Supplementary Table 1. Epidemiological evidence

Study highlight	Author	Year of publication	Study population	Number of participants M/F	Median/Mean follow-up	Type of remnant lipoprotein measured	Fasting vs Nonfasting	RLP measurement	End point	risk association HR, OR (95% CI)
Atherogenicity of RLP	Phillips N R et al.[51]	1993	Montreal Heart Institute	Total: 335 M:272 W: 63	5 years	remnant VLDL	Fasting	Analytical Ultracentrifugation	CAD progression	1.021(1.01-1.03) per 1 mg/dl difference
RLP as a predictor Coronary Events in Patients With CAD	Kugiyama K et al.[153]	1999	Kumamoto University Institution	Total:147 M:97 F:50	26.8 months	RLP	Fasting	Immunoseparation	Coronary events	6.38 (2.3-17.6) for highest tertile compared to lowest tertile
RLP independent CVD risk factor in women	McNamara J R et al.[52]	2001	Framingham heart study-women	W: 1567	N/A	RLP-C and RLP-TG	Fasting	Immunoseparation	CVD prevalence	2.27(1.37-3.77) for RLP-C>75th percentile
RLP-C as a risk of CAD in patients with CAD and type 2 diabetes	Fukushima et al.[154]	2004	Kumamoto University Institution	Total:240 Total with CAD:120 M:151 F:89	20.5 months	RLP-C	Fasting	immunoseparation	coronary events	2.2 (1.2-6.4) For high RLP-C levels
RLP-C predict CHD incidence	C. Imke et al.[53]	2005	The Honolulu Heart Study	Total:1156	17 years	RLP-C, RLP-TG	Fasting	immunoseparation	CHD events	RLP-C and RLP-TG levels on CHD relative risk (P=0.0022, P=0.0045, respectively)
CVD risk prediction associated with lipoprotein profiles	Mora et al.[155]	2009	Women's Health Study	Total:27 673	11 years	VLDL	Nonfasting	nuclear magnetic resonance spectroscopy	CAD events	1.71(1.38-2.12) for the highest quintile of total VLDL compared to the lowest quintile
Genetically elevated RLP-C as causal risk factors	Jorgensen et al.[54]	2013	Copenhagen City Heart Study (CCHS),	CGPS: 36,853 CCHS: 36,853 CIHDS: 2804	Varies between cohorts.	RLP-C	Nonfasting	Calculated	MI events	1.87 (1.25-2.81) for genotype

for myocardial infarction			Copenhagen General population study (CGPS), Copenhagen Ischaemic Heart Disease Study (CIHDS)		(1976-2003)					combination 10 vs. 1
RLP-C as a causal risk factor for IHD	Varbo et al. [55]	2013	CCHS, CGPS, CIHDS	CGPS:47,351 CCHS:10,609 CIHDS:10,609	Varies between studies. Data collected (1976-2010)	RLP-C	Nonfasting	Calculated	IHD events	The causal OR for a 1 mmol/l (39 mg/dl) genetic increase of RLP-C 2.8 (1.9-4.2), observational HR of 1.4 (1.3-1.5).
RLP-C associated with low-grade inflammation and with IHD	Varbo et al. [56]	2013	CCHS, CGPS, CIHDS	CGPS: 48,250 CCHS: 7417 CIHDS: 4941	Varies between studies. (1976-2010)	RLP-C	Nonfasting	Calculated	IHD events	causal OR for IHD for a 1-mmol/L (39-mg/dL) 3.3 (2.1-5.2)
RLP-C as a mediator From obesity to IHD.	Varbo et al. [57]	2014	CCHS, CGPS, CIHDS	CGPS: 69 535 CCHS: 10,099 CIHDS: 5050	Varies between studies. (1976-2013)	RLP-C	Nonfasting	Calculated	IHD events	observational HR of 1.10 (1.08–1.11) genetically derived risk ratios of 1.20 (1.07–1.34) as an intermediate variable of a 10 kg/m2 higher BMI
Extreme RLP-C vs Extreme LDL-C as Contributors to CVD and All-Cause Mortality	Varbo et al. [58]	2015	CCHS, CGPS	CGPS: 88,404 CCHS: 9558	Varies between studies. (1977-2013)	RLP-C	Nonfasting	Calculated	IHD, MI, and all-cause mortality	2.4 (1.9-2.9) for Extreme RLP-C ≥1.5 mmol/L (58 mg/dL).
RLP-C and Incident CHD	Joshi et al. [59]	2016	Jackson Heart Study,	Total:4932 M:1858	8 years	RLP-C	Fasting	vertical auto profile method	CHD events	1.23 (1.06-1.42)

