

SUPPLEMENTARY DATA

Supplementary Table 1A. The SNPs included in the 13SNP(*) and 30SNP GRS including the source of data, minor allele frequency (MAF) and Hardy Weinberg Equilibrium p-value (HWE). Previously reported association p-values and published effects (as odds ratios (OR)) used for weighting are also shown. Single SNP association effect sizes and p-values in the Diabetes Heart Study (DHS) for associations with self-reported history of prior CVD (effect reported as OR) and coronary artery calcified plaque (CAC; effect reported as β value) are shown. Associations are reported for the risk allele as used in the GRS. †effect allele in bold.

Chr	Position	SNP	Gene	DHS Data				Reported Assoc.		DHS Single SNP association Results				Reference
				Source	Alleles (Maj/Min) †	MAF	HWE	Effect	p-value	Prior CVD		CAC		
										Effect (OR)	p-value	Effect (β)	p-value	
1	55496039	rs11206510*	PCSK9	Exome	A/G	0.211	1.00	1.15	9.60x10 ⁻⁹	1.02	0.76	0.15	0.22	[4]
1	109818530	rs646776*	CELSR2	Exome	A/G	0.230	0.80	1.19	7.90x10 ⁻¹²	1.06	0.40	0.24	0.04	[4]
1	222823529	rs17465637*	MIA3	GWAS	C/A	0.276	0.82	1.20	1.27x10 ⁻⁶	1.03	0.58	0.12	0.25	[5]
1	109822166	rs599839	SORT1	Exome	A/G	0.236	0.53	1.29	4.05x10 ⁻⁹	1.06	0.43	0.27	0.02	[5]
2	203745885	rs6725887*	WDR12	GWAS	T/C	0.137	0.43	1.16	1.30x10 ⁻⁸	1.02	0.83	0.16	0.26	[4]
2	227068080	rs2943634	IRS1	GWAS	C/A	0.312	0.67	1.22	1.19x10 ⁻⁵	1.12	0.06	0.06	0.55	[5]
3	138119952	rs2306374	MRAS	GWAS	T/C	0.164	0.61	1.15	3.34x10 ⁻⁸	1.01	0.85	0.14	0.29	[6]
3	138122122	rs9818870*	MRAS	GWAS	C/T	0.165	0.73	1.15	7.44x10 ⁻¹³	1.00	0.98	0.10	0.46	[2]
6	12927544	rs12526453*	PHACTR1	GWAS	C/G	0.346	1.00	1.13	1.30x10 ⁻⁹	1.06	0.31	0.05	0.66	[4]
6	35034800	rs17609940	ANKS1A	GWAS	G/C	0.200	1.00	1.07	1.36x10 ⁻⁸	1.00	0.94	0.15	0.21	[6]
