

Supplemental materials

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Supplement to: Association between genetic risk and development of type 2 diabetes in a general Japanese population: The Hisayama Study

Short title: Genetic risk and incident type 2 diabetes.

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Table of Contents	Page
1. Supplementary Tables S1-8	4-13
Supplementary Table 1	
Components of the genetic risk score	
Supplementary Table 2	
Baseline characteristics according to the quintile of type 2 diabetes genetic risk score using a European coefficient	
Supplementary Table 3	
The associations of type 2 diabetes genetic risk score using a Japanese coefficient with development of type 2 diabetes in subjects with normal glucose tolerance at baseline	
Supplementary Table 4	
The associations of type 2 diabetes genetic risk score using a Japanese coefficient with development of prediabetes in subjects with normal glucose tolerance at baseline	
Supplementary Table 5	
The associations of type 2 diabetes genetic risk score using a European coefficient with development of type 2 diabetes	
Supplementary Table 6	
The associations of type 2 diabetes genetic risk score using a European coefficient with development of type 2 diabetes in subjects with normal glucose tolerance at baseline	
Supplementary Table 7	
The associations of type 2 diabetes genetic risk score using a European coefficient with development of prediabetes in subjects with normal glucose tolerance at baseline	
Supplementary Table 8	

Improvement of the risk assessment ability for the development of type 2 diabetes by adding contributions of genetic risk score using a European coefficient to the environmental risk model

2. Supplementary Figures S1-4 14-17

Supplementary Figure 1

Flow chart for survival analyses of subjects with normal glucose tolerance at baseline for incident type 2 diabetes

Supplementary Figure 2

Flow chart for survival analyses of subjects with normal glucose tolerance at baseline for incident prediabetes defined by OGTT

Supplementary Figure 3

Age- and sex-adjusted incidence rate of diabetes mellitus according to the quintile of type 2 diabetes genetic risk score using a European coefficient

Supplementary Figure 4

Comparisons of the influence of a genetic risk score using a European coefficient on the development of type 2 diabetes between subgroups of environmental risk factors

Supplementary Table 1. Components of the genetic risk score

#	Locus	SNP (literature)	SNP (in BBJ)	CHR	POS_b37	Risk Allele	Other Allele	European OR from DIAGRAM	European coefficient	Japanese OR from BBJ	Japanese coefficient	Risk allele frequency in BBJ
#01	<i>TCF7L2</i>	rs7903146	rs7903146	10	114758349	T	C	1.40	0.34	1.43	0.357	0.05
#02	<i>TLE4</i>	rs17791513	rs17791513	9	81905590	A	G	1.21	0.19	1.16	0.152	0.95
#03	<i>DMRTA1</i>	rs1575972	rs1575972	9	22301092	T	A	1.20	0.18	1.20	0.185	0.94
#04	<i>CDKAL1</i>	rs7756992	rs7756992	6	20679709	G	A	1.20	0.18	1.18	0.169	0.49
#05	<i>CDKN2A/B</i>	rs10811661	rs10811661	9	22134094	T	C	1.18	0.17	1.22	0.197	0.56
#06	<i>PPARG</i>	rs1801282 [p.Pro12Ala]	rs1801282	3	12393125	C	G	1.16	0.15	1.19	0.177	0.97
#07	<i>SLC30A8</i>	rs3802177	rs3802177	8	118185025	G	A	1.16	0.15	1.11	0.104	0.58
#08	<i>HMGA2</i>	rs2261181	rs2261181	12	66212318	T	C	1.16	0.15	1.03	0.027	0.13
#09	<i>HHEX-IDE</i>	rs1111875	rs1111875	10	94462882	C	T	1.15	0.14	1.15	0.136	0.29
#10	<i>BCAR1</i>	rs7202877	rs7202877	16	75247245	T	G	1.15	0.14	0.99	-0.011	0.79
#11	<i>THADA</i>	rs10203174	rs112801539 (r ² =1.00)	2	43700827	A	C	1.15	0.14	0.97	-0.030	0.99
#12	<i>CENTD2-ARAP1</i>	rs1552224	rs1552224	11	72433098	A	C	1.13	0.12	1.21	0.187	0.96
#13	<i>IGF2BP2</i>	rs4402960	rs4402960	3	185511687	T	G	1.13	0.12	1.18	0.162	0.32
#14	<i>FTO</i>	rs9936385	rs9936385	16	53819169	C	T	1.13	0.12	1.15	0.144	0.20
#15	<i>DGKB</i>	rs17168486	rs17168486	7	14898282	T	C	1.13	0.12	1.05	0.048	0.40
#16	<i>CILP2-GATAD2A</i>	rs10401969	rs10401969	19	19407718	C	T	1.13	0.12	1.01	0.006	0.10
#17	<i>ZBED3</i>	rs6878122	rs6878122	5	76427311	G	A	1.13	0.12	0.98	-0.023	0.02
#18	<i>MAEA</i>	rs6815464	rs6815464	4	1309901	C	G	1.12	0.11	1.11	0.103	0.65
#19	<i>MTNR1B</i>	rs10830963	rs10830963	11	92708710	G	C	1.11	0.10	1.03	0.030	0.42
#20	<i>RBMS1</i>	rs7593730	rs7593730	2	161171454	G	A	1.11	0.10	1.02	0.015	0.85
#21	<i>HNF1B (TCF2)</i>	rs11651052	rs11651052	17	36102381	A	G	1.10	0.10	1.14	0.127	0.33
#22	<i>UBE2E2</i>	rs7612463	rs7612463	3	23336450	C	A	1.10	0.10	1.16	0.151	0.84
#23	<i>ANK1</i>	rs515071	rs515071	8	41519462	G	A	1.10	0.10	1.10	0.100	0.81
#24	<i>FAF1</i>	rs17106184	rs17106184	1	50909985	G	A	1.10	0.10	1.10	0.092	0.90
#25	<i>SPRY2</i>	rs1359790	rs1359790	13	80717156	G	A	1.10	0.10	1.09	0.082	0.73
#26	<i>NOTCH2</i>	rs10923931	rs10923931	1	120517959	T	G	1.10	0.10	1.06	0.059	0.02
#27	<i>CCND2</i>	rs11063069	rs11063069	12	4374373	G	A	1.10	0.10	1.05	0.048	0.02
#28	<i>KLF14</i>	rs13233731	rs13233731	7	130437689	G	A	1.10	0.10	1.02	0.024	0.70
#29	<i>KCNQ1</i>	rs163184	rs163184	11	2847069	G	T	1.09	0.09	1.21	0.193	0.44
#30	<i>WFS1</i>	rs4458523	rs4458523	4	6289986	G	T	1.09	0.09	1.09	0.090	0.98
#31	<i>ZMIZ1</i>	rs12571751	rs12571751	10	80942631	A	G	1.09	0.09	1.08	0.079	0.53
#32	<i>POU5F1-TCF19</i>	rs3130501	rs3130501	6	31136453	G	A	1.09	0.09	1.08	0.075	0.60
#33	<i>KLHDC5</i>	rs10842994	rs10842994	12	27965150	C	T	1.09	0.09	1.06	0.054	0.81

