

SUPPLEMENTARY TABLES

Supplementary Table 1. Basic characteristics of the genotyped participants of European ancestry in the selected studies over all available longitudinal measurements.

Study	Source	<i>N</i>	Men (%)	Age (SD, SE), years	A β 40 (SD, SE), pg/ml	A β 42 (SD, SE), pg/ml	Tau (SD, SE), pg/ml	pTau (SD, SE), pg/ml
ADNI-1	Plasma	2077	1269 (61.1)	76.6 (6.6, 0.1)	164.4 (46.7, 1.0)	39.9 (10.9, 0.2)	NA	NA
ADNI-1	CSF	948	571 (60.2)	76.7 (6.9, 0.2)	7844.7 (2326.7, 97.1)	768.6 (365.6, 11.9)	307.6 (122.3, 4.0)	29.7 (13.7, 0.4)
ADNI-2/GO	CSF	636	357 (56.1)	73.9 (7.4, 0.3)	8652.0 (2492.9, 105.0)	901.4 (369.0, 14.6)	279.6 (121.9, 4.8)	26.3 (13.3, 0.5)

Abbreviation: CSF: cerebrospinal fluid; SD: standard deviation; SE: standard error. *N* denotes the total number of observations of Alzheimer's disease (AD) biomarkers at four (plasma) and up to eight (CSF) examinations. ADNI-1 and ADNI-2/GO denote the AD Neuroimaging Initiative initial and extended cohorts, respectively. Age was defined at the time of the AD biomarker measurement.

Supplementary Table 2. Pearson pair-wise correlation estimates between Alzheimer's disease (AD) biomarkers in selected studies.

Study	Biomarker_1	Biomarker_2	<i>N</i>	Correlation, <i>r</i>	<i>P</i> value
ADNI-1	A β 40_plasma	A β 42_plasma	608	0.703	6.80E-92
ADNI-1	A β 40_plasma	Tau_plasma	449	0.127	7.03E-03
ADNI-1	A β 42_plasma	Tau_plasma	450	0.064	1.73E-01
ADNI-1	A β 40_CSF	A β 42_CSF	305	0.304	6.41E-08
ADNI-1	A β 40_CSF	Tau_CSF	339	0.524	2.85E-25
ADNI-1	A β 40_CSF	pTau_CSF	339	0.460	4.01E-19
ADNI-1	A β 42_CSF	Tau_CSF	308	-0.275	9.27E-07
ADNI-1	A β 42_CSF	pTau_CSF	308	-0.314	1.78E-08
ADNI-1	Tau_CSF	pTau_CSF	345	0.980	9.17E-244
ADNI-1	A β 42_plasma	A β 42_CSF	280	0.074	2.19E-01
ADNI-1	A β 40_plasma	A β 40_CSF	313	0.005	9.24E-01
ADNI-1	Tau_CSF	Tau_plasma	334	0.155	4.51E-03
ADNI-2/GO	A β 40_CSF	A β 42_CSF	274	0.253	2.22E-05
ADNI-2/GO	A β 40_CSF	Tau_CSF	351	0.542	3.78E-28
ADNI-2/GO	A β 40_CSF	pTau_CSF	351	0.464	4.13E-20
ADNI-2/GO	A β 42_CSF	Tau_CSF	283	-0.269	4.39E-06
ADNI-2/GO	A β 42_CSF	pTau_CSF	283	-0.326	2.04E-08
ADNI-2/GO	Tau_CSF	pTau_CSF	360	0.979	3.03E-250
FHS_C1	A β 40_plasma	A β 42_plasma	636	0.613	7.16E-67
FHS_C1	A β 40_plasma	Tau_plasma	128	0.103	2.49E-01
FHS_C1	A β 42_plasma	Tau_plasma	128	0.096	2.80E-01
FHS_C2	A β 40_plasma	A β 42_plasma	3095	0.500	9.43E-196
FHS_C2	A β 40_plasma	Tau_plasma	2554	0.108	5.04E-08
FHS_C2	A β 42_plasma	Tau_plasma	2554	0.068	5.77E-04
FHS_C3	A β 40_plasma	A β 42_plasma	3029	0.388	1.40E-109
FHS_C3	A β 40_plasma	Tau_plasma	3026	0.021	2.45E-01
FHS_C3	A β 42_plasma	Tau_plasma	3026	0.043	1.91E-02

N denotes the number of subjects. Abbreviation: CSF: cerebrospinal fluid. FHS_C1, FHS_C2, and FHS_C3 denote the Framingham Heart Study parental, offspring, and grandchildren cohorts, respectively; ADNI-1 and ADNI-2/GO denote the AD Neuroimaging Initiative initial and extended cohorts, respectively.

