

Longitudinal relationships between glycemic status and body mass index in a multiethnic study: evidence from observational and genetic epidemiology

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Supplementary Table 1. Description of the 23 SNPs selected in EpiDREAM.

Gene	SNP	Risk Allele	Other Allele	Trait	Chromosome	Publication
<i>TNNI3K</i>	rs1514176	G	A	BMI	1	Speliotes, Nat Genet 2010
<i>PCSK1</i>	rs6235	C	G	Obesity	5	Benzinou, Nat Genet 2008
	rs6232	G	A			
<i>CDKALI</i>	rs2206734	C	T	BMI	6	Okada, Nat Genet 2012
<i>BDNF</i>	rs6265	G	A	BMI	11	Thorleifsson, Nat Genet 2009
	rs1401635	C	G			
<i>FTO</i>	rs9939609	A	T	BMI	16	Frayling, Science 2007
	rs7203521	A	G			Thorleifsson Nat Genet 2009
<i>NPC1</i>	rs1805081	A	G	Obesity	18	Meyre Nat Genet 2009
<i>TFAP2PB</i>	rs2272903	G	A	BMI	6	Speliotes, Nat Genet 2010
<i>NTRK2</i>	rs1211166	A	G	BMI	9	Guo, Hum Mol Genet 2013
<i>MAP2K5</i>	rs997295	T	G	BMI	15	Speliotes, Nat Genet 2010
<i>APOE</i>	rs2075650	A	G	BMI	19	Guo, Hum Mol Genet 2013
<i>GIPR</i>	rs11671664	G	A	BMI	19	Speliotes, Nat Genet 2010
<i>TALI</i>	rs2984618	T	G	BMI	1	Locke et al., Nat Genet 2015
<i>LEPR</i>	rs1011527	A	G	Obesity	1	Wheeler Nat Genet 2013
<i>POMC</i>	rs7605927	G	C	BMI	2	Graff Hum Mol Genet 2013
<i>USP37</i>	rs611203	G	A	BMI	2	Locke et al., Nat Genet 2015
<i>ITIH4</i>	rs2535633	G	C	BMI	3	Wen Hum Mol Genet 2014
<i>NT5C2</i>	rs3824755	C	G	BMI	10	Wen Hum Mol Genet 2014
<i>TCF7L2</i>	rs7903146	C	T	BMI	10	Locke et al., Nat Genet 2015
<i>FANCL</i>	rs12617233	C	T	BMI	2	Locke et al., Nat Genet 2015
<i>KAT8</i>	rs749767	A	G	BMI	16	Locke et al., Nat Genet 2015

Supplementary Table 2. Genotype distributions of 23 obesity SNPs in the EpiDREAM study.

