Supplementary Material

Lithovius R, Antikainen AA, Mutter S ,Valo E, Forsblom C, Harjutsalo V, Sandholm N, Groop PH, on behalf of the FinnDiane Study Group. Genetic risk score enhances coronary artery disease risk prediction in individuals with type 1 diabetes

Contents

Supplemental Tables

Supplemental Table S1. Physicians and nurses at each of the FinnDiane centers participating in patient recruitment and characterization

The Finnish Diabetic Nephropathy Study Center	Physicians and nurses
Anjalankoski Health Center	S.Koivula, T.Uggeldahl
Central Finland Central Hospital, Jyväskylä	T.Forslund, A.Halonen, A.Koistinen, P.Koskiaho, M.Laukkanen, J.Saltevo, M.Tiihonen
Central Hospital of Åland Islands, Mariehamn	M.Forsen, H.Granlund, A.-C.Jonsson, B.Nyroos
Central Hospital of Kanta-Häme, Hämeenlinna	P.Kinnunen, A.Orvola, T.Salonen, A.Vähänen
Central Hospital of Kymenlaakso, Kotka	R.Paldanius, M.Riihelä, L.Ryysy
Central Hospital of Länsi-Pohja, Kemi	H.Laukkanen, P.Nyländen, A.Sademies
Central Ostrobothnian Hospital District, Kokkola	S.Anderson, B.Asplund, U.Byskata, P.Liedes, M.Kuusela, T.Virkkala
City of Espoo Health Center:	
Espoonlahti	A.Nikkola, E.Ritola
Tapiola	M.Niska, H.Saarinen
Samaria	E.Oukko-Ruponen, T.Virtanen
Viherlaakso	A.Lyytinen
City of Helsinki Health Center:	
Puistola	H.Kari, T.Simonen
Suutarila	A.Kaprio, J.Kärkkäinen, B.Rantaeskola
Töölö	P.Kääriäinen, J.Haaga, A-L.Pietiläinen
City of Hyvinkää Health Center	S.Klemetti, T.Nyandoto, E.Rontu, S.Satuli-Autere
City of Vantaa Health Center:	
Korso	R.Toivonen, H.Virtanen
Länsimäki	R.Ahonen, M.Ivaska-Suomela, A.Jauhiainen
Martinlaakso	M.Laine, T.Pellonpää, R.Puranen
Myyrmäki	A.Airas, J.Laakso, K.Rautavaara
Rekola	M.Erola, E.Jatkola
Tikkurila	R.Lönnblad, A.Malm, J.Mäkelä, E.Rautamo
Heinola Health Center	P.Hentunen, J.Lagerstam
Helsinki University Central Hospital, Department of Medicine, Division of Nephrology	M.Feodoroff, D.Gordin, O.Heikkilä, K.Hietala, J.Fagerudd, M.Korolainen, L.Kyllönen, J.Kytö, S.Lindh, K.Pettersson-Fernholm, M.Rosengård-Bärlund, A.Sandelin, L.Thorn, J.Tuomikangas, T.Vesisenaho, J.Wadén
Herttoniemi Hospital, Helsinki	V.Sipilä
Hospital of Lounais-Häme, Forssa	T.Kalliomäki, J.Koskelainen, R.Nikkanen, N.Savolainen, H.Sulonen, E.Valtonen
Hyvinkää Hospital	L. Norvio, A.Hämäläinen
Iisalmi Hospital	E.Toivanen
Jokilaakso Hospital, Jämsä	A.Parta, I.Pirttiniemi
Jorvi Hospital, Helsinki University Central Hospital	S.Aranko, S.Ervasti, R.Kauppinen-Mäkelin, A.Kuusisto, T.Leppälä, K.Nikkilä, L.Pekkonen
Jyväskylä Health Center, Kyllö	K.Nuorva, M.Tiihonen
Kainuu Central Hospital, Kajaani	S.Jokelainen, K.Kananen, M.Karjalainen, P.Kemppainen, A-M.Mankinen, A.Reponen M.Sankari
Kerava Health Center	H.Stuckey, P.Suominen
Kirkkonummi Health Center	A.Lappalainen, M.Liimatainen, J.Santaholma
Kivelä Hospital, Helsinki	A.Aimolahti, E.Huovinen
Koskela Hospital, Helsinki	V.Ilkka, M.Lehtimäki
Kotka Health Center	E.Pälikkö-Kontinen, A.Vanhanen
Kouvola Health Center	E.Koskinen, T.Siitonen
Kuopio University Hospital	E.Huttunen, R.Ikäheimo, P.Karhapää, P.Kekäläinen, M.Laakso, T.Lakka, E.Lampainen, L.Moilanen, S. Tanskanen, L.Niskanen, U.Tuovinen, I.Vauhkonen, E.Voutilainen
Kuusamo Health Center	T.Kääriäinen, E.Isopoussu
Kuusankoski Hospital	E.Kilkki, I.Koskinen, L.Riihelä
Laakso Hospital, Helsinki	T.Meriläinen, P.Poukka, R.Savolainen, N.Uhlenius
Lahti City Hospital	A.Mäkelä, M.Tanner
Lapland Central Hospital, Rovaniemi	L.Hyvärinen, K.Lampela, S.Pöykkö, T.Rompasaari, S.Severinkangas, T.Tulokas
Lappeenranta Health Center	P. Erola, L.Härkönen, P.Linkola, T.Pekkanen, I.Pulli, E.Repo
Lohja Hospital	T.Granlund, K.Hietanen, M.Porrassalmi, M.Saari, T.Salonen, M.Tiikkainen,
Länsi-Uusimaa Hospital, Tammisaari	I.-M.Jousmaa, J.Rinne
Loimaa Health Center	A.Mäkelä, P.Eloranta
Malmi Hospital, Helsinki	H.Lanki, S.Moilanen, M.Tilly-Kiesi
Mikkeli Central Hospital	A.Gynther, R.Manninen, P.Nironen, M.Salminen, T.Vänttinen
Mänttä Regional Hospital	I.Pirttiniemi, A-M.Hänninen
North Karelian Hospital, Joensuu	U-M.Henttula, P.Kekäläinen, M.Pietarinen, A.Rissanen, M.Voutilainen
Nurmijärvi Health Center	A.Burgos, K.Urtamo
Oulaskangas Hospital, Oulainen	E.Jokelainen, P-L.Jylkkä, E.Kaarlela, J.Vuolaspuro
Oulu Health Center	L.Hiltunen, R.Häkkinen, S.Keinänen-Kiukaanniemi
Oulu University Hospital	R.Ikäheimo
Päijät-Häme Central Hospital	H.Haapamäki, A.Helanterä, S.Hämäläinen, V.Ilvesmäki, H.Miettinen
Palokka Health Center	P.Sopanen, L.Welling
Pieksämäki Hospital	V.Sevtsenko, M.Tamminen
Pietarsaari Hospital	M-L.Holmbäck, B.Isomaa, L.Sarelin

Pori City Hospital	P.Ahonen, P.Merisalo, E.Muurinen, K.Sävelä
Porvoo Hospital	M.Kallio, B.Rask, S.Rämö
Raahe Hospital	A.Holma, M.Honkala, A.Tuomivaara, R.Vainionpää
Rauma Hospital	K.Laine, K.Saarinen, T.Salminen
Riihimäki Hospital	P.Aalto, E.Immonen, L.Juurinen
Salo Hospital	A.Alanko, J.Lapinleimu, P.Rautio, M.Virtanen
Satakunta Central Hospital, Pori	M.Asola, M.Juhola, P.Kunelius, M.-L.Lahdenmäki, P.Pääkkönen, M.Rautavirta
Savonlinna Central Hospital	T.Pulli, P.Sallinen, M.Taskinen, E.Tolvanen, T.Tuominen, H.Valtonen, A.Vartia, S-L. Viitanen
Seinäjoki Central Hospital	O.Antila, E.Korpi-Hyövälti, T.Latvala, E.Leijala, T.Leikkari, M.Punkari, N.Rantamäki, H.Vähävuori
South Karelia Central Hospital, Lappeenranta	T.Ensala, E.Hussi, R.Härkönen, U.Nyholm, J.Toivanen
Tampere Health Center	A.Vaden, P.Alarotu, E.Kujansuu, H.Kirkkopelto-Jokinen, M.Helin, S.Gummerus, L.Calonius, T.Niskanen, T.Kaitala, T.Vatanen
Tampere University Hospital	P. Hannula, I.Ala-Houhala, R.Kannisto, T.Kuningas, P.Lampinen, M.Määttä, H.Oksala, T.Oksanen, A.Putila, H.Saha, K.Salonen, H.Tauriainen, S.Tulokas
Tiirismaa Health Center, Hollola	T.Kivelä, L.Petlin, L.Savolainen
Turku Health Center	A.Artukka, I.Hämäläinen, L.Lehtinen, E.Pyysalo, H.Virtamo, M.Viinikkala, M.Vähätalo
Turku University Central Hospital	K.Breitholz, R.Eskola, K.Metsärinne, U.Pietilä, P.Saarinen, R.Tuominen, S.Äyräpää
Vaajakoski Health Center	K.Mäkinen, P.Sopanen
Valkeakoski Regional Hospital	S.Ojanen, E.Valtonen, H.Ylönen, M.Rautiainen, T.Immonen
Vammala Regional Hospital	I.Isomäki, R.Kroneld, L.Mustaniemi, M.Tapiolinna-Mäkelä
Vaasa Central Hospital	S.Bergkulla, U.Hautamäki, V-A.Myllyniemi, I.Rusk

