ORIGINAL RESEARCH

American Heart Association | American Stroke Association

# Effect of Change in Total Cholesterol Levels on Cardiovascular Disease Among Young Adults

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***Background*—**Although high serum cholesterol in young adults is known to be a predictor for cardiovascular events, there is not enough evidence for the association of cholesterol level change with cardiovascular disease (CVD). This study aimed to evaluate whether the change in cholesterol is associated with incidence of CVD among young adults.

***Methods and Results*—**We examined 2 682 045 young adults (aged 20–39 years) who had undergone 2 consecutive national health check-ups provided by Korean National Health Insurance Service between 2002 and 2005. Cholesterol levels were classified into low (<180 mg/dL), middle (180–240 mg/dL) and high (≥240 mg/dL). CVD events were defined as ≥2 days hospitalization attributable to CVD for 10 years follow-up. Increased cholesterol levels were significantly associated with elevated ischemic heart disease risk (adjusted hazard ration [aHR]=1.21; 95% confidence interval [CI]=1.03–1.42 in low-high group and aHR=1.21; 95% CI=1.15–1.27 in middle-high group) and cerebrovascular disease (CEVD) risk (aHR=1.24; 95% CI=1.05–1.47 in low-high group and aHR=1.09; 95% CI=1.02–1.16 in middle-high group). Decreased cholesterol levels were associated with reduced ischemic heart disease risk (aHR=0.91; 95% CI=0.88–0.95 in middle-low group, aHR=0.65; 95% CI=0.56–0.75 in high-low group and aHR=0.68; 95% CI=0.65–0.73 in high-middle group). Furthermore, lower cerebrovascular disease risk (aHR=0.76; 95% CI=0.62–0.92) was observed in the high-low group compared with patients with sustained high cholesterol.

***Conclusions*—**The findings of our study indicate that increased cholesterol levels were associated with high CVD risk in young adults. Furthermore, young adults with decreased cholesterol levels had reduced risk for CVD. **(*J Am Heart Assoc*. 2018;7: e008819. DOI: 10.1161/JAHA.118.008819.)**

**Key Words:** cardiovascular disease • cerebrovascular disease/stroke • cholesterol • coronary artery disease

Although cardiovascular disease (CVD) mortality has gradually decreased in developed countries because of therapeutic advances, CVD mortality nonetheless accounts for one-thirds of all deaths in adults aged ≥35 years.[1] One of the major risk factors for CVD is dyslipidemia, which precipitates atherosclerotic change in vessels.[2] In this context, strategies for lowering cholesterol, such as statins have shown to reduce cardiovascular events in meta-analysis.[3,4] However, most studies have focused on middle-aged or elderly participants. In 2016, the United States Preventive Services Task Force stated that direct evidence on the benefits and harms of screening or treatment of dyslipidemia in young adults aged 21 to 39 years old remains insufficient.[5]

The prevalence of dyslipidemia in young adults is relatively high, with estimations ranging from 12.0% to 13.0%.[6,7] Furthermore, several studies have reported that high serum cholesterol in young adults is associated with cardiovascular events in the future.[8–11] In CARDIA (Coronary Artery Risk Development in Young Adults) study for young people aged 18 to 30 years, the risk for coronary calcium, a strong predictor of future coronary heart disease, was elevated for those with low-density lipoprotein (LDL) levels of more than 160 mg/dL compared with those with LDL levels of <70 mg/mL.[8] In a prospective study of 1071 young male medical students with a

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Accompanying Tables S1 through S5 are available at http://jaha.ahajournals.org/content/7/12/e008819/DC1/embed/inline-supplementary-material-1.pdf

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## Clinical Perspective

### What Is New?

- This study investigated the association between change in cholesterol and cardiovascular disease incidence among young adults (aged 20–39 years).
- Increased cholesterol levels were associated with elevated cardiovascular disease risk, while decreased cholesterol levels were associated with reduced cardiovascular risk among young adults.

### What Are the Clinical Implications?

- These results suggest that lowering cholesterol in young adults may contribute to reduced cardiovascular disease risk.

mean age of 22 years, higher total cholesterol at baseline was associated with increased risk of CVD.[11] Young men in 3 large cohorts demonstrated that those with total cholesterol levels <200 mg/dL had longer estimated life expectancy.[10] Although many previous studies have evaluated the effect of baseline cholesterol to CVD risk or mortality, the population size was small and limited to men.[10,11] In addition, most studies did not evaluate the association between change in cholesterol levels and CVD outcomes.

Therefore, we aimed to investigate the association between change in cholesterol among young adults and cardiovascular events using a nationwide claims database.

## Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

### Study Population

The Korean National Health Insurance (KNHI), which covers ≈97% of the Korean population, provides periodic National Health Screening Programs (NHSPs) to workers and householders in young adults in their 20s and 30s.[12] The NHSP consists of screening tests for several target diseases, including anemia, liver disease, and kidney disease, as well as cardiovascular risk factors, such as blood pressure, lipid profile, and fasting glucose. Since Korea has a single national payer, all information on utilization of medical facilities, including outpatients as well as admissions, under the national insurance is sent to KNHI with *International Classification of Diseases, 10th revision* (*ICD-10*) codes. This KNHI database has been used in epidemiological studies[13] and is described in detail elsewhere.[14]

Among 16 087 032 entire young adults aged 20 to 39 years in 2002, 8 796 348 (49.1%) were eligible for NHSP. Participation rate in NHSP among eligible people is generally known to be about 75%.[15] We identified 2 692 151 participants who had consecutively undergone national health check-ups for both the first (2002 or 2003) and second (2004 or 2005) health examination periods. Index date was set on January 1, 2006 with follow-up until December 31, 2015. We excluded people with missing cholesterol levels (n=1738), those who passed away (n=90), and those who had ischemic heart disease (IHD) (n=6164) or cerebrovascular disease (CEVD) (n=2581) before the index date, ultimately resulting in a final study population of 2 682 045 subjects (Figure). IHD (I20–I25) and CEVD (I60–I69) for exclusion were defined by using *ICD-10* diagnosis based on claim data for KNHI. This study was approved by the Seoul National University Hospital Institutional Review Board (IRB number: 1703-039-836), and consent from individual patients was waived as the data are anonymized under confidentiality guidelines.

### Change in Cholesterol Levels

Enzymatic method was used to measure serum cholesterol levels after 8 hours of fasting. Both baseline (2002–2003) and follow-up (2004–2005) cholesterol levels were classified into low (cholesterol <180 mg/dL), middle (180≤ cholesterol <240 mg/dL), and high (cholesterol ≥240 mg/dL).[16,17] Participants were then divided into 9 categories according to the change in cholesterol levels between the 2 periods (sustained low, low-middle, low-high, middle-low, sustained middle, middle-high, high-low, high-middle, and sustained high groups). Those who stayed in the same category of cholesterol during first and second examination were established as the reference groups (sustained low, sustained middle, and sustained high).

