Supplementary appendix

Title: Contribution of life course circumstances to the acceleration of phenotypic and functional aging: A retrospective study

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Supplementary Methods.

Health indicators

We considered health indicators including mobility, activities of daily living (ADL), handgrip strength, walking speed, full-tandem stand (FTS), repeated chair stand (RCS), global cognition, depression, self-rated health, and short-term mortality. All health indicators (except short-term mortality) were standardized (mean=0, standard deviation [SD]=1) for analyses.

- Subjective physical function

Mobility. We measured mobility by 7 activities, including extending arms up, lifting 5 kg, picking up a small coin, walking 100 m, climbing several flights of stairs, getting up from a chair, and stooping or kneeling or crouching.[1] Adults who had difficulty in performing an activity received a score of 1, and otherwise, received a score of 0. The summary score ranges from 0 to 7, with higher scores indicating higher level of mobility disability.

Activities of daily living (ADL). We measured ADL by 5 daily activities, including eating, dressing, getting in/out of bed, using the toilet, and bathing.[2] Adults who needed assistance with activity received a score of 1, and otherwise, received a score of 0. The summary score ranges from 0 to 5, with higher scores indicating higher level of ADL disability.

- Objective physical function

Handgrip strength. We measured handgrip strength with the arm bent at 90 degrees in a standing position using the dynamometer (Yuejian WL-1000, Nantong, China) twice in each hand.[3] We calculated an average absolute handgrip strength value from both hands across 2 trials for each participant.

Walking speed. We measured walking speed by two-timed walk tests over a 2·5-m course, at the usual pace.[3] We calculated the average absolute walking speed across 2 tests.

Full-tandem stand (FTS). We measured FTS by asking adults to stand with one foot in front of the other and heel touching toe for 30 seconds (for adults aged ≥70 years) or 60 seconds (for adults aged <70 years).[3] Adults who completed the task received a score of 1, and those who failed received a score of 0.

Repeated chair stand (RCS). We measured RCS by asking adults to fold their arms across their chest (i.e., the armrests were not used) and stand up from the chair 5 times with their fastest speed.[3] The time from the initial sitting position to the final standing position at the last stand was rated on a scale of 0 to 4, with higher value indicating better balance ability.

- Cognitive function

Global cognition. We measured global cognition by three tests, including the Telephone Interview of Cognitive Status-10 (TICS-10), word recall, and figure drawing. Ten items from TICS-10 included date (month, day, and year), day of the week, the season of the year, and serial subtraction of 7 from 100 (up to five times). Summing the number of correct answers to these questions resulted in a TICS-10 score, ranging from 0 to 10. For word recall, adults were asked to immediately recall as many words as they could in any order immediately after interviewers read 10 Chinese nouns (i.e., immediate recall). Four to ten minutes later, adults were asked to recall as many of the original words as possible (i.e., delayed recall).[4,5] The episodic memory was assessed by the average number of immediate and delayed word recalls, ranging from 0 to 10.[6] The visuospatial ability was assessed by figure drawing. Adults were shown a picture of two overlapped pentagons and asked to draw a similar figure.[7] Adults who completed the task received a score of 1, and those who failed received a score of 0. The summary score ranges from 0 to 21, with higher scores indicating better cognitive function.[4,8]

- Mental health

Depression. We measured depression by the 10-item Center for Epidemiologic Studies Depression Scale (CESD-10).[3] The 10 items evaluated the depressive behaviors and feelings of adults during the last week as follows: (1) “Felt depressed,” (2) “Felt everything I did was an effort,” (3) “Sleep was restless,” (4) “Was happy,” (5) “Felt lonely,” (6) “Bothered by little things,” (7) “Could not get going,” (8) “Had trouble keeping mind,” (9) “Feel hopeful about the future,” (10) “Felt fearful.” The scales for each of the ten items were slightly modified to 0 to 3, instead of 1 to 4, as done in previous literature.[9] Then, the summary score ranges from 0 to 30, with higher scores indicating more severe depressive symptoms during the last week. The reliability and validity of the CESD-10 have been verified in the Chinese population.[9]

- Self-rated health

Self-rated health. We measured self-rated health by asking adults to rate their health status on a scale of 1-5 (very good, good, fair, poor, or very poor).

- Mortality

Mortality

In CHARLS, death information was collected from the exit interviews in the 2018 wave. However, in the 2018 wave, the exact date of death was not available. Therefore, in this study, we constructed a binary variable to denote the occurrence of death over the approximately 3 years of follow-up since 2015, as we did before.[1]

Statistical Analyses

We analyzed associations of two aging measures (i.e., physiological dysregulation [PD], and frailty index [FI]) with health indicators using linear regression models (all indicators except short-term mortality), and logistic regression models (short-term mortality), respectively. Models adjusted for chronological age and gender. Effect sizes (i.e., β coefficients or odds ratio [OR]) were plotted using bar charts or forest plot.

The Shapley Value Decomposition

The Shapley Value Decomposition (hereafter referred to as Shapley method) is carried out on the basis of regression. The Shapley method tests the statistical significance of specific independent variables, while also enabling researchers to measure the shares (and their confidence interval) of changes in health outcomes attributable to the respective life course circumstances or areas of these life course circumstances. We introduce the application of the Shapley method in this study below.

The outcomes of interest in our study are the two aging measures, PD, and FI, which represent aging acceleration (*Aging.Accel*) after accounting for chronological age. As a measure of the degree of inequality in *Aging.Accel*, the mean logarithmic deviation (MLD) of an *Aging.Accel* distribution $F(Aging.Accel)$, i.e. $MLD(F)$, represents the total inequality of outcomes. As a popular measure of inequality in statistics and econometrics, MLD has been used to measure multidimensional well-being.[10-14] MLD is a special case of the Generalized Entropy. It is one of the widely accepted series of inequality measures, which enables us to completely decompose the changes in health outcomes into observed and unobserved factors.[15-18] As described by Roemer and Trannoy,[19] the Shapley method could be extended to other continuous measurements, such as the three aging measures in our study.

$$MLD = \frac{1}{N}\sum_{i=1}^{N}(\ln\bar{x} - \ln x_i) = \ln\bar{x} - \overline{lnx}$$

where N is the number of adults, x_i is the health status of the person *i*. $\bar{x}$ is the mean of x_i. $\overline{lnx}$ is the mean of $\ln x_i$. The logarithmic form has some characteristics, the ones most relevant to this study include: 1) It takes into account an aversion to higher health inequality. Considering the mean *Aging.Accel* $\underline{\bar{x}}$ (i.e. the first term of MLD fixed), the more unequal the health status, the larger the corresponding second term, and therefore the higher the MLD. This can be explained by a mathematical theorem, i.e., the second term increases with inequality ($-(\ln x_1 + \ln x_2)/2 > -\ln[(x_1 + x_2)/2]$, x1 and x2 represent the health status of two adults); 2) the logarithmic form allows us to mitigate the possible excessive influence of outliers.

Simply speaking, the MLD measures the average difference between $\ln\bar{x}$ and $\ln x_i$. The MLD is non-negative. The MLD is equal to zero when everyone has the same health status, and the MLD is more positive when the health status becomes more unequal. The reason for using MLD in the Shapley method is that it can well distinguish the changes in health outcomes caused by life course circumstances from those caused by unobserved factors,[19] so it is helpful for cross-study comparisons.

In essence, the Shapley method based on regression divides the sample into different types of adults corresponding to the set of adults with the same independent variable value (i.e., life course circumstances in this study). Each type has its own *Aging.Accel* distribution. Let the type distributions be $\{F^t(Aging.Accel), t \in T\}$ where T is the set of types, and let type t have the frequency f_t in the population and mean *Aging.Accel* μ^t, summarized by the vectors $f = f^1, \ldots, f^T$ and $\mu = \mu^1, \ldots, \mu^T$. In this paper, we construct a hypothetical distribution, expressed as $\Phi_{(\mu,f)}$, in which all members of each type t receive the mean *Aging.Accel* μ^t of that type. $\Phi_{(\mu,f)}$ has a cumulative distribution function, which is a step function with the same number of steps and types; it is often referred to as the 'smoothed' distribution of *F* related to the typology (f, μ). MLD of total inequality can be decomposed as follows:

$$MLD(F) = MLD(\Phi) + \sum_{t=1}^{T} f_t MLD(F_t) \qquad (1)$$

Through observable life course circumstances (the first term on the right-hand side) and other unobserved characteristics (the second term on the right-hand side), a MLD can be completely decomposed into inequality. Therefore, the ratio r can be used to measure *Aging.Accel* inequality by the degree of observed life course circumstances.

$$r = \frac{MLD(\Phi)}{MLD(F)}$$

A Simple Illustrating Example: Suppose we have two binary childhood and adulthood circumstances in total, i.e. childhood socioeconomic status (SES) (high/low) and adulthood SES (high/low). Therefore, there are four types, i.e. (high, high), (high, low), (low, high), (low, low). All adults are partitioned into these four groups. This paper assumes that all adults within each type have the same *Aging.Accel* value, which means that adults with the same childhood and adulthood SES have the same level of *Aging.Accel*, so the difference between the four types of *Aging.Accel* can only be due to the difference in childhood and adulthood SES. This variation is the numerator. The proportion of health inequality, which can be explained by the observed childhood and adulthood SES, was measured by the ratio of these two indicators.

Note that this example is for the sake of simplicity and only two life course circumstances are considered. In the implementation of this study, we used the regression-based Shapley method to consider about 70 life course circumstances simultaneously.

Conditional on using a rich set of life course circumstances, our regression-based Shapley method follows procedures from Ferreira and Gignoux,[11,12] Niehues and Peichl,[20] and Roemer and Trannoy[19] to specify the model

$$ln\ Aging.Accel_i = \boldsymbol{\alpha V_i} + u_i, \qquad (2)$$

i represents the person i. Since the MLD decomposition only allows positive health outcome measures (due to its component of the logarithmic form), but has scale invariance, we convert all the values of *Aging.Accel* to positive by adding a positive number without changing its distribution. To ensure that the results are robust to our conversion and basically remain unchanged, we tested multiple such positive values.

This reduced form estimation enables us to derive *Aging.Accel*'s overall fraction of variance, which is derived from a vector $\boldsymbol{V_i}$ of childhood ($\boldsymbol{C_i}$) and adulthood ($\boldsymbol{A_i}$) factors, where $\boldsymbol{V} = (\boldsymbol{C}, \boldsymbol{A})$. Based on this estimation, we construct a parametric estimate of the smoothed distribution Φ defined earlier by replacing *Aging.Accel* outcomes by their predictions:

$$\widehat{Aging.Accel} = \exp(\hat{\boldsymbol{\alpha}}\boldsymbol{V_i}) \qquad (3)$$

Let Φ be the distribution of estimated *Aging.Accel*. In this counterfactual, all adults with the same childhood and adulthood characteristics have the same *Aging.Accel*. Thus r can be rewritten as:

$$r = \frac{MLD(\{\widehat{Aging.Accel}\})}{MLD(\{Aging.Accel\})}$$

The overall contribution $\hat{r}$ can be neatly decomposed into components for each category $\hat{r}^j$ in the childhood and adulthood vector $\boldsymbol{V}$.

$$\hat{r} = \sum_j \hat{r}^j = \sum_j (var\ Aging.Accel)^{-1} \left[a_j^2\, var\ V^j + \frac{1}{2}\sum_k a_k a_j\, cov(V^k, V^j)\right] \quad (4)$$

where *j*, *k*=1, 2, … as categories of childhood and adulthood characteristics. α_j and α_k are coefficients of categories *j* and *k* in equation (2). Equation (4) gives an example of a Shapley method. This method provides an appropriate way to assign roles to sources in generating health inequality.[12,14-16,19]

A particular category *j*'s overall contribution to the variance in *Aging.Accel* – $\hat{r}^j$ – corresponds to an average between two channels. Intuitively, the childhood environment may directly affect the health of the adults, and it may also play an indirect role by shaping other childhood and adulthood characteristics. Formally, all $V^j_{j \neq J}$ are held constant in the *direct* contribution of category *j*, i.e. $a_j^2 (var\ Aging.Accel)^{-1} var\ V^j$. Regarding the *indirect* contribution, category *j* itself is held constant, and its indirect contribution, i.e. $\frac{1}{2}(var\ Aging.Accel)^{-1} \sum_k a_k a_j\, cov(V^k, V^j)$, is regarded as the difference between the total variance and the ensuing variance.

