

Supplementary Table 1 List of proxy SNPs used in MR analyses

MR analyses of Exposure - Outcome	proxy SNP RSID	query SNP RSID	Proxy SNP chromosome:bp	r²
Neuroticism - PD	rs10045812	rs13168838	chr5:46026057	1.00
	rs11022725	rs4757136	chr11:13273156	1.00
	rs11563463	rs11766965	chr7:127006928	1.00
	rs11903494	rs1226574	chr2:157145541	1.00
	rs12967878	rs7240682	chr18:57826570	1.00
	rs1439320	rs12898855	chr15:48013713	1.00
	rs1782170	rs1778377	chr14:41674903	1.00
	rs2217731	rs11875397	chr18:39305562	1.00
	rs58879558	rs77804065	chr17:44095467	1.00
	rs72704544	rs17611770	chr4:176853286	1.00
	rs72841270	rs3740393	chr10:104642237	1.00
	rs7961279	rs938496	chr12:74358554	1.00
	rs11646847	rs12926477	chr16:13088905	0.95
	rs3742021	rs11608355	chr12:109883117	0.95
	rs10814852	rs2380937	chr9:4144772	0.94
	rs329671	rs167915	chr11:133801262	0.92
	rs10896647	rs10896636	chr11:57571883	0.91
	rs35715151	rs2407746	chr8:4944600	0.91
	rs10830225	rs10830220	chr11:88885945	0.88
	rs521746	rs655836	chr3:136103920	0.88
	rs11039216	rs7107356	chr11:47406592	0.83
	rs13176710	rs11740246	chr5:115448982	0.83
Neuroticism - Smoking	rs10045812	rs13168838	chr5:46026057	1.00
	rs11022725	rs4757136	chr11:13273156	1.00
	rs11563463	rs11766965	chr7:127006928	1
	rs11903494	rs1226574	chr2:157145541	1
	rs12967878	rs7240682	chr18:57826570	1
	rs1439320	rs12898855	chr15:48013713	1
	rs1782170	rs1778377	chr14:41674903	1
	rs2217731	rs11875397	chr18:39305562	1
	rs72704544	rs17611770	chr4:176853286	1
	rs72841270	rs3740393	chr10:104642237	1
	rs77588756	rs12426113	chr12:125084956	1
	rs7961279	rs938496	chr12:74358554	1
	rs4121744	rs10830220	chr11:88874969	0.98
	rs11646847	rs12926477	chr16:13088905	0.95
	rs329671	rs167915	chr11:133801262	0.92
	rs10896647	rs10896636	chr11:57571883	0.91

	rs13176710	rs11740246	chr5:115448982	0.83
Smoking - PD				
	rs10012501	rs55900829	chr4:35523111	1.00
	rs10021088	rs1160685	chr4:94059475	1.00
	rs10224126	rs10259715	chr7:3325368	1.00
	rs10455528	rs17554906	chr6:92213245	1.00
	rs10509757	rs111842178	chr10:104752960	1.00
	rs1056668	rs6932350	chr6:26510605	1.00
	rs10795754	rs7920501	chr10:10063553	1.00
	rs10883756	rs28408682	chr10:104400112	1.00
	rs11130380	rs2306866	chr3:53758950	1.00
	rs11191270	rs11191269	chr10:104124605	1.00
	rs11620029	rs1108130	chr13:100655432	1.00
	rs11712680	rs4543050	chr3:75009019	1.00
	rs12194023	rs1737329	chr6:163816903	1.00
	rs12445937	rs61537885	chr16:75699820	1.00
	rs12668101	rs76841737	chr7:91285428	1.00
	rs12894123	rs8005334	chr14:79562860	1.00
	rs13237811	rs79631993	chr7:69429577	1.00
	rs13248395	rs3850736	chr8:64909495	1.00
	rs1335180	rs10969352	chr9:29753733	1.00
	rs141102492	rs112913817	chr7:115457246	1.00
	rs1602798	rs1389171	chr4:28815914	1.00
	rs17534089	rs72789626	chr5:106829219	1.00
	rs17609347	rs62052916	chr16:72532362	1.00
	rs1931427	rs1931431	chr9:11159953	1.00
	rs1937455	rs1937443	chr1:66416939	1.00
	rs1947161	rs2734390	chr3:60441079	1.00
	rs2192363	rs4140932	chr4:15465978	1.00
	rs301805	rs301807	chr1:8481016	1.00
	rs35937770	rs17692129	chr17:44808360	1.00
	rs41264285	rs45444697	chr1:155033918	1.00
	rs4840525	rs4326350	chr8:10765635	1.00
	rs4948487	rs7921378	chr10:63669865	1.00
	rs6103271	rs6073075	chr20:42015848	1.00
	rs6549362	rs2196356	chr3:70886989	1.00
	rs78081759	rs117734003	chr19:51130909	1.00
	rs9627290	rs9627272	chr22:46443040	1.00
	rs10268837	rs13237637	chr7:3467366	0.98
	rs2382252	rs6474609	chr9:10988832	0.98
	rs10455621	rs79180767	chr6:67539129	0.98
	rs10075489	rs10805858	chr5:88872383	0.98
	rs12986535	rs34399632	chr2:137590406	0.98

rs1473624	rs12633090	chr3:83169976	0.97
rs71627577	rs35375873	chr5:43125795	0.96
rs10511087	rs74664784	chr3:85439136	0.96
rs11631953	rs4310804	chr15:96862761	0.95
rs359249	rs359247	chr2:60480237	0.94
rs10891480	rs2155646	chr11:112830526	0.94
rs1014228	rs13319205	chr3:47652639	0.94
rs140285472	rs11692435	chr2:98512189	0.92
rs9302534	rs9941217	chr16:18048710	0.91
rs10052591	rs986714	chr5:50812738	0.90
rs1899491	rs7585579	chr2:60000394	0.90
rs12614651	rs75210106	chr2:113252403	0.90
rs12923427	rs9922607	chr16:17575065	0.89
rs4676964	rs11128203	chr3:71034748	0.87
rs6706713	rs7598402	chr2:50721511	0.86
rs41533650	rs62340589	chr4:176869252	0.86
rs10242758	rs10233018	chr7:117522956	0.85
rs7553439	rs11587399	chr1:50861622	0.82
rs72778145	rs10858334	chr9:137973402	0.81
rs4937001	rs76460663	chr11:111928053	0.80

