatase (U/L), blood urea nitrogen (mg/dL), creatinine (mg/dL), glycated hemoglobin (%), total cholesterol (mg/dL), lymphocyte percentage (%), white blood cell count (10^9 cells/L), and mean corpuscular volume (fL). This indicator derives from regression analyses of each biomarker against chronological age in a reference population, integrating biomarker deviations weighted by their regression parameters:

$$\text{Biological age} = \frac{\sum_{j=1}^{n}(x_j - q_j)\left(\frac{k_j}{S_j^2}\right) + \frac{CA}{S_{BA}^2}}{\sum_{j=1}^{n}(k_j)^2 + \frac{1}{S_{BA}^2}} \quad (4)$$

where x_j is the measured value of the j-th biomarker; CA is chronological age; k_j and q_j are the slope and intercept of the regression between the j-th biomarker and chronological age; S_j is the root mean square error of that regression; and S_{BA} is the variance of chronological age in the reference population.

3.5 Covariates Assessment

Covariate information was extracted from NHANES demographic, physical examination, and questionnaire data [59]. Based on prior research, we included potential confounders linked to accelerated biological aging: age, sex, race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other), and education level (less than 9th grade, 9-11th grade, high school graduate/GED, some college/associate degree, college graduate or above). Anthropometric and clinical measures included height, weight, and body mass index (BMI), categorized as normal (18.5–23.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥30.0 kg/m^2). Blood pressure variables included systolic and diastolic readings. Socioeconomic status was represented by the poverty income ratio (PIR), defined as household income relative to the federal poverty level and categorized as low (0–1.0), middle (1.1–3.0), and high (>3.0). Smoking status was classified as current smoker or non-smoker, and alcohol consumption as drinker or non-drinker.

3.6 Statistical Analysis

Data from the 2013–2014 and 2015–2016 NHANES cycles were combined using adjusted sample weights, calculated as the average of the 2-year MEC weights (WTMEC2YR) following NHANES guidelines [60, 61]:

$$\text{MEC4YR} = \frac{1}{2} \times \text{WTMEC2YR} \quad (5)$$

Continuous variables with normal distributions are presented as mean ± standard deviation (Mean ± SD), and differences between groups were compared using

one-way analysis of variance (ANOVA). Non-normally distributed variables are reported as median and interquartile range [M (Q1, Q3)] and were compared using the Kruskal–Wallis H test. Categorical variables are expressed as frequency and percentage $[n(\%)]$. Unordered categorical variables were analyzed using Pearson's χ^2 test or Fisher's exact test, whereas ordered categorical variables were compared using the Kruskal–Wallis H test. Standardized mean differences (SMDs) were used to assess group imbalance and were interpreted as follows: SMD < 0.10, acceptable balance; 0.10–0.34, small difference; 0.35–0.64, moderate difference; 0.65–1.19, large difference; and ≥ 1.20, very large difference [62].

Threshold effects for phenotypic age acceleration and biological age acceleration were explored using standard and piecewise linear regression models via the segmented R package [63]. Restricted cubic splines (RCS) were used to model nonlinear associations with the rms R package [64]. Spearman correlation analysis was performed to assess interrelationships among the 74 EEBs [65].

WQS regression was used to estimate the relative contribution of each EEB to aging acceleration; chemicals with weights above the bootstrap average threshold (0.013) were considered significant and included in subsequent analyses. The gWQS R package was used for WQS modeling [66]. Logistic regression was used to estimate odds ratios (ORs) for the associations between EEBs and aging acceleration [67]. Multivariable Cox proportional hazards models were applied to estimate hazard ratios (HRs) for aging acceleration in relation to disease risk and mortality [68].

LASSO regression with 10-fold cross-validation was used to identify disease-specific variables [69]. BKMR was applied to assess the joint effects of EEB mixtures on aging acceleration, with 10,000 Markov Chain Monte Carlo iterations performed for model estimation [70]. To ensure model convergence and reduce computational burden, only EEBs with WQS weights above the bootstrap threshold were included in the BKMR analysis [71]. All exposures were standardized using Z-score normalization before model fitting [72], and BKMR analyses were implemented using the bkmr R package.

In addition to evaluating statistical associations, we considered the computational characteristics of the applied methods. Compared with conventional single-pollutant regression models, the present analytical framework is more computationally demanding because it integrates variable selection, mixture-effect estimation, and downstream risk modeling. Among the applied methods, LASSO regression is relatively efficient for high-dimensional variable selection, whereas WQS regression provides a practical balance between interpretability and computational burden for mixture analysis. In contrast, BKMR is substantially more computationally intensive because it relies on Bayesian estimation and iterative Markov Chain Monte Carlo sampling, although it offers important advantages in capturing nonlinear and interaction effects within exposure mixtures. Therefore, the combined use of LASSO, WQS, and BKMR in this study reflects a trade-off between computational efficiency, interpretability, and modeling flexibility (Table 2).

To further examine the robustness and interpretability of the findings, subgroup analyses and single-pollutant analyses were additionally conducted as supplementary analyses. All statistical analyses were performed using R version 4.5.0 (R Foundation for Statistical Computing, Vienna, Austria) [73]. A two-sided P value < 0.05 was considered statistically significant.

4 Results

4.1 Demographic Characteristics

This study included a total of 8,582 participants (Table 3). Based on exposure levels, the population was divided into a high-exposure group ($n = 1,472$) and a low-exposure group ($n = 7,110$). The analysis revealed that while the median age was 47 years in both groups, the phenotypic age (SMD $= 0.172$) and physiological age (SMD $= 0.173$) were significantly higher in the high-exposure group compared to the low-exposure group ($P < 0.001$). The high-exposure group had a higher proportion of males (SMD $= 0.213$, $P < 0.001$) and a greater percentage of non-Hispanic Black individuals (SMD $= 0.196$, $P = 0.03$). Regarding socioeconomic characteristics, the high-exposure group had a higher proportion of individuals with a high school education or below (SMD $= 0.188$, $P < 0.001$), a lower proportion of married individuals (SMD $= 0.162$, $P < 0.001$), and a lower median poverty-to-income ratio (PIR) (SMD $= 0.170$, $P < 0.001$). In terms of lifestyle factors, the high-exposure group exhibited a lower alcohol consumption rate (SMD $= 0.104$, $P < 0.001$), but no statistically significant difference was observed in smoking status between the two groups (SMD $=$

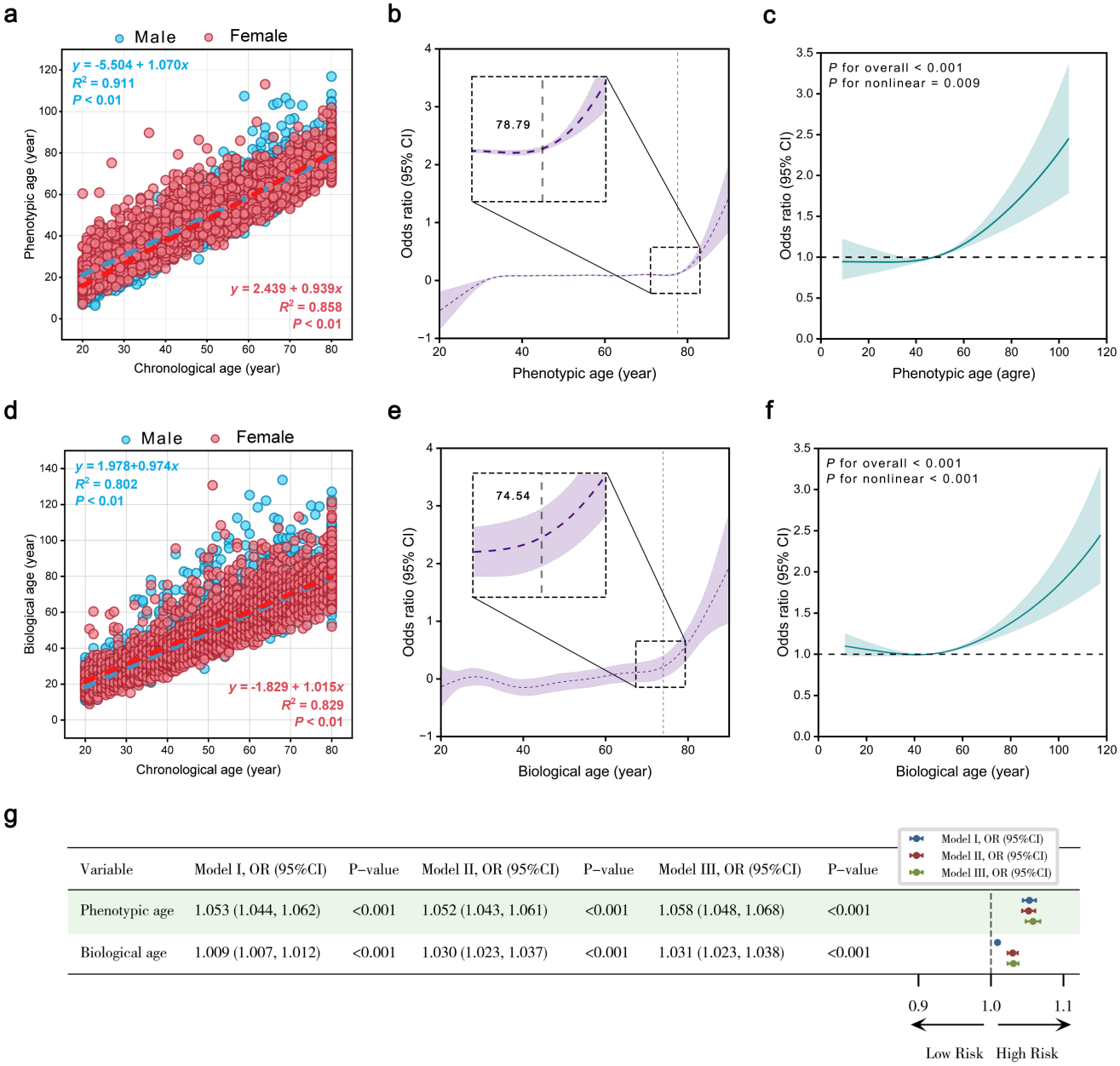
Table 2. Comparison of the analytical methods used in this study.

Method	Main purpose	Can assess mixture effects	Can capture nonlinearity /interaction	Relative computational burden	Main advantage
Single-pollutant regression	Assess association of each exposure separately	No	Limited	Low	Simple and easy to interpret
LASSO regression	Variable selection in high-dimensional data	Partial	No	Low-Moderate	Efficient screening of important variables
WQS regression	Evaluate overall mixture effect and variable weights	Yes	Limited	Moderate	Interpretable mixture contribution estimates
BKMR	Model joint effects of exposure mixtures	Yes	Yes	High	Flexible modeling of nonlinear and interaction effects
Logistic/Cox regression	Estimate disease and mortality risks	No	Limited	Low-Moderate	Widely used for downstream risk estimation

Table 3. Demographic characteristics of participants in NHANES 2013-2016.

Variables	Total (n = 8582)	Low-exposure (n = 7110)	High-exposure (n = 1472)	Statistics	*P*-value	*SMD*
Chronological age (years), Median (IQR)	47.000 (34.000, 63.000)	47.000 (34.000, 63.000)	47.000 (34.000, 63.000)	-1.736[1]	0.083	0.053
Phenotypic age (years), Median (IQR)	47.094 (32.660, 61.798)	46.787 (32.220, 61.347)	48.289 (34.598, 64.028)	-4.570[1]	<0.001	0.172
Biological age (years), Median (IQR)	47.226 (32.994, 62.699)	46.909 (32.702, 62.468)	48.539 (34.566, 64.347)	-3.771[1]	<0.001	0.173
Gender, n (%)				54.741[3]	<0.001	0.213
Male	4133 (48.159)	3295 (46.343)	838 (56.929)			
Female	4449 (51.841)	3815 (53.657)	634 (43.071)			
Race, n (%)				-2.167[1]	0.030	0.196
Mexican American	1298 (15.125)	1110 (15.612)	188 (12.772)			
Other Hispanic	920 (10.720)	780 (10.970)	140 (9.511)			
Non-Hispanic White	3355 (39.093)	2765 (38.889)	590 (40.082)			
Non-Hispanic Black	1736 (20.228)	1356 (19.072)	380 (25.815)			
Other Race	1273 (14.833)	1099 (15.457)	174 (11.821)			
Education, n (%)				5.833[1]	<0.001	0.188
Less than 9th grade	788 (9.182)	644 (9.058)	144 (9.783)			
9-11th grade	1095 (12.759)	861 (12.110)	234 (15.897)			
High school graduate	1915 (22.314)	1547 (21.758)	368 (25.000)			
AA degree	2625 (30.588)	2191 (30.815)	434 (29.484)			
College graduate or above	2159 (25.157)	1867 (26.259)	292 (19.837)			
Marital status, n (%)				-3.864[1]	<0.001	0.162
Married	5175 (60.301)	4328 (60.872)	847 (57.541)			
Widowed	587 (6.840)	461 (6.484)	126 (8.560)			
Divorced	1213 (14.134)	983 (13.826)	230 (15.625)			
Never married	1607 (18.725)	1338 (18.819)	269 (18.274)			
Living with partner	687 (8.005)	536 (7.539)	151 (10.258)			
Drinking status, n (%)				12.285[3]	<0.001	0.104
Yes	5593 (70.914)	4700 (71.723)	893 (66.942)			
No	2294 (29.086)	1853 (28.277)	441 (33.058)			
Smoking status, n (%)				3.837[3]	0.050	0.056
Yes	3674 (42.845)	3078 (43.322)	596 (40.544)			
No	4901 (57.155)	4027 (56.678)	874 (59.456)			
Poverty to income ratio, Median (IQR)	2.100 (1.070, 4.040)	2.160 (1.100, 4.120)	1.770 (0.980, 3.450)	5.621[1]	<0.001	0.170
BMI (Kg/m^2), Mean ± SD	29.306±7.051	29.307±7.049	29.303±7.065	0.019[4]	0.985	<0.001
Systolic pressure (mmHg), Mean ± SD	124.045±18.183	123.690±17.975	125.785±19.084	-3.923[4]	<0.001	0.113
Diastolic pressure (mmHg), Mean ± SD	69.448±13.110	69.525±12.789	69.070±14.582	1.082[2]	0.279	0.033
TC (mmol/L), Mean ± SD	189.603±41.333	189.715±41.049	189.059±42.686	0.554[4]	0.579	0.016
TG (mmol/L), Median (IQR)	94.000 (64.000, 142.000)	93.000 (64.000, 139.500)	97.000 (64.000, 152.000)	-1.600[1]	0.110	0.070
LDL-C (mmol/L), Median (IQR)	108.000 (86.000, 133.000)	109.000 (87.000, 133.000)	106.000 (84.000, 134.000)	0.719[1]	0.472	0.023
HDL-C (mmol/L), Mean ± SD	53.258±16.611	53.544±16.477	51.876±17.187	3.510[4]	<0.001	0.099
Albumin (g/L), Mean ± SD	42.705±3.442	42.816±3.372	42.170±3.715	6.168[2]	<0.001	0.182
WBC (10^9 cells/L) Median (IQR)	7.000 (5.800, 8.500)	7.000 (5.800, 8.400)	7.300 (6.000, 9.000)	-5.989[1]	<0.001	0.153
RDW (%), Mean ± SD	13.760±1.296	13.721±1.248	13.946±1.494	-5.408[2]	<0.001	0.164
Creatinine (μmol/L), Median (IQR)	74.700 (62.760, 89.280)	74.260 (61.880, 87.520)	78.680 (66.300, 93.700)	-9.205[1]	<0.001	0.244
ALP (U/L), Median (IQR)	64.000 (52.000, 78.000)	64.000 (52.000, 77.000)	67.000 (55.000, 81.000)	-5.393[1]	<0.001	0.147
Lymphocyte percentage (%), Mean ± SD	30.597±8.556	30.796±8.442	29.635±9.028	4.539[2]	<0.001	0.133
MCV (fL), Mean ± SD	88.924±6.022	88.816±5.970	89.445±6.241	-3.543[2]	<0.001	0.103
Hemoglobin (g/dL), Mean ± SD	13.961±1.532	13.956±1.507	13.985±1.649	-0.622[2]	0.534	0.018
BUN (mg/dL), Median (IQR)	4.640 (3.570, 5.710)	4.640 (3.570, 5.710)	4.640 (3.570, 6.070)	-2.097[1]	0.036	0.184

