

Supplementary material

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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, 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 $\geq 4\%$ 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) $< 5 \times 10^{-8}$ and those in Hardy-Weinberg disequilibrium ($P < 5 \times 10^{-8}$).

Association analysis and meta-analysis

Among 35 sites participating to the Courage-PD consortium, we excluded Asian studies (as rs4988235-T frequency is very low), case-only studies, and those with less than 50 cases and 50 controls. Our analyses are therefore restricted to 26 sites that provided samples for both cases and controls and included participants of Caucasian ancestry. 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 10,198 cases and 8,686 controls from 26 sites are shown in Table S1.

Our analyses are based on a single SNP (rs4988235) that was genotyped (not imputed) in all individuals from all sites (Table S2). For each site, logistic regression adjusted for sex and the first four principal components was performed for each SNP under a dominant genetic model (TC+TT vs CC carriers) using PLINK software (version 1.9).⁷

Summary statistics of the 23 studies with more than 5 cases and controls with the TC+TT or CC genotypes were meta-analysed using the GWAMA software.⁸ Effects size and standard errors were combined using a fixed-effect model in case of low heterogeneity across studies ($I^2 \leq 25\%$), while we used a random-effects model in case of high heterogeneity ($I^2 > 25\%$).

Sensitivity analyses

Analyses were first performed overall. We then performed several sets of sensitivity analyses:

- As the association between dairy intake and PD is stronger in men than women⁹, we performed sex-stratified analyses.
- To examine the potential for survival bias,¹⁰ we stratified analyses by median age at study in controls from all studies (≤ 67 years, > 67 years).
- Analyses were stratified by median disease duration in cases from all studies (≤ 7 years, > 7 years) to rule out incidence-prevalence bias (if rs4988235 had a different effect on survival in PD patients than controls);¹¹ cases from each group were compared to all controls.
- rs4988235-T frequency was heterogeneous across countries. We performed analyses stratified by median allele frequency in controls from all studies to assess whether associations varied by allele frequency.
- We used exact logistic regression (unadjusted for sex and principal components using SAS v9.4) for sites with ≤ 5 TC+TT or CC carriers, instead of excluding them (10,198 cases and 8,686 controls from 26 studies).
- We performed a leave-one-out meta-analysis by leaving out one study to assess how each individual study affects the overall estimate.

In stratified analyses, we compared MR estimates across strata.¹² For disease duration, they were not independent and we computed a p-value for the difference between the two duration groups by comparing cases-only.

Statistical power

Statistical power is shown in Table S7, overall and separately in men and women:

- Statistical power to detect a genetic association between rs4988235 and PD under a dominant model, assuming a frequency of 70% of the TC+TT genotypes in controls (based on a meta-analysis of the frequency of TC+TT genotypes in each study).
- Statistical power of MR analyses, considering that the standard deviation of dairy consumption is of 1.07 servings per day and that the R^2 for rs4988235 is of 1.75%.

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Table S1: 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	
					Male	Female	Mean	SD	MD	Mean	SD	MD	Mean	SD	MD	Mean	SD
Africa	Bardien/Carr	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	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	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	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	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	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	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	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/Mutez	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		-	-		-	-		-	-
	Deuschländer	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	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	Germany	Cases	1074	63.3	36.7	65.8	10.3		60.1	10.9		61.2	10.6	576	5.7	5.7
			Controls	746	51.7	48.3	61.5	7.3		-	-		-	-		-	-
	Duga/Cilia	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	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	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	
					Male	Female	Mean	SD	MD	Mean	SD	MD	Mean	SD	MD	Mean	SD
	Kruger	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		-	-		-	-		-	-
	Morris/Wood	United Kingdom	Cases	1307	67.8	32.2			1307				1307				
			Controls	559	24.9	75.1			559	-	-		-	-		-	-
	Pastor/Diez-Fairen	Spain	Cases	336	59.2	40.8	67.5	10.6		59.7	11.9				336	7.8	6.9
			Controls	325	40.3	59.7	66.2	11.4		-	-		-	-		-	-
	Puschmann	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	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		-	-		-	-		-	-
	Toft	Norway	Cases	407	63.9	36.1	65.8	9.0		56.2	11.5		54.2	10.1	137	9.5	6.8
			Controls	426	55.4	44.6	61.9	11.2		-	-		-	-		-	-
	Tolosa	Spain	Cases	278	62.6	37.4	66.0	10.6		58.5	11.4				278	7.5	6.3
			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	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	-	-		-	-		-	-

Abbreviation: MD = missing data; SD = standard deviation.

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

The following sites participate to the Geo-PD consortium: Bardien/Carr, Farrer, Rogaeva/Lang, Mellick, Aasly, Annesi, Brice/Corvol/Lesage, Carmine Belin/Ran, Chartier-Harlin/Mutez, Deutschländer, Elbaz, Duga/Cilia, Hadjigeorgiou, Koks/Tabata, Kruger, Puschmann, Stefanis/Simitsi, Wirdefeldt.

Table S2: Distribution of rs4988235 genotypes in cases and controls in each study from the Courage-PD consortium

