

Supplemental Table I. Definitions of coronary heart disease across studies.

Study	CHD Cases	Controls	CHD Definition	Control Definition
ATVB	1763	1693	EOMI in male or female $\leq 45y$	No history of thromboembolic disease
BBJ	9957	5641	History of CHD validated by an evidence of left ventricular wall motion abnormalities on echocardiography and a coronary angiography.	Free of CHD individuals with 5 diseases (cerebral aneurysm, esophageal cancer, endometrial cancer, chronic obstructive pulmonary disease or glaucoma).
CAGE-CAD Stage1	1291	1314	The CHD criteria include (i) a validated history of either MI or coronary revascularization (coronary artery bypass grafting or percutaneous coronary intervention), or (ii) subjective symptoms of angina pectoris with 1 or more major coronary vessels showing $\geq 75\%$ stenosis documented by coronary angiography.	Free of CHD
CAGE-CAD Stage2	3038	6320		
DiscovEHR	4199	19939	EOCAD in male $\leq 55y$ or female $\leq 65y$	Free of CAD
DHM	400	399	EOMI in male $\leq 40y$ or female $\leq 55y$	Controls without CAD, men $\geq 65y$ and women $\geq 75y$
ESP-EOMI	962	1426	EOMI (male $\leq 50y$ or female $\leq 60y$)	Hospital-based, no report of MI by history
JHS	20	900	Combination of prevalent CHD (self-reported or electrocardiographic evidence of MI) and incident CHD (MI or coronary revascularization) in $\leq 50y$ or female $\leq 60y$.	Free of CHD during follow-up
Leicester	1148	1058	EOMI (male $\leq 50y$ or female $\leq 60y$)	
Lubeck	857	871	EOMI (male $\leq 50y$ or female $\leq 60y$)	Controls without CAD; male and female \leq age 65
OHS	593	966	EOMI (male $\leq 50y$ female $\leq 60y$)	Asymptomatic
PROCARDIS	912	904	EOMI (male $\leq 50y$ or female $\leq 60y$)	No history of CAD
PROMIS	3946	5671	EOMI (male $\leq 50y$ or female $\leq 60y$)	Age and gender frequency-matched. No history of MI/CVD
REGICOR	382	402	EOMI (male $\leq 50y$ or female $\leq 60y$)	Controls from a population-based study; free of MI, coronary revascularization; ≥ 55 and $< 80y$
TAICHI	3635	5423	CAD (history of MI/CABG/PCI, or at least 1 major vessel with stenosis $\geq 50\%$)	Free of CAD

Abbreviations: CAD, coronary artery disease; CHD, coronary heart disease; CABG, Coronary artery bypass grafting; CVD, cardiovascular disease; EOCAD, early-onset coronary artery disease; EOMI, early-onset myocardial infarction; MI, myocardial infarction.

Supplemental Table II. Baseline characteristics of MIGen, DiscovEHR, BBJ, CAGE-CAD, and TAICHI.

