

Supplemental Material

High Remnant Cholesterol Level Potentiates the Development of Hypertension

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Table S1 Baseline characteristic of 24252 participants in longitudinal analysis

	Total (N=24252)
Age (year, mean (SD))	45.15(11.27)
Gender, male (%)	15371(63.38)
Heart rate (bpm, mean (SD))	72.73(10.14)
BMI (kg/m ² , mean (SD))	24.12(3.28)
WC (cm, mean (SD))	83.67(10.31)
SBP (mmHg, mean (SD))	121.37(16.82)
DBP (mmHg, mean (SD))	77.51(11.28)
FBG (mmol/L, mean (SD))	5.50(1.19)
TC (mmol/L, mean (SD))	4.90(0.96)
TG (mmol/L, mean (SD))	1.78(1.59)
LDL-C (mmol/L, mean (SD))	2.71(0.73)
RC (mmol/L, mean (SD))	0.81(0.59)
ALT (IU/L, mean (SD))	27.80(24.12)
AST (IU/L, mean (SD))	26.99(14.90)
γ-GGT (IU/L, mean (SD))	36.07(41.01)
Scr (μmol/L, mean (SD))	71.50(15.98)
SUA (μmol/L, mean (SD))	344.11(90.75)
BUN (mmol/L, mean (SD))	5.15(1.31)
RBC (×10 ¹² /L, mean (SD))	4.77(0.49)
LEU (×10 ⁹ /L, mean (SD))	6.02(2.00)
HGB (g/L, mean (SD))	144.49(14.83)
PLT (×10 ⁹ /L, mean (SD))	199.56(53.94)
HRC (%)	10541(43.46)
Type 2 diabetes (%)	1621(6.70)
Hypertension (%)	5071(20.91)
Dyslipidemia (%)	9975(41.13)
MetS (%)	8309(34.33)

Abbreviations: SD, standard deviation; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol; ALT, alanine aminotransferase; AST, aspartate transaminase; γ-GGT, γ-glutamyltranspeptidase; Scr, serum creatinine; SUA, serum uric acid; BUN, blood urea nitrogen; RBC, red blood cell; LEU, leukocyte count; HGB, haemoglobin; PLT, platelet count; HRC, high remnant cholesterol; MetS, metabolic syndrome.

Table S2 Baseline characteristics of study variables in Cohort 1

	Total (N=19181)	NRC (N=11405)	HRC (N=7776)	<i>P-value</i> *
Age (year, mean (SD))	43.69(10.69)	43.56(10.81)	43.90(10.52)	0.032
Gender, male (%)	11500(59.96)	6164(54.05)	5336(68.62)	<0.001
Heart rate (bpm, mean (SD))	72.32(9.78)	73.22(8.94)	69.24(11.74)	<0.001
BMI (kg/m², mean (SD))	23.67(3.15)	23.18(3.11)	24.38(3.08)	<0.001
WC (cm, mean (SD))	82.24(10.06)	80.62(10.20)	84.30(9.48)	<0.001
SBP (mmHg, mean (SD))	115.18(11.04)	113.96(10.73)	116.98(11.24)	<0.001
DBP (mmHg, mean (SD))	73.60(8.05)	73.12(7.77)	74.31(8.39)	<0.001
FBG (mmol/L, mean (SD))	5.40(1.06)	5.30(0.90)	5.54(1.25)	<0.001
TC (mmol/L, mean (SD))	4.83(0.94)	4.51(0.81)	5.31(0.91)	<0.001
TG (mmol/L, mean (SD))	1.65(1.45)	1.20(0.57)	2.32(1.99)	<0.001
LDL-C (mmol/L, mean (SD))	2.68(0.72)	2.66(0.75)	2.71(0.67)	<0.001
RC (mmol/L, mean (SD))	0.77(0.56)	0.42(0.21)	1.28(0.53)	<0.001
ALT (IU/L, mean (SD))	26.37(21.36)	23.63(19.81)	30.40(22.86)	<0.001
AST (IU/L, mean (SD))	26.03(12.97)	23.94(10.54)	28.03(14.66)	<0.001
γ-GGT (IU/L, mean (SD))	32.94(36.90)	27.42(30.18)	39.97(42.99)	<0.001
Scr (μmol/L, mean (SD))	70.55(15.54)	68.51(15.32)	73.55(15.38)	<0.001
SUA (μmol/L, mean (SD))	335.46(88.69)	315.20(83.34)	354.86(89.33)	<0.001
BUN (mmol/L, mean (SD))	5.09(1.29)	5.01(1.28)	5.20(1.30)	<0.001
RBC (×10¹²/L, mean (SD))	4.74(0.49)	4.66(0.48)	4.84(0.48)	<0.001
LEU (×10⁹/L, mean (SD))	5.98(2.10)	5.85(1.51)	6.17(2.73)	<0.001
HGB (g/L, mean (SD))	143.42(14.89)	141.50(15.24)	146.32(13.85)	<0.001
PLT (×10⁹/L, mean (SD))	200.74(53.92)	204.31(53.77)	195.45(53.71)	<0.001
HRC (%)	7776(40.54)	0(0.00)	7776(100.00)	<0.001
Type 2 diabetes (%)	966(5.05)	476(4.18)	490(6.33)	<0.001
Hypertension (%)	0(0.00)	0(0.00)	0(0.00)	-
Dyslipidemia (%)	7218(37.63)	3310(29.02)	3908(50.26)	<0.001
MetS (%)	4616(24.11)	1986(17.45)	2630(33.89)	<0.001

