

Supplementary material

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Supplementary Methods 1 Calculations of PhenoAge and PhenoAgeAccel.

The resulting final equations for calculating PhenoAge and PhenoAgeAccel in this study are as follows:

$$\text{PhenoAge} = 141.50 + \frac{\ln[-0.00553 \times \ln(1 - \text{Mortality risk})]}{0.090165}$$

$$\text{PhenoAgeAccel} = \text{Phenotypic Age} - \text{Chronological Age}$$

Where:

$$\text{Mortality risk} = 1 - \exp\left(\frac{-1.51714 \times \exp(\text{xb})}{0.0076927}\right)$$

And:

$$\begin{aligned} \text{xb} = & -19.907 - 0.0336 \times \text{albumin} + 0.0095 \times \text{Creatinine} + 0.1953 \times \text{Glucose} \\ & + 0.0954 \times \ln(\text{C-reactive protein}) - 0.0120 \times \text{Lymphocyte Percent} \\ & + 0.0268 \times \text{Mean Cell Volume} + 0.3306 \times \text{Red Cell Distribution Width} \\ & + 0.00188 \times \text{Alkaline Phosphatase} + 0.0554 \times \text{White Blood Cell Count} \\ & + 0.0804 \times \text{Chronological Age} \end{aligned}$$

Supplementary Methods 2 The multivariable models for linear regression and Cox proportional hazards regression analysis.

Three multivariate regression models were constructed:

Model 1: unadjusted.

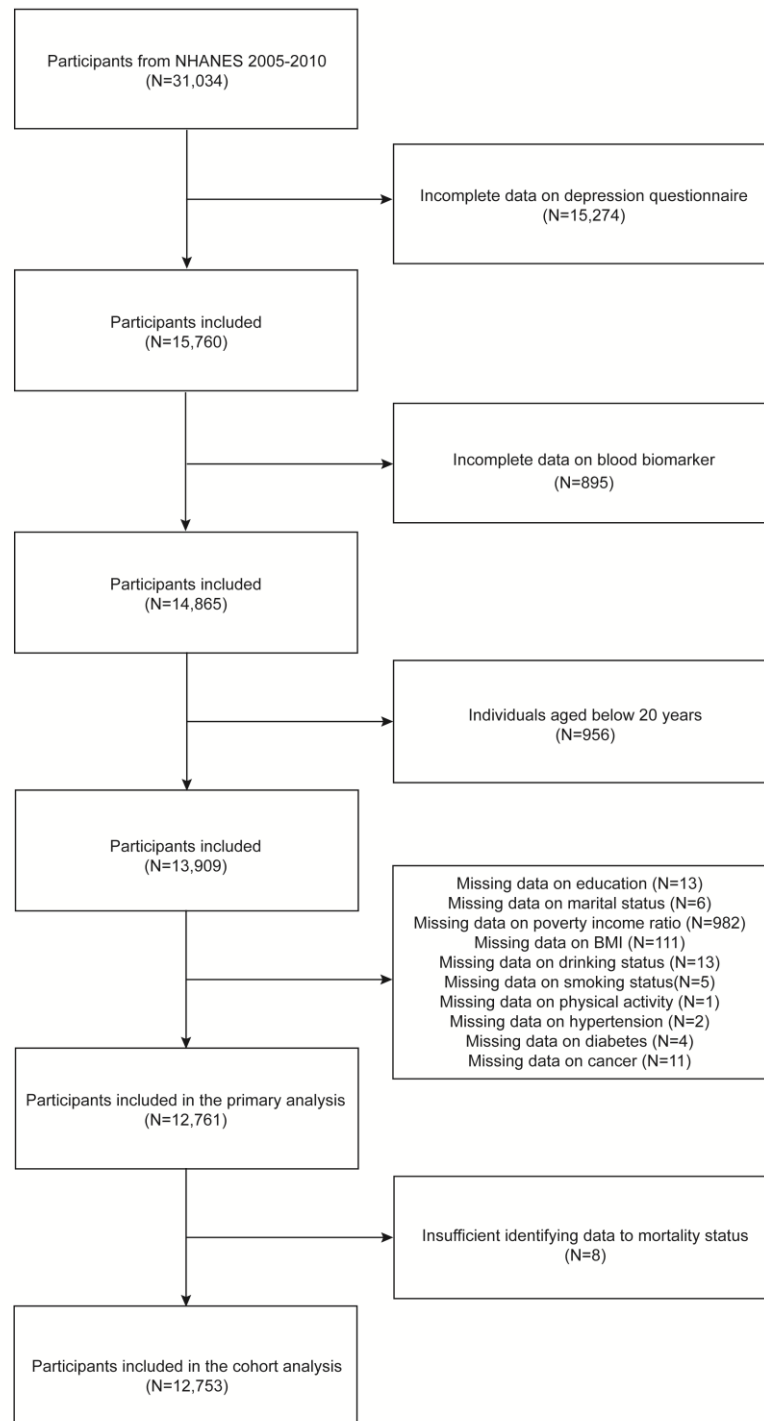
Model 2: adjusted for age, gender, and race.

