## DATA SUPPLEMENT

## U-shaped association of high-density lipoprotein cholesterol with all-cause and cardiovascular mortality in patients with hypertension

Table S1. Threshold effect analysis of HDL-C on all-cause and cardiovascular mortality by subgroups

Figure S1. Kaplan-Meier curves of the event-free survival for all-cause mortality (A) and cardiovascular mortality (B) according to HDL-C categories.

Figure S2. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in participants $<65$ years old.

Figure S3. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in participants $\geq 65$ years old.

Figure S4. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in men.

Figure S5. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in women.

Figure S6. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in Non-white participants.

Figure S7. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in white participants.

Table S1. Threshold effect analysis of HDL-C on all-cause and cardiovascular mortality by subgroups

|  | All-cause mortality |  |  | Cardiovascular mortality |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Model I <br> HR ( $95 \% \mathrm{CI}$ ), P- <br> value | Model II <br> HR ( $95 \% \mathrm{CI}$ ), P- <br> value | Model III <br> HR ( $95 \% \mathrm{CI}$ ), P- <br> value | Model I <br> HR ( $95 \% \mathrm{CI}$ ), P- <br> value | Model II <br> HR ( $95 \% \mathrm{CI}$ ), P- <br> value | Model III <br> HR (95\%CI), P- <br> value |
| Age $\geq 65$ year |  |  |  |  |  |  |
| HDL-C per mmol/L increment | 0.91 (0.82, 1.01) | 0.93 (0.83, 1.03) | 1.05 (0.94, 1.17) | 0.75 (0.61, 0.93) | 0.79 (0.63, 0.99) | 0.92 (0.73, 1.17) |
|  | 0.0674 | 0.1538 | 0.3928 | 0.0073 | 0.0383 | 0.5062 |
| Inflection point, mmol/L | 1.33 | 1.33 | 1.33 | 1.10 | 1.10 | 1.10 |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants with HDL-C $<$ inflection point | $\begin{aligned} & 0.51(0.39,0.65) \\ & <0.0001 \end{aligned}$ | $\begin{aligned} & 0.51(0.40,0.66) \\ & <0.0001 \end{aligned}$ | $\begin{aligned} & 0.65(0.50,0.85) \\ & 0.0015 \end{aligned}$ | $\begin{aligned} & 0.21(0.09,0.48) \\ & 0.0002 \end{aligned}$ | $\begin{aligned} & 0.21(0.09,0.47) \\ & 0.0002 \end{aligned}$ | $\begin{aligned} & 0.28(0.12,0.66) \\ & 0.0035 \end{aligned}$ |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants with HDL-C > inflection point | $\begin{aligned} & 1.21(1.05,1.40) \\ & 0.0093 \end{aligned}$ | $\begin{aligned} & 1.22(1.05,1.41) \\ & 0.0094 \end{aligned}$ | $\begin{aligned} & 1.30(1.12,1.52) \\ & 0.0006 \end{aligned}$ | $\begin{aligned} & 0.95(0.74,1.22) \\ & 0.6730 \end{aligned}$ | $\begin{aligned} & 1.00(0.77,1.30) \\ & 0.9898 \end{aligned}$ | $\begin{aligned} & 1.13(0.87,1.48) \\ & 0.3610 \end{aligned}$ |
| P for log likelihood ratio test | $<0.001$ | $<0.001$ | $<0.001$ | 0.003 | 0.002 | 0.006 |
| Age $<65$ year |  |  |  |  |  |  |
| HDL-C per mmol/L increment | 0.99 (0.83, 1.19) | 1.05 (0.86, 1.27) | 1.32 (1.08, 1.60) | 0.76 (0.50, 1.16) | 0.94 (0.61, 1.46) | 1.37 (0.88, 2.12) |
|  | 0.9412 | 0.6506 | 0.0061 | 0.2001 | 0.7858 | 0.1627 |
| Inflection point, mmol/L | 1.74 | 1.74 | 1.74 | 0.83 | 0.83 | 0.83 |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants with HDL-C $<$ inflection point | $\begin{aligned} & 0.63(0.49,0.82) \\ & 0.0006 \end{aligned}$ | $\begin{aligned} & 0.64(0.49,0.85) \\ & 0.0018 \end{aligned}$ | $\begin{aligned} & 0.94(0.71,1.25) \\ & 0.6694 \end{aligned}$ | $\begin{array}{lr} 1.13 & (0.01, \\ 144.82) & 0.9594 \end{array}$ | $\begin{array}{lr} 1.09 & (0.01, \\ 168.62) & 0.9723 \end{array}$ | $\begin{array}{lr} 6.96 & (0.04, \\ 1306.39) & 0.4674 \end{array}$ |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants with HDL-C > inflection point | $\begin{aligned} & 2.33(1.64,3.31) \\ & <0.0001 \end{aligned}$ | $\begin{aligned} & 2.50(1.75,3.59) \\ & <0.0001 \end{aligned}$ | $\begin{aligned} & 2.32(1.61,3.36) \\ & <0.0001 \end{aligned}$ | $\begin{aligned} & 0.75(0.48,1.18) \\ & 0.2089 \end{aligned}$ | $\begin{aligned} & 0.94(0.59,1.49) \\ & 0.7828 \end{aligned}$ | $\begin{aligned} & 1.31(0.82,2.08) \\ & 0.2593 \end{aligned}$ |
| P for log likelihood ratio test | $<0.001$ | $<0.001$ | 0.002 | 0.868 | 0.953 | 0.520 |


