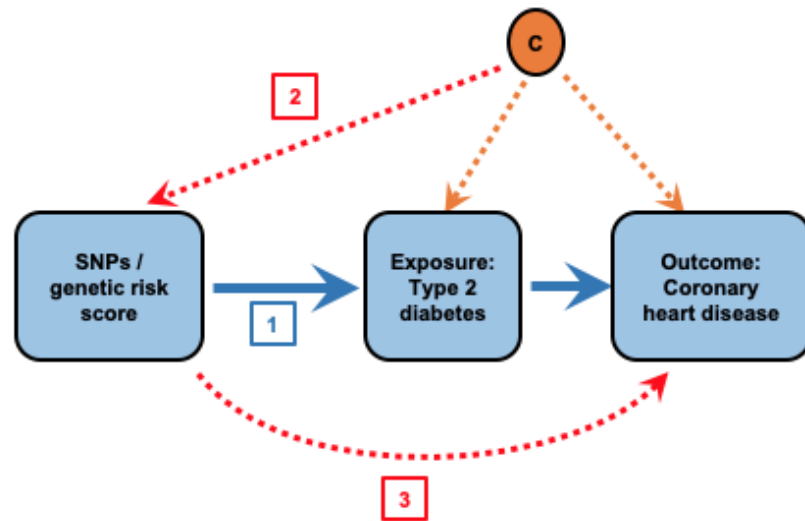


Supplemental Figure 1.



Assumptions of Mendelian randomization: 1) The variants must be associated with the exposure of interest; 2) The variants must not be associated with confounders of the relationship between the exposure and the outcome; 3) The variants must be independent of the outcome except for their association via the exposure. SNP: single nucleotide polymorphism; C: Confounders

Supplemental Table 1. Details of the 270 single nucleotide polymorphisms (SNP) used as a genetic instrument for type 2 diabetes in Mendelian randomization analyses. Beta coefficients and standard errors (SE) for the association of each SNP with type 2 diabetes from the European DIAMANTE genome-wide association study. Outlier SNPs identified using radial MR.

SNP*	Locus	Chr [†]	Effect Allele	Non-effect Allele	WOMEN		MEN		OUTLIER [‡]
					Beta	SE	Beta	SE	
rs1005752	<i>HMG20A</i>	15	A	C	0.082	0.013	0.076	0.012	W,M
rs10096633	<i>LPL</i>	8	C	T	0.086	0.019	0.056	0.017	W
rs10097617	<i>TP53INP1</i>	8	T	C	0.05	0.012	0.043	0.011	
rs10193538	<i>BNIP1</i>	2	T	G	0.025	0.012	0.033	0.011	
rs10195252	<i>GRB14/COBLL1</i>	2	T	C	0.066	0.012	0.036	0.011	
rs10228066	<i>DGKB</i>	7	T	C	0.058	0.012	0.061	0.011	
rs10406327	<i>PEPD</i>	19	C	G	0.01	0.012	0.043	0.011	
rs10406431	<i>GIPR</i>	19	A	G	0.041	0.012	0.06	0.011	W
rs1042725	<i>HMGA2</i>	12	T	C	0.053	0.012	0.04	0.011	
rs1061810	<i>HSD17B12</i>	11	A	C	0.041	0.013	0.078	0.012	
rs10750397	<i>ETS1</i>	11	A	G	0.031	0.013	0.053	0.012	
rs10757283	<i>CDKN2A/B</i>	9	T	C	0.017	0.012	0.029	0.011	
rs10830963	<i>MTNR1B</i>	11	G	C	0.1	0.013	0.1	0.013	
rs10842994	<i>KLHDC5</i>	12	C	T	0.079	0.015	0.089	0.014	
rs10882101	<i>HHEX/IDE</i>	10	T	C	0.1	0.012	0.11	0.011	
rs10893829	<i>ETS1</i>	11	T	C	0.022	0.017	0.06	0.016	
rs10908278	<i>HNF1B</i>	17	T	A	0.052	0.012	0.083	0.011	
rs10937721	<i>WFS1</i>	4	C	G	0.071	0.012	0.096	0.011	
rs10938398	<i>GNPDA2</i>	4	A	G	0.056	0.012	0.042	0.011	
rs10954772	<i>PURG</i>	8	T	C	0.037	0.013	0.026	0.012	
rs10962	<i>HNF1B</i>	17	C	G	0.021	0.015	0.053	0.014	
rs10974438	<i>GLIS3</i>	9	C	A	0.035	0.013	0.055	0.012	

