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ORIGINAL RESEARCH

Changes in Cardiovascular Risk Factors and Cardiovascular Events in the Elderly Population

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BACKGROUND: This study examines changes in the ideal cardiovascular health (CVH) status and whether these changes are associated with incident cardiovascular disease (CVD) and mortality in the elderly Asian population.

METHODS AND RESULTS: In the Korea National Health Insurance Service–Senior cohort aged ≥60 years, 208 673 participants without prior CVD, including 109 431 who showed changes in CVH status, were assessed. The association of the changes in cardiovascular risk factors with incident CVD was assessed from 2004 to 2014 in the elderly (aged 60–74 years) and very elderly (≥75 years) groups. During the follow-up period (7.1 years for CVD and 7.2 years for mortality), 19 429 incident CVD events and 24 225 deaths occurred. In both the elderly and very elderly participants, higher CVH status resulted in a lower risk of CVD and mortality. In the very elderly participants, compared with consistently low CVH, consistently high CVH (subhazard ratio, 0.41; 95% CI, 0.23–0.73) was associated with a lower risk of CVD. This trend was consistently observed in the elderly population. In the very elderly participants, total cholesterol level was not informative enough for the prediction of CVD events. In both the elderly and very elderly groups, body mass index and total cholesterol were not informative enough for the prediction of all-cause mortality.

CONCLUSIONS: In both the elderly and very elderly Asian populations without CVD, a consistent relationship was observed between the improvement of a composite metric of CVH and the reduced risk of CVD. Body mass index and total cholesterol were not informative enough for the prediction of all-cause mortality in both the elderly and very elderly groups.

Key Words: cardiovascular disease ■ cardiovascular health ■ elderly ■ mortality

The leading cause of death in the elderly is cardiovascular disease (CVD). Prevention of cardiovascular events in elderly participants presents a therapeutic challenge that goes beyond the general underrepresentation of the elderly in clinical trials.[1,2]

As a complementary prevention strategy for CVD, primary prevention, which prevents the development of CVD, is increasingly being emphasized.[3] The American Heart Association developed a simple tool consisting of 7 metrics (nonsmoking, ideal body weight, physical activity, diet, blood pressure, fasting blood glucose, and total cholesterol level) to promote ideal cardiovascular health (CVH). The substantial benefits of high CVH and ideal metrics for the prevention of incident CVD events and mortality have been reported.[4–6] Among a group of middle-aged participants without CVD, there was a significant reduction of the CVD risk with the increase of ideal metrics and CVH score.[6] However, whether changes in CVH status are related to the development of incident CVD and mortality is unknown in the elderly population.

By using the serial examination data of the Korean National Health Insurance Service (NHIS)–Senior cohort,[7] this study examined changes in the ideal CVH

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CLINICAL PERSPECTIVE

What Is New?

- In both the elderly (aged 60–74 years) and very elderly (aged ≥75 years) populations, a consistent relationship was observed between the improvement of a composite metric of cardiovascular health and reducing the risk of cardiovascular disease.
- However, among the individual health factors, body mass index and total cholesterol were not informative enough for the prediction of all-cause mortality in both the elderly and very elderly populations.

What Are the Clinical Implications?

- Our findings highlight that improving the status of cardiovascular health is beneficial for the elderly and very elderly as well.

Nonstandard Abbreviations and Acronyms

ARIC	Atherosclerosis Risk in Communities
CVH	cardiovascular health
NHIS	National Health Insurance Service
sHR	subhazard ratio

status and whether the improvement of CVH status was beneficial for the prevention of incident CVD and mortality in the elderly Asian population.

METHODS

All data and materials have been made publicly available at the NHIS of Korea. The data can be accessed on the National Health Insurance Data Sharing Service homepage of the NHIS (http://nhiss.nhis.or.kr). Applications to use the NHIS data will be reviewed by the inquiry committee of research support and, once approved, raw data will be provided to the authorized researcher for a fee at several permitted sites.

Data were collected from the NHIS–Senior database, which included data for 558 147 individuals selected by a 10% simple random sampling method from a total of 5.5 million subjects aged ≥60 years in the National Health Information Database.[8,9] The NHIS–Senior database covers the following parameters: sociodemographic and socioeconomic information, insurance status, health checkup examinations, and records of participants' medical and dental histories. These parameters were stratified to cover 13 years (2002–2014) and anonymized to protect the privacy of individuals within the cohort study. This study was approved by the institutional review board of the Yonsei University Health System (4-2020-0674). The need for informed consent was waived. The NHIS–Senior database used in this study was established by the NHIS in Korea.

Study Population

From the Korean NHIS–Senior database, 312 736 participants who had a health checkup between 2005 and 2012 were selected, and follow-up data were reviewed until December 2014. The exclusion criteria were as follows: (1) participants who had an ischemic stroke or transient ischemic attack before enrollment (n=41 993), (2) participants who had a myocardial infarction before enrollment (n=6359), (3) participants who had a hemorrhagic stroke before enrollment (n=1357), (4) participants with vascular disease (n=10 498), (5) participants who had a malignancy before enrollment (n=27 514), (6) participants with a body mass index (BMI) of <18.5 kg/m^2 (n=10 139); and (7) those with missing data (n=6203). Finally, we included 208 673 participants, of whom 109 431 had at least 2 health checkups and were without CVD between the first and second examination.

CVH Metrics and Status

To characterize the ideal CVH status, we applied 6 American Heart Association guideline metrics (total cholesterol level, fasting blood glucose level, blood pressure, BMI, cigarette smoking, and exercise) and the cutoff definition for ideal, intermediate, or poor status for each CVH metric (Table S1).[3] Information on these 6 metrics was obtained through routine health checks and laboratory measurements. At each test cycle, an interview and physical examination were performed for each patient, and information on medical history and drug use was collected.

We stratified the participants into 3 groups according to the number of ideal metrics as follows: high (5+ ideal metrics), moderate (3 or 4 metrics), and low (≤2 metrics).[4,5] A continuous 12-point CVH score assigning 0 points for poor metrics, 1 point for intermediate metrics, and 2 points for ideal metrics was also calculated.[10] Change in CVH status was examined between the first and second health checkups of the participants with 6 metrics at both time points. All the participants were required to be free of a CVD event between the first and second examinations (Figure S1).

Covariates

The sociodemographic variables included age, sex, economic status, and living in metropolitan cities. The baseline economic status was determined on the basis of the relative economic levels categorized

into 10 levels according to their health insurance premiums in the index year. We obtained information on selected comorbid conditions from inpatient and outpatient hospital diagnoses. Baseline comorbidities were defined using the medical claims and prescription drug information before the index date. To ensure diagnostic accuracy, the participants were considered to have comorbidities when their condition was a discharge diagnosis or had been confirmed at least twice in an outpatient setting, in line with previous studies that used data from the NHIS database (Table S2).[11,12]

Outcomes

The primary outcome was time to first CVD (combination of coronary heart disease and ischemic stroke or systemic embolism). Coronary heart disease was defined from any discharge diagnoses (*International Classification of Diseases , Tenth Revision* (*ICD-10*) codes for acute myocardial infarction [I21x and I22x], chronic ischemic heart disease [I25.2, I25.5, I25.6, I25.8, and I25.9], or procedure codes for coronary revascularization [M6551, M6552, M6561, M6563, M6562, M6564, M6571, M6572, M6634, O1641, OA641, O1642, OA642, O1647, and OA647]). Ischemic stroke was defined from any discharge diagnoses (*ICD-10* codes I63 and I64) with concomitant brain imaging studies. The accuracy of the diagnosis of an ischemic stroke based on the NHIS claims data was previously validated.[9,12–16] The definitions of the clinical outcomes are presented in Table S2. The same patient could have >1 study outcome during the study duration, but only the first event of each outcome was considered in the study.

The secondary outcome was mortality. Information on death (date and causes of death) was confirmed from the National Population Registry of the Korea National Statistical Office with unique personal identification numbers, in which the central registration of death was conducted on the basis of death certificates.[9,12–16] The NHIS and National Statistical Office are national agencies serving all Korean residents, so this approach provides a complete event check. Follow-ups for CVD and mortality were conducted until December 2014. We also analyzed cause-specific mortality based on causes of death confirmed by Korean National Statistical Office, because health metrics can be related to non–CVD-related mortality.

Sensitivity Analysis

The analysis was repeated with 4 groups of changes in CVH status, as used in the Framingham Offspring Study.[17] The change in the number of ideal metrics between the first and second health checkups as the exposure was evaluated in the Cox analysis by using the unchanged category as reference. We also investigated the associations of time-varying CVH and changes in the individual CVH metrics with the outcomes.

Statistical Analysis

The 2 steps of the analysis conducted in this study are summarized in Figure S1.

In the Cox proportional hazard regression analysis, CVH status between the first and fifth tests were used as time-varying variables. Of the 3 versions of CVH status (category CVH status [low, medium, and high], ideal number of metrics [range, 0–6], and 12-point CVH score), only 1 version of CVH status was used in each Cox proportional hazard regression according to the purpose of each analysis. At each date of an event (CVD or death), the model used the CVH exposure before the event. Coronary heart disease and ischemic stroke/systemic embolism were investigated as a composite CVD end point as well as separate results. In the analysis of the composite CVD end point, the 2025 participants had both the occurrence of coronary heart disease and ischemic stroke/systemic embolism. In this case, on the date of the first event, follow-up was stopped, and the composite CVD end point was measured. The Fine and Gray method was used to consider death as a competing risk when assessing the composite CVD end point, coronary heart disease, and ischemic stroke or systemic embolism.[18] The proportional hazards assumption was tested on the basis of Schoenfeld residuals.[19]

The changes in CVH categories between the first and second health examination yielded 9 possible combinations of CVH statuses. In these analyses, follow-up for CVD and mortality began from the second examination. Participants with at least 1 missing CVH metric in the second examination were removed from analysis. The subhazard ratio (sHR) of CVD and hazard ratio of all-cause mortality for each combination of changes in CVH status were computed in the models using the consistently low CVH as the reference category. All models were adjusted for sex, age, economic status, Hospital Frailty Score, and living in metropolitan cities. The proportional hazard assumption was evaluated by visual inspection of the survival curves and the Kolmogorov test.

The individuals without a second health checkup or those with CVD between the first and second health checkup were excluded from the analysis of the changes in CVH status. To account for attrition between included and excluded subjects, we conducted an additional analysis using inverse probability of attrition weights. The weights for each individual were calculated at the first and second health checkup using

the inverse of the estimated probabilities of being without CVD and receiving the next health checkup. The weights were stabilized by the baseline variables of sex, age, economic status, Hospital Frailty Score, living in metropolitan cities, and comorbidities.

Because multiple comparisons were made on the CVH variables, we used the Bonferroni correction, the most conservative approach for declaring significance. Differences were significant if $P<0.0083$. The statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and R version 3.3.2 (The R Foundation for Statistical Computing, Vienna, Austria; www.R-project.org).

RESULTS

Baseline Characteristics

The study population included 208 673 participants free of CVD who had data on all 6 CVH metrics at baseline. The mean (SD) age of the study population at baseline was 70.6 years (5.4 years), and 42.5% of the population were men. The comparison of the baseline characteristics between the elderly (aged 60–74 years) and very elderly participants (≥75 years) are presented in Table 1. Compared with the elderly participants, very elderly participants had more comorbidities including hypertension, diabetes mellitus, dyslipidemia, and osteoporosis (Table 1).

Table 1. Baseline Characteristics

Characteristics	Elderly, 60–74 y, N=167 317	Very Elderly, ≥75 y, N=41 356	*P* Value
Age, mean (SD), y	68.5 (3.1)	79.2 (3.8)	<0.001
Men	74 288 (44.4)	14 383 (34.8)	<0.001
Economic status, 0–10	7.0 (4.0–9.0)	7.0 (3.0–9.0)	<0.001
Low, 0–4	52 329 (31.3)	13 235 (32.0)	
Middle, 5–7	39 700 (23.7)	8404 (20.3)	
High, 8–10	75 288 (45.0)	19 717 (47.7)	
Living area			
Small city or rural area	100 798 (60.2)	26 198 (63.3)	<0.001
Metropolitan city	66 519 (39.8)	15 158 (36.7)	
Hypertension	69 373 (41.5)	21 622 (52.3)	<0.001
Diabetes mellitus	22 790 (13.6)	5874 (14.2)	0.002
Dyslipidemia	52 086 (31.1)	11 714 (28.3)	<0.001
Osteoporosis	46 229 (27.6)	14 646 (35.4)	<0.001
CVH status no. of ideal metrics			
Low, 0–2	69 905 (41.8)	15 824 (38.3)	<0.001
Moderate, 3–4	87 769 (52.5)	23 279 (56.3)	
High, 5–6	9643 (5.8)	2253 (5.4)	
No. of ideal metrics, median (IQR)*	3.0 (2.0–4.0)	3.0 (2.0–4.0)	<0.001
12-Point CVH score, median (IQR)†	7.0 (6.0–9.0)	8.0 (6.0–9.0)	<0.001

Values are reported as number (%) unless otherwise indicated. The relative economic levels categorized into 10 levels according to their health insurance premiums. CVH indicates cardiovascular health; and IQR, interquartile range.

*The CVH metrics included nonsmoking, body weight, physical activity, blood pressure, fasting blood glucose, and total cholesterol.

†The continuous 12-point CVH score (range, higher score indicating higher CVH) was calculated by assigning 0 (poor), 1 (intermediate), and 2 (ideal) points to each of the 6 metrics and summing them.

Prevalence of CVH Status During the Total Follow-Up Period

The baseline characteristics of the study population and the characteristics at each examination are presented in Table S3. The proportion of high CVH status was 5.7% at the first checkup. Those who attended 5 examinations (the maximum) were more likely to be healthy, with the proportion of participants with a high CVH status of 14.1%. Distribution of the number of ideal cardiovascular health metrics at each wave was same in the total study population, and elderly and very elderly population.

