Supplementary Table 1. Variable names in each neuropathology dataset

Neuropathology	NACC	ADNI	ROSMAP
Amyloid plaques	NPTHAL		plaq_d[†]
0	Phase 0 (A0)		0
1	Phase 1-2 (A1)		≤0.5
2	Phase 3 (A2)		≤1
3	Phase 4-5 (A3)		>1
Tau neurofibrillary tangles	NACCBRAA	NPBRAAK	braaksc
0	Stage 0 (B0)		
1	Stage I-II (B1)		
2	Stage III-IV (B2)		
3	Stage V-VI (B3)		
Neocortical neuritic plaques	NACCNEUR	NPNEUR	ceradsc
0	No (C0)		No
1	Sparse (C1)		Possible
2	Moderate (C2)		Probable
3	Frequent (C3)		Definite
TDP-43 in amygdala	NPTDPB		tdp_st4
0	No		None
1	Yes		Amygdala /Amygdala + Limbic /Amygdala + Limbic + Neocortical
TDP-43 in limbic	NPTDPC/NPTDPD		
0	No		None/Amygdala
1	Yes		Amygdala + Limbic /Amygdala + Limbic + Neocortical
TDP-43 in neocortex	NPTDPE		
0	No		None/Amygdala /Amygdala + Limbic
1	Yes		Amygdala + Limbic + Neocortical
Lewy bodies	NACCLEWY	NPLBOD	dlbdx
0	No		Not present
1	Other regions		Nigral-predominant/ Limbic-type
2	Neocortical region		neocortical-type
Hippocampal sclerosis	NPHIPSCL		hspath_typ
0	None		Not present
1	Unilateral/Bilateral/present		Definitely present

[†] Diffuse plaques across regions were used in ROSMAP instead of Thal phase ratings

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project; NFT = neurofibrillary tangle

Supplementary Table 2. Filtering criteria for whole genome sequencing genotype calling data

Description		ID	Criteria
INFO			
	Allele count in genotypes	AC	<2
	Approximate read depth	DP	<10
	RMS Mapping Quality	MQ	<40
	Z-score From Wilcoxon rank sum test of Alt vs. Ref read mapping qualities	MQRankSum	<-12.5
	Z-score from Wilcoxon rank sum test of Alt Vs. Ref base qualities	BaseQRankSum	<-10 or >10
	Phred-scaled p-value using Fisher's exact test to detect strand bias	FS	>100
	Symmetric Odds Ratio of 2x2 contingency table to detect strand bias	SOR	>5
	Z-score from Wilcoxon rank sum test of Alt vs. Ref read position bias	ReadPosRankSum	<-10 or >10
	Variant Confidence/Quality by Depth	QD	<2
FORMAT			
	Approximate read depth	DP	<10
	Genotype Quality	GQ	<30

```
bcftools filter -e 'INFO/AC<2 || INFO/DP<10 || INFO/MQ<40 || INFO/MQRankSum<-12.5 ||
INFO/BaseQRankSum<-10 || INFO/BaseQRankSum>10 || INFO/FS>100 || INFO/SOR>5 ||
INFO/ReadPosRankSum<-10 || INFO/ReadPosRankSum>10 || INFO/QD<2' -O z -o
output.vcf.gz --threads 100 input.vcf.gz
```

```
bcftools annotate -x ^FORMAT/GT,FORMAT/AD,FORMAT/DP,FORMAT/GQ,FORMAT/PL
input.vcf.gz | bcftools filter -S . -i '\''FORMAT/DP>=10 & FORMAT/GQ>=30'\'' - | gzip -c >
output.vcf.gz'
```

Supplementary Table 3. Characteristics of included and excluded participant groups due to missing data

Characteristics	Participants without missing data (n = 1,304)	Participants with at least one missing data (n = 1,387)	P-value
Age at death, mean ± SD	83.0 ± 9.1	84.1 ± 9.0	0.0024
Years in education, mean ± SD	16.5 ± 8.5	16.5 ± 9.4	0.99
Sex, n (%)			
Male	641 (49.2)	722 (52.1)	0.14
Female	663 (50.8)	665 (47.9)	
Thal phase / diffuse plaques*, n (%)			
0 / 0	102 (7.8)	18 (1.3)	3.8×10^{-9}
1-2 / ≤0.5	115 (8.8)	202 (14.7)	
3 / ≤1	114 (8.7)	312 (22.7)	
4-5 / >1	973 (74.6)	843 (61.3)	
Braak NFT stage, n (%)			
0	25 (1.9)	18 (1.3)	0.20
I-II	177 (13.6)	202 (14.7)	
III-IV	266 (20.4)	312 (22.7)	
V-VI	836 (64.1)	843 (61.3)	
Neuritic plaques, n (%)			
No	196 (15.0)	233 (16.9)	5.6×10^{-9}
Sparse	140 (10.7)	137 (9.9)	
Moderate	222 (17.0)	334 (24.2)	
Frequent	746 (57.2)	676 (49.0)	
TDP-43 in amygdala, n (%)			
No	860 (66.0)	262 (82.6)	1.1×10^{-8}
Yes	444 (34.0)	55 (17.4)	
TDP-43 in hippocampus and/or entorhinal/inferior temporal cortex, n (%)			
No	884 (67.8)	112 (47.1)	1.2×10^{-9}
Yes	420 (32.2)	126 (52.9)	
TDP-43 in neocortex, n (%)			
No	1240 (95.1)	341 (95.5)	0.85
Yes	64 (4.9)	16 (4.5)	
Lewy bodies, n (%)			
No	713 (54.7)	842 (61.4)	7.4×10^{-4}
Other regions	384 (29.4)	322 (23.5)	
Neocortex	207 (15.9)	208 (15.2)	
Hippocampal sclerosis, n (%)			
No	1109 (85.0)	1132 (87.3)	0.10
Yes	195 (15.0)	164 (12.7)	

SD = standard deviation; NFT = neurofibrillary tangle

Supplementary Table 4. Rotated factor loadings with the oblimin rotation in NACC/ADNI and ROSMAP

Neuropathology	NACC/ADNI			ROSMAP		
	F1	F2	F3	F1	F2	F3
Braak NFT stage	-0.014	0.881	0.023	-0.074	0.629	0.014
Neuritic plaques	0.044	0.890	-0.012	0.078	0.618	0.065
Thal phase	-0.021	0.959	-0.012	0.004	0.894	-0.022
TDP-43 in amygdala	0.922	0.056	0.099	0.747	-0.045	0.072
TDP-43 in limbic	0.995	0.035	-0.039	0.997	-0.020	0.008
TDP-43 in neocortex	0.935	-0.080	-0.033	0.996	0.012	-0.021
Hippocampal sclerosis	0.671	-0.027	-0.024	0.988	0.031	-0.018
Lewy bodies	0.002	-0.004	0.974	-0.001	0.003	0.984

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project; NFT = neurofibrillary tangle

Supplementary Table 5. Number of missing data in each single nucleotide variant displayed in Tables 2 and 3

	CHR	Gene	SNV	Position	# of missing			
					≥ 65 at death		≥ 80 at death	
					NACC/ADNI	ROSMAP	NACC/ADNI	ROSMAP
Table 2								
	1	*GBA*	rs140335079	155237596	0	0		
	2	*BIN1*	rs6733839	127135234	2	1		
	7	*TMEM106B*	rs10950392	12223912	0	10		
	17	*GRN*	rs5848	44352876	2	0		
	19	*APOE*	rs429358	44908684	2	2		
Table 3								
Factor 1								
	1	*KAZN*	rs72643142	14148707	1	0	0	0
	5	*ARHGEF28*	rs80190672	73973002	0	0	0	0
	15	*UNC13C*	rs141108370	54631819	0	1	0	1
Factor 2								
	1	*C1orf185*	rs72692278	51129361	1	1	0	1
	1	*ZNF281*	rs188482877	200431363	0	4	0	4
	12	*GRIN2B*	rs71457202	13748154	0	0	0	0
	13	*LINC00559*	rs145442832	89883465	1	0	0	0
	14	*TTLL5*	rs745536628	75760859	1	0	0	0
Factor 3								
	6	*TNFRSF21*	rs78794444	47311493	1	0	0	0
Table 4								
Factor 1								
	8	*TMEM68*	rs28610182	55751840	2	4		
	19	*SDHAF1*	rs17706479	35994474	1	0		
Factor 2								
	10	*BMS1*	rs3128722	4288490	0	0		

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project

Supplementary Table 6. Significant and suggestive significant single nucleotide variants associated with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score in subjects aged 65 years or older at death and in subjects aged 80 years or older at death as a sensitivity analysis

					≥ 65 at death								≥ 80 at death	
CHR	Gene	SNV	Position	Effect /reference	Meta-analysis		NACC/ADNI			ROSMAP			Meta-analysis	
					$\hat{\beta}$	P-value	AF	$\hat{\beta}$	P-value	AF	$\hat{\beta}$	P-value	$\hat{\beta}$	P-value
1	***KAZN***	**rs72643142**	**14148707**	**T/C**	**-0.40**	**7.1×10^{-7}**	**0.101**	**-0.35**	**0.0033**	**0.103**	**-0.45**	**6.4×10^{-5}**	**-0.48**	**5.6×10^{-7}**
1	*LPHN2*	rs17472472	82013634	C/T	0.24	3.9×10^{-6}	0.385	0.22	0.0045	0.347	0.25	3.0×10^{-4}	0.25	3.5×10^{-5}
2	*KLHL29*	rs55869619	23200869	C/G	0.44	6.8×10^{-6}	0.067	0.52	1.9×10^{-4}	0.063	0.37	0.0097	0.42	3.3×10^{-4}
2	*DDX18*	rs554736674	116872180	A/G	0.70	2.6×10^{-6}	0.023	1.02	7.1×10^{-6}	0.030	0.45	0.025	0.66	4.9×10^{-4}
4	*MSANTD1*	rs362285	3256594	A/G	-0.90	4.9×10^{-6}	0.011	-0.97	0.0046	0.018	-0.86	3.7×10^{-4}	-0.79	2.3×10^{-4}
5	***ARHGEF28***	**rs80190672**	**73973002**	**G/A**	**-0.64**	**4.7×10^{-8}**	**0.046**	**-0.59**	**6.6×10^{-4}**	**0.041**	**-0.69**	**2.3×10^{-5}**	**-0.76**	**5.8×10^{-8}**
7	*TMEM106B*	rs10950392	12223912	C/T	-0.22	7.2×10^{-6}	0.431	-0.23	0.0010	0.414	-0.21	0.0025	-0.25	3.0×10^{-5}
8	*TMEM68*	rs28610182	55751840	A/G	-0.29	1.1×10^{-6}	0.208	-0.23	0.0075	0.216	-0.36	3.1×10^{-5}	-0.31	2.5×10^{-5}
9	*RNU6ATAC*	rs147951468	134200170	A/G	0.79	3.7×10^{-6}	0.020	0.82	0.0012	0.021	0.77	0.0010	0.63	3.6×10^{-4}
12	*CD9*	rs140383201	6164511	T/C	0.93	3.1×10^{-6}	0.016	0.77	0.0043	0.014	1.11	1.8×10^{-4}	1.22	6.8×10^{-5}
12	*MGAT4C*	rs11615307	87047504	C/T	0.34	6.2×10^{-6}	0.128	0.41	2.2×10^{-4}	0.120	0.27	0.0067	0.39	1.2×10^{-5}
15	***UNC13C***	**rs141108370**	**54631819**	**G/A**	**-1.06**	**5.7×10^{-7}**	**0.013**	**-1.09**	**4.3×10^{-4}**	**0.014**	**-1.02**	**4.5×10^{-4}**	**-1.25**	**2.8×10^{-7}**
16	*PARN*	rs77639069	14418707	T/C	0.82	5.8×10^{-6}	0.019	0.90	7.4×10^{-4}	0.017	0.75	0.0026	0.94	3.8×10^{-5}
18	*MIR4318*	rs77579757	37626039	T/C	-0.44	6.1×10^{-6}	0.061	-0.37	0.014	0.069	-0.49	1.4×10^{-4}	-0.45	6.7×10^{-5}
19	*SDHAF1*	rs17706479	35994474	A/G	0.31	1.8×10^{-6}	0.184	0.38	3.5×10^{-5}	0.151	0.24	0.012	0.30	9.2×10^{-5}
19	*CLIP3*	rs113229403	36021913	T/C	0.30	4.5×10^{-6}	0.179	0.38	3.3×10^{-5}	0.153	0.21	0.025	0.28	2.4×10^{-4}

Bolded results indicate single nucleotide variants which were confirmed as a suggestive significance in the sensitivity analysis for people who died 80 years or older.

CHR = chromosome; SNV = single nucleotide variant; NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project; AF = allele frequency

Supplementary Table 7. Significant and suggestive significant single nucleotide variants associated with the estimated factor 2 (Alzheimer's disease neuropathologic change related) score in subjects aged 65 years or older at death and in subjects aged 80 years or older at death as a sensitivity analysis

					≥ 65 at death								≥ 80 at death	
CHR	Gene	SNV	Position	Effect /reference	Meta-analysis		NACC/ADNI			ROSMAP			Meta-analysis	
					$\hat{\beta}$	P-value	AF	$\hat{\beta}$	P-value	AF	$\hat{\beta}$	P-value	$\hat{\beta}$	P-value
1	***C1orf185***	**rs72692278**	**51129361**	**A/G**	**-0.50**	**6.6×10^{-6}**	**0.052**	**-0.50**	**0.0020**	**0.058**	**-0.49**	**0.0012**	**-0.58**	**7.2×10^{-6}**
1	*LRRC7*	rs79165012	69428372	T/C	-1.05	1.7×10^{-6}	0.013	-1.12	3.8×10^{-4}	0.014	-0.99	0.0015	-1.11	1.3×10^{-5}
1	***ZNF281***	**rs188482877**	**200431363**	**T/A**	**-1.00**	**3.2×10^{-6}**	**0.015**	**-1.14**	**1.4×10^{-4}**	**0.014**	**-0.84**	**0.0066**	**-1.12**	**3.3×10^{-6}**
4	*SPINK2*	rs34986806	56843293	C/T	-0.66	5.3×10^{-6}	0.037	-0.65	6.2×10^{-4}	0.026	-0.67	0.0031	-0.61	7.7×10^{-4}
5	*PARP8*	rs149949227	50746672	A/T	-0.88	5.1×10^{-6}	0.020	-1.05	4.7×10^{-5}	0.015	-0.65	0.0266	-0.58	0.0089
5	*LOC101928448*	rs462520	56558051	A/G	-0.24	2.1×10^{-6}	0.402	-0.27	2.7×10^{-4}	0.396	-0.22	0.0025	-0.23	2.0×10^{-4}
5	*CTB-118N6.3*	rs150918584	116478466	G/A	0.91	4.3×10^{-6}	0.017	0.89	0.0018	0.016	0.94	8.5×10^{-4}	0.95	6.2×10^{-5}
7	*ASNS*	rs185792646	97833130	T/C	-1.08	6.1×10^{-6}	0.011	-0.90	0.0094	0.012	-1.25	1.8×10^{-4}	-1.01	1.1×10^{-4}
7	*MIR29A*	rs34484449	130843576	A/G	0.45	5.9×10^{-6}	0.067	0.57	9.2×10^{-5}	0.074	0.34	0.012	0.40	3.4×10^{-4}
9	*PTPRD*	rs79814862	9653882	C/T	-0.35	6.1×10^{-6}	0.126	-0.27	0.012	0.116	-0.44	1.1×10^{-4}	-0.34	2.3×10^{-4}
9	*LCN15*	rs9411227	136759203	A/G	-0.30	1.8×10^{-6}	0.196	-0.28	0.0026	0.216	-0.33	2.3×10^{-4}	-0.32	1.6×10^{-5}
10	*BMS1*	rs3128722	42884908	G/T	-0.22	8.3×10^{-6}	0.490	-0.23	0.0010	0.487	-0.22	0.0029	-0.22	2.4×10^{-4}
12	***GRIN2B***	**rs71457202**	**13748154**	**A/G**	**0.81**	**3.8×10^{-6}**	**0.028**	**0.82**	**1.9×10^{-4}**	**0.015**	**0.78**	**0.0074**	**0.99**	**1.1×10^{-6}**
13	***LINC00559***	**rs145442832**	**89883465**	**T/C**	**-0.39**	**4.6×10^{-6}**	**0.085**	**-0.37**	**0.0033**	**0.105**	**-0.41**	**4.8×10^{-4}**	**-0.52**	**2.2×10^{-7}**
14	***TTLL5***	**rs745536628**	**75760859**	**A/AT**	**-1.04**	**5.4×10^{-6}**	**0.012**	**-0.93**	**0.0044**	**0.013**	**-1.14**	**4.0×10^{-4}**	**-1.21**	**6.3×10^{-6}**
15	*FBN1*	rs12591575	48478822	T/C	0.94	1.0×10^{-5}	0.013	0.94	0.0014	0.014	0.94	0.0025	0.73	0.0027
19	*PVRL2*	rs6857	44888997	T/C	0.41	7.5×10^{-12}	0.309	0.35	4.7×10^{-6}	0.171	0.50	3.3×10^{-7}	0.54	3.9×10^{-13}
19	*TOMM40*	rs157582	44892962	T/C	0.33	8.8×10^{-9}	0.356	0.34	1.2×10^{-5}	0.229	0.32	2.6×10^{-4}	0.40	1.2×10^{-8}
19	*APOE*	rs429358	44908684	C/T	0.50	9.1×10^{-17}	0.338	0.42	2.0×10^{-8}	0.141	0.63	8.5×10^{-10}	0.60	6.9×10^{-15}

Bolded results indicate single nucleotide variants which were confirmed as a suggestive significance in the sensitivity analysis for people who died 80 years or older.