6	151252985	rs6922269	MTHFD1L	GWAS	G/A	0.285	0.03	1.23	6.33x10 ⁻⁶	1.00	0.96	0.20	0.08	[5]
6	160961137	rs3798220*	LPA	Exome	A/G	0.016	1.00	1.92	9.0x10 ⁻⁷	1.33	0.20	0.59	0.13	[1]
7	129663496	rs11556924	ZC3HC1	GWAS	C/T	0.388	0.33	1.09	9.18x10 ⁻¹⁸	1.05	0.41	0.14	0.17	[6]
9	22098574	rs4977574*	CDKN2B-AS1	GWAS	A/G	0.472	0.35	1.29	2.7x10 ⁻⁴⁴	1.10	0.09	0.12	0.22	[4]
9	136154168	rs579459	ABO	Exome	A/G	0.212	0.28	1.10	4.08x10 ⁻¹⁴	1.05	0.48	0.13	0.31	[6]
10	44753867	rs501120	LOC100130539	Exome	A/G	0.124	0.49	1.24	1.31x10 ⁻³	1.02	0.82	0.15	0.30	[5]
10	44775824	rs1746048*	CXCL12	GWAS	C/T	0.123	0.66	1.33	5.73x10 ⁻⁷	1.02	0.83	0.14	0.35	[6]
10	104719096	rs12413409	CNNM2	GWAS	G/A	0.084	0.77	1.12	1.03x10 ⁻⁹	1.04	0.67	0.12	0.49	[6]
11	116648917	rs964184	ZNF259	Exome	C/G	0.153	0.73	1.13	1.02x10 ⁻¹⁷	1.03	0.67	0.06	0.68	[6]
12	111884608	rs3184504*	SH2B3	Exome	G/A	0.497	0.35	1.13	8.6x10 ⁻⁸	1.08	0.14	0.14	0.15	[3]
12	121435587	rs2259816*	HNF1A	GWAS	G/T	0.344	0.26	1.08	4.81x10 ⁻⁷	1.03	0.62	0.04	0.67	[2]
13	110960712	rs4773144	COL4A1	Exome	A/G	0.417	0.44	1.07	3.84x10 ⁻⁹	1.13	0.03	0.04	0.70	[6]
14	100133942	rs2895811	HHIPL1	Exome	A/G	0.415	0.51	1.07	1.14x10 ⁻⁷	1.02	0.69	0.16	0.11	[6]
15	67458639	rs17228212	SMAD3	GWAS	T/C	0.306	0.16	1.19	1.18x10 ⁻⁴	1.08	0.19	0.13	0.24	[5]
15	79089111	rs3825807	ADAMTS7	Exome	A/G	0.464	0.26	1.08	1.07x10 ⁻¹²	1.06	0.26	0.18	0.06	[6]
17	2126504	rs216172	SMG6	Exome	G/C	0.366	0.77	1.07	1.15x10 ⁻⁹	1.09	0.13	0.03	0.72	[6]
17	17543722	rs12936587	PEMT	Exome	G/A	0.441	0.93	1.07	4.45x10 ⁻¹⁰	1.04	0.48	0.14	0.16	[6]
17	46988597	rs46522	UBE2Z	Exome	A/G	0.460	0.35	1.06	1.81x10 ⁻⁸	1.05	0.39	0.08	0.41	[6]
19	11163601	rs1122608*	SMARCA4	Exome	C/A	0.256	0.90	1.14	1.90x10 ⁻⁹	1.04	0.52	0.13	0.22	[4]
21	35599128	rs9982601*	MRPS6	Imputed	C/T	0.122	0.92	1.20	6.4x10 ⁻¹¹	1.07	0.44	0.11	0.49	[4]

