Supplementary Methods

Participating studies

GENIUS-CHD consortium

The following member cohort of GENIUS-CHD were included for the meta-analysis in the present analyses:

Study/Cohort Name	Study Institution	Country	Reference(s)
CDCS – Coronary Disease Cohort Study	University of Otago, Chirstchurch	New Zealand	[1]
Corogene	University of Helsinki	Finland	[2]
CURE – Genetics study	PHRI, McMaster University	Canada	[3,4]
CTMM	UMC Utrecht	The Netherlands	
DECODE	deCODE genetics	Iceland	[5]
Emory Cardiovascular Biobank	Emory University	USA	[6]
GENEBANK	Cleveland Clinic	USA	[7-9]
INVEST Genes	University of Florida	USA	[10]
LIFE-Heart	Heart Centre University of Leipzig	Germany	[11]
LURIC	Heidelberg University	Germany	[12]
MDCS – Malmo Diet Cancer Study	Lund University	Sweden	[13]
Christchurch Post-Myocardial Infarction (PMI) study	Christchurch	New Zealand	[1]
OHGS	University of Ottawa	Canada	[14]
PLATO	Uppsala	Sweden	[15]
GENESIS PRAXY	McGill University Health Center, Quebec	Canada	[16]
PROSPER	Leiden University Medical Center	The Netherlands	[17]
RISCA	McGill University	Canada	[18]
STABILITY	Uppsala Clinical Research Centre	Sweden	[19]
Krakow Cohort	Jagiellonian University, Medical College	Poland	
TexGen	Baylor College of Medicine, Houston	USA	[20,21]
TRIUMPH	Washington University and MAHI	USA	[22]
VHS – Verona Heart Study	University of Verona	Italy	[23-25]
VIVIT	Vorarlberg Institute of Vascular Investigation and Treatment, VIVIT	Austria	[26]
WTCCC CAD	University of Leicester	United Kingdom	[27]

The Homburg Cream and Sugar (HCS) Study

The study design and the methods of the Homburg Cream and Sugar (HCS) study (NCT00628524) have been described elsewhere[28]. In summary, 514 patients with clinically stable CAD documented by angiography were enrolled in this prospective, observational study from February 2008 to July 2009. Blood samples were drawn at the time of coronary angiography. The study was approved by the ethics committee of the Saarland (170/07). All participants gave written informed consent.

Standardized telephone interviews were performed 12, 24, and 48 months after enrollment to obtain follow up data. Median follow-up was 4·0 years. No patients were lost to follow-up. The composite cardiovascular end-point was defined as cardiovascular death and hospitalization for ACS or unplanned, symptom-induced coronary angiography and revascularization including bypass surgery.

The KAROLA study

The KAROLA-study is an observational prospective cohort study, which recruited 1206 participants in two rehabilitation clinics in Germany. As described previously, in Germany, patients who experienced an ACS or who underwent elective coronary artery bypass grafting (CABG) are offered a three week in-hospital rehabilitation program[29,30]. All patients who were admitted within this program in 2 collaborating rehabilitation clinics (Schwabenland-Klinik, Isny, and Klinik im Suedpark, Bad Nauheim, Germany) and were aged between 30-70 years meeting the ICD-9 codes 410-414 (CAD) were invited to participate in the study (initial response rate 58%). We included patients who started their rehabilitation program within the first 3 months after having experienced their first ACS or CABG. Blood was drawn at discharge from the rehabilitation center on average 43 days after the acute event (inter quartile range 36 days and 51 days, respectively) in a fasting state. Written informed consent was obtained from all participants. The study was approved by the ethics committees of the Universities of Ulm and Heidelberg, and by the ethics boards of the chambers of physicians of the Federal States of Hessen and Baden-Wuerttemberg, Germany.

Standardized questionnaires were sent to the participants and their primary care physicians during follow-up at 1, 3, 4·5, 6, 8, 10, and 13 years after discharge from the rehabilitation clinic. For patients deceased during follow-up, death certificates were retrieved from local health authorities. 1045 participants with available blood samples were included in the present analysis. Median follow-up was 9·9 years and n=1,045 of the initially n=1,204 recruited patients could be included in the present analyses. Composite cardiovascular end-point was defined as CVD as the main cause of death and non-fatal stroke or MI as obtained from the primary care physicians.

The Western Norway B Vitamin Interventional Trail (WENBIT)

The combined WENBIT/WECAC cohort includes 4164 patients who underwent coronary angiography due to suspected stable angina pectoris at two Norwegian university hospitals in the period 1999-2004. Approximately 2/3 of the patients were enrolled into WENBIT, a double-blinded, placebo-controlled, 2-center trial with patients randomly assigned to four groups receiving folic acid plus vitamin B12 and vitamin B6, folic acid plus vitamin B12, vitamin B6 or placebo[31]. For the current analysis, median follow-up time was 10·3 years, with no patient lost to follow-up. The blood samples in the WENBIT/WECAC were drawn either 1-2 days before (most patients) or immediately after the

coronary angiography procedure. All participants provided written informed consent. The Regional Committee for Medical and Health Research Ethics, the Norwegian Medicines Agency, and the Data Inspectorate approved WENBIT/WECAC. The Clinical Trials.gov identifier was NCT00354081.

The PROspective Study of Pravastatin in the Elderly at Risk (PROSPER)

The PROSPER enrolled 5804 participants between the ages of 70 and 82 years, with either preexisting vascular disease (coronary, cerebral, or peripheral) or an increased risk for vascular disease due to the presence of smoking, hypertension, or diabetes. Participants were recruited in Scotland, Ireland, and the Netherlands, and subsequently randomized to either placebo or 40 mg of pravastatin. The study was approved by the institutional ethics review boards of each center, and all participants gave written informed consent. The study design has been described in detail elsewhere[17]. 1,860 participants of PROSPER with myocardial infarction, CABG, PTCA or angina at baseline were included. Lp(a) was measured at baseline. Median follow-up time was 3·2 years, with no patients lost to follow-up. Cardiovascular mortality was defined as definite or suspect coronary heart disease death, as well as fatal stroke.

ATHEROGENE study

Between 1996 and 2004 all patients presenting with chest pain, dyspnea and pathologic imaging studies, or ECG alterations suggestive for ischemia, undergoing coronary angiography at the Department of Cardiology at the University Medical Center of the Johannes Gutenberg-University in Mainz, Germany, and the Department of Internal Medicine of the Federal Armed Forces Central Hospital in Koblenz, Germany, were screened for the AtheroGene study cohort as described previously[32]. Blood was drawn in the cath lab under standardized conditions directly before coronary angiography. All patients with at least one stenosis of ≥30% angiographic lumen reduction in one main native coronary artery were included. Exclusion criteria were coronary revascularisation within the previous four weeks, severe valvular heart disease, surgery or trauma within the previous month, use of oral anticoagulation in the previous four weeks, known malignancies, febrile conditions, and severe renal dysfunction with a serum creatinine concentration >2.5 mg/dL. Furthermore, all patients with venous thromboembolism, sepsis or cardio-pulmonary-reanimation during the previous 12 weeks were excluded. Each participant gave written informed consent. The study protocol was approved by the ethic committee of Rhineland-Palatinate, Germany, and the local ethic review board of the Johannes Gutenberg-University Mainz.