### Outcome: Cardiovascular Disease Incidence

To identify CVD incidence, hospital admission records were used between January 1, 2006 and December 31, 2015. CVD events were defined as hospitalization for at least 2 days with *ICD-10* codes pertaining to CVD.[18] IHD (I20–I25), which includes acute myocardial infarction (I21) and CEVD (I60–69), which includes stroke (I60–I64) were included in CVD.

### Covariates

Age was grouped into 4 categories, 20 to 24, 25 to 29, 30 to 34, ≥35 years old. Body mass index (BMI) was calculated weight (kg) divided by height (m) squared and classified into <18.5, 18.5 to 22.9, 23.0 to 24.9, and ≥25.0 kg/m$^2$ according to the Asian-Pacific obesity classification.[19] Smoking status was classified into never, former, and current smokers. Drinking status was divided into yes or no. Status of

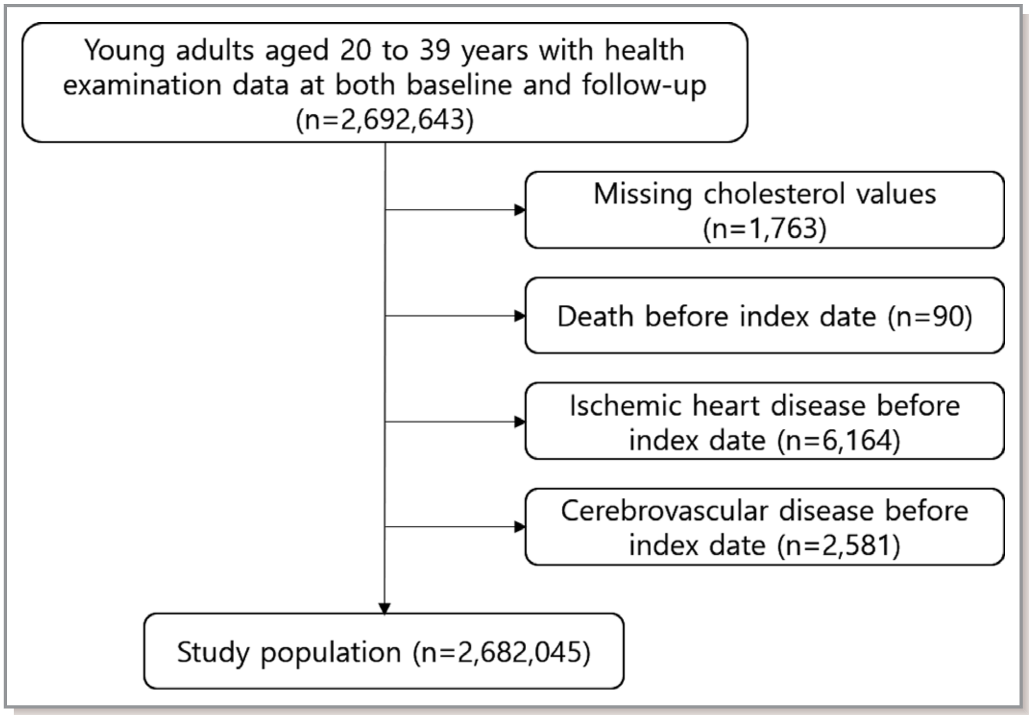


**Figure.** Flow chart of inclusion in the study population.

physical activity was classified according to the frequency per week (none, 1–2, 3–4, and 5–7 times). Quartiles of insurance premium was used to assess income status. Comorbidities were determined by the Charlson comorbidity index (CCI)[20] with *ICD-10* codes before the index date.

Statin use was defined with defined daily dose (DDD). Defined daily dose is the average maintenance dose per day to compare dosing of different statins, which was standardized by the World Health Organization.[21] The sum of defined daily dose through 2002–2005 was used and subjects with statin prescription history of >30 cumulative defined daily doses were defined as statin users.[22] Hypertension was defined as diagnosis by a physician, taking anti-hypertensive medication based on self-questionnaire or blood pressure ≥140/90 mm Hg. Diabetes mellitus was defined as diagnosis by a physician, taking oral hypoglycemic agents or insulin injections based on self-questionnaire or fasting blood sugar (FBG) ≥126 mg/dL.

## Statistical Analysis

The mean (standard deviation [SD]) for continuous variables and number of subjects with percentage with categorical variables were determined. We used Cox proportional hazards regression analysis to evaluate the risk of CVD according to change in cholesterol levels. We adjusted for age and sex in model 1. We additionally adjusted for lifestyle variables (BMI, smoking status, drinking status and physical activity), socioeconomic factors (income status) and medical information (Charlson comorbidity index, statin medication, history of hypertension, diabetes mellitus, systolic blood pressure, and FBG level) in model 2. We also performed subgroup analyses stratified by age, sex, statin medication, hypertension and diabetes mellitus. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

# Results

## Baseline Characteristics

The mean age of the total population was 34.3 (SD 5.5) years and 68.8% of the participants were male (Table 1). The mean cholesterol levels at baseline was 186.2 mg/dL (SD 42.2). The number participants in baseline low, middle, and high cholesterol level groups were 1 232 472 (46.0%), 1 259 264 (47.0%), and 189 843 (7.0%), respectively. Participants in the high cholesterol group were more likely to be old, male, have high Charlson comorbidity index, and have hypertension or diabetes mellitus. Moreover, statin prescription rate was higher in the high cholesterol group at 8.0%.