#34	<i>IRS1</i>	rs2943640	rs2943640	2	227093585	C	A	1.09	0.09	1.05	0.047	0.92
#35	<i>BCL11A</i>	rs243088	rs243088	2	60568745	T	A	1.09	0.09	1.03	0.034	0.68
#36	<i>ZFAND6</i>	rs11634397	rs11634397	15	80432222	G	A	1.09	0.09	1.02	0.017	0.12
#37	<i>PRC1</i>	rs12899811	rs12899811	15	91544076	G	A	1.09	0.09	0.98	-0.018	0.99
#38	<i>TSPAN8/LGR5</i>	rs7955901	rs7955901	12	71433293	C	T	1.09	0.09	0.98	-0.018	0.66
#39	<i>ARL15</i>	rs702634	rs702634	5	53271420	A	G	1.08	0.08	1.07	0.066	0.83
#40	<i>HMG20A</i>	rs7178572	rs7178572	15	77747190	G	A	1.08	0.08	1.06	0.060	0.41
#41	<i>MC4R</i>	rs12970134	rs12970134	18	57884750	A	G	1.08	0.08	1.05	0.052	0.16
#42	<i>KCNJ11</i>	rs5215 [p.Val337Ile]	rs5215	11	17408630	C	T	1.08	0.08	1.05	0.045	0.37
#43	<i>TMEM154</i>	rs6813195	rs6813195	4	153520475	C	T	1.08	0.08	1.04	0.042	0.48
#44	<i>TP53INP1</i>	rs7845219	rs7845219	8	95937502	T	C	1.08	0.08	1.04	0.041	0.29
#45	<i>PROX1</i>	rs2075423	rs2075423	1	214154719	G	T	1.08	0.08	1.03	0.027	0.87
#46	<i>SSR1-RREB1</i>	rs9505118	rs9505118	6	7290437	A	G	1.08	0.08	1.00	0.003	0.58
#47	<i>TLE1</i>	rs2796441	rs2796441	9	84308948	G	A	1.07	0.07	1.08	0.075	0.38
#48	<i>HNF4A</i>	rs4812829	rs4812829	20	42989267	A	G	1.07	0.07	1.07	0.063	0.46
#49	<i>ADAMTS9</i>	rs6795735	rs6795735	3	64705365	C	T	1.07	0.07	1.02	0.020	0.16
#50	<i>CDC123-CAMK1D</i>	rs11257655	rs11257655	10	12307894	T	C	1.06	0.06	1.12	0.111	0.45
#51	<i>C2CD4A/B</i>	rs7172432	rs7172432	15	62396389	A	G	1.06	0.06	1.09	0.086	0.58
#52	<i>GIPR</i>	rs8108269	rs8108269	19	46158513	G	T	1.06	0.06	1.08	0.078	0.64
#53	<i>MACF1</i>	rs2296172 [p.M2290V]	rs2296172	1	39835817	G	A	1.06	0.06	1.06	0.056	0.17
#54	<i>MPHOSPH9</i>	rs4275659	rs4275659	12	123447928	C	T	1.06	0.06	1.02	0.024	0.69
#55	<i>TH-INS</i>	rs10770141	rs10770141	11	2193840	A	G	1.05	0.05	1.16	0.144	0.07
#56	<i>ANKRD55</i>	rs459193	rs459193	5	55806751	G	A	1.05	0.05	1.11	0.101	0.47
#57	<i>BCL2</i>	rs12454712	rs12454712	18	60845884	T	C	1.05	0.05	1.06	0.055	0.49
#58	<i>GLIS3</i>	rs7041847	rs7041847	9	4287466	A	G	1.05	0.05	1.05	0.044	0.48
#59	<i>GCK</i>	rs10278336	rs10278336	7	44245363	A	G	1.05	0.05	1.01	0.011	0.69
#60	<i>GRB14-COBL1</i>	rs3923113	rs3923113	2	165501849	A	C	1.04	0.04	1.10	0.098	0.91
#61	<i>GCKR</i>	rs780094	rs780094	2	27741237	C	T	1.04	0.04	1.07	0.072	0.44
#62	<i>AP3S2</i>	rs2028299	rs2028299	15	90374257	C	A	1.04	0.04	1.07	0.071	0.23
#63	<i>SREBF1</i>	rs4925115	rs4925115	17	17721457	A	G	1.04	0.04	1.02	0.023	0.83
#64	<i>ATP8B2</i>	rs67156297	rs67156297	1	154336716	A	G	1.04	0.04	1.16	0.152	0.09
#65	<i>PSMD6</i>	rs831571	rs831571	3	64048297	C	T	1.03	0.03	1.05	0.052	0.65
#66	<i>ST6GAL1</i>	rs16861329	rs16861329	3	186666461	G	A	1.03	0.03	1.04	0.041	0.80
#67	<i>PEPD</i>	rs3786897	rs3786897	19	33893008	A	G	1.02	0.02	1.06	0.057	0.55
#68	<i>RASGRP1</i>	rs7403531	rs7403531	15	38822905	T	C	1.02	0.02	1.04	0.037	0.47
#69	<i>VPS26A</i>	rs1802295	rs1802295	10	70931474	A	G	1.02	0.02	1.01	0.012	0.10