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Supplementary Table 1B. The SNPs included in the 13SNP(*) and 30SNP GRS including the source of data, minor allele frequency (MAF) and Hardy Weinberg Equilibrium p-value (HWE). Previously reported association p-values and published effects (as odds ratios (OR)) used for weighting are also shown. Single SNP association effect sizes and p-values in the Diabetes Heart Study (DHS) for associations with all-cause mortality and CVD-mortality are shown. Associations are reported for the risk allele as used in the GRS. †effect allele in bold.

Chr	Position	SNP	Gene	DHS Data				Reported Assoc.		DHS Single SNP association Results				Reference
				Source	Alleles (Maj/Min) †	MAF	HWE	Effect	p-value	All-cause mortality		CVD mortality		
										Effect	p-value	Effect	p-value	
1	55496039	rs11206510*	PCSK9	Exome	A/G	0.211	1.00	1.15	9.60x10 ⁻⁹	1.02	0.80	1.10	0.32	[4]
1	109818530	rs646776*	CELSR2	Exome	A/G	0.230	0.80	1.19	7.90x10 ⁻¹²	1.05	0.55	1.16	0.11	[4]
1	222823529	rs17465637*	MIA3	GWAS	C/A	0.276	0.82	1.20	1.27x10 ⁻⁶	1.08	0.27	1.09	0.11	[5]
1	109822166	rs599839	SORT1	Exome	A/G	0.236	0.53	1.29	4.05x10 ⁻⁹	1.04	0.64	1.13	0.17	[5]
2	203745885	rs6725887*	WDR12	GWAS	T/C	0.137	0.43	1.16	1.30x10 ⁻⁸	1.13	0.18	1.07	0.54	[4]
2	227068080	rs2943634	IRS1	GWAS	C/A	0.312	0.67	1.22	1.19x10 ⁻⁵	1.03	0.61	1.09	0.29	[5]
3	138119952	rs2306374	MRAS	GWAS	T/C	0.164	0.61	1.15	3.34x10 ⁻⁸	1.03	0.77	1.12	0.29	[6]
3	138122122	rs9818870*	MRAS	GWAS	C/T	0.165	0.73	1.15	7.44x10 ⁻¹³	1.01	0.87	1.12	0.31	[2]
6	12927544	rs12526453*	PHACTR1	GWAS	C/G	0.346	1.00	1.13	1.30x10 ⁻⁹	1.03	0.67	1.12	0.16	[4]
6	35034800	rs17609940	ANKS1A	GWAS	G/C	0.200	1.00	1.07	1.36x10 ⁻⁸	1.05	0.54	1.10	0.32	[6]
6	151252985	rs6922269	MTHFD1L	GWAS	G/A	0.285	0.03	1.23	6.33x10 ⁻⁶	1.05	0.52	1.05	0.59	[5]
6	160961137	rs3798220*	LPA	Exome	A/G	0.016	1.00	1.92	9.0x10 ⁻⁷	1.17	0.50	1.07	0.82	[1]
7	129663496	rs11556924	ZC3HC1	GWAS	C/T	0.388	0.33	1.09	9.18x10 ⁻¹⁸	1.04	0.56	1.01	0.92	[6]
9	22098574	rs4977574*	CDKN2B-AS1	GWAS	A/G	0.472	0.35	1.29	2.7x10 ⁻⁴⁴	1.08	0.23	1.13	0.13	[4]
9	136154168	rs579459	ABO	Exome	A/G	0.212	0.28	1.10	4.08x10 ⁻¹⁴	1.08	0.35	1.06	0.52	[6]
10	44753867	rs501120	LOC100130539	Exome	A/G	0.124	0.49	1.24	1.31x10 ⁻³	1.32	0.006	1.23	0.09	[5]
10	44775824	rs1746048*	CXCL12	GWAS	C/T	0.123	0.66	1.33	5.73x10 ⁻⁷	1.31	0.007	1.23	0.10	[6]
10	104719096	rs12413409	CNNM2	GWAS	G/A	0.084	0.77	1.12	1.03x10 ⁻⁹	1.23	0.08	1.30	0.09	[6]
11	116648917	rs964184	ZNF259	Exome	C/G	0.153	0.73	1.13	1.02x10 ⁻¹⁷	1.00	0.95	1.07	0.50	[6]
12	111884608	rs3184504*	SH2B3	Exome	G/A	0.497	0.35	1.13	8.6x10 ⁻⁸	1.07	0.27	1.03	0.70	[3]
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13	110960712	rs4773144	COL4A1	Exome	A/G	0.417	0.44	1.07	3.84x10 ⁻⁹	1.15	0.03	1.19	0.02	[6]
14	100133942	rs2895811	HHIPL1	Exome	A/G	0.415	0.51	1.07	1.14x10 ⁻⁷	1.06	0.33	1.03	0.72	[6]
15	67458639	rs17228212	SMAD3	GWAS	T/C	0.306	0.16	1.19	1.18x10 ⁻⁴	1.04	0.54	1.18	0.04	[5]
15	79089111	rs3825807	ADAMTS7	Exome	A/G	0.464	0.26	1.08	1.07x10 ⁻¹²	1.03	0.59	1.04	0.62	[6]
17	2126504	rs216172	SMG6	Exome	G/C	0.366	0.77	1.07	1.15x10 ⁻⁹	1.00	0.99	1.07	0.37	[6]
17	17543722	rs12936587	PMT	Exome	G/A	0.441	0.93	1.07	4.45x10 ⁻¹⁰	1.05	0.41	1.04	0.62	[6]
17	46988597	rs46522	UBE2Z	Exome	A/G	0.460	0.35	1.06	1.81x10 ⁻⁸	1.04	0.55	1.04	0.63	[6]
19	11163601	rs1122608*	SMARCA4	Exome	C/A	0.256	0.90	1.14	1.90x10 ⁻⁹	1.11	0.15	1.03	0.72	[4]
21	35599128	rs9982601*	MRPS6	Imputed	C/T	0.122	0.92	1.20	6.4x10 ⁻¹¹	1.02	0.80	1.01	0.96	[4]