Supplementary Table 2. Instruments for Neuroticism

snp	chr	pos	beta	se
rs12137398	1	7790548	0.017454	0.002952
rs11576073	1	37200680	0.015811	0.002295
rs12747763	1	49339602	0.017814	0.003743
rs17096778	1	75809970	0.032966	0.005602
rs11184994	1	107383738	0.013314	0.002452
rs7536102	1	174465939	0.015098	0.002506
rs199933	1	181747349	0.013716	0.002662
rs2488401	1	197702401	-0.01659	0.002819
rs17432675	1	201887721	0.013449	0.002449
rs17502858	1	225781230	0.025849	0.00519
rs4396680	2	10178236	0.016756	0.002813
rs4665244	2	24102691	0.012099	0.002383
rs10188070	2	58299326	-0.01455	0.002442
rs11127043	2	86738324	0.016126	0.003093
rs10048736	2	144239303	-0.01232	0.002362
rs2042555	2	148555489	0.017439	0.002304
rs11903494	2	157145541	-0.0177	0.002804
rs1018154	2	164072337	-0.02145	0.004739
rs10497655	2	185462041	0.013653	0.002438
rs138218528	2	212676884	0.013218	0.002523
rs78720888	2	215498326	-0.01804	0.003258
rs6737187	2	226360417	-0.01433	0.002528
rs9867227	3	16866253	0.01672	0.002538
rs1542212	3	35683935	-0.01591	0.00233
rs6776145	3	50316119	-0.01868	0.003468
rs2015971	3	52546820	-0.01228	0.002299
rs9852417	3	65161154	-0.01233	0.002379
rs9870448	3	85416384	0.014193	0.002796
rs836927	3	107201428	0.01661	0.002372
rs59382200	3	116959274	0.013037	0.002387
rs521746	3	136103920	0.015603	0.002297
rs4585149	3	157493952	-0.01712	0.002988
rs4697241	4	21855941	-0.01148	0.002349
rs9291211	4	42139132	0.014332	0.002656
rs6828271	4	90750025	0.014093	0.002322
rs57360718	4	118936191	-0.02442	0.00461
rs1595693	4	139043652	0.01359	0.002466
rs72704544	4	176853286	-0.01419	0.002883
rs10045812	5	46026057	0.012508	0.002335
rs1501673	5	87963600	0.020736	0.003302
rs11240962	5	107721366	0.017719	0.002778
rs13176710	5	115448982	-0.01392	0.003464

rs4868748	5	164437147	-0.01575	0.002532
rs2031595	6	11980752	-0.015	0.002544
rs2071303	6	26091336	0.013741	0.002377
rs200965	6	27866384	-0.01754	0.002907
rs28986304	6	29566082	-0.02133	0.003484
rs2503775	6	98521600	0.021456	0.003355
rs240769	6	101012187	-0.01394	0.002322
rs2056477	7	2079744	-0.01527	0.002751
rs11509880	7	12261911	0.014987	0.002441
rs6948810	7	21523194	0.012973	0.002542
rs10274968	7	38939254	0.012705	0.002273
rs274632	7	86269181	-0.01314	0.002341
rs35763039	7	97718650	-0.01355	0.002511
rs35048193	7	126382539	0.016759	0.002318
rs11563463	7	127006928	0.009572	0.002351
rs3812479	8	1495947	0.01138	0.002272
rs35715151	8	4944600	0.016686	0.002608
rs2921036	8	8363897	0.010792	0.002338
rs7818437	8	10209623	-0.01835	0.002686
rs28639817	8	14151407	-0.02002	0.00338
rs76288073	8	65568214	-0.01642	0.003151
rs2737219	8	116635688	0.012841	0.002312
rs13262595	8	143316970	0.011906	0.00229
rs10814852	9	4144772	-0.01172	0.002322
rs62550480	9	11449346	-0.01802	0.002822
rs10811883	9	23291526	-0.01747	0.002382
rs10119773	9	23736400	-0.01533	0.002322
rs12344656	9	28604268	-0.01401	0.002413
rs78046549	9	96268478	0.024292	0.003796
rs75614054	9	98275789	0.031285	0.004132
rs7025144	9	120496387	0.018433	0.002553
rs60393230	9	122655283	-0.0116	0.002371
rs11256385	10	9962206	-0.01218	0.002278
rs2093623	10	10922977	-0.01229	0.002299
rs72841270	10	104642237	0.015917	0.003353
rs860626	10	119301703	0.01501	0.002566
rs11022725	11	13273156	0.015577	0.002339
rs297343	11	16354653	0.01593	0.002409
rs10835565	11	29783941	0.01256	0.002413
rs1806153	11	31850105	0.016927	0.002704
rs12283653	11	46231998	-0.01327	0.002334
rs11039216	11	47406592	0.013219	0.002329
rs10896647	11	57571883	0.015426	0.002482
rs10830225	11	88885945	-0.01298	0.002322

