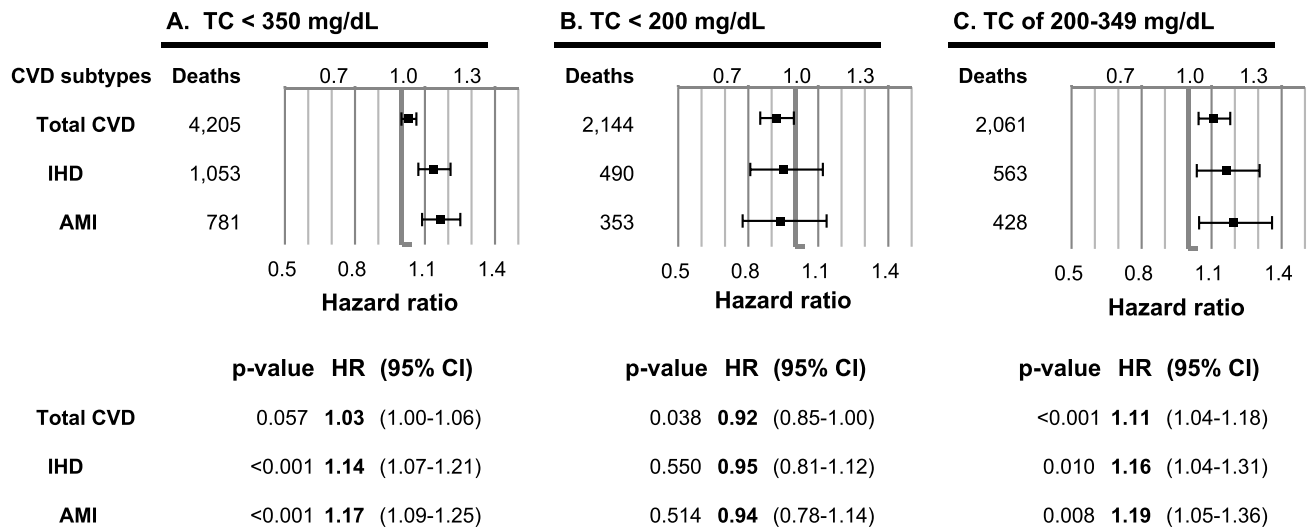
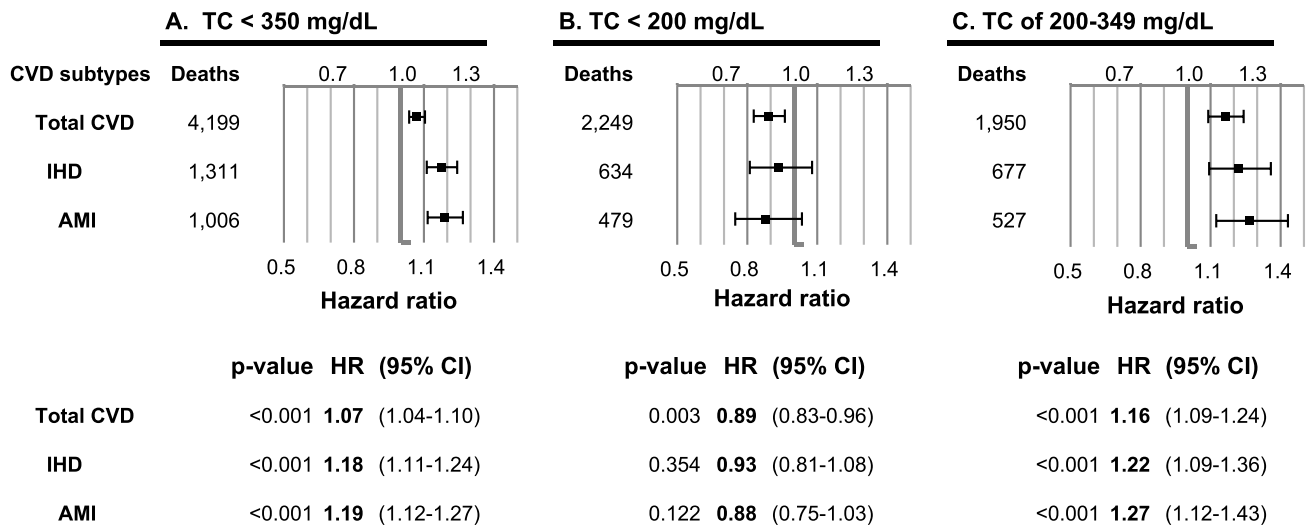