rs11042596	<i>INS/IGF2</i>	11	G	T	0.057	0.013	0.032	0.012	
rs11063028	<i>CCND2</i>	12	C	T	0.046	0.016	0.057	0.015	M
rs11070332	<i>LTK</i>	15	A	G	0.045	0.013	0.044	0.012	
rs11137820	<i>MTND2P8</i>	9	C	G	0.026	0.012	0.059	0.011	
rs11257655	<i>CDC123/CAMK1D</i>	10	T	C	0.08	0.014	0.09	0.013	
rs1127215	<i>PTGFRN</i>	1	C	T	0.048	0.012	0.046	0.011	
rs11496066	<i>FBXL13</i>	7	T	C	0.049	0.016	0.037	0.015	
rs115505614	<i>PAM</i>	5	T	C	0.15	0.029	0.17	0.026	M
rs11642430	<i>FAM57B</i>	16	G	C	0.034	0.012	0.048	0.011	
rs11680058	<i>FAM49A</i>	2	A	G	0.049	0.019	0.056	0.018	
rs11688682	<i>GLI2</i>	2	G	C	0.072	0.014	0.036	0.013	
rs11699802	<i>CEBPB</i>	20	C	T	0.037	0.012	0.041	0.011	
rs117001013	<i>YWHAH</i>	22	C	T	0.07	0.022	0.03	0.02	
rs11708067	<i>ADCY5</i>	3	A	G	0.1	0.015	0.08	0.014	
rs11709077	<i>PPARG</i>	3	G	A	0.11	0.019	0.11	0.017	
rs117483894	<i>TCF12</i>	15	G	A	0.12	0.031	0.077	0.029	
rs11759026	<i>CENPW</i>	6	G	A	0.062	0.014	0.059	0.013	W
rs11820019	<i>CCND1</i>	11	T	C	0.1	0.04	0.15	0.038	
rs11842871	<i>HMGB1</i>	13	G	T	0.051	0.014	0.028	0.013	
rs11926707	<i>KIF9</i>	3	C	T	0.048	0.013	0.029	0.012	
rs11967262	<i>VEGFA</i>	6	G	C	0.035	0.013	0.039	0.011	W
rs12001437	<i>UBAP2</i>	9	C	T	0.047	0.012	0.043	0.011	
rs12048743	<i>DSTYK</i>	1	G	C	0.043	0.012	0.039	0.011	
rs12140153	<i>PATJ</i>	1	G	T	0.065	0.021	0.039	0.02	
rs12454712	<i>BCL2A</i>	18	T	C	0.051	0.013	0.045	0.012	
rs1260326	<i>GCKR</i>	2	C	T	0.047	0.012	0.062	0.012	
rs12640250	<i>LCORL</i>	4	C	A	0.054	0.013	0.035	0.013	
rs12680028	<i>TRHR</i>	8	C	G	0.042	0.012	0.023	0.011	
rs12719778	<i>BOP1</i>	8	T	C	0.028	0.012	0.031	0.011	
rs12811407	<i>FBRSL1</i>	12	A	G	0.05	0.014	0.043	0.013	
rs12910825	<i>PRC1</i>	15	G	A	0.053	0.013	0.055	0.012	
rs12920022	<i>SPG7</i>	16	A	T	0.051	0.017	0.042	0.016	