## Association Between Baseline Cholesterol Levels and Incidence of CVD

The median follow-up period to CVD incidence was 9.9 years. The risk of IHD was higher in the high cholesterol group (adjusted HR [aHR]=1.75; 95% confidence interval [CI]=1.69–

**Table 1.** Baseline Characteristics of Study Populations

| | Total | Baseline Total Cholesterol | | | P Value |
|---|---|---|---|---|---|
| | | Low (TC <180 mg/dL) | Middle (180< TC <240 mg/dL) | High (TC ≥240 mg/dL) | |
| All subjects, n (%) | 2 682 045 | 1 232 668 (46.0) | 1 259 503 (47.0) | 189 874 (7.0) | |
| Age, mean (SD), y | 34.3 (5.5) | 33.3 (5.6) | 35.0 (5.2) | 36.2 (4.7) | <0.001 |
| 20 to 24 | 106 383 (4.0) | 71 246 (5.8) | 33 170 (2.6) | 1967 (1.0) | <0.001 |
| 25 to 29 | 470 240 (17.5) | 278 983 (22.6) | 176 482 (14.0) | 14 775 (7.8) | |
| 30 to 34 | 771 097 (28.8) | 358 818 (29.1) | 361 115 (28.7) | 51 164 (27.0) | |
| ≥35 | 1 334 325 (49.8) | 523 621 (42.5) | 688 736 (54.7) | 121 968 (64.2) | |
| Sex, n (%) | | | | | |
| Male | 1 845 940 (68.8) | 758 861 (61.6) | 928 045 (73.7) | 159 034 (83.8) | <0.001 |
| Female | 836 105 (31.2) | 473 807 (38.4) | 331 458 (26.3) | 30 840 (16.2) | |
| Baseline TC, mean (SD), mg/dL | 186.2 (42.2) | 156.7 (16.7) | 203 (15.9) | 266.8 (87.3) | <0.001 |
| Body mass index, n (%), kg/m$^2$ | | | | | |
| <18.5 | 143 392 (5.4) | 93 516 (7.6) | 46 758 (3.7) | 3118 (1.6) | <0.001 |
| 18.5 to 22.9 | 1 182 734 (44.1) | 655 341 (53.2) | 481 210 (38.2) | 46 183 (24.3) | |
| 23.0 to 24.9 | 605 482 (22.6) | 249 955 (20.3) | 308 552 (24.5) | 46 975 (24.7) | |
| ≥25.0 | 749 971 (28.0) | 233 660 (19.0) | 422 744 (33.6) | 93 567 (49.3) | |
| N/A | 466 (0.0) | 196 (0.0) | 239 (0.0) | 31 (0.0) | |
| Physical activity, n (%), times per week | | | | | |
| None | 1 322 132 (49.3) | 640 911 (52.0) | 596 868 (49.4) | 84 353 (44.4) | <0.001 |
| 1 to 2 | 882 017 (32.9) | 386 118 (31.3) | 427 996 (34.0) | 67 903 (35.8) | |
| 3 to 4 | 299 699 (11.2) | 127 897 (10.4) | 147 765 (11.7) | 24 037 (12.7) | |
| 5 to 6 | 57 021 (2.1) | 24 447 (2.0) | 28 063 (2.2) | 4511 (2.4) | |
| 7 | 68 934 (2.6) | 30 278 (2.5) | 33 527 (2.7) | 5129 (2.7) | |
| N/A | 52 242 (2.0) | 23 017 (1.9) | 25 284 (2.0) | 3941 (2.1) | |
| Smoking status, n (%) | | | | | |
| Never | 1 433 222 (53.4) | 713 388 (57.9) | 647 532 (50.6) | 82 302 (43.4) | <0.001 |
| Former | 286 770 (10.7) | 115 123 (9.3) | 146 391 (11.6) | 25 256 (13.3) | |
| Current | 914 282 (34.1) | 381 349 (30.9) | 453 663 (36.0) | 79 270 (41.8) | |
| N/A | 47 771 (1.8) | 22 808 (1.9) | 21 917 (1.7) | 3046 (1.6) | |
| Drinking, n (%) | | | | | |
| No | 1 000 221 (37.3) | 492 101 (39.9) | 446 677 (35.5) | 61 443 (32.4) | <0.001 |
| Yes | 1 647 770 (61.4) | 725 014 (58.8) | 796 736 (63.3) | 126 020 (66.4) | |
| N/A | 34 054 (1.3) | 15 553 (1.3) | 15 553 (1.3) | 2411 (1.3) | |
| Income status, n (%) | | | | | |
| 1st quartile (lowest) | 317 404 (11.8) | 156 338 (12.7) | 141 307 (11.2) | 19 759 (10.4) | <0.001 |
| 2nd quartile | 583 864 (21.8) | 302 457 (24.5) | 249 161 (19.8) | 32 246 (17.0) | |
| 3rd quartile | 969 043 (36.1) | 447 712 (36.3) | 452 887 (36.0) | 68 444 (36.1) | |
| 4th quartile (highest) | 811 734 (30.3) | 326 161 (26.5) | 416 148 (33.0) | 69 425 (36.6) | |
| Charlson comorbidity index, n (%) | | | | | |
| 0 | 1 362 127 (50.8) | 633 427 (51.4) | 637 084 (50.6) | 91 616 (48.3) | <0.001 |
| 1 | 921 844 (34.4) | 424 741 (34.5) | 431 927 (34.3) | 65 176 (34.3) | |
| ≥2 | 398 074 (14.8) | 174 500 (14.2) | 190 492 (15.1) | 33 082 (17.4) | |

Continued

**Table 1.** Continued

| | Total | Baseline Total Cholesterol | | | *P* Value |
|---|---|---|---|---|---|
| | | Low (TC <180 mg/dL) | Middle (180< TC <240 mg/dL) | High (TC ≥240 mg/dL) | |
| Statin medication, n (%) | | | | | |
| No | 2 648 797 (98.8) | 1 229 354 (99.7) | 1 244 710 (98.8) | 174 733 (92.0) | <0.001 |
| Yes | 33 248 (1.2) | 3314 (0.3) | 14 793 (1.2) | 15 141 (8.0) | |
| Hypertension, n (%) | | | | | |
| No | 2 258 949 (84.2) | 1 086 832 (88.2) | 1 032 016 (81.9) | 140 101 (73.8) | <0.001 |
| Yes | 423 096 (15.8) | 145 836 (11.8) | 227 487 (18.1) | 49 773 (26.2) | |
| Diabetes mellitus, n (%) | | | | | |
| No | 2 599 939 (96.9) | 1 206 990 (97.9) | 1 216 029 (96.6) | 176 920 (93.2) | <0.001 |
| Yes | 82 106 (3.1) | 25 678 (2.1) | 43 474 (3.5) | 12 954 (6.8) | |
| Systolic blood pressure, mean (SD), mm Hg | 119.6 (13.8) | 117.6 (13.2) | 120.9 (13.8) | 124.3 (14.5) | <0.001 |
| Fasting blood glucose, mean (SD), mg/dL | 75.7 (10.0) | 74.2 (9.6) | 76.6 (10.0) | 79.0 (10.5) | <0.001 |

n indicates number of people; N/A, not available; SD, standard deviation; TC, total cholesterol.

1.82) and middle cholesterol group (aHR=1.17; 95% CI=1.14–1.20) compared with the low cholesterol group at baseline (Table S1). The risk of CEVD was also higher in the high cholesterol group (aHR=1.19; 95% CI=1.14–1.25) and middle cholesterol group (aHR=1.05; 95% CI=1.02–1.08) compared with the low cholesterol group at baseline.