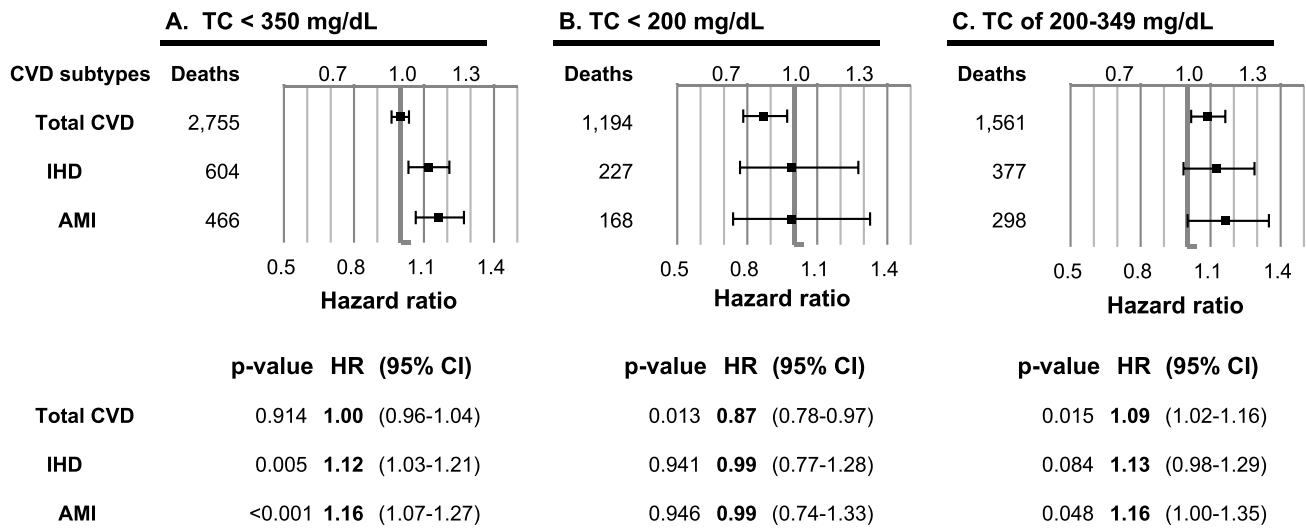
Supplementary Figure 1. HRs* per each 39 mg/dL (1 mmol/L) increase in total cholesterol (TC), according to TC range in the middle-aged persons (40-64 years) *HRs and 95% CIs were calculated using Cox proportional hazard models stratified by baseline age (years: 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85-99; if applicable), after adjustment for age at baseline (continuous variable), sex, smoking status, alcohol use, physical activity, body-mass index, systolic blood pressure, and fasting glucose levels. AMI indicates acute myocardial infarction; CI, confidence interval; HR, hazard ratio; ICH, intracerebral hemorrhage; IHD, ischemic heart disease; SAH, subarachnoid hemorrhage. To convert glucose from mg/dL to mmol/L, multiply by 0.0259.



Supplementary Figure 2. HRs* per each 39 mg/dL (1 mmol/L) increase in total cholesterol (TC), according to TC range in the elderly persons (≥65 years) *The same statistical methods and abbreviations as in supplementary figure 1 were used. To convert glucose from mg/dL to mmol/L, multiply by 0.0259.



