

Supplemental Digital Contents

Total cholesterol and all-cause mortality by sex and age: a prospective cohort

study among 12.8 million adults

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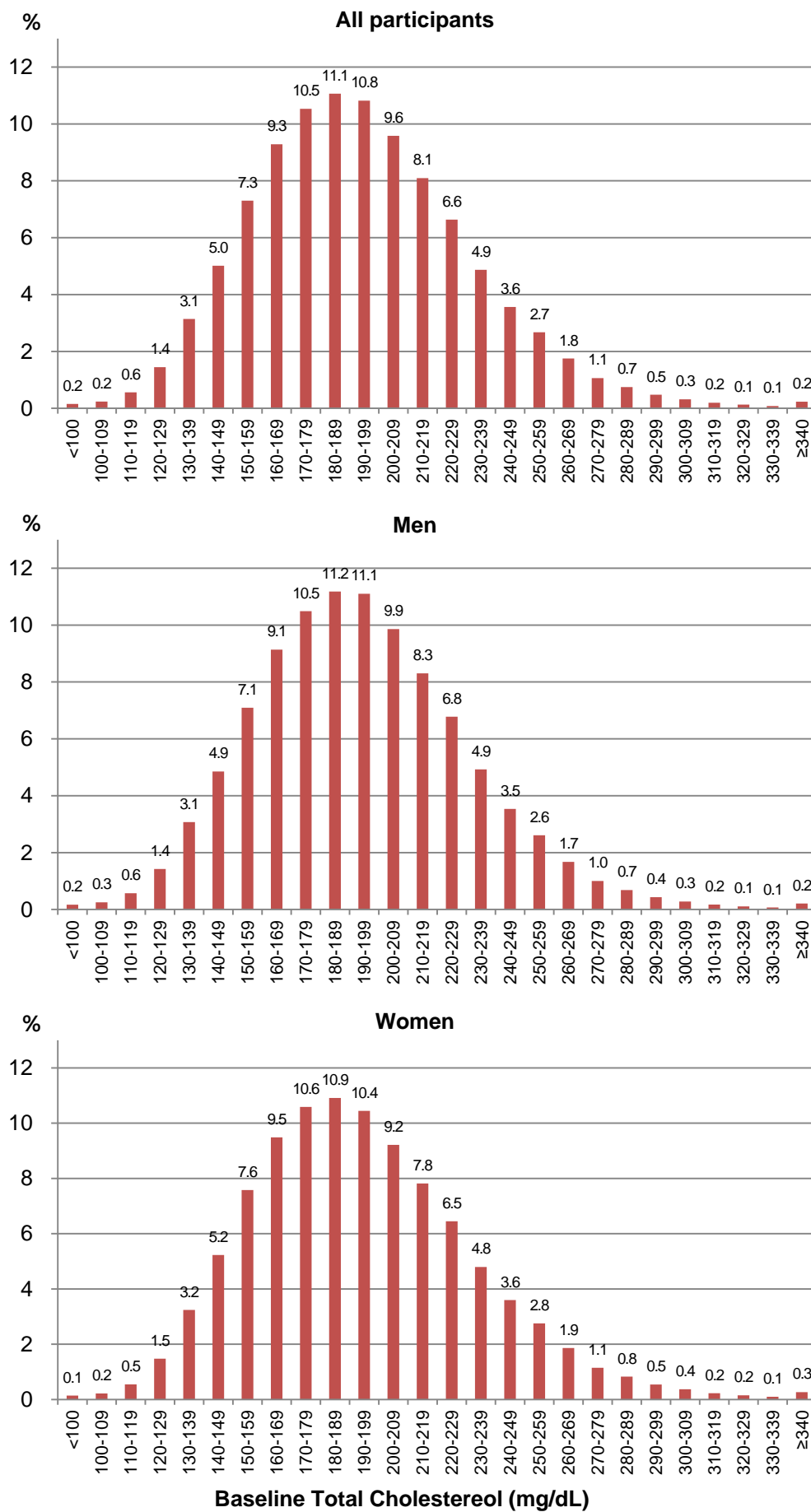


Figure S1. Distribution of total concentration in Korean adults.
 To convert cholesterol from mg/dL to mmol/L, multiply by 0.02586.

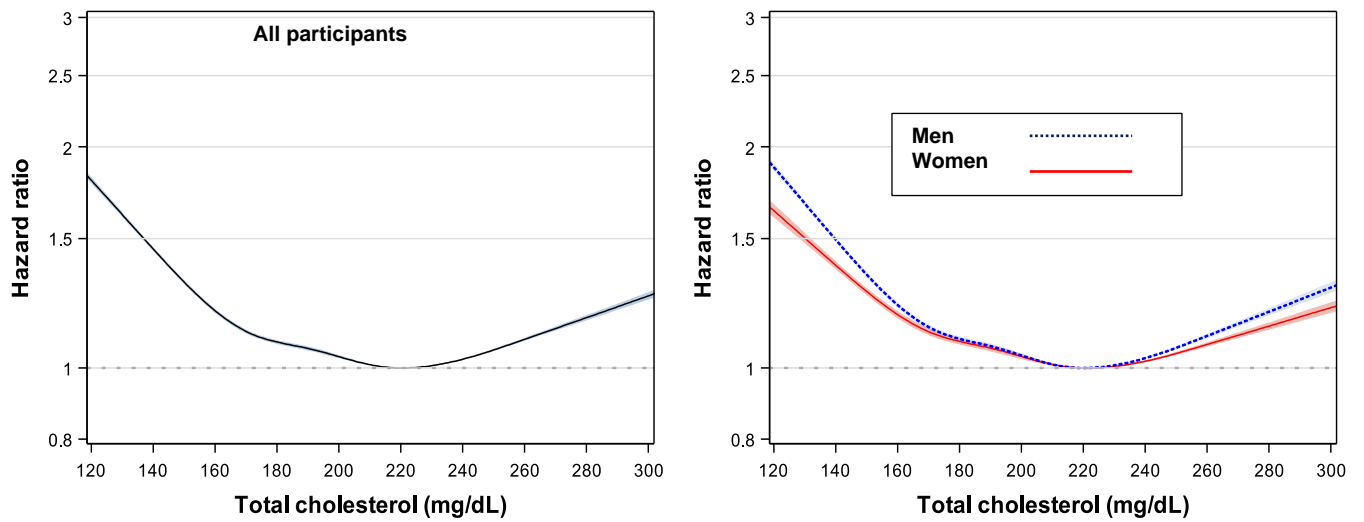


Figure S2. Hazard ratios^a for all-cause mortality according to sex by restricted cubic splines of total cholesterol with five knots (138, 170, 191, 213, and 260 mg/dL) and 220 mg/dL as a reference

^aHazard ratios and 95% confidence intervals were calculated using Cox hazards models after adjustment for age at baseline (continuous variable), sex (when applicable), smoking status, alcohol use, physical activity, known history of heart disease, stroke, or cancer, body-mass index, systolic blood pressure, and fasting glucose levels. To convert cholesterol from mg/dL to mmol/L, multiply by 0.02586.