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Supplementary Table 2. Association of 13 SNP and 30 SNP genetic risk scores with history of prior CVD, all-cause mortality, CVD-mortality and CAC in European Americans (n=1175) from the Diabetes Heart Study. Effect estimates are reported as odds ratios (OR), hazard ratios (HR) and β -coefficient (β) based on a single unit increase in the GRS i.e. per risk allele.

Trait	Unadjusted		Partially Adjusted*		Fully Adjusted†	
	Effect (95% CI)	p-value	Effect (95% CI)	p-value	Effect (95% CI)	p-value
13 SNP Unweighted GRS						
Prior CVD	OR: 1.06 (1.00-1.13)	0.05	OR: 1.08 (1.01-1.14)	0.02	OR: 1.09 (1.03-1.16)	0.006
All-cause Mortality	HR: 0.99 (0.93-1.06)	0.80	HR: 1.02 (0.96-1.09)	0.47	HR: 1.02 (0.96-1.09)	0.46
CVD Mortality	HR: 1.06 (0.98-1.15)	0.18	HR: 1.08 (1.00-1.18)	0.06	HR: 1.09 (1.00-1.19)	0.05
CAC	β : 0.02 (-0.06-0.11)	0.60	β : 0.03 (-0.03-0.10)	0.34	β : 0.04 (-0.02-0.11)	0.22
13 SNP Weighted GRS						
Prior CVD	OR: 1.08 (1.01-1.16)	0.02	OR: 1.10 (1.03-1.18)	0.007	OR: 1.11 (1.04-1.20)	0.003
All-cause Mortality	HR: 1.01 (0.94-1.09)	0.78	HR: 1.04 (0.97-1.12)	0.26	HR: 1.04 (0.97-1.12)	0.24
CVD Mortality	HR: 1.07 (0.97-1.17)	0.18	HR: 1.09 (0.99-1.20)	0.07	HR: 1.10 (1.00-1.21)	0.06
CAC	β : 0.05 (-0.05-0.15)	0.33	β : 0.06 (-0.02-0.13)	0.14	β : 0.07 (-0.01-0.14)	0.08
30 SNP Unweighted GRS						
Prior CVD	OR: 1.03 (1.00-1.07)	0.07	OR: 1.04 (1.00-1.08)	0.04	OR: 1.04 (1.00-1.09)	0.02
All-cause Mortality	HR: 1.02 (0.99-1.06)	0.24	HR: 1.03 (0.99-1.06)	0.11	HR: 1.03 (0.99-1.06)	0.11
CVD Mortality	HR: 1.06 (1.01-1.12)	0.03	HR: 1.06 (1.01-1.12)	0.02	HR: 1.07 (1.02-1.13)	0.01
CAC	β : 0.05 (0.01-0.10)	0.02	β : 0.06 (0.02-0.09)	0.005	β : 0.06 (0.02-0.10)	0.002
30 SNP Weighted GRS						
Prior CVD	OR: 1.03 (1.00-1.07)	0.07	OR: 1.04 (1.00-1.08)	0.04	OR: 1.04 (1.01-1.09)	0.02
All-cause Mortality	HR: 1.03 (0.99-1.07)	0.14	HR: 1.04 (1.00-1.08)	0.04	HR: 1.04 (1.00-1.08)	0.03
CVD Mortality	HR: 1.05 (1.00-1.10)	0.06	HR: 1.06 (1.00-1.11)	0.03	HR: 1.06 (1.01-1.11)	0.02
CAC	β : 0.05 (0.00-0.09)	0.06	β : 0.05 (0.01-0.09)	0.02	β : 0.05 (0.01-0.09)	0.007

*adjusted for age, sex, type 2 diabetes affection status; †adjusted for age, sex, type 2 diabetes affection status, BMI, current smoking, hypertension, dyslipidemia

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Supplementary Table 3. Association between unweighted 13SNP low (n=339), moderate (mod; n=618) and high (n=218) genetic risk score groups and history of prior CVD, all-cause mortality, CVD mortality and CAC in European Americans from the Diabetes Heart Study. Effect estimates (odds ratio (OR); hazard ratio (HR); β -coefficient (β)) are reported relative to the low risk group.

