SUPPLEMENTARY DATA

SUPPLEMENTARY METHOD

Algorithms for KDM biological and phenotypic age

1. KDM biological age

The values j and i represent the number of biomarkers and the number of samples, respectively. The values k, q, and s represent the regression slopes, intercepts, and root-mean-square errors of a biomarker regressed on chronological age, respectively. The value r_j^2 denotes the variance explained by regression of chronological age (CA) on biomarkers.[1]

$$BA_E = \frac{\Sigma_{j=1}^{m}(x_j - q_j)\left(\frac{k_j}{s_j^2}\right)}{\Sigma_{j=1}^{m}\left(\frac{k_j}{s_j}\right)^2}$$

$$r_{char} = \frac{\Sigma_{j=1}^{m}\frac{r_j^2}{\sqrt{1-r_j^2}}}{\Sigma_{j=1}^{m}\frac{r_j}{\sqrt{1-r_j{}^2}}}$$

$$S_{BA}^2 = \frac{\Sigma_{j=1}^{n}\left(\left(BA_{E_j} - CA_j\right) - \frac{\Sigma_{i=1}^{n}(BA_{E_j} - CA_i)}{n}\right)^2}{n} - \left(\frac{1-r_{char}^2}{r_{char}^2}\right) \times \left(\frac{(CA_{max} - CA_{min})^2}{12m}\right)$$

$$BA = \frac{\Sigma_{j=1}^{m}(x_j - q_j)\left(\frac{k_j}{s_j^2}\right) + \frac{CA}{S_{BA}^2}}{\sum_{j=1}^{m}\left(\frac{k_j}{s_j}\right)^2 + \frac{1}{S_{BA}^2}}$$

2. Phenotypic age

xb = −19.9067 − 0.0336 × albumin (g/L) + 0.0095 × creatinine (μmoL/L) + 0.1953 × glucose (mmoL/L) + 0.0954 × LnCRP (mg/dL) − 0.0120 × lymphocyte percent (%) + 0.0268 × mean cell volume (fL) + 0.3306 × red cell distribution width (%) + 0.0019 × alkaline phosphatase (U/L) + 0.0554 × white blood cell count (1000 cells/μL) + 0.0804 × CA (y).[2]

$$\mathrm{PA} = 141.50 + \frac{Ln\left[-0.00553 \times Ln(\exp(\frac{-1.51714 \times \exp(\mathrm{xb})}{0.0076927}))\right]}{0.09165}$$

SUPPLEMENTARY METHOD

Covariates

The covariates included in the study were age, sex, race/ethnicity, educational level, marital status, PIR, CVD history, and drinking status. Race/ethnicity was self-reported and categorized as Mexican American, non-Hispanic black, non-Hispanic white, other Hispanic, or other. Marital status included married, never married, living with a partner, or other (widowed, divorced, or separated). Educational level was classified as less than high school, high school, or equivalent, and above high school. The PIR was grouped into 3 categories: ≤ 1.30, 1.31-3.50, or > 3.50. CVD history was based on self-reports of heart failure, coronary heart disease, angina, heart attack, or stroke. Drinking status was self-reported and classified as follows: never (had < 12 drinks in a lifetime), former (had ≥ 12 drinks in 1 year but did not

drink in the last year, or did not drink in the last year but had ≥ 12 drinks in a lifetime), mild (female drinking ≤ 1 and male drinking ≤ 2 per day), moderate (female drinking ≤ 2 and male drinking ≤ 3 per day), or heavy (female drinking ≥ 3 and male drinking ≥ 4 per day). Age was treated as a continuous variable in the main analysis and categorized into <40 years, 40-64 years, and ≥ 65 years for subgroup analyses.

SUPPLEMENTARY METHOD

Statistical analysis

1. Weighted weights

Weighted analysis is a statistical method that assigns different weights to observations within a sample, reflecting their significance and representativeness in the overall dataset. This approach enhances the accuracy and efficiency of estimates, providing a deeper understanding of the relationships between aggregate characteristics and variables, and serving as a foundation for informed decision-making by policymakers.[3,4]

Furthermore, weighted analysis effectively accommodates complex sample designs, such as multistage and stratified sampling, ensuring that the sample accurately represents the larger population. It also addresses issues related to nonrandom missing data by assigning appropriate weights to missing observations, thus improving estimation precision and mitigating selection bias.[5]

Through the adjustment of sample weights, weighted analysis corrects estimation bias, resulting in more precise estimates. Additionally, it optimizes estimation efficiency by

assigning distinct weights to observations based on their relative importance. Consequently, it guarantees the representativeness of the sample, leading to more accurate overall estimates.[5]

Weighted analysis empowers researchers to explore relationships between variables, uncover hidden patterns, and identify trends. Furthermore, it facilitates group comparisons, allowing for a comprehensive understanding of disparities and commonalities among different groups.

2. Chi-square test

Chi-square tests are characterized by test statistics whose distribution approximates a chi-square distribution asymptotically as sample sizes increase, assuming the null hypothesis holds true.[6,7]

When dealing with large sample sizes, the chi-square test, often referred to as the χ^2 test, is a statistical hypothesis test employed in the analysis of contingency tables. In essence, its primary aim is to ascertain whether 2 categorical variables (corresponding to the dimensions of the contingency table) exert independent influences on the test statistic (cell values within the table). This test, notably the Pearson chi-square test and its variations, is valid when the test statistic conforms to a chi-square distribution under the null hypothesis. If a statistically significant disparity emerges between the anticipated and observed frequencies within 1 or more categories of a contingency table, it can be discerned using the Pearson chi-

square test. For smaller sample sizes in contingency tables, a Fisher exact test is employed as an alternative.[6,7]

In conventional applications of this examination, observations are sorted into mutually exclusive classes. The test statistic derived from these observations follows a chi-square distribution when the null hypothesis—indicating no population-level differences among the classes—is true. The objective of the text is to ascertain the likelihood of observing the given frequencies under this null hypothesis.

In cases of unrelated observations, the test generates test statistics with chi-square distributions. Moreover, depending on the nature of the observed pairings, there are chi-square tests designed to evaluate the independence of a pair of random variables.

