Appendix 1: Supplementary tables [posted as supplied by author]

Table A. Table showing the primary haplotypes representing the totality of variation in the CRP gene in European descent populations.

	rs3093077	rs3093068	**rs1205**	**rs1130864**	**rs1800947**	rs1417938	rs3091244	rs2794521	**Frequency**
Haplotype 1	**T**	C	**C**	**T**	**G**	A	T	T	0.30
Haplotype 2	**T**	C	**C**	**C**	**G**	T	C	C	0.24
Haplotype 3	**G**	G	**C**	**C**	**G**	T	A	T	0.05
Haplotype 4	**T**	C	**T**	**C**	**G**	T	C	T	0.13
Haplotype 5	**T**	C	**T**	**C**	**C**	T	C	T	0.03
Haplotype 6[§]	**?**	?	**C**	**C**	**G**	T	?	?	0.07
Haplotype 7[‡]	**T**	C	**T**	**C**	**?**	T	C	T	0.18

These haplotypes explain 98% of the variability in the CRP gene in European descent populations. The four pre-specified tagging SNPs are in bold and the remaining SNPs were used as surrogate markers in 100% linkage disequilibrium with the primary SNPs. Haplotypes were identified using 40 SNPs from 39 studies in the CCGC who provided individual participant data on at least two SNPs, supplemented by information from SeattleSNPs (NHLBI Program for Genomic Applications, SeattleSNPs, Seattle, WA. http://pga.gs.washington.edu [last accessed Nov, 2009]) and The International HapMap Consortium (*Nature* 2007;449:851-861). § Haplotype 6 comprises participants who cannot be allocated to haplotypes 2 or 3 due to insufficient data on the following SNPs: rs3093077, rs3093068, rs3091244 and rs2794521. ‡ Haplotype 7 comprises participants who cannot be allocated to haplotypes 4 or 5 due to insufficient data on rs1800947.

Table B. Descriptive summary by study for 47 studies in the CRP CHD Genetics Collaboration.

Study / design	Location	Population source	Years of baseline survey	Total subjects	Duration of follow up mean (SD)	No. SNPs	Age (years) mean (SD)	No. (%) Male	Incident cases‡	Prevalent cases‡
Prospective Studies: *Case-cohort*										
ARIC	USA	Household listings	1987-89	14246	13.1 (3.2)	2	55 (5.8)	6419 (45)	1118	0
MONICAKORA	Germany	Population register	1984-1995	1688	10.5 (4.8)	10	53 (10.3)	971 (58)	275	0
Cohort										
AGES*	Iceland	Population register	1967-1994; 2002-	3207	–	20	76 (6)	1366 (42)	0	793
BRHS	UK	GP lists	1978-80	3943	25.3 (4.5)	4	49 (5.5)	3943 (100)	496	70
BWHHS[1]	UK	Population register	1999-2001	3786	4.2 (0.8)	4	69 (5.5)	0 (0)	52	262
CCHS[2]	Denmark	Population register	1991-94	10259	11.1 (4.5)	4	57 (16.1)	4531 (44)	693	228
CGPS[2]	Denmark	Population register	2003-present	32038	1.8 (1.0)	4	57 (13.6)	13,757 (43)	188	899
CHS[3]	USA	GP lists	1989-93	5342	9.5 (3.6)	5	73 (5.3)	2256 (42)	920	515
EAS	Scotland	GP lists	1987-88	907	12.5 (4.9)	3	64 (5.6)	449 (50)	61	28
ELSA	England	Household listings	1998-2001	5496	6.6 (1.5)	3	61 (9.5)	2509 (46)	105	230
FRAMOFF	USA	Household listings	1991-95	1680	6.6 (1.4)	13	62 (9.4)	840 (50)	48	84
HEALTHABC*	USA	Population screening	2000-present	1660	–	7	70-79 (range)	~830 (50)	584	0
NPHSII[4]	England	GP lists	1989-94	2282	11.9 (3.1)	3	57 (3.5)	2282 (100)	108	0
PROSPER[†]	UK,	Population screening	1998	5777	3.1 (0.8)	3	75 (3.4)	2794 (48)	480	772
ROTTERDAM[5]	Netherlands	Population register	1990-93	5732	10.3 (3.8)	3	69 (8.4)	2379 (42)	282	667
WHITEII[1]	England	Occupational	1985-88	5988	11.3 (0.5)	3	49 (6.0)	4282 (72)	0	230
WOSCOPS[4,†]	Scotland	Population screening	1989-91	1451	4.4 (1.3)	1	57 (5.2)	1451 (100)	279	0
Nested case-control: *Individually matched*										
EPICNL	Netherlands	Population register	1993-1997	3507	9.6 (2.5)	4	53 (10.9)	952 (27)	426	0
EPICNOR	England	GP lists	1993-98	3298	–	3	65 (7.8)	2106 (64)	1102	0
HPFS[6]	USA	Occupational	1994	781	12.9 (1.7)	6	57 (8.4)	781 (100)	231	0
NHS[6]	USA	Occupational	1990	744	10.7 (2.3)	6	57 (6.5)	0 (0)	243	0
NSC	Sweden	Population register	1985-99	1673	3.6 (2.5)	4	55 (7.8)	1215 (73)	585	0
Frequency										
CAPS[1]	England	Electoral rolls	1979-83	1157	9.0 (3.5)	3	57 (4.4)	1157 (100)	202	3
4D[†]	Germany	GP lists	1998-2002	897	3.0 (1.5)	25	66 (8.0)	492 (55)	273	0
MALMO	Sweden	Population screening	1991-94	2148	5.8 (2.2)	4	63 (6.4)	1637 (76)	613	459
SPEED[1]	England	GP lists	1979-82	854	24.0 (4.0)	4	54 (4.2)	854 (100)	93	1
WHIOS	USA	Population screening	1991	4390	8.6 (3.4)	4	68 (7.0)	0 (0)	1524	0
Subtotal (27 studies)				124,931	9.6 (2.7)		61 (10.3)	60,253 (48)	10,981	5241