		Unadjusted		Partially Adjusted*		Fully Adjusted†	
	n (%) or mean \pm SD	Effect (95% CI)	p-value	Effect (95% CI)	p-value	Effect (95% CI)	p-value
Prior CVD							
low	117 (34.5%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	247 (40.0%)	OR: 1.30 (0.99-1.71)	0.06	OR: 1.39 (1.03-1.86)	0.03	OR: 1.43 (1.06-1.94)	0.02
high	95 (43.6%)	OR: 1.51 (1.05-2.15)	0.02	OR: 1.67 (1.15-2.42)	0.007	OR: 1.77 (1.21-2.59)	0.003
All-cause Mortality							
low	75 (22.1%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	126 (20.4%)	HR: 0.95 (0.71-1.27)	0.71	HR: 1.05 (0.79-1.38)	0.75	HR: 1.07 (0.81-1.40)	0.64
high	45 (20.6%)	HR: 0.93 (0.63-1.36)	0.70	HR: 1.11 (0.77-1.60)	0.58	HR: 1.17 (0.77-1.62)	0.56
CVD Mortality							
low	28 (8.3%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	59 (9.5%)	HR: 1.18 (0.73-1.90)	0.50	HR: 1.28 (0.80-2.07)	0.30	HR: 1.31 (0.81-2.11)	0.27
high	20 (9.2%)	HR: 1.10 (0.61-1.97)	0.75	HR: 1.26 (0.70-2.26)	0.44	HR: 1.30 (0.72-2.32)	0.38
CAC							
low	1598 \pm 2821	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	1731 \pm 2952	β : 0.14 (-0.22-0.50)	0.44	β : 0.15 (-0.14-0.45)	0.31	β : 0.17 (-0.12-0.45)	0.25
high	1462 \pm 2528	β : 0.004 (-0.49-0.50)	0.99	β : 0.08 (-0.32-0.49)	0.70	β : 0.11 (-0.28-0.51)	0.58

*adjusted for age, sex; †adjusted for age, sex, BMI, current smoking, hypertension, dyslipidemia

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Supplementary Table 4. Association between unweighted 30SNP low (n=193), moderate (mod; n=707) and high (n=275) genetic risk score groups and history of prior CVD, all-cause mortality, CVD mortality and CAC in European Americans from the Diabetes Heart Study. Effect estimates (odds ratio (OR); hazard ratio (HR); β -coefficient (β)) are reported relative to the low risk group.

		Unadjusted		Partially Adjusted*		Fully Adjusted†	
	n (%) or mean \pm SD	Effect (95% CI)	p-value	Effect (95% CI)	p-value	Effect (95% CI)	p-value
Prior CVD							
low	60 (31.1%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	326 (39.6%)	OR: 1.49 (1.05-2.11)	0.02	OR: 1.60 (1.12-2.28)	0.009	OR: 1.66 (1.15-2.38)	0.006
high	73 (45.9%)	OR: 1.91 (1.19-3.05)	0.007	OR: 1.99 (1.24-3.18)	0.004	OR: 2.10 (1.29-3.40)	0.003
All-cause Mortality							
low	28 (14.5%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	179 (21.7%)	HR: 1.59 (1.06-2.36)	0.02	HR: 1.70 (1.17-2.45)	0.005	HR: 1.70 (1.18-2.45)	0.005
high	39 (24.5%)	HR: 1.71 (1.02-2.86)	0.04	HR: 1.82 (1.21-2.95)	0.02	HR: 1.75 (1.08-2.86)	0.02
CVD-Mortality							
low	10 (5.2%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	76 (9.2%)	HR: 1.88 (0.91-3.87)	0.08	HR: 2.00 (0.98-4.07)	0.06	HR: 2.06 (1.01-4.19)	0.05
high	21 (13.2%)	HR: 2.56 (1.14-5.76)	0.02	HR: 2.67 (1.20-5.92)	0.02	HR: 2.76 (1.23-6.21)	0.01
CAC							
low	1362 \pm 2696	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	1655 \pm 2821	β : 0.37 (-0.06-0.80)	0.09	β : 0.46 (0.12-0.80)	0.009	β : 0.45 (0.12-0.79)	0.008
high	1911 \pm 3074	β : 0.96 (0.41-1.50)	0.0006	β : 0.91 (0.46-1.35)	6.98x10 ⁻⁵	β : 0.89 (0.45-1.33)	8.03x10 ⁻⁵