CHR = chromosome; SNV = single nucleotide variant; NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project; AF = allele frequency

Supplementary Table 8. Suggestive significant single nucleotide variants associated with the estimated factor 3 (Lewy body pathology related) score in subjects aged 65 years or older at death and in subjects aged 80 years or older at death as a sensitivity analysis

					≥ 65 at death								≥ 80 at death	
CHR	Gene	SNV	Position	Effect /reference	Meta-analysis		NACC/ADNI			ROSMAP			Meta-analysis	
					$\hat{\beta}$	P-value	AF	$\hat{\beta}$	P-value	AF	$\hat{\beta}$	P-value	$\hat{\beta}$	P-value
2	*NBAS*	rs145028924	15232755	G/A	0.92	3.2×10^{-6}	0.019	0.91	5.1×10^{-4}	0.016	0.93	0.0023	1.05	2.5×10^{-5}
4	*HS3ST1*	rs73227761	11527873	A/G	0.40	6.2×10^{-6}	0.096	0.40	8.9×10^{-4}	0.087	0.41	0.0025	0.35	8.4×10^{-4}
4	*PABPC4L*	rs13134385	133792235	A/G	0.37	6.8×10^{-6}	0.101	0.41	6.6×10^{-4}	0.121	0.33	0.0033	0.39	1.8×10^{-5}
6	***TNFRSF21***	**rs78794444**	**47311493**	**T/G**	**-0.71**	$\mathbf{3.0\times10^{-6}}$	**0.027**	**-0.41**	**0.056**	**0.031**	**-1.04**	$\mathbf{2.8\times10^{-6}}$	**-0.87**	$\mathbf{1.5\times10^{-6}}$
7	*ADAP1*	rs112886046	947886	G/A	-0.58	8.5×10^{-6}	0.049	-0.59	3.6×10^{-4}	0.029	-0.56	0.0087	-0.60	3.9×10^{-5}
7	*EPHB4*	rs75881054	100808585	T/G	-0.59	9.3×10^{-6}	0.036	-0.64	8.7×10^{-4}	0.046	-0.54	0.0036	-0.48	0.0011
7	*SLC12A9*	rs1235649855	100843125	A/ACT	-0.57	9.9×10^{-6}	0.041	-0.64	4.2×10^{-4}	0.046	-0.50	0.0076	-0.43	0.0026
9	*SH3GL2*	rs60097187	17998212	T/C	0.72	3.4×10^{-6}	0.034	0.66	0.0012	0.025	0.83	8.6×10^{-4}	0.68	3.0×10^{-4}
12	*RERGL*	rs117137691	17933738	C/T	0.82	4.8×10^{-6}	0.025	0.68	0.0032	0.017	1.04	3.3×10^{-4}	0.72	3.9×10^{-4}
12	*SLC5A8*	rs79398551	101212178	A/C	-0.50	3.4×10^{-6}	0.057	-0.50	0.0011	0.065	-0.50	0.0011	-0.47	1.1×10^{-4}
12	*LOC101928416*	rs28677872	132408886	G/A	0.24	5.9×10^{-6}	0.422	0.24	7.2×10^{-4}	0.436	0.23	0.0029	0.23	1.1×10^{-4}
13	*FLT3*	rs117990166	28013358	T/C	0.88	5.0×10^{-6}	0.013	1.12	3.1×10^{-4}	0.024	0.72	0.0035	0.80	1.6×10^{-4}
13	*MIR5007*	rs73202898	54904307	A/G	0.60	8.2×10^{-6}	0.036	0.75	6.2×10^{-5}	0.036	0.43	0.027	0.49	0.0011
14	*LOC642426*	rs28394359	18651775	G/A	0.98	9.4×10^{-6}	0.013	0.97	0.0025	0.016	0.98	0.0014	0.94	1.3×10^{-4}
16	*PLLP*	rs12929504	57320578	C/T	-0.26	8.4×10^{-6}	0.295	-0.30	1.4×10^{-4}	0.258	-0.21	0.018	-0.26	1.0×10^{-4}
16	*PLCG2*	rs146614066	81977696	A/G	1.03	5.8×10^{-6}	0.013	1.11	3.2×10^{-4}	0.013	0.93	0.0061	0.85	0.0010
19	*LINC01233*	rs116885812	22545387	G/A	1.15	9.7×10^{-7}	0.011	1.03	7.3×10^{-4}	0.011	1.31	3.9×10^{-4}	1.44	4.0×10^{-5}

Bolded result indicates a single nucleotide variant which was confirmed as a suggestive significance in the sensitivity analysis for people who died 80 years or older.

CHR = chromosome; SNV = single nucleotide variant; NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project; AF = allele frequency

Supplementary Table 9. Quality score of significant and suggestive significant single nucleotide variants associated with the estimated factor 1 (TDP-43 and hippocampal sclerosis related) score

CHR	Gene	SNV	Position	Location	FILTER	MQ	FS	SOR	QD	P_HWE
1	*KAZN*	rs72643142	14148707	Intron	PASS	60	0	0.716	15.09	0.072
1	*LPHN2*	rs17472472	82013634	Intergenic	PASS	.	0	0.704	17.96	1.0×10^{-5}
2	*KLHL29*	rs55869619	23200869	Promoter	PASS	60	0	0.715	14.85	4.0×10^{-5}
2	*DDX18*	rs554736674	116872180	Intergenic	PASS	42.32	0	0.758	13.83	1
4	*MSANTD1*	rs362285	3256594	3’ UTR	PASS	60	0.516	0.671	14.55	7.5×10^{-8}
5	*ARHGEF28*	rs80190672	73973002	Intergenic	PASS	60	0	0.714	14.25	0.16
7	*TMEM106B*	rs10950392	12223912	Intron	PASS	.	0	0.682	28.77	2.1×10^{-6}
8	*TMEM68*	rs28610182	55751840	Promoter	PASS	60	0	0.695	16.3	2.3×10^{-6}
9	*RNU6ATAC*	rs147951468	134200170	Intergenic	PASS	60	0.517	0.661	14.31	0.0033
12	*CD9*	rs140383201	6164511	Intergenic	PASS	59.96	0	0.701	13.22	0.0062
12	*MGAT4C*	rs11615307	87047504	Intergenic	PASS	60	0	0.696	15.17	0.0087
15	*UNC13C*	rs141108370	54631819	Intergenic	PASS	60	0	0.701	13.86	1
16	*PARN*	rs77639069	14418707	Promoter	PASS	59.83	0	0.703	14.54	1.7×10^{-4}
18	*MIR4318*	rs77579757	37626039	Intron	PASS	59.98	0	0.695	14.35	1.4×10^{-4}
19	*SDHAF1*	rs17706479	35994474	Promoter	PASS	60	0	0.68	15.21	0.0048
19	*CLIP3*	rs113229403	36021913	Intron	PASS	59.95	0	0.668	15.11	0.0037

CHR = chromosome; SNV = single nucleotide variant; MQ = RMS mapping quality; FS = Phred-scaled p-value using Fisher's exact test to detect strand bias; SOR = symmetric odds ratio of 2×2 contingency table to detect strand bias; QD = variant confidence/quality by depth; P_HWE = p-value from Hardy-Weinberg equilibrium test

Supplementary Table 10. Quality score of significant and suggestive significant single nucleotide variants associated with the estimated factor 2 (Alzheimer's disease neuropathologic change related) score

CHR	Gene	SNV	Position	Location	FILTER	MQ	FS	SOR	QD	P_HWE
1	*C1orf185*	rs72692278	51129361	Intron	PASS	60	0	0.672	14.12	9.6×10^{-4}
1	*LRRC7*	rs79165012	69428372	Intergenic	PASS	60	0	0.717	13.68	1
1	*ZNF281*	rs188482877	200431363	Intron	PASS	59.99	0.521	0.756	14.33	0.37
4	*SPINK2*	rs34986806	56843293	Intergenic	PASS	60.02	0.528	0.622	13.78	0.47
5	*PARP8*	rs149949227	50746672	Intron	PASS	60	0	0.677	13.94	0.39
5	*LOC101928448*	rs462520	56558051	Intron	PASS	.	0	0.703	23.26	0.79
5	*CTB-118N6.3*	rs150918584	116478466	Intron	PASS	60	0	0.687	13.07	0.044
7	*ASNS*	rs185792646	97833130	Intergenic	PASS	59.99	0	0.735	14.27	0.12
7	*MIR29A*	rs34484449	130843576	Promoter	PASS	60.23	0.525	0.661	15.05	0.22
9	*PTPRD*	rs79814862	9653882	Intron	PASS	60	0	0.707	14.66	5.3×10^{-5}
9	*LCN15*	rs9411227	136759203	Promoter	PASS	60.08	0	0.729	16.98	0.0039
10	*BMS1*	rs3128722	42884908	Intergenic	PASS	.	0	0.692	21.29	0.045
12	*GRIN2B*	rs71457202	13748154	Intron	PASS	60	0	0.72	14.14	0.73
13	*LINC00559*	rs145442832	89883465	Intergenic	PASS	59.98	0	0.673	15.47	0.064
14	*TTLL5*	rs745536628	75760859	Intron	PASS	60.07	0.521	0.762	18.94	0.038
15	*FBN1*	rs12591575	48478822	Intron	PASS	60	0	0.68	14.84	5.1×10^{-7}
19	*PVRL2*	rs6857	44888997	3' UTR	PASS	59.24	0.575	0.788	16.23	0.030
19	*TOMM40*	rs157582	44892962	Promoter	PASS	.	0	0.692	18.82	6.0×10^{-6}
19	*APOE*	rs429358	44908684	Coding	PASS	.	0	0.688	16.75	0.38

CHR = chromosome; SNV = single nucleotide variant; MQ = RMS mapping quality; FS = Phred-scaled p-value using Fisher's exact test to detect strand bias; SOR = symmetric odds ratio of 2×2 contingency table to detect strand bias; QD = variant confidence/quality by depth; P_HWE = p-value from Hardy-Weinberg equilibrium test

Supplementary Table 11. Quality score of significant and suggestive significant single nucleotide variants associated with the estimated factor 3 (Lewy body pathology related) score

CHR	Gene	SNV	Position	Location	FILTER	MQ	FS	SOR	QD	P_HWE
2	*NBAS*	rs145028924	15232755	-	PASS	60.04	0	0.683	13.26	0.28
4	*HS3ST1*	rs73227761	11527873	-	PASS	60	0	0.701	14.79	4.3×10^{-4}
4	*PABPC4L*	rs13134385	133792235	Intergenic	PASS	60.04	0.532	0.748	14.72	0.0015
6	*TNFRSF21*	rs78794444	47311493	Promoter	PASS	60	0.517	0.65	14.32	0.12
7	*ADAP1*	rs112886046	947886	Intron	PASS	60.01	0.522	0.621	13.8	0.25
7	*EPHB4*	rs75881054	100808585	Promoter	PASS	60	0	0.663	14.37	0.0019
7	*SLC12A9*	rs1235649855	100843125	Intron	PASS	59.94	0	0.686	19.59	0.17
9	*SH3GL2*	rs60097187	17998212	Intron	PASS	60	0	0.694	15.27	5.3×10^{-5}
12	*RERGL*	rs117137691	17933738	Intergenic	PASS	60.11	0	0.715	13.51	1
12	*SLC5A8*	rs79398551	101212178	Promoter	PASS	60	0	0.679	14.98	1.4×10^{-4}
12	*LOC101928416*	rs28677872	132408886	Intergenic	PASS	.	0	0.682	19.65	0.42
13	*FLT3*	rs117990166	28013358	-	PASS	60	0.516	0.678	13.82	0.57
13	*MIR5007*	rs73202898	54904307	Intergenic	PASS	60	0	0.688	14.25	0.70
14	*LOC642426*	rs28394359	18651775	Intergenic	VQSRTranche SNP99.80to99.90	55.57	45.651	3.211	3.41	0.063
16	*PLLP*	rs12929504	57320578	Promoter	PASS	.	0.534	0.71	18.27	2.2×10^{-6}
16	*PLCG2*	rs146614066	81977696	Intergenic	PASS	58.95	0	0.73	17.16	8.9×10^{-4}
19	*LINC01233*	rs116885812	22545387	Intergenic	PASS	60	0	0.689	14.2	0.019

CHR = chromosome; SNV = single nucleotide variant; MQ = RMS mapping quality; FS = Phred-scaled p-value using Fisher's exact test to detect strand bias; SOR = symmetric odds ratio of 2×2 contingency table to detect strand bias; QD = variant confidence/quality by depth; P_HWE = p-value from Hardy-Weinberg equilibrium test

Supplementary Table 12. Results on colocalization analyses from multi resources for significant and suggestive significant single nucleotide variants associated with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score in subjects aged 65 years or older at death

Chr	Gene	SNV	Source	Gene expression	Tissue	$\hat{\beta}^*$	P-value	PPH4		
								10^{-4}	10^{-5}	10^{-6}
1	*LPHN2*	rs17472472	GTEx	*ADGRL2*	Muscle Skeletal	-0.20	3.4×10^{-8}	0.86	0.39	0.059
4	*MSANTD1*	rs362285	TOPMed	*MSANTD1*	Whole blood	-0.23	1.1×10^{-8}	0.25	0.032	0.0033
7	*TMEM106B*	rs10950392	GTEx	*TMEM106B*	Adrenal Gland	0.17	1.4×10^{-7}	0.99	0.95	0.66
7	*TMEM106B*	rs10950392	GTEx	*TMEM106B*	Artery Tibial	0.11	4.1×10^{-7}	0.99	0.89	0.46
7	*TMEM106B*	rs10950392	GTEx	*TMEM106B*	Colon Transverse	0.14	1.4×10^{-6}	0.99	0.95	0.64
7	*TMEM106B*	rs10950392	GTEx	*TMEM106B*	Esophagus Muscularis	0.12	1.8×10^{-7}	0.99	0.94	0.63
7	*TMEM106B*	rs10950392	GTEx	*TMEM106B*	Heart Atrial Appendage	0.16	1.1×10^{-8}	0.53	0.10	0.011
7	*TMEM106B*	rs10950392	GTEx	*TMEM106B*	Heart Left Ventricle	0.14	2.4×10^{-8}	0.99	0.90	0.49
7	*TMEM106B*	rs10950392	GTEx	*TMEM106B*	Whole Blood	0.23	3.8×10^{-23}	>0.99	0.96	0.68
7	*TMEM106B*	rs10950392	TOPMed	*TMEM106B*	Lung	-0.07	8.5×10^{-17}	0.40	0.063	0.0066
7	*TMEM106B*	rs10950392	TOPMed	*TMEM106B*	Monocyte	-0.17	7.6×10^{-12}	0.95	0.64	0.15
7	*TMEM106B*	rs10950392	TOPMed	*TMEM106B*	Nasal epithelial	-0.12	1.5×10^{-6}	0.82	0.32	0.044
7	*TMEM106B*	rs10950392	TOPMed	*TMEM106B*	T cell	0.12	3.9×10^{-10}	0.97	0.76	0.24
7	*TMEM106B*	rs10950392	TOPMed	*TMEM106B*	Whole blood	-0.07	3.6×10^{-76}	0.93	0.59	0.13
8	*TMEM68*	rs28610182	GTEx	*LYN*	Artery Aorta	-0.18	1.1×10^{-6}	0.94	0.59	0.13
8	*TMEM68*	rs28610182	GTEx	*TMEM68*	Brain Frontal Cortex BA9	0.42	1.0×10^{-7}	>0.99	0.99	0.91
8	*TMEM68*	rs28610182	GTEx	*TMEM68*	Brain Hypothalamus	0.48	3.3×10^{-8}	>0.99	0.99	0.89
8	*TMEM68*	rs28610182	GTEx	*TMEM68*	Cells Cultured fibroblasts	0.26	4.1×10^{-9}	>0.99	0.99	0.93
8	*TMEM68*	rs28610182	GTEx	*TMEM68*	Colon Transverse	0.21	5.5×10^{-7}	>0.99	0.99	0.90
8	*TMEM68*	rs28610182	GTEx	*TMEM68*	Esophagus Mucosa	0.25	2.9×10^{-11}	>0.99	0.99	0.93
8	*TMEM68*	rs28610182	GTEx	*LYN*	Esophagus Muscularis	-0.31	2.3×10^{-12}	0.87	0.40	0.062
8	*TMEM68*	rs28610182	GTEx	*TMEM68*	Nerve Tibial	0.20	1.5×10^{-6}	>0.99	0.99	0.89
8	*TMEM68*	rs28610182	GTEx	*TMEM68*	Thyroid	0.29	4.4×10^{-11}	0.14	0.016	0.0016