Study / design	Location	Population source	Years of baseline survey	Total subjects	No. SNPs	Age (years) mean (SD)	No. (%) Male	Prevalent cases‡
Retrospective studies								
Case-control, *frequency matched*								
BHF-FHS	England	Population register	1998-2003	4548	4	51 (13.3)	2896 (64)	2157
CHAOS	England	Hospital admissions/ general population	1992-94	2475	4	56 (9.4)	1283 (52)	650
CIHDS[2]	Denmark	Hospital admissions/ general population	1991-2004	6716	4	61 (10.5)	4861 (72)	2236
CRPHANS	China	Hospital admissions/ general population	2008-2010	902	2	60 (9.6)	652 (72)	479
CUDAS	Australia	Electoral rolls	1998; 1995-96	1107	2	53 (12.7)	557 (50)	59
CUPID	Australia	Hospital admissions	1995	555	2	50 (5.1)	484 (87)	353
GERMIFS*	Germany	Population screening	1997-2002	2911	12	58 (8.7)	1979 (68)	1084
GISSI-P ŧ	Italy	Hospital admission / general population	1993-95	4034	4	59 (9.8)	3274 (81)	3054
HIFMECH[4]	Europe	Hospital admissions/ general population	1996-98	1008	1	52 (5)	1006 (100)	490
HIMS[1]	Australia	Population register	2004-04	4194	3	72 (4.2)	4194 (100)	585
HVHS	USA	GP lists	1995-2002	4833	11	65 (9.8)	2111 (44)	1162
INTERHEART[7]	International	Hospital admissions/ general population	1999-2003	8666	16	56 (12)	6904 (80)	3969
ISIS[7]	UK	Hospital admissions/ general population	1989-91	3618	8	50 (8.7)	2239 (62)	2107
LOLIPOP*,[7]	UK	General population	2000-	4712	26	59 (9.7)	3864 (82)	2538
LURIC[8]	Germany	Hospital admissions	1997-2000	2808	24	63 (11)	1942 (69)	1167
PENNCATH*	USA	Hospital admissions	1998-2003	1516	16	59 (10)	1000 (66)	1027
PROCARDIS[7]	Europe	Hospital admissions/ general population	1998-present	6505	17	61 (8.8)	3860 (59)	3156
PROMIS	Pakistan	Hospital admissions	2006-09	3694	26	53 (10.6)	3055 (83)	1813
UCP ŧ	Netherlands	Population register	1985-present	2014	4	64 (10.1)	1322 (66)	1089
SHEEP	Sweden	GP lists, electoral roles	1992-94	2671	3	60 (7.2)	1840 (69)	1160
Subtotal (20 studies)				69,487		58 (9.8)	49,323 (71)	30,335
TOTAL (47 studies)				194,418	41	59 (10.1)	109,576 (56)	35,576