*adjusted for age, sex; †adjusted for age, sex, BMI, current smoking, hypertension, dyslipidemia

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Supplementary Table 5. T2D-affected only analysis. Association between unweighted 13SNP low (n=284), moderate (mod; n=513) and high (n=186) genetic risk score groups and history of prior CVD, all-cause mortality, CVD mortality and CAC in T2D affected European Americans from the Diabetes Heart Study. Effect estimates (odds ratio (OR); hazard ratio (HR); β -coefficient (β)) are reported relative to the low risk group. (compare to Supplementary Table 3).

		Unadjusted		Partially Adjusted*		Fully Adjusted†	
	n (%) or mean \pm SD	Effect (95% CI)	p-value	Effect (95% CI)	p-value	Effect (95% CI)	p-value
Prior CVD							
low	111 (39.1%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	219 (42.7%)	OR: 1.19 (0.89-1.60)	0.25	OR: 1.28 (0.94-1.75)	0.12	OR: 1.34 (0.97-1.85)	0.07
high	89 (47.8%)	OR: 1.46 (1.00-2.12)	0.05	OR: 1.66 (1.12-2.46)	0.01	OR: 1.79 (1.20-2.69)	0.005
All-cause Mortality							
low	69 (24.3%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	118 (23.0%)	HR: 0.99 (0.72-1.35)	0.92	HR: 1.08 (0.80-1.45)	0.61	HR: 1.11 (0.83-1.49)	0.48
high	42 (22.6%)	HR: 0.93 (0.62-1.38)	0.70	HR: 1.12 (0.76-1.65)	0.56	HR: 1.13 (0.77-1.67)	0.53
CVD Mortality							
low	28 (9.9%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	55 (10.7%)	HR: 1.12 (0.69-1.82)	0.64	HR: 1.21 (0.75-1.95)	0.43	HR: 1.25 (0.78-2.01)	0.36
high	18 (9.7%)	HR: 0.97 (0.53-1.79)	0.93	HR: 1.14 (0.62-2.10)	0.67	HR: 1.18 (0.64-2.18)	0.59
CAC							
low	2025 \pm 4243	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	1884 \pm 3086	β : 0.01 (-0.37-0.37)	0.98	β : 0.11 (-0.20-0.43)	0.48	β : 0.15 (-0.16-0.45)	0.35
high	1697 \pm 2660	β : -0.02 (-0.52-0.49)	0.95	β : 0.16 (-0.28-0.60)	0.48	β : 0.20 (-0.23-0.63)	0.35

*adjusted for age, sex; †adjusted for age, sex, BMI, current smoking, hypertension, dyslipidemia

SUPPLEMENTARY DATA

Supplementary Table 6. T2D-affected only analysis. Association between weighted 13SNP low (n=189), moderate (mod; n=602) and high (n=192) genetic risk score groups and history of prior CVD, all-cause mortality, CVD mortality and CAC in T2D affected European Americans from the Diabetes Heart Study. Effect estimates (odds ratio (OR); hazard ratio (HR); β -coefficient (β)) are reported relative to the low risk group. (compare to Table 3).

