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| Supplemental Table S1 cardiovascular disease event incidence (per 1000 person-year) of different serum lipid markers and lipid indices among men, women and total participants (n=5054); Tehran Lipid and Glucose Study (TLGS) (2001-2012). | | | | | | | | | | | |
|  | |  | | **Lipid limits** | | **Event/At risk** | | **Person-year** | | **CVD incidence\***  **(95% CI)** | |
| Men (N=458) | |  | |  | |  | |  | |  | |
| TC | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <5.15 | | 145/965 | | 9744 | | 14.9(12.6-17.5) | |
|  | T2 | |  | | 5.15-6.14 | | 156/774 | | 8316 | | 18.8(16.0-21.9) | |
|  | T3 | |  | | ≥6.14 | | 157/541 | | 5805 | | 27.0(23.1-31.6) | |
| LDL-C | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <3.49 | | 135/919 | | 9283 | | 14.5(12.3-14.2) | |
|  | T2 | |  | | 3.49-4.32 | | 159/766 | | 8216 | | 19.3(16.7-22.6) | |
|  | T3 | |  | | ≥4.32 | | 164/595 | | 6365 | | 25.8(22.1-30.0) | |
| HDL-C | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <0.93 | | 228/1122 | | 11691 | | 19.5(17.1-22.2) | |
|  | T2 | |  | | 0.93-1.19 | | 124/630 | | 6582 | | 18.8(15.8-22.5) | |
|  | T3 | |  | | ≥1.19 | | 106/528 | | 5591 | | 18.9(15.7-22.9) | |
| Non-HDL-C | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <4.09 | | 1.5/899 | | 9085 | | 14.8(12.5-17.6) | |
|  | T2 | |  | | 4.09-5.08 | | 159/773 | | 8287 | | 19.2(16.4-22.4) | |
|  | T3 | |  | | ≥5.08 | | 164/608 | | 6492 | | 25.3(21.7-29.4) | |
| TGs | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <1.5 | | 138/797 | | 8078 | | 17.1(14.4-20.2) | |
|  | T2 | |  | | 1.5-2.33 | | 144/723 | | 7616 | | 18.9(16.0-22.2) | |
|  | T3 | |  | | ≥2.33 | | 176/760 | | 8171 | | 21.5(18.6-24.9) | |
| TC/HDL-C | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <4.75 | | 103/662 | | 6761 | | 15.2(12.5-18.5) | |
|  | T2 | |  | | 4.75-6.12 | | 153/771 | | 8150 | | 18.8(16.0-22.0) | |
|  | T3 | |  | | ≥6.12 | | 202/847 | | 8953 | | 22.7(19.6-25.9) | |
| TGs/HDL-C | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <1.35 | | 117/688 | | 7136 | | 16.4(13.7-19.6) | |
|  | T2 | |  | | 1.35-2.39 | | 148/731 | | 7559 | | 19.6(16.7-23.0) | |
|  | T3 | |  | | ≥2.39 | | 193/861 | | 9170 | | 21.0(18.3-24.2) | |
|  | |  | |  | |  | |  | |  | |
| Women(N=331) | |  | |  | |  | |  | |  | |
| TC | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <5.15 | | 39/751 | | 7917 | | 4.9(3.6-6.7) | |
|  | T2 | |  | | 5.15-6.14 | | 91/874 | | 9447 | | 9.6(7.8-11.8) | |
|  | T3 | |  | | ≥6.14 | | 201/1149 | | 12685 | | 15.8(13.8-18.2) | |
| LDL-C | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <3.49 | | 42/810 | | 8545 | | 4.9(3.6-6.5) | |
|  | T2 | |  | | 3.49-4.32 | | 103/908 | | 9891 | | 10.4(8.6-12.6) | |