#70	<i>MIR4686</i>	rs7107784	rs7107784	11	2215089	G	A	1.02	0.02	1.17	0.155	0.09
#71	<i>LEP-MIR129</i>	rs791595	rs791595	7	127862802	A	G	1.01	0.01	1.14	0.127	0.10
#72	<i>ASB3</i>	rs9309245	rs9309245	2	53397048	G	C	1.01	0.01	1.12	0.113	0.18
#73	<i>CCDC85A</i>	rs1116357	rs1116357	2	57287411	G	A	1.01	0.01	1.11	0.104	0.29
#74	<i>INAFM2</i>	rs67839313	rs67839313	15	40619724	C	T	1.01	0.01	1.09	0.089	0.27
#75	<i>KCNK16</i>	rs1535500	rs1535500	6	39284050	T	G	1.01	0.01	1.07	0.068	0.37
#76	<i>SRR</i>	rs391300	rs391300	17	2216258	G	A	1.00	0.00	1.00	-0.004	0.77
#77	<i>PTPRD</i>	rs17584499	rs17584499	9	8879118	T	C	1.00	0.00	0.97	-0.034	0.15
#78	<i>ZFAND3</i>	rs9470794	rs9470794	6	38106844	C	T	0.99	-0.01	1.08	0.077	0.19
#79	<i>GCCI-PAX4</i>	rs6467136	rs6467136	7	127164958	G	A	0.99	-0.01	1.07	0.068	0.77
#80	<i>GRK5</i>	rs10886471	rs10886471	10	121149403	C	T	0.99	-0.01	1.00	0.000	0.74
#81	<i>SLC16A11/A13</i>	rs312457	rs312457	17	6940393	G	A	no proxy	NA	1.19	0.178	0.09
#82	<i>GPSM1</i>	rs11787792	rs11787792	9	139252148	A	G	no proxy	NA	1.14	0.135	0.88
#83	<i>FAM60A</i>	rs147538848	rs147538848	12	31466613	A	G	monoallelic in CEU	NA	1.11	0.107	0.19
#84	<i>TOMM40-APOE</i>	rs157582	rs157582	19	45396219	C	T	no proxy	NA	1.03	0.033	0.76

OR, odds ratio. The genetic risk score (GRS) using a Japanese coefficient included 84 single nucleotide polymorphisms (SNPs). In the GRS using a European coefficient, 4 SNPs were dropped from the GRS, since proxies in 3 SNPs were not available and one SNP was monomorphic in Europeans. The average GRS using the Japanese coefficient was 2.96 and that using the European coefficient was 3.23. BBJ, Biobank Japan Project; DIAGRAM, DIAbetes Genetics Replication And Meta-analysis Consortium.