Time-Varying CVH and Risks of CVD and Mortality

The median follow-up period starting from baseline was 7.1 years (interquartile range [IQR], 4.6–7.9 years) for CVD and 7.2 years (IQR, 4.9–8.0 years) for mortality. During the follow-up period, 19 429 incident CVD events (9932 coronary heart disease events and 11 522 ischemic stroke or systemic embolism events) and 24 225 deaths occurred. The median times to CVD (2.6 years [IQR, 1.3–4.0 years] versus 2.8 years [IQR, 1.3–4.3 years], $P=0.009$) and all-cause death (3.1 years [IQR, 1.7–4.5 years] versus 3.3 years [IQR, 1.9–4.7 years], $P=0.001$) were significantly short in the very elderly than elderly. The time to CVD and all-cause mortality according to baseline cardiovascular health is presented in Table S4. After adjustment of clinical variables and competing risk of mortality, in the very elderly participants, compared with low CVH, moderate CVH (sHR, 0.82; 95% CI, 0.77–0.87), and high CVH (sHR, 0.53; 95% CI, 0.46–0.61) were associated with a lower risk of CVD (Table 2). Similarly, CVD risk was significantly reduced for each additional time-varying ideal metric (sHR, 0.86; 95% CI, 0.84–0.89) and point in the 12-point CVH score (sHR, 0.87; 95% CI, 0.85–0.88; Table 2). Similar results were observed for all-cause mortality (Table 2), coronary heart disease, ischemic stroke/systemic embolism (Table S5), and cause-specific mortality (Table S6). This trend was consistently observed in the elderly population (aged 60–74 years). The incidence rates for CVD and all-cause mortality according to the CVH category,

Table 2. Time-Varying Cox Proportional Hazard Model for Incident Cardiovascular Disease and All-Cause Mortality

	CVH Status, No. of Ideal Metrics			Per Additional Ideal Metric*	Per 1-Point Increase in the CVH Score*
	Low, 0–2	Moderate, 3–4	High, 5–6		
Cardiovascular disease	Adjusted subhazard ratio (95% CI)†				
Elderly 60~74 y, n/total n=13 761/167 317	1 [Reference]	0.73 (0.71–0.75)‡	0.44 (0.41–0.47)‡	0.82 (0.81–0.83)‡	0.85 (0.85–0.86)‡
Very elderly ≥75 y, n/total n=5668/41 356	1 [Reference]	0.82 (0.77–0.87)‡	0.52 (0.46–0.60)‡	0.86 (0.84–0.88)‡	0.87 (0.85–0.88)‡
All-cause mortality	Adjusted hazard ratio (95% CI)§				
Elderly 60~74 y, n/total n=14 438/99 532	1 [Reference]	0.86 (0.82–0.90)‡	0.55 (0.51–0.58)‡	0.93 (0.91–0.94)‡	0.90 (0.89–0.90)‡
Very elderly ≥75 y, n/total n=9787/41 356	1 [Reference]	0.95 (0.90–1.00)	0.71 (0.66–0.77)‡	0.95 (0.93–0.97)‡	0.93 (0.92–0.94)‡

CVH, indicates cardiovascular health.
*A linear model was used for the analysis, per additional ideal metric and per 1-point increase in the 12-point CVH score.
†Cardiovascular disease was adjusted for sex, age, economic status, Hospital Frailty Score, and living in metropolitan cities, and competing risk of death.
‡$P<0.0083$ for differences reported.
§All-cause mortality was adjusted for sex, age, economic status, Hospital Frailty Score, and living in metropolitan cities.

number of ideal metrics, and level of 12-point CVH score at baseline are presented in Table 3.

The time-varying Cox proportional risk model for the association of individual CVH metrics with the occurrence of CVD event and all-cause mortality is presented in Table S7. In the very elderly participants, BMI and total cholesterol level were not appropriate for the prediction of CVD events and all-cause mortality. In the elderly participants, all 6 metrics were appropriate for the prediction of CVD events.

Table 3. Incidence Rates for Cardiovascular Disease and All-Cause Mortality According to Measures of Baseline Cardiovascular Health

	Incidence Rate per 1000 Person-Years (95% CI)			
	Cardiovascular Disease		All-Cause Mortality	
	Elderly, 60~74 y, N/Total N=14 260/173 109	Very Elderly, ≥75 y, N/Total N=6234/45 379	Elderly, 60~74 y, N/Total N=15 641/173 109	Very Elderly, ≥75 y, N/Total N=11 507/45 379
CVH status, no. of ideal metrics				
Low, 0–2	15.5 (15.1–15.9)	29.3 (28.2–30.5)	13.8 (13.5–14.2)	43.2 (41.8–44.6)
Moderate, 3–4	11.3 (11.0–11.6)	25.0 (24.1–25.9)	12.6 (12.3–12.5)	43.9 (42.8–45.1)
High, 5–6	6.4 (5.8–7.1)	18.8 (16.3–21.6)	9.8 (9.0–10.6)	40.7 (37.0–44.6)
CVH status per no. of ideal metrics				
0	22.2 (19.8–24.8)	41.8 (33.2–51.9)	18.8 (16.7–21.2)	53.3 (43.9–64.1)
1	16.8 (16.1–17.6)	31.4 (29.1–33.8)	13.8 (13.2–14.5)	40.3 (37.8–42.9)
2	14.6 (14.2–15.1)	28.1 (26.8–29.5)	13.6 (13.2–14.0)	43.9 (42.3–45.6)
3	12.2 (11.8–12.6)	26.2 (25.1–27.4)	13.2 (12.8–13.5)	44.0 (42.5–45.5)
4	9.9 (9.5–10.3)	23 (21.6–24.4)	11.7 (11.2–12.1)	43.8 (41.9–45.7)
5	6.5 (5.8–7.2)	19.6 (16.9–22.6)	9.7 (8.9–10.5)	42.1 (38.2–46.3)
6	5.4 (3.5–7.9)	9.3 (4.0–18.4)	11.1 (8.4–13.5)	24.1 (14.9–36.8)
CVH status per points on the CVH score				
1 or 2	33.6 (27.3–40.9)	49.5 (31.4–74.4)	27.1 (21.7–33.4)	78.9 (56.4–107.4)
3 or 4	22.8 (21.5–24.1)	39.1 (35.3–43.1)	19.7 (18.5–20.9)	52.1 (47.9–56.6)
5 or 6	16.1 (15.6–16.6)	31.2 (29.7–32.8)	15.2 (14.8–15.7)	46.2 (44.4–48.0)
7 or 8	12.3 (12.0–12.6)	25.4 (24.4–26.5)	12.6 (12.3–12.9)	42.7 (41.5–44.0)
9 or 10	8.8 (8.4–9.1)	21.4 (20.2–22.7)	10.2 (9.8–10.6)	40.5 (38.8–42.3)
≥11	6.4 (5.5–3.5)	17.3 (14.0–21.2)	9.0 (8.0–10.1)	37.3 (32.4–42.7)

CVH, indicates cardiovascular health.

Changes in CVH Status from the First and Second Health Examinations

Changes in CVH status were investigated and calculated in 109 431 individuals. The median interval for participants with all 6 metrics at both time points was 2.0 years (IQR, 1.6–2.8 years). The characteristics of the individuals included in this analysis, as compared with those of the participants, were not examined in the second checkup (n=97 566) and with CVD in the interval (n=1676), and are shown in Table S8.

Figures 1A and 1B and Figure S2 show that 22.1% (n=3740) of the very elderly participants had improved CVH mostly from low to moderate status (15.6%) and from moderate to high status (5.6%), and only 0.8% improved from low to high status. In 15.8% (n=2674) of the very elderly participants with worse cardiovascular health over time, 11.8% went from moderate to low, 3.4% from high to moderate, and 1.5% from high to low cardiovascular health. Stable moderate CVH was more prevalent in the elderly women than in the elderly men (Figures 2A and 2B) but was similarly prevalent regardless of high or low economic status (Figures 2C and 2D). The baseline characteristics of the participants according to the patterns of the changes in CVH status are shown in Table S9.

Changes in CVH (First to Second) and Subsequent Incidence of CVD and Mortality

The median follow-up of the outcomes starting from the second checkup was 5.1 years (IQR, 3.2–6.0 years) for CVD and 5.2 (IQR, 3.5–6.1 years) for mortality, which resulted in 7745 incident CVD events (elderly, 5980 and very elderly, 1765) and 8930 deaths (elderly, 6099 and very elderly, 2831). Heatmaps (Figures 1 and 2) and Kaplan–Meier curves (Figure S3A and S3B)s were used to depict the crude rates of CVD incidence and all-cause mortality according to the patterns of change in CVH status in the different age groups. The incidence, absolute difference rates, and adjusted sHRs for CVD and HRs for all-cause mortality are reported in Table 4 and Figure 3. After weighting to account for

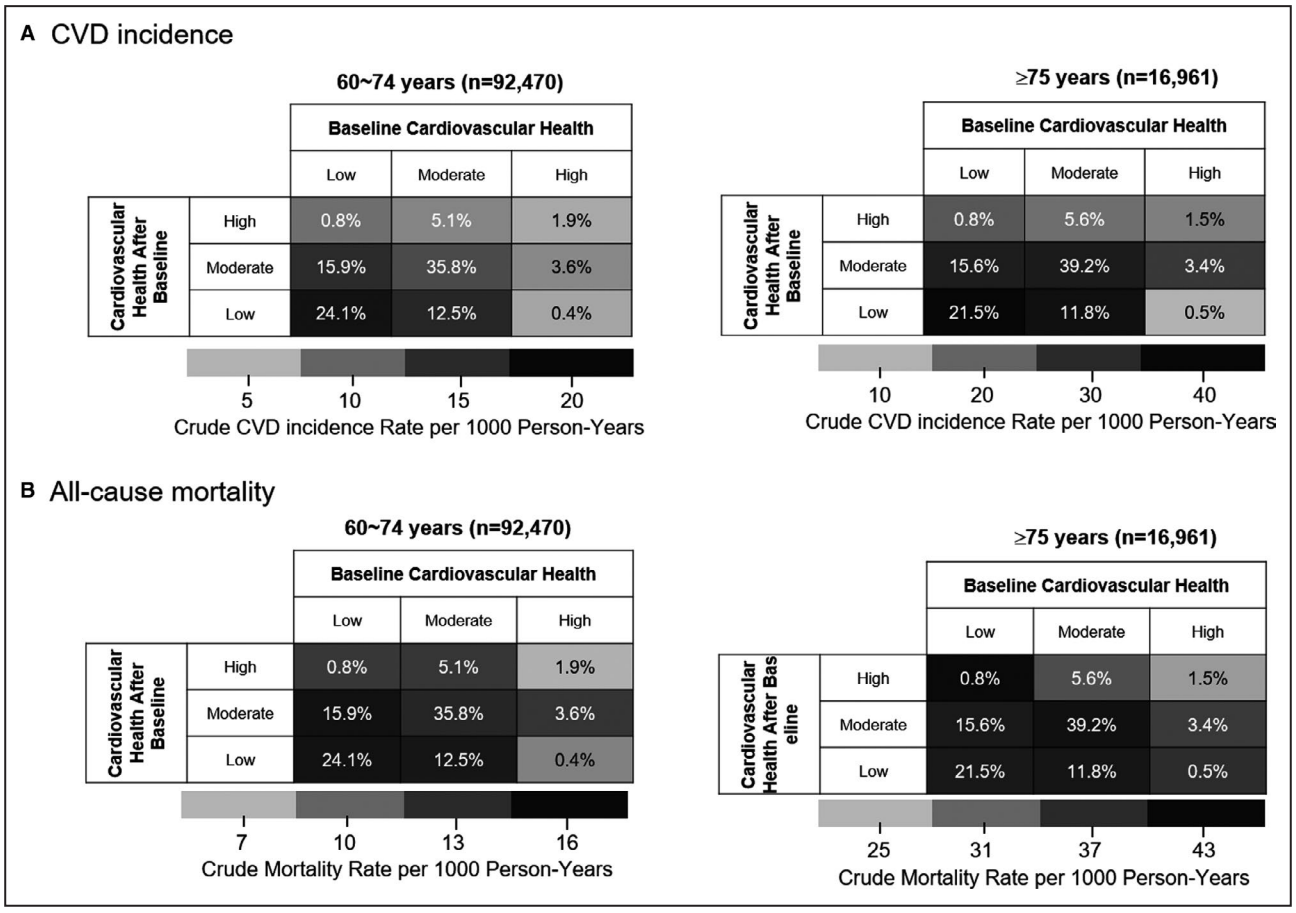

Figure 1. Heatmap of the unadjusted incidence rates of cardiovascular disease (CVD) (A) and all-cause mortality (B) according to the patterns of change in cardiovascular health between the first and second examinations in the elderly (60–74 years) and very elderly (≥75 years) populations.

Values indicate the percentage of participants in each category, and colors indicate rate per 1000 person-years.