Supplementary Figure 3. HRs* per each 39 mg/dL (1 mmol/L) increase in total cholesterol (TC), according to TC range in men. *The same statistical methods and abbreviations as in supplementary figure 1 were used. To convert glucose from mg/dL to mmol/L, multiply by 0.0259.



Supplementary Figure 4. HRs* per each 39 mg/dL (1 mmol/L) increase in total cholesterol (TC), according to TC range in women *The same statistical methods and abbreviations as in supplementary figure 1 were used. To convert glucose from mg/dL to mmol/L, multiply by 0.0259.

Supplementary Table 1. Characteristics of participants according to total cholesterol categories.

| Variables | Characteristics | TC categories | <140 mg/dL | 140-159 mg/dL | 160-179 mg/dL | 180-199 mg/dL | 200-219 mg/dL | 220-239 mg/dL | 240-259 mg/dL | ≥ 260 mg/dL |
|-----------------------------|-------------------|------------------|-----------------|-----------------|-----------------|------------------|-----------------|-----------------|-----------------|-----------------|
| | | N=503,340 | N=19,167 | N=46,068 | N=86,874 | N=109,349 | N=99,108 | N=69,991 | N=39,913 | N=32,870 |
| Total cholesterol | mg/dL | 200.4 ±38.7 | 126.9 ±12.8 | 151.0 ±5.6 | 170.2 ±5.7 | 189.6 ±5.7 | 209.1 ±5.7 | 228.5 ±5.6 | 248.5 ±5.8 | 284.5 ±35.9 |
| Age | years | 52.9 ±9.7 | 52.8 ±10.4 | 52.0 ±10.0 | 52.1 ±9.8 | 52.5 ±9.6 | 53.0 ±9.5 | 53.5 ±9.4 | 54.0 ±9.4 | 54.7 ±9.4 |
| Systolic blood pressure | mm Hg | 127.1 ±18.2 | 124.7 ±18.4 | 124.4 ±17.9 | 125.1 ±18.0 | 126.4 ±17.9 | 127.6 ±18.1 | 128.8 ±18.2 | 129.8 ±18.4 | 131.3 ±18.9 |
| Fasting serum glucose | mg/dL | 98.3 ±34.6 | 98.7 ±51.0 | 95.5 ±31.3 | 95.9 ±30.3 | 96.7 ±29.9 | 98.2 ±31.4 | 99.6 ±33.8 | 101.3 ±34.6 | 107.4 ±55.1 |
| Body mass index | kg/m ² | 24.0 ±3.0 | 22.9 ±3.0 | 23.2 ±2.9 | 23.5 ±2.9 | 23.9 ±2.9 | 24.2 ±2.9 | 24.5 ±2.9 | 24.6 ±2.9 | 24.9 ±2.9 |
| Sex | Women | 229,865 (45.7) | 7,776 (40.6) | 19,938 (43.3) | 38,266 (44.0) | 48,897 (44.7) | 45,336 (45.7) | 32,899 (47.0) | 19,470 (48.8) | 17,283 (52.6) |