In the first step, we estimated all possible permutation inequality measures of childhood and adulthood variables (domains in this study). In a second step, we computed the average marginal effect of each domain on inequality in *Aging.Accel*.[17] This process is very computationally intensive because 2^K (K= number of domains) have to be calculated. Finally, we repeated these steps to obtain the bootstrap standard errors.

Compared with other decomposition methods, this approach has great advantages. First, it is order-independent, which means that the order of feature decomposition does not affect the result. Second, it is additive, which means that the total contribution of each field to the inequality in *Aging.Accel* is the total contribution to the inequality in *Aging.Accel*. Although the decomposition should not be regarded as causality,

it provides the concept of the relative importance of factors.[12] Third, the Shapley method has always been a basic built-in toolkit in popular statistical software, such as STATA and R, which further simplifies the analysis and dissemination.

Notable that the Shapley method may provide a lower-bound estimate of the contribution to health inequality, as changes in health may not be fully explained due to *unobserved* characteristics. To obtain population-based estimates, we incorporated survey weights in the 2014 life course survey of CHARLS in this analysis. Moreover, the function form of MLD implicitly assumes increasing disutility from more *Aging.Accel*. Our results are robust to the square variance decomposition, and variance decomposition is an alternative decomposition method, which assumes that the function form has no specific curvature. For a description of variance decomposition and its comparison with MLD decomposition, see.[17]

Principal components analysis (PCA) and hierarchal cluster analysis (HCA)

Principal components analysis (PCA) is a statistical method that helps convert potentially correlated variables into a set of linearly unrelated variables named PCs. We performed PCA to reduce the dimension of potentially correlated variables concerning childhood and adulthood circumstances. A total of 70 circumstance variables from domains of childhood SES, childhood war, childhood health, childhood trauma, childhood relationship, childhood parents' health, adulthood SES, adulthood adversity, and adulthood social support were included. We chose the top 4 PCs with eigenvalues >2 via scree plot. The proportion of variance explained was 16.6%.

We performed a hierarchal clustering analysis (HCA) for all adults using the top 4 PCs with the WGCNA R package[21] to cluster adults into distinct subpopulations that having different levels of *Aging.Accel*. Adults in the same subpopulation shared similar life course circumstances. Finally, we got 6 optimal subpopulations/clusters with a cut height of 0·80 and a minimum size of 20. We presented these subpopulations/clusters (the subpopulation 1 to 6) using different colors: "turquoise", "green", "orange", "yellow", "blue", and "red". To show how these subpopulations/clusters differed in characteristics, we used several main circumstances including gender, childhood family poverty, childhood war, childhood health (summarized score), childhood trauma (summarized score), childhood relationship (summarized score), childhood parents' health (summarized score), education, adulthood adversity (summarized score), adulthood social support (summarized score), and obesity, and draw the cluster dendrogram with these circumstance variables. All values of these circumstance variables were indicated by various colors in the cluster dendrogram, the closer to "darkorange", the higher dose of exposure to circumstance risk factors (except gender). For example, an adult with an education level above senior school was indicated by "darkmagenta", whereas an adult with an education level below middle school was indicated by "darkorange". Through WGCNA,[21] we estimated adults' cluster membership for each subpopulation using a continuous measure which ranged from -1 to 1 and indicates how similar the profile of an adult is to the characteristics of the subpopulation. For example, an adult has a score of 0·9 for the subpopulation 6 and -0·7 for the subpopulation 1, meaning that she/he is very similar to the profile represented by the subpopulation 6, but different from the subpopulation 1. Using these cluster membership values, we also examined the correlation between these subpopulations/clusters.

Sensitivity analysis

To assess the robustness of our findings, we performed several sensitivity analyses. First, we compared the characteristics of included and excluded study populations. Second, we repeated the Shapley method in those who fasted (N=5369). Third, because an individual weight with non-response adjustment was available in the main survey of CHARLS, we used it as an alternative weight in the Shapley method. Fourth, to account for the influence of chronological age, we calculated residuals resulting from linear models when regressing PD and FI on chronological age (hereafter, PD.resid and FI.resid), respectively. We performed the Shapley method using these residuals (i.e., PD.resid, and FI.res) as outcomes. Finally, to estimate whether the results varied by gender, we performed the Shapley method stratified by gender. Also, the distributions of PD and FI across six subpopulations were plotted for male and female separately.

Supplementary Results

Associations of two aging measures with health indicators

The associations of the two aging measures with health indicators are presented in appendix p 19. The two aging measures were positively associated with subjective physical disability in mobility and ADL, depressive symptoms, and self-rated poor health status. Additionally, the two aging measures were negatively associated with better objective physical functioning and global cognition. We demonstrated that PD and FI were significantly associated with short-term mortality risk, as found in previous studies.[22,23] After accounting for chronological age and gender, PD, and FI were positively associated with short-term mortality, with ORs of 1·91 (95% confidence interval [CI]: 1·62-2·26), and 1·034 (95% CI: 1·025-1·044), respectively.

The characteristics of the study population

There was a considerable proportion of adults who self-reported low levels of childhood SES. For example, 37·4% reported financially poor status during childhood. The prevalence of terrible health conditions ranged from 0·8% (ever hospitalized more than 3 times within 1-year) to 5·1% (ever confined to bed or home for a month or more). About 13·6% to 15·4% of adults were born in the war era. The proportion of experiencing childhood trauma varied widely, ranging from 0·6% (parents divorced) to 55·1% (parents had smoking problems). The majority of the adults enjoyed a harmonious relationship with their neighborhood, friends, and parents in childhood. For example, 96·0% of adults self-rated somewhat or very close-knit relationship with the neighborhood. The prevalence of parents' terrible health conditions during childhood ranged from 3·6% (had abnormality of mind) to 21·0 % (continued signs of sadness or depression).

In adulthood, about 25·1% were illiterate, 49·4% engaged in agricultural work, and 64·3% lived in rural areas. The exposure to adulthood adversity was also variable. For example, 4·9% reported being hospitalized more than 3 times within 1-year, while 17·0% reported leaving a job for one month or more because of health conditions. As for adulthood social support, 6·9% reported receiving financial support for work, and 15·5% reported receiving positive support or mentoring for interpersonal relationship.

About 10% of adults ever experienced obesity over the study period. Over 46% of adults consumed alcohol. About 16·5% of adults were former smokers, and 27·7% were current smokers.

Sensitivity analyses

The differences in characteristics of included and excluded populations are shown in appendix p 18. Those who were excluded were more likely to be younger, Han ethnicity, have illiteracy, and live in an urban area. When limiting the sample to those who fasted (appendix p 24) or using an individual weight with adjustment for non-response as an alternative weight (appendix p 25), we did not observe substantial changes in the contributions of life course circumstances to the two aging measures. The contribution of life course circumstances to PD.resid and FI.resid are presented in appendix p 26. Overall, all the 11 domains contributed 5·5% (bootstrap standard error=0·0006), and 25·4% (bootstrap standard error=0·002) of variance in PD.resid, and FI.resid, respectively. The results did not change substantially. Moreover, the results were similar between male and female (appendix p 27-28).

Table S1: Questions and responses for variables included in the childhood and adulthood circumstances and behaviors.

Variables names	Questions	Responses/description
Childhood circumstances		
Childhood SES		
Parental education	What is the highest level of education your biological father/mother completed?	0=literate; 1=illiterate
Parental occupation	What was your male guardian's usual occupation when you were growing up before you were 17?	0=nonfarming; 1=farming
House type at birth	What is the architectural type of your first residence?	1=concrete; 2=adobe; 3=wood or others
First hukou type	What was your first hukou type?	0=agricultural; 1= non-agricultural
Regional status	Since your birth, the first county for living more than six months is?	1= Eastern China; 2=Central China; 3=Western China
Family's financial situation	When you were a child before age 17, compared to the average family in the same community/village at that time, how was your family's financial situation?	1=a lot/somewhat better; 2=same; 3=somewhat worse/a lot worse
Food deficiency	When you were a child before age 17 was there ever a time when your family did not have enough food to eat?	0=no; 1=yes
Family starved to death	During those days, had any of your family (including your grandparents, parents, siblings, children and so on) starved to death?	0=no; 1=yes
Parents political status	Is (Was) any of your parents a Communist Party member?	0= yes; 1= no
Childhood health		
Self-reported health status	Before you were 15 years old (including 15 years old), would you say that compared to other children of the same age, you were healthier, same, or less healthy?	1=healthier; 2=same; 3= less healthy
Ever confined to bed	Before you were 15 years old (including 15 years old), because of a health condition, were you ever confined to bed or home for a month or more?	0=no; 1=yes
Ever hospitalized for ≥1 month	Before you were 15 years old (including 15 years old), because of a health condition, were you ever hospitalized for a month or more?	0=no; 1=yes
Ever hospitalized ≥3 times	Were you ever hospitalized more than three times within a 12-month period before you were 15 years old (including 15 years old)?	0=no; 1=yes
Received vaccinations	Before you were 15 years old (including 15 years old), have you received any vaccinations?	0=yes; 1=no
Had a usual source of care	Before you were 15 years old (including 15 years old), have you always had a usual source of care, that is, a particular person or a place that you went to when you were sick or you needed advice about your health?	0=have usual source of care; 1=don't have usual source of care
Childhood war		
Born in the Civil War era	Born in the Civil War era. (1946-1949)	0=no; 1=yes
Born in the Second Sino-Japanese era	Born in the Second Sino-Japanese era. (1937-1945)	0=no; 1=yes
Childhood trauma		
Parents died	Before age 16 did you one or both parents die?	0=no; 1=yes
Parents divorced	Before age 16 did your biological parents divorce?	0=no; 1=yes
Sibling died	Do you have any sibling who died before age 6?	0=no; 1=yes
Parents had alcoholism problem	During the years you were growing up, did female/male dependents have alcoholism problem?	0=no; 1=yes
Parents had smoking problem	During the years you were growing up, did female/male dependents have smoking problem?	0=no; 1=yes
Parents had gambling problem	During the years you were growing up, did female/male dependents have gambling problem?	0=no; 1=yes
Abused by neighbor kids	When you were a child, how often were you picked on or bullied by kids in your neighborhood?	0=not very often/never; 1=often/sometimes
Hit by mother	When you were growing up, did your female guardian ever hit you?	0=not very often/never; 1=often/sometimes
Hit by father	When you were growing up, did your male guardian ever hit you?	0=not very often/never; 1=often/sometimes
Hit by siblings	When you were growing up, how often did your brother or sister ever hit you?	0=not very often/never; 1=often/sometimes