Note: TC: Total cholesterol; TG: Triglyceride; LDL-C: LDL-cholesterol; HDL-C: HDL-cholesterol; WBC: White blood cell; RDW: Red cell distribution; ALP: Alkaline phosphatase; MCV: Mean corpuscular volume; BUN: Blood urea nitrogen. [1]Mann Whitney U test; [2]Variance-corrected independent samples t-test; [3]Pearson's chi-square (χ^2) test; [4]Independent samples t-test.



Variable	Model I, OR (95%CI)	P–value	Model II, OR (95%CI)	P–value	Model III, OR (95%CI)	P–value
Phenotypic age	1.053 (1.044, 1.062)	<0.001	1.052 (1.043, 1.061)	<0.001	1.058 (1.048, 1.068)	<0.001
Biological age	1.009 (1.007, 1.012)	<0.001	1.030 (1.023, 1.037)	<0.001	1.031 (1.023, 1.038)	<0.001

Figure 2. Construction of biological aging metrics. (a) Phenotypic age estimated using eight clinical biomarkers; (b) Threshold analysis of phenotypic age in relation to aging; (c) RCS analysis depicting the association between phenotypic age acceleration and aging, adjusted for age, sex, race/ethnicity, education level, marital status, PIR, smoking status, alcohol consumption, and BMI; (d) Physiological age estimated using ten blood biomarkers; (e) Threshold analysis of physiological age in relation to aging; (f) RCS analysis showing the association between physiological age acceleration and aging, adjusted for the same covariates as in panel (c); (g) Multivariable logistic regression analyses of biological aging metrics across three models: Model I, unadjusted; Model II, adjusted for demographic factors (age, sex, race/ethnicity, education, marital status, PIR); Model III, further adjusted for lifestyle factors (smoking, alcohol consumption, BMI).

0.056, $P = 0.05$). Conversely, high-density lipoprotein cholesterol (HDL-C) and lymphocyte percentage were lower in the high-exposure group ($P < 0.001$). These findings are consistent with previous research [74, 75].

4.2 Construction of Biological Aging Indicators

We constructed phenotypic age and physiological age indicators based on a variety of biomarkers to assess individuals' levels of biological aging and to explore their relationships with chronological age and accelerated aging. The results showed a positive correlation between phenotypic age and chronological age (Figure 2a), with high goodness of fit for both males ($R^2 = 0.911$) and females ($R^2 = 0.858$). Similarly, physiological age was also positively correlated with chronological age (Figure 2d), though

the correlation was slightly weaker for males ($R^2 = 0.802$) and females ($R^2 = 0.829$).

To examine potential thresholds in phenotypic age and physiological age, we employed both standard linear regression and two-piecewise linear regression models. The results revealed a significant inflection point for phenotypic age at 78.79 years (likelihood ratio test $P < 0.001$). The regression coefficient before the inflection point was 1.020 (95% CI: 1.020–1.020, $P < 0.001$), which increased markedly to 6.340 after the threshold (95% CI: 4.520–9.280, $P < 0.001$) (Figure 2b). In contrast, the threshold for physiological age was identified at 74.54 years ($P < 0.001$), with regression coefficients of 1.004 before (95% CI: 1.001–1.007, $P = 0.005$) and 1.157 after the threshold (95% CI: 1.106–1.210, $P < 0.001$) (Figure 2c). Both phenotypic age and physiological ages exhibited nonlinear aging trajectories, but phenotypic age showed a more pronounced acceleration post-threshold (Supplementary Table S5).

To further investigate the dose–response relationship between the two indicators and accelerated aging, we applied RCS models. After adjusting for confounding factors such as age, sex, race, education level, marital status, poverty income ratio (PIR), smoking, alcohol consumption, and BMI, both phenotypic age (Figure 2c) and physiological age (Figure 2f) showed a nonlinear positive association with accelerated aging ($P_{\text{nonlinear}} < 0.01$, $P_{\text{overall}} < 0.01$).

Finally, we conducted multivariable logistic regression analyses, including an unadjusted model (Model I), a partially adjusted model (Model II), and a fully adjusted model (Model III). Throughout all models, phenotypic age consistently showed a stronger effect on accelerated aging than physiological age (Figure 2g). Specifically, in the fully adjusted model, each 1-year increase in phenotypic age was associated with a 5.8% higher risk of accelerated aging (OR = 1.058, 95% CI: 1.048-1.068, P <0.001), whereas physiological age was associated with a 3.1% increase in risk (OR = 1.031, 95% CI: 1.023-1.038, P <0.001).

4.3 Potential Associations Between EEBs and Accelerated Biological Aging

A co-exposure network of EEBs was constructed based on Pearson correlation analysis (Figure 3). The results revealed strong correlations among certain EEBs. For instance, 2,2-DCVMA and 2-Naphthol ($\rho = 0.97$), MEOHP and MEHHP ($\rho = 0.87$), as well as PGA and MA ($\rho = 0.74$) exhibited high intercorrelations, suggesting that these compounds may originate from common environmental sources or share similar metabolic pathways.

We further employed the WQS regression model to evaluate the contribution weights of EEBs in the context of phenotypic and biological age acceleration. For phenotypic age acceleration, Arsenobetaine ($\omega = 0.233$) and Copper ($\omega = 0.161$) had the highest weights, suggesting that metal pollutants may play a key role in accelerating phenotypic aging.

Additionally, Tin ($\omega = 0.054$), Manganese ($\omega = 0.049$), and several organic metabolites such as PMA and 2,2-DCVMA also contributed to the mixture effect, indicating that inorganic metals and organic pollutants may synergistically promote aging through co-exposure mechanisms (Figure 4a). For biological age acceleration, Selenium ($\omega = 0.245$) and Zinc ($\omega = 0.163$) exhibited the highest weights (Figure 4b). Although these are essential trace elements, previous studies have reported potential toxic effects when levels exceed physiological thresholds [75]. Moreover, phthalate metabolites, including MHNCH ($\omega = 0.096$), MiBP ($\omega = 0.043$), and BPMA ($\omega = 0.041$), represented the major group of organic pollutants contributing to biological age acceleration (Supplementary Table S6).

Based on multivariable linear regression analysis, multiple EEBs were significantly associated with both phenotypic and biological age acceleration (Supplementary Figure S2). Specifically, increased concentrations of 2-Hydroxyfluorene, 2-Naphthol, AAMA, Acrylamide, AMCC, Cadmium, Cobalt, Copper, CYMA, Ethylene Oxide, Glycideamide, HEMA, HPMMA, MA, MCiOP, MCPP, MECPP, MEOHP, MEP, MHBMA3, MnBP, PHEMA, TCPy, and Thiocyanate were significantly associated with phenotypic age acceleration (P < 0.05).

4.4 Potential Association Between Accelerated Biology Aging and Disease Risk

LASSO regression was employed to assess the disease risks associated with phenotypic age acceleration (Figure 5a) and biological age acceleration (Figure 5b) under mixed EEB exposure. The results indicated that individuals in the highest quartile (Q4) of phenotypic age acceleration exhibited significantly increased mortality risk, primarily driven by metabolic disorder-related diseases, including oral health problems ($\omega = 0.140$), dyslipidemia ($\omega = 0.130$), and

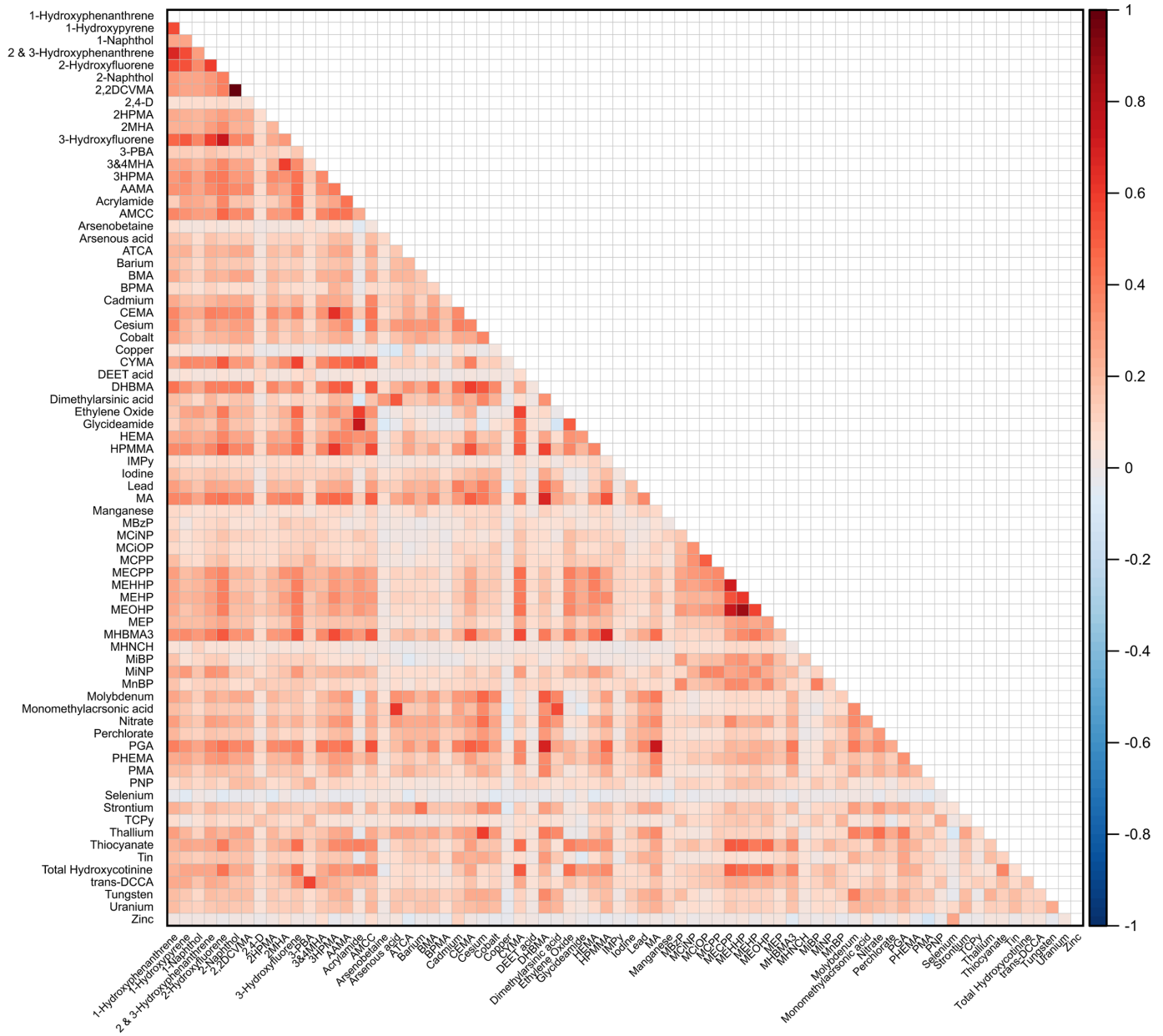


Figure 3. Pearson correlation heatmap among 74 EEBs.

metabolic dysfunction-associated fatty liver disease ($\omega = 0.018$). In contrast, individuals in the lowest quartile (Q1) of biological age acceleration showed increased mortality risk mainly associated with respiratory and hematological disorders, with chronic obstructive pulmonary disease ($\omega = 0.571$), anemia ($\omega = 0.413$), and oral health problems ($\omega = 0.138$) being the major contributors (Supplementary Table S7, Supplementary Figure S3). In the BKMR analysis, phenotypic age acceleration showed an upward trend when exposure levels were at or above the 55th percentile; however, the difference compared to the 50th percentile was not statistically significant. Biological age acceleration demonstrated a significant positive association with higher levels of mixed EEB exposure.