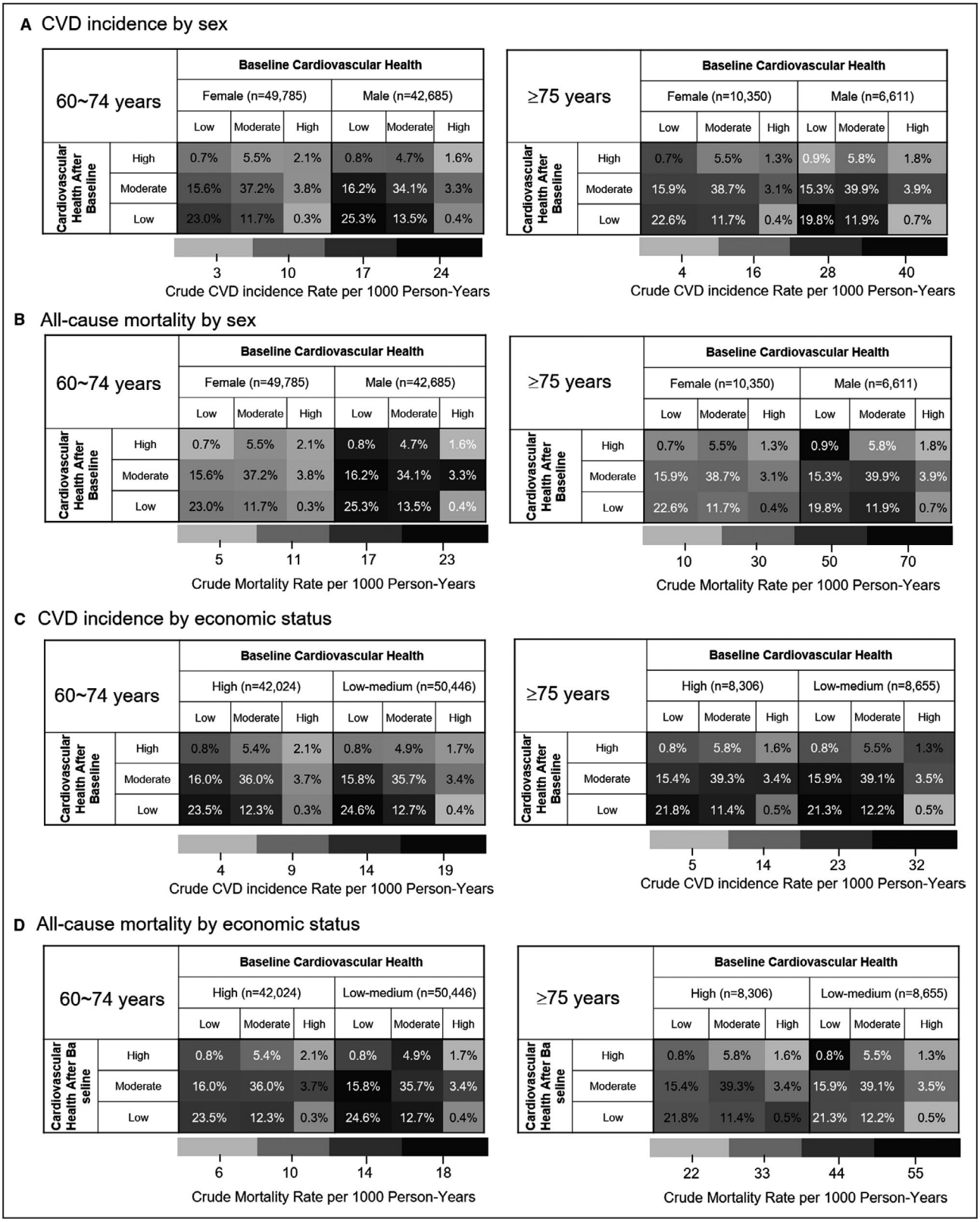

Figure 2. Heatmap of the unadjusted incidence rates of cardiovascular disease (CVD) and all-cause mortality according to the patterns of change in cardiovascular health between the first and second examinations for comparison between women and men (A and B) and between high and low-to-moderate economic status (C and D).
Values indicate the percentage of participants in each category, and black and gray indicate rate per 1000 person-years.

Table 4. Change in CVH Status, and Association With Subsequent Incident Cardiovascular Disease and All-Cause Mortality

Change in CVH Status	Cardiovascular Disease				All-Cause Mortality			
	N/Total N	Incidence Rate per 1000 Person-Years (95% CI)	ARD per 1000 Person-Years (95% CI)	Adjusted sHR (95% CI)*	N/Total N	Incidence Rate per 1000 Person-Years (95% CI)	ARD per 1000 Person-Years (95% CI)	Adjusted HR (95% CI)†\
Elderly, 60–74 y	5980/92 470				6099/92 470			
Consistently low	1914/22 258	18.0 (17.2-18.8)	Ref	1 [Reference]	1607/22 258	14.5 (13.8-15.2)	Ref	1 [Reference]
Low to moderate	1008/14 680	14.8 (13.9-15.8)	−3.2 (−4.4 to −1.9)	0.81 (0.75-0.88)‡	1020/14 680	14.6 (13.7-15.5)	-0.1 (−1.1 to 1.2)	1.00 (0.92-1.08)
Low to high	29/720	9.2 (6.1-13.2)	−8.8 (−13.5 to −4.1)	0.51 (0.35-0.73)‡	39/720	12.1 (8.6-16.6)	-2.4 (−6.6 to 1.8)	0.86 (0.63-1.18)
Moderate to low	862/11 556	15.3 (14.3-16.3)	−2.7 (−4.0 to −1.4)	0.84 (0.77-0.91)‡	830/11 556	14.2 (13.-15.2)	-0.3 (−1.5 to 0.9)	0.95 (0.87-1.03)
Consistently moderate	1845/33 115	11.9 (11.3-12.4)	−6.1 (−7.0 to −5.2)	0.66 (0.61-0.70)‡	2089/33 115	13.1 (12.6-13.7)	-1.4 (−2.3 to −0.5)	0.91 (0.85-0.97)‡
Moderate to high	160/4755	7.7 (6.6-9.0)	−10.3 (−12.2 to −8.4)	0.43 (0.37-0.51)‡	256/4755	12.2 (10.7-13.8)	-2.3 (−4.1 to −0.6)	0.88 (0.77-1.01)
High to low	10/354	5.8 (2.8-10.6)	−12.2 (−18.5 to −5.9)	0.32 (0.17-0.59)‡	16/354	9.1 (5.2-14.8)	-5.4 (−11.1 to 0.2)	0.59 (0.36-0.96)
High to moderate	113/3288	7.5 (6.2-9.0)	−10.5 (−12.7 to −8.3)	0.42 (0.35-0.51)‡	188/3288	12.3 (10.6-14.2)	-2.2 (−4.2 to −0.1)	0.87 (0.75-1.02)
Consistently high	39/1744	5.5 (3.9-7.6)	−12.5 (−15.6 to −9.3)	0.32 (0.23-0.44)‡	54/1744	7.5 (5.7-9.8)	-6.9 (−9.8 to −4.1)	0.58 (0.44-0.76)‡
Very elderly, ≥75 y	1765/16 961				2831/16 961			
Consistently low	463/3651	30.1 (27.4-33.0)	Ref	1 [Reference]	637/3651	39.5 (36.5-42.7)	Ref	1 [Reference]
Low to moderate	269/2651	24.9 (22.1-28.1)	−5.2 (−9.3 to −1.0)	0.80 (0.69-0.93)‡	441/2651	39.3 (35.7-43.2)	-0.2 (−4.9 to 4.6)	0.96 (0.84-1.08)
Low to high	9/136	17.0 (7.8-32.3)	−13.1 (−28.0 to 1.8)	0.54 (0.28-1.05)	23/136	42.3 (26.9-63.6)	2.9 (−14.1 to 19.9)	1.04 (0.68-1.58)
Moderate to low	231/2004	27.7 (24.3-31.5)	−2.4 (−6.9 to 2.2)	0.89 (0.76-1.05)	350/2004	40.0 (35.9-44.4)	0.5 (−4.7 to 5.7)	0.95 (0.84-1.09)
Consistently moderate	680/6645	25.3 (23.4-27.3)	−4.8 (−8.1 to −1.6)	0.81 (0.72-0.91)‡	1141/6645	40.8 (38.5-43.3)	1.4 (−2.5 to 5.3)	0.97 (0.88-1.07)
Moderate to high	53/953	14.6 (10.9-19.1)	−15.5 (−21.5 to −9.6)	0.47 (0.35-0.62)‡	123/953	33.1 (27.5-39.5)	-6.3 (−13.3 to 0.6)	0.81 (0.66-0.98)
High to low	3/86	8.5 (1.8-24.9)	−21.6 (−39.8 to −3.4)	0.27 (0.09-0.81)	13/86	36.6 (19.5-62.6)	-2.8 (−23.7 to 18.0)	0.79 (0.46-1.37)
High to moderate	45/584	20.8 (15.2-27.9)	−9.3 (−17.0 to −1.6)	0.66 (0.49-0.91)‡	78/584	35.1 (27.8-43.9)	-4.3 (−13.1 to 4.4)	0.81 (0.64-1.02)
Consistently high	12/251	13.0 (6.7-22.7)	−17.1 (−28.5 to −5.8)	0.41 (0.23-0.73)‡	25/251	26.7 (17.3-39.5)	-12.7 (−25.7 to 0.3)	0.60 (0.40-0.90)

ARD indicates absolute rate difference; CVH, cardiovascular health; HR, hazard ratio; Ref, reference; and sHR, subhazard ratio.

*Cardiovascular disease was adjusted for sex, age, economic status, Hospital Frailty Score, living in metropolitan cities, and competing risk of death.

†All-cause mortality was adjusted for sex, age, economic status, Hospital Frailty Score, and living in metropolitan cities.

‡$P<0.0083$ for differences reported.

attrition, the incidence, absolute difference rates, and adjusted sHRs for CVD and hazard ratios for all-cause mortality are reported in Table S10.

For the very elderly population (aged ≥75 years), the multivariable analysis with adjustment of competing risk of death showed that compared with the individuals with consistently low CVH status (CVD incident rate per 1000 person-years, 30.1; 95% CI, 27.4–33.0), the low-to-moderate (sHR, 0.80; 95% CI, 0.69–0.93), consistently moderate (sHR, 0.80; 95% CI, 0.72–0.91), moderate-to-high (sHR, 0.47; 95% CI, 0.35–0.62), high-to-low (sHR, 0.27; 95% CI, 0.09–0.80), high-to-moderate (sHR, 0.66; 95% CI, 0.49–0.90), and consistently high CVH status groups (sHR, 0.42; 95% CI, 0.23–0.74) showed lower CVD risks (Table 4). In the elderly groups, compared with the individuals with consistently low CVH status, a lower CVD risk was observed in all of the other groups with the improvement of CVH status. The results were similar for all-cause mortality.

Number of participants according to changes in the levels of individual CVH metrics between the first and second examinations are presented in Table S11. The associations of the changes in the individual CVH metrics with the subsequent occurrence of incident CVD events and all-cause mortality are presented in Table 5 and Table S12. Compared with the low-low group, the high-high group of total cholesterol level was associated lower risk of CVD event in elderly but not in the very elderly population (*P* interaction=0.005). In both the elderly and very elderly groups, compared with the low-low group, the high-high group of BMI and total cholesterol were not informative enough for prediction of all-cause mortality.

Sensitivity Analysis

The results for 4 groups of changes in the CVH score showed that the high (score of ≥8)-to-low (score of <8), low-to-high, and consistently high CVH status groups had lower risks of CVD and mortality compared with the consistently low group (Table S13).

DISCUSSION

Principal Findings

In this study, time-varying moderate and high measures of CVH were associated with lower risks of CVD and mortality than low CVH status in both the elderly and very elderly populations. In both the elderly and

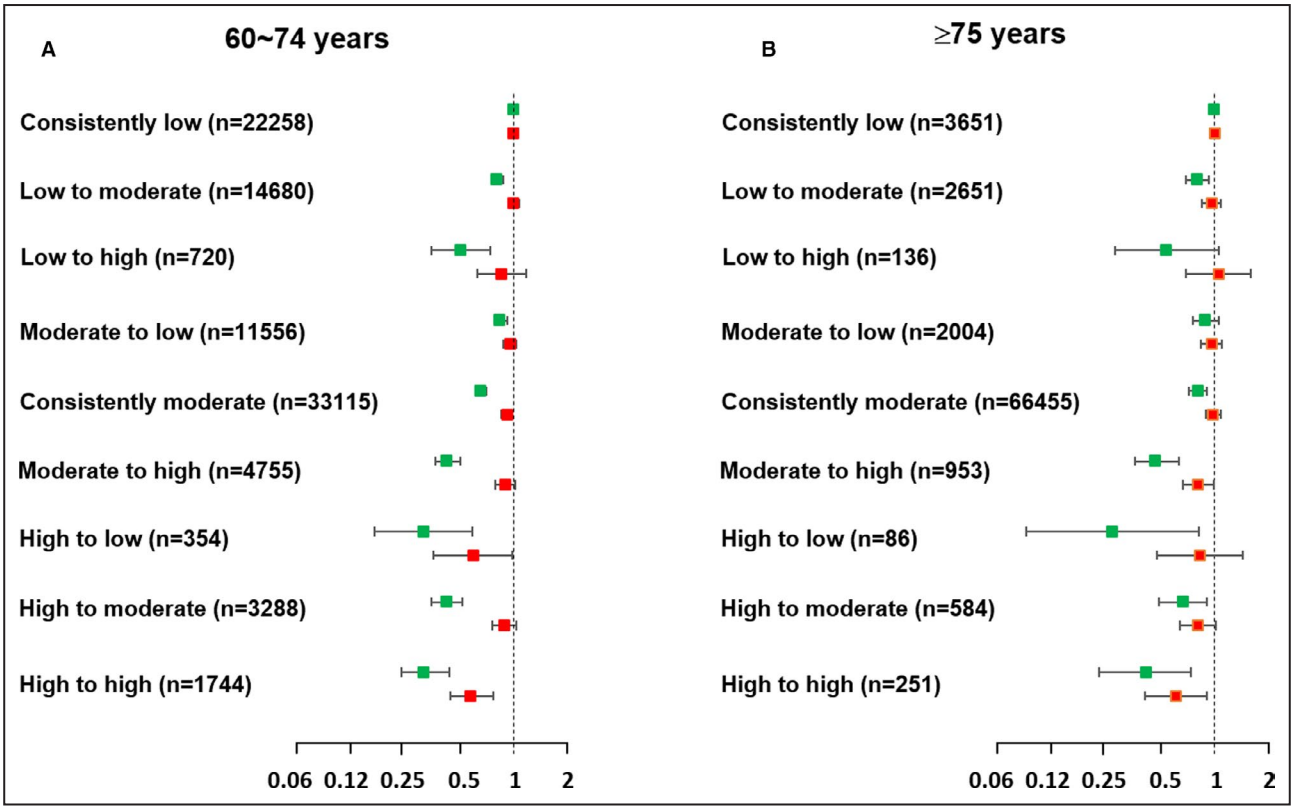

Figure 3. Hazard ratios of cardiovascular disease (green dots) and all-cause mortality (red dots) according to the pattern of change in the cardiovascular health status between the first and second health examinations in the elderly (60–74 years) (A) and very elderly (≥75 years) (B) populations.