Lp(a) concentrations were successfully measured in fresh blood samples of 2,993 consecutive patients collected at fasting state. Of these, all patients with available variables for adjustment of the Cox models (age, sex, diabetes, hypertension, BMI, smoking status, eGFR, LDL, lipid-lowering medication) were included, resulting in 2,614 patients for the present analysis.

Follow-up data were assessed by medical technicians via postal questionnaires or telephone interviews. Endpoint events were validated by three cardiologists based on written medical reports obtained from general practitioners or from hospital records.

Laboratory methods and procedures

For laboratory analyses in LURIC, fasting blood samples were obtained immediately upon admission and before angiography. Enzymatic reagents from WAKO (Neuss, Germany) on an Olympus AU640 analyser were used to measure cholesterol and triglycerides; apolipoproteins B was measured by turbidimetry with reagents from Greiner (Flacht, Germany). Lipoproteins were separated with a combined ultracentrifugation-precipitation method (β-quantification). Removal of very low-density lipoprotein (VLDL) was performed by ultracentrifugation at d = 1·063 kg/l, LDL were precipitated from the infranate with phosphotungstic acid/$MgCl_2$, high density lipoprotein (HDL) cholesterol was measured in the supernate. LDL cholesterol was calculated as the difference between cholesterol in the d = 1·063 kg/l infranate (LDL plus HDL) and the supernatant of the phosphotungstic acid/$MgCl_2$ precipitation (HDL). Serum creatinine was determined by liquid chromatography tandem mass spectrometry (LC-MS/MS). Cystatin C concentrations were assessed using a nephelometric assay (N LATEX Cystatin C) on a Behring nephelometer II (Dade Behring GmbH, Marburg, Germany). ´High sensitivity´ C-reactive protein (hsCRP) was measured by immunonephelometry on a Behring nephelometer II (N High Sensitivity CRP, Dade Behring, Marburg, Germany).

CAD was assessed by investigating the maximal luminal narrowing by visual analysis during coronary angiography. Clinically relevant CAD was defined as the presence of one or more stenoses of ≥20 % in one or more of 15 coronary segments. The Friesinger score was used to determine the severity of CAD [33]. To build the Friesinger sore, lesion sizes are quantified in three regions (left anterior descending artery [LAD], left circumflex artery [LCX] and right coronary artery [RCA] of the coronary circulation. The lesions sizes in these three regions are graded from 0 to 5 (0 – no disease; 1 – lesions < 50 % lumen area stenosis; 2 – single lesion >50 % but < 90 %; 3 – multiple lesions >50 % but <90 %; 4 – 90 % lesion area; 5 – 100 %). The Friesinger score is then calculated as the sum of most severe lesion grade for each of three regions. The maximum Friesinger score is 15. ACS was defined as unstable angina within seven days before coronary angiography, non-ST segment elevation MI or ST segment elevation MI. Diabetes mellitus was defined as a fasting plasma glucose >1·25 g/L or >2·00 g/L after oral administration of a glucose dose. Furthermore a glycated hemoglobin ≥6·5 % or the use of oral antidiabetics, or insulin was also a definition for diabetes mellitus. High-performance liquid chromatography (Diamat, Chromsystem Instruments & Chemicals GmbH, Martinsried, Germany) was used to determine glycated hemoglobin. Arterial hypertension was diagnosed if the mean diastolic and systolic blood pressure out of six measurements, performed by an automated oscillometric device (Omron MX4, Omron Health Care GmbH, Hamburg, Germany), exceeded 140 and/or 90 mmHg.
Lp(a) was determined using a photometric assay with an anti-human Lp(a) antibody (LPA Test, Rolf Greiner Biochemica, Flacht, Germany), as described previously [34].

In KAROLA, at the time of discharge from the rehabilitation center, blood was drawn following a standardized protocol (e.g. fasting state). Consecutively, these samples were stored at -80°C and served for biomarker measurements later on. hsCRP and cystatin C were measured as previously reported [29]. All markers were measured in a blinded fashion. Creatinine and blood lipids were obtained from the routine blood drawings at the two cooperating rehabilitation centers.

Lp(a) plasma levels in LURIC and HCS were measured by the same assay (LPA Test, Rolf Greiner Biochimica, Flacht, Germany) as described in the methods section. Lp(a) in KAROLA was measured with another Lp(a) assay (Lp(a)-LATEX "SEIKEN", Denka Seiken Co., LTD, Tokyo Japan). Both assays show a strong correlation with the Northwest Lipid Research Laboratory NWRL a-40 ELISA as reference (r=0·997 for the Rolf Greiner assay and r=0·999 for the Denka Seiken assay, respectively) according to the suppliers. Therefore, both methods highly correlate with each other. The inter-assay coefficient of variation for the Rolf Greiner assay is 1·01 % and 1·26 % for the Denka Seiken assay, which indicates a high degree of reproducibility. In PROSPER, Lp(a) was measured using a latex agglutination assay (Bio-Stat Diagnostics Ltd., Stockport, UK). In ATHEROGENE Lp(a) was measured using the particle-enhanced immunoturbidimetric Tina-quant assay (Roche Diagnostics, Mannheim, Germany) on a Hitachi 911 and 917 platform. Serum levels of Lp(a) were measured immunoturbidimetrically on a Hitachi 917 system (Roche Diagnostics GmbH, Mannheim, Germany) using the lipoprotein(a) kit from Roche Diagnostics.

Genotyping in LURIC

Genotyping in LURIC was performed as described previously [35]. Briefly, genomic DNA was obtained from peripheral blood. To genotype the *LPA* SNPs *rs10455872* and *rs3798220* were extracted from the Affymetrix genome wide SNP array 6·0.

Supplementary Tables

Supplemental table 1
Logistic regression analyses for risk of CHD according to carrier status of *LPA* SNPs in the LURIC study.