rs10790767	11	99392678	0.011207	0.00232
rs7111031	11	113377488	0.01962	0.00236
rs11605020	11	126980865	0.012683	0.002304
rs329671	11	133801262	-0.01177	0.002443
rs4337088	12	22881333	0.011761	0.002286
rs9971907	12	23779061	-0.0136	0.002379
rs7961279	12	74358554	-0.01142	0.002365
rs3742021	12	109883117	-0.01991	0.002472
rs3741475	12	117669914	0.017143	0.00283
rs6490177	12	118796085	0.018107	0.002934
rs12426113	12	125081259	-0.01772	0.003283
rs3124426	13	55937346	-0.01546	0.00275
rs4444227	13	59116160	-0.01745	0.002763
rs1892350	13	68080614	-0.01364	0.002269
rs7999314	13	69370301	0.014184	0.0025
rs9516861	13	97854889	0.017969	0.003336
rs3783007	13	99109816	-0.01068	0.002399
rs9521987	13	111555592	0.01113	0.002341
rs1782170	14	41674903	-0.01488	0.002547
rs11627348	14	57295404	0.018285	0.003184
rs1275411	14	69594913	0.014143	0.002452
rs9972151	14	72101765	-0.01338	0.002592
rs9671386	14	75151047	0.019754	0.002593
rs12442330	15	47504742	0.012888	0.002281
rs1439320	15	48013713	-0.01226	0.002408
rs8033552	15	60843585	0.015033	0.002966
rs4360891	15	78018854	-0.01503	0.002271
rs11852334	15	97003989	0.012403	0.002382
rs3785232	16	7667538	0.017519	0.002449
rs11646847	16	13088905	-0.01204	0.002581
rs3751855	16	31091209	0.015075	0.002316
rs9933638	16	52539597	0.011988	0.002274
rs1424144	16	71349498	-0.0145	0.002626
rs2042395	16	87446053	-0.01499	0.002708
rs529900	16	88976968	0.011881	0.002405
rs12938775	17	2574821	-0.0155	0.002316
rs35982947	17	38214275	0.014133	0.00243
rs58879558	17	44095467	-0.03004	0.002777
rs1980119	17	64520406	-0.01307	0.002442
rs56084168	17	79084574	-0.02443	0.003265
rs10460051	18	31413679	0.014642	0.002318
rs11082011	18	35145122	-0.02263	0.002451
rs2217731	18	39305562	0.016358	0.002956
rs4632195	18	50746748	0.014665	0.002269

rs12958048	18	53101598	0.014968	0.002443
rs12967878	18	57826570	0.014775	0.002775
rs1861777	19	31213030	-0.01218	0.002424
rs62212171	20	32987687	-0.01811	0.003368
rs2425752	20	44702120	0.016951	0.002595
rs9611519	22	41613188	0.018847	0.002509

Supplementary Table 3. Instruments for Smoking initiation

Chr	Position	rsID	Pvalue	Beta	SE
1	7791461	rs12130857	3.65E-11	-0.018	0.00272
1	8484823	rs301807	2.5E-12	0.01801	0.00257
1	18436657	rs3820277	1.57E-13	-0.0188	0.00255
1	32195819	rs1889571	4.19E-09	0.02218	0.00378
1	33795572	rs10914684	6.32E-09	-0.0158	0.00272
1	38757237	rs2637869	6.54E-11	0.01822	0.00279
1	41776623	rs12755632	1.93E-08	-0.0154	0.00274
1	44011737	rs951740	3.82E-29	0.02954	0.00263
1	46496709	rs925524	2.94E-08	0.01556	0.00281
1	50603995	rs12022778	3.18E-17	0.02682	0.00318
1	50861071	rs11587399	7.25E-09	-0.0178	0.00308
1	58815243	rs4912332	2.94E-08	0.01412	0.00255
1	66469643	rs1937443	1.79E-15	0.02044	0.00257
1	71490122	rs1022528	8.48E-11	0.0174	0.00268
1	72752073	rs12740789	1.18E-17	-0.0285	0.00333
1	72900406	rs80054503	3.1E-09	-0.0241	0.00407
1	73824909	rs10789369	3.39E-19	-0.0234	0.00262
1	74991596	rs1514176	7.67E-14	-0.0193	0.00258
1	76689019	rs10873871	2.82E-08	0.01745	0.00314
1	87913176	rs11162019	5.06E-09	-0.0155	0.00265
1	91189731	rs1008078	1.63E-18	0.02282	0.0026
1	96414335	rs1935571	6.99E-10	-0.0157	0.00255
1	154206358	rs12027999	5.33E-10	-0.0244	0.00392
1	155034632	rs45444697	2.72E-10	0.01969	0.00312
1	174104743	rs2901785	1.47E-11	-0.0173	0.00256
1	179783167	rs147052174	2.3E-10	0.06231	0.00983
1	190957480	rs35656245	2.23E-08	0.01595	0.00285
1	210302043	rs12739243	4.45E-12	-0.0213	0.00307
1	236872829	rs12563365	1.05E-10	0.01656	0.00256
1	237852083	rs876793	5.69E-11	-0.0179	0.00274
2	264621	rs114976176	6.04E-09	-0.0155	0.00267
2	417167	rs62106258	3.33E-14	-0.0455	0.006