Principal investigator	rs4988235 N (%)	Overall		Men		Women		Age ≤ 67y		Age > 67y		PD duration ≤ 7y	PD duration > 7y
		Cases (N=10198)	Controls (N=8686)	Cases (N=6290)	Controls (N=3915)	Cases (N=3908)	Controls (N=4771)	Cases (N=3523)	Controls (N=3734)	Cases (N=3878)	Controls (N=3047)	Cases (N=4503)	Cases (N=4353)
Aasly	N	463	487	276	264	187	223					20	443
	EAF (%)	79.5	78.3	78.8	77.1	80.5	79.8					85	79.2
	CC	15 (3.2)	23 (4.7)	8 (2.9)	14 (5.3)	7 (3.7)	9 (4)					0 (0)	15 (3.4)
	TC	160 (34.6)	165 (33.9)	101 (36.6)	93 (35.2)	59 (31.6)	72 (32.3)					6 (30)	154 (34.8)
	TT	288 (62.2)	299 (61.4)	167 (60.5)	157 (59.5)	121 (64.7)	142 (63.7)					14 (70)	274 (61.9)
	TC+TT	448 (96.8)	464 (95.3)	268 (97.1)	250 (94.7)	180 (96.3)	214 (96)					20 (100)	428 (96.6)
Annesi	N	89	93	58	43	31	50	42	45	47	48	51	38
	EAF (%)	9.6	10.2	6.9	9.3	14.5	11	7.1	7.8	11.7	12.5	11.8	6.6
	CC	73 (82)	76 (81.7)	50 (86.2)	35 (81.4)	23 (74.2)	41 (82)	37 (88.1)	38 (84.4)	36 (76.6)	38 (79.2)	40 (78.4)	33 (86.8)
	TC	15 (16.9)	15 (16.1)	8 (13.8)	8 (18.6)	7 (22.6)	7 (14)	4 (9.5)	7 (15.6)	11 (23.4)	8 (16.7)	10 (19.6)	5 (13.2)
	TT	1 (1.1)	2 (2.2)	0 (0)	0 (0)	1 (3.2)	2 (4)	1 (2.4)	0 (0)	0 (0)	2 (4.2)	1 (2)	0 (0)
	TC+TT	16 (18)	17 (18.3)	8 (13.8)	8 (18.6)	8 (25.8)	9 (18)	5 (11.9)	7 (15.6)	11 (23.4)	10 (20.8)	11 (21.6)	5 (13.2)
Bardien/Carr	N	117	80	70	46	47	34	43	73	74	7	64	53
	EAF (%)	65.4	58.8	60	62	73.4	54.4	72.1	58.9	61.5	57.1	68	62.3
	CC	16 (13.7)	16 (20)	12 (17.1)	7 (15.2)	4 (8.5)	9 (26.5)	5 (11.6)	15 (20.5)	11 (14.9)	1 (14.3)	10 (15.6)	6 (11.3)
	TC	49 (41.9)	34 (42.5)	32 (45.7)	21 (45.7)	17 (36.2)	13 (38.2)	14 (32.6)	30 (41.1)	35 (47.3)	4 (57.1)	21 (32.8)	28 (52.8)
	TT	52 (44.4)	30 (37.5)	26 (37.1)	18 (39.1)	26 (55.3)	12 (35.3)	24 (55.8)	28 (38.4)	28 (37.8)	2 (28.6)	33 (51.6)	19 (35.8)
	TC+TT	101 (86.3)	64 (80)	58 (82.9)	39 (84.8)	43 (91.5)	25 (73.5)	38 (88.4)	58 (79.5)	63 (85.1)	6 (85.7)	54 (84.4)	47 (88.7)
Brice/Corvol/ Lesage	N	745	275	444	155	301	120	507	182	213	93	332	388
	EAF (%)	50.1	48.2	49.6	45.8	50.8	51.3	49.8	48.4	51.2	47.9	49	51.3
	CC	205 (27.5)	73 (26.5)	123 (27.7)	48 (31)	82 (27.2)	25 (20.8)	143 (28.2)	48 (26.4)	53 (24.9)	25 (26.9)	96 (28.9)	100 (25.8)
	TC	334 (44.8)	139 (50.5)	202 (45.5)	72 (46.5)	132 (43.9)	67 (55.8)	223 (44)	92 (50.5)	102 (47.9)	47 (50.5)	147 (44.3)	178 (45.9)
	TT	206 (27.7)	63 (22.9)	119 (26.8)	35 (22.6)	87 (28.9)	28 (23.3)	141 (27.8)	42 (23.1)	58 (27.2)	21 (22.6)	89 (26.8)	110 (28.4)
	TC+TT	540 (72.5)	202 (73.5)	321 (72.3)	107 (69)	219 (72.8)	95 (79.2)	364 (71.8)	134 (73.6)	160 (75.1)	68 (73.1)	236 (71.1)	288 (74.2)
Carmine Belin/ Ran	N	214	611	136	335	78	276					111	103
	EAF (%)	74.8	71.4	76.1	72.1	72.4	70.7					74.8	74.8
	CC	15 (7)	54 (8.8)	10 (7.4)	29 (8.7)	5 (6.4)	25 (9.1)					7 (6.3)	8 (7.8)
	TC	78 (36.4)	241 (39.4)	45 (33.1)	129 (38.5)	33 (42.3)	112 (40.6)					42 (37.8)	36 (35)
	TT	121 (56.5)	316 (51.7)	81 (59.6)	177 (52.8)	40 (51.3)	139 (50.4)					62 (55.9)	59 (57.3)
	TC+TT	199 (93)	557 (91.2)	126 (92.6)	306 (91.3)	73 (93.6)	251 (90.9)					104 (93.7)	95 (92.2)

Principal investigator	rs4988235	Overall		Men		Women		Age ≤ 67y		Age > 67y		PD duration ≤ 7y	PD duration > 7y
	N (%)	Cases (N=10198)	Controls (N=8686)	Cases (N=6290)	Controls (N=3915)	Cases (N=3908)	Controls (N=4771)	Cases (N=3523)	Controls (N=3734)	Cases (N=3878)	Controls (N=3047)	Cases (N=4503)	Cases (N=4353)
Chartier-Harlin/ Mutez	N	285	217	159	84	126	133	176	147	109	70	68	217
	EAF (%)	62.5	59.9	62.6	60.7	62.3	59.4	59.9	59.5	66.5	60.7	53.7	65.2
	CC	50 (17.5)	38 (17.5)	29 (18.2)	15 (17.9)	21 (16.7)	23 (17.3)	35 (19.9)	27 (18.4)	15 (13.8)	11 (15.7)	19 (27.9)	31 (14.3)
	TC	114 (40)	98 (45.2)	61 (38.4)	36 (42.9)	53 (42.1)	62 (46.6)	71 (40.3)	65 (44.2)	43 (39.4)	33 (47.1)	25 (36.8)	89 (41)
	TT	121 (42.5)	81 (37.3)	69 (43.4)	33 (39.3)	52 (41.3)	48 (36.1)	70 (39.8)	55 (37.4)	51 (46.8)	26 (37.1)	24 (35.3)	97 (44.7)
	TC+TT	235 (82.5)	179 (82.5)	130 (81.8)	69 (82.1)	105 (83.3)	110 (82.7)	141 (80.1)	120 (81.6)	94 (86.2)	59 (84.3)	49 (72.1)	186 (85.7)
Deutschlander	N	264	40	163	13	101	27	101	22	163	18	131	133
	EAF (%)	58.1	66.3	62.3	57.7	51.5	70.4	60.4	65.9	56.8	66.7	55.3	60.9
	CC	56 (21.2)	4 (10)	27 (16.6)	2 (15.4)	29 (28.7)	2 (7.4)	19 (18.8)	2 (9.1)	37 (22.7)	2 (11.1)	33 (25.2)	23 (17.3)
	TC	109 (41.3)	19 (47.5)	69 (42.3)	7 (53.8)	40 (39.6)	12 (44.4)	42 (41.6)	11 (50)	67 (41.1)	8 (44.4)	51 (38.9)	58 (43.6)
	TT	99 (37.5)	17 (42.5)	67 (41.1)	4 (30.8)	32 (31.7)	13 (48.1)	40 (39.6)	9 (40.9)	59 (36.2)	8 (44.4)	47 (35.9)	52 (39.1)
	TC+TT	208 (78.8)	36 (90)	136 (83.4)	11 (84.6)	72 (71.3)	25 (92.6)	82 (81.2)	20 (90.9)	126 (77.3)	16 (88.9)	98 (74.8)	110 (82.7)
Duga/Cilia	N	1340	1328	795	455	545	873	665	883	675	445	872	468
	EAF (%)	19.5	20	20.6	17.8	17.9	21.2	18.7	19.4	20.3	21.2	19.2	20.1
	CC	879 (65.6)	859 (64.7)	512 (64.4)	311 (68.4)	367 (67.3)	548 (62.8)	443 (66.6)	581 (65.8)	436 (64.6)	278 (62.5)	578 (66.3)	301 (64.3)
	TC	400 (29.9)	406 (30.6)	239 (30.1)	126 (27.7)	161 (29.5)	280 (32.1)	196 (29.5)	261 (29.6)	204 (30.2)	145 (32.6)	254 (29.1)	146 (31.2)
	TT	61 (4.6)	63 (4.7)	44 (5.5)	18 (4)	17 (3.1)	45 (5.2)	26 (3.9)	41 (4.6)	35 (5.2)	22 (4.9)	40 (4.6)	21 (4.5)
	TC+TT	461 (34.4)	469 (35.3)	283 (35.6)	144 (31.6)	178 (32.7)	325 (37.2)	222 (33.4)	302 (34.2)	239 (35.4)	167 (37.5)	294 (33.7)	167 (35.7)
Elbaz	N	387	998	234	589	153	409	116	309	271	689	299	88
	EAF (%)	48.5	48.4	49.4	49.8	47.1	46.3	50	49	47.8	48.1	50.2	42.6
	CC	99 (25.6)	276 (27.7)	62 (26.5)	157 (26.7)	37 (24.2)	119 (29.1)	27 (23.3)	88 (28.5)	72 (26.6)	188 (27.3)	70 (23.4)	29 (33)
	TC	201 (51.9)	478 (47.9)	113 (48.3)	277 (47)	88 (57.5)	201 (49.1)	62 (53.4)	139 (45)	139 (51.3)	339 (49.2)	158 (52.8)	43 (48.9)
	TT	87 (22.5)	244 (24.4)	59 (25.2)	155 (26.3)	28 (18.3)	89 (21.8)	27 (23.3)	82 (26.5)	60 (22.1)	162 (23.5)	71 (23.7)	16 (18.2)
	TC+TT	288 (74.4)	722 (72.3)	172 (73.5)	432 (73.3)	116 (75.8)	290 (70.9)	89 (76.7)	221 (71.5)	199 (73.4)	501 (72.7)	229 (76.6)	59 (67)
Farrer	N	262	394	174	122	88	272	125	151	136	243	94	167
	EAF (%)	64.3	63.2	65.2	66	62.5	62	67.6	61.9	61	64	60.6	66.2
	CC	40 (15.3)	46 (11.7)	28 (16.1)	15 (12.3)	12 (13.6)	31 (11.4)	15 (12)	18 (11.9)	25 (18.4)	28 (11.5)	16 (17)	24 (14.4)
	TC	107 (40.8)	198 (50.3)	65 (37.4)	53 (43.4)	42 (47.7)	145 (53.3)	51 (40.8)	79 (52.3)	56 (41.2)	119 (49)	42 (44.7)	65 (38.9)
	TT	115 (43.9)	150 (38.1)	81 (46.6)	54 (44.3)	34 (38.6)	96 (35.3)	59 (47.2)	54 (35.8)	55 (40.4)	96 (39.5)	36 (38.3)	78 (46.7)
	TC+TT	222 (84.7)	348 (88.3)	146 (83.9)	107 (87.7)	76 (86.4)	241 (88.6)	110 (88)	133 (88.1)	111 (81.6)	215 (88.5)	78 (83)	143 (85.6)