Supplementary Table 3. Associations of the APOE ϵ 4 allele with Alzheimer's disease (AD) biomarkers.

Study	Type	Biomarker	Source	Genotype	<i>N</i> subjects	<i>N</i> observations	Beta	SE	<i>P</i> value
ADNI-1	Baseline	A β 40	CSF	e4	171	171	-0.047	0.034	1.76E-01
ADNI-1	Baseline	A β 40	CSF	e33	149	149	Reference		
ADNI-2/GO	Baseline	A β 40	CSF	e4	133	133	0.022	0.033	5.06E-01
ADNI-2/GO	Baseline	A β 40	CSF	e33	185	185	Reference		
Meta	Baseline	A β 40	CSF	e4	304	304	-0.011	0.024	6.49E-01
Meta	Baseline	A β 40	CSF	e33	334	334	Reference		
ADNI-1	Longitudinal	A β 40	CSF	e4	173	271	-0.051	0.049	2.97E-01
ADNI-1	Longitudinal	A β 40	CSF	e33	152	267	Reference		
ADNI-2/GO	Longitudinal	A β 40	CSF	e4	134	216	0.034	0.045	4.58E-01
ADNI-2/GO	Longitudinal	A β 40	CSF	e33	186	290	Reference		
Meta	Longitudinal	A β 40	CSF	e4	307	487	-0.005	0.033	8.70E-01
Meta	Longitudinal	A β 40	CSF	e33	338	557	Reference		
ADNI-1	Baseline	A β 40	Plasma	e4	291	291	-0.795	4.345	8.55E-01
ADNI-1	Baseline	A β 40	Plasma	e33	270	270	Reference		
FHS_C1	Baseline	A β 40	Plasma	e4	114	114	-8.986	4.397	4.15E-02
FHS_C1	Baseline	A β 40	Plasma	e33	432	432	Reference		
FHS_C2	Baseline	A β 40	Plasma	e4	630	630	0.666	1.827	7.16E-01
FHS_C2	Baseline	A β 40	Plasma	e33	1982	1982	Reference		
FHS_C3	Baseline	A β 40	Plasma	e4	674	674	-2.299	2.609	3.78E-01
FHS_C3	Baseline	A β 40	Plasma	e33	1916	1916	Reference		
ARIC	Baseline	A β 40	Plasma	e4	400	400	-2.837	4.938	5.66E-01
ARIC	Baseline	A β 40	Plasma	e33	1083	1083	Reference		
Meta	Baseline	A β 40	Plasma	e4	2109	2109	-1.287	1.300	3.22E-01
Meta	Baseline	A β 40	Plasma	e33	5683	5683	Reference		
ADNI-1	Longitudinal	A β 40	Plasma	e4	296	961	-1.237	3.270	7.05E-01
ADNI-1	Longitudinal	A β 40	Plasma	e33	277	942	Reference		
Meta	Longitudinal	A β 40	Plasma	e4	296	961	-1.237	3.270	7.05E-01
Meta	Longitudinal	A β 40	Plasma	e33	277	942	Reference		
ADNI-1	Baseline	A β 42	CSF	e4	165	165	-0.407	0.048	7.15E-16
ADNI-1	Baseline	A β 42	CSF	e33	125	125	Reference		
ADNI-2/GO	Baseline	A β 42	CSF	e4	127	127	-0.256	0.049	3.94E-07
ADNI-2/GO	Baseline	A β 42	CSF	e33	134	134	Reference		
Meta	Baseline	A β 42	CSF	e4	292	292	-0.334	0.034	1.50E-22
Meta	Baseline	A β 42	CSF	e33	259	259	Reference		
ADNI-1	Longitudinal	A β 42	CSF	e4	178	433	-0.478	0.062	4.85E-14
ADNI-1	Longitudinal	A β 42	CSF	e33	151	374	Reference		
ADNI-2/GO	Longitudinal	A β 42	CSF	e4	132	223	-0.274	0.069	9.49E-05
ADNI-2/GO	Longitudinal	A β 42	CSF	e33	142	231	Reference		
Meta	Longitudinal	A β 42	CSF	e4	310	656	-0.387	0.046	7.32E-17
Meta	Longitudinal	A β 42	CSF	e33	293	605	Reference		
ADNI-1	Baseline	A β 42	Plasma	e4	291	291	-1.987	0.944	3.57E-02
ADNI-1	Baseline	A β 42	Plasma	e33	273	273	Reference		
FHS_C1	Baseline	A β 42	Plasma	e4	114	114	-3.912	1.194	1.12E-03