|  | T3 | |  | | ≥4.32 | | 186/1056 | | 11613 | | 16.0(13.9-18.5) | |
| HDL-C | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <0.93 | | 74/679 | | 7314 | | 10.12(8.0-12.7) | |
|  | T2 | |  | | 0.93-1.18 | | 101/790 | | 8411 | | 12.0(9.9-14.6) | |
|  | T3 | |  | | ≥1.18 | | 156/1305 | | 14329 | | 10.9(9.3-12.7) | |
| Non-HDL-C | |  | |  | |  | |  | |  | |
|  | T1 | |  | | <4.09 | | 43/810 | | 8523 | | 5.0(3.7-6.8) | |
|  | T2 | |  | | 4.09-5.08 | | 98/917 | | 10018 | | 9.8(8.0-11.9) | |
|  | T3 | |  | | ≥5.08 | | 190/1047 | | 11507 | | 10.5(14.3-19.0) | |
| CVD: cardiovascular disease, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, TGs: triglycerides.  \*Per 1000 person-year. | | | | | | | | | | | |

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| Supplemental Table S1 (continued) | | | | | | |
|  | |  | **Lipid limits** | **Event/At risk** | **Person-year** | **CVD incidence \***  **(95% CI)** |
| TGs | |  |  |  |  |  |
|  | T1 |  | <1.5 | 64/915 | 9868 | 6.8(5.3-8.6) |
|  | T2 |  | 1.5-2.33 | 105/942 | 101146 | 10.3(8.5-12.5) |
|  | T3 |  | ≥2.33 | 159/917 | 10035 | 15.8(13.7-18.5) |
| TC/HDL-C | |  |  |  |  |  |
|  | T1 |  | <4.75 | 80/1061 | 11353 | 7.0(5.6-8.8) |
|  | T2 |  | 4.75-6.12 | 113/906 | 9900 | 11.4(9.5-13.7) |
|  | T3 |  | ≥6.12 | 138/807 | 8796 | 15.7(13.3-18.5) |
| TGs/HDL-C | |  |  |  |  |  |
|  | T1 |  | <1.35 | 88/1027 | 11126 | 7.9(6.4-9.7) |
|  | T2 |  | 1.35-2.39 | 121/950 | 10210 | 11.8(9.9-14.2) |
|  | T3 |  | ≥2.39 | 122/797 | 8713 | 14.0(11.7-16.7) |
|  | |  |  |  |  |  |
| Total (N=789) | |  |  |  |  |  |
| TC | |  |  |  |  |  |
|  | T1 |  | <5.15 | 184/1716 | 17661 | 10.4(9.0-12.0) |
|  | T2 |  | 5.15-6.14 | 247/1648 | 17762 | 13.9(12.3-15.7) |
|  | T3 |  | ≥6.14 | 358/1690 | 18490 | 19.4(17.4-21.5) |
| LDL-C | |  |  |  |  |  |
|  | T1 |  | <3.49 | 177/1729 | 17828 | 9.9(8.7-11.5) |
|  | T2 |  | 3.49-4.32 | 262/1674 | 18108 | 14.5(12.8-16.3) |
|  | T3 |  | ≥4.32 | 350/1651 | 17978 | 19.5(17.5-21.6) |
| HDL-C | |  |  |  |  |  |
|  | T1 |  | <0.93 | 302/1801 | 19005 | 15.9(14.2-17.8) |
|  | T2 |  | 0.93-1.19 | 225/1420 | 14993 | 15.0(13.2-17.1) |
|  | T3 |  | ≥1.19 | 262/833 | 19915 | 13.1(11.6-14.8) |
| Non-HDL-C | |  |  |  |  |  |
|  | T1 |  | <4.09 | 178/1709 | 17609 | 10.1(8.7-11.7) |
|  | T2 |  | 4.09-5.08 | 257/1690 | 18305 | 14.0(12.4-18.9) |
|  | T3 |  | ≥5.08 | 354/1655 | 17999 | 19.7(17.7-21.8) |
| TGs | |  |  |  |  |  |
|  | T1 |  | <1.5 | 205/1712 | 17946 | 11.4(9.9-13.1) |
|  | T2 |  | 1.5-2.33 | 249/1665 | 17762 | 14.0(12.4-15.9) |
|  | T3 |  | ≥2.33 | 335/1677 | 18206 | 18.4(16.5-20.5) |
| TC/HDL-C | |  |  |  |  |  |
|  | T1 |  | <4.75 | 183/1723 | 18114 | 10.1(8.7-11.7) |
