Supplementary Material

Mendelian Randomisation Study of Smoking, Alcohol, and Coffee Drinking in Relation to Parkinson's Disease

Supplementary Methods

Courage-PD international consortium

The Courage-PD (COmprehensive Unbiased Risk Factor Assessment for Genetics and Environment in Parkinson's Disease) international consortium pooled individual-level data from 35 studies on Parkinson's disease (PD) from different populations worldwide and used the same array to genotype their participants.

The Geo-PD (Genetic Epidemiology Of Parkinson's disease; https://geopd.biomedinfo.org/) consortium represents one of the components of Courage-PD. This consortium aims at conducting collaborative studies on genetic susceptibility in PD; one of its main features is that participating sites are distributed in the five continents, therefore representing a highly diverse population. In addition, several other studies from Europe contributed to Courage-PD. PD was diagnosed using standard criteria (United Kingdom Parkinson's Disease Society Brain Bank - UKPDSBB, Gelb, Bower) [1-3].

All studies were approved by local ethical committees following the procedures of each country, and material transfer agreements were set up between participating sites and the University of Tübingen (Germany).

According to the study's consortium agreement, participating sites contributed DNA and demographic/environmental data. DNAs (25µl of DNA at a concentration of 50 to 100 ng/µl) were shipped for quality control to University of Tübingen (Germany) and genotyped in a central

laboratory in Munich (Institute of Human Genetics, Helmholtz Zentrum, Germany). The samples from two sites (Gasser, Morris/Wood) were genotyped at the Laboratory of Neurogenetics (National Institute on Aging, National Institutes of Health, Bethesda, MD, USA). Demographic data were harmonized and collected using a standardized form and cleaned at Inserm U1018 (Villejuif, France).

Genotyping

The Neurochip chip was used to genotype all the samples [4]. Briefly, this chip is a custom-designed array containing a tagging variant backbone with good genome-wide resolution of about 306,670, complemented with a manually curated custom content comprised of 179,467 variants implicated in diverse neurological diseases, including PD.

Genotyping was performed with an automated protocol according to the manufacturer's instructions (Illumina, San Diego, CA, USA). All arrays were scanned with an Illumina iScan and raw data were analyzed with the Illumina Beeline and GenomeStudio software packages using the manifest file Neuro_Consortium_20013217_A1.bpm. Clustering was performed in GenomeStudio with the GenTrain cluster 2.0 algorithm. Genotypes were post-processed with zCall (DOI: 10.1093/bioinformatics/bts479) to improve detection of rare alleles.

Quality control

Genotyped data exported from Genome Studio to PLINK format were used for quality control and downstream analysis. The pooled dataset from the 35 sites consists of 27,538 subjects. Phenotypic data were missing for 245 subjects and three sites were removed as they only included cases, leaving 26,535 subjects (14,859 cases, 11,431 controls) for quality control using

"COMRARE" an automated pipeline under development at the University of Tübingen. The pipeline uses PLINK (https://www.cog-genomics.org/plink) and R scripts (R Foundation for Statistical Computing, Vienna, Austria) and the following steps were implemented separately for each site:

1- *Per individual quality control:*

- Identification of individuals with elevated missing genotyping rates or outlying heterozygosity rate: individuals with a genotype failure rate ≥4% or heterozygosity rate ± 4 standard deviations from the mean were excluded.
- Identification of Individuals with discordant sex information: the homozygosity rate was calculated for X-linked SNPs for each individual and compared to the expected rate. Participants for whom phenotypic and genotypic sex were discordant were removed.
- Identification of duplicated or related Individuals: pairs of individuals with an identity by descent (IBD) greater than 0.185 were removed.
- Eigensoft software was used to compute principal components in order to correct for population stratification by merging our dataset with HapMap [5, 6]. A scatter plot of the first two principal components was used to identify outliers in each study.

2- *Per marker quality control:*

- Identification of markers with high missing data rate: a call-rate threshold of 4% was used and SNPs with a lower rate were removed.
- SNPs with a significant ($p<10^{-5}$) difference in rates of missing values between cases and controls were removed.

- We excluded variants with a minor allele frequency (MAF) $<5\times10^{-8}$ and those in Hardy-Weinberg disequilibrium ($p<5\times10^{-8}$).

Imputation

After QC, we used the HRC/1000G imputation preparation and checking tool (https://www.well.ox.ac.uk/~wrayner/tools/HRC-1000G-check-bim-v4.3.0.zip) to check for Ref/Alt allele assignments, incorrect strands, deviation from allele frequency, and palindromic SNPs. Imputation of autosomal variants was performed separately for each dataset based on based on 271,398 to 373,664 SNPs in each study, through the Michigan Imputation server using the HRC reference panel and the GRCh37/hg19 assembly with a R^2 filter of 0.3. The mean of the number of SNPs available in each study after imputation was 13,710,549 (SD=2,986,478).

Association analysis and meta-analysis

We excluded from our analyses samples overlapping with the international Parkinson Disease Genomics Consortium (iPDGC) which included all the samples from three sites (Pastor/Diez-Fairen, Spain; Toft, Norway; Morris/Wood, UK) as well as 1,000 samples from the Gasser/Sharma (Germany) site (642 cases, 358 controls) and 137 samples of PD cases from the Tolosa site (Spain). Analyses are also restricted to sites that provided samples for both cases and controls and to participants of Caucasian ancestry; only sites with at least 50 cases or 50 controls were included. In addition, as the role of environmental factors may be different in carriers of Mendelian PD mutations, we excluded participants with GBA/LRRK2 mutations or positive family history of PD. The main characteristics of 7,369 cases and 7,018 controls from 23 sites included in the analyses are shown in Supplementary Table 1.

We excluded SNPs with a MAF <1%, in Hardy-Weinberg disequilibrium ($P<5\times10^{-8}$), and those with low imputation quality ($r^2<0.8$). The final number of SNPs available for analysis in each study was comprised between 5,934,239 and 7,168,307. Only SNPs available in 75% (n=17) of the studies or more were retained for further analyses.

For our MR analyses, we selected a total of 411 SNPs, of which 6 were not available and 37 excluded (Supplementary Table 5). Therefore, the final number of SNPs used in the analyses was of 368 SNPs, of which 93% were available in all studies. Of these SNPs, 27 were genotyped and 341 were imputed; when genotyped SNPs were available, we selected them in priority.

For each site, logistic regression adjusted for sex and the first four principal components was performed for each SNP under an additive genetic model (number of alleles for genotyped SNPs, dosage for imputed SNPs) using PLINK software (version 1.9) [7].

Summary statistics from the GWAS of the 23 studies were meta-analysed using the GWAMA software [8]. To assess heterogeneity of genetic associations with each SNP in Courage-PD, we used the I^2 statistic; I^2 values of 0 to 24% suggest little heterogeneity, 25 to 49% reflect moderate heterogeneity, 50 to 74% reflect large heterogeneity, and >75% reflect very large heterogeneity. Effects size and standard errors of SNPs with little heterogeneity across studies ($I^2\leq25\%$) were combined using a fixed-effect model, while we used a random-effects model for SNPs with higher heterogeneity ($I^2>25\%$). Of 368 SNPs used in our MR analyses, 324 (88%) displayed little heterogeneity and 44 (12%) had moderate heterogeneity; there were no SNPs with I^2 above 50%.

Analyses were first performed overall. We then repeated our analyses: (*i*) in two groups defined by median age at study (≤67 years, >67 years; 6,086 cases and 5,672 controls from 19 studies); (*ii*) in two groups defined by median disease duration in PD cases (≤7 years, N=3,633; >7 years, N=3,271) from 22 studies (cases from each group were compared to all controls).

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Supplementary Table 1. Characteristics of cases and controls from the Courage-PD consortium by study site (after quality control).

Continent	Principal investigators	Country	Status	N	Sex (%)		Age at study			Age at PD onset			Age at PD diagnosis			Disease duration[b]	
					Male	Female	Mean	SD	MD	Mean	SD	MD	Mean	SD	MD	Mean	SD
Africa	Bardien/Carr[a]	South Africa	Cases	117	59.8	40.2	68.2	11.2		59.6	12.6		59.6	12.6		8.5	6.7
			Controls	80	57.5	42.5	50.8	12.6		-	-		-	-		-	-
North America	Farrer[a]	United States	Cases	262	66.4	33.6	66.9	10.4	1	55.8	11.5	1	58.6	11.5	96	11.0	6.5
			Controls	394	31.0	69.0	69.4	12.2		-	-		-	-		-	-
	Rogaeva/Lang[a]	Canada	Cases	159	66.0	34.0	62.6	13.0	5	52.8	12.8	5			159	9.8	5.9
			Controls	149	38.9	61.1	74.0	8.6		-	-		-	-		-	-
Australia	Mellick[a]	Australia	Cases	399	64.9	35.1	68.2	9.3		59.1	11.5		60.7	10.8	8	9.2	7.1
			Controls	399	48.4	51.6	67.7	9.0		-	-		-	-		-	-
Europe	Aasly[a]	Norway	Cases	463	59.6	40.4	78.2	11.2		61.1	10.8				463	17.1	5.4
			Controls	487	54.2	45.8	73.2	14.1	74	-	-		-	-		-	-
	Annesi[a]	Italy	Cases	89	65.2	34.8	66.8	9.0		59.6	10.1		66.8	9.0		7.2	5.6
			Controls	93	46.2	53.8	58.6	20.1		-	-		-	-		-	-
	Brice/Corvol/Lesage[a]	France	Cases	745	59.6	40.4	61.1	10.8	25	52.1	11.0	25			745	8.9	6.3
			Controls	275	56.4	43.6	62.4	10.6		-	-		-	-		-	-
	Carmine Belin/Ran[a]	Sweden	Cases	214	63.6	36.4	67.2	10.3		58.6	11.0				214	8.6	6.2
			Controls	611	54.8	45.2	66.3	9.8	583	-	-		-	-		-	-
	Chartier-Harlin/Muttez[a]	France	Cases	285	55.8	44.2	64.3	9.0		52.3	10.3		53.3	10.1		12	5.9
			Controls	217	38.7	61.3	59.8	12.5		-	-		-	-		-	-
	Deutschländer[a]	Germany	Cases	264	61.7	38.3	69.6	9.9		60.7	11.4		59.6	10.7	199	8.9	6.6
			Controls	40	32.5	67.5	66.3	10.2		-	-		-	-		-	-
	Elbaz[a]	France	Cases	387	60.5	39.5	70.1	7.3		65	7.6		65.9	7.4	1	5.2	4.1
			Controls	998	59.0	41.0	69.8	7.6		-	-		-	-		-	-
	Ferreira	Portugal	Cases	313	58.5	41.5	69.1	10.1		58.5	11.7		60.2	11.8		10.6	7.2
			Controls	53	26.4	73.6	46.9	18.7		-	-		-	-		-	-
	Gasser/Sharma[c]	Germany	Cases	432	65.0	35.0	65.8	10.8		60.4	11.2		60.4	11.2	129	5.3	5.1
			Controls	388	43.0	57.0	62.9	7.3		-	-		-	-		-	-
	Duga/Cilia[a]	Italy	Cases	1340	59.3	40.7	65.9	10.9		59.1	11.3		60.7	11.1		6.8	5.6
			Controls	1328	34.3	65.7	61.9	10.9		-	-		-	-		-	-
	Hadjigeorgiou[a]	Greece	Cases	256	48.4	51.6	67.6	10.4		62.8	10.3		63.7	10.4		4.8	4.4
			Controls	310	47.4	52.6	69.8	8.7		-	-		-	-		-	-
	Koks/Taba[a]	Estonia	Cases	210	40.0	60.0	73.0	8.2		66.7	9.8				210	6.3	5.4
			Controls	163	41.1	58.9	72.6	10.1		-	-		-	-		-	-

Continent	Principal investigators	Country	Status	N	Sex (%)		Age at study			Age at PD onset			Age at PD diagnosis			Disease duration[b]	
					Male	Female	Mean	SD	MD	Mean	SD	MD	Mean	SD	MD	Mean	SD
	Kruger[a]	Luxembourg	Cases	285	69.5	30.5	67.7	11.3		60.1	12.8		62.3	12.0	10	7.2	6.2
			Controls	283	57.2	42.8	58.5	12.1		-	-		-	-		-	-
	Puschmann[a]	Sweden	Cases	50	70.0	30.0	69.0	10.4		61.5	11.3				49	7.4	4.8
			Controls	105	29.5	70.5	66.7	8.9		-	-		-	-		-	-
	Stefanis/Simitsi[a]	Greece	Cases	174	62.1	37.9	67.7	13.3		61.5	13.6		61.9	12.7	44	6.2	6.3
			Controls	178	36.0	64.0	67.0	9.6		-	-		-	-		-	-
	Tolosa[d]	Spain	Cases	141	62.4	37.6	67.4	10.3		60.4	11.1				141	7.0	5.9
			Controls	66	16.7	83.3	61.9	12.1	8	-	-		-	-		-	-
	Valente	Italy	Cases	223	60.1	39.9	67.1	12.7	4	54.3	10.8	4	59.1	7.8	144	12.7	8.2
			Controls	54	38.9	61.1	78.4	9.6		-	-		-	-		-	-
	Wirdefeldt[a]	Sweden	Cases	61	55.7	44.3	75.9	8.1		66.8	9.9				61	8.6	5.6
			Controls	165	46.1	53.9	73.9	9.6		-	-		-	-		-	-
	Zimprich	Austria	Cases	500	63.0	37.0			500	59.1	11.2				500		
			Controls	182	40.1	59.9			182	-	-		-	-		-	-
	Total		**Cases**	**7,369**													
			Controls	**7,018**													

MD, missing data; SD, standard deviation.

[a] Sites from the Geo-PD consortium.

[b] Duration disease = age at study - age at PD onset. Missing values are the same as those for age at study.

[c] For the Gasser/Sharma site, we excluded 1,000 samples overlapping with iPDGC (642 cases, 358 controls).

[d] For the Tolosa site, we excluded 137 samples of PD cases overlapping with iPDGC.

Supplementary Table 2. Statistical power to detect odds ratios comprised between 0.3 and 0.9 for two values of type-1 error in Mendelian randomization analyses in the Courage-PD consortium (7,369 cases, 7,018 controls).

		Type-1 error=1.7% Odds ratio							**Type-1 error=5% Odds ratio**						
Exposure	**R^2**	**0.30**	**0.40**	**0.50**	**0.60**	**0.70**	**0.80**	**0.90**	**0.30**	**0.40**	**0.50**	**0.60**	**0.70**	**0.80**	**0.90**
Smoking initiation	2.95%	**1.00**	**1.00**	**1.00**	**1.00**	**0.91**	0.47	0.10	**1.00**	**1.00**	**1.00**	**1.00**	**0.96**	0.64	0.19
Lifetime smoking index	0.49%	**1.00**	**0.95**	0.73	0.42	0.19	0.07	0.03	**1.00**	**0.98**	**0.85**	0.59	0.33	0.16	0.07
Alcohol drinking	0.48%	**1.00**	**0.94**	0.72	0.41	0.19	0.07	0.03	**1.00**	**0.98**	**0.84**	0.58	0.32	0.15	0.07
Coffee drinking	0.21%	**0.88**	0.60	0.33	0.17	0.08	0.04	0.02	**0.95**	0.75	0.50	0.30	0.17	0.09	0.06

R^2 is the sum of the proportion of the variance of the exposure explained by each individual genetic variants (Supplementary Table 3).
Bold values are ≥0.80.
Statistical power was computed according to Brion MJ et al. (Int J Epidemiol 2013;42:1497-1501).

Supplementary Table 3. SNPs used for Mendelian randomization analyses: individual associations with exposures and PD.

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
Alcohol drinking (per 1-SD increase of ln(drinks per week))														
rs705687	1:4548453	G/A	0.22	0.011	0.002	8.15E-10	23	14387	0.79	0.031	0.032	3.28E-01	0	4.01E-05
rs58107686	1:33837334	A/C	0.67	0.010	0.002	7.79E-10	23	14387	0.34	0.020	0.027	4.59E-01	11.1	4.19E-05
rs12088813	1:66407700	C/A	0.73	0.009	0.002	1.58E-08	23	14387	0.26	0.044	0.029	1.26E-01	0	3.41E-05
rs5024204	1:71491890	A/T	0.28	0.010	0.002	2.55E-09	23	14387	0.28	0.045	0.028	1.16E-01	0	3.78E-05
rs10753661	1:165119792	A/G	0.32	0.009	0.002	3.76E-08	23	14387	0.68	0.033	0.028	2.40E-01	0	3.23E-05
rs28680958	1:173848808	A/G	0.78	0.011	0.002	5.13E-10	23	14387	0.22	0.004	0.031	8.96E-01	0	4.11E-05
rs823114	1:205719532	G/A	0.55	0.009	0.001	2.31E-09	23	14387	0.42	-0.032	0.026	2.22E-01	0	3.80E-05
rs77165542	2:430975	T/C	0.97	0.026	0.004	5.63E-11	3	1179	Excluded for MR					
rs1260326[b]	2:27730940	T/C	0.60	0.021	0.001	8.05E-45	23	14387	0.46	**-0.069**	**0.026**	**8.41E-03**	0	2.09E-04
rs13383034	2:45155276	C/T	0.33	0.015	0.002	6.31E-22	23	14387	0.68	-0.061	0.035	8.17E-02	28.4	9.84E-05
rs13032049	2:63581507	A/G	0.28	0.010	0.002	3.00E-10	23	14387	0.70	0.055	0.038	1.47E-01	32.8	4.22E-05
rs828867	2:74334462	G/A	0.54	0.009	0.001	2.15E-09	16	9769	Excluded for MR					
rs11692435	2:98275354	G/A	0.09	0.017	0.003	2.53E-11	NA in COURAGE-PD							
rs13024996	2:144225215	A/C	0.64	0.011	0.002	5.72E-13	23	14387	0.37	0.009	0.027	7.43E-01	14.9	5.51E-05
rs72859280	2:147956293	G/T	0.04	0.023	0.004	4.44E-09	20	11260	0.96	-0.131	0.081	1.06E-01	0	3.65E-05
rs56337305	2:225475560	C/T	0.62	0.010	0.001	1.63E-10	23	14387	0.38	-0.014	0.026	5.83E-01	24.8	4.35E-05
rs13094887	3:70968431	T/A	0.70	0.010	0.002	8.57E-11	23	14387	0.69	-0.037	0.028	1.77E-01	0	4.47E-05
rs62250685	3:85457240	G/A	0.39	0.014	0.002	1.05E-21	23	14387	0.61	-0.017	0.026	5.09E-01	0	9.77E-05
rs9838144	3:131576287	C/G	0.79	0.010	0.002	2.65E-08	23	14387	0.80	-0.050	0.032	1.26E-01	15.8	3.28E-05
rs2011092	3:141124607	C/T	0.66	0.009	0.002	7.35E-09	23	14387	0.30	-0.006	0.028	8.19E-01	0	3.55E-05
rs6787172	3:158187811	G/T	0.45	0.008	0.001	4.27E-08	23	14387	0.54	0.022	0.025	3.77E-01	0	3.19E-05
rs3748034	4:3446091	T/G	0.86	0.012	0.002	1.67E-08	23	14387	0.14	-0.009	0.037	8.16E-01	23.3	3.38E-05
rs11940694[a]	4:39414993	A/G	0.60	0.026	0.001	3.03E-68	23	14387	0.43	-0.031	0.028	2.70E-01	6.3	3.24E-04
rs4501255	4:42151306	C/G	0.23	0.011	0.002	4.83E-10	23	14387	0.23	-0.030	0.031	3.30E-01	0	4.11E-05
rs1229984[a]	4:100239319	T/C	0.96	0.151	0.004	<1.00E-300	21	14004	0.06	-0.011	0.055	8.49E-01	0	1.61E-03
rs2165670	4:100286085	G/A	0.11	0.023	0.002	1.67E-22	22	14205	0.91	0.047	0.061	4.37E-01	36.6	1.01E-04
rs13107325[a]	4:103188709	T/C	0.93	0.028	0.003	1.53E-22	23	14387	0.07	**-0.104**	**0.051**	**4.04E-02**	0	1.01E-04
rs4690727	4:143648579	C/G	0.72	0.011	0.002	2.43E-11	23	14387	0.70	-0.009	0.028	7.63E-01	0	4.74E-05
rs12651313	4:171086393	G/C	0.56	0.009	0.001	3.79E-09	23	14387	0.56	Excluded for MR				
rs4916723	5:87854395	C/A	0.58	0.010	0.001	1.72E-11	23	14387	0.40	-0.044	0.027	1.06E-01	0	4.81E-05
rs12655091	5:144412335	A/G	0.47	0.008	0.001	1.25E-08	23	14387	0.52	-0.021	0.026	4.13E-01	6.1	3.44E-05
rs55872084	5:155902003	G/T	0.23	0.010	0.002	6.32E-09	23	14387	0.78	0.012	0.031	7.03E-01	0	3.58E-05
rs6460047	7:73042443	T/C	0.21	0.012	0.002	9.69E-11	23	14387	0.81	-0.021	0.041	6.08E-01	26.8	4.45E-05
rs10236149	7:98977515	G/A	0.88	0.013	0.002	1.18E-09	23	14387	0.13	0.032	0.038	4.00E-01	9.7	3.93E-05
rs35034355	7:103840115	A/G	0.48	0.008	0.001	2.87E-08	23	14387	0.49	-0.013	0.026	6.24E-01	0	3.27E-05
rs6951574	7:153489744	T/C	0.46	0.013	0.001	1.58E-19	23	14387	0.53	0.010	0.026	6.99E-01	0	8.68E-05
rs13250583	8:20949917	T/C	0.79	0.010	0.002	4.70E-08	23	14387	0.20	-0.011	0.033	7.34E-01	15.1	3.17E-05
rs1217091	8:64527399	T/C	0.81	0.012	0.002	7.05E-11	23	14387	0.20	**0.073**	**0.033**	**2.53E-02**	0	4.52E-05
rs28601761	8:126500031	C/G	0.42	0.009	0.001	7.17E-10	23	14387	0.42	Excluded for MR				
rs55932213	9:108755622	A/G	0.74	0.009	0.002	9.55E-09	21	13853	0.30	-0.019	0.030	5.29E-01	13.5	3.50E-05
rs10978550[a]	9:109345993	C/T	0.79	0.012	0.002	7.15E-11	23	14387	0.20	0.014	0.032	6.64E-01	0	4.52E-05

