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SUPPLEMENTAL MATERIAL

Supplementary table 1. Characteristics of the study participants per cohort

	ARIC	B58C-WTCCC	B58C-T1DGC	FHS	LBC 1921	LBC 1936	ORCADES	PROSPER	PREVEND	RS I	RS II	CROATIA-VIS
Count	9257	1461	2484	2806	176	757	677	5047	3621	5974	1895	766
Age, y (SD)	54.3 (5.7)	44.9 (0.4)	45.3 (0.3)	54.2 (9.7)	86.6 (0.4)	72.5 (0.7)	53.5 (15.3)	75.4 (3.4)	49.7 (12.4)	72.3 (7.0)	64.9 (8.1)	56.6(15.6)
Men, (%)	47.1	50.0	48.3	45.4	45.5	52.4	46.4	47.9	51.1	42.8	45.7	41.4
Current smoker, (%)	24.6	22.9	23.0	18.6	2.8	7.9	8.5	26.5	35.6	16.7	20.3	28.0
Body mass index, kg/m2 (SD)	27.0 (4.8)	27.4 (4.94)	27.4 (4.9)	27.4 (5.0)	26.1 (4.2)	27.9 (4.2)	27.6 (4.8)	26.8 (4.2)	26.1 (4.3)	26.8 (3.9)	27.3 (4.2)	27.4 (4.4)
Waist circumference, cm (SD)	96.1 (13.3)	92.2(13.3)	91.9 (13.6)	92.4 (14.2)	N/A	N/A	93.8 (14.0)	N/A	89.0 (13.3)	93.5 (11.5)	94.0 (11.6)	95.7 (11.7)
Systolic blood pressure, mm Hg (SD)	118.4 (17.0)	126.7(15.3)	126.7 (14.7)	125.5 (18.6)	157.0 (23.2)	147.1 (18.3)	130.2 (19.3)	154.5 (21.8)	129.1 (19.8)	143.5 (21.0)	142.9 (20.9)	137.4 (24.2)
Total/HDL cholesterol, ratio(SD)	4.7 (1.7)	4.0 (1.1)	4.0 (1.2)	4.4 (1.5)	N/A	3.8 (1.1)	3.6 (0.9)	4.7 (1.3)	N/A	4.5 (1.3)	4.5 (1.3)	3.9(0.9)

Fasting glucose, mg/dL(SD)	106.9 (30.8)	N/A	N/A	100.0 (26.6)	N/A	N/A	97.9 (17.6)	N/A	88.34 (20.0)	6.0 (1.5)	6.0 (1.7)	102.8 (25.3)
Triglycerides, mg/dL (SD)	137.2 (92.4)	183.3 (132.5)	183.3 (152.6)	145.7 (113.1)	N/A	145.84 (72.5)	118.8 (59.0)	155 (71.0)	127.8 (87.4)	152 (74.0)	161 (89.0)	137.4 (80.9)
Diabetes, (%)	8.4	1.9	1.3	7.5	6.3	11.2	3.0	10.3	1.6	14.5	11.1	6.7
Hypertension, (%)	26.8	4.2	4.8	15.9	47.7	49.3	21.2	62.2	30.0	42	28.5	25
Lipid treatment, (%)	3.4	N/A	N/A	6	N/A	N/A	11.5	0	4.4	16.1	13.3	3.2
Hormone replacement (women), (%)	21.4	2.3	2.5	17	N/A	16.4	N/A	N/A	24.5	11.1	N/A	N/A
Prevalent cardiovascular disease, (%)	4.8	N/A†	N/A††	5.3	24.4	29.3	8.60	44.6	4.0‡	11	5.2	13.8
Median VWF:Ag, % (IQR)	105 (81-134)	117 (93-146)	116 (93-144)	121 (92-156)	147 (119-180)	120 (95-149)	110 (86-140)	136 (109-168)	65 (36-110)	125 (95-166)	114 (89-148)	131 (103-160)

No. of subjects with low VWF:Ag	476	72	123	141	8	40	37	254	181	163	100	40
Blood group O, N (%)	3916 (42)	643 (44)	1150 (46)	1327 (47)	96 (55)	419 (55)	297 (44)	2703 (53)	1644 (45)	1547 (45)	954 (46)	289 (38)

Table presents baseline characteristics of all subjects per cohort. Summary statistics for continuous variables are presented as means and standard deviations (SD), unless otherwise specified. Categorical data are summarized as percentages.

