

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Clarke R, Peden JF, Hopewell JC, et al. Genetic variants associated with Lp(a) lipoprotein level and coronary disease. *N Engl J Med* 2009;361:2518-28.

Supplementary Methods

PROCARDIS case definition

The PROCARDIS “genetically-enriched” case collection is composed of sibships (proband and at least one affected sibling) with coronary disease. Ascertainment criteria for PROCARDIS probands were myocardial infarction (MI) or symptomatic acute coronary syndrome (SACS) before the age of 66 years. Diagnosis of MI required documentation of two or more of: (a) typical ischaemic chest pain, pulmonary oedema, syncope or shock; (b) development of pathological Q-waves and/or appearance or disappearance of localized ST elevation followed by T-wave inversion in two or more standard electrocardiograph leads; (c) increase in concentration of serum enzymes consistent with MI (e.g. creatine kinase more than twice the upper limit of normal). Diagnosis of SACS required documentation on hospitalization for one of the following indications: (a) unstable angina diagnosed by typical ischemic chest pain at rest associated with reversible ST depression in two or more standard electrocardiograph leads; (b) thrombolysis for suspected MI (as indicated by localized ST elevation in two or more standard electrocardiograph leads) even without later development of T-wave inversion, Q-waves or a significant enzyme rise; (c) emergency revascularization following presentation with typical ischaemic chest pain at rest. Each proband also had a sibling with coronary disease (MI, SACS, coronary revascularization or angina) before age 66 years.

PROCARDIS control collection

For each of the coronary disease cases included in the “genetically-enriched” case-control study, it was planned to recruit one control of the same sex, ethnicity and within 5 years of age of cases, with no personal or sibling history of coronary disease

before age 66 years. In the UK, controls were identified by mailing a self-administered questionnaire to spouses or siblings of spouses or male friends of any individuals who had previously returned a completed questionnaire to the PROCARDIS study. Eligible respondents were asked to attend their general practice to have their blood pressure, height and weight recorded, and to provide a blood sample. In Sweden, Italy and Germany, controls were selected from population registers and invited to attend a special clinic to have their blood pressure, height and weight recorded, to provide a blood sample and to complete a self-administered questionnaire. The questionnaire sought information on demography, medical history and lifestyle. Self-reported medical history collected information on history of MI, coronary artery bypass surgery, coronary angioplasty, stroke, hypertension and diabetes mellitus. Prevalence of diabetes mellitus was supplemented if participants reported use of medication specifically indicated for the treatment of diabetes, irrespective of the information provided in the questionnaire. Current smokers were defined as individuals reporting any cigarette smoking activity within a year of completion of the questionnaire; ex-smokers were defined as individuals reporting quitting smoking at least one year prior to completion of the questionnaire; never smokers were defined as individuals who had no evidence of any smoking. Comparable definitions were also used to classify smoking habits 10 years prior to completing the questionnaire.

PROCARDIS “trio family” collection

For the “trio family” study design, index cases (cases with coronary disease consistent with the PROCARDIS proband definition) completed a questionnaire to establish the availability of their parents and siblings. Both parents whenever

possible, or one parent and at least one sibling (affected or unaffected), were then invited to participate, along with any further affected siblings.

ISIS cases and control collection

Cases in the International Study of Infarct Survival (ISIS) study had early onset myocardial infarction, but were not selected on the basis of family history. They were men or women aged 30-64 with non-fatal myocardial infarction confirmed by cardiac enzymes or electrocardiographic criteria (or both). The ISIS controls were spouses of the siblings or children of the cases (i.e. unrelated to cases except by marriage), and with no history of myocardial infarction, angina, or other heart disease.

SHEEP case and control collection

The Stockholm Heart Epidemiology Programme (SHEEP) study, a population-based case control study of MI (first events only), recruited cases and gender- and age-matched controls aged 45 to 70 living in Stockholm County during a 3-year period (2 years for men and 3 years for women to increase the number of female patients). All coronary care units in the greater Stockholm area participated in the recruitment of patients, and randomly selected control subjects were enrolled from the same catchment areas.

SCARF cases and control collection

The Stockholm Coronary Artery Risk Factor (SCARF) study enrolled all survivors of a first MI event before the age of 60 years admitted to three CCUs in the greater Stockholm area during a 5-year period. Gender- and age-matched healthy

individuals from the general population were recruited as controls. Thus, SCARF targeted subjects with premature MI, but family history was not an inclusion criterion.

DNA extraction and Beadchip genotyping

DNA was extracted from buffy coats as has been previously described^{S1,S2}.

Genotyping was carried out using automated laboratory systems at the Centre Nationale de Genotypage (CNG) in Evry, France without knowledge of case-control status. Genotypes were automatically called with the BeadStudio genotyping module (Illumina Inc.).

The following HumanCVD BeadChip SNPs in *LPA* were excluded from analysis due to low call-rates (<95%) or minimum allele frequency (≤ 0.0015): rs7449940, rs9457933, rs6922557, rs9347412, rs1801693, rs9457943, rs6922216, rs7755463, rs12182517, rs6921912, rs6455697, rs1800769 and rs1853021. The 27 *LPA* SNPs that passed quality control map within, or immediately upstream or downstream of, *LPA* on chromosome 6 (160,860,000 -161,012,000 bp) (see Supplementary Figure 1). Out of a total of 78 HapMap SNPs in this region with MAF > 1% in the CEU samples, these 27 SNPs tagged 69 SNPs at $r^2 > 0.8$ and 75 SNPs at $r^2 > 0.5$ (CEU - HapMap phase 2 release 22, April 2007).