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
rs7074871	10:110507806	A/G	0.74	0.009	0.002	1.86E-08	23	14387	0.25	0.009	0.029	7.48E-01	0	3.36E-05
rs17665139	10:125093880	T/C	0.85	0.012	0.002	1.59E-08	23	14387	0.14	-0.007	0.037	8.45E-01	14.3	3.39E-05
rs7950166	11:8642218	T/C	0.36	0.010	0.002	9.89E-11	23	14387	0.60	-0.019	0.027	4.76E-01	13.6	4.44E-05
rs11030084	11:27643725	T/C	0.82	0.011	0.002	1.72E-08	23	14387	0.20	-0.035	0.032	2.82E-01	0	3.38E-05
rs56030824	11:47397353	A/G	0.68	0.012	0.002	1.15E-13	23	14387	0.32	0.006	0.027	8.26E-01	24.9	5.88E-05
rs10750025[a]	11:113424042	C/T	0.69	0.010	0.002	4.89E-11	23	14387	0.34	-0.004	0.027	8.85E-01	0	4.59E-05
rs4938230	11:116075001	C/A	0.84	0.013	0.002	1.48E-10	14	6683	Excluded for MR					
rs682011[a]	11:121544285	T/C	0.56	0.008	0.001	2.22E-08	23	14387	0.46	-0.021	0.026	4.21E-01	0	3.33E-05
rs12795042	11:133658168	C/A	0.38	0.008	0.002	3.25E-08	23	14387	0.58	-0.012	0.036	7.33E-01	31.3	3.25E-05
rs3809162	12:54674235	A/G	0.40	0.009	0.001	1.19E-09	23	14387	0.64	-0.014	0.027	6.00E-01	8.5	3.93E-05
rs10506274	12:81601464	T/G	0.52	0.009	0.001	5.78E-10	23	14387	0.48	0.017	0.025	5.13E-01	19.7	4.08E-05
rs4842786	12:92170791	A/G	0.42	0.009	0.001	2.73E-09	23	14387	0.56	0.000	0.027	9.99E-01	22.8	3.76E-05
rs500321	13:27124360	T/A	0.26	0.010	0.002	4.92E-09	23	14387	0.28	0.009	0.029	7.70E-01	11.5	3.63E-05
rs1123285	14:57274519	G/C	0.66	0.009	0.002	8.14E-09	23	14387	0.66	-0.041	0.027	1.35E-01	10.4	3.53E-05
rs28929474	14:94844947	T/C	0.98	0.037	0.005	1.34E-11	16	9567	Excluded for MR					
rs2472297[a,b]	15:75027880	C/T	0.25	0.011	0.002	3.10E-10	23	14387	0.81	-0.032	0.033	3.30E-01	0	4.21E-05
rs12907323	15:86796012	A/G	0.41	0.008	0.001	9.93E-09	23	14387	0.56	0.010	0.026	7.11E-01	2	3.50E-05
rs17177078[a]	16:24810681	T/C	0.94	0.022	0.003	1.27E-13	23	14387	0.08	-0.027	0.048	5.78E-01	0	5.84E-05
rs378421	16:28754684	A/G	0.60	0.011	0.001	4.83E-14	23	14387	0.38	-0.030	0.027	2.56E-01	8.6	6.05E-05
rs62044525	16:64872590	G/C	0.82	0.012	0.002	1.03E-10	23	14387	0.82	**0.079**	**0.033**	**1.77E-02**	0	4.45E-05
rs1104608	16:73912588	C/G	0.58	0.011	0.001	1.05E-13	11	5990	Excluded for MR					
rs4548913	17:2209888	A/G	0.37	0.008	0.002	3.11E-08	23	14387	0.60	-0.014	0.027	5.91E-01	9.7	3.25E-05
rs3803800[a]	17:7462969	A/G	0.79	0.011	0.002	1.50E-10	23	14387	0.20	0.005	0.032	8.82E-01	0	4.36E-05
rs2854334	17:29715500	A/G	0.62	0.009	0.001	7.51E-10	20	13362	0.39	0.035	0.030	2.38E-01	0	4.03E-05
rs10438820	17:78524597	C/T	0.70	0.009	0.002	1.76E-08	23	14387	0.30	0.029	0.028	3.03E-01	6.3	3.37E-05
rs9950000	18:53052169	T/C	0.60	0.009	0.001	9.38E-10	23	14387	0.40	-0.009	0.026	7.41E-01	0	3.97E-05
rs4092465	18:55080437	G/A	0.36	0.008	0.002	4.39E-08	NA in COURAGE-PD							
rs281379	19:49214274	G/A	0.51	0.014	0.001	4.91E-21	23	14387	0.54	0.016	0.026	5.43E-01	0	9.41E-05
rs4815364	20:25035711	G/A	0.62	0.009	0.001	1.02E-08	23	14387	0.37	0.044	0.027	1.04E-01	6.3	3.48E-05
rs9607814	22:41946519	A/C	0.80	0.010	0.002	4.31E-08	23	14387	0.21	**-0.121**	**0.032**	**1.83E-04**	4.2	3.32E-05
Coffee drinking (per ln(cups per day))														
rs574367	1:177873210	T/G	0.21	0.010	0.002	8.06E-09	23	14387	0.18	**-0.139**	**0.051**	**6.63E-03**	47	3.32E-05
rs10865548	2:631606	G/A	0.83	0.015	0.002	4.46E-15	23	14387	0.80	0.014	0.033	6.77E-01	10.4	6.35E-05
rs1260326[b]	2:27730940	C/T	0.61	0.014	0.002	2.62E-19	23	14387	0.54	**0.069**	**0.026**	**8.41E-03**	0	9.33E-05
rs4410790	7:17284577	C/T	0.63	0.039	0.002	5.59E-141	23	14387	0.61	-0.009	0.027	7.22E-01	3.6	7.09E-04
rs34060476	7:73037956	G/A	0.13	0.019	0.002	5.06E-18	23	14387	0.11	0.045	0.041	2.72E-01	15.6	8.17E-05
rs1057868	7:75615006	T/C	0.29	0.020	0.002	5.26E-33	23	14387	0.28	0.041	0.028	1.48E-01	0	1.65E-04
rs597045	11:56272114	A/T	0.70	0.011	0.002	6.62E-11	23	14387	0.70	-0.035	0.037	3.42E-01	33.2	5.08E-05
rs1956218	14:33075243	G/A	0.56	0.008	0.002	3.62E-08	23	14387	0.53	-0.027	0.026	2.96E-01	0	3.15E-05
rs2472297[a,b]	15:75027880	T/C	0.26	0.044	0.002	5.19E-155	23	14387	0.19	0.032	0.033	3.30E-01	0	7.45E-04
rs66723169	18:57808978	A/C	0.23	0.015	0.002	9.88E-17	23	14387	0.23	-0.019	0.031	5.47E-01	9.5	7.97E-05
rs2330783	22:24747031	G/T	0.99	0.044	0.006	1.57E-12	18	11562	0.98	0.168	0.119	1.57E-01	4.6	3.83E-05

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
Lifetime smoking index														
rs1193237	1:7526486	C/G	0.56	0.008	0.001	2.80E-08	23	14387	0.57		Excluded for MR			
rs4949465	1:32178489	C/T	0.13	0.012	0.002	1.70E-08	23	14387	0.12	0.002	0.040	9.59E-01	0	3.06E-05
rs549845	1:44076469	G/A	0.30	0.011	0.002	8.30E-14	23	14387	0.33	-0.054	0.028	5.20E-02	23.8	5.34E-05
rs1933270	1:49977965	T/G	0.36	0.009	0.001	1.50E-10	23	14387	0.37	**0.057**	**0.027**	**3.23E-02**	0	3.93E-05
rs7528604	1:66407352	G/A	0.57	0.010	0.001	5.70E-12	23	14387	0.56	-0.002	0.026	9.32E-01	0.4	4.58E-05
rs11210229	1:73860028	A/G	0.38	0.012	0.001	2.00E-16	23	14387	0.45	-0.025	0.026	3.48E-01	17.4	6.48E-05
rs7553348	1:75005067	G/A	0.44	0.010	0.001	5.20E-12	23	14387	0.44	0.009	0.026	7.44E-01	4.8	4.57E-05
rs10922907	1:91193049	A/T	0.45	0.010	0.001	3.00E-13	23	14387	0.48		Excluded for MR			
rs1931263	1:96175101	T/G	0.49	0.008	0.001	4.00E-08	23	14387	0.50	-0.026	0.026	3.16E-01	2.8	2.89E-05
rs7519626	1:99514554	C/T	0.32	0.008	0.001	1.20E-08	23	14387	0.36	0.005	0.028	8.64E-01	12	3.10E-05
rs9435340	1:107593201	T/A	0.34	0.008	0.001	1.20E-08	23	14387	0.35	0.013	0.028	6.37E-01	0	3.15E-05
rs10918701	1:162090536	G/A	0.37	0.008	0.001	2.10E-08	23	14387	0.40	-0.017	0.026	5.25E-01	17	3.01E-05
rs2867112	2:651349	T/G	0.83	0.015	0.002	4.80E-15	23	14387	0.82	0.015	0.034	6.59E-01	5.9	6.03E-05
rs6741228	2:22548774	T/C	0.43	0.008	0.001	1.60E-08	23	14387	0.44	-0.015	0.026	5.56E-01	10.9	3.09E-05
rs62135536	2:44326028	C/T	0.97	0.024	0.004	8.00E-10	18	13065	0.97	-0.006	0.086	9.49E-01	13.6	3.64E-05
rs7569203	2:45154418	C/A	0.31	0.011	0.002	7.40E-13	23	14387	0.32	0.058	0.035	9.40E-02	27.7	4.96E-05
rs13016665	2:57995348	A/C	0.42	0.008	0.001	1.80E-09	23	14387	0.42	0.041	0.027	1.19E-01	0	3.52E-05
rs4671357[a]	2:60136176	C/T	0.48	0.009	0.001	1.10E-11	23	14386	0.47	-0.018	0.026	4.82E-01	0	4.45E-05
rs359243	2:60475509	C/T	0.61	0.009	0.001	9.50E-10	23	14387	0.57	-0.013	0.035	7.03E-01	32.1	3.63E-05
rs2678670	2:104469564	A/T	0.49	0.009	0.001	3.10E-10	23	14387	0.50		Excluded for MR			
rs62155874	2:105973094	G/A	0.13	0.017	0.002	5.20E-16	23	14387	0.12	-0.023	0.039	5.63E-01	0	6.32E-05
rs3811038	2:113240183	C/T	0.28	0.010	0.002	8.90E-10	23	14387	0.28	-0.004	0.029	8.90E-01	9.1	3.64E-05
rs2890772	2:146175106	T/G	0.59	0.014	0.001	2.10E-22	23	14387	0.55	0.009	0.026	7.20E-01	0	9.10E-05
rs62175972	2:161362830	T/C	0.97	0.022	0.004	1.70E-08	23	14387	0.96	0.050	0.069	4.66E-01	0	3.11E-05
rs3769949	2:166199284	A/T	0.47	0.008	0.001	2.50E-09	23	14387	0.47		Excluded for MR			
rs13009008	2:174043233	A/G	0.33	0.009	0.001	4.60E-09	23	14387	0.35	0.045	0.027	9.27E-02	0	3.28E-05
rs4473348	2:182073742	T/A	0.75	0.010	0.002	6.40E-11	23	14387	0.76	-0.037	0.030	2.21E-01	13.6	4.08E-05
rs12623702	2:202885506	G/A	0.39	0.010	0.001	7.70E-12	23	14387	0.37	-0.048	0.027	6.88E-02	0	4.53E-05
rs6779302	3:16859710	T/G	0.37	0.009	0.001	1.20E-09	23	14387	0.35	0.041	0.027	1.25E-01	0	3.56E-05
rs6778080[a]	3:49317338	T/C	0.27	0.011	0.002	1.30E-12	23	14387	0.27	-0.018	0.030	5.39E-01	2.8	4.84E-05
rs775758	3:77582005	A/T	0.43	0.008	0.001	1.10E-08	23	14387	0.43		Excluded for MR			
rs421983	3:84892866	T/C	0.52	0.009	0.001	3.30E-10	23	14387	0.50	0.004	0.025	8.64E-01	14.2	3.79E-05
rs326341	3:107811142	G/A	0.52	0.009	0.001	1.20E-11	23	14387	0.55	-0.012	0.026	6.48E-01	0	4.44E-05
rs73220544	3:131074511	C/A	0.16	0.011	0.002	1.50E-08	21	13998	0.18	-0.062	0.037	9.73E-02	0	3.11E-05
rs9842947	3:157412246	T/C	0.67	0.009	0.001	3.10E-09	23	14387	0.70	0.033	0.029	2.51E-01	0	3.38E-05
rs624833[a]	4:2881256	T/G	0.69	0.009	0.002	6.60E-10	23	14387	0.69	**-0.076**	**0.031**	**1.30E-02**	10.7	3.66E-05
rs61796681	4:23678196	T/A	0.09	0.013	0.002	4.20E-08	23	14387	0.07	0.025	0.049	6.17E-01	6.7	2.88E-05
rs317021	4:35418368	A/T	0.19	0.012	0.002	1.10E-10	23	14387	0.16	0.030	0.035	3.96E-01	15.1	4.05E-05
rs72678864	4:112422145	G/A	0.83	0.012	0.002	1.60E-11	23	14387	0.85	0.025	0.037	4.88E-01	0	4.36E-05
rs17576594	4:147952241	G/A	0.72	0.011	0.002	1.70E-12	23	14387	0.74	-0.044	0.029	1.27E-01	0	4.80E-05
rs11948770	5:13246336	C/T	0.23	0.010	0.002	4.90E-10	23	14387	0.23	-0.045	0.030	1.38E-01	23.6	3.73E-05
rs71627581	5:43161351	G/A	0.89	0.013	0.002	1.60E-09	15	8384			Excluded for MR			

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
rs10052591	5:50812738	T/C	0.57	0.008	0.001	2.10E-09	23	14387	0.57	0.026	0.026	3.10E-01	0	3.45E-05
rs2080870	5:60388313	A/T	0.26	0.009	0.002	4.90E-08	23	14387	0.25	**0.062**	**0.030**	**3.68E-02**	0	2.85E-05
rs4571506[a]	5:87756918	C/T	0.54	0.008	0.001	1.50E-08	23	14385	0.51	**-0.053**	**0.026**	**4.10E-02**	0	3.08E-05
rs4957528	5:106420589	C/A	0.79	0.010	0.002	4.20E-09	10	5308	Excluded for MR					
rs329120[a]	5:133861756	C/T	0.58	0.010	0.001	6.30E-12	23	14387	0.57	-0.045	0.026	8.41E-02	0	4.54E-05
rs986391	5:166993972	G/A	0.37	0.011	0.001	9.40E-15	23	14387	0.38	-0.020	0.027	4.73E-01	0	5.76E-05
rs13153393	5:167604213	G/A	0.12	0.014	0.002	2.50E-10	23	14387	0.11	0.054	0.041	1.88E-01	10.7	3.88E-05
rs245774	5:170530930	G/A	0.73	0.009	0.002	7.40E-09	23	14387	0.71	-0.053	0.029	6.81E-02	0	3.22E-05
rs6935954	6:26255451	A/G	0.42	0.010	0.001	8.20E-12	23	14387	0.39	0.028	0.033	4.01E-01	25.5	4.48E-05
rs2254710	6:37477000	C/A	0.24	0.009	0.002	3.50E-08	23	14387	0.23	0.028	0.042	5.05E-01	33.1	2.92E-05
rs2894808	6:52861990	A/T	0.08	0.015	0.003	3.50E-09	23	14387	0.10	0.007	0.044	8.70E-01	0	3.36E-05
rs12202536	6:67475273	G/A	0.49	0.008	0.001	2.80E-09	23	14387	0.46	**-0.068**	**0.026**	**8.41E-03**	20.2	3.39E-05
rs7766610	6:111707821	C/A	0.18	0.013	0.002	2.20E-12	23	14387	0.19	-0.058	0.043	1.84E-01	29.6	4.73E-05
rs1922018	7:3560401	C/T	0.36	0.010	0.001	3.00E-12	23	14387	0.35	-0.014	0.027	6.11E-01	0	4.66E-05
rs10226228	7:32315613	G/A	0.37	0.011	0.001	2.00E-15	23	14387	0.36	-0.034	0.027	2.04E-01	0	6.07E-05
rs11768481	7:96629103	C/A	0.67	0.009	0.001	9.90E-10	5	3107	Excluded for MR					
rs6962772	7:99081730	A/G	0.85	0.011	0.002	7.80E-09	23	14387	0.85	-0.012	0.036	7.28E-01	0	3.20E-05
rs10282292[a]	7:111092478	C/T	0.36	0.009	0.001	5.90E-10	23	14386	0.37	0.019	0.027	4.73E-01	0	3.71E-05
rs2401924	7:115057862	G/C	0.50	0.011	0.001	2.70E-14	23	14387	0.51	Excluded for MR				
rs7807019	7:117543063	G/A	0.46	0.010	0.001	6.70E-14	23	14387	0.45	0.020	0.026	4.32E-01	5.5	5.39E-05
rs6957896[a]	7:132309592	T/C	0.50	0.008	0.001	4.50E-08	22	13529	0.50	-0.039	0.035	2.67E-01	32	2.88E-05
rs4731925	7:132664757	T/C	0.68	0.008	0.001	2.60E-08	23	14387	0.69	-0.035	0.028	2.06E-01	0	2.97E-05
rs35169606	8:9604066	T/G	0.61	0.009	0.001	1.20E-09	16	9769	Excluded for MR					
rs11783093	8:27425349	C/T	0.84	0.016	0.002	1.20E-16	23	14387	0.84	-0.021	0.035	5.46E-01	21.5	6.67E-05
rs2062882[a]	8:91839576	A/G	0.41	0.008	0.001	1.10E-08	23	14387	0.43	-0.022	0.026	3.87E-01	0	3.19E-05
rs72674867	8:95578201	A/T	0.76	0.009	0.002	3.80E-08	23	14387	0.73	0.015	0.029	6.04E-01	15.3	2.91E-05
rs4543592	9:3014254	C/T	0.48	0.009	0.001	4.50E-10	23	14387	0.48	-0.026	0.026	3.25E-01	17.6	3.75E-05
rs7039819	9:82430418	G/A	0.43	0.009	0.001	5.10E-10	23	14387	0.42	-0.009	0.027	7.52E-01	0	3.73E-05
rs1246265	9:86761745	C/T	0.70	0.009	0.002	4.20E-09	23	14387	0.69	-0.020	0.035	5.77E-01	26.2	3.33E-05
rs1221148	9:122046875	C/G	0.59	0.009	0.001	7.30E-11	23	14387	0.61	0.026	0.027	3.38E-01	0	4.07E-05
rs13296519	9:128471924	T/G	0.39	0.010	0.001	8.10E-12	23	14387	0.39	-0.024	0.027	3.56E-01	10	4.49E-05
rs113382419	9:136463019	A/C	0.11	0.028	0.002	3.00E-37	23	14387	0.10	-0.017	0.044	6.92E-01	0	1.57E-04
rs11255908	10:8802912	G/T	0.26	0.010	0.002	2.30E-10	23	14387	0.26	-0.015	0.029	6.13E-01	0	3.87E-05
rs2675638[a]	10:63576286	G/A	0.58	0.008	0.001	1.30E-09	23	14385	0.61	-0.021	0.026	4.22E-01	0	3.52E-05
rs10823968	10:74738269	A/T	0.63	0.008	0.001	2.10E-08	23	14387	0.65	0.009	0.027	7.29E-01	3.1	3.08E-05
rs17553262[c]	10:92912773	C/A	0.12	0.013	0.002	5.30E-09	9	4488	Excluded for MR					
rs7077678	10:104438565	C/T	0.62	0.009	0.001	2.60E-09	23	14387	0.62	0.000	0.026	9.93E-01	0	3.43E-05
rs12244388	10:104640052	A/G	0.34	0.013	0.001	1.40E-19	23	14387	0.37	**-0.055**	**0.026**	**3.57E-02**	0	7.87E-05
rs3896224[a]	10:106467853	A/G	0.59	0.010	0.001	1.10E-11	23	14387	0.54	-0.008	0.026	7.52E-01	0	4.50E-05
rs34866095	11:16377356	G/A	0.31	0.009	0.002	1.20E-08	23	14387	0.33	-0.044	0.028	1.11E-01	12.6	3.16E-05
rs75742406	11:17070365	G/A	0.74	0.010	0.002	1.30E-09	23	14387	0.77	-0.024	0.039	5.50E-01	29.7	3.57E-05
rs17309874	11:27667236	A/G	0.26	0.011	0.002	9.70E-13	23	14387	0.22	-0.037	0.031	2.33E-01	0	4.90E-05
rs4391802	11:28674592	A/G	0.71	0.010	0.002	1.40E-11	23	14387	0.71	**0.057**	**0.029**	**4.64E-02**	0	4.41E-05

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
rs112282219	11:46632809	A/G	0.04	0.023	0.004	3.80E-11	22	14205	0.04	0.023	0.069	7.38E-01	0	4.23E-05
rs9919670	11:112877304	A/G	0.39	0.015	0.001	7.60E-27	23	14387	0.39	-0.013	0.026	6.26E-01	0	1.10E-04
rs74086911	12:50015942	G/A	0.93	0.015	0.003	2.10E-08	23	14387	0.93	-0.045	0.050	3.73E-01	0	3.02E-05
rs7297175	12:56473808	C/T	0.57	0.008	0.001	6.60E-09	23	14387	0.58	0.011	0.027	6.96E-01	0	3.23E-05
rs10879871	12:75380511	G/T	0.66	0.010	0.001	5.00E-11	23	14387	0.60	-0.012	0.027	6.69E-01	0	4.14E-05
rs12831617	12:84758368	T/C	0.24	0.009	0.002	1.90E-08	23	14387	0.25	0.023	0.029	4.42E-01	0	3.04E-05
rs6562474	13:67332812	C/G	0.65	0.008	0.001	1.00E-08	23	14387	0.65	-0.004	0.027	8.86E-01	0	3.18E-05
rs7333559	13:100546450	G/A	0.21	0.011	0.002	3.20E-10	21	13839	0.24	-0.034	0.033	2.96E-01	7.9	3.85E-05
rs860326	14:57342912	C/T	0.43	0.008	0.001	2.70E-09	23	14387	0.42	0.011	0.026	6.83E-01	18	3.40E-05
rs7155595	14:77502546	C/A	0.33	0.009	0.001	2.50E-09	23	14387	0.32	-0.012	0.028	6.75E-01	0	3.44E-05
rs3742365	14:104198251	C/T	0.40	0.011	0.001	2.50E-14	23	14387	0.37	0.001	0.027	9.77E-01	0	5.61E-05
rs35175834	15:47680815	A/G	0.21	0.016	0.002	4.60E-22	23	14387	0.22	-0.043	0.031	1.62E-01	10.2	8.98E-05
rs28485305	15:74044197	C/T	0.63	0.008	0.001	2.60E-08	23	14387	0.60	0.015	0.026	5.61E-01	0	2.98E-05
rs8042849	15:78817929	C/T	0.34	0.019	0.001	1.80E-39	23	14387	0.39	-0.019	0.027	4.81E-01	0	1.66E-04
rs8042134	15:97514404	G/T	0.46	0.010	0.001	1.30E-12	23	14387	0.44	0.047	0.026	7.40E-02	0	4.91E-05
rs6598539	15:99204483	C/T	0.51	0.008	0.001	4.50E-09	23	14387	0.49	-0.019	0.026	4.64E-01	23.9	3.32E-05
rs11861214	16:746611	G/T	0.78	0.009	0.002	2.00E-08	22	14161	0.79	0.046	0.032	1.49E-01	17.8	3.03E-05
rs12708665	16:24728227	G/A	0.72	0.009	0.002	3.50E-09	23	14387	0.68	-0.013	0.028	6.36E-01	0	3.36E-05
rs57611503	16:31165795	G/A	0.48	0.008	0.001	4.00E-08	20	13192	0.46	**-0.100**	**0.029**	**4.95E-04**	12.5	3.00E-05
rs889398	16:69556715	C/T	0.59	0.009	0.001	6.30E-11	18	10342	0.59	0.013	0.048	7.86E-01	45.4	4.14E-05
rs60952428	16:75640521	T/C	0.91	0.013	0.002	3.00E-08	14	6978	Excluded for MR					
rs1050847	16:87443734	C/T	0.43	0.008	0.001	1.40E-08	23	14387	0.49	-0.013	0.026	6.21E-01	11.3	3.11E-05
rs369230	16:89645437	T/G	0.69	0.009	0.002	1.80E-09	22	14161	0.74	-0.043	0.030	1.55E-01	3	3.52E-05
rs8614	17:27588806	A/C	0.18	0.011	0.002	1.80E-10	22	13821	0.17	**0.084**	**0.037**	**2.24E-02**	0	3.92E-05
rs732083	17:37834367	G/A	0.33	0.008	0.001	1.50E-08	23	14387	0.36	-0.028	0.028	3.23E-01	15.4	3.10E-05
rs9904288	17:47031973	T/C	0.71	0.008	0.002	3.10E-08	23	14387	0.71	-0.018	0.028	5.38E-01	0	2.94E-05
rs67596067	17:50333733	A/G	0.35	0.009	0.001	1.20E-09	23	14387	0.33	0.009	0.027	7.47E-01	0	3.59E-05
rs12967855	18:35138245	A/G	0.33	0.008	0.001	3.10E-08	23	14387	0.35	-0.040	0.028	1.52E-01	1.3	2.97E-05
rs62098013	18:50863861	A/G	0.36	0.009	0.001	4.10E-09	23	14387	0.36	0.043	0.027	1.14E-01	23.6	3.38E-05
rs71367545	18:77576337	A/G	0.21	0.010	0.002	1.40E-09	23	14387	0.17	0.023	0.034	4.98E-01	0	3.53E-05
rs76608582	19:4474725	C/A	0.95	0.022	0.003	3.20E-10	NA in COURAGE-PD							
rs35343344	19:18471610	C/A	0.73	0.009	0.002	8.80E-09	23	14387	0.75	0.056	0.031	7.27E-02	0	3.30E-05
rs4814873	20:19616429	C/T	0.77	0.010	0.002	2.90E-09	23	14387	0.75	-0.013	0.030	6.68E-01	0	3.38E-05
rs6119897	20:31145415	A/G	0.24	0.013	0.002	3.60E-15	23	14387	0.21	-0.018	0.032	5.89E-01	0	5.95E-05
rs12481282	20:44761377	C/G	0.28	0.009	0.002	7.80E-09	23	14387	0.26	-0.020	0.030	5.15E-01	0	3.21E-05
rs348809	20:59032097	G/A	0.65	0.008	0.001	1.30E-08	23	14387	0.62	-0.012	0.027	6.62E-01	0	3.11E-05
rs6011779	20:61984317	C/T	0.19	0.019	0.002	2.30E-27	22	14161	0.22	-0.017	0.032	6.00E-01	0	1.13E-04
rs147412694	21:40702786	A/G	0.15	0.012	0.002	2.90E-09	23	14387	0.14	-0.024	0.038	5.22E-01	0	3.41E-05
rs2838834	21:46665208	T/C	0.30	0.009	0.002	6.30E-10	23	14387	0.29	0.016	0.028	5.61E-01	19.7	3.69E-05
rs136233	22:31212410	G/A	0.19	0.010	0.002	1.80E-08	23	14387	0.19	-0.037	0.032	2.50E-01	0	3.06E-05
rs202645	22:41798520	G/A	0.80	0.010	0.002	3.90E-09	23	14387	0.77	**0.122**	**0.032**	**1.47E-04**	3.5	3.34E-05

Smoking initiation (per 1-SD increase in the prevalence of ever smoking)