Using the Cox proportional hazards model, we further evaluated the association between accelerated biological aging and the risk of disease onset (Figure 6a). After adjusting for potential confounders, including age, sex, race, education level, alcohol consumption, smoking status, and BMI, each one-year increase in phenotypic age was associated with a 30.0% higher risk of dyslipidemia (HR = 1.300, 95% CI: 1.211–1.395, $P < 0.001$) and a 14.3% higher risk of metabolic-associated fatty liver disease (HR = 1.143, 95% CI: 1.065–1.228, $P < 0.001$). Although phenotypic age acceleration also showed a trend toward increased risk of oral health problems (HR

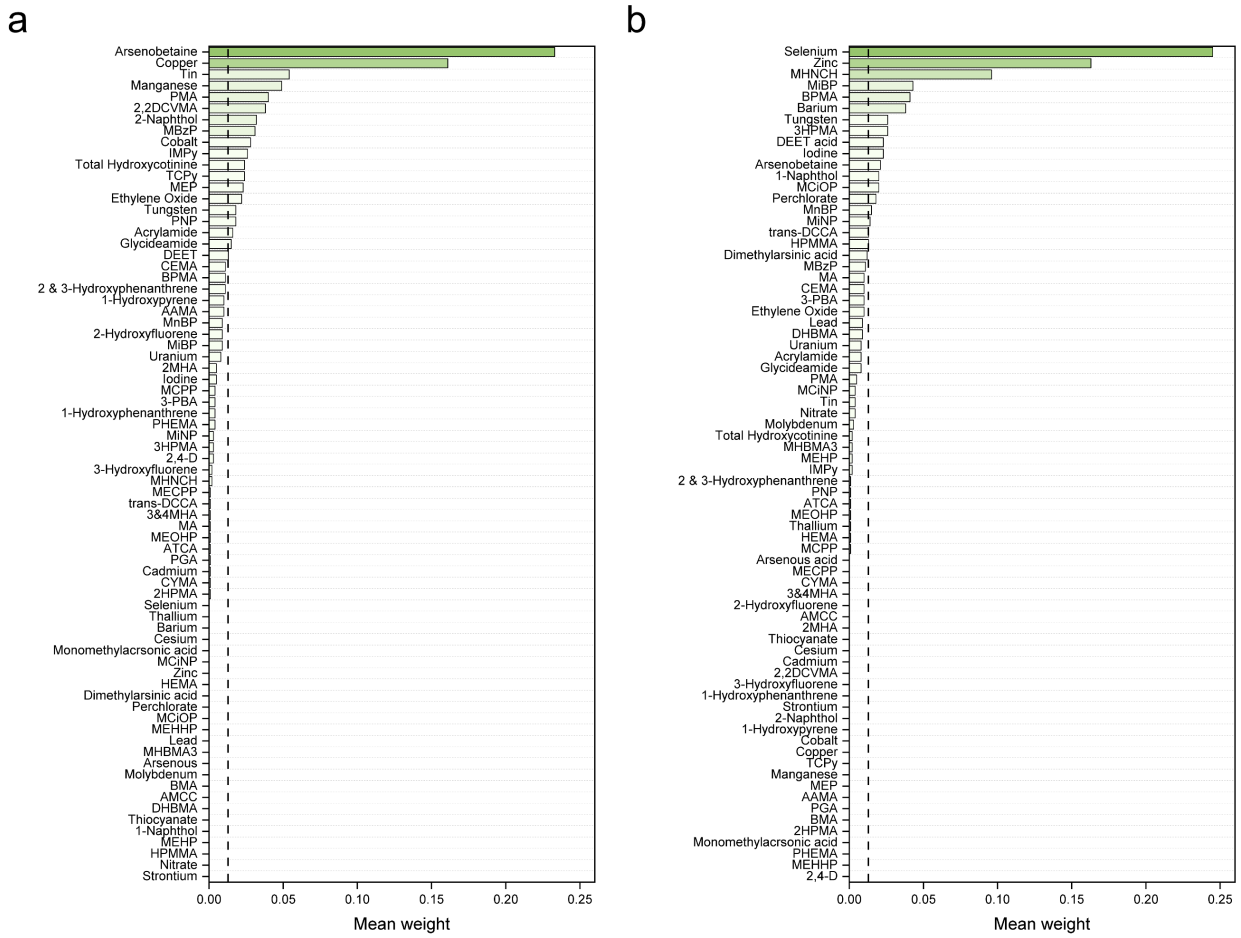


Figure 4. WQS weights of EEBs exposure. (a) Phenotypic age acceleration; (b) Biological age acceleration.

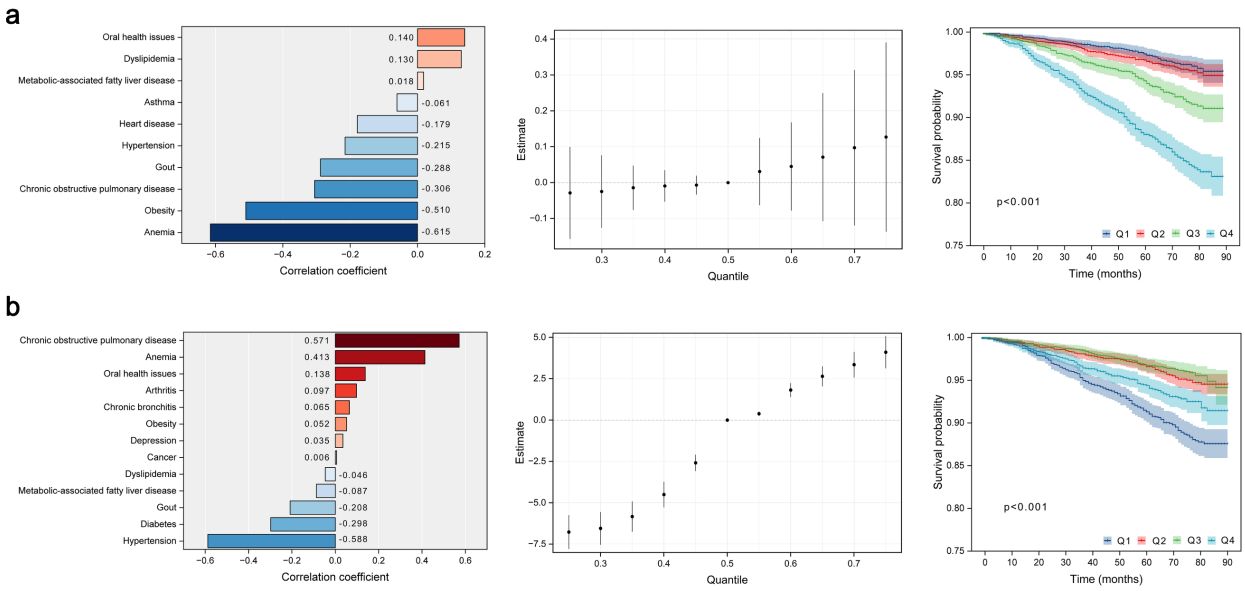
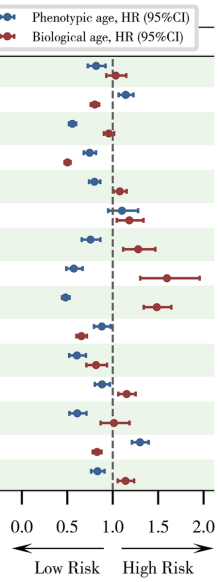


Figure 5. Associations between accelerated biology aging and disease risk. (a) Disease burden weights associated with phenotypic age acceleration; mixture effects of EEBs on phenotypic age acceleration; Kaplan-Meier curve of mortality risk. (b) Disease burden weights associated with biological age acceleration; mixture effects of EEBs on biological age acceleration; Kaplan-Meier curve of mortality risk.

= 1.102, 95% CI: 0.950–1.279), the association was not statistically significant ($P = 0.201$). In contrast, each one-year increase in physiological age was significantly associated with a 59.7% increased risk of chronic

a

Variable	Phenotypic age, HR (95%CI)	P–value	Biological age, HR (95%CI)	P–value
Cancer	0.817 (0.725, 0.921)	<0.001	1.033 (0.929, 1.149)	0.546
Metabolic–associated fatty liver disease	1.143 (1.065, 1.228)	<0.001	0.803 (0.758, 0.850)	<0.001
Obesity	0.556 (0.518, 0.598)	<0.001	0.957 (0.902, 1.015)	0.141
Hypertension	0.746 (0.682, 0.816)	<0.001	0.502 (0.471, 0.536)	<0.001
Arthritis	0.799 (0.739, 0.863)	<0.001	1.078 (1.008, 1.153)	0.028
Oral health issues	1.102 (0.950, 1.279)	0.201	1.183 (1.045, 1.338)	0.008
Chronic bronchitis	0.755 (0.659, 0.864)	<0.001	1.280 (1.115, 1.469)	<0.001
Chronic obstructive pulmonary disease	0.572 (0.489, 0.668)	<0.001	1.597 (1.303, 1.957)	<0.001
Anemia	0.481 (0.442, 0.525)	<0.001	1.485 (1.341, 1.645)	<0.001
Diabetes	0.880 (0.794, 0.976)	0.015	0.655 (0.601, 0.715)	<0.001
Gout	0.606 (0.521, 0.705)	<0.001	0.816 (0.710, 0.937)	0.004
Asthma	0.882 (0.803, 0.969)	0.009	1.153 (1.061, 1.252)	<0.001
Heart disease	0.610 (0.523, 0.711)	<0.001	1.014 (0.867, 1.185)	0.865
Dyslipidemia	1.300 (1.211, 1.395)	<0.001	0.827 (0.780, 0.876)	<0.001
Depression	0.833 (0.762, 0.910)	<0.001	1.141 (1.055, 1.235)	0.001



b

Variable	Phenotypic age, OR (95%CI)	P for interaction	Biological age, OR (95%CI)	P for interaction
Age		0.198		0.455
⩽65	1.352 (1.024 ~ 1.803)		0.943 (0.724 ~ 1.231)	
>65	1.684 (1.483 ~ 1.907)		1.124 (0.973 ~ 1.283)	
Gender		0.132		0.407
Male	1.882 (1.603 ~ 2.204)		1.032 (0.874 ~ 1.194)	
Female	1.583 (1.334 ~ 1.882)		0.913 (0.772 ~ 1.074)	
BMI		0.002		0.288
⩽25	2.284 (1.835 ~ 2.862)		0.942 (0.763 ~ 1.153)	
25–30	1.503 (1.217 ~ 1.864)		1.123 (0.915 ~ 1.354)	
>30	1.384 (1.157 ~ 1.673)		1.204 (0.993 ~ 1.423)	
Drinking		0.191		0.029
Yes	1.663 (1.437 ~ 1.923)		1.153 (0.974 ~ 1.302)	
No	1.404 (1.127 ~ 1.743)		0.872 (0.703 ~ 1.073)	
Smoking		0.985		0.571
Yes	1.623 (1.364 ~ 1.953)		1.125 (0.943 ~ 1.302)	
No	1.643 (1.417 ~ 1.902)		1.074 (0.913 ~ 1.214)	

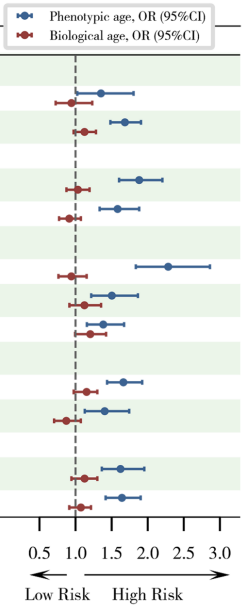


Figure 6. Association analyses between accelerated biology aging and disease risk. (a) Cox proportional hazards regression models examining the association between biological aging acceleration and disease risk. Models were adjusted for age, sex, race/ethnicity, education level, alcohol consumption, smoking status, and BMI. Participants diagnosed with specific diseases at baseline were excluded. (b) Subgroup analyses of associations between EEBs and phenotypic age acceleration and biological age acceleration.

obstructive pulmonary disease (HR = 1.597, 95% CI: 1.303–1.957, $P < 0.001$), a 48.5% increased risk of anemia (HR = 1.485, 95% CI: 1.341–1.645, $P < 0.001$), and a 28.0% increased risk of chronic bronchitis (HR = 1.280, 95% CI: 1.115–1.469, $P < 0.001$). These findings suggest distinct patterns of disease susceptibility associated with different dimensions of biological age acceleration.

Subgroup analysis revealed no significant interactions between phenotypic age acceleration and factors such as age or sex. However, a significant interaction with BMI was observed ($P_{\text{interaction}} < 0.05$). In contrast, physiological age acceleration showed a significant interaction only with alcohol consumption status ($P_{\text{interaction}} < 0.05$) (Figure 6b). Taken together, these findings suggest that phenotypic age acceleration may more strongly reflect the risk of metabolism-related chronic diseases, while physiological age acceleration appears to be more sensitive to abnormalities in the respiratory and hematologic systems. These two measures demonstrate distinct orientations and

mechanisms in predicting biological aging and disease risk [76].

5 Conclusion

This study comprehensively evaluated the associations between EEBs and biological aging using multiple statistical approaches. The results indicate that mixed environmental exposures are significantly associated with accelerated biological aging and increased risks of metabolic, respiratory, and hematological diseases. By integrating WQS regression, BKMR, and logistic regression models, we identified several key pollutants—including cadmium, lead, and volatile organic compounds—as important contributors to aging acceleration. These findings support previous evidence suggesting that environmental pollutants may promote aging processes through mechanisms such as oxidative stress, mitochondrial dysfunction, chronic inflammation, and DNA damage.

Our results further demonstrate that different aging indicators capture distinct aspects of environmental health effects. Phenotypic age appears to be more strongly related to metabolic and inflammatory dysregulation, whereas biological age may better reflect functional decline in organ systems. The clustering analysis also revealed that individuals with higher environmental exposure levels exhibited more pronounced aging acceleration and lower socioeconomic status, suggesting that environmental exposure disparities may contribute to health inequality. These findings highlight the importance of evaluating mixed environmental exposures rather than focusing on single pollutants in environmental health research.

Despite these strengths, several limitations should be acknowledged. First, the cross-sectional design of NHANES limits the ability to infer causal relationships between environmental exposures and accelerated aging. Second, exposure biomarkers were measured at a single time point, which may not fully capture long-term exposure patterns, particularly for pollutants with long biological half-lives. Third, the aging indicators were constructed using biomarker data from specific NHANES cycles, which may restrict generalizability across different populations or time periods. In addition, the experimental validation in this study relied primarily on publicly available datasets. Independent external datasets were not available for validation, which may limit the robustness of the findings. Future studies should incorporate independent cohorts and longitudinal data to further verify these associations.

Overall, this study provides new evidence that mixed environmental exposures may play an important role in biological aging and related disease risks. Future research integrating longitudinal cohort data, independent validation datasets, and mechanistic studies will help clarify the causal pathways linking environmental pollutants and aging processes.

Data Availability Statement

The data used in this study are publicly available from the National Health and Nutrition Examination Survey (NHANES) at: https://www.cdc.gov/nchs/nhanes/.

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Conflicts of Interest

The authors declare no conflicts of interest.

AI Use Statement

The authors declare that no generative AI was used in the preparation of this manuscript.

Ethical Approval and Consent to Participate

Not applicable (secondary analysis of publicly available, de-identified NHANES data).