rs1296328	<i>PABPC4L</i>	4	A	C	0.02	0.012	0.034	0.011	
rs13024606	<i>GRB14/COBLL1</i>	2	T	C	0.05	0.029	0.074	0.028	
rs13041756	<i>NKX2.2</i>	20	C	T	0.088	0.019	0.063	0.018	
rs13085136	<i>SHQ1</i>	3	C	T	0.05	0.025	0.058	0.023	
rs1316776	<i>DMGDH</i>	5	C	A	0.041	0.013	0.059	0.012	M
rs13426680	<i>CYTIP</i>	2	A	G	0.13	0.026	0.034	0.023	
rs1359790	<i>SPRY2</i>	13	G	A	0.057	0.013	0.085	0.013	
rs13737	<i>PTPN9</i>	15	G	T	0.04	0.014	0.044	0.014	
rs1377807	<i>ZZEF1</i>	17	C	G	0.059	0.013	0.054	0.012	W
rs140242150	<i>TCF7L2</i>	10	A	G	0.25	0.11	0.22	0.11	
rs1412234	<i>LINGO2</i>	9	C	T	0.061	0.013	0.032	0.012	
rs141521721	<i>PDE3B</i>	11	A	C	0.11	0.04	0.085	0.039	
rs1421085	<i>FTO</i>	16	C	T	0.13	0.012	0.11	0.011	
rs1426371	<i>WSCD2</i>	12	G	A	0.059	0.014	0.035	0.013	
rs145678014	<i>QSER1</i>	11	G	T	0.15	0.032	0.1	0.029	
rs145904381	<i>FAM63A</i>	1	T	C	0.11	0.061	0.3	0.056	
rs149364428	<i>CPQ</i>	8	A	G	0.27	0.061	0.18	0.058	
rs1493694	<i>NOTCH2</i>	1	T	C	0.084	0.019	0.087	0.018	M
rs1531583	<i>PCGF3</i>	4	T	G	0.11	0.028	0.095	0.026	
rs1561927	<i>PVT1</i>	8	C	T	0.038	0.013	0.046	0.013	
rs1562396	<i>KLF14</i>	7	G	A	0.081	0.013	0.029	0.012	
rs1580278	<i>SLC9B1</i>	4	C	A	0.052	0.012	0.029	0.011	
rs17013314	<i>UBE2E2</i>	3	G	A	0.13	0.033	0.12	0.031	
rs1708302	<i>JAZF1</i>	7	C	T	0.086	0.012	0.097	0.011	
rs17122772	<i>SLC7A7</i>	14	G	C	0.038	0.015	0.043	0.014	
rs17168486	<i>DGKB</i>	7	T	C	0.052	0.015	0.07	0.014	
rs17250977	<i>ANKH</i>	5	G	A	0.12	0.034	0.099	0.033	M
rs17261179	<i>ITGA1</i>	5	T	C	0.038	0.012	0.041	0.011	
rs17522122	<i>AKAP6</i>	14	T	G	0.031	0.012	0.045	0.011	
rs17684074	<i>WDR7</i>	18	G	C	0.033	0.014	0.046	0.013	M
rs17689007	<i>MSRA</i>	8	G	A	0.056	0.012	0.037	0.011	
rs177045	<i>NEUROG3</i>	10	G	A	0.064	0.013	0.054	0.012	