Abbreviations: NRC, normal remnant cholesterol; HRC, high remnant cholesterol; SD, standard deviation; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol; ALT, alanine aminotransferase; AST, aspartate transaminase; γ-GGT, γ-glutamyltranspeptidase; Scr, serum creatinine; SUA, serum uric acid; BUN, blood urea nitrogen; RBC, red blood cell; LEU, leukocyte count; HGB, haemoglobin; PLT, platelet count; MetS, metabolic syndrome.

* *P-values* were calculated by student's t-test for normally distributed variables and the Wilcoxon rank-sum test for non-normal distributed variables, as well as the chi-square test or Fisher's exact test for categorical variables.

Table S3 Baseline characteristics of study variables in Cohort 2

	Total (N=13711)	Non-hypertension (N=11405)	Hypertension (N=2306)	<i>P-value</i> *
Age (year, mean (SD))	44.92(11.42)	43.56(10.81)	51.63(11.99)	<0.001
Gender, male (%)	7816(57.01)	6164(54.05)	1652(71.64)	<0.001
Heart rate (bpm, mean (SD))	73.45(9.14)	73.22(8.94)	74.56(10.01)	<0.001
BMI (kg/m ² , mean (SD))	23.55(3.22)	23.18(3.11)	25.35(3.18)	<0.001
WC (cm, mean (SD))	81.83(10.55)	80.62(10.20)	87.97(10.12)	<0.001
SBP (mmHg, mean (SD))	118.74(15.47)	113.96(10.73)	142.37(13.47)	<0.001
DBP (mmHg, mean (SD))	76.17(10.40)	73.12(7.77)	91.24(8.48)	<0.001
FBG (mmol/L, mean (SD))	5.37(0.99)	5.30(0.90)	5.71(1.31)	<0.001
TC (mmol/L, mean (SD))	4.54(0.82)	4.51(0.81)	4.71 (0.86)	<0.001
TG (mmol/L, mean (SD))	1.24(0.59)	1.20(0.57)	1.45(0.64)	<0.001
LDL-C (mmol/L, mean (SD))	2.70(0.77)	2.66(0.75)	2.90(0.80)	<0.001
RC (mmol/L, mean (SD))	0.42(0.21)	0.42(0.21)	0.44 (0.21)	<0.001
ALT (IU/L, mean (SD))	24.58(21.66)	23.63(19.81)	29.27 (28.66)	<0.001
AST (IU/L, mean (SD))	24.60(12.16)	23.94(10.54)	27.80(17.79)	<0.001
γ-GGT (IU/L, mean (SD))	29.23(32.17)	27.42(30.18)	37.87(39.20)	<0.001
Scr (μmol/L, mean (SD))	69.27(15.46)	68.51(15.32)	72.99(15.59)	<0.001
SUA (μmol/L, mean (SD))	321.90(85.06)	315.20(83.34)	354.75(85.78)	<0.001
BUN (mmol/L, mean (SD))	5.07(1.29)	5.01(1.28)	5.35(1.32)	<0.001
RBC (×10 ¹² /L, mean (SD))	4.69(0.48)	4.66(0.48)	4.83(0.47)	<0.001
LEU (×10 ⁹ /L, mean (SD))	5.88(1.52)	5.85(1.51)	6.06(1.55)	<0.001
HGB (g/L, mean (SD))	142.46(15.24)	141.50(15.24)	147.22(14.33)	<0.001
PLT (×10 ⁹ /L, mean (SD))	203.62(53.89)	204.31(53.77)	200.18(54.39)	0.001
HRC (%)	0(0.00)	0(0.00)	0(0.00)	-
Type 2 diabetes (%)	708(5.17)	476(4.18)	232(10.07)	<0.001
Hypertension (%)	2306(16.82)	0(0.00)	2306(100.00)	<0.001
Dyslipidemia (%)	4277(31.19)	3310(29.02)	967(41.93)	<0.001
MetS (%)	3431(25.08)	1986(17.45)	1445(62.94)	<0.001