Principal investigator	rs4988235	Overall		Men		Women		Age ≤ 67y		Age > 67y		PD duration ≤ 7y	PD duration > 7y
	N (%)	Cases (N=10198)	Controls (N=8686)	Cases (N=6290)	Controls (N=3915)	Cases (N=3908)	Controls (N=4771)	Cases (N=3523)	Controls (N=3734)	Cases (N=3878)	Controls (N=3047)	Cases (N=4503)	Cases (N=4353)
Ferreira	N	313	53	183	14	130	39	125	43	188	10	129	184
	EAF (%)	40.7	41.5	40.7	42.9	40.8	41	39.6	41.9	41.5	40	39.2	41.9
	CC	119 (38)	16 (30.2)	67 (36.6)	4 (28.6)	52 (40)	12 (30.8)	49 (39.2)	13 (30.2)	70 (37.2)	3 (30)	51 (39.5)	68 (37)
	TC	133 (42.5)	30 (56.6)	83 (45.4)	8 (57.1)	50 (38.5)	22 (56.4)	53 (42.4)	24 (55.8)	80 (42.6)	6 (60)	55 (42.6)	78 (42.4)
	TT	61 (19.5)	7 (13.2)	33 (18)	2 (14.3)	28 (21.5)	5 (12.8)	23 (18.4)	6 (14)	38 (20.2)	1 (10)	23 (17.8)	38 (20.7)
	TC+TT	194 (62)	37 (69.8)	116 (63.4)	10 (71.4)	78 (60)	27 (69.2)	76 (60.8)	30 (69.8)	118 (62.8)	7 (70)	78 (60.5)	116 (63)
Gasser/ Sharma	N	1074	746	683	386	391	360	540	587	534	159	767	307
	EAF (%)	59	54.2	59.4	53.1	58.3	55.3	57.7	54.6	60.4	52.5	58.2	61.1
	CC	176 (16.4)	159 (21.3)	109 (16)	83 (21.5)	67 (17.1)	76 (21.1)	95 (17.6)	127 (21.6)	81 (15.2)	32 (20.1)	130 (16.9)	46 (15)
	TC	528 (49.2)	366 (49.1)	336 (49.2)	196 (50.8)	192 (49.1)	170 (47.2)	267 (49.4)	279 (47.5)	261 (48.9)	87 (54.7)	381 (49.7)	147 (47.9)
	TT	370 (34.5)	221 (29.6)	238 (34.8)	107 (27.7)	132 (33.8)	114 (31.7)	178 (33)	181 (30.8)	192 (36)	40 (25.2)	256 (33.4)	114 (37.1)
	TC+TT	898 (83.6)	587 (78.7)	574 (84)	303 (78.5)	324 (82.9)	284 (78.9)	445 (82.4)	460 (78.4)	453 (84.8)	127 (79.9)	637 (83.1)	261 (85)
Hadjigeorgiou	N	256	310	124	147	132	163	98	129	158	181	198	58
	EAF (%)	20.9	16.5	23	14.3	18.9	18.4	18.4	16.3	22.5	16.6	19.4	25.9
	CC	162 (63.3)	219 (70.6)	74 (59.7)	106 (72.1)	88 (66.7)	113 (69.3)	66 (67.3)	90 (69.8)	96 (60.8)	129 (71.3)	128 (64.6)	34 (58.6)
	TC	81 (31.6)	80 (25.8)	43 (34.7)	40 (27.2)	38 (28.8)	40 (24.5)	28 (28.6)	36 (27.9)	53 (33.5)	44 (24.3)	63 (31.8)	18 (31)
	TT	13 (5.1)	11 (3.5)	7 (5.6)	1 (0.7)	6 (4.5)	10 (6.1)	4 (4.1)	3 (2.3)	9 (5.7)	8 (4.4)	7 (3.5)	6 (10.3)
	TC+TT	94 (36.7)	91 (29.4)	50 (40.3)	41 (27.9)	44 (33.3)	50 (30.7)	32 (32.7)	39 (30.2)	62 (39.2)	52 (28.7)	70 (35.4)	24 (41.4)
Koks/Taba	N	210	163	84	67	126	96	44	54	166	109	140	70
	EAF (%)	41.7	45.4	39.9	48.5	42.9	43.2	44.3	47.2	41	44.5	43.2	38.6
	CC	71 (33.8)	48 (29.4)	29 (34.5)	16 (23.9)	42 (33.3)	32 (33.3)	14 (31.8)	17 (31.5)	57 (34.3)	31 (28.4)	47 (33.6)	24 (34.3)
	TC	103 (49)	82 (50.3)	43 (51.2)	37 (55.2)	60 (47.6)	45 (46.9)	21 (47.7)	23 (42.6)	82 (49.4)	59 (54.1)	65 (46.4)	38 (54.3)
	TT	36 (17.1)	33 (20.2)	12 (14.3)	14 (20.9)	24 (19)	19 (19.8)	9 (20.5)	14 (25.9)	27 (16.3)	19 (17.4)	28 (20)	8 (11.4)
	TC+TT	139 (66.2)	115 (70.6)	55 (65.5)	51 (76.1)	84 (66.7)	64 (66.7)	30 (68.2)	37 (68.5)	109 (65.7)	78 (71.6)	93 (66.4)	46 (65.7)
Kruger	N	285	283	198	162	87	121	115	213	170	70	184	101
	EAF (%)	59	49.3	60.1	49.4	56.3	49.2	61.3	50	57.4	47.1	56.3	63.9
	CC	53 (18.6)	71 (25.1)	38 (19.2)	38 (23.5)	15 (17.2)	33 (27.3)	21 (18.3)	52 (24.4)	32 (18.8)	19 (27.1)	36 (19.6)	17 (16.8)
	TC	128 (44.9)	145 (51.2)	82 (41.4)	88 (54.3)	46 (52.9)	57 (47.1)	47 (40.9)	109 (51.2)	81 (47.6)	36 (51.4)	89 (48.4)	39 (38.6)
	TT	104 (36.5)	67 (23.7)	78 (39.4)	36 (22.2)	26 (29.9)	31 (25.6)	47 (40.9)	52 (24.4)	57 (33.5)	15 (21.4)	59 (32.1)	45 (44.6)
	TC+TT	232 (81.4)	212 (74.9)	160 (80.8)	124 (76.5)	72 (82.8)	88 (72.7)	94 (81.7)	161 (75.6)	138 (81.2)	51 (72.9)	148 (80.4)	84 (83.2)