## Association Between Change in Total Cholesterol and Incidence of CVD

Increased cholesterol levels to the high cholesterol group was significantly associated with elevated IHD risk (aHR=1.21; 95% CI=1.03–1.42 in low-high group and aHR=1.21; 95% CI=1.15–1.27 in middle-high group) and high CEVD risk (aHR=1.24; 95% CI=1.05–1.47 in low-high group and aHR=1.09; 95% CI=1.02–1.16 in middle-high group) (Table 2).

Decreased cholesterol levels were associated with reduced IHD risk (aHR=0.91; 95% CI=0.88–0.95 in the middle-low group, aHR=0.65; 95% CI=0.56–0.75 in the high-low group and aHR=0.68; 95% CI=0.65–0.73 in the high-middle group). Furthermore, decreased CEVD risk (aHR=0.76; 95% CI=0.62–0.92) was observed in the high-low cholesterol group compared with the sustained high cholesterol group.

The mean changes for each group were 11.0 (SD, 24.6), −4.8 (SD, 27.2) and −28.3 (SD, 37.2) in the low-, middle-, and high-cholesterol group, respectively (Table 3). Significantly, high risk for IHD was observed in each group (aHR=1.02; 95% CI 1.00–1.05 in low-, aHR=1.04; 95% CI=1.02–1.06 in middle- and aHR=1.09; 95% CI=1.06–1.11 in high-cholesterol group per 1 SD [29.1 mg/dL] increase).

## Subgroup Analysis for Incidence of CVD

In subgroup analysis stratified by baseline characteristics such as age, sex, statin medication, hypertension, and diabetes mellitus, incidence rates were shown for each stratified group. Women between the ages of 20 to 29 years, who were statin non-users without hypertension and diabetes mellitus had lower incidence rates for CVD (Table S2).

Increased or decreased cholesterol levels in their 20s were not significantly associated with incidence of CVD (Table S3). Meanwhile, increased cholesterol levels in their 30s were associated with elevated risk of CVD (aHR=1.28; 95% CI=1.09–1.51 in the low-high group for IHD) and decreased cholesterol levels were associated with reduced risk of CVD (aHR=0.62; 95% CI=0.54–0.72 in high-low group for IHD). Consistent results were observed in men compared with no significant association in women. Decreased cholesterol levels from baseline high cholesterol levels were associated with low CVD risk in both statin users and non-users compared with the sustained high cholesterol group. Moreover, the magnitude of risk lowering effect was larger in statin users (aHR=0.60; 95% CI=0.44–0.83 in high-low group for IHD) than statin non-users (aHR=0.68; 95% CI=0.57–0.80 in the high-low group for IHD).

## Discussion

In this nationwide cohort study, we have revealed that increased cholesterol levels and decreased cholesterol levels in young adults were associated with elevated and reduced risk of CVD, respectively. These findings were more robust in men aged >30 years irrespective of statin medication.

**Table 2.** Hazard Ratios for Cardiovascular Diseases Incidence by Change of Total Cholesterol

| Baseline TC | Low (TC <180 mg/dL) | | | Middle (180≤ TC <240 mg/dL) | | | High (TC ≥240 mg/dL) | | |
|---|---|---|---|---|---|---|---|---|---|
| Follow-Up TC | Low | Middle | High | Low | Middle | High | Low | Middle | High |
| Change, mg/dL, mean (SD) | 1.0 (18.1) | 32.8 (19.3) | 112.2 (147.8) | −32.0 (18.1) | 0.3 (19.0) | 44.1 (69.7) | −130.8 (198.4) | −46.6 (90.2) | −0.9 (59.1) |
| Number of people (%) | 866 178 (70.2) | 353 605 (28.7) | 12 885 (1.0) | 325 271 (25.8) | 835 005 (66.3) | 99 227 (7.9) | 12 504 (6.6) | 99 103 (52.2) | 78 267 (41.2) |
| Ischemic heart disease | | | | | | | | | |
| Cases, n | 6370 | 3231 | 155 | 3227 | 10 738 | 1824 | 200 | 2000 | 2557 |
| Incidence rates* | 0.74 | 0.92 | 1.21 | 1.00 | 1.30 | 1.86 | 1.62 | 2.05 | 3.33 |
| Model 1 | | | | | | | | | |
| aHR | 1.00 | 1.11 | 1.52 | 0.88 | 1.00 | 1.35 | 0.64 | 0.64 | 1.00 |
| 95% CI | | 1.06 to 1.16 | 1.30 to 1.78 | 0.84 to 0.91 | | 1.29 to 1.42 | 0.55 to 1.74 | 0.61 to 0.68 | |
| *P*-value | | <0.001 | <0.001 | <0.001 | | <0.001 | <0.001 | <0.001 | |
| Model 2 | | | | | | | | | |
| aHR | 1.00 | 1.05 | 1.21 | 0.91 | 1.00 | 1.21 | 0.65 | 0.68 | 1.00 |
| 95% CI | | 1.00 to 1.09 | 1.03 to 1.42 | 0.88 to 0.95 | | 1.15 to 1.27 | 0.56 to 0.75 | 0.65 to 0.73 | |
| *P*-value | | 0.059 | 0.022 | <0.001 | | <0.001 | <0.001 | <0.001 | |
| Cerebrovascular disease | | | | | | | | | |
| Cases, n | 5910 | 2863 | 138 | 2822 | 7998 | 1170 | 115 | 1270 | 1136 |
| Incidence rates* | 0.69 | 0.82 | 1.08 | 0.87 | 0.97 | 1.18 | 0.92 | 1.28 | 1.47 |
| Model 1 | | | | | | | | | |
| aHR | 1.00 | 1.09 | 1.49 | 0.98 | 1.00 | 1.20 | 0.73 | 0.90 | 1.00 |
| 95% CI | | 1.05 to 1.14 | 1.26 to 1.77 | 0.93 to 1.02 | | 1.13 to 1.27 | 0.60 to 0.89 | 0.83 to 0.97 | |
| *P*-value | | <0.001 | <0.001 | 0.241 | | <0.001 | 0.002 | 0.009 | |
| Model 2 | | | | | | | | | |
| aHR | 1.00 | 1.03 | 1.24 | 1.02 | 1.00 | 1.09 | 0.76 | 0.95 | 1.00 |
| 95% CI | | 0.98 to 1.08 | 1.05 to 1.47 | 0.97 to 1.06 | | 1.02 to 1.16 | 0.62 to 0.92 | 0.87 to 1.03 | |
| *P*-value | | 0.205 | 0.014 | 0.515 | | 0.008 | 0.005 | 0.195 | |

Model 1: adjusted for age and sex. Model 2: additionally adjusted for body mass index, Charlson comorbidity index, statin medication, alcohol consumption, smoking habit, physical activity, income status, hypertension, diabetes mellitus, blood pressure, and fasting serum glucose. aHR indicates adjusted hazard ratio; CI, confidence interval; SD, standard deviation; TC, total cholesterol.
*Cases per 1000 person-years.