Supplementary Table 2. Baseline characteristics according to the quintile of type 2 diabetes genetic risk score using a European coefficient

Environmental factors	Genetic risk score using a European coefficient					P for trend
	Q1 (≤ 3.0364) (N=293)	Q2 (3.0365-3.1661) (N=293)	Q3 (3.1662-3.2806) (N=293)	Q4 (3.2807-3.4162) (N=293)	Q5 (≥ 3.4163) (N=293)	
Age, y	57.6 (9.9)	58.4 (9.2)	57.9 (9.2)	57.1 (10)	57.2 (10.4)	0.47
Men, %	42.0%	39.6%	33.8%	35.5%	35.2%	0.20
Family history of diabetes mellitus, %	9.6%	10.6%	14.3%	15.7%	12.6%	0.14
Fasting plasma glucose, mmol/l	5.65 (0.44)	5.66 (0.41)	5.71 (0.49)	5.74 (0.46)	5.78 (0.47)	0.003
2-h postload glucose, mmol/l	6.69 (1.49)	6.84 (1.69)	6.81 (1.63)	6.81 (1.53)	7.03 (1.61)	0.14
Hypertension, %	38.6%	37.5%	35.5%	32.4%	31.7%	0.32
Serum total cholesterol, mmol/l	5.33 (0.90)	5.24 (0.82)	5.30 (0.93)	5.33 (0.93)	5.37 (1.00)	0.49
Serum HDL cholesterol, mmol/l	1.67 (0.44)	1.64 (0.41)	1.65 (0.41)	1.67 (0.44)	1.67 (0.41)	0.89
Serum triglycerides, mmol/l	1.05 (0.73-1.65)	1.07 (0.76-1.56)	1.06 (0.79-1.46)	1.04 (0.73-1.37)	1.03 (0.77-1.46)	0.86
Use of lipid-modifying medication, %	8.2%	5.8%	6.1%	6.8%	5.8%	0.75
Body mass index, kg/m ²	23.3 (3.1)	23.3 (3.3)	22.9 (3.2)	22.9 (3)	22.7 (2.8)	0.04
Smoking habits, %	23.9%	19.8%	21.5%	19.8%	18.4%	0.53
Alcohol intake, %	45.1%	45.7%	43.3%	44.7%	45.7%	0.98
Regular exercise, %	13.3%	6.1%	13.7%	11.3%	10.9%	0.03
Times of received health examination during follow-up	10 (6-11)	9 (5-11)	9 (6-11)	9 (5-11)	10 (7-11)	0.77

HDL, high-density lipoprotein.

Serum triglycerides and times of received health examination during follow-up are presented as the median (interquartile range).

All other values are presented as the mean (standard deviations) or percentages.

Supplementary Table 3. The associations of type 2 diabetes genetic risk score using a Japanese coefficient with development of type 2 diabetes in subjects with normal glucose tolerance at baseline

GRS levels	No. of events /subjects	Model 1			Model 2			Model 3		
		HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend
Q1	6/183	1.00 (reference)	-		1.00 (reference)	-		1.00 (reference)	-	
Q2	2/183	0.36 (0.07, 1.81)	0.22		0.36 (0.07, 1.78)	0.21		0.36 (0.07, 1.78)	0.21	
Q3	12/183	2.20 (0.82, 5.87)	0.12	0.02	2.22 (0.83, 5.99)	0.11	0.02	2.52 (0.92, 6.91)	0.07	0.03
Q4	8/183	1.62 (0.56, 4.71)	0.37		1.63 (0.55, 4.79)	0.38		1.61 (0.53, 4.86)	0.40	
Q5	11/183	2.29 (0.84, 6.24)	0.11		2.32 (0.83, 6.45)	0.11		2.40 (0.85, 6.74)	0.10	

HR, hazard ratio; CI, confidence interval; GRS, genetic risk score.

Model 1: Adjustment was made for age and sex.

Model 2: Adjustment was made for age, sex, family history of diabetes mellitus, hypertension, serum total cholesterol, serum high-density lipoprotein cholesterol, serum triglycerides, use of lipid-modifying medication, body mass index, smoking habits, alcohol intake, and regular exercise.

Model 3: Adjustment was made for covariates included in model 2 plus fasting plasma glucose and 2-h postload glucose.

Supplementary Table 4. The associations of type 2 diabetes genetic risk score using a Japanese coefficient with development of prediabetes in subjects with normal glucose tolerance at baseline

GRS levels	No. of events /subjects	Model 1			Model 2			Model 3		
		HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend
Q1	63/171	1.00 (reference)	-		1.00 (reference)	-		1.00 (reference)	-	
Q2	64/171	1.15 (0.81, 1.63)	0.44		1.22 (0.86, 1.73)	0.28		1.26 (0.89, 1.80)	0.20	
Q3	70/172	1.21 (0.86, 1.71)	0.27	0.002	1.24 (0.88, 1.75)	0.22	0.002	1.26 (0.89, 1.78)	0.19	0.01
Q4	74/171	1.45 (1.03, 2.04)	0.03		1.50 (1.06, 2.11)	0.02		1.45 (1.03, 2.05)	0.03	
Q5	79/171	1.63 (1.17, 2.28)	0.004		1.67 (1.19, 2.34)	0.003		1.54 (1.10, 2.15)	0.01	

HR, hazard ratio; CI, confidence interval; GRS, genetic risk score.

Model 1: Adjustment was made for age and sex.

Model 2: Adjustment was made for age, sex, family history of diabetes mellitus, hypertension, serum total cholesterol, serum high-density lipoprotein cholesterol, serum triglycerides, use of lipid-modifying medication, body mass index, smoking habits, alcohol intake, and regular exercise.