Table S1. Mean and median of total cholesterol (mg/dL) (Including numerical version of Figure 1).

| Age, years | Men and women | | | | Men | | | | Women | | | | Sex difference ^a | |
|------------|---------------|--------|-------|--------|-----------|--------|-------|--------|-----------|--------|-------|--------|-----------------------------|-------|
| | n | Median | Mean | (SD) | n | Median | Mean | (SD) | n | Median | Mean | (SD) | Median | Mean |
| 18-99 | 12,815,006 | 191 | 194.2 | (49.0) | 7,292,064 | 191 | 194.1 | (47.4) | 5,522,942 | 190 | 194.3 | (51.1) | 1 | -0.2 |
| 18-19 | 50,235 | 166 | 168.5 | (32.5) | 10,472 | 156 | 159.0 | (29.2) | 39,763 | 168 | 171.1 | (32.9) | -12 | -12.0 |
| 20-21 | 168,383 | 166 | 168.6 | (34.5) | 56,062 | 162 | 164.8 | (35.5) | 112,321 | 168 | 170.5 | (33.8) | -6 | -5.7 |
| 22-23 | 327,931 | 168 | 170.9 | (37.8) | 112,041 | 167 | 169.9 | (39.4) | 215,890 | 169 | 171.4 | (36.9) | -2 | -1.5 |
| 24-25 | 496,965 | 171 | 174.3 | (38.5) | 206,778 | 172 | 175.4 | (39.4) | 290,187 | 171 | 173.5 | (37.8) | 1 | 1.9 |
| 26-27 | 566,542 | 176 | 179.0 | (40.6) | 323,129 | 178 | 181.3 | (41.8) | 243,413 | 173 | 176.0 | (38.8) | 5 | 5.3 |
| 28-29 | 620,505 | 180 | 183.8 | (42.0) | 432,261 | 183 | 186.3 | (42.8) | 188,244 | 174 | 177.9 | (39.6) | 9 | 8.4 |
| 30-31 | 610,405 | 184 | 187.0 | (41.6) | 458,754 | 187 | 189.8 | (41.8) | 151,651 | 175 | 178.4 | (39.9) | 12 | 11.4 |
| 32-33 | 587,101 | 186 | 189.2 | (42.9) | 456,532 | 189 | 192.1 | (43.1) | 130,569 | 175 | 178.7 | (40.7) | 14 | 13.4 |
| 34-35 | 544,672 | 187 | 190.7 | (43.0) | 424,512 | 191 | 194.0 | (43.8) | 120,160 | 176 | 179.3 | (37.9) | 15 | 14.6 |
| 36-37 | 508,630 | 189 | 192.0 | (42.6) | 394,652 | 192 | 195.2 | (43.2) | 113,978 | 178 | 180.9 | (38.3) | 14 | 14.4 |
| 38-39 | 489,834 | 191 | 193.7 | (43.5) | 375,014 | 194 | 196.9 | (43.8) | 114,820 | 180 | 183.2 | (40.9) | 14 | 13.7 |
| 40-41 | 771,454 | 189 | 192.3 | (45.0) | 430,586 | 195 | 197.8 | (44.9) | 340,868 | 182 | 185.4 | (44.3) | 13 | 12.3 |
| 42-43 | 750,228 | 191 | 194.3 | (47.3) | 420,327 | 196 | 199.1 | (47.3) | 329,901 | 185 | 188.2 | (46.5) | 11 | 10.9 |
| 44-45 | 693,916 | 193 | 196.0 | (47.8) | 379,106 | 197 | 200.1 | (47.3) | 314,810 | 188 | 191.1 | (48.0) | 9 | 9.1 |
| 46-47 | 638,709 | 195 | 198.1 | (48.4) | 343,520 | 198 | 200.8 | (45.9) | 295,189 | 192 | 195.0 | (51.0) | 6 | 5.8 |
| 48-49 | 572,787 | 197 | 200.4 | (48.8) | 298,490 | 198 | 201.2 | (47.4) | 274,297 | 196 | 199.6 | (50.3) | 2 | 1.6 |
| 50-51 | 505,007 | 200 | 203.1 | (51.8) | 261,436 | 198 | 201.4 | (50.4) | 243,571 | 202 | 205.0 | (53.2) | -4 | -3.6 |
| 52-53 | 454,406 | 202 | 204.8 | (52.4) | 236,260 | 198 | 200.7 | (48.9) | 218,146 | 206 | 209.1 | (55.6) | -8 | -8.4 |
| 54-55 | 450,635 | 203 | 205.6 | (51.0) | 235,215 | 198 | 200.5 | (48.5) | 215,420 | 208 | 211.2 | (53.1) | -10 | -10.7 |
| 56-57 | 390,911 | 203 | 206.1 | (53.6) | 198,187 | 197 | 200.0 | (52.1) | 192,724 | 209 | 212.4 | (54.4) | -12 | -12.4 |
| 58-59 | 347,132 | 202 | 205.3 | (52.5) | 174,366 | 196 | 198.7 | (49.5) | 172,766 | 209 | 212.0 | (54.6) | -13 | -13.3 |
| 60-61 | 384,271 | 201 | 204.6 | (54.4) | 189,991 | 194 | 197.4 | (52.2) | 194,280 | 209 | 211.7 | (55.5) | -15 | -14.4 |
| 62-63 | 361,062 | 201 | 204.2 | (58.0) | 174,138 | 193 | 196.3 | (56.1) | 186,924 | 208 | 211.5 | (58.7) | -15 | -15.2 |
| 64-65 | 323,187 | 200 | 203.6 | (56.6) | 155,662 | 192 | 195.4 | (53.3) | 167,525 | 208 | 211.2 | (58.6) | -16 | -15.9 |
| 66-67 | 280,786 | 200 | 203.0 | (55.9) | 132,790 | 191 | 194.4 | (53.3) | 147,996 | 207 | 210.7 | (57.0) | -16 | -16.3 |
| 68-69 | 239,383 | 199 | 202.6 | (57.8) | 111,671 | 190 | 193.5 | (57.0) | 127,712 | 207 | 210.5 | (57.3) | -17 | -17.0 |
| 70-71 | 185,926 | 199 | 202.6 | (62.2) | 84,436 | 189 | 193.4 | (65.3) | 101,490 | 207 | 210.3 | (58.4) | -18 | -17.0 |
| 72-73 | 142,558 | 198 | 201.8 | (57.8) | 61,930 | 188 | 191.6 | (56.0) | 80,628 | 206 | 209.7 | (58.0) | -18 | -18.1 |
| 74-75 | 112,889 | 198 | 201.9 | (64.2) | 48,880 | 187 | 191.3 | (63.8) | 64,009 | 206 | 210.0 | (63.3) | -19 | -18.7 |
| 76-77 | 82,237 | 197 | 200.6 | (59.7) | 35,677 | 186 | 189.2 | (54.9) | 46,560 | 205 | 209.3 | (61.7) | -19 | -20.1 |
| 78-79 | 57,463 | 196 | 198.6 | (48.8) | 25,735 | 185 | 187.6 | (43.1) | 31,728 | 204 | 207.6 | (51.2) | -19 | -20.0 |
| 80-81 | 42,346 | 194 | 198.1 | (57.8) | 18,802 | 184 | 186.9 | (52.2) | 23,544 | 203 | 207.0 | (60.4) | -19 | -20.1 |
| 82-83 | 26,015 | 193 | 197.0 | (62.9) | 11,568 | 182 | 186.4 | (62.3) | 14,447 | 201 | 205.5 | (62.1) | -19 | -19.2 |
| 84-85 | 14,482 | 191 | 195.8 | (63.7) | 6,482 | 180 | 184.9 | (69.2) | 8,000 | 201 | 204.6 | (57.4) | -21 | -19.7 |
| 86-99 | 16,013 | 190 | 193.3 | (51.6) | 6,602 | 179 | 182.3 | (51.0) | 9,411 | 198 | 201.0 | (50.5) | -19 | -18.7 |