‡ Cases were defined as fatal or non-fatal myocardial infarction, coronary death or ≥ 50% stenosis of at least 1 major coronary vessel (details in **eTable 5**); * Studies have contributed tabular data; ŧ Randomised controlled trials; [1] Lawlor, *PLoS One* 2008; [2] Zacho, *NEJM* 2008; [3] Lange, *JAMA* 2006; [4] Casas, *IJE* 2006; [5] Kardys, *Eur Heart J*, 2006; [6] Pai, *PLoS One* 2008; [7] Elliot, *JAMA* 2009; [8] Grammer, *Eur Heart J*, 2009. Overall standard deviations (SD) for age were estimated accounting for sample size of contributing studies; Study acronyms are listed in **eAppendix 1**.

Table C. Median CRP concentration and laboratory methods for biochemical analysis in 36 studies with circulating CRP measurements in the CCGC.

Study	Median CRP concentration (5^{th}, 95^{th} pctiles)	Fasting status at blood sampling / duration	Sampling source	Time between collection and measurement	Sample state before analyses, storage temperature (°C) if frozen	Assay method (source)	Assay standard
AGES	2.0 (0.4 to 10.8)	Fasted / > 8hrs	Serum	> 10 yrs	Frozen, -20	ITA (Roche Diagnostics)	Manufacturer
ARIC	2.1 (0.3 to 11.3)	Fasted / > 8 hrs	Plasma	> 10 yrs	Frozen, -70	ITA (Denka Seiken)	Manufacturer
BRHS	1.2 (0.2 to 8.5)	Non-fasted	Serum	> 10 yrs	Frozen, -20	MEIA (Abbott)	WHO 85/506
BWHHS	1.8 (0.2 to 9.8)	Fasted / > 8 hrs	Serum	1 - 2 yrs	Frozen, -80	INA (Behring)	Manufacturer
CAPS	1.7 (0.3 to 8.2)	Fasted / > 8 hrs	Plasma	> 10 yrs	Frozen, -70	INA (Behring)	Who 85/506
CCHS	1.7 (0.7 to 9.6)	Non-fasted	Plasma	> 10 yrs	Fresh or frozen	INA, ITA (Dade Behring)	Manufacturer
CGPS	1.5 (0.4 to 8.8)	Non-fasted	Plasma	Fresh	Fresh	INA, ITA (Dade Behring)	Manufacturer
CHS	2.5 (0.5 to 15.5)	Fasted / > 8 hrs	Plasma	5 - 10 yrs	Frozen, -70	ELISA (In-house)	WHO 85/506
CIHDS	1.6 (0.4 to 8.9)	Non-fasted	Plasma	Fresh	Fresh	INA, ITA (Dade Behring)	Manufacturer
CUDAS	1.7 (0.3 to 11.8)	Fasted / > 8 hrs	Serum	NS	Frozen, -70	ITA (Roche Diagnostics)	Manufacturer
CUPID	2.0 (0.4 to 12.0)	Fasted / > 8 hrs	Serum	NS	Frozen, -70	ITA (Roche Diagnostics)	Manufacturer
4D	4.9 (0.7 to 39.1)	Non-fasted	NS	NS	Frozen, -80	ITA (Roche Diagnostics)	Manufacturer
EAS	1.8 (0.4 to 10.8)	Fasted / > 8 hrs	Serum	> 10 yrs	Frozen, -50	INA (Behring)	Manufacturer
ELSA	1.9 (0.3 to 12.4)	Fasted / NS	Serum	Fresh	Fresh	INA (Behring)	Manufacturer
EPICNL	1.5 (0.3 to 9.4)	Non-fasted	Plasma	Fresh	Fresh	ITA (Beckman Coulter)	Manufacturer