2	624205	rs6731872	5.35E-21	0.0316	0.00336
2	22067213	rs1022376	1.66E-08	-0.0147	0.00261
2	22582968	rs61533748	2.82E-11	0.01744	0.00262
2	29513404	rs72790288	3.28E-09	-0.0455	0.0077
2	32808804	rs2710634	3.36E-12	-0.0178	0.00255
2	44250149	rs62137126	1.31E-09	-0.0237	0.00391
2	45159091	rs1004787	1.11E-28	0.02841	0.00256
2	50735943	rs7598402	7.38E-09	-0.0147	0.00255
2	51341259	rs10490159	3.86E-11	0.01724	0.00261
2	58171220	rs1518393	1.3E-10	0.01686	0.00262
2	59022210	rs17616642	0.000000021	-0.0166	0.00295
2	59315828	rs6730325	0.000000021	-0.0146	0.00261
2	59819545	rs2539706	1.95E-10	0.01625	0.00255
2	60024857	rs7585579	5.48E-15	0.0204	0.00261
2	60139524	rs1863161	2.34E-09	0.01534	0.00257
2	60477052	rs359247	9.89E-17	0.02203	0.00265
2	63416606	rs62180324	3.91E-10	-0.0195	0.00312
2	80748807	rs6750107	0.000000026	0.01457	0.00262
2	80999398	rs12714017	3.65E-09	0.0154	0.00261
2	83247997	rs56208390	2.68E-08	0.02156	0.00388
2	98275354	rs11692435	4.47E-08	0.02505	0.00458
2	100672408	rs13392222	1.93E-10	-0.0234	0.00368
2	104126983	rs1901477	2.07E-31	0.03044	0.00261
2	104432494	rs11889814	3.44E-08	-0.021	0.00381
2	113240183	rs3811038	1.58E-11	0.01914	0.00284
2	113246436	rs75210106	2.33E-08	-0.0187	0.00334
2	137571174	rs34399632	1.46E-10	0.01935	0.00302
2	145412271	rs74697736	2.43E-15	0.0223	0.00282
2	146140132	rs6756212	3.49E-40	-0.0339	0.00255
2	146283610	rs3076896	1.99E-16	0.02265	0.00275
2	147825689	rs16826827	9.17E-09	-0.0222	0.00387
2	155682556	rs1445649	8.48E-16	0.02057	0.00256
2	161816880	rs1722666	2.17E-08	0.01609	0.00288
2	162101261	rs11678980	5.19E-12	0.01767	0.00256
2	162802993	rs12474587	4.83E-21	0.02423	0.00257
2	164862639	rs357304	5.4E-09	0.01668	0.00286
2	166250244	rs13007361	2.29E-08	0.01753	0.00314
2	172521827	rs7600835	0.000000018	-0.0151	0.00269
2	182027603	rs6750529	9.26E-12	0.01991	0.00292
2	199523122	rs17229285	1.27E-09	-0.0155	0.00255
2	200936399	rs3115418	2.79E-08	-0.0142	0.00256

2	202843875	rs62193862	1.99E-08	0.02385	0.00425
2	225365635	rs4674916	3.06E-11	-0.018	0.00271
2	226332033	rs4674993	4.85E-14	-0.024	0.00319
3	2365026	rs11713899	3.15E-08	0.01872	0.00338
3	16851202	rs748832	6.6E-11	0.01721	0.00264
3	25725501	rs10446419	5.05E-10	-0.0196	0.00314
3	47800216	rs13319205	3.77E-09	0.01654	0.00281
3	48731487	rs3172494	3.4E-13	-0.0291	0.004
3	50192760	rs2526390	3.62E-14	0.02047	0.0027
3	52886605	rs2276825	1.89E-10	0.01888	0.00296
3	53766212	rs2306866	1.89E-10	-0.0167	0.00262
3	55988394	rs73831818	5.46E-09	0.03204	0.0055
3	59434420	rs1910236	9.91E-09	0.01464	0.00255
3	59966156	rs7640107	3.46E-08	-0.0142	0.00257
3	60459291	rs2734390	2.09E-08	0.01477	0.00264
3	64234307	rs221988	1.43E-08	-0.0149	0.00262
3	70890288	rs2196356	2.45E-11	-0.0188	0.00281
3	71064431	rs11128203	1.29E-15	0.02041	0.00255
3	71483084	rs62246017	3.03E-09	-0.0162	0.00273
3	74954560	rs4543050	1.45E-11	0.0222	0.00329
3	77176032	rs6782116	1.46E-08	-0.0147	0.00259
3	81325861	rs13066050	1.93E-09	0.01883	0.00314
3	83241365	rs12633090	3.16E-12	-0.023	0.0033
3	85460131	rs1549979	8.8E-21	-0.0245	0.00262
3	85475292	rs74664784	9.34E-13	-0.0199	0.00279
3	85902536	rs57153235	1.56E-12	-0.0194	0.00274
3	107997514	rs6437769	3.74E-08	0.01421	0.00258
3	114147927	rs9288999	1.5E-09	0.01744	0.00289
3	117822149	rs6438436	5.33E-14	0.02474	0.00329
3	118302515	rs12053870	1.02E-09	0.01562	0.00256
3	131945722	rs9826984	3.87E-08	-0.0141	0.00256
3	147106319	rs2279829	2.05E-08	-0.0174	0.0031
3	147719648	rs2319545	8.3E-11	0.02324	0.00358
3	149543102	rs10935779	2.95E-08	-0.0143	0.00259
3	157393770	rs963354	4.21E-08	0.01505	0.00275
3	158284861	rs1714521	3.07E-10	-0.0163	0.00259
3	159048333	rs1449012	1.77E-09	-0.0154	0.00256
3	161761866	rs9850597	1.65E-08	-0.0186	0.00329
3	173072584	rs1187820	2.69E-08	-0.0143	0.00257
3	173353739	rs16828799	1.83E-08	0.01977	0.00351
3	175718927	rs9841807	1.35E-08	0.01625	0.00286