SD, standard deviation.

^a Concentration in men minus concentration in women.

To convert cholesterol from mg/dL to mmol/L, multiply by 0.02586.

Table S2. HRs^a for death associated with fasting glucose, after adjustment for potential risk factors (Including numerical version of Figure 2).

| sex | TC group, mg/dL | Person year | No. of death | Sex, and age adjusted ^b | | Fully adjusted ^c | |
|---------------|-----------------|-------------|--------------|------------------------------------|------------------|-----------------------------|------------------|
| | | | | p-value | HR (95% CI) | p-value | HR (95% CI) |
| Men and Women | <120 | 1,251,757 | 13,600 | <0.001 | 2.26 (2.22-2.31) | <0.001 | 2.03 (1.99-2.07) |
| Women | 120-129 | 1,929,661 | 13,287 | <0.001 | 1.81 (1.77-1.84) | <0.001 | 1.68 (1.65-1.71) |
| | 130-139 | 4,219,402 | 24,511 | <0.001 | 1.59 (1.57-1.61) | <0.001 | 1.49 (1.47-1.52) |
| | 140-149 | 6,754,049 | 34,398 | <0.001 | 1.41 (1.39-1.43) | <0.001 | 1.35 (1.33-1.37) |
| | 150-159 | 9,857,135 | 47,598 | <0.001 | 1.29 (1.27-1.30) | <0.001 | 1.25 (1.23-1.26) |
| | 160-169 | 12,552,009 | 58,289 | <0.001 | 1.19 (1.18-1.21) | <0.001 | 1.17 (1.15-1.18) |
| | 170-179 | 14,239,120 | 66,208 | <0.001 | 1.12 (1.11-1.14) | <0.001 | 1.11 (1.09-1.12) |
| | 180-189 | 14,964,456 | 69,918 | <0.001 | 1.07 (1.06-1.09) | <0.001 | 1.06 (1.05-1.08) |
| | 190-199 | 14,633,057 | 69,776 | <0.001 | 1.05 (1.03-1.06) | <0.001 | 1.04 (1.03-1.06) |
| | 200-209 | 12,952,005 | 64,340 | <0.001 | 1.03 (1.02-1.04) | <0.001 | 1.03 (1.02-1.04) |
| | 210-219 | 10,934,462 | 55,757 | 0.065 | 1.01 (1.00-1.02) | 0.098 | 1.01 (1.00-1.02) |
| | 220-229 | 8,960,734 | 46,623 | | 1.00 (Reference) | | 1.00 (Reference) |
| | 230-239 | 6,568,184 | 35,346 | 0.381 | 1.01 (0.99-1.02) | 0.446 | 1.01 (0.99-1.02) |
| | 240-249 | 4,799,485 | 26,936 | 0.063 | 1.01 (1.00-1.03) | 0.208 | 1.01 (0.99-1.02) |
| | 250-259 | 3,593,413 | 21,662 | <0.001 | 1.06 (1.05-1.08) | <0.001 | 1.06 (1.04-1.07) |
| | 260-269 | 2,353,108 | 14,499 | <0.001 | 1.07 (1.05-1.09) | <0.001 | 1.05 (1.03-1.07) |
| | 270-279 | 1,423,317 | 9,300 | <0.001 | 1.13 (1.10-1.15) | <0.001 | 1.10 (1.07-1.12) |
| | ≥280 | 2,915,081 | 22,375 | <0.001 | 1.28 (1.26-1.30) | <0.001 | 1.23 (1.21-1.25) |
| Men | <120 | 723,347 | 11,239 | <0.001 | 2.45 (2.40-2.51) | <0.001 | 2.14 (2.09-2.19) |
| | 120-129 | 1,068,428 | 10,648 | <0.001 | 1.91 (1.87-1.95) | <0.001 | 1.73 (1.69-1.77) |
| | 130-139 | 2,328,158 | 19,185 | <0.001 | 1.67 (1.64-1.70) | <0.001 | 1.53 (1.50-1.56) |
| | 140-149 | 3,700,041 | 26,152 | <0.001 | 1.47 (1.45-1.50) | <0.001 | 1.38 (1.36-1.41) |
| | 150-159 | 5,432,347 | 35,199 | <0.001 | 1.33 (1.31-1.35) | <0.001 | 1.27 (1.25-1.29) |
| | 160-169 | 7,018,011 | 41,965 | <0.001 | 1.23 (1.21-1.25) | <0.001 | 1.18 (1.17-1.20) |
| | 170-179 | 8,070,894 | 46,155 | <0.001 | 1.15 (1.13-1.16) | <0.001 | 1.12 (1.10-1.13) |
| | 180-189 | 8,617,076 | 47,166 | <0.001 | 1.09 (1.07-1.11) | <0.001 | 1.07 (1.06-1.09) |
| | 190-199 | 8,568,492 | 45,737 | <0.001 | 1.06 (1.04-1.07) | <0.001 | 1.05 (1.03-1.06) |
| | 200-209 | 7,613,334 | 40,632 | <0.001 | 1.03 (1.02-1.05) | <0.001 | 1.03 (1.01-1.04) |
| | 210-219 | 6,413,884 | 33,878 | 0.210 | 1.01 (0.99-1.03) | 0.386 | 1.01 (0.99-1.02) |
| | 220-229 | 5,235,961 | 27,495 | | 1.00 (Reference) | | 1.00 (Reference) |
| | 230-239 | 3,805,814 | 20,099 | 0.528 | 1.01 (0.99-1.02) | 0.559 | 1.01 (0.99-1.02) |
| | 240-249 | 2,729,948 | 14,776 | 0.108 | 1.02 (1.00-1.04) | 0.216 | 1.01 (0.99-1.03) |