Variables names	Questions	Responses/description
Parents ever quarreled	When you were growing up, how often did your parents ever quarrel?	0=not very often/never; 1=often/sometimes
Parents hit each other	Have your parents hit each other?	0=not very often/never; 1=often/sometimes
Childhood Relationship		
Self-rated neighborhood safety	Was it safe being out alone at night in the neighborhood where you lived as a child?	0=not very/not at all; 1=very/somewhat
Self-rated neighborhood willingness to help	Were the neighbors of the place where you lived as a child willing to help each other out?	0=not very/not at all; 1=very/somewhat
Self-rated neighborhood close-knit relationship	Were the neighbors of the place where you lived as a child very close-knit?	0=not very/not at all; 1=very/somewhat
Self-rated neighborhood cleanness	Was the neighborhood of the place where you lived as a child very clean and attractive?	0=not very/not at all; 1=very/somewhat
Felt lonely	When you were a child, how often did you feel lonely for not having friends?	0=sometimes/often; 1=never/not very often
Had a group of friends	When you were a child, did you often have a group of friends that you felt comfortable spending time with?	0=never/not very often; 1=sometimes/often
Had a good friend	When you were a child, did you have a good friend?	0=no; 1=yes
Self-rated relationship with mother	How would you rate your relationship with your female guardian when you were growing up?	1=poor, 2=fair, 3=good, 4= very good, 5=excellent
Mother's love and affection	How much love and affection did your female guardian give you while you were growing up?	0=rarely/never; 1=Often/sometimes
Mother's effort put into watching over you	How much effort did your female guardian put into watching over you?	0=a little/not at all; 1=A lot/some
Mother's preference for siblings	Did your female guardian treat your siblings better than you when you were growing up?	0=very much/somewhat; 1=a little / not at all
Mother's preference for boy	Did your female guardian prefer boys to girls?	0=very much/somewhat; 1=a little/not at all
Self-rated relationship with father	How would you rate your relationship with your male guardian when you were growing up?	1=poor, 2=fair, 3=good, 4= very good, 5=excellent
Father's preference for siblings	Did your male guardian treat your siblings better than you when you were growing up?	0=a little/not at all; 1=very much/somewhat
Father's preference for boy	Did your male guardian prefer boys to girls?	0=a little/not at all; 1=very much/somewhat
Childhood parents' health		
Parental sadness or depression	During the years you were growing up, had your female/male guardian showed continued signs of sadness or depression that lasted 2 weeks or more?	0=no; 1=yes
Parents' sick on bed	Did your female/male guardian have a long time be sick on bed when you were young?	0=no; 1=yes
Parents' deformity	Did your female/male guardian have a serious deformity when you were young?	0=no; 1=yes
Parents' abnormality of mind	Did your female/male guardian have abnormality of mind when you were young?	0=no; 1=yes
Mother is alive	Is Your Biological Mother Living?	0=others; 1=yes
Father is alive	Is Your Biological Father Living?	0=others;1=yes
Alive mother's longevity	Alive mother's longevity (≥80 years)	0=others;1=yes
Dead mother's longevity	Dead mother's longevity (≥80 years)	0=others;1=yes
Alive mother's longevity	Alive mother's longevity (≥80 years)	0=others;1=yes
Dead mother's longevity	Dead mother's longevity (≥80 years)	0=others;1=yes
Adulthood circumstances		
Adulthood SES		
Individual's education attainment	What is the highest level of education you attained now?	1=illiteracy; 2=elementary; 3=middle; 4=senior; 5≥college

Variables names	Questions	Responses/description
Individual's occupation	What is the main labor force status?	1=agricultural; 3=Non-agricultural employed; 3=others
Residence	What is your residence: Rural or urban?	0=urban; 1=rural
Adulthood adversity		
Child died	Death of child.	0=no; 1=yes
Physically injury	Have you ever received a physical injury that has led to any permanent handicap, disability or limitations in what you can do in daily in adulthood?	0=no; 1=yes
Experienced lifetime discrimination	After you were 16 years old, because of ill health, did you experience any of the following (Denied promotions, Assignment to a task with fewer responsibilities, working on tasks below your qualifications, Harassment by your boss or colleagues, Pay cuts, Dismissed)?	0=no; 1=yes
Ever confined to bed	After you were 16 years old, because of a health condition, were you ever confined to bed or home for one month or more?	0=no; 1=yes
Ever hospitalized for ≥1 month	After you were 16 years old, because of a health condition, were you ever hospitalized for a month or more?	0=no; 1=yes
Ever hospitalized ≥3 times	Were you ever hospitalized more than three times within a 12-month period after you were 16 years old?	0=no; 1=yes
Ever left job for health condition	After you were 16 years old, because of a health condition, did you leave your job for one month or more?	0=no; 1=yes
Had a usual source of care	When you were between 16-55 years old, have you always had a usual source of care, that is, a particular person or a place that you went to when you were sick or you needed advice about your health?	0=have usual source of care; 1= don't have usual source of care
Social support		
Financial support for your work	When you were a young adult, was there anyone who provided you with financial support for your work such as starting a business?	0=no; 1=yes
Positive nonfinancial support for your work	When you were a young adult, was there anyone who provided you with positive nonfinancial support or mentoring for your work such as starting a business?	0=no; 1=yes
Positive support for interpersonal relationships	When you were a young adult, was there anyone who provided you with positive support or mentoring for your interpersonal relationships, such as marriage or a marriage-like relationship?	0=no; 1=yes
Behaviors		
Proportion of obesity	Proportion of obesity (BMI≥28kg/m^2)	Cont. (proportion)
Smoking status	Smoking status.	0=never smoking; 1=ever smoking; 2=current smoking
Drinking status	Have you ever drunk any alcohol before	0=no;1=yes

BMI=body mass index.

Table S2: The components of frailty index in CHARLS.

No.	Items
1	Has hypertension.
2	Has dyslipidemia.
3	Has diabetes or high blood glucose.
4	Has chronic lung diseases.
5	Has liver disease.
6	Has heart disease.
7	Has stroke.
8	Has kidney disease.
9	Has stomach or other digestive diseases.
10	Has emotional, nervous, or psychiatric problems.
11	Has memory-related disease.
12	Has arthritis or rheumatism.
13	Has asthma.
14	Physical disabilities.
15	Brain damage/mental retardation.
16	Permanent vision damage.
17	Permanent hearing damage.
18	Self-rating of health.
19	Limitations in dressing.
20	Limitations in eating.
21	Limitations in bathing or showering.
22	Limitations in getting into or out of bed.
23	Limitations in using the toilet.
24	Difficulty with controlling urination and defecation.
25	Limitations in doing household chores.
26	Limitations in preparing hot meals.
27	Limitations in shopping.
28	Limitations in managing money.
29	Limitations in taking medications.
30	Limitations in running/jogging 1 kilometer.
31	Limitations in walking 1 kilometer.
32	Limitations in climbing several flights of stairs.
33	Limitations in getting up from a chair after sitting for a long period.
34	Limitations in crouching, kneeling, or stooping.
35	Limitations in reaching or extending arms.
36	Limitations in lifting weights over 5 kilograms.
37	Limitations in picking up a coin from a table.
38	Has depressive symptom (the score of CESD-10 >10)
39	Cognitive decline (1-(the cognition score/21))

CHARLS=the China Health and Retirement Longitudinal Study. CESD-10=The 10-item Center for Epidemiologic Studies Depression Scale**.**

Table S3. Characteristics of the study population in CHARLS (N=6224).

Characteristics	Mean±SD or n (%)
Demographics	
Chronological age, years	61·6±8·5
Gender	
Male	2911 (46·8)
Female	3313 (53·2)
Ethnicity	
Han	5788 (93·0)
Others	436 (7·0)
Childhood circumstances	
Childhood SES	
Parental education	
Literate	607 (9·8)
Illiterate	5617 (90·3)
Parental occupation	
Non-farmer	1129 (18·1)
Farmer	5095 (81·9)
House type at birth	
Concrete	670 (10·8)
Adobe	3925 (63·1)
wood or others	1629 (26·2)
First hukou type	
Non-agricultural	464 (7·5)
Agricultural	5760 (92·5)
Regional status	
Eastern China	1984 (31·9)
Central China	2266 (36·4)
Western China	1974 (31·7)
Family financial status	
A lot / somewhat better	600 (9·6)
Same	3295 (52·9)
Somewhat / a lot worse	2329 (37·4)
Ever experienced food deficiency, yes	4499 (72·3)
Ever experienced family starved to death, yes	650 (10·4)
Parents political status	
Any party member	878 (14·1)
None	5346 (85·9)
Childhood health	
Self-reported health status before age 15	
Healthier	2312 (37·1)
Same	3167 (50·9)
Less healthy	745 (12·0)
Ever confined to bed or home for a month or more, yes	318 (5·1)
Ever hospitalized for a month or more, yes	107 (1·7)
Ever hospitalized more than three times within 1-year, yes	50 (0·8)
Didn't receive vaccination before age 15, yes	878 (14·1)
Didn't have a usual source of care, yes	566 (9·1)
Childhood war	
Born in the Civil War era (1946-1949), yes	844 (13·6)
Born in the Second Sino-Japanese era (1937-1945), yes	957 (15·4)
Childhood trauma	
Parents died, yes	2569 (41·3)
Parents divorced, yes	34 (0·5)
Siblings died, yes	1432 (23·0)
Parents had alcoholism problem, yes	449 (7·2)
Parents had smoking problem, yes	3427 (55·1)
Parents had gambling problem, yes	116 (1·9)
Bullied by neighbor kids, yes	706 (11·3)
Female guardian ever hit you, yes	1477 (23·7)
Male guardian ever hit you, yes	980 (15·7)
Siblings ever hit you, yes	366 (5·9)
Parents ever quarreled, yes	1403 (22·5)
Parents hit each other, yes	527 (8·5)
Childhood relationship	
Self-rated neighborhood safety	
Not at all / not very	493 (7·9)
Somewhat / very	5731 (92·1)
Self-rated neighborhood willingness to help	
Not at all / not very	680 (10·9)