References

[1] López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2013). The hallmarks of aging. *Cell, 153*(6), 1194-1217. [CrossRef]

[2] Li, X., & Ma, L. (2024). From biological aging to functional decline: Insights into chronic inflammation and intrinsic capacity. *Ageing Research Reviews, 93*, 102175. [CrossRef]

[3] Kirkwood, T. B. L., & Austad, S. N. (2000). Why do we age? *Nature, 408*(6809), 233-238. [CrossRef]

[4] Horvath, S., & Raj, K. (2018). DNA methylation-based biomarkers and the epigenetic clock theory of ageing. *Nature reviews genetics, 19*(6), 371-384. [CrossRef]

[5] Sorrentino, J. A., Sanoff, H. K., & Sharpless, N. E. (2014). Defining the toxicology of aging. *Trends in Molecular Medicine, 20*(7), 375-384. [CrossRef]

[6] Belsky, D. W., & Baccarelli, A. A. (2023). To promote healthy aging, focus on the environment. *Nature Aging, 3*(11), 1334-1344. [CrossRef]

[7] Wahl, H.-W., Iwarsson, S., & Oswald, F. (2012). Aging well and the environment: Toward an integrative

model and research agenda for the future. *The Gerontologist, 52*(3), 306-316. [CrossRef]

[8] Kim, E. S., Tkatch, R., Martin, D., MacLeod, S., Sandy, L., & Yeh, C. (2021). Resilient aging: Psychological well-being and social well-being as targets for the promotion of healthy aging. *Gerontology and Geriatric Medicine, 7*, 23337214211002951. [CrossRef]

[9] Ferrucci, L., Levine, M. E., Kuo, P.-L., & Simonsick, E. M. (2018). Time and the metrics of aging. *Circulation Research, 123*(7), 740-744. [CrossRef]

[10] Wu, H., Eckhardt, C. M., & Baccarelli, A. A. (2023). Molecular mechanisms of environmental exposures and human disease. *Nature Reviews Genetics, 24*(5), 332-344. [CrossRef]

[11] Wang, C., Koutrakis, P., Gao, X., Baccarelli, A., & Schwartz, J. (2020). Associations of annual ambient PM2.5 components with DNAm PhenoAge acceleration in elderly men: The Normative Aging Study. *Environmental Pollution, 258*, 113690. [CrossRef]

[12] Nwanaji-Enwerem, J. C., Van Ngu, T., Cardenas, A., Baccarelli, A. A., & Nunez-Smith, M. (2021). Adopting a "compound" exposome approach in environmental aging biomarker research: A call to action for advancing racial health equity. *Environmental Health Perspectives, 129*(4), 045001. [CrossRef]

[13] Wang, S., Ma, N., Kawanishi, S., Hiraku, Y., Oikawa, S., Xie, Y., Zhang, Z., Huang, G., & Murata, M. (2024). Particulate matter 2.5 accelerates aging: Exploring cellular senescence and age-related diseases. *Ecotoxicology and Environmental Safety, 284*, 116920. [CrossRef]

[14] Davalli, P., Mitic, T., Caporali, A., Lauriola, A., & D'Arca, D. (2016). ROS, cell senescence, and novel molecular mechanisms in aging and age-related diseases. *Oxidative Medicine and Cellular Longevity, 2016*(1), 3565127. [CrossRef]

[15] Rottenberg, H., & Hoek, J. B. (2017). The path from mitochondrial ROS to aging runs through the mitochondrial permeability transition pore. *Aging Cell, 16*(5), 943-955. [CrossRef]

[16] Santos, A. L., Sinha, S., & Lindner, A. B. (2018). The good, the bad, and the ugly of ROS: New insights on aging and aging-related diseases from eukaryotic and prokaryotic model organisms. *Oxidative Medicine and Cellular Longevity, 2018*(1), 1941285. [CrossRef]

[17] Andrade, B., Jara-Gutiérrez, C., Paz-Araos, M., Vásquez-Trincado, C., & Radojkovic, C. (2022). The relationship between reactive oxygen species and the cGAS/STING signaling pathway in the inflammaging process. *International Journal of Molecular Sciences, 23*(23), 15182. [CrossRef]

[18] Guachalla, L. M., & Rudolph, K. L. (2010). ROS induced DNA damage and checkpoint responses: Influences on aging? *Cell Cycle, 9*(20), 4058-4060. [CrossRef]

[19] Afanas'ev, I. (2013). New nucleophilic mechanisms of ROS-dependent epigenetic modifications: Comparison of aging and cancer. *Aging and Disease, 5*(1), 52. [CrossRef]

[20] Wu, Z., Du, Y., Xue, H., Wu, Y., & Zhou, B. (2012). Aluminum induces neurodegeneration and its toxicity arises from increased iron accumulation and reactive oxygen species (ROS) production. *Neurobiology of Aging, 33*(1), 199.e1-199.e12. [CrossRef]

[21] MacNee, W. (2016). Is chronic obstructive pulmonary disease an accelerated aging disease? *Annals of the American Thoracic Society, 13*(Supplement 5), S429-S437. [CrossRef]

[22] Blackburn, E. H., Epel, E. S., & Lin, J. (2015). Human telomere biology: A contributory and interactive factor in aging, disease risks, and protection. *Science, 350*(6265), 1193-1198. [CrossRef]

[23] Guo, J., Huang, X., Dou, L., Yan, M., Shen, T., Tang, W., & Li, J. (2022). Aging and aging-related diseases: From molecular mechanisms to interventions and treatments. *Signal Transduction and Targeted Therapy, 7*(1), 391. [CrossRef]

[24] Cao, Q., Wu, S., & Xiao, T. (2024). Biological aging mediates the association between volatile organic compounds and cardiovascular disease. *BMC Public Health, 24*(1), 2928. [CrossRef]

[25] Cakmak, S., Cole, C., Hebbern, C., Andrade, J., & Dales, R. (2020). Associations between blood volatile organic compounds, and changes in hematologic and biochemical profiles, in a population-based study. *Environment International, 145*, 106121. [CrossRef]

[26] Ogbodo, J. O., Arazu, A. V., Iguh, T. C., Onwodi, N. J., & Ezike, T. C. (2022). Volatile organic compounds: A proinflammatory activator in autoimmune diseases. *Frontiers in Immunology, 13*, 928379. [CrossRef]

[27] Chen, X., Ren, H., Wang, C., & Zhang, J. (2024). Associations between ethylene oxide exposure and biological age acceleration: Evidence from NHANES 2013–2016. *Frontiers in Public Health, 12*, 1488558. [CrossRef]

[28] Fu, Z., Liu, Y., & Xu, Q. (2024). Association between single and mixed exposure to polycyclic aromatic hydrocarbons and biological aging. *Frontiers in Public Health, 12*, 1379252. [CrossRef]

[29] Yang, G., Weng, Z., & Chen, X. (2025). Biological age acceleration and interaction with genetic predisposition in the risk of type 2 diabetes and coronary artery disease. *Geroscience*, 1-16. [CrossRef]

[30] Ahluwalia, N., Dwyer, J., Terry, A., Moshfegh, A., & Johnson, C. (2016). Update on NHANES dietary data: Focus on collection, release, analytical considerations, and uses to inform public policy. *Advances in Nutrition, 7*(1), 121-134. [CrossRef]

[31] Yao, X., Xu, X., Wang, G., Lei, M., Qu, L., & Huo, X. (2021). Stratification of population in NHANES 2009-2014 based on exposure pattern of lead, cadmium, mercury, and arsenic and their

association with cardiovascular, renal and respiratory outcomes. *Environment International, 149*, 106410. [CrossRef]

[32] Park, H. S., & Jun, C. H. (2009). A simple and fast algorithm for K-medoids clustering. *Expert systems with applications, 36*(2), 3336-3341. [CrossRef]

[33] World Medical Association. (2025). World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human participants. *JAMA, 333*(1), 71-74. [CrossRef]

[34] Dong, H., Yang, X., Zhang, S., Wang, X., Guo, C., Zhang, X., ... & Chen, T. (2021). Associations of low level of fluoride exposure with dental fluorosis among US children and adolescents, NHANES 2015–2016. *Ecotoxicology and environmental safety, 221*, 112439. [CrossRef]

[35] Chobanian, A. V., Bakris, G. L., Black, H. R., Cushman, W. C., Green, L. A., Izzo Jr, J. L., ... & National High Blood Pressure Education Program Coordinating Committee, T. (2003). The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *Jama, 289*(19), 2560-2571. [CrossRef]

[36] Dang, K., Wang, X., Hu, J., Zhang, Y., Cheng, L., Qi, X., ... & Li, Y. (2024). The association between triglyceride-glucose index and its combination with obesity indicators and cardiovascular disease: NHANES 2003–2018. *Cardiovascular diabetology, 23*(1), 8. [CrossRef]

[37] Ba, Y., Yu, H., Wu, F., Wang, L., & Ren, X. (2023). Association of exposures to serum terpenes with the prevalence of dyslipidemia: A population-based analysis. *Environmental Science and Pollution Research, 30*(54), 115295-115309. [CrossRef]

[38] Mach, F., Baigent, C., Catapano, A. L., Koskinas, K. C., Casula, M., Badimon, L., ... & Wiklund, O. (2020). 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). *European heart journal, 41*(1), 111-188. [CrossRef]

[39] Langsted, A., Madsen, C. M., & Nordestgaard, B. G. (2020). Contribution of remnant cholesterol to cardiovascular risk. *Journal of Internal Medicine, 288*(1), 116-127. [CrossRef]

[40] Wang, Y. F., Xie, B., & Zou, Y. X. (2023). Association between PFAS congeners exposure and asthma among US children in a nationally representative sample. *Environmental Geochemistry and Health, 45*(8), 5981-5990. [CrossRef]

[41] Rahman, H. H., Niemann, D., & Munson-McGee, S. H. (2022). Association between environmental toxic metals, arsenic and polycyclic aromatic hydrocarbons and chronic obstructive pulmonary disease in the US adult population. *Environmental Science and Pollution Research, 29*(36), 54507-54517. [CrossRef]

[42] Shiue, I. (2016). Urinary polyaromatic hydrocarbons are associated with adult emphysema, chronic bronchitis, asthma, and infections: US NHANES, 2011-2012. *Environmental Science and Pollution Research, 23*, 25494-25500. [CrossRef]

[43] Guo, J., Wan, Z., Cui, G., Pan, A., & Liu, G. (2021). Association of exposure to ethylene oxide with risk of diabetes mellitus: results from NHANES 2013–2016. *Environmental Science and Pollution Research, 28*(48), 68551-68559. [CrossRef]

[44] Yin, T., Xu, F., Shi, S., Liao, S., Tang, X., Zhang, H., ... & Li, X. (2022). Vitamin D mediates the association between acrylamide hemoglobin biomarkers and obesity. *Environmental Science and Pollution Research, 29*(12), 17162-17172. [CrossRef]

[45] Nehme, R., Nahas, P. C., & de Oliveira, E. P. (2023). Association between serum uric acid and muscle strength in older adults with or without gout diagnosis: NHANES 2011-2014. *Aging Clinical and Experimental Research, 35*(9), 1967-1972. [CrossRef]

[46] Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine, 16*(9), 606-613. [CrossRef]

[47] Spitzer, R. L., Kroenke, K., Williams, J. B., & Patient Health Questionnaire Primary Care Study Group. (1999). Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. *Jama, 282*(18), 1737-1744. [CrossRef]

[48] Hou, K., Song, W., He, J., & Ma, Z. (2024). The association between non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) and prevalence of periodontitis among US adults: a cross-sectional NHANES study. *Scientific Reports, 14*(1), 5558. [CrossRef]

[49] Lin, L., Xie, Y., Lin, Z., Lin, C., & Yang, Y. (2025). Machine learning for predicting metabolic-associated fatty liver disease including NHHR: a cross-sectional NHANES study. *Plos one, 20*(3), e0319851. [CrossRef]

[50] Sheng, G., Liu, D., Kuang, M., Zhong, Y., & Zhang, Y. (2022). Utility of non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio in evaluating incident diabetes risk. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 15*, 1677-1686. [CrossRef]

[51] Liu, B., Wang, J., Li, Y. Y., Li, K. P., & Zhang, Q. (2023). The association between systemic immune-inflammation index and rheumatoid arthritis: evidence from NHANES 1999–2018. *Arthritis research & therapy, 25*(1), 34. [CrossRef]

[52] Dye, B. A., Afful, J., Thornton-Evans, G., & Iafolla, T. (2019). Overview and quality assurance for the oral health component of the National Health and Nutrition Examination Survey (NHANES), 2011–2014.

BMC Oral Health, 19(1), 95. [CrossRef]

[53] Le, C. H. H. (2016). The prevalence of anemia and moderate-severe anemia in the US population (NHANES 2003-2012). *PloS one, 11*(11), e0166635. [CrossRef]

[54] Steele, C. C., Steele, T. J., Rosenkranz, S. K., Lee, J., & Ade, C. J. (2021). Health behaviors and patient–practitioner communication in cancer patients and the general population: an analysis of the National Health and Nutrition Examination Survey (NHANES) 2005–2014. *Supportive Care in Cancer, 29*(7), 3877-3884. [CrossRef]

[55] Zhu, M., & Chen, A. (2024). Epidemiological characteristics of asthma-COPD overlap, its association with all-cause mortality, and the mediating role of depressive symptoms: Evidence from NHANES 2005-2018. *BMC Public Health, 24*(1), 1423. [CrossRef]

[56] Xing, W., Gao, W., Zhao, Z., Xu, X., Bu, H., Su, H., ... & Chen, J. (2023). Dietary flavonoids intake contributes to delay biological aging process: analysis from NHANES dataset. *Journal of Translational Medicine, 21*(1), 492. [CrossRef]

[57] Levine, M. E., Lu, A. T., Quach, A., Chen, B. H., Assimes, T. L., Bandinelli, S., ... & Horvath, S. (2018). An epigenetic biomarker of aging for lifespan and healthspan. *Aging (albany NY), 10*(4), 573. [CrossRef]

[58] Klemera, P., & Doubal, S. (2006). A new approach to the concept and computation of biological age. *Mechanisms of ageing and development, 127*(3), 240-248. [CrossRef]

[59] Liu, Z., Kuo, P.-L., Horvath, S., Crimmins, E., Ferrucci, L., & Levine, M. (2018). A new aging measure captures morbidity and mortality risk across diverse subpopulations from NHANES IV: A cohort study. *PLoS Medicine, 15*(12), e1002718. [CrossRef]

[60] Chen, T. C., Parker, J. D., Clark, J., Shin, H. C., Rammon, J. R., & Burt, V. L. (2018). National Health and Nutrition Examination Survey: Estimation Procedures, 2011-2014. *Vital and health statistics. Series 2, Data evaluation and methods research*, (177), 1-26.