Principal investigator	rs4988235 N (%)	Overall		Men		Women		Age ≤ 67y		Age > 67y		PD duration ≤ 7y	PD duration > 7y
		Cases (N=10198)	Controls (N=8686)	Cases (N=6290)	Controls (N=3915)	Cases (N=3908)	Controls (N=4771)	Cases (N=3523)	Controls (N=3734)	Cases (N=3878)	Controls (N=3047)	Cases (N=4503)	Cases (N=4353)
Mellick	N	399	399	259	193	140	206	171	192	228	207	191	208
	EAF (%)	71.2	73.4	71.2	72.5	71.1	74.3	70.8	74.5	71.5	72.5	70.7	71.6
	CC	46 (11.5)	27 (6.8)	26 (10)	18 (9.3)	20 (14.3)	9 (4.4)	23 (13.5)	9 (4.7)	23 (10.1)	18 (8.7)	21 (11)	25 (12)
	TC	138 (34.6)	158 (39.6)	97 (37.5)	70 (36.3)	41 (29.3)	88 (42.7)	54 (31.6)	80 (41.7)	84 (36.8)	78 (37.7)	70 (36.6)	68 (32.7)
	TT	215 (53.9)	214 (53.6)	136 (52.5)	105 (54.4)	79 (56.4)	109 (52.9)	94 (55)	103 (53.6)	121 (53.1)	111 (53.6)	100 (52.4)	115 (55.3)
	TC+TT	353 (88.5)	372 (93.2)	233 (90)	175 (90.7)	120 (85.7)	197 (95.6)	148 (86.5)	183 (95.3)	205 (89.9)	189 (91.3)	170 (89)	183 (88)
Morris/Wood	N	1307	559	886	139	421	420						
	EAF (%)	75.1	73.4	74.9	71.6	75.4	73.9						
	CC	85 (6.5)	45 (8.1)	56 (6.3)	13 (9.4)	29 (6.9)	32 (7.6)						
	TC	482 (36.9)	208 (37.2)	333 (37.6)	53 (38.1)	149 (35.4)	155 (36.9)						
	TT	740 (56.6)	306 (54.7)	497 (56.1)	73 (52.5)	243 (57.7)	233 (55.5)						
	TC+TT	1222 (93.5)	514 (91.9)	830 (93.7)	126 (90.6)	392 (93.1)	388 (92.4)						
Pastor/ Diez-Fairen	N	336	325	199	131	137	194	141	178	195	147	193	143
	EAF (%)	49	47.4	47.2	42	51.5	51	45.4	48.3	51.5	46.3	49.7	47.9
	CC	87 (25.9)	99 (30.5)	54 (27.1)	47 (35.9)	33 (24.1)	52 (26.8)	45 (31.9)	51 (28.7)	42 (21.5)	48 (32.7)	50 (25.9)	37 (25.9)
	TC	169 (50.3)	144 (44.3)	102 (51.3)	58 (44.3)	67 (48.9)	86 (44.3)	64 (45.4)	82 (46.1)	105 (53.8)	62 (42.2)	94 (48.7)	75 (52.4)
	TT	80 (23.8)	82 (25.2)	43 (21.6)	26 (19.8)	37 (27)	56 (28.9)	32 (22.7)	45 (25.3)	48 (24.6)	37 (25.2)	49 (25.4)	31 (21.7)
	TC+TT	249 (74.1)	226 (69.5)	145 (72.9)	84 (64.1)	104 (75.9)	142 (73.2)	96 (68.1)	127 (71.3)	153 (78.5)	99 (67.3)	143 (74.1)	106 (74.1)
Puschmann	N	50	105	35	31	15	74	21	50	29	55	30	20
	EAF (%)	80	78.6	81.4	69.4	76.7	82.4	88.1	79	74.1	78.2	83.3	75
	CC	2 (4)	5 (4.8)	0 (0)	2 (6.5)	2 (13.3)	3 (4.1)	0 (0)	1 (2)	2 (6.9)	4 (7.3)	1 (3.3)	1 (5)
	TC	16 (32)	35 (33.3)	13 (37.1)	15 (48.4)	3 (20)	20 (27)	5 (23.8)	19 (38)	11 (37.9)	16 (29.1)	8 (26.7)	8 (40)
	TT	32 (64)	65 (61.9)	22 (62.9)	14 (45.2)	10 (66.7)	51 (68.9)	16 (76.2)	30 (60)	16 (55.2)	35 (63.6)	21 (70)	11 (55)
	TC+TT	48 (96)	100 (95.2)	35 (100)	29 (93.5)	13 (86.7)	71 (95.9)	21 (100)	49 (98)	27 (93.1)	51 (92.7)	29 (96.7)	19 (95)
Rogaeva/ Lang	N	159	149	105	58	54	91	90	33	64	116	51	103
	EAF (%)	61.6	67.5	59.1	71.6	66.7	64.8	64.4	59.1	60.9	69.8	58.8	65.1
	CC	25 (15.7)	20 (13.4)	20 (19)	8 (13.8)	5 (9.3)	12 (13.2)	10 (11.1)	7 (21.2)	12 (18.8)	13 (11.2)	10 (19.6)	12 (11.7)
	TC	72 (45.3)	57 (38.3)	46 (43.8)	17 (29.3)	26 (48.1)	40 (44)	44 (48.9)	13 (39.4)	26 (40.6)	44 (37.9)	22 (43.1)	48 (46.6)
	TT	62 (39)	72 (48.3)	39 (37.1)	33 (56.9)	23 (42.6)	39 (42.9)	36 (40)	13 (39.4)	26 (40.6)	59 (50.9)	19 (37.3)	43 (41.7)
	TC+TT	134 (84.3)	129 (86.6)	85 (81)	50 (86.2)	49 (90.7)	79 (86.8)	80 (88.9)	26 (78.8)	52 (81.3)	103 (88.8)	41 (80.4)	91 (88.3)

