Supplementary Material

Insights on Genetic and Environmental Factors in Parkinson's Disease from a Regional Swedish Case-Control Cohort

Supplementary Table 1. Frequency of self-reported symptoms in MPBC.

Symptoms	Control % (N yes/no)	Patient % (N yes/no)	p
Motor			
Muscle stiffness	10.0 (89/797)	72.7 (647/243)	1.23E-157
Slowness of movement	1.9 (17/863)	72.4 (643/245)	1.96E-205
Balance problems	11.9 (106/784)	65.4 (581/308)	4.53E-118
Tremor	6.0 (53/829)	64.8 (577/313)	6.07E-147
Non-motor			
Nocturia	58.4 (540/385)	71.6 (659/261)	3.26E-09
Leg swelling	16.5 (151/765)	70.4 (273/648)	3.22E-11
Urgent urination	23.5 (215/701)	51.9 (474/440)	9.11E-36
Vertigo, dizziness or feeling of weakness when standing up from supine or sitting	21.9 (200/715)	50.2 (460/457)	3.11E-36
Reduced ability to taste or smell	6.9 (63/852)	45.0 (414/506)	6.85E-77
Feeling depressed	17.5 (159/750)	44.6 (410/510)	1.32E-35
Slow thinking	12.8 (116/792)	43.5 (396/515)	1.17E-47
Forgetfulness	19.7 (178/727)	42.3 (388/529)	2.69E-25
Unpleasant sensations in legs in the evening or when resting, and an urge to move	19.1 (175/739)	41.7 (384/537)	1.60E-25
Sexual dysfunction	28.1 (248/636)	41.0 (350/503)	1.70E-08
Speaking or moving during sleep as when "acting out" dreams	8.1 (73/826)	39.7 (365/555)	2.02E-55
Insomnia	31.2 (285/628)	39.5 (365/558)	2.31E-04
Increased or decreased libido	28.7 (260/646)	36.0 (319/567)	1.13E-03
Drooling	3.3 (30/885)	34.6 (319/603)	3.49E-65
Concentration difficulties	6.2 (57/860)	34.4 (316/603)	1.77E-50
Vivid dreams or nightmares	8.8 (81/835)	33.4 (307/612)	1.16E-37
Constipation	5.6 (51/865)	33.3 (305/612)	2.22E-50
Falling	7.0 (64/850)	30.3 (278/638)	3.10E-37
Feeling of incomplete evacuation of stools	11.2 (102/812)	28.6 (261/653)	1.98E-20
Idiopathic pain	7.8 (71/841)	26.9 (245/666)	8.70E-27
Feeling anxious/worried/scared or panicky	6.7 (61/846)	26.0 (239/681)	2.36E-28
Difficulties swallowing food/drinks	5.9 (54/862)	24.6 (226/691)	1.37E-28
Loss of interest	3.1 (28/889)	21.6 (198/720)	3.70E-33
Excessive sweating	8.4 (77/838)	18.8 (173/746)	1.29E-10
Difficulties judging physical distance	2.7 (25/887)	17.4 (159/755)	5.49E-25
Diplopia	2.1 (19/888)	17.1 (157/760)	3.93E-27
Hallucinations	1.1 (10/904)	16.8 (155/765)	1.17E-31
Difficulties staying awake during activities such as eating or driving	2.4 (22/897)	13.0 (120/806)	3.59E-17
Unexplained weight loss	1.4 (13/900)	11.2 (103/815)	1.77E-17
Fecal incontinence	3.4 (31/884)	7.3 (66/834)	2.81E-04
Nausea	1.8 (16/898)	7.0 (64/854)	8.63E-08
Delusions	0.5 (5/909)	6.0 (55/860)	1.29E-10

Supplementary Table 2. Risk factors for PD in Sweden displayed as OR and 95% CI for both non-adjusted and adjusted complete-case logistic regression analyses

Risk factor	Control (n)	Patient (n)	Non-adjusted		Adjusted	
			OR	95% CI	OR	95% CI
Coffee age <41 years	881	878				
Nothing	55	81	1.00	Referent	1.00	Referent
1-2 cups/day	323	348	0.73	0.50 - 1.06	0.82	0.56 - 1.20
3-5 cups/day	422	397	0.64	0.44 - 0.92	0.71	0.49 - 1.04
>5 cups/day	81	52	0.44	0.27 - 0.71	0.52	0.31 - 0.86
Coffee age 41-64 years	881	874				
Nothing	44	70	1.00	Referent	1.00	Referent
1-2 cups/day	287	351	0.77	0.51 - 1.15	0.88	0.57 - 1.33
3-5 cups/day	472	408	0.54	0.36 - 0.81	0.62	0.41 - 0.94
>5 cups/day	78	45	0.36	0.21 - 0.61	0.43	0.25 - 0.74
Coffee age >64 years	776	717				
Nothing	44	72	1.00	Referent	1.00	Referent
1-2 cups/day	361	385	0.65	0.43 - 0.97	0.74	0.49 - 1.11
3-5 cups/day	331	240	0.44	0.29 - 0.67	0.49	0.32 - 0.74
>5 cups/day	40	20	0.31	0.16 - 0.58	0.36	0.18 - 0.70
Snus	828	820				
Ever vs. never	127/701	74/746	0.55	0.40 - 0.74	0.53	0.38 - 0.73
Tobacco	838	835				
Ever vs. never	508/330	424/411	0.67	0.55 - 0.81	0.72	0.59 - 0.88
Smoking	828	820				
Current vs. never	51/342	40/415	0.65	0.42 - 1.00	0.76	0.47 - 1.21
Ever vs. never	486/342	405/415	0.69	0.57 - 0.83	0.82	0.67 - 1.01
Past vs. never	435/342	365/415	0.69	0.57 - 0.84	0.83	0.67 - 1.02
Pack-years (Ever-smokers)	433	335	0.99	0.98 - 1.00	0.99	0.98 - 1.00
Well-water	847	738				
Ever vs. never	370/477	334/404	0.94	0.78 - 1.13	1.02	0.83 - 1.26
BMI age 20	861	841	1.05	1.02 - 1.09	1.05	1.01 - 1.09
BMI highest	875	864	1.01	0.99 - 1.03	1.01	0.99 - 1.03
Farming	847	738				
Ever vs. never	68/779	85/653	1.30	0.94 - 1.81	1.09	0.74 - 1.61
Head trauma	925	918				
Ever vs. never	296/629	351/567	1.32	1.09 - 1.59	1.30	1.08 - 1.58
Loss of consciousness	133/157	134/209	0.76	0.55 - 1.04	0.76	0.55 - 1.04
PD family history	850	743				
1st degree	59/791	66/677	1.31	0.91 - 1.89	1.31	0.91 - 1.90
Any relative	93/757	148/595	2.02	1.53 - 2.69	2.00	1.51 - 2.67
Pesticides	847	738				
Ever vs. never	31/816	61/677	2.37	1.53 - 3.74	2.26	1.39 - 3.72

Supplementary Table 3. Associations between various variables and PD. Analyzed variables were obtained from questions regarding exposure/use within the past year prior to study inclusion. Associations are indicated in OR and 95% CI (adjusted for sex and age at inclusion).

