

Supplemental Data

Psoriasis and cardiometabolic traits: modest association but distinct genetic architectures

Manja Koch¹, PhD; Hansjörg Baurecht², MSc; Janina S. Ried³, PhD; Elke Rodriguez², PhD; Sabrina Schlesinger¹, PhD; Natalie Volks, MD²; Christian Gieger^{4,5}, PhD; Ina-Maria Rückert⁴, PhD; Luise Heinrich⁶, MSc; Christina Willenborg, PhD⁷; Catherine Smith⁸, MD; Annette Peters⁴, PhD; Barbara Thorand⁴, PhD; Wolfgang Koenig⁹, MD; Claudia Lamina¹⁰, PhD; Henning Jansen¹¹, PhD; Florian Kronenberg¹⁰, MD; Jochen Seissler¹², MD; Joachim Thiery¹³, MD; Wolfgang Rathmann¹⁴, MD; Heribert Schunkert¹¹, MD; Jeanette Erdmann⁷, PhD; Jonathan Barker⁸, MD; Rajan P Nair¹⁵, PhD; Lam C Tsoi¹⁶, PhD; James T Elder^{15,17}, MD; Ulrich Mrowietz², MD; Michael Weichenthal², MD; Sören Mucha¹⁸, MSc; Stefan Schreiber^{18,19}, MD; Andre Franke¹⁸, PhD; Jochen Schmitt^{*6}, MD, Wolfgang Lieb^{*1}, MD, MSc; Stephan Weidinger^{*2}, MD

* denotes equal contribution

¹Institute of Epidemiology, Christian-Albrechts University Kiel, Kiel, Germany.

²Department of Dermatology, Allergology, and Venerology, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany.

³Institute of Genetic Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.

⁴Institute of Epidemiology II, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.

⁵Research Unit of Molecular Epidemiology, Helmholtz Zentrum München- German Research Center for Environmental Health, Neuherberg, Germany

⁶Center for Evidence-Based Healthcare, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany.

⁷Institute for Integrative und Experimental Genomics and DZHK (German Research Centre for Cardiovascular Research), partner site Hamburg/Lübeck/Kiel, University Hospital Schleswig-Holstein, Campus Lübeck, Germany.

⁸St John's Institute of Dermatology, Division of Genetics and Molecular Medicine, Kings College London.

⁹Department of Internal Medicine II-Cardiology, University of Ulm Medical Center, Ulm, Germany.

¹⁰Division of Genetic Epidemiology, Department of Medical Genetics, Molecular and Clinical Pharmacology, Innsbruck Medical University, Schoepfstr. 41, A-6020 Innsbruck, Austria.

¹¹Deutsches Herzzentrum Munich, Technische Universität Munich, Munich, Germany.

¹²Medizinische Klinik und Poliklinik IV, Diabetes Zentrum, Klinikum der Ludwig-Maximilians-Universität, Munich, Germany.

¹³Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, University Hospital Leipzig, Leipzig, Germany.

¹⁴German Diabetes Center, Leibniz Institute at Heinrich Heine University Düsseldorf, Institute of Biometrics and Epidemiology, Düsseldorf, Germany.

¹⁵Department of Dermatology, University of Michigan Medical School, Ann Arbor, Michigan, USA

¹⁶Department of Biostatistics, Center for Statistical Genetics, University of Michigan, Ann Arbor, Michigan, USA

¹⁷Ann-Arbor Veteran Affairs Hospital, Ann Arbor, MI, USA

¹⁸Institute of Clinical Molecular Biology, Christian-Albrechts-University of Kiel, Kiel, Germany.

¹⁹Department of Internal Medicine I, University Medical Center Schleswig-Holstein, Kiel, Germany

Table S1. Multivariable-adjusted beta coefficient for waist circumference and OR (95% confidence interval in parentheses) for type 2 diabetes or myocardial infarction per increment of predictor variables (n=4,180).

Table S2. Multivariable-adjusted Risk Ratios (RR; 95% confidence interval in parentheses) for cardiometabolic diseases per increment of predictor variables (n= 1,811,098)¹.

Table S3: Systemic Therapies received by psoriasis patients of the longitudinal cohort in 2005/2006.

Table S4: Association of known CAD SNPs with psoriasis in psoriasis GWAS cohorts.

Table S5: Association of known psoriasis SNPs with CAD in the Coronary Artery Disease Genome-Wide Replication And Meta-Analysis (CARDIoGRAM).

Table S6: Cardiometabolic susceptibility loci (MetaboChip analysis) associated with psoriasis at a genome-wide significance level.

Table S7: SNPs with suggestive evidence ($P < 5 \times 10^{-6}$) for association with psoriasis from the MetaboChip analysis.

Table S8: Results from the MetaboChip analysis for established psoriasis loci (GWASCatalog 2013-01).

Figure S1: Forest plot displaying the associations of each psoriasis single nucleotide polymorphism (SNP) with coronary artery disease (CAD) in the Coronary Artery Disease Genome-Wide Replication And Meta-Analysis (CARDIoGRAM).

Supplementary Methods

Table S1. Multivariable-adjusted beta coefficient for waist circumference and OR (95% confidence interval in parentheses) for type 2 diabetes or myocardial infarction per increment of predictor variables (n=4,185)¹.

Predictor variables	Outcome variable					
	Change in waist circumference; Beta Coefficient (95% CI)		OR (95% CI) for type 2 diabetes		OR (95% CI) for myocardial infarction	
	Model 1 ²	Model 2 ³	Model 1	Model 2 ⁴	Model 1	Model 2 ⁴
Psoriasis (yes as compared to no)	2.03 (0.36, 3.70)	1.70 (0.14, 3.26)	2.31 (1.41, 3.80)	2.37 (1.40, 4.02)	2.29 (1.17, 4.46)	2.26 (1.03, 4.96)
Sex (Female as compared to male)	-11.65 (-12.36, -10.93)	-10.38 (-11.13, -9.62)	0.76 (0.58, 1.01)	0.77 (0.56, 1.08)	0.36 (0.23, 0.55)	0.28 (0.17, 0.48)
Age (per 1-unit increase)	0.30 (0.27, 0.33)	0.09 (0.05, 0.12)	1.08 (1.07, 1.09)	1.05 (1.03, 1.06)	1.09 (1.07, 1.11)	1.03 (1.01, 1.06)
Smoking status						
Former (as compared to never)	1.68 (0.88, 2.49)	1.53 (0.77, 2.28)	1.28 (0.94, 1.75)	1.28 (0.92, 1.78)	1.85 (1.18, 2.90)	1.70 (1.04, 2.78)
Current (as compared to never)	0.19 (-0.83, 1.21)	-0.02 (-0.99, 0.95)	1.50 (0.95, 2.37)	1.63 (1.01, 2.63)	1.96 (1.01, 3.83)	2.23 (1.07, 4.65)
Years of Education						
10 y (as compared to ≤9 y)	-3.00 (-3.88, -2.12) ³	-2.59 (-3.43, -1.76)	0.66 (0.45, 0.87)	0.70 (0.47, 0.93)	0.60 (0.34, 0.86)	0.63 (0.34, 0.92)