Principal investigator	rs4988235 N (%)	Overall		Men		Women		Age ≤ 67y		Age > 67y		PD duration ≤ 7y	PD duration > 7y
		Cases (N=10198)	Controls (N=8686)	Cases (N=6290)	Controls (N=3915)	Cases (N=3908)	Controls (N=4771)	Cases (N=3523)	Controls (N=3734)	Cases (N=3878)	Controls (N=3047)	Cases (N=4503)	Cases (N=4353)
Stefanis/ Simitsi	N	174	178	108	64	66	114	72	91	102	87	122	52
	EAF (%)	12.4	12.6	12	11.7	12.9	13.2	9.7	11	14.2	14.4	11.5	14.4
	CC	134 (77)	135 (75.8)	84 (77.8)	50 (78.1)	50 (75.8)	85 (74.6)	58 (80.6)	72 (79.1)	76 (74.5)	63 (72.4)	97 (79.5)	37 (71.2)
	TC	37 (21.3)	41 (23)	22 (20.4)	13 (20.3)	15 (22.7)	28 (24.6)	14 (19.4)	18 (19.8)	23 (22.5)	23 (26.4)	22 (18)	15 (28.8)
	TT	3 (1.7)	2 (1.1)	2 (1.9)	1 (1.6)	1 (1.5)	1 (0.9)	0 (0)	1 (1.1)	3 (2.9)	1 (1.1)	3 (2.5)	0 (0)
	TC+TT	40 (23)	43 (24.2)	24 (22.2)	14 (21.9)	16 (24.2)	29 (25.4)	14 (19.4)	19 (20.9)	26 (25.5)	24 (27.6)	25 (20.5)	15 (28.8)
Toft	N	407	426	260	236	147	190	220	303	187	123	183	224
	EAF (%)	81.3	77.2	82.7	78.2	78.9	76.1	79.6	77.1	83.4	77.6	81.2	81.5
	CC	15 (3.7)	13 (3.1)	9 (3.5)	6 (2.5)	6 (4.1)	7 (3.7)	11 (5)	11 (3.6)	4 (2.1)	2 (1.6)	7 (3.8)	8 (3.6)
	TC	122 (30)	168 (39.4)	72 (27.7)	91 (38.6)	50 (34)	77 (40.5)	68 (30.9)	117 (38.6)	54 (28.9)	51 (41.5)	55 (30.1)	67 (29.9)
	TT	270 (66.3)	245 (57.5)	179 (68.8)	139 (58.9)	91 (61.9)	106 (55.8)	141 (64.1)	175 (57.8)	129 (69)	70 (56.9)	121 (66.1)	149 (66.5)
	TC+TT	392 (96.3)	413 (96.9)	251 (96.5)	230 (97.5)	141 (95.9)	183 (96.3)	209 (95)	292 (96.4)	183 (97.9)	121 (98.4)	176 (96.2)	216 (96.4)
Tolosa	N	278	66	174	11	104	55					177	101
	EAF (%)	39.9	36.4	39.1	31.8	41.4	37.3					40.1	39.6
	CC	106 (38.1)	29 (43.9)	66 (37.9)	6 (54.5)	40 (38.5)	23 (41.8)					68 (38.4)	38 (37.6)
	TC	122 (43.9)	26 (39.4)	80 (46)	3 (27.3)	42 (40.4)	23 (41.8)					76 (42.9)	46 (45.5)
	TT	50 (18)	11 (16.7)	28 (16.1)	2 (18.2)	22 (21.2)	9 (16.4)					33 (18.6)	17 (16.8)
	TC+TT	172 (61.9)	37 (56.1)	108 (62.1)	5 (45.5)	64 (61.5)	32 (58.2)					109 (61.6)	63 (62.4)
Valente	N	223	54	134	21	89	33	101	8	118	46	67	152
	EAF (%)	12.6	13	12.7	16.7	12.4	10.6	13.4	18.8	11.9	12	9.7	13.8
	CC	169 (75.8)	42 (77.8)	102 (76.1)	15 (71.4)	67 (75.3)	27 (81.8)	75 (74.3)	5 (62.5)	91 (77.1)	37 (80.4)	55 (82.1)	111 (73)
	TC	52 (23.3)	10 (18.5)	30 (22.4)	5 (23.8)	22 (24.7)	5 (15.2)	25 (24.8)	3 (37.5)	26 (22)	7 (15.2)	11 (16.4)	40 (26.3)
	TT	2 (0.9)	2 (3.7)	2 (1.5)	1 (4.8)	0 (0)	1 (3)	1 (1)	0 (0)	1 (0.8)	2 (4.3)	1 (1.5)	1 (0.7)
	TC+TT	54 (24.2)	12 (22.2)	32 (23.9)	6 (28.6)	22 (24.7)	6 (18.2)	26 (25.7)	3 (37.5)	27 (22.9)	9 (19.6)	12 (17.9)	41 (27)
Wirdefeldt	N	61	165	34	76	27	89	10	41	51	124	29	32
	EAF (%)	82	79.7	82.4	77	81.5	82	85	78.1	81.4	80.2	84.5	79.7
	CC	1 (1.6)	6 (3.6)	0 (0)	4 (5.3)	1 (3.7)	2 (2.2)	0 (0)	3 (7.3)	1 (2)	3 (2.4)	0 (0)	1 (3.1)
	TC	20 (32.8)	55 (33.3)	12 (35.3)	27 (35.5)	8 (29.6)	28 (31.5)	3 (30)	12 (29.3)	17 (33.3)	43 (34.7)	9 (31)	11 (34.4)
	TT	40 (65.6)	104 (63)	22 (64.7)	45 (59.2)	18 (66.7)	59 (66.3)	7 (70)	26 (63.4)	33 (64.7)	78 (62.9)	20 (69)	20 (62.5)
	TC+TT	60 (98.4)	159 (96.4)	34 (100)	72 (94.7)	26 (96.3)	87 (97.8)	10 (100)	38 (92.7)	50 (98)	121 (97.6)	29 (100)	31 (96.9)

Principal	rs4988235	Overall		Men		Women		Age ≤ 67y		Age > 67y		PD duration ≤ 7y	PD duration > 7y
investigator	N (%)	Cases (N=10198)	Controls (N=8686)	Cases (N=6290)	Controls (N=3915)	Cases (N=3908)	Controls (N=4771)	Cases (N=3523)	Controls (N=3734)	Cases (N=3878)	Controls (N=3047)	Cases (N=4503)	Cases (N=4353)
Zimprich													
	N	500	182	315	73	185	109						
	EAF (%)	54.5	57.1	54.4	51.4	54.6	61						
	CC	114 (22.8)	35 (19.2)	77 (24.4)	17 (23.3)	37 (20)	18 (16.5)						
	TC	227 (45.4)	86 (47.3)	133 (42.2)	37 (50.7)	94 (50.8)	49 (45)						
	TT	159 (31.8)	61 (33.5)	105 (33.3)	19 (26)	54 (29.2)	42 (38.5)						
	TC+TT	386 (77.2)	147 (80.8)	238 (75.6)	56 (76.7)	148 (80)	91 (83.5)						

Abbreviations: EAF = effect allele frequency (T allele).

In italic: not included in the main analyses because there were ≤5 cases or controls with the CC or TC+TT genotypes.

Table S3: Genetic association between rs4988235 and PD, and causal effect of genetically-predicted dairy products intake on PD, overall and by sex, age, and PD duration: exact logistic regression for sites with ≤ 5 cases or controls with the TC+TT or CC genotypes

Characteristics	N studies	N cases	N controls	Genetic association				MR estimate per 1-serving/day		
				OR (95% CI) TC+TT vs. CC	P-value	I ² (%)	P-het.	OR (95% CI) TC+TT vs. CC	P-value	P-diff.
All participants	26	10,198	8,686	1.11 (1.02-1.20)	0.017	23.9	0.14	1.66 (1.09-2.53)	0.017	
Men	24	6,221	3,808	1.20 (1.06-1.35)	0.003	0.0	0.80	2.45 (1.35-4.43)	0.003	--
Women	26	3,908	4,771	1.01 (0.86-1.19)	0.89	28.2	0.092	1.06 (0.48-2.34)	0.89	0.096
Age ≤ 67 years	19	3,492	3,643	1.08 (0.95-1.23)	0.24	20.5	0.21	1.47 (0.77-2.78)	0.24	--
Age > 67 years	21	3,878	3,047	1.11 (0.97-1.27)	0.12	20.2	0.20	1.70 (0.88-3.31)	0.12	0.75
PD duration ≤ 7 years	22	4,454	7,293	1.09 (0.99-1.21)	0.088	9.8	0.33	1.55 (0.94-2.56)	0.088	--
PD duration > 7 years	24	3,853	7,945	1.13 (0.96-1.33)	0.14	33.6	0.057	1.83 (0.82-4.09)	0.14	0.099

Abbreviations: OR = odds ratio; CI = confidence interval; P-het. = P-value for heterogeneity; P-diff. = P-value for the difference between subgroups.