EPICNOR	1.7 (0.3 to 14.7)	Non-fasted	Serum	NS	Frozen, -80	ELISA (Sanquin Res)	Manufacturer
FRAMOFF	2.2 (0.4 to 14.3)	Fasted / > 8 hrs	Plasma	1 - 4 yrs	Frozen, -70	ELISA (Behring)	WHO 85/506
HIFMECH	1.2 (0.1 to 8.0)	Fasted / > 8 hrs	Plasma	1 - 4 yrs	Frozen, -70	ELISA (Dako)	Manufacturer
HIMS	1.9 (0.4 to 11.9)	Fasted / NS	NS	Fresh	Fresh	INA (Dade Behring)	Manufacturer
HPFS	1.3 (0.2 to 11.6)	Fasted / NS	Plasma	5 - 10 yrs	Frozen, -130	ITA (Denka Seiken)	Manufacturer
ISIS	1.1 (0.2 to 7.6)	Non-fasted	Plasma	> 10 yrs	Frozen, -40	INA (Dade Behring)	Manufacturer
LURIC	2.8 (0.4 to 26.5)	Fasted / NS	Plasma	1 - 4 yrs	Frozen, -80	INA (Behring)	Manufacturer
MALMO	1.6 (0.3 to 13.0)	Fasted / > 8 hrs	Plasma	>10 yrs	Frozen, -80	ITA (Roche Diagnostics)	Manufacturer
MONICAKORA	1.6 (0.2 to 9.5)	Non-fasted	Plasma	2 - 12 yrs	Frozen, -80	IRMA, INA (Dade Behring)	WHO 85/506
NHS	2.4 (0.3 to 15.2)	Fasted / NS	Plasma	5 - 10 yrs	Frozen, -130	ITA (Denka Seiken)	Manufacturer
NPHSII	2.6 (0.5 to 12.6)	Non-fasted	Serum	> 5 yrs	Frozen, -40	ELISA (Cordia)	Manufacturer
NSC	1.5 (0.3 to 9.2)	Fasted / 4-8 hrs	Plasma	> 5 yrs	Frozen, -80	CIA (Immulite)	WHO 85/506
PROCARDIS	1.2 (0.2 to 8.0)	Non-fasted	Plasma	5 - 10 yrs	Frozen, -80	INA (Dade Behring)	Manufacturer
PROMIS	2.3 (0.4 to 32.2)	Non-fasted	Serum	1 week - 1 yr	Frozen, -80	ELISA (Dako)	Manufacturer
PROSPER	3.1 (0.5 to 19.4)	Fasted / > 8 hrs	Plasma	1 - 5 yrs	Frozen, -80	ITA (Roche Diagnostics)	cFas calibrator
ROTTERDAM	1.8 (0.3 to 9.6)	Non-fasted	Serum	> 10 yrs	Frozen, -20	INA (Immage)	Manufacturer
SHEEP	1.2 (0.2 to 8.7)	Fasted / NS	Plasma	5 - 10 yrs	Frozen, -70	INA (Dade-Behring)	NS
SPEED	1.2 (0.2 to 8.2)	Fasted / > 8 hrs	Plasma	NS	Frozen, -20	INA (Behring)	WHO 85/506
WHIOS	1.7 (0.1 to 15.1)	Fasted / > 8 hrs	Plasma	< 10 yrs	Frozen, -70	ITA (Roche Diagnostics)	Manufacturer
WHITEII	0.8 (0.1 to 6.5)	Fasted / NS	Serum	> 10 yrs	Frozen, -80	INA (Behring)	Manufacturer
WOSCOPS	2.0 (0.3 to 10.4)	Fasted / > 8 hrs	Plasma	10 yrs	Frozen, -70	ELISA (In-house)	IFCC CRM470

CIA = chemiluminescence immunoassay; ELISA = enzyme-linked immunosorbent assay; INA = immunonephelometric assay; IRMA = immunoradiometric assay; ITA = immunoturbidimetry assay; WHO = World Health Organization; NS = not specified; Study acronyms are listed in appendix 2.

Table D Laboratory methods and quality control measures for measurement of CRP SNPs in 47 studies in the CCGC.