			Framingham offspring study	F:3074				RLP-C (VLDL3-C+IDL-C)		per 1-SD increase of RLP-C 1.26 (1.08-1.47) per 1-SD increase of IDL-C
Atherogenic Lipoprotein and CVD	Lawler P et al.[156]	2017	Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER)	Total: 11,984 M: 7624 F: 4360	2 years	VLDL particles	Nonfasting	nuclear magnetic resonance (NMR) spectroscopy	CVD events	Total VLDL 1.21 (1.04-1.41) per 1 SD increase
RLP-C and MI stratified by weight	Varbo et al. [157]	2018	CGPS	Total:106216 W: 58,472 M: 47,744	6 years	RLP-C	Nonfasting	Calculated	MI	2.31 (1.4-3.5) for Obese participants
Lipids profile and PAD	Aday A et al. [158]	2018	Women's Health Study	Total: 27,888	15.1 years	VLDL particles	Nonfasting	NMR spectroscopy for VLDL	PAD	medium VLDL 1.98 (1.15 to 3.41)] for extreme tertile
RLP-C and the risk of MI and stroke	Holmes M et al. [159]	2018	Chinese Kadoorie Biobank Nested Case-Control Study	Total:4662	N/A	RLP-C (VLDL-C + IDL-C	Nonfasting	(NMR) spectroscopy for VLDL	MI, IS	MI 1.27 (1.15-1.39) per SD increase IS 1.20 (1.09 - 1.32) per SD increase
RLP-C and incident CVD	Saeed A et al. [60]	2018	Atherosclerosis Risk in Communities Study (ARIC)	Total: 9334 M:3807 W:5527	CVD, CHD 15.6 IS 15.8	RLP-C	Fasting	Homogeneous assay	CHD, CVD, IS	CHD: 1.06(0.88-1.27) CVD 1.05(0.89-1.23) IS 1.07(0.78-1.45) For the highest quartile

										compared to lowest quartile
TRL-C and Risk of CVD in Patients Receiving Statin	Vallejo-Vaz et al. [160]	2018	Treating to New Targets	Total: 9993 M: 8092 W: 1901	4.9 years	TRL-C	Fasting	Calculated	MACE	1.48 (1.15–1.92) for the highest quartile compared to lowest quartile
RLP-C and Ischaemic stroke	Varbo et al. [161]	2019	CGPS, CCHS	CGPS:102,964 CCHS: 9,548	CGPS:8.7 years CCHS:19.3 years	RLP-C	Nonfasting	Calculated Homogeneous assay (TRL-C)	IS	1.99 (1.49-2.67) for RLP-C ≥1.5 mmol/l
VLDL-C Associated with MI and other apoB containing lipoproteins	Balling M et al.[162]	2020	CGPS	Total: 25,480 W: 13,504 M: 11,976	11 years	(VLDL, IDL) Cholesterol, TG	Nonfasting	NMR spectroscopy for VLDL, IDL	MI	Per 1-mmol/l higher levels, VLDL-C: 2.07 (1.81-2.36) VLDL-TG: 1.19 (1.14-1.25) IDL-C: 5.38 (3.73-7.75)
The association of RLP-C with cardiovascular outcomes in patients with diabetes and pre-diabetes	Cao et al. [66]	2020	Multicentre study in China	Total: 4331 M:3078 F:1253	5.1 years	RLP-C	Fasting	Homogenous assay	MACE	DM: 2.05 (1.28-3.29 Pre-DM: 1.98- (1.19-3.29) For high RLP-C levels
TRL-C and incident CVD	Duran EK et al. [163]	2020	Women's Health Study	Total:976	15.7 years	TRL-C	Nonfasting	Homogenous assay	Total CVD	MI: 3.05 (1.46 to 6.39) PAD: 2.58 (1.18-5.63) For the highest quartile