	MIGen	DiscovEHR	TAICHI	BBJ	CAGE-CAD Stage 1	CAGE-CAD Stage 2
	N = 25,273	N = 24,138	N = 9,058	N = 15,598	N = 2,605	N = 9,358
Age, years, mean (SD)	53.3 (13)	46.2 (12)	60.9 (15)	65.2 (10)	65.9 (8.4)	62.5 (8.0)
Male gender, n (%)	18,413 (73)	5,786 (24)	6,128 (68)	11,021 (71)	1,723 (66)	6,089 (65)
BMI, kg/m ² , median (IQR)	26.2 (24–29)	31.2 (26–37)	24.9 (23–28)	23.4 (21–26)	23.3 (21–25)	23.2 (21–25)
Current smoker, n (%)	7,396 (29)	5051	N/A	10,360 (66)	1,347 (51)	4,788 (51)
Ancestry						
African	1,548 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
European	14,108 (56)	24,138 (100)	0 (0)	0 (0)	0 (0)	0 (0)
South Asian	9,617 (38)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
East Asian	0 (0)	0 (0)	9,058 (100)	15,598 (100)	2,605 (100)	9,358 (100)
Medical history						
Coronary heart disease, n (%)	10,983 (43)	4,199 (17)	3,635 (40)	9,957 (64)	1,291 (49)	3038 (32)
Hypertension, n (%)	9,511 (38)	12,940 (54)	4,789 (53)	6,462 (41)	1,188 (45)	4799 (51)
Type 2 diabetes, n (%)	5,077 (20)	4,131 (17)	4,351 (48)	8,646 (55)	926 (35)	2190 (23)
Lipid-lowering medication*, n (%)	3,683 (14)	6,133 (25)	1,784 (22)	5,207 (33)	383 (14)	N/A
Lipid profile						
LDL cholesterol, mean (SD)	130 (48)	124 (38)	120 (50)	125 (38)	130 (38)	N/A
HDL cholesterol, mean (SD)	41 (14)	51 (15)	45 (14)	50 (15)	58 (16)	N/A
Triglycerides, median (IQR)	150 (102–222)	126 (89–177)	121 (83–176)	145 (86–175)	109 (79–154)	N/A
Total cholesterol, mean (SD)	206 (54)	205 (42)	190 (53)	232 (61)	214 (41)	N/A

*At the time of lipid measurement.

Abbreviations: Same as Table 1.

Supplemental Table III. Clinical characteristics of each study by case-control status.

	MIGen		DiscovEHR		TAICHI		BBJ		CAGE-CAD Stage1		CAGE-CAD Stage2	
	CHD	CHD-free	CHD	CHD-free	CHD	CHD-free	CHD	CHD-free	CHD	CHD-free	CHD	CHD-free
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
	N = 10,983	N = 14,290	N = 4,199	N = 19,939	N = 3,635	N = 5,423	N = 9,957	N = 5,641	N = 1,291	N = 1,314	N = 3,038	N = 6,320
Age, years, mean (SD)	46.6 (8.5)	58.3 (13)	51.8 (7.3)	45.0 (12)	67.2 (11)	56.7 (16)	66.6 (10.4)	62.8 (9.8)	66.4 (9)	65.5 (7)	62.6 (9)	62.4 (6)
Male gender, n (%)	8,263 (75)	10,150 (71)	1,938 (46)	3,848 (19)	2,886 (79)	3,242 (60)	8,133 (82)	2,888 (51)	998 (77)	725 (55)	2364 (77)	3725 (58)
BMI, kg/m ² , median (IQR)	26.7 (24–30)	25.9 (24–29)	32.3 (28–38)	31.0 (26–37)	25.5 (23–28)	24.5 (22–27)	24.0 (22–26)	22.5 (20–25)	23.5 (21–25)	23.1 (21–25)	23.6 (21–25)	23.0 (21–24)
Current smoker, n (%)	4,509 (41)	2,887 (20)	986 (23)	4,065 (20)	N/A	N/A	7,164 (72)	3,196 (57)	809 (62)	538 (40)	1999 (65)	2789 (44)
Medical history												
Hypertension, n (%)	4,331 (39)	5,180 (36)	3,373 (80)	12444 (34)	2,184 (60)	2,605 (48)	3,941 (40)	2,521 (45)	774 (59)	414 (31)	1635 (53)	3164 (50)
Type 2 Diabetes, n (%)	2,679 (24)	2,398 (17)	1,520 (36)	2611 (13)	1,702 (47)	2,648 (49)	4,338 (44)	4,308 (76)	603 (46)	323 (24)	1153 (37)	1037 (16)
Lipid-lowering medication*, n (%)	3,176 (29)	507 (4)	2,494 (59)	3639 (18)	1,226 (34)	738 (14)	4,712 (47)	495 (9)	171 (13)	212 (16)	N/A	N/A
Lipid profile												
LDL cholesterol, mean (SD)	146 (54)	120 (41)	130 (40)	122 (37)	124 (53)	117 (48)	126 (37)	124 (38)	124 (37)	132 (37)	N/A	N/A
HDL cholesterol, mean (SD)	38 (13)	43 (15)	46 (13)	52 (15)	43 (12)	46 (15)	49 (14)	58 (18)	52 (15)	61 (16)	N/A	N/A
Triglycerides, median (IQR)	168 (117–248)	138 (94–206)	154 (112–215)	119 (85–167)	124 (87–178)	118 (81–174)	150 (91–181)	132 (77–158)	133 (97–181)	103 (76–140)	N/A	N/A
Total cholesterol, mean (SD)	222 (57)	196 (48)	214 (43)	203 (42)	192 (52)	189 (53)	234 (62)	223 (58)	207 (41)	216 (41)	N/A	N/A