|  | T2 |  | 4.75-6.12 | 266/1677 | 18051 | 14.7(13.1-16.6) |
|  | T3 |  | ≥6.12 | 340/1654 | 17748 | 19.1(17.2-21.3) |
| TGs/HDL-C | |  |  |  |  |  |
|  | T1 |  | <1.35 | 205/1715 | 18262 | 11.2(9.8-12.9) |
|  | T2 |  | 1.35-2.39 | 269/1681 | 17768 | 15.1(13.4-17.1) |
|  | T3 |  | ≥2.39 | 315/1658 | 17883 | 17.6(15.8-19.7) |
| CVD: cardiovascular disease, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, TGs: triglycerides.  \*Per 1000 person-year. | | | | | | |

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| Supplemental Table S2 cardiovascular mortality rate (per 1000 person-year) of different serum lipid markers and lipid indices among total participants (n=5518); Tehran Lipid and Glucose Study (TLGS) (2001-2012). | | | | | | |
|  | |  | **Lipid limits** | **Event/At risk** | **Person-year** | **Mortality rate\***  **(95% CI)** |
| CV mortality (n=279) | | |  |  |  |  |
| TC | |  |  |  |  |  |
|  | T1 |  | <5.15 | 71/1831 | 18709 | 3.8(3.0-4.8) |
|  | T2 |  | 5.15-6.14 | 92/1807 | 19297 | 4.8(3.9-5.8) |
|  | T3 |  | ≥6.14 | 116/1880 | 20391 | 5.7(4.7-6.8) |
| LDL-C | |  |  |  |  |  |
|  | T1 |  | <3.49 | 72/1840 | 18843 | 3.8(3.0-4.8) |
|  | T2 |  | 3.49-4.32 | 94/1839 | 19707 | 4.8(3.9-5.8) |
|  | T3 |  | ≥4.32 | 113/1839 | 19847 | 5.7(4.7-6.8) |
| HDL-C | |  |  |  |  |  |
|  | T1 |  | <0.93 | 106/1980 | 20676 | 5.1(4.2-6.2) |
|  | T2 |  | 0.93-1.19 | 73/1558 | 16341 | 4.5(3.5-5.6) |
|  | T3 |  | ≥1.19 | 100/1980 | 21380 | 4.7(3.8-5.7) |
| Non-HDL-C | |  |  |  |  |  |
|  | T1 |  | <4.09 | 73/1824 | 18674 | 3.9(3.1-4.9) |
|  | T2 |  | 4.09-5.08 | 97/1855 | 19887 | 4.9(4.0-5.9) |
|  | T3 |  | ≥5.08 | 109/1839 | 19835 | 5.5(4.5-6.6) |
| TGs | |  |  |  |  |  |
|  | T1 |  | <1.5 | 98/1838 | 19174 | 5.1(4.2-6.2) |
|  | T2 |  | 1.5-2.33 | 84/1822 | 19254 | 4.4(3.5-5.4) |
|  | T3 |  | ≥2.33 | 97/1858 | 19968 | 4.8(4.0-5.9) |
| TC/ HDL-C | |  |  |  |  |  |
|  | T1 |  | <4.75 | 85/1842 | 19258 | 4.4(3.6-5.4) |
|  | T2 |  | 4.75-6.12 | 87/1834 | 19552 | 4.4(3.6-5.5) |
|  | T3 |  | ≥6.12 | 107/1842 | 19587 | 5.5(4.5-6.6) |
| TGs/ HDL-C | |  |  |  |  |  |
|  | T1 |  | <1.35 | 89/1840 | 19499 | 4.6(3.7-5.6) |
|  | T2 |  | 1.35-2.39 | 105/1839 | 19257 | 5.4(4.5-5.6) |
|  | T3 |  | ≥2.39 | 85/1839 | 19641 | 4.3(3.5-5.3) |
| CV: cardiovascular, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, TGs: triglycerides.  \*Per 1000 person-year. | | | | | | |

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| Supplemental Table S3 Non-cardiovascular mortality rate (per 1000 person-year) of different serum lipid markers and lipid indices among total participants (n=5518); Tehran Lipid and Glucose Study (TLGS) (2001-2012). | | | | | | | |
|  | |  | **Lipid limits** | **Event/At risk** | **Person-year** | **Mortality rate\***  **(95% CI)** | |