| | Men | 273,475 (54.3) | 11,391 (59.4) | 26,130 (56.7) | 48,608 (56.0) | 60,452 (55.3) | 53,772 (54.3) | 37,092 (53.0) | 20,443 (51.2) | 15,587 (47.4) |
| Smoking status | Never smoker | 322,696 (64.1) | 11,879 (62.0) | 29,374 (63.8) | 55,459 (63.8) | 69,897 (63.9) | 63,561 (64.1) | 45,077 (64.4) | 25,734 (64.5) | 21,715 (66.1) |
| | Past smoker | 42,543 (8.5) | 1,518 (7.9) | 3,663 (8.0) | 7,270 (8.4) | 9,405 (8.6) | 8,522 (8.6) | 6,061 (8.7) | 3,373 (8.5) | 2,731 (8.3) |
| | Current smoker | 116,820 (23.2) | 5,047 (26.3) | 11,221 (24.4) | 20,685 (23.8) | 25,436 (23.3) | 22,662 (22.9) | 15,816 (22.6) | 8,928 (22.4) | 7,025 (21.4) |
| | Missing | 21,281 (4.2) | 723 (3.8) | 1,810 (3.9) | 3,460 (4.0) | 4,611 (4.2) | 4,363 (4.4) | 3,037 (4.3) | 1,878 (4.7) | 1,399 (4.3) |
| Alcohol use frequency, days | ≤ 1/month | 278,394 (55.3) | 10,387 (54.2) | 25,137 (54.6) | 47,440 (54.6) | 59,657 (54.6) | 54,763 (55.3) | 38,993 (55.7) | 22,681 (56.8) | 19,336 (58.8) |
| | 2/month-2/week | 158,360 (31.5) | 5,629 (29.4) | 14,373 (31.2) | 27,812 (32.0) | 35,400 (32.4) | 31,551 (31.8) | 22,089 (31.6) | 12,214 (30.6) | 9,292 (28.3) |
| | 3-7/week | 57,128 (11.3) | 2,831 (14.8) | 5,715 (12.4) | 10,083 (11.6) | 12,259 (11.2) | 10,980 (11.1) | 7,542 (10.8) | 4,202 (10.5) | 3,516 (10.7) |
| | Missing | 9,458 (1.9) | 320 (1.7) | 843 (1.8) | 1,539 (1.8) | 2,033 (1.9) | 1,814 (1.8) | 1,367 (2.0) | 816 (2.0) | 726 (2.2) |
| Physical activity | ≥1 times/week | 206,821 (41.1) | 7,083 (37.0) | 18,201 (39.5) | 35,617 (41.0) | 45,528 (41.6) | 41,444 (41.8) | 29,286 (41.8) | 16,459 (41.2) | 13,203 (40.2) |
| Income status, decile | <4 (low-income) | 115,882 (23.0) | 4,795 (25.0) | 10,846 (23.5) | 19,920 (22.9) | 24,713 (22.6) | 22,520 (22.7) | 16,044 (22.9) | 9,136 (22.9) | 7,908 (24.1) |
| | 4-7 | 163,984 (32.6) | 6,743 (35.2) | 15,588 (33.8) | 28,952 (33.3) | 35,390 (32.4) | 31,727 (32.0) | 22,317 (31.9) | 12,681 (31.8) | 10,586 (32.2) |
| | >7 (high-income) | 223,474 (44.4) | 7,629 (39.8) | 19,634 (42.6) | 38,002 (43.7) | 49,246 (45.0) | 44,861 (45.3) | 31,630 (45.2) | 18,096 (45.3) | 14,376 (43.7) |