Model 3: adjusted for age, gender, race, education, marital status, poverty income ratio, BMI, drinking status, smoking status, physical activity, and the history of hypertension, diabetes, cardiovascular disease, and cancer.

Supplementary Table1 PhenoAgeAccel as mediators in the associations between depression and mortality outcomes.

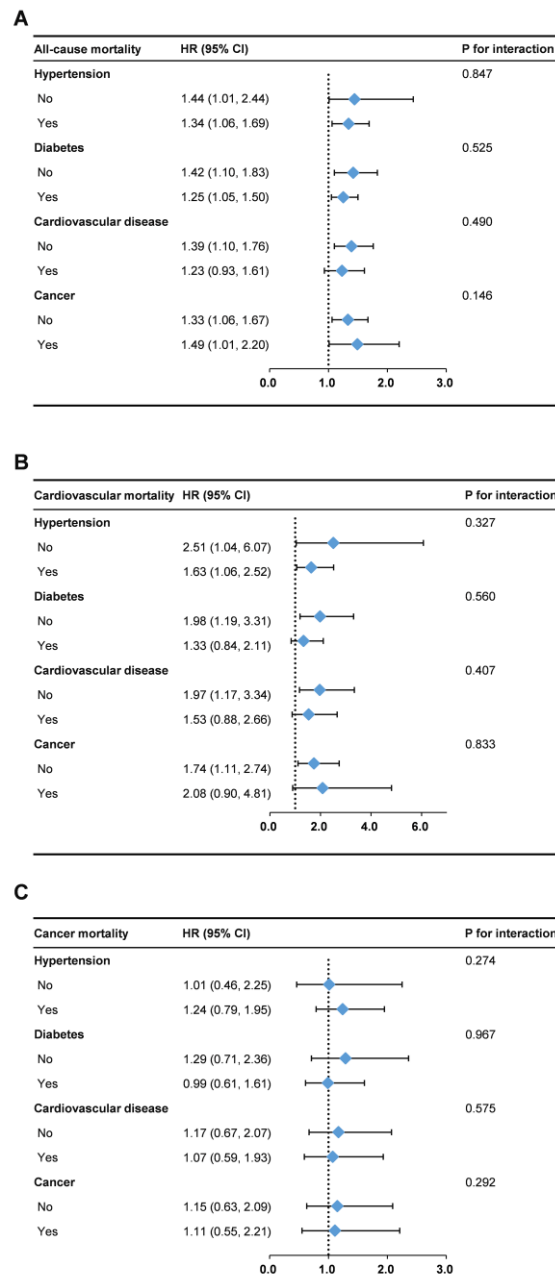
Mortality outcome	Total effect (95% CI)	Indirect effect (95% CI)	Direct effect (95% CI)	Mediation (%)	<i>P</i> value
All-cause mortality	0.0322 (0.0050, 0.0373)	0.0033 (0.0010, 0.0039)	0.0289 (0.0030, 0.0347)	10.32	0.008
Cardiovascular mortality	0.0282 (0.0047, 0.0273)	0.0014 (0.0004, 0.0014)	0.0268 (0.0041, 0.0264)	5.12	0.010
Cancer mortality	0.0040 (-0.0043, 0.0134)	0.0009 (0.0002, 0.0009)	0.0031 (-0.0046, 0.0128)	21.54	0.416

The analysis adjusted for age, gender, race, education, marital status, poverty income ratio, BMI, drinking status, smoking status, physical activity, and the history of hypertension, diabetes, cardiovascular disease, and cancer. A *P* value <0.05 indicates that a statistically significant proportion of the total effect is mediated through the mediator.



Supplementary Figure 1 Flow chart of participants selection.

Abbreviation: NHANES, National Health and Nutrition Examination Survey



Supplementary Figure 2 Subgroup analysis for the association between major depression and (A) all-cause mortality, (B) cardiovascular mortality, and (C) cancer mortality.

The analysis adjusted for age, gender, race, education, marital status, poverty income ratio, BMI, drinking status, smoking status, physical activity, and the history of hypertension, diabetes, cardiovascular disease, and cancer, except for the stratification variable itself.