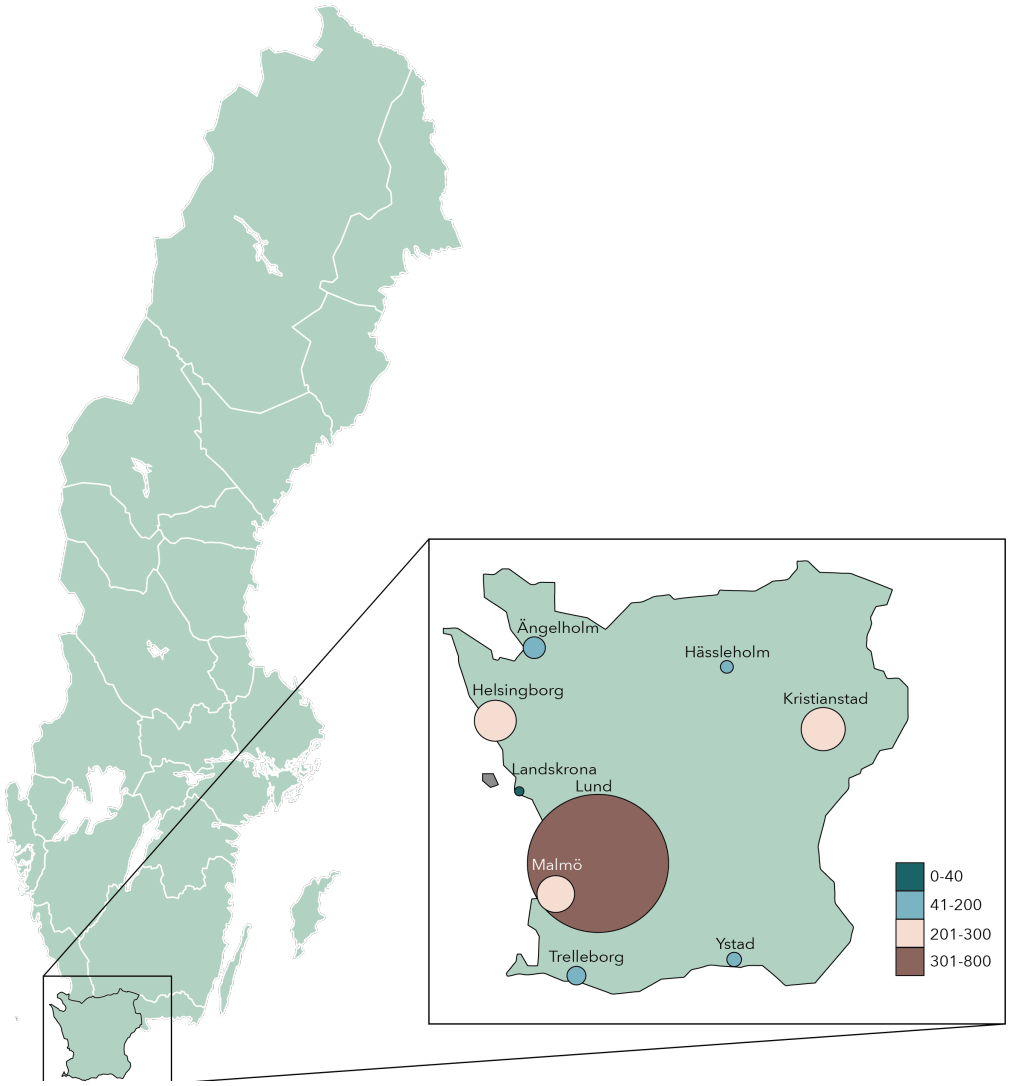
Variable	Control % (N)	Patient % (N)	OR	95% CI
Alcohol				
Nothing	9.1 (84)	16.1 (149)	1.00	Referent
Low	48.2 (447)	52.5 (481)	0.58	0.43 - 0.78
Moderate	29.1 (270)	25.1 (230)	0.45	0.33 - 0.62
High	13.6 (126)	6.2 (57)	0.23	0.15 - 0.34
Red Wine				
Nothing	11.8 (99)	12.9 (99)	1.00	Referent
Low	59.0 (497)	63.6 (489)	0.99	0.73 - 1.35
Moderate	22.0 (185)	21.0 (161)	0.88	0.62 - 1.25
High	7.2 (61)	2.6 (20)	0.32	0.18 - 0.57
BMI				
Inclusion	100.0 (921)	100.0 (914)	0.99	0.96 - 1.00
Physical activity				
Sedentary	7.9 (73)	19.5 (179)	1.00	Referent
Moderate	52.3 (484)	51.9 (469)	0.38	0.28 - 0.51
Moderate but regular	24.0 (222)	18.2 (167)	0.28	0.20 - 0.39
Regular	15.8 (146)	11.4 (105)	0.26	0.18 - 0.38
Physical activity - Hours/week				
Nothing	3.2 (29)	9.8 (84)	1.00	Referent
< 1 hour/week	10.3 (93)	15.0 (129)	0.44	0.26 - 0.72
1-3 hours/week	27.4 (248)	28.8 (248)	0.31	0.20 - 0.49
>3 - <5 hours/week	24.5 (222)	21.6 (186)	0.26	0.16 - 0.42
≥5 hours/week	34.6 (313)	24.9 (214)	0.21	0.13 - 0.33
Comorbidities				
Hyperlipidemia	24.6 (230/705)	13.9 (129/800)	0.51	0.40 - 0.64
Hypertension	43.7 (409/526)	29.9 (278/651)	0.57	0.47 - 0.69
Osteoarthritis	29.4 (275/660)	21.0 (195/734)	0.66	0.53 - 0.82
Migraine	7.1 (66/869)	5.9 (55/874)	0.81	0.55 - 1.17
Back pain	8.1 (76/859)	11.8 (110/819)	1.56	1.15 - 2.13
Depression	7.5 (70/865)	13.3 (124/805)	1.89	1.39 - 2.59
Bowel problems	3.5 (33/902)	11.9 (111/818)	3.93	2.66 - 5.97
Ibuprofen				
Never	69.6 (514)	78.5 (693)	1.00	Referent
< 2 times/week	24.8 (183)	138 (15.6)	0.53	0.41 - 0.68
≥ 2 times/week	5.7 (42)	5.9 (52)	0.89	0.58 - 1.37

Supplementary Table 4. Results from GWA analysis in MPBC for the 90 risk variants reported to be associated with PD in cohorts of European ancestry