rs17772814	<i>CASC11</i>	8	G	A	0.081	0.024	0.12	0.022	
rs17791513	<i>TLE4</i>	9	A	G	0.094	0.025	0.12	0.022	
rs17802463	<i>DTNB</i>	2	G	T	0.037	0.014	0.043	0.013	
rs17819328	<i>PPARG</i>	3	G	T	0.035	0.012	0.029	0.011	
rs1783541	<i>MAP3K11</i>	11	T	C	0.076	0.015	0.036	0.014	
rs17836088	<i>NRXN3</i>	14	C	G	0.058	0.015	0.049	0.014	
rs1796330	<i>TSPAN8/LGR5</i>	12	G	C	0.049	0.012	0.062	0.011	
rs1800574	<i>HNF1A</i>	12	T	C	0.16	0.036	0.18	0.033	
rs1800961	<i>HNF4A</i>	20	T	C	0.17	0.032	0.11	0.029	
rs1801645	<i>PIM3</i>	22	C	T	0.041	0.014	0.045	0.013	
rs184509201	<i>TCF7L2</i>	10	C	G	0.18	0.052	0.15	0.048	
rs1903002	<i>FAM13A</i>	4	G	C	0.032	0.012	0.05	0.011	
rs2028150	<i>CEP68</i>	2	C	G	0.045	0.012	0.059	0.011	
rs2066827	<i>CDKN1B</i>	12	G	T	0.022	0.016	0.055	0.015	
rs2102278	<i>USP46</i>	4	G	A	0.038	0.013	0.011	0.012	
rs2197973	<i>USP44</i>	12	T	C	0.031	0.012	0.02	0.011	
rs2237895	<i>KCNQ1</i>	11	C	A	0.068	0.013	0.098	0.012	
rs2237897	<i>KCNQ1</i>	11	C	T	0.16	0.033	0.19	0.029	
rs2238689	<i>GIPR</i>	19	C	T	0.04	0.013	0.037	0.012	
rs2249105	<i>CEP68</i>	2	A	G	0.046	0.013	0.057	0.012	W
rs2258238	<i>HMGA2</i>	12	T	A	0.13	0.02	0.084	0.019	
rs2268078	<i>RALY</i>	20	A	G	0.029	0.013	0.051	0.012	M
rs2272163	<i>ROBO2</i>	3	C	A	0.044	0.012	0.033	0.012	
rs2280141	<i>PLEKHA1</i>	10	T	G	0.039	0.012	0.071	0.011	
rs2283220	<i>KCNQ1</i>	11	A	G	0.041	0.014	0.024	0.012	
rs2307111	<i>POC5</i>	5	T	C	0.07	0.012	0.039	0.011	
rs231349	<i>KCNQ1</i>	11	T	C	0.078	0.02	0.053	0.019	
rs231361	<i>KCNQ1</i>	11	A	G	0.052	0.014	0.06	0.013	M
rs243024	<i>BCL11A</i>	2	A	G	0.044	0.012	0.068	0.011	
rs2431115	<i>ANKRD55</i>	5	A	G	0.024	0.012	0.026	0.011	
rs2456530	<i>ONECUT1</i>	15	T	C	0.028	0.018	0.042	0.017	
rs2581787	<i>RFT1</i>	3	T	G	0.043	0.012	0.039	0.011	

rs2642588	<i>NEUROG3</i>	10	G	T	0.042	0.013	0.066	0.012	
rs2767036	<i>PDHX</i>	11	C	A	0.032	0.013	0.044	0.012	
rs2796441	<i>TLE1</i>	9	G	A	0.034	0.012	0.069	0.011	
rs279744	<i>ARL15</i>	5	C	A	0.049	0.013	0.03	0.012	
rs2800733	<i>SOGA3</i>	6	A	G	0.028	0.014	0.061	0.013	
rs2820446	<i>LYPLAL1</i>	1	C	G	0.068	0.013	0.057	0.012	M
rs28505901	<i>GPSM1</i>	9	G	A	0.076	0.016	0.086	0.015	
rs2872246	<i>ABCC5</i>	3	A	C	0.03	0.012	0.029	0.011	
rs28819812	<i>PDGFC</i>	4	C	A	0.032	0.015	0.05	0.014	
rs291367	<i>GNG4</i>	1	G	A	0.058	0.014	0.045	0.013	
rs2925979	<i>CMIP</i>	16	T	C	0.094	0.013	0.039	0.012	
rs2972144	<i>IRS1</i>	2	G	A	0.089	0.013	0.11	0.012	M
rs3111316	<i>FARSA</i>	19	A	G	0.053	0.012	0.025	0.011	
rs3217792	<i>CCND2</i>	12	C	T	0.08	0.024	0.1	0.022	
rs3217860	<i>CCND2</i>	12	G	A	0.042	0.014	0.051	0.013	
rs329122	<i>PHF15</i>	5	A	G	0.024	0.012	0.041	0.011	
rs340874	<i>PROX1</i>	1	C	T	0.049	0.012	0.07	0.011	
rs34298980	<i>LRFN2</i>	6	T	C	0.035	0.013	0.024	0.012	
rs34454109	<i>TSHZ2</i>	20	A	T	0.054	0.014	0.047	0.013	W
rs34584161	<i>RNF6</i>	13	A	G	0.025	0.014	0.068	0.013	M
rs34715063	<i>RASGRP1</i>	15	C	T	0.043	0.02	0.066	0.018	M
rs348330	<i>ABCB10</i>	1	G	A	0.032	0.013	0.058	0.012	
rs34855406	<i>MLX</i>	17	C	G	0.047	0.013	0.035	0.013	
rs34855922	<i>TCF7L2</i>	10	A	G	0.017	0.014	0.044	0.013	
rs34965774	<i>KSR2</i>	12	A	G	0.039	0.017	0.069	0.016	
rs35352848	<i>UBE2E2</i>	3	T	C	0.056	0.015	0.052	0.014	
rs35895680	<i>TTLL6</i>	17	C	A	0.05	0.013	0.05	0.012	M
rs35913461	<i>TMEM18</i>	2	C	T	0.06	0.016	0.042	0.015	
rs35999103	<i>PABPC1P2</i>	2	T	C	0.047	0.016	0.019	0.015	
rs362307	<i>HTT</i>	4	T	C	0.092	0.023	0.044	0.021	
rs3751837	<i>CLUAP1</i>	16	T	C	0.058	0.015	0.029	0.013	
rs3768321	<i>MACF1</i>	1	T	G	0.086	0.015	0.084	0.014	

