Interaction of genetic risk and lifestyle on the incidence of atrial fibrillation

SUPPLEMENTAL MATERIAL

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Supplemental Table 1 – Lifestyle risk factor scores

Lifestyle risk factor	**Score**	**Definition**
Smoking	0	Current smoking
	1	Former smoking
	2	Never smoking
Body mass index	0	≥30 kg/m^2
	1	25.0–29.99 kg/m^2
	2	<25.0 kg/m^2
Physical activity	0	No exercise
	1	1–149 min of moderate exercise or 1–74 min of vigorous exercise/week
	2	150+ min of moderate exercise or 75+ min of vigorous exercise/week
Diet	0	0-1 components of healthy diet
	1	2 components of healthy diet
	2	3 components of healthy diet
Alcohol consumption	0	>14 drinks for women and >21 drinks/week for men
	1	1-14 drinks/week for women and 1-21 drinks/week for men
	2	<1 drink/week for women and men
Total cholesterol	0	≥240 mg/dL
	1	200–239 mg/dL or treated to <200 mg/dL
	2	<200 mg/dL, unmedicated
Blood pressure	0	SBP ≥140 mmHg or DBP ≥90 mmHg
	1	SBP 120–139 mmHg or DBP 80–89 mmHg or treated to <120/80 mmHg
	2	<120/80 mm Hg, unmedicated

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Supplemental Table 2 – Components of the genetic risk score

Variant and risk allele	Risk allele	Reference allele	P-value	RAF	OR	CI	Mapped gene	Location
rs284277	C	A	1 x 10-9	0.383	1.04	[1.03-1.06]	*CASZ1*	1:10730740
rs1545300	C	T	1 x 10-14	0.691	1.06	[1.04-1.07]	*KCND3*	1:111921382
rs4073778	A	C	5 x 10-13	0.564	1.05	[1.04-1.06]	*CASQ2*	1:115755137
rs10465885	C	T	1 x 10-10	0.472	1.04	[1.03-1.06]	*GJA5*	1:147760632
rs79187193	G	A	3 x 10-14	0.943	1.12	[1.09-1.16]	*GJA5, GJA8*	1:147783720
rs6689306	A	G	1 x 10-18	0.413	1.06	[1.05-1.08]	*IL6R*	1:154423470
rs4999127	A	G	2 x 10-23	0.839	1.1	[1.08-1.12]	*KCNN3*	1:154741530
rs11264280	T	C	3 x 10-79	0.333	1.14	[1.13-1.16]	*KCNN3, PMVK*	1:154890476
rs72700114	C	G	3 x 10-54	0.076	1.22	[1.19-1.26]	*LINC01681*	1:170224684
rs72700118	A	C	2 x 10-36	0.127	1.14	[1.12-1.16]	*LINC01681*	1:170225682
rs577676	C	T	2 x 10-20	0.562	1.07	[1.05-1.08]	*GORAB, PRRX1*	1:170618199
rs10753933	T	G	1 x 10-19	0.448	1.06	[1.05-1.08]	*PPFIA4*	1:203057086
rs4951258	A	G	2 x 10-8	0.416	1.04	[1.02-1.05]	*NUCKS1*	1:205722188
rs7529220	C	T	2 x 10-10	0.847	1.06	[1.04-1.08]	*CELA3B, HSPG2*	1:21956126
rs2885697	G	T	3 x 10-10	0.352	1.04	[1.03-1.06]	*SCMH1*	1:41078607
rs11590635	A	G	4 x 10-9	0.024	1.16	[1.10-1.21]	*AGBL4*	1:48844092
rs146518726	A	G	8 x 10-15	0.033	1.17	[1.13-1.22]	*MIR6500, C1orf185*	1:51069367
rs55693294	T	C	4 x 10-9	0.061	1.09	[1.06-1.12]	*NEURL1*	10:103517717
rs11598047	G	A	9 x 10-66	0.162	1.17	[1.15-1.19]	*NEURL1*	10:103582915
rs35176054	A	T	8 x 10-41	0.130	1.15	[1.12-1.17]	*SH3PXD2A*	10:103720629
rs10749053	T	C	1 x 10-8	0.158	1.06	[1.04-1.08]	*RBM20*	10:110816937
rs12245149	C	A	2 x 10-12	0.526	1.05	[1.03-1.06]	*REEP3*	10:63561387
rs7096385	T	C	5 x 10-8	0.092	1.07	[1.05-1.10]	*SIRT1*	10:67905124
rs60212594	G	C	9 x 10-35	0.856	1.12	[1.10-1.15]	*SYNPO2L-AS1, SYNPO2L*	10:73654586
rs10458660	G	A	7 x 10-10	0.173	1.06	[1.04-1.07]	*LRMDA*	10:76176818
rs4935786	T	A	5 x 10-9	0.267	1.05	[1.03-1.06]	*'-*	11:121790799
rs76097649	A	G	1 x 10-20	0.093	1.12	[1.10-1.15]	*KCNJ5*	11:128894675
rs10741807	T	C	2 x 10-20	0.245	1.08	[1.06-1.09]	*NAV2*	11:19989899
rs883079	T	C	3 x 10-40	0.707	1.1	[1.09-1.12]	*TBX5*	12:114355435
rs10773657	C	A	3 x 10-8	0.138	1.06	[1.04-1.08]	*HIP1R*	12:122843353
rs6560886	C	T	1 x 10-8	0.788	1.05	[1.03-1.07]	*FBRSL1*	12:132573624
rs2291437	G	T	2 x 10-17	0.105	1.09	[1.07-1.12]	*SOX5*	12:24562114
rs4963776	G	T	2 x 10-25	0.818	1.1	[1.08-1.11]	*RN7SL38P, KNOP1P1*	12:24626557
rs17380837	C	T	5 x 10-12	0.693	1.05	[1.04-1.07]	*SSPN*	12:26192593
rs12809354	C	T	3 x 10-14	0.144	1.07	[1.05-1.09]	*PKP2*	12:32825503
rs11614818	C	T	2 x 10-8	0.363	1.04	[1.03-1.05]	*PSMB3P1, METTL7B*	12:55662031