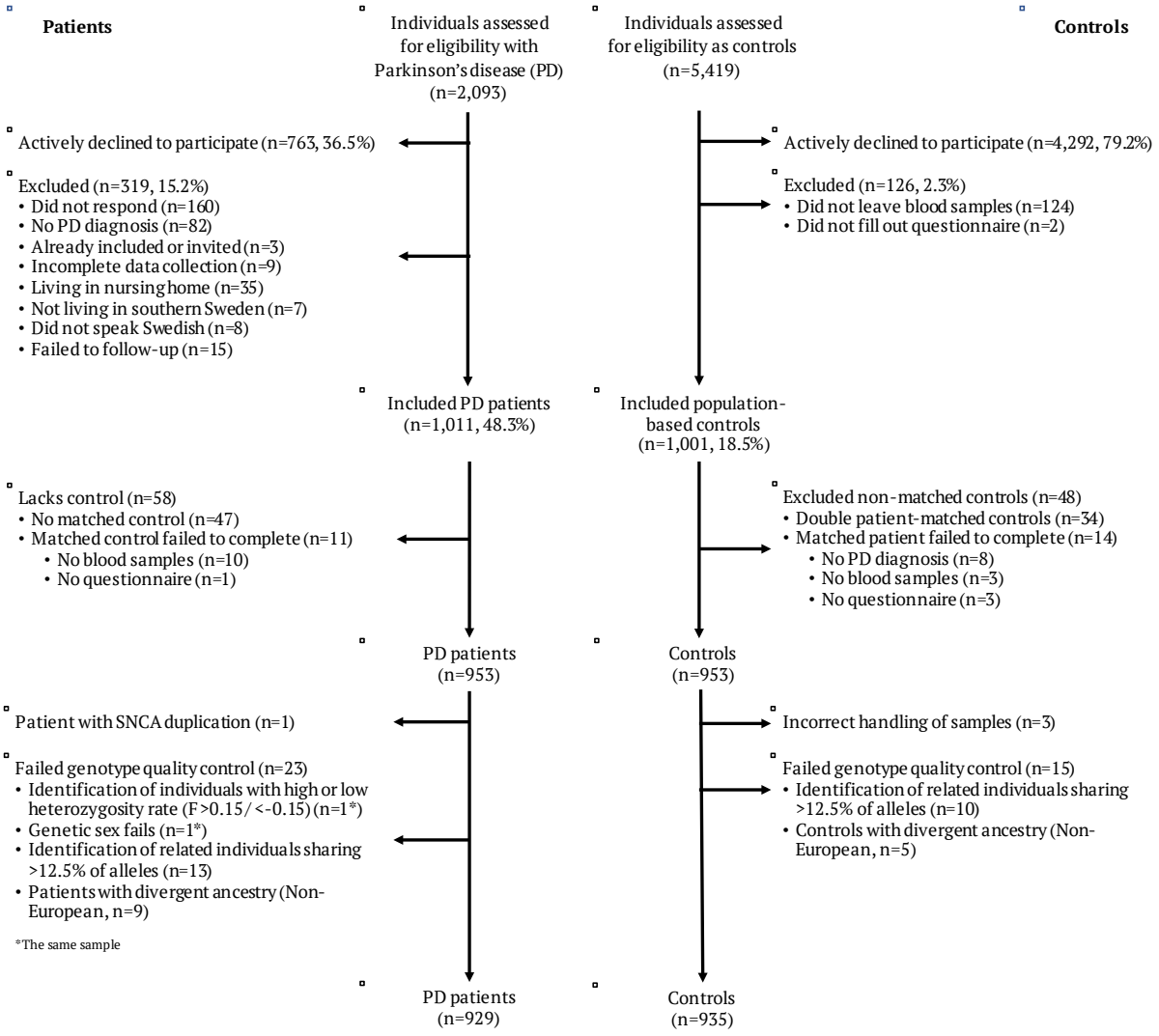
Nearest gene(s)	SNP	CHR	POS	Effect allele	Alt. allele	EAF	MAF	Genotyped	Rsq	Beta	OR	SE	P	EAF[a]	MAF[a]	Beta[a]	OR[a]	SE[a]	P[a]	EAF[b]	MAF[b]	Beta[b]	OR[b]	SE[b]	P[b]
PMVK	rs114138760	1	154898185	C	G	0.007	0.007	Imputed	0.914	-0.136	0.873	0.411	7.40E-01	0.011	0.011	0.311	1.365	0.084	2.25E-04	0.011	0.011	0.281	1.324	0.048	4.19E-09
KRTCAP2	rs35749011	1	155135036	A	G	0.024	0.024	Imputed	0.997	0.649	1.914	0.229	4.52E-03	0.019	0.019	0.751	2.119	0.066	5.02E-30	0.017	0.017	0.607	1.835	0.034	1.72E-70
GBAP1	rs76763715	1	155205634	T	C	0.998	0.002	Imputed	0.826	-1.832	0.160	1.026	7.42E-02	0.993	0.007	-0.491	0.612	0.143	5.76E-04	0.995	0.005	-0.747	0.474	0.077	1.59E-22
FCGR2A	rs6658353	1	161469054	C	G	0.505	0.495	Imputed	0.986	0.120	1.127	0.066	6.92E-02	0.501	0.499	0.072	1.075	0.017	2.42E-05	0.501	0.499	0.065	1.067	0.009	6.10E-12
VAMP4	rs11578699	1	171719769	T	C	0.179	0.179	Imputed	0.988	-0.034	0.967	0.087	7.00E-01	0.196	0.196	-0.078	0.925	0.022	4.24E-04	0.195	0.195	-0.070	0.932	0.012	4.47E-09
NUCKS1	rs823118	1	205723572	C	T	0.560	0.440	Genotyped	1.000	0.141	1.151	0.066	3.37E-02	0.575	0.425	0.100	1.105	0.017	4.94E-09	0.566	0.434	0.107	1.113	0.009	1.11E-29
RAB29	rs11557080	1	205737739	A	G	0.109	0.109	Imputed	0.972	0.194	1.214	0.108	7.19E-02	0.143	0.143	0.135	1.145	0.024	2.12E-08	0.139	0.139	0.132	1.141	0.014	2.50E-22
ITPKB	rs4653767	1	226916078	T	C	0.739	0.261	Imputed	0.991	0.022	1.022	0.076	7.76E-01	0.716	0.284	0.073	1.076	0.019	8.67E-05	0.720	0.280	0.083	1.087	0.010	1.38E-15
SIPA1L2	rs10797576	1	232664611	T	C	0.107	0.107	Genotyped	0.999	0.122	1.130	0.106	2.48E-01	0.143	0.143	0.100	1.105	0.024	3.53E-05	0.140	0.140	0.111	1.117	0.013	6.84E-17
KCNS3	rs76116224	2	18147848	A	T	0.895	0.105	Imputed	0.952	0.154	1.166	0.109	1.58E-01	0.911	0.090	0.155	1.168	0.040	1.19E-04	0.904	0.096	0.110	1.116	0.019	1.27E-08
KCNIP3	rs2042477	2	96000943	A	T	0.241	0.241	Imputed	0.877	0.048	1.049	0.078	5.43E-01	0.237	0.237	-0.058	0.944	0.022	6.89E-03	0.242	0.242	-0.066	0.936	0.012	1.38E-08
MAP4K4	rs11683001	2	102396963	A	T	0.339	0.339	Imputed	0.987	0.068	1.070	0.070	3.30E-01	0.332	0.332	0.076	1.079	0.018	2.11E-05	0.337	0.337	0.071	1.074	0.010	8.04E-13
TMEM163	rs57891859	2	135464616	A	G	0.768	0.232	Imputed	0.976	0.097	1.102	0.079	2.23E-01	0.715	0.285	0.111	1.118	0.019	4.93E-09	0.719	0.281	0.081	1.084	0.011	4.55E-14
STK39	rs1474055	2	169110394	T	C	0.123	0.123	Imputed	0.985	0.140	1.150	0.101	1.63E-01	0.133	0.133	0.176	1.193	0.025	1.14E-12	0.131	0.131	0.180	1.197	0.014	2.54E-39
SATB1	rs73038319	3	18361759	A	C	0.933	0.067	Imputed	0.972	-0.048	0.953	0.135	7.19E-01	0.961	0.039	-0.195	0.823	0.045	1.30E-05	0.959	0.041	-0.169	0.845	0.024	5.94E-13
LINC00693	rs6808178	3	28705690	T	C	0.390	0.390	Imputed	0.972	0.165	1.179	0.068	1.55E-02	0.377	0.377	0.086	1.090	0.017	7.20E-07	0.379	0.379	0.066	1.068	0.010	8.09E-12
IP6K2	rs12497850	3	48748989	T	C	0.619	0.381	Imputed	0.976	-0.018	0.982	0.068	7.92E-01	0.647	0.353	0.049	1.050	0.018	5.74E-03	0.648	0.352	0.064	1.066	0.010	1.36E-10
KPNA1	rs55961674	3	122196892	T	C	0.134	0.134	Imputed	0.930	0.106	1.112	0.100	2.90E-01	0.179	0.179	0.083	1.087	0.023	2.49E-04	0.172	0.172	0.086	1.090	0.013	9.98E-12
MED12L	rs11707416	3	151108965	A	T	0.375	0.375	Imputed	0.994	-0.051	0.950	0.067	4.48E-01	0.370	0.370	-0.072	0.931	0.018	4.53E-05	0.367	0.367	-0.063	0.939	0.010	1.13E-10
SPTSSB	rs1450522	3	161077630	A	G	0.678	0.322	Imputed	0.995	0.029	1.029	0.071	6.89E-01	0.673	0.327	-0.047	0.954	0.018	8.63E-03	0.674	0.326	-0.062	0.940	0.010	5.01E-10
MCCC1	rs10513789	3	182760073	T	G	0.783	0.217	Genotyped	1.000	0.156	1.169	0.081	5.38E-02	0.817	0.183	0.160	1.173	0.022	3.19E-13	0.811	0.189	0.149	1.161	0.012	1.22E-34
GAK	rs873786	4	925376	T	C	0.102	0.102	Imputed	0.948	-0.281	0.755	0.114	1.38E-02	0.100	0.100	-0.135	0.874	0.030	8.70E-06	0.099	0.099	-0.173	0.841	0.018	1.79E-21
TMEM175	rs34311866	4	951947	T	C	0.803	0.197	Imputed	0.986	-0.332	0.717	0.085	1.02E-04	0.804	0.196	-0.227	0.797	0.023	7.97E-23	0.807	0.193	-0.213	0.808	0.012	9.98E-70
BST1	rs4698412	4	15737348	A	G	0.564	0.436	Imputed	0.980	0.098	1.103	0.067	1.44E-01	0.553	0.447	0.126	1.134	0.017	7.05E-14	0.553	0.447	0.104	1.110	0.009	2.06E-28
LCORL	rs34025766	4	17968811	A	T	0.129	0.129	Imputed	0.997	-0.217	0.805	0.098	2.66E-02	0.162	0.162	-0.068	0.934	0.024	4.57E-03	0.159	0.159	-0.084	0.919	0.013	2.87E-10
SCARB2	rs6825004	4	77110365	C	G	0.706	0.294	Imputed	0.975	0.116	1.123	0.073	1.11E-01	0.692	0.308	0.035	1.035	0.018	6.05E-02	0.691	0.309	0.062	1.064	0.010	1.17E-09
FAM47E	rs4101061	4	77147969	A	G	0.707	0.293	Imputed	0.987	-0.164	0.849	0.073	2.40E-02	0.715	0.286	-0.096	0.909	0.019	2.96E-07	0.711	0.289	-0.091	0.913	0.010	4.97E-19
FAM47E-STBD1	rs6854006	4	77198054	T	C	0.353	0.353	Imputed	0.996	-0.187	0.829	0.069	6.65E-03	0.363	0.363	-0.097	0.908	0.018	3.50E-08	0.363	0.363	-0.091	0.913	0.010	5.82E-21
SNCA	rs356182*	4	90626111	A	G	0.617	0.383	Genotyped	0.997	-0.377	0.686	0.069	5.64E-08	0.616	0.384	-0.255	0.775	0.021	9.41E-34	0.628	0.372	-0.277	0.758	0.011	3.89E-154
SNCA	rs5019538	4	90636630	A	G	0.689	0.311	Imputed	0.971	-0.206	0.814	0.071	3.65E-03	0.687	0.313	-0.169	0.844	0.018	2.82E-20	0.679	0.321	-0.157	0.855	0.012	1.13E-36
CAMK2D	rs13117519	4	114369065	T	C	0.184	0.184	Imputed	0.958	0.103	1.108	0.089	2.46E-01	0.179	0.179	0.072	1.075	0.022	1.10E-03	0.174	0.174	0.088	1.092	0.012	9.82E-13
CLCN3	rs62333164	4	170583157	A	G	0.326	0.326	Imputed	0.976	-0.072	0.931	0.070	3.03E-01	0.322	0.322	-0.058	0.943	0.018	1.44E-03	0.326	0.326	-0.064	0.938	0.010	2.00E-10
ELOVL7	rs1867598	5	60137959	A	G	0.901	0.099	Imputed	0.994	-0.018	0.982	0.114	8.78E-01	0.899	0.101	-0.198	0.821	0.028	8.74E-13	0.902	0.098	-0.155	0.856	0.016	2.52E-23
PAM	rs26431	5	102365794	C	G	0.718	0.282	Imputed	0.934	0.123	1.131	0.076	1.06E-01	0.701	0.300	0.063	1.065	0.018	5.37E-04	0.703	0.297	0.062	1.064	0.010	1.57E-09
C5orf24	rs11950533	5	134199105	A	C	0.122	0.122	Imputed	0.946	-0.150	0.861	0.107	1.61E-01	0.101	0.101	-0.088	0.915	0.028	1.81E-03	0.102	0.102	-0.092	0.912	0.016	7.16E-09
LOC100131289	rs4140646	6	27738801	A	G	0.245	0.245	Imputed	0.995	0.091	1.095	0.075	2.23E-01	0.222	0.222	0.073	1.076	0.022	8.35E-04	0.208	0.208	0.083	1.087	0.012	5.62E-12
TRIM40	rs9261484	6	30108683	T	C	0.284	0.284	Genotyped	1.000	-0.095	0.909	0.073	1.91E-01	0.240	0.240	-0.046	0.956	0.021	3.26E-02	0.245	0.245	-0.064	0.938	0.011	1.62E-08
HLA-DRB5	rs112485576	6	32578772	A	C	0.186	0.186	Imputed	0.993	-0.175	0.839	0.084	3.78E-02	0.155	0.155	-0.187	0.829	0.029	1.36E-10	0.163	0.163	-0.168	0.845	0.015	6.96E-28
RIMS1	rs12528068	6	72487762	T	C	0.296	0.296	Imputed	0.992	-0.025	0.975	0.073	7.31E-01	0.286	0.286	0.083	1.086	0.019	8.37E-06	0.284	0.284	0.066	1.068	0.010	1.63E-10
FYN	rs997368	6	112243291	A	G	0.815	0.185	Imputed	0.976	0.026	1.026	0.085	7.62E-01	0.801	0.199	0.053	1.055	0.021	1.19E-02	0.805	0.195	0.071	1.074	0.012	1.84E-09
RPS12	rs75859381	6	133210361	T	C	0.954	0.046	Imputed	0.965	-0.261	0.770	0.165	1.14E-01	0.970	0.030	-0.285	0.752	0.067	1.95E-05	0.967	0.033	-0.221	0.802	0.034	1.04E-10
GPNMB	rs199351	7	23300049	A	C	0.607	0.393	Imputed	0.989	0.058	1.060	0.067	3.84E-01	0.591	0.409	0.099	1.104	0.017	1.28E-08	0.594	0.406	0.102	1.107	0.010	5.25E-26
GS1-124K5.11	rs76949143	7	66009851	A	T	0.067	0.067	Imputed	0.985	-0.357	0.700	0.135	8.21E-03	0.058	0.058	-0.118	0.889	0.052	2.23E-02	0.051	0.051	-0.143	0.867	0.025	1.43E-08
CTSB	rs1293298	8	11712443	A	C	0.759	0.241	Imputed	0.929	0.151	1.163	0.081	6.12E-02	0.749	0.251	0.089	1.093	0.022	3.73E-05	0.744	0.256	0.093	1.097	0.011	3.99E-16
FGF20	rs620513	8	16697593	T	G	0.274	0.274	Imputed	0.979	-0.060	0.942	0.074	4.15E-01	0.268	0.268	-0.115	0.892	0.019	2.14E-09	0.268	0.268	-0.086	0.918	0.011	2.72E-15