			0.97) ⁴	1.04)	1.05) ⁴	1.14)
≥11 y (as compared to ≤9 y)	-4.37 (-5.28, -3.46) ³	-3.55 (-4.42, -2.67)	0.73 (0.49, 1.08) ⁴	0.83 (0.55, 1.26)	0.50 (0.28, 0.90) ⁴	0.50 (0.27, 0.95)
Alcohol intake (per 1 unit increase)	0.01 (-0.01, 0.03)	0.01 (-0.01, 0.03)	0.99 (0.98, 1.00) ⁴	0.99 (0.98, 1.00)	0.98 (0.97, 0.99)	0.98 (0.97, 0.99)
Physical activity						
Low activity (as compared to no activity)	0.14 (-1.09, 1.37)	0.80 (-0.37, 1.97)	1.04 (0.67, 1.62)	1.08 (0.68, 1.71)	0.67 (0.33, 1.37)	0.70 (0.33, 1.50)
Moderate activity (as compared to no activity)	-2.05 (-2.99, -1.10)	-1.20 (-2.10, -0.30)	0.80 (0.57, 1.11)	0.87 (0.62, 1.23)	0.73 (0.45, 1.17)	0.78 (0.47, 1.31)
High activity (as compared to no activity)	-4.77 (-5.80, -3.73)	-3.55 (-4.54, -2.56)	0.39 (0.25, 0.61)	0.41 (0.26, 0.66)	0.65 (0.38, 1.12)	0.74 (0.41, 1.34)
Systolic blood pressure (per 1-unit increase)	0.11 (0.09, 0.13)	0.09 (0.07, 0.11)	1.01 (1.01, 1.02)	1.01 (1.01, 1.02)	0.99 (0.98, 1.00)	0.99 (0.98, 1.00)
Hypertension treatment (yes as compared to no)	7.36 (6.49, 8.22)	6.54 (5.66, 7.41)	3.94 (2.81, 5.54)	2.95 (2.07, 4.20)	15.80 (7.85, 31.78)	8.34 (4.04, 17.20)
Type 2 diabetes (yes as compared to no)	7.43 (5.84, 9.01)	2.25 (-1.10, 5.59)	NA	NA	2.57 (1.57, 4.20)	0.57 (0.10, 3.14)
Type 2 diabetes treatment (yes as	8.15 (6.40, 9.90)	3.06 (-0.61, 6.74)	NA	NA	2.82 (1.69, 4.71)	2.11 (0.36,

compared to no)						12.22)
Lipid-lowering treatment (yes as compared	1.64 (0.49, 2.79)	-0.74 (-1.86, 0.38)	3.30 (2.45,	2.67 (1.94,	12.59 (8.15,	8.00 (5.08,
to no)			4.44)	3.66)	19.45)	12.59)

¹Model 1 was adjusted for sex and age (continuous). Model 2 was mutually adjusted for psoriasis (no, yes), sex, age (continuous), smoking status (never, former, current), years of education (≤ 9 y, 10 y, or ≥ 11 y), alcohol intake (continuous), physical activity (no activity, low activity, moderate activity, high activity), systolic blood pressure (continuous), hypertension treatment (no, yes), type 2 diabetes (no, yes; except type 2 diabetes), type 2 diabetes treatment (no, yes; except type 2 diabetes), lipid-lowering treatment (no, yes). ²n=4173. ³n=4168. ⁴n=4180.

Table S2. Multivariable-adjusted Risk Ratios (RR; 95% confidence interval in parentheses) for cardiometabolic diseases per increment of predictor variables (n= 1,811,098)¹.

	RR (95%CI)	
	Model 1	Model 2
Type 2 diabetes 2007-2012²		
Psoriasis (yes as compared to no)	1.21 (1.18, 1.25)	1.11 (1.08, 1.14)
Psoriasis, no medication (as compared to no psoriasis)	1.16 (1.08, 1.23)	1.06 (0.99, 1.13)
Psoriasis, exclusively topical medication (as compared to no psoriasis)	1.21 (1.17, 1.25)	1.10 (1.07, 1.14)
Psoriasis, systemic medication (as compared to no psoriasis)	1.38 (1.26, 1.51)	1.25 (1.14, 1.37)
Sex (male as compared to female)	1.24 (1.23, 1.25)	1.30 (1.29, 1.32)
Age (per 1-unit increase)	1.04 (1.04, 1.04)	1.03 (1.03, 1.03)
Obesity (yes as compared to no)	2.41 (2.38, 2.44)	2.03 (2.01, 2.06)
Disorders of lipoprotein metabolism and other lipidaemias (yes as compared to no)	1.42 (1.40, 1.44)	1.19 (1.17, 1.20)
Hypertension (yes as compared to no)	1.93 (1.90, 1.96)	1.65 (1.63, 1.67)
Myocardial infarction 2007-2012³		
Psoriasis (yes as compared to no)	1.24 (1.15, 1.33)	1.14 (1.06, 1.22)
Psoriasis, no medication (as compared to no psoriasis)	1.10 (0.94, 1.30)	1.01 (0.86, 1.19)