Abbreviations: SD, standard deviation; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol; ALT, alanine aminotransferase; AST, aspartate transaminase; γ-GGT, γ-glutamyltranspeptidase; Scr, serum creatinine; SUA, serum uric acid; BUN, blood urea nitrogen; RBC, red blood cell; LEU, leukocyte count; HGB, haemoglobin; PLT, platelet count; HRC, high remnant cholesterol; MetS, metabolic syndrome.

* *P-values* were calculated by student's t-test for normally distributed variables and the Wilcoxon rank-sum test for non-normal distributed variables, as well as the chi-square test or Fisher's exact test for categorical variables.

Table S4 Baseline hypertension was associated with subsequent HRC in Cohort 2

	Non-hypertension	hypertension	
Incident cases of HRC, n (%)	4341(38.06)	1030(44.67)	
Incident rate (per 1000 person-years)	90.30	106.22	
Model	HR(95% CI)	HR(95% CI)	P-value
Crude	ref	1.20(1.12,1.29)	<0.001
Model 1*	ref	1.23(1.15,1.32)	<0.001
Model 2†	ref	1.25(1.17,1.35)	<0.001

Abbreviations: HRC, high remnant cholesterol; HR, hazard ratio; CI, confidence interval.

* In Model 1, the adjustment factors included age, sex and heart rate.

† In Model 2, the adjustment factors included age, sex, heart rate, body mass index, fasting blood glucose, alanine aminotransferase, leukocyte count, and serum creatinine.

Table S5 Cross-lagged standard regression coefficient of RC and blood pressure levels in the IV sensitivity analysis

Variables	$\beta_{RC\text{-blood pressure}}$(95% CI)	$\beta_{blood\ pressure\text{-RC}}$(95% CI)	<i>P-value</i> [*]	CFI
Hypertension	0.025(0.013,0.037)	0.007(-0.005,0.019)	<0.001	0.944
SBP	0.031(0.019,0.043)	0.011(-0.001,0.023)	<0.001	0.933
DBP	0.068(0.056,0.079)	0.024(0.012,0.036)	<0.001	0.935
MAP	0.055(0.044,0.067)	0.020(0.008,0.032)	<0.001	0.930

Abbreviations: RC, remnant cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; CI, confidence interval; CFI, comparative fit index.

* Test the difference of the cross-lagged path coefficients between $\beta_{RC\text{-blood pressure}}$ and $\beta_{blood\ pressure\text{-RC}}$ by the t-test.

The adjustment factors included age, sex, heart rate, body mass index, fasting blood glucose, alanine aminotransferase, leukocyte count, serum creatinine, waist circumference, coronary heart diseases, stroke, and fatty liver disease.