Characteristics	Mean±SD or n (%)
Somewhat / very	5544 (89·1)
Self-rated neighborhood close-knit relationship	
Not at all / not very	250 (4·0)
Somewhat / very	5974 (96·0)
Self-rated neighborhood cleanness	
Not at all / not very	2203 (35·4)
Somewhat / very	4021 (64·6)
Felt lonely for not having friends?	
Never / not very often	5536 (89·0)
Sometimes / often	688 (11·1)
Had a group of friends	
ever / not very often	1361 (21·9)
Sometimes / often	4863 (78·1)
Had a good friend	
No	3013 (48·4)
Yes	3211 (51·6)
Self-rated relationship with the female guardian	
Excellent	2067 (33·2)
Very good	1997 (32·1)
Good	1045 (16·8)
Fair	1058 (17·0)
Poor	57 (0·9)
Female guardian's love and affection	
Never / rarely	1226 (19·7)
Sometimes / Often	4998 (80·3)
Female guardian's effort put into watching over you	
Not at all / a little	1377 (22·1)
Some / a lot	4847 (77·9)
Female guardian treated your siblings better than you	
Not at all / a little	5488 (88·2)
Somewhat / very much	736 (11·8)
Female guardian preferred boys to girls	
Not at all / a little	5702 (91·6)
Somewhat / very much	522 (8·4)
Self-rated relationship with the male guardian	
Excellent	1827 (29·4)
Very good	2053 (33·0)
Good	1112 (17·9)
Fair	1160 (18·6)
Poor	72 (1·2)
Male guardian treated your siblings better than you	
Not at all / a little	5649 (90·8)
Somewhat / very much	575 (9·3)
Male guardian preferred boys to girls	
Not at all / a little	5708 (91·7)
Somewhat / very much	516 (8·3)
Childhood parents' health	
Parents showed continued signs of sadness or depression, yes	1305 (21·0)
Parents had a long time be sick on bed, yes	1130 (18·2)
Parents had a serious deformity, yes	302 (4·9)
Parents had abnormality of mind, yes	226 (3·6)
Was biological mother alive, yes	1444 (23·2)
Was biological father alive, yes	793 (12·7)
Alive mother's longevity (≥80 years), yes	776 (12·5)
Dead mother's longevity (≥80 years), yes	1405 (22·6)
Alive father's longevity (≥80 years), yes	426 (6·8)
Dead father's longevity (≥80 years), yes	1281 (20·6)
Adulthood circumstances	
Adulthood SES	
Education	
Illiteracy	1560 (25·1)
Elementary	2552 (41·0)
Middle	1426 (22·9)
Senior	614 (9·9)
≥College	72 (1·2)
Occupation	
Agricultural work	3059 (49·4)
Non-agricultural employed	1204 (19·4)
Others	1931 (31·2)

Characteristics	Mean±SD or n (%)
Residence	
Urban	2224 (35·7)
Rural	4000 (64·3)
Adulthood adversity	
Ever experienced the death of a child, yes	796 (12·8)
Ever received a physical injury, yes	429 (6·9)
Ever experienced lifetime discrimination, yes	596 (9·6)
Ever confined to bed or home for one month or more, yes	954 (15·3)
Ever hospitalized for a month or more, yes	718 (11·5)
Ever hospitalized more than three times within 1-year, yes	307 (4·9)
Ever left your job for one month or more because of health condition, yes	1060 (17·0)
Didn't have a usual source of care, yes	458 (7·4)
Adulthood social support	
Was there financial support for your work, yes	429 (6·9)
Was there positive nonfinancial support or mentoring for your work, yes	734 (11·8)
Was there positive support or mentoring for your interpersonal relationships, yes	963 (15·5)
Adulthood behaviors	
Proportion of obesity, 0-1	0·1±0·3
Smoking	
Non-smoker	3473 (55·8)
Ever smoker	1028 (16·5)
Current smoker	1723 (27·7)
Drinking	
Non-drinker	3337 (53·6)
Drinker	2887 (46·4)

SD=standard deviation. SES=socioeconomic status.

Table S4: Characteristics of the study population in CHARLS by identified subpopulations (N=6224).

Characteristics	Subpopulation 1 (N=1407)	Subpopulation 2 (N=587)	Subpopulation 3 (N=1208)	Subpopulation 4 (N=1132)	Subpopulation 5 (N=1354)	Subpopulation 6 (N=536)
Demographics						
Chronological age, years	59·0±7·4	55·3±5·6	59·7±7·8	62·2±8·2	67·5±7·5	62·9±8·4
Gender						
Male	584 (41·5)	329 (56·0)	578 (47·8)	529 (46·7)	584 (43·1)	307 (57·3)
Female	823 (58·5)	258 (44·0)	630 (52·2)	603 (53·3)	770 (56·9)	229 (42·7)
Ethnicity						
Han	1311 (93·2)	543 (92·5)	1133 (93·8)	1003 (88·6)	1292 (95·4)	506 (94·4)
Others	96 (6·8)	44 (7·5)	75 (6·2)	129 (11·4)	62 (4·6)	30 (5·6)
Childhood circumstances						
Childhood SES						
Parental education						
Literate	109 (7·7)	152 (25·9)	230 (19·0)	40 (3·5)	33 (2·4)	43 (8·0)
Illiterate	1298 (92·3)	435 (74·1)	978 (81·0)	1092 (96·5)	1321 (97·6)	493 (92·0)
Parental occupation						
Non-farmer	108 (7·7)	178 (30·3)	570 (47·2)	47 (4·2)	91 (6·7)	135 (25·2)
Farmer	1299 (92·3)	409 (69·7)	638 (52·8)	1085 (95·8)	1263 (93·3)	401 (74·8)
House type at birth						
Concrete	117 (8·3)	67 (11·4)	294 (24·3)	39 (3·4)	90 (6·6)	63 (11·8)
Adobe	961 (68·3)	395 (67·3)	721 (59·7)	650 (57·4)	854 (63·1)	344 (64·2)
wood or others	329 (23·4)	125 (21·3)	193 (16·0)	443 (39·1)	410 (30·3)	129 (24·1)
First hukou type						
Non-agricultural	1401 (99·6)	549 (93·5)	854 (70·7)	1127 (99·6)	1340 (99·0)	489 (91·2)
Agricultural	6 (0·4)	38 (6·5)	354 (29·3)	5 (0·4)	14 (1·0)	47 (8·8)
Regional status						
Eastern China	552 (39·2)	213 (36·3)	430 (35·6)	250 (22·1)	398 (29·4)	141 (26·3)
Central China	507 (36·0)	161 (27·4)	498 (41·2)	289 (25·5)	594 (43·9)	217 (40·5)
Western China	348 (24·7)	213 (36·3)	280 (23·2)	593 (52·4)	362 (26·7)	178 (33·2)
Family financial status						
A lot / somewhat better	106 (7·5)	77 (13·1)	255 (21·1)	45 (4·0)	69 (5·1)	48 (9·0)
Same	910 (64·7)	340 (57·9)	688 (57·0)	442 (39·0)	687 (50·7)	228 (42·5)
Somewhat / a lot worse	391 (27·8)	170 (29·0)	265 (21·9)	645 (57·0)	598 (44·2)	260 (48·5)
Ever experienced food deficiency, yes	910 (64·7)	366 (62·4)	713 (59·0)	974 (86·0)	1092 (80·6)	444 (82·8)
Ever experienced family starved to death, yes	65 (4·6)	50 (8·5)	56 (4·6)	206 (18·2)	195 (14·4)	78 (14·6)
Parents political status						
Any party member	170 (12·1)	175 (29·8)	270 (22·4)	112 (9·9)	69 (5·1)	82 (15·3)
None	1237 (87·9)	412 (70·2)	938 (77·6)	1020 (90·1)	1285 (94·9)	454 (84·7)
Childhood health						
Self-reported health status before age 15						
Healthier	587 (41·7)	230 (39·2)	549 (45·4)	290 (25·6)	471 (34·8)	185 (34·5)
Same	737 (52·4)	282 (48·0)	558 (46·2)	602 (53·2)	740 (54·7)	248 (46·3)
Less healthy	83 (5·9)	75 (12·8)	101 (8·4)	240 (21·2)	143 (10·6)	103 (19·2)
Ever confined to bed or home for a month or more, yes	11 (0·8)	36 (6·1)	21 (1·7)	134 (11·8)	39 (2·9)	77 (14·4)

Characteristics	Subpopulation 1 (N=1407)	Subpopulation 2 (N=587)	Subpopulation 3 (N=1208)	Subpopulation 4 (N=1132)	Subpopulation 5 (N=1354)	Subpopulation 6 (N=536)
Ever hospitalized for a month or more, yes	2 (0·1)	23 (3·9)	6 (0·5)	46 (4·1)	1 (0·1)	29 (5·4)
Ever hospitalized more than three times within 1-year, yes	1 (0·1)	9 (1·5)	5 (0·4)	18 (1·6)	1 (0·1)	16 (3·0)
Didn't receive vaccination before age 15, yes	171 (12·2)	24 (4·1)	80 (6·6)	186 (16·4)	361 (26·7)	56 (10·4)
Didn't have a usual source of care, yes	59 (4·2)	26 (4·4)	31 (2·6)	241 (21·3)	175 (12·9)	34 (6·3)
Childhood war						
Born in the Civil War era (1946-1949), yes	131 (9·3)	13 (2·2)	133 (11·0)	158 (14·0)	322 (23·8)	87 (16·2)
Born in the Second Sino-Japanese era (1937-1945), yes	98 (7·0)	9 (1·5)	115 (9·5)	174 (15·4)	459 (33·9)	102 (19·0)
Childhood trauma						
Parents died, yes	437 (31·1)	102 (17·4)	402 (33·3)	542 (47·9)	844 (62·3)	242 (45·1)
Parents divorced, yes	5 (0·4)	3 (0·5)	7 (0·6)	4 (0·4)	8 (0·6)	7 (1·3)
Siblings died, yes	170 (12·1)	138 (23·5)	269 (22·3)	329 (29·1)	336 (24·8)	190 (35·4)
Parents had alcoholism problem, yes	70 (5·0)	65 (11·1)	83 (6·9)	109 (9·6)	65 (4·8)	57 (10·6)
Parents had smoking problem, yes	721 (51·2)	345 (58·8)	671 (55·5)	640 (56·5)	703 (51·9)	347 (64·7)
Parents had gambling problem, yes	9 (0·6)	14 (2·4)	21 (1·7)	19 (1·7)	29 (2·1)	24 (4·5)
Bullied by neighbor kids, yes	54 (3·8)	103 (17·5)	121 (10·0)	179 (15·8)	116 (8·6)	133 (24·8)
Female guardian ever hit you, yes	160 (11·4)	183 (31·2)	386 (32·0)	208 (18·4)	323 (23·9)	217 (40·5)
Male guardian ever hit you, yes	104 (7·4)	136 (23·2)	238 (19·7)	149 (13·2)	181 (13·4)	172 (32·1)
Siblings ever hit you, yes	33 (2·3)	63 (10·7)	79 (6·5)	58 (5·1)	61 (4·5)	72 (13·4)
Parents ever quarreled, yes	142 (10·1)	176 (30·0)	361 (29·9)	216 (19·1)	280 (20·7)	228 (42·5)
Parents hit each other, yes	34 (2·4)	45 (7·7)	121 (10·0)	74 (6·5)	126 (9·3)	127 (23·7)
Childhood relationship						
Self-rated neighborhood safety						
Not at all / not very	51 (3·6)	26 (4·4)	71 (5·9)	140 (12·4)	139 (10·3)	66 (12·3)
Somewhat / very	1356 (96·4)	561 (95·6)	1137 (94·1)	992 (87·6)	1215 (89·7)	470 (87·7)
Self-rated neighborhood willingness to help						
Not at all / not very	83 (5·9)	17 (2·9)	59 (4·9)	156 (13·8)	277 (20·5)	88 (16·4)
Somewhat / very	1324 (94·1)	570 (97·1)	1149 (95·1)	976 (86·2)	1077 (79·5)	448 (83·6)
Self-rated neighborhood close-knit relationship						
Not at all / not very	21 (1·5)	8 (1·4)	26 (2·2)	45 (4·0)	108 (8·0)	42 (7·8)
Somewhat / very	1386 (98·5)	579 (98·6)	1182 (97·8)	1087 (96·0)	1246 (92·0)	494 (92·2)
Self-rated neighborhood cleanness						
Not at all / not very	448 (31·8)	217 (37·0)	412 (34·1)	433 (38·3)	478 (35·3)	215 (40·1)
Somewhat / very	959 (68·2)	370 (63·0)	796 (65·9)	699 (61·7)	876 (64·7)	321 (59·9)
Felt lonely for not having friends?						
Never / not very often	1340 (95·2)	527 (89·8)	1132 (93·7)	908 (80·2)	1184 (87·4)	445 (83·0)
Sometimes / often	67 (4·8)	60 (10·2)	76 (6·3)	224 (19·8)	170 (12·6)	91 (17·0)
Had a group of friends						
ever / not very often	193 (13·7)	35 (6·0)	115 (9·5)	335 (29·6)	575 (42·5)	108 (20·1)
Sometimes / often	1214 (86·3)	552 (94·0)	1093 (90·5)	797 (70·4)	779 (57·5)	428 (79·9)
Had a good friend						
No	665 (47·3)	124 (21·1)	373 (30·9)	621 (54·9)	986 (72·8)	244 (45·5)
Yes	742 (52·7)	463 (78·9)	835 (69·1)	511 (45·1)	368 (27·2)	292 (54·5)