	Genetic analysis of C-reactive protein		Quality control		
Study	**DNA source/Type**	**Genotyping methods**	**Scrambling of cases and controls**	**Negative controls**	**Positive controls**
AGES	Whole blood/Native	Illumina 370CNV BeadChip array	✓	☐	☐
ARIC	Whole blood/Native	TaqMan	✓	☐	✓
BHF-FHS	Leukocyte DNA/Native	Multiplex	☐	☐	
BRHS	Whole blood/Native	TaqMan	✓	✓	✓
BWHHS	Whole blood/Native	Kbioscience	✓	✓	✓
CAPS	Whole blood/Native	Kbioscience	✓	✓	✓
CCHS	Whole blood/Native	TaqMan	✓	✓	NS
CGPS	Whole blood/Native	TaqMan	✓	✓	NS
CHAOS	Whole blood/Native	TaqMan	✓	✓	✓
CHS	Whole blood/Native	TaqMan	✓	✓	NS
CIHDS	Whole blood/Native	TaqMan	✓	✓	NS
CRPHANS	Whole blood/WGA	TaqMan	✓	✓	✓
CUDAS	Whole blood/Native	TaqMan	✓	✓	NS
CUPID	Whole blood/Native	TaqMan	✓	✓	NS
4D	Whole blood/Native	Illumina IBC 50K SNP array	☐	☐	☐
EAS	Whole blood/Native	TaqMan	✓	✓	✓
ELSA	Whole blood/Native	TaqMan	✓	✓	✓
EPICNL	Whole blood/Native	Illumina IBC 50K SNP array	☐	✓	✓
EPICNOR	Whole blood/Native	TaqMan	✓	✓	✓
FRAMOFF	Whole blood/Native	Multiplex	☐	☐	✓
GERMIFS	Whole blood/Native	Affymetrix 500K or 6.0 Chip	☐	☐	☐
GISSI-P	Whole blood/Native	TaqMan	✓	✓	✓
HEALTHABC	Whole blood/Native	Illumina Human 1-MDuo	✓	✓	✓
HIFMECH	Whole blood/Native	PCR / RFLP	✓	✓	NS
HIMS	Whole blood/Native	TaqMan	✓	✓	NS
HPFS	Whole blood/Native	TaqMan	✓	✓	NS
HVHS	Whole blood/Native	Illumina Golden Gate, Sequenom iPLEX	☐	☐	☐
INTERHEART	Whole blood/Native	Illumina Golden Gate, Sequenom iPLEX	✓	☐	☐
ISIS	Whole blood/Native	Taqman	✓	✓	✓
LOLIPOP	Whole blood/Native	Illumina IBC 50K SNP array	☐	☐	☐
LURIC	Whole blood/Native	Illumina IBC 50K SNP array	☐	☐	☐
MALMO	Granulocyte preparation/Native	Multiplex	✓	NS	NS
MONICAKORA	Whole blood/Native	Illumina IBC 50K SNP array	✓	☐	☐
NHS	Whole blood/Native	TaqMan	✓	✓	NS
NPHSII	Whole blood/Native	PCR / RFLP	✓	✓	NS
NSC	Whole blood/Native	TaqMan	✓	✓	✓
PENNCATH	Whole blood/Native	Illumina IBC 50K SNP array	☐	☐	☐
PROCARDIS	Whole blood/Native	Illumina IBC 50K SNP array	☐	☐	☐
PROMIS	Whole blood/Native	Illumina IBC 50K SNP array	☐	☐	☐
PROSPER	Whole blood/Native	TaqMan	✓	✓	☐
ROTTERDAM	Whole blood/Native	TaqMan	NS	✓	✓
SHEEP	Whole blood/Native	TaqMan	✓	✓	✓
SPEED	Whole blood/Native	Kbioscience	✓	✓	✓
UCP	Buccal swab (saliva) /Native	Illumina IBC 50K SNP array	✓	✓	✓
WHIOS	Whole blood/Native	Illumina IBC 50K SNP array	✓	✓	✓
WHITEII	Whole blood/Native	TaqMan, Geneservice	✓	✓	✓
WOSCOPS	Whole blood/Native	PCR / RFLP	☐	☐	☐

IBC = ITMAT-Broad-CARe; PCR = polymerase chain reaction; RFLP = restriction fragment length polymorphism; WGA = whole genome amplification; SNP = single nucleotide polymorphism; ✓ = Criterion included in quality control; ☐ = Criterion not included in quality control or not applicable. NS = not specified; Study acronyms are listed in appendix 2.