Table 5. Association of Change in the Individual Cardiovascular Health Metrics With the Risk of Subsequent Incident Cardiovascular Disease Events and All-Cause Mortality

Pattern of Change	Low-Low	Low-Moderate	Low-High	Moderate-Low	Moderate-Moderate	Moderate-High	High-Low	High-Moderate	High-High
Incident cardiovascular disease, adjusted sHR (95% CI)*									
Elderly 60–74, y									
Smoking	1 [Reference]	0.84 (0.69–1.02)	0.84 (0.74–0.96)	0.87 (0.70–1.09)	0.77 (0.65–0.91)†	0.74 (0.64–0.85)†	0.81 (0.71–0.93)†	0.76 (0.67–0.87)†	0.68 (0.63–0.74)†
Body mass index	1 [Reference]	0.80 (0.58–1.09)	1.67 (0.78–3.57)	0.82 (0.60–1.12)	0.82 (0.69–0.98)	0.80 (0.66–0.97)	1.66 (0.87–3.15)	0.74 (0.61–0.91)†	0.74 (0.63–0.88)†
Physical activity	1 [Reference]	0.87 (0.80–0.94)†	0.87 (0.79–0.95)†	0.91 (0.82–1.01)	0.68 (0.62–0.76)†	0.78 (0.70–0.87)†	0.87 (0.76–1.00)	0.84 (0.74–0.96)†	0.75 (0.68–0.83)†
Blood pressure	1 [Reference]	0.89 (0.82–0.96)†	0.70 (0.58–0.86)†	0.87 (0.80–0.95)†	0.79 (0.73–0.85)†	0.55 (0.48–0.63)†	0.81 (0.66–0.99)	0.58 (0.51–0.66)†	0.44 (0.37–0.51)†
Total cholesterol	1 [Reference]	0.73 (0.64–0.84)†	0.81 (0.67–0.98)†	0.70 (0.61–0.80)†	0.66 (0.59–0.74)†	0.65 (0.58–0.73)†	0.88 (0.72–1.08)	0.67 (0.59–0.75)†	0.56 (0.51–0.62)† ‡
Fasting glucose	1 [Reference]	0.84 (0.74–0.97)	0.63 (0.50–0.79)†	0.84 (0.73–0.97)	0.66 (0.59–0.73)†	0.52 (0.46–0.59)†	0.76 (0.61–0.94)†	0.54 (0.48–0.60)†	0.50 (0.45–0.55)†
Very elderly, ≥75 y									
Smoking	1 [Reference]	0.97 (0.67–1.41)	0.80 (0.62–1.03)	0.67 (0.39–1.15)	0.67 (0.46–0.96)	0.76 (0.58–0.99)	0.66 (0.50–0.89)†	0.69 (0.53–0.90)†	0.67 (0.57–0.80)†
Body mass index	1 [Reference]	0.79 (0.42–1.49)	1.30 (0.40–4.25)	1.06 (0.59–1.93)	0.67 (0.46–0.98)	0.91 (0.62–1.36)	1.05 (0.37–2.98)	0.85 (0.57–1.28)	0.78 (0.54–1.12)
Physical activity	1 [Reference]	0.92 (0.80–1.06)	0.81 (0.69–0.95)	0.86 (0.69–1.06)	0.80 (0.66–0.98)	0.76 (0.61–0.95)	1.09 (0.87–1.38)	0.80 (0.62–1.03)	0.75 (0.62–0.92)†
Blood pressure	1 [Reference]	0.98 (0.85–1.13)	0.69 (0.48–1.01)	0.97 (0.83–1.13)	0.82 (0.71–0.93)†	0.71 (0.54–0.92)	0.95 (0.67–1.35)	0.61 (0.46–0.82)†	0.51 (0.37–0.72)†
Total cholesterol	1 [Reference]	1.01 (0.77–1.32)	0.94 (0.66–1.35)	1.03 (0.79–1.35)	0.90 (0.73–1.12)	0.80 (0.63–1.02)	1.06 (0.68–1.64)	0.92 (0.72–1.18)	0.81 (0.66–1.01)†
Fasting glucose	1 [Reference]	0.75 (0.57–0.99)	0.83 (0.59–1.17)	0.82 (0.63–1.08)	0.65 (0.52–0.81)†	0.56 (0.45–0.71)†	0.65 (0.44–0.95)	0.60 (0.48–0.75)†	0.56 (0.46–0.69)†
All-cause mortality, adjusted HR (95% CI)§									
Elderly, 60–74 y									
Smoking	1 [Reference]	0.86 (0.73–1.02)	0.89 (0.80–1.00)	0.70 (0.57–0.87)†	0.60 (0.50–0.71)†	0.58 (0.50–0.66)†	0.78 (0.69–0.89)†	0.61 (0.53–0.69)†	0.59 (0.55–0.64)†
Body mass index	1 [Reference]	0.89 (0.63–1.26)	1.16 (0.43–3.14)	1.11 (0.80–1.54)	0.77 (0.63–0.95)	1.01 (0.81–1.25)	0.55 (0.18–1.74)	0.82 (0.66–1.03)	1.03 (0.84–1.25)
Physical activity	1 [Reference]	0.92 (0.85–1.00)	0.87 (0.80–0.96)†	0.86 (0.77–0.95)†	0.67 (0.60–0.74)†	0.75 (0.67–0.84)†	0.84 (0.74–0.96)	0.79 (0.70–0.90)	0.75 (0.68–0.83)†
Blood pressure	1 [Reference]	1.00 (0.92–1.09)	0.99 (0.83–1.19)	0.97 (0.89–1.07)	0.98 (0.88–1.02)	0.86 (0.76–0.97)	0.98 (0.80–1.19)	0.86 (0.76–0.97)	0.91 (0.80–1.03)
Total cholesterol	1 [Reference]	0.92 (0.78–1.07)	0.99 (0.81–1.22)	0.91 (0.77–1.06)	0.79 (0.69–0.90)†	0.95 (0.83–1.09)	1.28 (1.04–1.59)	0.88 (0.76–1.01)	1.00 (0.89–1.13)
Fasting glucose	1 [Reference]	0.86 (0.75–1.00)	0.88 (0.71–1.08)	0.79 (0.69–0.92)†	0.68 (0.61–0.76)†	0.62 (0.55–0.70)†	0.85 (0.70–1.05)	0.59 (0.52–0.66)†	0.56 (0.51–0.62)†
Very elderly, ≥75 y									
Smoking	1 [Reference]	0.83 (0.62–1.12)	0.85 (0.70–1.01)	1.04 (0.75–1.44)	0.70 (0.53–0.93)	0.65 (0.53–0.80)†	0.75 (0.61–0.93)†	0.73 (0.60–0.89)†	0.65 (0.58–0.74)†
Body mass index	1 [Reference]	1.22 (0.63–2.38)	2.40 (0.82–7.00)	1.51 (0.81–2.84)	1.16 (0.75–1.80)	1.91 (1.22–3.00)†	1.91 (0.72–4.40)	1.56 (0.99–2.46)	1.68 (1.09–2.59)
Physical activity	1 [Reference]	0.94 (0.84–1.05)	0.80 (0.70–0.91)†	0.83 (0.70–0.97)	0.83 (0.71–0.96)	0.75 (0.62–0.90)†	0.93 (0.77–1.13)	0.78 (0.63–0.95)	0.67 (0.57–0.79)†
Blood pressure	1 [Reference]	1.10 (0.97–1.24)	1.23 (0.96–1.58)	1.06 (0.93–1.20)	1.00 (0.89–1.11)	1.04 (0.86–1.26)	1.06 (0.80–1.40)	1.03 (0.84–1.25)	0.94 (0.75–1.16)
Total cholesterol	1 [Reference]	0.92 (0.73–1.17)	1.05 (0.79–1.41)	1.00 (0.79–1.26)	0.80 (0.66–0.97)	0.94 (0.77–1.15)	1.49 (1.07–2.07)	0.98 (0.80–1.20)	1.04 (0.87–1.24)
Fasting glucose	1 [Reference]	0.72 (0.58–0.89)†	0.66 (0.49–0.88)†	0.84 (0.68–1.04)	0.63 (0.53–0.75)†	0.58 (0.49–0.70)†	0.74 (0.56–0.99)	0.58 (0.49–0.70)†	0.57 (0.48–0.66)†

HR indicates hazard ratio; and sHR, subhazard ratio.

*Cardiovascular disease was adjusted for sex, age, economic status, Hospital Frailty Score, living in metropolitan cities, and competing risk of death.

†$P<0.0083$ for differences reported.

‡Compared with low-low group, high-high group of total cholesterol level was associated lower risk of CVD event in elderly but not in the very elderly population (P interaction=0.005).

§All-cause mortality was adjusted for sex, age, economic status, Hospital Frailty Score, and living in metropolitan cities.

very elderly populations, consistent relationships were found between the improvement of the composite metric of CVH and the reduced risk of CVD. However, among the individual health factors, total cholesterol level was not appropriate for the prediction of CVD events in the very elderly participants. BMI and total cholesterol level were not appropriate for the prediction of all-cause mortality in both the elderly and very elderly groups. This study is showing that improving CVH status is beneficial for both the elderly and very elderly populations.

CVH Metrics in the Very Elderly Population

The recently published European Society of Cardiology and European Atherosclerosis Society guidelines extended the age of the risk assessment system from 65 years to 70 years and recommended statin use for primary prevention according to the individual level of risk until aged 75 years.[20] With this in mind, we have defined very elderly as referring to individuals aged >75 years herein.

The present study found that in the overall Asian very elderly population, 61.8%, 21.8%, and 16.3% of the participants showed stable, improved, and deteriorated CVH, respectively. This trend is consistently observed in both the very elderly and elderly populations. This study had a higher number of participants with improved health metrics than other studies.[6,21,22] This can be related with the high proportion of participants with intermediate or ideal BMI and physical activity in the Asian elderly cohort. Worldwide, 31.1% (95% CI, 30.9–31.2) of adults are physically inactive, with proportions ranging from 17.0% (95% CI, 16.8–17.2) in Southeast Asia to about 43% in the Americas and Eastern Mediterranean regions. Adults aged 60 years or older from Southeast Asia are much more active than are individuals of the same age from all other regions, and more active than are young adults (aged 15–29 years) from the Americas, the Eastern Mediterranean, Europe, and the western Pacific regions.[23]

The National Health and Nutrition Examination Surveys[21] of the United States found that the prevalence of smoking, hypercholesterolemia, and hypertension decreased significantly, but the prevalence of obesity and diabetes mellitus increased significantly. However, dietary and physical activity levels were unchanged from 1988/1994 to 2008. In the elderly Asian cohort of this study, the proportion of participants with ideal body weights was >60%. Moreover, those of the participants with intermediate or ideal physical activity levels were 28.5% and 64.2% in the first and second health examinations, respectively. This can be explained by the fact that this study included only individuals aged >60 years. In the ARIC (Atherosclerosis Risk in Communities) study,[22] the general trend was a decrease in the number of ideal metrics, with only 7% of the participants showing improved CVH over 26 years from 1987 to 2013. In a UK general community (Whitehall II), 13% of the participants showed improved CVH. The baseline mean ages of the participants in the ARIC and Whitehall II studies were 52.1 and 44.8 years, respectively.[6] Moreover, the ideal other individual CVH metrics, including smoking habit, were high in this study.

CVH Change and CVD Disease

The relationship between change of CVH and CVD event is still controversial. In the ARIC study,[22] the improvement in CVH through follow-up over 26 years was associated with a lower prevalence of CVD (no data on incident CVD) and better cardiac structure and function. In addition, in the Framingham Heart Study,[10] loss of ideal CVH metrics over 6 years was not statistically significantly associated with coronary artery calcification progression after adjustment for the number of baseline ideal metrics. In the Whitehall II study,[6] time-varying moderate and high measures of CVH were associated with a lower CVD risk than low CVH. However, no consistent relationship was observed between the direction of change in the category of a composite metric of CVH and the risk of CVD.

In this study, the time-varying moderate and high measures of CVH were associated with lower CVD and mortality risks than low CVH status in both the elderly and very elderly populations. In the elderly group, compared with the persistently low CVH group, the CVD risk was decreased in all of the other groups. By contrast, compared with the very elderly individuals with persistently low CVH status (consistently low group), all of the other groups except the low-to-moderate and low-to-high groups had a decreased CVD risk. Because the very elderly population with low baseline CVH status did not show decreased CVD risk even after improvement of their health metrics, the effect of baseline health condition might be more important in the very elderly population.

Individual CVH Metrics and CVD Risk in the Very Elderly Population

Because of the lack of data in the very elderly participants, there are no clinical support tools specifically designed to assess cardiovascular risk in this population. Statin therapy, blood pressure control, smoking cessation, physical activity, and maintaining a normal body weight are interventions that have been shown to reduce the incidence of primary cardiovascular events in the very elderly. The present study showed that maintaining optimal BMI and cholesterol level were not related with reduced mortality in both the elderly and very

elderly population. No significant association of BMI with outcomes might be attributable to the obesity paradox.[24,25] For example, obesity is associated with mortality at a younger age, but not at an older age. Thus, the association might be driven by this age difference.

The association between weight loss and cardiovascular mortality is less clear in the very elderly population. Ghaem Maralani et al reported that obesity increased risk of CVD-related death only in those aged <70 years, but not in those aged ≥70 years.[26] Takata et al observed a similar outcome that cardiovascular mortality was 78% less in overweight octogenarians than in those who were underweight.[27] Thus, although dietary recommendations can be made for the very elderly participants, weight loss recommendations for this population are not well supported by the literature.