8	*TMEM68*	rs28610182	ROSMAP	*TMEM68*	Brain Prefrontal Cortex	0.10	4.4×10^{-19}	>0.99	0.99	0.87
8	*TMEM68*	rs28610182	TOPMed	*TMEM68*	Lung	0.10	4.2×10^{-10}	0.34	0.049	0.0052
8	*TMEM68*	rs28610182	TOPMed	*TMEM68*	Nasal epithelial	0.16	3.5×10^{-11}	>0.99	0.99	0.91
8	*TMEM68*	rs28610182	TOPMed	*TMEM68*	PBMC	0.12	2.7×10^{-8}	0.069	0.0074	7.5×10^{-4}
8	*TMEM68*	rs28610182	TOPMed	*TMEM68*	Whole blood	0.08	1.0×10^{-19}	0.076	0.0082	8.2×10^{-4}
8	*TMEM68*	rs28610182	TOPMed	*TGS1*	Whole blood	0.06	8.1×10^{-12}	0.078	0.0084	8.5×10^{-4}
8	*TMEM68*	rs28610182	TOPMed	*LYN*	Whole blood	-0.04	6.7×10^{-29}	0.046	0.0048	4.8×10^{-4}
16	*PARN*	rs77639069	TOPMed	*NPIPA1*	Lung	0.41	1.3×10^{-7}	0.31	0.044	0.0045
16	*PARN*	rs77639069	TOPMed	*NPIPA5*	Lung	-0.59	1.8×10^{-7}	0.32	0.045	0.0047
16	*PARN*	rs77639069	TOPMed	*NPIPA1*	Whole blood	0.28	6.9×10^{-12}	0.30	0.042	0.0043
16	*PARN*	rs77639069	TOPMed	*NPIPP1*	Whole blood	0.17	2.6×10^{-8}	0.61	0.13	0.015
19	*SDHAF1*	rs17706479	GTEx	*CLIP3*	Adipose Subcutaneous	0.23	2.9×10^{-6}	0.87	0.41	0.065
19	*SDHAF1*	rs17706479	GTEx	*CLIP3*	Artery Tibial	0.23	1.3×10^{-8}	0.87	0.40	0.062
19	*SDHAF1*	rs17706479	GTEx	*TBCB*	Heart Left Ventricle	-0.25	3.3×10^{-6}	0.98	0.81	0.30
19	*SDHAF1*	rs17706479	GTEx	*WDR62*	Heart Left Ventricle	-0.20	1.4×10^{-6}	0.87	0.40	0.062
19	*SDHAF1*	rs17706479	GTEx	*WDR62*	Muscle Skeletal	-0.33	4.8×10^{-23}	0.87	0.41	0.065
19	*SDHAF1*	rs17706479	GTEx	*TBCB*	Muscle Skeletal	-0.24	1.1×10^{-14}	0.87	0.41	0.064
19	*SDHAF1*	rs17706479	GTEx	*WDR62*	Skin Not Sun Exposed Suprapubic	0.42	1.4×10^{-16}	0.87	0.40	0.063
19	*SDHAF1*	rs17706479	GTEx	*CLIP3*	Skin Not Sun Exposed Suprapubic	0.16	9.7×10^{-6}	0.87	0.40	0.063
19	*SDHAF1*	rs17706479	GTEx	*THAP8*	Skin Not Sun Exposed Suprapubic	0.20	1.4×10^{-6}	0.09	0.010	0.0010
19	*SDHAF1*	rs17706479	GTEx	*WDR62*	Skin Sun Exposed Lower leg	0.40	8.4×10^{-18}	0.87	0.40	0.062
19	*SDHAF1*	rs17706479	GTEx	*THAP8*	Skin Sun Exposed Lower leg	0.23	2.2×10^{-9}	0.09	0.010	0.0010
19	*SDHAF1*	rs17706479	GTEx	*CLIP3*	Thyroid	0.23	1.4×10^{-9}	0.87	0.40	0.062
19	*SDHAF1*	rs17706479	TOPMed	*CLIP3*	Lung	0.18	4.8×10^{-23}	0.87	0.39	0.061
19	*SDHAF1*	rs17706479	TOPMed	*SDHAF1*	Lung	-0.10	1.3×10^{-7}	>0.99	0.99	0.93
19	*SDHAF1*	rs17706479	TOPMed	*CLIP3*	Nasal epithelial	0.52	3.3×10^{-7}	0.09	0.010	0.0010

19	*SDHAF1*	rs17706479	TOPMed	*WDR62*	PBMC	-0.19	9.5×10^{-7}	0.87	0.40	0.062
19	*SDHAF1*	rs17706479	TOPMed	*CLIP3*	PBMC	0.44	2.4×10^{-15}	0.87	0.40	0.063
19	*SDHAF1*	rs17706479	TOPMed	*CLIP3*	T cell	0.60	3.5×10^{-8}	0.88	0.42	0.068
19	*SDHAF1*	rs17706479	TOPMed	*SDHAF1*	Whole blood	-0.07	3.8×10^{-21}	>0.99	0.99	0.94
19	*SDHAF1*	rs17706479	TOPMed	*POLR2I*	Whole blood	-0.05	2.3×10^{-17}	0.07	0.0075	7.6×10^{-4}
19	*SDHAF1*	rs17706479	TOPMed	*CLIP3*	Whole blood	0.28	6.2×10^{-44}	0.87	0.40	0.063
19	*SDHAF1*	rs17706479	TOPMed	*U2AF1L4*	Whole blood	0.06	1.0×10^{-6}	0.49	0.087	0.0094

[*] The effect allele is the same as that shown in Supplementary Table 5.

PPH4 = posterior probability for a hypothesis that both traits are associated and share the same single nucleotide variants

Supplementary Table 13. Results on colocalization analyses from multi resources for significant and suggestive significant single nucleotide variants associated with the estimated factor 2 (Alzheimer's disease neuropathologic change related) score in subjects aged 65 years or older at death

Chr	Gene	SNV	Source	Gene expression	Tissue	$\hat{\beta}$	P-value	PPH4		
								10^{-4}	10^{-5}	10^{-6}
1	*C1orf185*	rs72692278	TOPMed	*TTC39A*	Lung	-0.19	1.1×10^{-8}	0.66	0.17	0.019
1	*C1orf185*	rs72692278	TOPMed	*TTC39A*	Nasal epithelial	-0.41	7.9×10^{-6}	0.68	0.18	0.021
1	*C1orf185*	rs72692278	TOPMed	*NRDC*	Whole blood	-0.06	6.7×10^{-8}	0.75	0.23	0.029
4	*SPINK2*	rs34986806	TOPMed	*POLR2B*	Lung	0.16	1.5×10^{-6}	0.45	0.076	0.0082
7	*MIR29A*	rs34484449	TOPMed	ENSG00000285106	Whole blood	-0.12	1.9×10^{-11}	0.26	0.033	0.0034
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Adipose Subcutaneous	0.34	1.6×10^{-10}	0.18	0.022	0.0022
10	*BMS1*	rs3128722	GTEx	*ZNF33B*	Adipose Subcutaneous	-0.22	1.3×10^{-12}	0.74	0.22	0.028
10	*BMS1*	rs3128722	GTEx	*LOC441666*	Adipose Subcutaneous	0.32	9.1×10^{-8}	0.23	0.029	0.0030
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Adipose Visceral Omentum	0.29	4.7×10^{-7}	0.33	0.047	0.0049
10	*BMS1*	rs3128722	GTEx	*ZNF33B*	Adipose Visceral Omentum	-0.14	7.2×10^{-8}	0.77	0.25	0.033
10	*BMS1*	rs3128722	GTEx	*CCNYL2*	Artery Aorta	0.57	2.0×10^{-12}	0.53	0.10	0.011
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Artery Aorta	0.46	7.8×10^{-10}	0.53	0.10	0.011
10	*BMS1*	rs3128722	GTEx	*CCNYL2*	Artery Tibial	0.49	1.6×10^{-15}	0.57	0.12	0.013
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Artery Tibial	0.46	9.8×10^{-16}	0.33	0.047	0.0049
10	*BMS1*	rs3128722	GTEx	*ZNF33B*	Artery Tibial	-0.13	1.1×10^{-7}	0.77	0.25	0.033
10	*BMS1*	rs3128722	GTEx	*LOC441666*	Artery Tibial	0.24	5.7×10^{-6}	0.23	0.028	0.0029
10	*BMS1*	rs3128722	GTEx	ENSG00000259869	Artery Tibial	-0.31	9.5×10^{-7}	0.99	0.95	0.65
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Brain Caudate basal ganglia	0.40	4.1×10^{-6}	0.95	0.65	0.16
10	*BMS1*	rs3128722	GTEx	*LOC441666*	Brain Caudate basal ganglia	0.35	8.6×10^{-6}	0.26	0.035	0.0036
10	*BMS1*	rs3128722	GTEx	*BMS1*	Brain Cerebellum	-0.42	1.3×10^{-7}	0.99	0.94	0.60
10	*BMS1*	rs3128722	GTEx	*BMS1*	Brain Cortex	-0.32	2.1×10^{-6}	0.77	0.25	0.032
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Brain Cortex	0.40	4.0×10^{-6}	0.51	0.093	0.010

10	*BMS1*	rs3128722	GTEx	*LOC441666*	Brain Cortex	0.49	4.0×10^{-6}	0.23	0.029	0.0030
10	*BMS1*	rs3128722	GTEx	*BMS1*	Brain Frontal Cortex BA9	-0.29	6.2×10^{-6}	0.58	0.12	0.014
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Brain Nucleus accumbens basal ganglia	0.52	3.0×10^{-8}	0.98	0.85	0.37
10	*BMS1*	rs3128722	GTEx	*LOC441666*	Brain Putamen basal ganglia	0.49	3.6×10^{-6}	0.26	0.035	0.0036
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Breast Mammary Tissue	0.37	1.3×10^{-11}	0.33	0.047	0.0049
10	*BMS1*	rs3128722	GTEx	*CCNYL2*	Cells Cultured fibroblasts	0.37	4.4×10^{-8}	0.25	0.033	0.0034
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Cells Cultured fibroblasts	0.45	9.1×10^{-11}	0.17	0.021	0.0021
10	*BMS1*	rs3128722	GTEx	*ZNF33B*	Cells Cultured fibroblasts	-0.15	8.4×10^{-7}	0.77	0.25	0.033
10	*BMS1*	rs3128722	GTEx	*LOC441666*	Cells Cultured fibroblasts	0.40	2.9×10^{-9}	0.24	0.031	0.0032
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Esophagus Gastroesophageal Junction	0.43	2.1×10^{-7}	0.54	0.10	0.012
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Esophagus Mucosa	0.34	2.3×10^{-7}	0.30	0.041	0.0043
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Esophagus Muscularis	0.55	5.4×10^{-15}	0.56	0.11	0.012
10	*BMS1*	rs3128722	GTEx	*ZNF33B*	Esophagus Muscularis	-0.17	1.2×10^{-7}	0.75	0.23	0.029
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Heart Atrial Appendage	0.41	6.1×10^{-8}	0.54	0.11	0.012
10	*BMS1*	rs3128722	GTEx	*ZNF33B*	Heart Left Ventricle	-0.15	4.1×10^{-6}	0.77	0.25	0.033
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Lung	0.36	1.3×10^{-12}	0.18	0.022	0.0022
10	*BMS1*	rs3128722	GTEx	*LOC441666*	Lung	0.28	8.5×10^{-7}	0.26	0.034	0.0036
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Muscle Skeletal	0.35	1.5×10^{-11}	0.56	0.11	0.013
10	*BMS1*	rs3128722	GTEx	*ZNF33B*	Muscle Skeletal	-0.29	2.2×10^{-16}	0.77	0.25	0.033
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Nerve Tibial	0.29	1.7×10^{-7}	0.61	0.14	0.016
10	*BMS1*	rs3128722	GTEx	*ZNF33B*	Nerve Tibial	-0.19	3.3×10^{-8}	0.77	0.25	0.032
10	*BMS1*	rs3128722	GTEx	*LOC441666*	Nerve Tibial	0.32	2.9×10^{-7}	0.22	0.028	0.0029

10	*BMS1*	rs3128722	GTEx	*LOC441666*	Pituitary	0.41	6.7×10^{-7}	0.26	0.035	0.0036
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Prostate	0.52	5.0×10^{-9}	0.19	0.023	0.0023
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Skin Not Sun Exposed Suprapubic	0.39	5.3×10^{-11}	0.30	0.041	0.0043
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Skin Sun Exposed Lower leg	0.43	3.8×10^{-13}	0.18	0.021	0.0021
10	*BMS1*	rs3128722	GTEx	*LOC441666*	Skin Sun Exposed Lower leg	0.28	4.8×10^{-7}	0.25	0.033	0.0034
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Testis	0.35	5.9×10^{-7}	0.67	0.17	0.020
10	*BMS1*	rs3128722	GTEx	*LINC00839*	Thyroid	0.22	6.9×10^{-6}	0.50	0.092	0.010
10	*BMS1*	rs3128722	ROSMAP	*BMS1*	Brain Prefrontal Cortex	-0.07	3.7×10^{-15}	0.85	0.37	0.055
10	*BMS1*	rs3128722	ROSMAP	*LINC00839*	Brain Prefrontal Cortex	0.19	3.2×10^{-12}	0.54	0.11	0.012
10	*BMS1*	rs3128722	TOPMed	*CCNYL2*	Lung	0.21	1.5×10^{-9}	0.21	0.026	0.0026
10	*BMS1*	rs3128722	TOPMed	*LINC00839*	Lung	0.32	7.5×10^{-27}	0.17	0.020	0.0021
10	*BMS1*	rs3128722	TOPMed	*ZNF33B*	Lung	-0.10	1.4×10^{-14}	0.76	0.24	0.030
10	*BMS1*	rs3128722	TOPMed	*LOC441666*	Lung	0.17	4.7×10^{-9}	0.27	0.036	0.0037
10	*BMS1*	rs3128722	TOPMed	*LINC02623*	Lung	0.14	2.6×10^{-7}	0.38	0.059	0.0062
10	*BMS1*	rs3128722	TOPMed	*ENSG00000259869*	Lung	-0.14	2.6×10^{-7}	0.43	0.071	0.0076
10	*BMS1*	rs3128722	TOPMed	*ZNF33B*	PBMC	-0.08	8.2×10^{-6}	0.66	0.16	0.019
10	*BMS1*	rs3128722	TOPMed	*RET*	Whole blood	0.06	5.2×10^{-6}	0.21	0.026	0.0027
10	*BMS1*	rs3128722	TOPMed	*BMS1*	Whole blood	-0.03	4.5×10^{-9}	0.57	0.12	0.013
10	*BMS1*	rs3128722	TOPMed	*ZNF33B*	Whole blood	-0.07	1.5×10^{-36}	0.77	0.25	0.033
10	*BMS1*	rs3128722	TOPMed	*LOC105378268*	Whole blood	-0.16	5.3×10^{-35}	0.17	0.020	0.0021
15	*FBN1*	rs12591575	TOPMed	*DUT*	Whole blood	-0.07	6.9×10^{-7}	0.30	0.041	0.0042
15	*FBN1*	rs12591575	TOPMed	*FBN1*	Whole blood	-0.23	7.1×10^{-16}	0.24	0.031	0.0032
19	*APOE*	rs429358	TOPMed	*APOE*	Lung	0.16	1.7×10^{-12}	4.5×10^{-10}	4.5×10^{-11}	4.5×10^{-12}

[*] The effect allele is the same as that shown in Supplementary Table 7.

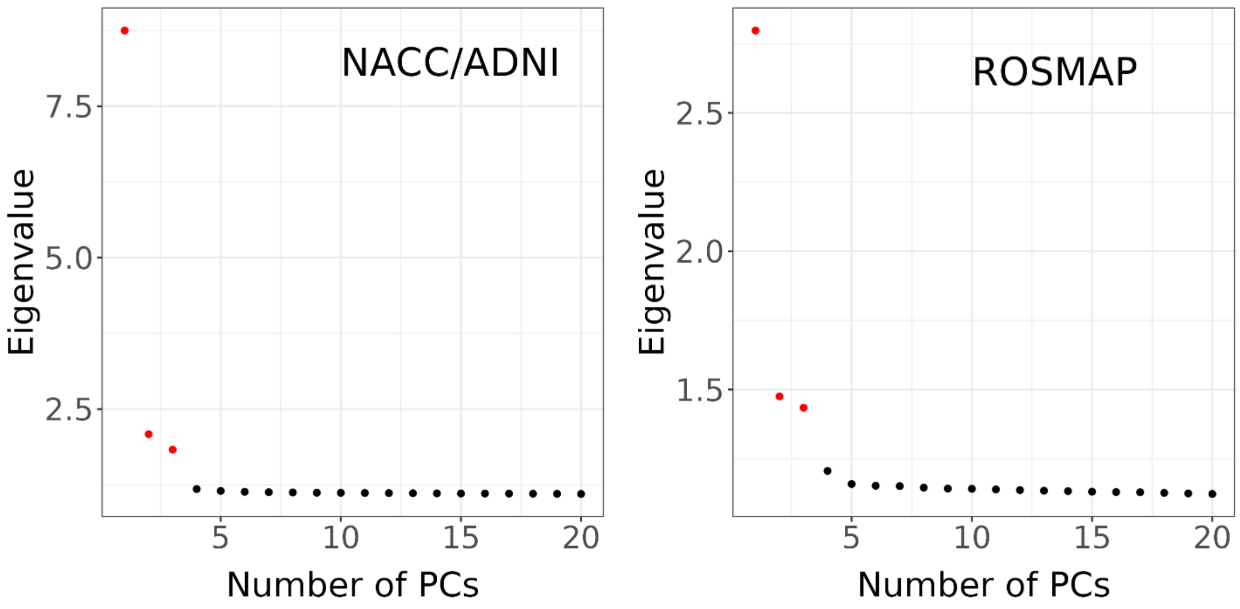
PPH4 = posterior probability for a hypothesis that both traits are associated and share the same single nucleotide variants

Supplementary Table 14. Results on colocalization analyses from multi resources for significant and suggestive significant single nucleotide variants associated with the estimated factor 3 (Lewy body pathology related) score in subjects aged 65 years or older at death