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Variant and risk allele	Risk allele	Reference allele	P-value	RAF	OR	CI	Mapped gene	Location
rs2860482	A	C	1 x 10-12	0.274	1.06	[1.04-1.07]	*PTGES3, NACA*	12:56712154
rs71454237	G	A	2 x 10-13	0.791	1.06	[1.05-1.08]	*BEST3, LRRC10*	12:69619635
rs775498	G	A	9 x 10-9	0.280	1.04	[1.03-1.06]	*BEST3*	12:69677733
rs12426679	C	T	5 x 10-9	0.472	1.04	[1.03-1.05]	*'-*	12:75844207
rs35569628	T	C	1 x 10-8	0.777	1.05	[1.03-1.06]	*CUL4A*	13:113218398
rs9506925	T	C	3 x 10-9	0.267	1.05	[1.03-1.06]	*DDX39AP1, SNORD36*	13:22794804
rs422068	C	T	4 x 10-10	0.349	1.04	[1.03-1.06]	*MYH6*	14:23395595
rs1957021	C	T	5 x 10-15	0.222	1.06	[1.05-1.08]	*AKAP6*	14:32455299
rs11156751	C	T	7 x 10-21	0.285	1.07	[1.06-1.09]	*AKAP6*	14:32521231
rs73241997	T	C	3 x 10-15	0.142	1.08	[1.06-1.10]	*CFL2, RPL23AP8*	14:34704569
rs2738413	A	G	3 x 10-31	0.495	1.08	[1.07-1.10]	*ESR2, SYNE2*	14:64213242
rs74884082	C	T	3 x 10-10	0.75	1.05	[1.03-1.07]	*DPF3*	14:72782711
rs10873298	C	T	7 x 10-9	0.366	1.04	[1.03-1.06]	*LINC01629*	14:76960182
rs147301839	C	A	2 x 10-10	0.007	1.39	[1.26-1.55]	*MYZAP, GCOM1*	15:57632516
rs7170477	A	G	5 x 10-8	0.304	1.04	[1.03-1.05]	*HERC1*	15:63811578
rs74022964	T	C	4 x 10-36	0.157	1.12	[1.10-1.14]	*HCN4, REC114*	15:73384923
rs12908004	G	A	4 x 10-16	0.164	1.08	[1.06-1.10]	*LINC00927, ARNT2*	15:80384583
rs2759301	A	G	9 x 10-9	0.454	1.04	[1.03-1.05]	*ABHD17C*	15:80701947
rs4965430	C	G	1 x 10-10	0.386	1.05	[1.03-1.06]	*IGF1R*	15:98725621
rs118159104	G	T	2 x 10-8	0.014	1.2	[1.13-1.28]	*CRAMP1*	16:1626803
rs140185678	A	G	2 x 10-14	0.035	1.18	[1.13-1.23]	*RPL3L*	16:1953015
rs77316573	T	C	2 x 10-8	0.199	1.05	[1.03-1.07]	*PGP, E4F1*	16:2215270
rs2359171	A	T	5 x 10-91	0.176	1.19	[1.17-1.21]	*ZFHX3*	16:73019123
rs876727	T	G	7 x 10-9	0.791	1.05	[1.03-1.07]	*ZFHX3*	16:73033862
rs72811294	G	C	1 x 10-11	0.887	1.07	[1.05-1.10]	*MYOCD*	17:12715363
rs7225165	G	A	3 x 10-9	0.887	1.07	[1.04-1.09]	*CRK, YWHAE*	17:1406556
rs11658278	T	C	3 x 10-11	0.479	1.05	[1.03-1.06]	*ZPBP2*	17:39874911
rs1563304	T	C	3 x 10-12	0.178	1.07	[1.05-1.09]	*WNT3*	17:46797087
rs9899183	T	C	2 x 10-9	0.714	1.05	[1.03-1.06]	*TNFSF12-TNFSF13, TNFSF12*	17:7549660
rs12604076	T	C	4 x 10-8	0.478	1.04	[1.02-1.05]	*CYTH1*	17:78777556
rs9953366	C	T	2 x 10-11	0.663	1.05	[1.04-1.07]	*SMAD7*	18:48947822
rs9963878	C	T	2 x 10-8	0.085	1.07	[1.04-1.09]	*SRSF10P1, SMAD4*	18:51153152
rs8088085	A	C	5 x 10-8	0.535	1.04	[1.02-1.05]	*MEX3C*	18:51182178
rs28387148	T	C	6 x 10-11	0.105	1.08	[1.05-1.10]	*GYPC*	2:126675889
rs67969609	G	C	2 x 10-8	0.071	1.07	[1.05-1.10]	*TEX41*	2:145002786
rs56181519	C	T	6 x 10-18	0.732	1.07	[1.05-1.08]	*WIPF1, H3P6*	2:174690986
rs2288327	G	A	7 x 10-25	0.156	1.1	[1.08-1.12]	*TTN-AS1, TTN*	2:178546938