Supplemental Table S2. ICD and procedure codes used for ascertaining coronary artery disease (CAD) during the whole study period (by the end of 2015) and ICD codes used for ascertaining previous stroke events prior to the FinnDiane baseline visit (for the clinical risk score calculation)

Code type	Register	Codes	Explanation
ICD-10	Finnish Causes of Death Register and Finnish Care Register for Health Care (Hospital Discharge Register until 1993)	I21, I22, I23	myocardial infraction
		I60, I61, I62, I63, I64	stroke
ICD-8/9		410, 412	myocardial infraction
		430, 431, 432, 433, 434	stroke
Procedure code	Care Register for Health Care (Hospital Discharge Register until 1993)	FNA01, FNA02, FNA03, FNA04, FNA05, FNA10, FNA20, FNA96 FNB01, FNB02, FNB20, FNB96 FNC10, FNC20, FNC30, FNC40, FNC50, FNC60, FNC96 FND10, FND20, FND96 FNE01, FNE02, FNE03, FNE10, FNE11, FNE20, FNE21, FNE96	coronary bypass surgery (GABG)
	Care Register for Health Care (Hospital Discharge Register until 1993)	FN1AT, FN1BT, FN1YT TFN40,TFN50	coronary balloon angioplasty (PTCA/PCI)
	Care Register for Health Care (Hospital Discharge Register until 1993)	5311, 5312, 5313, 5314, 5315, 5329	coronary operations (coronary bypass surgery or balloon angioplasty) before 1996

CAD was defined as a hard CAD event (myocardial infarction, coronary bypass surgery or coronary balloon angioplasty) and controls were individuals without hard CAD events. In the original study cohort (1) only 5% of cases had CAD event before age of 35 years, and thus, controls with age <35 years (N = 322) or diabetes duration <15 years (N = 151) were excluded from the case–control CAD analysis (1). Stroke was defined as a hard stroke event prior to the FinnDiane baseline visit.

Supplemental Table S3. Variants in the genetic risk score (1, 2)

Variant	Variant position (GRCh37)	Effect allele	Close genes	Known variant EAF	Known variant OR	Reference
rs2493298	1:3325912	A	PRDM16, PEX10, PLCH2, RER1	0.14	1.06	4
rs61776719	1:38461319	A	FHL3, UTP11, SF3A3, MANEAL, INPP5B	0.53	1.04	4
rs11206510	1:55496039	T	PCSK9	0.82	1.08	6
rs17114036	1:56962821	A	PPAP2B	0.91	1.17	6
rs599839	1:109822166	A	SORT1, PSCR1, CELSR2	0.78	1.11	6
rs11806316	1:115753482	G	NGF, CASQ2	0.63	1.04	4
rs11810571	1:151762308	G	TDRKH, RP11-98D18.9	0.79	1.07	5
rs4845625	1:154422067	T	IL6R, AQP10, ATP8B2, CHTOP, UBAP2L	0.47	1.06	13
rs1892094	1:169094459	C	ATP1B1, BLZF1, CCDC181, F5, NME7, SELP, SLC19A2	0.5	1.04	7
rs6700559	1:200646073	C	DDX59, CAMSAP2, KIF14	0.53	1.04	7
rs2820315	1:201872264	T	LMOD1, IPO9, NAV1, SHISA4, TIMM17A	0.3	1.05	7
rs60154123	1:210468999	T	HHAT, SERTAD4, DIEXF	0.15	1.05	4
rs17465637	1:222823529	C	MIA3, AIDA, C1orf58	0.74	1.14	6
rs699	1:230845794	G	AGT, CAPN9, GNPAT	0.42	1.04	4
rs515135	2:21286057	C	APOB	0.83	1.07	13
rs6544713	2:44073881	T	ABCG5, ABCG8	0.29	1.06	11
rs582384	2:45896437	A	PRKCE, TMEM247	0.53	1.03	4
rs1561198	2:85809989	T	VAMP5, VAMP8, GGCX	0.45	1.06	13
rs2252641	2:145801461	C	ZEB2, TEX41	0.46	1.06	13
rs12999907	2:164957251	A	FIGN	0.82	1.06	4
rs840616	2:188196469	C	CALCRL, TFPI	0.65	1.04	4
rs6725887	2:203745885	C	WDR12, CARF, FAM117B, ICA1L, NBEAL1	0.15	1.14	6
rs1250229	2:216304384	T	FN1, ATIC, LOC102724849, ABCA12, LINC00607	0.26	1.07	11
rs2571445	2:218683154	A	TNS1, CXCR2, RUFY4	0.39	1.04	7
rs2972146	2:227100698	T	LOC646736, IRS1, MIR5702	0.65	1.06	10
rs1801251	2:233633460	A	KCNJ13, GIGYF2	0.35	1.05	14
rs11677932	2:238223955	G	COL6A3	0.68	1.03	4
rs748431	3:14928077	G	FGD5	0.36	1.05	10
rs7633770	3:46688562	A	ALS2CL, RTP3	0.41	1.03	4
rs7617773	3:48193515	T	CDC25A, SPINK8, MAP4, ZNF589	0.67	1.04	4
rs7623687	3:49448566	A	RHOA, AMT, TCTA, CDHRA, KLHDC8B	0.86	1.07	5
rs142695226	3:124475201	G	UMPS, ITGB5	0.14	1.08	5
rs10512861	3:132257961	G	DNAJC13, NPHP3, ACAD11, UBA5	0.86	1.04	4
rs667920	3:136069472	T	STAG1, MSL2, NCK1, PPP2R3A	0.78	1.05	4
rs2306374	3:138119952	C	MRAS, CEP70	0.18	1.12	6
rs12493885	3:153839866	C	ARHGEF26	0.85	1.08	10
rs4266144	3:156852592	G	CCNL1, TIPARP	0.32	1.03	4
rs12897	3:172115902	G	FNDC3B	0.41	1.04	4
rs16844401	4:3449652	A	HGFAC, RGS12, MSANTD1	0.07	1.07	4
rs17087335	4:57838583	T	REST, NOA1	0.21	1.06	8
rs12500824	4:77416627	A	SHROOM3, SEPT11, FAM47E, STBD1	0.36	1.04	4
rs10857147	4:81181072	T	PRDM8, FGF5	0.29	1.06	10
rs11099493	4:82587050	A	HNRNPD, RASGEF1B	0.69	1.04	4
rs3775058	4:96117371	A	UNC5C	0.23	1.04	4
rs35879803	4:146782837	C	ZNF827	0.7	1.05	5
rs1878406	4:148393664	T	EDNRA	0.15	1.1	13
rs7692387	4:156635309	G	GUCY1A1	0.81	1.08	13
rs7696431	4:169687725	T	PALLD, DDX60L	0.51	1.04	4
rs1508798	5:9556694	T	SEMA5A, TAS2R1	0.81	1.05	4
rs3936511	5:55860781	G	MAP3K1, MIER3	0.18	1.04	4
rs1800449	5:121413208	T	LOX	0.17	1.07	10