3. Analysis of variance (ANOVA)

Analysis of variance (ANOVA) is a statistical method used to assess differences in means. It encompasses a range of statistical models and associated estimation techniques, including the examination of "variation" within and between groups. This valuable tool was developed by the eminent statistician Ronald Fisher. Anchored in the principle of total variance, which dissects the observed variance in a given variable into distinct sources of variation, ANOVA extends the scope of the t-test by providing a statistical means to evaluate the equality of 2 or more population means. In essence, ANOVA serves as a statistical test to ascertain whether multiple means exhibit significant differences from each other.[8]

4. Restricted cubic splines

A restricted cubic spline (RCS) is a statistical method used to model nonlinear relationships between an outcome variable and 1 or more independent variables. It involves segmenting the range of values of an independent variable using "knots" to define the end of 1 segment and the start of the next. Separate curves are then fitted to each segment. The resulting curve is smooth and continuous, providing a flexible description of nonlinearity. The method ensures that the relationship is adequately captured without introducing excessive complexity. RCSs are a transformation of an independent variable and can be used in various regression contexts, including ordinary least squares, logistic regression, and survival analysis.[9]

Researchers typically choose knot positions based on quantiles of the continuous variable. While the location of knots is essential, the number of knots is a more critical factor. Research suggests that a minimum of 3 to 5 knots can be sufficient for most practical datasets. However, the specific dataset characteristics and the complexity of the relationship might necessitate more knots.

The benefits of using RCSs include their ability to effectively capture nonlinear relationships, their flexibility in different regression models, and their capacity to provide insights into the relationships between predictors and outcomes. By providing a smooth and continuous curve, RCSs help avoid model misspecification, allowing for more accurate inferences in

statistical analyses. They are especially useful when the relationship between the variables is not linear and cannot be adequately described using simple linear models or polynomial functions.

5. Weighted quantile sum (WQS) regression

The WQS regression model built a weighted index to estimate the combined effects of all predictive factors related to the outcomes, demonstrating high sensitivity and specificity in identifying significant exposures. Bootstrapping with 1000 iterations was employed to construct the WQS index and the contribution weights of each component to the overall impact of the LE8 metrics were calculated. The dataset was randomly divided, with 40% allocated to the training set and the remaining 60% used as the validation set. Set the seed to 2024.[10]

6. Stratified analysis

Stratification, in the context of data analysis, involves the systematic categorization of data, individuals, or objects into distinct groups or layers. This essential technique is often used in conjunction with other data analysis tools to enhance comprehension and pattern identification. When data originating from diverse sources or categories are amalgamated, the inherent meaning can become obscured, making it challenging to discern underlying patterns. Stratification emerges as a pivotal data collection and analysis method, capable of ameliorating this issue by partitioning the data into stratified groups. This process reveals

hidden patterns and is regarded as one of the foundational tools for quality control and data analysis. Stratification serves a dual purpose in evaluating and mitigating confounding variables. It necessitates the division of the sample into subgroups, or strata, predicated on the confounding variable of interest (eg, age, sex, race/ethnicity) to facilitate a more comprehensive evaluation and control of potential confounding factors.[11]

SUPPLEMENTARY DISCUSSION

Mechanism

The mechanism underlying the ability of adherence to ideal LE8 metrics to decelerate biological aging can be explained through the following aspects. Telomere attrition, genomic instability, epigenetic modifications, mitochondrial impairments, and cellular senescence are prominent aging hallmarks,[12] while adequate PA and sleep, may slow biological aging through cellular self-repair, DNA protection, and gene expression regulation.[13,14] Meanwhile, PA, diet, and low nicotine exposure have the potential to reduce inflammation and suppress immune system activation,[15-17] leading to a suppression in chronic low-grade inflammation and immune system activation, which could slow the process of biological aging.

SUPPLEMENTARY DISCUSSION

Limitations

However, it is important to acknowledge some limitations in our study. First, in a cross-sectional study, we were unable to establish a causal relationship between CVH and

biological aging. Additionally, self-reported information is often influenced by social expectations, and people tend to optimize their behavior.[18] When participants recall their CVH metrics, they may underreport socially undesirable behaviors. Furthermore, multiple socioeconomic conditions and lifestyle factors were included in the multivariable model to minimize the effects of residual confounding. However, there may be other factors associated with CVH, such as individual-level socioeconomic and social indicators (occupational status, subjective social status, social isolation, experiences of racial discrimination, and incarceration) and neighborhood factors (resources, social cohesion, and built environment.[19] Due to the lack of data for these factors in the NHANES database, they were not adjusted in the multivariate model.

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Table 1 of the supplementary data

Scoring criteria for the DASH-style diet score

Component	Foods (NHANES 24-h recall)	Scoring criteria	Note
Fruits	All fruits and fruit juices	Quintile 1: 1 point Quintile 2: 2 points Quintile 3: 3 points Quintile 4: 4 points Quintile 5: 5 points	Higher score represents more ideal intake. Quintile 1 is lowest consumption and Quintile 5 is highest consumption
Vegetables	All vegetables except potatoes and legumes		
Nuts and legumes	Nuts and peanut butter, dried beans, peas, and tofu		
Whole grains	Brown rice, dark breads, cooked cereal, whole grain cereal, other grains, popcorn, wheat germ, and bran		
Low-fat dairy	Skim milk, yogurt, cottage cheese		
Sodium	Sum of sodium content of all foods reported as consumed	Quintile 1: 5 points Quintile 2: 4 points Quintile 3: 3 points Quintile 4: 2 points Quintile 5: 1 point	Reverse scoring as higher quintiles represent less ideal intake. Quintile 1 is lowest consumption and Quintile 5 is highest consumption
Red and processed meats	Beef, pork, lamb, deli m eats, organ meats, hot dogs, and bacon		
Sweetened beverages	Carbonated and noncarbonated sweetened beverages		

DASH, dietary approaches to stop hypertension; NHANES, National Health and Nutrition Examination Survey.