Chr	Gene	SNV	Source	Gene expression	Tissue	$\hat{\beta}$	P-value	PPH4		
								10^{-4}	10^{-5}	10^{-6}
7	*ADAP1*	rs112886046	GTEx	*ADAP1*	Esophagus Muscularis	-0.32	5.2×10^{-6}	0.62	0.14	0.016
7	*ADAP1*	rs112886046	TOPMed	*ADAP1*	Whole blood	-0.11	2.6×10^{-17}	0.92	0.55	0.11
7	*ADAP1*	rs112886046	TOPMed	*COX19*	Whole blood	-0.10	1.6×10^{-9}	0.92	0.55	0.11
7	*EPHB4*	rs75881054	GTEx	*GNB2*	Cells Cultured fibroblasts	-0.25	3.5×10^{-9}	0.91	0.51	0.093
7	*EPHB4*	rs75881054	GTEx	*EPHB4*	Whole Blood	-0.44	7.1×10^{-8}	0.28	0.037	0.0038
7	*EPHB4*	rs75881054	TOPMed	*PILRB*	Lung	0.11	5.7×10^{-6}	0.41	0.066	0.0070
7	*EPHB4*	rs75881054	TOPMed	*GNB2*	Lung	-0.13	5.3×10^{-12}	0.88	0.42	0.068
7	*EPHB4*	rs75881054	TOPMed	*STAG3L5P*	Lung	0.15	2.2×10^{-7}	0.41	0.065	0.0069
7	*EPHB4*	rs75881054	TOPMed	*UFSP1*	PBMC	0.43	5.9×10^{-7}	0.99	0.91	0.51
7	*EPHB4*	rs75881054	TOPMed	*STAG3*	Whole blood	-0.06	4.4×10^{-10}	0.34	0.049	0.0052
7	*EPHB4*	rs75881054	TOPMed	*TRIP6*	Whole blood	-0.12	1.3×10^{-7}	0.20	0.024	0.0025
7	*EPHB4*	rs75881054	TOPMed	*TFR2*	Whole blood	0.12	3.6×10^{-7}	0.18	0.022	0.0022
7	*EPHB4*	rs75881054	TOPMed	*PILRB*	Whole blood	0.12	5.6×10^{-9}	0.40	0.063	0.0067
7	*EPHB4*	rs75881054	TOPMed	*EPO*	Whole blood	0.23	6.3×10^{-9}	0.97	0.79	0.27
7	*EPHB4*	rs75881054	TOPMed	*MEPCE*	Whole blood	-0.06	6.4×10^{-8}	0.32	0.045	0.0047
7	*EPHB4*	rs75881054	TOPMed	*UFSP1*	Whole blood	0.17	4.1×10^{-9}	0.18	0.021	0.0022
7	*EPHB4*	rs75881054	TOPMed	*EPHB4*	Whole blood	-0.15	1.1×10^{-7}	0.25	0.031	0.0032
7	*EPHB4*	rs75881054	TOPMed	*PVRIG*	Whole blood	-0.05	5.7×10^{-9}	0.34	0.049	0.0051
7	*EPHB4*	rs75881054	TOPMed	*PCOLCE-AS1*	Whole blood	0.18	9.9×10^{-6}	0.23	0.028	0.0029
7	*EPHB4*	rs75881054	TOPMed	ENSG00000235333	Whole blood	0.07	2.8×10^{-6}	0.43	0.069	0.0074
16	*PLCG2*	rs146614066	TOPMed	*SDR42E1*	Whole blood	-0.17	1.3×10^{-8}	0.66	0.16	0.019

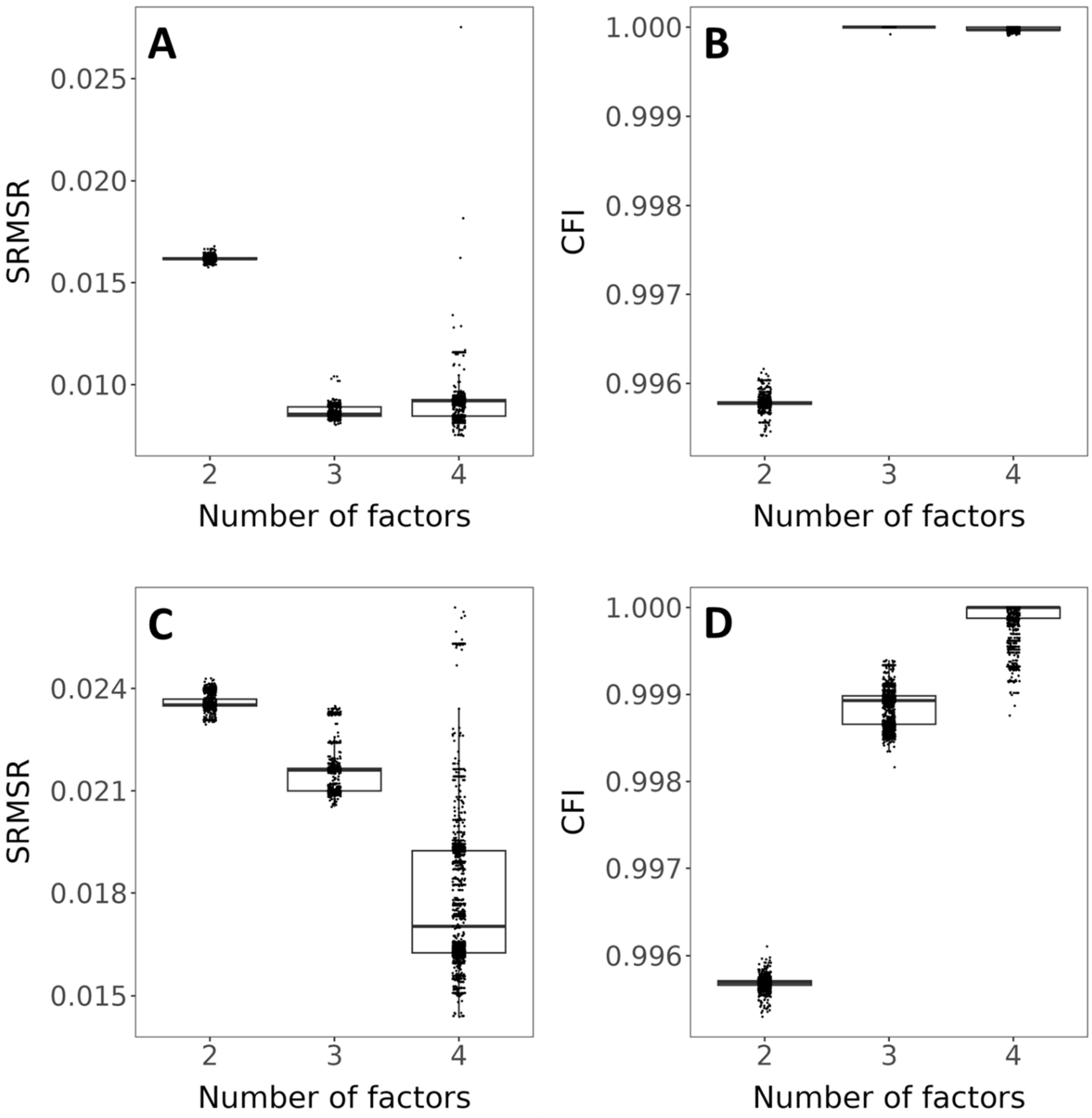
[*] The effect allele is the same as that shown in Supplementary Table 9.

PPH4 = posterior probability for a hypothesis that both traits are associated and share the same single nucleotide variants



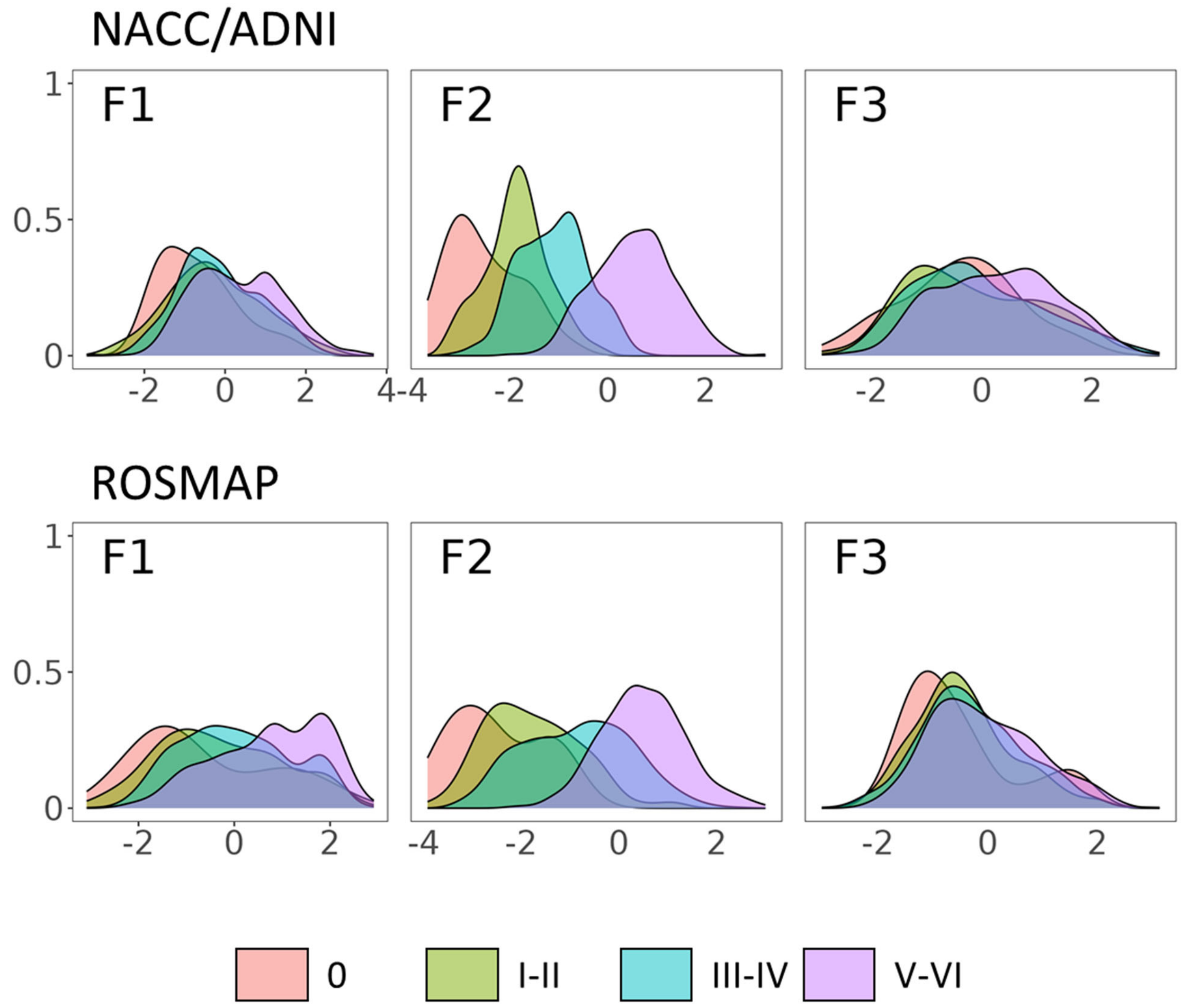
Supplementary Figure 1. Principal component analysis scree plots in NACC/ADNI and ROSMAP

PC = principal component; NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project



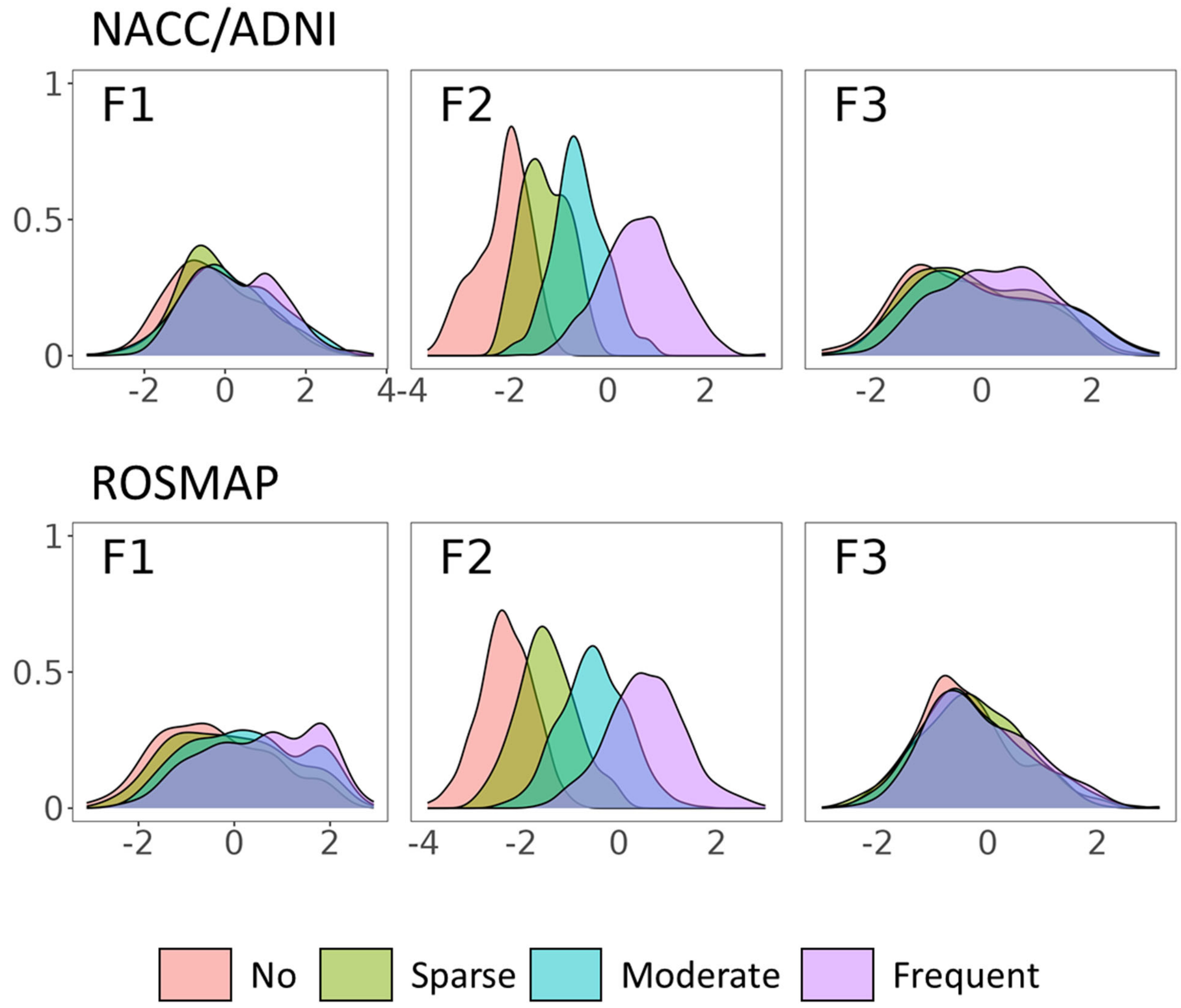
Supplementary Figure 2. Comparisons in model fit indices among two-, three-, and four-dimensional generalized partial credit models using leave-one-out cross-validation in NACC/ADNI (A and B) and ROSMAP (C and D)

SRMSR = standardized root mean square residual; CFI = comparative fit index



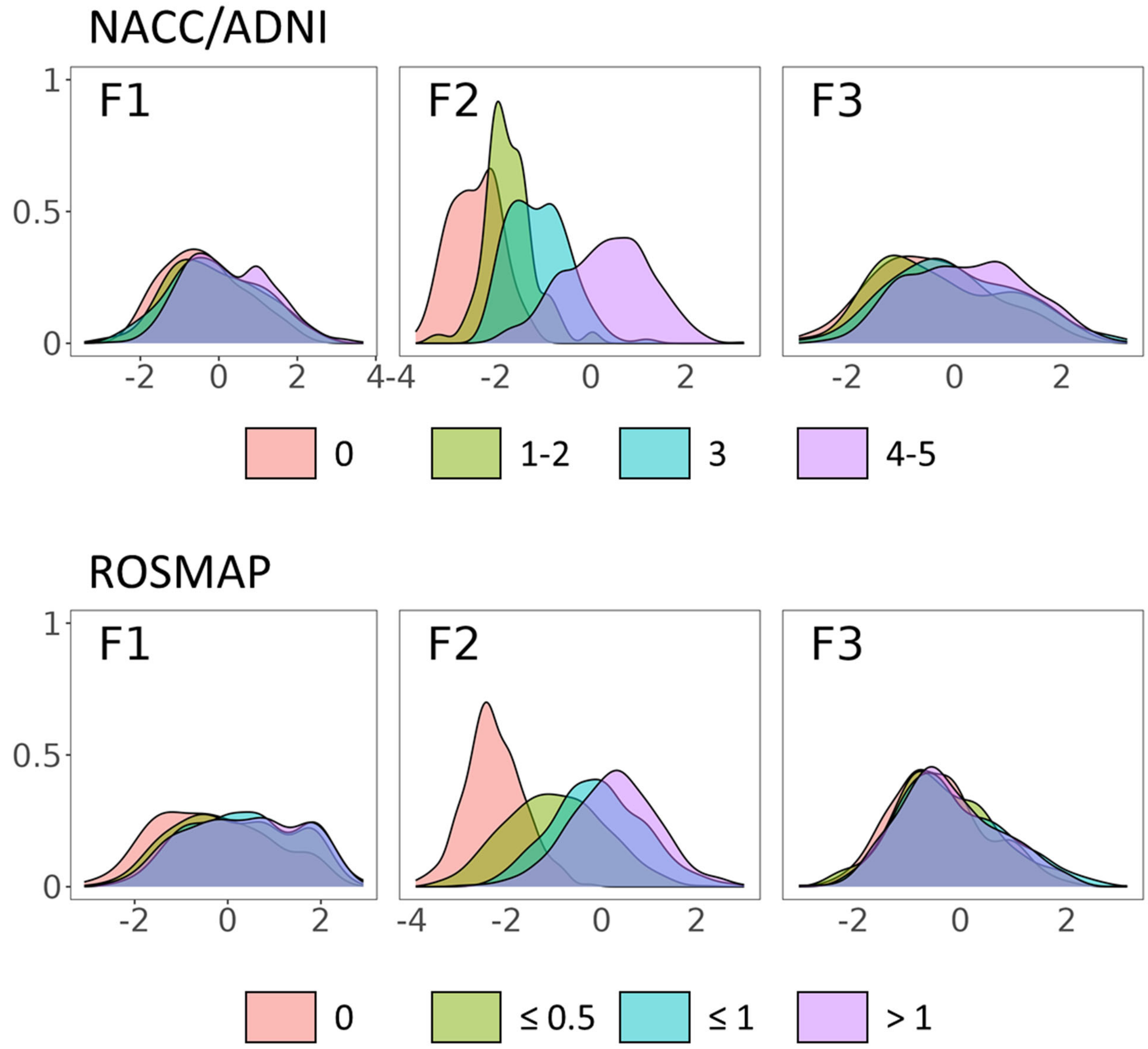
Supplementary Figure 3. Density plots in each estimated factor score by Braak neurofibrillary tangle Stage