Psoriasis, exclusively topical medication (as compared to no psoriasis)	1.23 (1.14, 1.34)	1.13 (1.05, 1.23)
Psoriasis, systemic medication (as compared to no psoriasis)	1.62 (1.30, 2.01)	1.48 (1.19, 1.84)
Sex (male as compared to female)	2.61 (2.54, 2.69)	2.58 (2.51, 2.65)
Age (per 1-unit increase)	1.05 (1.05, 1.05)	1.04 (1.04, 1.04)
Obesity (yes as compared to no)	1.43 (1.38, 1.48)	1.12 (1.07, 1.16)
Disorders of lipoprotein metabolism and other lipidaemias (yes as compared to no)	1.82 (1.77, 1.87)	1.63 (1.59, 1.68)
Type 2 diabetes (yes as compared to no)	1.55 (1.51, 1.60)	1.35 (1.31, 1.39)
Hypertension (yes as compared to no)	1.62 (1.57, 1.68)	1.33 (1.29, 1.38)

Angina pectoris 2007-2012⁴

Psoriasis (yes as compared to no)	1.38 (1.30, 1.45)	1.27 (1.20, 1.34)
Psoriasis, no medication (as compared to no psoriasis)	1.29 (1.14, 1.46)	1.17 (1.04, 1.33)
Psoriasis, exclusively topical medication (as compared to no psoriasis)	1.38 (1.29, 1.47)	1.28 (1.20, 1.36)
Psoriasis, systemic medication (as compared to no psoriasis)	1.57 (1.32, 1.86)	1.43 (1.21, 1.70)
Sex (male as compared to female)	1.38 (1.35, 1.41)	1.37 (1.34, 1.40)
Age (per 1-unit increase)	1.04 (1.04, 1.04)	1.03 (1.03, 1.03)
Obesity (yes as compared to no)	1.56 (1.51, 1.60)	1.27 (1.23, 1.31)

Disorders of lipoprotein metabolism and other lipidaemias (yes as compared to no)	1.87 (1.83, 1.91)	1.67 (1.63, 1.71)
Type 2 diabetes (yes as compared to no)	1.15 (1.12, 1.18)	0.95 (0.93, 0.98)
Hypertension (yes as compared to no)	1.78 (1.73, 1.83)	1.52 (1.48, 1.56)

Stroke 2007-2012⁵

Psoriasis (yes as compared to no)	1.17 (1.11, 1.23)	1.11 (1.06, 1.17)
Psoriasis, no medication (as compared to no psoriasis)	1.10 (0.99, 1.24)	1.05 (0.94, 1.18)
Psoriasis, exclusively topical medication (as compared to no psoriasis)	1.19 (1.12, 1.26)	1.13 (1.07, 1.20)
Psoriasis, systemic medication (as compared to no psoriasis)	1.14 (0.95, 1.36)	1.08 (0.90, 1.29)
Sex (male as compared to female)	1.33 (1.31, 1.36)	1.32 (1.30, 1.35)
Age (per 1-unit increase)	1.06 (1.06, 1.06)	1.06 (1.06, 1.06)
Obesity (yes as compared to no)	1.23 (1.19, 1.26)	1.04 (1.01, 1.07)
Disorders of lipoprotein metabolism and other lipidaemias (yes as compared to no)	1.24 (1.22, 1.27)	1.13 (1.11, 1.16)
Type 2 diabetes (yes as compared to no)	1.43 (1.40, 1.46)	1.33 (1.30, 1.35)
Hypertension (yes as compared to no)	1.45 (1.42, 1.49)	1.33 (1.30, 1.36)

¹Model was adjusted for sex and age (continuous). Model 2 was mutually adjusted for psoriasis (no, yes), sex, age (continuous), hypertension (no, yes); type 2 diabetes (no, yes; except for outcome type 2 diabetes); obesity and disorders of lipoprotein metabolism and other lipidaemias (no, yes).

²n=1,514,541. ³n=1,773,833. ⁴n=1,715,269. ⁵n=1,746,355.

Table S3: Systemic Therapies received by Psoriasis Patients of the longitudinal cohort in 2005/2006.

Systemic Therapy 2005/2006	No. of Patients with Psoriasis	% of Patients with Psoriasis (n= 44,623)	% of Patients with Psoriasis and Systemic Therapy (n=4,271)
UV Therapy	2,127	4.8%	49.8%
Adalimumab	84	0.2%	2.0%
Etanercept	125	0.3%	2.9%
Infliximab	42	0.1%	1.0%
Acitretin	232	0.5%	5.4%
Cyclosporine	124	0.3%	2.9%
Fumaric Acid	801	1.8%	18.8%
Methotrexate	1,324	3.0%	31.0%

Table S4. Association of known CAD SNPs (CARDIoGRAM & GWASCatalog 2013-01) with psoriasis in psoriasis GWAS cohorts.

SNP	CHR	POS	EA/OA	Effect Allele Freq	OR (95% CI) for psoriasis	P value	Direction	Gene
rs11206510	1	55496039	T/C	0.8115	0.988 (0.919-1.062)	0.745	++	PCSK9
rs17114036	1	56962821	A/G	0.9126	1.105 (0.998-1.224)	0.05414	+++	PPAP2B
rs12740374	1	109817590	T/G	0.2229	0.994 (0.929-1.064)	0.8667	+/-	CELSR2
rs646776	1	109818530	T/C	0.7765	1.004 (0.938-1.075)	0.9009	++	CELSR2
rs599839	1	109822166	A/G	0.7685	1.002 (0.935-1.074)	0.9492	++	SORT1
rs4845625	1	154422067	T/C	0.4281	1.034 (0.976-1.095)	0.2563	+++	IL6R
rs17465637	1	222823529	A/C	0.2881	0.992 (0.924-1.065)	0.8203	++	MIA3
rs2123536	2	19945577	T/C	0.0512	1.014 (0.888-1.158)	0.8395	++	TTC32-WDR35
rs515135	2	21286057	T/C	0.1806	1.008 (0.934-1.086)	0.845	++	APOB
rs6544713	2	44073881	T/C	0.3173	0.991 (0.932-1.054)	0.7697	+-	ABCG5-ABCG8
rs1561198	2	85809989	T/C	0.4592	1.019 (0.963-1.079)	0.5054	++	VAMP5-VAMP8-GGCX
rs2252641	2	145801461	T/C	0.5513	1.041 (0.984-1.103)	0.1626	+++	ZEB2-AC074093.1
rs6725887	2	203745885	T/C	0.8683	0.953 (0.864-1.051)	0.3322	-?+	WDR12
rs2306374	3	138119952	T/C	0.843	0.992 (0.905-1.087)	0.8624	+?-	MRAS
rs9818870	3	138122122	T/C	0.154	1.006 (0.929-1.089)	0.8915	++	MRAS
rs1878406	4	148393664	T/C	0.1402	0.982 (0.905-1.067)	0.669	---	EDNRA
rs1842896	4	156511459	T/G	0.5261	0.962 (0.908-1.019)	0.1894	++	MTND1P22-GUCY1A3
rs7692387	4	156635309	A/G	0.1884	0.979 (0.91-1.053)	0.5649	+/-	GUCY1A3
rs273909	5	131667353	A/G	0.8874	1.074 (0.966-1.194)	0.1879	+?-	SLC22A4-SLC22A5
rs6903956	6	11774583	A/G	0.3807	1.042 (0.982-1.106)	0.1759	++	C6orf105
rs9349379	6	12903957	A/G	0.6005	0.934 (0.873-1)	0.05082	-?-	PHACTR1
rs2894181 ¹	6	31174527	A/G	0.5615	1.413(1.318-1.514)	1.58x10 ⁻²²	+?+	HLA-C, HLA-B, HCG27
rs6932542 ²	6	32380262	A/G	0.547	1.488(1.389-1.595)	1.51x10 ⁻²⁹	-?-	BTNL2
rs12190287	6	134214525	C/G	0.6227	0.994 (0.934-1.059)	0.8622	++	TCF21
rs6922269	6	151252985	A/G	0.267	0.99 (0.928-1.056)	0.7554	++	MTHFD1L
rs2023938	7	19036775	T/C	0.9029	1.013 (0.906-1.134)	0.8146	-?+	HDAC9