Table 2 of the supplementary data

Life's Essential 8 components and criteria for scoring

Domain	CVH metric	Method of measurement	Quantification of CVH metric	Score, points
Health Behaviors	Diet	Quantiles of HEI-2015 (population) Example tools: 24-hour dietary recall	1st-24th	0
			25th-49th	25
			50th-74th	50
			75th-94th	80
			≥ 95th	100
	PA	Self-reported minutes of moderate or vigorous PA per week Example tools: NHANES PAQ	0	0
			1-29	20
			30-59	40
			60-89	60
			90-119	80
			120-149	90
			≥ 150	100
	Nicotine exposure	Self-reported use of cigarettes or inhaled NDS Example tools: NHANES SMQ and SMQFAM	Current smoker	0
			Former smoker quit < 1 y, or currently using inhaled NDS, with active indoor smoker	5
			Former smoker, quit < 1 y, or currently using inhaled NDS, without active indoor smoker	25
			Former smoker, quit 1 ≤ 5 y, with active indoor smoker	30
			Former smoker, quit 1 ≤ 5 y, without active indoor smoker	50
			Former smoker, quit ≥ 5 y, with active indoor smoker	55
			Former smoker, quit ≥ 5 y, without active indoor smoker	75
			Never smoker, with active indoor smoker	80
			Never smoker, without active indoor smoker	100
	Sleep health	Self-reported average hours of sleep per night Example tools: NHANES SLQ	< 4	0
			4 ≤ 5	20
			5 ≤ 6 or ≥ 10	40
			6 ≤ 7	70
			9 ≤ 10	90
			7 ≤ 9	100
Health factors	BMI	Body weight (kilograms) divided by height squared (meters squared) Example tools: NHANES BMX	≥ 40.0	0
			35.0-39.9	15
			30.0-34.9	30
			25.0-29.9	70
			< 25	100

	Blood lipids	Plasma total and HDL cholesterol with calculation of non-HDL cholesterol Example tools: NHANES TCHOL, HDL and BPQ	≥ 220 or 190-219 (takes medication)	0
			190-219(no medication) or 160-189 (takes medication)	20
			160-189(no medication) or 130-159(takes medication)	40
			130-159(no medication)	60
			< 130(takes medication)	80
			< 130(no medication)	100
	Blood glucose	Casual HbA1c (%) Example tools: NHANES GHB and DIQ	Diabetes with HbA1c ≥ 10.0	0
			Diabetes with HbA1c 9.0-9.9	10
			Diabetes with HbA1c 8.0-8.9	20
			Diabetes with HbA1c 7.0-7.9	30
			Diabetes with HbA1c < 7.0	40
			No diabetes and HbA1c 5.7-6.4)	60
			No history of diabetes and HbA1c < 5.7	100
	BP	Appropriately measured systolic and diastolic BPs Example tools: NHANES BPX and BPQ	≥160 or ≥100	0
			140-159 or 90-99(takes medication)	5
			140-159 or 90-99(no medication)	25
			130-139 or 80-89(takes medication)	30
			130-139 or 80-89(no medication)	50
			120-129/< 80 (takes medication)	55
			120-129/< 80 (no medication)	75
			<120/< 80(takes medication)	80
			<120/< 80(no medication)	100

BMI, body mass index; BP, blood pressure; BPQ, blood pressure and cholesterol questionnaire; BPX, blood pressure examination; CVH, cardiovascular health; DIQ, diabetes questionnaire; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; GHB, glycohemoglobin; HEI, healthy eating index; NDS, nicotine-delivery system; NHANES, National Health and Nutrition Examination Surveys; PA, physical activity; PAQ, Physical Activity Questionnaire; SMQ, smoking-cigarette use questionnaire; SMQFAM, Smoking - Household Smokers Questionnaire; SLQ, sleep disorders questionnaire; BMX, body measures examination; TCHOL, total cholesterol .

Table 3 of the supplementary data

Baseline characteristics by cardiovascular health score

Characteristics	Total (N = 18 261)	Low CVH (n = 2801)	Moderate CVH (n= 12 259)	High CVH (n = 3201)	*P*
AHA LE8 scores					
Total CVH score	67.16 ± 0.30	42.45 ± 0.16	65.47 ± 0.13	86.82 ± 0.12	< .001
Health behaviors score	64.09 ± 0.42	38.55 ± 0.48	62.35 ± 0.29	84.40 ± 0.26	< .001
Diet score	44.93 ± 0.45	26.53 ± 0.71	41.86 ± 0.43	65.13 ± 0.69	< .001
Physical activity score	57.36 ± 0.80	14.56 ± 0.81	55.24 ± 0.73	88.98 ± 0.62	< .001
Nicotine exposure score	70.49 ± 0.60	45.11 ± 1.24	68.75 ± 0.54	90.70 ± 0.57	< .001
Sleep health score	83.57 ± 0.34	67.98 ± 0.83	83.55 ± 0.30	92.80 ± 0.41	< .001
Health factors score	70.23 ± 0.25	46.35 ± 0.39	68.60 ± 0.22	89.23 ± 0.22	< .001
BMI score	60.80 ± 0.50	33.16 ± 0.87	58.09 ± 0.47	85.33 ± 0.64	< .001
Blood lipids score	64.75 ± 0.39	44.02 ± 0.82	62.31 ± 0.47	84.38 ± 0.50	< .001
Blood glucose score	85.50 ± 0.28	62.96 ± 0.84	85.97 ± 0.30	97.27 ± 0.22	< .001
Blood pressure score	69.86 ± 0.36	45.25 ± 0.69	68.02 ± 0.38	89.93 ± 0.52	< .001
KDM biological age, y	46.89 ± 0.29	55.84 ± 0.48	47.92 ± 0.32	38.48 ± 0.38	< .001
KDM biological age acceleration					< .001
No	11 356 ± 62.19	1069 ± 38.29	7756 ± 64.32	2531 ± 79.24	
Yes	6905 ± 37.81	1732 ± 61.71	4503 ± 35.68	670 ± 20.76	
Phenotypic age, y	45.34 ± 0.33	56.75 ± 0.60	46.36 ± 0.37	35.53 ± 0.47	< .001
Phenotypic age acceleration					< .001
No	9784 ± 53.58	850 ± 29.29	6665 ± 53.05	2269 ± 70.06	
Yes	8477 ± 46.42	1951 ± 70.71	5594 ± 46.95	932 ± 29.94	

AHA, the American Heart Association; CVD, cardiovascular disease; CVH, cardiovascular health; PIR, poverty income ratio; SE, standard error; KDM, Klemera-Doubal method; LE8, Life's Essential 8.

The data are expressed as mean ± standard error.