Variant and risk allele	Risk allele	Reference allele	P-value	RAF	OR	CI	Mapped gene	Location
rs3820888	C	T	6 x 10-24	0.392	1.07	[1.06-1.09]	*SPATS2L*	2:200315300
rs35544454	A	T	1 x 10-11	0.808	1.06	[1.04-1.08]	*ERBB4*	2:212401279
rs7578393	T	C	2 x 10-12	0.796	1.06	[1.05-1.08]	*KIF3C*	2:25942659
rs11125871	C	T	6 x 10-9	0.605	1.04	[1.03-1.05]	*USP34*	2:61242991
rs2540949	A	T	3 x 10-22	0.615	1.07	[1.05-1.08]	*CEP68*	2:65057097
rs6747542	T	C	1 x 10-16	0.536	1.06	[1.04-1.07]	*GMCL1*	2:69879700
rs72926475	G	A	2 x 10-11	0.877	1.07	[1.05-1.09]	*U8, KDM3A*	2:86367364
rs2834618	T	G	3 x 10-17	0.894	1.1	[1.08-1.12]	*LINC01426*	21:34746814
rs464901	T	C	2 x 10-12	0.665	1.05	[1.04-1.07]	*TUBA8*	22:18114735
rs133902	T	C	9 x 10-10	0.427	1.04	[1.03-1.06]	*MYO18B*	22:25768112
rs10804493	A	G	2 x 10-15	0.651	1.06	[1.04-1.07]	*PHLDB2, PLCXD2*	3:111835579
rs7650482	G	A	2 x 10-24	0.64	1.07	[1.06-1.09]	*CAND2*	3:12800305
rs1278493	G	A	9 x 10-9	0.436	1.04	[1.03-1.05]	*PPP2R3A*	3:136095167
rs7612445	T	G	5 x 10-9	0.188	1.05	[1.03-1.07]	*GNB4, MTHFD2P7*	3:179455191
rs60902112	T	C	2 x 10-8	0.226	1.05	[1.03-1.06]	*XXYLT1*	3:195080124
rs73041705	T	C	2 x 10-9	0.702	1.05	[1.03-1.06]	*THRB*	3:24421744
rs7374540	A	C	7 x 10-12	0.607	1.05	[1.03-1.06]	*SCN5A*	3:38592651
rs7373065	T	C	3 x 10-16	0.049	1.23	[1.17-1.29]	*SCN5A, SCN10A*	3:38668824
rs6790396	G	C	2 x 10-20	0.596	1.06	[1.05-1.08]	*SCN10A*	3:38730434
rs34080181	G	A	1 x 10-10	0.621	1.05	[1.03-1.06]	*LRIG1*	3:66403767
rs17005647	T	C	3 x 10-9	0.364	1.04	[1.03-1.06]	*FRMD4B*	3:69357030
rs6771054	T	C	2 x 10-11	0.596	1.05	[1.03-1.06]	*EPHA3*	3:89440379
rs10006327	C	T	4 x 10-8	0.49	1.04	[1.02-1.05]	*SLC9B1*	4:102969823
rs244017	T	G	8 x 10-11	0.776	1.06	[1.04-1.08]	*ENPEP, ZBED1P1*	4:110334761
rs61501369	T	C	1 x 10-28	0.234	1.1	[1.09-1.12]	*PANCR*	4:110603473
rs6850025	A	G	9 x 10-11	0.049	1.12	[1.08-1.16]	*PITX2, ANAPC10*	4:110675204
rs67249485	T	A	7 x 10-443	0.199	1.44	[1.42-1.46]	*LINC01438*	4:110778529
rs3853445	T	C	4 x 10-52	0.734	1.16	[1.13-1.18]	*MIR297, LINC01438*	4:110840331
rs79399769	C	T	2 x 10-18	0.966	1.24	[1.18-1.30]	*LYPLA1P2*	4:111004500
rs1532170	G	A	8 x 10-18	0.451	1.07	[1.05-1.08]	*RNU6-289P*	4:111244056
rs138311480	C	T	3 x 10-9	0.978	1.18	[1.12-1.25]	'-	4:111533139
rs114904067	G	A	9 x 10-9	0.972	1.13	[1.09-1.18]	'-	4:111683665
rs7687819	A	G	9 x 10-9	0.771	1.05	[1.03-1.06]	*ALPK1*	4:112408189
rs6829664	G	A	2 x 10-13	0.262	1.06	[1.04-1.07]	*CAMK2D*	4:113527500
rs10213171	G	C	1 x 10-11	0.061	1.1	[1.07-1.12]	*ARHGAP10*	4:148016386
rs10520260	A	G	6 x 10-10	0.679	1.05	[1.03-1.06]	*HAND2*	4:173526198
rs12648245	T	C	3 x 10-13	0.924	1.1	[1.07-1.12]	*LINC02269*	4:173720033