**Table 3.** Hazard Ratios for Cardiovascular Diseases Incidence by Change in Total Cholesterol as a Continuous Variable

| Baseline TC | Low (TC <180 mg/dL) | Middle (180≤ TC <240 mg/dL) | High (TC ≥240 mg/dL) |
|---|---|---|---|
| Mean change of TC (SD), mg/dL | 11.0 (24.6) | −4.8 (27.2) | −28.3 (37.2) |
| Adjusted HR (95% CI) per 1 SD of change* | | | |
| Ischemic heart disease | 1.02 (1.00–1.05) | 1.04 (1.02–1.06) | 1.09 (1.06–1.11) |
| Cerebrovascular disease | 1.02 (0.99–1.04) | 1.01 (0.99–1.03) | 1.01 (0.98–1.04) |

Adjusted for age, sex, body mass index, Charlson comorbidity index, statin medication, alcohol consumption, smoking habit, physical activity, income status, hypertension, diabetes mellitus, blood pressure, and fasting serum glucose. CI indicates confidence interval; HR, hazard ratio; SD, standard deviation; TC, total cholesterol.
*1 SD of change was calculated as 29.1 mg/dL.

While many previous studies have evaluated the association between cholesterol levels and CVD risk in young adults,[8–11] there was no randomized controlled trial targeted to young adults. Although guidelines recommend high-intensity statin treatment in adults aged >21 years with LDL-C ≥190 mg/dL, the benefits were extrapolated from results in middle and elderly participants because of the lack of studies in young adults.[23] The results from our study could add evidence that reducing cholesterol levels may be beneficial and necessary for those with high cholesterol levels to reduce CVD risk in young adults. However, our significant result was limited to men aged >30 years, possibly because of low incidence rates in female participants in their 20s.

Participants with increased cholesterol levels were associated with higher risk of CVD compared with those in sustained low or sustained middle cholesterol groups. Furthermore, decreased cholesterol levels were associated with lower CVD risk. Although the reasons for change in cholesterol levels cannot be determined, we can assume that such decrease would be achieved mostly by statin medication or lifestyle intervention. Well-established lifestyle management includes diet, increased physical activity, and weight control.[24,25] However, only 10% to 42% of young adults meet the optimal physical activity levels recommended[26,27] and the prevalence of obesity among young adults is persistently increasing not only in Korea[28] but also globally.[29] Therefore, lifestyle modification should be emphasized in those with high cholesterol levels. However, cholesterol lowering effects by lifestyle modification can decrease only 7% to 18% of cholesterol.[30] Decreased cholesterol levels to the low-cholesterol group were associated with lower risk of CVD compared with decreased cholesterol levels to the middle-cholesterol group from the high-cholesterol group. Therefore, lifestyle modification alone may not be sufficient to completely benefit from reduced risk of CVD upon cholesterol level reduction.

Meanwhile, there is a lack of definitive evidence to support the prescription of statin at a young age in terms of unconfirmed long-term benefits, harms, and cost-effectiveness.[31] Steinberg suggested that early intervention should be considered particularly among those with high lifetime risk and low 10-year atherosclerotic CVD.[32] The author stressed the "cumulative damage hypothesis" which assumes that atherosclerotic change begins at a young age.[33] However, despite American College of Cardiology/American Heart Association guidelines,[23] statin prescription rates in people <40 years were estimated to be <45% among those with LDL-C≥190 mg/dL, which is lower than that in middle-aged and elderly adults.[34]

The main strength of this study lies in the nature of the nationwide database with a large study population of young adults. We confirmed CVD risk according to not only baseline cholesterol levels but also the change in cholesterol levels with a relatively long observation period. In addition, we adjusted for various cardiovascular risk factors encompassing lifestyle variables and clinical information.

There are several limitations that need to be considered when interpreting our study. First, since national data are not intentionally collected solely for this study, it is difficult to determine the exact cause of cholesterol change. Unintentionally decreased cholesterol levels may partly reflect poor health condition that can affect cholesterol synthesis.[16] However, it is reasonable to assume that cholesterol levels have been reduced by positive health effects because most of the study population are composed of working young adults. Second, we do not have information on specific composition of lipoprotein particles, such as LDL-C and high-density lipoprotein-cholesterol. Although a previous report showed that total cholesterol and LDL-C were linearly associated (correlation coefficient=0.84),[35] the number of atherogenic particles (LDL-C) or ratio of lipoproteins (LDL/high-density lipoprotein) may be more important determinants for atherosclerosis than total cholesterol levels.[36] Third, since NHSP is provided to workers and householders among young adults, only half of young adults were eligible for the NHSP. Therefore, the results from our study may be partly reflected by characteristics of study population, which is mainly composed of men aged ≥30 years.

Fourth, we could not reflect specific information on statin use. However, to supplement simple adjustment for statin use (yes or no), adjusted values for average treatment effects were used to reclassify statin users (Table S4). The results were in accordance with the main findings. Fifth, the change in cholesterol could reflect the "regression to mean" phenomenon rather than reflecting an actual biological effect.[37] Particularly, 52.2% of subjects in the high cholesterol group at baseline reduced to the middle cholesterol group. Multiple measurements at baseline could partly relieve the regression to mean effect. However, changes in other factors, which could be affected by lifestyle modification, including BMI, FBG, and systolic blood pressure, were accompanied by the change in cholesterol levels (Table S5).

## Conclusion

Increased cholesterol levels were associated with elevated CVD risk, while decreased cholesterol levels were associated with reduced CVD risk among young adults. Future studies should elucidate the effect of lowering cholesterol levels on CVD risk using interventions such as statins among young adults.

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## Disclosures

None.