rs3772071	<i>RBMS1</i>	2	T	C	0.055	0.013	0.044	0.013	
rs3774723	<i>PSMD6</i>	3	G	A	0.046	0.017	0.052	0.015	
rs3798519	<i>TFAP2B</i>	6	C	A	0.057	0.015	0.036	0.014	
rs3802177	<i>SLC30A8</i>	8	G	A	0.1	0.013	0.11	0.012	
rs3810291	<i>ZC3H4</i>	19	A	G	0.042	0.013	0.05	0.012	M
rs3811978	<i>ITGA1</i>	5	G	A	0.028	0.016	0.054	0.015	M
rs3845281	<i>ANKH</i>	5	G	A	0.068	0.021	0.058	0.019	
rs3887925	<i>ST6GAL1</i>	3	T	C	0.052	0.012	0.051	0.011	
rs39328	<i>RELN</i>	7	T	C	0.033	0.012	0.024	0.011	M
rs4148856	<i>MPHOSPH9</i>	12	C	G	0.053	0.015	0.049	0.014	
rs4238013	<i>CCND2</i>	12	C	T	0.062	0.015	0.059	0.014	
rs4279506	<i>IGF2BP3</i>	7	G	C	0.028	0.012	0.04	0.011	
rs4281707	<i>FTO</i>	16	G	A	0.028	0.012	0.029	0.011	
rs429358	<i>TOMM40/APOE</i>	19	T	C	0.079	0.018	0.1	0.016	W, M
rs4457053	<i>ZBED3</i>	5	G	A	0.065	0.013	0.067	0.012	
rs465002	<i>ANKRD55</i>	5	T	C	0.068	0.014	0.069	0.013	
rs4686471	<i>LPP</i>	3	C	T	0.058	0.012	0.047	0.011	
rs4688760	<i>RBM6</i>	3	T	C	0.027	0.013	0.039	0.012	
rs4709746	<i>QKI</i>	6	C	T	0.059	0.018	0.051	0.017	
rs474513	<i>SLC22A3</i>	6	A	G	0.043	0.012	0.032	0.011	W
rs4776970	<i>MAP2K5</i>	15	A	T	0.05	0.013	0.058	0.012	
rs4804833	<i>MAP2K7</i>	19	A	G	0.045	0.013	0.04	0.012	
rs4810426	<i>HNF4A</i>	20	T	C	0.092	0.019	0.072	0.018	
rs4925109	<i>RAI1</i>	17	A	G	0.066	0.013	0.038	0.012	
rs4929965	<i>INS/IGF2</i>	11	A	G	0.066	0.013	0.056	0.012	
rs4932265	<i>AP3S2</i>	15	T	C	0.052	0.013	0.078	0.013	
rs4946812	<i>BEND3</i>	6	G	A	0.038	0.013	0.036	0.012	
rs4977213	<i>BOP1</i>	8	C	T	0.05	0.013	0.056	0.012	
rs505922	<i>ABO</i>	9	C	T	0.066	0.013	0.044	0.012	
rs5213	<i>KCNJ11</i>	11	C	T	0.083	0.012	0.058	0.011	
rs523288	<i>MC4R</i>	18	T	A	0.037	0.014	0.041	0.013	
rs528350911	<i>WDR72</i>	15	G	C	0.31	0.078	0.27	0.075	