Statistical analysis

Identity-by-state (IBS) analysis and other genotyping QC checks were performed using software and scripts written by SCH. Statistical genetic analyses were carried out using custom scripts and functions for the Stata™ software (version 10.0). An

exact Hardy-Weinberg equilibrium test was performed in Stata™ using the *genhw* program^{S3}. The 3145 CAD cases in PROCARDIS were drawn from 2128 sib-ships and the 3352 controls from 2971 sib-ships, and robust sandwich estimators of variance were used to allow for this familial clustering^{S4}. Country of origin was included as a categorical main-effect to model differences in SNP allele frequencies across different populations. Additive and non-additive effects were modelled by defining continuous variables with levels 0, 1 and 2 or 0, 1 and 0, respectively, corresponding to genotypes AA, AB and BB^{S5}. Additive logistic regression models were used to estimate the log odds ratio of CAD associated with alleles for each SNP (which is equivalent to an allelic-dosage model). Inclusion of non-additive effects was used to model genotype associations^{S5}. Odds ratios (OR) for the *LPA* genotype score in PROCARDIS are presented as “floating absolute risks” with 95% confidence intervals (CI) where indicated^{S6}. Meta-analysis was carried out using standard fixed-effects (inverse-variance-weighting) methods and heterogeneity tests^{S7}. Family-based association tests were performed with the TRANSMIT software^{S8}; estimates of odds ratios and their standard errors were calculated for combination with case-control results^{S9}.

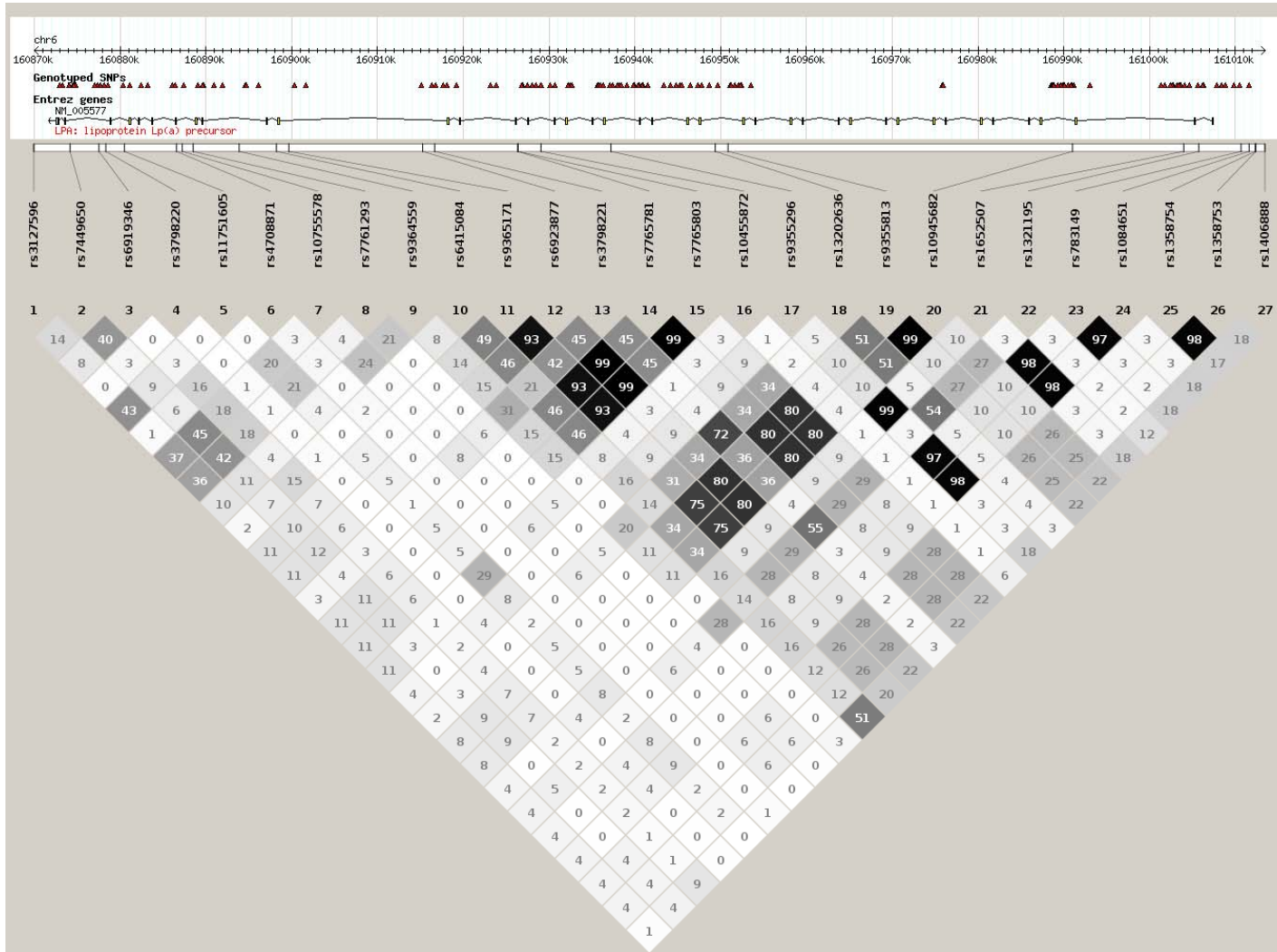
Linkage disequilibrium analysis

A systematic scan using the GLIDERS application (author Dr. R. Lawrence: <http://mather.well.ox.ac.uk/GLIDERS/>) in the HapMap phase 2 build 36 database failed to detect any *cis*-chromosome SNPs in strong linkage disequilibrium ($r^2 \geq 0.8$) with rs10455872. The best proxy SNP in Illumina GWAS SNP arrays is rs11751605 ($r^2 = 0.55$); the best proxy SNP in Affymetrix GWAS SNP arrays is rs3120139 ($r^2 = 0.34$).