Table E. Characterisation of coronary disease outcomes in studies contributing to the CCGC.

	Definition of Endpoints				
	Death	Non-fatal MI			
Study		Clinical features	ECG	Cardiac markers	Coronary Stenosis[+]
AGES	***	✓	✓	✓	-
ARIC	***	✓	✓	✓	-
BHF-FHS	*	✓	✓	✓	>50%
BRHS	**	✓	✓	✓	-
BWHHS	***	✓	✓	✓	-
CAPS	***	✓	✓	-	-
CCHS	***	✓	✓	✓	-
CGPS	***	✓	✓	✓	-
CHAOS	*	✓	✓	✓	>50%
CHS	***	✓	✓	✓	-
CIHDS	***	✓	✓	✓	>50%
CRPHANS	***	✓	✓	✓	-
CUDAS	*	-[1]	-	-	-
CUPID	*	-[2]	-	-	-
4D	***	✓	✓	✓	-
EAS	***	✓	✓	✓	-
ELSA	*	-[3]	-	-	-
EPICNL	**	-[1]	-	-	-
EPICNOR	**	✓	✓	✓	-
FRAMOFF	***	✓	✓	✓	-
GERMIFS	*	✓	✓	✓	-
GISSI-P	*	✓	✓	✓	-
HEALTHABC	***	✓	✓	✓	-
HIFMECH	*	✓	✓	✓	-
HIMS	***	-[1]	-	-	-
HPFS	***	✓	✓	✓	-
HVHS	*	✓	✓	✓	-
INTERHEART	*	✓	✓	✓	-
ISIS	*	✓	✓	✓	-
LOLIPOP	*	✓	✓	✓	-
LURIC	***	✓	✓	✓	-
MALMO	***	✓	✓	✓	-
MONICAKORA	***	✓	✓	✓	-
NHS	***	✓	✓	✓	-
NPHSII	***	✓	✓	✓	-
NSC	***	✓	✓	✓	-
PENNCATH	*	-	✓	✓	>50%
PROCARDIS	*	✓	✓	✓	>50%
PROMIS	*	✓	✓	✓	-
PROSPER	***	✓	✓	✓	-
ROTTERDAM	***	✓	✓	✓	-
SHEEP	*	✓	✓	✓	-
SPEED	***	✓	✓	✓	-
UCP	*	-[1]	-	-	-
WHIOS	*	✓	✓	✓	-
WHITE2	**	✓	✓	✓	-
WOSCOPS	***	✓	✓	✓	-

*: Non-fatal events only; **: death certificate only; ***: death certificate supplemented by medical record
✓: Feature included in criteria; - : feature not included in criteria
[+] As determined by angiography, reported stenosis of at least 1 major coronary vessel
[1] Diagnosis obtained from hospital case records; [2] History of hospitalization with MI; [3] self-reported history of MI
Study acronyms are listed in appendix 2.

Table F. Association of CRP SNPs or haplotypes with CRP levels and categorical variables.

		Minor allele Frequency	Per allele or in comparison with reference haplotype % change in CRP (95% CI)	P-value for association with: Sex	Ethnicity	Diabetes mellitus	Smoking status	Alcohol consumption
SNPs								
	rs3093077	0.06	22.9% (19.0%, 27.0%)	0.854	$1.00x10^{-40}$	0.921	0.537	0.051
	rs1205	0.33	19.4% (17.4%, 21. 5%)	0.107	$4.41x10^{-21}$	0.685	0.005	0.017
	rs1130864	0.30	14.1% (12.5%, 15.8%)	0.973	$1.00x10^{-40}$	0.890	0.038	0.793
	rs1800947	0.06	29.9% (25.6%, 34.3%)	0.305	$1.25x10^{-30}$	0.903	0.679	0.960
Haplotypes								
(1)	T / C / T / G	0.30	Reference*	Ref	-	Ref	Ref	Ref
(2)	T / C / C / G	0.24	-9.3% (-10.8%, -7.8%)	0.703	-	0.682	0.820	0.428
(3)	G / C / C / G	0.05	10.9% (8.3%, 13.5%)	0.662	-	0.649	0.766	0.032
(4)	T / T / C / G	0.13	-17.7% (-19.3%, -16.1%)	0.524	-	0.094	0.048	0.420
(5)	T / T / C / C	0.03	-29.0% (-31.8%, -26.1%)	0.217	-	0.732	0.246	0.985
(6)	? / C / C / G	0.07	-6.7% (-10.4%, -2.9%)	0.532	-	0.391	0.049	0.324
(7)	T / T / C / ?	0.18	-17.9% (-20.1%, -15.7%)	0.189	-	0.211	0.049	0.104