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
rs12130857	1:7791461	G/A	0.68	0.018	0.003	3.65E-11	23	14387	0.69	-0.027	0.028	3.34E-01	0	1.42E-04
rs3820277	1:18436657	G/T	0.47	0.019	0.003	1.57E-13	23	14387	0.50	-0.032	0.037	3.90E-01	42.3	1.77E-04
rs1889571	1:32195819	G/T	0.13	0.022	0.004	4.19E-09	23	14387	0.12	0.010	0.040	8.13E-01	0	1.12E-04
rs10914684	1:33795572	G/A	0.68	0.016	0.003	6.32E-09	23	14387	0.66	-0.027	0.027	3.16E-01	9.1	1.09E-04
rs951740	1:44011737	A/G	0.62	0.030	0.003	3.82E-29	23	14387	0.61	-0.041	0.026	1.24E-01	5.5	4.09E-04
rs12022778	1:50603995	C/A	0.20	0.027	0.003	3.18E-17	23	14387	0.18	0.060	0.033	6.97E-02	5	2.32E-04
rs4912332	1:58815243	T/C	0.49	0.014	0.003	2.94E-08	23	14387	0.47	0.028	0.026	2.82E-01	0	9.97E-05
rs80054503	1:72900406	T/C	0.88	0.024	0.004	3.10E-09	NA in COURAGE-PD							
rs10789369	1:73824909	A/G	0.38	0.023	0.003	3.39E-19	23	14387	0.43	-0.041	0.026	1.21E-01	12.5	2.60E-04
rs1514176	1:74991596	G/A	0.42	0.019	0.003	7.67E-14	23	14387	0.42	0.007	0.026	8.02E-01	16.3	1.81E-04
rs11162019	1:87913176	C/T	0.64	0.015	0.003	5.06E-09	23	14387	0.65	-0.026	0.027	3.35E-01	10.5	1.11E-04
rs1008078	1:91189731	T/C	0.40	0.023	0.003	1.63E-18	23	14387	0.40	-0.025	0.040	5.27E-01	48.6	2.50E-04
rs12027999	1:154206358	T/C	0.88	0.024	0.004	5.33E-10	23	14387	0.89	0.001	0.042	9.77E-01	0	1.25E-04
rs45444697	1:155034632	G/C	0.21	0.020	0.003	2.72E-10	23	14387	0.20	-0.019	0.033	5.69E-01	21.8	1.30E-04
rs2901785	1:174104743	G/A	0.55	0.017	0.003	1.47E-11	23	14387	0.54	-0.008	0.026	7.60E-01	10.4	1.48E-04
rs147052174	1:179783167	T/G	0.02	0.062	0.010	2.30E-10	13	7882	Excluded for MR					
rs35656245	1:190957480	A/G	0.28	0.016	0.003	2.23E-08	23	14387	0.29	-0.003	0.028	9.14E-01	0	1.02E-04
rs12739243	1:210302043	T/C	0.78	0.021	0.003	4.45E-12	23	14387	0.78	0.017	0.031	5.70E-01	0	1.56E-04
rs876793	1:237852083	T/C	0.65	0.018	0.003	5.69E-11	23	14387	0.66	0.051	0.028	6.89E-02	17	1.46E-04
rs6731872	2:624205	G/T	0.83	0.032	0.003	5.35E-21	23	14387	0.80	0.016	0.033	6.34E-01	0	2.87E-04
rs1022376	2:22067213	T/C	0.48	0.015	0.003	1.66E-08	23	14387	0.51	0.002	0.026	9.33E-01	0	1.09E-04
rs61533748	2:22582968	C/T	0.38	0.017	0.003	2.82E-11	23	14387	0.37	-0.012	0.027	6.58E-01	8	1.44E-04
rs2710634	2:32808804	T/C	0.48	0.018	0.003	3.36E-12	23	14387	0.51	-0.039	0.026	1.31E-01	0	1.57E-04
rs7598402	2:50735943	C/G	0.51	0.015	0.003	7.38E-09	23	14387	0.50	Excluded for MR				
rs10490159	2:51341259	T/C	0.39	0.017	0.003	3.86E-11	23	14387	0.39	-0.027	0.026	3.04E-01	0	1.42E-04
rs359247	2:60477052	T/A	0.64	0.022	0.003	9.89E-17	23	14387	0.61	-0.017	0.027	5.36E-01	24.7	2.24E-04
rs12714017	2:80999398	C/T	0.51	0.015	0.003	3.65E-09	23	14387	0.52	0.011	0.026	6.71E-01	0	1.18E-04
rs13392222	2:100672408	A/C	0.86	0.023	0.004	1.93E-10	23	14387	0.87	0.012	0.039	7.53E-01	0	1.31E-04
rs1901477	2:104126983	G/A	0.51	0.030	0.003	2.07E-31	23	14387	0.52	0.024	0.038	5.33E-01	45.5	4.63E-04
rs3811038	2:113240183	C/T	0.28	0.019	0.003	1.58E-11	23	14387	0.28	-0.004	0.029	8.90E-01	9.1	1.47E-04
rs34399632	2:137571174	G/A	0.23	0.019	0.003	1.46E-10	23	14387	0.17	-0.035	0.044	4.30E-01	26.8	1.33E-04
rs6756212	2:146140132	C/T	0.47	0.034	0.003	3.49E-40	23	14387	0.46	-0.023	0.026	3.72E-01	3.4	5.71E-04
rs16826827	2:147825689	T/C	0.88	0.022	0.004	9.17E-09	23	14387	0.89	-0.041	0.040	3.08E-01	0	1.07E-04
rs1445649	2:155682556	C/T	0.54	0.021	0.003	8.48E-16	23	14387	0.54	-0.023	0.026	3.58E-01	0	2.10E-04
rs12474587	2:162802993	T/G	0.43	0.024	0.003	4.83E-21	23	14387	0.40	0.043	0.027	1.08E-01	5	2.88E-04
rs13007361	2:166250244	A/G	0.21	0.018	0.003	2.29E-08	23	14387	0.21	0.014	0.031	6.52E-01	9.7	1.01E-04
rs6750529	2:182027603	T/C	0.74	0.020	0.003	9.26E-12	23	14387	0.75	-0.025	0.030	3.96E-01	10.5	1.51E-04
rs17229285	2:199523122	C/T	0.50	0.015	0.003	1.27E-09	23	14387	0.52	0.013	0.026	6.11E-01	0	1.20E-04
rs62193862	2:202843875	A/G	0.10	0.024	0.004	1.99E-08	12	6492	Excluded for MR					
rs4674993	2:226332033	A/G	0.80	0.024	0.003	4.85E-14	23	14387	0.80	-0.006	0.044	8.84E-01	33.7	1.84E-04
rs11713899	3:2365026	C/A	0.17	0.019	0.003	3.15E-08	23	14387	0.17	-0.032	0.034	3.49E-01	0	9.93E-05
rs748832	3:16851202	G/A	0.37	0.017	0.003	6.60E-11	23	14387	0.34	0.051	0.027	5.61E-02	0	1.38E-04
rs2526390	3:50192760	T/C	0.33	0.020	0.003	3.62E-14	23	14387	0.33	-0.007	0.027	7.88E-01	0	1.86E-04

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
rs221988	3:64234307	A/C	0.62	0.015	0.003	1.43E-08	23	14387	0.62	0.024	0.027	3.90E-01	0	1.05E-04
rs11128203	3:71064431	A/T	0.53	0.020	0.003	1.29E-15	10	4792	Excluded for MR					
rs62246017	3:71483084	G/A	0.68	0.016	0.003	3.03E-09	23	14387	0.67	-0.045	0.029	1.18E-01	7.9	1.14E-04
rs12633090	3:83241365	G/C	0.82	0.023	0.003	3.16E-12	23	14387	0.80	0.065	0.043	1.31E-01	31.5	1.58E-04
rs1549979	3:85460131	C/T	0.38	0.025	0.003	8.80E-21	23	14387	0.39	0.019	0.026	4.69E-01	0	2.85E-04
rs6437769	3:107997514	T/C	0.58	0.014	0.003	3.74E-08	23	14387	0.59	0.024	0.026	3.54E-01	12.9	9.84E-05
rs9288999	3:114147927	A/G	0.74	0.017	0.003	1.50E-09	23	14387	0.73	-0.043	0.029	1.47E-01	0	1.18E-04
rs6438436	3:117822149	T/C	0.82	0.025	0.003	5.33E-14	23	14387	0.82	0.058	0.035	9.38E-02	16.4	1.84E-04
rs9826984	3:131945722	G/A	0.46	0.014	0.003	3.87E-08	23	14387	0.44	0.017	0.026	5.24E-01	0.3	9.80E-05
rs2279829	3:147106319	C/T	0.78	0.017	0.003	2.05E-08	23	14387	0.80	0.024	0.033	4.57E-01	0	1.02E-04
rs2319545	3:147719648	A/C	0.15	0.023	0.004	8.30E-11	23	14387	0.13	0.017	0.052	7.45E-01	34.6	1.37E-04
rs1714521	3:158284861	A/C	0.59	0.016	0.003	3.07E-10	23	14387	0.61	-0.007	0.026	8.01E-01	22.4	1.29E-04
rs1449012	3:159048333	C/T	0.54	0.015	0.003	1.77E-09	23	14387	0.53	-0.010	0.036	7.82E-01	37.8	1.18E-04
rs1187820	3:173072584	C/T	0.56	0.014	0.003	2.69E-08	23	14387	0.57	0.015	0.038	6.84E-01	34.4	1.00E-04
rs7631379	3:181409057	C/T	0.21	0.021	0.003	3.94E-11	23	14387	0.19	-0.059	0.047	2.12E-01	36.2	1.42E-04
rs4140932	4:15458598	T/A	0.57	0.014	0.003	4.89E-08	23	14387	0.57	Excluded for MR				
rs59537158	4:28246049	T/C	0.21	0.022	0.003	4.62E-13	23	14387	0.20	-0.001	0.033	9.73E-01	12.1	1.70E-04
rs58400863	4:31184484	G/A	0.65	0.020	0.003	4.89E-14	23	14387	0.63	0.018	0.027	5.09E-01	3.3	1.84E-04
rs112725451	4:68017710	T/C	0.17	0.026	0.003	1.65E-14	23	14387	0.18	0.010	0.033	7.69E-01	0	1.91E-04
rs1160685	4:94052854	G/C	0.45	0.015	0.003	2.31E-09	23	14387	0.49	Excluded for MR				
rs3934797	4:112467612	G/A	0.82	0.021	0.003	1.12E-10	23	14387	0.83	0.015	0.035	6.77E-01	18.4	1.35E-04
rs71602617	4:136406155	C/T	0.78	0.018	0.003	2.10E-08	23	14387	0.80	-0.010	0.032	7.58E-01	0	1.07E-04
rs7696257	4:137474783	A/G	0.37	0.015	0.003	6.78E-09	23	14387	0.35	-0.006	0.027	8.13E-01	7	1.09E-04
rs1116690	4:143510148	G/A	0.74	0.016	0.003	2.16E-08	21	13928	0.71	-0.020	0.030	5.05E-01	0	1.02E-04
rs13110073	4:147797913	T/C	0.60	0.025	0.003	3.24E-21	23	14387	0.62	**-0.055**	**0.026**	**3.61E-02**	0	2.90E-04
rs62340589	4:176875795	C/G	0.20	0.017	0.003	4.31E-08	23	14387	0.19	-0.002	0.033	9.48E-01	0	9.74E-05
rs12517438	5:30842054	G/T	0.54	0.015	0.003	1.89E-09	23	14387	0.52	0.005	0.026	8.46E-01	0	1.17E-04
rs35375873	5:43190647	G/C	0.89	0.027	0.004	3.29E-11	15	8384	Excluded for MR					
rs71592686	5:60121271	C/T	0.27	0.021	0.003	3.85E-13	23	14387	0.26	0.055	0.029	5.69E-02	19.2	1.71E-04
rs6874731	5:80263865	G/T	0.48	0.015	0.003	1.83E-09	23	14387	0.47	-0.002	0.026	9.45E-01	0	1.17E-04
rs6452785	5:87685500	C/T	0.53	0.027	0.003	4.69E-26	23	14387	0.51	-0.044	0.026	8.56E-02	0	3.60E-04
rs42417	5:94198290	T/C	0.69	0.017	0.003	8.27E-10	23	14387	0.70	**-0.079**	**0.037**	**3.33E-02**	29	1.22E-04
rs72780746	5:103929588	T/C	0.83	0.026	0.003	2.05E-14	23	14387	0.81	**-0.071**	**0.033**	**2.97E-02**	6.7	1.90E-04
rs329124	5:133865452	A/G	0.57	0.016	0.003	1.96E-10	23	14387	0.57	-0.042	0.026	1.01E-01	0	1.31E-04
rs1385108	5:154839646	T/C	0.24	0.019	0.003	3.84E-10	23	14387	0.22	-0.017	0.031	5.71E-01	0	1.27E-04
rs6890961	5:166778503	C/T	0.38	0.019	0.003	2.13E-13	23	14387	0.40	-0.038	0.028	1.68E-01	0	1.75E-04
rs4044321	5:166989513	A/G	0.36	0.023	0.003	1.75E-17	23	14387	0.37	-0.016	0.028	5.63E-01	0	2.35E-04
rs2173019	5:167614971	A/T	0.18	0.028	0.003	2.98E-17	23	14387	0.17	0.051	0.034	1.37E-01	0	2.32E-04
rs1150668	6:28129789	T/G	0.58	0.019	0.003	8.54E-13	23	14387	0.59	0.020	0.027	4.68E-01	0	1.67E-04
rs3218116	6:41901763	C/T	0.74	0.020	0.003	1.05E-11	23	14387	0.77	-0.010	0.030	7.49E-01	0	1.50E-04
rs160631	6:52895230	T/G	0.27	0.017	0.003	1.87E-09	23	14387	0.28	0.042	0.029	1.47E-01	0	1.17E-04
rs7743165	6:67521222	G/T	0.50	0.019	0.003	4.15E-14	23	14387	0.47	-0.060	0.034	8.30E-02	32.5	1.85E-04
rs10945141	6:69470709	A/G	0.26	0.018	0.003	3.59E-10	23	14387	0.26	0.001	0.029	9.68E-01	0	1.28E-04

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
rs17554906	6:92226609	C/G	0.44	0.014	0.003	3.14E-08	23	14387	0.42	Excluded for MR				
rs6568832	6:97702876	A/G	0.75	0.019	0.003	1.74E-10	23	14387	0.74	0.023	0.039	5.47E-01	28.9	1.32E-04
rs12195240	6:98636905	A/G	0.28	0.025	0.003	1.08E-18	23	14387	0.30	-0.041	0.028	1.39E-01	0	2.53E-04
rs6936160	6:100347745	T/C	0.70	0.020	0.003	4.20E-13	23	14387	0.69	0.018	0.028	5.17E-01	0	1.70E-04
rs118202	6:111658371	G/T	0.19	0.037	0.003	1.90E-29	23	14387	0.19	-0.060	0.043	1.63E-01	29.2	4.12E-04
rs1737329	6:163807748	G/C	0.74	0.017	0.003	5.08E-09	23	14387	0.73	-0.014	0.041	7.41E-01	36.1	1.11E-04
rs6948707	7:1870794	G/T	0.42	0.024	0.003	4.24E-21	23	14387	0.41	<0.001	0.026	9.93E-01	11	2.89E-04
rs7809303	7:69484366	G/A	0.68	0.021	0.003	3.48E-15	23	14387	0.70	-0.053	0.027	5.14E-02	0	2.01E-04
rs1030015[a]	7:78139581	T/G	0.52	0.014	0.003	2.15E-08	23	14387	0.52	0.009	0.031	7.75E-01	23.1	1.02E-04
rs4727189	7:88442568	C/T	0.34	0.015	0.003	3.00E-08	23	14387	0.36	0.031	0.027	2.40E-01	0	9.97E-05
rs11768481	7:96629103	C/A	0.66	0.019	0.003	5.23E-12	5	3107	Excluded for MR					
rs13437771	7:99071478	A/G	0.84	0.027	0.004	1.39E-14	23	14387	0.85	-0.012	0.036	7.27E-01	0	1.93E-04
rs10233018	7:117523709	G/A	0.52	0.025	0.003	4.77E-22	23	14387	0.50	0.014	0.026	5.76E-01	0	3.03E-04
rs10953957	7:121954709	A/G	0.39	0.014	0.003	3.66E-08	23	14387	0.39	0.036	0.027	1.77E-01	10.3	9.84E-05
rs77283305	7:132593831	G/A	0.69	0.015	0.003	3.91E-08	23	14387	0.70	-0.037	0.028	1.78E-01	0	9.80E-05
rs10279261	7:133589846	G/A	0.38	0.019	0.003	6.05E-13	23	14387	0.39	-0.010	0.027	7.05E-01	0	1.68E-04
rs4326350	8:10763655	C/G	0.51	0.018	0.003	5.16E-12	23	14387	0.53	Excluded for MR				
rs11783093	8:27425349	C/T	0.84	0.047	0.003	2.07E-41	23	14387	0.84	-0.021	0.035	5.46E-01	21.5	5.91E-04
rs7836565	8:52569449	C/T	0.28	0.016	0.003	4.36E-08	23	14387	0.29	**0.060**	**0.029**	**3.85E-02**	0	9.74E-05
rs13261666	8:59814666	G/T	0.48	0.020	0.003	4.36E-15	23	14387	0.48	-0.019	0.026	4.64E-01	0	2.00E-04
rs3850736	8:64912021	G/C	0.47	0.019	0.003	6.43E-14	23	14387	0.46	Excluded for MR				
rs2063976	8:91096366	C/T	0.34	0.020	0.003	7.45E-14	23	14387	0.34	-0.019	0.027	4.81E-01	0	1.81E-04
rs6986430	8:93048104	T/C	0.78	0.024	0.003	1.99E-15	23	14387	0.77	0.019	0.030	5.26E-01	0	2.05E-04
rs290601	8:115374642	T/C	0.27	0.016	0.003	1.14E-08	23	14387	0.27	-0.003	0.029	9.19E-01	0	1.06E-04
rs3847244	9:3025368	T/C	0.47	0.019	0.003	2.60E-13	23	14387	0.48	-0.026	0.027	3.34E-01	0	1.74E-04
rs11791671	9:3398679	T/C	0.07	0.028	0.005	4.24E-08	23	14387	0.07	0.019	0.073	8.00E-01	35.7	9.74E-05
rs7024924	9:8282399	C/T	0.17	0.019	0.003	1.90E-08	23	14387	0.17	-0.004	0.034	9.18E-01	0	1.03E-04
rs10966092	9:23831658	T/C	0.73	0.020	0.003	1.12E-12	23	14387	0.74	-0.023	0.029	4.35E-01	0	1.64E-04
rs4877285	9:81354129	G/A	0.33	0.018	0.003	2.10E-11	23	14387	0.36	-0.052	0.028	5.89E-02	0	1.46E-04
rs2378662	9:86707289	A/G	0.54	0.015	0.003	2.67E-09	23	14387	0.53	-0.010	0.034	7.70E-01	28.6	1.15E-04
rs4837631	9:122061948	C/T	0.55	0.015	0.003	2.03E-09	23	14387	0.58	0.022	0.027	4.08E-01	0	1.17E-04
rs34553878	9:134334588	G/A	0.11	0.025	0.004	1.17E-09	15	9465	Excluded for MR					
rs10858334	9:137989785	G/C	0.14	0.023	0.004	1.18E-09	23	14387	0.14	-0.045	0.054	4.05E-01	37.9	1.26E-04
rs7920501	10:10043159	T/A	0.54	0.016	0.003	1.25E-09	23	14387	0.53	Excluded for MR				
rs1291821	10:11133823	G/A	0.53	0.014	0.003	1.39E-08	23	14387	0.54	-0.015	0.026	5.60E-01	24.1	1.05E-04
rs7072776	10:22032942	A/G	0.29	0.022	0.003	5.66E-15	22	13367	0.33	0.011	0.030	7.11E-01	0	1.98E-04
rs2796793	10:36634124	A/G	0.45	0.014	0.003	1.55E-08	22	13367	0.42	0.059	0.035	8.98E-02	29.8	1.04E-04
rs1733760	10:56698174	C/T	0.51	0.015	0.003	6.70E-09	23	14387	0.50	0.024	0.026	3.68E-01	0	1.09E-04
rs7921378	10:63674885	G/C	0.52	0.023	0.003	6.10E-20	23	14387	0.53	Excluded for MR				
rs11594623	10:103960351	C/T	0.23	0.027	0.003	7.45E-20	23	14387	0.21	**-0.067**	**0.031**	**3.24E-02**	0	2.70E-04
rs12244388	10:104640052	A/G	0.35	0.026	0.003	4.31E-22	23	14387	0.37	**-0.055**	**0.026**	**3.57E-02**	0	3.03E-04
rs10885480	10:115378364	T/C	0.72	0.019	0.003	3.83E-11	23	14387	0.73	-0.014	0.029	6.46E-01	18.9	1.42E-04
rs4752018	10:118678712	A/C	0.23	0.019	0.003	4.42E-10	23	14387	0.24	-0.023	0.030	4.46E-01	21.6	1.26E-04

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
rs9423279	10:125680419	C/G	0.36	0.019	0.003	3.06E-12	1	950	Excluded for MR					
rs6265[a]	11:27679916	C/T	0.81	0.029	0.003	2.81E-19	23	14387	0.79	0.038	0.032	2.44E-01	0	2.62E-04
rs2939756	11:41436297	G/A	0.52	0.016	0.003	7.45E-10	23	14387	0.56	-0.007	0.026	7.96E-01	5.7	1.23E-04
rs1381775	11:42442826	T/C	0.29	0.016	0.003	2.79E-08	23	14387	0.29	-0.038	0.029	1.87E-01	0	1.00E-04
rs61886926	11:64133552	C/T	0.62	0.018	0.003	7.30E-12	23	14387	0.64	-0.004	0.035	9.05E-01	34.3	1.52E-04
rs644740	11:65561468	C/T	0.54	0.014	0.003	3.67E-08	23	14387	0.54	-0.007	0.026	7.95E-01	0	9.84E-05
rs7943721	11:73309393	G/A	0.17	0.021	0.003	3.58E-10	NA in COURAGE-PD							
rs7929518	11:85980958	G/A	0.77	0.019	0.003	2.55E-10	23	14387	0.77	-0.062	0.038	1.10E-01	27.6	1.30E-04
rs2155646	11:112912811	C/T	0.40	0.038	0.003	9.44E-48	23	14387	0.39	-0.012	0.026	6.61E-01	0	6.85E-04
rs1713676[a]	11:113660576	A/G	0.48	0.017	0.003	5.38E-11	23	14387	0.46	0.034	0.026	1.96E-01	0	1.40E-04
rs540860	11:121530888	G/A	0.54	0.018	0.003	5.75E-12	23	14387	0.52	0.038	0.026	1.40E-01	0	1.54E-04
rs1106363	11:131966264	T/C	0.34	0.017	0.003	9.20E-11	23	14387	0.37	0.013	0.026	6.14E-01	0	1.36E-04
rs2010921	11:132098205	A/G	0.31	0.017	0.003	2.47E-10	23	14387	0.30	0.034	0.028	2.25E-01	0	1.30E-04
rs11057005	12:16748721	A/G	0.56	0.016	0.003	9.12E-10	23	14387	0.58	-0.034	0.038	3.73E-01	40	1.22E-04
rs13906	12:49952394	C/T	0.89	0.025	0.004	1.98E-09	23	14387	0.89	0.019	0.042	6.56E-01	0	1.17E-04
rs4759229	12:56474480	G/A	0.66	0.016	0.003	6.53E-09	22	14205	0.66	<0.001	0.029	9.98E-01	0	1.09E-04
rs7969559	12:69655167	A/G	0.29	0.017	0.003	1.53E-09	23	14387	0.34	-0.016	0.028	5.67E-01	6.6	1.18E-04
rs7134009	12:75263193	T/C	0.71	0.016	0.003	4.30E-08	23	14387	0.70	-0.015	0.028	5.96E-01	0	1.02E-04
rs77215829	12:112618346	A/C	0.87	0.024	0.004	2.02E-10	18	9799	0.87	0.005	0.051	9.25E-01	16	1.32E-04
rs1109480	12:121083279	G/A	0.62	0.017	0.003	1.84E-10	23	14387	0.62	-0.030	0.027	2.63E-01	0	1.32E-04
rs11611651	12:133380790	A/G	0.09	0.027	0.005	2.05E-09	23	14387	0.08	-0.008	0.048	8.65E-01	0	1.17E-04
rs17197663	13:38172867	G/A	0.88	0.022	0.004	2.06E-08	23	14387	0.87	0.030	0.038	4.30E-01	23	1.02E-04
rs4264267	13:38359676	T/C	0.53	0.015	0.003	6.82E-09	23	14387	0.53	-0.025	0.026	3.46E-01	0	1.09E-04
rs61959481	13:55834929	G/A	0.79	0.020	0.003	7.95E-11	23	14387	0.79	-0.022	0.032	4.94E-01	0	1.37E-04
rs55786907	13:59871584	G/A	0.16	0.019	0.003	1.84E-08	23	14387	0.17	0.021	0.034	5.41E-01	0	1.03E-04
rs9540731[a]	13:66949370	C/T	0.49	0.018	0.003	3.42E-12	23	14387	0.50	-0.036	0.031	2.46E-01	20.4	1.57E-04
rs9545155	13:80191873	T/C	0.52	0.016	0.003	3.04E-10	23	14387	0.53	-0.004	0.026	8.70E-01	0	1.29E-04
rs1772572	13:81191176	C/A	0.68	0.017	0.003	5.62E-10	23	14387	0.68	-0.045	0.027	9.54E-02	0	1.25E-04
rs1108130	13:100648356	A/T	0.21	0.024	0.003	1.57E-14	23	14387	0.20	-0.022	0.033	5.06E-01	0	1.92E-04
rs12878369	14:28346502	A/C	0.41	0.017	0.003	1.60E-11	23	14387	0.42	-0.035	0.038	3.47E-01	42.9	1.48E-04
rs9323328[a]	14:58653514	A/G	0.46	0.014	0.003	2.55E-08	23	14387	0.45	0.003	0.026	9.21E-01	0	1.01E-04
rs1811739	14:77529375	A/G	0.25	0.018	0.003	5.97E-10	23	14387	0.25	0.022	0.030	4.67E-01	0	1.25E-04
rs8005334	14:79563654	G/T	0.36	0.017	0.003	3.44E-10	23	14387	0.35	-0.016	0.027	5.55E-01	0	1.28E-04
rs2925128	14:98362355	T/C	0.39	0.017	0.003	3.67E-10	23	14387	0.38	-0.028	0.040	4.90E-01	48.2	1.34E-04
rs1381287	14:98597552	T/C	0.47	0.018	0.003	1.81E-12	23	14387	0.49	0.020	0.026	4.39E-01	14.1	1.62E-04
rs1435672	15:36399479	C/T	0.56	0.014	0.003	3.82E-08	23	14387	0.54	-0.018	0.026	4.95E-01	0	9.80E-05
rs281296	15:47685010	A/G	0.36	0.025	0.003	1.59E-20	23	14387	0.37	-0.046	0.027	9.02E-02	0	2.80E-04
rs2289791	15:67476952	G/T	0.75	0.018	0.003	2.01E-09	10	4792	Excluded for MR					
rs62007780	15:78025464	G/T	0.58	0.016	0.003	7.48E-10	23	14387	0.60	-0.002	0.026	9.37E-01	0	1.23E-04
rs4310804	15:96858409	C/G	0.75	0.018	0.003	7.55E-10	20	11001	0.77	0.029	0.038	4.46E-01	24.5	1.23E-04
rs1139897	16:720986	G/A	0.77	0.024	0.003	1.77E-15	22	14161	0.78	0.050	0.032	1.20E-01	10.2	2.06E-04
rs11076962	16:5811367	C/T	0.28	0.018	0.003	1.20E-10	23	14387	0.26	0.010	0.029	7.27E-01	0	1.35E-04
rs9922607	16:17570220	C/T	0.80	0.022	0.003	3.42E-12	23	14387	0.80	-0.014	0.033	6.66E-01	0	1.57E-04