rs539515	<i>SEC16B</i>	1	C	A	0.082	0.015	0.028	0.014	
rs555759341	<i>INS/IGF2</i>	11	C	G	0.32	0.1	0.32	0.099	
rs55653563	<i>ZNF169</i>	9	A	C	0.042	0.013	0.048	0.013	
rs56337234	<i>MAEA</i>	4	C	T	0.067	0.013	0.039	0.012	
rs56348580	<i>HNF1A</i>	12	G	C	0.069	0.013	0.085	0.012	M
rs57235767	<i>MTNR1B</i>	11	C	T	0.038	0.013	0.046	0.012	
rs57327348	<i>XKR6</i>	8	A	T	0.068	0.015	0.043	0.014	
rs5758223	<i>EP300</i>	22	A	G	0.04	0.013	0.028	0.012	
rs576674	<i>KL</i>	13	G	A	0.061	0.016	0.061	0.015	
rs58432198	<i>FAF1</i>	1	C	T	0.041	0.019	0.061	0.018	
rs58730668	<i>ACSL1</i>	4	T	C	0.074	0.017	0.072	0.016	
rs601945	<i>MHC</i>	6	G	A	0.077	0.016	0.074	0.015	
rs60276348	<i>ACE</i>	17	T	C	0.042	0.018	0.061	0.017	
rs6063048	<i>EYA2</i>	20	G	A	0.044	0.013	0.039	0.013	
rs6070625	<i>GNAS</i>	20	G	C	0.03	0.012	0.041	0.011	
rs61676547	<i>BPTF</i>	17	C	G	0.05	0.015	0.082	0.014	
rs62007683	<i>MARK3</i>	14	G	T	0.035	0.013	0.031	0.012	
rs62080313	<i>COMMD9</i>	18	C	T	0.06	0.018	0.053	0.018	
rs62107261	<i>TMEM18</i>	2	T	C	0.13	0.032	0.071	0.029	
rs62271373	<i>TSC22D2</i>	3	A	T	0.12	0.028	0.052	0.026	
rs62492368	<i>AOC1</i>	7	A	G	0.044	0.013	0.037	0.012	
rs6458354	<i>VEGFA</i>	6	C	T	0.039	0.013	0.07	0.012	
rs6459733	<i>MNX1</i>	7	G	C	0.057	0.013	0.057	0.012	M
rs649961	<i>SLC12A8</i>	3	T	C	0.022	0.012	0.054	0.011	
rs6518681	<i>MTMR3/ASCC2</i>	22	G	A	0.096	0.023	0.09	0.021	
rs6545714	<i>BNIPL</i>	2	G	A	0.04	0.012	0.022	0.011	
rs6600191	<i>ITFG3</i>	16	T	C	0.062	0.016	0.06	0.015	
rs6708643	<i>THADA</i>	2	A	G	0.032	0.012	0.037	0.011	
rs67232546	<i>ETS1</i>	11	T	C	0.059	0.015	0.049	0.014	
rs6821438	<i>SMARCAD1</i>	4	A	G	0.048	0.012	0.044	0.011	M
rs6884702	<i>MRPS30</i>	5	G	A	0.05	0.012	0.045	0.011	
rs6885132	<i>ANKH</i>	5	C	G	0.051	0.021	0.055	0.02	