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project



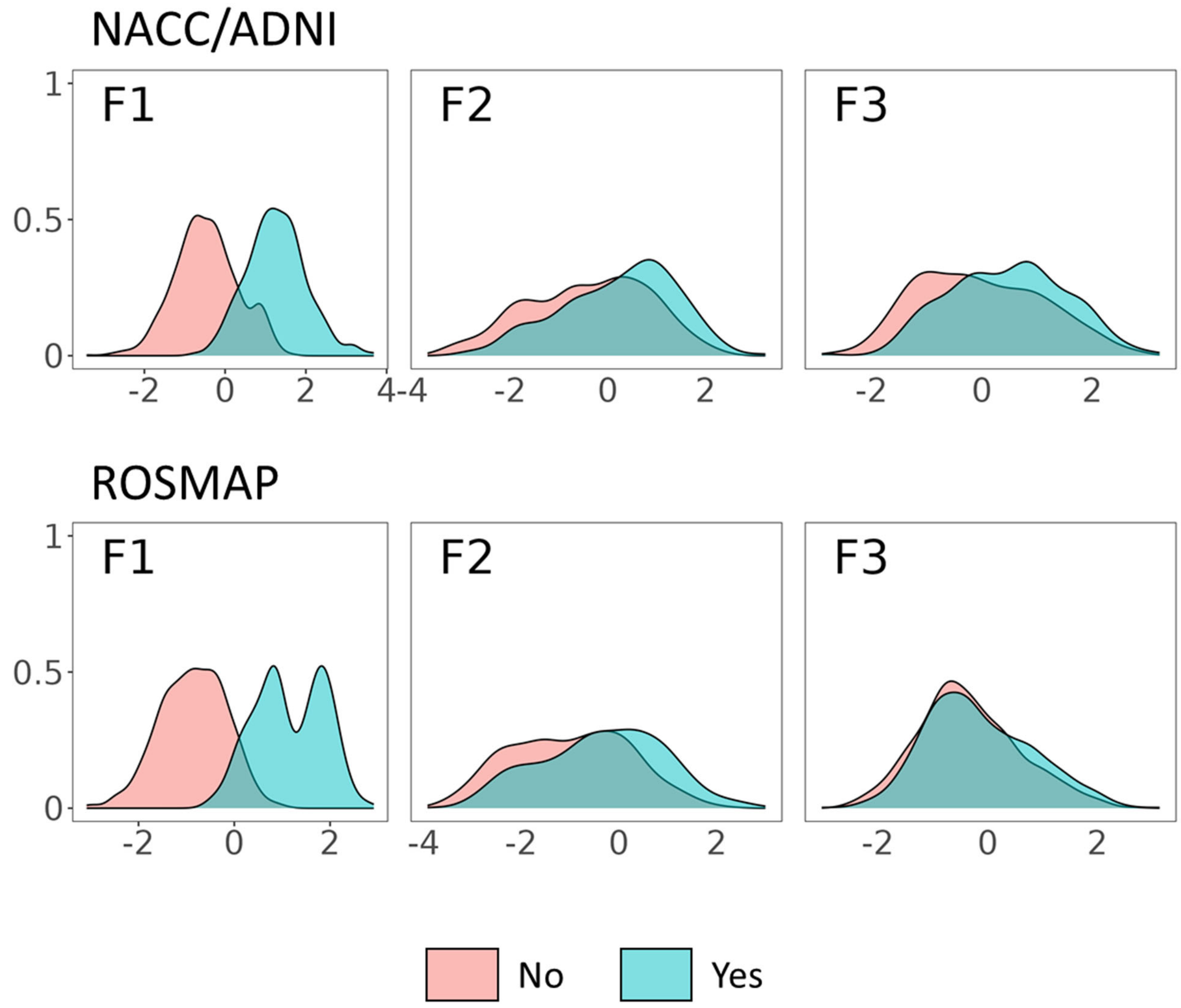
Supplementary Figure 4. Density plots in each estimated factor score by neuritic plaques

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project



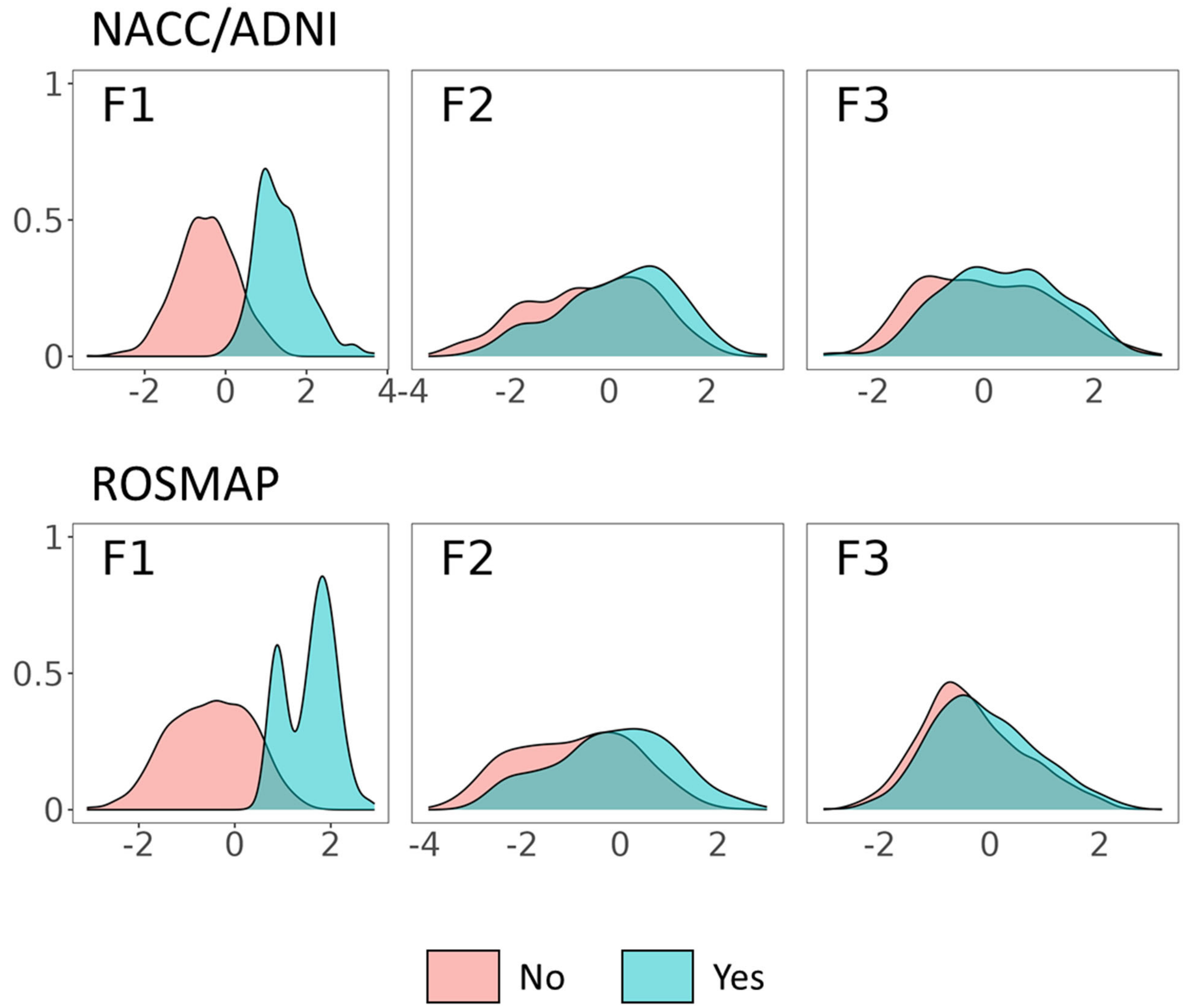
Supplementary Figure 5. Density plots in each estimated factor score colored by Thal phase in NACC and diffuse plaque across regions in ROSMAP

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project



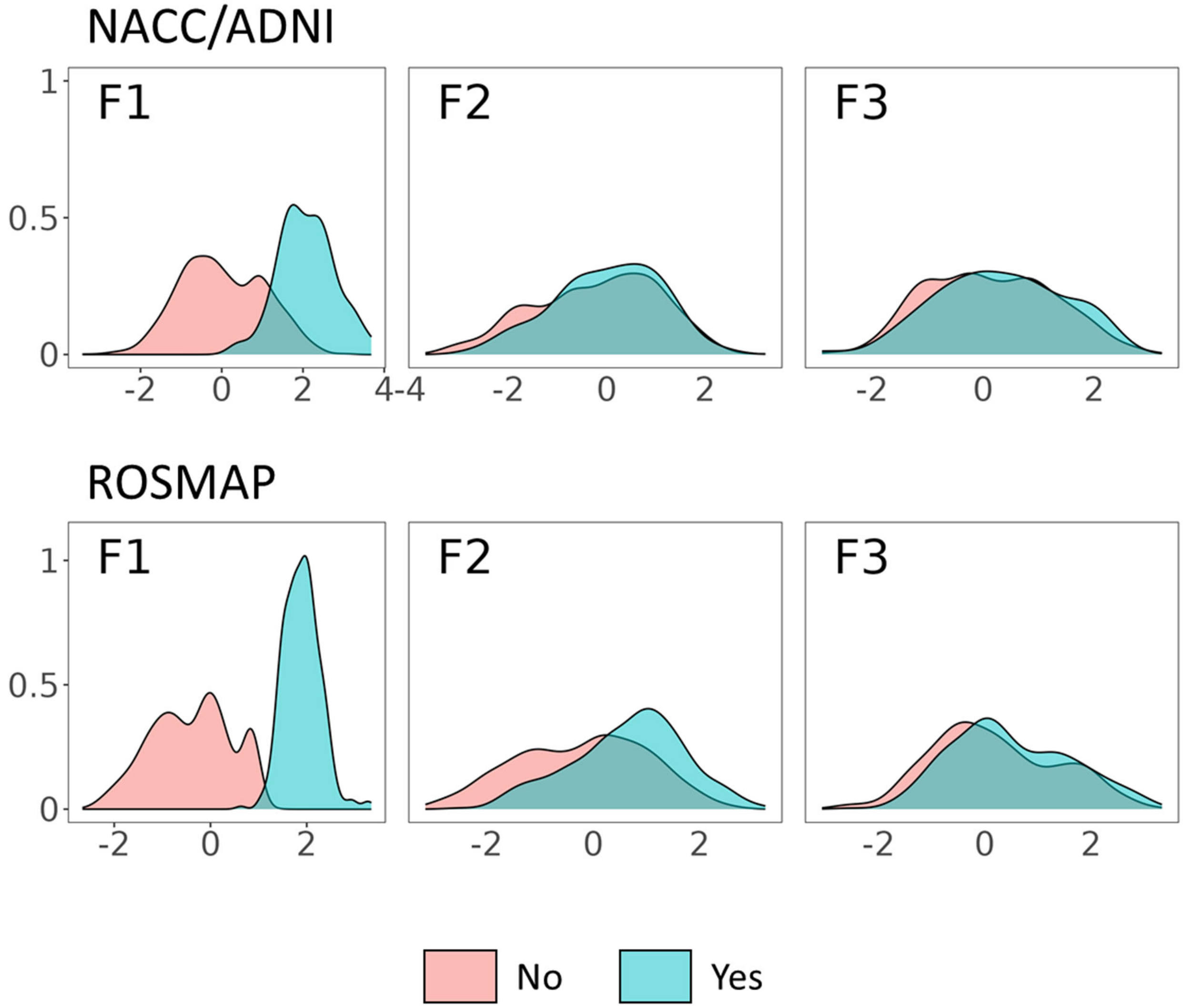
Supplementary Figure 6. Density plots in each estimated factor score colored by TDP-43 in amygdala

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project



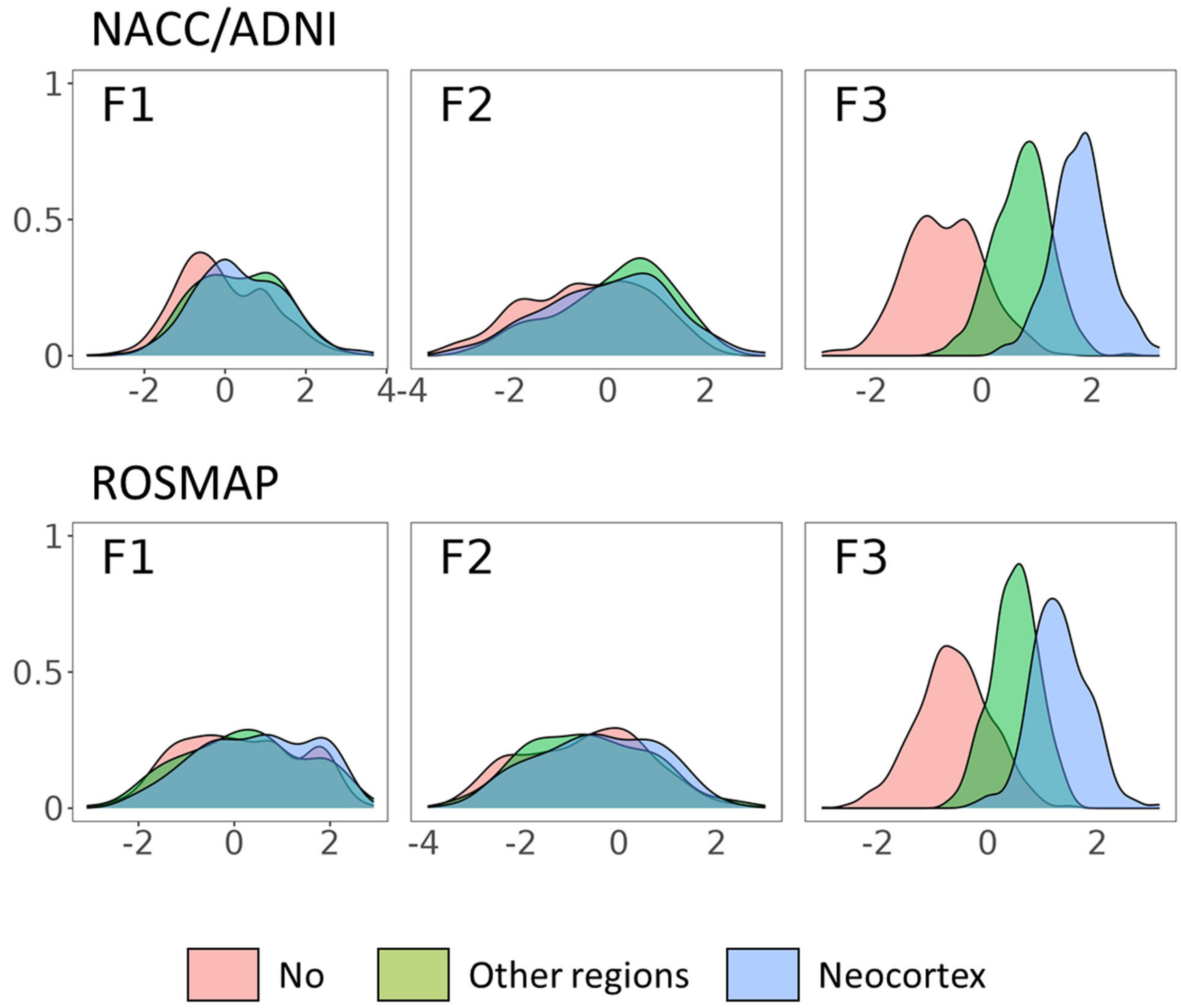
Supplementary Figure 7. Density plots in each estimated factor score colored by TDP-43 in limbic