Exact logistic regression did not converge for 2 sites in men, 2 sites for younger age, and 2 sites for shorter duration.

For genetic associations, ORs and their 95% CI were computed using fixed (if $I^2 \leq 25\%$) or random (if $I^2 > 25\%$) effects meta-analysis.

Table S4: Associations between rs4988235 and other traits at a genome-wide significant threshold (5×10^{-8}) using the PhenoScanner V2 database

Author, date	Traits	Beta	SE	P	N studies	N samples	Units
Nalls 2014	Parkinson's disease	0.117	0.02	7.41E-09	15	108,990	log OR
Locke 2015	Hip circumference	0.022	0.004	2.40E-08	101	207,713	IVNT
Willer 2013	Total cholesterol	-0.031	0.004	3.98E-14	60	183,761	IVNT
	Low density lipoprotein	-0.028	0.004	3.22E-11	60	169,531	IVNT
Neale 2017 (UKBB)	Whole body fat mass	0.016	0.003	1.41E-08	1	330,762	IVNT
	Body fat percentage	0.013	0.002	1.10E-09	1	331,117	IVNT
	Body mass index	0.016	0.003	2.59E-08	1	336,107	IVNT
	Leg fat mass left	0.013	0.002	2.95E-09	1	331,275	IVNT
	Leg fat mass right	0.013	0.002	6.09E-09	1	331,293	IVNT
	Leg fat percentage left	0.01	0.002	1.14E-08	1	331,278	IVNT
	Leg fat percentage right	0.011	0.002	5.03E-09	1	331,296	IVNT
	Trunk fat mass	0.016	0.003	1.18E-08	1	331,093	IVNT
	Trunk fat percentage	0.015	0.003	4.35E-09	1	331,113	IVNT
	Arm fat mass left	0.016	0.003	2.39E-08	1	331,164	IVNT
	Arm fat mass right	0.016	0.003	1.63E-08	1	331,226	IVNT
	Arm fat percentage left	0.012	0.002	3.22E-08	1	331,198	IVNT
	Arm fat percentage right	0.012	0.002	1.43E-08	1	331,249	IVNT
	Forced vital capacity	-0.015	0.002	2.27E-10	1	307,638	IVNT
	Forced expiratory volume in 1-second	-0.013	0.002	4.22E-08	1	307,638	IVNT

Abbreviations: SE = standard errors; IVNT = inverse normally rank transformed phenotype, UKBB = UK-Biobank. Effect allele, T; Other allele, C.

Table S5: SNPs used for reverse Mendelian randomization analyses: individual associations with PD (exposure) and milk intake (outcome)

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure: PD				Outcome: Milk intake			
			EAF	Beta	SE	P-value	EAF	Beta	SE	P-value
Chang et al. 2017										
rs35749011	1:155135036	A/G	0.01	0.545	0.044	2.59E-35	0.02	0.004	0.010	7.20E-01
rs823118	1:205723572	T/C	0.56	0.117	0.012	1.12E-23	0.55	-0.001	0.003	7.90E-01
rs4653767	1:226916078	T/C	0.69	0.083	0.013	1.63E-11	0.72	0.003	0.003	2.70E-01
rs10797576	1:232664611	T/C	0.14	0.113	0.016	8.41E-13	0.12	-0.005	0.004	2.20E-01
rs34043159	2:102413116	C/T	0.35	0.077	0.012	5.48E-11	0.34	0.005	0.003	4.40E-02
rs6430538	2:135539967	C/T	0.55	0.117	0.012	8.24E-24	0.61	0.004	0.003	1.40E-01
rs1474055	2:169110394	T/C	0.13	0.186	0.018	5.68E-26	0.12	-0.003	0.004	3.70E-01
rs4073221	3:18277488	G/T	0.13	0.095	0.017	1.57E-08	0.12	-0.005	0.004	1.70E-01
rs12497850	3:48748989	T/G	0.65	0.073	0.013	9.16E-09	0.65	-0.006	0.003	2.60E-02
rs115185635	3:87520857	C/G	0.04	0.191	0.052	1.22E-04	0.04	-0.011	0.007	9.70E-02
rs12637471	3:182762437	G/A	0.80	0.163	0.014	2.11E-30	0.81	0.003	0.003	4.20E-01
rs34311866	4:951947	C/T	0.18	0.207	0.014	1.47E-50	0.18	0.004	0.003	2.40E-01
rs11724635	4:15737101	A/C	0.55	0.105	0.012	1.22E-19	0.55	-0.001	0.003	6.80E-01
rs356182	4:90626111	G/A	0.35	0.285	0.012	5.21E-123	0.34	0.002	0.003	5.50E-01
rs78738012	4:114360372	C/T	0.11	0.122	0.019	4.78E-11	0.11	0.000	0.004	9.30E-01
rs2694528	5:60273923	C/A	0.12	0.140	0.018	4.84E-15	0.08	0.002	0.005	6.00E-01
rs9468199	6:27681215	A/G	0.17	0.104	0.015	1.46E-12	0.17	0.001	0.003	8.40E-01
rs9275326	6:32666660	C/T	0.90	0.163	0.022	1.26E-13	0.90	0.003	0.004	4.10E-01
rs199347	7:23293746	A/G	0.59	0.094	0.011	3.51E-18	0.59	-0.001	0.003	5.90E-01
rs591323	8:16697091	G/A	0.73	0.094	0.014	2.38E-11	0.72	-0.001	0.003	7.60E-01
rs2280104	8:22525980	T/C	0.37	0.068	0.012	2.53E-08	0.35	0.001	0.003	6.70E-01
rs13294100	9:17579690	G/T	0.63	0.083	0.012	4.84E-13	0.65	0.003	0.003	2.80E-01
rs10906923	10:15569598	A/C	0.69	0.073	0.013	1.35E-08	0.67	-0.002	0.003	5.60E-01
rs117896735	10:121536327	A/G	0.02	0.501	0.056	2.23E-19	0.02	-0.004	0.010	7.00E-01
rs3793947	11:83544472	G/A	0.56	0.073	0.013	3.72E-09	0.57	0.005	0.003	7.50E-02
rs329648	11:133765367	T/C	0.35	0.086	0.012	1.11E-13	0.35	0.000	0.003	9.10E-01
rs11060180	12:123303586	A/G	0.55	0.105	0.011	2.05E-20	0.56	-0.001	0.003	8.10E-01

SNP	Chr:Pos (GRCh37)	EA/BA	Exposure: PD				Outcome: Milk intake			
			EA/BA	Beta	SE	P-value	EA/BA	Beta	SE	P-value
rs11158026	14:55348869	C/T	0.67	0.094	0.012	4.30E-16	0.66	0.002	0.003	4.50E-01
rs1555399	14:67984370	T/A	0.51	0.086	0.014	9.61E-11	0.50	Excluded for reverse MR		
rs8005172	14:88472612	T/C	0.42	0.077	0.012	8.77E-11	0.42	-0.001	0.003	8.40E-01
rs2414739	15:61994134	A/G	0.73	0.094	0.013	3.94E-14	0.74	-0.003	0.003	3.80E-01
rs11343	16:19279464	T/G	0.45	0.068	0.011	9.13E-11	0.44	0.002	0.003	5.00E-01
rs14235	16:31121793	A/G	0.38	0.077	0.011	5.44E-12	0.36	-0.002	0.003	3.50E-01
rs4784227	16:52599188	T/C	0.27	0.086	0.014	9.75E-11	0.24	0.005	0.003	7.20E-02
rs17649553	17:43994648	C/T	0.78	0.248	0.014	1.26E-68	0.77	0.005	0.003	1.00E-01
rs12456492	18:40673380	G/A	0.32	0.095	0.012	5.56E-16	0.31	0.001	0.003	6.10E-01
rs62120679	19:2363319	T/C	0.31	0.077	0.016	6.64E-07	0.31	-0.006	0.003	2.50E-02
rs67820322	20:3161010	C/T	0.56	0.068	0.015	1.99E-06	0.61	0.002	0.003	3.90E-01

EA/BA, effect allele/base allele; SE, standard error.