The best available evidence for the primary prevention of cardiovascular events in older adults supports the use of statin therapy and blood pressure control. This study showed ideal total cholesterol was positively associated with CVD events in elderly participants. It can be a benefit from lipid-lowering therapy. Statin therapy reduces the risk of myocardial infarction and stroke, although close monitoring for adverse events is warranted. It was the same in the Asian very elderly (≥75 years) population.[28] However, in participants aged >75 years because of the lack of evidence, the American College of Cardiology/American Heart Association guidelines on the treatment of blood cholesterol to reduce cardiovascular risk in adults do not recommend using their atherosclerotic risk calculator. It is suggested that therapy could be considered on the basis of a discussion of benefits and risks, adverse effects, drug interactions, and patient preference.[29]

LIMITATIONS

This study has several limitations. First, studies that use administrative databases might be susceptible to errors arising from coding inaccuracies. To minimize this problem, we applied the definition that has been previously validated in previous studies that used the Korean NHIS sample cohort.[9,12–16] Second, the individuals excluded from the analysis of the changes in CVH had a less favorable cardiovascular risk profile, which could lead to an underestimation of the reported associations. To check this problem, we did an analysis with weighting to account for attrition. The weighted result to account for attrition was consistent with the main result. Third, the changes in the distribution of CVH across repeated examinations might have partly been related to aging, temporal trends, and cohort attrition. Fourth, some categories of CVH change were small, which might explain why some associations are not statistically significant.

CONCLUSIONS

In both the elderly and very elderly populations, a consistent relationship was observed between the improvement of a composite metric of CVH and reducing the risk of CVD. However, among the individual health factors, total cholesterol level was not appropriate for the prediction of CVD events in the very elderly participants. BMI and total cholesterol level were not appropriate for the prediction of all-cause mortality in both the elderly and very elderly groups.

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Supplementary Material

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SUPPLEMENTAL MATERIAL

Table S1. Definition of cardiovascular health metrics according to the American Heart Association for ascertainment of cardiovascular health status.

Metric	Optimal	Intermediate	Poor
	2 point	1 point	0 point
Smoking	Never or quit ≥12 months	Quit <12 months	Current smokers
Body mass index	<25 kg/m^2	25-29.9 kg/m^2	≥30 kg/m^2
Physical activity [a]	≥75 min/week of vigorous activity, ≥150 min/week of moderate activity or a combination of the two	1–74 min/week vigorous activity, 1–149 min/week moderate activity or a combination of the two	None
Blood pressure [b]	<120/80 mmHg, untreated	<120/80 mmHg on treatment or 120-139/80-89 mmHg	≥140/90 mmHg
Fasting glucose [c]	<100 mg/dL, untreated	100-126 mg/dL or <100 mg/dL treated	≥126 mg/dL
Total cholesterol [c]	200mg/dL, untreated	200-240 mg/dL or <200mg/dL treated	>240 mg/dL

a. Physical activity was assessed using questions on frequency and duration of participation in mildly energetic (e.g., weeding, general housework, bicycle repair), moderately energetic (e.g., dancing, cycling, leisurely swimming), and vigorous physical activity (e.g., running, hard swimming, playing squash).

b. Systolic blood pressure was measured twice with a sphygmomanometer in the sitting position after 5 min rest, and the average of the two readings was used in the present analyses.

c. Fasting blood glucose and total cholesterol were measured using standardized methods.

SI conversion factor: To convert cholesterol to millimoles per liter, multiply by 0.0259.

SI conversion factor: To convert glucose to millimoles per liter, multiply by 0.0555.

Table S2. Definitions and ICD-10 codes used for defining the comorbidities and clinical outcomes.

	Definitions	ICD-10 codes or conditions
Comorbidities		
Atrial fibrillation [12,14,30]	Defined from diagnosis*	ICD-10: I48
Heart failure [14,30]	Defined from diagnosis*	ICD-10: I11.0, I50, I97.1
Hypertension [14,15, 30]	Defined from diagnosis*	ICD-10: I10, I11, I12, I13, I15 and antihypertensive medication
Diabetes mellitus [14, 30]	Defined from diagnosis* plus treatment	ICD-10: E10, E11, E12, E13, E14 Treatment: all kinds of oral antidiabetics and insulin.
Dyslipidemia [14, 30]	Defined from diagnosis*	ICD-10: E78
Ischemic stroke [14, 30]	Defined from diagnosis*	ICD-10: I63, I64
Transient ischemic attack [14, 30]	Defined from diagnosis*	ICD-10: G45
Hemorrhagic stroke	Defined from diagnosis*	ICD-10: I60, I61, I62
Myocardial infarction [31]	Defined from diagnosis*	ICD-10: I21, I22, I25.2
Coronary heart disease	Defined from a history of acute myocardial infarction, coronary revascularization, or chronic ischemic heart disease.	Acute myocardial infarction: admission diagnosis (ICD-10: I21, I22) concurrently with coronary angiography (HA670, HA680, HA681) Coronary revascularization: percutaneous coronary intervention (M6551, M6552, M6561, M6563, M6562, M6564, M6571, M6572), thrombolytic treatment (M6634), or coronary artery bypass graft (O1641, OA641, O1642, OA642, O1647, OA647) Chronic ischemic heart disease: diagnosis* (ICD-10: I25.2, I25.5, I25.6, I25.8, I25.9)
Peripheral arterial disease [14, 30]	Defined from diagnosis*	ICD-10: I70.0, I70.1, I70.2, I70.8, I70.9
Chronic kidney disease [14, 30]	Defined from eGFR or diagnosis* (if laboratory value was not available, diagnosis code was used)	eGFR <60mL/min per 1.73 m^2 ICD-10: N18, N19
End-stage renal disease [32]	Defined from national registry for severe illness.	Patients with end-stage renal disease undergoing chronic dialysis or received a kidney transplant.
Hypertrophic cardiomyopathy [33]	Defined from at least one records of either inpatient or outpatient diagnoses	ICD-10: I42.1, I42.2
Sleep apnea	Defined from diagnosis*	ICD-10: G47.3
Proteinuria	Defined from laboratory data (if laboratory value was not available, diagnosis code was used)	Urine dipstick proteinuria 1+ or higher (ICD-10: N06, N391, N392, R80)

Osteoporosis [34]	Defined from diagnosis*	ICD-10: M80, M81, M82 (except M82.0)
Hyperthyroidism	Defined from diagnosis*	ICD-10: E05
Hypothyroidism	Defined from diagnosis*	ICD-10: E03
Chronic Liver disease	Defined from diagnosis of chronic liver disease, cirrhosis, and hepatitis	ICD-10: B18, K70, K71, K72, K73, K74, K76.1
Chronic obstructive pulmonary disease [35]	Defined from diagnosis* plus treatment	ICD-10: J42, J43(except J43.0), J44 Treatment: SABA, SAMA, LABA, LAMA, ICS, ICS+LABA, or methylxanthine (>1 months).
Malignancy	Defined from diagnoses of cancer (non-benign)	ICD-10: C00-C97
Clinical outcomes		
Coronary heart disease	Defined from an event of acute myocardial infarction, coronary revascularization, or death of which the cause was recorded as a coronary artery disease or myocardial infarction	Acute myocardial infarction: admission diagnosis (ICD-10: I21, I22) concurrently with coronary angiography (HA670, HA680, HA681) Coronary revascularization: percutaneous coronary intervention (M6551, M6552, M6561, M6563, M6562, M6564, M6571, M6572), thrombolytic treatment (M6634), or coronary artery bypass graft (O1641, OA641, O1642, OA642, O1647, OA647) Coronary artery disease or myocardial infarction: ICD-10: I20, I21, I22, I23, I25
Ischemic stroke [12, 30]	Defined from any discharge diagnoses with concomitant imaging studies	ICD-10: I63, I64
Systemic embolism	Defined from admission diagnosis or related death	ICD-10: I74, N280 (including renal infarction)

Abbreviations: eGFR, estimated glomerular filtration rate; ICD-10, International Classification of Diseases-10th Revision.

*To ensure accuracy, comorbidities were established based on one inpatient or two outpatient records of ICD-10 codes in the database.

Table S3. Characteristics and cardiovascular health status at baseline and follow-up.

Characteristics	1st (n=208,673)	2nd (n=109,431)	3rd (n=119,826)	4th (n=92,731)	5th (n=34,265)
Age, mean (SD), year	70.6 (5.4)	72.5 (4.4)	73.1 (4.5)	74.4 (4.2)	75.6 (3.9)
Men	88671 (42.5)	44867 (41.0)	52484 (43.8)	44604 (48.1)	18263 (53.3)
Economic status, 0-10	7 (4, 9)	7 (4, 9)	8 (4, 9)	8 (4, 9)	8 (4, 9)
Low, 0-4	65564 (31.4)	33793 (29.9)	31813 (27.4)	23504 (26.1)	8679 (26.0)
Middle, 5-7	48104 (23.1)	24715 (21.9)	25416 (21.9)	19170 (21.3)	6745 (20.2)
High, 8-10	95005 (45.5)	54372 (48.2)	58715 (50.6)	47348 (52.6)	17911 (53.7)
Living area					
Small city or rural area	126996 (60.9)	65923 (58.4)	71273 (61.5)	58135 (64.6)	21319 (64.0)
Metropolitan city	81677 (39.1)	46957 (41.6)	44671 (38.5)	31887 (35.4)	12016 (36.0)
Hypertension	90995 (43.6)	59834 (58.1)	66663 (59.8)	56099 (64.5)	22009 (68.2)
Diabetes mellitus	28664 (13.7)	18134 (16.1)	20601 (17.8)	17694 (19.7)	7060 (21.2)
Dyslipidemia	63800 (30.6)	46957 (41.6)	57936 (50.0)	51774 (57.5)	20538 (61.6)
Osteoporosis	60875 (29.2)	42228 (37.4)	49993 (43.1)	43267 (48.1)	16697 (50.1)
CVH status, No. of ideal metrics [a]					
Low, 0-2	85729 (41.1)	44096 (40.3)	32602 (28.4)	23604 (26.3)	8509 (25.6)
Moderate, 3-4	111048 (53.2)	59028 (53.9)	67736 (58.9)	54012 (60.1)	20090 (60.4)
High, 5-6	11896 (5.7)	6307 (5.8)	14641 (12.7)	12283 (13.7)	4685 (14.1)
No. of ideal metrics, Median (IQR) [a]	3 (2, 4)	3 (2,4)	3 (2,4)	3 (2,4)	3 (2,4)
12-Point CVH score, Median (IQR) [b]	7 (6, 9)	8 (6,9)	9 (7,10)	9 (8,10)	9 (8,10)

Abbreviations: CVH, cardiovascular health; IQR, interquartile range, SD, standard deviation.

Values are reported as No. (%) unless otherwise indicated.

a. The cardiovascular health metrics included nonsmoking, body weight, physical activity, blood pressure, fasting blood glucose, and total cholesterol.

b. The continuous 12-point CVH score (range, higher score indicating higher CVH) was calculated by assigning 0 (poor), 1 (intermediate), and 2 (ideal) points to each of the 6 metrics and summing them.

Table S4. The time to cardiovascular disease and all-cause mortality according to measures of baseline cardiovascular health.

	The Time (years) to Cardiovascular Disease			The Time (years) to All-Cause Mortality		
	60~74 years (No./Total No.= 14,260/173,109)	**≥ 75 years (No./Total No.= 6,234/45,379)**	**p-value**	**60~74 years (No./Total No.= 15,641/173,109)**	**≥ 75 years (No./Total No.= 11,507/45,379)**	**p-value**
CVH status, No. of ideal metrics						
Low, 0-2	2.7 [1.2; 4.2]	2.6 [1.4; 4.0]	0.627	3.2 [1.8; 4.6]	3.2 [1.8; 4.7]	0.792
Moderate, 3-4	2.9 [1.4; 4.3]	2.5 [1.2; 4.1]	0.001	3.3 [2.0; 4.7]	3.1 [1.7; 4.4]	0.001
High, 5-6	2.6 [1.3; 4.2]	2.6 [1.5; 4.2]	0.963	3.4 [1.8; 4.8]	2.8 [1.6; 4.3]	0.139
CVH status per No. of ideal metrics						
0	2.5 [1.1; 3.9]	2.6 [1.4; 4.4]	0.614	3.6 [2.1; 4.7]	3.4 [1.3; 4.9]	0.611
1	2.6 [1.2; 4.1]	2.8 [1.3; 4.0]	0.714	3.3 [1.8; 4.6]	3.5 [1.8; 4.7]	0.423
2	2.7 [1.3; 4.2]	2.6 [1.4; 4.0]	0.623	3.2 [1.8; 4.6]	3.1 [1.8; 4.6]	0.566
3	2.8 [1.4; 4.3]	2.4 [1.2; 4.1]	0.003	3.3 [2.0; 4.7]	3.1 [1.7; 4.4]	0.001
4	2.9 [1.4; 4.4]	2.8 [1.3; 4.0]	0.108	3.4 [1.9; 4.7]	3.2 [1.8; 4.4]	0.018
5 & 6	2.6 [1.3; 4.2]	2.6 [1.5; 4.2]	0.963	3.4 [1.8; 4.8]	2.8 [1.6; 4.3]	0.139
CVH status per points on the CVH score						
≤4	2.6 [1.3; 4.1]	2.7 [1.4; 4.0]	0.724	3.4 [1.9; 4.7]	3.6 [1.7; 4.7]	0.927
5 or 6	2.8 [1.3; 4.2]	2.6 [1.2; 3.9]	0.070	3.3 [1.9; 4.7]	3.2 [1.8; 4.6]	0.365
7 or 8	2.8 [1.4; 4.3]	2.6 [1.3; 4.1]	0.081	3.3 [1.9; 4.7]	3.1 [1.8; 4.5]	0.037
9 or 10	2.8 [1.3; 4.4]	2.5 [1.3; 4.1]	0.375	3.3 [1.9; 4.6]	3.0 [1.6; 4.3]	0.003
≥11	2.3 [1.0; 3.9]	2.1 [1.4; 3.3]	0.865	3.1 [1.6; 4.8]	2.5 [1.6; 3.9]	0.357

Abbreviations: CVH, cardiovascular health.