			Exposure				Courage-PD							
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**N studies**	**N samples**	**EAF**	**Beta**	**SE**	**p**	**I² (%)**	**R²**
rs9941217	16:18050926	C/G	0.65	0.019	0.003	3.50E-12	23	14387	0.68	0.019	0.028	5.05E-01	20.7	1.57E-04
rs6497840	16:25351633	A/G	0.71	0.023	0.003	2.01E-15	23	14387	0.69	-0.012	0.028	6.61E-01	4.1	2.15E-04
rs12918191	16:50945156	A/G	0.76	0.020	0.003	3.14E-11	23	14387	0.76	-0.004	0.030	8.95E-01	0	1.43E-04
rs9302604	16:69576894	G/A	0.44	0.019	0.003	3.29E-13	23	14387	0.44	-0.016	0.033	6.41E-01	26.3	1.72E-04
rs117657830	16:75766873	A/G	0.96	0.038	0.006	3.18E-09	23	14387	0.96	0.003	0.066	9.64E-01	0	1.14E-04
rs1050847	16:87443734	C/T	0.44	0.015	0.003	7.37E-09	23	14387	0.49	-0.013	0.026	6.21E-01	11.3	1.08E-04
rs11642231	16:89608702	G/A	0.63	0.016	0.003	3.44E-09	23	14387	0.68	**0.072**	**0.028**	**1.06E-02**	0	1.13E-04
rs4790874	17:1995177	T/C	0.53	0.017	0.003	8.43E-12	23	14387	0.54	-0.035	0.026	1.85E-01	0	1.52E-04
rs28441558	17:7803118	T/C	0.94	0.036	0.006	1.24E-10	16	9769	Excluded for MR					
rs67777803	17:27323322	G/T	0.83	0.025	0.003	3.18E-13	23	14387	0.84	-0.014	0.035	6.79E-01	4.8	1.72E-04
rs3764351	17:37824339	G/A	0.34	0.015	0.003	3.89E-08	23	14387	0.37	-0.033	0.028	2.34E-01	13.7	9.80E-05
rs72836318	17:44121579	T/C	0.75	0.017	0.003	7.00E-09	23	14387	0.75	**-0.085**	**0.030**	**5.21E-03**	0	1.09E-04
rs75919030	17:50193197	T/C	0.73	0.021	0.003	3.35E-13	23	14387	0.74	0.003	0.029	9.27E-01	0	1.72E-04
rs2587507[a]	17:77790135	T/C	0.50	0.015	0.003	8.69E-09	23	14382	0.52	-0.042	0.026	9.96E-02	0	1.07E-04
rs34342129	18:5872472	T/C	0.49	0.014	0.003	2.13E-08	23	14387	0.50	-0.038	0.026	1.45E-01	0	1.02E-04
rs4476253	18:25253297	G/A	0.76	0.018	0.003	5.78E-10	23	14387	0.76	0.014	0.038	7.14E-01	26.8	1.25E-04
rs8096225	18:36921851	C/A	0.70	0.016	0.003	2.63E-08	23	14387	0.70	-0.006	0.028	8.23E-01	1.4	1.01E-04
rs67050670	18:39297254	A/G	0.77	0.020	0.003	2.34E-11	23	14387	0.74	0.051	0.030	8.56E-02	14.6	1.45E-04
rs1373178	18:49967811	T/G	0.41	0.020	0.003	4.16E-15	23	14387	0.42	-0.023	0.026	3.87E-01	0	2.00E-04
rs72938304	18:53661743	G/A	0.89	0.027	0.004	1.36E-11	23	14387	0.88	0.051	0.041	2.12E-01	18.7	1.48E-04
rs71367544	18:77574374	T/C	0.20	0.021	0.003	8.54E-11	23	14387	0.17	0.025	0.034	4.58E-01	0	1.37E-04
rs76608582	19:4474725	C/A	0.95	0.035	0.006	4.88E-09	NA in COURAGE-PD							
rs10853981	19:4965064	A/G	0.33	0.015	0.003	4.88E-08	23	14387	0.31	-0.016	0.028	5.72E-01	1.9	9.67E-05
rs113230003	19:18460956	G/A	0.74	0.019	0.003	1.05E-10	23	14387	0.76	0.055	0.031	7.61E-02	0	1.35E-04
rs117734003	19:51129745	C/G	0.07	0.030	0.005	2.57E-09	15	8384	Excluded for MR					
rs1126757[a]	19:55879872	T/C	0.47	0.014	0.003	2.92E-08	23	14369	0.47	-0.001	0.029	9.68E-01	12.9	1.00E-04
rs6050446[d]	20:25195509	G/A	0.97	0.054	0.008	8.80E-13	18	12644	0.98	-0.070	0.091	4.42E-01	0	2.81E-04
rs6073075	20:42015801	T/A	0.18	0.019	0.003	2.44E-08	23	14387	0.20	-0.008	0.033	8.05E-01	4.9	1.01E-04
rs3810496	20:62406886	C/T	0.62	0.016	0.003	1.54E-09	22	14205	0.63	-0.047	0.042	2.61E-01	44.2	1.19E-04
rs4818005	21:40588819	G/A	0.42	0.020	0.003	1.09E-14	23	14387	0.43	-0.036	0.026	1.70E-01	0	2.03E-04
rs4822102	22:42698430	C/T	0.38	0.017	0.003	2.78E-10	23	14387	0.38	0.022	0.036	5.34E-01	33.4	1.29E-04

NA, not available; EA/BA, effect allele/base allele; EAF, effect allele frequency; SE, standard error.

Bold coefficients with their corresponding SE and p-values are significant at $p \leq 0.05$; those underlined with a solid line are negative and those underlined with a dashed line are positive.

R^2 is the proportion of the variance of the exposure explained by the genetic variant according to the formula: $2 \times Beta_{exposure} \times EAF_{exposure} \times (1-EAF_{exposure})$.

[a] SNPs genotyped.

[b] SNPs associated with both alcohol and coffee consumption.

[c] Proxy SNP used in Courage-PD: rs61857951.

[d] Proxy SNP used in Courage-PD: rs117495226.

Supplementary Table 4. SNPs used for Mendelian randomization analyses: individual associations with PD stratified by age and disease duration.