3	181409057	rs7631379	3.94E-11	0.0208	0.00315
4	15458598	rs4140932	4.89E-08	-0.014	0.00257
4	28027176	rs12642744	2.82E-08	-0.0166	0.00299
4	28246049	rs59537158	4.62E-13	0.02249	0.00311
4	28822284	rs1389171	4.45E-09	-0.0175	0.00298
4	29082156	rs55944129	1.06E-09	-0.0176	0.00288
4	31184484	rs58400863	4.89E-14	-0.0202	0.00268
4	35501032	rs7657022	7.34E-13	0.01829	0.00255
4	35514712	rs55900829	5.63E-12	0.01913	0.00278
4	68017710	rs112725451	1.65E-14	0.02609	0.0034
4	94052854	rs1160685	2.31E-09	0.0153	0.00256
4	94550450	rs1435479	5.68E-09	0.01639	0.00282
4	112467612	rs3934797	1.12E-10	-0.0213	0.0033
4	136406155	rs71602617	0.000000021	-0.0178	0.00317
4	137474783	rs7696257	6.78E-09	0.01533	0.00264
4	140886963	rs13109980	3.37E-16	-0.0222	0.00272
4	143510148	rs1116690	2.16E-08	0.01629	0.00291
4	147797913	rs13110073	3.24E-21	-0.0246	0.00261
4	147985231	rs28717373	6.16E-10	-0.0165	0.00266
4	176875795	rs62340589	4.31E-08	0.01741	0.00318
5	30842054	rs12517438	1.89E-09	0.01535	0.00256
5	43190647	rs35375873	3.29E-11	-0.027	0.00407
5	50821338	rs986714	4.13E-10	-0.016	0.00256
5	60121271	rs71592686	3.85E-13	0.02074	0.00286
5	79308315	rs2028269	5.19E-10	0.01616	0.0026
5	80263865	rs6874731	1.83E-09	0.01532	0.00255
5	87685500	rs6452785	4.69E-26	-0.0269	0.00255
5	88873832	rs10805858	1.88E-11	0.01812	0.0027
5	91366274	rs181508347	4.95E-10	0.08108	0.01303
5	94198290	rs42417	8.27E-10	0.01693	0.00276
5	103929588	rs72780746	2.05E-14	-0.0258	0.00337
5	106455988	rs10060196	1.29E-12	0.01831	0.00258
5	106825618	rs72789626	5.13E-12	-0.0256	0.00372
5	107365642	rs17165769	9.56E-10	0.01594	0.00261
5	133865452	rs329124	1.96E-10	-0.0164	0.00257
5	154839646	rs1385108	3.84E-10	0.0187	0.00299
5	157707571	rs1173461	9.51E-10	0.01661	0.00272
5	161018271	rs11956866	7.82E-09	-0.0148	0.00257
5	165096435	rs3909281	1.62E-16	0.02107	0.00255
5	165427280	rs3843905	5.41E-09	-0.0151	0.0026
5	166063680	rs79476395	1.04E-11	0.03337	0.00491

5	166778503	rs6890961	2.13E-13	-0.0193	0.00263
5	166989513	rs4044321	1.75E-17	-0.0226	0.00266
5	167614971	rs2173019	2.98E-17	0.02821	0.00334
5	170299916	rs10042827	9.41E-10	0.01672	0.00273
5	173288534	rs359431	3.16E-08	-0.0142	0.00257
6	26171250	rs1059490	2.16E-12	-0.0186	0.00265
6	26571629	rs6932350	5.13E-09	0.01497	0.00256
6	28129789	rs1150668	8.54E-13	-0.0185	0.00259
6	29796685	rs1632941	6.67E-10	-0.0158	0.00256
6	41901763	rs3218116	1.05E-11	-0.0198	0.00292
6	52895230	rs160631	1.87E-09	-0.0173	0.00287
6	67521222	rs7743165	4.15E-14	0.01926	0.00255
6	67540984	rs79180767	7E-12	0.02009	0.00293
6	69470709	rs10945141	3.59E-10	0.01814	0.00289
6	92226609	rs17554906	3.14E-08	0.01418	0.00256
6	94175279	rs619087	0.000000031	0.01427	0.00258
6	97702876	rs6568832	1.74E-10	0.01887	0.00296
6	98636905	rs12195240	1.08E-18	0.02491	0.00282
6	100347745	rs6936160	4.2E-13	0.02011	0.00277
6	101329173	rs12530388	5.83E-13	-0.0184	0.00255
6	108994161	rs3800227	3.64E-09	0.01718	0.00291
6	111658371	rs118202	1.9E-29	-0.0367	0.00326
6	156431856	rs73008357	2.44E-08	-0.0223	0.004
6	157738258	rs9331343	0.000000039	-0.0141	0.00257
6	158882320	rs10698713	2.38E-09	-0.0335	0.00562
6	163807748	rs1737329	5.08E-09	0.01703	0.00291
7	1703675	rs10272990	1.27E-14	-0.0209	0.00271
7	1870794	rs6948707	4.24E-21	0.02435	0.00258
7	3329967	rs10259715	6.42E-09	-0.0187	0.00322
7	3503207	rs13237637	1.54E-20	-0.0237	0.00255
7	69432311	rs79631993	3.67E-08	-0.017	0.00309
7	69484366	rs7809303	3.48E-15	-0.0214	0.00272
7	77771983	rs7802996	1.06E-09	-0.0209	0.00342
7	78139581	rs1030015	2.15E-08	0.01429	0.00255
7	88442568	rs4727189	0.00000003	0.01486	0.00268
7	91281409	rs76841737	3.26E-08	-0.0231	0.00419
7	96629103	rs11768481	5.23E-12	-0.0186	0.00269
7	97707069	rs1799068	2.59E-10	0.01661	0.00263
7	99071478	rs13437771	1.39E-14	-0.0271	0.00352
7	111100585	rs11766326	1.79E-11	-0.0175	0.00261
7	114940159	rs6968380	1.05E-17	-0.0234	0.00273