[61] Chen, T. C., Clark, J., Riddles, M. K., Mohadjer, L. K., & Fakhouri, T. H. I. (2020). National Health and Nutrition Examination Survey, 2015-2018: Sample Design and Estimation Procedures. *Vital and Health statistics. Series 2, Data Evaluation and Methods Research*, (184), 1-35.

[62] Schober, P., Mascha, E. J., & Vetter, T. R. (2021). Statistics from A (agreement) to Z (z score): A guide to interpreting common measures of association, agreement, diagnostic accuracy, effect size, heterogeneity, and reliability in medical research. *Anesthesia & Analgesia, 133*(6), 1633-1641. [CrossRef]

[63] Muggeo, V. M., & Muggeo, M. V. M. (2017). Package 'segmented'. *Biometrika, 58*(525-534), 516.

[64] Gauthier, J., Wu, Q. V., & Gooley, T. A. (2020). Cubic splines to model relationships between continuous variables and outcomes: A guide for clinicians. *Bone Marrow Transplantation, 55*(4), 675-680. [CrossRef]

[65] De Winter, J. C. F., Gosling, S. D., & Potter, J. (2016). Comparing the Pearson and Spearman correlation coefficients across distributions and sample sizes: A tutorial using simulations and empirical data. *Psychological Methods, 21*(3), 273-290. [CrossRef]

[66] Carrico, C., Gennings, C., Wheeler, D. C., & Factor-Litvak, P. (2015). Characterization of weighted quantile sum regression for highly correlated data in a risk analysis setting. *Journal of Agricultural, Biological, and Environmental Statistics, 20*(1), 100-120. [CrossRef]

[67] LaValley, M. P. (2008). Logistic regression. *Circulation, 117*(18), 2395-2399. [CrossRef]

[68] Lin, D. Y., & Wei, L. J. (1989). The robust inference for the Cox proportional hazards model. *Journal of the American statistical Association, 84*(408), 1074-1078. [CrossRef]

[69] Tibshirani, R. (1996). Regression shrinkage and selection via the lasso. *Journal of the Royal Statistical Society Series B: Statistical Methodology, 58*(1), 267-288. [CrossRef]

[70] Bobb, J. F., Valeri, L., Claus Henn, B., Christiani, D. C., Wright, R. O., Mazumdar, M., ... & Coull, B. A. (2015). Bayesian kernel machine regression for estimating the health effects of multi-pollutant mixtures. *Biostatistics, 16*(3), 493-508. [CrossRef]

[71] Benoit, L., Koual, M., Tomkiewicz, C., Bats, A. S., Antignac, J. P., Coumoul, X., ... & Cano-Sancho, G. (2022). Impact of mixtures of persistent organic pollutants on breast cancer aggressiveness. *Environment International, 170*, 107615. [CrossRef]

[72] DeVore, G. R. (2017). Computing the Z score and centiles for cross-sectional analysis: A practical approach. *Journal of Ultrasound in Medicine, 36*(3), 459-473. [CrossRef]

[73] R Core Team. (2021). *R: A language and environment for statistical computing* [Computer software]. R Foundation for Statistical Computing.

[74] Chen, W. Y., Fu, Y. P., Tu, H., Zhong, W., & Zhou, L. (2023). The association between exposure to volatile organic compounds and serum lipids in the US adult population. *Lipids in Health and Disease, 22*(1), 129. [CrossRef]

[75] Prashanth, L., Kattapagari, K. K., Chitturi, R. T., Baddam, V. R. R., & Prasad, L. K. (2015). A review on role of essential trace elements in health and disease. *Journal of dr ntr university of health sciences, 4*(2), 75-85. [CrossRef]

[76] Kuo, C. L., Pilling, L. C., Liu, Z., Atkins, J. L., & Levine, M. E. (2021). Genetic associations for two biological age measures point to distinct aging phenotypes. *Aging Cell, 20*(6), e13376. [CrossRef]

Appendix

A Supplementary Figures

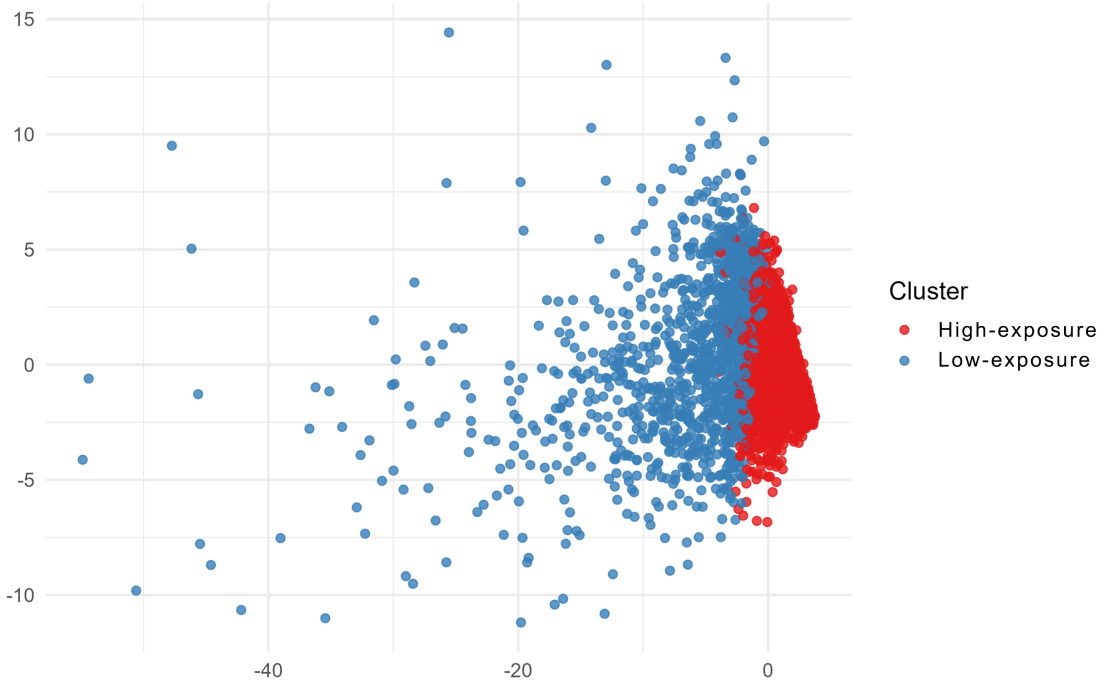

Figure S1. K-Medoids clustering visualization based on exposure to 83 environmental pollutants among 8,528 participants.

Variable	Phenotypic age, β (95%CI)	P-value	Biological age, β (95%CI)	P-value
1-Hydroxyphenanthrene	0.014 (0.003 ~ 0.024)	0.009	0.012 (0.002 ~ 0.023)	0.022
1-Hydroxypyrene	0.009 (-0.001 ~ 0.019)	0.076	0.008 (-0.002 ~ 0.019)	0.114
1-Naphthol	-0.001 (-0.011 ~ 0.009)	0.793	-0.003 (-0.008 ~ 0.013)	0.581
2 & 3-Hydroxyphenanthrene	0.009 (-0.001 ~ 0.019)	0.076	0.008 (-0.003 ~ 0.018)	0.162
2-Hydroxyfluorene	0.022 (0.011 ~ 0.032)	<0.001	0.020 (0.009 ~ 0.030)	<0.001
2-Naphthol	0.029 (0.019 ~ 0.039)	<0.001	0.015 (0.005 ~ 0.026)	0.004
2,2DCVMA	0.029 (0.019 ~ 0.039)	<0.001	0.015 (0.005 ~ 0.026)	0.004
2,4-D	0.003 (-0.007 ~ 0.013)	0.52	0.006 (-0.005 ~ 0.016)	0.288
2HPMA	-0.001 (-0.011 ~ 0.010)	0.917	0.002 (-0.009 ~ 0.012)	0.776
2MHA	0.004 (-0.006 ~ 0.014)	0.436	0.011 (0.001 ~ 0.021)	0.042
3-Hydroxyfluorene	0.022 (0.012 ~ 0.032)	<0.001	0.022 (0.011 ~ 0.032)	<0.001
3-PBA	0.010 (-0.000 ~ 0.020)	0.057	0.000 (-0.010 ~ 0.011)	0.959
3&4MHA	0.004 (-0.006 ~ 0.014)	0.477	0.006 (-0.004 ~ 0.017)	0.245
3HPMA	0.022 (0.012 ~ 0.032)	<0.001	0.010 (-0.001 ~ 0.020)	0.067
AAMA	0.027 (0.017 ~ 0.037)	<0.001	0.012 (0.002 ~ 0.023)	0.021
Acrylamide	0.024 (0.014 ~ 0.035)	<0.001	0.015 (0.005 ~ 0.026)	0.004
AMCC	0.030 (0.020 ~ 0.040)	<0.001	0.027 (0.017 ~ 0.038)	<0.001
Arsenocholine	-0.005 (-0.015 ~ 0.005)	0.307	-0.008 (-0.018 ~ 0.003)	0.149
Arsenous acid	-0.004 (-0.014 ~ 0.006)	0.445	0.001 (-0.010 ~ 0.011)	0.915
ATCA	0.022 (0.012 ~ 0.032)	<0.001	0.007 (-0.004 ~ 0.017)	0.211
Barium	0.007 (-0.004 ~ 0.017)	0.208	0.003 (-0.008 ~ 0.013)	0.58
BMA	0.007 (-0.003 ~ 0.017)	0.174	0.009 (-0.002 ~ 0.019)	0.099
BPMA	-0.002 (-0.012 ~ 0.008)	0.708	-0.005 (-0.015 ~ 0.006)	0.393
Cadmium	0.018 (0.008 ~ 0.028)	<0.001	0.019 (0.008 ~ 0.029)	<0.001
CEMA	0.023 (0.012 ~ 0.033)	<0.001	-0.002 (-0.013 ~ 0.009)	0.711
Cesium	0.007 (-0.003 ~ 0.017)	0.172	0.005 (-0.005 ~ 0.016)	0.318
Cobalt	0.024 (0.014 ~ 0.034)	<0.001	0.016 (0.006 ~ 0.027)	0.002
Copper	0.056 (0.046 ~ 0.066)	<0.001	0.039 (0.028 ~ 0.049)	<0.001
CYMA	0.029 (0.019 ~ 0.039)	<0.001	0.021 (0.011 ~ 0.032)	<0.001
DEET acid	-0.001 (-0.011 ~ 0.009)	0.815	-0.002 (-0.012 ~ 0.009)	0.721
DHBMA	0.029 (0.018 ~ 0.039)	<0.001	0.008 (-0.002 ~ 0.019)	0.125
Dimethylarsinic acid	-0.004 (-0.014 ~ 0.006)	0.455	-0.004 (-0.014 ~ 0.007)	0.488
Ethylene Oxide	0.035 (0.025 ~ 0.045)	<0.001	0.023 (0.013 ~ 0.034)	<0.001
Glycideamide	0.026 (0.016 ~ 0.036)	<0.001	0.011 (0.001 ~ 0.022)	0.037
HEMA	0.024 (0.014 ~ 0.034)	<0.001	0.016 (0.005 ~ 0.026)	0.004
HPMMA	0.028 (0.018 ~ 0.038)	<0.001	0.021 (0.011 ~ 0.032)	<0.001
IMPy	0.008 (-0.002 ~ 0.018)	0.106	0.008 (-0.003 ~ 0.018)	0.144
Iodine	0.007 (-0.003 ~ 0.017)	0.198	0.007 (-0.003 ~ 0.018)	0.167
Lead	-0.003 (-0.013 ~ 0.007)	0.518	0.002 (-0.008 ~ 0.013)	0.654
MA	0.026 (0.016 ~ 0.036)	<0.001	0.017 (0.007 ~ 0.028)	0.001
Manganese	0.011 (0.001 ~ 0.021)	0.037	0.012 (0.002 ~ 0.023)	0.022
MBzP	0.016 (0.006 ~ 0.026)	0.002	-0.000 (-0.011 ~ 0.010)	0.929
MCiNP	0.009 (-0.001 ~ 0.019)	0.086	0.009 (-0.002 ~ 0.019)	0.1
MCiOP	0.017 (0.007 ~ 0.028)	<0.001	0.011 (0.001 ~ 0.021)	0.045
MCPP	0.010 (0.001 ~ 0.020)	0.045	0.011 (0.001 ~ 0.021)	0.035
MECPP	0.028 (0.018 ~ 0.039)	<0.001	0.012 (0.002 ~ 0.023)	0.021
MEHHP	0.023 (0.013 ~ 0.033)	<0.001	0.010 (-0.000 ~ 0.021)	0.055
MEHP	0.019 (0.009 ~ 0.029)	<0.001	0.010 (-0.001 ~ 0.020)	0.072
MEOHP	0.026 (0.016 ~ 0.036)	<0.001	0.012 (0.002 ~ 0.023)	0.024
MEP	0.017 (0.007 ~ 0.027)	0.001	0.021 (0.011 ~ 0.032)	<0.001
MHBMA3	0.030 (0.020 ~ 0.040)	<0.001	0.020 (0.009 ~ 0.030)	<0.001
MHNCH	0.003 (-0.007 ~ 0.013)	0.524	-0.004 (-0.015 ~ 0.006)	0.405
MiBP	0.011 (0.001 ~ 0.021)	0.032	0.003 (-0.008 ~ 0.013)	0.618
MiNP	0.008 (-0.003 ~ 0.018)	0.142	0.007 (-0.003 ~ 0.018)	0.176
MnBP	0.011 (0.001 ~ 0.021)	0.029	0.007 (-0.003 ~ 0.018)	0.172
Molybdenum	0.004 (-0.006 ~ 0.014)	0.435	-0.000 (-0.011 ~ 0.010)	0.961
Monomethylacrsonic acid	-0.006 (-0.017 ~ 0.004)	0.212	0.003 (-0.008 ~ 0.013)	0.581
Nitrate	0.013 (0.003 ~ 0.023)	0.011	0.007 (-0.003 ~ 0.018)	0.177
Perchlorate	-0.004 (-0.014 ~ 0.006)	0.413	-0.011 (-0.021 ~ -0.001)	0.042
PGA	0.022 (0.012 ~ 0.033)	<0.001	0.010 (-0.001 ~ 0.020)	0.069
PHEMA	0.020 (0.010 ~ 0.031)	<0.001	0.013 (0.002 ~ 0.023)	0.019
PMA	0.006 (-0.004 ~ 0.016)	0.227	-0.004 (-0.015 ~ 0.006)	0.403
PNP	0.009 (-0.001 ~ 0.020)	0.069	0.008 (-0.002 ~ 0.019)	0.134
Selenium	-0.036 (-0.046 ~ -0.026)	<0.001	-0.033 (-0.044 ~ -0.023)	<0.001
Strontium	-0.000 (-0.010 ~ 0.010)	0.952	0.003 (-0.007 ~ 0.014)	0.572
TCPy	0.018 (0.008 ~ 0.028)	<0.001	0.011 (0.001 ~ 0.022)	0.034
Thallium	-0.002 (-0.012 ~ 0.008)	0.662	0.001 (-0.009 ~ 0.012)	0.787
Thiocyanate	0.023 (0.013 ~ 0.034)	<0.001	0.012 (0.002 ~ 0.023)	0.024
Tin	0.013 (0.002 ~ 0.023)	0.016	0.004 (-0.007 ~ 0.014)	0.509
Total Hydroxycotinine	0.020 (0.009 ~ 0.030)	<0.001	0.006 (-0.004 ~ 0.017)	0.24
trans-DCCA	0.009 (-0.001 ~ 0.020)	0.066	0.002 (-0.009 ~ 0.012)	0.762
Tungsten	0.015 (0.005 ~ 0.025)	0.004	0.001 (-0.009 ~ 0.012)	0.832
Uranium	0.013 (0.003 ~ 0.023)	0.013	-0.001 (-0.012 ~ 0.009)	0.844
Zinc	-0.039 (-0.050 ~ -0.029)	<0.001	-0.020 (-0.031 ~ -0.010)	<0.001