The rs7770628 SNP at the *LPA* locus, which has also been reported to be associated with quantitative variation in Lp(a) concentrations^{S10}, was not measured directly by the HumanCVD beadchip used in this study. However, it was tagged ($r^2 = 0.68$) by the measured rs1406888 SNP, which was associated ($p=0.00002$) with Lp(a) concentration (Table 1) but not with coronary disease risk (Figure 1).

A haplotype-based GWAS scan by Tregouet et al.^{S11} identified two coronary disease associated haplotypes (CTTG and CCTC) defined by 4 SNPs (rs2048327, rs3127599, rs7767084 and rs10755578) that overlie the *LPA* locus and neighbouring genes on chromosome 6q. An analysis of the HapMap (www.HapMap.org) data shows that the CTTG haplotype (population frequency = 15%; OR with coronary disease = 1.2)^{S11} partially tags ($r^2 = 0.52$) the rs10455872 risk allele (population frequency = 7%; OR ~ 1.5 in our study); conceivably all of this haplotype's effect could be explained by imperfect linkage disequilibrium with rs10455872. SNP rs3798220 (population frequency = 2%; OR ~ 1.8 in our study) is uninformative in the European ancestry HapMap data which precludes an attempt to link this SNP with the CCTC haplotype (population frequency = 2%; OR ~ 1.8)^{S11}. However, suitable genotype data are available from the Wellcome Trust Case Control Consortium (www.wtccc.org.uk) in which UK control samples have been genotyped with the Illumina 1M (which includes rs3798220) and Affymetrix 6.0 (which includes the 4 Tregouet SNPs) arrays. A haplotype analysis of these data shows that the CCTC haplotype is strongly correlated ($r^2 = 0.86$) with rs3798220 indicating consistency of the two coronary disease association studies.

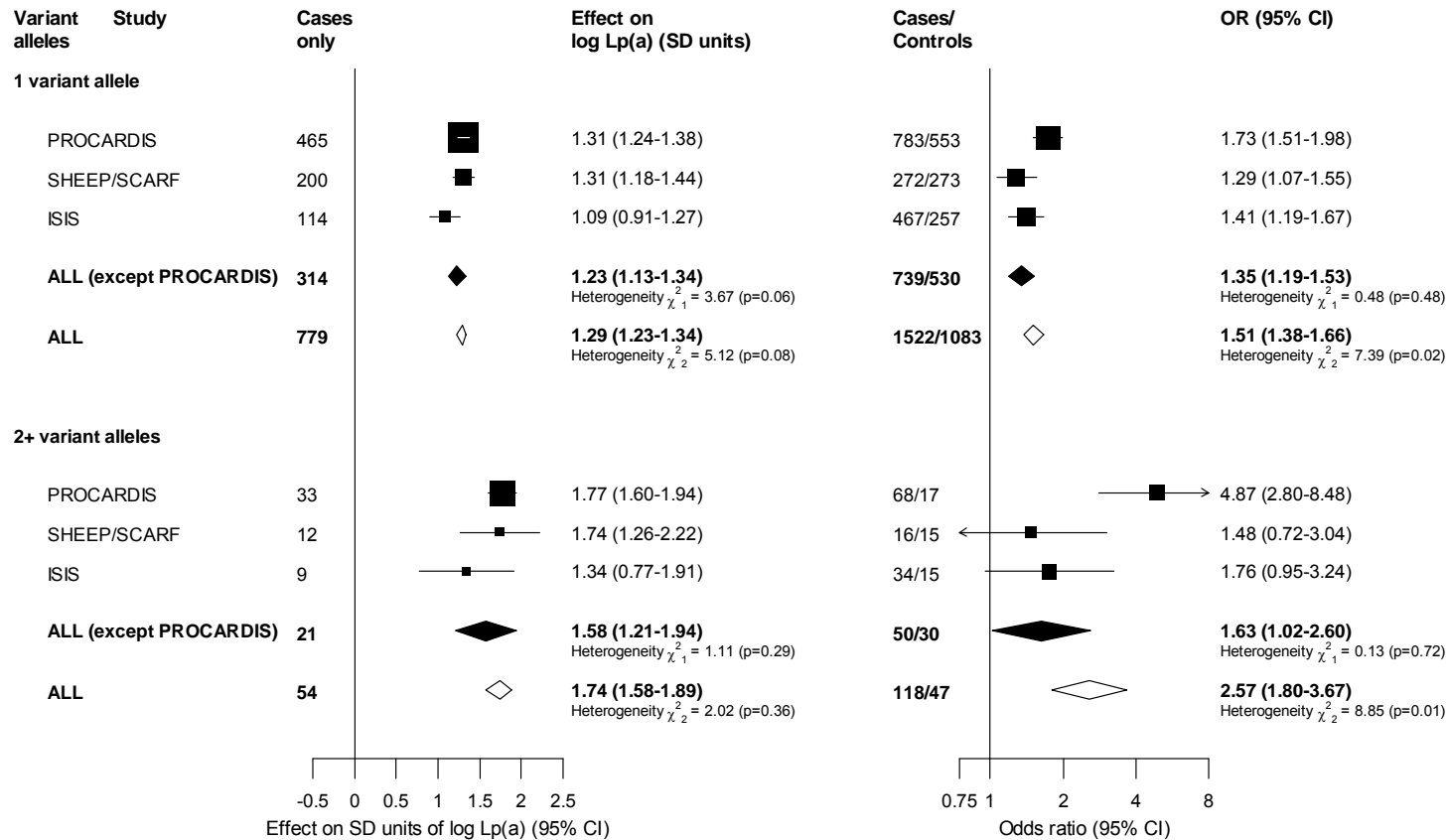
Supplementary Figure 1: Linkage disequilibrium analysis of 27 SNPs in *LPA*.