rs273909	5:131667353	G	SLC22A4	0.14	1.07	13
rs2706399	5:131867702	G	IL5, RAD50	0.51	1.07	15
rs246600	5:142516897	T	ARHGAP26	0.48	1.05	7
rs9501744	6:1617143	C	FOXC1	0.87	1.05	4
rs12526453	6:12927544	C	PHACTR1, EDN1	0.67	1.1	6
rs35541991	6:22583856	C	HDGFL1	0.31	1.05	5
rs3130683	6:31888367	T	C2, C4A	0.86	1.09	14
rs17609940	6:35034800	G	ANKS1A, UHRF1BP1	0.75	1.07	6
rs1321309	6:36638636	A	CDKN1A, PI16	0.49	1.03	4
rs10947789	6:39174922	T	KCNK5	0.76	1.07	13
rs6905288	6:43758873	A	VEGFA, MRPL14, TMEM63B	0.57	1.05	4
rs9367716	6:57160572	G	PRIM2, RAB23, DST, BEND6	0.68	1.04	4
rs4613862	6:82612271	A	FAM46A	0.53	1.03	4
rs1591805	6:126717064	A	CENPW	0.49	1.04	4
rs12190287	6:134214525	C	TCF21, TARID (EYA4−AS1)	0.62	1.08	6
rs17080091	6:150997401	C	PLEKHG1, IYD	0.92	1.05	4
rs4252120	6:161143608	T	PLG, LPAL2	0.73	1.07	13
rs10267593	7:1937261	G	MAD1L1	0.8	1.04	4
rs11509880	7:12261911	A	TMEM106B, THSD7A	0.36	1.04	4
rs2023938	7:19036775	C	HDAC9	0.1	1.08	13
rs2107732	7:45077978	G	CCM2, MYO1G	0.91	1.06	4
rs10953541	7:107244545	C	BCAP29, GPR22	0.8	1.08	12
rs975722	7:117332914	G	CTTNBP2, CFTR, ASZ1	0.4	1.03	4
rs11556924	7:129663496	C	ZC3HC1, KLHDC10	0.62	1.09	6
rs10237377	7:139757136	G	PARP12, TBXAS1	0.65	1.05	7
rs3918226	7:150690176	T	NOS3	0.06	1.14	8
rs6997340	8:18286997	T	NAT2	0.31	1.04	4
rs264	8:19813180	G	LPL	0.86	1.11	13
rs6984210	8:22033615	G	BMP1, SFTPC, DMTN, PHYHIP, DOK2, XPO7	0.06	1.09	4
rs10093110	8:106565414	G	ZFPM2	0.58	1.03	4
rs2954029	8:126490972	A	TRIB1	0.55	1.06	13
rs1333049	9:22125503	C	ANRIL, CDKN2B-AS	0.48	1.36	3
rs944172	9:110517794	C	KLF4	0.28	1.04	4
rs111245230	9:113169775	C	SVEP1	0.04	1.14	9
rs885150	9:124420173	C	DAB2IP	0.27	1.03	4
rs579459	9:136154168	C	ABO, SURF6, GBGT1	0.21	1.1	6
rs61848342	10:12303813	C	CDC123, NUDT5, OPTN	0.36	1.04	4
rs2505083	10:30335122	C	KIAA1462	0.38	1.07	12
rs1746048	10:44775824	C	CXCL12	0.87	1.09	6
rs17680741	10:82251514	T	TSPAN14, MAT1A, FAM213A	0.72	1.05	4
rs1412444	10:91002927	T	LIPA	0.42	1.09	12
rs12413409	10:104719096	G	CYP17A1, CNNM2, NT5C2	0.89	1.12	6
rs4918072	10:105693644	A	STN1, SH3PXD2A	0.27	1.04	4
rs4752700	10:124237612	G	HTRA1, PLEKHA1	0.45	1.03	4
rs11601507	11:5701074	A	TRIM5, TRIM22, TRIM6, OR52N1, OR52B6	0.07	1.09	4
rs10840293	11:9751196	A	SWAP70	0.55	1.06	8
rs11042937	11:10745394	T	MRVl1, CTR9	0.49	1.04	14
rs1351525	11:13301548	T	ARNTL	0.67	1.05	5
rs7116641	11:43696917	G	HSD17B12	0.31	1.03	4
rs12801636	11:65391317	G	PCNX3, POLA2, RELA, SIPA1	0.77	1.05	7
rs590121	11:75274150	T	SERPINH1	0.3	1.05	7
rs7947761	11:100624599	G	ARHGAP42	0.28	1.04	4
rs974819	11:103660567	T	PDGFD	0.32	1.07	12
rs964184	11:116648917	G	APOA1-C3-A4-A5	0.13	1.13	6
rs11838267	12:7175872	T	C1S	0.87	1.05	4
rs10841443	12:20220033	G	RP11-664H17.1	0.67	1.05	10
rs11170820	12:54513915	G	HOXC4	0.08	1.1	5

rs11172113	12:57527283	C	LRP1, STAT6	0.41	1.06	14
rs7306455	12:95355541	G	NDUFA12, FGD6	0.9	1.05	4
rs3184504	12:111884608	T	SH2B3, FLJ21127, ATXN2	0.44	1.07	6
rs2244608	12:121416988	G	HNF1A, OASL, C12orf43	0.35	1.06	5
rs11057401	12:124427306	T	CCDC92	0.69	1.06	10
rs11057830	12:125307053	A	SCARB1	0.15	1.08	14
rs9319428	13:28973621	A	FLT1	0.32	1.06	13
rs9591012	13:33058333	G	N4BP2L2, PDS5B	0.66	1.04	4
rs4773144	13:110960712	G	COL4A1, COL4A2	0.44	1.07	6
rs1317507	13:113631780	A	MCF2L, PCID2, CUL4A	0.26	1.04	4
rs2145598	14:58794001	G	ARID4A, PSMA3	0.42	1.03	4
rs3832966	14:75614504	I	TMED10, ZC2HC1C, RPS6KL1, NEK9, EIF2B2e, ACYP1	0.46	1.05	5
rs112635299	14:94838142	G	SERPINA2, SERPINA1	0.98	1.15	4
rs2895811	14:100133942	C	HHIPL1, YY1	0.43	1.07	6
rs6494488	15:65024204	A	OAZ2, RBPMS2, TRIP4	0.82	1.05	7
rs56062135	15:67455630	C	SMAD3	0.79	1.07	8
rs3825807	15:79089111	A	ADAMTS7	0.57	1.08	6
rs8042271	15:89574218	G	MFGE8, RP11-326A19.4, ABHD2	0.9	1.1	8
rs17514846	15:91416550	A	FURIN, FES	0.44	1.07	13
rs17581137	15:96146414	A	gene desert	0.75	1.04	4
rs1800775	16:56995236	C	CETP	0.51	1.04	14
rs1050362	16:72130815	A	DHX38, HP, DHODH	0.38	1.04	7
rs3851738	16:75387533	C	CFDP1, BCAR1	0.6	1.05	10
rs7199941	16:81906423	A	PLCG2, CENPN	0.4	1.04	4
rs7500448	16:83045790	A	CDH13	0.77	1.07	5
rs216172	17:2126504	C	SMG6, SRR	0.37	1.07	6
rs12936587	17:17543722	G	Ral1, PEMT, RASD1, SMCR3, TOM1L2	0.56	1.07	6
rs13723	17:27941886	G	CORO6, BLMH, ANKRD13B, GIT1, SSH2, EFCAB5	0.49	1.04	4
rs76954792	17:30033514	T	COPRS, RAB11FIP4	0.22	1.04	4
rs2074158	17:40257163	C	DHX58, KAT2A, RAB5, NKIRAS2, DNAJC7, KCNH4, HCRT, GHDC	0.18	1.05	4
rs17608766	17:45013271	C	GOSR2, MYL4, ARL17A	0.14	1.07	7
rs46522	17:46988597	T	UBE2Z, GIP, ATP5G1	0.53	1.06	6
rs7212798	17:59013488	C	BCAS3	0.15	1.08	8
rs1867624	17:62387091	T	PECAM1, DDX5, TEX2	0.61	1.04	7
rs9964304	18:47229717	C	ACAA2, RPL17	0.28	1.04	4
rs663129	18:57838401	A	PMAIP1, MC4R	0.26	1.06	8
rs116843064	19:8429323	G	ANGTPL4	0.98	1.16	9
rs1122608	19:11163601	G	LDLR, SMARCA4	0.77	1.14	6
rs73015714	19:17855763	G	FCHO1, COLGALT1	0.2	1.06	4
rs12976411	19:32882020	A	ZNF507, LOC400684	0.91	1.05	8
rs2075650	19:45395619	G	APOE, APOC1, TOMM40, PVRL2, COTL1	0.14	1.14	15
rs1964272	19:46190268	G	SNRPD2, GIPR	0.51	1.05	11
rs867186	20:33764554	A	PROCR, ASIP, NCOA6, ITGB4BP/EIF6	0.89	1.08	7
rs6102343	20:39924279	A	ZHX3, PLCG1, TOP1	0.25	1.04	4
rs3827066	20:44586023	T	PCIF1, ZNF335, NEURL2, PLTP, MMP9	0.14	1.04	4
rs260020	20:57714025	T	ZNF831	0.13	1.05	4
rs2832227	21:30533076	G	MAP3K7CL, BACH1	0.18	1.04	4
rs9982601	21:35599128	T	MRPS6, SLC5A3, KCNE2	0.15	1.18	6

Supplemental Table S4. Cox proportional hazards models according to the low and high genetic, clinical and combined risk score percentile comparisons. Models are adjusted for diabetes onset year and sex.