BIN3	rs2280104	8	22525980	T	C	0.369	0.369	Genotyped	0.999	0.049	1.050	0.068	4.72E-01	0.364	0.364	0.061	1.063	0.018	4.53E-04	0.360	0.360	0.056	1.058	0.010	1.16E-08
FAM49B	rs2086641	8	130901909	T	C	0.746	0.254	Imputed	0.955	-0.009	0.991	0.077	9.10E-01	0.721	0.279	-0.068	0.934	0.021	1.11E-03	0.723	0.277	-0.061	0.941	0.011	1.81E-08
SH3GL2	rs13294100	9	17579690	T	G	0.356	0.356	Imputed	0.969	-0.251	0.778	0.070	3.62E-04	0.341	0.341	-0.086	0.918	0.018	1.20E-06	0.342	0.342	-0.086	0.918	0.010	8.72E-18
SH3GL2	rs10756907	9	17727065	A	G	0.733	0.267	Imputed	0.957	-0.224	0.799	0.075	2.86E-03	0.760	0.240	-0.100	0.905	0.020	3.10E-07	0.767	0.233	-0.093	0.911	0.011	5.06E-17
UBAP2	rs6476434	9	34046391	T	C	0.741	0.259	Imputed	0.956	-0.022	0.978	0.075	7.73E-01	0.728	0.273	-0.043	0.958	0.019	2.52E-02	0.734	0.266	-0.062	0.940	0.011	6.58E-09
ITGA8	rs896435	10	15557406	T	C	0.681	0.319	Imputed	0.968	-0.092	0.912	0.072	2.03E-01	0.690	0.310	0.055	1.056	0.018	2.61E-03	0.689	0.311	0.074	1.077	0.010	3.41E-13
GBF1	rs10748818	10	104015279	A	G	0.840	0.160	Imputed	0.986	-0.077	0.926	0.089	3.87E-01	0.852	0.148	-0.050	0.952	0.024	3.59E-02	0.851	0.149	-0.079	0.924	0.013	1.05E-09
BAG3	rs72840788	10	121415685	A	G	0.248	0.248	Imputed	0.981	-0.061	0.941	0.077	4.27E-01	0.217	0.217	0.091	1.095	0.021	1.00E-05	0.216	0.216	0.076	1.079	0.011	1.57E-11
INPP5F	rs117896735	10	121536327	A	G	0.016	0.016	Imputed	0.946	0.811	2.250	0.293	5.73E-03	0.018	0.018	0.419	1.521	0.067	2.83E-10	0.017	0.017	0.435	1.545	0.039	2.36E-28
RNF141	rs7938782	11	10558777	A	G	0.899	0.101	Imputed	0.981	0.370	1.448	0.114	1.14E-03	0.873	0.127	0.077	1.080	0.026	2.94E-03	0.878	0.122	0.087	1.091	0.015	2.12E-09
DLG2	rs12283611	11	83487277	A	C	0.391	0.391	Imputed	0.974	-0.031	0.969	0.068	6.46E-01	0.417	0.417	-0.050	0.951	0.017	3.23E-03	0.415	0.415	-0.065	0.937	0.010	2.61E-10
IGSF9B	rs3802920	11	133787001	T	G	0.164	0.164	Imputed	0.992	0.107	1.113	0.090	2.35E-01	0.212	0.212	0.112	1.119	0.021	1.65E-07	0.205	0.205	0.107	1.113	0.012	6.26E-20
LRRK2	rs76904798	12	40614434	T	C	0.126	0.126	Genotyped	1.000	0.265	1.303	0.101	8.67E-03	0.149	0.149	0.135	1.145	0.024	9.22E-09	0.144	0.144	0.144	1.155	0.013	1.52E-28
LRRK2	rs34637584	12	40734202	A	G	0.001	0.001	Imputed	0.822	1.661	5.265	1.255	1.86E-01	0.005	0.005	2.124	8.365	0.300	1.33E-12	0.002	0.002	2.429	11.348	0.094	3.61E-148
LRRK2	*rs34637584*	*12*	*40734202*	*A*	*G*	*0.002*	*0.002*	*Genotyped*	-	-	-	-	-	*0.005*	*0.005*	*2.124*	*8.365*	*0.300*	*1.33E-12*	*0.002*	*0.002*	*2.429*	*11.348*	*0.094*	*3.61E-148*
SCAF11	rs7134559	12	46419086	T	C	0.353	0.353	Imputed	0.985	-0.030	0.970	0.071	6.72E-01	0.402	0.402	-0.074	0.928	0.017	1.51E-05	0.404	0.404	-0.054	0.947	0.010	3.96E-08
HIP1R	rs10847864	12	123326598	T	G	0.342	0.342	Imputed	0.913	0.158	1.171	0.073	3.09E-02	0.363	0.363	0.127	1.136	0.018	9.81E-13	0.364	0.364	0.148	1.160	0.012	1.47E-37
FBRSL1	rs11610045	12	133063768	A	G	0.554	0.446	Genotyped	0.999	0.141	1.151	0.067	3.61E-02	0.482	0.482	0.057	1.058	0.017	7.40E-04	0.490	0.490	0.060	1.062	0.009	1.77E-10
CAB39L	rs9568188	13	49927732	T	C	0.677	0.323	Imputed	0.993	0.040	1.041	0.070	5.72E-01	0.744	0.256	0.024	1.024	0.019	2.27E-01	0.740	0.260	0.062	1.064	0.011	1.15E-08
MBNL2	rs4771268	13	97865021	T	C	0.218	0.218	Imputed	0.940	-0.021	0.979	0.083	7.95E-01	0.232	0.232	0.072	1.075	0.020	2.74E-04	0.230	0.230	0.068	1.070	0.011	1.45E-09
MIPOL1	rs12147950	14	37989270	T	C	0.417	0.417	Imputed	0.950	-0.005	0.995	0.068	9.46E-01	0.436	0.436	-0.079	0.924	0.018	9.46E-06	0.438	0.438	-0.053	0.948	0.010	3.54E-08
GCH1	rs11158026	14	55348869	T	C	0.326	0.326	Genotyped	0.999	-0.138	0.871	0.070	4.94E-02	0.316	0.316	-0.066	0.936	0.018	2.59E-04	0.325	0.325	-0.084	0.919	0.010	1.66E-16
RPS6KL1	rs3742785	14	75373034	A	C	0.769	0.231	Imputed	0.988	0.006	1.006	0.078	9.34E-01	0.786	0.214	0.083	1.086	0.023	2.60E-04	0.787	0.213	0.071	1.074	0.012	1.92E-09
GALC	rs979812	14	88464264	T	G	0.430	0.430	Imputed	0.981	0.040	1.041	0.067	5.55E-01	0.445	0.445	0.036	1.036	0.017	3.44E-02	0.442	0.442	0.061	1.063	0.009	6.19E-11
VPS13C	rs2251086	15	61997385	T	C	0.144	0.144	Imputed	0.961	-0.103	0.902	0.094	2.73E-01	0.135	0.135	-0.128	0.880	0.025	2.53E-07	0.142	0.142	-0.119	0.888	0.014	6.08E-18
SYT17	rs6497339	16	19277493	A	T	0.504	0.497	Imputed	0.923	0.013	1.013	0.068	8.54E-01	0.461	0.461	0.045	1.046	0.017	8.61E-03	0.454	0.454	0.063	1.065	0.010	2.76E-11
CD19	rs2904880	16	28944396	C	G	0.333	0.333	Imputed	0.921	0.056	1.058	0.071	4.32E-01	0.305	0.305	-0.066	0.936	0.019	4.49E-04	0.309	0.309	-0.065	0.937	0.011	7.87E-10
SETD1A	rs11150601	16	30977799	A	G	0.642	0.358	Imputed	0.960	0.062	1.064	0.069	3.67E-01	0.653	0.347	0.112	1.119	0.018	9.02E-10	0.644	0.356	0.091	1.095	0.010	5.12E-20
NOD2	rs6500328	16	50736656	A	G	0.593	0.407	Imputed	0.990	0.012	1.012	0.067	8.57E-01	0.602	0.398	0.070	1.073	0.018	1.35E-04	0.599	0.401	0.059	1.061	0.010	1.82E-09
CASC16	rs3104783	16	52636242	A	C	0.376	0.376	Imputed	0.974	0.046	1.047	0.070	5.13E-01	0.437	0.437	0.081	1.084	0.017	1.94E-06	0.434	0.434	0.067	1.069	0.009	1.29E-12
CHD9	rs10221156	16	52969426	A	G	0.091	0.091	Imputed	0.986	-0.222	0.801	0.116	5.55E-02	0.090	0.090	-0.162	0.851	0.040	5.75E-05	0.093	0.093	-0.116	0.890	0.018	1.08E-10
CHRNB1	rs12600861	17	7355621	A	C	0.619	0.381	Imputed	0.974	-0.046	0.955	0.069	5.09E-01	0.645	0.355	-0.062	0.940	0.018	5.10E-04	0.648	0.352	-0.057	0.945	0.010	1.01E-08
RETREG3	rs12951632	17	40741013	T	C	0.724	0.276	Imputed	0.983	0.186	1.204	0.076	1.41E-02	0.733	0.267	0.072	1.075	0.019	1.35E-04	0.735	0.265	0.064	1.066	0.011	1.40E-09
UBTF	rs2269906	17	42294337	A	C	0.696	0.304	Imputed	0.987	0.104	1.110	0.072	1.52E-01	0.660	0.340	0.061	1.063	0.020	1.90E-03	0.653	0.347	0.063	1.065	0.010	6.24E-10
FAM171A2	rs850738	17	42434630	A	G	0.576	0.424	Imputed	0.956	-0.117	0.890	0.069	8.96E-02	0.604	0.396	-0.082	0.921	0.022	1.89E-04	0.606	0.394	-0.071	0.931	0.011	1.29E-11
CRHR1	rs62053943	17	43744203	T	C	0.110	0.110	Imputed	0.881	-0.156	0.856	0.112	1.63E-01	0.145	0.145	-0.229	0.795	0.031	5.86E-14	0.155	0.155	-0.270	0.763	0.016	3.58E-68
CRHR1	rs117615688	17	43798308	A	G	0.040	0.040	Imputed	0.729	-0.410	0.664	0.194	3.46E-02	0.072	0.072	-0.164	0.849	0.042	1.07E-04	0.067	0.067	-0.232	0.793	0.029	6.71E-16
WNT3	rs11658976	17	44866805	A	G	0.584	0.416	Genotyped	0.993	-0.087	0.917	0.067	1.96E-01	0.603	0.397	-0.061	0.941	0.023	7.81E-03	0.580	0.420	-0.062	0.940	0.011	3.52E-08
BRIP1	rs61169879	17	59917366	T	C	0.173	0.173	Imputed	0.973	-0.038	0.963	0.088	6.64E-01	0.167	0.167	0.067	1.069	0.030	2.45E-02	0.164	0.164	0.082	1.085	0.013	9.28E-10
DNAH17	rs666463	17	76425480	A	T	0.819	0.189	Imputed	0.986	0.019	1.019	0.085	8.27E-01	0.829	0.171	0.071	1.073	0.023	1.82E-03	0.833	0.167	0.076	1.079	0.013	3.20E-09
ASXL3	rs1941685	18	31304318	T	G	0.522	0.478	Imputed	0.954	0.212	1.236	0.068	1.82E-03	0.499	0.499	0.033	1.033	0.017	5.73E-02	0.498	0.498	0.053	1.054	0.009	1.69E-08
RIT2	rs12456492	18	40673380	A	G	0.660	0.340	Genotyped	0.999	-0.122	0.885	0.069	7.99E-02	0.674	0.326	-0.104	0.901	0.018	4.89E-09	0.682	0.318	-0.098	0.907	0.010	3.80E-23
MEX3C	rs8087969	18	48683589	T	G	0.518	0.482	Imputed	0.962	-0.120	0.887	0.067	7.34E-02	0.550	0.450	-0.057	0.945	0.023	1.26E-02	0.550	0.450	-0.058	0.944	0.010	1.41E-08
SPPL2B	rs55818311	19	2341047	T	C	0.688	0.312	Imputed	0.868	-0.034	0.967	0.076	6.54E-01	0.677	0.323	-0.059	0.943	0.021	6.11E-03	0.694	0.306	-0.070	0.932	0.011	4.18E-10
CRLS1	rs77351827	20	6006041	T	C	0.125	0.125	Imputed	0.979	0.003	1.003	0.102	9.76E-01	0.127	0.127	0.094	1.098	0.026	2.37E-04	0.128	0.128	0.080	1.083	0.014	8.87E-09
DYRK1A	rs2248244	21	38852361	A	G	0.277	0.277	Imputed	0.970	-0.048	0.953	0.077	5.29E-01	0.290	0.290	0.100	1.105	0.021	2.01E-06	0.283	0.283	0.071	1.074	0.011	2.74E-11