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# SUPPLEMENTAL MATERIAL

**Table S1**. **Hazard Ratios for cardiovascular disease by baseline total cholesterol.**

| Baseline TC | Low (TC < 180 mg/dL) | Middle (180 ≤ TC < 240 mg/dL) | *p*- value | High (TC ≥ 240 mg/dL) | *p*- value |
|---|---|---|---|---|---|
| Number of people | 1,232,668 | 1,259,503 | | 189,874 | |
| Ischemic heart disease | | | | | |
| Cases | 9,756 | 15,789 | | 4,757 | |
| Incidence rates* | 0.80 | 1.27 | | 2.55 | |
| Unadjusted HR (95% CI) | 1.00 | 1.59 (1.55-1.63) | <0.001 | 3.20 (3.09-3.31) | <0.001 |
| Model 1 | | | | | |
| aHR (95% CI) | 1.00 | 1.28 (1.25-1.32) | <0.001 | 2.23 (2.15-2.31) | <0.001 |
| Model 2 | | | | | |
| aHR (95% CI) | 1.00 | 1.17 (1.14-1.20) | <0.001 | 1.75 (1.69-1.82) | <0.001 |
| Cerebrovascular disease | | | | | |
| Cases | 8,911 | 11,991 | | 2,521 | |
| Incidence rates* | 0.73 | 0.96 | | 1.34 | |
| Unadjusted HR (95% CI) | 1.00 | 1.32 (1.28-1.36) | <0.001 | 1.85 (1.77-1.93) | <0.001 |
| Model 1 | | | | | |
| aHR (95% CI) | 1.00 | 1.13 (1.10-1.16) | <0.001 | 1.42 (1.36-1.49) | <0.001 |
| Model 2 | | | | | |
| aHR (95% CI) | 1.00 | 1.05 (1.02-1.08) | 0.001 | 1.19 (1.14-1.25) | <0.001 |

* Cases per 1,000 peson-years

Model 1: hazard ratio calculated by Cox proportional hazards regression adjusted for age and sex

Model 2: additionally adjusted for body mass index, Charlson comorbidity index, statin medication, alcohol consumption, smoking habit, physical activity, income status, hypertension, diabetes, blood pressure and fasting serum glucose.

Acronyms: TC, total cholesterol; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval

**Table S2**. **Incidence cases with incidence rates (1,000 person-years) for cardiovascular events by change of total cholesterol total with stratification by baseline characteristics.**

| Baseline TC | Low (TC < 180 mg/dL) | | | Middle (180 ≤ TC < 240 mg/dL) | | | High (TC ≥ 240 mg/dL) | | |
|---|---|---|---|---|---|---|---|---|---|
| Follow-up TC | Low | Middle | High | Low | Middle | High | Low | Middle | High |
| Number of people | 866,178 | 353,605 | 12,885 | 325,271 | 835,005 | 99,227 | 12,504 | 99,103 | 78,267 |
| | 887 (0.34) | 333 (0.40) | 7 (0.22) | 246 (0.36) | 596 (0.47) | 82 (0.67) | 11 (0.56) | 50 (0.56) | 56 (0.98) |
| Ischemic heart disease | | | | | | | | | |
| | 5,483 (0.92) | 2,898 | 148 (1.55) | 2,981 (1.18) | 10,142 | 1,742 (2.03) | 189 (1.82) | 1,950 | 2,501 (3.52) |
| Age | | | | | | | | | |
| | | (1.09) | | | (1.45) | | | (2.20) | |
| 20-29 | | | | | | | | | |
| | 4,797 (0.95) | | 136 (1.75) | 2,585 (1.25) | | 1,713 (2.12) | 169 (2.27) | | 2,458 (3.60) |
| 30-39 | | | | | | | | | |
| | 1,573 (0.45) | 2,679 | 19 (0.38) | 642 (0.55) | 9,595 (1.52) | 111 (0.65) | 31 (0.64) | 1,864 | 99 (1.18) |
| Sex | | | | | | | | | |
| | | (1.13) | | | 1,143 (0.58) | | | (2.32) | |
| Men | | | | | | | | | |
| | 6,321 (0.74) | 552 (0.49) | 138 (1.11) | 3,117 (0.97) | | 1,663 (1.77) | 158 (1.40) | 136 (0.78) | 2.073 (3.03) |
| Women | | | | | | | | | |
| | 49 (3.46) | | 17 (4.55) | 110 (4.42) | 10,404 | 161 (4.20) | 42 (4.13) | | 484 (5.81) |
| Statin medication | | | | | | | | | |
| | | 3,170 | | | (1.27) | | | 1,787 | |
| No | | | | | | | | | |
| | 4,998 (0.65) | (0.91) | 90 (0.88) | 2,281 (0.82) | 334 (4.15) | 1,100 (1.49) | 114 (1.16) | (1.94) | 1,505 (2.77) |
| Yes | | | | | | | | | |
| | 1,372 (1.53) | 61 (4.25) | 65 (2.55) | 956 (2.07) | | 724 (3.00) | 86 (3.47) | 213 (4.00) | 1,052 (4.72) |
| Hypertension | | | | | | | | | |
| | | | | | 7,059 (1.05) | | | | |
| No | | | | | | | | | |
| | 6,109 (0.72) | 2,323 | 134 (1.11) | 2,982 (0.95) | 3,679 (2.39) | 1,619 (1.75) | 174 (1.51) | 1,220 | 2,216 (3.13) |
| Yes | | | | | | | | | |
| | 261 (1.65) | (0.78) | 21 (3.24) | 245 (2.68) | | 205 (3.69) | 26 (3.13) | (1.65) | 341 (5.81) |
| Diabetes | | | | | | | | | |
| | | 908 (1.76) | | | 9,899 (1.24) | | | 780 (3.29) | |
| No | | | | | | | | | |
| | | | | | 839 (3.02) | | | | |
| Yes | | | | | | | | | |
| | | 3,032 | | | | | | 1,752 | |
| | | (0.89) | | | | | | (1.91) | |
| | | 65 (2.55) | | | | | | 248 (4.24) | |
| Cerebrovascular disease | | | | | | | | | |
| Age | | | | | | | | | |
| 20-29 | 887 (0.34) | 273 (0.32) | 17 (0.53) | 250 (0.36) | 521 (0.41) | 57 (0.47) | 9 (0.46) | 34 (0.38) | 42 (0.73) |
| 30-39 | 5,023 (0.84) | 2,590 | 121 (1.26) | 2,572 (1.01) | 7,478 (1.07) | 1,113 (1.29) | 106 (1.02) | 1,236 | 1,094 (1.53) |
| Sex | | (0.97) | | | | | | (1.39) | |
| Men | 3,880 (0.76) | | 106 (1.36) | 2,009 (0.97) | 6,431 (1.02) | 1,002 (1.23) | 86 (1.15) | | 1,027 (1.49) |
| Women | 2,030 (0.57) | 2,123 | 32 (0.64) | 813 (0.70) | 168 (0.98) | 168 (0.98) | 29 (0.59) | 1,102 | 109 (1.30) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Statin medication | | (0.89) | | | | | | (1.37) | |
| No | 5,880 (0.68) | 740 (0.65) | 132 (1.06) | 2,767 (0.86) | 7,836 (0.95) | 1,079 (1.14) | 100 (0.88) | 168 (0.97) | 958 (1.39) |
| Yes | 30 (2.10) | | 6 (1.58) | 55 (2.18) | 163 (2.00) | 91 (2.34) | 15 (1.45) | | 178 (2.10) |
| Hypertension | | 2,832 | | | | | | 1,164 | |
| No | 4,622 (0.60) | (0.81) | 96 (0.94) | 1,974 (0.71) | 5,312 (0.79) | 705 (0.95) | 70 (0.71) | (1.26) | 592 (1.08) |
| Yes | 1,288 (1.43) | 31 (2.13) | 42 (1.64) | 848 (1.85) | 2,687 (1.74) | 465 (1.91) | 45 (1.80) | 106 (1.97) | 544 (2.41) |
| Diabetes | | | | | | | | | |
| No | 5,705 (0.68) | 2,057 | 121 (1.00) | 2,649 (0.84) | 7,494 (0.94) | 1,018 (1.10) | 98 (0.85) | 759 (1.02) | 985 (1.38) |
| Yes | 205 (1.29) | (0.69) | 17 (2.61) | 173 (1.88) | 505 (1.80) | 152 (2.71) | 17 (2.02) | 511 (2.14) | 151 (2.53) |
| | | 806 (1.56) | | | | | | | |
| | | | | | | | | 1,122 | |
| | | 2,728 | | | | | | (1.22) | |
| | | (0.80) | | | | | | 148 (2.51) | |
| | | 135 (1.53) | | | | | | | |