Percentiles (Low / High)	Low Cases / Controls	High Cases / Controls	*P* value*	HR (95% CI)†	*P* value
GRS 5 / 95	8 / 157	35 / 130	2.1×10^{-5}	6.72 (3.08, 14.70)	1.8×10^{-6}
GRS 10 / 90	34 / 296	76 / 254	1.9×10^{-5}	2.99 (1.98, 4.50)	1.7×10^{-7}
GRS 20 / 80	66 / 593	126 / 533	4.1×10^{-6}	2.21 (1.64, 2.98)	2.2×10^{-7}
GRS 30 / 70	114 / 875	174 / 815	0.0002	1.76 (1.39, 2.24)	2.9×10^{-6}
Clinical risk score 20 / 80	4 / 655	243 / 416	2.5×10^{-63}	75.42 (25.80, 220.48)	2.8×10^{-15}
Clinical risk score 30 / 70	17 / 972	330 / 659	5.7×10^{-76}	15.98 (9.05, 28.22)	1.3×10^{-21}
Combined risk score 20 / 80	4 / 655	255 / 404	2.8×10^{-67}	85.48 (29.67, 246.26)	1.7×10^{-16}
Combined risk score 30 / 70	15 / 974	327 / 662	2.4×10^{-76}	16.92 (9.38, 30.50)	5.2×10^{-21}

**P* values represent comparisons of numbers of cases and controls between the top and the bottom percentiles and are calculated with χ^2 test, †All models adjusted for sex and type 1 diabetes onset year; GRS, genetic risk score

Supplemental Table S5. Characteristics of the individuals according to the medication status

Medication status	No antihypertensive or lipid-lowering drugs (A)	Antihypertensive drugs only (B)	Both antihypertensive and lipid-lowering drugs (C)	Lipid-lowering drugs only (D)	*P* value A vs. B	*P* value A vs. C	*P* value A vs. D	*P* value B vs. C
n	1,258	559	282	40				
Age (years)	33.6 ± 9.9	42.3 ± 10.5	47.3 ± 9.3	50.2 ± 8.4	5.9×10^{-55}	1.5×10^{-72}	1.8×10^{-15}	4.9×10^{-12}
Duration of diabetes (years)	16.9 ± 10.3	27.7 ± 9.8	31.9 ± 9.3	29.0 ± 12.5	4.7×10^{-85}	4.1×10^{-82}	3.8×10^{-7}	2.4×10^{-9}
Median type 1 diabetes onset year	1985 (1977–1991)	1973 (1965–1979)	1969 (1962–1976)	1974 (1965–1982)	2.7×10^{-86}	6.4×10^{-66}	3.7×10^{-7}	0.0003
Men n (%)	551 (43.8)	301 (53.8)	167 (59.2)	15 (37.5)	9.2×10^{-5}	3.7×10^{-6}	0.5	0.2
Median age at diabetes onset (years)	15.5 (10.1–22.7)	13.2 (8.6–19.4)	13.5 (9.0–21.3)	24.1 (14.0–28.1)	4.2×10^{-7}	0.01	0.003	0.2
Genetic risk score	0.0077 ± 0.0031	0.0079 ± 0.0032	0.0083 ± 0.0032	0.0070 ± 0.0028	0.3	0.01	0.1	0.09
Median clinical risk score	1.11 (0.63–2.19)	4.42 (2.17–9.22)	8.99 (4.65–16.28)	4.22 (2.81–10.16)	3.8×10^{-114}	2.7×10^{-115}	4.0×10^{-15}	1.8×10^{-20}
Diabetic nephropathy status n (%)					2.8×10^{-195}	4.2×10^{-160}	0.01	1.3×10^{-5}
Normal AER	1186 (94.3)	164 (29.3)	63 (22.3)	38 (95.0)	NA	NA	NA	NA
Microalbuminuria	61 (4.8)	153 (27.4)	47 (16.7)	0 (0.0)	NA	NA	NA	NA
Macroalbuminuria	8 (0.6)	165 (29.5)	125 (44.3)	0 (0.0)	NA	NA	NA	NA
ESRD	3 (0.2)	77 (13.8)	47 (16.7)	2 (5.0)	NA	NA	NA	NA
Chronic kidney disease n (%)					2.4×10^{-92}	1.1×10^{-139}	9.9×10^{-5}	6.9×10^{-7}
1 eGFR >90 (ml/min/1.73 m^2)	1037 (82.4)	251 (44.9)	86 (30.5)	23 (57.5)	NA	NA	NA	NA
2 eGFR 60 - 89	211 (16.8)	138 (24.7)	56 (19.9)	14 (35.0)	NA	NA	NA	NA
3 eGFR 30 - 59	6 (0.5)	65 (11.6)	55 (19.5)	1 (2.5)	NA	NA	NA	NA
4 eGFR 15 - 29	1 (0.1)	18 (3.2)	24 (8.5)	0 (0.0)	NA	NA	NA	NA
5 eGFR <15	3 (0.2)	87 (15.6)	61 (21.6)	2 (5.0)	NA	NA	NA	NA
Median eGFR (ml/min/1.73 m^2)	108.6 (95.8 – 118.6)	84.4 (47.4 – 105.2)	60.4 (19.0 – 94.3)	96.6 (80.1 – 104.3)	3.6×10^{-72}	2.1×10^{-84}	8.7×10^{-7}	1.5×10^{-8}
HbA_{1c} (%)	8.1 ± 1.4	8.4 ± 1.4	8.6 ± 1.4	8.1 ± 1.1	7.2×10^{-6}	4.9×10^{-9}	0.9	0.02
HbA_{1c} (mmol/mol)	65 ± 16	68 ± 16	71 ± 16	65 ± 12	7.2×10^{-6}	4.9×10^{-9}	0.9	0.02
Total cholesterol (mmol/l)	4.62 ± 0.81	4.96 ± 0.91	5.13 ± 1.09	4.99 ± 0.93	1.6×10^{-13}	8.2×10^{-13}	0.02	0.02
HDL cholesterol (mmol/l)	1.38 ± 0.37	1.34 ± 0.40	1.28 ± 0.40	1.42 ± 0.41	0.07	0.0004	0.5	0.06
Median Triglycerides (mmol/l)	0.88 (0.69 – 1.17)	1.02 (0.77 – 1.50)	1.32 (0.96 – 1.90)	1.00 (0.81 – 1.33)	4.0×10^{-13}	7.6×10^{-35}	0.06	1.96×10^{-10}
LDL cholesterol (mmol/l)	2.81 ± 0.76	3.09 ± 0.84	3.17 ± 0.98	3.11 ± 0.99	1.1×10^{-11}	1.4×10^{-8}	0.06	0.2
Systolic BP (mmHg)	126 ± 14	142 ± 19	148 ± 20	134 ± 14	4.6×10^{-62}	2.65×10^{-50}	0.0006	6.7×10^{-6}
Diastolic BP (mmHg)	77 ± 9	82 ± 10	82 ± 11	76 ± 8	5.0×10^{-24}	8.8×10^{-13}	0.6	0.9
Waist to height ratio	0.48 ± 0.05	0.51 ± 0.06	0.55 ± 0.07	0.53 ± 0.07	5.6×10^{-28}	1.4×10^{-44}	6.1×10^{-5}	2.6×10^{-12}
Current or history of smoking n (%)	510 (40.5)	279 (49.9)	159 (56.4)	17 (42.5)	0.0002	1.7×10^{-6}	0.9	0.09
CAD at the end of follow-up n (%)	67 (5.3)	132 (23.6)	93 (33.0)	7 (17.5)	2.7×10^{-30}	2.1×10^{-12}	0.006	0.005
Previous stroke n (%)	4 (0.3)	18 (3.2)	20 (7.1)	4 (10.0)	9.6×10^{-7}	5.3×10^{-12}	5.0×10^{-5}	0.02
Deceased, n (%)	57 (4.5)	161 (28.8)	92 (32.6)	6 (15.0)	2.2×10^{-48}	1.8×10^{-46}	0.01	0.3

Data are mean ± SD, median (IQR), or %. NA, not applicable

Supplemental Table S6. Cox proportional hazards models according to the low and the high genetic risk score (GRS) quintiles at each medication group

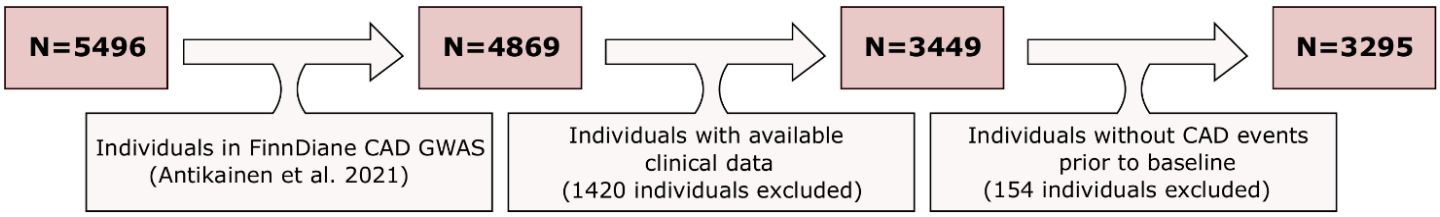
GRS Quintiles (%)	Low (0-20)	High (80-100)		Model 1†		Model 2‡	
	Cases/ Controls	Cases/ Controls	*P* value *	HR (95% CI)	*P* value	HR (95% CI)	*P* value
No antihypertensive or lipid-lowering drugs	7 / 245	25 /227	0.002	3.78 (1.63, 8.78)	0.002	3.68 (1.58, 8.56)	0.002
Antihypertensive drugs only	19 / 93	34 / 78	0.03	2.23 (1.24, 3.98)	0.007	2.69 (1.45, 5.00)	0.002
Both antihypertensive and lipid-lowering drugs	20 / 37	22 / 35	0.8	0.99 (0.54, 1.84)	0.99	1.06 (0.56, 1.97)	0.86

**P* values (calculated with the χ^2test) present comparisons of the numbers of cases and controls between low and high quintiles, †Adjusted for sex and type 1 diabetes onset year, ‡Adjusted for sex, type 1 diabetes onset year and clinical risk score.