		Unadjusted		Partially Adjusted*		Fully Adjusted†	
	n (%) or mean \pm SD	Effect (95% CI)	p-value	Effect (95% CI)	p-value	Effect (95% CI)	p-value
Prior CVD							
low	67 (35.4%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	255 (42.4%)	OR: 1.39 (0.97-1.99)	0.07	OR: 1.36 (0.93-1.98)	0.11	OR: 1.41 (0.95-2.08)	0.09
high	97 (50.5%)	OR: 1.93 (1.25-2.96)	0.003	OR: 2.17 (1.40-3.38)	0.0006	OR: 2.40 (1.52-3.79)	0.0002
All-cause Mortality							
low	34 (17.9%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	155 (25.7%)	HR: 1.60 (1.09-2.33)	0.02	HR: 1.61 (1.11-2.32)	0.01	HR: 1.62 (1.12-2.33)	0.01
high	40 (20.8%)	HR: 1.16 (0.72-1.87)	0.55	HR: 1.32 (0.83-2.11)	0.25	HR: 1.34 (0.84-2.15)	0.22
CVD Mortality							
low	11 (5.8%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	70 (11.6%)	HR: 2.20 (1.19-4.08)	0.01	HR: 2.18 (1.18-4.01)	0.01	HR: 2.20 (1.19-4.10)	0.01
high	20 (10.4%)	HR: 1.77 (0.84-3.72)	0.13	HR: 1.96 (0.93-4.15)	0.08	HR: 2.02 (0.94-4.34)	0.07
CAC							
low	1604 \pm 2909	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	1946 \pm 3069	β : 0.36 (-0.04-0.75)	0.08	β : 0.30 (-0.03-0.63)	0.07	β : 0.32 (-0.01-0.64)	0.06
high	1707 \pm 2685	β : 0.24 (-0.28-0.76)	0.37	β : 0.35 (-0.10-0.80)	0.13	β : 0.44 (0.01-0.87)	0.05

*adjusted for age, sex; †adjusted for age, sex, BMI, current smoking, hypertension, dyslipidemia

SUPPLEMENTARY DATA

Supplementary Table 7. T2D-affected only analysis. Association between unweighted 30SNP low (n=161), moderate (mod; n=684) and high (n=138) genetic risk score groups and history of prior CVD, all-cause mortality, CVD mortality and CAC in T2D-affected European Americans from the Diabetes Heart Study. Effect estimates (odds ratio (OR); hazard ratio (HR); β -coefficient (β)) are reported relative to the low risk group. (compare to Supplementary Table 4).

		Unadjusted		Partially Adjusted*		Fully Adjusted†	
	n (%) or mean \pm SD	Effect (95% CI)	p-value	Effect (95% CI)	p-value	Effect (95% CI)	p-value
Prior CVD							
low	59 (36.4%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	292 (42.7%)	OR: 1.31 (0.92-1.88)	0.14	OR: 1.39 (0.96-2.00)	0.08	OR: 1.45 (0.99-2.12)	0.06
high	68 (49.3%)	OR: 1.72 (1.05-2.79)	0.03	OR: 1.90 (1.16-3.11)	0.01	OR: 2.05 (1.23-3.44)	0.006
All-cause Mortality							
low	27 (16.7%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	167 (24.4%)	HR: 1.56 (1.05-2.33)	0.03	HR: 1.64 (1.13-2.39)	0.01	OR: 1.65 (1.13-2.40)	0.009
high	35 (25.4%)	HR: 1.54 (0.91-2.60)	0.11	HR: 1.70 (1.04-2.81)	0.04	OR: 1.66 (1.00-2.75)	0.05
CVD Mortality							
low	10 (6.2%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	71 (10.4%)	HR: 1.79 (0.87-3.67)	0.11	HR: 1.87 (0.92-3.81)	0.08	HR: 1.96 (0.96-4.00)	0.06
high	20 (14.5%)	HR: 2.35 (1.04-5.30)	0.04	HR: 2.56 (1.14-5.75)	0.02	HR: 2.71 (1.18-6.21)	0.02
CAC							
low	1556 \pm 2880	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	1933 \pm 3537	β : 0.41 (-0.03-0.84)	0.07	β : 0.47 (0.12-0.82)	0.009	β : 0.47 (0.13-0.81)	0.007
high	2048 \pm 3129	β : 0.97 (0.28-0.42)	0.0006	β : 1.06 (0.60-1.53)	7.29x10 ⁻⁶	β : 1.06 (0.60-1.51)	5.22x10 ⁻⁶