Legend to Supplementary Figure 1

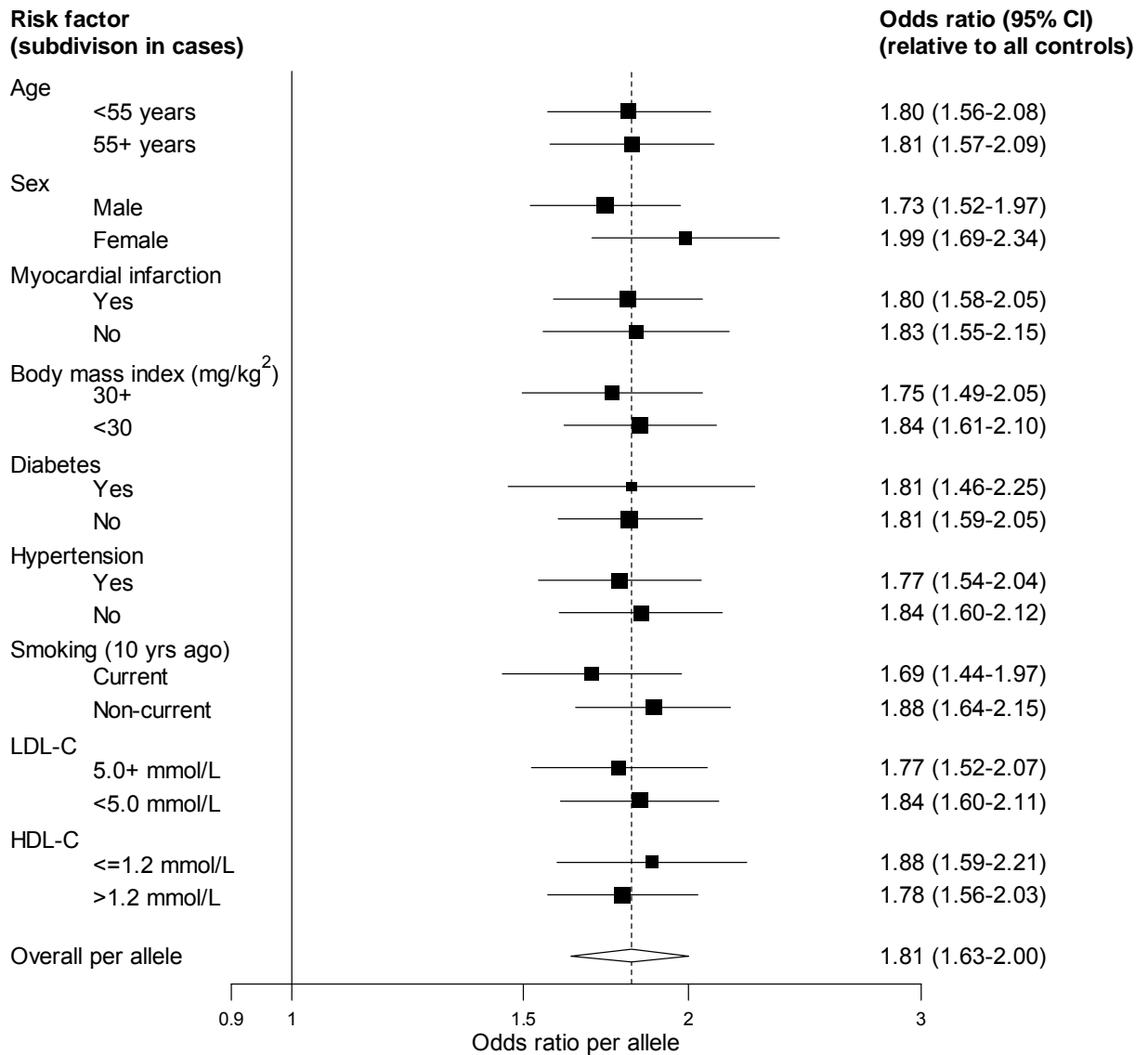
Linkage disequilibrium (LD) analysis of 27 SNPs in the apolipoprotein(a) gene (*LPA*) was performed using genotype data for 3352 PROCARDIS controls with the Haploview v4.1 program. The r^2 values ($\times 100$) are shown for each pair of SNPs in variably shaded boxes (shading in proportion to the strength of LD). The physical location of the SNPs is shown (NCBI build 36) on chromosome 6 along with a schematic of the *LPA* intron-exon structure. The genotyped SNPs track indicates SNPs present in the HapMap database.

