DATA

Data for the analyses in this article come from the National Health and Nutrition Examination Surveys (NHANES). NHANES surveys include collection of information from an interview, a clinical examination, and laboratory tests. NHANES III was a nationally representative, cross-sectional survey of the noninstitutionalized U.S. population from 1988 through 1994 (National Center for Health Statistics 1994). Beginning in 1999, NHANES moved to continuous surveying and now releases data in two-year modules. For the analysis of time change, we use data from 1999–2000, and then the combined information for 2003–2006. The NHANES III data are supplemented with mortality follow-up data from the National Death Index through the year 2000. These data are used for the mortality analysis.

Sample Size

The size of the sample (ages 65+) used in the time-trend analysis is shown in Table S1. Sample size varies somewhat because only fasting samples are used for low-density lipoprotein (LDL) cholesterol and triglycerides. In addition, serum homocysteine was included in only part of the time period (1991–1994).

Table S1. Sample Number for Analysis of Biomarkers Change (Ages 65+) in NHANES 1988–1994, 1999–2000, and 2003–2006

Indicator	NHANES 1988–1994	NHANES 1999–2000	NHANES 2003–2006
Systolic Blood Pressure	3,876	1,076	1,453
Diastolic Blood Pressure	3,823	1,052	1,437
Total Cholesterol	4,179	1,090	2,347
HDL Cholesterol	4,157	1,088	2,346
Fasting LDL Cholesterol	1,632	441	1,000
Fasting Triglycerides	1,751	451	1,017
Body Mass Index	4,461	1,156	2,405
Glycated Hemoglobin	4,228	1,112	2,376
C-Reactive Protein	3,626	1,090	2,021
Serum Homocysteine	1,723	1,115	2,373

Note: HDL = high-density lipoprotein; LDL = low-density lipoprotein.

The sample for the racial/ethnic groups for ages 40+ are shown in Table S2.

In the mortality analysis, we use data on the 9,479 sample members ages 40 and older who provide data on at least 4 of the 10 indicators of risk and all seven diseases. For the mortality analysis among those aged 60+, the 3,323 sample members also had to have information on the nine frailty indicators used in this analysis.

All analyses are weighted to reflect the noninstitutionalized population of older adults in the United States.

MEASURES

Biological Factors

Clinical risk is measured using 10 indicators of physiological status. Values in the range regarded as clinically significant (or empirically defined through other studies if no clinical

Table S2. Sample *N* by Race/Ethnicity in Biomarkers and Diseases (NHANES 1988–1994) and Frailty Indicators (NHANES 2003–2006)

	Ages 40+			Ages 60+		
Indicators	White/ Other	Black	Hispanic	White/ Other	Black	Hispanic
Biomarkers						
Systolic blood pressure	2,955	1,020	1,008	1,599	444	514
Diastolic blood pressure	2,955	1,020	1,008	1,599	444	514
Pulse rate at 60 sec.	3,425	1,176	1,157	1,951	529	613
Total cholesterol	3,406	1,140	1,158	1,934	516	604
HDL cholesterol	3,405	1,140	1,158	1,933	516	604
Body mass index	3,485	1,207	1,183	1,982	536	614
Glycated hemoglobin	3,433	1,155	1,165	1,956	526	608
C-reactive protein	2,981	924	1,015	1,684	410	521
Fibrinogen	—[a]			—[a]		
Albumin	3,390	1,132	1,153	1,924	510	601
Diseases						
Diabetes	3,485	1,214	1,190	1,983	543	623
Congestive heart failure	3,548	1,237	1,202	2,025	557	629
Heart attack	3,555	1,242	1,208	2,031	561	633
Stroke	3,558	1,242	1,208	2,034	561	633
Bronchitis/emphysema	3,566	1,242	1,210	2,040	561	635
Cancer	3,560	1,238	1,211	2,036	560	636
Angina	3,550	1,236	1,205	2,028	556	631
Frailty						
Cognitive function				2,962	1,007	1,051
Immune function				2,692	885	909
Kidney function				2,332	750	836
Lung function				2,981	1,014	1,055
Performance on timed walk test				2,827	969	1,012
Performance on chair stand				2,840	968	1,017
Performance on lock/unlock with a key				2,836	954	1,012
Performance on timed tandem stand				2,801	946	1,005

Note: HDL = high-density lipoprotein.