Characteristics	Subpopulation 1 (N=1407)	Subpopulation 2 (N=587)	Subpopulation 3 (N=1208)	Subpopulation 4 (N=1132)	Subpopulation 5 (N=1354)	Subpopulation 6 (N=536)
Self-rated relationship with the female guardian						
Excellent	608 (43·2)	222 (37·8)	316 (26·2)	510 (45·1)	279 (20·6)	132 (24·6)
Very good	475 (33·8)	233 (39·7)	374 (31·0)	357 (31·5)	411 (30·4)	147 (27·4)
Good	193 (13·7)	74 (12·6)	221 (18·3)	152 (13·4)	307 (22·7)	98 (18·3)
Fair	130 (9·2)	56 (9·5)	283 (23·4)	112 (9·9)	334 (24·7)	143 (26·7)
Poor	1 (0·1)	2 (0·3)	14 (1·2)	1 (0·1)	23 (1·7)	16 (3·0)
Female guardian's love and affection						
Never / rarely	175 (12·4)	63 (10·7)	361 (29·9)	95 (8·4)	371 (27·4)	161 (30·0)
Sometimes / Often	1232 (87·6)	524 (89·3)	847 (70·1)	1037 (91·6)	983 (72·6)	375 (70·0)
Female guardian's effort put into watching over you						
Not at all / a little	187 (13·3)	86 (14·7)	377 (31·2)	123 (10·9)	440 (32·5)	164 (30·6)
Some / a lot	1220 (86·7)	501 (85·3)	831 (68·8)	1009 (89·1)	914 (67·5)	372 (69·4)
Female guardian treated your siblings better than you						
Not at all / a little	1383 (98·3)	543 (92·5)	847 (70·1)	1109 (98·0)	1230 (90·8)	376 (70·1)
Somewhat / very much	24 (1·7)	44 (7·5)	361 (29·9)	23 (2·0)	124 (9·2)	160 (29·9)
Female guardian preferred boys to girls						
Not at all / a little	1391 (98·9)	566 (96·4)	934 (77·3)	1121 (99·0)	1242 (91·7)	448 (83·6)
Somewhat / very much	16 (1·1)	21 (3·6)	274 (22·7)	11 (1·0)	112 (8·3)	88 (16·4)
Self-rated relationship with the male guardian						
Excellent	570 (40·5)	193 (32·9)	269 (22·3)	472 (41·7)	224 (16·5)	99 (18·5)
Very good	505 (35·9)	247 (42·1)	396 (32·8)	355 (31·4)	409 (30·2)	141 (26·3)
Good	197 (14·0)	78 (13·3)	236 (19·5)	165 (14·6)	319 (23·6)	117 (21·8)
Fair	133 (9·5)	68 (11·6)	292 (24·2)	133 (11·7)	374 (27·6)	160 (29·9)
Poor	2 (0·1)	1 (0·2)	15 (1·2)	7 (0·6)	28 (2·1)	19 (3·5)
Male guardian treated your siblings better than you						
Not at all / a little	1390 (98·8)	548 (93·4)	942 (78·0)	1116 (98·6)	1268 (93·6)	385 (71·8)
Somewhat / very much	17 (1·2)	39 (6·6)	266 (22·0)	16 (1·4)	86 (6·4)	151 (28·2)
Male guardian preferred boys to girls						
Not at all / a little	1386 (98·5)	567 (96·6)	974 (80·6)	1112 (98·2)	1237 (91·4)	432 (80·6)
Somewhat / very much	21 (1·5)	20 (3·4)	234 (19·4)	20 (1·8)	117 (8·6)	104 (19·4)
Childhood parents' health						
Parents showed continued signs of sadness or depression, yes	90 (6·4)	115 (19·6)	157 (13·0)	445 (39·3)	293 (21·6)	205 (38·2)
Parents had a long time be sick on bed, yes	115 (8·2)	97 (16·5)	155 (12·8)	357 (31·5)	224 (16·5)	182 (34·0)
Parents had a serious deformity, yes	18 (1·3)	29 (4·9)	30 (2·5)	119 (10·5)	61 (4·5)	45 (8·4)
Parents had abnormality of mind, yes	16 (1·1)	25 (4·3)	23 (1·9)	73 (6·4)	49 (3·6)	40 (7·5)
Was biological mother alive, yes	503 (35·7)	380 (64·7)	315 (26·1)	181 (16·0)	14 (1·0)	51 (9·5)
Was biological father alive, yes	315 (22·4)	252 (42·9)	115 (9·5)	87 (7·7)	5 (0·4)	19 (3·5)
Alive mother's longevity (≥80 years), yes	286 (20·3)	197 (33·6)	155 (12·8)	109 (9·6)	6 (0·4)	23 (4·3)
Dead mother's longevity (≥80 years), yes	180 (12·8)	19 (3·2)	296 (24·5)	202 (17·8)	555 (41·0)	153 (28·5)
Alive father's longevity (≥80 years), yes	187 (13·3)	141 (24·0)	53 (4·4)	37 (3·3)	1 (0·1)	7 (1·3)
Dead father's longevity (≥80 years), yes	229 (16·3)	68 (11·6)	307 (25·4)	161 (14·2)	395 (29·2)	121 (22·6)

Characteristics	Subpopulation 1 (N=1407)	Subpopulation 2 (N=587)	Subpopulation 3 (N=1208)	Subpopulation 4 (N=1132)	Subpopulation 5 (N=1354)	Subpopulation 6 (N=536)
Adulthood circumstances						
Adulthood SES						
Education						
Illiteracy	351 (24·9)	39 (6·6)	101 (8·4)	409 (36·1)	546 (40·3)	114 (21·3)
Elementary	615 (43·7)	179 (30·5)	346 (28·6)	547 (48·3)	627 (46·3)	238 (44·4)
Middle	332 (23·6)	230 (39·2)	455 (37·7)	137 (12·1)	150 (11·1)	122 (22·8)
Senior	107 (7·6)	128 (21·8)	256 (21·2)	35 (3·1)	31 (2·3)	57 (10·6)
≥College	2 (0·1)	11 (1·9)	50 (4·1)	4 (0·4)	0 (0·0)	5 (0·9)
Occupation						
Agricultural work	898 (64·0)	184 (31·6)	236 (19·7)	787 (69·8)	750 (55·6)	204 (38·3)
Non-agricultural employed	218 (15·5)	281 (48·2)	434 (36·2)	74 (6·6)	97 (7·2)	100 (18·8)
Others	288 (20·5)	118 (20·2)	528 (44·1)	267 (23·7)	502 (37·2)	228 (42·9)
Residence						
Urban	329 (23·4)	263 (44·8)	872 (72·2)	149 (13·2)	366 (27·0)	245 (45·7)
Rural	1078 (76·6)	324 (55·2)	336 (27·8)	983 (86·8)	988 (73·0)	291 (54·3)
Adulthood adversity						
Ever experienced the death of a child, yes	89 (6·3)	28 (4·8)	56 (4·6)	224 (19·8)	329 (24·3)	70 (13·1)
Ever received a physical injury, yes	7 (0·5)	72 (12·3)	28 (2·3)	159 (14·0)	42 (3·1)	121 (22·6)
Ever experienced lifetime discrimination, yes	27 (1·9)	78 (13·3)	32 (2·6)	251 (22·2)	69 (5·1)	139 (25·9)
Ever confined to bed or home for one month or more, yes	16 (1·1)	139 (23·7)	53 (4·4)	379 (33·5)	52 (3·8)	315 (58·8)
Ever hospitalized for a month or more, yes	8 (0·6)	107 (18·2)	56 (4·6)	241 (21·3)	34 (2·5)	272 (50·7)
Ever hospitalized more than three times within 1-year, yes	2 (0·1)	32 (5·5)	21 (1·7)	115 (10·2)	28 (2·1)	109 (20·3)
Ever left your job for one month or more because of health condition, yes	21 (1·5)	155 (26·4)	67 (5·5)	454 (40·1)	68 (5·0)	295 (55·0)
Didn't have a usual source of care, yes	38 (2·7)	16 (2·7)	19 (1·6)	212 (18·7)	143 (10·6)	30 (5·6)
Adulthood social support						
Was there financial support for your work, yes	44 (3·1)	89 (15·2)	110 (9·1)	84 (7·4)	40 (3·0)	62 (11·6)
Was there positive nonfinancial support or mentoring for your work, yes	80 (5·7)	176 (30·0)	199 (16·5)	137 (12·1)	54 (4·0)	88 (16·4)
Was there positive support or mentoring for your interpersonal relationships, yes	130 (9·2)	178 (30·3)	224 (18·5)	212 (18·7)	94 (6·9)	125 (23·3)
Adulthood behaviors						
Proportion of obesity, 0-1	0·1±0·3	0·2±0·4	0·2±0·3	0·1±0·3	0·1±0·3	0·2±0·3
Smoking						
Non-smoker	847 (60·2)	314 (53·5)	678 (56·1)	614 (54·2)	768 (56·7)	252 (47·0)
Ever smoker	206 (14·6)	94 (16·0)	194 (16·1)	192 (17·0)	227 (16·8)	115 (21·5)
Current smoker	354 (25·2)	179 (30·5)	336 (27·8)	326 (28·8)	359 (26·5)	169 (31·5)
Drinking						
Non-drinker	835 (59·3)	280 (47·7)	598 (49·5)	619 (54·7)	755 (55·8)	250 (46·6)
Drinker	572 (40·7)	307 (52·3)	610 (50·5)	513 (45·3)	599 (44·2)	286 (53·4)

SD=standard deviation. SES=socioeconomic status.

Table S5. Characteristics of the included and excluded study populations.