Supplementary Figure 2: Replication of the association of the *LPA* genotype score with Lp(a) concentrations and with coronary disease risk in independent populations



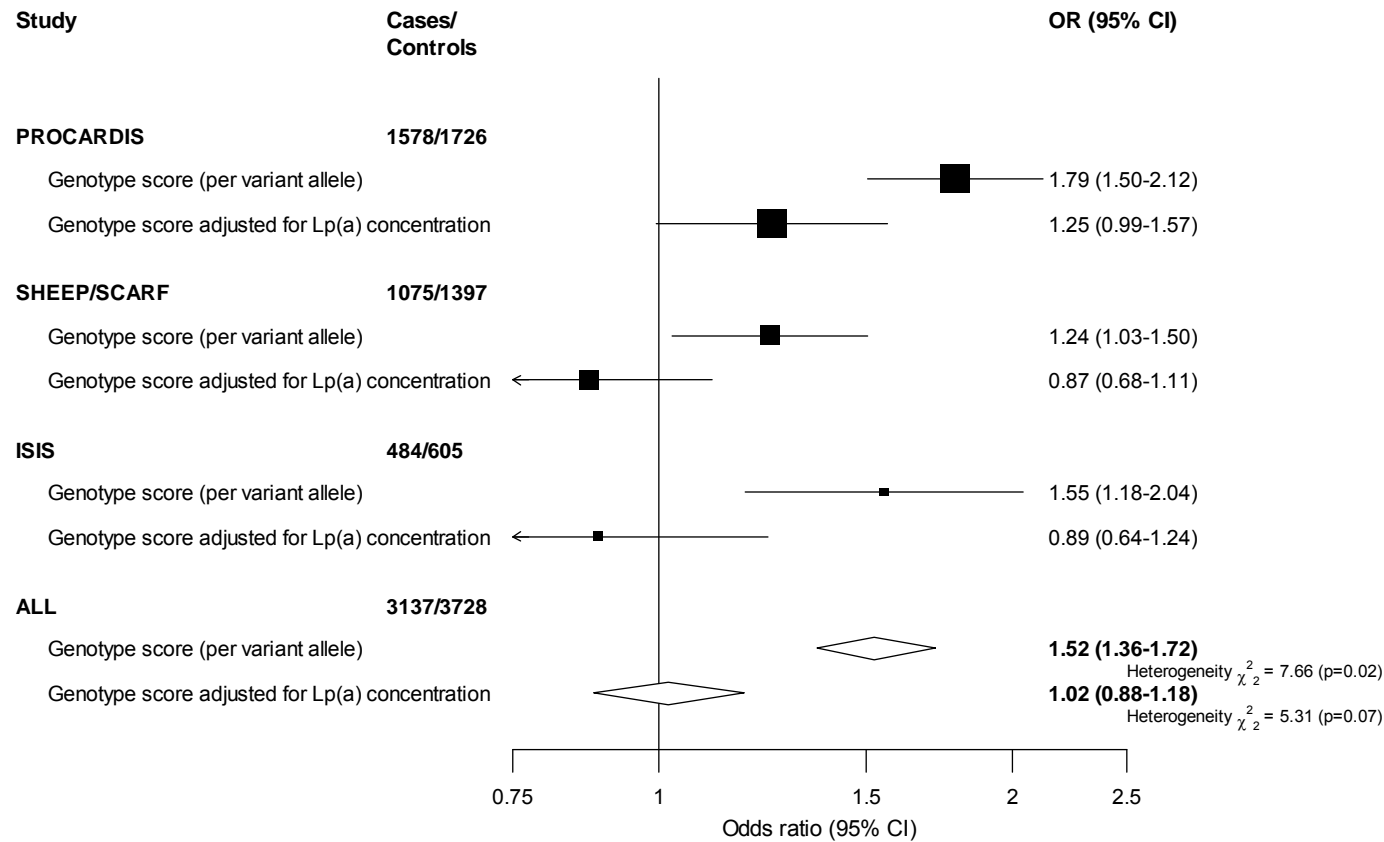
The values shown are the regression coefficients for Lp(a) in standard deviation (SD) units of log Lp(a) and odds ratios (OR) for coronary disease and 95% confidence intervals for *LPA* genotype score. The combined odds ratios and 95%CI are indicated by the diamonds.

Supplementary Figure 3: Association of the *LPA* genotype score with coronary disease risk in PROCARDIS sub-groups by levels of established risk factors.



The values shown are the odds ratios and 95% confidence intervals (CI) for *LPA* genotype score adjusted for country of origin.

Supplementary Figure 4: Association of *LPA* genotype score with coronary disease risk, before and after adjustment for Lp(a) concentrations.



The values shown are the odds ratios (OR) and 95% CI for coronary disease per variant allele for *LPA* genotype score after adjustment for age and sex. The combined odds ratios and 95%CI are indicated by the diamonds.

Supplementary Table 1: Association of 33 SNPs on the Human CVD chip with coronary disease risk in PROCARDIS