Associations of SNPs with PD come from Chang et al. (2017) and associations of SNPs with milk intake come from the UK Biobank.

Table S6: Reverse Mendelian randomization analysis

Method	OR (95%CI)	P-value	P-het.	P-pleio.
IVW (random)	1.01 (0.99-1.02)	0.23	0.24	
Weighted median	1.01 (0.99-1.02)	0.32		
Weighted mode	1.01 (0.99-1.02)	0.15		
MR-Egger	1.02 (0.99-1.03)	0.40		0.73
MR-PRESSO	-	-		0.32

OR, odds ratio per 1-unit increase in log odds of liability to PD; IVW, inverse-variance weighted (random-effect); CI, confidence interval; p-het., p for heterogeneity (IVW); p-pleio., p for pleiotropy (MR-Egger and MR-PRESSO).

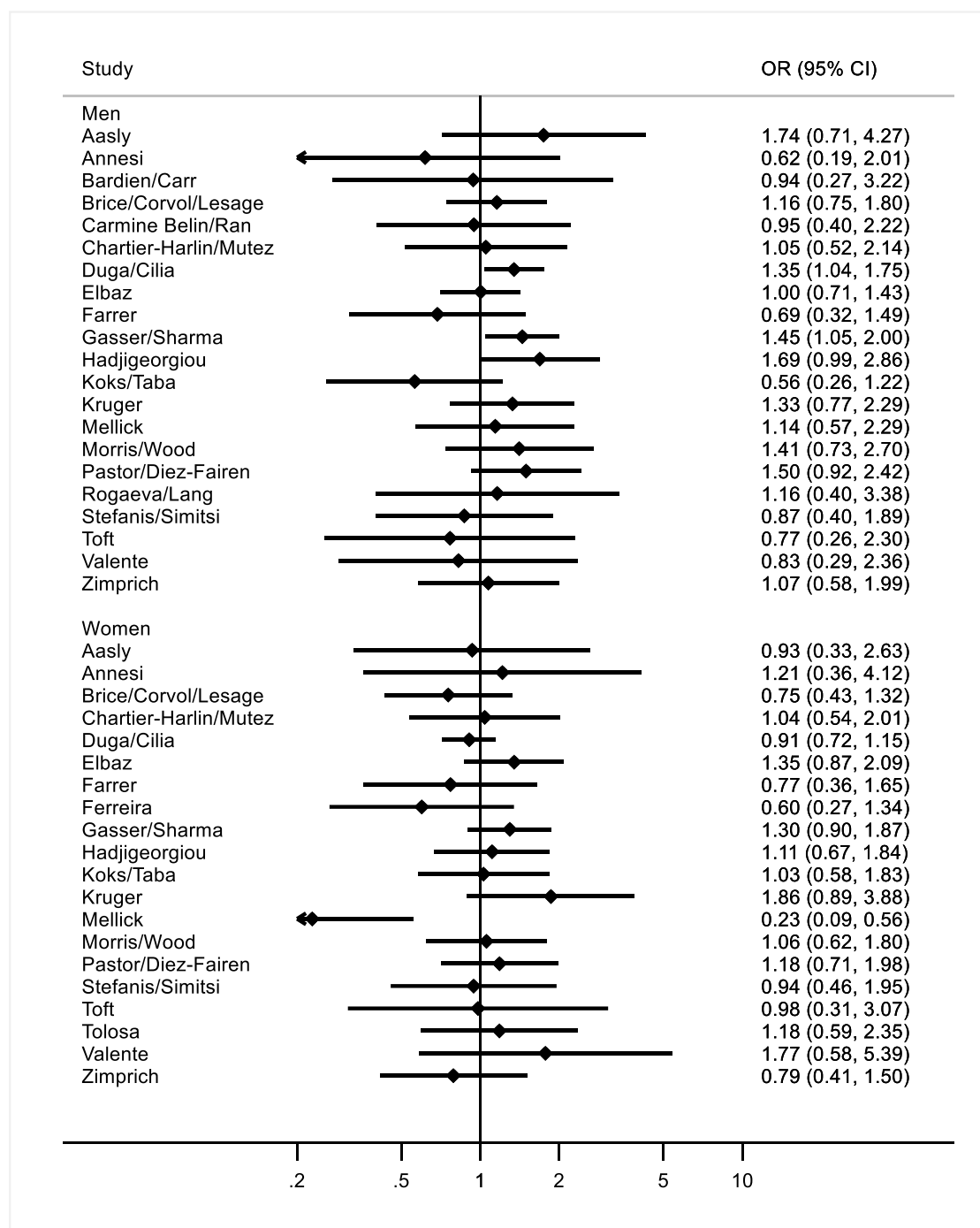
Table S7: Statistical power of the study

Group	MR analysis OR per 1-serving per day^a						Genetic association OR TT/TC vs. CC^b			
	1.40	1.50	1.60	1.70	1.80	1.90	1.10	1.15	1.20	1.30
Overall	0.88	0.97	0.99	1.00	1.00	1.00	0.83	0.99	1.00	1.00
Men	0.59	0.75	0.86	0.93	0.96	0.98	0.56	0.85	0.98	1.00
Women	0.56	0.73	0.85	0.93	0.97	0.99	0.48	0.80	0.95	1.00

^a Statistical power computed according to Brion et al (Int J Epidemiol 42, 1497-1501) based on a R^2 for rs4988235 of 1.75%, and assuming that the standard deviation of dairy intake is of 1.07 servings per day (based on a meta-analysis of the studies included in Mendelian Randomization of Dairy Consumption Working Group. Clin Chem 2018;64:183-191).