† In B58C-WTCCC 4.2% has medication for heart disease or high blood pressure

†† In B58C-T1DGC 4.75% has medication for heart disease or high blood pressure

‡Percentage of prevalent myocardial infarction or cerebrovascular accident.

Supplementary table 2. VWF antigen assay used in each cohort

Cohort	Assay description
ARIC	Antigen was determined by an ELISA kit from American Bioproducts Co (Parsippany, NJ). The reliability coefficient obtained from repeated 39 testing of individuals over several weeks was 0.68, and the method CV was 18.5%. No reference range available.
B58C	Antigen was measured by ELISA assays that used a double-antibody sandwich (DAKO, Copenhagen, Denmark). The standard curve was constructed using the 9th British standard for Blood Cogulation Factors from National Institute for Biological Standards and Controls (NIBSC), South Mimms, Herefordshire UK, and the results were expressed as International units/decilitre (IU/dl). As a control, the pooled plasma of 20 healthy middle-aged persons was run on each ELISA plate. The intra-assay CV was 6%, the inter-assay CV was 8%, and reference range was 50 to 200 IU/dl.
FHS	The von Willebrand Factor was assessed using ELISA. In our laboratory, the intra-assay coefficient of variation was 8.8%. No reference range available.
LBC	The VWF antigen method is an in-house ELISA using reagents from Dako, High Wycombe, UK. The intra-assay coefficient of variation was 3.2% and inter-assay was 4.2%.
ORKNEY	Same as B58C
PROSPER	Von Willebrand factor antigen was measured with an in-house ELISA with polyclonal rabbit anti-human VWF antibodies (DAKO, Copenhagen, Denmark). No reference range available.
PREVEND	Antigen was determined by an ELISA kit from Dade Behring of vWf antigen (Ag) was measured by immunoturbidimetric determination using the Dade

	Behring vWF:Ag test kit (Dade Behring Marburg GmbH, Marburg, Germany) using EDTA anticoagulated plasma.
RS	Von Willebrand factor antigen was measured with an in-house ELISA with polyclonal rabbit anti-human VWF antibodies (DAKO, Copenhagen, Denmark). The intra-assay CV was 1.9%, inter-assay CV was 6.3%, and the reference range was 0.60-1.40 IU/ml.
VIS	Same as B58C

Supplemental Table 3. Genotyping and imputation methods for autosomal chromosomes by study

	ARIC	B58C-WTCCC	B58C-T1DGC	FHS	LBC1921	LBC1936	ORCADES	PROSPER	PREVEND	RS	VIS
N	9257	1461	2484	2806	176	757	677	5047	3621	5558	766
Platform	Affymetrix	Affymetrix	Illumina	Affymetrix	Illumina	Illumina	Illumina	Illumina	Illumina	Illumina	Illumina
Chip	6.0	500K	550K (v3)	500K, MIPS 50K	Human 610_Quadv1	Human 610_Quadv1	HumanHap300 (v2)	660k (quad)	CytoSNP12 v2	V3 Illumina Infinium II HumanHap550	HumanHap300 (v1)
SNP exclusion criteria:											
MAF	< 1%	None	None	< 1%	< 1%	< 1%	< 1%	< 1%	< 1%	< 1%	< 1%
HWE p-value	$< 1.0 \times 10^{-5}$	None	None	$< 1.0 \times 10^{-6}$	$< 1.0 \times 10^{-3}$	$< 1.0 \times 10^{-3}$	$< 1.0 \times 10^{-6}$	$< 1.0 \times 10^{-5}$	$< 1.0 \times 10^{-3}$	$< 1.0 \times 10^{-5}$	$< 1.0 \times 10^{-6}$
Call rate	< 0.95	None	None	< 0.97	≤ 0.98	≤ 0.98	≤ 0.98	≤ 0.975	≤ 0.95	≤ 0.90	≤ 0.98

Total number SNPs	597,357	419,829	539,458	378,163	542,050	542,050	285,491	557,192	232,571	530,683	305,068
Imputation software	MACH	IMPUTE	MACH	MACH	MACH	MACH	MACH	MACH	Beagle	MACH	MACH
Imp. software version	1.0.16	0.2.0	1.0.16	1.0.15	1.0.16	1.0.16	1.0.16	1.0.15	3.3.2	1.0.15	1.0.15

Abbreviations used in this table are MAF for minor allele frequency and HWE for Hardy-Weinberg equilibrium