Locus	rsid	Odds ratio (95% CI)	Risk allele (frequency)	p-value
6q26-27	rs10455872	1.70 (1.49 - 1.95)	G (0.07)	3E-15
	rs3798220	1.92 (1.48 - 2.49)	C (0.02)	9E-07
9p21	rs10757272	1.32 (1.20 - 1.41)	T (0.48)	2E-11
	rs7859727	1.30 (1.20 - 1.41)	T (0.48)	4E-11
	rs2891168	1.30 (1.20 - 1.41)	G (0.48)	6E-11
	rs10757274	1.30 (1.20 - 1.41)	G (0.48)	7E-11
	rs4977574	1.30 (1.20 - 1.41)	G (0.48)	8E-11
	rs1333042	1.30 (1.19 - 1.39)	G (0.5)	1E-10
	rs1333048	1.30 (1.19 - 1.39)	C (0.49)	2E-10
	rs1537375	1.28 (1.19 - 1.39)	C (0.50)	3E-10
	rs10511701	1.28 (1.19 - 1.39)	C (0.50)	3E-10
	rs9632885	1.28 (1.19 - 1.39)	A (0.47)	3E-10
	rs9632884	1.28 (1.19 - 1.39)	C (0.48)	4E-10
	rs10757278	1.28 (1.19 - 1.39)	G (0.48)	6E-10
	rs2383206	1.28 (1.19 - 1.39)	G (0.51)	7E-10
	rs1333049	1.28 (1.19 - 1.39)	C (0.47)	8E-10
	rs10116277	1.28 (1.18 - 1.39)	T (0.48)	8E-10
	rs10757269	1.28 (1.18 - 1.39)	G (0.48)	8E-10
	rs944797	1.28 (1.18 - 1.39)	C (0.51)	8E-10
	rs6475606	1.28 (1.18 - 1.39)	T (0.48)	8E-10
	rs1537370	1.28 (1.18 - 1.39)	T (0.48)	9E-10
	rs10965224	1.27 (1.18 - 1.37)	A (0.59)	2E-09
	rs4977756	1.27 (1.18 - 1.37)	A (0.59)	3E-09
	rs1333040	1.23 (1.15 - 1.33)	T (0.58)	1E-07
	rs1537372	1.22 (1.13 - 1.32)	T (0.43)	4E-07
	rs1412832	1.25 (1.14 - 1.35)	T (0.69)	5E-07
	rs2157719	1.22 (1.12 - 1.32)	T (0.57)	1E-06
	1p13	rs4970834	1.33 (1.20 - 1.49)	C (0.81)
rs602633		1.32 (1.19 - 1.45)	G (0.79)	9E-08
rs646776		1.30 (1.18 - 1.43)	T (0.78)	2E-07
rs12740374		1.30 (1.18 - 1.43)	G (0.78)	2E-07
rs583104		1.28 (1.18 - 1.43)	T (0.78)	3E-07
rs7528419		1.30 (1.18 - 1.43)	A (0.78)	3E-07

Supplementary Table 2: Effect of individual SNPs on plasma concentrations of Lp(a) in PROCARDIS and the replication cohorts

		Effects of individual SNPs on Lp(a) concentrations Geometric mean of Lp(a) * (no. studied)			
Cohort (no studied)	rs3798220	rs10455872			All
		AA	AG	GG	
PROCARDIS	TT	17.26 (1324)	61.96 (363)	100.33 (28)	23.28 (1715)
	CT	76.06 (102)	104.78 (4)	(0)	76.98 (106)
	CC	148.64 (1)	(0)	(0)	148.64 (1)
	All	19.22 (1427)	62.31 (367)	100.33 (28)	
ISIS (Cases)	TT	50.11 (361)	149.19 (84)	166.25 (7)	62.52 (452)
	CT	145.09 (30)	270.53 (2)	(0)	150.86 (32)
	CC	(0)	(0)	(0)	(0)
	All	54.36 (391)	151.27 (86)	166.25 (7)	
ISIS (Controls)	TT	36.53 (499)	122.36 (85)	160.99 (5)	44.05 (589)
	CT	113.46 (16)	(0)	(0)	113.46 (16)
	CC	(0)	(0)	(0)	(0)
	All	37.84 (515)	122.36 (85)	160.99 (5)	
SHEEP/SCARF (Cases)	TT	4.73 (863)	16.67 (157)	27.48 (6)	5.79 (1026)
	CT	21.02 (43)	26.97 (6)	(0)	21.67 (49)
	CC	(0)	(0)	(0)	(0)
	All	5.07 (906)	16.97 (163)	27.48 (6)	
SHEEP/SCARF (Controls)	TT	4.32 (1171)	15.77 (173)	26.87 (6)	5.15 (1350)
	CT	12.58 (41)	20.21 (4)	(0)	13.12 (45)
	CC	7.13 (1)	10.33 (1)	(0)	8.59 (2)
	All	4.49 (1213)	15.82 (178)	26.87 (6)	

*Geometric mean of Lp(a) calculated as the exponential of mean log Lp(a) in study-specific SD units

Supplementary Table 3: Mean (SE) concentrations of blood lipids and biomarkers of inflammation by LPA genotypes in PROCARDIS statin-free controls

<i>LPA</i> Genotypes	Frequency	Apo B (mg/dL)	Apo A ₁ (mg/dL)	LDL-C (mmol/L)	HDL-C (mmol/L)	CRP (mg/L)	Fibrinogen (mg/L)
rs3798220							
TT	2992	103.4 (0.49)	173.9 (0.59)	3.33 (0.02)	1.43 (0.01)	2.60 (0.10)	3.89 (0.02)
CT	96	106.4 (2.38)	172.0 (3.09)	3.46 (0.09)	1.44 (0.05)	1.99 (0.27)	3.96 (0.09)
CC	0	-	-	-	-	-	-
P-value for heterogeneity		0.270	0.585	0.200	0.958	0.291	0.530
rs10455872							
AA	2663	103.3 (0.52)	173.5 (0.62)	3.32 (0.02)	1.43 (0.01)	2.63 (0.11)	3.89 (0.02)
AG	415	104.7 (1.26)	175.1 (1.59)	3.37 (0.05)	1.47 (0.02)	2.29 (0.22)	3.89 (0.05)
GG	11	107.2 (7.47)	205.3 (13.3)	3.53 (0.27)	1.85 (0.20)	2.31 (1.10)	4.04 (0.23)
P-value for heterogeneity		0.512	0.003	0.534	0.003	0.502	0.893
LPA genotype score							
0	2570	103.2 (0.54)	173.6 (0.64)	3.32 (0.02)	1.43 (0.01)	2.65 (0.12)	3.89 (0.02)
1	503	104.9 (1.13)	174.1 (1.43)	3.37 (0.04)	1.46 (0.02)	2.25 (0.19)	3.91 (0.04)
2	15	109.8 (6.47)	202.8 (9.83)	3.70 (0.27)	1.83 (0.14)	2.05 (0.82)	3.98 (0.19)
P-value for heterogeneity		0.274	0.002	0.184	0.002	0.305	0.909