Ethnicity	Major allele	Minor allele	Obesity risk allele	Genotype count			Obesity risk allele frequency	Genotype call rate	HWE P-value
rs9939609 – FTO									
				AA	AT	TT			
South Asian	T	A	A	323	1182	1251	0.332	100 %	0.088
East Asian				5	69	151	0.176	100 %	0.373
European				1698	4468	3214	0.419	100 %	0.035
African				293	640	314	0.491	100 %	0.345
Latin American				392	1440	1455	0.338	100 %	0.218
Native North American				32	166	301	0.230	100 %	0.165
Total				2743	7965	6686	0.387	100 %	N.A.
rs7203521 – FTO									
				AA	GA	GG			
South Asian	A	G	A	521	1325	909	0.429	99.96%	0.328
East Asian				15	86	124	0.258	100 %	0.986
European				3538	4370	1472	0.610	100 %	0.045
African				503	569	175	0.632	100 %	0.489
Latin American				769	1548	969	0.469	99.97 %	0.002
Native North American				93	202	203	0.389	99.80 %	0.001
Total				5439	8100	3852	0.546	99.98 %	N.A.
rs1514176 – TNNT3K									
				AA	GA	GG			
South Asian	A	G	G	565	1357	834	0.549	100 %	0.762
East Asian				35	70	120	0.689	100 %	3.90x10 ⁻⁵
European				3173	4555	1652	0.419	100 %	0.804
African				137	551	559	0.669	100 %	0.944
Latin American				805	1564	918	0.517	100 %	0.010
Native North American				97	245	157	0.560	100 %	0.935
Total				4812	8342	4240	0.484	100 %	N.A.
rs6265 – BDNF									
				AA	AG	GG			
South Asian	G	A	G	146	952	1658	0.774	100 %	0.540
East Asian				46	117	62	0.536	100 %	0.497
European				345	2807	6228	0.814	100 %	0.194
African				4	74	1169	0.967	100 %	0.018
Latin American				94	859	2334	0.841	100 %	0.166
Native North American				14	128	357	0.844	100 %	0.539
Total				649	4937	11808	0.821	100 %	N.A.
rs1401635 – BDNF									
				CC	CG	GG			
South Asian	G	C	C	424	1255	1076	0.382	99.96 %	0.067
East Asian				4	28	193	0.080	100 %	0.020
European				826	3801	4752	0.291	99.99 %	0.094
African				77	478	692	0.253	100 %	0.645
Latin American				156	1119	2012	0.218	100 %	0.979
Native North American				28	168	303	0.224	100 %	0.462
Total				1515	6849	9028	0.284	99.99 %	N.A.
rs1805081 – NPC1									
				AA	GA	GG			
South Asian	A	G	A	1628	973	155	0.767	100 %	0.545
East Asian				133	77	15	0.762	100 %	0.402
European				3552	4385	1443	0.612	100 %	0.140
African				1083	158	6	0.92	100 %	0.928
Latin American				1588	1372	327	0.692	100 %	0.226
Native North American				224	231	44	0.680	100 %	0.151
Total				8208	7196	1990	0.679	100 %	N.A.
rs6232 – PCSK1									
				AA	GA	GG			
South Asian	A	G	G	2431	309	16	0.062	100 %	0.074
East Asian				223	2	0	0.004	100 %	0.947
European				8491	866	23	0.049	100 %	0.853