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
Alcohol drinking (per 1-SD increase of ln(drinks per week))													
rs705687	G/A	0.024	0.051	6.36E-01	-0.013	0.052	8.09E-01	0.033	0.040	4.07E-01	0.037	0.042	3.81E-01
rs58107686	A/C	-0.014	0.043	7.42E-01	0.014	0.043	7.40E-01	0.031	0.033	3.60E-01	-0.010	0.036	7.72E-01
rs12088813	C/A	-0.024	0.065	7.11E-01	0.026	0.046	5.80E-01	0.042	0.036	2.36E-01	0.045	0.038	2.41E-01
rs5024204	A/T	0.088	0.045	5.11E-02	0.012	0.046	7.90E-01	0.042	0.035	2.30E-01	**0.080**	**0.037**	**3.34E-02**
rs10753661	A/G	0.026	0.045	5.65E-01	0.080	0.045	7.70E-02	0.032	0.035	3.65E-01	0.026	0.037	4.90E-01
rs28680958	A/G	-0.013	0.049	7.83E-01	0.012	0.049	8.09E-01	-0.007	0.038	8.60E-01	0.019	0.040	6.39E-01
rs823114	G/A	**-0.082**	**0.041**	**4.63E-02**	0.002	0.042	9.71E-01	-0.015	0.033	6.48E-01	-0.064	0.035	6.42E-02
rs77165542	T/C	Excluded for MR											
rs1260326	T/C	**-0.103**	**0.042**	**1.35E-02**	-0.072	0.042	8.51E-02	**-0.075**	**0.032**	**2.05E-02**	**-0.070**	**0.035**	**4.42E-02**
rs13383034	C/T	-0.033	0.044	4.49E-01	**-0.088**	**0.044**	**4.66E-02**	**-0.077**	**0.034**	**2.46E-02**	-0.029	0.036	4.18E-01
rs13032049	A/G	0.049	0.044	2.67E-01	0.069	0.046	1.30E-01	0.037	0.045	4.12E-01	0.055	0.038	1.44E-01
rs828867	G/A	Excluded for MR											
rs11692435	G/A	NA in COURAGE-PD											
rs13024996	A/C	0.064	0.043	1.30E-01	-0.005	0.043	9.10E-01	0.010	0.033	7.54E-01	0.022	0.035	5.37E-01
rs72859280	G/T	Excluded for MR						-0.134	0.104	1.97E-01	-0.147	0.105	1.62E-01
rs56337305	C/T	-0.045	0.042	2.84E-01	-0.014	0.042	7.34E-01	0.005	0.033	8.76E-01	-0.039	0.035	2.64E-01
rs13094887	T/A	0.013	0.043	7.72E-01	**-0.101**	**0.044**	**2.26E-02**	-0.033	0.034	3.35E-01	-0.035	0.037	3.34E-01
rs62250685	G/A	-0.036	0.041	3.82E-01	-0.014	0.042	7.39E-01	0.012	0.032	7.06E-01	-0.048	0.034	1.61E-01
rs9838144	C/G	-0.075	0.070	2.86E-01	-0.053	0.070	4.47E-01	-0.029	0.041	4.74E-01	**-0.099**	**0.042**	**2.04E-02**
rs2011092	C/T	-0.037	0.045	4.08E-01	0.036	0.060	5.50E-01	0.026	0.035	4.49E-01	-0.054	0.037	1.40E-01
rs6787172	G/T	0.047	0.040	2.48E-01	0.019	0.041	6.35E-01	0.012	0.031	6.94E-01	0.044	0.034	1.88E-01
rs3748034	T/G	-0.071	0.061	2.44E-01	0.038	0.060	5.24E-01	0.003	0.047	9.51E-01	0.009	0.049	8.53E-01
rs11940694	A/G	-0.016	0.058	7.86E-01	-0.029	0.042	4.92E-01	-0.017	0.039	6.54E-01	-0.020	0.034	5.65E-01
rs4501255	C/G	-0.017	0.072	8.12E-01	-0.024	0.050	6.24E-01	0.005	0.038	8.99E-01	-0.063	0.041	1.29E-01
rs1229984	T/C	-0.092	0.083	2.70E-01	0.023	0.086	7.90E-01	0.022	0.098	8.23E-01	-0.056	0.077	4.66E-01
rs2165670	G/A	0.019	0.075	7.99E-01	0.114	0.118	3.33E-01	Excluded for MR			0.008	0.059	8.92E-01
rs13107325	T/C	**-0.221**	**0.081**	**6.28E-03**	-0.012	0.093	8.95E-01	**-0.122**	**0.062**	**4.81E-02**	-0.040	0.068	5.58E-01
rs4690727	C/G	-0.016	0.045	7.21E-01	-0.016	0.046	7.30E-01	-0.043	0.035	2.22E-01	0.043	0.038	2.52E-01
rs12651313	G/C	Excluded for MR											
rs4916723	C/A	-0.051	0.056	3.56E-01	-0.056	0.044	1.97E-01	-0.023	0.034	4.87E-01	-0.056	0.036	1.13E-01
rs12655091	A/G	-0.013	0.041	7.56E-01	0.005	0.053	9.24E-01	-0.035	0.032	2.76E-01	-0.022	0.034	5.24E-01
rs55872084	G/T	0.085	0.050	9.28E-02	-0.014	0.051	7.87E-01	0.019	0.039	6.35E-01	-0.021	0.041	6.17E-01
rs6460047	T/C	0.019	0.053	7.27E-01	-0.001	0.069	9.93E-01	-0.003	0.041	9.41E-01	-0.034	0.043	4.23E-01
rs10236149	G/A	0.058	0.060	3.29E-01	0.039	0.061	5.15E-01	0.086	0.046	6.46E-02	0.045	0.051	3.77E-01
rs35034355	A/G	0.009	0.040	8.24E-01	-0.015	0.041	7.19E-01	-0.011	0.032	7.22E-01	-0.013	0.034	7.10E-01
rs6951574	T/C	-0.007	0.042	8.71E-01	-0.008	0.042	8.42E-01	-0.030	0.033	3.52E-01	0.030	0.035	3.87E-01
rs13250583	T/C	-0.022	0.052	6.80E-01	-0.009	0.053	8.68E-01	-0.018	0.041	6.55E-01	-0.009	0.043	8.37E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs1217091	T/C	0.049	0.052	3.51E-01	0.090	0.054	9.42E-02	**0.090**	**0.041**	**2.72E-02**	0.063	0.043	1.45E-01
rs28601761	C/G	Excluded for MR											
rs55932213	A/G	-0.051	0.048	2.87E-01	0.002	0.049	9.70E-01	-0.014	0.037	7.17E-01	-0.020	0.040	6.15E-01
rs10978550	C/T	0.017	0.052	7.39E-01	0.004	0.071	9.50E-01	0.008	0.045	8.54E-01	0.028	0.042	5.09E-01
rs7074871	A/G	0.014	0.068	8.41E-01	0.001	0.047	9.81E-01	0.033	0.036	3.65E-01	-0.013	0.039	7.35E-01
rs17665139	T/C	0.033	0.059	5.78E-01	0.002	0.058	9.68E-01	0.061	0.058	2.91E-01	-0.039	0.049	4.30E-01
rs7950166	T/C	-0.039	0.042	3.50E-01	0.011	0.043	7.96E-01	-0.020	0.042	6.35E-01	-0.038	0.035	2.74E-01
rs11030084	T/C	-0.059	0.051	2.48E-01	0.020	0.052	7.04E-01	-0.031	0.040	4.42E-01	-0.024	0.043	5.80E-01
rs56030824	A/G	0.016	0.043	7.06E-01	<0.001	0.044	9.92E-01	<0.001	0.048	9.94E-01	0.050	0.036	1.63E-01
rs10750025	C/T	0.008	0.045	8.67E-01	-0.056	0.044	2.02E-01	-0.025	0.034	4.62E-01	0.004	0.040	9.13E-01
rs4938230	C/A	Excluded for MR											
rs682011	T/C	-0.053	0.041	1.99E-01	-0.012	0.041	7.72E-01	-0.038	0.035	2.73E-01	-0.017	0.034	6.14E-01
rs12795042	C/A	-0.002	0.044	9.60E-01	-0.034	0.044	4.40E-01	0.018	0.034	6.06E-01	-0.043	0.036	2.34E-01
rs3809162	A/G	-0.014	0.043	7.52E-01	-0.034	0.044	4.38E-01	-0.054	0.034	1.10E-01	0.010	0.046	8.30E-01
rs10506274	T/G	0.054	0.041	1.84E-01	-0.013	0.041	7.55E-01	0.036	0.032	2.53E-01	-0.013	0.034	7.10E-01
rs4842786	A/G	-0.020	0.042	6.27E-01	0.012	0.043	7.80E-01	0.002	0.033	9.57E-01	-0.002	0.035	9.52E-01
rs500321	T/A	<0.001	0.046	9.98E-01	0.026	0.048	5.91E-01	0.037	0.036	3.03E-01	-0.045	0.039	2.50E-01
rs1123285	G/C	0.024	0.064	7.06E-01	-0.066	0.044	1.34E-01	-0.059	0.034	8.19E-02	0.002	0.036	9.56E-01
rs28929474	T/C	Excluded for MR											
rs2472297	C/T	-0.022	0.056	6.93E-01	-0.011	0.072	8.75E-01	-0.077	0.046	9.74E-02	-0.021	0.045	6.43E-01
rs12907323	A/G	-0.016	0.041	6.94E-01	0.039	0.042	3.51E-01	0.045	0.032	1.65E-01	-0.010	0.034	7.59E-01
rs17177078	T/C	-0.035	0.074	6.35E-01	-0.001	0.079	9.90E-01	-0.020	0.059	7.30E-01	-0.015	0.064	8.18E-01
rs378421	A/G	-0.036	0.043	4.02E-01	0.006	0.043	8.93E-01	-0.034	0.033	3.07E-01	-0.038	0.035	2.76E-01
rs62044525	G/C	**0.119**	**0.053**	**2.42E-02**	0.071	0.053	1.81E-01	**0.098**	**0.041**	**1.76E-02**	0.053	0.044	2.27E-01
rs1104608	C/G	Excluded for MR											
rs4548913	A/G	-0.019	0.042	6.57E-01	0.024	0.044	5.87E-01	0.005	0.048	9.21E-01	-0.046	0.035	1.98E-01
rs3803800	A/G	0.037	0.053	4.91E-01	-0.004	0.052	9.40E-01	0.018	0.050	7.18E-01	-0.001	0.043	9.75E-01
rs2854334	A/G	Excluded for MR						**0.076**	**0.037**	**4.14E-02**	-0.018	0.039	6.37E-01
rs10438820	C/T	**0.088**	**0.044**	**4.55E-02**	0.019	0.046	6.78E-01	0.027	0.035	4.48E-01	0.061	0.037	1.00E-01
rs9950000	T/C	-0.023	0.041	5.82E-01	-0.011	0.042	7.96E-01	-0.040	0.032	2.18E-01	0.019	0.035	5.89E-01
rs4092465	G/A	NA in COURAGE-PD											
rs281379	G/A	0.052	0.058	3.67E-01	0.038	0.042	3.57E-01	0.054	0.032	9.22E-02	-0.013	0.034	6.96E-01
rs4815364	G/A	0.042	0.043	3.27E-01	0.063	0.043	1.48E-01	0.050	0.033	1.33E-01	0.011	0.036	7.65E-01
rs9607814	A/C	**-0.162**	**0.051**	**1.56E-03**	**-0.116**	**0.051**	**2.41E-02**	**-0.118**	**0.040**	**3.19E-03**	**-0.144**	**0.058**	**1.34E-02**
Coffee drinking (per ln(cups per day))													
rs574367	T/G	-0.105	0.077	1.73E-01	-0.094	0.055	8.85E-02	**-0.148**	**0.061**	**1.43E-02**	-0.103	0.061	9.03E-02
rs10865548	G/A	-0.037	0.052	4.76E-01	0.083	0.072	2.48E-01	-0.005	0.040	9.10E-01	0.032	0.044	4.66E-01
rs1260326	C/T	**0.103**	**0.042**	**1.35E-02**	0.072	0.042	8.51E-02	**0.075**	**0.032**	**2.05E-02**	**0.070**	**0.035**	**4.42E-02**
rs4410790	C/T	-0.027	0.042	5.17E-01	0.008	0.043	8.48E-01	-0.030	0.044	4.94E-01	-0.008	0.035	8.24E-01
rs34060476	G/A	0.067	0.066	3.07E-01	0.002	0.066	9.76E-01	0.020	0.052	6.95E-01	0.082	0.053	1.18E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs1057868	T/C	0.005	0.061	9.28E-01	0.031	0.045	4.86E-01	0.019	0.035	5.93E-01	0.031	0.037	4.02E-01
rs597045	A/T	0.011	0.044	7.99E-01	-0.015	0.045	7.39E-01	-0.039	0.050	4.40E-01	0.006	0.037	8.64E-01
rs1956218	G/A	-0.048	0.041	2.45E-01	0.002	0.041	9.61E-01	-0.036	0.032	2.59E-01	-0.026	0.034	4.51E-01
rs2472297	T/C	0.022	0.056	6.93E-01	0.011	0.072	8.75E-01	0.077	0.046	9.74E-02	0.021	0.045	6.43E-01
rs66723169	A/C	-0.004	0.049	9.38E-01	-0.057	0.050	2.53E-01	0.005	0.038	8.91E-01	-0.057	0.041	1.64E-01
rs2330783	G/T	Excluded for MR											
Lifetime smoking index													
rs1193237	C/G	Excluded for MR											
rs4949465	C/T	-0.007	0.064	9.13E-01	0.004	0.064	9.54E-01	0.016	0.049	7.50E-01	0.010	0.052	8.48E-01
rs549845	G/A	-0.102	0.066	1.19E-01	0.030	0.045	5.05E-01	-0.060	0.046	1.93E-01	-0.046	0.047	3.27E-01
rs1933270	T/G	0.044	0.042	3.00E-01	0.020	0.042	6.34E-01	0.038	0.033	2.49E-01	**0.075**	**0.035**	**3.33E-02**
rs7528604	G/A	0.018	0.040	6.57E-01	-0.005	0.041	9.01E-01	0.007	0.032	8.13E-01	0.014	0.042	7.39E-01
rs11210229	A/G	-0.041	0.042	3.19E-01	-0.005	0.042	9.08E-01	-0.015	0.032	6.43E-01	-0.008	0.035	8.21E-01
rs7553348	G/A	0.003	0.042	9.41E-01	-0.018	0.043	6.65E-01	0.008	0.033	8.07E-01	0.008	0.035	8.29E-01
rs10922907	A/T	Excluded for MR											
rs1931263	T/G	0.010	0.041	8.15E-01	-0.048	0.041	2.47E-01	-0.027	0.032	3.91E-01	-0.041	0.034	2.28E-01
rs7519626	C/T	0.007	0.044	8.68E-01	0.001	0.044	9.84E-01	-0.015	0.044	7.30E-01	0.035	0.036	3.32E-01
rs9435340	T/A	NA			-0.010	0.044	8.16E-01	0.002	0.034	9.44E-01	0.019	0.036	5.96E-01
rs10918701	G/A	0.004	0.042	9.15E-01	-0.077	0.042	6.64E-02	0.002	0.043	9.54E-01	-0.018	0.035	6.11E-01
rs2867112	T/G	-0.044	0.054	4.11E-01	0.095	0.074	1.99E-01	-0.002	0.042	9.67E-01	0.028	0.045	5.42E-01
rs6741228	T/C	-0.021	0.057	7.13E-01	0.035	0.042	4.02E-01	-0.025	0.032	4.38E-01	0.009	0.034	7.82E-01
rs62135536	C/T	Excluded for MR						0.034	0.112	7.60E-01	-0.102	0.108	3.48E-01
rs7569203	C/A	0.025	0.044	5.65E-01	**0.093**	**0.044**	**3.61E-02**	**0.073**	**0.034**	**3.18E-02**	0.029	0.036	4.31E-01
rs13016665	A/C	0.006	0.042	8.87E-01	**0.103**	**0.043**	**1.58E-02**	0.046	0.033	1.61E-01	0.042	0.035	2.34E-01
rs4671357	C/T	0.002	0.042	9.70E-01	0.001	0.041	9.74E-01	0.018	0.032	5.84E-01	-0.030	0.036	3.99E-01
rs359243	C/T	-0.031	0.042	4.70E-01	0.050	0.043	2.49E-01	0.047	0.042	2.65E-01	-0.031	0.047	5.06E-01
rs2678670	A/T	Excluded for MR											
rs62155874	G/A	0.003	0.062	9.66E-01	-0.069	0.063	2.71E-01	-0.032	0.049	5.15E-01	-0.006	0.052	9.08E-01
rs3811038	C/T	-0.049	0.046	2.84E-01	-0.008	0.061	8.91E-01	0.001	0.036	9.82E-01	-0.011	0.038	7.74E-01
rs2890772	T/G	0.006	0.041	8.91E-01	0.040	0.042	3.38E-01	0.013	0.032	6.87E-01	-0.004	0.034	9.00E-01
rs62175972	T/C	0.075	0.111	5.03E-01	0.016	0.111	8.82E-01	0.093	0.087	2.85E-01	-0.009	0.090	9.19E-01
rs3769949	A/T	Excluded for MR											
rs13009008	A/G	0.057	0.042	1.77E-01	0.046	0.043	2.84E-01	0.008	0.033	8.02E-01	**0.079**	**0.036**	**2.72E-02**
rs4473348	T/A	0.006	0.048	8.95E-01	-0.085	0.049	8.13E-02	-0.071	0.037	5.79E-02	-0.014	0.040	7.24E-01
rs12623702	G/A	-0.035	0.042	4.06E-01	-0.012	0.043	7.74E-01	-0.028	0.033	3.92E-01	-0.054	0.035	1.26E-01
rs6779302	T/G	0.032	0.042	4.51E-01	0.049	0.043	2.55E-01	0.047	0.033	1.59E-01	0.011	0.035	7.45E-01
rs6778080	T/C	-0.014	0.046	7.67E-01	0.005	0.047	9.20E-01	0.005	0.042	8.97E-01	-0.023	0.038	5.52E-01
rs775758	A/T	Excluded for MR											
rs421983	T/C	-0.029	0.040	4.71E-01	0.020	0.041	6.25E-01	0.007	0.031	8.30E-01	-0.004	0.034	9.16E-01
rs326341	G/A	**-0.086**	**0.042**	**3.86E-02**	0.025	0.042	5.50E-01	-0.028	0.032	3.89E-01	-0.005	0.034	8.73E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs73220544	C/A	-0.086	0.060	1.50E-01	-0.050	0.085	5.54E-01	-0.037	0.047	4.26E-01	**-0.114**	**0.050**	**2.21E-02**
rs9842947	T/C	0.026	0.046	5.79E-01	0.020	0.046	6.69E-01	0.020	0.036	5.77E-01	0.045	0.038	2.39E-01
rs624833	T/G	-0.046	0.045	2.97E-01	-0.088	0.063	1.62E-01	**-0.113**	**0.034**	**1.02E-03**	-0.039	0.047	4.06E-01
rs61796681	T/A	0.068	0.078	3.85E-01	0.065	0.080	4.15E-01	0.074	0.061	2.27E-01	-0.007	0.066	9.17E-01
rs317021	A/T	0.007	0.075	9.23E-01	0.049	0.057	3.91E-01	**0.093**	**0.044**	**3.50E-02**	0.012	0.046	7.94E-01
rs72678864	G/A	0.050	0.057	3.86E-01	0.015	0.060	7.96E-01	0.065	0.046	1.54E-01	-0.008	0.048	8.68E-01
rs17576594	G/A	-0.059	0.046	2.01E-01	-0.009	0.047	8.42E-01	-0.026	0.036	4.67E-01	-0.063	0.038	9.77E-02
rs11948770	C/T	-0.026	0.049	6.00E-01	-0.045	0.049	3.57E-01	-0.017	0.038	6.52E-01	**-0.091**	**0.040**	**2.52E-02**
rs71627581	G/A	Excluded for MR											
rs10052591	T/C	0.036	0.041	3.74E-01	-0.008	0.041	8.45E-01	0.005	0.032	8.73E-01	0.059	0.034	8.25E-02
rs2080870	A/T	0.067	0.047	1.50E-01	0.080	0.048	9.20E-02	**0.086**	**0.037**	**1.91E-02**	0.051	0.039	1.95E-01
rs4571506	C/T	-0.072	0.052	1.67E-01	0.004	0.058	9.44E-01	-0.019	0.036	5.95E-01	**-0.076**	**0.034**	**2.58E-02**
rs4957528	C/A	Excluded for MR											
rs329120	C/T	-0.056	0.042	1.78E-01	-0.034	0.042	4.12E-01	**-0.070**	**0.032**	**2.94E-02**	0.009	0.034	7.96E-01
rs986391	G/A	-0.005	0.043	9.07E-01	-0.022	0.044	6.22E-01	-0.019	0.034	5.67E-01	-0.042	0.036	2.46E-01
rs13153393	G/A	0.046	0.102	6.54E-01	0.052	0.065	4.22E-01	0.002	0.071	9.75E-01	**0.134**	**0.054**	**1.30E-02**
rs245774	G/A	-0.060	0.046	1.88E-01	-0.054	0.046	2.40E-01	**-0.094**	**0.035**	**8.18E-03**	0.004	0.039	9.08E-01
rs6935954	A/G	0.021	0.042	6.24E-01	0.012	0.043	7.77E-01	-0.019	0.043	6.52E-01	**0.084**	**0.035**	**1.57E-02**
rs2254710	C/A	0.028	0.073	7.05E-01	0.055	0.051	2.87E-01	0.022	0.039	5.78E-01	0.041	0.041	3.18E-01
rs2894808	A/T	0.034	0.067	6.09E-01	-0.020	0.071	7.74E-01	0.004	0.054	9.36E-01	0.043	0.057	4.55E-01
rs12202536	G/A	-0.043	0.041	2.99E-01	**-0.106**	**0.042**	**1.11E-02**	**-0.068**	**0.032**	**3.45E-02**	**-0.067**	**0.034**	**4.87E-02**
rs7766610	C/A	-0.101	0.074	1.71E-01	-0.044	0.055	4.18E-01	**-0.090**	**0.042**	**3.33E-02**	-0.014	0.067	8.34E-01
rs1922018	C/T	0.010	0.043	8.22E-01	0.001	0.044	9.77E-01	-0.004	0.033	8.98E-01	0.009	0.035	8.06E-01
rs10226228	G/A	-0.050	0.042	2.31E-01	-0.035	0.044	4.32E-01	-0.024	0.033	4.67E-01	-0.033	0.036	3.61E-01
rs11768481	C/A	Excluded for MR											
rs6962772	A/G	-0.059	0.057	2.95E-01	-0.019	0.057	7.36E-01	-0.058	0.044	1.90E-01	-0.026	0.047	5.80E-01
rs10282292	C/T	-0.026	0.043	5.40E-01	0.027	0.050	5.95E-01	0.006	0.033	8.52E-01	0.005	0.038	8.99E-01
rs2401924	G/C	Excluded for MR											
rs7807019	G/A	0.013	0.041	7.56E-01	0.004	0.042	9.21E-01	-0.006	0.032	8.59E-01	0.044	0.034	1.98E-01
rs6957896	T/C	-0.027	0.052	6.07E-01	-0.039	0.052	4.57E-01	-0.040	0.047	3.97E-01	-0.022	0.040	5.86E-01
rs4731925	T/C	-0.014	0.044	7.50E-01	-0.042	0.044	3.42E-01	0.026	0.045	5.54E-01	**-0.084**	**0.036**	**2.07E-02**
rs35169606	T/G	Excluded for MR											
rs11783093	C/T	-0.004	0.080	9.61E-01	0.011	0.055	8.47E-01	0.010	0.043	8.19E-01	-0.048	0.057	4.02E-01
rs2062882	A/G	0.007	0.042	8.71E-01	-0.024	0.041	5.56E-01	-0.007	0.035	8.41E-01	-0.054	0.044	2.21E-01
rs72674867	A/T	0.033	0.045	4.70E-01	0.042	0.047	3.75E-01	0.028	0.036	4.42E-01	-0.017	0.048	7.16E-01
rs4543592	C/T	-0.036	0.041	3.84E-01	-0.071	0.042	9.30E-02	-0.023	0.033	4.74E-01	-0.036	0.034	2.91E-01
rs7039819	G/A	-0.009	0.043	8.27E-01	0.002	0.043	9.58E-01	0.010	0.033	7.74E-01	-0.001	0.036	9.69E-01
rs1246265	C/T	0.061	0.045	1.76E-01	-0.006	0.045	8.95E-01	0.011	0.035	7.42E-01	-0.005	0.037	8.98E-01
rs1221148	C/G	0.056	0.043	1.89E-01	0.030	0.055	5.93E-01	0.050	0.034	1.34E-01	-0.031	0.035	3.86E-01
rs13296519	T/G	-0.016	0.059	7.89E-01	-0.044	0.043	3.01E-01	-0.020	0.033	5.53E-01	-0.010	0.035	7.76E-01
rs113382419	A/C	0.037	0.068	5.87E-01	-0.045	0.070	5.21E-01	0.036	0.054	5.01E-01	-0.073	0.060	2.24E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs11255908	G/T	0.008	0.045	8.66E-01	-0.036	0.048	4.45E-01	-0.014	0.036	6.93E-01	0.027	0.039	4.92E-01
rs2675638	G/A	0.014	0.064	8.32E-01	0.014	0.042	7.48E-01	-0.040	0.033	2.19E-01	-0.010	0.037	7.88E-01
rs10823968	A/T	0.002	0.044	9.55E-01	0.029	0.044	4.98E-01	0.028	0.034	4.09E-01	-0.010	0.036	7.76E-01
rs61857951	C/A	Excluded for MR											
rs7077678	C/T	-0.010	0.041	8.09E-01	-0.020	0.043	6.42E-01	-0.013	0.033	6.97E-01	0.007	0.035	8.40E-01
rs12244388	A/G	**-0.098**	**0.042**	**2.00E-02**	-0.048	0.042	2.57E-01	**-0.086**	**0.033**	**8.52E-03**	-0.036	0.035	2.95E-01
rs3896224	A/G	0.028	0.042	5.08E-01	-0.019	0.042	6.57E-01	-0.006	0.032	8.55E-01	0.004	0.034	9.12E-01
rs34866095	G/A	**-0.101**	**0.044**	**2.38E-02**	-0.051	0.045	2.49E-01	-0.020	0.034	5.70E-01	**-0.085**	**0.037**	**2.27E-02**
rs75742406	G/A	-0.050	0.049	3.10E-01	-0.063	0.051	2.19E-01	-0.033	0.039	4.01E-01	-0.052	0.050	2.97E-01
rs17309874	A/G	-0.059	0.051	2.45E-01	-0.032	0.051	5.30E-01	-0.054	0.039	1.67E-01	0.003	0.041	9.48E-01
rs4391802	A/G	0.003	0.045	9.41E-01	**0.113**	**0.046**	**1.34E-02**	0.051	0.035	1.51E-01	0.050	0.038	1.85E-01
rs112282219	A/G	-0.061	0.108	5.69E-01	Excluded for MR			0.022	0.087	7.97E-01	0.051	0.091	5.75E-01
rs9919670	A/G	-0.019	0.042	6.49E-01	-0.028	0.042	5.09E-01	-0.019	0.033	5.69E-01	-0.013	0.035	7.17E-01
rs74086911	G/A	**-0.201**	**0.079**	**1.13E-02**	0.116	0.083	1.60E-01	0.006	0.063	9.21E-01	**-0.134**	**0.065**	**3.97E-02**
rs7297175	C/T	0.042	0.043	3.25E-01	-0.044	0.044	3.16E-01	0.011	0.034	7.40E-01	0.029	0.036	4.21E-01
rs10879871	G/T	0.045	0.043	2.95E-01	-0.046	0.044	2.99E-01	-0.003	0.034	9.34E-01	-0.005	0.036	8.85E-01
rs12831617	T/C	-0.033	0.045	4.66E-01	0.047	0.047	3.18E-01	0.029	0.036	4.27E-01	0.021	0.039	5.84E-01
rs6562474	C/G	0.001	0.043	9.72E-01	0.041	0.043	3.45E-01	0.024	0.033	4.64E-01	-0.010	0.035	7.73E-01
rs7333559	G/A	-0.064	0.053	2.26E-01	-0.027	0.052	6.06E-01	-0.079	0.041	5.14E-02	0.009	0.055	8.73E-01
rs860326	C/T	0.049	0.063	4.35E-01	-0.023	0.043	5.97E-01	0.011	0.033	7.32E-01	-0.030	0.035	3.95E-01
rs7155595	C/A	0.009	0.045	8.44E-01	0.021	0.045	6.35E-01	-0.008	0.035	8.11E-01	0.004	0.048	9.26E-01
rs3742365	C/T	-0.012	0.043	7.80E-01	0.015	0.043	7.33E-01	0.001	0.033	9.72E-01	0.013	0.035	7.09E-01
rs35175834	A/G	-0.027	0.049	5.78E-01	-0.062	0.050	2.13E-01	-0.036	0.038	3.55E-01	-0.037	0.041	3.68E-01
rs28485305	C/T	0.036	0.042	3.86E-01	0.001	0.042	9.87E-01	0.058	0.033	7.68E-02	-0.040	0.035	2.41E-01
rs8042849	C/T	-0.035	0.043	4.26E-01	0.053	0.043	2.23E-01	0.032	0.034	3.33E-01	-0.041	0.036	2.60E-01
rs8042134	G/T	0.009	0.056	8.79E-01	0.067	0.042	1.11E-01	0.041	0.033	2.07E-01	0.026	0.035	4.49E-01
rs6598539	C/T	<0.001	0.042	9.98E-01	-0.017	0.042	6.94E-01	-0.021	0.033	5.27E-01	-0.013	0.047	7.88E-01
rs11861214	G/T	0.011	0.051	8.31E-01	0.050	0.052	3.35E-01	0.047	0.040	2.42E-01	0.044	0.042	2.91E-01
rs12708665	G/A	<0.001	0.044	9.99E-01	-0.065	0.045	1.51E-01	-0.038	0.035	2.68E-01	0.009	0.037	8.18E-01
rs57611503	G/A	Excluded for MR						**-0.111**	**0.036**	**2.14E-03**	-0.080	0.049	9.86E-02
rs889398	C/T	Excluded for MR						0.019	0.061	7.52E-01	0.019	0.060	7.47E-01
rs60952428	T/C	Excluded for MR											
rs1050847	C/T	0.006	0.042	8.81E-01	-0.014	0.043	7.39E-01	0.019	0.033	5.69E-01	**-0.074**	**0.035**	**3.51E-02**
rs369230	T/G	-0.019	0.048	6.94E-01	-0.057	0.049	2.47E-01	-0.036	0.038	3.44E-01	-0.044	0.050	3.75E-01
rs8614	A/C	**0.141**	**0.059**	**1.65E-02**	0.011	0.061	8.52E-01	**0.098**	**0.046**	**3.27E-02**	0.064	0.048	1.86E-01
rs732083	G/A	-0.041	0.044	3.57E-01	-0.015	0.045	7.45E-01	-0.035	0.035	3.06E-01	-0.031	0.037	4.04E-01
rs9904288	T/C	-0.016	0.045	7.19E-01	-0.038	0.046	4.13E-01	-0.037	0.035	2.92E-01	-0.007	0.038	8.61E-01
rs67596067	A/G	-0.026	0.043	5.42E-01	0.047	0.044	2.86E-01	0.008	0.034	8.12E-01	0.035	0.036	3.31E-01
rs12967855	A/G	**-0.102**	**0.044**	**2.06E-02**	0.010	0.045	8.31E-01	-0.052	0.035	1.33E-01	0.002	0.037	9.47E-01
rs62098013	A/G	0.067	0.044	1.22E-01	0.025	0.044	5.78E-01	**0.102**	**0.034**	**2.81E-03**	-0.014	0.050	7.77E-01
rs71367545	A/G	-0.063	0.054	2.41E-01	0.077	0.055	1.63E-01	-0.014	0.043	7.40E-01	0.062	0.044	1.64E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs76608582	C/A	NA in COURAGE-PD											
rs35343344	C/A	0.030	0.069	6.64E-01	0.068	0.050	1.76E-01	0.037	0.039	3.46E-01	0.040	0.041	3.31E-01
rs4814873	C/T	-0.008	0.048	8.62E-01	-0.043	0.049	3.80E-01	0.013	0.038	7.35E-01	**-0.079**	**0.040**	**4.76E-02**
rs6119897	A/G	0.034	0.053	5.18E-01	-0.061	0.053	2.42E-01	-0.032	0.041	4.40E-01	0.003	0.042	9.52E-01
rs12481282	C/G	-0.010	0.048	8.38E-01	-0.080	0.048	9.98E-02	-0.041	0.038	2.71E-01	-0.013	0.040	7.43E-01
rs348809	G/A	-0.024	0.043	5.77E-01	-0.005	0.043	9.07E-01	-0.037	0.044	4.06E-01	0.009	0.035	8.03E-01
rs6011779	C/T	-0.107	0.072	1.38E-01	0.042	0.051	4.17E-01	-0.056	0.040	1.63E-01	0.036	0.042	3.96E-01
rs147412694	A/G	-0.072	0.060	2.31E-01	0.053	0.060	3.76E-01	-0.024	0.047	6.03E-01	-0.032	0.050	5.20E-01
rs2838834	T/C	0.037	0.044	3.97E-01	-0.013	0.059	8.27E-01	0.003	0.035	9.26E-01	0.038	0.050	4.41E-01
rs136233	G/A	0.034	0.051	5.04E-01	**-0.114**	**0.052**	**2.98E-02**	-0.035	0.040	3.85E-01	-0.025	0.042	5.52E-01
rs202645	G/A	**0.172**	**0.051**	**7.11E-04**	0.100	0.067	1.37E-01	**0.121**	**0.039**	**2.13E-03**	**0.138**	**0.055**	**1.17E-02**
Smoking initiation (per 1-SD increase in the of prevalence of ever smoking)													
rs12130857	G/A	-0.028	0.043	5.16E-01	-0.009	0.045	8.38E-01	-0.038	0.034	2.70E-01	0.003	0.037	9.43E-01
rs3820277	G/T	-0.036	0.041	3.79E-01	-0.041	0.057	4.74E-01	-0.042	0.048	3.83E-01	-0.035	0.034	3.02E-01
rs1889571	G/T	-0.002	0.065	9.81E-01	0.009	0.065	8.91E-01	0.030	0.050	5.48E-01	0.011	0.053	8.27E-01
rs10914684	G/A	0.010	0.043	8.11E-01	-0.023	0.044	5.93E-01	-0.039	0.034	2.45E-01	0.006	0.036	8.72E-01
rs951740	A/G	-0.109	0.059	6.57E-02	0.033	0.043	4.44E-01	-0.039	0.033	2.43E-01	-0.055	0.046	2.28E-01
rs12022778	C/A	0.068	0.052	1.93E-01	-0.012	0.054	8.26E-01	0.042	0.041	3.11E-01	0.078	0.061	2.05E-01
rs4912332	T/C	0.074	0.057	1.95E-01	0.036	0.042	3.91E-01	**0.084**	**0.032**	**8.77E-03**	-0.031	0.034	3.67E-01
rs80054503	T/C	NA in COURAGE-PD											
rs10789369	A/G	-0.046	0.042	2.72E-01	-0.047	0.043	2.74E-01	-0.034	0.033	2.93E-01	-0.018	0.035	5.99E-01
rs1514176	G/A	-0.001	0.042	9.82E-01	0.023	0.055	6.72E-01	0.005	0.033	8.82E-01	0.014	0.035	6.99E-01
rs11162019	C/T	-0.010	0.043	8.17E-01	-0.031	0.044	4.86E-01	-0.016	0.034	6.38E-01	-0.034	0.036	3.45E-01
rs1008078	T/C	-0.052	0.041	2.07E-01	0.047	0.042	2.61E-01	-0.038	0.041	3.54E-01	0.008	0.055	8.86E-01
rs12027999	T/C	-0.007	0.067	9.15E-01	0.096	0.086	2.67E-01	0.028	0.052	5.98E-01	-0.009	0.056	8.70E-01
rs45444697	G/C	-0.013	0.053	8.02E-01	-0.011	0.075	8.78E-01	-0.016	0.042	6.98E-01	0.005	0.043	9.04E-01
rs2901785	G/A	0.041	0.054	4.44E-01	0.004	0.053	9.37E-01	0.052	0.045	2.47E-01	-0.015	0.034	6.67E-01
rs147052174	T/G	Excluded for MR											
rs35656245	A/G	0.006	0.044	8.97E-01	-0.019	0.045	6.79E-01	-0.006	0.046	8.90E-01	-0.007	0.037	8.44E-01
rs12739243	T/C	0.003	0.048	9.44E-01	-0.017	0.050	7.41E-01	0.035	0.038	3.65E-01	0.013	0.040	7.50E-01
rs876793	T/C	0.034	0.045	4.43E-01	0.084	0.045	6.08E-02	0.005	0.051	9.27E-01	**0.074**	**0.037**	**4.37E-02**
rs6731872	G/T	-0.026	0.051	6.20E-01	0.058	0.053	2.71E-01	0.005	0.040	9.04E-01	0.029	0.044	5.08E-01
rs1022376	T/C	0.020	0.041	6.25E-01	0.015	0.042	7.27E-01	-0.005	0.032	8.74E-01	0.023	0.035	5.12E-01
rs61533748	C/T	-0.011	0.057	8.50E-01	0.042	0.043	3.29E-01	-0.020	0.034	5.53E-01	0.021	0.036	5.53E-01
rs2710634	T/C	-0.035	0.041	4.02E-01	-0.031	0.042	4.52E-01	-0.027	0.032	4.00E-01	-0.054	0.034	1.12E-01
rs7598402	C/G	Excluded for MR											
rs10490159	T/C	-0.009	0.041	8.29E-01	**-0.124**	**0.055**	**2.37E-02**	-0.006	0.032	8.42E-01	-0.061	0.034	7.61E-02
rs359247	T/A	-0.009	0.042	8.32E-01	0.022	0.043	6.13E-01	0.020	0.033	5.49E-01	-0.025	0.035	4.88E-01
rs12714017	C/T	0.042	0.041	3.10E-01	-0.018	0.042	6.76E-01	-0.019	0.032	5.63E-01	0.059	0.034	8.36E-02
rs13392222	A/C	0.067	0.065	3.01E-01	0.005	0.088	9.54E-01	0.022	0.050	6.57E-01	-0.032	0.052	5.34E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs1901477	G/A	-0.031	0.041	4.48E-01	0.047	0.041	2.57E-01	<0.001	0.043	9.94E-01	0.034	0.050	5.03E-01
rs3811038	C/T	-0.049	0.046	2.84E-01	-0.008	0.061	8.91E-01	0.001	0.036	9.82E-01	-0.011	0.038	7.74E-01
rs34399632	G/A	0.050	0.059	3.98E-01	-0.026	0.084	7.58E-01	0.001	0.059	9.81E-01	-0.052	0.046	2.50E-01
rs6756212	C/T	-0.022	0.041	5.97E-01	0.027	0.041	5.15E-01	-0.015	0.032	6.33E-01	-0.015	0.034	6.52E-01
rs16826827	T/C	-0.003	0.065	9.68E-01	-0.086	0.064	1.79E-01	-0.054	0.049	2.77E-01	-0.017	0.052	7.41E-01
rs1445649	C/T	0.005	0.041	9.11E-01	-0.059	0.041	1.51E-01	-0.014	0.032	6.50E-01	-0.033	0.034	3.25E-01
rs12474587	T/G	0.081	0.042	5.53E-02	0.019	0.043	6.63E-01	0.062	0.033	6.28E-02	0.021	0.035	5.59E-01
rs13007361	A/G	0.047	0.072	5.12E-01	0.007	0.049	8.93E-01	**0.082**	**0.038**	**2.98E-02**	-0.053	0.042	2.05E-01
rs6750529	T/C	0.004	0.047	9.30E-01	-0.066	0.048	1.66E-01	-0.054	0.037	1.43E-01	-0.006	0.039	8.79E-01
rs17229285	C/T	0.058	0.065	3.73E-01	-0.038	0.042	3.62E-01	-0.016	0.032	6.17E-01	0.040	0.035	2.49E-01
rs62193862	A/G	Excluded for MR											
rs4674993	A/G	0.015	0.052	7.70E-01	0.034	0.075	6.51E-01	0.044	0.057	4.37E-01	-0.048	0.053	3.67E-01
rs11713899	C/A	-0.049	0.053	3.55E-01	-0.006	0.055	9.18E-01	-0.082	0.042	5.29E-02	0.016	0.045	7.20E-01
rs748832	G/A	0.045	0.043	2.91E-01	0.054	0.044	2.15E-01	0.062	0.034	6.52E-02	0.020	0.035	5.64E-01
rs2526390	T/C	-0.061	0.062	3.29E-01	0.049	0.044	2.62E-01	-0.001	0.034	9.69E-01	-0.006	0.036	8.58E-01
rs221988	A/C	0.047	0.066	4.75E-01	-0.017	0.044	7.02E-01	0.049	0.034	1.52E-01	-0.009	0.036	8.02E-01
rs11128203	A/T	Excluded for MR											
rs62246017	G/A	-0.028	0.045	5.31E-01	-0.046	0.046	3.14E-01	-0.038	0.036	2.84E-01	-0.050	0.048	2.92E-01
rs12633090	G/C	0.087	0.052	9.46E-02	0.014	0.052	7.87E-01	0.072	0.057	2.06E-01	0.021	0.059	7.17E-01
rs1549979	C/T	0.037	0.042	3.75E-01	0.017	0.042	6.91E-01	-0.009	0.033	7.83E-01	0.050	0.035	1.51E-01
rs6437769	T/C	-0.028	0.057	6.21E-01	0.086	0.058	1.40E-01	0.032	0.033	3.31E-01	0.013	0.034	7.11E-01
rs9288999	A/G	0.018	0.046	6.98E-01	**-0.137**	**0.048**	**4.24E-03**	-0.044	0.036	2.31E-01	-0.067	0.038	7.91E-02
rs6438436	T/C	0.028	0.084	7.40E-01	0.075	0.057	1.86E-01	0.016	0.043	7.09E-01	0.071	0.046	1.24E-01
rs9826984	G/A	0.017	0.042	6.89E-01	0.029	0.042	4.82E-01	-0.019	0.032	5.65E-01	**0.069**	**0.034**	**4.42E-02**
rs2279829	C/T	0.057	0.053	2.82E-01	0.027	0.053	6.13E-01	0.026	0.041	5.31E-01	-0.004	0.043	9.28E-01
rs2319545	A/C	-0.025	0.063	6.86E-01	-0.020	0.062	7.46E-01	-0.019	0.066	7.70E-01	0.032	0.050	5.31E-01
rs1714521	A/C	-0.034	0.042	4.12E-01	-0.036	0.043	4.06E-01	0.002	0.033	9.41E-01	-0.036	0.044	4.10E-01
rs1449012	C/T	0.034	0.054	5.29E-01	-0.048	0.042	2.57E-01	-0.024	0.044	5.79E-01	0.066	0.034	5.49E-02
rs1187820	C/T	0.031	0.044	4.84E-01	0.069	0.061	2.61E-01	0.002	0.035	9.57E-01	0.037	0.053	4.82E-01
rs7631379	C/T	0.010	0.076	8.92E-01	-0.133	0.074	7.15E-02	0.006	0.043	8.86E-01	**-0.093**	**0.046**	**4.13E-02**
rs4140932	T/A	Excluded for MR											
rs59537158	T/C	**-0.109**	**0.053**	**4.12E-02**	0.070	0.054	1.96E-01	-0.049	0.042	2.43E-01	0.048	0.043	2.69E-01
rs58400863	G/A	0.018	0.043	6.85E-01	0.048	0.044	2.68E-01	-0.003	0.034	9.39E-01	0.029	0.036	4.24E-01
rs112725451	T/C	-0.016	0.052	7.54E-01	0.055	0.054	3.04E-01	-0.013	0.041	7.51E-01	0.030	0.044	4.97E-01
rs1160685	G/C	Excluded for MR											
rs3934797	G/A	0.020	0.055	7.12E-01	0.010	0.058	8.60E-01	0.041	0.044	3.54E-01	0.003	0.068	9.60E-01
rs71602617	C/T	-0.016	0.052	7.64E-01	0.047	0.064	4.60E-01	-0.035	0.040	3.84E-01	0.033	0.042	4.42E-01
rs7696257	A/G	0.020	0.043	6.40E-01	-0.035	0.044	4.17E-01	0.024	0.034	4.68E-01	-0.041	0.036	2.53E-01
rs1116690	G/A	-0.061	0.048	2.03E-01	-0.046	0.050	3.58E-01	-0.049	0.038	1.95E-01	0.001	0.040	9.78E-01
rs13110073	T/C	-0.010	0.042	8.02E-01	-0.074	0.042	7.85E-02	-0.054	0.032	9.92E-02	-0.052	0.035	1.38E-01
rs62340589	C/G	-0.067	0.054	2.14E-01	0.048	0.053	3.65E-01	0.014	0.042	7.40E-01	-0.011	0.044	8.02E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs12517438	G/T	0.040	0.041	3.23E-01	-0.003	0.042	9.36E-01	0.026	0.032	4.05E-01	-0.009	0.034	7.92E-01
rs35375873	G/C	Excluded for MR											
rs71592686	C/T	0.048	0.046	2.94E-01	0.053	0.046	2.50E-01	**0.085**	**0.036**	**1.71E-02**	0.023	0.038	5.57E-01
rs6874731	G/T	0.017	0.041	6.81E-01	-0.020	0.041	6.28E-01	0.008	0.032	7.94E-01	-0.022	0.034	5.22E-01
rs6452785	C/T	-0.066	0.041	1.05E-01	0.013	0.058	8.20E-01	-0.012	0.032	7.16E-01	-0.065	0.034	5.53E-02
rs42417	T/C	-0.070	0.046	1.32E-01	-0.129	0.072	7.50E-02	**-0.116**	**0.052**	**2.51E-02**	-0.055	0.038	1.52E-01
rs72780746	T/C	**-0.134**	**0.051**	**9.26E-03**	0.002	0.052	9.64E-01	-0.063	0.040	1.15E-01	-0.049	0.043	2.53E-01
rs329124	A/G	-0.040	0.041	3.31E-01	-0.045	0.042	2.78E-01	-0.061	0.032	5.71E-02	0.004	0.034	9.07E-01
rs1385108	T/C	-0.011	0.049	8.25E-01	0.033	0.050	5.11E-01	-0.005	0.038	8.96E-01	-0.016	0.040	6.92E-01
rs6890961	C/T	-0.109	0.066	1.00E-01	0.007	0.044	8.74E-01	-0.018	0.034	5.91E-01	-0.064	0.036	7.78E-02
rs4044321	A/G	-0.003	0.043	9.46E-01	-0.016	0.044	7.20E-01	-0.010	0.034	7.62E-01	-0.045	0.036	2.18E-01
rs2173019	A/T	0.050	0.080	5.29E-01	0.021	0.055	7.03E-01	0.018	0.043	6.71E-01	**0.091**	**0.045**	**4.15E-02**
rs1150668	T/G	-0.027	0.042	5.20E-01	0.034	0.044	4.34E-01	0.021	0.033	5.31E-01	-0.006	0.035	8.69E-01
rs3218116	C/T	-0.045	0.079	5.65E-01	0.013	0.049	7.85E-01	0.001	0.038	9.78E-01	-0.026	0.040	5.14E-01
rs160631	T/G	0.063	0.046	1.71E-01	0.040	0.047	3.88E-01	**0.071**	**0.036**	**4.84E-02**	0.011	0.038	7.71E-01
rs7743165	G/T	<0.001	0.062	9.94E-01	**-0.104**	**0.042**	**1.26E-02**	**-0.065**	**0.032**	**4.49E-02**	-0.059	0.044	1.85E-01
rs10945141	A/G	-0.002	0.046	9.72E-01	0.017	0.047	7.21E-01	-0.011	0.036	7.59E-01	0.040	0.038	2.90E-01
rs17554906	C/G	Excluded for MR											
rs6568832	A/G	**-0.096**	**0.048**	**4.55E-02**	0.006	0.049	9.01E-01	-0.022	0.038	5.57E-01	-0.026	0.040	5.11E-01
rs12195240	A/G	0.009	0.045	8.37E-01	**-0.096**	**0.044**	**3.03E-02**	-0.031	0.034	3.68E-01	-0.023	0.037	5.24E-01
rs6936160	T/C	0.080	0.045	7.41E-02	-0.001	0.045	9.80E-01	0.053	0.035	1.26E-01	-0.025	0.037	4.99E-01
rs118202	G/T	-0.098	0.075	1.91E-01	-0.045	0.055	4.08E-01	**-0.093**	**0.042**	**2.82E-02**	-0.016	0.067	8.08E-01
rs1737329	G/C	-0.041	0.047	3.84E-01	0.011	0.067	8.70E-01	-0.024	0.037	5.14E-01	-0.001	0.053	9.85E-01
rs6948707	G/T	-0.003	0.041	9.51E-01	-0.032	0.057	5.73E-01	0.002	0.032	9.45E-01	0.007	0.035	8.48E-01
rs7809303	G/A	**-0.104**	**0.043**	**1.68E-02**	-0.020	0.044	6.52E-01	**-0.068**	**0.034**	**4.63E-02**	-0.063	0.036	8.17E-02
rs1030015	T/G	-0.028	0.049	5.61E-01	0.014	0.051	7.81E-01	0.026	0.048	5.80E-01	-0.011	0.034	7.56E-01
rs4727189	C/T	**0.083**	**0.042**	**4.58E-02**	-0.005	0.043	9.08E-01	-0.004	0.033	8.94E-01	0.068	0.035	5.47E-02
rs11768481	C/A	Excluded for MR											
rs13437771	A/G	-0.060	0.057	2.93E-01	-0.018	0.057	7.46E-01	-0.058	0.044	1.88E-01	-0.025	0.047	5.92E-01
rs10233018	G/A	0.011	0.041	7.88E-01	0.008	0.042	8.42E-01	-0.017	0.032	5.93E-01	0.054	0.034	1.13E-01
rs10953957	A/G	0.071	0.055	1.99E-01	-0.017	0.043	6.83E-01	0.023	0.033	4.76E-01	0.048	0.035	1.75E-01
rs77283305	G/A	-0.018	0.044	6.84E-01	-0.047	0.044	2.92E-01	0.015	0.035	6.60E-01	**-0.085**	**0.036**	**1.86E-02**
rs10279261	G/A	-0.011	0.062	8.58E-01	-0.019	0.044	6.62E-01	0.011	0.034	7.33E-01	-0.037	0.036	3.10E-01
rs4326350	C/G	Excluded for MR											
rs11783093	C/T	-0.004	0.080	9.61E-01	0.011	0.055	8.47E-01	0.010	0.043	8.19E-01	-0.048	0.057	4.02E-01
rs7836565	C/T	0.038	0.046	4.09E-01	**0.114**	**0.046**	**1.37E-02**	0.047	0.036	1.90E-01	0.083	0.038	2.82E-02
rs13261666	G/T	-0.052	0.055	3.41E-01	-0.020	0.041	6.28E-01	-0.014	0.032	6.54E-01	-0.020	0.034	5.59E-01
rs3850736	G/C	Excluded for MR											
rs2063976	C/T	0.021	0.043	6.34E-01	-0.059	0.044	1.79E-01	0.001	0.034	9.71E-01	-0.030	0.036	4.14E-01
rs6986430	T/C	-0.034	0.048	4.73E-01	0.068	0.049	1.63E-01	-0.010	0.037	7.85E-01	0.053	0.040	1.86E-01
rs290601	T/C	0.040	0.046	3.85E-01	0.032	0.047	4.89E-01	0.039	0.035	2.76E-01	-0.027	0.038	4.80E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs3847244	T/C	-0.046	0.042	2.72E-01	-0.058	0.043	1.78E-01	-0.028	0.033	3.99E-01	-0.036	0.035	3.10E-01
rs11791671	T/C	-0.027	0.130	8.34E-01	-0.016	0.088	8.57E-01	-0.012	0.096	9.00E-01	0.078	0.088	3.78E-01
rs7024924	C/T	-0.061	0.054	2.61E-01	-0.014	0.055	7.92E-01	-0.010	0.042	8.15E-01	-0.002	0.045	9.71E-01
rs10966092	T/C	-0.009	0.047	8.53E-01	-0.046	0.046	3.24E-01	-0.048	0.046	2.95E-01	0.018	0.039	6.42E-01
rs4877285	G/A	-0.069	0.074	3.53E-01	-0.046	0.060	4.47E-01	-0.036	0.034	2.92E-01	**-0.088**	**0.037**	**1.58E-02**
rs2378662	A/G	0.019	0.043	6.51E-01	-0.019	0.067	7.81E-01	-0.017	0.044	6.96E-01	0.011	0.035	7.57E-01
rs4837631	C/T	0.049	0.042	2.44E-01	0.028	0.043	5.08E-01	0.045	0.033	1.72E-01	-0.028	0.035	4.29E-01
rs34553878	G/A	Excluded for MR											
rs10858334	G/C	-0.076	0.060	2.11E-01	-0.124	0.079	1.14E-01	-0.068	0.048	1.55E-01	-0.076	0.069	2.72E-01
rs7920501	T/A	Excluded for MR											
rs1291821	G/A	-0.012	0.041	7.65E-01	0.004	0.042	9.20E-01	-0.024	0.032	4.64E-01	-0.009	0.034	7.95E-01
rs7072776	A/G	0.020	0.047	6.77E-01	-0.019	0.048	6.98E-01	-0.014	0.037	6.99E-01	0.040	0.040	3.10E-01
rs2796793	A/G	**0.100**	**0.043**	**2.11E-02**	0.011	0.043	7.88E-01	**0.081**	**0.033**	**1.55E-02**	0.038	0.053	4.73E-01
rs1733760	C/T	-0.005	0.042	8.98E-01	0.008	0.043	8.57E-01	-0.014	0.033	6.73E-01	0.052	0.035	1.38E-01
rs7921378	G/C	Excluded for MR											
rs11594623	C/T	-0.043	0.050	3.89E-01	**-0.133**	**0.051**	**9.75E-03**	-0.076	0.039	5.41E-02	-0.032	0.042	4.36E-01
rs12244388	A/G	**-0.098**	**0.042**	**2.00E-02**	-0.048	0.042	2.57E-01	**-0.086**	**0.033**	**8.52E-03**	-0.036	0.035	2.95E-01
rs10885480	T/C	-0.072	0.047	1.28E-01	0.046	0.047	3.35E-01	0.003	0.037	9.34E-01	-0.044	0.039	2.54E-01
rs4752018	A/C	-0.040	0.048	4.02E-01	0.017	0.049	7.27E-01	-0.049	0.050	3.33E-01	-0.030	0.040	4.63E-01
rs9423279	C/G	Excluded for MR											
rs6265	C/T	0.060	0.052	2.46E-01	-0.012	0.052	8.17E-01	0.039	0.040	3.30E-01	0.023	0.043	5.88E-01
rs2939756	G/A	-0.019	0.041	6.33E-01	-0.010	0.042	8.17E-01	-0.019	0.032	5.52E-01	-0.017	0.034	6.28E-01
rs1381775	T/C	-0.006	0.046	9.02E-01	-0.071	0.047	1.26E-01	-0.034	0.036	3.45E-01	-0.060	0.038	1.14E-01
rs61886926	C/T	-0.056	0.042	1.82E-01	-0.003	0.064	9.63E-01	-0.020	0.033	5.38E-01	-0.001	0.044	9.78E-01
rs644740	C/T	-0.015	0.041	7.21E-01	-0.008	0.041	8.48E-01	-0.015	0.032	6.42E-01	-0.003	0.034	9.33E-01
rs7943721	G/A	NA in COURAGE-PD											
rs7929518	G/A	<0.001	0.048	9.99E-01	-0.027	0.048	5.75E-01	-0.042	0.037	2.55E-01	-0.014	0.040	7.20E-01
rs2155646	C/T	-0.018	0.042	6.63E-01	-0.027	0.042	5.27E-01	-0.018	0.033	5.81E-01	-0.012	0.035	7.24E-01
rs1713676	A/G	0.019	0.042	6.49E-01	0.060	0.045	1.86E-01	0.048	0.032	1.31E-01	0.039	0.034	2.56E-01
rs540860	G/A	0.061	0.040	1.34E-01	0.030	0.042	4.67E-01	0.034	0.032	2.82E-01	0.055	0.034	1.04E-01
rs1106363	T/C	-0.013	0.042	7.62E-01	0.057	0.043	1.83E-01	-0.026	0.033	4.26E-01	0.067	0.035	5.57E-02
rs2010921	A/G	0.017	0.045	6.98E-01	0.034	0.045	4.48E-01	0.037	0.035	2.88E-01	0.037	0.037	3.29E-01
rs11057005	A/G	-0.045	0.061	4.57E-01	-0.082	0.043	6.05E-02	-0.033	0.048	4.92E-01	-0.021	0.036	5.62E-01
rs13906	C/T	**-0.139**	**0.066**	**3.55E-02**	0.122	0.068	7.26E-02	0.058	0.052	2.72E-01	-0.057	0.054	2.95E-01
rs4759229	G/A	0.008	0.060	8.94E-01	-0.005	0.046	9.20E-01	<0.001	0.036	9.94E-01	0.008	0.037	8.29E-01
rs7969559	A/G	-0.018	0.044	6.75E-01	-0.038	0.045	3.88E-01	-0.065	0.035	6.19E-02	0.041	0.037	2.70E-01
rs7134009	T/C	-0.006	0.044	8.96E-01	-0.030	0.044	4.95E-01	-0.030	0.034	3.79E-01	<0.001	0.037	9.92E-01
rs77215829	A/C	Excluded for MR						0.041	0.084	6.22E-01	-0.030	0.066	6.45E-01
rs1109480	G/A	-0.021	0.043	6.22E-01	-0.041	0.043	3.33E-01	-0.043	0.033	1.99E-01	-0.026	0.035	4.61E-01
rs11611651	A/G	-0.054	0.077	4.82E-01	Excluded for MR			-0.005	0.060	9.28E-01	0.032	0.063	6.13E-01
rs17197663	G/A	0.092	0.059	1.17E-01	0.023	0.060	7.06E-01	0.018	0.072	8.04E-01	-0.021	0.051	6.83E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs4264267	T/C	-0.046	0.042	2.72E-01	-0.008	0.043	8.58E-01	-0.031	0.033	3.44E-01	-0.017	0.035	6.16E-01
rs61959481	G/A	0.046	0.050	3.60E-01	-0.049	0.052	3.40E-01	-0.040	0.039	3.01E-01	0.020	0.042	6.34E-01
rs55786907	G/A	-0.030	0.054	5.75E-01	0.102	0.055	6.43E-02	0.037	0.042	3.82E-01	0.025	0.045	5.74E-01
rs9540731	C/T	-0.027	0.057	6.37E-01	-0.042	0.055	4.44E-01	-0.033	0.035	3.48E-01	-0.031	0.047	5.10E-01
rs9545155	T/C	-0.032	0.041	4.37E-01	0.007	0.042	8.72E-01	0.013	0.043	7.57E-01	0.005	0.034	8.89E-01
rs1772572	C/A	-0.040	0.043	3.51E-01	-0.017	0.044	7.04E-01	-0.047	0.044	2.83E-01	-0.060	0.036	8.98E-02
rs1108130	A/T	0.031	0.053	5.54E-01	-0.037	0.054	4.94E-01	0.024	0.041	5.59E-01	-0.030	0.043	4.84E-01
rs12878369	A/C	-0.005	0.041	9.07E-01	-0.044	0.053	4.10E-01	-0.028	0.045	5.33E-01	-0.029	0.043	5.10E-01
rs9323328	A/G	-0.037	0.042	3.76E-01	0.022	0.041	5.89E-01	-0.026	0.032	4.25E-01	0.016	0.034	6.31E-01
rs1811739	A/G	0.058	0.047	2.18E-01	0.069	0.048	1.52E-01	0.044	0.037	2.33E-01	0.019	0.039	6.20E-01
rs8005334	G/T	0.018	0.064	7.82E-01	-0.041	0.044	3.45E-01	0.004	0.034	9.14E-01	-0.025	0.036	4.84E-01
rs2925128	T/C	-0.067	0.065	3.05E-01	-0.017	0.042	6.92E-01	-0.040	0.033	2.17E-01	0.015	0.045	7.36E-01
rs1381287	T/C	0.004	0.041	9.31E-01	0.024	0.042	5.58E-01	0.026	0.032	4.23E-01	0.033	0.034	3.37E-01
rs1435672	C/T	0.012	0.042	7.65E-01	-0.032	0.042	4.44E-01	-0.022	0.033	5.07E-01	-0.027	0.048	5.75E-01
rs281296	A/G	-0.080	0.043	6.09E-02	-0.038	0.043	3.76E-01	-0.045	0.033	1.73E-01	-0.052	0.036	1.47E-01
rs2289791	G/T	Excluded for MR											
rs62007780	G/T	-0.025	0.042	5.53E-01	0.036	0.042	3.87E-01	-0.007	0.032	8.39E-01	-0.008	0.035	8.07E-01
rs4310804	C/G	Excluded for MR											
rs1139897	G/A	-0.001	0.051	9.90E-01	0.070	0.052	1.83E-01	0.065	0.040	1.05E-01	0.035	0.042	4.13E-01
rs11076962	C/T	0.020	0.047	6.64E-01	-0.011	0.047	8.18E-01	-0.002	0.036	9.61E-01	0.004	0.038	9.17E-01
rs9922607	C/T	0.018	0.051	7.31E-01	-0.027	0.075	7.21E-01	-0.044	0.040	2.66E-01	0.002	0.044	9.71E-01
rs9941217	C/G	0.004	0.044	9.33E-01	0.029	0.046	5.24E-01	-0.004	0.047	9.24E-01	-0.016	0.047	7.28E-01
rs6497840	A/G	-0.082	0.071	2.44E-01	0.055	0.046	2.25E-01	0.022	0.035	5.35E-01	-0.048	0.038	2.00E-01
rs12918191	A/G	-0.009	0.047	8.44E-01	-0.007	0.048	8.85E-01	-0.016	0.037	6.57E-01	0.006	0.040	8.84E-01
rs9302604	G/A	-0.051	0.042	2.26E-01	-0.068	0.055	2.13E-01	-0.017	0.047	7.14E-01	0.021	0.035	5.44E-01
rs117657830	A/G	0.108	0.107	3.16E-01	-0.041	0.104	6.94E-01	-0.050	0.081	5.32E-01	0.037	0.090	6.82E-01
rs1050847	C/T	0.006	0.042	8.81E-01	-0.014	0.043	7.39E-01	0.019	0.033	5.69E-01	**-0.074**	**0.035**	**3.51E-02**
rs11642231	G/A	0.032	0.045	4.86E-01	**0.094**	**0.045**	**3.95E-02**	0.056	0.035	1.12E-01	0.057	0.037	1.29E-01
rs4790874	T/C	-0.050	0.042	2.33E-01	-0.020	0.042	6.43E-01	0.002	0.033	9.46E-01	-0.064	0.035	6.59E-02
rs28441558	T/C	Excluded for MR											
rs67777803	G/T	0.056	0.054	3.08E-01	-0.065	0.057	2.50E-01	-0.049	0.054	3.69E-01	-0.006	0.046	8.91E-01
rs3764351	G/A	-0.043	0.044	3.35E-01	0.001	0.058	9.86E-01	-0.026	0.035	4.62E-01	-0.045	0.037	2.26E-01
rs72836318	T/C	-0.062	0.073	3.94E-01	**-0.135**	**0.049**	**5.54E-03**	-0.068	0.038	7.09E-02	**-0.124**	**0.040**	**1.85E-03**
rs75919030	T/C	-0.019	0.047	6.84E-01	0.003	0.048	9.55E-01	0.014	0.037	7.12E-01	-0.030	0.039	4.33E-01
rs2587507	T/C	-0.029	0.044	5.03E-01	-0.037	0.041	3.61E-01	-0.046	0.034	1.72E-01	-0.022	0.034	5.08E-01
rs34342129	T/C	-0.011	0.042	7.92E-01	-0.079	0.042	6.03E-02	-0.057	0.032	7.66E-02	-0.026	0.034	4.50E-01
rs4476253	G/A	0.042	0.049	3.83E-01	-0.021	0.075	7.81E-01	-0.010	0.038	7.88E-01	0.024	0.056	6.73E-01
rs8096225	C/A	-0.021	0.045	6.34E-01	0.045	0.045	3.18E-01	0.016	0.035	6.47E-01	-0.033	0.037	3.76E-01
rs67050670	A/G	0.036	0.046	4.40E-01	0.057	0.048	2.35E-01	0.038	0.051	4.64E-01	0.051	0.039	1.94E-01
rs1373178	T/G	-0.001	0.042	9.81E-01	-0.057	0.043	1.82E-01	-0.042	0.033	2.01E-01	-0.010	0.035	7.64E-01
rs72938304	G/A	0.034	0.065	6.07E-01	0.113	0.067	9.06E-02	0.104	0.070	1.38E-01	-0.033	0.054	5.47E-01

		Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)			PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
SNP	**EA/BA**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**	**Beta**	**SE**	**p**
rs71367544	T/C	-0.059	0.054	2.74E-01	0.078	0.055	1.62E-01	-0.011	0.043	8.03E-01	0.063	0.044	1.59E-01
rs76608582	C/A	NA in COURAGE-PD											
rs10853981	A/G	0.001	0.045	9.90E-01	-0.054	0.045	2.35E-01	0.004	0.044	9.22E-01	-0.020	0.037	5.79E-01
rs113230003	G/A	0.020	0.071	7.78E-01	0.073	0.050	1.41E-01	0.031	0.039	4.22E-01	0.047	0.041	2.59E-01
rs117734003	C/G	Excluded for MR											
rs1126757	T/C	0.030	0.042	4.73E-01	-0.050	0.058	3.87E-01	0.015	0.035	6.75E-01	-0.017	0.039	6.61E-01
rs117495226	G/A	Excluded for MR						-0.090	0.113	4.20E-01	-0.041	0.121	7.40E-01
rs6073075	T/A	0.063	0.052	2.26E-01	-0.060	0.053	2.59E-01	0.020	0.041	6.28E-01	-0.010	0.044	8.23E-01
rs3810496	C/T	-0.031	0.065	6.31E-01	-0.026	0.059	6.63E-01	-0.047	0.046	3.07E-01	-0.038	0.053	4.67E-01
rs4818005	G/A	-0.075	0.041	6.81E-02	0.018	0.042	6.68E-01	-0.026	0.032	4.26E-01	-0.056	0.034	1.06E-01
rs4822102	C/T	0.071	0.060	2.36E-01	-0.006	0.043	8.98E-01	0.011	0.050	8.31E-01	0.021	0.035	5.48E-01

NA, not available; EA/BA, effect allele/base allele; SE, standard error.
Bold coefficients with their corresponding SE and p-values are significant at p≤0.05; those underlined with a solid line are negative and those underlined with a dashed line are positive.

Supplementary Table 5. Number of SNPs retained for each exposure in Mendelian randomization analyses and distribution of F-statistics.

	Number of SNPs				F-statistic[c]
Exposure	Total[a]	Not available in Courage-PD	Excluded[b]	Retained for MR	
Smoking initiation	203	3	18	182	205.75
Lifetime smoking index	126	1	12	113	20.03
Alcohol	71	2	7	62	73.68
Coffee	11	-	-	11	70.47

[a] SNPs selected after clumping (r^2=0.001, genomic region=10,000 kb).

[b] Ambiguous palindromic SNPs with MAF≥0.42, SNPs with MAF<0.01, or SNPs available in less than 17 studies.

[c] For each instrument, the F-statistic is given by the formula $\left(\frac{n-k-1}{k}\right)\left(\frac{R^2}{1-R^2}\right)$, with R^2 the proportion of variance explained by the genetic variants, n the sample size, and k the number of instruments. (Burgess S et al., Int J Epidemiol 2011;40(3):755-64).

Supplementary Table 6. Mendelian randomization analyses stratified by age at study.

	Age ≤ 67y (2,878 cases; 2,944 controls)			Age > 67y (3,208 cases; 2,728 controls)		
Exposure	**OR_{IVW} (95% CI)**	**p**	**p-het.**	**OR_{IVW} (95% CI)**	**p**	**p-het.**
Smoking initiation	0.68 (0.48-0.97)	0.031	0.92	0.83 (0.58-1.18)	0.29	0.50
Lifetime smoking	0.46 (0.19-1.09)	0.077	0.66	0.88 (0.37-2.07)	0.76	0.59
Alcohol drinking	0.51 (0.22-1.16)	0.11	0.19	0.85 (0.39-1.83)	0.68	0.93
Alcohol drinking after exclusion of 2 SNPs associated with coffee	0.61 (0.27-1.38)	0.24	0.26	0.97 (0.44-2.13)	0.94	0.94
Coffee drinking	1.15 (0.25-5.33)	0.86	0.24	1.45 (0.34-6.14)	0.62	0.44
Coffee drinking after exclusion of 2 SNPs associated with alcohol	0.53 (0.10-2.88)	0.47	0.69	1.01 (0.19-5.42)	0.99	0.52

OR, odds ratio; IVW, inverse-variance weighted; CI, confidence interval; p-het., p for heterogeneity; IVW, inverse variance weighted.