All means and SEs for continuous variables and percentages for categorical variables were weighted. CVH scores range from 0 to 100 and are classified into low CVH (0-49), moderate CVH (50-79), and high CVH (80-100).

Table 4 of the supplementary data

Association of Life's Essential 8 component with KDM biological/phenotypic age and KDM biological/phenotypic age acceleration.

	KDM biological age		Phenotypic age		KDM biological age acceleration		Phenotypic age acceleration	
	β (95%CI)	*P*	β (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Diet score	−0.09 (−0.11, −0.06)	< .001	−0.21 (−0.25, −0.17)	< .001	0.96 (0.95, 0.97)	< .001	0.94 (0.93, 0.95)	< .001
Low	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate	−0.30 (−0.51, −0.09)	.005	−0.74 (−1.09, −0.38)	< .001	0.88 (0.78, 0.99)	.04	0.80 (0.71, 0.89)	< .001
High	−0.68 (−0.86, −0.50)	< .001	−1.47 (−1.79, −1.15)	< .001	0.73 (0.67, 0.80)	< .001	0.66 (0.60, 0.72)	< .001
Trend test		< .001		< .001		< .001		< .001
Physical activity score	−0.04 (−0.06, −0.02)	< .001	−0.17 (−0.20, −0.13)	< .001	0.99 (0.98, 0.99)	< .001	0.96 (0.95, 0.97)	< .001
Low	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate	−0.30 (−0.51, −0.09)	.005	−0.74 (−1.09, −0.38)	< .001	0.88 (0.78, 0.99)	.04	0.80 (0.71, 0.89)	< .001
High	−0.68 (−0.86, −0.50)	< .001	−1.47 (−1.79, −1.15)	< .001	0.73 (0.67, 0.80)	< .001	0.66 (0.60, 0.72)	< .001
Trend test		< .001		< .001		< .001		< .001
Nicotine exposure score	0.07 (0.05, 0.09)	< .001	−0.10 (−0.14, −0.06)	< .001	1.03 (1.02, 1.04)	< .001	0.98 (0.96, 0.99)	< .001
Low	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate	0.52 (0.28, 0.76)	< .001	−0.92 (−1.34, −0.51)	< .001	1.22 (1.08, 1.38)	.001	0.79 (0.69, 0.90)	< .001
High	0.69 (0.51, 0.86)	< .001	−0.94 (−1.29, −0.59)	< .001	1.34 (1.22, 1.46)	< .001	0.79 (0.71, 0.89)	< .001
Trend test		< .001		< .001		< .001		< .001

Sleep health score	−0.01 (−0.04, 0.02)	.69	−0.08 (−0.14, −0.02)	.01	1.00 (0.99, 1.02)	.78	0.98 (0.97, 1.00)	.03
Low	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate	−0.52 (−0.80, −0.24)	< .001	−1.80 (−2.29, −1.31)	< .001	0.84 (0.73, 0.96)	.01	0.67 (0.60, 0.75)	< .001
High	−0.17 (−0.40, 0.05)	.13	−0.85 (−1.26, −0.43)	< .001	0.97 (0.86, 1.09)	.57	0.85 (0.77, 0.94)	.002
Trend test		.93		.11		.60		.38
BMI score	−0.33 (−0.36, −0.31)	< .001	−0.70 (−0.75, −0.66)	< .001	0.85 (0.84, 0.86)	< .001	0.84 (0.82, 0.85)	< .001
Low	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate	−1.49 (−1.68, −1.31)	< .001	−3.73 (−4.08, −3.39)	< .001	0.52 (0.47, 0.58)	< .001	0.40 (0.37, 0.45)	< .001
High	−2.55 (−2.74, −2.37)	< .001	−5.07 (−5.46, −4.67)	< .001	0.28 (0.25, 0.31)	< .001	0.28 (0.24, 0.32)	< .001
Trend test		< .001		< .001		< .001		< .001
Blood lipids score	−0.39 (−0.42, −0.36)	< .001	0.01 (−0.05, 0.07)	.75	0.84 (0.82, 0.85)	< .001	1.00 (0.98, 1.02)	.73
Low	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate	−1.50 (−1.72, −1.29)	< .001	−0.20 (−0.55, 0.15)	.26	0.52 (0.47, 0.59)	< .001	0.99 (0.88, 1.12)	.90
High	−2.47 (−2.68, −2.27)	< .001	0.34 (−0.11, 0.79)	.14	0.33 (0.29, 0.37)	< .001	1.08 (0.95, 1.24)	.24
Trend test		< .001		.12		< .001		.23
Blood glucose score	−0.64 (−0.67, −0.60)	< .001	−1.27 (−1.35, −1.20)	< .001	0.79 (0.78, 0.80)	< .001	0.78 (0.77, 0.80)	< .001
Low	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate	−2.76 (−3.13, −2.38)	< .001	−7.49 (−8.28, −6.70)	< .001	0.48 (0.40, 0.57)	< .001	0.30 (0.25, 0.37)	< .001
High	−4.56 (−4.92, −4.19)	< .001	−10.13 (−10.85, −9.42)	< .001	0.21 (0.18, 0.24)	< .001	0.15 (0.13, 0.18)	< .001
Trend test		< .001		< .001		< .001		< .001

Blood pressure score	−0.77 (−0.80, −0.75)	< .001	−0.31 (−0.36, −0.26)	< .001	0.67 (0.66, 0.69)	< .001	0.94 (0.92, 0.95)	< .001
Low	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate	−2.85 (−3.08, −2.62)	< .001	−1.43 (−1.88, −0.99)	< .001	0.31 (0.27, 0.36)	< .001	0.82 (0.74, 0.91)	< .001
High	−5.69 (−5.91, −5.47)	< .001	−2.13 (−2.54, −1.72)	< .001	0.06 (0.05, 0.07)	< .001	0.65 (0.58, 0.72)	< .001
Trend test		< .001		< .001		< .001		< .001

BMI, body mass index; OR, odd ratio; 95%CI, 95% confidence interval; KDM, Klemera-Doubal method; NHANES, National Health and Nutrition Examination Survey.

All models were adjusted for age, sex, race/ethnicity, marital status, educational level, cardiovascular disease history, poverty income ratio group, and drinking status. Diet score, physical activity score, nicotine exposure score and sleep health score, body mass index score, blood lipids score, blood glucose score, and blood pressure score were entered as a continuous variable per 10 points increase, and were classified into low (0-49), moderate (50-79), and high (80-100).