| sex | TC group, mg/dL | Person year | No. of death | Sex, and age adjusted ^b | | Fully adjusted ^c | |
|-------|-----------------|-------------|--------------|------------------------------------|------------------|-----------------------------|------------------|
| | | | | p-value | HR (95% CI) | p-value | HR (95% CI) |
| | 250-259 | 2,012,779 | 11,438 | <0.001 | 1.06 (1.04-1.09) | <0.001 | 1.05 (1.03-1.08) |
| | 260-269 | 1,288,280 | 7,368 | <0.001 | 1.07 (1.04-1.10) | <0.001 | 1.06 (1.03-1.08) |
| | 270-279 | 768,371 | 4,699 | <0.001 | 1.15 (1.12-1.19) | <0.001 | 1.12 (1.09-1.16) |
| | ≥280 | 1,500,690 | 10,715 | <0.001 | 1.33 (1.30-1.36) | <0.001 | 1.26 (1.23-1.29) |
| Women | <120 | 528,410 | 2,361 | <0.001 | 1.83 (1.75-1.91) | <0.001 | 1.74 (1.66-1.81) |
| | 120-129 | 861,232 | 2,639 | <0.001 | 1.64 (1.58-1.71) | <0.001 | 1.60 (1.54-1.67) |
| | 130-139 | 1,891,244 | 5,326 | <0.001 | 1.49 (1.44-1.53) | <0.001 | 1.45 (1.41-1.49) |
| | 140-149 | 3,054,008 | 8,246 | <0.001 | 1.32 (1.29-1.36) | <0.001 | 1.30 (1.27-1.34) |
| | 150-159 | 4,424,787 | 12,399 | <0.001 | 1.24 (1.21-1.27) | <0.001 | 1.22 (1.20-1.25) |
| | 160-169 | 5,533,997 | 16,324 | <0.001 | 1.16 (1.13-1.18) | <0.001 | 1.15 (1.13-1.17) |
| | 170-179 | 6,168,225 | 20,053 | <0.001 | 1.11 (1.09-1.13) | <0.001 | 1.11 (1.08-1.13) |
| | 180-189 | 6,347,380 | 22,752 | <0.001 | 1.07 (1.05-1.09) | <0.001 | 1.07 (1.05-1.09) |
| | 190-199 | 6,064,564 | 24,039 | <0.001 | 1.04 (1.02-1.06) | <0.001 | 1.04 (1.03-1.07) |
| | 200-209 | 5,338,670 | 23,708 | <0.001 | 1.03 (1.01-1.05) | 0.003 | 1.03 (1.01-1.05) |
| | 210-219 | 4,520,578 | 21,879 | 0.065 | 1.02 (1.00-1.04) | 0.064 | 1.02 (1.00-1.04) |
| | 220-229 | 3,724,774 | 19,128 | | 1.00 (Reference) | | 1.00 (Reference) |
| | 230-239 | 2,762,370 | 15,247 | 0.381 | 1.00 (0.98-1.02) | 0.797 | 1.00 (0.98-1.02) |
| | 240-249 | 2,069,537 | 12,160 | 0.063 | 1.00 (0.98-1.03) | 0.966 | 1.00 (0.98-1.02) |
| | 250-259 | 1,580,634 | 10,224 | <0.001 | 1.06 (1.03-1.08) | <0.001 | 1.05 (1.03-1.08) |
| | 260-269 | 1,064,828 | 7,131 | <0.001 | 1.06 (1.03-1.09) | 0.001 | 1.05 (1.02-1.07) |
| | 270-279 | 654,946 | 4,601 | <0.001 | 1.09 (1.06-1.13) | <0.001 | 1.07 (1.03-1.10) |
| | ≥280 | 1,414,390 | 11,660 | <0.001 | 1.23 (1.20-1.26) | <0.001 | 1.18 (1.16-1.21) |

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

^a HRs were calculated by Cox 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 risk factors.

^b Adjustment for age at baseline, and sex (when applicable)

^c Adjustment for age at baseline, sex (when applicable), smoking status, alcohol use, physical activity, known history of heart disease, stroke, or cancer, body mass index, systolic blood pressure, and fasting glucose.

To convert cholesterol from mg/dL to mmol/L, multiply by 0.02586.

Table S3. HRs^a for death associated with total cholesterol in men and women, according to age. (Including numerical version of Figure 3).