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rs1458038	T	C	2 x 10-9	0.309	1.04	[1.03-1.06]	*FGF5, PRDM8*	4:80243569
rs6596717	C	A	3 x 10-9	0.395	1.04	[1.03-1.06]	*LINC01950*	5:107091908
rs337705	G	T	2 x 10-16	0.375	1.06	[1.04-1.07]	*KCNN2*	5:114401365
rs2012809	G	A	5 x 10-10	0.79	1.06	[1.04-1.08]	*SLC27A6*	5:128854670
rs2040862	T	C	1 x 10-35	0.178	1.11	[1.10-1.13]	*WNT8A*	5:138084300
rs6580277	G	A	2 x 10-17	0.237	1.07	[1.05-1.09]	*NR3C1*	5:143438558
rs12188351	A	G	3 x 10-9	0.056	1.09	[1.06-1.12]	*SLIT3*	5:168959084
rs6891790	G	T	5 x 10-22	0.717	1.08	[1.06-1.09]	*Y_RNA, NKX2-5*	5:173243742
rs28439930	G	C	2 x 10-11	0.517	1.05	[1.03-1.06]	*CPEB4, C5orf47*	5:173966108
rs3951016	A	T	2 x 10-22	0.459	1.07	[1.05-1.08]	*SLC35F1*	6:118238495
rs9401451	G	A	3 x 10-11	0.900	1.08	[1.05-1.10]	*HMGB3P18, RPL23AP48*	6:121778006
rs13195459	G	A	4 x 10-19	0.638	1.06	[1.05-1.08]	*'-*	6:122082413
rs117984853	T	G	1 x 10-24	0.101	1.13	[1.10-1.16]	*UST, TAB2*	6:149077964
rs73366713	G	A	2 x 10-25	0.86	1.11	[1.09-1.13]	*ATXN1*	6:16415520
rs34969716	A	G	2 x 10-19	0.305	1.07	[1.06-1.09]	*KDM1B*	6:18209878
rs3176326	G	A	1 x 10-13	0.802	1.06	[1.05-1.08]	*CDKN1A*	6:36679512
rs2031522	A	G	1 x 10-10	0.624	1.04	[1.03-1.06]	*RCN1P1, CGA*	6:87111783
rs11773845	A	C	2 x 10-55	0.586	1.11	[1.10-1.13]	*CAV1*	7:116551247
rs55985730	G	T	5 x 10-9	0.06	1.09	[1.06-1.12]	*OPN1SW, CCDC136*	7:128776990
rs55734480	A	G	2 x 10-12	0.249	1.06	[1.04-1.07]	*DGKB*	7:14332384
rs7789146	G	A	2 x 10-11	0.821	1.06	[1.04-1.08]	*KCNH2*	7:150964321
rs6462079	A	G	9 x 10-10	0.721	1.05	[1.03-1.06]	*CREB5*	7:28376208
rs35005436	C	T	3 x 10-10	0.155	1.06	[1.04-1.08]	*GTF2I*	7:74720592
rs56201652	G	A	2 x 10-12	0.733	1.05	[1.04-1.07]	*CDK6*	7:92648802
rs35620480	C	A	5 x 10-9	0.157	1.06	[1.04-1.07]	*LINC00208, GATA4*	8:11642399
rs62521286	G	A	4 x 10-19	0.066	1.13	[1.10-1.16]	*FBXO32*	8:123539735
rs4871397	G	C	1 x 10-9	0.089	1.09	[1.06-1.12]	*KLHL38, RN7SKP155*	8:123622957
rs6994744	C	A	1 x 10-9	0.495	1.04	[1.03-1.05]	*PTK2*	8:140730769
rs7508	A	G	2 x 10-21	0.711	1.07	[1.06-1.09]	*ASAH1*	8:18056461
rs7834729	G	T	4 x 10-10	0.885	1.07	[1.05-1.09]	*XPO7*	8:21964267
rs2274115	G	A	2 x 10-10	0.7	1.05	[1.03-1.07]	*LHX3*	9:136202927
rs10821415	A	C	3 x 10-34	0.413	1.09	[1.07-1.10]	*AOPEP*	9:94951177

The genetic variants presented in the table were derived from summary statistics from Nielsen, J.B., Thorolfsdottir, R.B., Fritsche, L.G. *et al.* Biobank-driven genomic discovery yields new insight into atrial fibrillation biology. *Nat Genet* **50**, 1234–1239 (2018).

Supplemental Table 3 – ICD codes for outcome and covariates

	ICD-10 codes	**ICD-8 codes**
Heart failure	I50, I50.0, I50.0A, I50.1, I50.1A, I50.1B, I50.1C, I50.1D, I50.9, I11.0, I13.0, I13.2, I42.0	427.09, 427.10, 427.11, 42719, 428.99, 782.49
Hypertension	I10, I10.9, I11, I11.0, I11.9, I11.9A, I12, I12.0, I12.9, I12.9A, I13, I13.0, I13.1, I13.2, I13.9, I15, I15.0, I15.1, I15.2, I15.8, I15.9	400.09, 400.19, 400.29, 400.39, 400.99, 401.99, 402.99, 403.99, 404.99, 410.09, 411.09, 412.09, 413.09, 414.09, 430.00, 430.01, 430.08, 430.09, 431.00, 431.01, 431.08, 431.09, 432.00, 432.01, 432.02, 432.08, 432.09, 433.09, 434.09, 435.09, 436.00, 436.01, 436.09, 437.00, 437.01, 437.08, 437.09, 438.09
Ischemic stroke	I63, I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9, I64, I64.9	433.09, 433.99, 434.09, 434.99, 436.01, 436.90
Diabetes Mellitus	E10, E10.0, E10.1, E10.2, E10.3, E10.4, E10.5, E10.5A, E10.5B, E10.5C, E10.5D, E10.6, E10.7, E10.8, E10.9, E10.9A, E11, E11.0, E11.1, E11.2, E11.3, E11.4, E11.5, E11.5A, E11.5B, E11.5C, E11.5D, E11.6, E11.7, E11.8, E11.9, E11.9A, E14, E14.0, E14.1, E14.2, E14.3, E14.4, E14.5, E14.5A, E14.5B, E14.5C, E14.5D, E14.6, E14.7, E14.8, E14.9	249.00, 249.08, 249.09, 250.00, 250.08, 250.09
Myocardial infarction	I20.0, I20.0B, I20.0C I21, I21.0, I21.0A, I21.0B, I21.1, I21.1A, I21.1B, I21.3, I21.3A, I21.3B, I21.3C, I21.4, I21.9, I21.9A, I23, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.6A, I23.6B, I23.8, I23.8A	410.09, 410.99
Atrial fibrillation	I48, I48.0, I48.1, I48.2, I48.3, I48.4, I48.9	427.93, 427.94