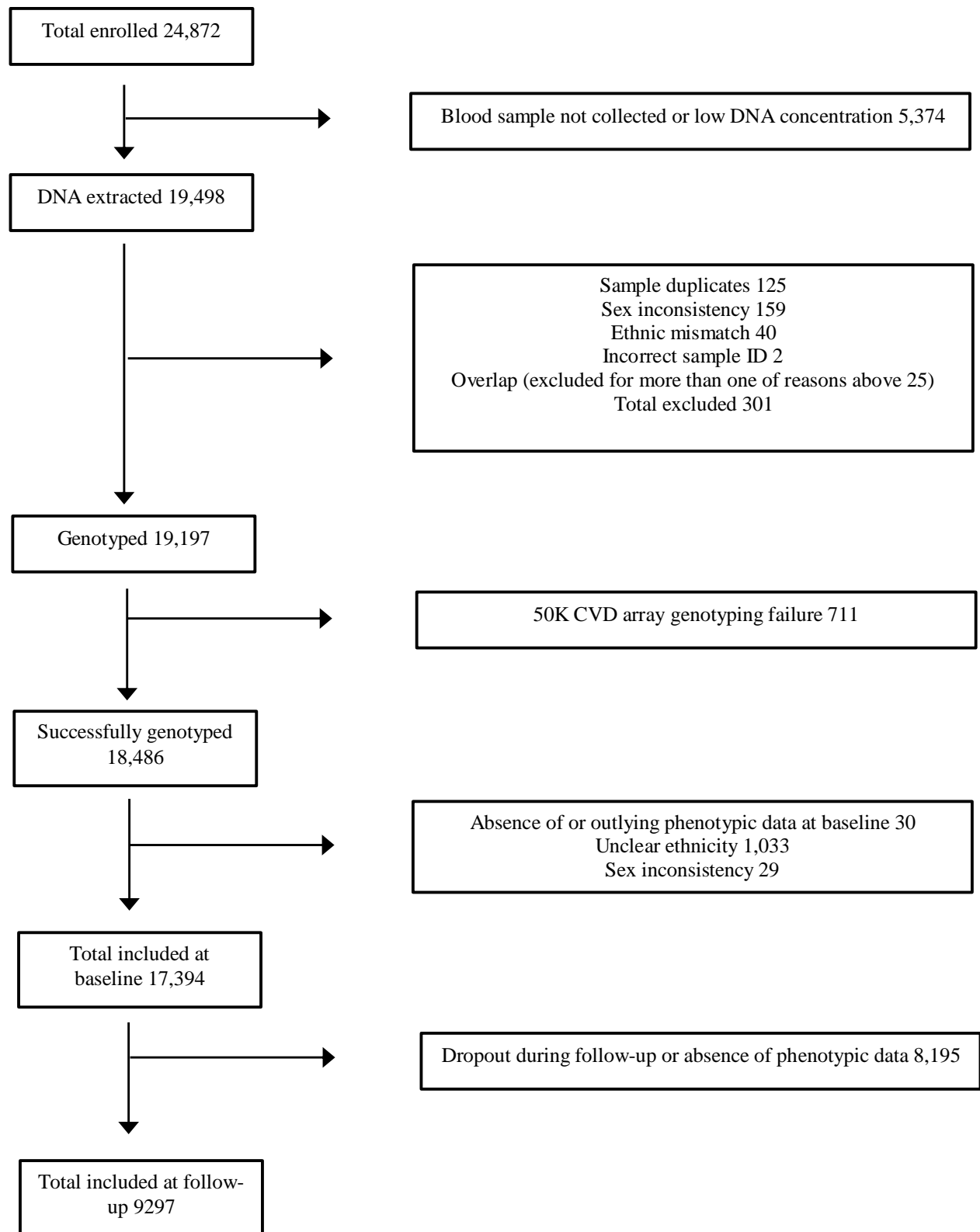
African				1229	18	0	0.007	100 %	0.797
Latin American				3099	185	3	0.029	100 %	0.889
Native North American				470	29	0	0.029	100 %	0.504
Total				15943	1409	42	0.043	100 %	N.A.
rs6235 – PCSKI									
				CC	CG	GG			
South Asian	G	C	C	262	1096	1397	0.294	99.96 %	0.029
East Asian				20	93	112	0.296	100 %	0.912
European				684	3612	5083	0.265	99.99 %	0.225
African				27	329	891	0.154	100 %	0.600
Latin American				157	1084	2046	0.213	100 %	0.384
Native North American				27	188	284	0.242	100 %	0.568
Total				1177	6402	9813	0.252	99.99 %	N.A.
rs2206734 – CDKALI									
				CC	TC	TT			
South Asian	C	T	C	1623	974	159	0.766	100 %	0.421
East Asian				102	94	29	0.662	100 %	0.321
European				6015	3018	346	0.802	99.99 %	0.174
African				715	460	72	0.758	100 %	0.861
Latin American				2104	1047	136	0.799	100 %	0.689
Native North American				299	182	18	0.782	100 %	0.128
Total				10858	5775	760	0.790	99.99 %	N.A.
rs2075650 – APOE									
				AA	GA	GG			
South Asian	A	G	A	2084	621	51	0.869	100 %	0.549
East Asian				173	47	5	0.873	100 %	0.402
European				6951	2248	181	0.861	100 %	0.962
African				956	278	13	0.878	100 %	0.144
Latin American				2593	647	47	0.887	100 %	0.361
Native North American				398	96	5	0.894	100 %	0.767
Total				13155	3937	302	0.870	100 %	N.A.
rs2272903 – TFAP2B									
				AA	AG	GG			
South Asian	G	A	G	132	945	1679	0.781	100 %	0.948
East Asian				8	77	140	0.793	100 %	0.513
European				118	1778	7484	0.893	100 %	0.286
African				120	487	640	0.709	100 %	0.054
Latin American				72	783	2432	0.859	100 %	0.338
Native North American				4	99	396	0.893	100 %	0.417
Total				454	4169	12771	0.854	100 %	N.A.
rs997295 – MAP2K5									
				GG	GT	TT			
South Asian	T	G	T	835	1336	585	0.455	100 %	0.239
East Asian				151	63	11	0.189	100 %	0.196
European				1597	4495	3288	0.590	100 %	0.363
African				261	616	370	0.544	100 %	0.876
Latin American				994	1584	708	0.456	99.97 %	0.102
Native North American				168	222	109	0.441	100 %	0.029
Total				4006	8316	5071	0.531	99.99 %	N.A.
rs1211166 – NTRK2									
				AA	GA	GG			
South Asian	A	G	A	1436	1105	215	0.722	100 %	0.905
East Asian				151	63	11	0.811	100 %	0.196
European				6115	2898	365	0.806	99.98 %	0.351
African				567	540	139	0.671	99.92 %	0.542
Latin American				2114	1019	154	0.798	100 %	0.030
Native North American				378	111	10	0.869	100 %	0.582
Total				10761	5736	894	0.784	99.98 %	N.A.
rs11671664 – GIPR									
				AA	AG	GG			
South Asian	G	A	G	33	521	2202	0.894	100 %	0.727
East Asian				41	89	95	0.620	100 %	0.016