Data are expressed as mean±SD or n (%). BMI, body mass index; FSG, fasting serum glucose; P values, which were calculated by the chi-square test and one-way ANOVA between cholesterol groups, were <0.001 for each variable. To convert total cholesterol from mg/dL to mmol/L, multiply by 0.0259. To convert glucose from mg/dL to mmol/L, multiply by 0.0555.

Supplementary Table 2. HRs for mortality from IHD and overall CVD associated with eight categories of total cholesterol.

| Stroke subtypes | TC group, mg/dL | Men and women | | | Men | | | Women | | |
|-----------------------------------|-----------------|---------------|---------|------------------|------------|---------|------------------|------------|---------|------------------|
| | | No. deaths | p-value | HR (95% CI) | No. deaths | p-value | HR (95% CI) | No. deaths | p-value | HR (95% CI) |
| Overall CVD (I00-I99) | <140 | 337 | 0.002 | 1.20 (1.07-1.36) | 236 | 0.042 | 1.16 (1.01-1.35) | 101 | <0.001 | 1.50 (1.21-1.85) |
| | 140-159 | 661 | 0.032 | 1.11 (1.01-1.22) | 481 | 0.008 | 1.17 (1.04-1.30) | 180 | 0.490 | 1.06 (0.90-1.26) |
| | 160-179 | 1096 | 0.739 | 1.01 (0.94-1.10) | 720 | 0.639 | 1.02 (0.93-1.13) | 376 | 0.624 | 1.03 (0.91-1.18) |
| | 180-199 | 1349 | | 1.00 (Reference) | 812 | | 1.00 (Reference) | 537 | | 1.00 (Reference) |
| | 200-219 | 1301 | 0.263 | 1.04 (0.97-1.13) | 778 | 0.038 | 1.11 (1.01-1.22) | 523 | 0.378 | 0.95 (0.84-1.07) |
| | 220-239 | 1000 | 0.007 | 1.12 (1.03-1.21) | 558 | 0.001 | 1.20 (1.07-1.33) | 442 | 0.950 | 1.00 (0.89-1.14) |
| | 240-259 | 613 | 0.005 | 1.15 (1.04-1.26) | 333 | <0.001 | 1.28 (1.12-1.45) | 280 | 0.858 | 0.99 (0.85-1.14) |
| | ≥260 | 619 | <0.001 | 1.33 (1.20-1.46) | 288 | <0.001 | 1.43 (1.24-1.63) | 331 | 0.013 | 1.19 (1.04-1.37) |
| Ischemic Heart diseases (I20-I25) | <140 | 75 | 0.800 | 1.03 (0.80-1.33) | 58 | 0.704 | 1.06 (0.79-1.41) | 17 | 0.529 | 1.18 (0.71-1.97) |
| | 140-159 | 167 | 0.383 | 1.09 (0.90-1.31) | 132 | 0.176 | 1.16 (0.94-1.44) | 35 | 0.954 | 1.01 (0.69-1.48) |
| | 160-179 | 276 | 0.936 | 0.99 (0.85-1.16) | 212 | 0.454 | 1.07 (0.89-1.29) | 64 | 0.326 | 0.86 (0.63-1.17) |
| | 180-199 | 343 | | 1.00 (Reference) | 232 | | 1.00 (Reference) | 111 | | 1.00 (Reference) |
| | 200-219 | 399 | 0.001 | 1.27 (1.10-1.47) | 262 | 0.003 | 1.30 (1.09-1.55) | 137 | 0.163 | 1.19 (0.93-1.53) |
| | 220-239 | 298 | <0.001 | 1.34 (1.15-1.56) | 194 | <0.001 | 1.43 (1.18-1.73) | 104 | 0.400 | 1.12 (0.86-1.47) |
| | 240-259 | 171 | 0.006 | 1.30 (1.08-1.56) | 122 | <0.001 | 1.60 (1.28-1.99) | 49 | 0.264 | 0.83 (0.59-1.16) |
| | ≥260 | 190 | <0.001 | 1.67 (1.39-2.00) | 101 | <0.001 | 1.71 (1.35-2.16) | 89 | 0.006 | 1.49 (1.12-1.97) |
| Acute myocardial infarction (I21) | <140 | 63 | 0.222 | 1.19 (0.90-1.57) | 50 | 0.136 | 1.27 (0.93-1.75) | 13 | 0.553 | 1.20 (0.66-2.16) |
| | 140-159 | 120 | 0.562 | 1.07 (0.86-1.33) | 94 | 0.301 | 1.14 (0.89-1.47) | 26 | 0.985 | 1.00 (0.65-1.56) |
| | 160-179 | 213 | 0.618 | 1.05 (0.87-1.26) | 166 | 0.176 | 1.16 (0.94-1.44) | 47 | 0.369 | 0.85 (0.59-1.21) |
| | 180-199 | 251 | | 1.00 (Reference) | 169 | | 1.00 (Reference) | 82 | | 1.00 (Reference) |
| | 200-219 | 307 | 0.001 | 1.34 (1.13-1.58) | 201 | 0.003 | 1.37 (1.12-1.68) | 106 | 0.118 | 1.26 (0.94-1.68) |
| | 220-239 | 233 | <0.001 | 1.43 (1.20-1.71) | 150 | <0.001 | 1.51 (1.21-1.89) | 83 | 0.196 | 1.22 (0.90-1.66) |
| | 240-259 | 135 | 0.002 | 1.40 (1.14-1.73) | 95 | <0.001 | 1.70 (1.32-2.19) | 40 | 0.676 | 0.92 (0.63-1.35) |
| | ≥260 | 153 | <0.001 | 1.84 (1.50-2.26) | 83 | <0.001 | 1.92 (1.48-2.51) | 70 | 0.004 | 1.61 (1.16-2.21) |