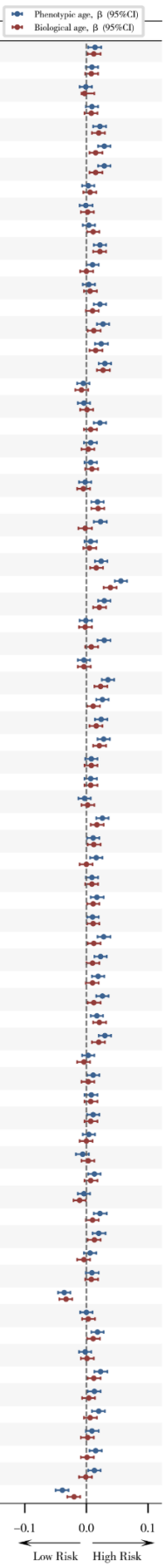

Figure S2. The association between EEBs and accelerated biological aging.

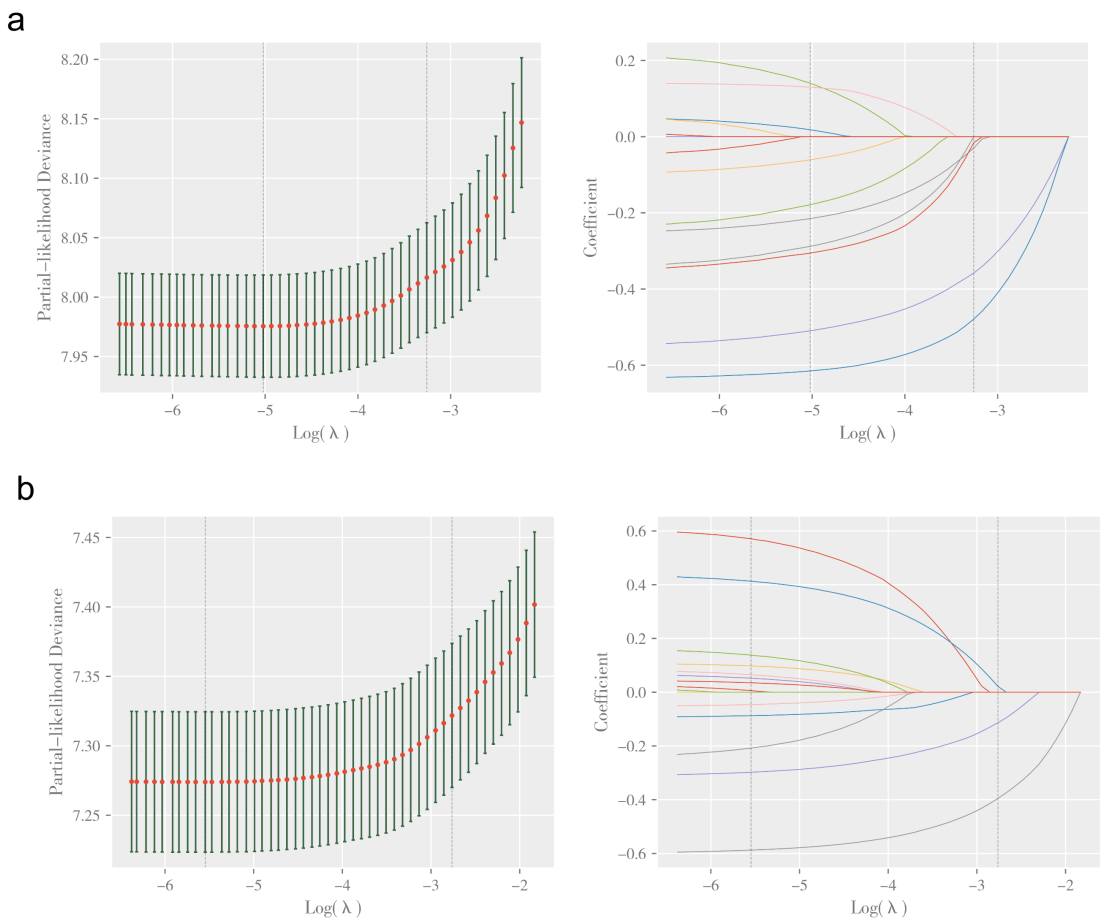

Figure S3. Lambda and residual relationship curves and LASSO regression coefficient curves. (a) Phenotypic age; (b) Biological age.

B Supplementary Tables

Table S1. Characteristics of the study population categorized by exposure levels.

Variables	Total (n = 8582)	Low-exposure (n = 7110)	High-exposure (n = 1472)	Statistics	P-value	SMD
1-Hydroxyphenanthrene (μg/L)	0.102 (0.060, 0.175)	0.091 (0.054, 0.151)	0.192 (0.116, 0.320)	-31.806[1]	<0.001	0.555
1-Hydroxypyrene (μg/L)	0.110 (0.050, 0.192)	0.096 (0.050, 0.162)	0.223 (0.113, 0.445)	-29.336[1]	<0.001	0.498
1-Naphthol (μg/L)	1.338 (0.621, 4.123)	1.150 (0.566, 2.950)	4.937 (1.357, 13.500)	-26.534[1]	<0.001	0.067
2 3-Hydroxyphenanthrene (μg/L)	0.121 (0.068, 0.208)	0.106 (0.062, 0.176)	0.252 (0.150, 0.458)	-33.883[1]	<0.001	0.549
2-Hydroxyfluorene (μg/L)	0.167 (0.087, 0.319)	0.145 (0.079, 0.247)	0.634 (0.240, 1.294)	-38.757[1]	<0.001	0.806
2-Naphthol (μg/L)	4.954 (2.345, 10.540)	4.293 (2.120, 8.581)	12.053 (5.700, 20.905)	-29.804[1]	<0.001	0.615
2,2DCVMA (ng/mL)	4.954 (2.345, 10.540)	4.293 (2.120, 8.581)	12.053 (5.700, 20.905)	-29.804[1]	<0.001	0.615
2,4-D (μg/L)	0.283 (0.154, 0.501)	0.270 (0.150, 0.488)	0.330 (0.184, 0.620)	-7.894[1]	<0.001	0.173
2HPMA (ng/mL)	29.200 (15.100, 56.400)	25.350 (13.700, 47.800)	54.900 (30.500, 99.125)	-25.979[1]	<0.001	0.220
2MH (ng/mL)	29.100 (12.600, 66.850)	24.300 (11.200, 52.300)	76.300 (30.175, 146.250)	-28.697[1]	<0.001	0.614
3-Hydroxyfluorene (μg/L)	0.065 (0.033, 0.135)	0.056 (0.030, 0.103)	0.302 (0.089, 0.772)	-37.766[1]	<0.001	0.817
3-PB (μg/L)	0.655 (0.300, 1.500)	0.609 (0.290, 1.350)	1.000 (0.373, 3.200)	-13.048[1]	<0.001	0.355
34MHA (ng/mL)	193.000 (82.500, 464.000)	164.000 (74.900, 372.750)	530.000 (197.000, 998.500)	-28.188[1]	<0.001	0.518
3HPMA (ng/mL)	236.000 (127.000, 440.000)	202.500 (113.000, 356.000)	623.500 (340.750, 1210.000)	-38.612[1]	<0.001	0.764
AAMA (ng/mL)	43.300 (23.000, 81.100)	36.800 (20.900, 65.100)	109.500 (59.975, 193.000)	-36.900[1]	<0.001	0.794
Acrylamide (pmol/g Hb)	40.200 (31.600, 54.400)	38.700 (30.900, 49.800)	59.600 (37.800, 114.000)	-24.877[1]	<0.001	0.730
AMCC (ng/mL)	131.000 (71.300, 243.000)	112.000 (64.400, 193.000)	346.000 (176.000, 569.750)	-37.834[1]	<0.001	0.993
Arsenocholine (μg/L)	0.080 (0.080, 0.080)	0.080 (0.080, 0.080)	0.080 (0.080, 0.080)	-6.820[1]	<0.001	0.146
Arsenous acid (μg/L)	0.300 (0.080, 0.640)	0.240 (0.080, 0.590)	0.540 (0.110, 0.870)	-18.413[1]	<0.001	0.511
ATCA (ng/mL)	104.500 (53.125, 205.000)	95.350 (50.300, 185.000)	165.000 (80.050, 343.500)	-18.071[1]	<0.001	0.537
Barium (μg/L)	0.960 (0.500, 1.870)	0.900 (0.480, 1.720)	1.475 (0.690, 2.890)	-15.654[1]	<0.001	0.368
BMA (ng/mL)	6.450 (3.410, 12.400)	5.940 (3.183, 10.900)	10.050 (5.370, 18.625)	-18.453[1]	<0.001	0.287
BPMA (ng/mL)	3.455 (1.240, 9.718)	3.320 (0.850, 9.138)	4.540 (1.492, 12.500)	-6.430[1]	<0.001	0.149
Cadmium (μg/L)	0.193 (0.094, 0.380)	0.173 (0.086, 0.336)	0.331 (0.169, 0.669)	-21.796[1]	<0.001	0.557
CEMA: (ng/mL)	99.300 (53.500, 169.000)	86.600 (48.000, 144.000)	202.500 (124.000, 365.500)	-35.475[1]	<0.001	0.821
Cesium (μg/L)	4.390 (2.850, 6.340)	4.050 (2.687, 5.880)	6.114 (4.183, 8.480)	-23.423[1]	<0.001	0.547
Cobalt (μg/L)	0.390 (0.238, 0.617)	0.363 (0.222, 0.574)	0.549 (0.343, 0.815)	-19.272[1]	<0.001	0.277
Copper (μg/L)	1206.628±303.087	1202.972±300.083	1224.284±316.710	-2.456[4]	0.014	0.069
CYMA (ng/mL)	1.530 (0.749, 3.810)	1.300 (0.654, 2.520)	40.050 (2.080, 155.250)	-37.230[1]	<0.001	0.789
DEET acid (μg/L)	1.850 (0.614, 6.540)	1.780 (0.574, 6.250)	2.500 (0.800, 7.672)	-5.483[1]	<0.001	0.079
DHBMA (ng/mL)	306.000 (198.000, 455.000)	282.000 (183.000, 395.000)	544.000 (368.000, 768.000)	-36.718[1]	<0.001	1.099
Dimethylarsinic acid (μg/L)	3.295 (1.350, 5.520)	3.090 (1.350, 4.980)	4.615 (2.720, 8.050)	-17.803[1]	<0.001	0.394
Ethylene Oxide (pmol/g Hb)	20.120 (14.720, 32.040)	19.240 (14.320, 27.412)	38.890 (17.803, 166.360)	-24.277[1]	<0.001	0.765
Glycideamide (pmol/g Hb)	34.800 (26.200, 46.300)	33.400 (25.600, 43.700)	46.750 (30.900, 76.650)	-21.586[1]	<0.001	0.673
HEMA (ng/mL)	0.559 (0.559, 1.350)	0.559 (0.559, 1.090)	1.460 (0.559, 3.183)	-29.383[1]	<0.001	0.608
HPMMA (ng/mL)	236.000 (137.000, 398.000)	206.000 (122.000, 319.000)	616.000 (326.000, 1340.000)	-40.313[1]	<0.001	0.874
IMP (μg/L)	0.070 (0.070, 0.070)	0.070 (0.070, 0.070)	0.070 (0.070, 0.146)	-6.492[1]	<0.001	0.190
Iodine (μg/L)	124.200 (69.625, 233.300)	116.000 (66.300, 218.550)	160.250 (94.200, 296.000)	-12.540[1]	<0.001	0.110
Lead (μg/L)	0.340 (0.190, 0.570)	0.310 (0.170, 0.520)	0.510 (0.320, 0.860)	-22.589[1]	<0.001	0.354
MA (ng/mL)	129.000 (78.400, 204.000)	115.000 (70.200, 172.000)	273.000 (174.000, 416.000)	-39.159[1]	<0.001	0.991
Manganese (μg/L)	0.092 (0.092, 0.130)	0.092 (0.092, 0.130)	0.092 (0.092, 0.160)	-9.697[1]	<0.001	0.125
MBz (ng/mL)	3.900 (1.600, 9.200)	3.700 (1.500, 8.300)	5.600 (2.200, 14.225)	-11.689[1]	<0.001	0.295
MCiNP (ng/mL)	2.000 (1.000, 3.900)	1.900 (1.000, 3.600)	2.500 (1.200, 6.000)	-10.755[1]	<0.001	0.314
MCiOP (ng/mL)	10.650 (4.600, 29.775)	9.800 (4.300, 25.700)	16.600 (6.000, 71.575)	-13.529[1]	<0.001	0.451
MCPP (ng/mL)	1.300 (0.600, 3.100)	1.200 (0.500, 2.700)	2.100 (0.800, 6.700)	-16.090[1]	<0.001	0.384
MECPP (ng/mL)	10.100 (5.400, 18.600)	9.000 (4.900, 15.100)	30.000 (11.875, 59.800)	-34.045[1]	<0.001	0.877
MEHHP (ng/mL)	6.700 (3.400, 12.200)	5.700 (3.100, 10.000)	18.750 (7.600, 38.400)	-33.602[1]	<0.001	0.819
MEHP (ng/mL)	1.100 (0.570, 2.500)	1.000 (0.570, 2.000)	3.400 (1.100, 8.000)	-31.160[1]	<0.001	0.716
MEOHP (ng/mL)	4.200 (2.200, 7.700)	3.600 (2.000, 6.200)	11.650 (4.600, 25.000)	-32.847[1]	<0.001	0.871
MEP (ng/mL)	39.300 (15.700, 126.800)	35.650 (14.600, 105.800)	68.350 (22.600, 527.450)	-15.274[1]	<0.001	0.544
MHBMA3 (ng/mL)	4.600 (2.450, 8.300)	4.060 (2.210, 6.520)	14.800 (6.357, 32.625)	-38.984[1]	<0.001	0.878
MHNCH (ng/mL)	0.280 (0.280, 0.700)	0.280 (0.280, 0.600)	0.280 (0.280, 0.700)	-2.750[1]	0.006	0.147
MiBP (ng/mL)	8.500 (3.900, 16.400)	8.000 (3.800, 15.100)	11.600 (5.075, 24.450)	-11.808[1]	<0.001	0.355
MiNP (ng/mL)	0.640 (0.640, 1.400)	0.640 (0.640, 1.200)	1.000 (0.640, 5.225)	-18.420[1]	<0.001	0.417
MnBP (ng/mL)	10.600 (5.200, 20.100)	9.700 (4.900, 18.100)	16.300 (7.275, 32.200)	-15.810[1]	<0.001	0.290
Molybdenum (μg/L)	37.110 (20.270, 61.300)	33.860 (18.793, 55.500)	57.800 (32.508, 94.120)	-22.277[1]	<0.001	0.608
Monomethylacrsonic acid (μg/L)	0.410 (0.140, 0.740)	0.360 (0.140, 0.680)	0.680 (0.310, 1.093)	-20.874[1]	<0.001	0.508
Nitrate (ng/mL)	43100.000 (25300.000, 65900.000)	39050.000 (24000.000, 60100.000)	66800.000 (44600.000, 101000.000)	-27.439[1]	<0.001	0.704
Perchlorate (ng/mL)	2.340 (1.410, 4.180)	2.210 (1.340, 3.830)	3.280 (1.877, 5.768)	-15.778[1]	<0.001	0.152
PGA (ng/mL)	191.000 (120.000, 306.000)	173.000 (109.000, 260.000)	402.000 (263.000, 571.000)	-39.671[1]	<0.001	1.051
PHEMA (ng/mL)	0.495 (0.495, 1.240)	0.495 (0.495, 1.010)	1.400 (0.706, 2.473)	-32.227[1]	<0.001	0.457
PMA (ng/mL)	0.424 (0.424, 0.967)	0.424 (0.424, 0.840)	0.841 (0.424, 1.490)	-21.238[1]	<0.001	0.430
PNP (μg/L)	0.600 (0.330, 1.200)	0.571 (0.321, 1.100)	0.804 (0.370, 1.652)	-10.247[1]	<0.001	0.317
Selenium (μg/L)	130.089±17.756	129.985±17.614	130.592±18.421	-1.159[2]	0.247	0.034
Strontium (μg/L)	89.780 (49.670, 147.070)	82.300 (46.460, 133.780)	132.185 (77.838, 221.673)	-20.143[1]	<0.001	0.401
TCPy (μg/L)	1.090 (0.590, 2.000)	1.010 (0.580, 1.860)	1.300 (0.690, 2.500)	-8.832[1]	<0.001	0.329
Thallium (μg/L)	0.159 (0.097, 0.238)	0.149 (0.092, 0.220)	0.212 (0.134, 0.309)	-18.837[1]	<0.001	0.313
Thiocyanate (ng/mL)	848.000 (419.000, 1770.000)	737.500 (374.000, 1420.000)	2645.000 (982.000, 6127.500)	-32.311[1]	<0.001	0.760
Tin (μg/L)	0.430 (0.200, 0.980)	0.390 (0.180, 0.890)	0.645 (0.320, 1.380)	-14.687[1]	<0.001	0.222
Total Hydroxycotinine (ng/mL)	0.653 (0.200, 20.775)	0.506 (0.177, 4.390)	654.500 (0.644, 5592.500)	-30.186[1]	<0.001	0.699
trans-DCCA (μg/L)	0.420 (0.420, 1.000)	0.420 (0.420, 0.804)	0.657 (0.420, 4.360)	-18.934[1]	<0.001	0.383
Tungsten (μg/L)	0.055 (0.024, 0.117)	0.051 (0.022, 0.104)	0.088 (0.043, 0.164)	-16.874[1]	<0.001	0.272
Uranium (μg/L)	0.005 (0.002, 0.010)	0.004 (0.002, 0.009)	0.007 (0.004, 0.015)	-17.329[1]	<0.001	0.262
Zinc (μg/L)	810.634±156.346	811.405±156.775	806.909±154.253	1.004[4]	0.315	0.029