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project



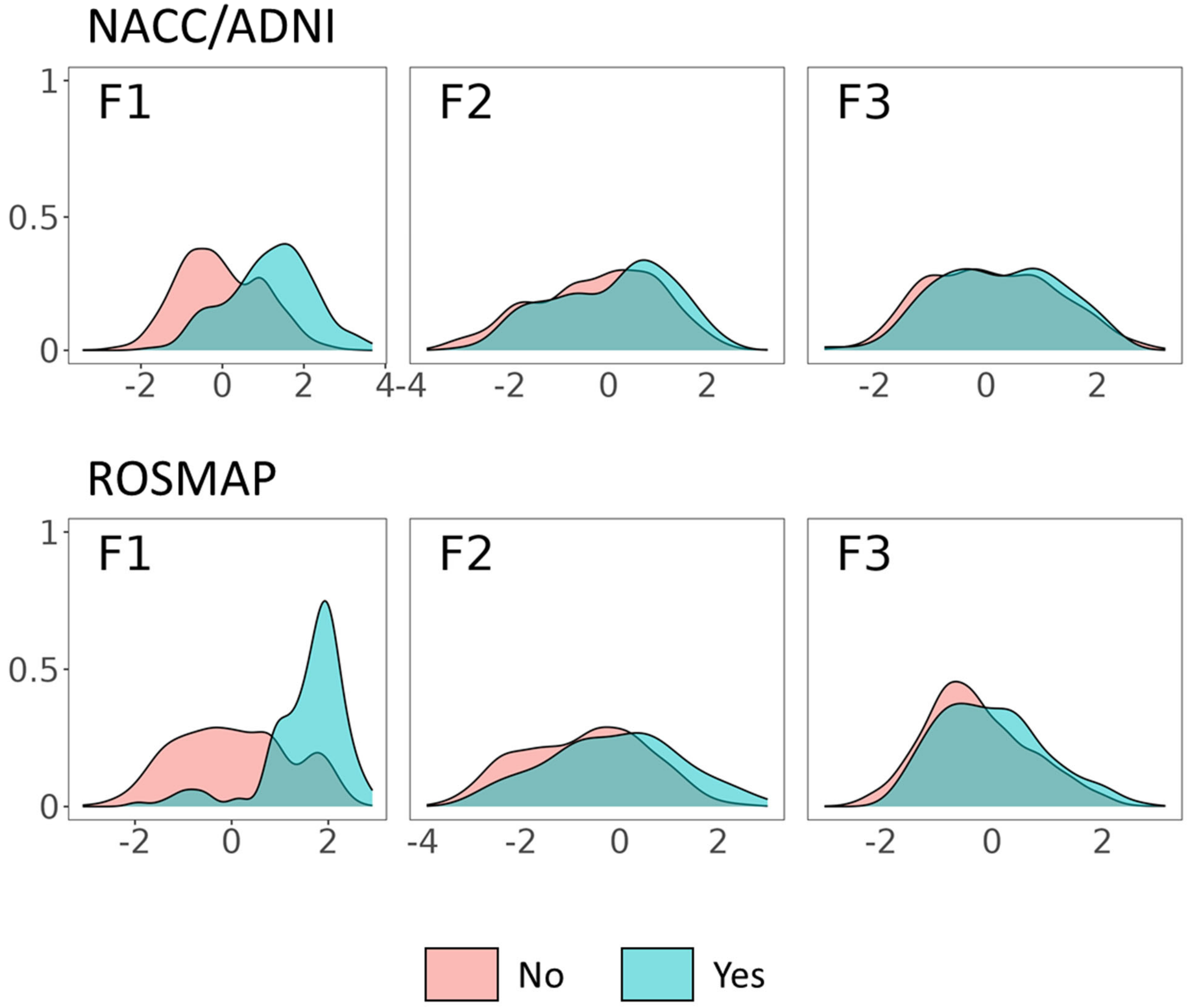
Supplementary Figure 8. Density plots in each estimated factor score colored by TDP-43 in neocortex

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project



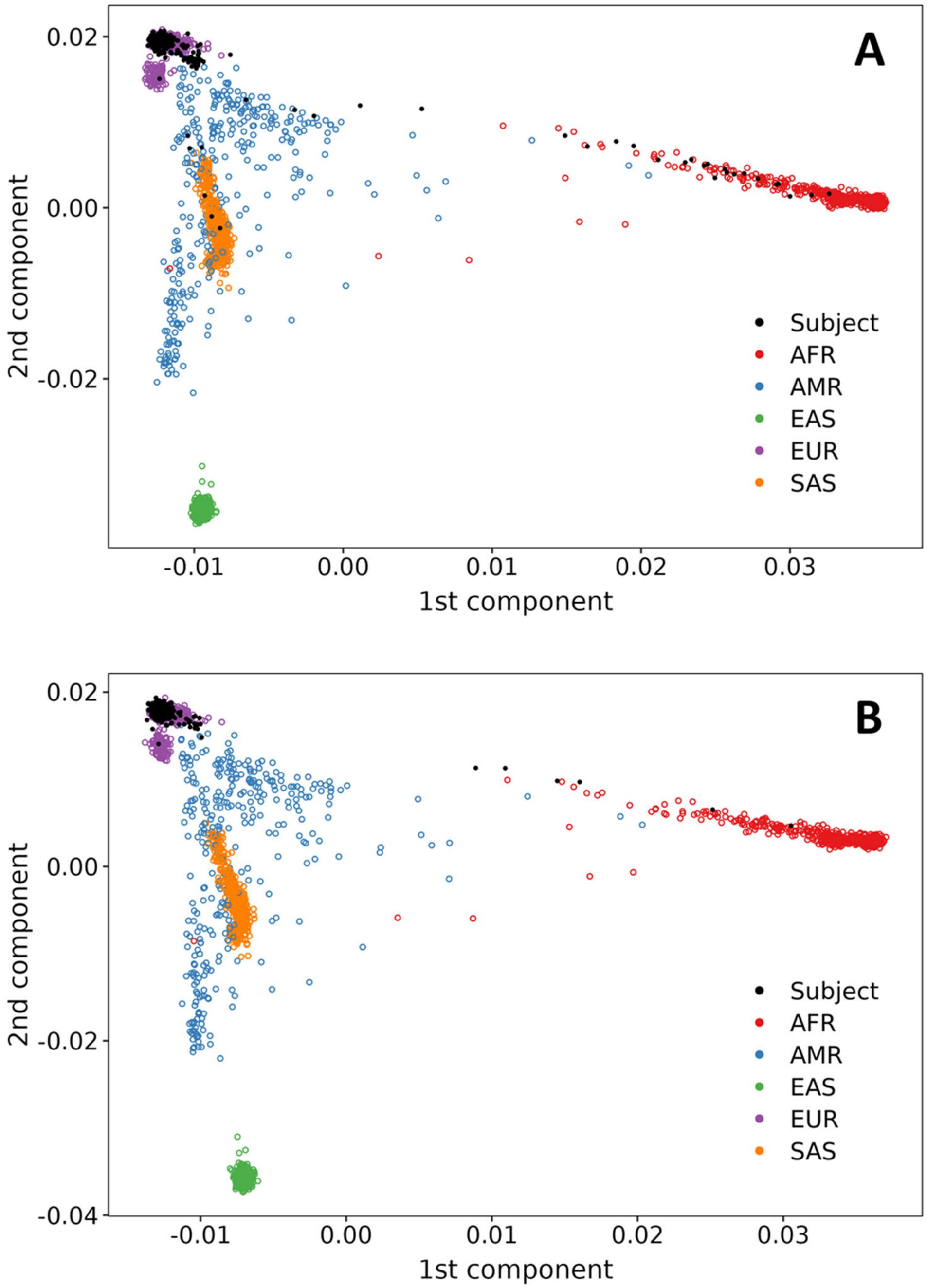
Supplementary Figure 9. Density plots in each estimated factor score colored by Lewy bodies

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project



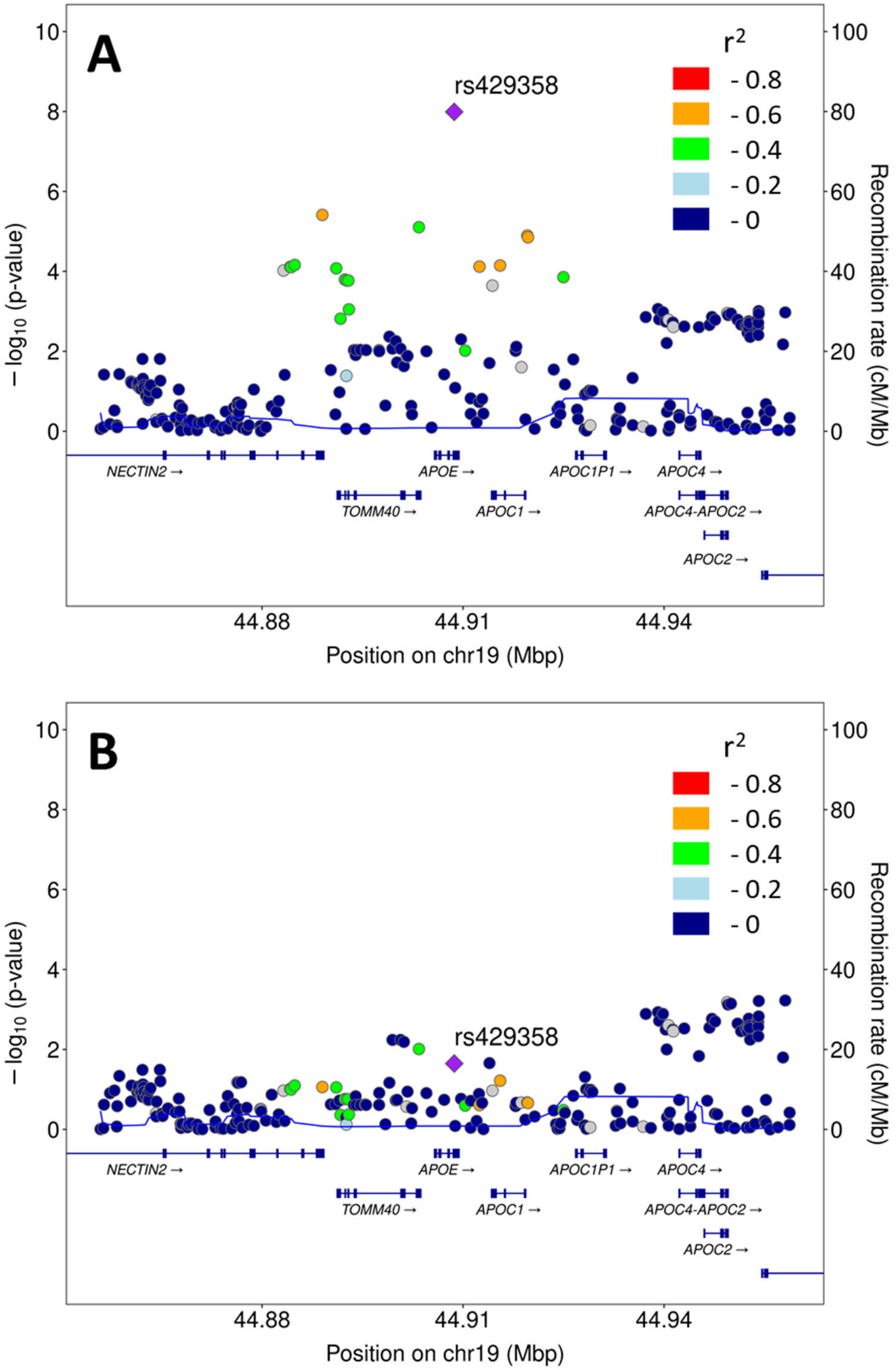
Supplementary Figure 10. Density plots in each estimated factor score colored by hippocampal sclerosis

NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study and Rush Memory and Aging Project

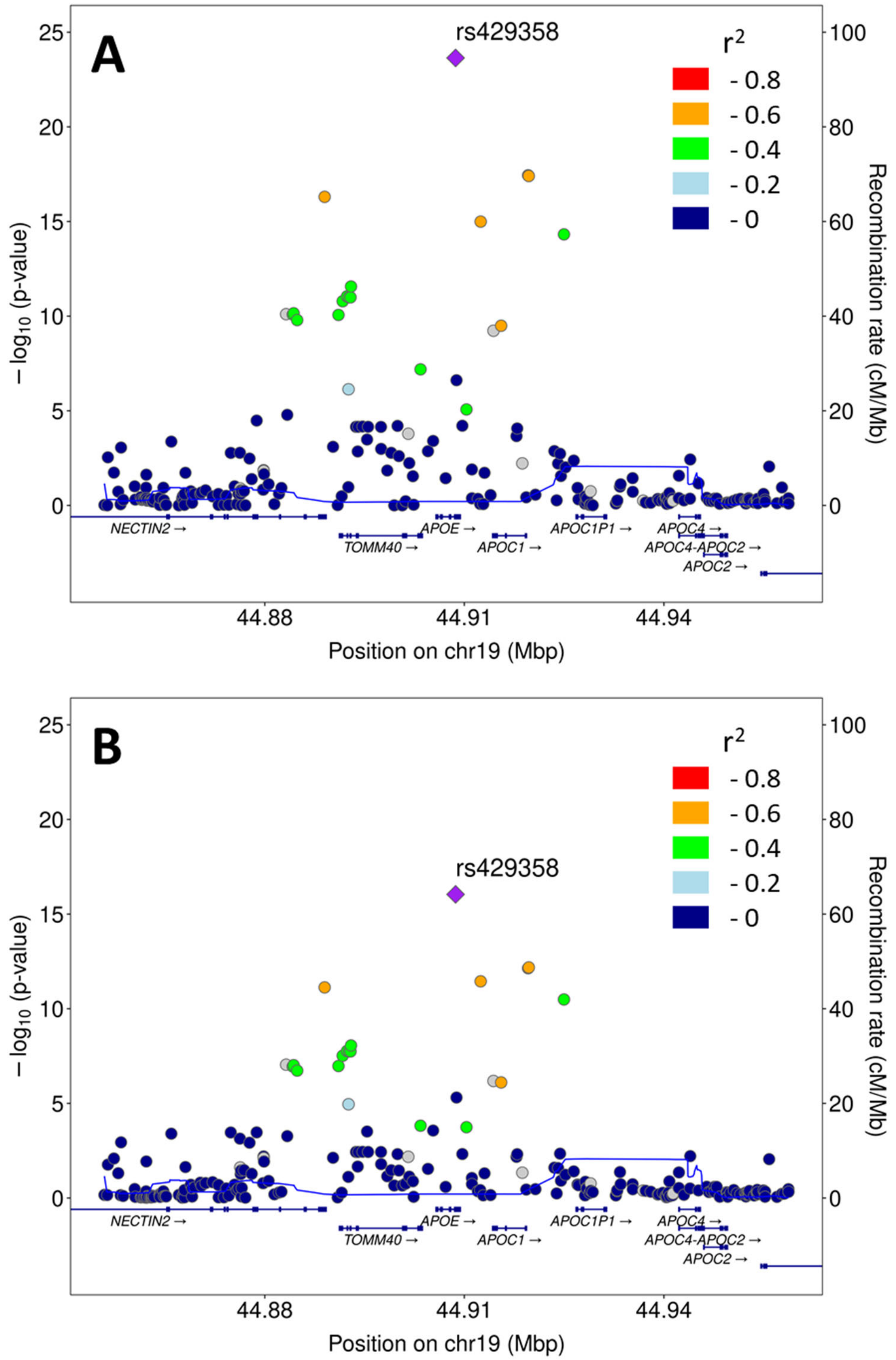


Supplementary Figure 11. First and second principal components plots along with 1000 genome reference samples. Block dots indicate individuals in the NACC/ADNI (A) and ROSMAP (B) dataset

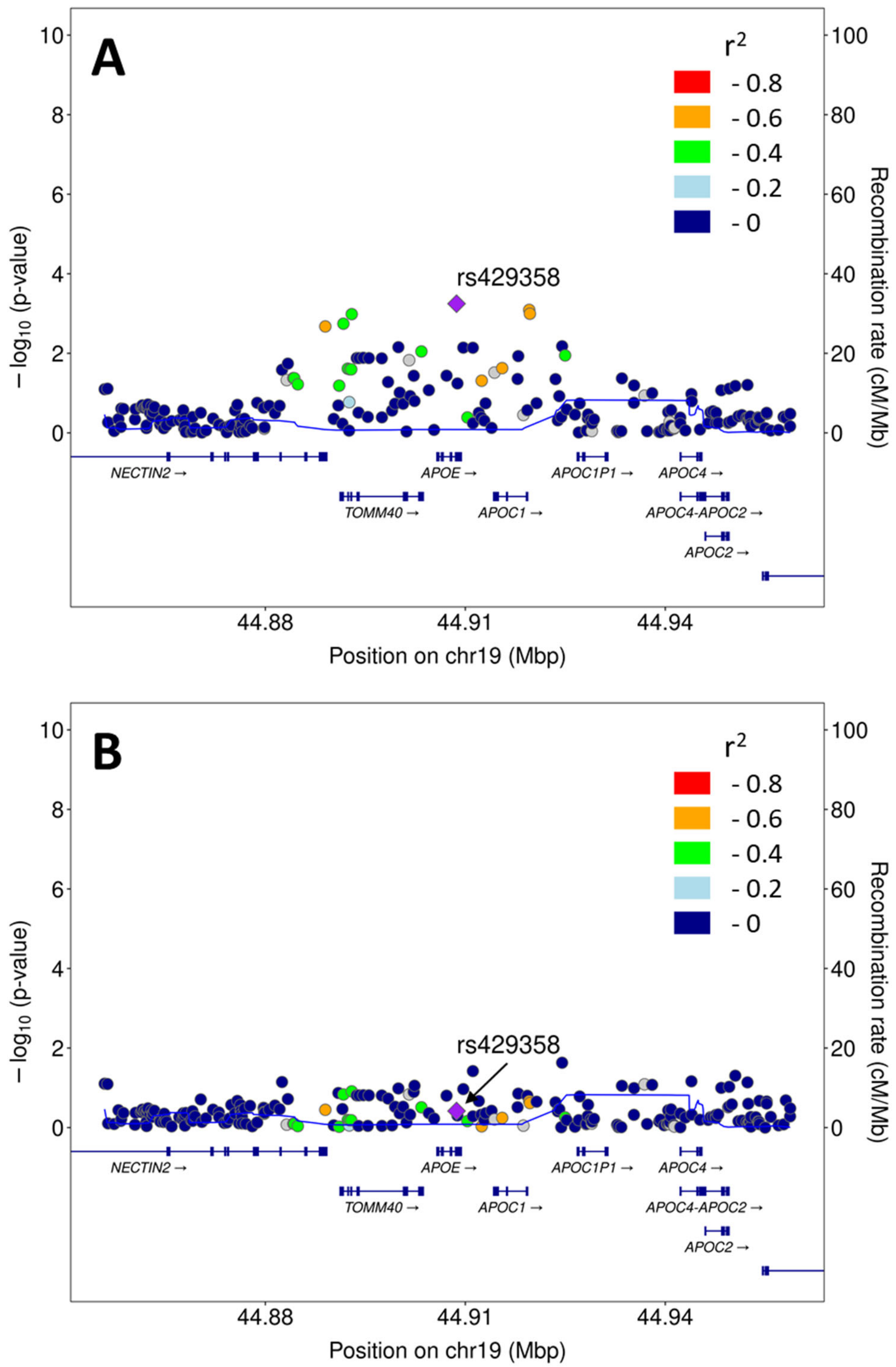
NACC = National Alzheimer's Coordinating Center; ADNI = Alzheimer's Disease Neuroimaging Initiative; ROSMAP = Religious Orders Study (ROS) and Rush Memory and Aging Project (MAP); AFR = African; AMR = Admixed American; EAS = East Asian; EUR = European; SAS = South Asian