CI, confidence interval; HR, hazard ratio; TC, total cholesterol

^a HRs were calculated by Cox proportional hazard models stratified by age (baseline age, years: 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85-99), after adjustment for age at baseline, sex (if applicable), smoking status, alcohol use, physical activity, body mass index, systolic blood pressure, and fasting glucose.

To convert cholesterol from mg/dL to mmol/L, multiply by 0.0259.

Supplementary Table 3. HRs for mortality from IHD and overall CVD associated with eight categories of total cholesterol after additional adjustment of lipid-lowering medication use at baseline.

| Stroke subtypes | TC group, mg/dL | Men and women | | | Men | | | Women | | |
|-----------------------------------|-----------------|---------------|---------|------------------|------------|---------|------------------|------------|---------|------------------|
| | | No. deaths | p-value | HR (95% CI) | No. deaths | p-value | HR (95% CI) | No. deaths | p-value | HR (95% CI) |
| Overall CVD (I00-I99) | <140 | 337 | 0.003 | 1.20 (1.06-1.35) | 236 | 0.050 | 1.16 (1.00-1.34) | 101 | <0.001 | 1.49 (1.20-1.85) |
| | 140-159 | 661 | 0.038 | 1.10 (1.01-1.21) | 481 | 0.010 | 1.16 (1.04-1.30) | 180 | 0.515 | 1.06 (0.89-1.25) |
| | 160-179 | 1096 | 0.739 | 1.01 (0.94-1.10) | 720 | 0.632 | 1.02 (0.93-1.13) | 376 | 0.628 | 1.03 (0.91-1.18) |
| | 180-199 | 1349 | | 1.00 (Reference) | 812 | | 1.00 (Reference) | 537 | | 1.00 (Reference) |
| | 200-219 | 1301 | 0.256 | 1.05 (0.97-1.13) | 778 | 0.036 | 1.11 (1.01-1.23) | 523 | 0.382 | 0.95 (0.84-1.07) |
| | 220-239 | 1000 | 0.007 | 1.12 (1.03-1.21) | 558 | 0.001 | 1.20 (1.08-1.33) | 442 | 0.948 | 1.00 (0.89-1.14) |
| | 240-259 | 613 | 0.006 | 1.14 (1.04-1.26) | 333 | <0.001 | 1.27 (1.12-1.45) | 280 | 0.850 | 0.99 (0.85-1.14) |