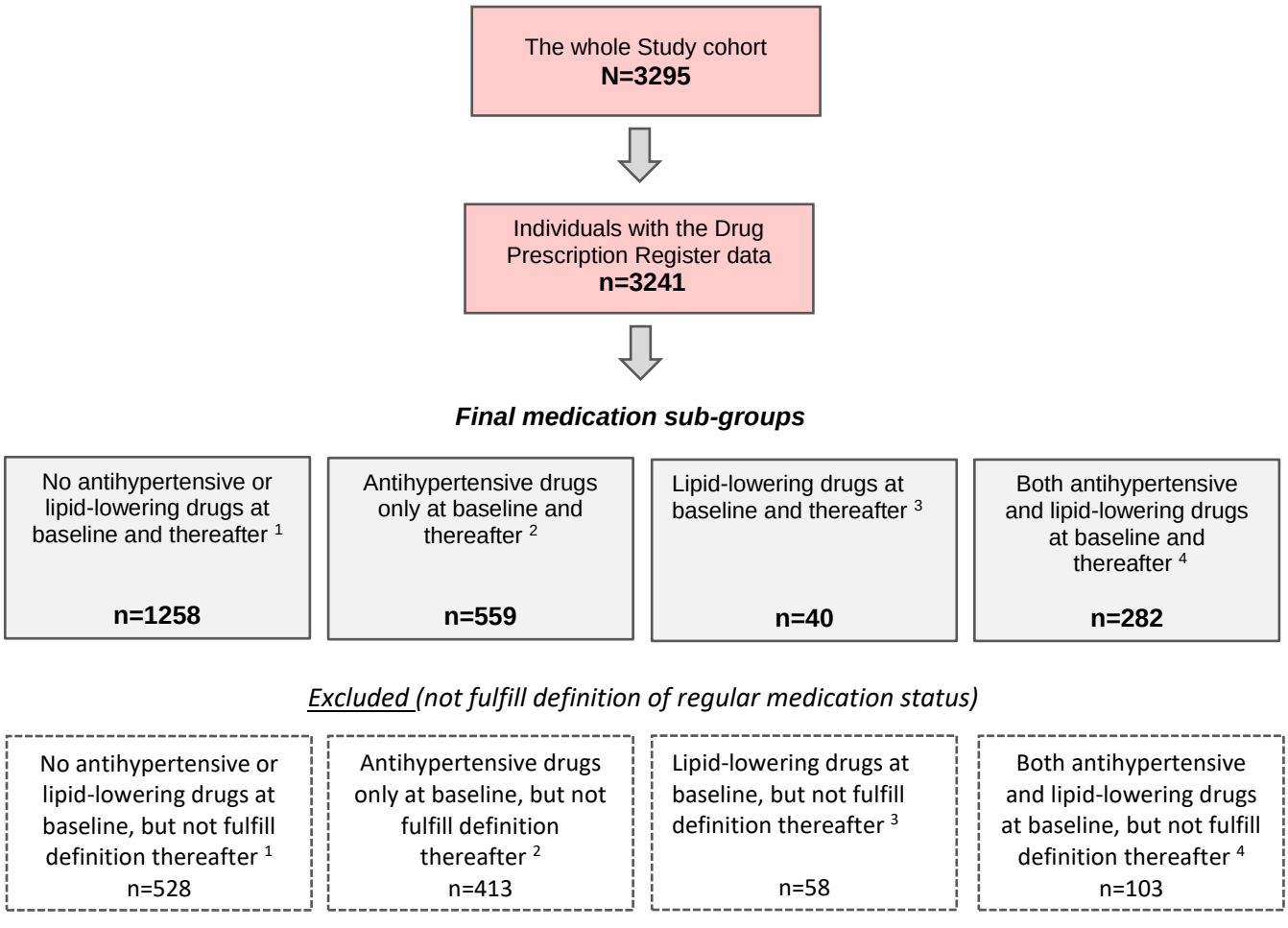
Supplementary Figures

Supplemental Figure S1. Flow chart of the study cohort inclusion process starting from the entire FinnDiane cohort (N=5496) (**A**) and sub-cohort selection process according to the pharmacological treatment (**B**)