| Age group, years | TC group, mg/dL | Men (n=7,292,064) | | | | | Women (n=5,522,942) | | | | |
|------------------|-----------------|-------------------|--------------|------------------|------------------|------------------|---------------------|--------------|------------------|------------------|------------------|
| | | Person year | No. of death | CDR ^b | p-value | HR (95% CI) | Person year | No. of death | CDR ^b | p-value | HR (95% CI) |
| 18-34 | <120 | 303,032 | 278 | 92 | <0.001 | 1.53 (1.33-1.76) | 243,846 | 87 | 36 | 0.350 | 1.13 (0.87-1.47) |
| | 120-129 | 511,449 | 403 | 79 | <0.001 | 1.33 (1.18-1.50) | 452,588 | 143 | 32 | 0.874 | 1.02 (0.81-1.28) |
| | 130-139 | 1,090,672 | 748 | 69 | 0.004 | 1.16 (1.05-1.28) | 958,414 | 298 | 31 | 0.983 | 1.00 (0.83-1.22) |
| | 140-149 | 1,664,807 | 1,130 | 68 | 0.003 | 1.15 (1.05-1.26) | 1,462,502 | 408 | 28 | 0.244 | 0.90 (0.74-1.08) |
| | 150-159 | 2,287,566 | 1,467 | 64 | 0.084 | 1.08 (0.99-1.18) | 1,933,275 | 542 | 28 | 0.230 | 0.90 (0.75-1.07) |
| | 160-169 | 2,755,016 | 1,717 | 62 | 0.349 | 1.04 (0.96-1.13) | 2,144,521 | 602 | 28 | 0.199 | 0.89 (0.75-1.06) |
| | 170-179 | 2,902,400 | 1,814 | 62 | 0.396 | 1.04 (0.95-1.13) | 2,068,039 | 621 | 30 | 0.543 | 0.95 (0.79-1.13) |
| | 180-189 | 2,856,258 | 1,644 | 58 | 0.195 | 0.95 (0.87-1.03) | 1,798,297 | 524 | 29 | 0.300 | 0.91 (0.76-1.09) |
| | 190-199 | 2,660,488 | 1,692 | 64 | 0.424 | 1.03 (0.95-1.12) | 1,452,647 | 388 | 27 | 0.046 | 0.83 (0.69-1.00) |
| | 200-209 | 2,155,762 | 1,349 | 63 | 0.865 | 1.01 (0.92-1.10) | 1,004,278 | 308 | 31 | 0.530 | 0.94 (0.78-1.14) |
| | 210-219 | 1,693,293 | 1,039 | 61 | 0.559 | 0.97 (0.89-1.07) | 693,825 | 232 | 33 | 0.907 | 1.01 (0.83-1.24) |
| | 220-229 | 1,293,881 | 826 | 64 | | 1.00 (Reference) | 467,354 | 156 | 33 | | 1.00 (Reference) |
| | 230-239 | 898,251 | 630 | 70 | 0.136 | 1.08 (0.98-1.20) | 281,607 | 87 | 31 | 0.516 | 0.92 (0.71-1.19) |
| | 240-249 | 603,822 | 423 | 70 | 0.273 | 1.07 (0.95-1.20) | 172,996 | 65 | 38 | 0.526 | 1.10 (0.82-1.47) |
| | 250-259 | 429,928 | 316 | 74 | 0.149 | 1.10 (0.97-1.25) | 112,227 | 34 | 30 | 0.507 | 0.88 (0.61-1.28) |
| | 260-269 | 264,699 | 225 | 85 | 0.003 | 1.25 (1.08-1.45) | 64,721 | 28 | 43 | 0.304 | 1.23 (0.83-1.85) |
| 270-279 | 154,923 | 129 | 83 | 0.053 | 1.20 (1.00-1.45) | 37,995 | 18 | 47 | 0.216 | 1.36 (0.84-2.22) | |
| ≥280 | 288,329 | 296 | 103 | <0.001 | 1.44 (1.26-1.64) | 89,389 | 46 | 51 | 0.032 | 1.43 (1.03-1.99) | |
| 35-44 | <120 | 150,536 | 725 | 482 | <0.001 | 3.13 (2.88-3.40) | 128,381 | 146 | 114 | <0.001 | 1.40 (1.16-1.67) |
| | 120-129 | 224,297 | 683 | 305 | <0.001 | 2.11 (1.94-2.30) | 206,714 | 183 | 89 | 0.152 | 1.13 (0.96-1.33) |
| | 130-139 | 528,158 | 1,313 | 249 | <0.001 | 1.76 (1.65-1.89) | 470,783 | 439 | 93 | 0.006 | 1.19 (1.05-1.35) |
| | 140-149 | 897,321 | 1,846 | 206 | <0.001 | 1.47 (1.39-1.57) | 785,221 | 612 | 78 | 0.836 | 0.99 (0.88-1.11) |
| | 150-159 | 1,391,295 | 2,590 | 186 | <0.001 | 1.34 (1.27-1.42) | 1,157,387 | 955 | 83 | 0.453 | 1.04 (0.94-1.15) |
| | 160-169 | 1,884,628 | 3,174 | 168 | <0.001 | 1.22 (1.16-1.29) | 1,465,788 | 1,158 | 79 | 0.779 | 0.99 (0.89-1.09) |
| | 170-179 | 2,266,431 | 3,729 | 165 | <0.001 | 1.18 (1.12-1.24) | 1,614,337 | 1,238 | 77 | 0.243 | 0.94 (0.85-1.04) |
| | 180-189 | 2,506,509 | 3,981 | 159 | <0.001 | 1.14 (1.08-1.20) | 1,603,757 | 1,239 | 77 | 0.188 | 0.94 (0.85-1.03) |
| | 190-199 | 2,549,803 | 3,916 | 154 | <0.001 | 1.09 (1.04-1.15) | 1,445,618 | 1,106 | 77 | 0.072 | 0.91 (0.83-1.01) |
| | 200-209 | 2,318,389 | 3,535 | 152 | 0.006 | 1.08 (1.02-1.13) | 1,182,447 | 915 | 77 | 0.059 | 0.91 (0.82-1.00) |
| | 210-219 | 1,984,850 | 2,919 | 147 | 0.383 | 1.02 (0.97-1.08) | 904,568 | 733 | 81 | 0.195 | 0.93 (0.84-1.04) |
| | 220-229 | 1,640,599 | 2,379 | 145 | | 1.00 (Reference) | 666,631 | 591 | 89 | | 1.00 (Reference) |
| | 230-239 | 1,202,907 | 1,895 | 158 | 0.023 | 1.07 (1.01-1.14) | 443,147 | 358 | 81 | 0.082 | 0.89 (0.78-1.02) |
| | 240-249 | 869,950 | 1,324 | 152 | 0.496 | 1.02 (0.96-1.09) | 292,766 | 264 | 90 | 0.760 | 0.98 (0.85-1.13) |
| | 250-259 | 643,394 | 1,100 | 171 | <0.001 | 1.13 (1.05-1.21) | 200,016 | 201 | 100 | 0.486 | 1.06 (0.90-1.24) |