7	115077394	rs112913817	9.28E-11	0.07806	0.01204
7	117523709	rs10233018	4.77E-22	0.02461	0.00255
7	121954709	rs10953957	3.66E-08	0.01441	0.00262
7	132593831	rs77283305	3.91E-08	-0.0152	0.00277
7	133589846	rs10279261	6.05E-13	-0.0189	0.00262
7	133840652	rs1561112	3.84E-09	-0.0152	0.00259
8	10143164	rs2952251	4.24E-08	0.01641	0.003
8	10763655	rs4326350	5.16E-12	-0.0176	0.00255
8	27344719	rs11780471	1.57E-13	-0.0387	0.00524
8	27425349	rs11783093	2.07E-41	-0.0471	0.00349
8	27426077	rs1565735	1.33E-09	-0.0192	0.00316
8	52569449	rs7836565	4.36E-08	-0.0155	0.00283
8	59814666	rs13261666	4.36E-15	-0.02	0.00255
8	64912021	rs3850736	6.43E-14	0.01913	0.00255
8	91096366	rs2063976	7.45E-14	-0.0202	0.0027
8	92733282	rs6993429	9.87E-14	-0.0191	0.00256
8	93048104	rs6986430	1.99E-15	-0.0243	0.00306
8	93190014	rs9987376	2.01E-15	-0.0205	0.00258
8	115374642	rs290601	1.14E-08	0.01631	0.00286
9	3025368	rs3847244	2.6E-13	0.01867	0.00255
9	3398679	rs11791671	4.24E-08	0.02785	0.00508
9	8282399	rs7024924	0.000000019	0.01889	0.00336
9	10981069	rs6474609	1.71E-09	-0.0156	0.00259
9	11161799	rs1931431	8.56E-13	0.01823	0.00255
9	20676454	rs7867822	2.76E-08	-0.0151	0.00272
9	23831658	rs10966092	1.12E-12	-0.0205	0.00288
9	29747488	rs10969352	1.82E-08	0.01435	0.00255
9	81354129	rs4877285	2.1E-11	-0.0181	0.00271
9	81444104	rs1930371	7.09E-09	-0.0172	0.00298
9	86707289	rs2378662	2.67E-09	0.01521	0.00256
9	120519111	rs1927901	0.000000031	-0.0142	0.00256
9	122061948	rs4837631	2.03E-09	-0.0154	0.00256
9	128073097	rs1759433	1.69E-09	0.01536	0.00255
9	134334588	rs34553878	1.17E-09	0.02467	0.00406
9	134907263	rs7026534	2.68E-09	-0.0166	0.00279
9	137989785	rs10858334	1.18E-09	0.02287	0.00376
10	8803551	rs10905461	2.36E-08	-0.0164	0.00293
10	10043159	rs7920501	1.25E-09	-0.0155	0.00255
10	11133823	rs1291821	1.39E-08	0.01449	0.00255
10	13533053	rs11258417	2.71E-08	-0.0145	0.00261
10	22032942	rs7072776	5.66E-15	-0.022	0.00281

10	36634124	rs2796793	1.55E-08	0.01448	0.00256
10	56698174	rs1733760	6.7E-09	0.01477	0.00255
10	63674885	rs7921378	6.1E-20	-0.0233	0.00255
10	103186838	rs7901883	1.98E-10	-0.0193	0.00303
10	103960351	rs11594623	7.45E-20	0.02744	0.00301
10	104120522	rs11191269	4.61E-08	0.01764	0.00323
10	104403310	rs28408682	1.41E-10	0.01667	0.0026
10	104640052	rs12244388	4.31E-22	0.02582	0.00267
10	104852121	rs111842178	2.24E-12	0.02245	0.0032
10	106078937	rs34970111	1.28E-08	-0.0146	0.00256
10	106460460	rs9787523	1.42E-09	-0.0156	0.00258
10	106929313	rs11192347	6.15E-10	-0.0265	0.00427
10	115378364	rs10885480	3.83E-11	-0.0187	0.00283
10	118678712	rs4752018	4.42E-10	0.01885	0.00302
10	125680419	rs9423279	3.06E-12	-0.0186	0.00266
11	27679916	rs6265	2.81E-19	-0.0293	0.00326
11	28652996	rs4275621	3.76E-16	-0.0214	0.00262
11	32956492	rs62618693	2.09E-08	-0.0353	0.00629
11	41436297	rs2939756	7.45E-10	-0.0157	0.00255
11	42442826	rs1381775	2.79E-08	-0.0156	0.00281
11	46078656	rs2959084	9.82E-10	0.01708	0.00279
11	46393574	rs3740977	1.17E-08	0.01947	0.00342
11	64133552	rs61886926	7.3E-12	-0.0179	0.00262
11	64485193	rs61884449	2.32E-08	0.01998	0.00358
11	65561468	rs644740	3.67E-08	-0.0141	0.00256
11	73309393	rs7943721	3.58E-10	-0.0212	0.00338
11	85980958	rs7929518	2.55E-10	0.01924	0.00304
11	92289734	rs586699	7.29E-09	-0.0148	0.00256
11	111979741	rs76460663	4.15E-11	-0.0423	0.00642
11	112912811	rs2155646	9.44E-48	0.03778	0.0026
11	112984491	rs78239456	9.37E-12	-0.0185	0.00271
11	113660576	rs1713676	5.38E-11	-0.0167	0.00255
11	113994505	rs238896	3.65E-11	-0.0169	0.00255
11	121530888	rs540860	5.75E-12	0.01761	0.00256
11	121634334	rs1944689	1.27E-08	0.01768	0.00311
11	122023187	rs1834306	1.96E-08	-0.0145	0.00258
11	131966264	rs1106363	9.2E-11	0.01737	0.00268
11	132098205	rs2010921	2.47E-10	0.01743	0.00275
12	16748721	rs11057005	9.12E-10	-0.0157	0.00257
12	49952394	rs13906	1.98E-09	-0.0245	0.00409
12	56474480	rs4759229	6.53E-09	0.01557	0.00268