| | ≥260 | 619 | <0.001 | 1.32 (1.20-1.45) | 288 | <0.001 | 1.41 (1.23-1.62) | 331 | 0.015 | 1.19 (1.03-1.36) |
| Ischemic Heart diseases (I20-I25) | <140 | 75 | 0.845 | 1.03 (0.80-1.32) | 58 | 0.742 | 1.05 (0.79-1.40) | 17 | 0.548 | 1.17 (0.70-1.96) |
| | 140-159 | 167 | 0.416 | 1.08 (0.90-1.30) | 132 | 0.190 | 1.15 (0.93-1.43) | 35 | 0.998 | 1.00 (0.68-1.46) |
| | 160-179 | 276 | 0.932 | 0.99 (0.85-1.16) | 212 | 0.454 | 1.07 (0.89-1.29) | 64 | 0.323 | 0.86 (0.63-1.17) |
| | 180-199 | 343 | | 1.00 (Reference) | 232 | | 1.00 (Reference) | 111 | | 1.00 (Reference) |
| | 200-219 | 399 | <0.001 | 1.28 (1.10-1.47) | 262 | 0.003 | 1.30 (1.09-1.56) | 137 | 0.160 | 1.20 (0.93-1.54) |
| | 220-239 | 298 | <0.001 | 1.34 (1.15-1.57) | 194 | <0.001 | 1.44 (1.19-1.74) | 104 | 0.393 | 1.12 (0.86-1.47) |
| | 240-259 | 171 | 0.006 | 1.29 (1.07-1.55) | 122 | <0.001 | 1.59 (1.28-1.98) | 49 | 0.258 | 0.82 (0.59-1.15) |
| | ≥260 | 190 | <0.001 | 1.65 (1.38-1.97) | 101 | <0.001 | 1.69 (1.33-2.14) | 89 | 0.007 | 1.47 (1.11-1.95) |
| Acute myocardial infarction (I21) | <140 | 63 | 0.237 | 1.18 (0.90-1.56) | 50 | 0.145 | 1.27 (0.92-1.74) | 13 | 0.565 | 1.19 (0.66-2.14) |
| | 140-159 | 120 | 0.587 | 1.06 (0.85-1.32) | 94 | 0.314 | 1.14 (0.88-1.47) | 26 | 0.989 | 1.00 (0.64-1.55) |
| | 160-179 | 213 | 0.621 | 1.05 (0.87-1.26) | 166 | 0.177 | 1.16 (0.94-1.44) | 47 | 0.368 | 0.85 (0.59-1.21) |
| | 180-199 | 251 | | 1.00 (Reference) | 169 | | 1.00 (Reference) | 82 | | 1.00 (Reference) |
| | 200-219 | 307 | <0.001 | 1.34 (1.13-1.58) | 201 | 0.003 | 1.37 (1.12-1.68) | 106 | 0.116 | 1.26 (0.94-1.68) |
| | 220-239 | 233 | <0.001 | 1.43 (1.20-1.71) | 150 | <0.001 | 1.52 (1.22-1.89) | 83 | 0.194 | 1.22 (0.90-1.66) |
| | 240-259 | 135 | 0.002 | 1.40 (1.13-1.72) | 95 | <0.001 | 1.69 (1.31-2.18) | 40 | 0.669 | 0.92 (0.63-1.34) |
| | ≥260 | 153 | <0.001 | 1.83 (1.49-2.24) | 83 | <0.001 | 1.90 (1.46-2.48) | 70 | 0.004 | 1.59 (1.16-2.20) |