*: At the time of lipid measurement.

Abbreviations: Same as Table 1.

Supplemental Table IV. List of protein truncating variants in the *CETP* gene and coronary heart disease.

Chr	BP (b37)	REF	ALT	rsID	Consequence	AA change	MIGen		DiscovEHR		TAICHI		BBJ		CAGE-CAD-1		CAGE-CAD-2	
							CHD	Controls	CHD	Controls	CHD	Controls	CHD	Controls	CHD	Controls	CHD	Controls
							N = 10,983	N = 14,290	N = 4,199	N = 19,939	N = 3,635	N = 5,423	N = 9,957	N = 5,641	N = 1,291	N = 1,314	N = 3,038	N = 6,320
16	56995902	CCA	C	rs766825140	Frameshift	T5SfsX95	0	1	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	56996963	C	T	rs780627434	Premature stop	D54X	1	0	0	0	0	1	N/A	N/A	N/A	N/A	N/A	N/A
16	56996966	GC	G	rs753876598	Frameshift	A55fsX	0	0	1	1	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	56997025	T	G	rs201790757	Premature stop	Y74X	0	2	1	1	0	1	N/A	N/A	N/A	N/A	N/A	N/A
16	57003374	C	T	rs759621654	Premature stop	Q104X	0	1	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57003536	C	T	rs781363517	Premature stop	Q128X	1	0	0	2	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57003581	AAC	A	.	Frameshift	Q145AfsX4	1	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57003587	C	T	.	Premature stop	Q145X	0	1	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57003859	CT	C	rs781445411	Frameshift	D159TfsX34	1	3	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57003914	G	A	.	Splice donor	INT5+1G>A	0	1	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57004961	C	T	rs142750310	Premature stop	Q182X	1	1	0	2	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57005015	G	T	rs777194816	Splice donor	INT6+1G>T	0	1	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57005910	TC	T	rs759929211	Frameshift	L223FfsX12	1	0	0	2	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57007274	ACCTC	A	rs767971569	Frameshift	D261fsX	0	0	0	0	2	5	N/A	N/A	N/A	N/A	N/A	N/A
16	57007345	C	T	rs748488549	Premature stop	R285X	0	3	0	2	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57012122	TC	T	rs769850349	Frameshift	P367fsX	0	0	0	0	2	7	N/A	N/A	N/A	N/A	N/A	N/A
16	57012151	C	CT	.	Frameshift	A377fsX	0	0	1	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57015573	CTG	C	rs760384575	Frameshift	T410fsX	0	0	0	1	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57016086	G	T	.	Premature stop	E420X	0	0	0	1	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57016107	C	T	rs780936328	Premature stop	Q427X	1	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57016150	G	A	rs5742907	Splice donor	IVS14+1G>A	1	0	0	1	0	0	72	50	6	15	17	59
16	57017236	A	G	.	Splice acceptor	IVS14-2A>G	1	0	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A
16	57017318	C	T	rs577301331	Premature stop	R468X	2	1	0	0	0	0	N/A	N/A	N/A	N/A	N/A	N/A

Abbreviations: AA, amino acid; ALT, alternative allele; BP, base-pair position; CHD, coronary heart disease; Chr, chromosome; REF, reference allele.

Supplemental Figure. Meta-analysis evaluating effects of *CETP* protein truncating variant carrier status on lipid traits.