Absolute cases with incidence rates (1,000 person-years) were noted.

**Table S3. Hazard Ratios for incidence of cardiovascular events according to the change of total cholesterol in with stratification by baseline characteristics.**

| Baseline TC | | Low (TC < 180 mg/dL) | | | Middle (180 ≤ TC < 240 mg/dL) | | | High (TC ≥ 240 mg/dL) | |
|---|---|---|---|---|---|---|---|---|---|
| Follow-up TC | Low | Middle | High | Low | Middle | High | Low | Middle | High |
| Ischemic heart disease | | | | | | | | | |
| Age | | | | | | | | | |
| 20-29 | 1.00 | 1.08 | 0.61 | 0.92 | 1.00 | 1.14 | 0.99 | 0.75 | 1.00 |
| | | 0.95 – 1.22 | 0.29 – 1.22 | 0.79-1.07 | | 0.90-1.44 | 0.51-1.93 | 0.51-1.11 | |
| ≥ 30 | 1.00 | 1.06 | 1.28 | 0.90 | 1.00 | 1.21 | 0.62 | 0.69 | 1.00 |
| | | 1.01 – 1.11 | 1.09 – 1.51 | 0.87-0.94 | | 1.15-1.28 | 0.54-0.72 | 0.65-0.73 | |
| Sex | | | | | | | | | |
| Men | 1.00 | 1.07 | 1.32 | 0.88 | 1.00 | 1.23 | 0.63 | 0.68 | 1.00 |
| | | 1.02 – 1.12 | 1.11 – 1.57 | 0.84-0.92 | | 1.17-1.29 | 0.54-0.74 | 0.64-0.72 | |
| Women | 1.00 | 0.95 | 0.76 | 1.09 | 1.00 | 0.94 | 0.82 | 0.80 | 1.00 |
| | | 0.86 – 1.05 | 0.48 – 1.20 | 0.99-1.20 | | 0.77-1.14 | 0.54-1.25 | 0.61-1.04 | |
| Statin medication | | | | | | | | | |
| No | 1.00 | 1.04 | 1.21 | 0.91 | 1.00 | 1.22 | 0.68 | 0.70 | 1.00 |
| | | 0.99 – 1.09 | 1.02 – 1.43 | 0.88-0.95 | | 1.16-1.28 | 0.57-0.80 | 0.66-0.75 | |
| Yes | 1.00 | 1.10 | 1.17 | 0.97 | 1.00 | 1.07 | 0.60 | 0.63 | 1.00 |
| | | 0.75 – 1.61 | 0.67 – 2.04 | 0.78-1.20 | | 0.88-1.29 | 0.44-0.83 | 0.54-0.74 | |
| Hypertension | | | | | | | | | |
| No | 1.00 | 1.03 | 1.13 | 0.93 | 1.00 | 1.23 | 0.62 | 0.67 | 1.00 |
| | | 0.98 – 1.16 | 0.92 – 1.40 | 0.88-0.97 | | 1.16-1.31 | 0.51-0.76 | 0.62-0.73 | |
| Yes | 1.00 | 1.07 | 1.34 | 0.88 | 1.00 | 1.17 | 0.69 | 0.71 | 1.00 |
| | | 0.98 – 1.16 | 1.04 – 1.72 | 0.82-0.95 | | 1.08-1.27 | 0.55-0.87 | 0.64-0.77 | |
| Diabetes | | | | | | | | | |
| No | 1.00 | 1.03 | 1.16 | 0.92 | 1.00 | 1.21 | 0.70 | 0.69 | 1.00 |
| | | 0.99 – 1.08 | 0.98 – 1.38 | 0.88-0.95 | | 1.15-1.28 | 0.60-0.81 | 0.64-0.73 | |
| Yes | 1.00 | 1.23 | 1.67 | 0.89 | 1.00 | 1.17 | 0.44 | 0.69 | 1.00 |
| | | 1.02 – 1.48 | 1.06 – 2.62 | 0.77-1.03 | | 1.00-1.36 | 0.30-0.67 | 0.58-0.81 | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cerebrovascular disease | | | | | | | | | |
| Age | | | | | | | | | |
| 20-29 | 1.00 | 0.90 | 1.45 | 0.99 | 1.00 | 0.96 | 0.82 | 0.61 | 1.00 |
| | | 0.79 – 1.04 | 0.89 – 2.35 | 0.85-1.16 | | 0.96-1.26 | 0.39-1.73 | 0.38-0.97 | |
| ≥ 30 | 1.00 | 1.07 | 1.22 | 1.03 | 1.00 | 1.10 | 0.71 | 0.97 | 1.00 |
| | | 1.02 – 1.12 | 1.01 – 1.46 | 0.96-1.05 | | 1.03-1.17 | 0.58-0.87 | 0.89-1.05 | |
| Sex | | | | | | | | | |
| Men | 1.00 | 1.05 | 1.32 | 1.01 | 1.00 | 1.09 | 0.78 | 0.96 | 1.00 |
| | | 0.99 – 1.11 | 1.09 – 1.61 | 0.96-1.07 | | 1.02-1.17 | 0.63-0.97 | 0.88-1.05 | |
| Women | 1.00 | 0.98 | 1.04 | 1.02 | 1.00 | 1.07 | 0.66 | 0.85 | 1.00 |
| | | 0.90 – 1.07 | 0.73 – 1.47 | 0.94-1.11 | | 0.91-1.25 | 0.43-0.99 | 0.67-1.09 | |
| Statin medication | | | | | | | | | |
| No | 1.00 | 1.03 | 1.27 | 1.02 | 1.00 | 1.08 | 0.80 | 0.97 | 1.00 |
| | | 0.98 – 1.08 | 1.07 – 1.51 | 0.97-1.06 | | 1.01-1.15 | 0.65-0.99 | 0.89-1.06 | |
| Yes | 1.00 | 0.97 | 0.69 | 0.98 | 1.00 | 1.22 | 0.58 | 0.85 | 1.00 |
| | | 0.58 – 1.62 | 0.28 – 1.67 | 0.72-1.34 | | 0.94-1.57 | 0.34-0.99 | 0.66-1.08 | |
| Hypertension | | | | | | | | | |
| No | 1.00 | 1.03 | 1.40 | 0.99 | 1.00 | 1.11 | 0.81 | 1.01 | 1.00 |
| | | 0.98 – 1.09 | 1.14 – 1.72 | 0.94-1.05 | | 1.02-1.20 | 0.63-1.04 | 0.91-1.13 | |
| Yes | 1.00 | 1.02 | 0.97 | 1.07 | 1.00 | 1.06 | 0.71 | 0.88 | 1.00 |
| | | 0.93 – 1.12 | 0.71 – 1.33 | 0.99-1.16 | | 0.96-1.17 | 0.52-0.97 | 0.78-0.99 | |
| Diabetes | | | | | | | | | |
| No | 1.00 | 1.03 | 1.20 | 1.01 | 1.00 | 1.05 | 0.76 | 0.95 | 1.00 |
| | | 0.98 – 1.08 | 1.00 – 1.44 | 0.97-1.06 | | 0.99-1.12 | 0.62-0.94 | 0.87-1.03 | |
| Yes | 1.00 | 1.08 | 1.66 | 1.08 | 1.00 | 1.43 | 0.74 | 0.97 | 1.00 |
| | | 0.86 – 1.34 | 1.00 – 2.75 | 0.91-1.28 | | 1.19-1.72 | 0.44-1.24 | 0.77-1.23 | |