CI, confidence interval; HR, hazard ratio; TC, total cholesterol

^a HRs were calculated by Cox proportional hazard models stratified by age (baseline age, years: 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85-99), after adjustment for age at baseline, sex (if applicable), smoking status, alcohol use, physical activity, body mass index, systolic blood pressure, fasting glucose, and lipid-lowering medication use at baseline.

To convert cholesterol from mg/dL to mmol/L, multiply by 0.0259.

Supplementary Table 4. HRs for mortality from IHD and overall CVD associated with three categories of total cholesterol according to sex.

| Stroke subtypes | TC group, mg/dL | Men and women | | | Men | | | Women | | |
|-----------------------------|-----------------|---------------|---------|------------------|------------|---------|------------------|------------|---------|------------------|
| | | No. deaths | p-value | HR (95% CI) | No. deaths | p-value | HR (95% CI) | No. deaths | p-value | HR (95% CI) |
| Overall CVD | <200 | 3443 | | 1.00 (Reference) | 2249 | | 1.00 (Reference) | 1194 | | 1.00 (Reference) |
| | 200-239 | 2301 | 0.222 | 1.03 (0.98-1.09) | 1336 | 0.019 | 1.09 (1.01-1.16) | 965 | 0.082 | 0.93 (0.85-1.01) |
| | ≥240 | 1232 | <0.001 | 1.18 (1.11-1.26) | 621 | <0.001 | 1.27 (1.16-1.39) | 611 | 0.475 | 1.04 (0.94-1.14) |
| Ischemic | <200 | 861 | | 1.00 (Reference) | 634 | | 1.00 (Reference) | 227 | | 1.00 (Reference) |
| Heart diseases | 200-239 | 697 | <0.001 | 1.28 (1.16-1.42) | 456 | <0.001 | 1.28 (1.13-1.44) | 241 | 0.048 | 1.20 (1.00-1.44) |
| | ≥240 | 361 | <0.001 | 1.44 (1.27-1.64) | 223 | <0.001 | 1.56 (1.33-1.82) | 138 | 0.103 | 1.19 (0.96-1.48) |
| Acute myocardial infarction | <200 | 647 | | 1.00 (Reference) | 479 | | 1.00 (Reference) | 168 | | 1.00 (Reference) |
| | 200-239 | 540 | <0.001 | 1.32 (1.18-1.48) | 351 | <0.001 | 1.29 (1.13-1.49) | 189 | 0.017 | 1.29 (1.05-1.59) |
| | ≥240 | 288 | <0.001 | 1.54 (1.33-1.77) | 178 | <0.001 | 1.63 (1.37-1.94) | 110 | 0.030 | 1.31 (1.03-1.67) |

CI, confidence interval; HR, hazard ratio; TC, total cholesterol

^a HRs were calculated by the same Cox models as in supplementary table 2.

To convert cholesterol from mg/dL to mmol/L, multiply by 0.0259.

Supplementary Table 5. HRs for mortality from IHD and overall CVD associated with three categories of total cholesterol according to age.

| Stroke subtypes | TC group, mg/dL | Total | | | Aged < 65 years old | | | Aged ≥ 65 years old | | |
|-----------------------------|-----------------|------------|---------|------------------|---------------------|---------|------------------|---------------------|---------|------------------|
| | | No. deaths | p-value | HR (95% CI) | No. deaths | p-value | HR (95% CI) | No. deaths | p-value | HR (95% CI) |
| Overall CVD | <200 | 3443 | | 1.00 (Reference) | 1299 | | 1.00 (Reference) | 2144 | | 1.00 (Reference) |
| | 200-239 | 2301 | 0.222 | 1.03 (0.98-1.09) | 954 | 0.152 | 1.06 (0.98-1.16) | 1347 | 0.948 | 1.00 (0.93-1.07) |
| | ≥240 | 1232 | <0.001 | 1.18 (1.11-1.26) | 506 | <0.001 | 1.23 (1.10-1.36) | 726 | 0.005 | 1.13 (1.04-1.23) |
| Ischemic | <200 | 861 | | 1.00 (Reference) | 371 | | 1.00 (Reference) | 490 | | 1.00 (Reference) |
| Heart diseases | 200-239 | 697 | <0.001 | 1.28 (1.16-1.42) | 328 | <0.001 | 1.31 (1.13-1.52) | 369 | 0.004 | 1.22 (1.07-1.40) |
| | ≥240 | 361 | <0.001 | 1.44 (1.27-1.64) | 165 | <0.001 | 1.46 (1.21-1.76) | 196 | <0.001 | 1.38 (1.16-1.63) |
| Acute myocardial infarction | <200 | 647 | | 1.00 (Reference) | 294 | | 1.00 (Reference) | 353 | | 1.00 (Reference) |
| | 200-239 | 540 | <0.001 | 1.32 (1.18-1.48) | 261 | 0.001 | 1.32 (1.12-1.56) | 279 | 0.002 | 1.28 (1.09-1.50) |
| | ≥240 | 288 | <0.001 | 1.54 (1.33-1.77) | 137 | <0.001 | 1.55 (1.26-1.90) | 151 | <0.001 | 1.46 (1.20-1.78) |

CI, confidence interval; CVD, cardiovascular disease; IHD, ischemic heart disease; HR, hazard ratio; TC, total cholesterol

^a HRs were calculated by the same Cox models as in supplementary table 2.

To convert cholesterol from mg/dL to mmol/L, multiply by 0.0259.