|  | All-cause mortality |  |  | Cardiovascular mortality |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Model I <br> HR ( $95 \% \mathrm{CI}$ ), P- <br> value | Model II <br> HR ( $95 \% \mathrm{CI}$ ), P - <br> value | Model III <br> HR ( $95 \% \mathrm{CI}$ ), P- <br> value | Model I <br> HR ( $95 \% \mathrm{CI}$ ), P- <br> value | Model II <br> HR (95\%CI), P- <br> value | Model III <br> HR (95\%CI), P- <br> value |
| Male |  |  |  |  |  |  |
| HDL-C per mmol/L increment | $\begin{aligned} & 1.26(1.11,1.43) \\ & 0.0005 \end{aligned}$ | $\begin{aligned} & 1.06(0.92,1.21) \\ & 0.4385 \end{aligned}$ | $\begin{aligned} & 1.26(1.09,1.45) \\ & 0.0015 \end{aligned}$ | $\begin{aligned} & 1.00(0.77,1.30) \\ & 0.9999 \end{aligned}$ | $\begin{aligned} & 0.81(0.61,1.07) \\ & 0.1420 \end{aligned}$ | $\begin{aligned} & 1.01(0.76,1.35) \\ & 0.9453 \end{aligned}$ |
| Inflection point, mmol/L | 1.26 | 1.26 | 1.26 | 1.19 | 1.19 | 1.19 |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants with HDL-C < inflection point | $\begin{aligned} & 0.81(0.59,1.09) \\ & 0.1667 \end{aligned}$ | $\begin{aligned} & 0.46(0.34,0.62) \\ & <0.0001 \end{aligned}$ | $\begin{aligned} & 0.69(0.50,0.96) \\ & 0.0255 \end{aligned}$ | $\begin{aligned} & 0.58(0.30,1.14) \\ & 0.1158 \end{aligned}$ | $\begin{aligned} & 0.32(0.16,0.62) \\ & 0.0008 \end{aligned}$ | $\begin{aligned} & 0.49(0.24,0.98) \\ & 0.0437 \end{aligned}$ |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants with HDL-C > inflection point P for log likelihood ratio test | $\begin{aligned} & 1.58(1.31,1.90) \\ & <0.0001 \\ & 0.002 \end{aligned}$ | $\begin{aligned} & 1.69(1.39,2.06) \\ & <0.0001 \\ & <0.001 \end{aligned}$ | $\begin{aligned} & 1.73(1.41,2.11) \\ & <0.0001 \\ & <0.001 \end{aligned}$ | $\begin{aligned} & 1.27(0.88,1.83) \\ & 0.2052 \\ & 0.094 \end{aligned}$ | $\begin{aligned} & 1.27(0.86,1.87) \\ & 0.2330 \\ & 0.004 \end{aligned}$ | $\begin{aligned} & 1.40(0.94,2.07) \\ & 0.0938 \\ & 0.028 \end{aligned}$ |
| Female |  |  |  |  |  | 0.028 |
| HDL-C per mmol/L increment | $\begin{aligned} & 1.16(1.02,1.31) \\ & 0.0193 \end{aligned}$ | $\begin{aligned} & 0.89(0.78,1.01) \\ & 0.0660 \end{aligned}$ | $\begin{aligned} & 1.00(0.87,1.14) \\ & 0.9672 \end{aligned}$ | $\begin{aligned} & 1.15(0.88,1.50) \\ & 0.2907 \end{aligned}$ | $\begin{aligned} & 0.84(0.64,1.11) \\ & 0.2226 \end{aligned}$ | $\begin{aligned} & 0.93(0.69,1.24) \\ & 0.6071 \end{aligned}$ |
| Inflection point, mmol/L | 1.71 | 1.71 | 1.71 | 1.66 | 1.66 | 1.66 |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants with HDL-C < inflection point | $\begin{aligned} & 0.86(0.70,1.06) \\ & 0.1548 \end{aligned}$ | $\begin{aligned} & 0.58(0.47,0.72) \\ & <0.0001 \end{aligned}$ | $\begin{aligned} & 0.68(0.55,0.85) \\ & 0.0005 \end{aligned}$ | $\begin{aligned} & 0.94(0.58,1.52) \\ & 0.8014 \end{aligned}$ | $\begin{aligned} & 0.59(0.36,0.98) \\ & 0.0395 \end{aligned}$ | $\begin{aligned} & 0.68(0.41,1.13) \\ & 0.1343 \end{aligned}$ |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants with HDL-C > inflection point P for log likelihood ratio test | $\begin{aligned} & 1.64(1.32,2.04) \\ & <0.0001 \\ & <0.001 \end{aligned}$ | $\begin{aligned} & 1.51(1.20,1.91) \\ & 0.0004 \\ & <0.001 \\ & \hline \end{aligned}$ | $\begin{aligned} & 1.59(1.26,2.01) \\ & <0.0001 \\ & <0.001 \end{aligned}$ | $\begin{aligned} & 1.43(0.88,2.31) \\ & 0.1469 \\ & 0.326 \\ & \hline \end{aligned}$ | $\begin{aligned} & 1.23(0.74,2.05) \\ & 0.4199 \\ & 0.104 \\ & \hline \end{aligned}$ | $\begin{aligned} & 1.29(0.77,2.16) \\ & 0.3262 \\ & 0.149 \\ & \hline \end{aligned}$ |