Model 3: Adjustment was made for covariates included in model 2 plus fasting plasma glucose and 2-h postload glucose.

Supplementary Table 5. The associations of type 2 diabetes genetic risk score using a European coefficient with development of type 2 diabetes

GRS levels	No. of events /subjects	Model 1			Model 2			Model 3		
		HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend
Q1	30/293	1.00 (reference)	-		1.00 (reference)	-		1.00 (reference)	-	
Q2	31/293	1.06 (0.64, 1.76)	0.81		1.10 (0.66, 1.82)	0.72		0.99 (0.60, 1.65)	0.97	
Q3	36/293	1.35 (0.83, 2.19)	0.23	<0.001	1.45 (0.89, 2.37)	0.13	<0.001	1.10 (0.67, 1.80)	0.70	0.004
Q4	44/293	1.69 (1.06, 2.69)	0.03		1.82 (1.14, 2.90)	0.01		1.37 (0.85, 2.19)	0.19	
Q5	58/293	2.33 (1.50, 3.62)	<0.001		2.71 (1.73, 4.23)	<0.001		1.72 (1.09, 2.69)	0.02	

HR, hazard ratio; CI, confidence interval; GRS, genetic risk score.

Model 1: Adjustment was made for age and sex.

Model 2: Adjustment was made for age, sex, family history of diabetes mellitus, hypertension, serum total cholesterol, serum high-density lipoprotein cholesterol, serum triglycerides, use of lipid-modifying medication, body mass index, smoking habits, alcohol intake, and regular exercise.

Model 3: Adjustment was made for covariates included in model 2 plus fasting plasma glucose and 2-h postload glucose.

Supplementary Table 6. The associations of type 2 diabetes genetic risk score using a European coefficient with development of type 2 diabetes in subjects with normal glucose tolerance at baseline

GRS levels	No. of events /subjects	Model 1			Model 2			Model 3		
		HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend
Q1	8/183	1.00 (reference)	-		1.00 (reference)	-		1.00 (reference)	-	
Q2	5/183	0.65 (0.21, 1.99)	0.45		0.63 (0.20, 1.93)	0.41		0.61 (0.20, 1.91)	0.40	
Q3	3/183	0.43 (0.11, 1.64)	0.22	0.02	0.42 (0.11, 1.63)	0.21	0.02	0.47 (0.12, 1.84)	0.28	0.02
Q4	8/183	1.19 (0.44, 3.20)	0.73		1.19 (0.43, 3.27)	0.74		1.16 (0.42, 3.24)	0.77	
Q5	15/183	2.35 (0.99, 5.60)	0.053		2.38 (0.97, 5.86)	0.06		2.23 (0.89, 5.60)	0.09	

HR, hazard ratio; CI, confidence interval; GRS, genetic risk score.

Model 1: Adjustment was made for age and sex.

Model 2: Adjustment was made for age, sex, family history of diabetes mellitus, hypertension, serum total cholesterol, serum high-density lipoprotein cholesterol, serum triglycerides, use of lipid-modifying medication, body mass index, smoking habits, alcohol intake, and regular exercise.

Model 3: Adjustment was made for covariates included in model 2 plus fasting plasma glucose and 2-h postload glucose.

Supplementary Table 7. The associations of type 2 diabetes genetic risk score using a European coefficient with development of prediabetes in subjects with normal glucose tolerance at baseline

GRS levels	No. of events /subjects	Model 1			Model 2			Model 3		
		HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend	HR (95% CI)	P	P for trend
Q1	63/171	1.00 (reference)	-		1.00 (reference)	-		1.00 (reference)	-	
Q2	60/171	1.03 (0.72, 1.47)	0.87		1.04 (0.72, 1.48)	0.85		1.01 (0.71, 1.45)	0.96	
Q3	78/172	1.42 (1.01, 1.98)	0.04	<0.001	1.43 (1.02, 2.01)	0.04	<0.001	1.45 (1.03, 2.03)	0.03	0.002
Q4	70/171	1.43 (1.02, 2.02)	0.04		1.45 (1.02, 2.06)	0.04		1.39 (0.98, 1.98)	0.06	
Q5	79/171	1.71 (1.22, 2.38)	0.002		1.81 (1.28, 2.54)	<0.001		1.57 (1.11, 2.21)	0.01	

HR, hazard ratio; CI, confidence interval; GRS, genetic risk score.

Model 1: Adjustment was made for age and sex.

Model 2: Adjustment was made for age, sex, family history of diabetes mellitus, hypertension, serum total cholesterol, serum high-density lipoprotein cholesterol, serum triglycerides, use of lipid-modifying medication, body mass index, smoking habits, alcohol intake, and regular exercise.

Model 3: Adjustment was made for covariates included in model 2 plus fasting plasma glucose and 2-h postload glucose.