[a]Nalls 2019 without 23andMe data; [b]Nalls 2019 with 23andMe data; *SNCA rs356182 can also be found in Table 3. LRRK2 G2019S (rs34637584) is occurring twice in the table, the italic being the genotyped data and the non-italic the imputed data.

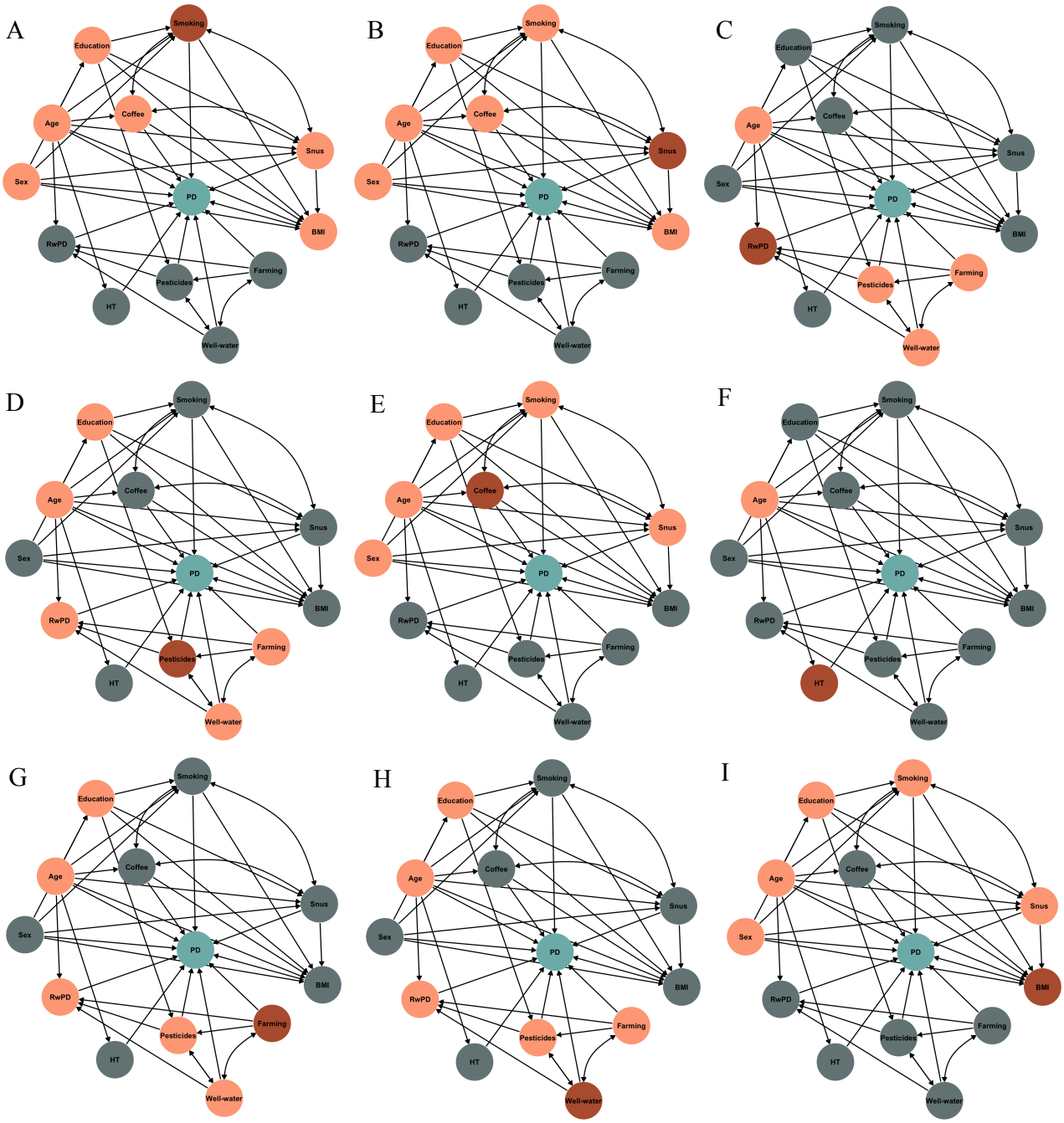
Nalls MA, Blauwendraat C, Vallerga CL, Heilbron K, Bandres-Ciga S, Chang D, Tan M, Kia DA, Noyce AJ, Xue A, et al. (2019) Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies. *Lancet Neurol* **18**, 1091-1102.