Supplementary Table 7. Mendelian randomization analyses stratified by disease duration in PD cases.

	PD duration ≤ 7y (3,633 cases; 6,836 controls)			PD duration > 7y (3,271 cases; 6,836 controls)		
Exposure	**OR_{IVW} (95% CI)**	**p**	**p-het.**	**OR_{IVW} (95% CI)**	**p**	**p-het.**
Smoking initiation	0.70 (0.53-0.91)	0.009	0.59	0.74 (0.56-1.00)	0.046	0.46
Lifetime smoking	0.69 (0.32-1.48)	0.34	0.008	0.61 (0.29-1.30)	0.20	0.17
Alcohol drinking	0.81 (0.36-1.83)	0.61	0.032	0.53 (0.27-1.02)	0.057	0.36
Alcohol drinking after exclusion of 2 SNPs associated with coffee	1.03 (0.46-2.31)	0.95	0.075	0.59 (0.30-1.16)	0.13	0.38
Coffee drinking	1.77 (0.37-8.56)	0.48	0.066	1.53 (0.41-5.70)	0.52	0.17
Coffee drinking after exclusion of 2 SNPs associated with alcohol	0.55 (0.11-2.85)	0.48	0.31	1.05 (0.22-4.98)	0.95	0.24

OR, odds ratio; IVW, inverse-variance weighted; CI, confidence interval; p-het., p for heterogeneity; IVW, inverse variance weighted.

Supplementary Table 8. SNPs used for reverse Mendelian randomization analyses: individual associations with PD (exposure) and smoking, alcohol, and coffee drinking (outcomes).

			PD (Nalls et al., 2019)				Outcome				
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**EAF**	**Beta**	**SE**	**p**	**R^2**
Outcome: Alcohol drinking											
rs35749011	1:155135036	A/G	0.02	0.607	0.034	1.72E-70	0.01	-0.002	0.008	7.80E-01	1.22E-02
rs6658353	1:161469054	C/G	0.50	0.065	0.009	6.10E-12	Excluded for reverse MR				
rs11578699	1:171719769	C/T	0.81	0.070	0.012	4.47E-09	0.80	0.002	0.002	3.08E-01	1.56E-03
rs823118	1:205723572	T/C	0.57	0.107	0.009	1.11E-29	0.55	**0.008**	**0.002**	**3.21E-05**	5.58E-03
rs4653767	1:226916078	T/C	0.72	0.083	0.010	1.38E-15	0.70	<0.001	0.002	9.60E-01	2.80E-03
rs10797576	1:232664611	T/C	0.14	0.111	0.013	6.84E-17	0.14	0.001	0.003	7.80E-01	2.99E-03
rs76116224	2:18147848	A/T	0.90	0.110	0.019	1.27E-08	0.91	0.003	0.003	4.29E-01	2.11E-03
rs2042477	2:96000943	T/A	0.76	0.066	0.012	1.38E-08	0.75	0.001	0.002	8.15E-01	1.58E-03
rs11683001	2:102396963	A/T	0.34	0.070	0.010	8.04E-13	0.33	0.002	0.002	2.71E-01	2.22E-03
rs57891859	2:135464616	A/G	0.72	0.081	0.011	4.55E-14	0.69	0.001	0.002	7.86E-01	2.63E-03
rs1474055	2:169110394	T/C	0.13	0.180	0.014	2.54E-39	0.13	0.004	0.003	2.29E-01	7.35E-03
rs73038319	3:18361759	C/A	0.04	0.169	0.024	5.94E-13	0.04	0.008	0.005	1.07E-01	2.24E-03
rs6808178	3:28705690	T/C	0.38	0.066	0.010	8.09E-12	0.36	0.002	0.002	3.26E-01	2.04E-03
rs12497850	3:48748989	T/G	0.65	0.064	0.010	1.36E-10	0.64	-0.001	0.002	5.16E-01	1.85E-03
rs55961674	3:122196892	T/C	0.17	0.086	0.013	9.98E-12	0.16	0.003	0.003	2.21E-01	2.11E-03
rs11707416	3:151108965	T/A	0.63	0.063	0.010	1.13E-10	0.64	0.003	0.002	9.36E-02	1.83E-03
rs10513789	3:182760073	T/G	0.81	0.148	0.012	1.22E-34	0.79	0.003	0.002	2.03E-01	6.75E-03
rs34311866	4:951947	C/T	0.19	0.213	0.012	9.98E-70	0.18	-0.004	0.003	1.03E-01	1.41E-02
rs4698412	4:15737348	A/G	0.55	0.104	0.009	2.06E-28	0.54	0.003	0.002	1.84E-01	5.30E-03
rs6854006	4:77198054	C/T	0.64	0.091	0.010	5.82E-21	0.64	**-0.006**	**0.002**	**1.21E-03**	3.85E-03
rs356182	4:90626111	G/A	0.37	0.277	0.011	3.89E-154	0.35	0.002	0.002	4.42E-01	3.60E-02
rs13117519	4:114369065	T/C	0.17	0.088	0.012	9.82E-13	0.16	**-0.008**	**0.003**	**3.76E-03**	2.20E-03
rs62333164	4:170583157	G/A	0.67	0.064	0.010	2.00E-10	0.67	-0.001	0.002	7.06E-01	1.79E-03
rs1867598	5:60137959	G/A	0.10	0.155	0.016	2.52E-23	0.09	-0.002	0.003	4.85E-01	4.27E-03
rs26431	5:102365794	C/G	0.70	0.062	0.010	1.57E-09	0.70	-0.002	0.002	3.76E-01	1.61E-03
rs11950533	5:134199105	C/A	0.90	0.092	0.016	7.16E-09	0.88	-0.003	0.003	3.20E-01	1.54E-03
rs12528068	6:72487762	T/C	0.28	0.066	0.010	1.63E-10	0.28	0.004	0.002	9.82E-02	1.76E-03
rs997368	6:112243291	A/G	0.80	0.071	0.012	1.84E-09	0.79	-0.001	0.003	7.74E-01	1.60E-03
rs75859381	6:133210361	C/T	0.03	0.221	0.034	1.04E-10	0.03	0.005	0.006	3.97E-01	3.08E-03
rs199351	7:23300049	A/C	0.59	0.102	0.010	5.25E-26	0.57	<0.001	0.002	9.38E-01	4.98E-03
rs76949143	7:66009851	T/A	0.95	0.143	0.025	1.43E-08	0.94	**0.009**	**0.004**	**4.49E-02**	1.97E-03
rs1293298	8:11712443	A/C	0.74	0.093	0.011	3.99E-16	0.76	-0.003	0.002	1.75E-01	3.29E-03
rs2280104	8:22525980	T/C	0.36	0.056	0.010	1.16E-08	0.35	-0.004	0.002	5.44E-02	1.43E-03
rs2086641	8:130901909	C/T	0.28	0.060	0.011	1.81E-08	0.26	-0.002	0.002	2.82E-01	1.47E-03
rs13294100	9:17579690	G/T	0.66	0.086	0.010	8.72E-18	0.63	0.001	0.002	6.44E-01	3.32E-03
rs6476434	9:34046391	C/T	0.27	0.062	0.011	6.58E-09	0.26	**0.008**	**0.002**	**2.06E-04**	1.48E-03
rs896435	10:15557406	T/C	0.69	0.074	0.010	3.41E-13	0.67	-0.003	0.002	1.39E-01	2.31E-03
rs10748818	10:104015279	G/A	0.15	0.079	0.013	1.05E-09	0.14	**-0.006**	**0.003**	**4.30E-02**	1.58E-03
rs117896735	10:121536327	A/G	0.02	0.435	0.039	2.36E-28	0.01	0.003	0.007	6.47E-01	6.19E-03

			PD (Nalls et al., 2019)				Outcome				
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**EAF**	**Beta**	**SE**	**p**	**R^2**
rs7938782	11:10558777	A/G	0.88	0.087	0.015	2.12E-09	0.86	0.001	0.003	7.58E-01	1.63E-03
rs12283611	11:83487277	C/A	0.59	0.064	0.010	2.61E-10	0.57	-0.001	0.002	5.01E-01	2.02E-03
rs3802920	11:133787001	T/G	0.21	0.107	0.012	6.26E-20	0.20	0.004	0.002	1.10E-01	3.76E-03
rs76904798	12:40614434	T/C	0.14	0.144	0.013	1.52E-28	0.13	0.003	0.003	3.17E-01	5.12E-03
rs7134559	12:46419086	C/T	0.60	0.054	0.010	3.96E-08	0.61	**0.007**	**0.002**	**4.06E-04**	1.40E-03
rs10847864	12:123326598	T/G	0.36	0.148	0.012	1.47E-37	0.35	0.004	0.002	8.08E-02	1.01E-02
rs9568188	13:49927732	T/C	0.74	0.062	0.011	1.15E-08	0.72	**0.007**	**0.002**	**8.55E-04**	1.47E-03
rs4771268	13:97865021	T/C	0.23	0.068	0.011	1.45E-09	0.24	0.004	0.002	5.31E-02	1.61E-03
rs12147950	14:37989270	C/T	0.56	0.053	0.010	3.54E-08	0.56	0.003	0.002	1.74E-01	1.38E-03
rs11158026	14:55348869	C/T	0.68	0.084	0.010	1.66E-16	0.66	-0.001	0.002	7.35E-01	3.11E-03
rs3742785	14:75373034	A/C	0.79	0.071	0.012	1.92E-09	0.77	-0.004	0.002	1.27E-01	1.68E-03
rs979812	14:88464264	T/G	0.44	0.061	0.009	6.19E-11	0.44	**0.004**	**0.002**	**2.31E-02**	1.84E-03
rs2251086	15:61997385	C/T	0.86	0.119	0.014	6.08E-18	0.84	**0.008**	**0.003**	**5.45E-03**	3.42E-03
rs6497339	16:19277493	A/T	0.45	0.063	0.010	2.76E-11	Excluded for reverse MR				
rs11150601	16:30977799	A/G	0.64	0.091	0.010	5.12E-20	0.63	**0.004**	**0.002**	**3.90E-02**	3.77E-03
rs3104783	16:52636242	A/C	0.43	0.067	0.009	1.29E-12	0.44	-0.003	0.002	1.95E-01	2.19E-03
rs12600861	17:7355621	C/A	0.35	0.056	0.010	1.01E-08	0.35	-0.003	0.002	1.04E-01	1.46E-03
rs850738	17:42434630	G/A	0.39	0.071	0.011	1.29E-11	0.39	0.003	0.002	1.89E-01	2.41E-03
rs62053943	17:43744203	C/T	0.84	0.270	0.016	3.58E-68	0.86	**0.017**	**0.003**	**6.83E-10**	1.91E-02
rs61169879	17:59917366	T/C	0.16	0.082	0.013	9.28E-10	0.17	**0.005**	**0.003**	**4.52E-02**	1.84E-03
rs666463	17:76425480	A/T	0.83	0.076	0.013	3.20E-09	0.84	<0.001	0.003	9.20E-01	1.61E-03
rs1941685	18:31304318	T/G	0.50	0.053	0.009	1.69E-08	0.52	<0.001	0.002	8.23E-01	1.41E-03
rs12456492	18:40673380	G/A	0.32	0.098	0.010	3.80E-23	0.32	**0.007**	**0.002**	**9.12E-04**	4.19E-03
rs8087969	18:48683589	G/T	0.45	0.058	0.010	1.41E-08	0.44	0.001	0.002	4.92E-01	1.65E-03
rs55818311	19:2341047	C/T	0.31	0.070	0.011	4.18E-10	0.33	0.002	0.002	2.27E-01	2.06E-03
rs77351827	20:6006041	T/C	0.13	0.080	0.014	8.87E-09	0.12	-0.001	0.003	8.50E-01	1.43E-03
rs2248244	21:38852361	A/G	0.28	0.071	0.011	2.74E-11	0.28	-0.003	0.002	1.28E-01	2.07E-03
Outcome: Coffee drinking											
rs35749011	1:155135036	A/G	0.02	0.607	0.034	1.72E-70	0.01	<0.001	0.007	9.60E-01	1.22E-02
rs6658353	1:161469054	C/G	0.50	0.065	0.009	6.10E-12	Excluded for reverse MR				
rs11578699	1:171719769	C/T	0.81	0.070	0.012	4.47E-09	0.80	0.002	0.002	4.16E-01	1.56E-03
rs823118	1:205723572	T/C	0.57	0.107	0.009	1.11E-29	0.55	-0.001	0.002	3.79E-01	5.58E-03
rs4653767	1:226916078	T/C	0.72	0.083	0.010	1.38E-15	0.72	<0.001	0.002	8.75E-01	2.80E-03
rs10797576	1:232664611	T/C	0.14	0.111	0.013	6.84E-17	0.12	-0.002	0.002	3.16E-01	2.99E-03
rs76116224	2:18147848	A/T	0.90	0.110	0.019	1.27E-08	0.90	-0.002	0.003	3.66E-01	2.11E-03
rs2042477	2:96000943	T/A	0.76	0.066	0.012	1.38E-08	0.74	0.002	0.002	1.90E-01	1.58E-03
rs11683001	2:102396963	A/T	0.34	0.070	0.010	8.04E-13	0.34	<0.001	0.002	7.90E-01	2.22E-03
rs57891859	2:135464616	A/G	0.72	0.081	0.011	4.55E-14	0.75	0.002	0.002	3.94E-01	2.63E-03
rs1474055	2:169110394	T/C	0.13	0.180	0.014	2.54E-39	0.12	0.003	0.002	2.51E-01	7.35E-03
rs73038319	3:18361759	C/A	0.04	0.169	0.024	5.94E-13	0.04	<0.001	0.004	9.15E-01	2.24E-03
rs6808178	3:28705690	T/C	0.38	0.066	0.010	8.09E-12	0.38	0.001	0.002	4.74E-01	2.04E-03
rs12497850	3:48748989	T/G	0.65	0.064	0.010	1.36E-10	0.65	**0.004**	**0.002**	**6.44E-03**	1.85E-03

			PD (Nalls et al., 2019)				Outcome				
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**EAF**	**Beta**	**SE**	**p**	**R²**
rs55961674	3:122196892	T/C	0.17	0.086	0.013	9.98E-12	0.15	0.002	0.002	3.26E-01	2.11E-03
rs11707416	3:151108965	T/A	0.63	0.063	0.010	1.13E-10	0.63	-0.001	0.002	5.21E-01	1.83E-03
rs10513789	3:182760073	T/G	0.81	0.148	0.012	1.22E-34	0.81	<0.001	0.002	9.52E-01	6.75E-03
rs34311866	4:951947	C/T	0.19	0.213	0.012	9.98E-70	0.18	0.001	0.002	6.12E-01	1.41E-02
rs4698412	4:15737348	A/G	0.55	0.104	0.009	2.06E-28	0.55	<0.001	0.002	8.79E-01	5.30E-03
rs6854006	4:77198054	C/T	0.64	0.091	0.010	5.82E-21	0.62	-0.001	0.002	7.34E-01	3.85E-03
rs356182	4:90626111	G/A	0.37	0.277	0.011	3.89E-154	0.34	<0.001	0.002	8.71E-01	3.60E-02
rs13117519	4:114369065	T/C	0.17	0.088	0.012	9.82E-13	0.17	-0.001	0.002	6.43E-01	2.20E-03
rs62333164	4:170583157	G/A	0.67	0.064	0.010	2.00E-10	0.67	0.002	0.002	2.01E-01	1.79E-03
rs1867598	5:60137959	G/A	0.10	0.155	0.016	2.52E-23	0.08	**0.007**	**0.003**	**2.38E-02**	4.27E-03
rs26431	5:102365794	C/G	0.70	0.062	0.010	1.57E-09	0.69	-0.001	0.002	3.83E-01	1.61E-03
rs11950533	5:134199105	C/A	0.90	0.092	0.016	7.16E-09	0.90	0.003	0.003	2.36E-01	1.54E-03
rs112485576	6:32578772	C/A	0.84	0.168	0.015	6.96E-28	0.81	**0.005**	**0.002**	**1.63E-02**	7.66E-03
rs12528068	6:72487762	T/C	0.28	0.066	0.010	1.63E-10	0.28	0.003	0.002	1.28E-01	1.76E-03
rs997368	6:112243291	A/G	0.80	0.071	0.012	1.84E-09	0.82	0.003	0.002	1.87E-01	1.60E-03
rs75859381	6:133210361	C/T	0.03	0.221	0.034	1.04E-10	0.03	0.001	0.005	8.48E-01	3.08E-03
rs199351	7:23300049	A/C	0.59	0.102	0.010	5.25E-26	0.59	-0.001	0.002	5.75E-01	4.98E-03
rs76949143	7:66009851	T/A	0.95	0.143	0.025	1.43E-08	0.95	-0.004	0.004	2.38E-01	1.97E-03
rs1293298	8:11712443	A/C	0.74	0.093	0.011	3.99E-16	0.74	**0.004**	**0.002**	**3.34E-02**	3.29E-03
rs2280104	8:22525980	T/C	0.36	0.056	0.010	1.16E-08	0.35	-0.001	0.002	4.61E-01	1.43E-03
rs2086641	8:130901909	C/T	0.28	0.060	0.011	1.81E-08	0.26	<0.001	0.002	8.43E-01	1.47E-03
rs13294100	9:17579690	G/T	0.66	0.086	0.010	8.72E-18	0.65	0.001	0.002	6.77E-01	3.32E-03
rs6476434	9:34046391	C/T	0.27	0.062	0.011	6.58E-09	0.27	-0.001	0.002	4.28E-01	1.48E-03
rs896435	10:15557406	T/C	0.69	0.074	0.010	3.41E-13	0.68	0.002	0.002	3.35E-01	2.31E-03
rs10748818	10:104015279	G/A	0.15	0.079	0.013	1.05E-09	0.15	-0.001	0.002	8.14E-01	1.58E-03
rs117896735	10:121536327	A/G	0.02	0.435	0.039	2.36E-28	0.02	-0.002	0.006	7.05E-01	6.19E-03
rs7938782	11:10558777	A/G	0.88	0.087	0.015	2.12E-09	0.88	**0.007**	**0.002**	**3.36E-03**	1.63E-03
rs12283611	11:83487277	C/A	0.59	0.064	0.010	2.61E-10	0.59	0.001	0.002	6.20E-01	2.02E-03
rs3802920	11:133787001	T/G	0.21	0.107	0.012	6.26E-20	0.20	-0.002	0.002	2.51E-01	3.76E-03
rs76904798	12:40614434	T/C	0.14	0.144	0.013	1.52E-28	0.14	-0.003	0.002	2.09E-01	5.12E-03
rs7134559	12:46419086	C/T	0.60	0.054	0.010	3.96E-08	0.60	0.001	0.002	4.01E-01	1.40E-03
rs10847864	12:123326598	T/G	0.36	0.148	0.012	1.47E-37	0.35	-0.001	0.002	3.89E-01	1.01E-02
rs9568188	13:49927732	T/C	0.74	0.062	0.011	1.15E-08	0.73	<0.001	0.002	7.92E-01	1.47E-03
rs4771268	13:97865021	T/C	0.23	0.068	0.011	1.45E-09	0.22	<0.001	0.002	8.36E-01	1.61E-03
rs12147950	14:37989270	C/T	0.56	0.053	0.010	3.54E-08	0.57	0.001	0.002	4.10E-01	1.38E-03
rs11158026	14:55348869	C/T	0.68	0.084	0.010	1.66E-16	0.66	0.002	0.002	2.33E-01	3.11E-03
rs3742785	14:75373034	A/C	0.79	0.071	0.012	1.92E-09	0.78	**-0.005**	**0.002**	**1.13E-02**	1.68E-03
rs979812	14:88464264	T/G	0.44	0.061	0.009	6.19E-11	0.42	-0.001	0.002	4.81E-01	1.84E-03
rs2251086	15:61997385	C/T	0.86	0.119	0.014	6.08E-18	0.86	0.004	0.002	7.31E-02	3.42E-03
rs6497339	16:19277493	A/T	0.45	0.063	0.010	2.76E-11	Excluded for reverse MR				
rs11150601	16:30977799	A/G	0.64	0.091	0.010	5.12E-20	0.63	-0.001	0.002	6.47E-01	3.77E-03
rs3104783	16:52636242	A/C	0.43	0.067	0.009	1.29E-12	0.41	<0.001	0.002	9.08E-01	2.19E-03
rs12600861	17:7355621	C/A	0.35	0.056	0.010	1.01E-08	0.36	<0.001	0.002	7.89E-01	1.46E-03

			PD (Nalls et al., 2019)				Outcome				
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**EAF**	**Beta**	**SE**	**p**	**R²**
rs850738	17:42434630	G/A	0.39	0.071	0.011	1.29E-11	0.39	0.002	0.002	1.81E-01	2.41E-03
rs62053943	17:43744203	C/T	0.84	0.270	0.016	3.58E-68	0.84	-0.001	0.002	6.85E-01	1.91E-02
rs61169879	17:59917366	T/C	0.16	0.082	0.013	9.28E-10	0.16	**0.012**	**0.002**	**4.00E-08**	1.84E-03
rs666463	17:76425480	A/T	0.83	0.076	0.013	3.20E-09	0.83	0.001	0.002	6.75E-01	1.61E-03
rs1941685	18:31304318	T/G	0.50	0.053	0.009	1.69E-08	0.50	<0.001	0.002	9.46E-01	1.41E-03
rs12456492	18:40673380	G/A	0.32	0.098	0.010	3.80E-23	0.31	**-0.005**	**0.002**	**1.98E-03**	4.19E-03
rs8087969	18:48683589	G/T	0.45	0.058	0.010	1.41E-08	0.46	<0.001	0.002	9.20E-01	1.65E-03
rs55818311	19:2341047	C/T	0.31	0.070	0.011	4.18E-10	0.32	0.001	0.002	4.97E-01	2.06E-03
rs77351827	20:6006041	T/C	0.13	0.080	0.014	8.87E-09	0.12	0.001	0.002	7.28E-01	1.43E-03
rs2248244	21:38852361	A/G	0.28	0.071	0.011	2.74E-11	0.28	**0.006**	**0.002**	**3.86E-04**	2.07E-03
Outcome: Lifetime smoking index											
rs35749011	1:155135036	A/G	0.02	0.607	0.034	1.72E-70	0.01	-0.005	0.006	4.10E-01	1.22E-02
rs6658353	1:161469054	C/G	0.50	0.065	0.009	6.10E-12	Excluded for reverse MR				
rs11578699	1:171719769	C/T	0.81	0.070	0.012	4.47E-09	0.80	-0.001	0.002	6.90E-01	1.56E-03
rs823118	1:205723572	T/C	0.57	0.107	0.009	1.11E-29	0.55	**0.004**	**0.001**	**6.50E-03**	5.58E-03
rs4653767	1:226916078	T/C	0.72	0.083	0.010	1.38E-15	0.72	-0.001	0.002	3.60E-01	2.80E-03
rs10797576	1:232664611	T/C	0.14	0.111	0.013	6.84E-17	0.12	**0.006**	**0.002**	**8.50E-03**	2.99E-03
rs76116224	2:18147848	A/T	0.90	0.110	0.019	1.27E-08	0.90	<0.001	0.002	8.60E-01	2.11E-03
rs2042477	2:96000943	T/A	0.76	0.066	0.012	1.38E-08	0.74	-0.001	0.002	7.10E-01	1.58E-03
rs11683001	2:102396963	A/T	0.34	0.070	0.010	8.04E-13	0.34	**0.004**	**0.001**	**5.00E-03**	2.22E-03
rs57891859	2:135464616	A/G	0.72	0.081	0.011	4.55E-14	0.75	<0.001	0.002	7.80E-01	2.63E-03
rs1474055	2:169110394	T/C	0.13	0.180	0.014	2.54E-39	0.12	0.004	0.002	6.00E-02	7.35E-03
rs73038319	3:18361759	C/A	0.04	0.169	0.024	5.94E-13	0.04	0.005	0.004	1.90E-01	2.24E-03
rs6808178	3:28705690	T/C	0.38	0.066	0.010	8.09E-12	0.38	0.001	0.001	6.30E-01	2.04E-03
rs12497850	3:48748989	T/G	0.65	0.064	0.010	1.36E-10	0.65	**-0.006**	**0.001**	**1.50E-05**	1.85E-03
rs55961674	3:122196892	T/C	0.17	0.086	0.013	9.98E-12	0.15	0.002	0.002	2.40E-01	2.11E-03
rs11707416	3:151108965	T/A	0.63	0.063	0.010	1.13E-10	0.63	**0.003**	**0.001**	**2.20E-02**	1.83E-03
rs10513789	3:182760073	T/G	0.81	0.148	0.012	1.22E-34	0.81	**0.003**	**0.002**	**4.80E-02**	6.75E-03
rs34311866	4:951947	C/T	0.19	0.213	0.012	9.98E-70	0.18	<0.001	0.002	8.90E-01	1.41E-02
rs4698412	4:15737348	A/G	0.55	0.104	0.009	2.06E-28	0.55	-0.001	0.001	3.10E-01	5.30E-03
rs6854006	4:77198054	C/T	0.64	0.091	0.010	5.82E-21	0.62	**-0.004**	**0.001**	**6.00E-03**	3.85E-03
rs356182	4:90626111	G/A	0.37	0.277	0.011	3.89E-154	0.34	-0.001	0.001	6.20E-01	3.60E-02
rs13117519	4:114369065	T/C	0.17	0.088	0.012	9.82E-13	0.17	0.001	0.002	5.40E-01	2.20E-03
rs62333164	4:170583157	G/A	0.67	0.064	0.010	2.00E-10	0.67	-0.001	0.001	4.00E-01	1.79E-03
rs1867598	5:60137959	G/A	0.10	0.155	0.016	2.52E-23	0.08	0.002	0.003	5.60E-01	4.27E-03
rs26431	5:102365794	C/G	0.70	0.062	0.010	1.57E-09	0.69	-0.002	0.002	2.60E-01	1.61E-03
rs11950533	5:134199105	C/A	0.90	0.092	0.016	7.16E-09	0.90	-0.003	0.002	1.50E-01	1.54E-03
rs112485576	6:32578772	C/A	0.84	0.168	0.015	6.96E-28	0.81	-0.002	0.002	3.00E-01	7.66E-03
rs12528068	6:72487762	T/C	0.28	0.066	0.010	1.63E-10	0.28	-0.001	0.002	6.20E-01	1.76E-03
rs997368	6:112243291	A/G	0.80	0.071	0.012	1.84E-09	0.82	0.002	0.002	2.30E-01	1.60E-03
rs75859381	6:133210361	C/T	0.03	0.221	0.034	1.04E-10	0.03	-0.002	0.004	6.90E-01	3.08E-03
rs199351	7:23300049	A/C	0.59	0.102	0.010	5.25E-26	0.59	-0.001	0.001	3.70E-01	4.98E-03