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Supplemental Table 4 – Baseline characteristics according to lifestyle status in the random subcohort

	Ideal (N=402, 10%)	**Intermediate** (N=1,185, 29%)	**Poor** (N=2,449, 61%)
Age (years)	54 (51-58)	55 (52-59)	56 (52-60)
Women	243 (60%)	712 (60%)	1,223 (50%)
School education < 8 years	91 (23%)	320 (27%)	864 (35%)
Body mass index (kg/m^2)	23.2 (21.5-24.5)	24.1 (22.4-26.1)	26.2 (24.1-28.7)
Systolic blood pressure (mmHg)	118 (112-128)	129 (119-142)	143 (131-156)
Diastolic blood pressure (mmHg)	74 (68-80)	80 (73-86)	84 (78-91)
Total cholesterol (mmol/L)	5 (4.6-5.7)	5.6 (5.0-6.2)	6.4 (5.7-7.0)
Physical activity (hours/week)	15 (10.5-22)	15 (10.5-22)	14 (9.5-21.5)
Alcohol intake (drinks/week)	6 (2-11)	8 (4-13)	11 (5-25)
Smoking			
Current	20 (5%)	233 (20%)	1,159 (47%)
Prior	67 (17%)	310 (26%)	754 (31%)
Never	310 (78%)	642 (54%)	536 (22%)
Diabetes mellitus	8 (2%)	22 (2%)	69 (3%)
Heart failure	2 (0.5%)	4 (0.3%)	12 (0.5%)
Myocardial infarction	3 (1%)	14 (1%)	56 (2%)
Stroke	1 (0.2%)	5 (0.4%)	20 (1%)

Values are n (%) and median (25^{th}-75^{th} percentile).

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Supplemental Table 5 – Hazard ratios of atrial fibrillation according to genetic risk score in the cases and the random subcohort and stratified by sex

	Total			**Women**	**Men**
	Hazard ratio (Age and sex adjusted)	**Hazard ratio#** (Multivariable adjusted)	**Subhazard ratio*** (Multivariable adjusted)	**Hazard ratio** (Multivariable adjusted)	**Hazard ratio** (Multivariable adjusted)
Genetic risk score					
Low	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**
Intermediate	1.99 (1.73-2.29)	1.97 (1.71-2.27)	2.00 (1.74-2.29)	2.22 (1.77-2.78)	1.86 (1.55-2.23)
High	4.22 (3.56-5.00)	4.27 (3.61-5.06)	4.22 (3.57-4.98)	4.39 (3.37-5.73)	4.19 (3.37-5.21)

Multivariable adjusted models were adjusted for age, sex, educational level, heart failure, stroke, diabetes mellitus, and myocardial infarction at baseline. Hazard ratios are weighted.
#) Harrell's C-index = 0.68 (95% CI 0.68-0.70)
*) Adjusted for competing risk of death

Supplemental Table 6 – Hazard ratios of atrial fibrillation according to lifestyle status in the cases and the random subcohort and stratified by sex

	Total			**Women**	**Men**
	Hazard ratio (Age and sex adjusted)	**Hazard ratio#** (Multivariable adjusted)	**Subhazard ratio*** (Multivariable adjusted)	**Hazard ratio** (Multivariable adjusted)	**Hazard ratio** (Multivariable adjusted)
Lifestyle status					
Ideal	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**
Intermediate	1.33 (1.07-1.65)	1.32 (1.05-1.65)	1.31 (1.05-1.64)	1.23 (0.90-1.69)	1.37 (1.01-1.86)
Poor	1.99 (1.62-2.45)	1.92 (1.56-2.36)	1.88 (1.53-2.31)	1.73 (1.28-2.33)	2.04 (1.54-2.71)

Multivariable-adjusted models were adjusted for age, sex, educational level, heart failure, stroke, diabetes mellitus, and myocardial infarction. Hazard ratios are weighted.
#) Harrell's C-index=0.67 (95% CI 0.66-0.68)
*) Adjusted for competing risk of death

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Supplemental Table 7 – Hazard ratios of atrial fibrillation according to genetic risk score and lifestyle status in the cases and the random subcohort adjusting for competing risk of death

	Genetic risk score Hazard ratio (95% CI)		
	Low	**Intermediate**	**High**
Lifestyle status			
Ideal	**Reference**	2.86 (1.50-5.47)	6.38 (3.10-13.10)
Intermediate	1.73 (0.91-3.29)	3.88 (2.11-7.14)	8.05 (4.25-15.26)
Poor	2.83 (1.53-5.22)	5.34 (2.93-9.73)	11.33 (6.15-20.85)

Multivariable adjusted models were adjusted for age, sex, educational level, heart failure, stroke, diabetes mellitus, and myocardial infarction and for competing risk of death. Hazard ratios are weighted.