Table 5 of the supplementary data

Comparison of effect values for each of Life's Essential 8 components using 2-independent-samples t-test based on bootstrapped estimates (n = 100).

A. KDM biological age (*P* value)

Diet							
4.10E-85	*Physical activity*						
1.04E-180	3.39E-161	*Nicotine exposure*					
5.74E-96	5.65E-48	1.19E-82	*Sleep health*				
1.12E-203	7.59E-209	2.09E-244	6.26E-198	*BMI*			
4.84E-231	4.43E-242	1.41E-268	3.23E-201	6.09E-97	*Blood lipids*		
3.18E-205	4.68E-193	1.57E-218	2.55E-246	1.44E-165	7.81E-161	*Blood glucose*	
2.34E-291	1.61E-281	2.42E-307	3.38E-264	2.24E-254	5.74E-239	4.70E-114	*Blood pressure*

B. Phenotypic age (*P* value)

Diet							
3.21E-32	*Physical activity*						
2.44E-94	5.72E-79	*Nicotine exposure*					
1.05E-90	4.42E-66	6.39E-09	*Sleep health*				
1.83E-213	2.86E-226	4.32E-238	2.61E-210	*BMI*			
1.44E-139	8.63E-122	1.10E-85	1.53E-68	7.45E-239	*Blood lipids*		
1.74E-198	3.21E-176	5.70E-196	3.07E-222	9.47E-157	8.93E-218	*Blood glucose*	
7.88E-73	3.53E-94	6.49E-128	1.05E-128	8.17E-178	5.55E-161	2.55E-210	*Blood pressure*

BMI, body mass index; KDM, Klemera-Doubal method.

The comparison of bootstrapped estimates is based on the adjusted model in table 2.

Table 6 of the supplementary data

Association of Life's Essential 8 with KDM biological/phenotypic age and KDM biological/phenotypic age acceleration in different subgroups[a]

	KDM biological age		Phenotypic age		KDM biological age acceleration		Phenotypic age acceleration	
	β (95%CI)	*P*	β (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Age, y		< .001*		.002*		.01*		.02*
< 40	−1.01 (−1.08, −0.93)	< .001	−1.47 (−1.68, −1.26)	< .001	0.57 (0.55, 0.60)	< .001	0.70 (0.66, 0.74)	< .001
40-64	−1.25 (−1.33, −1.17)	< .001	−1.76 (−1.90, −1.62)	< .001	0.55 (0.52, 0.58)	< .001	0.64 (0.61, 0.68)	< .001
≥ 65	−1.56 (−1.71, −1.41)	< .001	−1.97 (−2.23, −1.71)	< .001	0.56 (0.52, 0.60)	< .001	0.61 (0.57, 0.66)	< .001
Sex		.12*		.36*		.03*		.72*
Female	−1.16 (−1.22, −1.09)	< .001	−1.75 (−1.90, −1.60)	< .001	0.59 (0.56, 0.62)	< .001	0.64 (0.61, 0.68)	< .001
Male	−1.20 (−1.29, −1.11)	< .001	−1.57 (−1.70, −1.43)	< .001	0.57 (0.54, 0.59)	< .001	0.69 (0.66, 0.72)	< .001
Race/ethnicity[b]		< .001*		.73*		.26*		< .001*
Mexican American	−1.26 (−1.37, −1.14)	< .001	−1.76 (−2.00, −1.52)	< .001	0.56 (0.51, 0.60)	< .001	0.70 (0.64, 0.75)	< .001
Non-Hispanic Black	−1.38 (−1.55, −1.21)	< .001	−1.84 (−2.19, −1.49)	< .001	0.60 (0.56, 0.64)	< .001	0.72 (0.68, 0.76)	< .001
Non-Hispanic White	−1.16 (−1.22, −1.10)	< .001	−1.58 (−1.71, −1.45)	< .001	0.57 (0.55, 0.60)	< .001	0.65 (0.62, 0.69)	< .001
Other Hispanic	−0.99 (−1.19, −0.79)	< .001	−1.75 (−2.16, −1.34)	< .001	0.65 (0.59, 0.72)	< .001	0.71 (0.63, 0.80)	< .001
Other[c]	−1.33 (−1.55, −1.12)	< .001	−1.54 (−1.86, −1.22)	< .001	0.54 (0.48, 0.60)	< .001	0.71 (0.64, 0.79)	< .001
Educational level		.005*		.03*		.28*		.39*