European				122	1767	7488	0.892	99.97 %	0.126
African				15	256	976	0.885	100 %	0.696
Latin American				29	531	2726	0.910	99.97 %	0.577
Native North American				3	102	394	0.892	100 %	0.187
Total				243	3266	13881	0.892	99.98 %	N.A.
rs2984618- TALI									
				GG	GT	TT			
South Asian	G	T	T	554	1313	889	0.561	100 %	0.084
East Asian				3	19	203	0.944	100 %	0.003
European				3414	4445	1521	0.399	100 %	0.245
African				87	484	676	0.736	100 %	0.977
Latin American				766	1513	1008	0.537	100 %	2.0x10 ⁻⁵
Native North American				115	248	136	0.521	100 %	0.924
Total				4939	8022	4433	0.485	100 %	N.A.
rs1011527- LEPR									
				GG	GA	AA			
South Asian	G	A	A	1362	1144	250	0.299	100 %	0.660
East Asian				184	40	1	0.093	100 %	0.449
European				8038	1284	56	0.074	99.98 %	0.544
African				928	293	26	0.138	100 %	0.612
Latin American				2845	428	13	0.069	99.97 %	0.467
Native North American				450	47	2	0.051	100 %	0.520
Total				13807	3236	348	0.113	99.98 %	N.A.
rs7605927- POMC									
				GG	CG	CC			
South Asian	C	G	C	586	1364	794	0.536	99.56 %	0.996
East Asian				73	113	39	0.424	100 %	0.675
European				577	3386	5413	0.758	99.96 %	0.123
African				263	578	406	0.557	100 %	0.032
Latin American				508	1491	1282	0.617	99.82 %	0.031
Native North American				77	215	207	0.630	100 %	0.092
Total				2084	7147	8141	0.673	99.87 %	N.A.
rs611203- USP37									
				AA	GA	GG			
South Asian	A	G	G	1351	1101	303	0.310	99.96 %	0.001
East Asian				149	66	10	0.191	100 %	0.442
European				3264	4517	1599	0.411	100 %	0.591
African				452	616	179	0.391	100 %	0.183
Latin American				1094	1630	563	0.420	100 %	0.292
Native North American				218	219	62	0.344	100 %	0.544
Total				6528	8149	2716	0.390	99.99 %	N.A.
rs2535633- ITIH4									
				GG	CG	CC			
South Asian	G	C	C	456	1287	1013	0.399	100 %	0.168
East Asian				27	111	87	0.367	100 %	0.351
European				1565	4503	3309	0.407	99.97 %	0.618
African				584	538	125	0.684	100 %	0.946
Latin American				774	1618	894	0.482	99.97 %	0.426
Native North American				123	245	131	0.492	100 %	0.691
Total				3529	8302	5559	0.442	99.98 %	N.A.
rs3824755- NT5C2									
				GG	CG	CC			
South Asian	G	C	C	178	961	1617	0.761	100 %	0.030
East Asian				15	100	110	0.711	100 %	0.220
European				103	1671	7606	0.900	100 %	0.297
African				45	395	807	0.806	100 %	0.696
Latin American				93	903	2291	0.834	100 %	0.723
Native North American				8	122	369	0.862	100 %	0.562
Total				442	4152	12800	0.855	100 %	N.A.
rs7903146- TCFL72									
				TT	CT	CC			
South Asian	C	T	C	272	1170	1314	0.689	100 %	0.624