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Supplemental Table 8 – Hazard ratios of atrial fibrillation according to lifestyle status in the cases and the random subcohort stratified by genetic risk score

	Genetic risk score Hazard ratio (95% CI)		
	Low	**Intermediate**	**High**
Lifestyle status			
Ideal	**Reference**	**Reference**	**Reference**
Intermediate	1.86 (0.95-3.63)	1.36 (1.02-1.81)	1.09 (0.68-2.56)
Poor	2.91 (1.55-5.46)	1.93 (1.48-2.53)	1.68 (1.10-2.56)

Multivariable adjusted models were adjusted for age, sex, educational level, heart failure, stroke, diabetes mellitus, and myocardial infarction at baseline. Hazard ratios are weighted.

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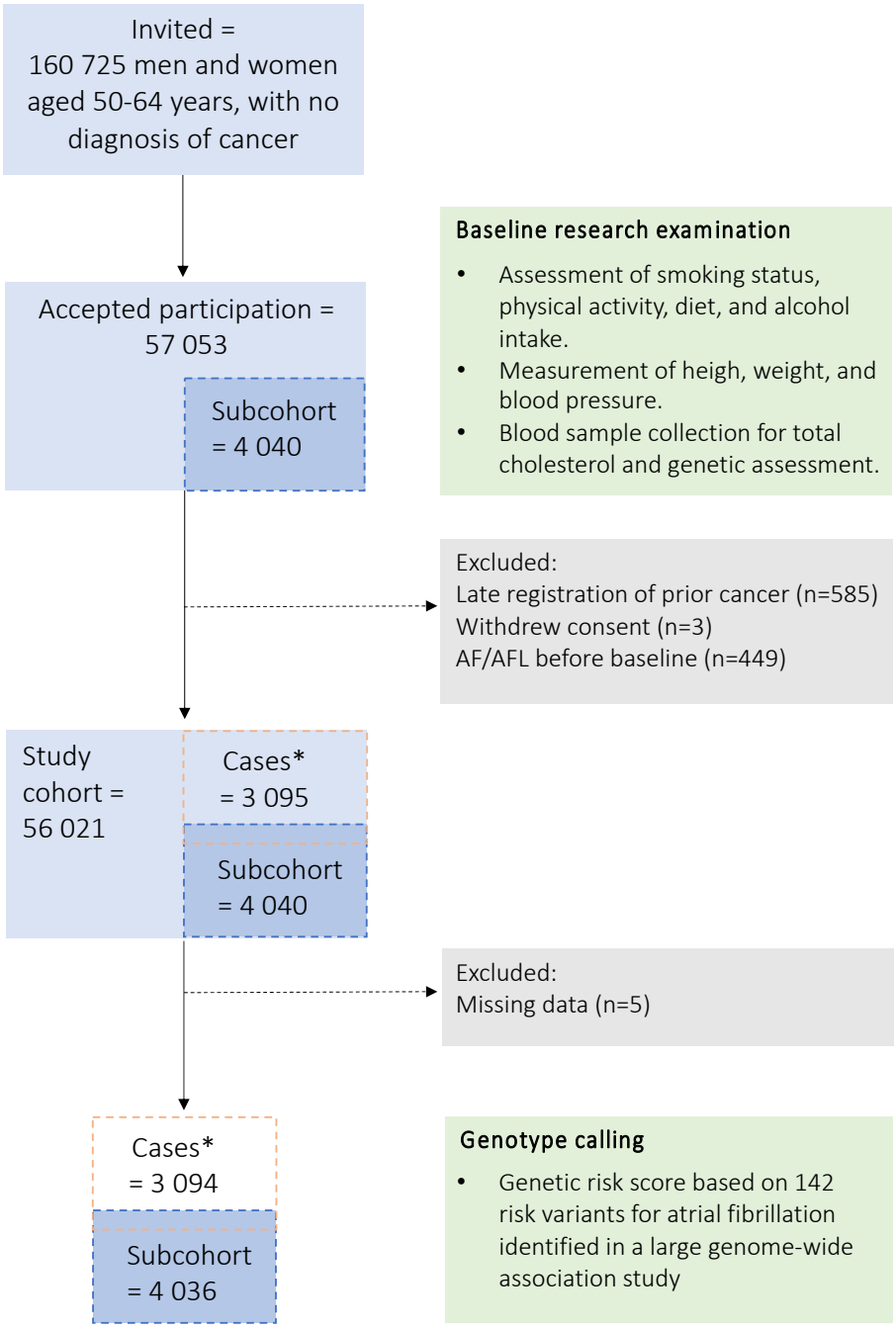
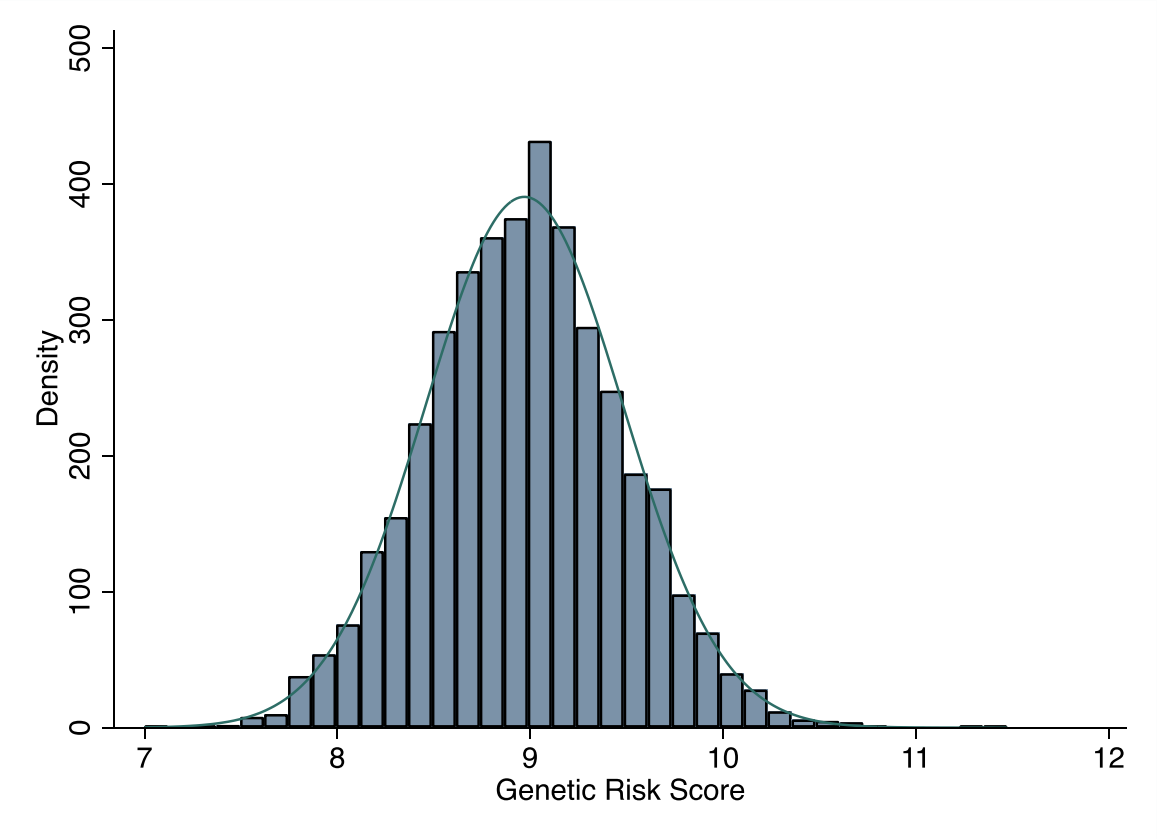
Supplemental Figure 1 – Study flowchart