rs6976111	<i>CTTNBP2</i>	7	A	C	0.033	0.015	0.03	0.014	
rs7022807	<i>HAUS6</i>	9	G	A	0.056	0.012	0.023	0.011	
rs702634	<i>ARL15</i>	5	A	G	0.056	0.013	0.054	0.012	
rs703972	<i>ZMIZ1</i>	10	G	C	0.061	0.012	0.059	0.011	
rs7115753	<i>CRY2</i>	11	A	G	0.03	0.012	0.039	0.011	
rs7124681	<i>ELF1</i>	11	A	C	0.047	0.012	0.02	0.011	
rs71372253	<i>NF1</i>	17	C	T	0.045	0.025	0.11	0.024	
rs7178762	<i>USP3</i>	15	C	T	0.028	0.012	0.045	0.011	
rs718314	<i>ITPR2</i>	12	G	A	0.05	0.014	0.034	0.013	
rs7222481	<i>GLP2R</i>	17	C	G	0.044	0.013	0.03	0.012	
rs7240767	<i>LAMA1</i>	18	C	T	0.045	0.012	0.025	0.012	
rs7249758	<i>UHRF1</i>	19	A	G	0.044	0.015	0.04	0.014	
rs72802342	<i>BCAR1</i>	16	C	A	0.088	0.023	0.14	0.022	W
rs72926932	<i>TCF4</i>	18	C	A	0.085	0.021	0.087	0.02	
rs73226260	<i>HNF1A</i>	12	G	A	0.084	0.037	0.097	0.034	
rs738408	<i>PNPLA3</i>	22	T	C	0.037	0.014	0.066	0.013	
rs74452128	<i>MC4R</i>	18	C	A	0.17	0.042	0.14	0.038	
rs74653713	<i>MBNL1</i>	3	C	A	0.083	0.03	0.091	0.027	
rs75253922	<i>INSR</i>	19	C	T	0.041	0.015	0.029	0.015	
rs76263492	<i>CACNA2D3</i>	3	T	G	0.047	0.029	0.11	0.028	
rs7629630	<i>EGFEM1P</i>	3	A	T	0.041	0.017	0.065	0.016	
rs7645517	<i>ST6GAL1</i>	3	A	G	0.011	0.026	0.066	0.025	
rs76549217	<i>ANKH</i>	5	T	C	0.11	0.041	0.074	0.039	
rs7669833	<i>TMEM154</i>	4	T	A	0.044	0.013	0.07	0.012	
rs76895963	<i>CCND2</i>	12	T	G	0.42	0.056	0.51	0.052	
rs7719891	<i>RASA1</i>	5	G	A	0.034	0.014	0.046	0.013	
rs77464186	<i>CENTD2/ARAP1</i>	11	A	C	0.09	0.017	0.1	0.015	
rs7756992	<i>CDKAL1</i>	6	G	A	0.15	0.013	0.14	0.012	M
rs77864822	<i>RMST</i>	12	A	G	0.075	0.025	0.065	0.023	
rs78020297	<i>FTO</i>	16	A	G	0.041	0.028	0.038	0.025	
rs7867635	<i>FOCAD</i>	9	C	T	0.029	0.012	0.041	0.011	
rs7918400	<i>TCF7L2</i>	10	C	T	0.0092	0.012	0.021	0.011	