Table S5. Time-varying Cox proportional hazard model for incident coronary heart disease and ischemic stroke / systemic embolism as separate outcomes.

	Adjusted Subhazard Ratio [a] (95% CI)				
	CVH Status, No. of Ideal Metrics			Per Additional Ideal Metric	Per 1-Point Increase in the CVH Score
	Low, 0-2	Moderate, 3-4	High, 5-6		
Coronary heart disease					
Elderly (60~74 years) (No./total No.= 6,764/167,317)	1 (Ref)	0.66 (0.56-0.76)	0.80 (0.75-0.86)	0.79 (0.78-0.81)	0.83 (0.81-0.84)
Very-elderly (≥ 75 years) (No./total No.=3,168/41,356)	1 (Ref)	0.81 (0.56-1.18)	0.83 (0.69-0.99)	0.87 (0.84-0.91)	0.88 (0.85-0.90)
Ischemic stroke / systemic embolism					
Elderly (60~74 years) (No./total No.=8,192/167,317)	1 (Ref)	0.86 (0.73-1.01)	0.90 (0.83-0.97)	0.84 (0.82-0.86)	0.85 (0.84-0.86)
Very-elderly (≥ 75 years) (No./total No.= 3,330/41,356)	1 (Ref)	0.70 (0.80-0.97)	0.78 (0.67-0.91)	0.88 (0.84-0.91)	0.87 (0.85-0.89)

Abbreviations: CI, confidence interval; CVH, cardiovascular health.

a. Subhazard ratios were adjusted for sex, age, economic status, Hospital Frailty Score, living in metropolitan cities, and competing risk of death.

Table S6. Time-varying Cox proportional hazard model for cause-specific mortality.

Cause of death	Elderly (60~74 years) (n=167,317)		Very-elderly (≥ 75 years) (n=41,356)	
	No. event	Adjusted HR (95% CI)	No. event	Adjusted HR (95% CI)
Cardiovascular death	2774		2421	
Cardiovascular health status				
Low (0-2 ideal metrics)		1 (Ref)		1 (Ref)
Moderate (3-4 ideal metrics)		0.79 (0.73-0.86)		0.86 (0.79-0.93)
High (5-6 ideal metrics)		0.56 (0.48-0.66)		0.63 (0.52-0.76)
Per additional ideal metric		0.86 (0.83-0.89)		0.90 (0.87-0.93)
Per end-point increase in CVH score		0.84 (0.83-0.86)		0.89 (0.87-0.91)
Cancer	6230		2588	
Cardiovascular health status				
Low (0-2 ideal metrics)		1 (Ref)		1 (Ref)
Moderate (3-4 ideal metrics)		0.97 (0.92-1.03)		1.01 (0.93-1.10)
High (5-6 ideal metrics)		0.84 (0.76-0.93)		1.01 (0.86-1.18)
Per additional ideal metric		0.97 (0.95-0.99)		1.0 (0.97-1.04)
Per end-point increase in CVH score		0.94 (0.93-0.95)		0.97 (0.95-0.99)
Other causes	5434		4778	
Cardiovascular health status				
Low (0-2 ideal metrics)		1 (Ref)		1 (Ref)
Moderate (3-4 ideal metrics)		0.87 (0.82-0.92)		0.95 (0.90-1.01)
High (5-6 ideal metrics)		0.73 (0.66-0.81)		0.73 (0.64-0.83)
Per additional ideal metric		0.93 (0.91-0.95)		0.95 (0.93-0.98)
Per end-point increase in CVH score		0.88 (0.87-0.90)		0.94 (0.92-0.95)

Abbreviations: CI, confidence interval; CVH, cardiovascular health; HR, hazard ratio.

Table S7. Time-varying Cox proportional hazard models for the association between individual cardiovascular health metrics and incident cardiovascular disease and all-cause mortality.

Level of cardiovascular health metric	Adjusted Subhazard Ratio (95% CI) [a]		Adjusted Hazard Ratio (95% CI) [b]	
	Incident cardiovascular disease		All-cause mortality	
	Elderly (60~74 years) (No./Total No.= 14,260/173,109)	Very-elderly (≥ 75 years) (No./Total No.= 6,234/45,379)	Elderly (60~74 years) (No./Total No.= 15,641/173,109)	Very-elderly (≥ 75 years) (No./Total No.= 11,507/45,379)
Smoking				
Poor	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Intermediate	0.79 (0.71-0.87)	0.79 (0.64-0.98)	0.71 (0.67-0.75)	0.71 (0.67-0.75)
Ideal	0.76 (0.71-0.81)	0.73 (0.64-0.83)	0.69 (0.67-0.71)	0.69 (0.67-0.71)
Body mass index				
Poor	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Intermediate	0.91 (0.78-1.04)	0.80 (0.59-1.08)	0.89 (0.80-0.99)	1.0 (0.86-1.18)
Ideal	0.81 (0.70-0.94)	0.87 (0.65-1.16)	1.08 (0.97-1.19)	1.29 (1.10-1.50)
Physical activity				
Poor	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Intermediate	0.82 (0.77-0.87)	0.82 (0.72-0.93)	0.75 (0.72-0.78)	0.92 (0.87-0.97)
Ideal	0.73 (0.68-0.78)	0.80 (0.70-0.92)	0.75 (0.71-0.78)	0.80 (0.75-0.85)
Blood pressure				
Poor	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Intermediate	0.82 (0.77-0.86)	0.87 (0.79-0.96)	0.93 (0.90-0.97)	0.96 (0.92-1.0)
Ideal	0.59 (0.54-0.65)	0.65 (0.53-0.78)	0.87 (0.82-0.91)	0.98 (0.91-1.05)
Total cholesterol				
Poor	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Intermediate	0.79 (0.73-0.85)	0.90 (0.78-1.04)	0.93 (0.88-0.98)	0.97 (0.90-1.03)
Ideal	0.72 (0.67-0.77)	0.87 (0.75-1.01)	1.06 (1.01-1.12)	1.13 (1.06-1.21)
Fasting glucose				
Poor	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Intermediate	0.71 (0.66-0.77)	0.73 (0.66-0.84)	0.69 (0.65-0.72)	0.76 (0.71-0.80)
Ideal	0.59 (0.55-0.64)	0.67 (0.58-0.77)	0.61 (0.58-0.64)	0.69 (0.65-0.73)

Abbreviations: CI, confidence interval.

a. Each individual cardiovascular health metric was included as a time-varying variable. Subhazard ratios were adjusted for sex, age, economic status, Hospital Frailty Score, living in metropolitan cities, and competing risk of death.

b. Each individual cardiovascular health metric was included as a time-varying variable. Hazard ratios were adjusted for sex, age, economic status, Hospital Frailty Score, and living in metropolitan cities.

Table S8. Baseline characteristics of included and excluded study participants for the analysis of change in cardiovascular health.

Characteristics	Included (N=109431)	Excluded [a]			P-value [b]
		All (N=99242)	Exclusion due to no second examination (N=97566)	Exclusion due to CVD event within interval (N=1676)	
Baseline characteristics					
Age, mean (SD), y	70.4 (4.4)	70.8 (6.3)	70.8 (6.3)	71.3 (4.6)	<0.001
Men	49296 (45.0)	39375 (39.7)	38431 (39.4)	944 (56.3)	<0.001
Economic status, 0-10	7 (4, 9)	7 (4, 9)	7 (4, 9)	7 (4, 9)	0.015
Hypertension	46978 (42.9)	44017 (44.4)	43103 (44.2)	914 (54.5)	<0.001
Diabetes mellitus	14207 (13.0)	14457 (14.6)	14115 (14.5)	342 (20.4)	<0.001
Dyslipidemia	33779 (30.9)	30021 (30.3)	29363 (30.1)	658 (39.3)	<0.001
Chronic kidney disease	1076 (1.0)	1144 (1.2)	1122 (1.1)	22 (1.3)	0.615
Anemia	16376 (15.0)	17420 (17.6)	17179 (17.6)	241 (14.4)	0.001
History of bleeding	2190 (2.0)	2177 (2.2)	2142 (2.2)	35 (2.1)	0.831
Hyperthyroidism	2614 (2.4)	2510 (2.5)	2470 (2.5)	40 (2.4)	0.767
Hypothyroidism	2701 (2.5)	2510 (2.5)	2469 (2.5)	41 (2.4)	0.889
COPD	7048 (6.4)	7176 (7.2)	7020 (7.2)	156 (9.3)	0.001
Liver disease	22698 (20.7)	19677 (19.8)	19271 (19.8)	406 (24.2)	<0.001
Hypertrophic cardiomyopathy	187 (0.2)	174 (0.2)	167 (0.2)	7 (0.4)	0.036
Osteoporosis	32097 (29.3)	28778 (29.0)	28305 (29.0)	473 (28.2)	0.497
Baseline cardiovascular health					
CVH status, No. of ideal metrics [c]					<0.001
Low, 0-2	44096 (40.3)	41633 (42.0)	40828 (41.8)	805 (48.0)	
Moderate, 3-4	59028 (53.9)	52020 (52.4)	51194 (52.5)	826 (49.3)	
High, 5-6	6307 (5.8)	5589 (5.6)	5544 (5.7)	45 (2.7)	
No. of ideal metrics, median (IQR) [c]	3 (2, 4)	3 (2, 4)	3 (2, 4)	3 (2, 3)	<0.001
12-Point CVH score, median (IQR) [d]	8 (6, 9)	7 (6, 9)	7 (6, 9)	7 (6, 8)	<0.001

Abbreviations: COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; CVH, cardiovascular health; IQR, interquartile range, SD, standard deviation.

a. Excluded participants are comprised of those who died in the interval (n=248), those who had a CVD event in the interval (n=468), those who dropped out (n=924) and those with incomplete CVH metrics (n=1290).

b. P-value for contrast between included and excluded participants, derived from Pearson, chi-square and t-test where appropriate.

c. The cardiovascular health metrics included nonsmoking, body weight, physical activity, blood pressure, fasting blood glucose, and total cholesterol.

d. The continuous 12-point CVH score (range, higher score indicating higher CVH) was calculated by assigning 0 (poor), 1 (intermediate), and 2 (ideal) points to each of the 6 metrics and summing them.

Table S9. Baseline characteristics by pattern of change in cardiovascular health.

Pattern of change	Low-Low (N=25909)	Low-Mod (N=17331)	Low-High (N=856)	Mod-Low (N=13560)	Mod-Mod (N=39760)	Mod-High (N=5708)	High-Low (N=440)	High-Mod (N=3872)	High-High (N=1995)
Age, mean (SD)	70.2 (4.3)	70.5 (4.4)	70.5 (4.4)	70.3 (4.4)	70.6 (4.5)	70.6 (4.4)	70.8 (4.7)	70.4 (4.4)	70.2 (4.1)
Men	12096 (46.7)	7940 (45.8)	416 (48.6)	6538 (48.2)	17211 (43.3)	2398 (42.0)	232 (52.7)	1658 (42.8)	807 (40.5)
Economic Status, 0-10	7 (3, 9)	7 (4, 9)	7 (4, 9)	7 (3, 9)	7 (4, 9)	7 (4, 9)	7 (4, 9)	7 (4, 9)	8 (4, 9)
Hypertension	15808 (61.0)	8246 (47.6)	159 (18.6)	5943 (43.8)	14934 (37.6)	1040 (18.2)	68 (15.5)	584 (15.1)	196 (9.8)
Diabetes mellitus	7171 (27.7)	2390 (13.8)	19 (2.2)	1522 (11.2)	2963 (7.5)	67 (1.2)	5 (1.1)	53 (1.4)	17 (0.9)
Dyslipidemia	11826 (45.6)	5592 (32.3)	150 (17.5)	4108 (30.3)	10112 (25.4)	974 (17.1)	65 (14.8)	610 (15.8)	342 (17.1)
Chronic kidney disease	348 (1.3)	154 (0.9)	7 (0.8)	139 (1.0)	348 (0.9)	47 (0.8)	3 (0.7)	21 (0.5)	9 (0.5)
Anemia	2891 (11.2)	2286 (13.2)	130 (15.3)	1873 (13.8)	6783 (17.1)	1077 (18.9)	84 (19.1)	807 (20.8)	445 (22.3)
History of bleeding	548 (2.1)	322 (1.9)	11 (1.3)	257 (1.9)	802 (2.0)	121 (2.1)	7 (1.6)	84 (2.2)	38 (1.9)
Hyperthyroidism	663 (2.6)	433 (2.5)	13 (1.5)	326 (2.4)	920 (2.3)	106 (1.9)	3 (0.7)	91 (2.4)	59 (3.0)
Hypothyroidism	632 (2.4)	459 (2.6)	6 (0.7)	322 (2.4)	987 (2.5)	126 (2.2)	10 (2.3)	100 (2.6)	59 (3.0)
COPD	1800 (6.9)	1182 (6.8)	50 (5.8)	926 (6.8)	2408 (6.1)	331 (5.8)	24 (5.5)	220 (5.7)	107 (5.4)
Liver disease	6207 (24.0)	3668 (21.2)	161 (18.8)	2777 (20.5)	7646 (19.2)	1029 (18.0)	84 (19.1)	742 (19.2)	384 (19.2)
Hypertrophic cardiomyopathy	51 (0.2)	40 (0.2)	0 (0.0)	18 (0.1)	61 (0.2)	14 (0.2)	0 (0.0)	2 (0.1)	1 (0.1)
Osteoporosis	7279 (28.1)	5090 (29.4)	251 (29.3)	3758 (27.7)	12018 (30.2)	1749 (30.6)	117 (26.6)	1169 (30.2)	666 (33.4)
Venous thromboembolism	189 (0.7)	124 (0.7)	5 (0.6)	89 (0.7)	221 (0.6)	30 (0.5)	3 (0.7)	19 (0.5)	6 (0.3)
Coagulation or platelet defect	227 (0.9)	148 (0.9)	9 (1.1)	105 (0.8)	330 (0.8)	63 (1.1)	4 (0.9)	36 (0.9)	14 (0.7)

Abbreviations: COPD, chronic obstructive pulmonary disease, SD, standard deviation.