Supplementary Table 8. Improvement of the risk assessment ability for the development of type 2 diabetes by adding contributions of genetic risk score using a European coefficient to the environmental risk model

Risk model	Harrell's C (95% CI)	P	IDI (95% CI)	P	cNRI (95% CI)	P	catNRI (95% CI)	P
Environmental risk model	0.681 (0.645-0.717)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Environmental risk model + GRS using a European coefficient	0.695 (0.660-0.730)	0.14	0.0242 (0.0167-0.0328)	<0.001	0.2558 (0.0192-0.495)	0.03	-0.0328 (-0.1115-0.0464)	0.48
Environmental risk model + FPG + 2hPG	0.818 (0.791-0.845)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Environmental risk model + FPG + 2hPG + GRS using a European coefficient	0.821 (0.794-0.848)	0.28	0.0063 (0.0007-0.0121)	0.03	-0.0218 (-0.2444-0.207)	0.88	0.0137 (-0.017-0.0452)	0.39

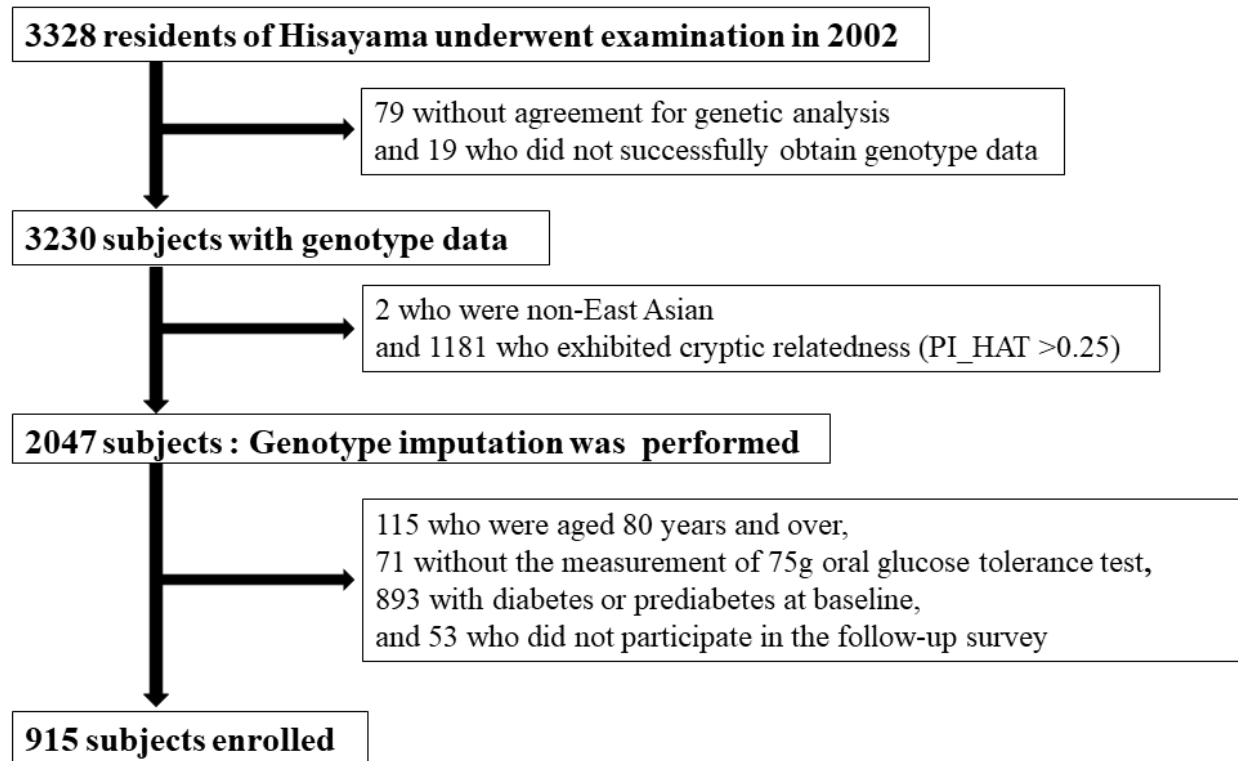
CI, confidence interval; FPG, fasting plasma glucose; 2hPG, 2-h postload glucose; IDI, integrated discrimination improvement; cNRI, continuous net reclassification improvement; GRS, genetic risk score; Ref, reference.

Categorical NRI(catNRI) was calculated using cutoff values of the tertiles of predicted risk with the environmental risk model over 10 years: 0.13 and 0.23 for the upper, and 0.08 and 0.19 for the lower comparison.