|  | All-cause mortality |  |  | Cardiovascular mortality |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Model I <br> HR (95\%CI), Pvalue | Model II <br> HR (95\%CI), Pvalue | Model III HR ( $95 \% \mathrm{CI}$ ), $\mathrm{P}-$ value | Model I HR (95\%CI), Pvalue | Model II HR ( $95 \% \mathrm{CI}$ ), Pvalue | Model III HR ( $95 \% \mathrm{CI}$ ), P value |
| Non-white |  |  |  |  |  |  |
| HDL-C per mmol/L increment | 1.13 (0.99, 1.30) | 1.11 (0.96, 1.29) | 1.26 (1.08, 1.46) | 1.14 (0.85, 1.51) | 1.17 (0.87, 1.58) | 1.29 (0.95, 1.76) |
|  | 0.0770 | 0.1536 | 0.0028 | 0.3775 | $0.2953$ | $0.1058$ |
| Inflection point, mmol/L | 1.32 | 1.32 | 1.32 | 0.93 | 0.93 | 0.93 |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants | 0.72 (0.50, 1.04) | 0.67 (0.46, 0.97) | 0.85 (0.58, 1.23) | 5.23 (0.20, | 7.60 (0.31, | 6.57 (0.24, |


| with HDL-C < inflection point | 0.0784 | 0.0340 | 0.3851 | 135.19) 0.3191 | 185.30) 0.2135 | 182.93) 0.2675 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants | 1.37 (1.13, 1.66) | 1.37 (1.13, 1.67) | 1.48 (1.21, 1.80) | 1.07 (0.79, 1.47) | 1.09 (0.79, 1.51) | 1.22 (0.87, 1.70) |
| with HDL-C > inflection point | 0.0012 | 0.0014 | 0.0001 | 0.6530 | 0.5976 | 0.2457 |
| P for log likelihood ratio test | 0.010 | 0.004 | 0.027 | 0.327 | 0.216 | 0.309 |
| White |  |  |  |  |  |  |
| HDL-C per mmol/L increment | 1.05 (0.94, 1.17) | 0.87 (0.77, 0.98) | 0.99 (0.87, 1.13) | 0.78 (0.62, 0.98$)$ | 0.66 (0.51, 0.86) | 0.81 (0.62, 1.07) |
|  | 0.3852 | 0.0236 | 0.8977 | 0.0339 | 0.0017 | 0.1367 |
| Inflection point, mmol/L | 2.15 | 2.15 | 2.15 | 1.17 | 1.17 | 1.17 |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants | 0.90 (0.80, 1.03) | 0.70 (0.60, 0.80) | $0.81(0.70,0.94)$ | 0.34 (0.17, 0.70) | 0.15 (0.07, 0.32) | 0.25 (0.12, 0.53) |
| with HDL-C < inflection point | 0.1220 | $<0.0001$ | 0.0066 | 0.0033 | $<0.0001$ | 0.0003 |
| Each $1 \mathrm{mmol} / \mathrm{L}$ increase in participants | 2.93 (1.85, 4.64) | 3.91 (2.45, 6.26) | 3.62 (2.24, 5.84) | 1.01 (0.74, 1.37) | 1.02 (0.74, 1.41) | 1.14 (0.82, 1.58) |
| with HDL-C $>$ inflection point | $<0.0001$ | $<0.0001$ | $<0.0001$ | 0.9681 | 0.8917 | 0.4264 |
| P for log likelihood ratio test | <0.001 | <0.001 | <0.001 | 0.021 | <0.001 | 0.001 |

HR, hazard ratio; CI, confidence interval; HDL-C, high density lipoprotein cholesterol.
Model I adjust for none
Model II adjust for age, gender, and race
Model III adjust for age, gender, race, education level, smoking, body mass index, energy, systolic blood pressure, estimated glomerular filtration rate, Creactive protein, total cholesterol, diabetes, cardiovascular disease, antihypertensive drugs, hypoglycemic agents, antiplatelet drugs, and lipid-lowering drugs except the variable itself.