* % change in CRP is shown per addition of each haplotype compared to 2 copies of reference haplotype 1.

Table G. Summary of data available on circulating biomarkers and associations with CRP levels.

	Summary of available data			Association with log_e CRP value
	No. of studies	No. of participants	Mean (SD) or %	Difference (95% CI) in log_e CRP levels per 1-SD increase or compared to reference category‡
Log_e CRP (mg/l)	35	111,158	0.62 (1.05)	
Age at survey (years)	35	111,158	60 (11)	0.16 (0.13 to 0.20)
Anthropometric markers				
Body Mass Index (kg/m2)	33	108,199	27 (4)	0.31 (0.28 to 0.34)
Height (cm)	31	103,730	170 (9)	-0.07 (-0.08 to -0.06)
Weight (kg)	30	101,440	76 (14)	0.28 (0.25 to 0.31)
Waist/hip ratio	20	85,204	0.90 (0.28)	0.91 (0.75 to 1.08)
Systolic Blood Pressure (mmHg)	33	108,054	138 (21)	0.12 (0.09 to 0.14)
Diastolic Blood Pressure (mmHg)	33	108,029	81 (11)	0.08 (0.06 to 0.11)
Lipid and metabolic markers				
Total cholesterol (mmol/l)	34	107,532	5.8 (1.1)	0.03 (0.01 to 0.05)
HDL cholesterol (mmol/l)	33	105,182	1.31 (0.44)	-0.26 (-0.29 to -0.23)
non-HDL cholesterol (mmol/l)	33	105,160	4.49 (1.11)	0.10 (0.08 to 0.12)
Apolipoprotein A-I (g/l)	16	71,404	1.49 (0.29)	-0.18 (-0.23 to -0.14)
Apolipoprotein B (g/l)	18	73,179	1.06 (0.31)	0.12 (0.09 to 0.16)
Log_e Triglycerides (mmol/l)	32	98,811	0.40 (0.52)	0.21 (0.18 to 0.23)
Fasting Glucose (mmol/l)	24	82,599	5.9 (1.6)	0.11 (0.09 to 0.13)
Inflammatory markers				
Fibrinogen (µmol/l)	25	82,885	9.7 (2.5)	0.67 (0.57 to 0.78)
Albumin (g/l)	9	22,467	43 (4)	-0.22 (-0.29 to -0.15)
Log_e interleukin 6 (ng/l)	13	22,148	0.73 (0.71)	0.54 (0.44 to 0.63)
Log_e leukocyte count (x10^9/l)	11	21,209	1.86 (0.27)	0.33 (0.30 to 0.37)
Categorical variables				
Sex	35	111,158		
Male	32	57,897	52%	Ref
Female	27	53,261	48%	0.09 (0.05 to 0.14)
Ethnicity	33	105,727		
White	33	107,304	97%	Ref
Black	8	1285	1%	0.42 (0.04 to 0.81)
Asian	5	1533	1%	-0.08 (-0.74 to 0.57)
Smoking status	35	109,551		
Not Current	35	96,979	89%	Ref
Current	32	12,572	11%	0.33 (0.28 to 0.37)
History of diabetes	35	108,469		
No	34	101,208	93%	Ref
Yes	34	7261	7%	0.31 (0.24 to 0.38)
Alcohol consumption	31	99,699		
Other	27	28,699	29%	
Current	27	7,1000	71%	-0.08 (-0.11 to -0.04)

‡ Difference in log_e CRP per 1 standard deviation (SD) increase in the row variable (or, for categorical variables, the difference in mean log_e CRP levels compared to the reference category) adjusted for sex and age. Study-specific estimates were combined using random effects meta-analysis. CI = confidence intervals; HDL = high density lipoprotein.