Less than high school	−1.34 (−1.45, −1.22)	< .001	−1.92 (−2.20, −1.65)	< .001	0.57 (0.53, 0.60)	< .001	0.67 (0.62, 0.72)	< .001
High school or equivalent	−1.20 (−1.30, −1.09)	< .001	−1.53 (−1.76, −1.31)	< .001	0.58 (0.55, 0.62)	< .001	0.68 (0.64, 0.72)	< .001
Above high school	−1.17 (−1.24, −1.09)	< .001	−1.61 (−1.76, −1.46)	< .001	0.57 (0.54, 0.60)	< .001	0.67 (0.64, 0.70)	< .001
PIR		< .001*		< .001*		.001*		.65*
≤ 1.3	−1.30 (−1.44, −1.16)	< .001	−2.03 (−2.27, −1.78)	< .001	0.60 (0.57, 0.64)	< .001	0.67 (0.64, 0.71)	< .001
1.3~3.5	−1.25 (−1.33, −1.16	< .001	−1.68 (−1.85, −1.51)	< .001	0.54 (0.51, 0.57)	< .001	0.66 (0.62, 0.70)	< .001
> 3.5	−1.09 (−1.18, −1.00)	< .001	−1.40 (−1.57, −1.24)	< .001	0.60 (0.56, 0.63)	< .001	0.68 (0.65, 0.72)	< .001
Marital status		< .001*		0.56*		< .001*		.22*
Married	−1.23 (−1.30, −1.16)	< .001	−1.70(−1.83, −1.56)	< .001	0.55(0.53, 0.58)	< .001	0.65(0.62, 0.69)	< .001
Never married	−1.07(−1.20, −0.94)	< .001	−1.65(−1.92, −1.38)	< .001	0.58(0.54, 0.63)	< .001	0.68(0.62, 0.74)	< .001
Living with partner	−1.0(−1.15, −0.85)	< .001	−1.56(−1.95, −1.16)	< .001	0.62(0.55, 0.71)	< .001	0.68(0.60, 0.76)	< .001
Other	−1.32(−1.43, −1.21)	< .001	−1.49(−1.72, −1.27)	< .001	0.58(0.54, 0.62)	< .001	0.70(0.66, 0.74)	< .001
CVD history[d]		< .001*		< .001*		< .001*		0.004*
Yes	−1.80(−2.01, −1.59)	< .001	−2.54(−2.91, −2.16)	< .001	0.51(0.45, 0.57)	< .001	0.58(0.53, 0.64)	< .001
No	−1.14(−1.20, −1.08)	< .001	−1.57(−1.69, −1.46)	< .001	0.58(0.56, 0.60)	< .001	0.68(0.65, 0.70)	< .001
Drinking status[e]		< .001*		< .001*		< .001*		.02*
Never	−1.45(−1.64, −1.26)	< .001	−1.74(−2.10, −1.38)	< .001	0.53(0.47, 0.59)	< .001	0.68(0.61, 0.75)	< .001
Former	−1.42(−1.55, −1.29)	< .001	−2.19(−2.50, −1.89)	< .001	0.55(0.51, 0.60)	< .001	0.59(0.55, 0.65)	< .001
Mild	−1.16(−1.24, −1.07)	< .001	−1.61(−1.79, −1.43)	< .001	0.57(0.54, 0.61)	< .001	0.66(0.62, 0.69)	< .001
Moderate	−1.08(−1.19, −0.97)	< .001	−1.58(−1.84, −1.32)	< .001	0.61(0.56, 0.65)	< .001	0.69(0.63, 0.75)	< .001
Heavy	−1.11(−1.22, −1.01)	< .001	−1.41(−1.63, −1.19)	< .001	0.57(0.53, 0.62)	< .001	0.70(0.65, 0.76)	< .001

95%CI, 95% confidence interval; CVD, cardiovascular disease; OR, odds ratio; PIR, poverty index ratio; KDM, Klemera-Doubal method.

[*] *P* for interaction.

[a] All participants aged < 20 years and those who were pregnant were excluded from this analysis.

[b] Race and ethnicity were self-reported.

[c] Included multi-racial participants. NHANES does not provide a detailed list of all races and ethnicities.

[d] Included congestive heart failure, coronary heart disease, angina, heart attack and stroke.

[e] Mild: female drinking ≤ 1 and male drinking ≤ 2 per day; moderate: female drinking ≤ 2 and male drinking ≤ 3 per day; heavy: female drinking ≥ 3 and male drinking ≥ 4 per day.

Table 7 of the supplementary data

Association of Life's Essential 8 with KDM biological/phenotypic age acceleration (defined by the residual between biological age and CA).

	KDM biological age acceleration				Phenotypic age acceleration			
	Crude model[a]		Adjusted model[b]		Crude model[a]		Adjusted model[b]	
	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*
Total CVH score[c]	−0.96 (−1.02, −0.89)	< .001	−1.19 (−1.24, −1.13)	< .001	−1.82 (−1.94, −1.69)	< .001	−1.63 (−1.74, −1.52)	< .001
Subgroups[d]								
Low CVH	0[Reference]		0[Reference]		0[Reference]		0[Reference]	
Moderate CVH	−2.94 (−3.25, −2.63)	< .001	−3.28 (−3.57, −2.99)	< .001	−5.4 (−5.92, −4.88)	< .001	−4.75 (−5.22, −4.29)	< .001
High CVH	−4.44 (−4.79, −4.10)	< .001	−5.20 (−5.50, −4.89)	< .001	−8.3 (−8.89, −7.71)	< .001	−7.03 (−7.51, −6.55)	< .001

Trend test		< .001		< .001		< .001		< .001
Health behaviors score[c]	−0.13 (−0.18, −0.09)	< .001	−0.06 (−0.10, −0.02)	.002	−0.69 (−0.78, −0.60)	< .001	−0.52 (−0.59, −0.44)	< .001
Diet score	−0.12 (−0.15, −0.10)	< .001	−0.09 (−0.11, −0.06)	< .001	−0.22 (−0.26, −0.18)	< .001	−0.21 (−0.25, −0.17)	< .001
Physical activity score	−0.02 (−0.04, −0.00)	.02	−0.04 (−0.06, −0.02)	< .001	−0.24 (−0.27, −0.20)	< .001	−0.17 (−0.20, −0.13)	< .001
Nicotine exposure score	0.003 (−0.02, 0.02)	.77	0.07 (0.05, 0.09)	< .001	−0.15 (−0.19, −0.11)	< .001	−0.10 (−0.14, −0.06)	< .001
Sleep health score	−0.06 (−0.09, −0.03)	< .001	−0.01 (−0.04, 0.02)	.69	−0.23 (−0.29, −0.16)	< .001	−0.08 (−0.14, −0.02)	.01
Health factors score[c]	−1.00 (−1.06, −0.94)	< .001	−1.37 (−1.41, −1.32)	< .001	−1.42 (−1.51, −1.33)	< .001	−1.36 (−1.46, −1.27)	< .001
BMI score	−0.32 (−0.35, −0.30)	< .001	−0.33 (−0.36, −0.31)	< .001	−0.76 (−0.80, −0.71)	< .001	−0.70 (−0.75, −0.66)	< .001
Blood lipids score	−0.32 (−0.35, −0.29)	< .001	−0.39 (−0.42, −0.36)	< .001	−0.03 (−0.09, 0.03)	.28	0.01 (−0.05, 0.07)	.75
Blood glucose score	−0.45 (−0.49, −0.41)	< .001	−0.64 (−0.67, −0.60)	< .001	−1.31 (−1.39, −1.24)	< .001	−1.27 (−1.35, −1.20)	< .001
Blood pressure score	−0.54 (−0.57, −0.52)	< .001	−0.77 (−0.80, −0.75)	< .001	−0.44 (−0.49, −0.40)	< .001	−0.31 (−0.36, −0.26)	< .001

BMI, body mass index; CVH, cardiovascular health; OR, odd ratio; 95%CI, 95% confidence interval; KDM, Klemera-Doubal method.