Note: 1-Naphtho: 1-Hydroxynaphthalene; 2-Naphthol: 2-Hydroxynaphthalene; 2,2DCVMA: N-acel-S-(2,2-dichlorvinyl)-L-cys; 2HPMA: N-ace-S-(2-hydroxypropyl)-L-cys; 2MHA: 2-methylhippuric acid; 3-PBA: 3-phenoxybenzoic acid; 3&4MHA: 3-methipurc acd & 4-methipurc acd; 3HPMA: N-ace-S-(3-hydroxypropyl)-L-cys; AAMA: N-ace-S-(2-carbamoylethyl)-L-cys(ng/mL); AMCC: N-ace-S-(N-methlcarbamoyl)-L-cys; ATCA: 2-amnothiazolne-4-carbxylic acid; BMA: N-acetyl-S-(benzyl)-L-cysteine; BPMA: N-acetyl-S-(n-propyl)-L-cysteine; CEMA: N-acetyl-S- (2-carbxyethyl)-L-cys; CYMA: N-acetyl-S-(2-cyanoethyl)-L-cyst; DHBMA: N-ace-S- (3,4-dihidxybutl)-L-cys; HEMA: N-ace-S-(2-hydroxyethyl)-L-cys; HPMMA: N-A-S-(3-hydrxprpl-1-metl)-L-cys; IMPy: Oxypyrimidine; MA: Mandelic acid; MBzP: Mono-benzyl phthalate; MCiNP: Mono(carboxynonyl) Phthalate; MCiOP: Mono(carboxyoctyl) Phthalate; MCPP: Mono-(3-carboxypropyl) phthalate; MECPP: MECP phthalate; MEHHP: MEHP phthalate; MEHP: Mono-(2-ethyl)-hexyl phthalate; MEOHP: MEOH phthalate; MEP: Mono-ethyl phthalate; MHBMA3: N-A-S-(4-hydrxy-2butn-l-yl)-L-cys; MiBP: Mono-isobutyl phthalate; MiNP: Mono-isononyl phthalate; MnBP: Mono-n-butyl phthalate; PGA: Phenylglyoxylic acid; PHEMA: N-ace-S-(phenl-2-hydxyetl)-L-cys; PMA: N-acetyl-S-(phenyl)-L-cysteine; PNP: para-Nitrophenol; TCPy: 3,5,6-trichloropyridinol; trans-DCCA: Dichlorovnl-dimeth prop carboacid. [1]Mann Whitney Utest; [2] Variance-corrected independent samples t-test; [3]Pearson's chi-square (χ^2) test; [4]Independent samples t-test.

Table S2. Exposure levels and detection characteristics of 74 environmental pollutants and metabolites.

No.	Chemical family	Common Abbreviation	Analyte Description	Unit	LOD	Matrix	Detection rate (%)	Variable Name
1		AAMA	N-Acetyl-S-(2-carbamoylethyl)-L-cysteine	µg/L	2.200	Urine	38.34	URXAAM
2		AMCC	N-Acetyl-S-(N-methylcarbamoyl)-L-cysteine	µg/L	6.260	Urine	39.00	URXAMC
3		ATCA	2-Aminothiazoline-4-carboxylic acid	µg/L	15.000	Urine	38.52	URXATC
4		BMA	N-Acetyl-S-(benzyl)-L-cysteine	µg/L	0.500	Urine	39.23	URXBMA
5		BPMA	N-Acetyl-S-(n-propyl)-L-cysteine	µg/L	1.200	Urine	38.86	URXBPM
6		CEMA	N-Acetyl-S-(2-carboxyethyl)-L-cysteine	µg/L	6.960	Urine	39.16	URXCEM
7		CYMA	N-Acetyl-S-(2-cyanoethyl)-L-cysteine	µg/L	0.500	Urine	38.91	URXCYM
8		2,2DCVMA	N-Acetyl-S-(2,2-dichlorovinyl)-L-cysteine	µg/L	4.700	Urine	37.50	URX2DC
9		DHBMA	N-Acetyl-S-(3,4-dihydroxybutyl)-L-cysteine	µg/L	5.250	Urine	37.30	URXDHB
10	Volatile organic compounds	HEMA	N-Acetyl-S-(2-hydroxyethyl)-L-cysteine	µg/L	0.791	Urine	39.09	URXHEM
11		3HPMA	N-Acetyl-S-(3-hydroxypropyl)-L-cysteine	µg/L	13.000	Urine	37.92	URXHPM
12		2HPMA	N-Acetyl-S-(2-hydroxypropyl)-L-cysteine	µg/L	5.300	Urine	39.04	URXHP2
13		HPMMA	N-Acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine	µg/L	1.700	Urine	38.91	URXPMM
14		MA	Mandelic acid	µg/L	12.000	Urine	38.66	URXMAD
15		2MHA	2-Methylhippuric acid	µg/L	5.000	Urine	37.33	URX2MH
16		34MHA	3- and 4-Methylhippuric acid	µg/L	8.000	Urine	39.27	URX34M
17		MHBMA3	N-Acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine	µg/L	0.600	Urine	38.37	URXMB3
18		PHEMA	N-Acetyl-S-(phenyl-2-hydroxyethyl)-L-cysteine	µg/L	0.700	Urine	38.48	URXPHE
19		PGA	Phenylglyoxylic acid	µg/L	12.000	Urine	38.79	URXPHG
20		PMA	N-Acetyl-S-(phenyl)-L-cysteine	µg/L	0.600	Urine	38.79	URXPMA
21		Barium	Barium	µg/L	0.060	Urine	39.58	URXUBA
22		Cadmium	Cadmium	µg/L	0.036	Urine	39.58	URXUCD
23		Cobalt	Cobalt	µg/L	0.023	Urine	39.58	URXUCO
24		Cesium	Cesium	µg/L	0.130	Urine	39.58	URXUCS
25		Manganese	Manganese	µg/L	0.800	Urine	39.59	URXUMN
26		Molybdenum	Molybdenum	µg/L	0.030	Urine	39.57	URXUMO
27		Lead	Lead	µg/L	0.022	Urine	39.57	URXUPB
28	Heavy metals	Strontium	Strontium	µg/L	0.018	Urine	39.58	URXUSR
29		Thallium	Thallium	µg/L	0.090	Urine	39.58	URXUTL
30		Tin	Tin	µg/L	0.018	Urine	39.57	URXUSN
31		Tungsten	Tungsten	µg/L	0.002	Urine	39.57	URXUTU
32		Uranium	Uranium	µg/L	0.060	Urine	39.58	URXUUR
33		Copper	Copper	µg/L	25.000	Serum	40.28	LBXSCU
34		Selenium	Selenium	µg/L	4.500	Serum	40.27	LBXSSE
35		Zinc	Zinc	µg/L	29.000	Serum	40.28	LBXSZN
36		1-Naphthol	1-Hydroxynapthalene	µg/L	0.060	Urine	38.31	URXP01
37		2-Naphthol	2-Hydroxynapthalene	µg/L	0.090	Urine	39.90	URXP02
38	Polycyclic Aromatic Hydrocarbons	3-Hydroxyfluorene	3-Hydroxyfluorene	µg/L	0.008	Urine	39.43	URXP03
39		2-Hydroxyfluorene	2-Hydroxyfluorene	µg/L	0.008	Urine	39.48	URXP04
40		1-Hydroxyphenanthrene	1-Hydroxyphenanthrene	µg/L	0.009	Urine	39.49	URXP06
41		1-Hydroxypyrene	1-Hydroxypyrene	µg/L	0.070	Urine	39.47	URXP10
42		2 3-Hydroxyphenanthrene	2-Hydroxyphenanthrene 3-Hydroxyphenanthrene	µg/L	0.010	Urine	39.49	URXP25
43	Perchlorate, Nitrate Thiocyanate	Nitrate	Nitrate	µg/L	700.000	Urine	39.42	URXNO3
44		Perchlorate	Perchlorate	µg/L	0.050	Urine	39.41	URXUP8
45		Thiocyanate	Thiocyanate	µg/L	20.000	Urine	39.31	URXSCN
46	Acrylamide Glycidamide	Acrylamide	Acrylamide	pmol/g Hb	3.900	Serum	38.52	LBXACR
47		Glycidamide	Glycidamide	pmol/g Hb	4.900	Serum	36.92	LBXGLY
48	Cotinine, Hydroxycotinine, Other Nicotine Metabolites and Analogs	Total Hydroxycotinine	Total Hydroxycotinine	µg/L	0.030	Urine	38.86	URXHCTT
49	Ethylene Oxide	Ethylene Oxide	Hemoglobin adducts of ethylene oxide	nmol/g Hb	8.200	Serum	39.35	LBXEOA
50		MCiNP	Mono(carboxyisononyl) phthalate	µg/L	0.200	Urine	39.07	URXCNP
51		MCiOP	Mono(carboxyisoctyl) phthalate	µg/L	0.300	Urine	39.07	URXCOP
52		MECPP	Mono-2-ethyl-5-carboxypentyl phthalate	µg/L	0.400	Urine	39.07	URXECP
53		MnBP	Mono-n-butyl phthalate	µg/L	0.400	Urine	39.07	URXMBP
54		MCPP	Mono-(3-carboxypropyl) phthalate	µg/L	0.400	Urine	39.07	URXMC1
55	Phthalates and Plasticizers Metabolites	MEP	Mono-ethyl phthalate	µg/L	1.200	Urine	39.07	URXMEP
56		MEHHP	Mono-(2-ethyl-5-hydroxyhexyl) phthalate	µg/L	0.400	Urine	39.07	URXMHH
57		MHINCH	Cyclohexane 1,2-dicarboxylic acid monohydroxy isononyl ester	µg/L	0.400	Urine	39.07	URXMHNC
58		MEHP	Mono-(2-ethyl)-hexyl phthalate	µg/L	0.800	Urine	39.07	URXMHP
59		MiBP	Mono-isobutyl phthalate	µg/L	0.800	Urine	39.07	URXMIB
60		MiNP	Mono-isononyl phthalate	µg/L	0.900	Urine	39.07	URXMNP
61		MEOHP	Mono-(2-ethyl-5-oxohexyl) phthalate	µg/L	0.200	Urine	39.07	URXMOH
62		MBzP	Mono-benzyl phthalate	µg/L	0.300	Urine	39.07	URXMZP
63		Arsenous acid	Arsenous Acid	µg/L	0.120	Urine	39.68	URXUAS3
64	Arsenic species	Arsenocholine	Arsenocholine	µg/L	0.110	Urine	39.68	URXUAC
65		Dimethylarsinic acid	Dimethylarsinic acid	µg/L	1.910	Urine	39.68	URXUDMA
66		Monomethylarsonic Acid	Monomethylarsonic Acid	µg/L	0.200	Urine	39.68	URXUMMA
67	DEET and Metabolites	DEET acid	DEET acid	µg/L	0.475	Urine	38.69	URXDEA
68	Iodine	Iodine	Iodine	µg/L	2.400	Urine	39.69	URXUIO
69		2,4-D	2,4-dichlorophenoxyacetic acid	µg/L	0.150	Urine	39.18	URX24D
70		TCPy	3,5,6-trichloropyridinol	µg/L	0.100	Urine	38.91	URXCPM
71	Pyrethroids, Herbicides, Organophosphorus Metabolites	3-PBA	3-phenoxybenzoic acid	µg/L	0.100	Urine	38.85	URXOPM
72		IMPy	2-isopropyl-4-methyl-pyrimidinol	µg/L	0.100	Urine	39.04	URXOXY
73		PNP	*para*-Nitrophenol	µg/L	0.100	Urine	38.49	URXPAR
74		trans-DCCA	*trans*-dichlorovinyl dimethylcyclopropane carboxylic acid	µg/L	0.600	Urine	39.57	URXTCC