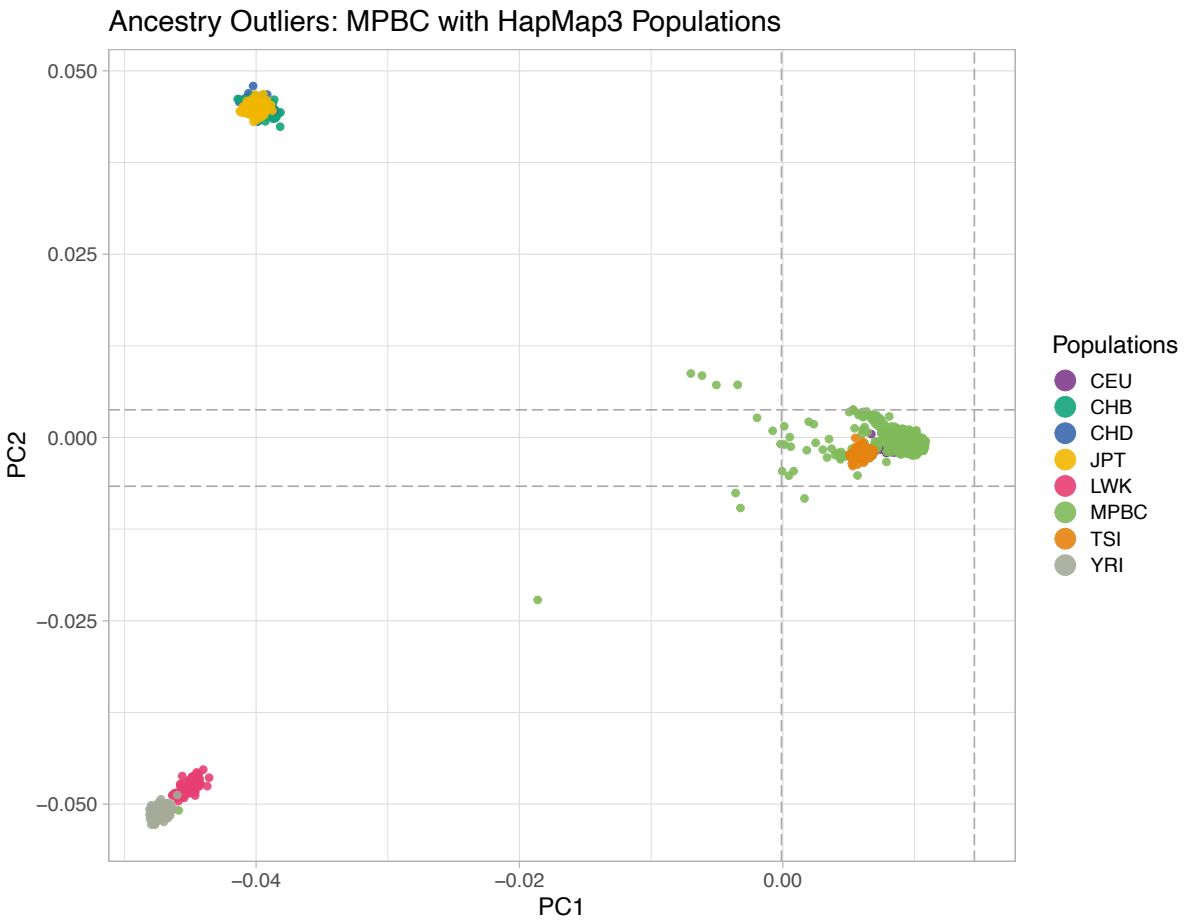
Supplementary Figure 1. Map over Sweden indicating the region of study inclusion. The inclusion region, the southernmost province of Sweden (Scania), is enlarged. The map over Scania shows the nine different cities of study recruitment (two neurological clinics were located in Malmö). The size and color of the circles indicates the number of study participants recruited from each city.



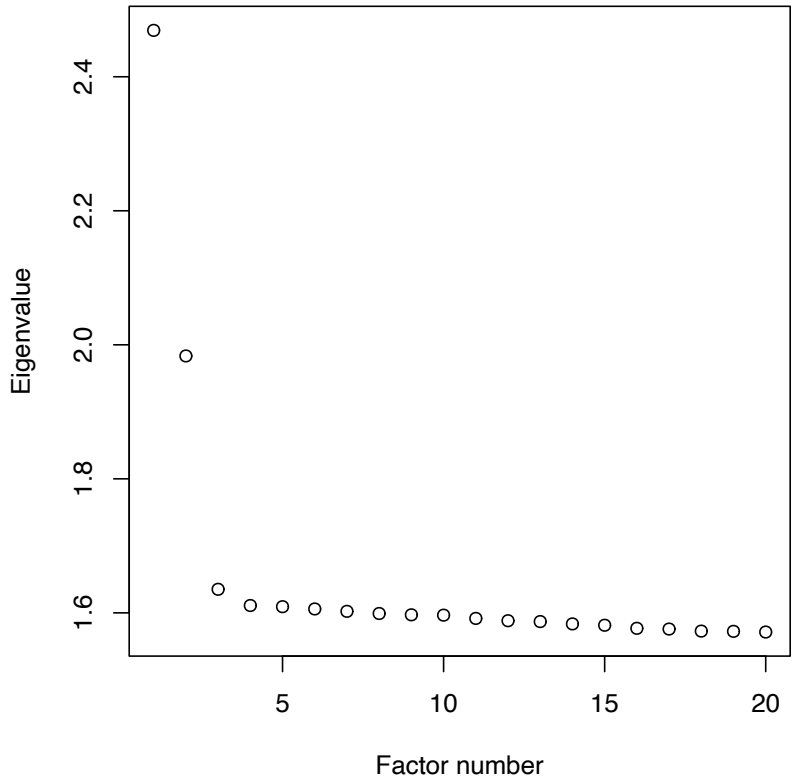
Supplementary Figure 2. Flowchart of the study participant inclusion process to MPBC



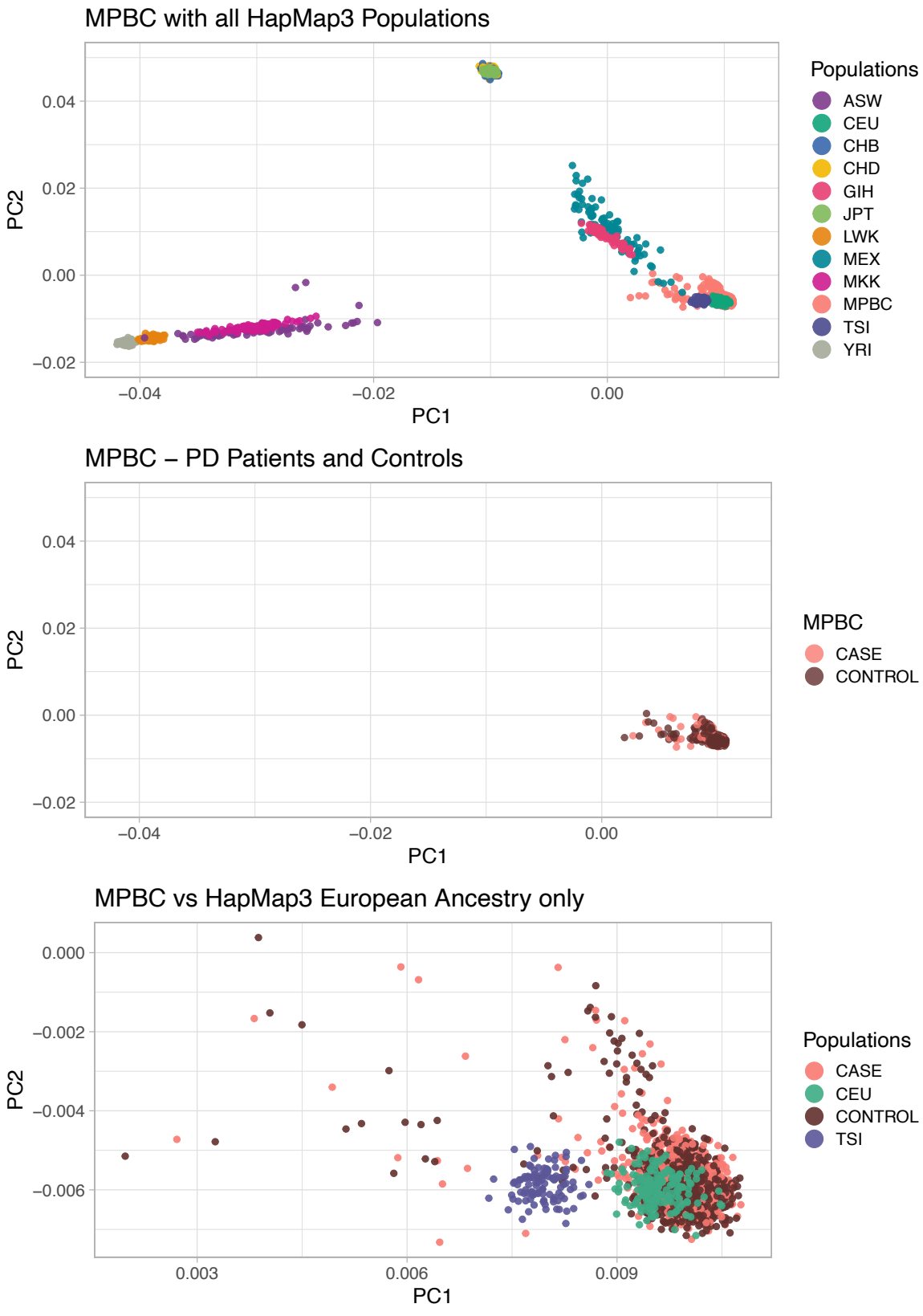
Supplementary Figure 3. Directed acyclic graphs (DAGs) for visualizing the minimal sufficient adjustment for estimating the direct effect of environmental factors on PD. A) Smoking, B) Snus, C) PD Heredity, D) Pesticides, E) Coffee, F) Head Trauma (HT), G) Farming, H) Well-Water, I) BMI. Red, Exposure of interest; turquoise, Outcome; PD, Orange, potential confounders to adjust for in the regression model; grey, Other variables. RwPD, Relative/s with PD; HT, Head trauma; BMI, Body mass index



Supplementary Figure 4. Exclusion of ancestry outliers using principal component analysis (PCA). Non-European individuals was defined as diverging >±6SD from the combined CEU/TSI population. Populations: CEU, Utah residents with Northern and Western European ancestry; CHB, Han Chinese in Beijing, China; CHD, Chinese in Metropolitan Denver, Colorado; JPT, Japanese in Tokyo, Japan; LWK, Luhya in Webuye, Kenya; TSI, Toscani in Italia; YRI, Yoruba in Ibadan, Nigeria