[a] Crude model.

[b] Adjusted for age, sex, race/ethnicity, marital status, educational level, cardiovascular disease history, poverty income ratio group, and drinking status.

[c] Total CVH score, health behaviors score (including diet score, physical activity score, nicotine exposure score and sleep health score), and health factors score (including BMI score, blood lipids score, blood glucose score, and blood pressure score) were entered as a continuous variable per 10 points increase.

[d] CVH scores range from 0 to 100 and are classified into low CVH (0-49), moderate CVH (50-79), and high CVH (80-100).

Table 8 of the supplementary data

Association of Life's Essential 8 with KDM biological/phenotypic age and KDM biological/phenotypic age acceleration, using multiple imputation by chained equations.

	KDM biological age		Phenotypic age		KDM biological age acceleration		Phenotypic age acceleration	
	β (95%CI)	*P*	β (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Total CVH score	−0.91 (−1.31, −0.51)	.008	−1.13 (−1.28, −0.99)	< .001	0.67 (0.57, 0.79)	.008	0.79 (0.75, 0.82)	< .001
Subgroups								
Low CVH	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate CVH	−2.33 (−3.38, −1.28)	.006	−2.96 (−3.50, −2.43)	< .001	0.40 (0.27, 0.60)	.009	0.56 (0.48, 0.65)	< .001
High CVH	−3.81 (−5.38, −2.25)	.005	−4.57 (−5.31, −3.84)	< .001	0.20 (0.10, 0.39)	.008	0.39 (0.32, 0.48)	< .001

CVH, cardiovascular health; OR, odd ratio; 95%CI, 95% confidence interval; KDM, Klemera-Doubal method.

Total CVH score were entered as a continuous variable per 10 points increase. CVH scores range from 0 to 100 and are classified into low CVH (0-49), moderate CVH (50-79), and high CVH (80-100). All models were adjusted for age, sex, race/ethnicity, marital status, educational level, CVD history, PIR group, and drinking status.

Table 9 of the supplementary data

Association of Life's Essential 8 with KDM biological/phenotypic age and KDM biological/phenotypic age acceleration (blood lipid, blood pressure, and blood glucose-related components of biological/phenotypic age were removed).

	KDM biological age		Phenotypic age		KDM biological age acceleration		Phenotypic age acceleration	
	β (95%CI)	*P* value	β (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Total CVH score	−0.30 (−0.41, −0.20)	< .001	−1.06 (−1.17, −0.96)	< .001	0.58 (0.56, 0.60)	< .001	0.67 (0.65, 0.70)	< .001
Subgroups								
Low CVH	0[Reference]		0[Reference]		1[Reference]		1[Reference]	
Moderate CVH	−1.39 (−1.91, −0.88)	< .001	−2.85 (−3.21, −2.48)	< .001	0.27 (0.24, 0.30)	< .001	0.37 (0.33, 0.42)	< .001
High CVH	−1.46 (−2.02, −0.89)	< .001	−4.49 (−4.93, −4.06)	< .001	0.10 (0.08, 0.11)	< .001	0.19(0.17, 0.23)	< .001
Trend test		< .001		< .001		< .001		< .001

CVH, cardiovascular health; OR, odd ratio; 95%CI, 95% confidence interval; KDM, Klemera-Doubal method.

Total CVH score were entered as a continuous variable per 10 points increase. CVH scores range from 0 to 100 and are classified into low CVH (0-49), moderate CVH (50-79), and high CVH (80-100). All models were adjusted for age, sex, race/ethnicity, marital status, educational level, cardiovascular disease history, poverty income ratio group, and drinking status.

Table 10 of the supplementary data

Association of Smoking Status and Serum Cotinine with KDM biological/Phenotypic Age Acceleration.

	KDM biological age acceleration				Phenotypic age acceleration			
	Crude model[a]		Adjusted model[b]		Crude model[a]		Adjusted model[b]	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Smoking status								
Never	1[Reference]		1[Reference]		1[Reference]		1[Reference]	
Former	0.88 (0.80, 0.96)	.01	0.94 (0.84, 1.04)	.21	1.16 (1.05, 1.28)	.004	1.03 (0.92, 1.14)	.64
Current	0.96 (0.88, 1.06)	.43	0.70 (0.64, 0.78)	< .001	1.42 (1.26, 1.59)	< .001	1.25 (1.11, 1.42)	< .001
Trend test		.12		< .001		< .001		.001
Serum cotinine, *Ln*	1.01 (1.00, 1.03)	.02	0.96 (0.95, 0.97)	< .001	1.03 (1.02, 1.05)	< .001	1.02 (1.01, 1.04)	.01

OR, odd ratio; 95%CI, 95% confidence interval; KDM, Klemera-Doubal method.

[a] Crude model.

[b] Adjusted for age, sex, race/ethnicity, marital status, educational level, cardiovascular disease history, poverty income ratio group, and drinking status.

Table 11 of the supplementary data

Association of Smoking Status and Serum Cotinine with KDM biological/Phenotypic Age.

	KDM biological age				Phenotypic age			
	Crude model[a]		Adjusted model[b]		Crude model[a]		Adjusted model[b]	
	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*
Smoking status								
Never	0[Reference]		0[Reference]		0[Reference]		0[Reference]	
Former	7.15 (6.31, 7.99)	< .001	−0.11 (−0.31, 0.09)	.26	8.14 (7.14, 9.13)	< .001	0.09 (−0.30, 0.47)	.65
Current	−3.83 (−4.63, −3.03)	< .001	−0.83 (−1.02, −0.65)	< .001	−2.04 (−2.98. −1.09)	< .001	0.99 (0.59, 1.38)	< .001
Trend test		.002		< .001		.36		< .001
Serum cotinine, Ln	−0.77 (−0.85, −0.68)	< .001	−0.08 (−0.10, −0.06)	< .001	−0.63 (−0.74, −0.53)	< .001	0.10 (0.06, 0.15)	< .001