		Risk of CHD	
Model	**SNP of *LPA***	**OR (95% CI)**	***P***
Crude	No	1	…
	Yes	1·86 (1·43-2·42)	<0·001
Adjusted 1	No	1	…
	Yes	1·88 (1·40-2·53)	<0·001

Adjustment 1: Age, sex, diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate, LDL-cholesterol, and lipid-lowering therapy.
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental table 2
Logistic regression analyses for risk of CHD according to tertiles of Lp(a) in the LURIC study

		Risk of CHD	
Model	**Tertile of Lp(a)**	**OR (95% CI)**	***P***
Crude	1	1	…
	2	1·02 (0·84-1·25)	0·808
	3	1·47 (1·20-1·80)	<0·001
Adjusted 1	1	1	…
	2	0·96 (0·77-1·20)	0·722
	3	1·44 (1·14-1·83)	0·002

Adjustment 1: Age, sex, diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate, LDL-cholesterol, and lipid-lowering therapy.
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental Table 3
Cox regression analyses for tertiles of Lp(a) and all-cause as well as cardiovascular mortality in the LURIC study

Model	Tertile of Lp(a)	All-cause mortality		Cardiovascular mortality	
		HR (95 % CI)	***P***	**HR (95 % CI)**	***P***
Crude	1	Reference	...	Reference	...
	2	0·99 (0·85–1·15)	0·842	0·88 (0·73–1·07)	0·206
	3	0·89 (0·77–1·04)	0·139	0·91 (0·75–1·10)	0·313
Adjusted 1	1	Reference	...	Reference	...
	2	0·99 (0·85–1·14)	0·840	0·88 (0·73–1·07)	0·199
	3	0·93 (0·80–1·09)	0·374	0·95 (0·79–1·15)	0·592
Adjusted 2	1	Reference	...	Reference	...
	2	1·01 (0·87–1·18)	0·905	0·91 (0·75–1·11)	0·339
	3	0·95 (0·81–1·11)	0·527	0·99 (0·81–1·20)	0·905

Adjustment 1: Adjusted for age and sex
Adjustment 2: Adjusted 1 + diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate, lipid-lowering therapy and LDL-cholesterol
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental table 4

Cox regression analyses for the association between tertiles of Lp(a) and all-cause as well as cardiovascular mortality in participants of the LURIC study divided into two groups at LDL-C 130 mg/dL or according to prevalent statin treatment.

	All-cause mortality			
	LDL-C < 130 mg/dL		**LDL ≥ 130 mg/dL**	
Tertile of Lp(a)	**HR (95 % CI)**	***P***	**HR (95 % CI)**	***P***
1	Reference		Reference	
2	1·00 (0·83-1·20)	0·996	1·04 (0·77-1·39)	0·809
3	0·88 (0·73-1·07)	0·201	1·02 (0·77-1·35)	0·904
	Cardiovascular mortality			
1	Reference		Reference	
2	0·85 (0·66-1·08)	0·185	0·93 (0·65-1·34)	0·691
3	0·94 (0·74-1·20)	0·610	0·93 (0·66-1·32)	0·685
	All-cause mortality			
	No Statin treatment		**Statin treatment**	
1	Reference		Reference	
2	0·94 (0·76-1·16)	0·556	1·01 (0·81-1·27)	0·919
3	0·94 (0·76-1·16)	0·581	0·84 (0·67-1·06)	0·138
	Cardiovascular mortality			
1	Reference		Reference	
2	0·87 (0·67-1·13)	0·291	0·85 (0·64-1·15)	0·291
3	0·92 (0·71-1·20)	0·537	0·91 (0·68-1·20)	0·490

Adjusted for age, sex, diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate, LDL-cholesterol, and lipid-lowering therapy (not for analysis in groups with/without statin treatment).

Supplemental table 5
Baseline characteristics of the **KAROLA** cohort, overall and stratified in tertiles of Lp(a).

	Overall (n=1045)	**Lp(a) Tertile 1 ≤ 4·2 mg/dL (n=350)**	**Lp(a) Tertile 2 4·2-12·3 mg/dL (n=347)**	**Lp(a) Tertile 3 >12·3 mg/dL (n=348)**	***P****
Age	59·0±7·9	58·6±7·9	59·6±7·7	58·8±8·1	0·26
Sex (% male)	84·6	86·9	85·3	81·6	0·14
BMI (kg/m^2)	26·9±3·2	27·1±3·2	26·9±3·3	26·7±3·3	0·30
Systolic blood pressure (mmHg)	118·9±16·5	119·2±16·6	118·7±16·6	118·6±16·3	0·72
Lp(a) (mg/dL)	6·8 (3·4-22·0)	2·4 (1·7-3·4)	6·8 (5·4-8·7)	30·7 (22·1-44·5)	<0·0001
Total cholesterol (mg/dL)	169·6±32·6	166·9±34·1	167·9±31·0	174·2±32·3	0·0025
Triglycerides (mg/dL)	144·2±71·7	157·8±87·3	133·5±57·3	141·3±65·1	0·0022
HDL cholesterol (mg/dL)	39·4±10·5	39·5±10·1	38·6±10·1	40·0±11·4	0·43
LDL cholesterol (mg/dL)	101·4±29·5	95·8±29·2	101·4±29·5	107·0±28·9	<0·0001
Glycosylated hemoglobin (%)	78·6±38·4	78·0±38·8	75·9±40·1	81·9±36·1	0·043
eGFR CKD-EPI (ml/min/1·73m^2)	83·4±17·3	85·1±17·3	81·3±17·5	83·7±16·8	0·0036
hsCRP (mg/L)	3·5 (1·3-8·3)	3·5 (1·2-8·3)	3·3 (1·3-8·3)	3·6 (1·4-8·2)	0·97
IL-6 (ng/L)	3·5 (2·2-7·1)	3·7 (2·2-7·1)	3·6 (2·2-7·4)	3·4 (2·2-6·7)	0·93
Previous myocardial infarction (%)	58·5	60·0	60·8	54·6	0·20
Diabetes mellitus (%)	17·4	19·1	18·4	14·7	0·24
Lipid lowering therapy (%)	77·6	76·3	74·0	82·4	0·022
Smoking (%)	68·6	70·0	69·5	66·4	0·54
Hypertension (%)	55·3	55·7	54·2	56·0	0·87

Values are presented as mean (SD), median (IQR) or number (%). BMI=body mass index. HDL=high-density lipoprotein. LDL=low-density lipoprotein· VLDL=very low-density lipoprotein. Lp(a)=lipoprotein(a). IL-6=interleukin-6. eGFR=estimated glomerular filtration rate. hsCRP=high sensitivity C-reactive protein.
* comparison between tertiles of Lp(a). $p < 0·05$ was considered significant

Supplemental table 6
Baseline characteristics of the **HCS** cohort, overall and stratified in tertiles of Lp(a).