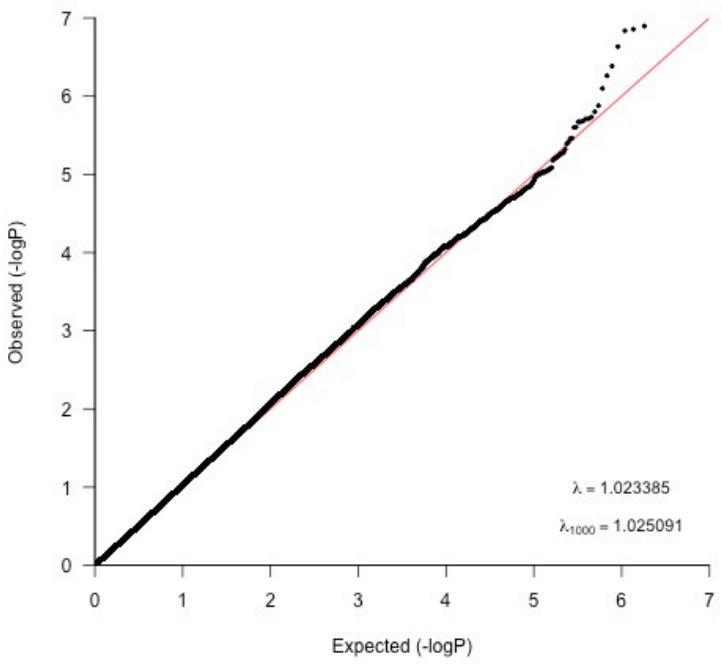


Supplementary Figure 5. Scree plot of the eigenvalues of principal components in the PCA. Used to determine the number of PCs to add as covariates in the GWA analyses.

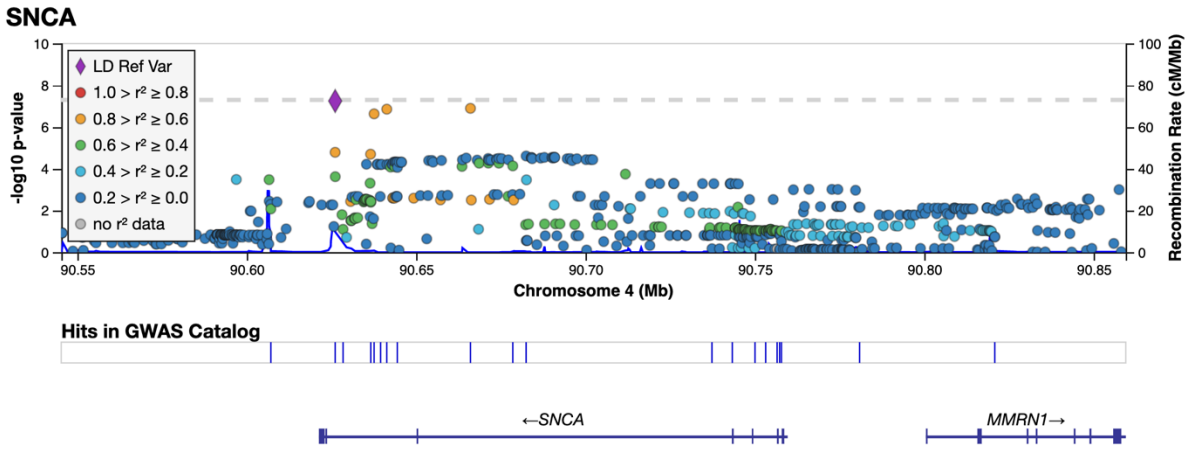

MPBC with all HapMap3 Populations
PC2
PC1
0.04
0.02
0.00
−0.02
−0.04
−0.02
0.00
Populations
ASW
CEU
CHB
CHD
GIH
JPT
LWK
MEX
MKK
MPBC
TSI
YRI
MPBC – PD Patients and Controls
MPBC
CASE
CONTROL
MPBC vs HapMap3 European Ancestry only
0.000
−0.002
−0.004
−0.006
0.003
0.006
0.009
Populations
CASE
CEU
CONTROL
TSI

Supplementary Figure 6. Swedish cohort MPBC population stratification with HapMap3 populations using PCA. Populations: ASW, African ancestry in Southwest USA; CEU, Utah residents with Northern and Western European ancestry; CHB, Han Chinese in Beijing, China;

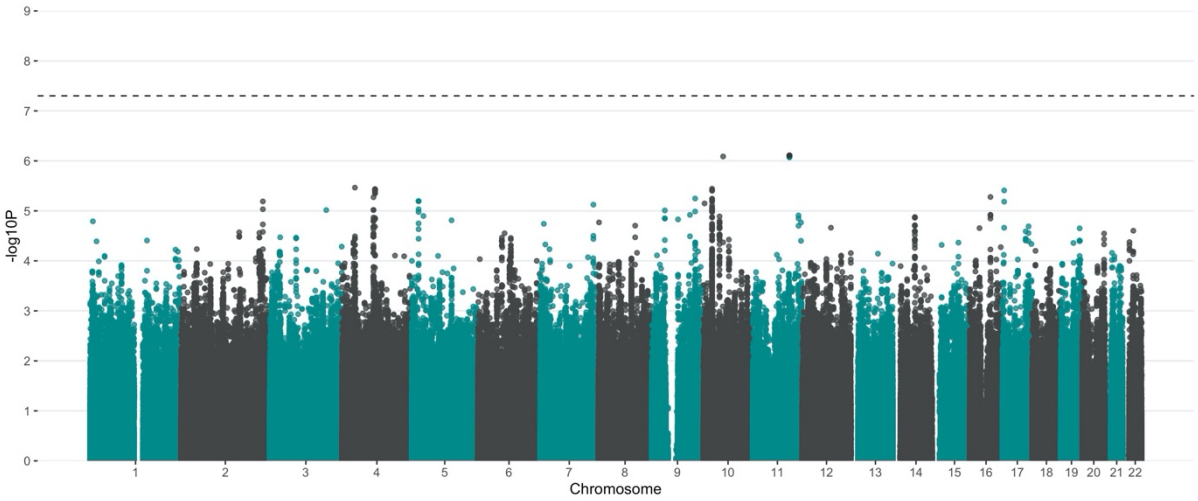
CHD, Chinese in Metropolitan Denver, Colorado; GIH, Gujarati Indians in Houston, Texas; JPT, Japanese in Tokyo, Japan; LWK, Luhya in Webuye, Kenya; MXL, Mexican ancestry in Los Angeles, California; MKK, Maasai in Kinyawa, Kenya; TSI, Toscani in Italia; YRI, Yoruba in Ibadan, Nigeria



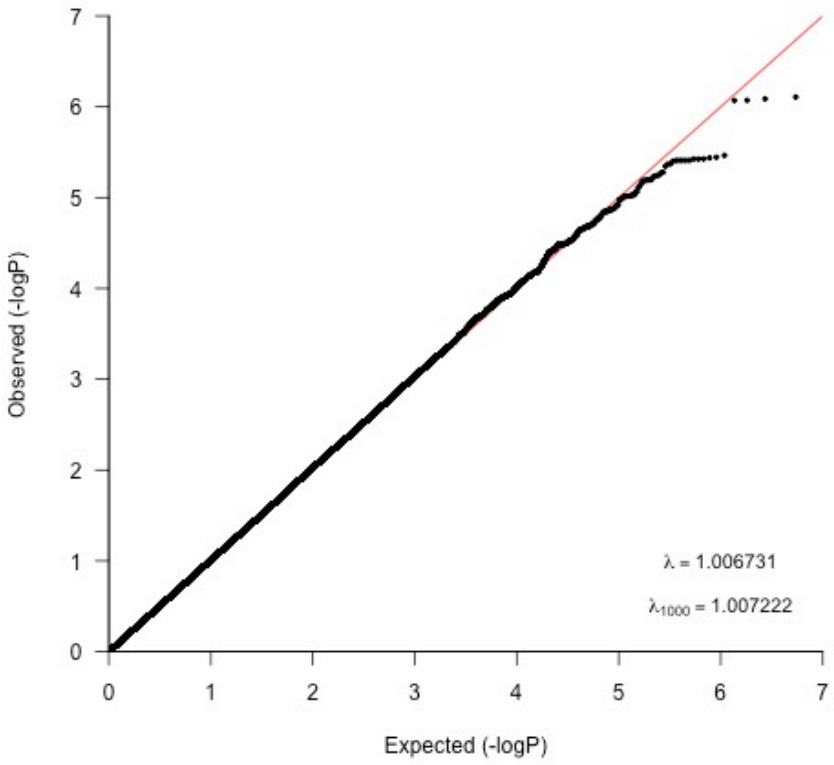
Supplementary Figure 7. Quantile-quantile-plot for PD GWAS with a total of 5,445,841 SNPs (MAF > 5%) tested for 929 PD patients vs. 935 controls.