FHS_C1	Baseline	Aβ42	Plasma	e33	432	432	Reference		
FHS_C2	Baseline	Aβ42	Plasma	e4	630	630	-1.891	0.466	5.04E-05
FHS_C2	Baseline	Aβ42	Plasma	e33	1982	1982	Reference		
FHS_C3	Baseline	Aβ42	Plasma	e4	674	674	-1.019	0.454	2.50E-02
FHS_C3	Baseline	Aβ42	Plasma	e33	1916	1916	Reference		
ARIC	Baseline	Aβ42	Plasma	e4	397	397	-3.114	0.654	2.10E-06
ARIC	Baseline	Aβ42	Plasma	e33	1076	1076	Reference		
Meta	Baseline	Aβ42	Plasma	e4	2106	2106	-1.903	0.271	2.18E-12
Meta	Baseline	Aβ42	Plasma	e33	5679	5679	Reference		
ADNI-1	Longitudinal	Aβ42	Plasma	e4	296	962	-1.995	0.799	1.26E-02
ADNI-1	Longitudinal	Aβ42	Plasma	e33	277	950	Reference		
Meta	Longitudinal	Aβ42	Plasma	e4	296	962	-1.995	0.799	1.26E-02
Meta	Longitudinal	Aβ42	Plasma	e33	277	950	Reference		
ADNI-1	Baseline	Tau	CSF	e4	167	167	0.204	0.043	3.04E-06
ADNI-1	Baseline	Tau	CSF	e33	149	149	Reference		
ADNI-2/GO	Baseline	Tau	CSF	e4	135	135	0.323	0.045	6.80E-12
ADNI-2/GO	Baseline	Tau	CSF	e33	192	192	Reference		
Meta	Baseline	Tau	CSF	e4	302	302	0.261	0.031	6.58E-17
Meta	Baseline	Tau	CSF	e33	341	341	Reference		
ADNI-1	Longitudinal	Tau	CSF	e4	179	435	0.217	0.059	2.36E-04
ADNI-1	Longitudinal	Tau	CSF	e33	165	433	Reference		
ADNI-2/GO	Longitudinal	Tau	CSF	e4	138	237	0.304	0.059	3.13E-07
ADNI-2/GO	Longitudinal	Tau	CSF	e33	194	334	Reference		
Meta	Longitudinal	Tau	CSF	e4	317	672	0.260	0.042	3.59E-10
Meta	Longitudinal	Tau	CSF	e33	359	767	Reference		
ADNI-1	Baseline	Tau	Plasma	e4	235	235	0.102	0.053	5.75E-02
ADNI-1	Baseline	Tau	Plasma	e33	223	223	Reference		
FHS_C1	Baseline	Tau	Plasma	e4	20	20	-0.113	0.082	1.72E-01
FHS_C1	Baseline	Tau	Plasma	e33	93	93	Reference		
FHS_C2	Baseline	Tau	Plasma	e4	556	556	0.019	0.019	3.25E-01
FHS_C2	Baseline	Tau	Plasma	e33	1721	1721	Reference		
FHS_C3	Baseline	Tau	Plasma	e4	673	673	-0.003	0.013	8.31E-01
FHS_C3	Baseline	Tau	Plasma	e33	1914	1914	Reference		
Meta	Baseline	Tau	Plasma	e4	1484	1484	0.006	0.011	5.67E-01
Meta	Baseline	Tau	Plasma	e33	3951	3951	Reference		

ARIC is the Atherosclerosis Risk in Communities Study. FHS_C1, FHS_C2, and FHS_C3 denote the Framingham Heart Study parental, offspring, and grandchildren cohorts, respectively. ADNI-1 and ADNI-2/GO denote the Alzheimer's disease Neuroimaging Initiative initial and extended cohorts, respectively. Meta shows the results of meta-analysis. Meta-analysis field was shown for consistency for each biomarker even if the analysis was performed in one study only. Column "Type" indicates biomarker measurements at baseline or longitudinally. Abbreviations: CSF: cerebrospinal fluid; SE: standard error. The APOE ε4 allele was defined as e34 and e44 genotypes. A gamma general linear model with a log link function was used for all biomarkers except Aβ40 and Aβ42 measured in plasma.