	Overall (n=514)	**Lp(a) Tertile 1 ≤ 3·0 mg/dL (n=237)**	**Lp(a) Tertile 2 3·0-9·8 mg/dL (n=99)**	**Lp(a) Tertile 3 >9·8 mg/dL (n=178)**	***P****
Age	66·4±10·1	66·1±9·6	68·1±9·7	65·9±10·8	0·19
Sex (% male)	82·9	83·5	84·8	80·9	0·66
BMI (kg/m^2)	28·9±4·2	29·0±4·2	28·3±4·1	29·0±4·3	0·34
Systolic blood pressure (mmHg)	126·7±15·8	126·6±15·3	124·8±16·6	127·8±16·0	0·31
Lp(a) (mg/dL)	13·0±17·1	3·0±0·1	5·3±1·7	31·5±18·9	<0·0001
Total cholesterol (mg/dL)	173·0±38·8	173·5±40·4	175·1±40·0	171·1±35·9	0·70
Triglycerides (mg/dL)	151·6±96·1	170·0±116·1	129·1±63·7	139·8±75·2	<0·0001
HDL cholesterol (mg/dL)	44·8±13·8	44·0±13·8	47·7±13·6	44·3±13·8	0·07
LDL cholesterol (mg/dL)	105·1±33·9	103·5±35·1	107·4±35·9	106·0±31·2	0·57
Glycosylated hemoglobin (%)	6·2±1·1	6·2±1·1	6·0±0·8	6·2±1·2	0·20
eGFR MDRD (ml/min/1·73m^2)	77·9±20·1	78·2±18·9	78·7±20·9	76·9±21·3	0·74
hsCRP (mg/L)	0·7±1·0	0·8±1·2	0·6±0·6	0·6±0·7	0·21
Previous myocardial infarction (%)	43·4	38·8	38·4	52·2	0·013
Diabetes mellitus (%)	32·5	35·4	30·3	29·8	0·42
Statin therapy (%)	94·6	93·2	98·0	94·4	0·22
Smoking (%)	18·9	18·6	17·2	20·2	0·81
Hypertension (%)	92·8	92·8	90·9	93·8	0·67

Values are presented as mean (SD) or number (%). BMI=body mass index. HDL=high-density lipoprotein. LDL=low-density lipoprotein. Lp(a)=lipoprotein(a). eGFR=estimated glomerular filtration rate. hsCRP=high sensitivity C-reactive protein. Smoking was defined as active smoking of within the past 12 months.
* comparison between tertiles of Lp(a). $p < 0·05$ was considered significant.

Supplemental table 7
Baseline characteristics of the **WENBIT/WECAC** cohort, overall and stratified in tertiles of Lp(a).

	Overall (n=4162)	**Lp(a) Tertile 1 ≤ 19·0 mg/dL (n=1392)**	**Lp(a) Tertile 2 20·0-47·0 mg/dL (n=1384)**	**Lp(a) Tertile 3 >47·0 mg/dL (n=1386)**	***P****
Age	61·8±10·4	61·9±10·3	62·0±10·3	61·4±10·5	0·26
Sex (% male)	71·9	72·4	73·5	69·9	0·10
BMI (kg/m^2)	26·8±4·0	26·6±3·9	26·8±4·0	26·9±3·9	0·16
Systolic blood pressure (mmHg)	141·1±20·8	140·9±20·5	141·5±20·7	141·0±21·0	0·62
Lp(a) (mg/dL)	29·6 (44·0)	10·4 (9·0)	29·8 (13·0)	76·0 (45·0)	<0·001
Total cholesterol (mg/dL)	197·2±42·5	189·4±42·5	193·3±42·5	204·9±46·4	<0·001
Triglycerides (mg/dL)	157·5±96·3	140·0±87·5	157·5±87·5	166·3±122·5	<0·001
HDL cholesterol (mg/dL)	49·9±14·7	51·4±15·1	48·7±14·7	49·9±13·9	<0·001
LDL cholesterol (mg/dL)	119·9±38·7	116·0±38·7	119·9±38·7	123·7±42·5	<0·001
Glycosylated hemoglobin (%)	6·22±1·38	6·15±1·40	6·24±1·37	6·25±1·38	0·15
eGFR MDRD (ml/min/1·73m^2)	87·8±17·3	88·1±16·8	87·4±17·4	87·8±17·7	0·56
hsCRP (mg/L)	1·8 (2·8)	1·6 (2·7)	1·8 (2·9)	1·9 (3·0)	0·47
Previous myocardial infarction (%)	40·3	38·4	40·8	41·8	0·17
Diabetes mellitus (%)	37·6	35·6	38·4	39·0	0·14
Statin therapy (%)	80·6	79·1	79·7	82·9	0·27
Smoking (%)	72·6	72·7	73·1	72·0	0·69
CAD (%)	74·9	72·3	73·3	79·0	<0·001

Values are presented as mean (SD) or number (%). BMI=body mass index. HDL=high-density lipoprotein. LDL=low-density lipoprotein. Lp(a)=lipoprotein(a). eGFR=estimated glomerular filtration rate. hsCRP=high sensitivity C-reactive protein.
* comparison between tertiles of Lp(a). $p < 0·05$ was considered significant.

Supplemental table 8
Baseline characteristics of the **PROSPER** cohort, overall and stratified in tertiles of Lp(a).

	Overall (n=1860)	**Lp(a) Tertile 1 ≤ 8·0 mg/dL (n=622)**	**Lp(a) Tertile 2 9·0-27·0 mg/dL (n=612)**	**Lp(a) Tertile 3 >27·0 mg/dL (n=626)**	***P****
Age	75·6±3·4	75·4±3·3	75·8±3·4	75·6±3·5	0·20
Sex (% male)	58·3	62·7	56·7	55·4	0·021
BMI (kg/m^2)	26·8±4·0	27·2±4·0	26·9±4·0	26·4±3·8	<0.001
Systolic blood pressure (mmHg)	150·2±22·3	150·6±22·6	150·5±22·0	149·6±22·4	0·69
Lp(a) (mg/dL)	14·0 (40·0)	4·0 (4·0)	13·5 (7·0)	61·0 (43·0)	<0·001
Total cholesterol (mg/dL)	218·0±32·2	212·9±33·0	218·4±35·0	222·7±34·1	<0·001
Triglycerides (mg/dL)	140·1±64·9	147·2±71·6	136·0±59·0	137·1±62·7	0·004
HDL cholesterol (mg/dL)	47·4±12·8	46·7±13·1	47·5±12·4	47·8±12·9	0·29
LDL cholesterol (mg/dL)	146·5±30·0	140·5±29·4	147·5±30·1	151·5±29·4	<0·001
Apolipoprotein B (mg/dL)	115·2±22·1	112·5±21·3	115·8±21·9	117·4±22·8	<0·001
eGFR MDRD (ml/min/1·73m^2)	55·1±13·4	55·9±13·8	54·4±13·1	54·9±13·2	0·11
hsCRP (mg/L)	3·2 (4·9)	2·9 (4·3)	3·0 (4·9)	3·3 (6·1)	0·044
Previous myocardial infarction (%)	41·1	41·2	41·7	40·6	0·93
Diabetes mellitus (%)	8·7	10·6	7·5	8·0	0·11
Lipid lowering therapy (%)	0	0	0	0	
Smoking (%)	16·1	17·4	16·8	14·1	0·23
Hypertension (%)	46·1	46·5	46·6	45·2	0·87

Values are presented as mean (SD) or number (%). BMI=body mass index. HDL=high-density lipoprotein. LDL=low-density lipoprotein. Lp(a)=lipoprotein(a). eGFR=estimated glomerular filtration rate. hsCRP=high sensitivity C-reactive protein.
* comparison between tertiles of Lp(a). $p < 0·05$ was considered significant.

