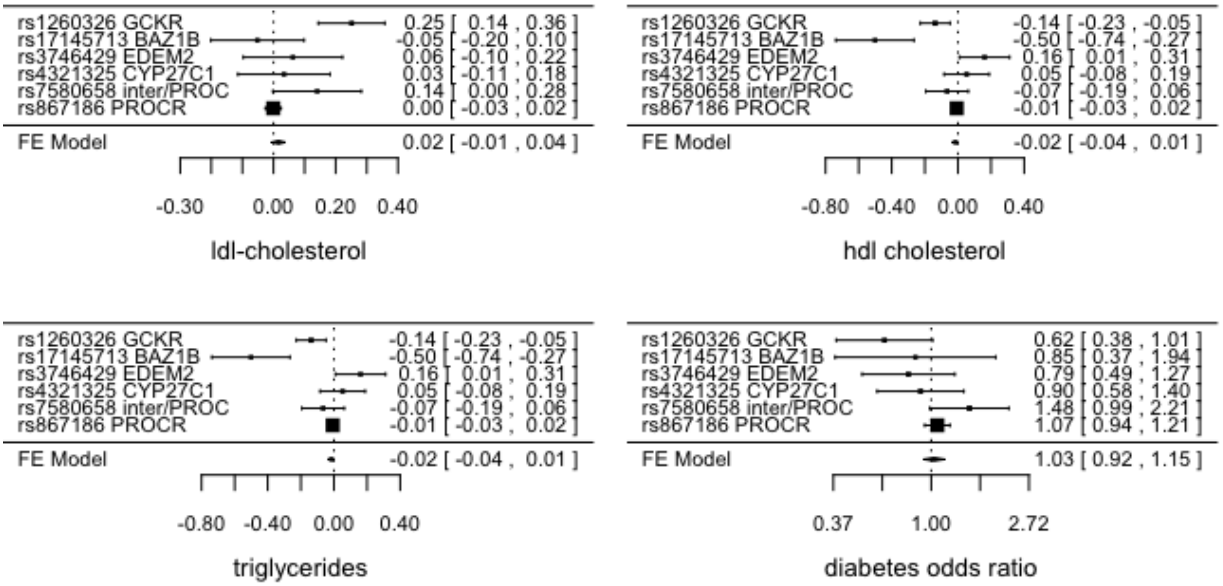
Supplementary Material to Schooling, Zhong: "Plasma levels of the anti-coagulation protein C and the risk of ischaemic heart disease. A Mendelian randomisation study" (Thromb Haemost 2017; 117.2)

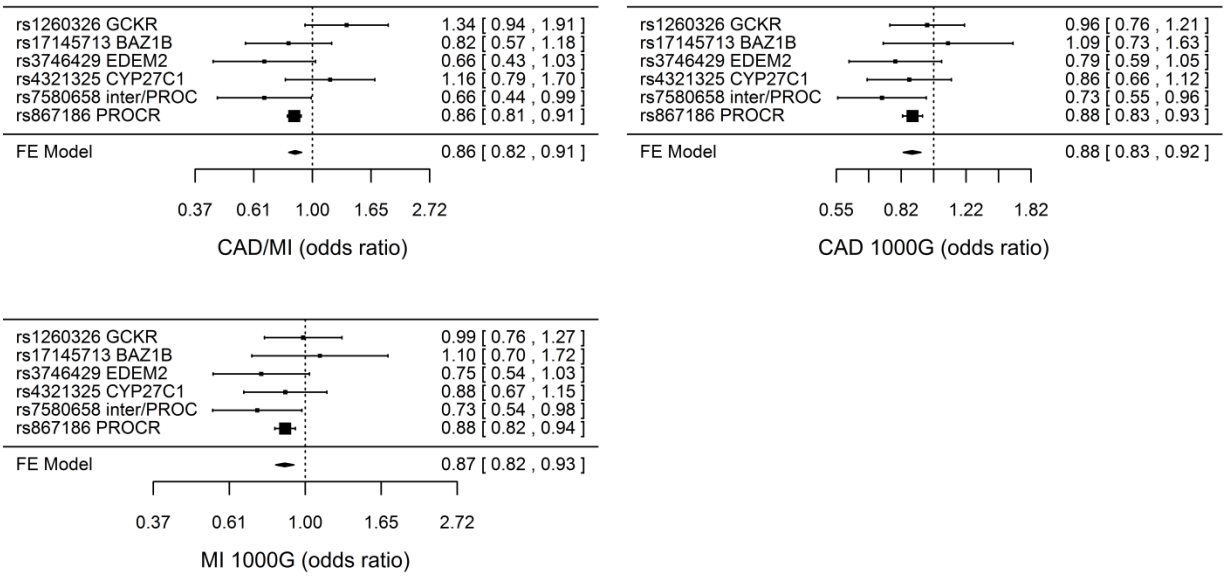
Suppl. Table 1: Associations per µg/mL protein C with CAD/MI, CAD, MI, diabetes, lipids, blood pressure, glycemic traits, adiposity, cognition and major depressive disorder, obtained from separate sample instrumental variable analysis using 3 and 6 genetic determinants of protein C [20, 34–36] applied to CARDIoGRAMplusC4D [23, 24], CARDIoGRAMplusC4D 1000 Genomes [25], DIAGRAM [27], the Global Lipids Genetics Consortium Results [26] GIANT [28, 29], SSGAC [30] and PGC [31] using a weighted median estimator