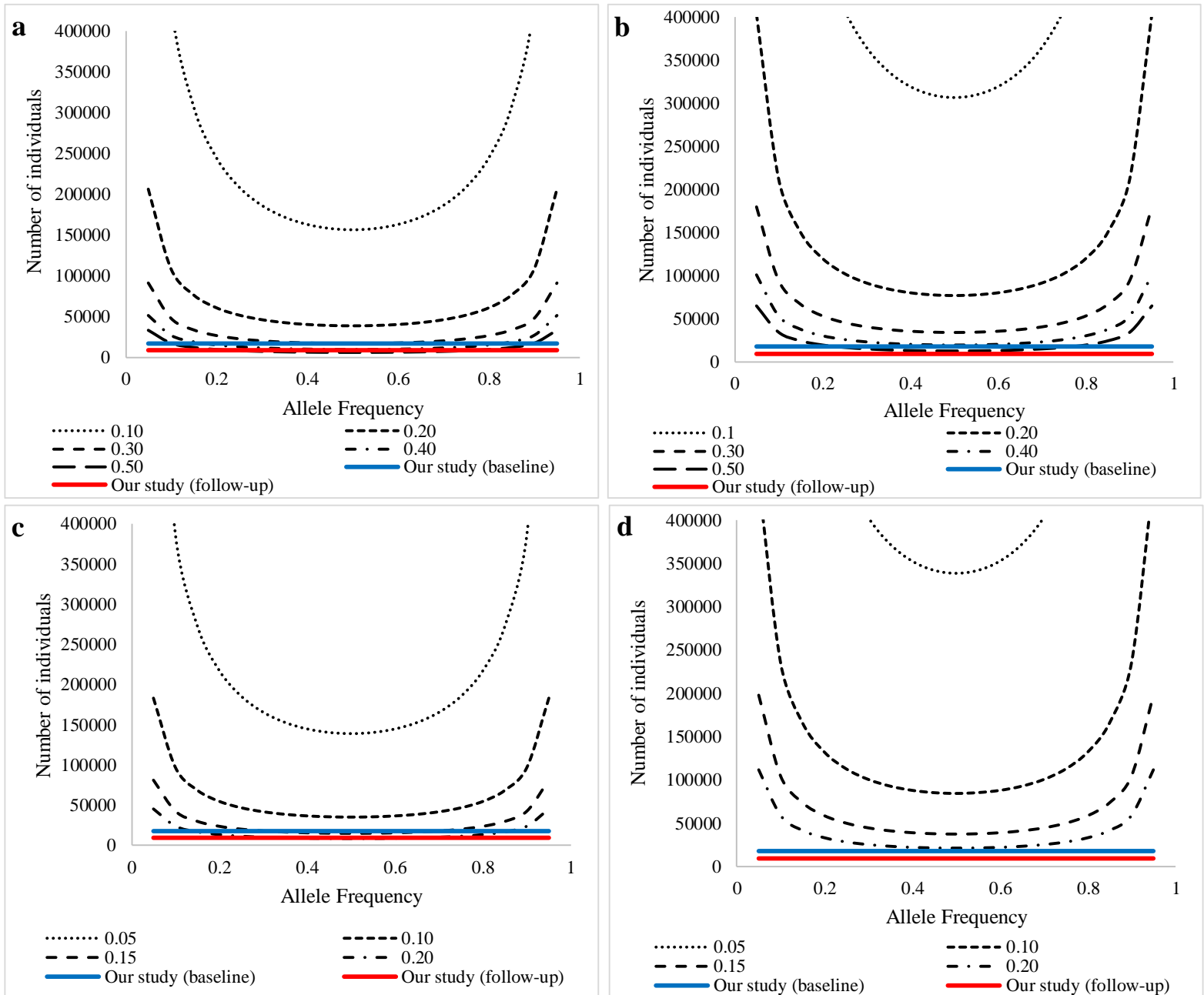
East Asian				2	22	201	0.942	100 %	0.126
European				956	3903	4521	0.690	100 %	0.01
African				112	520	615	0.702	100 %	0.890
Latin American				280	1304	1703	0.716	100 %	0.177
Native North American				10	145	344	0.835	100 %	0.238
Total				1632	7064	8698	0.703	100 %	N.A.
rs126172333- FANCL									
				TT	TC	CC			
South Asian	G	A	G	352	1301	1103	0.636	100 %	0.297
East Asian				67	119	39	0.438	100 %	0.264
European				1537	4480	3363	0.597	100 %	0.489
African				152	579	516	0.646	100 %	0.593
Latin American				638	1583	1066	0.565	100 %	0.247
Native North American				76	247	176	0.600	100 %	0.483
Total				2822	8309	6263	0.599	100 %	N.A.
rs749767- KAT8									
				GG	GA	AA			
South Asian	A	G	A	52	620	2082	0.868	99.93 %	0.461
East Asian				154	60	11	0.182	100 %	0.114
European				1437	4477	3466	0.608	100 %	0.889
African				111	496	640	0.712	100 %	0.291
Latin American				715	1559	1012	0.545	99.97 %	0.013
Native North American				109	232	158	0.549	100 %	0.172
Total				2578	7444	7369	0.638	99.98 %	N.A.