Figure S1

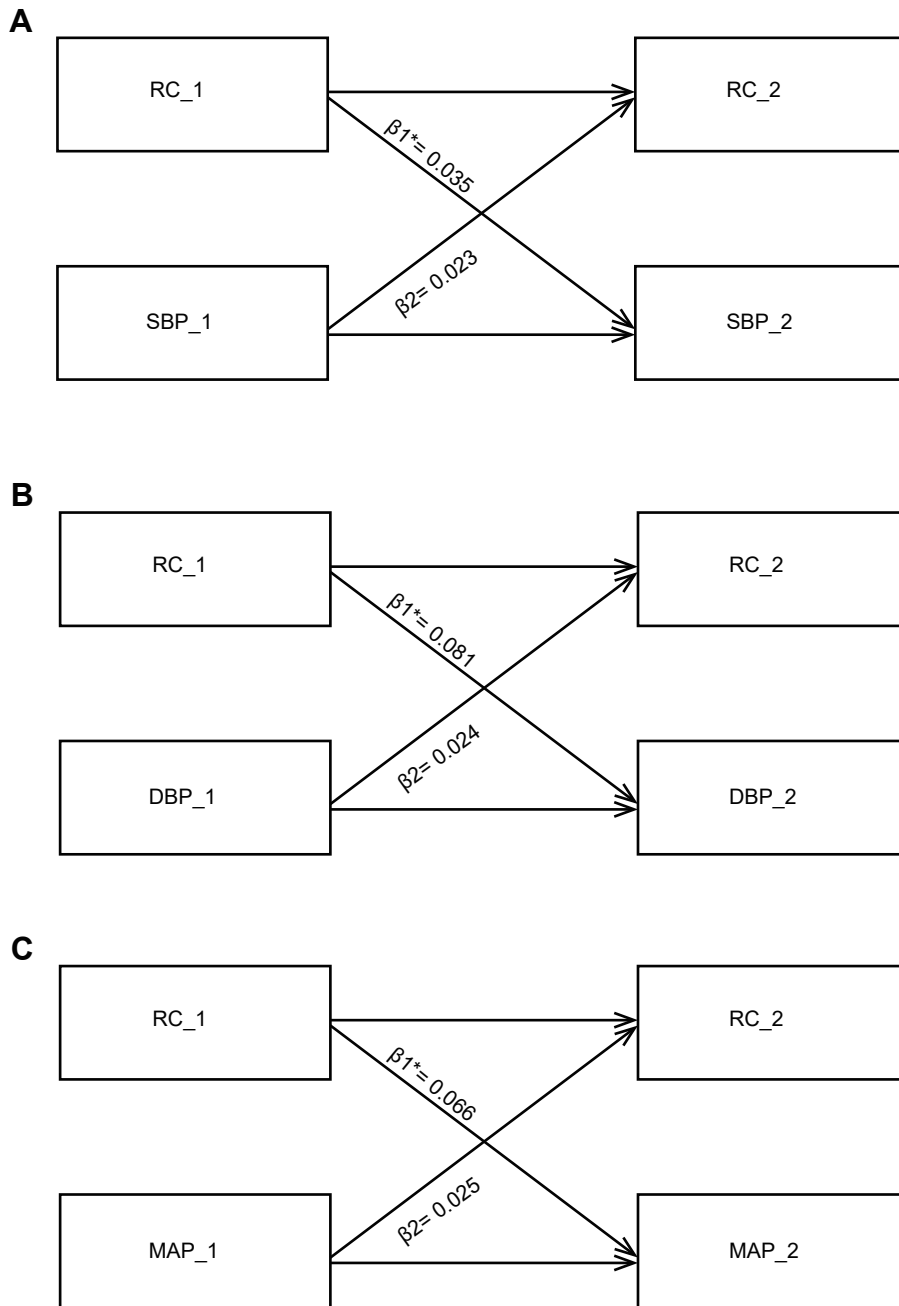


Figure S1 Cross-lagged standard regression coefficient of RC and blood pressure levels in the sensitivity analysis I. A, SBP; B, DBP; C, MAP The cross-lagged model was adjusted for age, sex, heart rate, body mass index, fasting blood glucose, alanine aminotransferase, leukocyte count, and serum creatinine. Abbreviations: RC, remnant cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure. * indicates $P < 0.001$ when comparing β_1 vs. β_2 .