Supplementary Table 4. Associations of the APOE ϵ 2 allele with Alzheimer’s disease (AD) biomarkers.

Study	Type	Biomarker	Source	Genotype	N subjects	N observations	Beta	SE	P value
ADNI-1	Baseline	A β 40	CSF	e4	25	25	0.063	0.069	3.62E-01
ADNI-1	Baseline	A β 40	CSF	e33	149	149	Reference		
ADNI-2/GO	Baseline	A β 40	CSF	e4	31	31	-0.032	0.055	5.68E-01
ADNI-2/GO	Baseline	A β 40	CSF	e33	185	185	Reference		
<i>Meta</i>	Baseline	A β 40	CSF	e4	56	56	0.006	0.043	8.99E-01
<i>Meta</i>	Baseline	A β 40	CSF	e33	334	334	Reference		
ADNI-1	Longitudinal	A β 40	CSF	e4	25	27	0.075	0.093	4.21E-01
ADNI-1	Longitudinal	A β 40	CSF	e33	152	267	Reference		
ADNI-2/GO	Longitudinal	A β 40	CSF	e4	31	54	-0.058	0.080	4.67E-01
ADNI-2/GO	Longitudinal	A β 40	CSF	e33	186	290	Reference		
<i>Meta</i>	Longitudinal	A β 40	CSF	e4	56	81	-0.002	0.060	9.80E-01
<i>Meta</i>	Longitudinal	A β 40	CSF	e33	338	557	Reference		
ADNI-1	Baseline	A β 40	Plasma	e4	36	36	0.679	8.602	9.37E-01
ADNI-1	Baseline	A β 40	Plasma	e33	270	270	Reference		
FHS_C1	Baseline	A β 40	Plasma	e4	74	74	-1.922	5.561	7.30E-01
FHS_C1	Baseline	A β 40	Plasma	e33	432	432	Reference		
FHS_C2	Baseline	A β 40	Plasma	e4	402	402	1.457	2.213	5.10E-01
FHS_C2	Baseline	A β 40	Plasma	e33	1982	1982	Reference		
FHS_C3	Baseline	A β 40	Plasma	e4	370	370	-6.513	3.022	3.12E-02
FHS_C3	Baseline	A β 40	Plasma	e33	1916	1916	Reference		
ARIC	Baseline	A β 40	Plasma	e4	230	230	-12.561	6.078	3.90E-02
ARIC	Baseline	A β 40	Plasma	e33	1083	1083	Reference		
<i>Meta</i>	Baseline	A β 40	Plasma	e4	1112	1112	-2.091	1.608	1.93E-01
<i>Meta</i>	Baseline	A β 40	Plasma	e33	5683	5683	Reference		
ADNI-1	Longitudinal	A β 40	Plasma	e4	36	123	-3.345	6.555	6.10E-01
ADNI-1	Longitudinal	A β 40	Plasma	e33	277	942	Reference		
<i>Meta</i>	Longitudinal	A β 40	Plasma	e4	36	123	-3.345	6.555	6.10E-01
<i>Meta</i>	Longitudinal	A β 40	Plasma	e33	277	942	Reference		
ADNI-1	Baseline	A β 42	CSF	e4	17	17	0.162	0.106	1.27E-01
ADNI-1	Baseline	A β 42	CSF	e33	125	125	Reference		
ADNI-2/GO	Baseline	A β 42	CSF	e4	20	20	0.130	0.086	1.31E-01
ADNI-2/GO	Baseline	A β 42	CSF	e33	134	134	Reference		
<i>Meta</i>	Baseline	A β 42	CSF	e4	37	37	0.143	0.067	3.18E-02
<i>Meta</i>	Baseline	A β 42	CSF	e33	259	259	Reference		
ADNI-1	Longitudinal	A β 42	CSF	e4	19	42	0.142	0.150	3.42E-01
ADNI-1	Longitudinal	A β 42	CSF	e33	151	374	Reference		
ADNI-2/GO	Longitudinal	A β 42	CSF	e4	20	38	0.084	0.144	5.61E-01
ADNI-2/GO	Longitudinal	A β 42	CSF	e33	142	231	Reference		
<i>Meta</i>	Longitudinal	A β 42	CSF	e4	39	80	0.112	0.104	2.80E-01
<i>Meta</i>	Longitudinal	A β 42	CSF	e33	293	605	Reference		
ADNI-1	Baseline	A β 42	Plasma	e4	36	36	0.278	2.062	8.93E-01
ADNI-1	Baseline	A β 42	Plasma	e33	273	273	Reference		
FHS_C1	Baseline	A β 42	Plasma	e4	74	74	-1.185	1.499	4.30E-01