Supplementary Table 3. Proportion of subjects with NGT, IFG/IGT and T2D within each ethnic groups at baseline.

<i>Ethnicity</i>	<i>NGT</i>	<i>IFG/IGT</i>	<i>T2D</i>	<i>All</i>
<i>South Asian</i>	1566 (56.5)	756 (27.4 %)	4454 (16.1 %)	2756 (100 %)
<i>East Asian</i>	74 (32.9 %)	100 (44.4 %)	51 (22.7 %)	225 (100 %)
<i>European</i>	3671 (39.1 %)	4355 (46.5 %)	1354 (14.4 %)	9380 (100 %)
<i>African</i>	465 (37.3 %)	557 (44.8 %)	225 (18.0 %)	1247 (100 %)
<i>Latino American</i>	1460 (44.4 %)	1402 (42.7 %)	425 (12.9 %)	3287 (100 %)
<i>Native North American</i>	221 (44.3 %)	219 (43.9 %)	59 (11.8 %)	499 (100 %)



Supplementary Figure 1. EpiDREAM study selection process overview.



Supplementary Figure 2. Number of individuals required for a statistical power of 80% based on obesity risk allele frequency and beta effect values. a) Main effect analysis using a P -value of 0.05, unadjusted for multiple testing; b) Main effect analysis after adjusting for multiple testing (adjusted P -value = 2.1×10^{-3}) with the Bonferroni correction method; c) Gene-environment interaction effect analysis using a P -value of 0.05, unadjusted for multiple testing; d) Gene-environment interaction effect after adjusting for multiple testing (adjusted P -value = 4.2×10^{-4} with the Bonferroni correction method).