Low stands for low cardiovascular health, mod for moderate cardiovascular health, high for high cardiovascular health.

Values are presented as median (Q1, Q3, quartiles [25th and 75th percentiles]) or number (%).

Table S10. Change in cardiovascular health status, and association with subsequent incident cardiovascular disease and all-cause mortality after weighting to account for attrition.

Change in CVH Status	Cardiovascular Disease				All-Cause Mortality			
	No./Total No.	Incidence Rate per 1000 Person-Years (95% CI)	ARD per 1000 Person-Years (95% CI)	Adjusted sHR (95% CI) [a]	No./Total No.	Incidence Rate per 1000 Person-Years (95% CI)	ARD per 1000 Person-Years (95% CI)	Adjusted HR (95% CI) [b]
Elderly (60~74 years)	5942/91634				6020/91634			
Consistently low	1937/22470	18.0 (17.2-18.8)	Ref	1 (Ref)	1619/22470	14.5 (13.8-15.2)	Ref	1 (Ref)
Low to moderate	1011/14715	14.9 (14.0-15.8)	-3.2 (-4.4 to -1.9)	0.81 (0.75-0.88) †	1019/14715	14.5 (13.7-15.5)	0.1 (-1.1 to 1.2)	1.00 (0.92-1.08)
Low to high	29/716	9.2 (6.2-13.2)	-8.8 (-13.5 to -4.1)	0.50 (0.35-0.73) †	38/716	11.9 (8.4-16.3)	-2.6 (-6.8 to 1.6)	0.84 (0.61-1.15)
Moderate to low	845/11329	15.3 (14.3-16.3)	-2.7 (-4.1 to -1.4)	0.83 (0.77-0.90) †	809/11329	14.2 (13.2-15.2)	-0.3 (-1.5 to 0.9)	0.95 (0.87-1.03)
Consistently moderate	1811/32576	11.8 (11.3-12.4)	-6.2 (-7.1 to -5.2)	0.65 (0.61-0.70) †	2043/32576	13.0 (12.5-13.6)	-1.4 (-2.3 to -0.5)	0.91 (0.85-0.97) †
Moderate to high	155/4658	7.6 (6.5-8.9)	-10.4 (-12.3 to -8.5)	0.43 (0.37-0.51) †	247/4658	12.0 (10.5-13.6)	-2.5 (-4.2 to -0.7)	0.88 (0.77-1.00)
High to low	9/336	5.5 (2.5-10.4)	-12.6 (-19.0 to -6.1)	0.30 (0.16-0.56) †	15/336	9.0 (5.0-14.8)	-5.5 (-11.3 to 0.3)	0.57 (0.35-0.94)
High to moderate	108/3160	7.5 (6.1-9.0)	-10.5 (-12.8 to -8.3)	0.42 (0.35-0.51) †	178/3160	12.2 (10.4-14.1)	-2.3 (-4.4 to -0.2)	0.87 (0.75-1.01)
Consistently high	38/1674	5.6 (4.0-7.7)	-12.4 (-15.6 to -9.2)	0.32 (0.23-0.44) †	52/1674	5.7 (5.7-9.9)	-6.9 (-9.8 to -4.0)	0.58 (0.44-0.77) †
Very-elderly (≥ 75 years)	1846/17695				2953/17695			
Consistently low	493/3898	30.0 (27.4-32.8)	Ref	1 (Ref)	679/3898	39.4 (36.5-42.5)	Ref	1 (Ref)
Low to moderate	286/2808	24.9 (22.1-28.2)	-4.9 (-8.9 to -0.9)	0.82 (0.70-0.95) †	467/2808	39.4 (35.9-43.1)	0.0 (-4.7 to 4.6)	0.96 (0.85-1.09)
Low to high	10/142	18.2 (8.7-33.4)	-11.8 (-26.5 to 2.8)	0.59 (0.31-1.15)	24/142	42.4 (27.2-63.1)	3.0 (-13.6 to 19.6)	1.03 (0.69-1.54)
Moderate to low	239/2077	27.7 (24.3-31.4)	-2.3 (-6.8 to 2.1)	0.90 (0.77-1.05)	362/2077	40.2 (36.2-44.6)	0.9 (-4.2 to 5.9)	0.95 (0.83-1.08)
Consistently moderate	704/6870	25.3 (23.5-27.3)	-4.7 (-7.8 to -1.5)	0.82 (0.73-0.92) †	1179/6870	40.9 (38.6-43.3)	1.5 (-2.3 to 5.3)	0.97 (0.88-1.07)

Moderate to high	54/980	14.5 (10.9-18.9)	-15.5 (-21.4 to -9.7)	0.48 (0.36-0.63) †	127/980	33.3 (27.8-39.7)	-6.1 (-12.9 to 0.8)	0.81 (0.67-0.99)
High to low	3/85	8.6 (1.8-25.2)	-21.4 (-40.0 to -3.1)	0.26 (0.09-0.79)	13/85	37.0 (19.7-63.3)	-2.4 (-23.3 to 18.6)	0.78 (0.45-1.32)
High to moderate	44/585	20.4 (14.8-27.4)	-9.6 (-17.2 to -2.0)	0.66 (0.49-0.90) †	77/585	34.8 (27.5-43.5)	-4.6 (-13.3 to 4.1)	0.81 (0.63-1.03)
Consistently high	12/250	13.0 (6.7-22.8)	-17.1 (-28.5 to -5.8)	0.42 (0.23-0.74) †	24/250	25.8 (16.5-38.3)	-13.6 (-26.6 to 0.7)	0.60 (0.39-0.91)

Abbreviations: ARD, absolute rate difference; CI, confidence interval, CVH, cardiovascular health; HR, hazard ratio; sHR, subhazard ratio.

a. sHRs were adjusted for sex, age, economic status, Hospital Frailty Score, living in metropolitan cities, and competing risk of death.

b. HRs were adjusted for sex, age, economic status, Hospital Frailty Score, and living in metropolitan cities.

† $P<0.0083$ for differences reported.

Table S11. Number of participants according to change in the level of individual cardiovascular health metrics between first and second examinations.

Pattern of change	Low-Low	Low-Mod	Low-High	Mod-Low	Mod-Mod	Mod-High	High-Low	High-Mod	High-High
Elderly (60~74 years)									
Smoking	10085 (10.9%)	1664 (1.8%)	3943 (4.3%)	940 (1%)	2722 (2.9%)	3082 (3.3%)	3182 (3.4%)	3926 (4.2%)	62926 (68.1%)
Body mass index	3662 (4%)	879 (1%)	1117 (1.2%)	828 (0.9%)	23167 (25.1%)	5855 (6.3%)	1319 (1.4%)	5336 (5.8%)	50307 (54.4%)
Physical activity	24819 (26.8%)	12130 (13.1%)	10247 (11.1%)	5349 (5.8%)	9910 (10.7%)	8642 (9.3%)	2945 (3.2%)	5528 (6%)	12900 (14%)
Blood pressure	30285 (32.8%)	15663 (16.9%)	4766 (5.2%)	14215 (15.4%)	11410 (12.3%)	2933 (3.2%)	4612 (5%)	3062 (3.3%)	5524 (6%)
Total cholesterol	4978 (5.4%)	5764 (6.2%)	1991 (2.2%)	5471 (5.9%)	22392 (24.2%)	10301 (11.1%)	1281 (1.4%)	9513 (10.3%)	30779 (33.3%)
Fasting glucose	4495 (4.9%)	3703 (4%)	1083 (1.2%)	3878 (4.2%)	14801 (16%)	10990 (11.9%)	1117 (1.2%)	12597 (13.6%)	39806 (43%)
Very-elderly (≥ 75 years)									
Smoking	1340 (7.9%)	259 (1.5%)	735 (4.3%)	127 (0.7%)	424 (2.5%)	643 (3.8%)	511 (3%)	788 (4.6%)	12134 (71.5%)
Body mass index	1009 (5.9%)	140 (0.8%)	481 (2.8%)	123 (0.7%)	2863 (16.9%)	1029 (6.1%)	619 (3.6%)	852 (5%)	9845 (58%)
Physical activity	4820 (28.4%)	2664 (15.7%)	2074 (12.2%)	734 (4.3%)	1652 (9.7%)	1414 (8.3%)	478 (2.8%)	1092 (6.4%)	2033 (12%)
Blood pressure	6055 (35.7%)	2996 (17.7%)	768 (4.5%)	2752 (16.2%)	2023 (11.9%)	445 (2.6%)	743 (4.4%)	447 (2.6%)	732 (4.3%)
Total cholesterol	877 (5.2%)	973 (5.7%)	383 (2.3%)	975 (5.7%)	3861 (22.8%)	1827 (10.8%)	218 (1.3%)	1681 (9.9%)	6166 (36.4%)
Fasting glucose	746 (4.4%)	722 (4.3%)	320 (1.9%)	705 (4.2%)	2776 (16.4%)	2136 (12.6%)	296 (1.7%)	2430 (14.3%)	6830 (40.3%)

Low stands for low cardiovascular health, mod for moderate cardiovascular health, high for high cardiovascular health.
Values are reported as No. (%).

Table S12. Incidence rates for cardiovascular disease and all-cause mortality according to change in the individual cardiovascular health metrics between first and second examinations.

	Incidence Rate per 1000 Person-Years (95% confidence intervals)								
Pattern of change	**Low-Low**	**Low-Mod**	**Low-High**	**Mod-Low**	**Mod-Mod**	**Mod-High**	**High-Low**	**High-Mod**	**High-High**
Incident cardiovascular disease									
Elderly (60~74 years)									
Smoking	20.5 (19.2-21.9)	17.3 (14.2-20.7)	16.7 (15.0-18.7)	18.2 (14.5-22.6)	15.8 (13.4-18.6)	16.0 (14.0-18.2)	16.4 (14.5-18.5)	16.1 (14.2-18.1)	12.0 (11.6-12.4)
Body mass index	15.4 (12.9-18.2)	13.0 (9.8-16.8)	29.4 (11.8-60.6)	13.3 (10.1-17.3)	14.0 (13.3-14.7)	14.2 (12.8-15.6)	30.3 (14.5-55.7)	13.2 (11.9-14.7)	13.6 (13.2-14.1)
Physical activity	15.6 (14.5-16.3)	13.6 (12.7-14.5)	13.7 (12.7-14.8)	14.3 (13.0-15.7)	10.7 (9.8-11.7)	12.4 (11.2-13.6)	13.9 (12.2-15.8)	13.2 (11.7-14.9)	12.0 (10.913.1)
Blood pressure	17.4 (16.5-18.4)	15.4 (14.5-16.3)	12.3 (10.1-14.9)	15.1 (14.1-16.1)	13.4 (12.8-14.0)	9.4 (8.3-10.6)	14.0 (11.4-17.0)	9.8 (8.7-11.0)	7.2 (6.2-8.4)
Total cholesterol	18.9 (17.2-20.8)	14.1 (12.8-15.6)	16.5 (14.0-19.3)	13.6 (12.2-15.1)	13.4 (12.7-14.1)	13.7 (12.7-14.8)	18.0 (14.8-21.7)	14.2 (13.1-15.3)	12.7 (12.2-13.3)
Fasting glucose	23.6 (21.5-25.9)	20.2 (18.1-22.5)	15.2 (12.1-18.9)	20.1 (18.1-22.3)	15.5 (14.6-16.5)	12.3 (11.3-13.3)	18.5 (15.1-22.5)	12.6 (11.8-13.6)	11.6 (11.1-12.1)
Very-elderly (≥ 75 years)									
Smoking	38.5 (33.1-44.6)	36.8 (25.4-51.7)	30.7 (24.9-37.6)	26.5 (14.5-44.4)	25.3 (17.5-35.3)	30.8 (24.2-38.6)	25.7 (19.5-33.1)	26.4 (20.8-33.0)	23.6 (22.3-24.9)
Body mass index	29.2 (19.7-41.6)	23.3 (12.8-39.1)	42.0 (8.7-122.6)	32.4 (18.9-51.9)	21.0 (18.6-23.7)	29.2 (24.5-34.5)	37.8 (10.3-9.7)	28.1 (23.0-33.9)	26.1 (24.7-27.7)
Physical activity	29.0 (27.0-31.2)	25.6 (22.8-28.7)	22.5 (19.4-25.9)	25.0 (20.3-30.5)	22.6 (18.6-27.1)	20.7 (16.6-25.6)	32.1 (25.4-40.1)	22.2 (17.2-28.2)	20.7 (17.1-24.8)
Blood pressure	29.3 (26.4-32.5)	28.6 (25.8-31.6)	20.6 (13.8-29.6)	28.1 (25.1-31.4)	23.5 (21.5-25.6)	20.5 (15.8-26.1)	28.0 (19.5-38.9)	17.9 (13.5-23.3)	15.4 (10.9-21.0)
Total cholesterol	26.9 (21.9-32.6)	27.4 (22.5-33.0)	27.1 (19.6-26.6)	27.7 (22.8-33.3)	24.9 (22.5-27.5)	23.3 (20.0-27.0)	29.1 (18.8-42.9)	26.9 (23.2-31.0)	25.3 (23.3-27.3)
Fasting glucose	39.0 (32.1-46.9)	30.7 (24.9-37.5)	34.2 (25.2-45.5)	33.7 (27.4-41.1)	26.5 (23.6-29.7)	23.1 (20.1-26.6)	28.0 (19.4-39.1)	24.4 (21.5-27.7)	23.0 (21.3-24.9)
All-cause mortality									
Elderly (60~74 years)									
Smoking	25.7 (24.3-27.3)	21.9 (18.5-25.7)	21.3 (19.4-23.5)	19.2 (15.4-23.5)	15.0 (12.7-17.7)	16.2 (14.2-18.4)	19.4 (17.4-21.6)	16.0 (14.2-18.0)	10.5 (10.1-10.9)
Body mass index	10.7 (8.7-13.0)	10.4 (7.6-13.8)	16.2 (4.4-41.4)	13.0 (9.8-16.9)	10.3 (9.7-10.9)	14.2 (12.8-15.6)	8.3 (1.8-24.3)	11.8 (10.5-13.1)	15.5 (15.0-16.0)
Physical activity	15.8 (15.2-16.5)	14.0 (13.1-15.0)	13.3 (12.3-14.4)	13.9 (12.6-15.3)	10.6 (9.7-11.6)	11.3 (10.2-12.5)	13.9 (12.2-15.8)	12.2 (10.7-13.7)	11.5 (10.5-12.6)
Blood pressure	14.8 (13.9-15.7)	14.5 (13.6-15.3)	14.7 (12.3-17.5)	14.0 (13.1-15.0)	13.3 (12.7-13.9)	12.3 (11.0-13.7)	14.2 (11.7-17.2)	11.9 (10.7-13.3)	12.1 (10.8-13.6)
Total cholesterol	12.2 (10.8-13.6)	11.4 (10.2-12.8)	13.6 (11.4-16.2)	11.6 (10.3-12.9)	10.7 (10.1-11.3)	14.0 (13.0-15.1)	18.2 (15.1-21.8)	13.1 (12.1-14.2)	16.7 (16.0-17.3)
Fasting glucose	21.5 (19.5-23.6)	18.9 (16.9-21.1)	19.8 (16.3-23.9)	17.5 (15.7-19.5)	14.7 (13.8-15.7)	13.2 (12.3-14.2)	19.7 (16.2-23.7)	12.6 (11.7-13.5)	11.7 (11.2-12.2)
Very-elderly (≥ 75 years)									
Smoking	66.5 (59.5-74.1)	53.1 (39.4-70.0)	55.0 (47.3-63.6)	74.4 (53.4-101.0)	45.7 (35.1-58.5)	49.2 (41.1-58.5)	49.8 (41.3-59.6)	48.3 (40.8-56.8)	33.6 (32.1-35.2)