| Age group, years | TC group, mg/dL | Men (n=7,292,064) | | | | | Women (n=5,522,942) | | | | |
|------------------|-----------------|-------------------|--------------|------------------|------------------|------------------|---------------------|--------------|------------------|------------------|------------------|
| | | Person year | No. of death | CDR ^b | p-value | HR (95% CI) | Person year | No. of death | CDR ^b | p-value | HR (95% CI) |
| | 260-269 | 410,907 | 710 | 173 | 0.011 | 1.12 (1.03-1.21) | 120,119 | 132 | 110 | 0.225 | 1.12 (0.93-1.36) |
| | 270-279 | 250,640 | 470 | 188 | <0.001 | 1.19 (1.08-1.32) | 67,067 | 83 | 124 | 0.059 | 1.25 (0.99-1.57) |
| | ≥280 | 484,058 | 1,146 | 237 | <0.001 | 1.42 (1.32-1.52) | 127,889 | 196 | 153 | <0.001 | 1.48 (1.26-1.74) |
| 45-54 | <120 | 102,907 | 1,542 | 1,498 | <0.001 | 3.39 (3.20-3.60) | 76,271 | 213 | 279 | <0.001 | 1.93 (1.67-2.23) |
| | 120-129 | 136,771 | 1,347 | 985 | <0.001 | 2.37 (2.23-2.52) | 107,313 | 255 | 238 | <0.001 | 1.72 (1.51-1.96) |
| | 130-139 | 309,813 | 2,499 | 807 | <0.001 | 2.01 (1.91-2.11) | 250,425 | 522 | 208 | <0.001 | 1.55 (1.40-1.71) |
| | 140-149 | 518,279 | 3,265 | 630 | <0.001 | 1.61 (1.54-1.69) | 437,913 | 783 | 179 | <0.001 | 1.33 (1.22-1.45) |
| | 150-159 | 826,178 | 4,576 | 554 | <0.001 | 1.45 (1.39-1.51) | 717,250 | 1,192 | 166 | <0.001 | 1.23 (1.14-1.33) |
| | 160-169 | 1,154,223 | 5,627 | 488 | <0.001 | 1.29 (1.24-1.35) | 1,013,582 | 1,590 | 157 | <0.001 | 1.15 (1.07-1.23) |
| | 170-179 | 1,441,776 | 6,343 | 440 | <0.001 | 1.18 (1.13-1.22) | 1,273,313 | 1,937 | 152 | 0.004 | 1.10 (1.03-1.18) |
| | 180-189 | 1,654,586 | 6,885 | 416 | <0.001 | 1.12 (1.08-1.16) | 1,453,665 | 2,161 | 149 | 0.090 | 1.06 (0.99-1.13) |
| | 190-199 | 1,736,882 | 6,772 | 390 | 0.005 | 1.06 (1.02-1.10) | 1,502,476 | 2,192 | 146 | 0.613 | 1.02 (0.95-1.08) |
| | 200-209 | 1,653,108 | 6,179 | 374 | 0.564 | 1.01 (0.97-1.05) | 1,436,978 | 2,128 | 148 | 0.736 | 1.01 (0.95-1.08) |
| | 210-219 | 1,455,496 | 5,444 | 374 | 0.748 | 1.01 (0.97-1.05) | 1,279,375 | 1,967 | 154 | 0.347 | 1.03 (0.97-1.10) |
| | 220-229 | 1,243,405 | 4,616 | 371 | | 1.00 (Reference) | 1,094,889 | 1,665 | 152 | | 1.00 (Reference) |
| | 230-239 | 929,267 | 3,454 | 372 | 0.725 | 0.99 (0.95-1.04) | 826,553 | 1,299 | 157 | 0.861 | 1.01 (0.94-1.08) |
| | 240-249 | 687,740 | 2,563 | 373 | 0.642 | 0.99 (0.94-1.04) | 629,500 | 1,003 | 159 | 0.942 | 1.00 (0.93-1.08) |
| | 250-259 | 518,194 | 2,038 | 393 | 0.214 | 1.03 (0.98-1.09) | 481,588 | 832 | 173 | 0.125 | 1.07 (0.98-1.16) |
| | 260-269 | 344,059 | 1,289 | 375 | 0.293 | 0.97 (0.91-1.03) | 325,387 | 545 | 167 | 0.826 | 1.01 (0.92-1.11) |
| | 270-279 | 202,709 | 886 | 437 | 0.003 | 1.12 (1.04-1.20) | 199,811 | 356 | 178 | 0.415 | 1.05 (0.94-1.18) |
| ≥280 | 409,263 | 2,141 | 523 | <0.001 | 1.28 (1.21-1.34) | 413,422 | 943 | 228 | <0.001 | 1.29 (1.19-1.39) | |
| 55-64 | <120 | 93,669 | 3,196 | 3,412 | <0.001 | 2.66 (2.55-2.77) | 45,155 | 502 | 1,112 | <0.001 | 2.42 (2.20-2.65) |
| | 120-129 | 111,297 | 2,746 | 2,467 | <0.001 | 2.06 (1.97-2.15) | 52,462 | 492 | 938 | <0.001 | 2.10 (1.91-2.31) |
| | 130-139 | 233,295 | 4,864 | 2,085 | <0.001 | 1.77 (1.71-1.84) | 119,125 | 858 | 720 | <0.001 | 1.64 (1.52-1.76) |
| | 140-149 | 370,775 | 6,413 | 1,730 | <0.001 | 1.54 (1.49-1.59) | 206,575 | 1,389 | 672 | <0.001 | 1.53 (1.43-1.62) |
| | 150-159 | 565,775 | 8,464 | 1,496 | <0.001 | 1.35 (1.31-1.40) | 352,304 | 2,132 | 605 | <0.001 | 1.40 (1.33-1.47) |
| | 160-169 | 765,792 | 10,235 | 1,337 | <0.001 | 1.24 (1.20-1.28) | 527,983 | 2,811 | 532 | <0.001 | 1.24 (1.18-1.30) |
| | 170-179 | 931,020 | 11,270 | 1,210 | <0.001 | 1.14 (1.11-1.18) | 709,592 | 3,529 | 497 | <0.001 | 1.16 (1.11-1.21) |
| | 180-189 | 1,040,344 | 11,731 | 1,128 | <0.001 | 1.08 (1.05-1.11) | 885,810 | 4,088 | 461 | <0.001 | 1.08 (1.04-1.13) |
| | 190-199 | 1,075,089 | 11,708 | 1,089 | <0.001 | 1.06 (1.03-1.09) | 990,752 | 4,498 | 454 | 0.001 | 1.07 (1.03-1.12) |
| | 200-209 | 996,941 | 10,515 | 1,055 | 0.042 | 1.03 (1.00-1.06) | 1,029,894 | 4,563 | 443 | 0.046 | 1.04 (1.00-1.09) |
| | 210-219 | 867,135 | 8,910 | 1,028 | 0.369 | 1.01 (0.98-1.05) | 993,073 | 4,277 | 431 | 0.592 | 1.01 (0.97-1.06) |
| | 220-229 | 725,119 | 7,313 | 1,009 | | 1.00 (Reference) | 907,481 | 3,865 | 426 | | 1.00 (Reference) |
| | 230-239 | 535,409 | 5,380 | 1,005 | 0.940 | 1.00 (0.96-1.03) | 742,031 | 3,019 | 407 | 0.068 | 0.96 (0.91-1.00) |
| 240-249 | 394,698 | 4,087 | 1,035 | 0.252 | 1.02 (0.98-1.06) | 594,659 | 2,573 | 433 | 0.743 | 1.01 (0.96-1.06) | |

