Table e-2. Investigating robustness and heterogeneity in the association signals.

		Block 1 rs73656147				Block 2 rs17763929			
	N	MAF	HR	P	P Het	MAF	HR	P	P Het
All	1950	0.013	1.95	3E-06		0.022	1.88	5E-08	
PD-associated risk factors									
Familial	424	0.013	1.84	0.05		0.023	2.09	3E-03	
Sporadic	1526	0.013	2.00	2E-05	0.81	0.022	1.84	4E-06	0.65
Male	1312	0.012	2.24	8E-06		0.020	1.81	9E-05	
Female	638	0.015	1.59	0.05	0.25	0.028	1.94	2E-04	0.77
Smokers	724	0.016	1.83	4E-03		0.027	1.89	2E-04	
Non-smokers	852	0.012	1.87	6E-03	0.94	0.019	1.74	5E-03	0.76
Coffee High	610	0.014	1.88	0.01		0.027	1.69	6E-03	
Coffee Low	828	0.013	1.86	4E-03	0.98	0.020	2.07	2E-04	0.47
OTC NSAIDs - ever	963	0.015	2.05	2E-04		0.026	1.70	7E-04	
OTC NSAIDs - never	582	0.011	1.63	0.08	0.50	0.016	1.79	0.02	0.86
Recruitment site									
New York	410	0.016	2.86	2E-04		0.024	2.83	1E-05	
Oregon	473	0.012	2.39	5E-03		0.025	1.88	4E-03	
Georgia	230	0.024	1.17	0.62		0.027	0.89	0.71	
Washington	837	0.010	1.93	9E-03	0.11	0.019	2.04	3E-04	3E-03
Ashkenazi Jewish									
Yes	88	0.017	2.88	0.09		0.069	1.24	0.51	
No	1862	0.013	1.95	6E-06	0.54	0.020	2.05	7E-09	0.15
Paternal or maternal ancestry									
Great Britain	527	0.009	2.67	3E-03		0.014	2.59	7E-04	
Germany / Austria	434	0.012	1.88	0.05		0.022	2.54	1E-04	
Ireland	245	0.019	1.22	0.57		0.038	1.37	0.22	
Scandinavia	223	0.005	1.83	0.38		0.013	2.28	0.09	
Eastern Europe	91	0.027	4.37	3E-03		0.033	2.39	0.06	
Italy	89	0.034	4.45	1E-03		0.041	4.14	6E-04	
France	80	0.016	4.79	0.03		0.028	5.53	2E-03	
Russia	62	0.008	4.28	0.16	0.35	0.049	0.69	0.44	1E-04

The NGRC dataset was stratified by variables relevant to PD, association of each SNP with age-at-diagnosis was tested within each stratum adjusted for PC 1-3, using Cox regression to generate hazard ratio (HR) and significance (P). The results across strata were then compared for evidence of heterogeneity (P Het). Association signal for block 1

(rs73656147) was relatively consistent across strata with so significant evidence for heterogeneity (this block was also robustly replicated in PAGE dataset with no evidence of heterogeneity). The signal for block 2 (rs17763929) varied significantly as a function of geographic origin of participants, both for their current residence within US and their European country of origin (this SNP was significantly associated with PC1 and PC3, and gave evidence for heterogeneity in PAGE dataset as well).

MAF=minor allele frequency. HR=hazard ratio using Cox regression. P=statistical significance of HR. P Het=statistical significance of heterogeneity across strata. Early-onset PD: age ≤50 years at onset of motor symptom. Late-onset PD: age >50 years at onset of motor symptom. Smoker: ≥100 cigarettes in lifetime. Coffee: Number of cups of caffeinated coffee drank per day multiplied by the number of years of consumption; high and low divided at the median in NGRC participants with PD. OTC NSAIDs: Ever or never use of over the counter non-steroidal anti-inflammatory drugs. Jewish/Non-Jewish: Defined by self-report, and verified by principal component analysis (the core of the Jewish cluster was defined within 0.04≤PC1≤0.055 and 0.001≤PC2≤0.013). Recruitment site: US states where participants were recruited from. Paternal or maternal ancestry: Self reports of the countries from which ancestors immigrated to US.