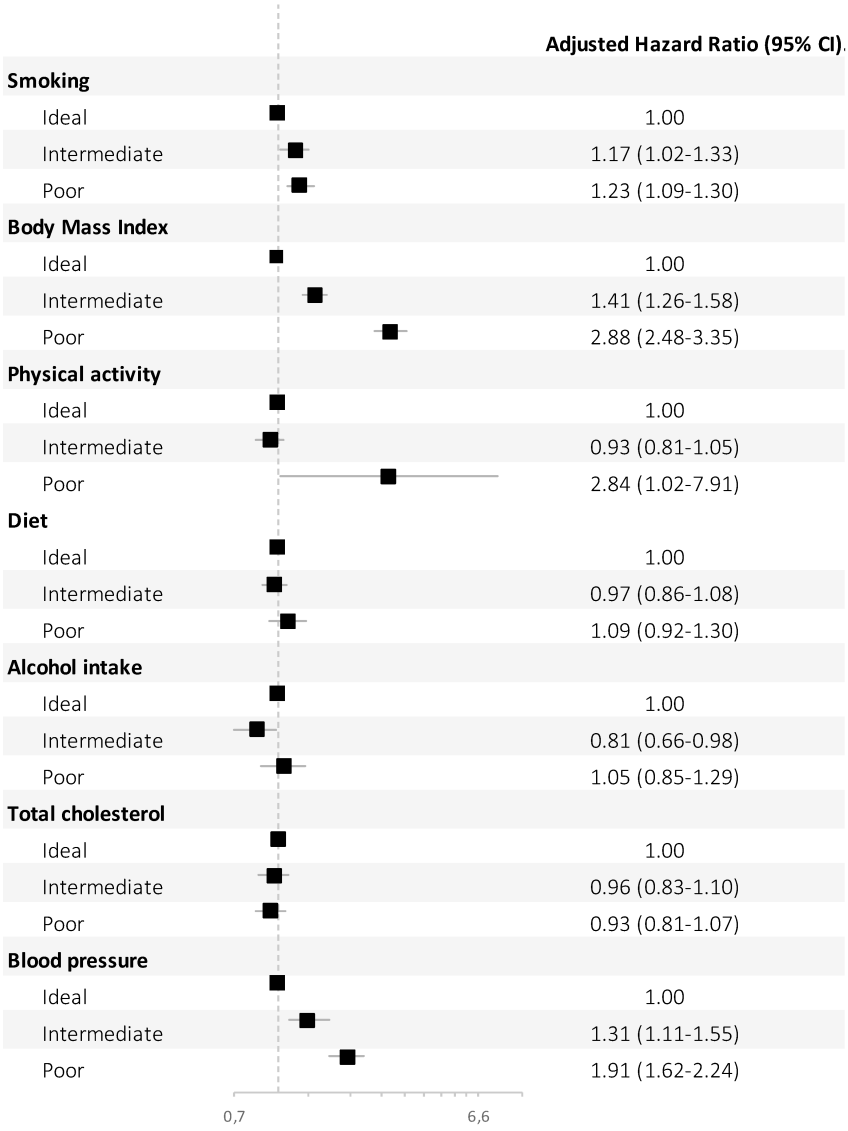
*= The overlap between cases and the random subcohort indicates that 234 individuals from the random subcohort had incident atrial fibrillation (AF) during follow-up and were also considered to be cases.