| Age group, years | TC group, mg/dL | Men (n=7,292,064) | | | | | Women (n=5,522,942) | | | | |
|------------------|-----------------|-------------------|--------------|------------------|---------|------------------|---------------------|--------------|------------------|---------|------------------|
| | | Person year | No. of death | CDR ^b | p-value | HR (95% CI) | Person year | No. of death | CDR ^b | p-value | HR (95% CI) |
| | 250-259 | 293,694 | 3,159 | 1,076 | 0.009 | 1.06 (1.01-1.10) | 481,307 | 2,151 | 447 | 0.179 | 1.04 (0.98-1.09) |
| | 260-269 | 188,688 | 2,024 | 1,073 | 0.034 | 1.05 (1.00-1.11) | 339,878 | 1,485 | 437 | 0.834 | 1.01 (0.95-1.07) |
| | 270-279 | 112,346 | 1,255 | 1,117 | 0.004 | 1.09 (1.03-1.16) | 214,995 | 1,007 | 468 | 0.092 | 1.06 (0.99-1.14) |
| | ≥280 | 225,289 | 2,996 | 1,330 | <0.001 | 1.25 (1.20-1.31) | 475,490 | 2,623 | 552 | <0.001 | 1.22 (1.16-1.28) |
| 65-74 | <120 | 58,893 | 3,669 | 6,230 | <0.001 | 1.81 (1.74-1.88) | 27,264 | 818 | 3,000 | <0.001 | 1.88 (1.74-2.02) |
| | 120-129 | 68,027 | 3,527 | 5,185 | <0.001 | 1.54 (1.48-1.60) | 33,862 | 897 | 2,649 | <0.001 | 1.68 (1.57-1.80) |
| | 130-139 | 134,291 | 6,217 | 4,630 | <0.001 | 1.37 (1.33-1.42) | 73,512 | 1,751 | 2,382 | <0.001 | 1.51 (1.43-1.59) |
| | 140-149 | 202,735 | 8,691 | 4,287 | <0.001 | 1.30 (1.26-1.34) | 128,720 | 2,720 | 2,113 | <0.001 | 1.36 (1.31-1.43) |
| | 150-159 | 294,436 | 11,541 | 3,920 | <0.001 | 1.22 (1.19-1.26) | 211,362 | 4,120 | 1,949 | <0.001 | 1.25 (1.21-1.30) |
| | 160-169 | 378,862 | 13,765 | 3,633 | <0.001 | 1.15 (1.12-1.18) | 307,739 | 5,459 | 1,774 | <0.001 | 1.15 (1.11-1.19) |
| | 170-179 | 440,573 | 14,938 | 3,391 | <0.001 | 1.08 (1.06-1.11) | 405,579 | 6,797 | 1,676 | <0.001 | 1.10 (1.06-1.14) |
| | 180-189 | 470,576 | 15,183 | 3,226 | <0.001 | 1.05 (1.02-1.08) | 492,988 | 8,035 | 1,630 | <0.001 | 1.07 (1.04-1.11) |
| | 190-199 | 462,377 | 14,479 | 3,131 | 0.023 | 1.03 (1.00-1.06) | 549,204 | 8,786 | 1,600 | <0.001 | 1.06 (1.02-1.09) |
| | 200-209 | 417,255 | 12,851 | 3,080 | 0.182 | 1.02 (0.99-1.05) | 559,797 | 8,848 | 1,581 | 0.002 | 1.05 (1.02-1.08) |
| | 210-219 | 353,837 | 10,679 | 3,018 | 0.600 | 1.01 (0.98-1.04) | 534,761 | 8,212 | 1,536 | 0.191 | 1.02 (0.99-1.05) |
| | 220-229 | 286,088 | 8,524 | 2,980 | | 1.00 (Reference) | 486,988 | 7,325 | 1,504 | | 1.00 (Reference) |
| | 230-239 | 208,036 | 6,090 | 2,927 | 0.466 | 0.99 (0.96-1.02) | 386,884 | 5,988 | 1,548 | 0.113 | 1.03 (0.99-1.06) |
| | 240-249 | 151,259 | 4,634 | 3,064 | 0.058 | 1.04 (1.00-1.07) | 314,853 | 4,816 | 1,530 | 0.383 | 1.02 (0.98-1.05) |
| | 250-259 | 110,620 | 3,411 | 3,084 | 0.031 | 1.04 (1.00-1.09) | 252,615 | 4,065 | 1,609 | <0.001 | 1.08 (1.04-1.12) |
| | 260-269 | 69,217 | 2,175 | 3,142 | 0.012 | 1.06 (1.01-1.11) | 178,782 | 2,921 | 1,634 | 0.002 | 1.07 (1.02-1.12) |
| | 270-279 | 41,365 | 1,399 | 3,382 | <0.001 | 1.13 (1.07-1.20) | 112,434 | 1,889 | 1,680 | <0.001 | 1.10 (1.05-1.16) |
| | ≥280 | 81,411 | 3,036 | 3,729 | <0.001 | 1.23 (1.18-1.29) | 255,780 | 4,718 | 1,845 | <0.001 | 1.18 (1.14-1.23) |
| 75-99 | <120 | 14,310 | 1,829 | 12,781 | <0.001 | 1.43 (1.36-1.52) | 7,492 | 595 | 7,942 | <0.001 | 1.32 (1.21-1.43) |
| | 120-129 | 16,586 | 1,942 | 11,708 | <0.001 | 1.31 (1.24-1.39) | 8,292 | 669 | 8,068 | <0.001 | 1.40 (1.29-1.51) |
| | 130-139 | 31,929 | 3,544 | 11,100 | <0.001 | 1.23 (1.18-1.29) | 18,985 | 1,458 | 7,680 | <0.001 | 1.34 (1.26-1.42) |
| | 140-149 | 46,123 | 4,807 | 10,422 | <0.001 | 1.17 (1.12-1.22) | 33,078 | 2,334 | 7,056 | <0.001 | 1.21 (1.15-1.27) |
| | 150-159 | 67,097 | 6,561 | 9,778 | <0.001 | 1.10 (1.06-1.15) | 53,209 | 3,458 | 6,499 | <0.001 | 1.13 (1.08-1.18) |
| | 160-169 | 79,491 | 7,447 | 9,368 | <0.001 | 1.07 (1.03-1.12) | 74,384 | 4,704 | 6,324 | <0.001 | 1.11 (1.07-1.15) |
| | 170-179 | 88,693 | 8,061 | 9,089 | 0.025 | 1.04 (1.01-1.09) | 97,366 | 5,931 | 6,091 | <0.001 | 1.08 (1.05-1.12) |
| | 180-189 | 88,804 | 7,742 | 8,718 | 0.321 | 1.02 (0.98-1.06) | 112,863 | 6,705 | 5,941 | 0.003 | 1.05 (1.02-1.09) |
| | 190-199 | 83,853 | 7,170 | 8,551 | 0.654 | 1.01 (0.97-1.05) | 123,867 | 7,069 | 5,707 | 0.095 | 1.03 (0.99-1.07) |
| | 200-209 | 71,879 | 6,203 | 8,630 | 0.153 | 1.03 (0.99-1.07) | 125,277 | 6,946 | 5,545 | 0.731 | 1.01 (0.97-1.04) |
| | 210-219 | 59,274 | 4,887 | 8,245 | 0.425 | 0.98 (0.94-1.03) | 114,976 | 6,458 | 5,617 | 0.246 | 1.02 (0.99-1.06) |
| | 220-229 | 46,869 | 3,837 | 8,187 | | 1.00 (Reference) | 101,430 | 5,526 | 5,448 | | 1.00 (Reference) |
| | 230-239 | 31,945 | 2,650 | 8,296 | 0.504 | 1.02 (0.97-1.07) | 82,147 | 4,496 | 5,473 | 0.461 | 1.01 (0.98-1.06) |