All laboratory measures are based on available data

Supplementary References

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Supplementary Appendix: Collaborators and participating centres

Collaborators and participating hospitals in the PROCARDIS study in the UK

Collaborators: *Aberdeen Royal:* J Webster, J Jamieson; *Addenbrooke's:* M Brown, S Blackwood; *Barnsley District General:* W Rhoden, C Simpson; *Bedford:* I Cooper, E Pickerell; *Birmingham Heartlands:* S Bain, A Jones, C Jewkes; *Bishop Auckland General:* M Bateson, P Gill; *Bristol Royal:* D Stansbie, G Andrews, M Halestrap; *Burnley General:* R Best, D Appleyard; *Castleford & Normanton:* C White, M Khalifa, J Woolford; *City General, Stoke-on-Trent:* J Creamer, C Butler, M Washington; *Coventry and Warwickshire:* R Mattu, L Gill, E Walton; *Cumberland:* H Robson, A Graham; *Derbyshire Royal:* A Scott, H Waterhouse, T Gibson, L Henshaw; *Derriford:* A Marshall, J Went, A Inman, J Simmonds; *Dewsbury:* T Kemp, G Roberts; *Ealing:* J Kooner, S Cahill; *Edinburgh Royal:* C Swainson, R Lindley, L Hillis, J Johnston, A Kenny; *Frenchay, Bristol:* M Papouchado, R Carpenter; *Glasgow Royal:* S Cobbe, C Campbell, J Hunter, H Young; *Gloucestershire Royal:* D Lindsay, A Halliday; *Guy's & St Thomas':* J Chambers, A Jones; *Hairmyres, Glasgow:* K Oldroyd, G Moreland, H Young, *HM Stanley, St Asaph:* J Green, N Jones; *Sutton-in-Ashfield:* R Lloyd-Mostyn, M Brown; *Leighton, Crewe:* S Mallya, M Nash, J Spruce; *Macclesfield:* E Davies, B Price, A Robinson; *Manor, Walsall:* A Cunnington, P Giles, J Sidaway; *Memorial, Darlington:* J Murphy, G Brennan; *Monklands, Airdrie:* C Rodger, J Hunter, A McNeilly; *Musgrove Park, Taunton:* T MacConnell, L Williams; *New Cross, Wolverhampton:* P Rylance, A Hodgson, L Robinson; *Ninewells, Dundee:* B Green, T Pringle, E Saunders; *North Manchester General:* J Swan, D Appleyard; *North Tyneside General:* R Curless, A Scott; *Northampton General:* J O'Donnell, S Dixon, E Tanqueray; *Oxford Radcliffe Hospitals:* H Watkins, J Armitage, S Beebe, J Fitzgerald, J Godden, A Lawson, H Lochhead, J Godden, H Lochead, A Taylor; *Pilgrim Hospital, Boston:* C Nyman, J Adams; *Poole General:* A McLeod, L Haimes; *Princess Royal, Telford:* N Capps, A Cook, D Donaldson; *Queen Margaret, Dunfermline:* D MacLeod, R Stuart; *Queen's Hospital, Burton-upon-Trent:* T Reynolds, J Maiden; *Raigmore, Inverness:* R MacFadyen, A Smith; *Rotherham General:* R Muthusamy, M Jones, S Dixon; *Royal Bolton:* A Hutchinson, K Morris; *Royal Bournemouth:* M Armitage, C Cope; *Royal Devon and Exeter:* K MacLeod, S Havill; *Royal Gwent:* J Davies, A Norris, M Williams; *Royal Sussex County:* R Vincent, E Joyce; *Royal United, Bath:* J Reckless, R Carpenter; *Russell Institute, Paisley:* I Findlay, C Campbell, J Hunter; *Russells Hall:* M Labib, J Sidaway; *St Helier:* J Barron, B Bradford, M McDonnell; *St Peter's, Chertsey:* M Baxter, R Chambers; *Sandwell General:* L Hughes, J Elson-Whittaker, C Verow, *Scunthorpe General:* J Dhawan, A Catchpole; *Singleton, Swansea:* P Thomas, R Thomas; *Southlands:* M Signy, E Joyce, J Sydenham; *Stepping Hill, Stockport:* P Lewis, J O'Toole; *Victoria Hospital, Blackpool:* D Roberts, C Davies, J Fitton; *Walton Centre:* P Humphrey, S Saminaden, D Watling; *Watford General:* M Clements, E Walker; *Western General, Edinburgh:* R Lindley, T Shaw, C Swainson; *Worcester Royal:* A Munro, J Cadwell; *Wycombe General:* S Price, M Aldersley.