Supplemental Figure 2 - Distribution of genetic risk score in the random subcohort



Mean genetic risk score (range) was 8.97 (6.99-11.47).

Supplemental Figure 3 - Hazard ratios of atrial fibrillation according to individual lifestyle risk factors in in the cases and the random subcohort



Multivariable-adjusted models were adjusted for age, sex, educational level, heart failure, stroke, diabetes mellitus, and myocardial infarction at baseline. The X-axis in the forest plot is logarithmic. Hazard ratios are weighted.

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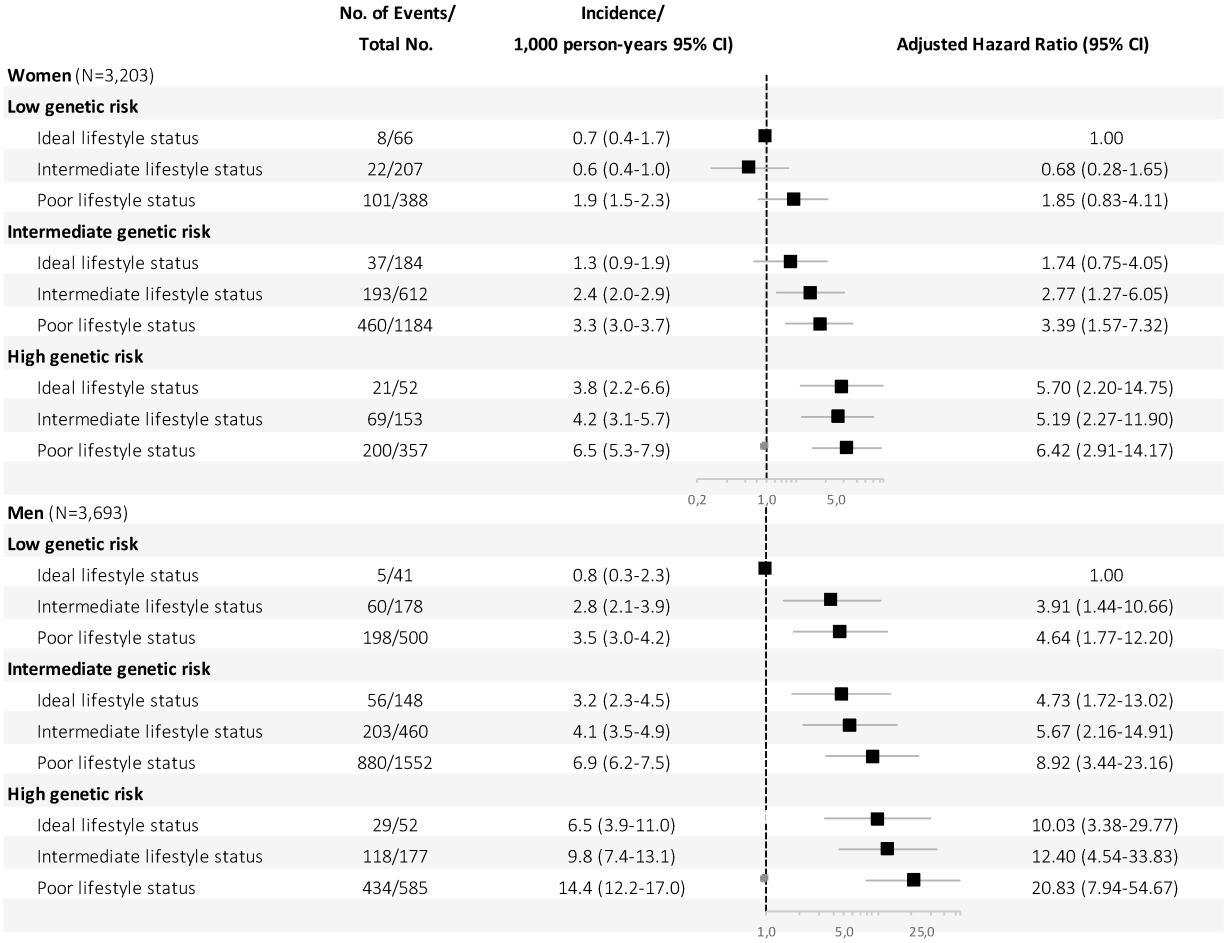
Supplemental Figure 4 - Incidence rates and hazard ratios of atrial fibrillation according to genetic risk score and lifestyle status in in the cases and the random subcohort stratified by sex



Multivariable-adjusted models were adjusted for age, educational level, heart failure, stroke, diabetes mellitus, and myocardial infarction at baseline. The X-axis in the forest plot is logarithmic. Incidence rates and hazard ratios are weighted.

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