| Age group, years | TC group, mg/dL | Men (n=7,292,064) | | | | | Women (n=5,522,942) | | | | |
|------------------|-----------------|----------------------|--------------|------------------|---------|------------------|------------------------|--------------|------------------|---------|------------------|
| | | Person year | No. of death | CDR ^b | p-value | HR (95% CI) | Person year | No. of death | CDR ^b | p-value | HR (95% CI) |
| 240-249 | | 22,481 | 1,745 | 7,762 | 0.111 | 0.96 (0.90-1.01) | 64,763 | 3,439 | 5,310 | 0.418 | 0.98 (0.94-1.03) |
| 250-259 | | 16,950 | 1,414 | 8,342 | 0.380 | 1.03 (0.97-1.09) | 52,881 | 2,941 | 5,561 | 0.113 | 1.04 (0.99-1.08) |
| 260-269 | | 10,709 | 945 | 8,824 | 0.033 | 1.08 (1.01-1.16) | 35,941 | 2,020 | 5,620 | 0.046 | 1.05 (1.00-1.11) |
| 270-279 | | 6,389 | 560 | 8,765 | 0.069 | 1.09 (0.99-1.19) | 22,643 | 1,248 | 5,512 | 0.365 | 1.03 (0.97-1.09) |
| ≥280 | | 12,340 | 1,100 | 8,914 | 0.005 | 1.10 (1.03-1.18) | 52,420 | 3,134 | 5,979 | <0.001 | 1.12 (1.07-1.17) |

CDR, crude death rate per 100,000 person-years; CI, confidence interval; TC, total cholesterol; HR, hazard ratio

^a HRs were calculated by Cox 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 (when applicable), smoking status, alcohol use, physical activity, known history of heart disease, stroke, or cancer, body mass index, systolic blood pressure, and fasting glucose.

^b per 100,000 person-years.

To convert cholesterol from mg/dL to mmol/L, multiply by 0.02586.

Table S4. HRs^a for death associated with three categories of total cholesterol, according to age.

| Age group, years | TC group, mg/dL | Men and women | | | Men | | | Women | | |
|------------------|-----------------|---------------|---------|------------------|--------------|---------|------------------|--------------|---------|------------------|
| | | No. of death | p-value | HR (95% CI) | No. of death | p-value | HR (95% CI) | No. of death | p-value | HR (95% CI) |
| 18-99 | <200 | 397,585 | | 1.00 (Reference) | 283,446 | | 1.00 (Reference) | 114,139 | | 1.00 (Reference) |
| all ages | 200-239 | 202,066 | <0.001 | 0.86 (0.86-0.87) | 122,104 | <0.001 | 0.84 (0.84-0.85) | 79,962 | <0.001 | 0.89 (0.88-0.90) |
| combined | ≥240 | 94,772 | <0.001 | 0.92 (0.92-0.93) | 48,996 | <0.001 | 0.91 (0.90-0.91) | 45,776 | <0.001 | 0.94 (0.93-0.95) |
| 18-34 | <200 | 14,506 | | 1.00 (Reference) | 10,893 | | 1.00 (Reference) | 3,613 | | 1.00 (Reference) |
| | 200-239 | 4,627 | 0.044 | 0.97 (0.93-1.00) | 3,844 | 0.013 | 0.95 (0.92-0.99) | 783 | 0.138 | 1.06 (0.98-1.15) |
| | ≥240 | 1,580 | <0.001 | 1.13 (1.07-1.19) | 1,389 | <0.001 | 1.12 (1.06-1.19) | 191 | 0.002 | 1.26 (1.09-1.46) |
| 35-44 | <200 | 29,033 | | 1.00 (Reference) | 21,957 | | 1.00 (Reference) | 7,076 | | 1.00 (Reference) |
| | 200-239 | 13,325 | <0.001 | 0.85 (0.83-0.87) | 10,728 | <0.001 | 0.83 (0.81-0.85) | 2,597 | 0.018 | 0.95 (0.90-0.99) |
| | ≥240 | 5,626 | <0.001 | 0.95 (0.92-0.98) | 4,750 | <0.001 | 0.92 (0.89-0.95) | 876 | <0.001 | 1.15 (1.07-1.23) |
| 45-54 | <200 | 49,701 | | 1.00 (Reference) | 38,856 | | 1.00 (Reference) | 10,845 | | 1.00 (Reference) |
| | 200-239 | 26,752 | <0.001 | 0.80 (0.78-0.81) | 19,693 | <0.001 | 0.77 (0.76-0.78) | 7,059 | <0.001 | 0.89 (0.86-0.92) |
| | ≥240 | 12,596 | <0.001 | 0.85 (0.83-0.87) | 8,917 | <0.001 | 0.82 (0.80-0.84) | 3,679 | 0.011 | 0.95 (0.92-0.99) |
| 55-64 | <200 | 90,926 | | 1.00 (Reference) | 70,627 | | 1.00 (Reference) | 20,299 | | 1.00 (Reference) |
| | 200-239 | 47,842 | <0.001 | 0.81 (0.80-0.82) | 32,118 | <0.001 | 0.80 (0.79-0.81) | 15,724 | <0.001 | 0.83 (0.81-0.85) |
| | ≥240 | 23,360 | <0.001 | 0.87 (0.86-0.88) | 13,521 | <0.001 | 0.86 (0.85-0.88) | 9,839 | <0.001 | 0.88 (0.86-0.90) |
| 65-74 | <200 | 131,393 | | 1.00 (Reference) | 92,010 | | 1.00 (Reference) | 39,383 | | 1.00 (Reference) |
| | 200-239 | 68,517 | <0.001 | 0.88 (0.87-0.89) | 38,144 | <0.001 | 0.87 (0.86-0.88) | 30,373 | <0.001 | 0.89 (0.88-0.90) |
| | ≥240 | 33,064 | <0.001 | 0.94 (0.93-0.96) | 14,655 | <0.001 | 0.94 (0.92-0.96) | 18,409 | <0.001 | 0.94 (0.93-0.96) |
| 75-99 | <200 | 82,026 | | 1.00 (Reference) | 49,103 | | 1.00 (Reference) | 32,923 | | 1.00 (Reference) |
| | 200-239 | 41,003 | <0.001 | 0.92 (0.91-0.93) | 17,577 | <0.001 | 0.93 (0.91-0.94) | 23,426 | <0.001 | 0.92 (0.90-0.94) |
| | ≥240 | 18,546 | <0.001 | 0.95 (0.94-0.97) | 5,764 | <0.001 | 0.95 (0.92-0.97) | 12,782 | <0.001 | 0.95 (0.93-0.97) |

CI, confidence interval; HR, hazard ratio; TC

^a HRs were calculated by Cox 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 (when applicable), known pre-existing diabetes, smoking status, alcohol use, physical activity, known history of heart disease, stroke, or cancer, body mass index, systolic blood pressure, and fasting glucose.

To convert cholesterol from mg/dL to mmol/L, multiply by 0.02586.