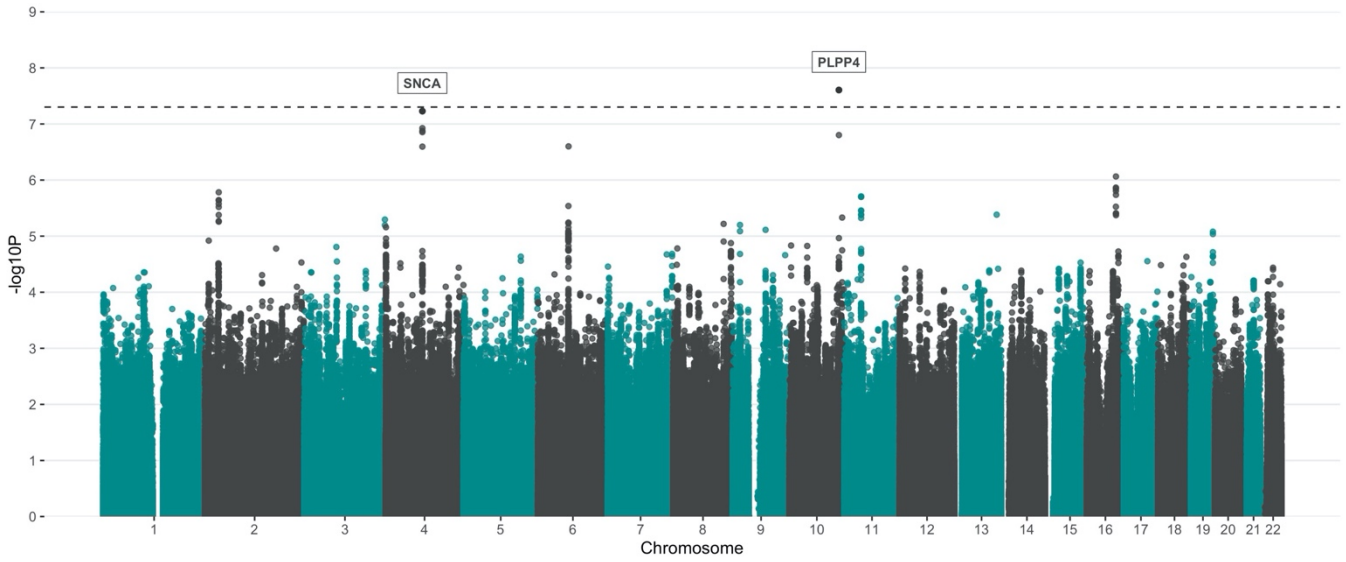
Supplementary Figure 8. LocusZoom plot for PD GWAS *SNCA* loci. Imputed and genotyped variants passing QC in the *SNCA* gene +/- 100 kb (chr4: 90545250 - 90859466) mapped to genome build GRCh37. The variant with lowest p-value (index) is indicated as a purple diamond. Marker colors indicate the strength of LD as r^2 between the index variant and other variants in the 1000 Genomes EUR population.



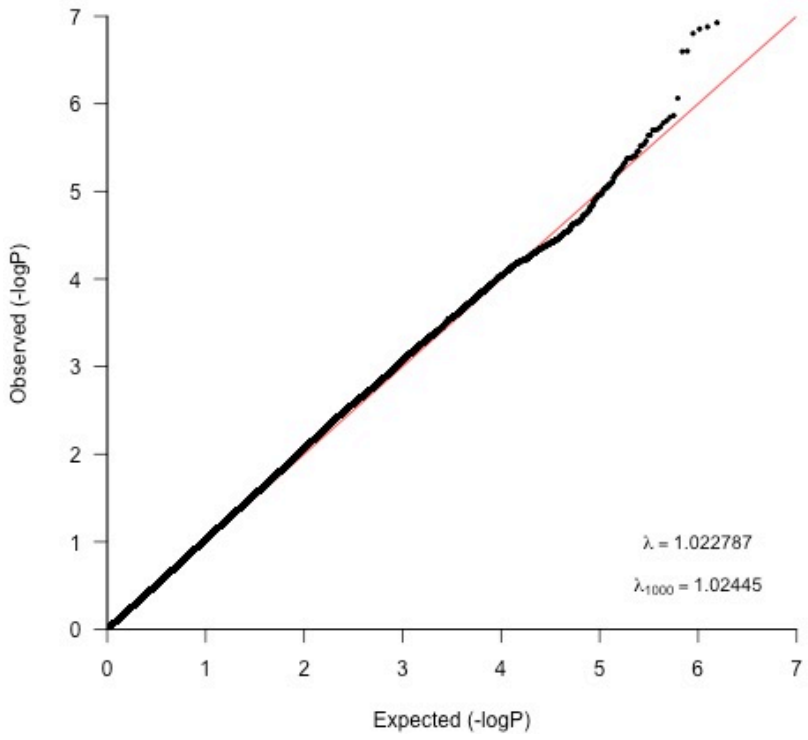
Supplementary Figure 9. Manhattan plot showing the results from the PD age at diagnosis (AAD) GWAS. Data for AAD was available for 792 of 929 PD patients (85.3%) in the cohort and the analysis was adjusted for sex and PC1-5. Analysis was run using 5,440,801 variants following exclusion of variants with a MAF <5% in the group.



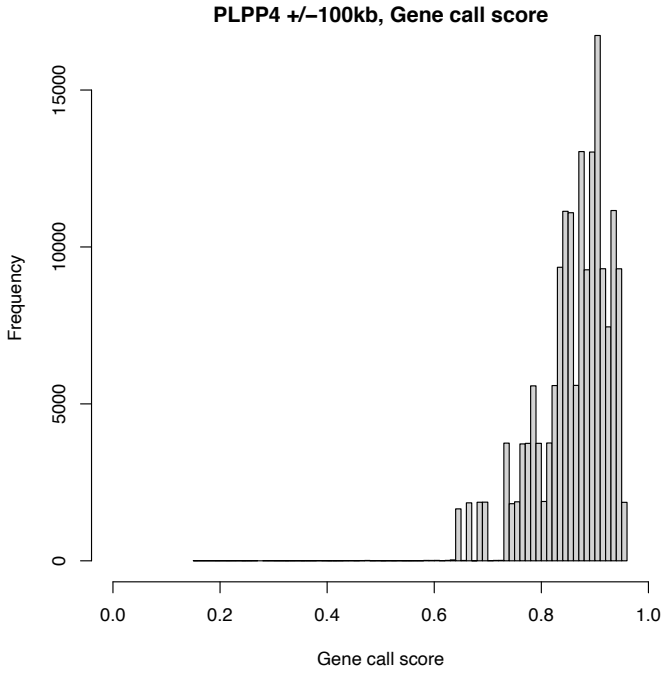
Supplementary Figure 10. Quantile-quantile-plot for the PD age at diagnosis GWAS.



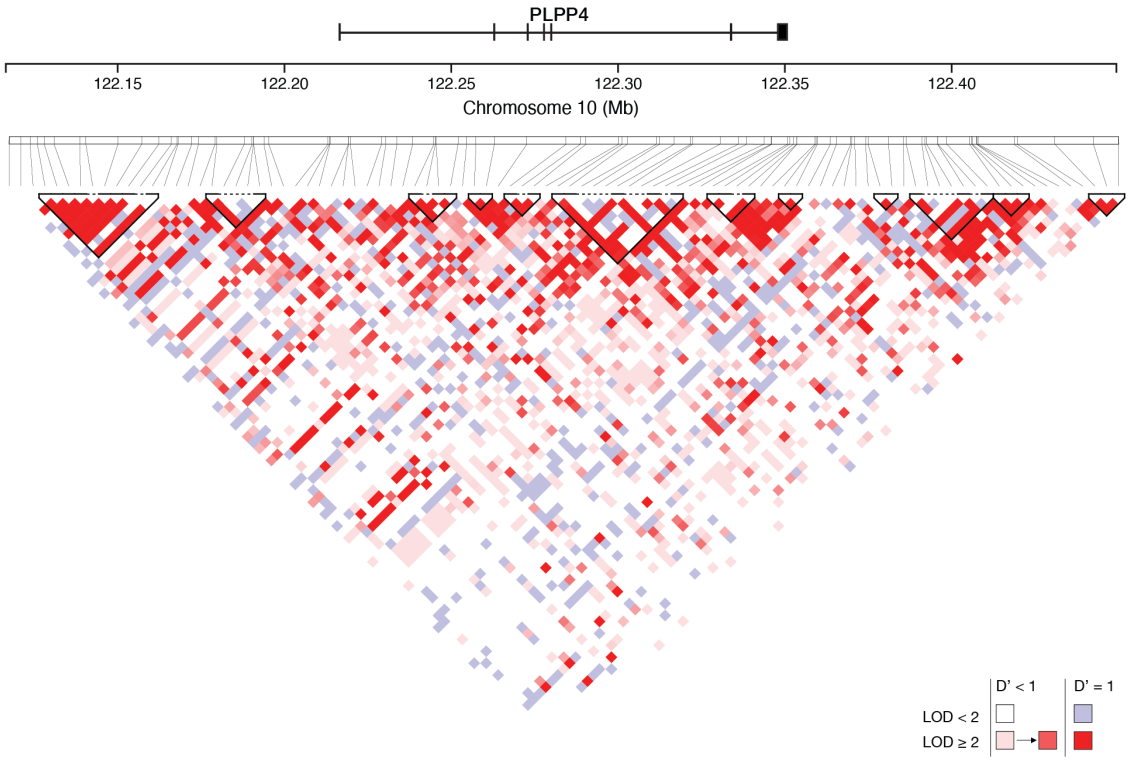
Supplementary Figure 11. Manhattan plot showing the result from PD GWA analysis following imputation with the TOPMed Imputation Reference panel. A total of 6,214,098 variants were included in the analysis following post-imputation QC (MAF > 5%, Rsq >0.3).



Supplementary Figure 12. Quantile-quantile-plot for PD GWAS following imputation with the TOPMed Imputation Reference panel and post-imputation QC (MAF > 5%, Rsq > 0.3)



Supplementary Figure 13. GenCall scores for genotyped variants (n=92) in *PLPP4* ±100 kb



Supplementary Figure 14. Linkage disequilibrium (LD) plot in the PLPP4 locus. LD heatmap showing the LD (D') between the genotyped variants in the region in the MPBC cohort. Note that the location of variants in the heatmap can be shifted relative to the chromosomal position.