Supplemental table 9
Baseline characteristics of the **ATHEROGENE** cohort, overall and stratified in tertiles of Lp(a).

	Overall (n=2,614)	**Lp(a) Tertile 1 ≤ 19·0 mg/dL** (n=907)	**Lp(a) Tertile 2 20·0-47·0 mg/dL** (n=845)	**Lp(a) Tertile 3 >47·0 mg/dL** (n=862)	***P****
Age	61·9±10·1	61·5±10·2	62·5±10·1	61·8±10·0	0·11
Sex (% male)	72·7	74·8	74·3	68·9	0·01
BMI (kg/m^2)	27·4±4·0	27·6±4·0	27·5±4·1	27·1±3·9	0·025
Systolic blood pressure (mmHg)	137·0±59·0	135·3±26·1	136·2±55·6	139·3±79·2	0·69
Lp(a) (mg/dL)	23·0 (45·0)	6·0 (8·0)	24·0 (12·0)	78·0 (46·0)	<0·001
Total cholesterol (mg/dL)	209·9±46·6	205·8±47·2	208·7±46·0	215·4±46·1	<0·001
Triglycerides (mg/dL)	159·5±105·7	172·2±127·3	157·6±95·4	148·1±87·2	<0·001
HDL cholesterol (mg/dL)	49·1±14·9	48·8±15·0	48·6±14·6	50·0±15·0	0·11
LDL cholesterol (mg/dL)	131·0±41·2	126·0±40·3	129·7±41·1	137·4±41·5	<0·001
Apolipoprotein B (mg/dL)	117·1±203·7	122·3±341·2	112·7±30·0	116·0±44·9	0·024
eGFR CKD-EPI (ml/min/1·73m^2)	74·7±18·1	75·2±17·6	74·4±18·2	74·4±18·5	0·80
hsCRP (mg/L)	3·9 (9·0)	3·6 (7·8)	4·3 (10·0)	3·9 (9·6)	0·072
Previous myocardial infarction (%)	43·0	43·1	43·2	42·7	0·98
Diabetes mellitus (%)	21·5	23·5	22·4	18·7	0·036
Statin therapy (%)	46·7	42·2	46·6	51·4	<0·001
Smoking (%)	30·2	32·1	30·5	27·8	0·15
CAD (%)	100·0	100·0	100·0	100·0	

Values are presented as mean (SD) or number (%). BMI=body mass index. HDL=high-density lipoprotein. LDL=low-density lipoprotein. Lp(a)=lipoprotein(a). eGFR=estimated glomerular filtration rate. hsCRP=high sensitivity C-reactive protein.
* comparison between tertiles of Lp(a). $p < 0·05$ was considered significant.

Supplemental table 10
Cox regression analyses for tertiles of Lp(a) and risk for fatal and composite cardiovascular end-point in the **KAROLA study**.

Model	**Tertile of Lp(a)**	**Composite cardiovascular end-point**	
		HR (95 % CI)	***P***
Crude	1	Reference	...
	2	1·00 (0·74-1·34)	0·99
	3	1·03 (0·77-1·39)	0·83
Adjusted 1	1	Reference	…
	2	0·97 (0·72-1·30)	0·82
	3	1·02 (0·76-1·37)	0·89
Adjusted 2	1	Reference	...
	2	0·95 (0·70-1·29)	0·74
	3	1·05 (0·77-1·43)	0·76

Adjustment 1: Adjusted for age and sex
Adjustment 2: Adjusted 1 + diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate and LDL-cholesterol
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental table 11
Cox regression analyses for tertiles of Lp(a) and risk for fatal and composite cardiovascular end-point in the **HCS**.

Model	**Tertile of Lp(a)**	**Composite cardiovascular end-point**	
		HR (95 % CI)	***P***
Crude	1	Reference	...
	2	0·89 (0·61-1·29)	0·52
	3	1·07 (0·80-1·43)	0·66
Adjusted 1	1	Reference	...
	2	0·89 (0·61-1·29)	0·53
	3	1·07 (0·79-1·43)	0·67
Adjusted 2	1	Reference	...
	2	0·93 (0·64-1·36)	0·71
	3	1·08 (0·80-1·44)	0·63

Adjustment 1: Adjusted for age and sex
Adjustment 2: Adjusted 1 + diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate and LDL-cholesterol
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental table 12
Cox regression analyses for tertiles of Lp(a) and cardiovascular mortality in **WENBIT/WECAC**.

Model	**Tertile of Lp(a)**	**Composite cardiovascular end-point**	
		HR (95 % CI)	***P***
Crude	1	Reference	...
	2	1·02 (0·80-1·30)	0·876
	3	1·10 (0·87-1·39)	0·431
Adjusted 1	1	Reference	...
	2	1·02 (0·80-1·30)	0·854
	3	1·15 (0·91-1·45)	0·252
Adjusted 2	1	Reference	...
	2	1·03 (0·81-1·31)	0·822
	3	1·02 (0·80-1·29)	0·902

Adjustment 1: Adjusted for age and sex
Adjustment 2: Adjusted 1 + diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate, LDL-cholesterol, and lipid-lowering therapy.
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental table 13
Cox regression analyses for tertiles of Lp(a) and cardiovascular mortality in the **PROSPER**.

Model	**Tertile of Lp(a)**	**Composite cardiovascular end-point**	
		HR (95 % CI)	***P***
Crude	1	Reference	...
	2	1·24 (0·81-1·90)	0·32
	3	1·23 (0·80-1·90)	0·34
Adjusted 1	1	Reference	...
	2	1·22 (0·79-1·87)	0·37
	3	1·23 (0·80-1·90)	0·34
Adjusted 2	1	Reference	...
	2	1·26 (0·81-1·94)	0·30
	3	1·31 (0·85-2·03)	0·22

Adjustment 1: Adjusted for age and sex
Adjustment 2: Adjusted 1 + diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate, LDL-cholesterol, and lipid-lowering therapy.
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental table 14
Cox regression analyses for tertiles of Lp(a) and cardiovascular mortality in the **ATHEROGENE study**.