Coordinating Centre for recruitment in the UK (Clinical Trial Service Unit, University of Oxford)

R Clarke, J Hopewell, S Parish, P Linksted, J Notman, H Gonzalez, A Young, T Ostley, A Munday, N Goodwin, V Verdon, S Shah, L Cobb, C Edwards, C Mathews,

R Gunter, J Benham, C Davies, M Cobb, L Cobb, J Crowther, A Richards, M Silver, S Tochlin, S Mozley, S Clark, M Radley, K Kourellias.

Collaborators and participating centres in the PROCARDIS study in Germany

1. Leibniz-Institut für Arteriosklerosforschung, Domagkstr. 3, 48149 Münster, Germany (Seedorf U., Schulte H., Epping H., Rust S., Assmann G.)
2. Institut für Klinische Chemie und Laboratoriumsmedizin – Zentrallabor, Universität Münster, Albert-Schweitzer-Str. 33, 48149 Münster, Germany (Assmann G., Fobker M.)
3. Klinik Königsfeld der Landesversicherungsanstalt Westfalen, Holthäuser Str. 2, 58256 Ennepetal, Germany (Karoff M.)
4. Klinikum Meiningen, Bergstr. 3, 98617 Meiningen, Germany (Köhler, E.)

Collaborators and participating centres in the PROCARDIS study in Sweden

All Swedish cases and controls were examined in the Clinical Cardiovascular Research Unit of the Department of Cardiology at the Karolinska University Hospital Solna. Cases were initially admitted to the hospitals in the greater Stockholm area with a coronary care unit.

Coordinating Centre for recruitment in Sweden (Atherosclerosis Research Unit, Department of Medicine Solna, Karolinska Institutet)

Anette Aly, Karolina Anner, Karin Björklund, Gun Blomgren, Barbro Cederschiöld, Karin Danell-Toverud, Per Eriksson, Ulla Grundstedt, Anders Hamsten, Merja Heinonen, Mai-Lis Hellénus, Ferdinand van't Hooft, Karin Husman, Jacob Lagercrantz, Anita Larsson, Magnus Mossfeldt, Angela Silveira, Birgitta Söderholm.

Collaborators and participating centres in the PROCARDIS study in Italy

GISSI – Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto, endorsed by ANMCO (Associazione Nazionale Medici Cardiologi Ospedalieri) and Istituto di Ricerche Farmacologiche Mario Negri (IRFMN)
 AVIS – Associazione Volontari Italiani Sanguine

Centre	City/Town	Investigator
IRFMN	Milano	G.Tognoni, M.G.Franzosi, S.Barlera, L.Crociati, E.Nicolis, S.Pietri, C.Specchia
Centro Diagnostico Italiano	Milano (MI)	L.Dionisio/ R.Colombo
Ospedale F. Lastaria	Lucera (FG)	M.Di Giovine/ C. Postiglione/ A.Villella
Ospedale Civile	S.Bonifacio (VR)	R. Rossi/ E.Carbonieri/ D.Bicego
Ospedale Gen.le Prov.le sC.G. Mazzoni	Ascoli Piceno (AP)	L. Capponi/ L. Moretti/ L. Falleroni
Cardio Centro Ticino	Lugano (Svizzera)	B.M. Colombo/T. Moccetti/ A.Anesini
Ospedale San Gerardo	Monza (MI)	V.E. Minolfi/ M.L. Carati
Ospedale Santa Croce	Castelnuovo in Garfagnana (LU)	M. Cabib/ D. Bernardi
Centro Diagnostico	Roma (RM)	M. Bambino/ M. Torella
Ospedale Misericordia e Dolce	Prato (PO)	D. Lami/R.P. Dabizzi
Ospedale Civile San Giuseppe	Albano Laziale (RM)	A. Felici/ G. Ruggeri
Ospedali Riuniti	Pistoia (PT)	E. Balli/ F. Del Citerna
Ospedale Santo Spirito	Roma (RM)	G. Greco/ V. Ceci
Ospedale San Leonardo	Castellammare di Stabia (NA)	R. Longobardi/ C. Esposito
Casa di Cura Eremo	Arco di Trento (TN)	G. Ferrario/ O. Alkhimovitch
Poliambulatorio Ex INAM	Barletta (BA)	G. Sarcina/ M. Palmieri
Ospedale V. Cervello	Palermo (PA)	A. Ledda/ A. Canonico
Ospedale E. Morelli	Sondalo (SO)	M. Maffi/ G.Campagnoli
Ospedale San Donato	Arezzo (AR)	S. Baldassarre/ M. Poggini
Ospedale Civile	Sondrio (SO)	G. Cucchi/ S.Giustiniani
Ospedale G.Giglio	Cefalù (PA)	G. Geraci/ F.Clemenza
Ospedale San Vincenzo	Taormina (ME)	R. Evola/ N. Russo
Ospedale Civile G. Tatarella	Cerignola (FG)	F. Di Biase
Ospedale Generale di Zona "Fatebenefratelli"	Erba (CO)	D. Agnelli
Ospedale Molinette- San Giovanni Battista	Torino (TO)	S. Bergerone
Ospedale Civile	Piombino(LI)	S. Bechi
Presidio Ospedaliero Villa Sofia	Palermo (PA)	V. Cirrincione
Fondazione S.Maugeri	Pavia (PA)	M. De Salvo
Ospedali Civili Riuniti	Venezia (VE)	A. Martino
Ospedale Sant'Anna	Como (CO)	R. Jemoli
Ospedale Civile	Ragusa (RG)	G. Iabichella
Ospedale S. Giovanni	Roma (RM)	N. Pagnoni
Ospedale Civile	Rho (MI)	A. Frisinghelli
Presidio Ospedaliero	Vasto (CH)	G. Levantesi