			PD (Nalls et al., 2019)				Outcome				
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**EAF**	**Beta**	**SE**	**p**	**R²**
rs76949143	7:66009851	T/A	0.95	0.143	0.025	1.43E-08	0.95	0.005	0.003	1.30E-01	1.97E-03
rs1293298	8:11712443	A/C	0.74	0.093	0.011	3.99E-16	0.74	**0.005**	**0.002**	**2.20E-03**	3.29E-03
rs2280104	8:22525980	T/C	0.36	0.056	0.010	1.16E-08	0.35	**-0.004**	**0.001**	**1.10E-02**	1.43E-03
rs2086641	8:130901909	C/T	0.28	0.060	0.011	1.81E-08	0.26	-0.002	0.002	1.70E-01	1.47E-03
rs13294100	9:17579690	G/T	0.66	0.086	0.010	8.72E-18	0.65	**0.005**	**0.001**	**2.00E-03**	3.32E-03
rs6476434	9:34046391	C/T	0.27	0.062	0.011	6.58E-09	0.27	0.001	0.002	6.50E-01	1.48E-03
rs896435	10:15557406	T/C	0.69	0.074	0.010	3.41E-13	0.68	<0.001	0.001	8.30E-01	2.31E-03
rs10748818	10:104015279	G/A	0.15	0.079	0.013	1.05E-09	0.15	**-0.006**	**0.002**	**3.40E-03**	1.58E-03
rs117896735	10:121536327	A/G	0.02	0.435	0.039	2.36E-28	0.02	-0.007	0.005	2.20E-01	6.19E-03
rs7938782	11:10558777	A/G	0.88	0.087	0.015	2.12E-09	0.88	<0.001	0.002	8.50E-01	1.63E-03
rs12283611	11:83487277	C/A	0.59	0.064	0.010	2.61E-10	0.59	-0.001	0.001	4.40E-01	2.02E-03
rs3802920	11:133787001	T/G	0.21	0.107	0.012	6.26E-20	0.20	-0.002	0.002	2.90E-01	3.76E-03
rs76904798	12:40614434	T/C	0.14	0.144	0.013	1.52E-28	0.14	-0.002	0.002	2.70E-01	5.12E-03
rs7134559	12:46419086	C/T	0.60	0.054	0.010	3.96E-08	0.60	<0.001	0.001	8.10E-01	1.40E-03
rs10847864	12:123326598	T/G	0.36	0.148	0.012	1.47E-37	0.35	-0.002	0.001	2.10E-01	1.01E-02
rs9568188	13:49927732	T/C	0.74	0.062	0.011	1.15E-08	0.73	-0.001	0.002	5.80E-01	1.47E-03
rs4771268	13:97865021	T/C	0.23	0.068	0.011	1.45E-09	0.22	0.001	0.002	5.90E-01	1.61E-03
rs12147950	14:37989270	C/T	0.56	0.053	0.010	3.54E-08	0.57	0.002	0.001	1.90E-01	1.38E-03
rs11158026	14:55348869	C/T	0.68	0.084	0.010	1.66E-16	0.66	-0.002	0.001	2.50E-01	3.11E-03
rs3742785	14:75373034	A/C	0.79	0.071	0.012	1.92E-09	0.78	-0.002	0.002	1.60E-01	1.68E-03
rs979812	14:88464264	T/G	0.44	0.061	0.009	6.19E-11	0.42	<0.001	0.001	8.90E-01	1.84E-03
rs2251086	15:61997385	C/T	0.86	0.119	0.014	6.08E-18	0.86	-0.003	0.002	7.80E-02	3.42E-03
rs6497339	16:19277493	A/T	0.45	0.063	0.010	2.76E-11	Excluded for reverse MR				
rs11150601	16:30977799	A/G	0.64	0.091	0.010	5.12E-20	0.63	**-0.004**	**0.001**	**1.30E-02**	3.77E-03
rs3104783	16:52636242	A/C	0.43	0.067	0.009	1.29E-12	0.42	0.001	0.001	3.10E-01	2.19E-03
rs12600861	17:7355621	C/A	0.35	0.056	0.010	1.01E-08	0.36	**-0.005**	**0.001**	**1.40E-03**	1.46E-03
rs850738	17:42434630	G/A	0.39	0.071	0.011	1.29E-11	0.39	0.002	0.001	2.00E-01	2.41E-03
rs62053943	17:43744203	C/T	0.84	0.270	0.016	3.58E-68	0.85	**0.006**	**0.002**	**8.50E-04**	1.91E-02
rs61169879	17:59917366	T/C	0.16	0.082	0.013	9.28E-10	0.16	-0.001	0.002	7.00E-01	1.84E-03
rs666463	17:76425480	A/T	0.83	0.076	0.013	3.20E-09	0.83	0.002	0.002	2.10E-01	1.61E-03
rs1941685	18:31304318	T/G	0.50	0.053	0.009	1.69E-08	0.50	-0.002	0.001	1.90E-01	1.41E-03
rs12456492	18:40673380	G/A	0.32	0.098	0.010	3.80E-23	0.31	**-0.003**	**0.001**	**2.80E-02**	4.19E-03
rs8087969	18:48683589	G/T	0.45	0.058	0.010	1.41E-08	0.46	-0.001	0.001	4.40E-01	1.65E-03
rs55818311	19:2341047	C/T	0.31	0.070	0.011	4.18E-10	0.32	-0.001	0.002	4.00E-01	2.06E-03
rs77351827	20:6006041	T/C	0.13	0.080	0.014	8.87E-09	0.12	**0.005**	**0.002**	**2.50E-02**	1.43E-03
rs2248244	21:38852361	A/G	0.28	0.071	0.011	2.74E-11	0.28	-0.001	0.002	3.60E-01	2.07E-03
Outcome: Smoking initiation											
rs35749011	1:155135036	A/G	0.02	0.607	0.034	1.72E-70	0.01	0.011	0.015	4.50E-01	1.22E-02
rs6658353	1:161469054	C/G	0.50	0.065	0.009	6.10E-12	Excluded for reverse MR				
rs11578699	1:171719769	C/T	0.81	0.070	0.012	4.47E-09	0.80	0.006	0.005	1.70E-01	1.56E-03
rs823118	1:205723572	T/C	0.57	0.107	0.009	1.11E-29	0.55	**0.011**	**0.004**	**2.75E-03**	5.58E-03
rs4653767	1:226916078	T/C	0.72	0.083	0.010	1.38E-15	0.70	0.002	0.004	5.68E-01	2.80E-03

			PD (Nalls et al., 2019)				Outcome				
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**EAF**	**Beta**	**SE**	**p**	**R²**
rs10797576	1:232664611	T/C	0.14	0.111	0.013	6.84E-17	0.14	0.009	0.005	9.08E-02	2.99E-03
rs76116224	2:18147848	A/T	0.90	0.110	0.019	1.27E-08	0.91	0.006	0.006	3.06E-01	2.11E-03
rs2042477	2:96000943	T/A	0.76	0.066	0.012	1.38E-08	0.75	0.002	0.004	5.47E-01	1.58E-03
rs11683001	2:102396963	A/T	0.34	0.070	0.010	8.04E-13	0.33	0.007	0.004	5.86E-02	2.22E-03
rs57891859	2:135464616	A/G	0.72	0.081	0.011	4.55E-14	0.69	-0.003	0.004	5.19E-01	2.63E-03
rs1474055	2:169110394	T/C	0.13	0.180	0.014	2.54E-39	0.13	**0.013**	**0.006**	**1.86E-02**	7.35E-03
rs73038319	3:18361759	C/A	0.04	0.169	0.024	5.94E-13	0.04	0.014	0.009	1.15E-01	2.24E-03
rs6808178	3:28705690	T/C	0.38	0.066	0.010	8.09E-12	0.36	-0.004	0.004	2.59E-01	2.04E-03
rs12497850	3:48748989	T/G	0.65	0.064	0.010	1.36E-10	0.64	**-0.012**	**0.004**	**1.76E-03**	1.85E-03
rs55961674	3:122196892	T/C	0.17	0.086	0.013	9.98E-12	0.16	0.003	0.005	5.79E-01	2.11E-03
rs11707416	3:151108965	T/A	0.63	0.063	0.010	1.13E-10	0.64	<0.001	0.004	9.17E-01	1.83E-03
rs10513789	3:182760073	T/G	0.81	0.148	0.012	1.22E-34	0.79	0.003	0.004	5.13E-01	6.75E-03
rs34311866	4:951947	C/T	0.19	0.213	0.012	9.98E-70	0.18	0.002	0.005	6.04E-01	1.41E-02
rs4698412	4:15737348	A/G	0.55	0.104	0.009	2.06E-28	0.54	0.002	0.004	6.16E-01	5.30E-03
rs6854006	4:77198054	C/T	0.64	0.091	0.010	5.82E-21	0.64	-0.007	0.004	6.93E-02	3.85E-03
rs356182	4:90626111	G/A	0.37	0.277	0.011	3.89E-154	0.35	<0.001	0.004	9.27E-01	3.60E-02
rs13117519	4:114369065	T/C	0.17	0.088	0.012	9.82E-13	0.16	-0.002	0.005	6.68E-01	2.20E-03
rs62333164	4:170583157	G/A	0.67	0.064	0.010	2.00E-10	0.67	0.006	0.004	1.22E-01	1.79E-03
rs1867598	5:60137959	G/A	0.10	0.155	0.016	2.52E-23	0.09	-0.005	0.006	4.08E-01	4.27E-03
rs26431	5:102365794	C/G	0.70	0.062	0.010	1.57E-09	0.70	-0.006	0.004	1.36E-01	1.61E-03
rs11950533	5:134199105	C/A	0.90	0.092	0.016	7.16E-09	0.88	-0.002	0.006	7.02E-01	1.54E-03
rs12528068	6:72487762	T/C	0.28	0.066	0.010	1.63E-10	0.28	0.003	0.004	4.49E-01	1.76E-03
rs997368	6:112243291	A/G	0.80	0.071	0.012	1.84E-09	0.79	0.003	0.005	4.65E-01	1.60E-03
rs75859381	6:133210361	C/T	0.03	0.221	0.034	1.04E-10	0.03	0.008	0.011	4.57E-01	3.08E-03
rs199351	7:23300049	A/C	0.59	0.102	0.010	5.25E-26	0.57	-0.003	0.004	4.13E-01	4.98E-03
rs76949143	7:66009851	T/A	0.95	0.143	0.025	1.43E-08	0.94	0.009	0.008	2.58E-01	1.97E-03
rs1293298	8:11712443	A/C	0.74	0.093	0.011	3.99E-16	0.76	0.004	0.004	3.41E-01	3.29E-03
rs2280104	8:22525980	T/C	0.36	0.056	0.010	1.16E-08	0.35	-0.006	0.004	1.04E-01	1.43E-03
rs2086641	8:130901909	C/T	0.28	0.060	0.011	1.81E-08	0.26	-0.005	0.004	2.01E-01	1.47E-03
rs13294100	9:17579690	G/T	0.66	0.086	0.010	8.72E-18	0.63	**0.009**	**0.004**	**1.65E-02**	3.32E-03
rs6476434	9:34046391	C/T	0.27	0.062	0.011	6.58E-09	0.26	-0.005	0.004	1.95E-01	1.48E-03
rs896435	10:15557406	T/C	0.69	0.074	0.010	3.41E-13	0.67	0.006	0.004	1.41E-01	2.31E-03
rs10748818	10:104015279	G/A	0.15	0.079	0.013	1.05E-09	0.14	**-0.011**	**0.005**	**2.47E-02**	1.58E-03
rs117896735	10:121536327	A/G	0.02	0.435	0.039	2.36E-28	0.01	0.007	0.013	5.92E-01	6.19E-03
rs7938782	11:10558777	A/G	0.88	0.087	0.015	2.12E-09	0.86	**0.015**	**0.006**	**8.85E-03**	1.63E-03
rs12283611	11:83487277	C/A	0.59	0.064	0.010	2.61E-10	0.57	-0.001	0.004	7.58E-01	2.02E-03
rs3802920	11:133787001	T/G	0.21	0.107	0.012	6.26E-20	0.20	-0.008	0.005	6.51E-02	3.76E-03
rs76904798	12:40614434	T/C	0.14	0.144	0.013	1.52E-28	0.13	-0.003	0.005	5.94E-01	5.12E-03
rs7134559	12:46419086	C/T	0.60	0.054	0.010	3.96E-08	0.61	**0.009**	**0.004**	**9.77E-03**	1.40E-03
rs10847864	12:123326598	T/G	0.36	0.148	0.012	1.47E-37	0.35	<0.001	0.004	9.56E-01	1.01E-02
rs9568188	13:49927732	T/C	0.74	0.062	0.011	1.15E-08	0.72	-0.003	0.004	4.18E-01	1.47E-03
rs4771268	13:97865021	T/C	0.23	0.068	0.011	1.45E-09	0.24	-0.003	0.004	5.51E-01	1.61E-03
rs12147950	14:37989270	C/T	0.56	0.053	0.010	3.54E-08	0.56	0.007	0.004	5.86E-02	1.38E-03

			PD (Nalls et al., 2019)				Outcome				
SNP	**Chr:Pos (GRCh37)**	**EA/BA**	**EAF**	**Beta**	**SE**	**p**	**EAF**	**Beta**	**SE**	**p**	**R²**
rs11158026	14:55348869	C/T	0.68	0.084	0.010	1.66E-16	0.66	-0.001	0.004	8.68E-01	3.11E-03
rs3742785	14:75373034	A/C	0.79	0.071	0.012	1.92E-09	0.77	-0.001	0.004	9.01E-01	1.68E-03
rs979812	14:88464264	T/G	0.44	0.061	0.009	6.19E-11	0.44	**0.008**	**0.004**	**2.96E-02**	1.84E-03
rs2251086	15:61997385	C/T	0.86	0.119	0.014	6.08E-18	0.84	<0.001	0.005	9.53E-01	3.42E-03
rs6497339	16:19277493	A/T	0.45	0.063	0.010	2.76E-11	Excluded for reverse MR				
rs11150601	16:30977799	A/G	0.64	0.091	0.010	5.12E-20	0.63	-0.005	0.004	1.72E-01	3.77E-03
rs3104783	16:52636242	A/C	0.43	0.067	0.009	1.29E-12	0.44	**-0.008**	**0.004**	**3.35E-02**	2.19E-03
rs12600861	17:7355621	C/A	0.35	0.056	0.010	1.01E-08	0.35	**-0.009**	**0.004**	**1.37E-02**	1.46E-03
rs850738	17:42434630	G/A	0.39	0.071	0.011	1.29E-11	0.39	0.006	0.004	9.01E-02	2.41E-03
rs62053943	17:43744203	C/T	0.84	0.270	0.016	3.58E-68	0.86	0.008	0.005	1.23E-01	1.91E-02
rs61169879	17:59917366	T/C	0.16	0.082	0.013	9.28E-10	0.17	0.001	0.005	7.83E-01	1.84E-03
rs666463	17:76425480	A/T	0.83	0.076	0.013	3.20E-09	0.84	-0.001	0.005	8.93E-01	1.61E-03
rs1941685	18:31304318	T/G	0.50	0.053	0.009	1.69E-08	0.52	-0.002	0.004	6.01E-01	1.41E-03
rs12456492	18:40673380	G/A	0.32	0.098	0.010	3.80E-23	0.32	-0.006	0.004	1.16E-01	4.19E-03
rs8087969	18:48683589	G/T	0.45	0.058	0.010	1.41E-08	0.44	0.002	0.004	5.22E-01	1.65E-03
rs55818311	19:2341047	C/T	0.31	0.070	0.011	4.18E-10	0.33	-0.004	0.004	2.87E-01	2.06E-03
rs77351827	20:6006041	T/C	0.13	0.080	0.014	8.87E-09	0.12	0.006	0.005	3.05E-01	1.43E-03
rs2248244	21:38852361	A/G	0.28	0.071	0.011	2.74E-11	0.28	0.004	0.004	2.79E-01	2.07E-03

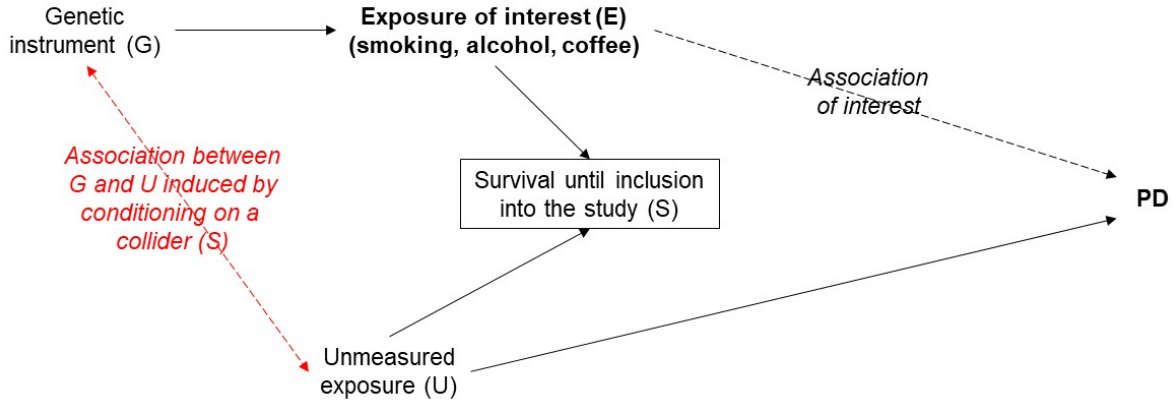
NA, not available; EA/BA, effect allele/base allele; EAF, effect allele frequency; SE, standard error.

SNPs associated with PD and corresponding betas come from Nalls et al., Lancet Neurol 2019:18,1091-1102. Associations with smoking, alcohol, and coffee come from Liu et al., Nat Genet 2019:51, 237-244; Zhong et al., Hum Mol Genet 2019:28, 2449-2457; and Wootton et al., Psychol Med 2019:50, 2435-2443.

Bold coefficients and corresponding SE and p-values are significant at $p \leq 0.05$; those underlined with a solid line are negative and those underlined with a dashed line are positive.

R^2 is the proportion of the variance of the exposure explained by the genetic variant according to the formula: $2 \times Beta_{exposure} \times EAF_{exposure} \times (1\text{-}EAF_{exposure})$.

Supplementary Figure 1. Survival bias in Mendelian randomization studies of diseases in elderly populations.

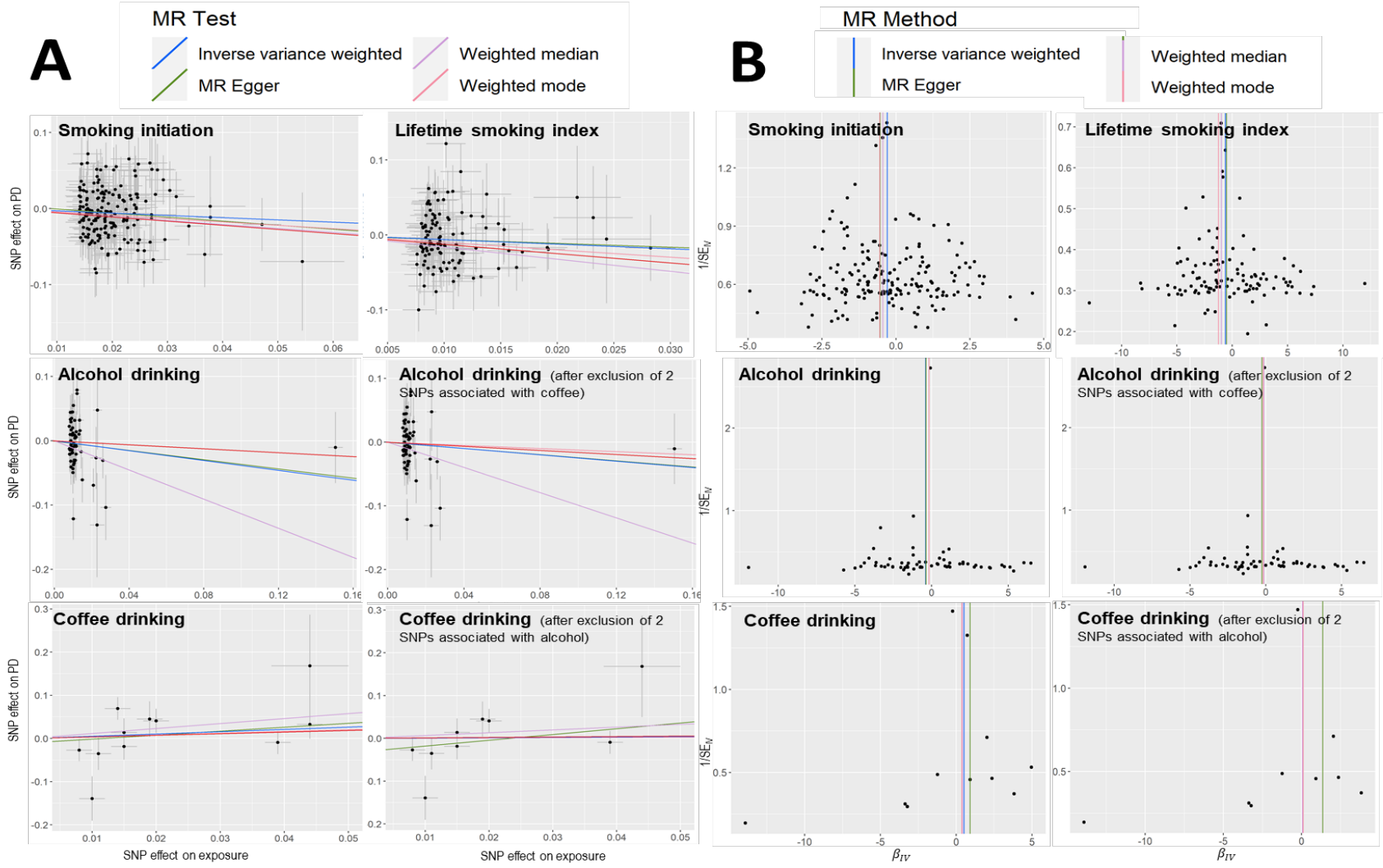


If both the exposure of interest (E) and an unmeasured exposure (U) influence survival (S), conditioning on survival up to the age at inclusion into the study creates an association between U and G (and E) (red dashed double arrow) because S is a collider. If U is not taken into account in the analysis, the association of G (and E) with PD is biased due to the association between U and G. The bias is more important for exposures that have an important effect on survival, and if there is an interaction between U and E in determining survival.

The importance and direction of the bias depends on the direction of the U-S and E-S associations (discordant or concordant) and of the U×E interaction for S. Depending on these parameters, the bias can go in any direction: it can distort associations towards the null (e.g., true associations that weaken as age increases), or it can create a false association between G and PD in situations where there is no true association (e.g., no association in younger subjects while there is one in older subjects) or make a true association seem stronger; in some extreme situations, it can even revert the direction of a true association (e.g., true positive association becomes negative as age increases).

MR estimates of the association between E and PD are based on the association between G and E, and the association between G and PD. In one-sample MR, both associations are estimated in the same sample and are likely to be similarly biased; therefore, taking the ratio of these associations cancels out much of the bias. Alternatively, in two-sample MR, only the association between G and PD is estimated in the study sample, and the bias of MR estimates equals the bias seen for the G and PD association (Smit RA et al., Epidemiology 2019;30(6):813-816).

Supplementary Figure 2. MR analyses of the relation of smoking, alcohol, and coffee drinking with PD: (A) Plots relating the effects sizes of the SNP-exposure (x-axis) and SNP-PD (y-axis, log OR) associations with standard error bars: the slope of the lines corresponds to causal estimates using different methods; (B) funnel plots of individual variant effects plotted against the inverse of their standard error.



Supplementary Figure 3. Reverse MR analyses of the relation of PD with smoking initiation, lifetime smoking index, and alcohol and coffee drinking: (A) Plots relating the effects sizes of the SNP-PD (x-axis) and SNP-outcomes (smoking, coffee, alcohol; y-axis, log OR) associations with standard error bars: the slope of the lines corresponds to causal estimates using different methods; (B) funnel plots of individual variant effects plotted against the inverse of their standard error.