rs10953541	7	107244545	T/C	0.2501	0.966 (0.904-1.031)	0.2982	---	BCAP29
rs11556924	7	129663496	T/C	0.3723	1.054 (0.943-1.177)	0.3526	?+?	ZC3HC1
rs6601299	8	9184691	T/C	0.0955	1.033 (0.938-1.138)	0.5136	++	LOC157273
rs264	8	19813180	A/G	0.1384	0.942 (0.866-1.026)	0.1697	---	LPL
rs2954029	8	126490972	A/T	0.5328	0.993 (0.938-1.051)	0.802	+-	TRIB1
rs7865618	9	22031005	A/G	0.5734	1.021 (0.917-1.138)	0.7028	?+?	CDKN2B-AS1
rs10757274	9	22096055	A/G	0.5111	0.965 (0.909-1.023)	0.2339	---	CDKN2B-AS1
rs4977574	9	22098574	A/G	0.511	0.961 (0.906-1.02)	0.1936	---	CDKN2B-AS1
rs944797	9	22115286	T/C	0.4937	0.96 (0.904-1.019)	0.179	---	CDKN2B-AS1
rs1333049	9	22125503	C/G	0.4761	1.024 (0.963-1.089)	0.449	+++	CDKN2A,CDKN2B
rs514659	9	136142203	A/C	0.6609	0.961 (0.905-1.02)	0.1914	---	ABO
rs579459	9	136154168	T/C	0.7834	0.946 (0.883-1.014)	0.1171	---	ABO
rs3739998	10	30316072	C/G	0.5681	0.999 (0.944-1.058)	0.9812	--+	KIAA1462
rs2505083	10	30335122	T/C	0.5727	0.989 (0.932-1.049)	0.7042	--+	KIAA1462
rs1746048	10	44775824	T/C	0.1317	0.93 (0.854-1.012)	0.0919	---	CXCL12
rs1412444	10	91002927	T/C	0.3374	1.019 (0.959-1.082)	0.5436	+++	LIPA
rs12413409	10	104719096	A/G	0.0862	0.944 (0.853-1.045)	0.2672	--+	CYP17A1,CNNM2,NT5C2
rs974819	11	103660567	T/C	0.2911	1.027 (0.965-1.093)	0.4104	++	PDGFD
rs964184	11	116648917	C/G	0.8648	1.035 (0.951-1.126)	0.4249	+++	ZNF259,APOA5-A4-C3-A1
rs7136259	12	90081188	T/C	0.4262	0.987 (0.931-1.047)	0.6755	+-	ATP2B1
rs3782889	12	111350655	A/G	0.9309	1.017 (0.891-1.16)	0.8033	+?-	MYL2
rs9319428	13	28973621	A/G	0.2954	1.004 (0.943-1.069)	0.9061	++	FLT1
rs4773144	13	110960712	A/G	0.5735	1.026 (0.965-1.091)	0.4045	+-	COL4A1,COL4A2
rs2895811	14	100133942	T/C	0.5754	0.985 (0.931-1.043)	0.6145	---	HHIPL1
rs1994016	15	79080234	T/C	0.4119	0.987 (0.93-1.048)	0.6712	+-	ADAMTS7
rs3825807	15	79089111	A/G	0.5603	1.006 (0.95-1.066)	0.8336	++	ADAMTS7
rs4380028	15	79111093	T/C	0.4003	0.985 (0.928-1.046)	0.6265	+-	ADAMTS7-RPL21P116
rs17514846	15	91416550	A/C	0.4664	0.995 (0.936-1.059)	0.8851	--+	FURIN-FES
rs1231206	17	2125605	A/G	0.3461	1.01 (0.952-1.072)	0.7422	++	SMG6
rs216172	17	2126504	C/G	0.3463	1.01 (0.951-1.072)	0.7492	++	SMG6, SRR

rs12936587	17	17543722	A/G	0.4611	0.994 (0.938-1.054)	0.8441	--+	RASD1,SMCR3,PEMT
rs46522	17	46988597	T/C	0.5294	1.03 (0.973-1.09)	0.3146	+-	UBE2Z,GIP,ATP5G1,SNF8
rs2075650	19	45395619	A/G	0.8542	0.985 (0.905-1.072)	0.7294	+-	APOE/TOMM40

¹rs2894181 is a proxy SNP for the CAD SNP rs3869109 ($r^2=0.736$ HapMap V3 release 27). The major allele of both SNPs increase the risk for CAD and psoriasis.

²rs6932542 is a proxy SNP for the CAD SNP rs9268402 ($r^2=0.659$ HapMap V3 release 27). The major allele of both SNPs increase the risk for CAD and psoriasis.