Table H. Subgroup analyses for associations between each SNP and CHD risk.

	rs3093077	rs1205	rs1130864	rs1800947
Individual-level characteristics	**P-value for interaction**			
Sex	0.303	0.152	0.402	0.507
Age at survey (yrs)	0.825	0.182	0.216	0.730
Smoking status (current vs. ex/never)	0.160	0.795	0.197	0.792
Alcohol status (Current vs. never)	0.311	0.876	0.715	0.754
History of diabetes (definite vs. other)	0.086	0.961	0.690	0.481
Ethnicity (white vs non-white)	0.500	0.961	0.616	0.931
Systolic BP (mmHg)	0.161	0.705	0.621	0.546
BMI (kg/m^2)	0.814	0.757	0.746	0.051
Non-HDL-C (mmol/l)	0.560	0.633	0.819	0.818
HDL-C (mmol/l)	0.470	0.885	0.076	0.896
Total cholesterol (mmol/l)	0.574	0.941	0.045	0.457
Log_e triglyceride (mmol/l)	0.999	0.241	0.637	0.174
Study-level characteristics	**Meta-regression P-value**			
Large vs. small studies (</> 500cases)	0.971	0.701	0.46	-*
Large vs. small studies (</> 1000 partic.)	0.272	0.78	0.418	-*
Study design	0.86	0.122	0.924	0.82
Geographical region	0.536	0.159	0.827	0.257
Population source	0.501	0.069	0.914	0.031
Year of baseline survey	0.33	0.1	0.862	0.201
Genotyping method	0.729	0.028	0.544	0.695
Negative controls used on assay plates	0.558	0.73	0.83	0.495
Scrambling of cases / controls	0.536	0.798	0.868	0.499
Strong vs. weak studies (F statistic >/< 10)	0.968	0.339	0.44	0.712
HWE P-value >/< 0.1	0.519	0.237	0.446	0.759

Continuous markers systolic blood pressure (BP), body mass index (BMI), non-high density lipoprotein cholesterol (HDL-C), HDL-C, total cholesterol and log_e triglyceride were assessed by comparing thirds of baseline levels; Age was divided into 3 groups, 40-59 years, 60-69 years and 70+ years. Studies were grouped by study design (cohort, individually matched case control, frequency matched case control and clinical trial), geographical region (Western Europe, North America, Other), population source (GP lists, hospital admissions / general population, household listings, population register, population screening), year of baseline survey (pre-1990, 1990-1995, 1996-2000 and post-2000), genotyping methods (TaqMan, KBioscience, Illumina IBC 50K SNP array, PCR/RFLP, other multiplex methods), use of negative controls (ie, blank spaces) on assay plates, scrambling of cases and controls on assay plates, Hardy Weinberg Equilibrium P-value more than or less than 0.1 and strength of each SNP as an instrument of CRP (as depicted by the F-statistic). *Insufficient data were available on subgroups of characteristic to estimate interaction with rs1800947.

Table I. Risk ratios for CHD per 1-SD higher $\log_e$ CRP progressively adjusted for conventional and novel vascular risk factors.

	No studies	No participants	No cases	RR (95% CI)	Wald X^2_1
Adjusted for age, sex and trial arm	13	56,411	3274	1.63 (1.52, 1.74)	212
...Plus conventional risk factors	13	56,411	3274	1.28 (1.18, 1.38)	37
...Plus fibrinogen	13	56,411	3274	1.22 (1.11, 1.33)	17
Adjusted for age, sex and trial arm	7	9327	1392	1.61 (1.36, 1.91)	30
...Plus conventional risk factors	7	9327	1392	1.35 (1.19, 1.54)	21
...Plus $\log_e$ interleukin-6	7	9327	1392	1.03 (0.85, 1.24)	0.1

RR = risk ratio; CI = confidence interval; Analyses were based on usual levels of circulating $\log_e$ CRP and baseline levels of confounders; Conventional vascular risk factors adjusted for in model include: systolic blood pressure, smoking status, history of diabetes mellitus, BMI, HDL-C, non-HDL-C and $\log_e$ triglyceride levels.