| Non-CV mortality (n=270) | | | |  |  |  | |
| TC | |  |  |  |  |  | |
|  | T1 |  | <5.15 | 106/1831 | 18709 | 5.5(4.7-6.8) | |
|  | T2 |  | 5.15-6.14 | 82/1807 | 19297 | 4.2(3.4-5.3) | |
|  | T3 |  | ≥6.14 | 82/1880 | 20391 | 4.0(3.2-5.0) | |
| LDL-C | |  |  |  |  |  | |
|  | T1 |  | <3.49 | 112/1840 | 18843 | 5.9(4.9-7.2) | |
|  | T2 |  | 3.49-4.32 | 74/1839 | 19707 | 3.7(3.0-4.7) | |
|  | T3 |  | ≥4.32 | 84/1839 | 19847 | 4.2(3.4-5.2) | |
| HDL-C | |  |  |  |  |  | |
|  | T1 |  | <0.93 | 94/1980 | 20676 | 4.5(3.7-5.6) | |
|  | T2 |  | 0.93-1.19 | 66/1558 | 16341 | 4.0(3.2-5.1) | |
|  | T3 |  | ≥1.19 | 110/1980 | 21380 | 5.1(4.3-6.2) | |
| Non-HDL-C | |  |  |  |  |  | |
|  | T1 |  | <4.09 | 113/1824 | 18674 | 6.1(5.0-7.3) | |
|  | T2 |  | 4.09-5.08 | 73/1855 | 19887 | 3.7(2.9-4.6) | |
|  | T3 |  | ≥5.08 | 84/1839 | 19835 | 4.2(3.4-5.2) | |
| TGs | |  |  |  |  |  | |
|  | T1 |  | <1.5 | 111/1838 | 19174 | 5.8(4.8-7.0) | |
|  | T2 |  | 1.5-2.33 | 89/1822 | 19254 | 4.6(3.8-5.7) | |
|  | T3 |  | ≥2.33 | 70/1858 | 19968 | 3.5(2.8-4.4) | |
| TC/HDL-C | |  |  |  |  |  | |
|  | T1 |  | <4.75 | 109/1842 | 19258 | 5.7(4.7-6.8) | |
|  | T2 |  | 4.75-6.12 | 89/1834 | 19552 | 4.6(3.7-5.6) | |
|  | T3 |  | ≥6.12 | 72/1842 | 19587 | 3.7(2.9-4.6) | |
| TGs/HDL-C | |  |  |  |  |  | |
|  | T1 |  | <1.35 | 107/1840 | 19499 | 5.5(4.5-6.6) | |
|  | T2 |  | 1.35-2.39 | 92/1839 | 19257 | 4.8(3.9-5.9) | |
|  | T3 |  | ≥2.39 | 71/1839 | 19641 | 3.6(2.9-5.7) | |
| CV: cardiovascular, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, TGs: triglycerides.  \*Per 1000 person-year. | | | | | | |

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| Supplemental Table S4 Hazard ratios of lipid measures for predicting first cardiovascular disease events among participants without prevalent CVD in those with available data on HOMA-IR (n=1548); Tehran Lipid and Glucose Study (TLGS) (2001-2012)\*. | | | | | | | |
|  |  | **Model 1** | | |  | **Model 2** | |  |
| **SD (mmol/L)** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| TC |  | 1.18 | 1.15(1.0-1.32) | 0.05 |  | 1.07(0.92-1.23) | 0.39 |  |
| LDL-C |  | 1.0 | 1.16(1.01-1.33) | 0.03 |  | 1.08(0.94-1.25) | 0.28 |  |
| HDL-C |  | 0.28 | 0.85(0.73-1.0) | 0.05 |  | 0.91(0.77-1.07) | 0.27 |  |
| Non-HDL-C |  | 1.17 | 1.18(1.03-1.35) | 0.01 |  | 1.05(0.91-1.21) | 0.49 |  |
| ln-TGs |  | 0.2 | 1.21(1.05-1.39) | 0.008 |  | 1.02(0.87-1.19) | 0.84 |  |
| TC/HDL-C |  | 1.64 | 1.20(1.05-1.38) | 0.007 |  | 1.13(0.97-1.32) | 0.12 |  |
| ln-TGs/HDL-C |  | 0.46 | 1.22(1.06-1.41) | 0.006 |  | 1.04(0.89-1.22) | 0.6 |  |