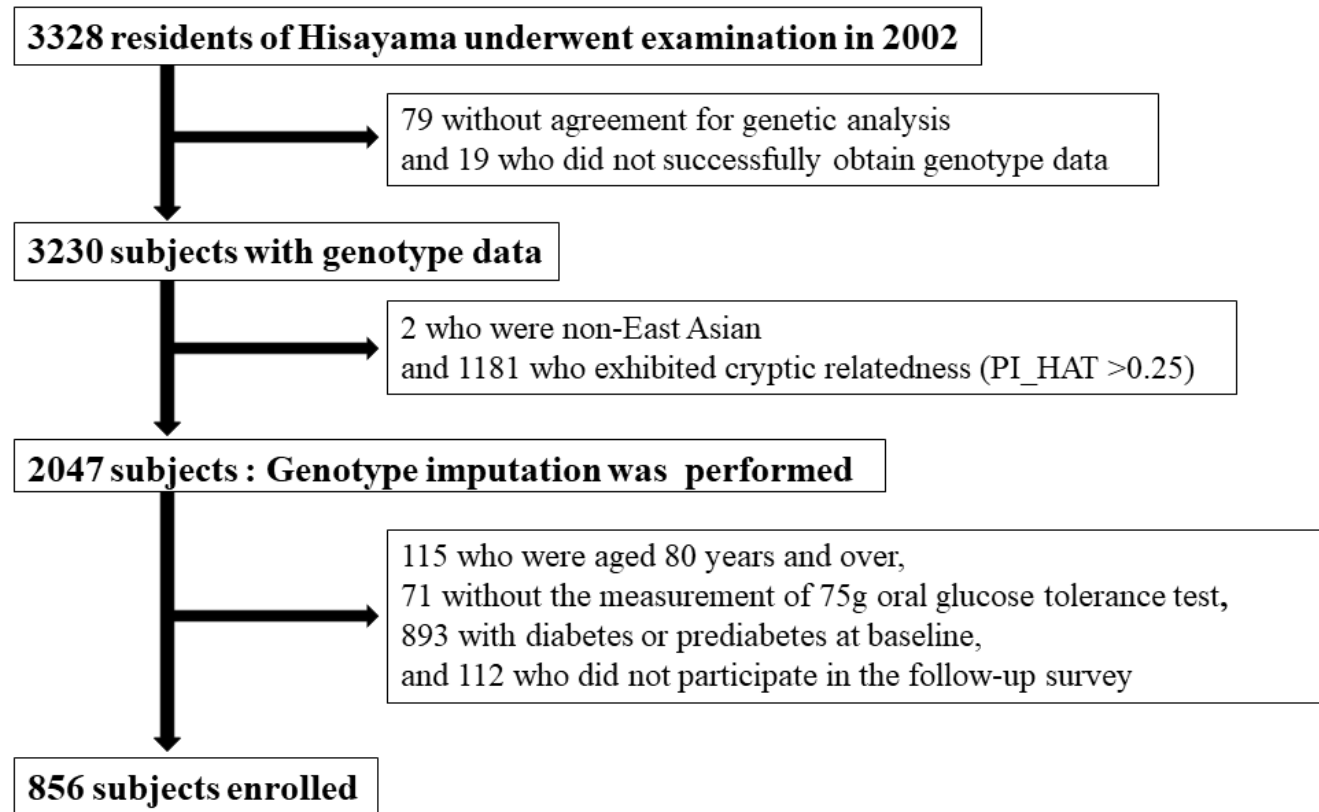
The environmental risk model included age, sex, family history of diabetes mellitus, hypertension, serum total cholesterol, serum high-density lipoprotein cholesterol, serum triglycerides, used of lipid-modifying medication, body mass index, smoking habits, alcohol intake, and regular exercise.

Table for Figure 2. Subgroup analysis

Supplementary Figure 1. Flow chart for survival analyses of subjects with normal glucose tolerance at baseline for incident type 2 diabetes