Abbreviations: OR, odds ratio; CI, confidence interval; SNP single nucleotide polymorphism. Effect directions are given for the 3 psoriasis studies included in the meta-analysis.

Table S5. Association of known psoriasis SNPs with CAD in the Coronary Artery Disease Genome-Wide Replication And Meta-Analysis (CARDIoGRAM).

SNP	CHR	POS	EA/OA	Effect Allele Freq	OR (95% CI) for CAD	P value	Gene
rs11121129	1	8268095	A/G	0.312	1.018(0.988-1.049)	0.24318	SLC45A1,TNFRSF9
rs7667	1	19718824	A/G	0.343	1.029(1.000-1.059)	0.04979	CAPZB
rs7552167	1	24518643	G/A	0.874	0.987(0.939-1.038)	0.61123	IL28RA
rs4649203	1	24519920	A/G	0.714	1.000(0.954-1.047)	0.98851	IL28RA
rs7536201	1	25293084	NA	NA	NA	NA	RUNX3
rs2201841	1	67694202	G/A	0.309	0.995(0.966-1.025)	0.73119	IL23R
rs11209026	1	67705958	G/A	0.909	1.040(0.982-1.101)	0.18466	IL23R
rs4085613	1	152550018	T/G	0.332	1.025(0.996-1.056)	0.09067	LCE3D,LCE3A
rs4112788	1	152551276	G/A	0.659	0.975(0.947-1.004)	0.09032	LCE3D
rs702873	2	61081542	C/T	0.576	1.002(0.975-1.030)	0.90074	REL
rs842636	2	61091950	G/A	0.568	1.000(0.973-1.028)	0.9962	NR
rs10865331	2	62551472	A/G	0.386	0.993(0.966-1.021)	0.61057	B3GNT2
rs17716942	2	163260691	T/C	0.864	1.057(1.012-1.105)	0.01276	IFIH1
rs6809854	3	18784423	G/A	0.179	1.019(0.983-1.056)	0.31118	Intergenic
rs1386478	3	113680951	A/G	0.731	0.990(0.960-1.021)	0.52654	ZDHHC23
rs27524	5	96101944	A/G	0.379	0.981(0.953-1.009)	0.17253	ERAP1
rs20541	5	131995964	G/A	0.792	1.018(0.984-1.054)	0.30554	IL13
rs17728338	5	150478318	A/G	0.089	1.052(0.993-1.113)	0.08479	TNIP1
rs2082412	5	158717789	G/A	0.791	1.004(0.970-1.038)	0.83254	IL12B
rs2546890	5	158759900	A/G	0.545	0.996(0.966-1.027)	0.79886	IL12B
rs12188300	5	158829527	T/A	0.084	1.026(0.971-1.085)	0.36263	IL12B
rs9504361	6	577820	A/G	0.542	1.007(0.979-1.035)	0.62986	EXOC2, IRF4
rs1265181	6	31155785	G/C	0.778	1.058(1.022-1.095)	0.00132	MHC
rs12191877	6	31252925	T/C	0.134	0.941(0.903-0.980)	0.00363	HLA-C
rs10484554	6	31274555	T/C	0.132	0.935(0.897-0.975)	0.00162	HLA-C

rs3134792	6	31312326	T/G	0.866	1.029(0.977-1.084)	0.28041	HLA-C
rs2395029	6	31431780	G/T	0.072	0.947(0.882-1.018)	0.14039	HLA-C
rs465969	6	111655530	G/A	0.882	0.991(0.944-1.040)	0.70507	REV3L
rs240993	6	111673714	T/C	0.271	1.027(0.996-1.059)	0.08786	TRAF3IP2
rs33980500	6	111913262	NA	NA	NA	NA	TRAF3IP2
rs610604	6	138199417	G/T	0.315	1.022(0.992-1.053)	0.16035	TNFAIP3
rs2451258	6	159506600	T/C	0.62	0.995(0.964-1.027)	0.74364	TAGAP
rs2700987	7	37386237	NA	NA	NA	NA	ELMO1
rs11795343	9	32523737	T/C	0.587	1.011(0.983-1.039)	0.4536	DDX58
rs10979182	9	110817020	A/G	0.566	0.979(0.952-1.006)	0.12773	KLF4
rs1076160	9	135776034	T/C	0.516	1.003(0.976-1.031)	0.84455	TSC1
rs1250544	10	81032885	G/A	0.622	0.973(0.945-1.003)	0.07432	ZMIZ1
rs4561177	11	109962432	A/G	0.582	0.986(0.959-1.014)	0.31664	ZC3H12C
rs3802826	11	128406438	NA	NA	NA	NA	ETS1
rs12580100	12	56439209	A/G	0.886	1.063(0.997-1.132)	0.06101	RPS26
rs2066808	12	56737973	A/G	0.924	1.047(0.993-1.104)	0.08791	IL23A
rs7993214	13	40350912	C/T	0.667	0.981(0.953-1.010)	0.20086	COG6
rs12586317	14	35682172	NA	NA	NA	NA	NFKBIA,PSMA6
rs8016947	14	35832666	G/T	0.559	1.000(0.972-1.028)	0.97265	NFKBIA
rs4780355	16	11347858	T/C	0.707	1.001(0.971-1.033)	0.92454	SOCS1
rs10782001	16	30942625	G/A	0.345	0.994(0.966-1.023)	0.67324	FBXL19,POL3S
rs1975974	17	21707060	G/A	0.212	1.005(0.971-1.040)	0.78707	NR
rs4795067	17	26106675	G/A	0.359	1.009(0.979-1.039)	0.57251	NOS2
rs963986	17	40561579	C/G	0.188	1.027(0.990-1.066)	0.15581	PTRF, STAT3,STAT5A/B
rs11652075	17	78178893	C/T	0.487	0.992(0.961-1.024)	0.61135	CARD14
rs545979	18	51819750	T/C	0.314	1.024(0.994-1.055)	0.11432	POL1, STARD6, MBD2
rs12720356	19	10469975	A/C	0.931	1.021(0.941-1.108)	0.61974	TYK2
rs280519	19	10472933	A/G	0.494	1.031(0.991-1.072)	0.12591	TYK2
rs892085	19	10818092	A/G	0.608	1.048(1.018-1.079)	0.00174	ILF3,CARM1
rs1008953	20	43980726	C/T	0.761	1.025(0.992-1.059)	0.13167	SDC4

rs495337	20	48522330	G/A	0.583	1.003(0.973-1.034)	0.85114	SPATA2
rs4821124	22	21979289	C/T	0.219	1.001(0.968-1.036)	0.94084	UBE2L3