| Model 1: lipid profile + gender; model 2= model 1 + blood pressure status (i.e. normotension, prehypertension and hypertension status), glucose tolerance status (normal glucose tolerance, prediabetes and diabetes), education status, low physical activity, current smoker, lipid lowering drugs, body mass index and HOMA-IR.  \*Hazard ratios (HR) indicate the increase risk for a 1-SD increase of each lipid parameter.  CVD: cardiovascular disease, HOMA-IR: homeostatic model assessment-insulin resistance, SD: standard deviation, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, ln-TGs: logarithm-transformed triglycerides, CI: confidence interval. | | | | | | | |

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| Supplemental Table S5 Hazard ratios of lipid measures for predicting first cardiovascular disease events among participants without prevalent CVD based on lipid profile tertiles CVD in those with available data on HOMA-IR (n=1548); Tehran Lipid and Glucose Study (TLGS) (2001-2012). | | | | | | | | | | |
|  |  | **Model 1** | | |  |  | **Model 2** | | |  |
|  |  | **Tertiles of variables** | | | **P for trend\*** |  | **Tertiles of variables** | | | **P for trend\*** |
|  |  | **1** | **2** | **3** |  |  | **1** | **2** | **3** |  |
| TC, mmol/L |  | Reference | 1.55(1.06-2.27) | 1.71(1.16-2.51) | 0.007 |  | Reference | 1.56(1.05-2.34) | 1.57(1.05-2.36) | 0.037 |
| LDL-C, mmol/L |  | Reference | 1.59(1.09-2.32) | 1.73(1.18-2.54) | 0.006 |  | Reference | 1.65(1.11-2.47) | 1.66(1.10-2.50) | 0.02 |
| HDL-C, mmol/L |  | Reference | 0.89(0.63-1.27) | 0.73(0.51-1.03) | 0.07 |  | Reference | 0.92(0.64-1.31) | 0.83(0.57-1.20) | 0.33 |
| Non-HDL-C |  | Reference | 1.61(1.10-2.34) | 1.73(1.18-2.53) | 0.007 |  | Reference | 1.61(1.08-2.40) | 1.58(1.05-2.39) | 0.04 |
| TGs, mmol/L |  | Reference | 1.15(0.79-1.68) | 1.62(1.14-2.30) | 0.006 |  | Reference | 0.95(0.65-1.39) | 1.10(0.75-1.62) | 0.57 |
| TC/HDL-C |  | Reference | 1.39(0.96-2.02) | 1.81(1.26-2.59) | 0.001 |  | Reference | 1.28(0.87-1.89) | 1.48(1.01-2.17) | 0.05 |
| TGs/HDL-C |  | Reference | 1.18(0.82-1.69) | 1.63(1.15-2.31) | 0.006 |  | Reference | 0.99(0.67-1.44) | 1.16(0.79-1.71) | 0.41 |
| Model 1: lipid profile tertiles + gender; model 2= model 1 + blood pressure status (i.e. normotension, prehypertension and hypertension status), glucose tolerance status (normal glucose tolerance, prediabetes and diabetes), education status, low physical activity, current smoker, lipid lowering drugs, body mass index and HOMA-IR.  CVD: cardiovascular disease, HOMA-IR: homeostatic model assessment-insulin resistance, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, TGs: triglycerides, CI: confidence interval.  \*P-values were calculated using age scale Cox proportional hazards regression models | | | | | | | | | | |