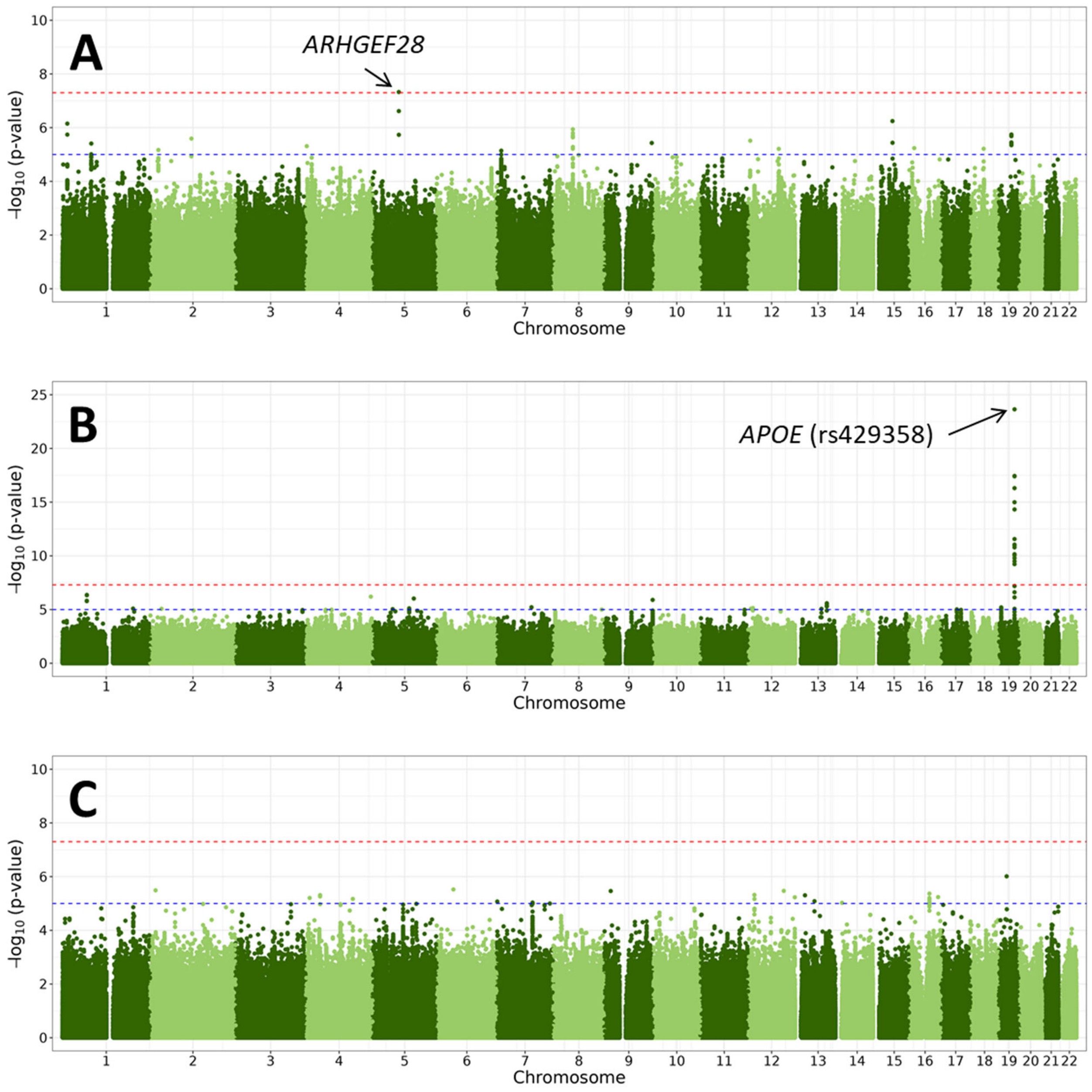
Supplementary Figure 12. Associations of single nucleotide variants in *APOE* with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score adjusted for age, sex, and the top three principal components (A), and additionally adjusted for the other factor scores (B) in subjects aged 65 years or older at death



Supplementary Figure 13. Associations of single nucleotide variants in *APOE* with the estimated factor 2 (Alzheimer's disease neuropathologic changes related) score adjusted for age, sex, and the top three principal components (A), and additionally adjusted for the other factor scores (B) in subjects aged 65 years or older at death

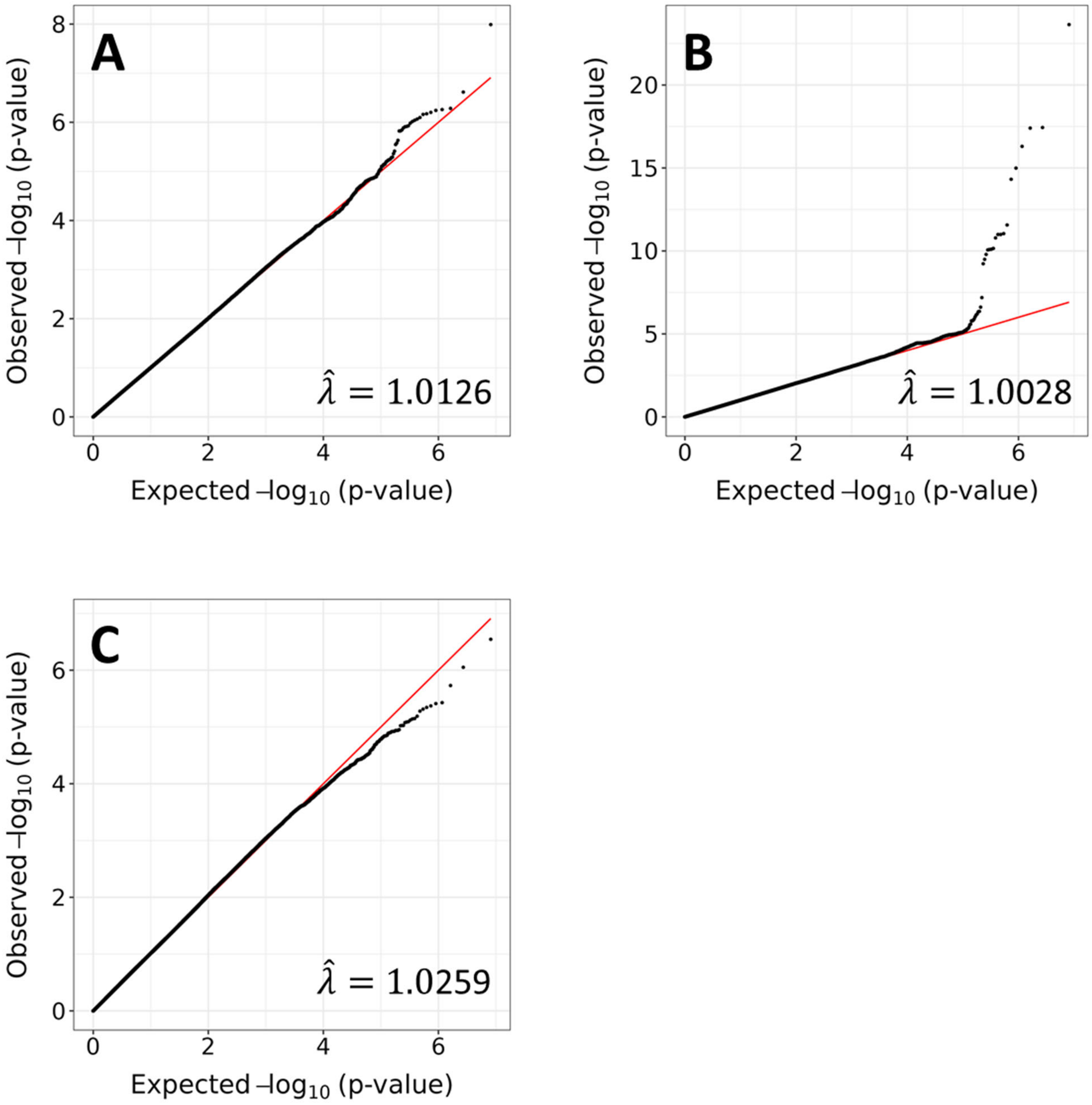


Supplementary Figure 14. Associations of single nucleotide variants in *APOE* with the estimated factor 3 (Lewy body pathology related) score adjusted for age, sex, and the top three principal components (A), and additionally adjusted for the other factor scores (B) in subjects aged 65 years or older at death



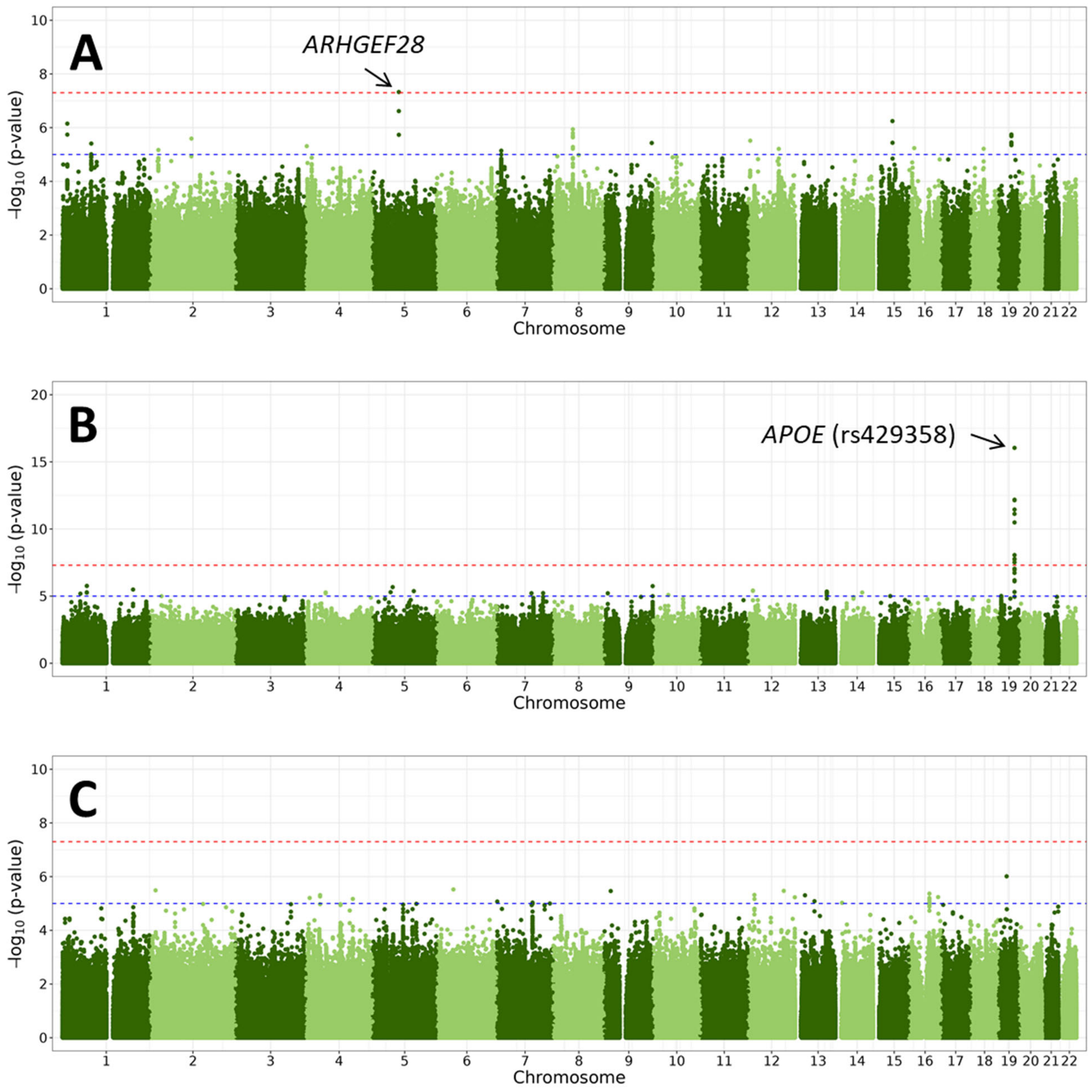
Supplementary Figure 15. Manhattan plot for associations with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score (A), the estimated factor 2 (Alzheimer's disease related) score (B), and the estimated factor 3 (Lewy body pathology related) score (C) adjusted for age, sex, and the top three principal components in subjects aged 65 years or older at death

The red dotted line indicates the significance level and the blue dotted line indicates the suggestively significance level.



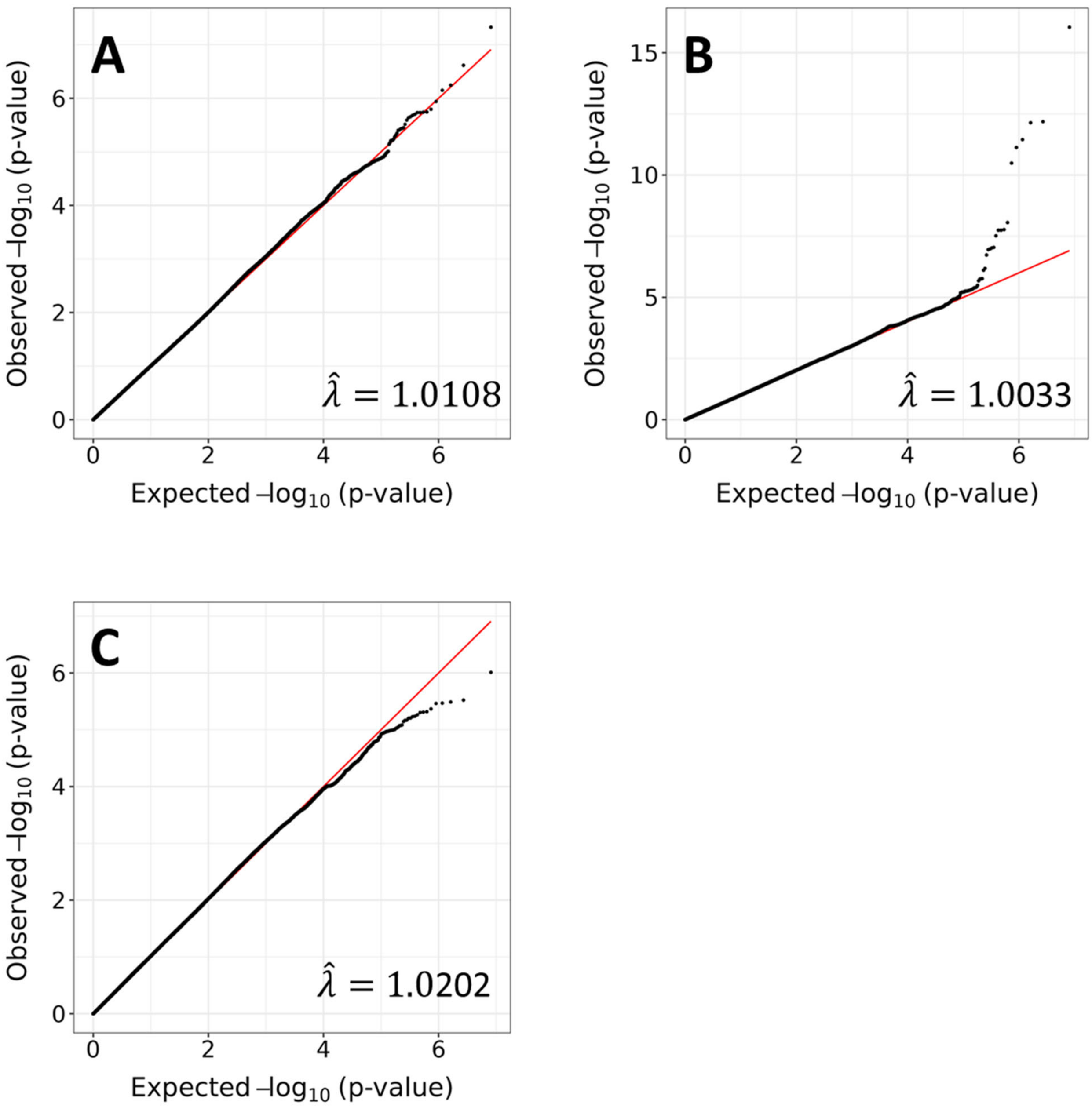
Supplementary Figure 16. QQ plot for associations with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score (A), the estimated factor 2 (Alzheimer's disease related) score (B), and the estimated factor 3 (Lewy body pathology related) score (C) adjusted for age, sex, and the top three principal components in subjects aged 65 years or older at death

Genomic inflation factor (λ) was estimated from the median of the chi-square statistic divided by 0.456.