Abbreviations: LOD, lower limit of detection.

Table S3. Diagnostic methods and criteria for the 15 diseases.

No.	Disease category	Specific disease	Diagnostic criteria (any one sufficient)
1	Cardiovascular Disease	Hypertension	1. Currently using antihypertensive medication; 2. Measured systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg.
2		Heart Disease	1. Standardized medical questionnaire (Has a doctor or other healthcare professional ever told you that you have congestive heart failure, coronary heart disease, angina, heart attack, or stroke?).
3		Dyslipidemia	1. Total cholesterol ≥5.18 mmol/L; 2. HDL-C (men 1.04 mmol/L, women 1.30 mmol/L); 3. Non-HDL-C ≥4.2 mmol/L; 4. Triglycerides ≥1.7 mmol/L; 5. LDL-C ≥3.37 mmol/L; 6. Residual cholesterol ≥1.0 mmol/L; 7. Apolipoprotein B ≥1.3 g/L.
4	Respiratory Disease	Asthma	1. Standardized medical questionnaire (Has a doctor or other healthcare professional ever told you that you have asthma?).
5		Chronic Obstructive Pulmonary Disease (COPD)	1. Standardized medical questionnaire (Has a doctor or other healthcare professional ever told you that you have COPD?).
6		Chronic Bronchitis	1. Standardized medical questionnaire (Has a doctor or other healthcare professional ever told you that you have chronic bronchitis?).
7	Endocrine and Metabolic Diseases	Diabetes	1. Fasting blood glucose ≥7.0 mmol/L; 2. 2-hour blood glucose during oral glucose tolerance test ≥11.1 mmol/L.
8		Obesity	1. BMI ≥30 kg/m²; 2. Waist circumference (men ≥102 cm, women ≥88 cm).
9		Gout	1. Standardized medical questionnaire (Has a doctor or other healthcare professional ever told you that you have gout?).
10	Nervous System Disease	Depression	1. Patient Health Questionnaire-9 (PHQ-9) score ≥10.
11	Digestive System Disease	Metabolic Associated Fatty Liver Disease (MAFLD)	1. Ratio of non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol (NHHR) ≥2.74.
12	Musculoskeletal Disease	Arthritis	1. Standardized medical questionnaire (Has a doctor or other healthcare professional ever told you that you have arthritis?).
13	Oral Disease	Oral Problems	1. General care advice: see a dentist as soon as convenient, see a dentist within the next two weeks, or see a dentist immediately.
14	Hematologic Disease	Anemia	1. Serum hemoglobin: (women 11 g/dL, men 13 g/dL).
15	Cancer	Cancer	1. Standardized medical questionnaire (Has a doctor or other healthcare professional ever told you that you have cancer or any type of malignant tumor?).

Table S4. Biomarkers of phenotypic age and biological age.

Variables	Total (n = 8582)	Low-exposure (n = 7110)	High-exposure (n = 1472)	Statistics	*P*-value	*SMD*
Phenotypic age (years)	47.094 (32.660, 61.798)	46.787 (32.220, 61.347)	48.289 (34.598, 64.028)	-4.570[2]	<0.001	0.172
Albumin (g/L)	42.705±3.442	42.816±3.372	42.170±3.715	6.168[1]	<0.001	0.182
Creatinine (μmol/L)	74.700 (62.760, 89.280)	74.260 (61.880, 87.520)	78.680 (66.300, 93.700)	-9.205[2]	<0.001	0.244
Glucose (mmol/L)	100.000 (93.000, 111.000)	100.000 (93.000, 110.000)	101.000 (94.000, 117.000)	-2.277[2]	0.023	0.206
Lymphocyte percentage (%)	30.597±8.556	30.796±8.442	29.635±9.028	4.539[1]	<0.001	0.133
Mean corpuscular volume (fL)	88.924±6.022	88.816±5.970	89.445±6.241	-3.543[1]	<0.001	0.103
Red cell distribution width (%)	13.760±1.296	13.721±1.248	13.946±1.494	-5.408[1]	<0.001	0.164
Alkaline phosphatase (U/L)	64.000 (52.000, 78.000)	64.000 (52.000, 77.000)	67.000 (55.000, 81.000)	-5.393[2]	<0.001	0.147
White blood cell count (10^9 cells/L)	7.000 (5.800, 8.500)	7.000 (5.800, 8.400)	7.300 (6.000, 9.000)	-5.989[2]	<0.001	0.153
Biological age (years)	47.226 (32.994, 62.699)	46.909 (32.702, 62.468)	48.539 (34.566, 64.347)	-3.771[2]	<0.001	0.173
Systolic blood pressure (mmHg)	124.045±18.183	123.690±17.975	125.785±19.084	-3.923[3]	<0.001	0.113
Albumin (g/dL)	42.705±3.442	42.816±3.372	42.170±3.715	6.168[2]	<0.001	0.182
Alkaline phosphatase (U/L)	64.000 (52.000, 78.000)	64.000 (52.000, 77.000)	67.000 (55.000, 81.000)	-5.393[3]	<0.001	0.147
Blood urea nitrogen (mg/dL)	4.640 (3.570, 5.710)	4.640 (3.570, 5.710)	4.640 (3.570, 6.070)	-2.097[2]	0.036	0.184
Creatinine (mg/dL)	74.700 (62.760, 89.280)	74.260 (61.880, 87.520)	78.680 (66.300, 93.700)	-9.205[2]	<0.001	0.244
Glycated hemoglobin (%)	5.776±1.113	5.744±1.051	5.930±1.365	-4.924[1]	<0.001	0.152
Total cholesterol (mg/dL)	189.603±41.333	189.715±41.049	189.059±42.686	0.554[3]	0.579	0.016
Lymphocyte percentage (%)	30.597±8.556	30.796±8.442	29.635±9.028	4.539[2]	<0.001	0.133
White blood cell count (10^9 cells/L)	7.000 (5.800, 8.500)	7.000 (5.800, 8.400)	7.300 (6.000, 9.000)	-5.989[3]	<0.001	0.153
Mean corpuscular volume (fL)	88.924±6.022	88.816±5.970	89.445±6.241	-3.543[2]	<0.001	0.103

Note: [1] Variance-corrected independent samples t-test; [2]Mann Whitney U text; [3] Independent samples t-test.

Table S5. Threshold characteristics of phenotypic age and biological age in aging and results of piecewise linear regression analysis.

Indicator	Model type	Inflection point	Interval	β (95% CI)	*P*-value
Biological Age	Model 1 Fitting model by standard linear regression	-	-	1.011 (1.009 – 1.014)	<0.001
	Model 2 Fitting model by two-piecewise linear regression	74.540	<74.540	1.004 (1.001 – 1.007)	0.005
			≥74.540	1.157 (1.106 – 1.210)	<0.001
	P for likelihood test				<0.001
Phenotypic Age	Model 1 Fitting model by standard linear regression	-	-	1.030 (1.030 – 1.030)	<0.001
	Model 2 Fitting model by two-piecewise linear regression	78.790	<78.790	1.020 (1.020 – 1.020)	<0.001
			≥78.790	6.340 (4.520 – 9.280)	<0.001
	P for likelihood test				<0.001

Table S6. Mean weights of environmental pollutants accelerating biological aging based on WQS model.

Phenotypic age				Biological age			
Chemicals	Weight	Chemicals	Weight	Chemicals	Weight	Chemicals	Weight
Arsenobetaine	0.233	MHNCH	0.002	Selenium	0.245	Total Hydroxycotinine	0.002
Copper	0.161	3-Hydroxyfluorene	0.002	Zinc	0.163	MCPP	0.001
Tin	0.054	2HPMA	0.001	MHNCH	0.096	HEMA	0.001
Manganese	0.049	CYMA	0.001	MiBP	0.043	Thallium	0.001
PMA	0.04	Cadmium	0.001	BPMA	0.041	MEOHP	0.001
2,2DCVMA	0.038	PGA	0.001	Barium	0.038	ATCA	0.001
2-Naphthol	0.032	ATCA	0.001	3HPMA	0.026	PNP	0.001
MBzP	0.031	MEOHP	0.001	Tungsten	0.026	2 3-Hydroxyphenanthrene	0.001
Cobalt	0.028	MA	0.001	Iodine	0.023	2,4-D	0
IMPy	0.026	34MHA	0.001	DEET acid	0.023	MEHHP	0
TCPy	0.024	trans-DCCA	0.001	Arsenobetaine	0.021	PHEMA	0
Total Hydroxycotinine	0.024	MECPP	0.001	MCiOP	0.02	Monomethylacrsonic acid	0
MEP	0.023	Strontium	0	1-Naphthol	0.02	2HPMA	0
Ethylene Oxide	0.022	Nitrate	0	Perchlorate	0.018	BMA	0
PNP	0.018	HPMMA	0	MnBP	0.015	PGA	0
Tungsten	0.018	MEHP	0	MiNP	0.014	AAMA	0
Acrylamide	0.016	1-Naphthol	0	HPMMA	0.013	MEP	0
Glycideamide	0.015	Thiocyanate	0	trans-DCCA	0.013	Manganese	0
DEET acid	0.013	DHBMA	0	Dimethylarsinic acid	0.012	TCPy	0
2 3-Hydroxyphenanthrene	0.011	AMCC	0	MBzP	0.011	Copper	0
BPMA	0.011	BMA	0	Ethylene Oxide	0.01	Cobalt	0
CEMA	0.011	Molybdenum	0	3-PBA	0.01	1-Hydroxypyrene	0
AAMA	0.01	Arsenous acid	0	CEMA	0.01	2-Naphthol	0
1-Hydroxypyrene	0.01	MHBMA3	0	MA	0.01	Strontium	0
MiBP	0.009	Lead	0	DHBMA	0.009	1-Hydroxyphenanthrene	0
2-Hydroxyfluorene	0.009	MEHHP	0	Lead	0.009	3-Hydroxyfluorene	0
MnBP	0.009	MCiOP	0	Glycideamide	0.008	2,2DCVMA	0
Uranium	0.008	Perchlorate	0	Acrylamide	0.008	Cadmium	0
Iodine	0.005	Dimethylarsinic acid	0	Uranium	0.008	Cesium	0
2MHA	0.005	HEMA	0	PMA	0.005	Thiocyanate	0
PHEMA	0.004	Zinc	0	Nitrate	0.004	2MHA	0
1-Hydroxyphenanthrene	0.004	MCiNP	0	Tin	0.004	AMCC	0
3-PBA	0.004	Monomethylacrsonic acid	0	MCiNP	0.004	2-Hydroxyfluorene	0
MCPP	0.004	Cesium	0	Molybdenum	0.003	34MHA	0
2,4-D	0.003	Barium	0	IMPy	0.002	CYMA	0
3HPMA	0.003	Thallium	0	MEHP	0.002	MECPP	0
MiNP	0.003	Selenium	0	MHBMA3	0.002	Arsenous acid	0

Table S7. LASSO regression results.

Type	Variable	Correlation coefficient
Phenotypic age	Anemia	-0.615134980531057
	Obesity	-0.509754688057163
	Chronic obstructive pulmonary disease	-0.30569480416062
	Gout	-0.288033647059623
	Hypertension	-0.215034167122041
	Heart disease	-0.178721657873439
	Asthma	-0.0607683137113985
	Metabolic-associated fatty liver disease	0.0181236353830542
	Dyslipidemia	0.130055699959009
	Oral health issues	0.140297991227631
Biological age	Hypertension	-0.587549424276646
	Diabetes	-0.2979467463893
	Gout	-0.208298085000463
	Metabolic-associated fatty liver disease	-0.0871967659462267
	Dyslipidemia	-0.0461824985520735
	Cancer	0.0062055959894831
	Depression	0.0351679419583314
	Obesity	0.0522174229803938
	Chronic bronchitis	0.0650875691231104
	Arthritis	0.0978517759573831
	Oral health issues	0.138178548784095
	Anemia	0.413208676219853
	Chronic obstructive pulmonary disease	0.571110993175399