Characteristics	Total (N=12270)	Included (N=6224)	Excluded (N=6046)	p value
Chronological age, years	60·5±9·6	61·6±8·5	59·3±10·6	<0·001
PD	1·8±0·7	1·8±0·8	1·8±0·7	0·25
FI	0·2±0·1	0·2±0·1	0·1±0·1	<0·0001
Gender				
Male	5779 (47·1)	2911 (46·8)	2868 (47·4)	0·47
Female	6491 (52·9)	3313 (53·2)	3178 (52·6)	
Ethnicity				
Han	11503 (93·8)	5788 (93·0)	5715 (94·5)	<0·0001
Others	767 (6·3)	436 (7·0)	331 (5·5)	
Education*				
Illiteracy	3193 (26·1)	1560 (25·1)	1633 (27·1)	<0·0001
Elementary	5474 (44·7)	2552 (41·0)	2922 (48·4)	
Middle	2393 (19·5)	1426 (22·9)	967 (16·0)	
Senior	1038 (8·5)	614 (9·9)	424 (7·0)	
≥College	161 (1·3)	72 (1·2)	89 (1·5)	
Residence				
Urban	4674 (38·1)	2224 (35·7)	2450 (40·5)	<0·0001
Rural	7596 (61·9)	4000 (64·3)	3596 (59·5)	
Drinking[a]				
Non-drinker	6595 (53·8)	3337 (53·6)	3258 (53·9)	0·76
Drinker	5674 (46·3)	2887 (46·4)	2787 (46·1)	
Smoking[a]				
Non-smoker	6938 (56·6)	3473 (55·8)	3465 (57·3)	0·03
Ever smoker	1923 (15·7)	1028 (16·5)	895 (14·8)	
Current smoker	3408 (27·8)	1723 (27·7)	1685 (27·9)	

PD=physiological dysregulation. FI=frailty index.

[a]There were missing data on education (N=11), drinking status (N=1), and smoking status (N=1).

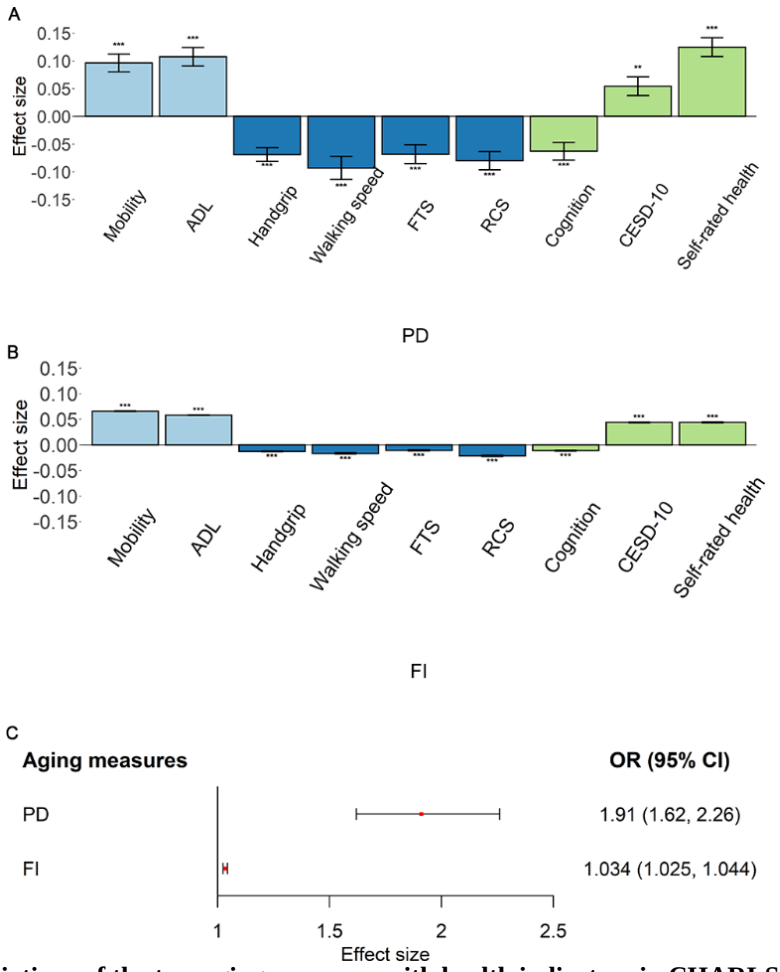

Figure S1: Associations of the two aging measures with health indicators in CHARLS.
(A) Bar chart shows the associations of PD with health indicators (except mortality). (B) Bar chart shows the associations of FI with health indicators (except mortality). The analysis of FI was performed using FI×100. In (A) and (B), effect sizes (β and corresponding 95% confidence intervals) were estimated for two measures of subjective physical functioning (mobility, and ADL), four measures of objective physical functioning (handgrip strength, walking speed, FTS, and RCS), cognitive function, mental health, and self-rated health. Groups of health indicators are denoted by different colors. Subjective physical functioning measures are shown in light blue. Objective physical functioning measures are shown in dark blue. Other aging measures are shown in green. **: p<0·01. ***: p<0·001 (C) Forest plot shows the associations of PD and FI with mortality. PD=physiological dysregulation. FI=frailty index. ADL=activities of daily living. FTS=full-tandem stand. RCS=repeated chair stand. CESD-10=The 10-item Center for Epidemiologic Studies Depression Scale. OR=odds ratio. CI=confidence interval.

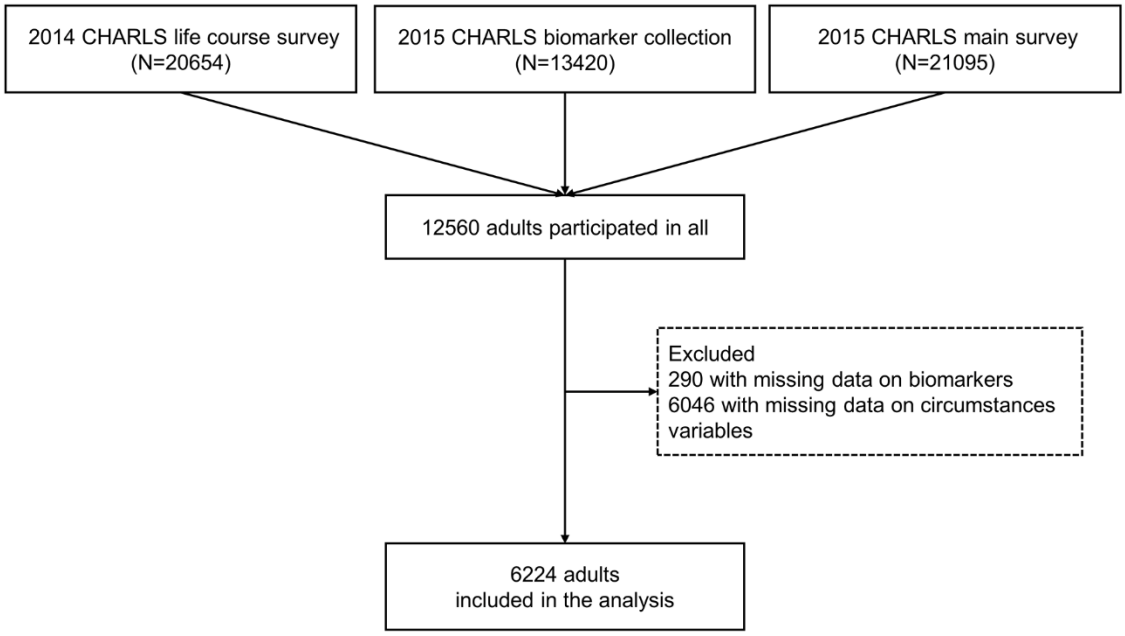

Figure S2: Flow chart of the study population.
CHARLS=the China Health and Retirement Longitudinal Study.

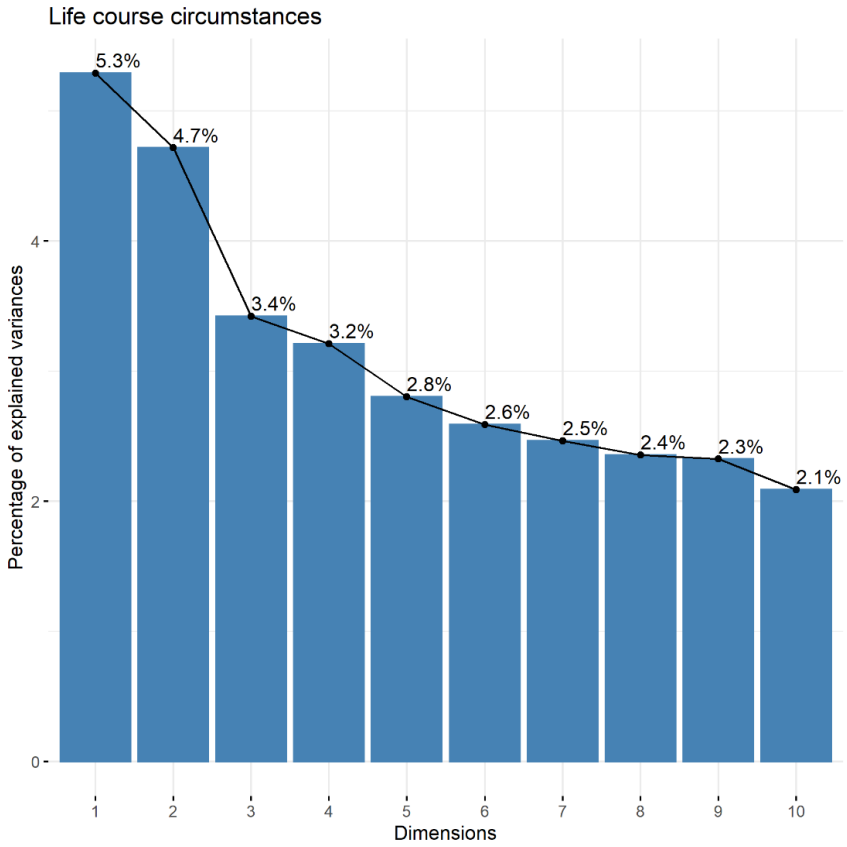

Figure S3: The scree plot of principal components analysis for life course circumstances.
The scree plot presents the percentage of explained variances for the top ten dimensions of the principal components analysis.