*adjusted for age, sex; †adjusted for age, sex, BMI, current smoking, hypertension, dyslipidemia

SUPPLEMENTARY DATA

Supplementary Table 8. T2D-affected only analysis. Association between weighted 30SNP low (n=159), moderate (mod; n=591) and high (n=233) genetic risk score groups and history of prior CVD, all-cause mortality, CVD mortality and CAC in T2D-affected European Americans from the Diabetes Heart Study. Effect estimates (odds ratio (OR); hazard ratio (HR); β -coefficient (β)) are reported relative to the low risk group. (compare to Table 4).

		Unadjusted		Partially Adjusted*		Fully Adjusted†	
	n (%) or mean \pm SD	Effect (95% CI)	p-value	Effect (95% CI)	p-value	Effect (95% CI)	p-value
Prior CVD							
low	60 (37.7%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	250 (42.3%)	OR: 1.23 (0.82-1.84)	0.26	OR: 1.32 (0.86-2.02)	0.15	OR: 1.37 (0.93-2.03)	0.11
high	109 (46.8%)	OR: 1.47 (0.96-2.25)	0.07	OR: 1.66 (1.06-2.59)	0.03	OR: 1.82 (1.14-2.89)	0.01
All-cause Mortality							
low	29 (18.2%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	140 (23.7%)	HR: 1.44 (0.95-2.17)	0.09	HR: 1.63 (1.11-2.40)	0.01	OR: 1.64 (1.12-2.40)	0.01
high	60 (25.8%)	HR: 1.46 (0.91-2.34)	0.12	HR: 1.72 (1.09-2.72)	0.02	OR: 1.75 (1.01-2.74)	0.02
CVD Mortality							
low	12 (7.5%)	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	58 (9.8%)	HR: 1.43 (0.75-2.73)	0.28	HR: 1.59 (0.84-3.01)	0.15	HR: 1.67 (0.88-3.17)	0.12
high	31 (13.3%)	HR: 1.81 (0.90-3.64)	0.10	HR: 2.08 (1.03-4.19)	0.04	HR: 2.21 (1.09-4.48)	0.03
CAC							
low	1665 \pm 3292	1.00 (ref)	-	1.00 (ref)	-	1.00 (ref)	-
mod	1954 \pm 3583	β : 0.42 (-0.02-0.86)	0.06	β : 0.53 (0.15-0.92)	0.007	β : 0.57 (0.20-0.94)	0.003
high	1871 \pm 2894	β : 0.50 (-0.03-1.03)	0.07	β : 0.66 (0.20-1.12)	0.005	β : 0.69 (0.25-1.13)	0.002

*adjusted for age, sex; †adjusted for age, sex, BMI, current smoking, hypertension, dyslipidemia

SUPPLEMENTARY DATA

Supplementary Table 9. Changes in risk classification as assessed using a net reclassification index (NRI) comparing fully adjusted models and fully adjusted models with the addition of genetic risk groups.

Trait	% reclassified	NRI	p-value
13 SNP Unweighted GRS			
Prior CVD	10.6%	0.041	0.04
All-cause Mortality	3.9%	0.020	0.12
CVD Mortality	13.3%	0.010	0.77
13 SNP Weighted GRS			
Prior CVD	12.1%	0.031	0.13
All-cause Mortality	6.8%	0.040	0.03
CVD Mortality	13.3%	0.062	0.06
30 SNP Unweighted GRS			
Prior CVD	10.0%	0.005	0.78
All-cause Mortality	9.4%	0.014	0.48
CVD Mortality	20.2%	0.065	0.17
30 SNP Weighted GRS			
Prior CVD	9.1%	0.002	0.93
All-cause Mortality	11.8%	0.055	0.02
CVD Mortality	16.0%	0.060	0.09