Adjusted hazard ratios with 95% confidence interval were noted.

Adjusted for age, sex, body mass index, Charlson comorbidity index, statin medication, alcohol consumption, smoking habit, physical activity, income status, hypertension, diabetes, blood pressure and fasting serum glucose

**Table S4. Hazard Ratios for incidence of cardiovascular events according to the change of total cholesterol with adjusted value.**

| Baseline TC | Low (TC < 180 mg/dL) | | | Middle (180 ≤ TC < 240 mg/dL) | | | High (TC ≥ 240 mg/dL) | | |
|---|---|---|---|---|---|---|---|---|---|
| Follow-up TC | Low | Middle | High | Low | Middle | High | Low | Middle | High |
| Number of people (%) | 864,818 | 352,289 | 12,587 | 323,238 | 830,213 | 97,578 | 11,983 | 100,149 | 89,190 |
| Ischemic heart disease | | | | | | | | | |
| Cases (N) | 6,323 | 3,179 | 142 | 3,143 | 10,545 | 1,760 | 181 | 2,053 | 2,976 |
| Incidence rates* | 0.73 | 0.90 | 1.13 | 0.97 | 1.27 | 1.80 | 1.51 | 2.05 | 3.34 |
| aHR | 1.00 | 1.05 | 1.22 | 0.91 | 1.00 | 1.23 | 0.66 | 0.70 | 1.00 |
| 95% CI | | 1.00-1.09 | 1.04-1.45 | 0.88-0.95 | | 1.16-1.29 | 0.57-0.77 | 0.66-0.74 | |
| *p*-value | | 0.058 | 0.018 | <0.001 | | <0.001 | <0.001 | <0.001 | |
| Cerebrovascular disease | | | | | | | | | |
| Cases (N) | 5,883 | 2,836 | 135 | 2,781 | 7,907 | 1,124 | 105 | 1,299 | 1,353 |
| Incidence rates* | 0.68 | 0.81 | 1.07 | 0.86 | 0.95 | 1.15 | 0.88 | 1.30 | 1.52 |
| aHR | 1.00 | 1.03 | 1.29 | 1.02 | 1.00 | 1.08 | 0.74 | 0.95 | 1.00 |
| 95% CI | | 0.98-1.08 | 1.08-1.53 | 0.97-1.06 | | 1.01-1.15 | 0.61-0.91 | 0.88-1.02 | |
| *p*-value | | 0.202 | 0.004 | 0.458 | | 0.023 | 0.004 | 0.177 | |

Acronyms: TC, total cholesterol; aHR, adjusted hazard ratio; CI, confidence interval

*Absolute cases with incidence rates (1,000 person-years) were noted.

Adjusted values were estimated by adding the average treatment effects to statin use group.

Adjusted for age, sex, body mass index, Charlson comorbidity index, statin medication, alcohol consumption, smoking habit, physical activity, income status, hypertension, diabetes, blood pressure and fasting serum glucose

**Table S5**. **Change of other covariates accompanied by the change of total cholesterol.**

| Baseline TC | Low (TC < 180 mg/dL) | | | Middle (180 ≤ TC < 240 mg/dL) | | | High (TC ≥ 240 mg/dL) | | |
|---|---|---|---|---|---|---|---|---|---|
| Follow-up TC | Low | Middle | High | Low | Middle | High | Low | Middle | High |
| BMI, mean of change (SD) | 0.1 (17.7) | 0.4 (13.2) | 1.3 (2.1) | -0.2 (15.5) | 0.1 (15.1) | 0.5 (10.0) | -0.74 (2.4) | -0.2 (11.5) | 0.2 (1.8) |
| FBG, mean of change (SD) | 1.0 (22.2) | 2.0 (26.7) | 3.1 (40.6) | -0.3 (23.3) | 1.4 (23.1) | 3.7 (27.9) | -14.1 (97.1) | -1.6 (41.9) | 2.3 (32.9) |
| SBP, mean of change (SD) | -0.2 (13.8) | 0.5 (14.1) | 0.9 (14.7) | -0.9 (14.1) | -0.1 (14.2) | 0.7 (14.7) | -1.7 (15.1) | -1.0 (14.8) | 0.1 (15.0) |

TC, total cholesterol; BMI, body mass index; FBG, fasting blood glucose; SBP, systolic blood pressure; SD, standard deviation.