Table S6. Cardiometabolic susceptibility loci (MetaboChip analysis) associated with psoriasis at a genome-wide significance level.¹

SNP	Chr	Position (hg18)	EA/OA	EAF	Effect	se (effect)	P value	R ²	Next Reference Gene
rs10484554	6	31382534	T/C	0.183	0.706	0.087	5.84E-16	1	HLA-C
rs4406273	6	31374069	A/G	0.121	0.841	0.113	8.57E-14	0.61	NA
rs9468929	6	31371195	A/G	0.195	0.618	0.086	5.51E-13	0.93	HLA-C
rs2245822	6	31338779	A/G	0.280	0.623	0.087	6.99E-13	0.57	HLA-C
rs9468928	6	31371022	G/A	0.239	0.458	0.075	8.52E-10	0.71	NA
rs28894987	6	31372281	C/A	0.237	0.451	0.075	1.56E-09	0.71	NA
rs2249742	6	31348700	T/C	0.495	0.434	0.072	1.68E-09	0.22	HLA-C
rs13437082	6	31462539	T/C	0.277	0.371	0.063	4.36E-09	0.06	HLA-B
rs4711268	6	31462483	T/C	0.277	0.369	0.063	5.32E-09	0.06	HLA-B
rs10947207	6	31469464	C/T	0.276	0.368	0.063	6.60E-09	0.06	HLA-B
rs6909321	6	31201169	A/G	0.138	0.597	0.103	7.20E-09	0.46	NA
rs3778639	6	31201755	G/A	0.140	0.584	0.101	7.48E-09	0.45	CDSN
rs887468	6	31249502	A/G	0.303	0.492	0.085	8.42E-09	0.48	POU5F1
rs4711269	6	31462798	T/C	0.278	0.363	0.063	8.62E-09	0.06	HLA-B
rs9501106	6	31496088	A/G	0.166	0.420	0.074	1.13E-08	0.16	HCP5
rs6932730	6	31462161	C/T	0.209	0.393	0.069	1.30E-08	0.12	HLA-B
rs2853926	6	31371030	C/T	0.281	0.400	0.071	1.56E-08	0.57	HLA-C
rs9469003	6	31515807	C/T	0.166	0.412	0.073	2.04E-08	0.16	HCP5
rs2596480	6	31533964	A/G	0.061	-0.719	0.129	2.61E-08	0.01	HCP5
rs6923313	6	31349349	C/T	0.408	0.391	0.071	3.14E-08	0.31	HLA-C
rs3094584	6	31491827	T/C	0.141	-0.478	0.087	3.97E-08	0.03	HCP5

Abbreviations: Chr, chromosome; EA, effect allele; EAF, effect allele frequency; OA, other allele.

¹For each SNP the LD (R²) to the SNP with the lowest p-value (rs10484554) is given.

Table S7. SNPs with suggestive evidence ($P < 5 \times 10^{-6}$) for association with psoriasis from the MetaboChip analysis.

SNP	Chr	Pos	EA/OA	EAF	OR	beta (SE)	P value	Gene	MAF	Call rate
rs3780605	9	73498209	T/C	0.1531	1.42	0.35 (0.07)	1.04E-06	TMEM2	0.153	0.996
rs10760553	9	100659831	A/G	0.3136	1.31	0.27 (0.06)	2.97E-06	none	0.314	0.995
rs1892497	10	80713713	T/C	0.2899	0.74	-0.31 (0.06)	1.29E-06	ZMIZ1	0.290	0.998
rs7927459	11	100204269	G/C	0.1155	1.44	0.36 (0.08)	4.50E-06	ARHGAP42	0.116	1.000
rs4772974	13	107926181	C/T	0.2961	1.32	0.28 (0.06)	2.90E-06	none	0.296	0.999

Abbreviations: BP, base pair; Chr, chromosome; EA, effect allele; EAF, effect allele frequency; MAF, minor allele frequency; OA, other allele; OR, odds ratio; Pos, position; SE, standard error; SNP single nucleotide polymorphism.

Table S8. Results from the MetaboChip analysis for established psoriasis loci (GWASCatalog 2013-01).¹

Reported gene	Previously reported SNP	SNP in 500kb region with good quality and best p-value ²	Chr	Position of SNP on metabochip (hg18)	Dist (KB)	Results for best SNP in region in our study				
						EA/OA	EAF	OR	P	r ²
Loci replicated meeting a Bonferroni corrected significance level of 0.05/45=0.0011¹										
RUNX3	rs7536201 (Tsoi <i>et al.</i> , 2012)	rs10903118	1	25167465	1.8	C/T	0.48	1.24	6.71E-05	1.000
TNIP1	rs17728338 (Nair <i>et al.</i> , 2009)	rs17728338	5	150458511	0.0	A/G	0.06	1.55	1.60E-05	1.000
IL12B	rs12188300 (Tsoi <i>et al.</i> , 2012)	rs3212218	5	158687174	74.9	T/G	0.20	0.76	1.06E-04	0.009
IL12B	rs2082412 (Nair <i>et al.</i> , 2009)	rs3212218	5	158687174	36.8	T/G	0.20	0.76	1.06E-04	1.000
IL12B	rs2546890 (Ellinghaus <i>et al.</i> , 2010)	rs3212218	5	158687174	5.3	T/G	0.20	0.76	1.06E-04	0.311
HLA-C	rs10484554 (Liu <i>et al.</i> , 2008; Strange <i>et al.</i> , 2010)	rs10484554	6	31382534	0.0	T/C	0.18	2.03	5.84E-16	1.000
HLA-C	rs12191877 (Ellinghaus <i>et al.</i> , 2010; Nair <i>et al.</i> , 2009)	rs10484554	6	31382534	21.6	T/C	0.18	2.03	5.84E-16	-
HLA-C	rs2395029 (Liu <i>et al.</i> , 2008)	rs10484554	6	31382534	157.2	T/C	0.18	2.03	5.84E-16	-
HLA-C	rs3134792 (Capon <i>et al.</i> , 2008)	rs10484554	6	31382534	37.8	T/C	0.18	2.03	5.84E-16	-
ZMIZ1	rs1250544 (Ellinghaus <i>et al.</i> , 2012)	rs1892497	10	80713713	10.8	T/C	0.29	0.74	1.29E-06	0.670