A

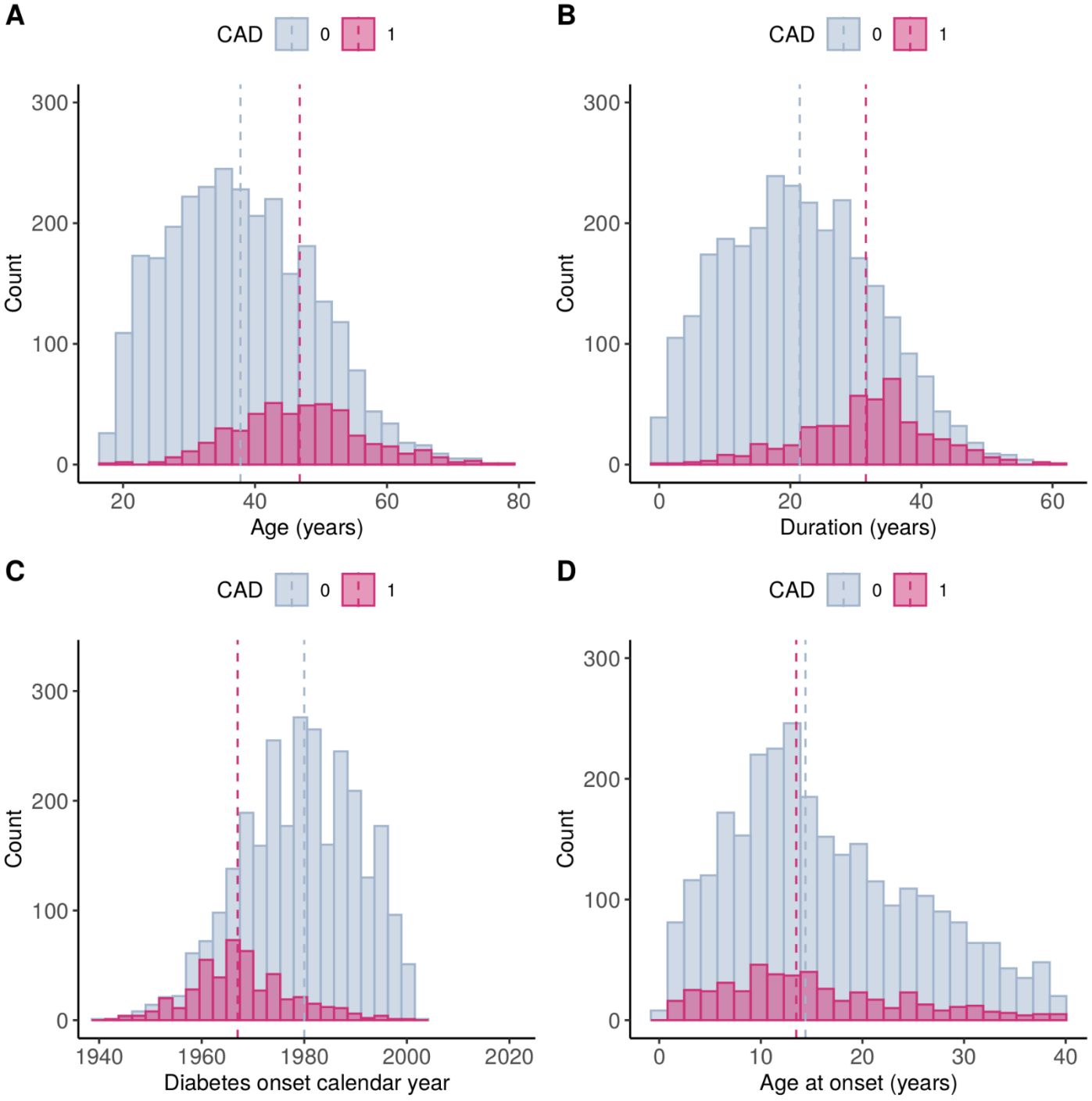


B

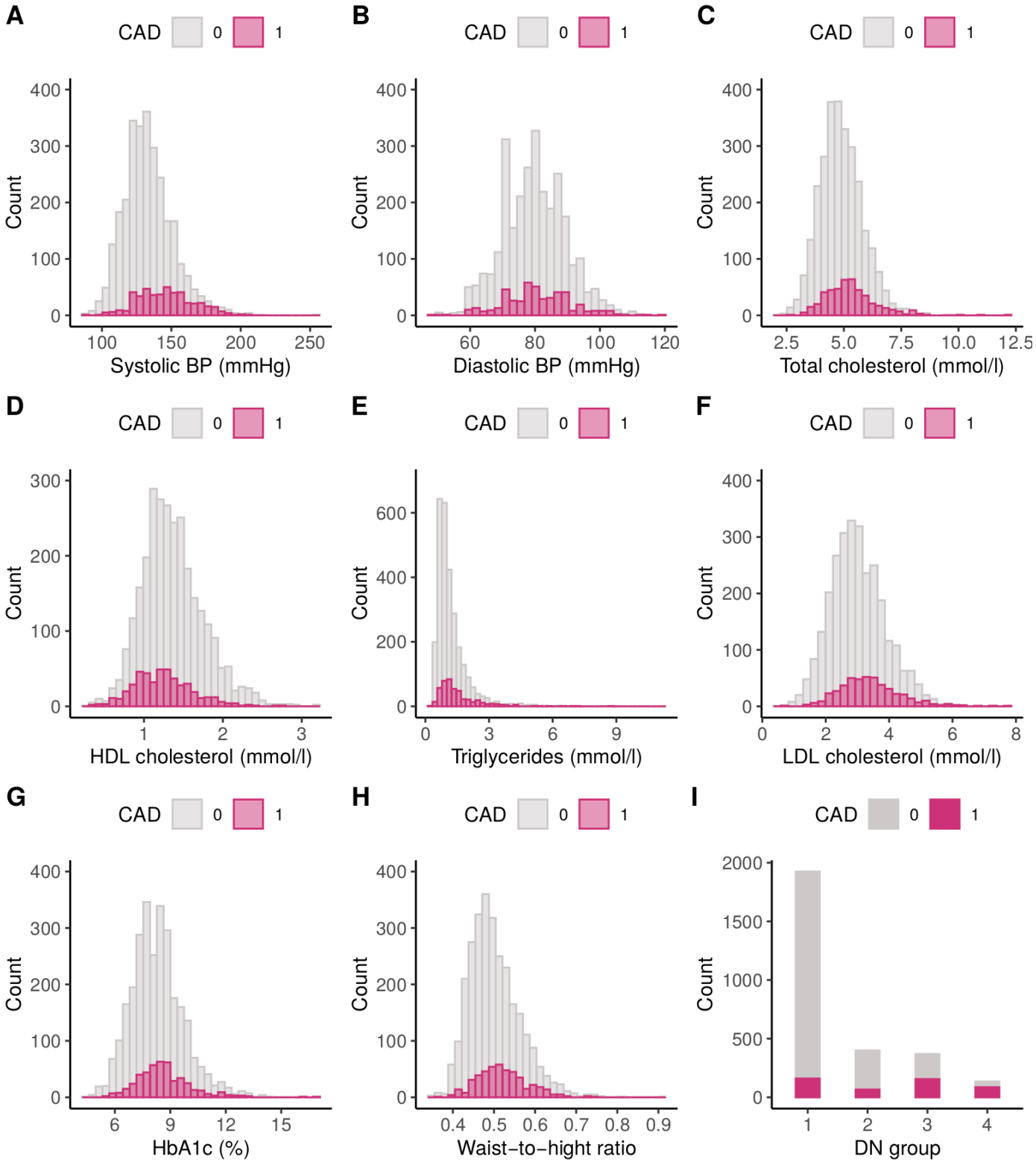


[1] No purchases of antihypertensive and lipid-lowering drugs at baseline and adherence <0.50 for both drugs during the follow-up
[2] Only purchases of antihypertensive drugs at baseline and adherence ≥0.80 for antihypertensive drugs, but <0.50 for lipid-lowering drugs during the follow-up
[3] Only purchases of lipid-lowering drugs at baseline and adherence for lipid-lowering drugs ≥0.80, but <0.50 for antihypertensive drugs during the follow-up
[4] Purchases of antihypertensive and lipid-lowering drugs at baseline and adherence ≥0.80 for both drugs

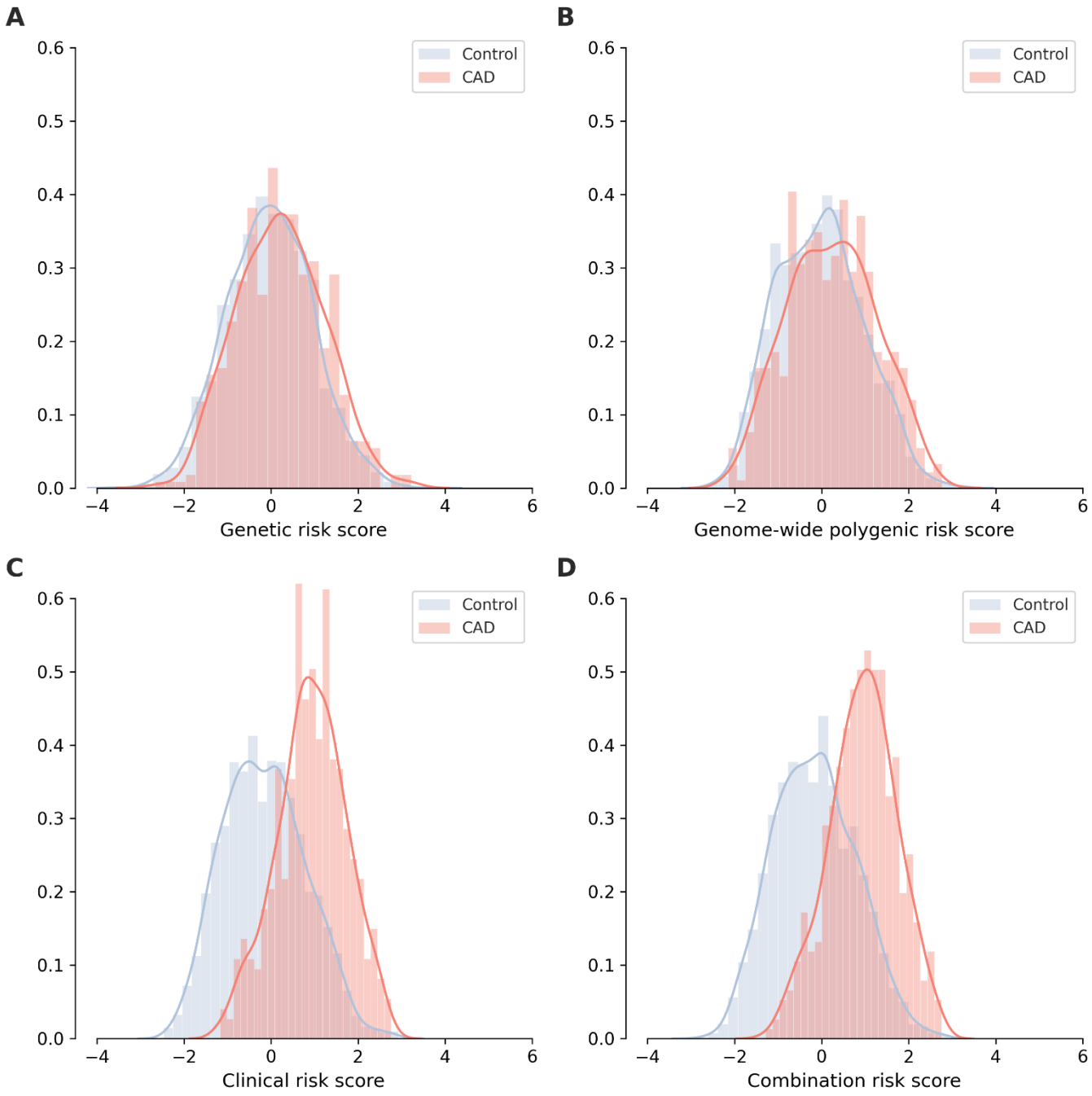
Supplemental Figure S2. Distribution of age (**A**), diabetes duration (**B**), calendar year of type 1 diabetes onset (**C**) and onset age of diabetes (**D**) for 467 CAD cases (red) and for 2,828 controls (grey) at the baseline