[a]Not available.

cutpoint is available) are coded as high-risk (see Appendix Table A1 of the main article). Individuals outside that range are not at high risk for that indicator. The 13 indicators include four indicators of cardiovascular health (high systolic blood pressure, high and low diastolic blood pressure, and high pulse); six indicators of metabolic risk (high and low total cholesterol, low high-density lipoprotein [HDL] cholesterol, high glycated hemoglobin

[HbA1c], and high and low body mass index [BMI]); and three indicators of inflammation (high fibrinogen, and C-reactive protein, and low albumin). Where available, homocysteine was also examined. Some of the indicators were collected in the physical exam: diastolic and systolic blood pressure, pulse, and BMI. Assays of blood samples were used to estimate levels of total and HDL cholesterol and HbA1c. Measures of inflammation were also obtained via blood samples.

Different assays were used to measure CRP in NHANES 1988–1994 and NHANES 1999 and after; NHANES 1999–2006 CRP assay values had to be adjusted to be comparable with NHANES 1988–1994, using information derived from comparisons in another sample made by the laboratory doing both assays. The correlation at levels above 3.0 mg/L between the two assays from two NHANES time periods was .993. The equation relating NHANES CRP values for 1988–1994 and 1999–2006 indicates we need to reduce the NHANES 1999–2006 values in the original data by 9.9%.

HDL analysis methods were changed between 1999–2002 and 2003–2006. In earlier dates, the HDL cholesterol was mostly analyzed using heparin manganese precipitation and a direct HDL immunoassay; in later dates, all HDL cholesterol samples were analyzed using the direct HDL cholesterol immunoassay method. Because the HDL cholesterol values showed an average increase of 3.0 mg/dL in NHANES 2003–2006 compared with NHANES 1999–2002, we adjusted this effect of different methods by subtracting 3 from the HDL values in NHANES 2003–2006.

Diseases

Sample members self-report during an interview whether a doctor has ever told them that they have a number of diseases, which include the major causes of death: heart attack, stroke, congestive heart failure, bronchitis and emphysema, cancer (except skin cancer) and diabetes. Presence of possible angina based on answers to the Rose Angina Questionnaire is also coded from responses to the Rose angina scale.

Frailty

There are eight frailty indicators, including biomarkers and performance measures of physical, cognitive, and organ functioning. Immune functioning is indicated by high levels of CMV virus: a CMV optimal density greater than 3.0 is defined as high. Lung function is measured by the ratio of the forced expiratory volume (FEV) at 1 second to the forced vital capacity (FVC), which provides a measure that controls for body size. The quartile with the lowest lung function is deemed frail. Kidney function is measured using cystatin C, and a level greater than 1.55 mg/L is defined as poor kidney function.

Cognitive functioning and measures of performance of physical functioning are available only for those aged 60+. Cognitive functioning was assessed based on tests of both immediate and delayed recall of details of a story, recall of words, and orientation. Scores ranged from 0 to 26, and the 10% with the worst cognitive functioning were designated as having poor functioning. Poor measured physical performance is indicated by problems with performance on a set of tasks related to mobility, strength, and balance. The 25% of the sample with the slowest completion on each of four tests are deemed as having poor performance on a test: an eight-foot walk performed twice at usual walking speed, a rise from an armless chair five times, the time able to stand (for up to 10 seconds) with the heel of one foot directly in front of the toes of the other foot (tandem stand), and the time to unlock and lock a lock with a key (within 60 seconds).

Mortality

NHANES III participants were linked to National Death Index reports of death through the year 2000. We examine deaths occurring within five years of interview. Deaths from violent causes are eliminated. Within the sample, 11.46% (N = 1,234) of persons aged 40+ died.

Missing

We describe the missing data specifically for the mortality analysis. Our sample includes those who have at least 4 (out of 10) markers of physiological dysregulation, which eliminates 30 cases. There are seven indicators of disease, and information on all seven is required to stay in the analytic sample, eliminating 158 cases. Missing data for the indicators of physiological dysregulation and disease eliminated 2.0% (N = 89) of individuals aged 40–59 and 1.9% (N = 99) of those aged 60+.

The indicators of cognitive performance and performance functioning tests were given only to the age 60+ group. Only 32 cases had missing data on the cognitive measure. Performance indicators of difficulty walking, chair stands, small motor ability, and balance had more missing data (277 for walking, 264 for chair stands, 279 for key-in-lock, 324 for tandem stand). There are no missing values on the measure of lung function for those ages 60+. The use of stored sera to perform assays long after the interview reduced the sample size by 628 for CMV and by 836 for cystatin C. Cystatin C was measured for all of the age 60+ with surplus sera, but it was only measured in a randomly selected quarter of the sample aged 12–59. The total reduction in the sample size for the missing frailty indicators is 1,203 of the 5,154 cases (23.3%).