RPS26	rs12580100 (Stuart <i>et al.</i> , 2010)	rs2066818	12	55040089	314.6	T/G	0.06	0.58	4.68E-05	0.205
IL23A	rs2066808 (Nair <i>et al.</i> , 2009; Strange <i>et al.</i> , 2010)	rs2066818	12	55040089	15.8	T/G	0.06	0.58	4.68E-05	1.000
NFKBIA, PSMA6	rs12586317 (Stuart <i>et al.</i> , 2010)	rs1712355	14	34417263	334.7	T/G	0.49	0.79	1.49E-05	0.169
NFKBIA	rs8016947 (Strange <i>et al.</i> , 2010; Tsoi <i>et al.</i> , 2012)	rs1712355	14	34417263	485.2	T/G	0.49	0.79	1.49E-05	0.098
FBXL19, POL3S	rs10782001 (Stuart <i>et al.</i> , 2010)	rs11865499	16	31039751	189.6	G/A	0.30	1.26	6.22E-05	0.377
Loci not replicated (but well covered by the Metabochip)										
IL28RA	rs4649203 (Strange <i>et al.</i> , 2010)	rs10794648	1	24390793	1.7	T/C	0.25	0.89	0.0736	0.954
Loci not replicated (and not well covered by the Metabochip)										
IL28RA	rs7552167 (Tsoi <i>et al.</i> , 2012)	rs10794648	1	24390793	0.4	T/C	0.25	0.89	0.0736	0.492
LCE3D	rs4112788 (Strange <i>et al.</i> , 2010)	rs4085613	1	150816642	1.3	A/C	0.37	0.90	0.0599	1.000
UBE2L3	rs4821124 (Tsoi <i>et al.</i> , 2012)	rs181360	22	20258916	50.4	C/A	0.20	1.10	0.1625	1.000
B3GNT2	rs10865331 (Tsoi <i>et al.</i> , 2012)	rs2129506	2	62641583	236.6	C/G	0.18	0.89	0.1010	0.016
ZDHHC23	rs1386478 (Ellinghaus <i>et al.</i> , 2012)	rs6438208	3	115652962	489.3	A/G	0.26	1.07	0.2892	0.010
TNFAIP3	rs610604 (Nair <i>et al.</i> , 2009; Strange <i>et al.</i> , 2010)	rs2327832	6	138014761	226.3	G/A	0.20	0.89	0.1046	0.025
TAGAP	rs2451258 (Tsoi <i>et al.</i> , 2012)	rs7749135	6	159784898	358.3	G/T	0.30	1.09	0.1595	0.079

ELMO1	rs2700987 (Tsoi <i>et al.</i> , 2012)	rs890111	7	37583608	230.8	A/G	0.37	0.91	0.0828	0.047
ZC3H12C	rs4561177 (Tsoi <i>et al.</i> , 2012)	rs11213393	11	109798387	330.7	T/C	0.07	1.21	0.0571	0.004
Intergenic	rs1975974 (Stuart <i>et al.</i> , 2010)	rs6587161	17	21372412	258.8	C/T	0.44	1.07	0.2165	0.009
SDC4	rs1008953 (Stuart <i>et al.</i> , 2010)	rs3091579	20	43380782	33.4	A/G	0.15	1.11	0.1767	0.001
SLC45A1, TNFRSF9	rs11121129 (Tsoi <i>et al.</i> , 2012)	rs500508	1	7850043	340.6	A/C	0.27	1.15	0.0217	0.122
CAPZB	rs7667 (Ellinghaus <i>et al.</i> , 2012)	rs4912122	1	19749025	157.6	A/G	0.35	1.13	0.0307	0.092
IL23R	rs11209026 (Strange <i>et al.</i> , 2010)	rs11209026	1	67478546	0.0	A/G	0.06	0.67	0.0014	1.000
IL23R	rs2201841 (Nair <i>et al.</i> , 2009)	rs11209026	1	67478546	11.8	A/G	0.06	0.67	0.0014	-
REL	rs702873 (Strange <i>et al.</i> , 2010)	chr2:60452604	2	60452604	482.4	G/C	0.32	0.86	0.0099	-
Intergenic	rs842636 (Stuart <i>et al.</i> , 2010)	chr2:60452604	2	60452604	492.9	G/C	0.32	0.86	0.0099	-
IFIH1	rs17716942 (Strange <i>et al.</i> , 2010; Tsoi <i>et al.</i> , 2012)	rs2111485	2	162818782	150.2	A/G	0.37	0.84	0.0026	0.194
Intergenic	rs6809854 (Strange <i>et al.</i> , 2010)	rs17005662	3	19105997	346.6	G/T	0.12	0.83	0.0380	0.037
ERAP1	rs27524 (Strange <i>et al.</i> , 2010)	rs30998	5	96521945	394.2	C/A	0.06	0.76	0.0255	0.044
IL13	rs20541 (Nair <i>et al.</i> , 2009)	rs848	5	132024399	0.5	T/G	0.21	0.80	0.0019	1.000
EXOC2, IRF4	rs9504361 (Tsoi <i>et al.</i> , 2012)	rs9505193	6	738060	215.2	C/A	0.31	1.20	0.0018	0.003
TRAF3IP2	rs240993 (Strange <i>et al.</i> , 2010)	rs2179070	6	111992445	212.0	C/T	0.07	1.37	0.0023	0.041