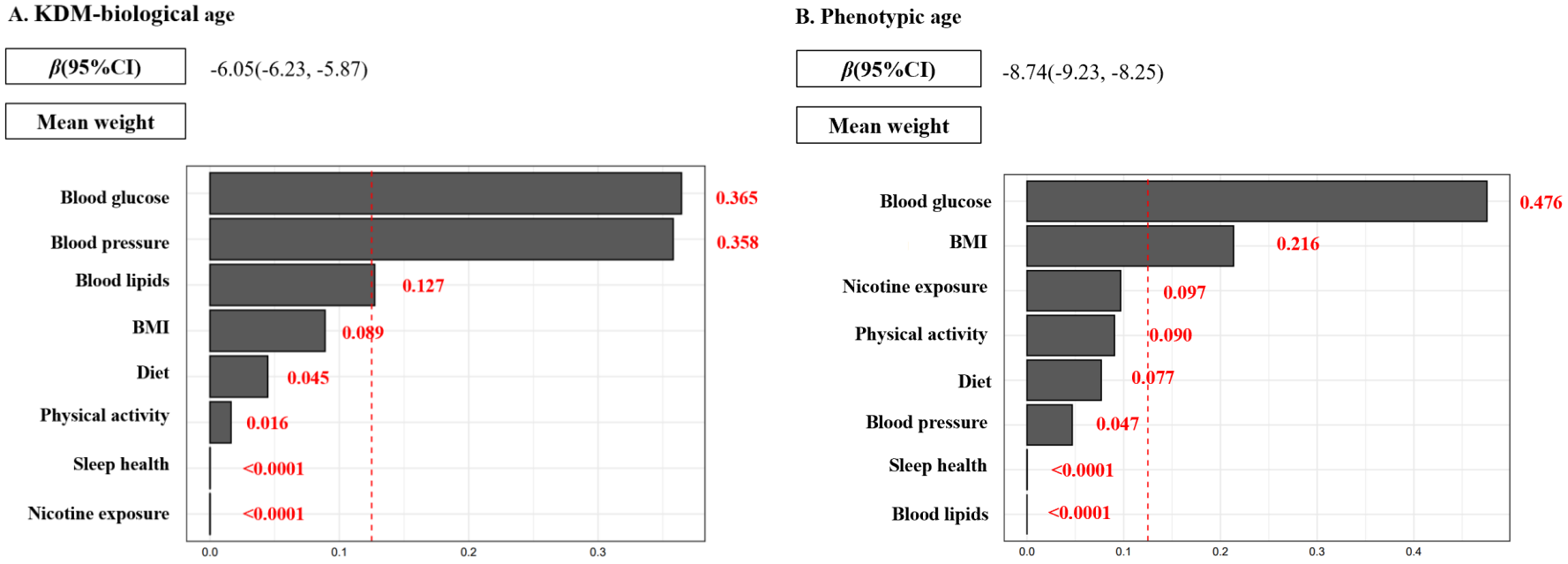
OR, odd ratio; 95%CI, 95% confidence interval; KDM, Klemera-Doubal method.

[a] Crude model.

[b] Adjusted for age, sex, race/ethnicity, marital status, educational level, cardiovascular disease history, poverty income ratio group, and drinking status.

Figure 1 of the supplemetary data.

Association of Life's Essential 8 with KDM biological age (A) and phenotypic age (B), using weighted quantile sum regression.

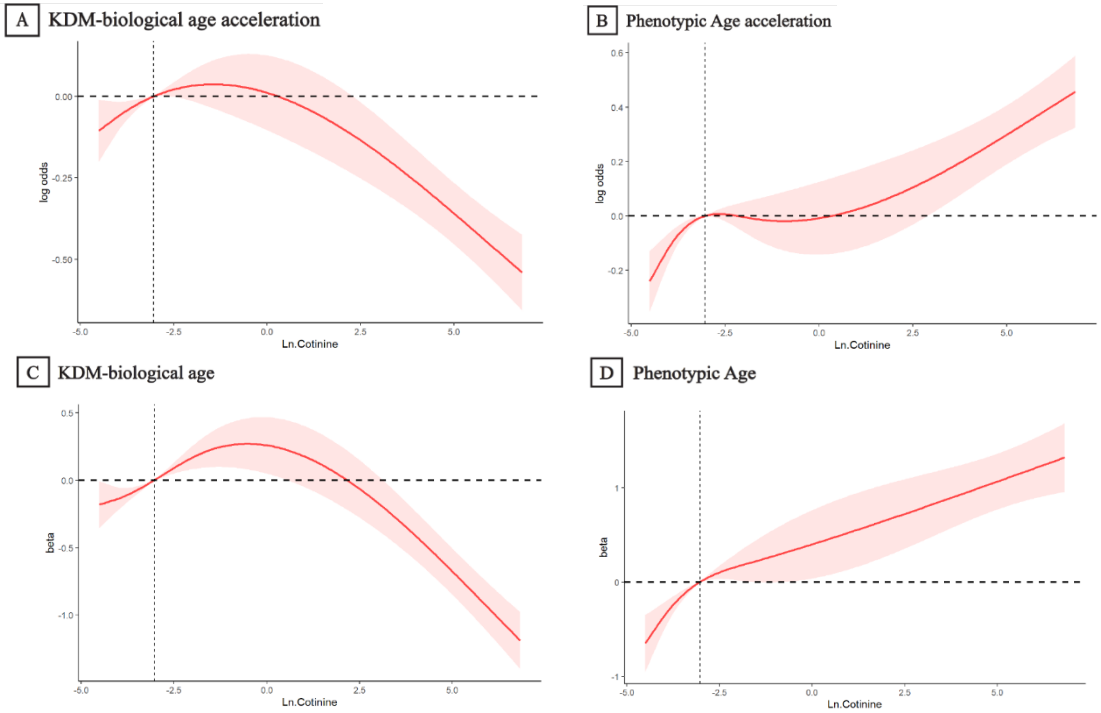


95%CI, 95% confidence interval; BMI, body mass index; KDM, Klemera-Doubal method.

All models were adjusted for age, sex, race/ethnicity, marital status, educational level, cardiovascular disease history, poverty income ratio group, and drinking status.

Figure 2 of the supplemetary data.

Association of serum cotinine with KDM biological age/phenotypic age acceleration (A, B) and KDM biological/phenotypic age (C, D)



KDM, Klemera-Doubal method.

Data were fited by a survey-weighted multivariable linear/logistic regression model based on restricted cubic splines. Data were adjusted for age, sex, race/ethnicity, poverty income ratio, marital status, educational level, cardiovascular disease history, and drinking status.