FHS_C1	Baseline	Aβ42	Plasma	e33	432	432	Reference		
FHS_C2	Baseline	Aβ42	Plasma	e4	402	402	0.228	0.567	6.88E-01
FHS_C2	Baseline	Aβ42	Plasma	e33	1982	1982	Reference		
FHS_C3	Baseline	Aβ42	Plasma	e4	370	370	-0.268	0.565	6.36E-01
FHS_C3	Baseline	Aβ42	Plasma	e33	1916	1916	Reference		
ARIC	Baseline	Aβ42	Plasma	e4	228	228	-0.198	0.830	8.12E-01
ARIC	Baseline	Aβ42	Plasma	e33	1076	1076	Reference		
Meta	Baseline	Aβ42	Plasma	e4	1110	1110	-0.105	0.346	7.61E-01
Meta	Baseline	Aβ42	Plasma	e33	5679	5679	Reference		
ADNI-1	Longitudinal	Aβ42	Plasma	e4	36	123	-0.982	1.751	5.75E-01
ADNI-1	Longitudinal	Aβ42	Plasma	e33	277	950	Reference		
Meta	Longitudinal	Aβ42	Plasma	e4	36	123	-0.982	1.751	5.75E-01
Meta	Longitudinal	Aβ42	Plasma	e33	277	950	Reference		
ADNI-1	Baseline	Tau	CSF	e4	24	24	-0.003	0.093	9.71E-01
ADNI-1	Baseline	Tau	CSF	e33	149	149	Reference		
ADNI-2/GO	Baseline	Tau	CSF	e4	31	31	-0.111	0.071	1.17E-01
ADNI-2/GO	Baseline	Tau	CSF	e33	192	192	Reference		
Meta	Baseline	Tau	CSF	e4	55	55	-0.072	0.056	2.02E-01
Meta	Baseline	Tau	CSF	e33	341	341	Reference		
ADNI-1	Longitudinal	Tau	CSF	e4	25	59	0.013	0.120	9.11E-01
ADNI-1	Longitudinal	Tau	CSF	e33	165	433	Reference		
ADNI-2/GO	Longitudinal	Tau	CSF	e4	31	61	-0.106	0.101	2.93E-01
ADNI-2/GO	Longitudinal	Tau	CSF	e33	194	334	Reference		
Meta	Longitudinal	Tau	CSF	e4	56	120	-0.057	0.077	4.64E-01
Meta	Longitudinal	Tau	CSF	e33	359	767	Reference		
ADNI-1	Baseline	Tau	Plasma	e4	32	32	-0.127	0.111	2.52E-01
ADNI-1	Baseline	Tau	Plasma	e33	223	223	Reference		
FHS_C1	Baseline	Tau	Plasma	e4	21	21	-0.127	0.055	2.12E-02
FHS_C1	Baseline	Tau	Plasma	e33	93	93	Reference		
FHS_C2	Baseline	Tau	Plasma	e4	350	350	0.011	0.020	5.77E-01
FHS_C2	Baseline	Tau	Plasma	e33	1721	1721	Reference		
FHS_C3	Baseline	Tau	Plasma	e4	370	370	0.037	0.019	4.80E-02
FHS_C3	Baseline	Tau	Plasma	e33	1914	1914	Reference		
Meta	Baseline	Tau	Plasma	e4	773	773	0.014	0.013	2.88E-01
Meta	Baseline	Tau	Plasma	e33	3951	3951	Reference		