Model	**Tertile of Lp(a)**	**Cardiovascular mortality**	
		HR (95 % CI)	***P***
Crude	1	Reference	...
	2	1·06 (0·78-1·43)	0·73
	3	0·83 (0·80-1·14)	0·25
Adjusted 1	1	Reference	…
	2	1·01 (0·74-1·37)	0·97
	3	0·83 (0·60-1·15)	0·26
Adjusted 2	1	Reference	…
	2	0·99 (0·73-1·35)	0·96
	3	0·85 (0·60-1·18)	0·34

Adjustment 1: Adjusted for age and sex
Adjustment 2: Adjusted 1 + diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate, LDL-cholesterol, and lipid-lowering therapy·
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental Table 15
Cox regression analyses for carrier status of *LPA* SNPs and all-cause as well as cardiovascular mortality in the LURIC study

Model	**SNP of *LPA***	**All-cause mortality**		**Cardiovascular mortality**	
		HR (95 % CI)	***P***	**HR (95 % CI)**	***P***
Crude	No	Reference	...	Reference	...
	Yes	1·03 (0·87–1·23)	0·720	1·06 (0·85–1·32)	0·594
Adjusted 1	No	Reference	...	Reference	...
	Yes	1·07 (0·90–1·27)	0·471	1·10 (0·88–1·36)	0·418
Adjusted 2	No	Reference	…	Reference	...
	Yes	1·10 (0·92–1·31)	0·312	1·13 (0·90–1·40)	0·290

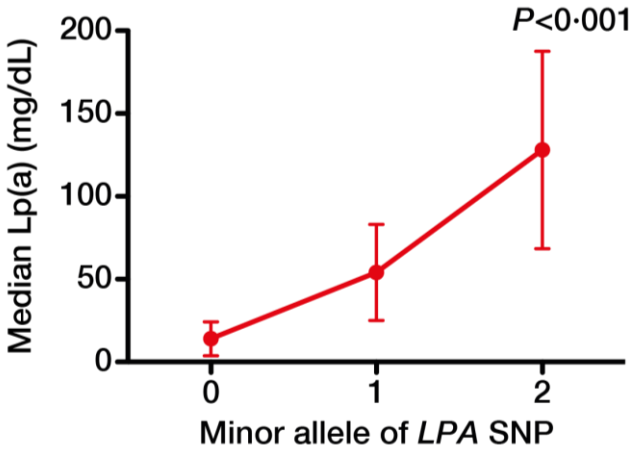
Adjustment 1: Adjusted for age and sex
Adjustment 2: Adjusted 1 + diabetes, systolic blood pressure, body mass index, smoking status, estimated glomerular filtration rate, lipid-lowering therapy and LDL-cholesterol
HR=Hazard ratio. 95% CI=95% confidence interval.

Supplemental table 16 – Baseline characteristics of cohorts/studies of the GENIUS-CHD consortium included for meta-analysis

Cohort	Number of participants	Age (years)	Sex (% male)	BMI (kg/m2)	Total cholesterol (mg/dL)	Triglycerides (mg/dL)	LDL-C (mg/dL)	HDL-C (mmol/L)	Creatinine (µmol/L)	CRP (mg/L)	rs3798220 TT (%)	rs3798220 TC (%)	rs3798220 CC (%)	rs10455872 AA (%)	rs10455872 AG (%)	rs10455872 GG (%)	Previous myocardial infarction (%)	Diabetes (%)	Statin use (%)	Current smoking (%)	Hypertension (%)	All-cause mortality (%)	Cardiovascular mortality (%)
CDCS	1976	67·4±12	71·3	27·3±4·7	193·7 ± 42·1	154 ± 83·1	114·1 ± 39·8	45·6 ± 13·1	100·8±41·4	0·5 (1·1)	94·5	5·4	0·1	79·8	19·3	1·0	30·4	12·5	46·0	5·8	66·2	24·1	13·4
Corogene	1489	64·7±11·9	70·9	27·6±4·8	177·1 ± 38·3		93·9 ± 34·0	48·3 ± 14·3	84±45·5	2·1(2·1)				90·9	8·9	0·2	NA	18·2	5·2	34·4	65·3	24·1	NA
CURE	10203	65·4±11·2	61·4	27·7±4·5					93·1±34·8		94·2	5·8	0				31·7	20·9	NA	23	57·3	5·5	1·7
CTMM	688	62·6±10·1	69	27·6±4·4	175·5 ± 41·0	137·4 ± 76·1	100·1 ± 37·9	44·1 ± 12·4	86·2±39·8	1·6(0·7)	95·5	4·3	0·2	83·4	15·6	1	30·3	21	NA	20·8	63·1	1·1	0·8
DECODE	11614	66±11·9	69	28·3±4·6							95·6	4·4	0·1	85·3	14·1	0·6	14·2	10·5	NA	26·4	56·5	33·1	NA
Emory	4230	65·4±11·7	68·8		173·2 ± 40·2	344·8 ± 228·4	93·6 ± 36·0	42·1 ± 13·1	100·2±55·5	1·6(2·1)				83·3	16·2	0·5	26·8	34·2	74·2	7·8	77·6	19·8	12·2
GENEBANK	2345	61·5±11·1	74·3	29·4±5·4	169·3 ± 36·0	331·6 ± 191·6	97·0 ± 31·7	34·8 ± 10·1		1·5(1·9)				84·1	15·3	0·6	56·1	11·8	71·8	16·8	73·5	6·5	NA
INVEST	2270	68·6±9·4	57	29·4±5·6							90·3	9·7	0	89·7	10·1	0·2	76·8	24·3	52·7	13·3	100	3·8	1·2
LIFE-Heart	5564	63·9±11·1	77·2	28·9±4·7	199·5 ± 46·0	166·3 ± 107·6	120·6 ± 40·6	47·6 ± 13·5	88·8±34·2	1·8 (2·1)	95·0	5·0	0	87·3	12·3	0·4	13·2	33·9	45·8	27·8	86·2	8·0	1·4
LURIC	2320	63·8±9·9	76·6	27·5±4	191·0 ± 38·3	174·1 ± 111·1	115·2 ± 34·4	37·1 ± 10·1	88·7±37·7	1·7(2·1)	95·9	4	0	86·1	13·5	0·5	57·8	44·1	58·9	24·7	54·7	34·5	22·1
MDCS	30441	58±7·6	39·8	25·8±4	238·5 ± 42·1	119·9 ± 70·0	160·8 ± 38·3	53·4 ± 14·3	84·8±16·3	0·1(0·2)	97·9	2·1	0	85·8	13·6	0·5	0	4·4	3	26·6	61·2	27·3	9·1
OHGS	546	65·6±11·1	73·8	28·5±4·9	215·3 ± 40·6	159·3 ± 118·1	133·8 ± 34·0	47·2 ± 13·1	89·1±20·6					84·2	15·1	0·8	23·3	5·5	91·6	19·3	65·8	4·8	4·4
PLATO	9814	62·6±11	69·5	28·2±4·5	208·8 ± 47·6	158·4 ± 117·3	126·4 ± 42·9	49·5 ± 13·5	85·6±26·3	1·9(2·1)	93·4	6·4	0·2	88·1	11·5	0·4	20·6	22·8	79·7	35·2	66	3·8	3·3