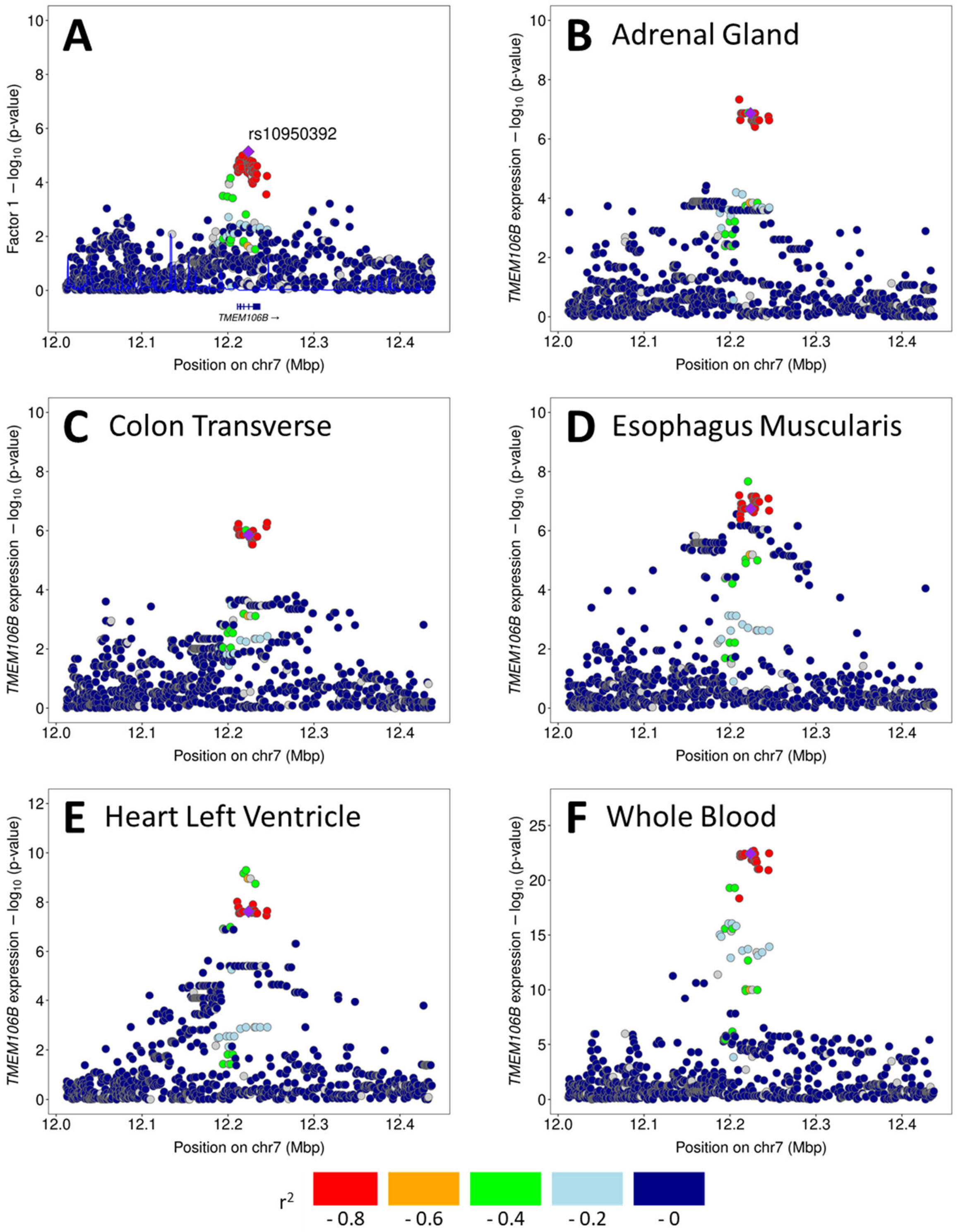
Supplementary Figure 17. Manhattan plot for associations with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score (A), the estimated factor 2 (Alzheimer's disease related) score (B), and the estimated factor 3 (Lewy body pathology related) score (C) adjusted for age, sex, the top three principal components, and the other factor scores in subjects aged 65 years or older at death

The red dotted line indicates the significance level and the blue dotted line indicates the suggestively significance level.

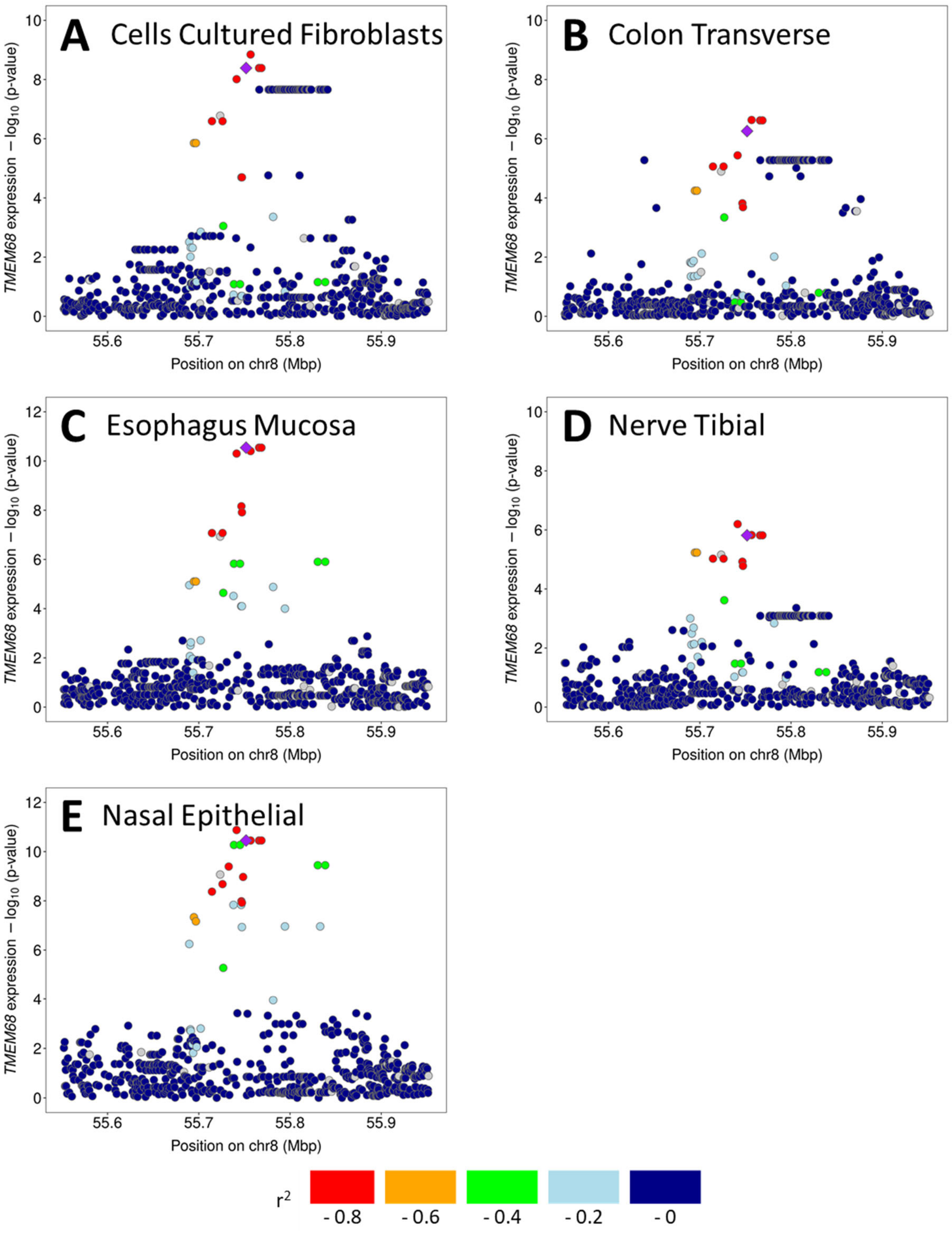


Supplementary Figure 18. QQ plot for associations with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score (A), the estimated factor 2 (Alzheimer's disease related) score (B), and the estimated factor 3 (Lewy body pathology related) score (C) adjusted for age, sex, the top three principal components, and the other factor scores in subjects aged 65 years or older at death

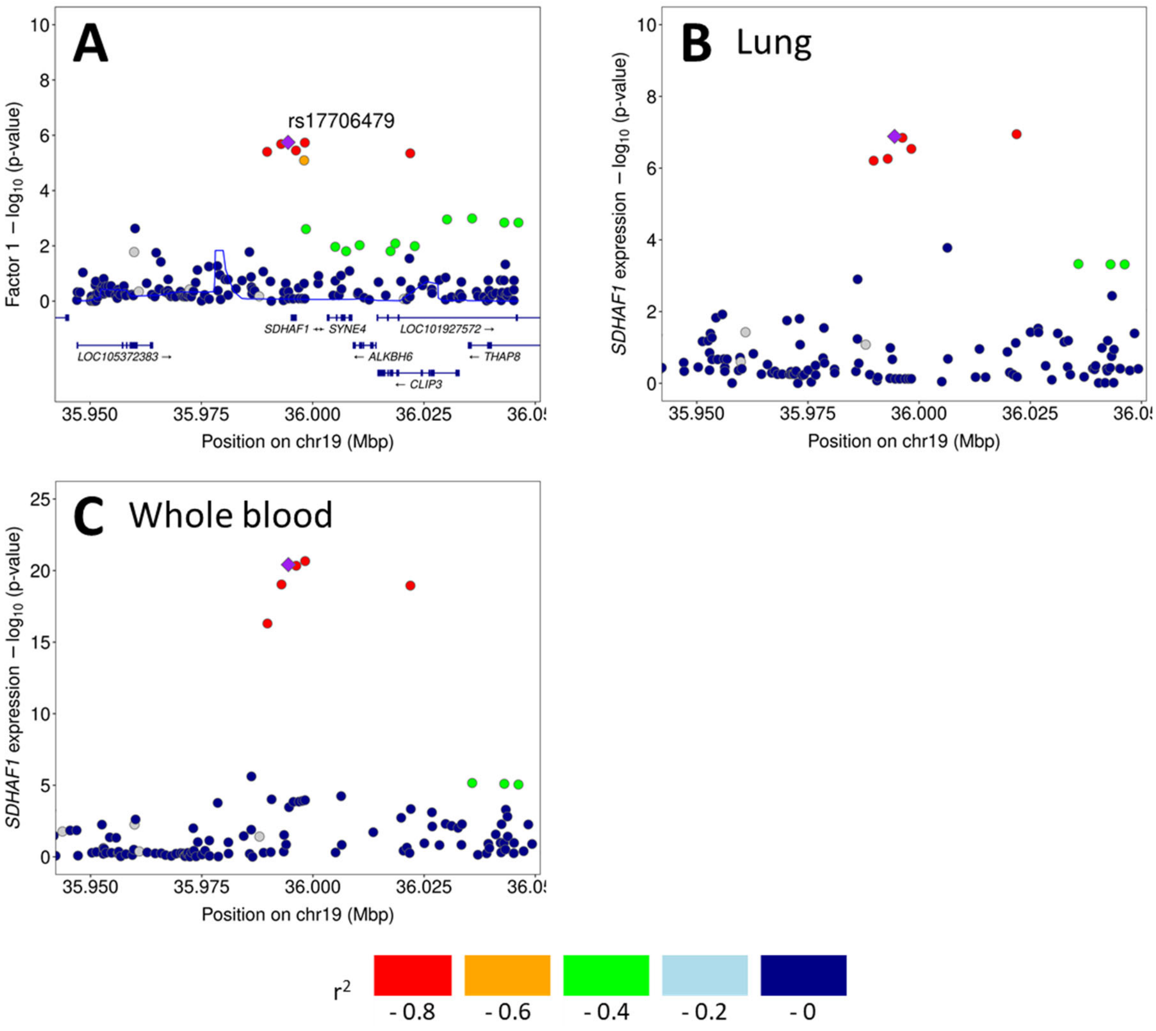
Genomic inflation factor (λ) was estimated from the median of the chi-square statistic divided by 0.456.



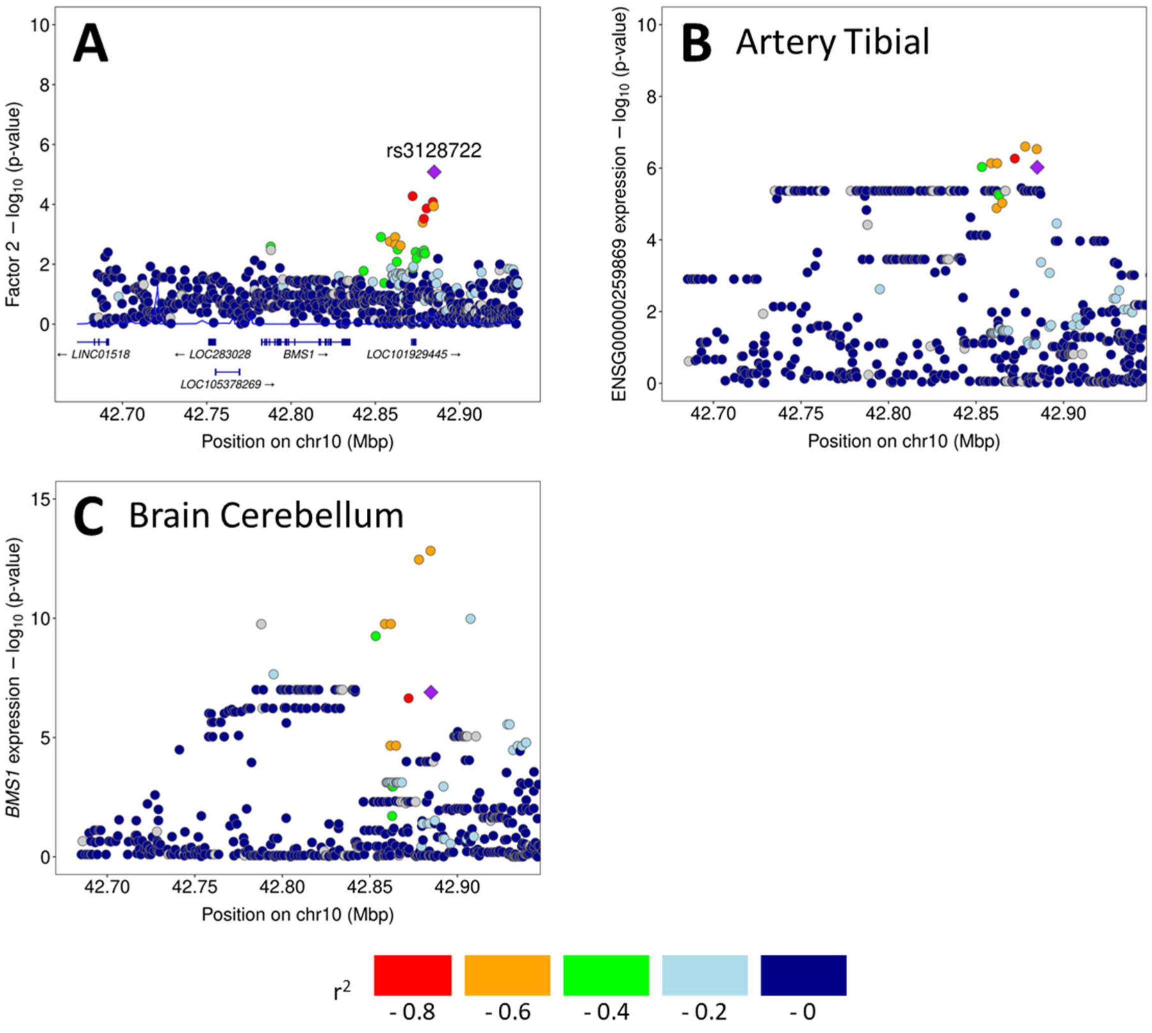
Supplementary Figure 19. LocusZoom plots for the association of single nucleotide variants with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score in *TMEM106B* (A) and with the *TMEM106B* expressions in Adrenal Gland (B), Colon Transverse (C), Esophagus Muscularis (D), Heart Left Ventricle (E), and Whole Blood (F) from GTEx



Supplementary Figure 20. LocusZoom plots for the association of single nucleotide variants with the *TMEM68* expressions in Cells Cultured Fibroblasts (A), Colon Transverse (B), Esophagus Mucosa (C), and Nerve Tibial (D) from GTEx, and Nasal Epithelial (F) from TOPMed



Supplementary Figure 21. LocusZoom plots for the association of single nucleotide variants with the estimated factor 1 (TDP-43 and hippocampal sclerosis) score in *SDHAF1* (A) and with the *SDHAF1* expressions in Lung (B) and Whole Blood (C) from TOPMed



Supplementary Figure 22. LocusZoom plots for the association of single nucleotide variants with the estimated factor 2 (Alzheimer's disease neuropathologic change) score in *BMS1* (A) and with ENSG00000259869 expressions in Artery Tibial (B) and with the BMS1 expression (C) from GTEx