ARIC is the Atherosclerosis Risk in Communities Study. FHS_C1, FHS_C2, and FHS_C3 denote the Framingham Heart Study parental, offspring, and grandchildren cohorts, respectively. ADNI-1 and ADNI-2/GO denote the Alzheimer's disease Neuroimaging Initiative initial and extended cohorts, respectively. Meta shows the results of meta-analysis. Meta-analysis field was shown for consistency for each biomarker even if the analysis was performed in one study only. Column "Type" indicates biomarker measurements at baseline or longitudinally. Abbreviations: CSF: cerebrospinal fluid; SE: standard error. The APOE ε2 allele was defined as e22 and e23 genotypes. A gamma general linear model with a log link function was used for all biomarkers except Aβ40 and Aβ42 measured in plasma.

Supplementary Table 5. Associations of compound genotypes with Alzheimer’s disease (AD) A β 42 and tau biomarkers measured at baseline.

Study	Biomarker	Source	Genotype	N	Beta	SE	P value
ADNI-1	A β 42	CSF	0XY	30	-0.029	0.079	7.14E-01
ADNI-1	A β 42	CSF	100+200	31	-0.347	0.084	6.82E-05
ADNI-1	A β 42	CSF	111+222	101	-0.411	0.055	1.64E-12
ADNI-1	A β 42	CSF	1XY+2XY	138	-0.450	0.050	1.08E-16
ADNI-1	A β 42	CSF	000	112	Reference		
ADNI-2/GO	A β 42	CSF	0XY	29	0.078	0.077	3.13E-01
ADNI-2/GO	A β 42	CSF	100+200	25	-0.208	0.078	8.82E-03
ADNI-2/GO	A β 42	CSF	111+222	77	-0.268	0.056	3.06E-06
ADNI-2/GO	A β 42	CSF	1XY+2XY	104	-0.288	0.053	1.77E-07
ADNI-2/GO	A β 42	CSF	000	125	Reference		
<i>Meta</i>	A β 42	CSF	0XY	59	0.026	0.055	6.37E-01
<i>Meta</i>	A β 42	CSF	100+200	56	-0.272	0.057	2.13E-06
<i>Meta</i>	A β 42	CSF	111+222	178	-0.341	0.039	2.46E-18
<i>Meta</i>	A β 42	CSF	1XY+2XY	242	-0.373	0.037	2.18E-24
<i>Meta</i>	A β 42	CSF	000	237	Reference		
ADNI-1	A β 42	Plasma	0XY	48	-2.137	1.752	2.23E-01
ADNI-1	A β 42	Plasma	100+200	51	-1.342	1.769	4.49E-01
ADNI-1	A β 42	Plasma	111+222	197	-2.598	1.067	1.53E-02
ADNI-1	A β 42	Plasma	1XY+2XY	252	-2.418	1.012	1.73E-02
ADNI-1	A β 42	Plasma	000	261	Reference		
FHS_C1	A β 42	Plasma	0XY	60	-2.829	1.588	7.54E-02
FHS_C1	A β 42	Plasma	100+200	22	-4.084	2.621	1.20E-01
FHS_C1	A β 42	Plasma	111+222	50	-4.227	1.776	1.78E-02
FHS_C1	A β 42	Plasma	1XY+2XY	77	-3.850	1.442	7.86E-03
FHS_C1	A β 42	Plasma	000	344	Reference		
FHS_C2	A β 42	Plasma	0XY	354	-0.582	0.585	3.20E-01
FHS_C2	A β 42	Plasma	100+200	133	-2.231	0.931	1.66E-02
FHS_C2	A β 42	Plasma	111+222	397	-1.670	0.573	3.59E-03
FHS_C2	A β 42	Plasma	1XY+2XY	504	-2.093	0.516	5.12E-05
FHS_C2	A β 42	Plasma	000	1843	Reference		
FHS_C3	A β 42	Plasma	0XY	292	1.460	0.626	1.98E-02
FHS_C3	A β 42	Plasma	100+200	128	-1.586	0.908	8.07E-02
FHS_C3	A β 42	Plasma	111+222	512	-0.848	0.494	8.63E-02
FHS_C3	A β 42	Plasma	1XY+2XY	615	-0.618	0.462	1.81E-01
FHS_C3	A β 42	Plasma	000	1994	Reference		
ARIC	A β 42	Plasma	0XY	197	1.809	0.860	3.56E-02
ARIC	A β 42	Plasma	100+200	62	-4.463	1.463	2.34E-03
ARIC	A β 42	Plasma	111+222	306	-2.109	0.724	3.65E-03
ARIC	A β 42	Plasma	1XY+2XY	373	-2.304	0.671	6.15E-04
ARIC	A β 42	Plasma	000	1107	Reference		
<i>Meta</i>	A β 42	Plasma	0XY	951	0.351	0.364	3.35E-01
<i>Meta</i>	A β 42	Plasma	100+200	396	-2.305	0.551	2.82E-05
<i>Meta</i>	A β 42	Plasma	111+222	1462	-1.582	0.312	4.14E-07
<i>Meta</i>	A β 42	Plasma	1XY+2XY	1821	-1.656	0.287	7.98E-09
<i>Meta</i>	A β 42	Plasma	000	5549	Reference		
ADNI-1	Tau	CSF	0XY	31	0.158	0.075	3.61E-02
ADNI-1	Tau	CSF	100+200	30	0.234	0.080	3.99E-03
ADNI-1	Tau	CSF	111+222	105	0.247	0.049	8.28E-07
ADNI-1	Tau	CSF	1XY+2XY	142	0.244	0.043	4.96E-08
ADNI-1	Tau	CSF	000	142	Reference		
ADNI-2/GO	Tau	CSF	0XY	39	0.031	0.068	6.46E-01
ADNI-2/GO	Tau	CSF	100+200	26	0.232	0.077	3.05E-03
ADNI-2/GO	Tau	CSF	111+222	84	0.342	0.050	5.86E-11