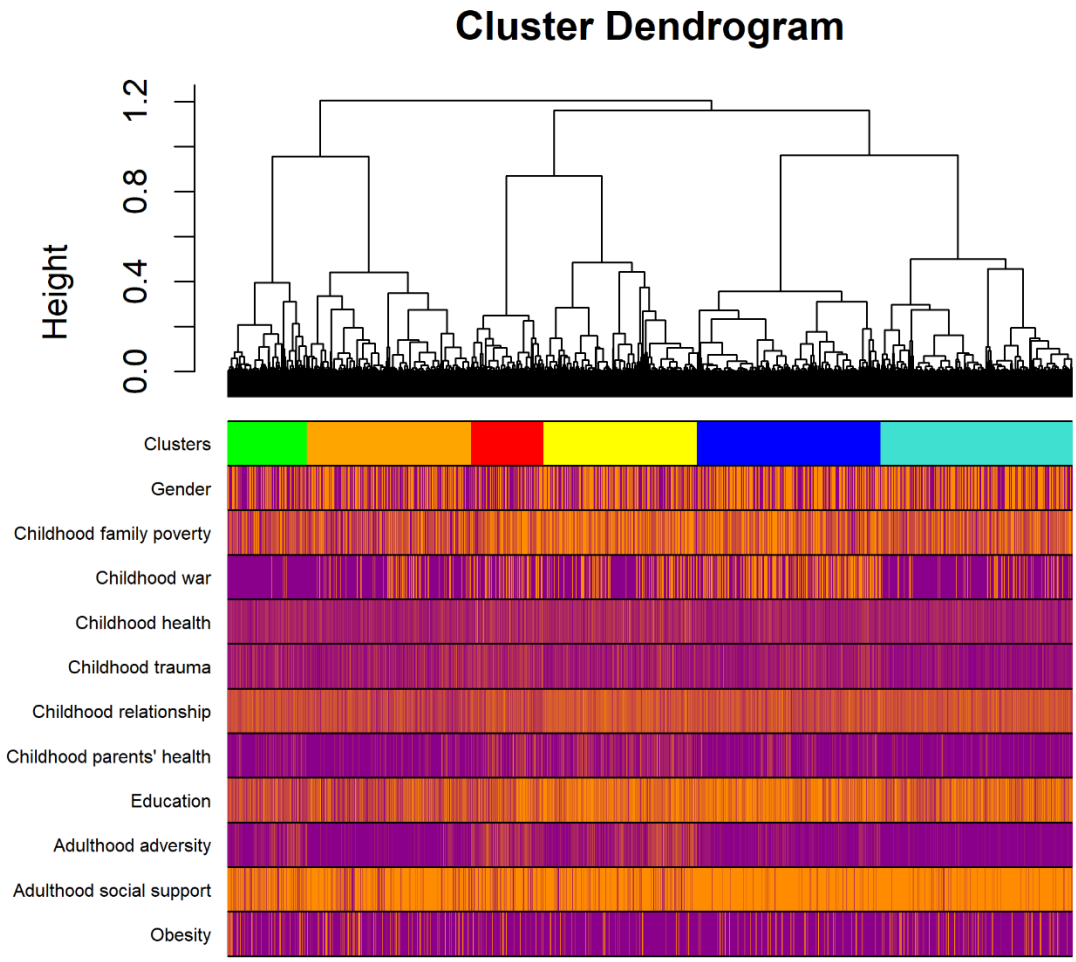

Figure S4: The cluster dendrogram.
Six subpopulations were identified including "blue" (i.e., subpopulation 5) (N=1354), "green" (i.e., subpopulation 2) (N=587), "orange" (i.e., subpopulation 3) (N=1208), "red" (i.e., subpopulation 6) (N=536), "turquoise" (i.e., subpopulation 1) (N=1407), and "yellow" (i.e., subpopulation 4) (N=1132). For the categories of these summarized measures, the closer to "darkorange", the higher dose of exposure to this risk factor (except gender).

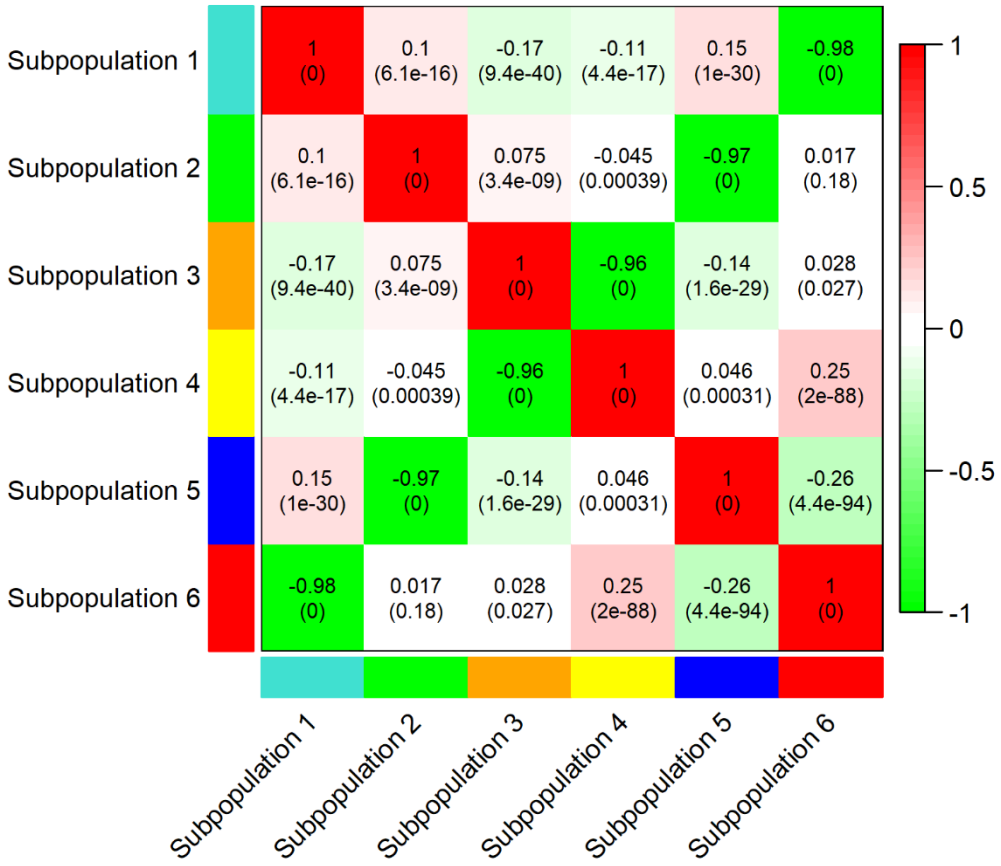

Figure S5: Correlations among the cluster memberships for the six subpopulations/clusters.
To determine what each subpopulation/cluster represents, we calculate a continuous measure (cluster membership) for each subpopulation/cluster (between -1 and 1) that indicates how strongly an adult belongs to that given subpopulation/cluster—for instance, an adult may have a score of 0·9 for the subpopulation 1 and -0·7 for the subpopulation 6, suggesting he/she is very similar to the profile representative of the subpopulation 1, but not the subpopulation 6. Each cell shows the correlation (and p value) between cluster memberships.

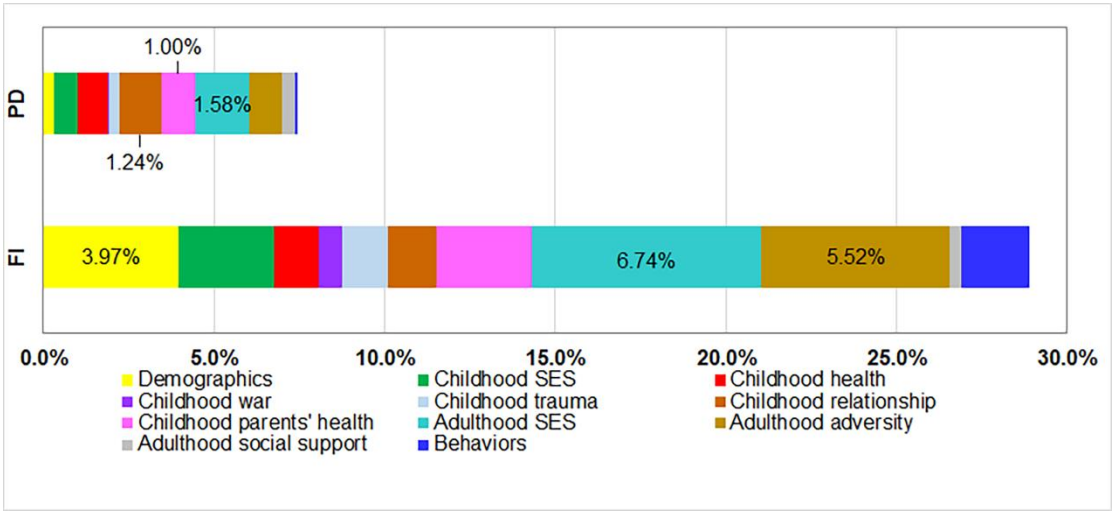

Figure S6: The contribution of all 11 study domains to PD, and FI in a sample of adults who fasted (N=5369).

The contribution values of the top three contributors were presented. Overall, all the 11 domains contributed 7·5% (bootstrap standard error=-0·0005), and 29·0% (bootstrap standard error=-0·007) of variance in PD, and FI, respectively. PD=physiological dysregulation. FI=frailty index. SES=socioeconomic status.

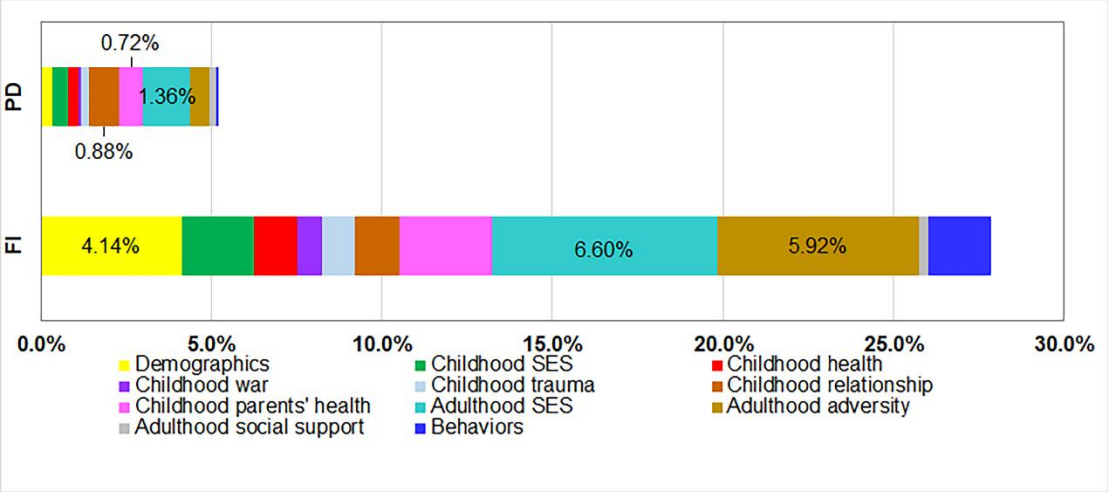

Figure S7: The contribution of all 11 study domains to PD, and FI using an individual weight with adjustment of non-response (N=6184).

The contribution values of the top three contributors were presented. Overall, all the 11 domains contributed 5·2% (bootstrap standard error=-0·0003), and 28·1% (bootstrap standard error=-0·005) of variance in PD, and FI, respectively. PD=physiological dysregulation. FI=frailty index. SES=socioeconomic status.