Figure S1. Kaplan-Meier curves of the event-free survival for all-cause mortality (A) and cardiovascular mortality (B) according to HDL-C categories.


Figure S2. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in participants $<65$ years old.

Models were adjusted for age, gender, race, education level, smoking, body mass index, energy, systolic blood pressure, estimated glomerular filtration rate, C-reactive protein, total cholesterol, diabetes, cardiovascular disease, antihypertensive drugs, hypoglycemic agents, antiplatelet drugs, and lipidlowering drugs.


Figure S3. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in participants $\geq 65$ years old.

Models were adjusted for age, gender, race, education level, smoking, body mass index, energy, systolic blood pressure, estimated glomerular filtration rate, C-reactive protein, total cholesterol, diabetes, cardiovascular disease, antihypertensive drugs, hypoglycemic agents, antiplatelet drugs, and lipidlowering drugs.


Figure S4. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in men.

Models were adjusted for age, gender, race, education level, smoking, body mass index, energy, systolic blood pressure, estimated glomerular filtration rate, C-reactive protein, total cholesterol, diabetes, cardiovascular disease, antihypertensive drugs, hypoglycemic agents, antiplatelet drugs, and lipidlowering drugs.


Figure S5. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in participants in women.

Models were adjusted for age, gender, race, education level, smoking, body mass index, energy, systolic blood pressure, estimated glomerular filtration rate, C-reactive protein, total cholesterol, diabetes, cardiovascular disease, antihypertensive drugs, hypoglycemic agents, antiplatelet drugs, and lipidlowering drugs.


Figure S6. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in Non-white participants.

Models were adjusted for age, gender, race, education level, smoking, body mass index, energy, systolic blood pressure, estimated glomerular filtration rate, C-reactive protein, total cholesterol, diabetes, cardiovascular disease, antihypertensive drugs, hypoglycemic agents, antiplatelet drugs, and lipidlowering drugs.


Figure S7. Adjusted cubic spline model of the association between hazard ratio of all-cause mortality (A), cardiovascular mortality (B) and HDL-C levels in white participants.

Models were adjusted for age, gender, race, education level, smoking, body mass index, energy, systolic blood pressure, estimated glomerular filtration rate, C-reactive protein, total cholesterol, diabetes, cardiovascular disease, antihypertensive drugs, hypoglycemic agents, antiplatelet drugs, and lipidlowering drugs.