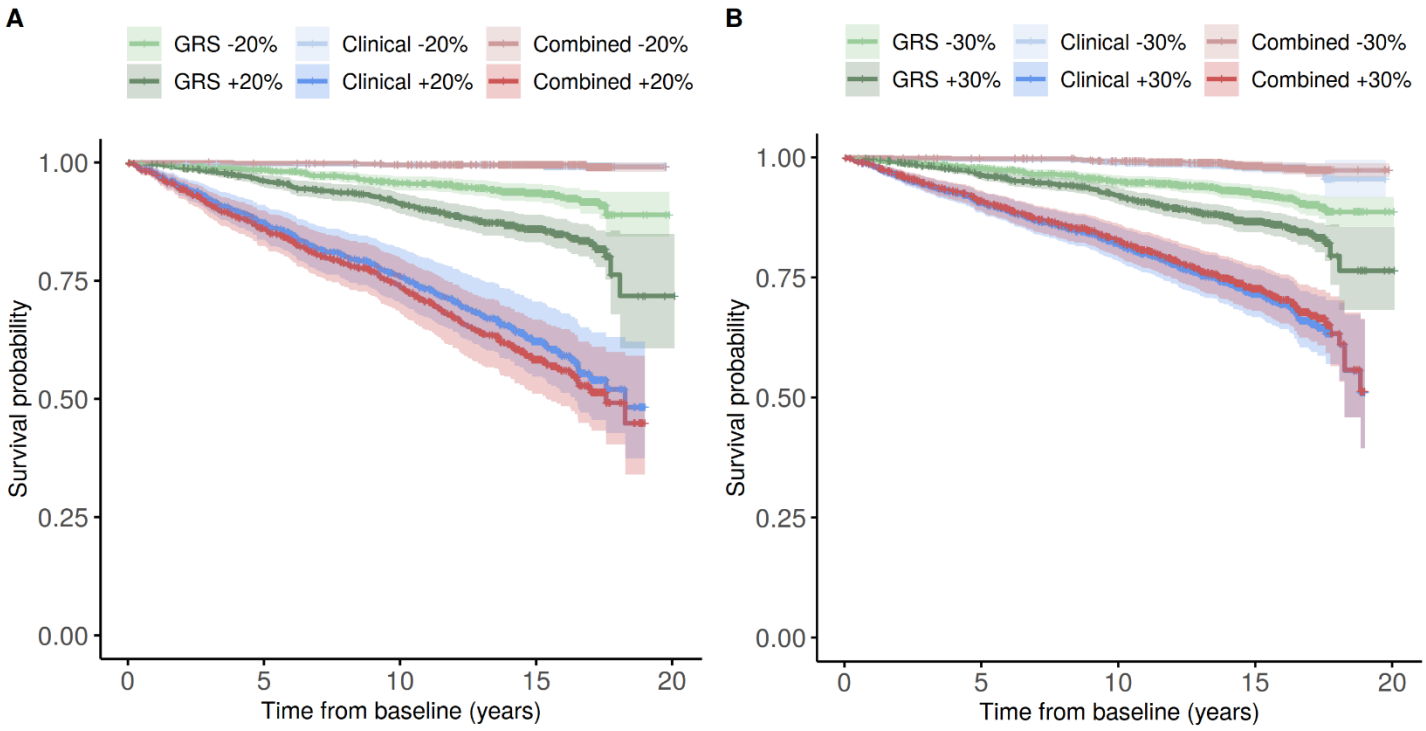
Supplemental Figure S3. Distributions of clinical variables. Systolic BP (**A**), diastolic BP (**B**), total cholesterol (**C**) HDL cholesterol (**D**) triglycerides (**E**), LDL cholesterol (**F**), HbA_{1c} (**G**), waist-to-height ratio (**H**) and diabetic nephropathy (DN) status (1. normal AER, 2. microalbuminuria, 3. macroalbuminuria and 4. end-stage renal disease (**I**) for 467 CAD cases (red) and for 2,828 controls (grey) at the baseline



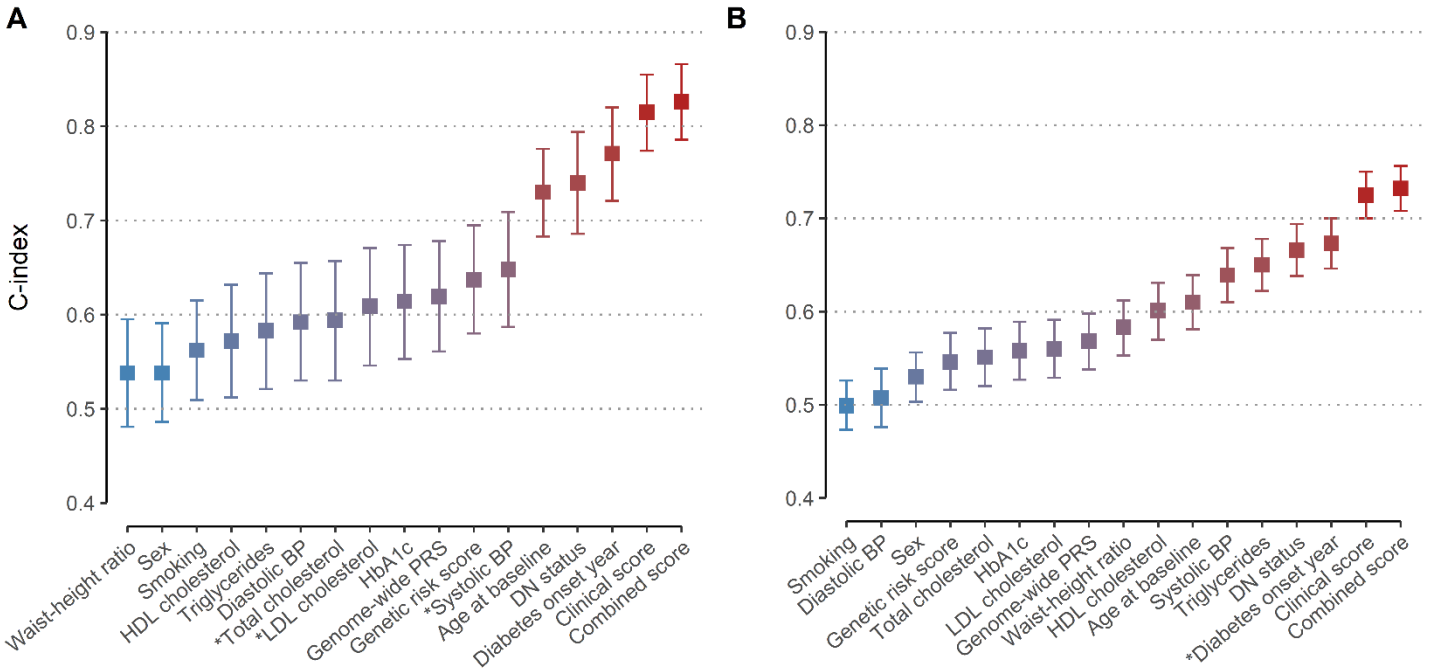
Supplemental Figure S4. Kernel density distribution of genetic (**A**), genome-wide polygenic (**B**), clinical (**C**) and combined (**D**) risk scores for 467 CAD cases (red) and for 2,828 controls (grey) at the baseline



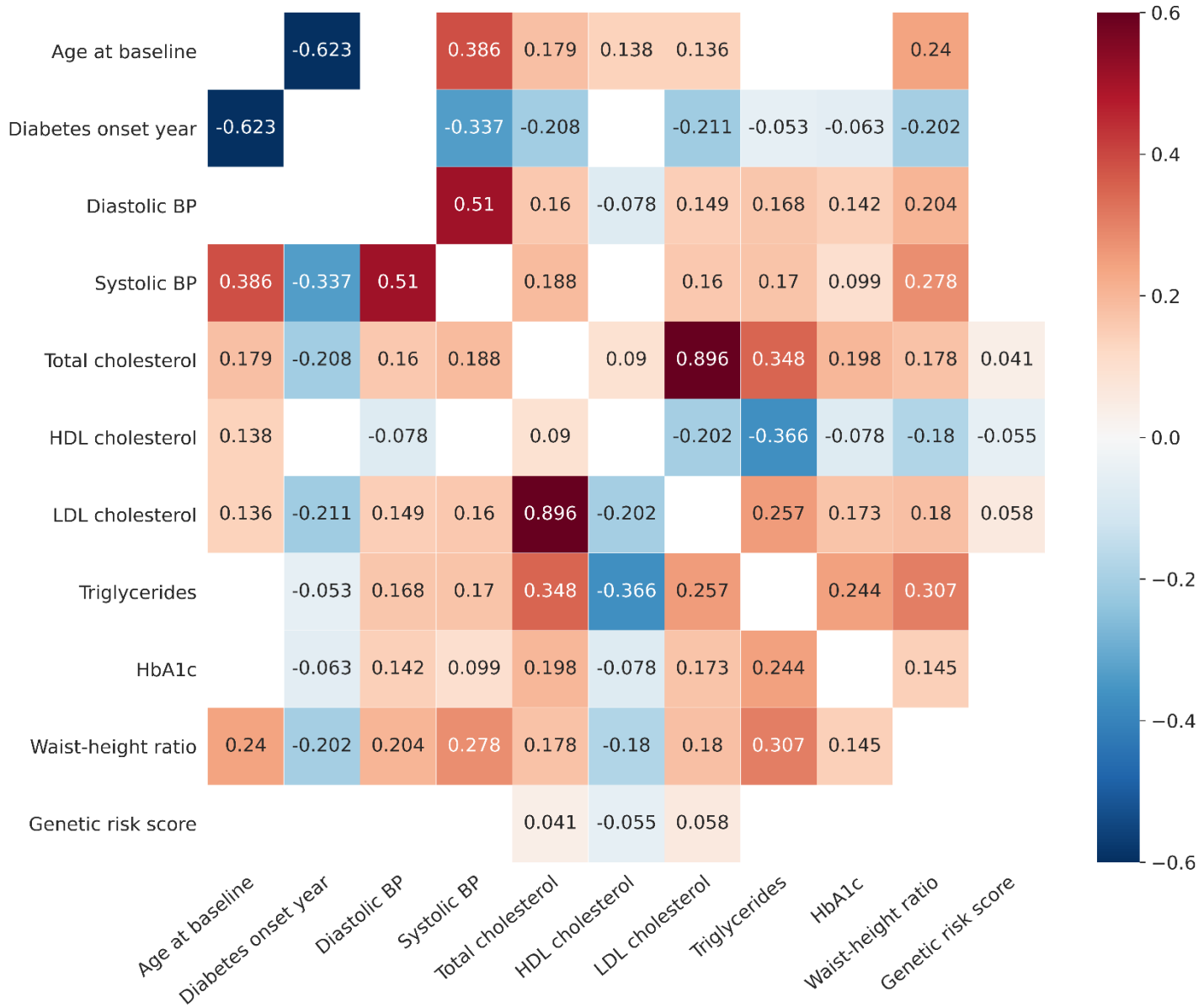
Supplemental Figure S5. Predicted survival functions of Cox proportional hazards models according to 20th percentiles of genetic (GRS), clinical- and combined scores (**A**), and 30th percentiles of GRS, clinical and combined risk scores (**B**). Models are adjusted for sex and type 1 diabetes onset year.