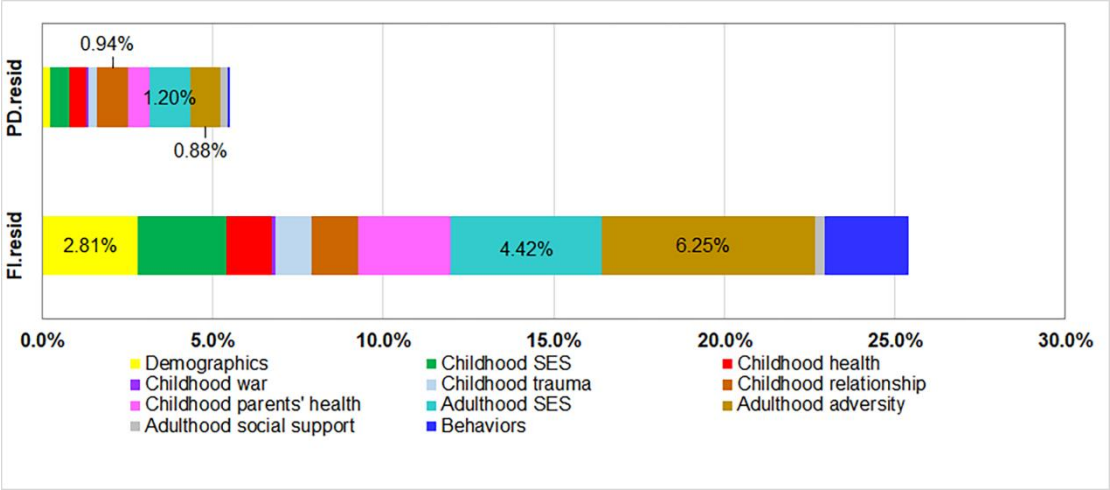

Figure S8: The contribution of all 11 study domains to PD.resid, and FI.resid (N=6224).
The contribution values of the top three contributors were presented. Overall, all the 11 domains contributed 5·5% (bootstrap standard error=0·0006), and 25·4% (bootstrap standard error=0·002) of variance in PD.resid, and FI.resid, respectively. PD.resid=residuals resulting from a linear model when regressing physiological dysregulation on chronological age. FI.resid=residuals resulting from a linear model when regressing frailty index on chronological age. SES=socioeconomic status.

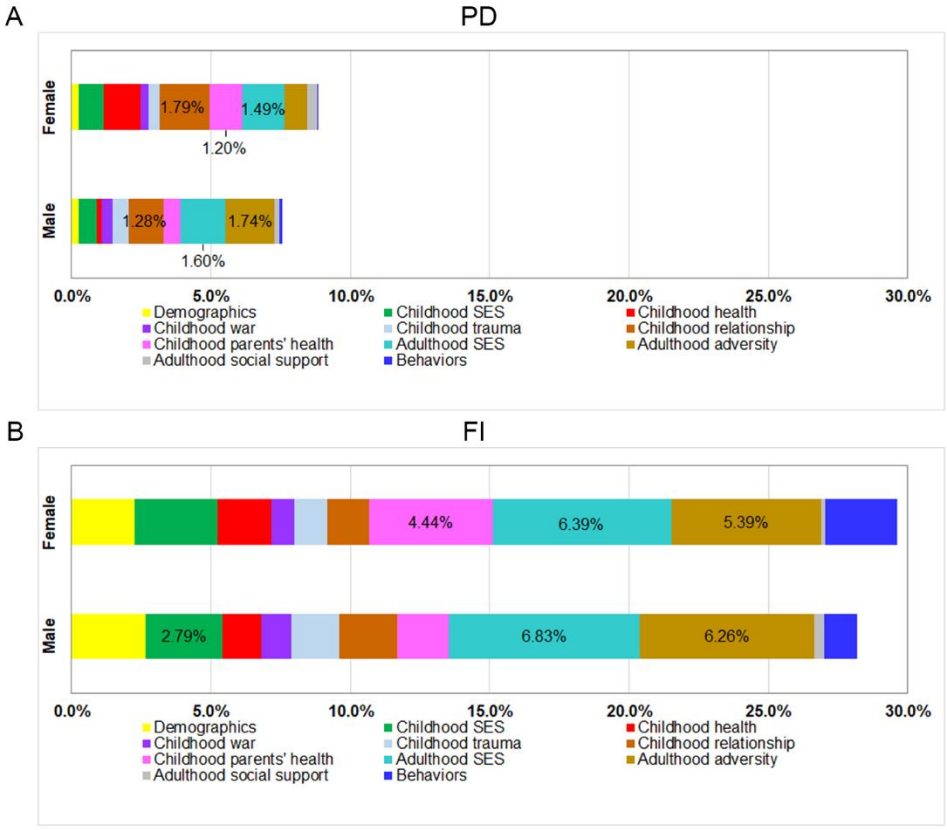

Figure S9: The contribution of all 11 study domains to PD and FI by gender.
(A) The stacked bar chart shows the contribution of 11 study domains to PD by gender. (B) The stacked bar chart shows the contribution of 11 study domains to FI by gender. The contribution values of the top three contributors were presented in (A) and (B). PD=physiological dysregulation. FI=frailty index. SES=socioeconomic status.

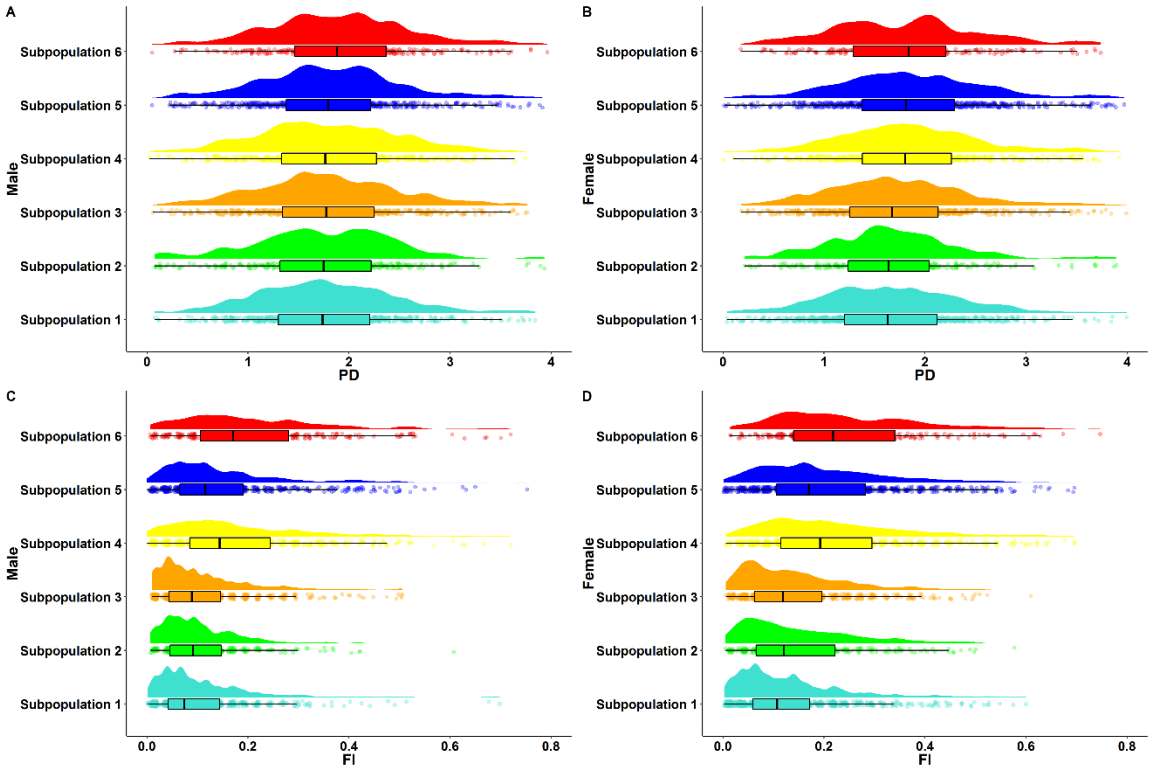

Figure S10: The distributions of PD and FI across six subpopulations by gender.
(A) The raincloud plot shows PD across the six subpopulations in male. (B) The raincloud plot shows PD across the six subpopulations in female. (C) The raincloud plot shows FI across the six subpopulations in male. (D) The raincloud plot shows FI across the six subpopulations in female. PD=physiological dysregulation. FI=frailty index.

Supplementary References

1 Chen C, Park J, Wu C, et al. Cognitive frailty in relation to adverse health outcomes independent of multimorbidity: results from the China health and retirement longitudinal study. *Aging (Albany NY)* 2020; **12**(22): 23129-45.

2 Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. *JAMA* 1963; **185**: 914-9.

3 Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). *Int J Epidemiol* 2014; **43**(1): 61-8.

4 Huang W, Zhou Y. Effects of education on cognition at older ages: evidence from China's Great Famine. *Soc Sci Med* 2013; **98**: 54-62.

5 Lei X, Smith JP, Sun X, Zhao Y. Gender Differences in Cognition in China and Reasons for Change over Time: Evidence from CHARLS. *J Econ Ageing* 2014; **4**: 46-55.

6 McArdle JJ, Fisher GG, Kadlec KM. Latent variable analyses of age trends of cognition in the Health and Retirement Study, 1992-2004. *Psychol Aging* 2007; **22**(3): 525-45.

7 Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W, Hodges JR. A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology* 2000; **55**(11): 1613-20.

8 Li J, Cacchione PZ, Hodgson N, et al. Afternoon Napping and Cognition in Chinese Older Adults: Findings from the China Health and Retirement Longitudinal Study Baseline Assessment. *J Am Geriatr Soc* 2017; **65**(2): 373-80.

9 Chen H, Mui AC. Factorial validity of the Center for Epidemiologic Studies Depression Scale short form in older population in China. *Int Psychogeriatr* 2014; **26**(1): 49-57.

10 Hufe P, Peichl A, Roemer J, Ungerer M. Inequality of income acquisition: the role of childhood circumstances. *Soc Choice Welf* 2017; **49**(3): 499-544.

11 Ferreira F, Gignoux J. The measurement of inequality of opportunity: theory and an application to Latin America. *Rev Income Wealth* 2011; **57**(4): 622-57.

12 Ferreira F, Gignoux J. The Measurement of Educational Inequality: Achievement and Opportunity. *World Bank Econ Rev* 2013; **28**: 210-46.

13 Haughton J, Khandker SR. Handbook on poverty and inequality. Washington, DC: World Bank; 2009.

14 Björklund A, Jäntti M, Roemer JE. Equality of opportunity and the distribution of long-run income in Sweden. *Soc Choice Welf* 2012; **39**(2): 675-96.

15 Shorrocks AF. Decomposition procedures for distributional analysis: a unified framework based on the Shapley value. *J Econ Inequal* 2013; **11**(1): 99-126.

16 Jusot F, Tubeuf S, Trannoy A. Circumstances and efforts: how important is their correlation for the measurement of inequality of opportunity in health? *Health Econ* 2013; **22**(12): 1470-95.

17 Juárez FWC, Soloaga I. iop: Estimating ex-ante inequality of opportunity. *Stata J* 2014; **14**(4): 830-46.

18 Shorrocks AF. The class of additively decomposable inequality measures. *Econometrica* 1980: 613-25.

19 Roemer J, Trannoy A. Equality of Opportunity: Theory and Measurement. *J Econ Lit* 2016; **54**(4): 1288-332.

20 Niehues J, Peichl A. Upper bounds of inequality of opportunity: theory and evidence for Germany and the US. *Soc Choice Welf* 2014; **43**(1): 73-99.

21 Langfelder P, Horvath S. WGCNA: an R package for weighted correlation network analysis. *BMC Bioinformatics* 2008; **9**: 559.

22 Cohen AA, Milot E, Yong J, et al. A novel statistical approach shows evidence for multi-system physiological dysregulation during aging. *Mech Ageing Dev* 2013; **134**(3-4): 110-7.

23 Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005; **173**(5): 489-95.