PMI	**893**	**62·8±10·6**	**78**	**26·5±3·8**	**230·8 ± 46·0**		**153·9 ± 41·4**		**88±28·5**		**95·3**	**4·5**	**0·3**	**82·8**	**16·0**	**1·2**	**18·4**	**12·5**	**44·5**	**28·0**	**72·3**	**49·3**	**31·5**
PRAXY	**774**	**48·3±5·6**	**69·1**		**188·3 ± 46·0**	**170·6 ± 119·0**	**111·7 ± 43·7**	**37·5 ± 11·6**	**75·9±19·9**	**2·4(2·3)**	**94·5**	**5·3**	**0·3**	**80·8**	**18·4**	**0·8**	**11·6**	**13·9**	**93·1**	**44·2**	**54·7**	**1**	**3·7**
PROSPER	**893**	**75·4±3·4**	**70·3**	**26·6±3·9**	**214·6 ± 32·5**	**139·1 ± 65·6**	**144·6 ± 28·6**	**45·2 ± 12·0**	**109·2±23·1**	**2·1(1·9)**	**95·3**	**4·7**	**0**				**86·9**	**10·4**	**0**	**17·2**	**42·3**	**15·5**	**9·9**
RISCA	**1054**	**61·8±11·5**	**75·9**	**27·2±4·4**					**100·6±28·5**	**1·8(2)**				**82·2**	**17·4**	**0·4**	**27·8**	**19·8**	**46·6**	**30·4**	**61·9**	**3·3**	**2·7**
STABILITY	**9287**	**64·7±9·1**	**82**	**29·9±5**			**87·0 ± 32·9**	**47·2 ± 12·4**		**1·2(1·6)**	**93·5**	**6·3**	**0·2**	**86·1**	**13·3**	**0·6**	**58·6**	**38·4**	**97·3**	**21·4**	**74**	**6·7**	**4·2**
Krakow Cohort	**747**	**68·3±10·3**	**71·6**	**26·3±4·5**	**192·1 ± 41·8**	**119·0 ± 63·0**	**120·2 ± 44·1**	**47·6 ± 14·3**	**91·3±41·7**	**1·6(2)**				**87·4**	**12·5**	**0·1**	**39·9**	**36·1**	**87·5**	**27·5**	**82·6**	**13·3**	**5·8**
TexGen	**2834**	**63·6±10·6**	**74·9**	**29·6±5·6**										**83·2**	**15·9**	**0·9**	**16·7**	**30·4**	**57·2**	**21·1**	**76·6**	**23**	
TRIUMPH	**2062**	**59·8±12·1**	**72·2**	**29·6±6**		**348·3 ± 240·6**	**104·4 ± 39·4**	**40·2 ± 12·8**	**113·7±81·3**		**94**	**5·8**	**0·2**	**84·3**	**15·3**	**0·3**	**18·5**	**29·1**	**89**	**37·4**	**61·5**	**4·9**	
VHS	**939**	**61·3±9·7**	**81**	**26·8±3·6**	**213·0 ± 43·7**	**167·1 ± 94·5**	**142·7 ± 38·7**	**45·2 ± 11·6**	**96·7±31·9**	**1·8(2)**							**59·4**	**18·4**	**46·4**	**69·1**	**65·5**	**20**	**14**
VIVIT	**1444**	**64·5±10·4**	**72**	**27·4±4·1**	**207·2 ± 44·5**	**150·5 ± 97·1**	**128·7 ± 39·4**	**52·2 ± 15·5**	**89·9±40·9**	**3(1·6)**	**95·4**	**4·4**	**0·2**				**30·4**	**31**	**49·9**	**19·4**	**65·3**	**24·7**	**11·9**
WTCCC CAD	**1926**	**60±8·1**	**79·3**	**27·6±4·2**	**205·3 ± 37·9**	**205·6 ± 116·4**	**120·6 ± 34·8**	**46·4 ± 147**			**94·3**	**5·6**	**0·1**	**87·3**	**12·4**	**0·4**	**72**	**11·7**	**71·6**	**12·8**	**43·1**	**21·4**	**NA**

Supplemental Figure 1: Median Lp(a) plasma concentration and sum of minor alleles of *LPA* SNPs (rs10455872 and rs3798220) in participants of the LURIC study (η^2 for rs10455872 = 9·0 %, P=8·2*10^{-62}, η^2 for rs3798220 = 12·7 %, P=1·9*10^{-83}, η^2 for rs10455872 and rs3798220 together = 24·5 %),.



References

1. Ellis KL, Pilbrow AP, Frampton CM, et al. A common variant at chromosome 9P21.3 is associated with age of onset of coronary disease but not subsequent mortality. *Circ Cardiovasc Genet* 2010; **3**(3): 286-93.
2. Vaara S, Nieminen MS, Lokki ML, et al. Cohort Profile: the Corogene study. *Int J Epidemiol* 2012; **41**(5): 1265-71.
3. Pare G, Mehta SR, Yusuf S, et al. Effects of CYP2C19 genotype on outcomes of clopidogrel treatment. *N Engl J Med* 2010; **363**(18): 1704-14.
4. Pare G, Ross S, Mehta SR, et al. Effect of PON1 Q192R genetic polymorphism on clopidogrel efficacy and cardiovascular events in the Clopidogrel in the Unstable Angina to Prevent Recurrent Events trial and the Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events. *Circ Cardiovasc Genet* 2012; **5**(2): 250-6.
5. Helgadottir A, Gretarsdottir S, Thorleifsson G, et al. Apolipoprotein(a) genetic sequence variants associated with systemic atherosclerosis and coronary atherosclerotic burden but not with venous thromboembolism. *J Am Coll Cardiol* 2012; **60**(8): 722-9.
6. Chan K, Patel RS, Newcombe P, et al. Association between the chromosome 9p21 locus and angiographic coronary artery disease burden: a collaborative meta-analysis. *J Am Coll Cardiol* 2013; **61**(9): 957-70.
7. Wang Z, Klipfell E, Bennett BJ, et al. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature* 2011; **472**(7341): 57-63.
8. Reiner AP, Hartiala J, Zeller T, et al. Genome-wide and gene-centric analyses of circulating myeloperoxidase levels in the charge and care consortia. *Hum Mol Genet* 2013; **22**(16): 3381-93.
9. Hartiala J, Bennett BJ, Tang WH, et al. Comparative genome-wide association studies in mice and humans for trimethylamine N-oxide, a proatherogenic metabolite of choline and L-carnitine. *Arterioscler Thromb Vasc Biol* 2014; **34**(6): 1307-13.
10. Beitelshees AL, Gong Y, Wang D, et al. KCNMB1 genotype influences response to verapamil SR and adverse outcomes in the INternational VErapamil SR/Trandolapril STudy (INVEST). *Pharmacogenet Genomics* 2007; **17**(9): 719-29.
11. Beutner F, Teupser D, Gielen S, et al. Rationale and design of the Leipzig (LIFE) Heart Study: phenotyping and cardiovascular characteristics of patients with coronary artery disease. *PLoS One* 2011; **6**(12): e29070.