12	69655167	rs7969559	1.53E-09	-0.017	0.00282
12	75263193	rs7134009	0.000000043	-0.0158	0.00288
12	112618346	rs77215829	2.02E-10	-0.024	0.00378
12	121083279	rs1109480	1.84E-10	-0.0167	0.00262
12	133380790	rs11611651	2.05E-09	0.02711	0.00453
13	38172867	rs17197663	2.06E-08	-0.0216	0.00385
13	38359676	rs4264267	6.82E-09	0.01479	0.00255
13	55834929	rs61959481	7.95E-11	-0.0203	0.00313
13	55931424	rs3098272	2.08E-08	-0.0178	0.00318
13	59265043	rs9538162	1.76E-11	0.01738	0.00258
13	59339281	rs1413119	4.77E-09	-0.0153	0.0026
13	59454139	rs56367474	4.2E-10	-0.0173	0.00277
13	59871584	rs55786907	1.84E-08	0.01945	0.00345
13	60705792	rs4886207	8.78E-10	-0.0162	0.00265
13	66949370	rs9540731	3.42E-12	-0.0177	0.00255
13	80191873	rs9545155	3.04E-10	-0.0161	0.00255
13	81191176	rs1772572	5.62E-10	-0.0169	0.00272
13	96823724	rs75674569	2.58E-09	-0.0253	0.00425
13	100546450	rs7333559	5.94E-14	-0.0232	0.00309
13	100648356	rs1108130	1.57E-14	0.02394	0.00312
13	101252635	rs12855717	1.22E-09	0.01552	0.00256
14	28346502	rs12878369	1.6E-11	0.01744	0.00259
14	29316842	rs2145451	5.44E-10	-0.02	0.00323
14	58653514	rs9323328	2.55E-08	-0.0142	0.00256
14	77529375	rs1811739	5.97E-10	0.01827	0.00295
14	79563654	rs8005334	3.44E-10	0.01667	0.00266
14	80102233	rs34940743	2.8E-09	0.01592	0.00268
14	98362355	rs2925128	3.67E-10	0.01682	0.00268
14	98597552	rs1381287	1.81E-12	0.01802	0.00256
14	99693843	rs55913542	3.25E-08	0.01856	0.00336
15	36399479	rs1435672	3.82E-08	0.01411	0.00257
15	47685010	rs281296	1.59E-20	0.02469	0.00266
15	47935843	rs1435741	1.09E-12	0.01831	0.00257
15	63898709	rs56902655	4.09E-09	-0.0219	0.00372
15	67476952	rs2289791	2.01E-09	-0.0177	0.00295
15	74048768	rs60833441	2.28E-08	-0.0143	0.00256
15	78025464	rs62007780	7.48E-10	-0.0159	0.00258
15	83893243	rs12442563	3.13E-14	-0.0232	0.00306
15	96858409	rs4310804	7.55E-10	-0.0182	0.00295
15	99204101	rs8027457	1.88E-09	0.01531	0.00255
16	720986	rs1139897	1.77E-15	-0.0241	0.00303

16	5811367	rs11076962	1.2E-10	0.0183	0.00284
16	10173748	rs7192140	3.4E-11	-0.0169	0.00255
16	17570220	rs9922607	3.42E-12	-0.0222	0.00319
16	18050926	rs9941217	3.5E-12	-0.0186	0.00267
16	24727064	rs7188873	8.46E-15	0.0203	0.00262
16	25351633	rs6497840	2.01E-15	0.02277	0.00287
16	49766772	rs4785187	6.55E-11	0.01998	0.00306
16	49891964	rs8050598	1.76E-10	0.01867	0.00293
16	50945156	rs12918191	3.14E-11	-0.0197	0.00297
16	69576894	rs9302604	3.29E-13	0.01871	0.00257
16	72230694	rs9936784	4.33E-08	0.01399	0.00255
16	72574550	rs62052916	1.62E-10	-0.0319	0.00499
16	72950468	rs4788676	4.92E-09	-0.0177	0.00303
16	75620118	rs61537885	8.06E-09	-0.0401	0.00694
16	75766873	rs117657830	3.18E-09	-0.0378	0.00637
16	87443734	rs1050847	7.37E-09	-0.0148	0.00257
16	89608702	rs11642231	3.44E-09	-0.0156	0.00264
17	1995177	rs4790874	8.43E-12	0.01745	0.00255
17	7795972	rs11078713	1.59E-08	-0.0146	0.00258
17	7803118	rs28441558	1.24E-10	-0.0356	0.00553
17	16235462	rs11651955	3.74E-08	-0.014	0.00255
17	27323322	rs67777803	3.18E-13	-0.0246	0.00338
17	30685935	rs2344976	7.98E-09	-0.0151	0.00261
17	37824339	rs3764351	3.89E-08	-0.0147	0.00268
17	44121579	rs72836318	0.000000007	-0.0171	0.00296
17	44793283	rs17692129	4.57E-13	0.0196	0.00271
17	50193197	rs75919030	3.35E-13	-0.021	0.00288
17	50243397	rs2938134	3.14E-10	-0.0175	0.00278
17	77790135	rs2587507	8.69E-09	-0.0147	0.00255
18	5872472	rs34342129	2.13E-08	-0.0143	0.00255
18	25253297	rs4476253	5.78E-10	-0.0185	0.00298
18	31696075	rs7505855	5.31E-11	-0.017	0.00259
18	36921851	rs8096225	2.63E-08	0.01552	0.00279
18	39297254	rs67050670	2.34E-11	-0.0203	0.00303
18	41314171	rs2359180	4.98E-08	-0.0144	0.00264
18	42658643	rs72898831	4.14E-12	-0.0244	0.00352
18	49874515	rs8083764	7.97E-09	-0.016	0.00276
18	49967811	rs1373178	4.16E-15	-0.0203	0.00259
18	50863861	rs62098013	2.24E-11	0.01771	0.00265
18	53661743	rs72938304	1.36E-11	-0.0272	0.00402
18	72535282	rs11872397	5.2E-09	-0.0171	0.00293