ADNI-2/GO	Tau	CSF	1XY+2XY	111	0.355	0.048	1.38E-12
ADNI-2/GO	Tau	CSF	000	184	Reference		
<i>Meta</i>	Tau	CSF	0XY	70	0.088	0.050	7.97E-02
<i>Meta</i>	Tau	CSF	100+200	56	0.233	0.056	2.85E-05
<i>Meta</i>	Tau	CSF	111+222	189	0.293	0.035	4.87E-17
<i>Meta</i>	Tau	CSF	1XY+2XY	253	0.294	0.032	6.75E-20
<i>Meta</i>	Tau	CSF	000	326	Reference		
ADNI-1	Tau	Plasma	0XY	39	-0.059	0.099	5.49E-01
ADNI-1	Tau	Plasma	100+200	38	0.048	0.102	6.37E-01
ADNI-1	Tau	Plasma	111+222	156	0.085	0.059	1.53E-01
ADNI-1	Tau	Plasma	1XY+2XY	204	0.117	0.059	4.83E-02
ADNI-1	Tau	Plasma	000	216	Reference		
FHS_C1	Tau	Plasma	0XY	17	-0.024	0.092	7.93E-01
FHS_C1	Tau	Plasma	100+200	5	-0.040	0.052	4.43E-01
FHS_C1	Tau	Plasma	111+222	9	-0.099	0.133	4.58E-01
FHS_C1	Tau	Plasma	1XY+2XY	14	-0.172	0.103	9.89E-02
FHS_C1	Tau	Plasma	000	91	Reference		
FHS_C2	Tau	Plasma	0XY	300	0.030	0.020	1.27E-01
FHS_C2	Tau	Plasma	100+200	118	-0.054	0.030	7.47E-02
FHS_C2	Tau	Plasma	111+222	357	-0.022	0.019	2.34E-01
FHS_C2	Tau	Plasma	1XY+2XY	448	-0.008	0.017	6.55E-01
FHS_C2	Tau	Plasma	000	1615	Reference		
FHS_C3	Tau	Plasma	0XY	291	-0.005	0.018	7.86E-01
FHS_C3	Tau	Plasma	100+200	128	-0.047	0.026	7.72E-02
FHS_C3	Tau	Plasma	111+222	511	-0.007	0.015	6.07E-01
FHS_C3	Tau	Plasma	1XY+2XY	614	-0.002	0.013	8.88E-01
FHS_C3	Tau	Plasma	000	1991	Reference		
<i>Meta</i>	Tau	Plasma	0XY	647	0.009	0.013	4.91E-01
<i>Meta</i>	Tau	Plasma	100+200	289	-0.045	0.018	1.28E-02
<i>Meta</i>	Tau	Plasma	111+222	1033	-0.010	0.011	3.66E-01
<i>Meta</i>	Tau	Plasma	1XY+2XY	1280	-0.002	0.010	8.42E-01
<i>Meta</i>	Tau	Plasma	000	3913	Reference		

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Supplementary Table 6. Comparative analysis of the associations of the selected compound genotypes with Alzheimer's disease (AD) A β 42 and tau biomarkers.