										compared to the lowest quartile
RLP-C predicts CVD beyond LDL and ApoB	Quispe R et al. [164]	2021	Multiethnic Study of Atherosclerosis (MESA) Coronary Artery Risk Development in Young Adults (CARDIA) ARIC	Total:17532 MESA:3049 ARIC:9748 CARDIA:4735	18.7 years	RLP-C	Fasting	Calculated	ASCVD	1.65 (1.45-1.89) for log RLP-C
IDL-C as a Predictor for Coronary Heart Disease	Yoshida H et al. [64]	2021	Tobu Medical Centre, Japan	Total:476	N/A	IDL	Fasting	anion exchange high-performance liquid chromatography	CHD prediction	1 SD increase in IDL-C was an independent predictor for 10-year CHD risk >10% of F-score 1.53 (1.26-1.85)
Association between RLP-C, hsCRP, and risk of ASCVD events (MESA)	Chevli et al. [62]	2022	MESA	Total: 6,720 W: 3548 M: 3172	15.6 years	RLP-C	Fasting/nonfasting	NMR spectroscopy	Incident ASCVD	1.20 (1.04-1.39) For RLP-C > Median (value >29.14 mg/dL)
RLP-C and the Risk of Coronary Artery Calcium Progression	Hao et al. [165]	2022	CARDIA and MESA	Total: 6544 CARDIA: 2635 MESA: 3909	8.6 years	RLP-C	Fasting	Calculated	Coronary Artery Calcium Progression	1.013 (1.008-1.017) per 1-mg/dL increase in RLP-C level
RLP-C and the risk of CVD in T2D	Huh et al. [63]	2022	Korean National Health Insurance Service database	Total: 1,956,452 M: 1,159,932 W: 1,159,932	8.1 years	RLP-C	Fasting	Calculated	MI, IS	MI: 1.28 (1.249-1.314) IS: 1.22 (1.195-1.247) For the highest RLP-C quartile
Elevated RLP-C increases the risk	Wadstrom et al. [61]	2022	CGPS, CCHS	CGPS:106,937 CCHS:13,974	CGPS: 9 years	RLP-C	Nonfasting	Calculated	**PAD, MI, IS**	CGPS

of peripheral artery disease, myocardial infarction, and ischaemic stroke.					CCHS: 24 years					-PAD 4.8 (3.1-7.5) -MI 4.2 (2.9-6.1) -IS 1.8 (1.4-2.5). CCHS -PAD 4.9 (2.9-8.5) -MI 2.6 (1.8-3.8) -IS 2.1 (1.5-3.1) for RLP-C levels ≥ 58 mg/dL vs. < 19 mg/dL.
RLP-C associated with cardiovascular mortality	Zhang et al. [166]	2022	National Health and Nutrition Examination Survey (NHANES)	Total:19650 M:9568 F:10,082	93 months	RLP-C	Fasting/nonfasting	Calculated	Cardiovascular mortality	2.82 (1.17-6.81) for log RLP-C

Abbreviations

RLP-C: remnant lipoprotein cholesterol, TRL-C: triglyceride-rich lipoprotein, TG: triglyceride, IDL: intermediate-density lipoprotein, LDL-C: low-density lipoprotein, VLDL: very low-density lipoprotein cholesterol, CAD: coronary artery disease, M: men, W: women, CVD: cardiovascular disease, CHD: coronary heart disease, MI: myocardial infarction, IHD: ischaemic heart disease. SD: standard deviation, IS: ischaemic stroke, PAD: peripheral artery disease, MACE: major adverse cardiac events, ASCVD: atherosclerotic cardiovascular disease, HR: hazard ratio, OR: odd ratio. CI: confidence interval.