18	77574374	rs71367544	8.54E-11	0.02055	0.00317
19	4474725	rs76608582	4.88E-09	-0.0345	0.00591
19	4965064	rs10853981	4.88E-08	0.01479	0.00271
19	18460956	rs113230003	1.05E-10	-0.0189	0.00292
19	18566395	rs8103660	3.03E-09	0.0158	0.00266
19	51129745	rs117734003	2.57E-09	0.0303	0.00509
19	55879872	rs1126757	2.92E-08	0.01416	0.00255
20	25195509	rs6050446	8.8E-13	0.05441	0.00761
20	29946968	rs6058782	1.78E-11	0.02971	0.00442
20	31175258	rs1555445	7.75E-12	0.01876	0.00274
20	42015801	rs6073075	2.44E-08	-0.0187	0.00335
20	54462393	rs910912	7.82E-09	-0.0168	0.00291
20	61984317	rs6011779	2.83E-09	-0.0192	0.00323
20	62406886	rs3810496	1.54E-09	0.01588	0.00263
21	40588819	rs4818005	1.09E-14	-0.0204	0.00264
22	38397797	rs139896	7.14E-09	0.01544	0.00267
22	42698430	rs4822102	2.78E-10	-0.0165	0.00262
22	46442288	rs9627272	2.42E-09	-0.0155	0.00259

Supplementary Table 4 Associations of neuroticism, smoking initiation, and Parkinson's disease using different Mendelian randomization methods.

Exposure - Outcome	# SNPs	Method	OR (β)*	95% CI		p-value	
Neuroticism - PD	107	IVW	0.89	0.68	1.16	0.39	
		No proxies	Weighted Median	0.99	0.79	1.25	0.94
			MR Egger _{slope}	1.15	0.29	4.60	0.85
			MR Egger _{intercept}	(-0,00)	-0,03	0,02	0.71
Neuroticism - Smoking Initiation	112	IVW	1.10	1.05	1.14	0.00	
		No proxies	Weighted Median	1.11	1.06	1.16	0.00
			MR Egger _{slope}	0.95	0.78	1.17	0.64
			MR Egger _{intercept}	(0.00)	0.00	0.01	0.17
Smoking Initiation - PD	304	IVW	0.76	0.62	0.93	0.01	
		No proxies	Weighted Median	0.72	0.57	0.91	0.01
			MR Egger _{slope}	0.54	0.26	1.12	0.01
			MR Egger _{intercept}	(0.00)	0.00	0.01	0.35

* Estimates are presented as ORs for causal effect estimates and β -values for the MR Egger intercept, which is a measure of directional pleiotropy.

Abbreviations: MR = Mendelian randomization; SNP = single nucleotide polymorphism; OR = odds ratio; CI = confidence interval; PD = Parkinson's disease; IVW = inverse variance weighting

Supplementary Table 5 Associations of neuroticism and smoking initiation with Parkinson’s disease (defined by clinical PD diagnosis or self-reported) using different Mendelian randomization methods.

Exposure-Outcome	Method	Clinical PD diagnosis				Self-reported PD diagnosis			
		OR (β)*	95% CI		p-value	OR (β)*	95% CI		p-value
Neuroticism - PD 128 SNPs	IVW	0.89	0.66	1.18	0.41	0.84	0.63	1.12	0.23
	Weighted median	1.02	0.77	1.35	0.92	0.98	0.72	1.34	0.92
	MR-Egger	0.60	0.13	2.73	0.51	1.30	0.30	5.74	0.73
	MR-Egger (intercept)	0.01	-0.02	0.03	0.61	-0.01	-0.03	0.02	0.55
Smoking initiation-PD 365 SNPs	IVW	0.77	0.61	0.97	0.02	0.73	0.58	0.92	0.01
	Weighted median	0.77	0.58	1.02	0.07	0.81	0.59	1.10	0.18
	MR-Egger	0.54	0.23	1.24	0.15	0.39	0.17	0.90	0.03
	MR-Egger (intercept)	0.00	-0.00	0.01	0.39	0.01	-0.00	0.01	0.13

* Estimates are presented as ORs for causal effect estimates and β -values for the MR Egger intercept, which is a measure of directional pleiotropy.

Abbreviations: MR = Mendelian randomization; SNP = single nucleotide polymorphism; OR = odds ratio; CI = confidence interval; PD = Parkinson’s disease; IVW = inverse variance weighting