		3 SNPs (rs867186, rs3746429, rs7580658)		6 SNPs (rs867186, rs3746429, rs7580658, rs1260326, rs4321325, rs17145713)	
		OR	95 % CI	OR	95 % CI
Cardiovascular disease	CAD/MI	**0.85**	**0.80 to 0.90**	**0.86**	**0.82 to 0.91**
	CAD 1000G	**0.87**	**0.82 to 0.92**	**0.88**	**0.83 to 0.93**
	MI 1000G	**0.86**	**0.81 to 0.92**	**0.88**	**0.82 to 0.93**
Diabetes		1.08	0.95 to 1.21	1.05	0.93 to 1.17
		β	95 % CI	β	95 % CI
Lipids	LDL-cholesterol (effect size)	-0.01	-0.03 to 0.02	0.01	-0.02 to 0.03
	HDL-cholesterol (effect size)	-0.01	-0.03 to 0.02	-0.01	-0.04 to 0.01
	Triglycerides (effect size)	0.01	-0.02 to 0.03	0.01	-0.02 to 0.03
Adiposity	BMI men (effect size)	**0.03**	**0.001 to 0.06**	0.03	-0.01 to 0.06
	BMI women (effect size)	-0.03	-0.06 to 0.001	-0.03	-0.06 to 0.001
	WHR men (effect size)	-0.01	-0.04 to 0.02	-0.01	-0.04 to 0.02
	WHR women (effect size)	0.03	-0.01 to 0.05	0.03	0.01 to 0.06
Other	Cognition z-score	0.01	-0.01 to 0.03	0.01	-0.01 to 0.03
		OR	95 % CI	OR	95 % CI
	Major depressive disorder(OR)	0.99	0.87 to 1.14	0.97	0.85 to 1.10

Suppl. Figure 1: SNP specific and total associations per µg/mL of protein C with a) low-density lipoprotein (LDL) cholesterol (inverse normal transformed effect size), b) high-density lipoprotein (HDL) cholesterol (inverse normal transformed effect size), c) triglycerides (inverse normal transformed effect size) and d) diabetes, obtained from separate sample instrumental variable analysis using 6 genetic determinants of protein C [20, 34–36] applied to the Global Lipids Genetics Consortium Results [26] and DIAGRAM [27]



Suppl. Figure 2: Associations per µg/mL protein C by SNP and overall with a) CAD/MI, b) CAD and c) MI, obtained from separate sample instrumental variable analysis using 6 genetic determinants of protein C [20, 34–36] applied to CARDIoGRAMplusC4D [23, 24], and CARDIoGRAMplusC4D 1000 Genomes [25]



Suppl. Figure 3: Associations per µg/mL protein C by SNP and overall with a) body mass index (BMI) in men (inverse normal standard transformed), b) BMI in women (inverse normal standard transformed c) waist-hip ratio (WHR) in men (inverse normal standard transformed, d) WHR in women (inverse normal standard transformed, e) cognition (z-score) and f) major depressive disorder, obtained from separate sample instrumental variable analysis using 6 genetic determinants of protein C [20, 34–36] applied to GIANT [28, 29], SSGAC [30] and PGC [31].