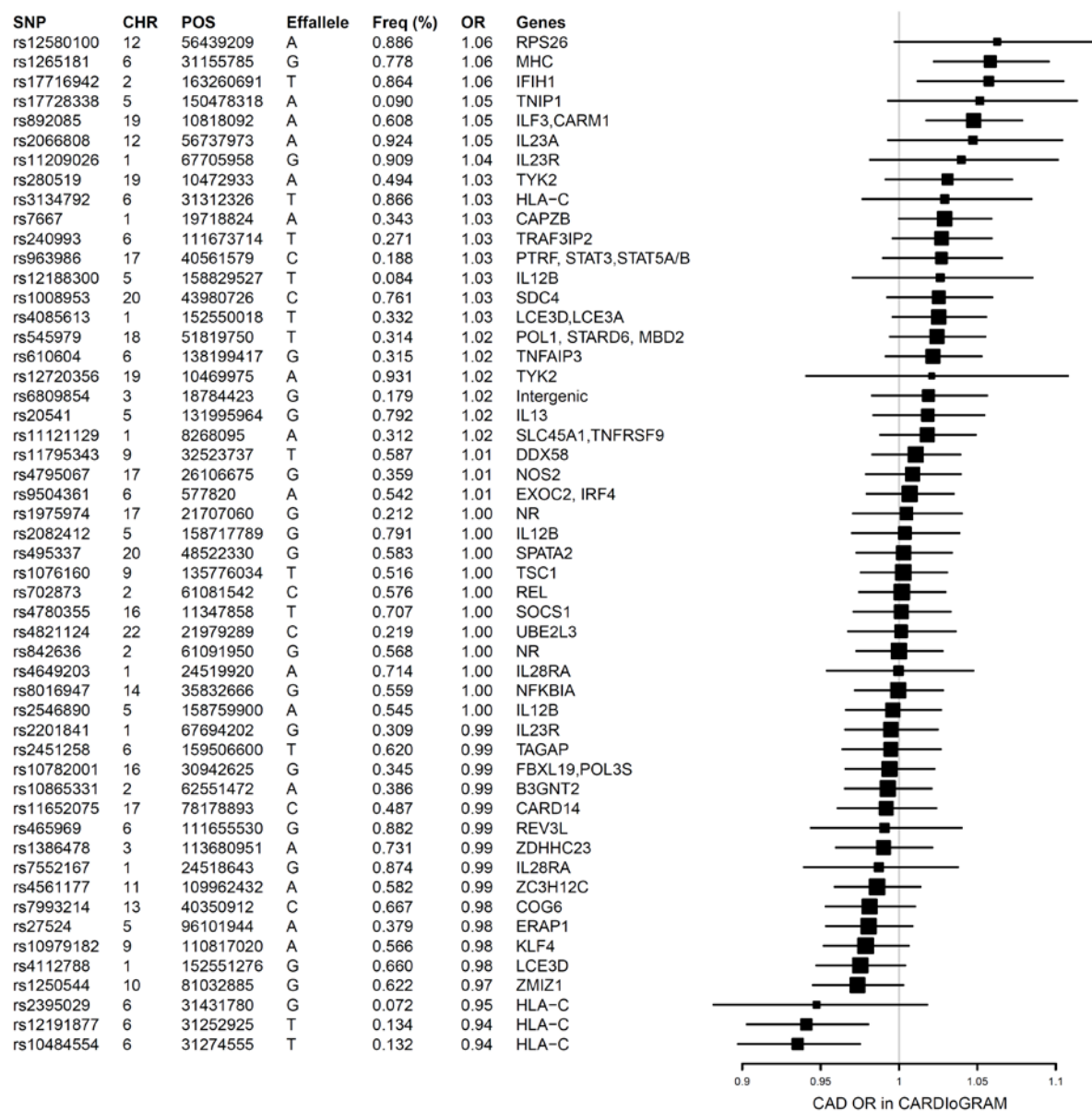
	<i>al.</i> , 2010)										
	rs33980500										
	(Ellinghaus <i>et al.</i> , 2010; Tsoi <i>et al.</i> , 2012)	rs2179070	6	111992445	27.5	C/T	0.07	1.37	0.0023	1.000	
TRAF3IP2	rs465969 (Strange <i>et al.</i> , 2010)	rs2179070	6	111992445	230.2	C/T	0.07	1.37	0.0023	0.546	
REV3L	rs11795343 (Tsoi <i>et al.</i> , 2012)	rs11795343	9	32513737	0.0	C/T	0.41	0.84	0.0015	1.000	
DDX58	rs10979182 (Tsoi <i>et al.</i> , 2012)	rs627610	9	109939112	82.3	A/C	0.24	1.18	0.0080	0.012	
KLF4	rs1076160 (Nair <i>et al.</i> , 2009)	rs7026201	9	134387619	378.2	G/A	0.10	1.24	0.0145	0.000	
TSC1	rs3802826 (Tsoi <i>et al.</i> , 2012)	rs1238566	11	128120696	209.0	G/A	0.45	1.17	0.0052	0.016	
ETS1	rs7993214 (Liu <i>et al.</i> , 2008)	rs9576804	13	38919841	329.1	G/C	0.45	1.15	0.0085	0.009	
COG6	rs4780355 (Ellinghaus <i>et al.</i> , 2012)	chr16:11596516	16	11596516	341.2	T/C	0.32	0.86	0.0123	-	
SOCS1	rs4795067 (Stuart <i>et al.</i> , 2010)	rs9909148	17	23334619	203.8	C/T	0.27	1.19	0.0040	0.001	
NOS2 PTRF, STAT3, STAT5A/B	rs963986 (Tsoi <i>et al.</i> , 2012)	rs8070945	17	37820177	5.1	T/C	0.22	1.14	0.0429	0.000	

Abbreviations: Chr, chromosome; Dist, distance; EA, effect allele; OA, other allele; EAF, effect allele frequency; OR, odds ratio; SNP single nucleotide polymorphism.

¹The MetaboChip covers 45 established psoriasis loci with SNPs in a region of 500kb.

²For each previously reported SNP the SNP with the best p-value (and good quality) within in a 500kb region around the reported SNP of the metabochip analyses is reported and r^2 -values between both are presented based on 1000genomes data.

Figure S1. Forest plot displaying the associations of each psoriasis single nucleotide polymorphism (SNP) with coronary artery disease (CAD) in the Coronary Artery Disease Genome-Wide Replication And Meta-Analysis (CARDIoGRAM).¹



Abbreviations: CHR, chromosome; POS, position; Effallele, effect allele; Freq, effect allele frequency, single nucleotide polymorphism, SNP.

¹Boxes represent the ORs for CAD by SNP variant and whiskers 95% confidence intervals.

Size of boxes is proportional to the inverse variance of ORs.