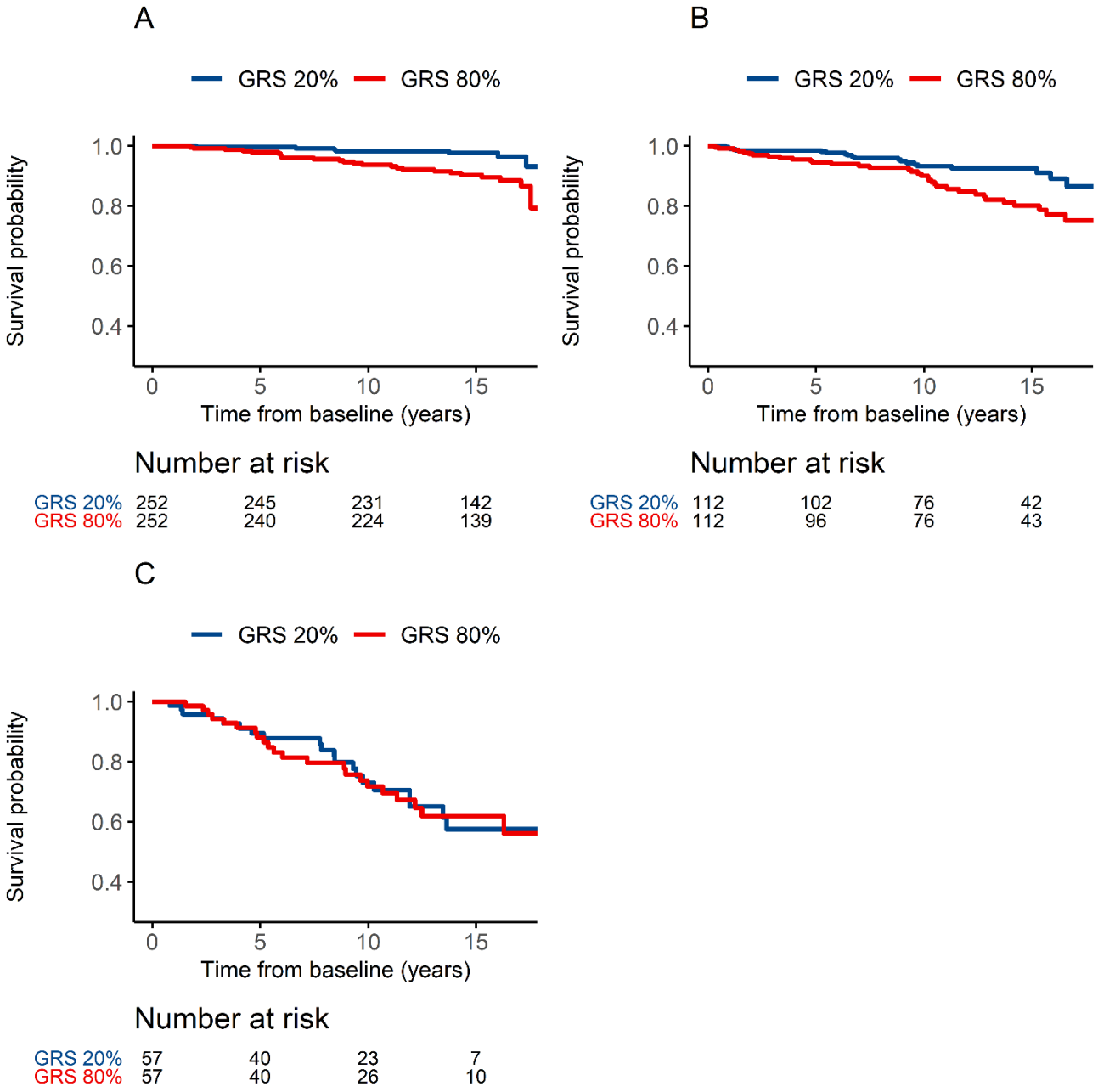
Supplemental Figure S6. C-indexes for clinical covariates, as well as genetic, clinical and combined risk scores according to the younger (i.e. median age at baseline <38.6 years) (**A**) and the older (i.e. median age at baseline ≥38.6 years) (**B**) age groups**.** Variables marked with an * violated the Cox proportional hazard assumption. Following the method from Zhang et al. (16) the follow-up time was split into three distinct periods as required for the model not to violate the assumption, however C-indexes were similar to ones reported. Notably, no differences were observed in C-indexes between the genetic risk score and the genome-wide polygenic risk score (PRS) neither in the younger (p-value 0.34) nor in the older (p-value 0.12) age groups.



Supplemental Figure S7. Correlation heatmap of clinical variables and genetic risk score (GRS). GRS correlates significantly only with HDL, LDL, and total cholesterol. Most of the clinical variables are inter-correlated with each other. These variables correlate at least with four other parameters (baseline age correlated with five other parameters, while the rest with more than five parameters).



Supplemental Figure S8. Predicted survival functions of Cox models according to the low and the high genetic risk score quintiles at each medication group. Models adjusted for sex and type 1 diabetes onset calendar year. A=no antihypertensive or lipid-lowering drugs, B=antihypertensive drug only, C=both antihypertensive and lipid-lowering drugs.



Supplemental references

1. Antikainen AAV, Sandholm N, Tregouet DA, et al. Genome-wide association study on coronary artery disease in type 1 diabetes suggests beta-defensin 127 as a risk locus. *Cardiovasc Res* 2021;117:600-612

2. Erdmann J, Kessler T, Munoz Venegas L, Schunkert H. A decade of genome-wide association studies for coronary artery disease: the challenges ahead. *Cardiovasc Res* 2018;114:1241-1257

3. Samani NJ, Erdmann J, Hall AS, et al. WTCCC, the Cardiogenics Consortium. Genomewide association analysis of coronary artery disease. *N Engl J Med* 2007;357:443453

4. van der Harst P, Verweij N. The identification of 64 novel genetic loci provides an expanded view on the genetic architecture of coronary artery disease. *Circ Res* 2017;122:433–443

5. Verweij N, Eppinga RN, Hagemeijer Y, van der Harst P. Identification of 15 novel risk loci for coronary artery disease and genetic risk of recurrent events, atrial fibrillation and heart failure. *Sci Rep* 2017;7:2761

6. Schunkert H, König IR, Kathiresan S, et al. Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease. *Nat Genet* 2011;43:333–338

7. Howson JMM, Zhao W, Barnes DR, et al. Fifteen new risk loci for coronary artery disease highlight arterial-wall-specific mechanisms. *Nat Genet* 2017;49:1113–1119

8. Nikpay M, Goel A, Won HH, et al. A comprehensive 1,000 Genomes-based genome-wide association meta-analysis of coronary artery disease. *Nat Genet* 2015;47:1121–1130

9. Myocardial Infarction Genetics and CARDIoGRAM Exome Consortia Investigators, Stitziel NO, Stirrups KE, Masca NG, et al. Coding Variation in ANGPTL4, LPL, and SVEP1 and the Risk of Coronary Disease. *N Engl J Med* 2016;374:1134-44

10. Klarin D, Zhu QM, Emdin CA, et al. Genetic analysis in UK Biobank links insulin resistance and transendothelial migration pathways to coronary artery disease. *Nat Genet* 2017;49:1392–1397

11. Nelson CP, Goel A, Butterworth AS, et al. Association analyses based on false discovery rate implicate new loci for coronary artery disease. *Nat Genet* 2017;49:1385–1391

12. Coronary Artery Disease (C4D) Genetics Consortium. A genome-wide association study in Europeans and South Asians identifies five new loci for coronary artery disease. *Nat Genet* 2011;43:339–344

13. Deloukas P, Kanoni S, Willenborg C, et al. Large-scale association analysis identifies new risk loci for coronary artery disease. *Nat Genet* 2013;45:25–33

14. Webb TR, Erdmann J, Stirrups KE, et al. Systematic evaluation of pleiotropy identifies 6 further loci associated with coronary artery disease. *J Am Coll Cardiol* 2017;69:823–836

15. Consortium IBC. Large-scale gene-centric analysis identifies novel variants for coronary artery disease. *PLoS Genet* 2011;7:e1002260

16. Zhang Z, Reinikainen J, Adeleke KA, Pieterse ME, Groothuis-Oudshoorn CGM. Time-varying covariates and coefficients in Cox regression models. *Ann Transl Med* 2018;6:121