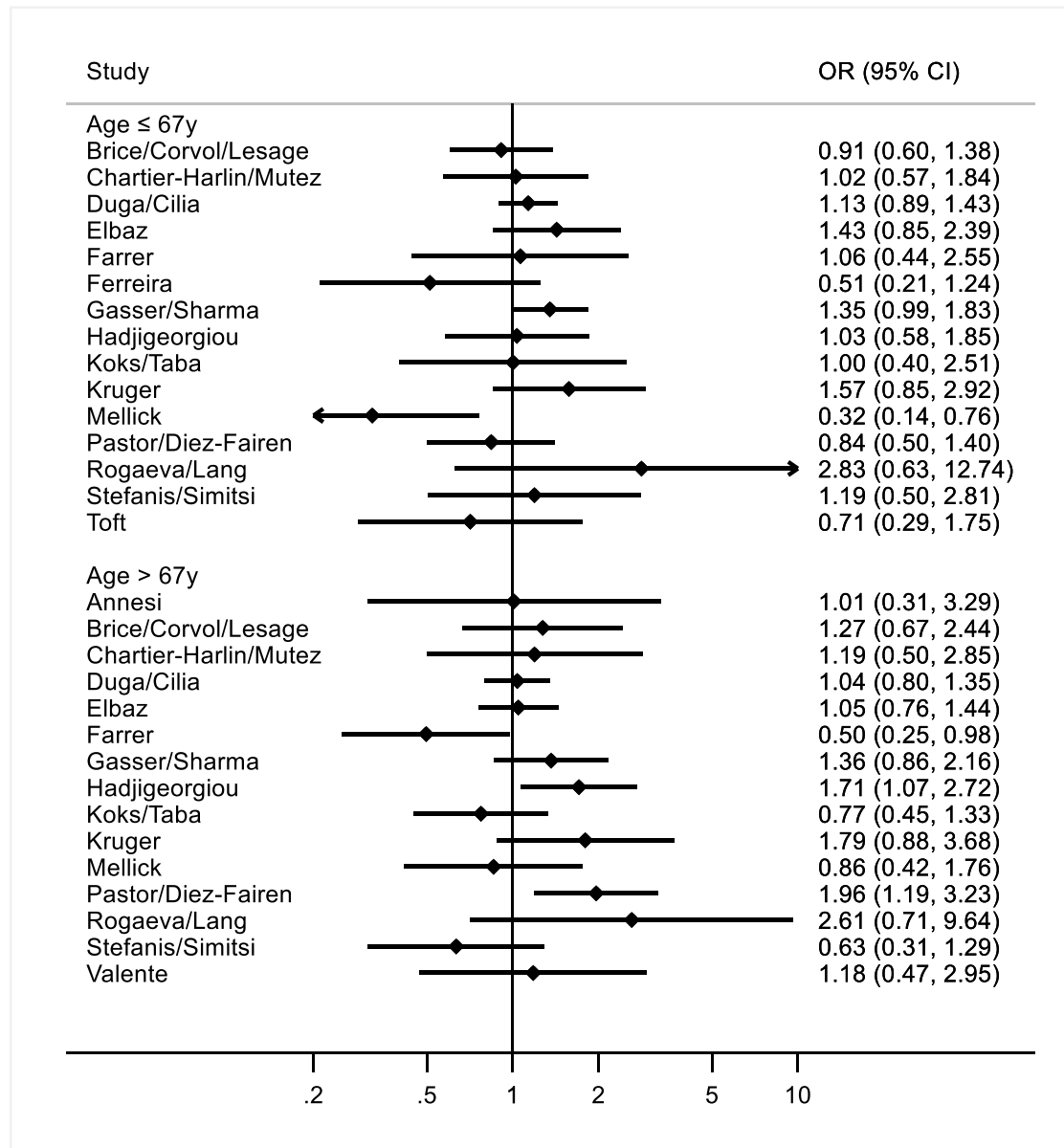
^b Computed using the Power software assuming a frequency of the TT/TC genotypes of 70% (<https://dceg.cancer.gov/tools/design/power>).

Figure S1: Forest plot of the association between rs4988235 and PD under a dominant model (TC+TT vs CC) by sex



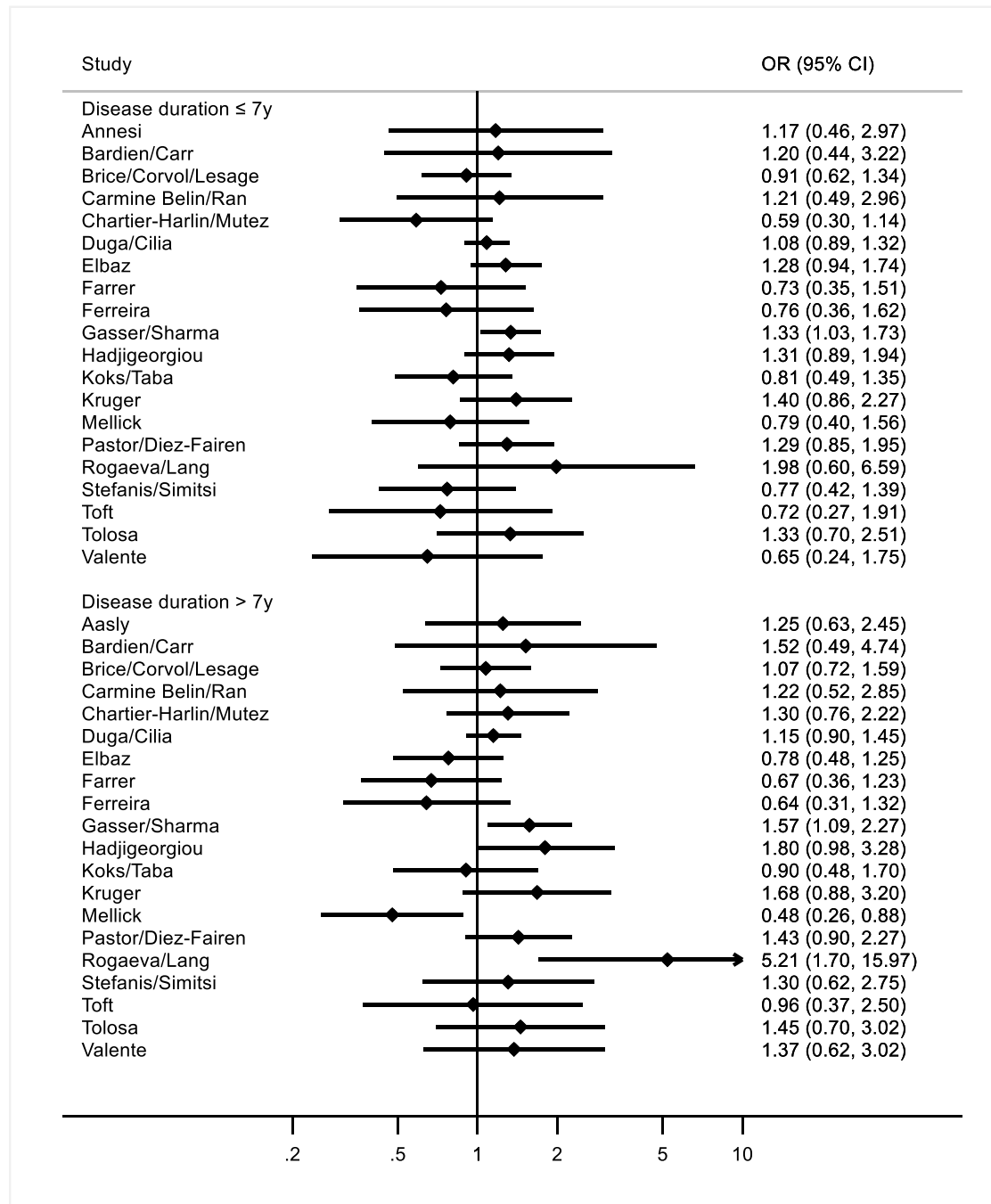
Abbreviations: OR = odds ratio; CI = confidence interval.
ORs were pooled using a fixed-effect meta-analysis.

Figure S2: Forest plot of the association between rs4988235 and PD under a dominant model (TC+TT vs CC) by median age at study



Abbreviations: OR = odds ratio; CI = confidence interval.
ORs were pooled using a fixed-effect meta-analysis.

Figure S3: Forest plot of the association between rs4988235 and PD under a dominant model (TC+TT vs CC) by median PD duration



Abbreviations: OR = odds ratio; CI = confidence interval.
ORs were pooled using a fixed-effect meta-analysis.