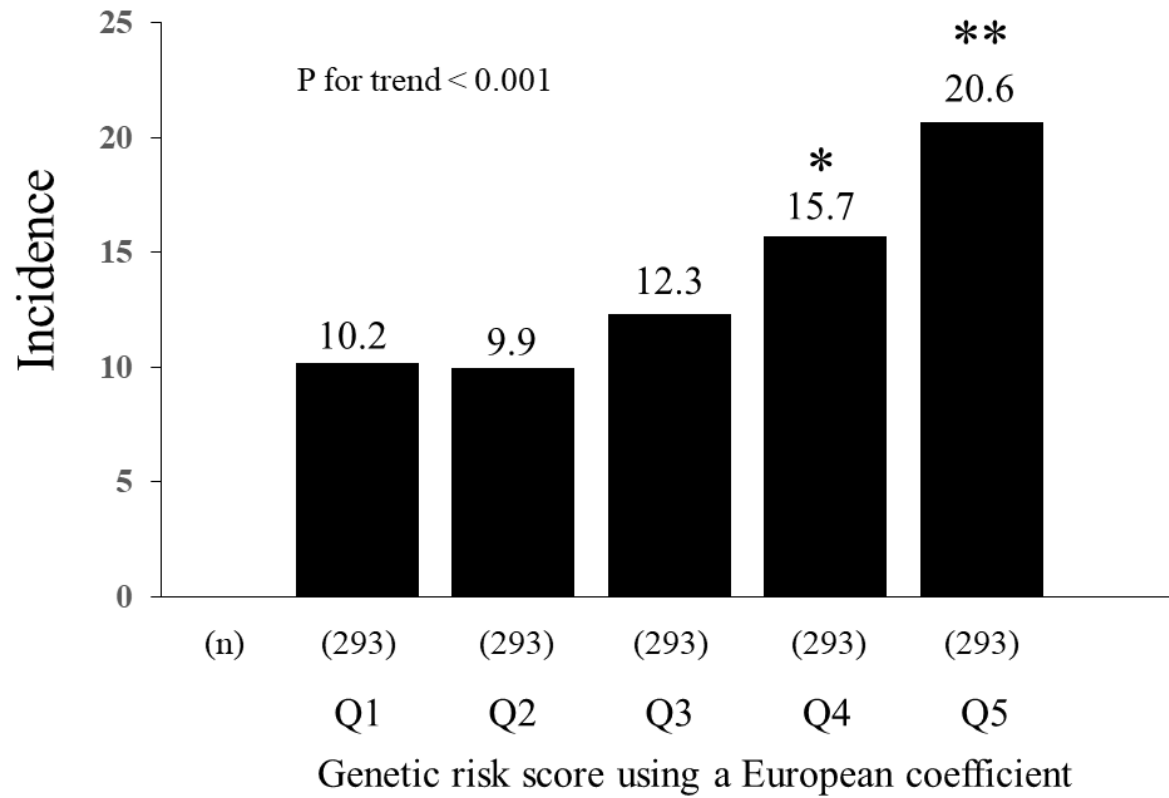


Supplementary Figure 2. Flow chart for survival analyses of subjects with normal glucose tolerance at baseline for incident prediabetes defined by OGTT



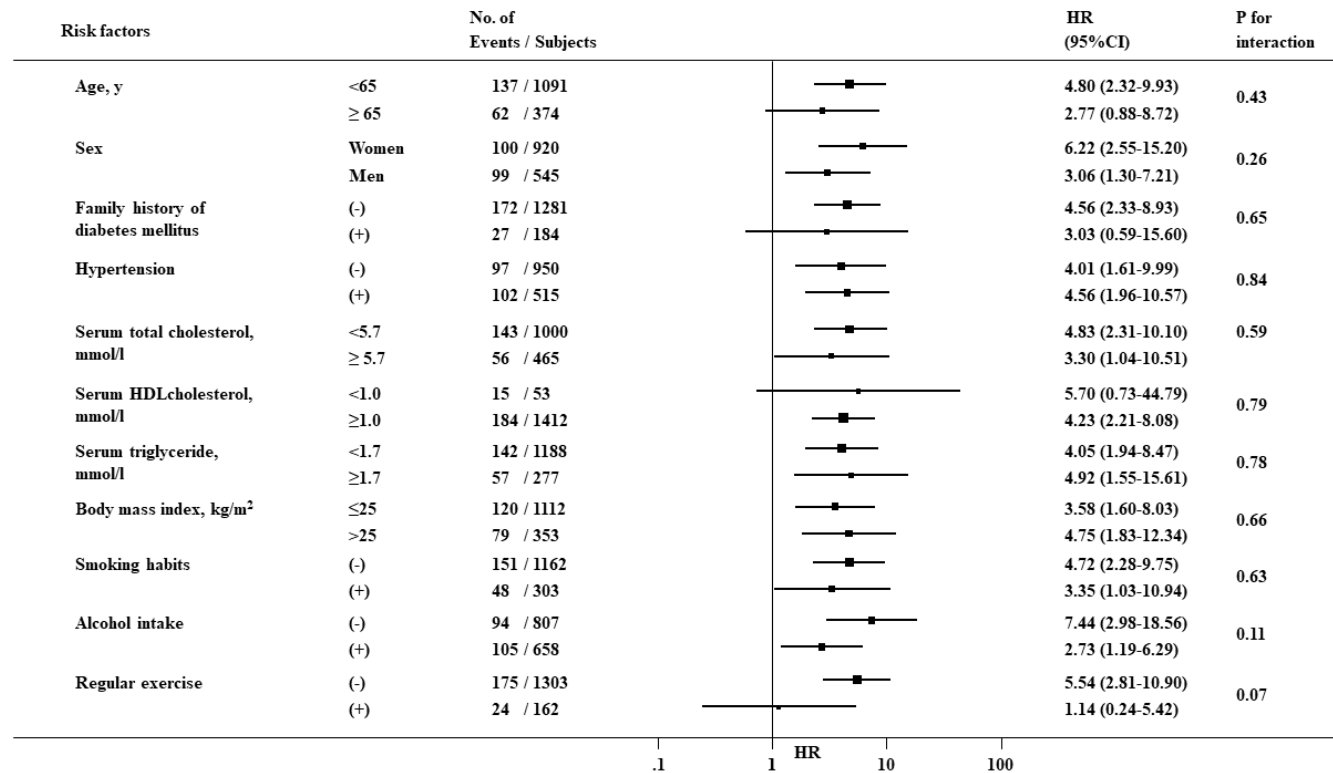
Supplementary Figure 3. Age- and sex-adjusted incidence rate of diabetes mellitus according to the quintile of type 2 diabetes genetic risk score using a European coefficient

per 1,000 person-years



* $P < 0.05$, ** $P < 0.01$ vs the 1st quintile.

Supplementary Figure 4. Comparisons of the influence of a genetic risk score using a European coefficient on the development of type 2 diabetes between subgroups of environmental risk factors



HR, hazard ratio; HDL, high-density lipoprotein.

The values are shown as hazard ratios and their 95% confidence interval per 1 standard deviation in genetic risk score using a European coefficient. The hazard ratios were adjusted for age, sex, family history of diabetes mellitus, hypertension, serum total cholesterol, serum high-density lipoprotein cholesterol, serum triglycerides, use of lipid-modifying medication, body mass index, smoking habits, alcohol intake, and regular exercise.