Body mass index	19.4 (12.0-29.6)	24.1 (13.5-39.8)	54.4 (14.8-13.9)	32.4 (19.2-51.2)	25.9 (23.3-28.8)	44.4 (38.7-50.7)	53.8 (19.7-11.7)	39.0 (33.2-45.6)	43.5 (41.7-45.5)
Physical activity	47.1 (44.5-49.8)	38.7 (35.2-42.4)	32.8 (29.1-36.8)	39.9 (34.0-46.6)	35.5 (30.6-41.0)	29.9 (25.0-35.6)	45.8 (37.9-54.9)	32.2 (26.2-39.1)	27.6 (23.5-32.2)
Blood pressure	39.0 (35.7-42.6)	42.1 (38.8-45.7)	48.1 (37.5-60.8)	40.2 (36.7-44.1)	37.0 (34.5-39.6)	39.5 (33.0-46.9)	41.5 (31.2-54.2)	39.1 (32.5-46.6)	38.2 (31.0-46.5)
Total cholesterol	34.7 (29.1-41.0)	32.8 (27.6-38.8)	42.0 (32.7-53.1)	34.7 (29.3-40.7)	29.7 (27.1-32.5)	38.2 (34.0-42.7)	53.4 (39.4-70.8)	40.2 (35.7-45.1)	47.8 (45.2-50.6)
Fasting glucose	57.5 (49.3-66.7)	45.5 (38.5-53.4)	41.4 (31.6-53.3)	53.9 (46.0-62.8)	39.6 (36.1-43.4)	37.3 (33.4-41.5)	52.4 (40.5-66.7)	37.1 (33.5-41.0)	36.0 (33.8-38.3)

Low stands for low cardiovascular health, mod for moderate cardiovascular health, high for high cardiovascular health.

Table S13. Associations between 4 groups of change in cardiovascular health as defined in the Framingham study and incident cardiovascular disease and all-cause mortality.

Change in CVH status [a]	Elderly (60~74 years)		Very-elderly (≥ 75 years)	
Incident cardiovascular disease	**No./Total No.**	**Adjusted sHR (95% CI) [b]**	**No./Total No.**	**Adjusted sHR (95% CI) [b]**
Low-low	1764/39326	1.97 (1.84-2.10)	569/7091	1.69 (1.50-1.90)
Low-high	524/7344	1.42 (1.33-1.51)	176/1546	1.12 (0.99-1.27)
High-low	1803/25893	1.55 (1.40-1.71)	464/4519	1.36 (1.15-1.61)
High-high	1889/19907	1 [Reference]	556/3805	1 [Reference]
All-cause mortality	**No./Total No.**	**Adjusted HR (95% CI) [c]**	**No./Total No.**	**Adjusted HR (95% CI) [c]**
Low-low	1997/39326	1.62 (1.52-1.73)	975/7091	1.46 (1.33-1.60)
Low-high	563/7344	1.11 (1.04-1.19)	320/1546	0.99 (0.90-1.09)
High-low	1658/25893	1.39 (1.27-1.53)	702/4519	1.39 (1.22-1.57)
High-high	1881/19907	1 [Reference]	834/3805	1 [Reference]

Abbreviations: CI, confidence interval; CVH, cardiovascular health; HR, hazard ratio; sHR, subhazard ratio.

a. The 4 groups of change in CVH were defined as high-high (those with CVH score ≥8 at baseline and last score of ≥8, reference category), high-low (≥8 baseline and ≤7 last), low-high (≤7 baseline and ≥8 last) and low-low (≤7 baseline and ≤7 last) as used in the Framingham Offspring Study.

b. sHRs were adjusted for sex, age, economic status, Hospital Frailty Score, living in metropolitan cities, and competing risk of death.

c. HRs were adjusted for sex, age, economic status, Hospital Frailty Score, and living in metropolitan cities.

Figure S1. Summary of the statistical analysis design. Gray lines represent the enrollment of patients in this study cohort. Red line represent analysis according to the changes in CVH categories between the first and the second visit. CVD, cardiovascular disease; CVH, cardiovascular health.

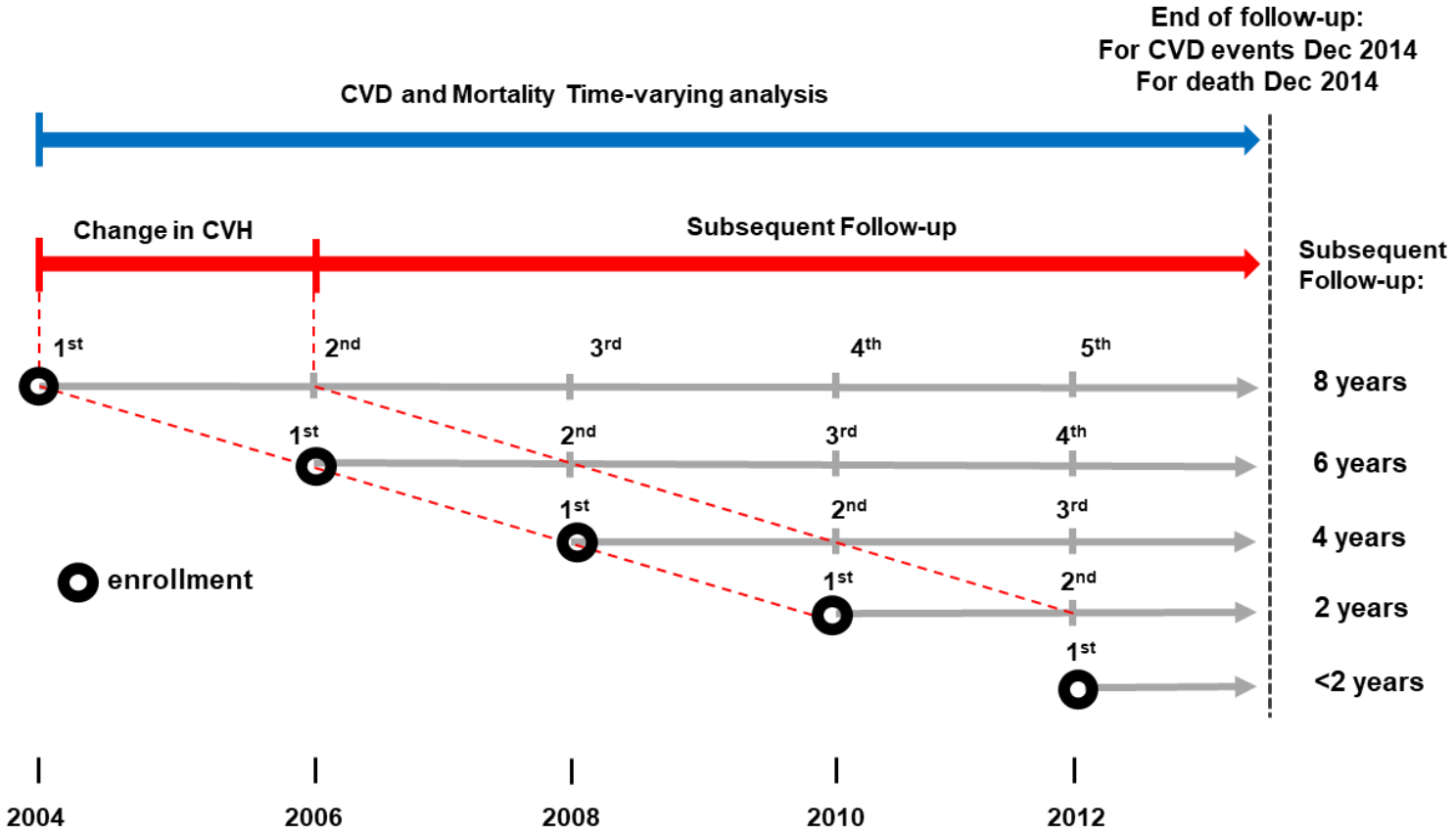

Figure S2. Distribution of the change in cardiovascular health between 1st and 2nd examination in the total study population (n=109,769) (A), in individuals aged <75 (n=92,490) and ≥70 years (n=16,961) (B), in women (n=60,135) and men (n=49,296) (C), and in high (n=50,330) and non-high (n=59,101) economic status (D). CVH, cardiovascular health.

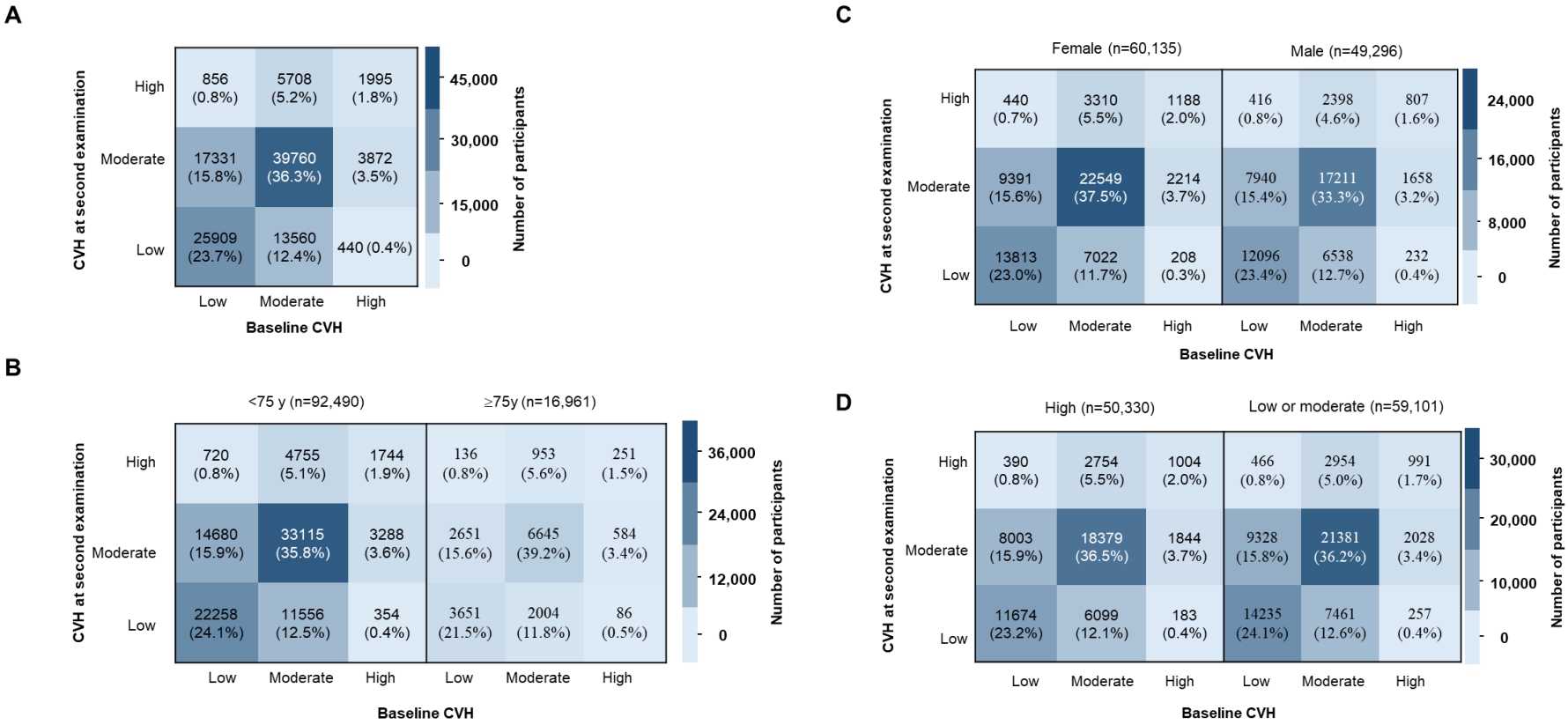

Figure S3. Kaplan–Meier curves of incident cardiovascular disease and all-cause mortality according to the patterns of change in cardiovascular health between the first and second health examinations.