12. Winkelmann BR, März W, Boehm BO, et al. Rationale and design of the LURIC study--a resource for functional genomics, pharmacogenomics and long-term prognosis of cardiovascular disease. *Pharmacogenomics* 2001; **2**(1 Suppl 1): S1-73.
13. Berglund G, Elmstahl S, Janzon L, Larsson SA. The Malmo Diet and Cancer Study. Design and feasibility. *Journal of internal medicine* 1993; **233**(1): 45-51.
14. Dandona S, Stewart AF, Chen L, et al. Gene dosage of the common variant 9p21 predicts severity of coronary artery disease. *J Am Coll Cardiol* 2010; **56**(6): 479-86.
15. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2009; **361**(11): 1045-57.
16. Pilote L, Karp I. GENESIS-PRAXY (GENdEr and Sex determInantS of cardiovascular disease: From bench to beyond-Premature Acute Coronary SYndrome). *Am Heart J* 2012; **163**(5): 741-6 e2.
17. Shepherd J, Blauw GJ, Murphy MB, et al. The design of a prospective study of Pravastatin in the Elderly at Risk (PROSPER). PROSPER Study Group. PROspective Study of Pravastatin in the Elderly at Risk. *Am J Cardiol* 1999; **84**(10): 1192-7.
18. Bogaty P, Boyer L, Simard S, et al. Clinical utility of C-reactive protein measured at admission, hospital discharge, and 1 month later to predict outcome in patients with acute coronary disease. The RISCA (recurrence and inflammation in the acute coronary syndromes) study. *J Am Coll Cardiol* 2008; **51**(24): 2339-46.
19. Investigators S, White HD, Held C, et al. Darapladib for preventing ischemic events in stable coronary heart disease. *N Engl J Med* 2014; **370**(18): 1702-11.
20. Virani SS, Brautbar A, Lee VV, et al. Usefulness of single nucleotide polymorphism in chromosome 4q25 to predict in-hospital and long-term development of atrial fibrillation and survival in patients undergoing coronary artery bypass grafting. *Am J Cardiol* 2011; **107**(10): 1504-9.
21. Virani SS, Brautbar A, Lee VV, et al. Chromosome 9p21 single nucleotide polymorphisms are not associated with recurrent myocardial infarction in patients with established coronary artery disease. *Circ J* 2012; **76**(4): 950-6.
22. Arnold SV, Chan PS, Jones PG, et al. Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH): design and rationale of a prospective multicenter registry. *Circ Cardiovasc Qual Outcomes* 2011; **4**(4): 467-76.

23. Olivieri O, Martinelli N, Girelli D, et al. Apolipoprotein C-III predicts cardiovascular mortality in severe coronary artery disease and is associated with an enhanced plasma thrombin generation. *J Thromb Haemost* 2010; **8**(3): 463-71.
24. Martinelli N, Girelli D, Lunghi B, et al. Polymorphisms at LDLR locus may be associated with coronary artery disease through modulation of coagulation factor VIII activity and independently from lipid profile. *Blood* 2010; **116**(25): 5688-97.
25. Girelli D, Russo C, Ferraresi P, et al. Polymorphisms in the factor VII gene and the risk of myocardial infarction in patients with coronary artery disease. *N Engl J Med* 2000; **343**(11): 774-80.
26. Muendlein A, Gasser K, Kinz E, et al. Evaluation of the prevalence and prospective clinical impact of the JAK2 V617F mutation in coronary patients. *Am J Hematol* 2014; **89**(3): 295-301.
27. Samani NJ, Erdmann J, Hall AS, et al. Genomewide association analysis of coronary artery disease. *N Engl J Med* 2007; **357**(5): 443-53.
28. Werner C, Filmer A, Fritsch M, et al. Risk prediction with triglycerides in patients with stable coronary disease on statin treatment. *Clinical research in cardiology : official journal of the German Cardiac Society* 2014; **103**(12): 984-97.
29. Koenig W, Breitling LP, Hahmann H, Wusten B, Brenner H, Rothenbacher D. Cardiac troponin T measured by a high-sensitivity assay predicts recurrent cardiovascular events in stable coronary heart disease patients with 8-year follow-up. *Clin Chem* 2012; **58**(8): 1215-24.
30. Rothenbacher D, Koenig W, Brenner H. Comparison of N-terminal pro-B-natriuretic peptide, C-reactive protein, and creatinine clearance for prognosis in patients with known coronary heart disease. *Archives of internal medicine* 2006; **166**(22): 2455-60.
31. Svingen GF, Ueland PM, Pedersen EK, et al. Plasma dimethylglycine and risk of incident acute myocardial infarction in patients with stable angina pectoris. *Arterioscler Thromb Vasc Biol* 2013; **33**(8): 2041-8.
32. Blankenberg S, Rupprecht HJ, Bickel C, et al. Glutathione peroxidase 1 activity and cardiovascular events in patients with coronary artery disease. *N Engl J Med* 2003; **349**(17): 1605-13.
33. Friesinger GC, Page EE, Ross RS. Prognostic significance of coronary arteriography. *Trans Assoc Am Physicians* 1970; **83**: 78-92.
34. Winkelmann BR, Marz W, Boehm BO, et al. Rationale and design of the LURIC study--a resource for functional genomics, pharmacogenomics and long-term prognosis of cardiovascular disease. *Pharmacogenomics* 2001; **2**(1 Suppl 1): S1-73.
35. Silbernagel G, Chapman MJ, Genser B, et al. High intestinal cholesterol absorption is associated with cardiovascular disease and risk alleles in ABCG8 and ABO: evidence from the LURIC and YFS cohorts and from a meta-analysis. *J Am Coll Cardiol* 2013; **62**(4): 291-9.