rs79687284	<i>PROX1</i>	1	C	G	0.15	0.035	0.17	0.033	
rs7987740	<i>IRS2</i>	13	T	C	0.042	0.012	0.013	0.011	
rs8010382	<i>SMEK1</i>	14	G	A	0.042	0.013	0.035	0.012	
rs80147536	<i>THADA</i>	2	A	T	0.08	0.021	0.16	0.02	
rs8017808	<i>CLEC14A</i>	14	G	T	0.043	0.014	0.015	0.013	
rs8032939	<i>RASGRP1</i>	15	C	T	0.058	0.014	0.026	0.013	
rs8037894	<i>C2CD4A/B</i>	15	G	C	0.046	0.012	0.051	0.011	
rs8046545	<i>ATP2A1</i>	16	G	A	0.033	0.013	0.028	0.012	
rs8107974	<i>TM6SF2</i>	19	T	A	0.061	0.022	0.11	0.021	M
rs862320	<i>NFAT5</i>	16	C	T	0.028	0.012	0.023	0.011	
rs878521	<i>GCK</i>	7	A	G	0.065	0.014	0.072	0.013	W
rs917195	<i>CRHR2</i>	7	C	T	0.055	0.015	0.052	0.014	
rs9379084	<i>RREB1</i>	6	G	A	0.099	0.02	0.051	0.019	
rs9430095	<i>SRGAP2</i>	1	C	G	0.015	0.012	0.043	0.011	
rs9494624	<i>SLC35D3</i>	6	A	G	0.041	0.013	0.059	0.012	
rs9505097	<i>RREB1</i>	6	C	T	0.032	0.015	0.054	0.014	
rs9537803	<i>PCDH17</i>	13	C	T	0.03	0.013	0.03	0.013	
rs9563615	<i>SRGAP2D</i>	13	A	T	0.032	0.013	0.023	0.012	
rs963740	<i>DLEU1</i>	13	A	T	0.024	0.013	0.056	0.013	
rs9687832	<i>ANKRD55</i>	5	A	G	0.076	0.015	0.041	0.014	
rs9828772	<i>TMCC1</i>	3	C	G	0.057	0.021	0.071	0.019	
rs9860730	<i>ADAMTS9</i>	3	A	G	0.067	0.013	0.066	0.012	M
rs9873618	<i>SLC2A2</i>	3	G	A	0.056	0.013	0.095	0.013	M
rs9957145	<i>GRP</i>	18	G	A	0.036	0.016	0.037	0.015	

*SNP: single nucleotide polymorphism

†Chr: Chromosome

‡Outliers identified using radial MR; W: women; M: men

Supplemental Table 2. Association of sex-specific genetic risk scores for type 2 diabetes with type 2 diabetes*. Genetic risk score comprised of 270 SNPs from the European DIAMANTE genome-wide association study.

	Women	Men
F statistic	683	1077
R-squared	0.02	0.03
Odds ratio (95% confidence interval)[†]	1.70 (1.66-1.73)	1.70 (1.67-1.73)

*Adjusted for age, genotype array, and four principal components of ancestry.

[†]Odds ratios for the risk of type 2 diabetes per standard deviation increase in type 2 diabetes genetic risk score.

Supplemental Table 3: Population Characteristics, UK Biobank (N=463 469), stratified by sex and coronary heart disease status.

	Women (N=251 420)		Men (N=212 049)	
	Without CHD (N=238 704)	With CHD (N=12 716)	Without CHD (N=185 705)	With CHD (N=26 344)
Age, mean (SD [*]), years	56.3 (8.0)	61.6 (6.1)	56.3 (8.2)	61.5 (6.2)
Array type, No. (%)				
BiLEVE	23 257 (9.7)	1663 (13.1)	21 256 (11.4)	3641 (13.8)
Axiom	215 436 (90.3)	11 053 (86.9)	164 446 (88.9)	22 701 (86.2)
Type 2 diabetes, No. (%)	8071 (3.3)	1893 (14.9)	11 705 (6.3)	5212 (19.8)
Body mass index, mean (SD), kg/m ²	26.9 (5.1)	29.3 (5.8)	27.7 (4.2)	29.1 (4.6)
Waist circumference, mean (SD), cm	84.2 (12.3)	90.8 (13.8)	96.5 (11.1)	100.9 (12.0)
Smoking history, No. (%)				
Never	140 460 (58.8)	6061 (47.7)	93 156 (51.8)	8983 (34.1)
Previous	76 325 (32.0)	4927 (38.7)	69 566 (37.5)	13 404 (50.9)
Current	20 937 (8.8)	1637 (12.9)	22 237 (12.0)	3774 (14.3)
Dyslipidemia, No. (%)	21 515 (9.0)	4034 (31.7)	24 773 (13.3)	9070 (34.4)
Hypertension, No. (%)	51 335 (21.5)	6386 (50.2)	51 029 (27.5)	13 639 (51.8)
Systolic BP [†] , mean (SD), mmHg	135.1 (19.1)	140.1 (19.7)	141.0 (17.2)	141.4 (18.7)
Diastolic BP, mean (SD), mmHg	80.6 (9.9)	79.8 (10.5)	84.3 (9.8)	81.7 (10.6)

*SD: standard deviation; [†]BP: blood pressure