Study	Biomarker	Source	Genotype	N	Beta	SE	P value
ADNI-1	A β 42	CSF	111+222	101	-0.047	0.081	5.62E-01
ADNI-1	A β 42	CSF	1XY+2XY	138	-0.087	0.077	2.64E-01
ADNI-1	A β 42	CSF	100+200	31	Reference		
ADNI-2/GO	A β 42	CSF	111+222	77	-0.065	0.095	4.99E-01
ADNI-2/GO	A β 42	CSF	1XY+2XY	104	-0.097	0.096	3.14E-01
ADNI-2/GO	A β 42	CSF	100+200	25	Reference		
<i>Meta</i>	A β 42	CSF	111+222	178	-0.054	0.062	3.77E-01
<i>Meta</i>	A β 42	CSF	1XY+2XY	242	-0.091	0.060	1.32E-01
<i>Meta</i>	A β 42	CSF	100+200	56	Reference		
ADNI-1	A β 42	Plasma	111+222	197	-1.200	1.626	4.61E-01
ADNI-1	A β 42	Plasma	1XY+2XY	252	-1.189	1.647	4.71E-01
ADNI-1	A β 42	Plasma	100+200	51	Reference		
FHS_C1	A β 42	Plasma	111+222	50	0.011	2.532	9.96E-01
FHS_C1	A β 42	Plasma	1XY+2XY	77	0.004	2.163	9.98E-01
FHS_C1	A β 42	Plasma	100+200	22	Reference		
FHS_C2	A β 42	Plasma	111+222	397	0.442	0.962	6.46E-01
FHS_C2	A β 42	Plasma	1XY+2XY	504	0.051	0.914	9.56E-01
FHS_C2	A β 42	Plasma	100+200	133	Reference		
FHS_C3	A β 42	Plasma	111+222	512	0.706	0.997	4.79E-01
FHS_C3	A β 42	Plasma	1XY+2XY	615	0.939	0.992	3.44E-01
FHS_C3	A β 42	Plasma	100+200	128	Reference		
ARIC	A β 42	Plasma	111+222	306	2.508	1.460	8.66E-02
ARIC	A β 42	Plasma	1XY+2XY	373	2.302	1.455	1.14E-01
ARIC	A β 42	Plasma	100+200	62	Reference		
<i>Meta</i>	A β 42	Plasma	111+222	1462	0.619	0.569	2.77E-01
<i>Meta</i>	A β 42	Plasma	1XY+2XY	1821	0.509	0.553	3.57E-01
<i>Meta</i>	A β 42	Plasma	100+200	396	Reference		
ADNI-1	Tau	CSF	111+222	105	0.041	0.072	5.70E-01
ADNI-1	Tau	CSF	1XY+2XY	142	0.030	0.066	6.50E-01
ADNI-1	Tau	CSF	100+200	30	Reference		
ADNI-2/GO	Tau	CSF	111+222	84	0.107	0.092	2.50E-01
ADNI-2/GO	Tau	CSF	1XY+2XY	111	0.121	0.095	2.04E-01
ADNI-2/GO	Tau	CSF	100+200	26	Reference		
<i>Meta</i>	Tau	CSF	111+222	189	0.066	0.057	2.46E-01
<i>Meta</i>	Tau	CSF	1XY+2XY	253	0.060	0.054	2.70E-01
<i>Meta</i>	Tau	CSF	100+200	56	Reference		
ADNI-1	Tau	Plasma	111+222	156	0.030	0.085	7.26E-01
ADNI-1	Tau	Plasma	1XY+2XY	204	0.063	0.098	5.18E-01
ADNI-1	Tau	Plasma	100+200	38	Reference		
FHS_C1	Tau	Plasma	111+222	9	0.075	0.288	8.02E-01
FHS_C1	Tau	Plasma	1XY+2XY	14	0.000	0.342	1.00E+00
FHS_C1	Tau	Plasma	100+200	5	Reference		

FHS_C2	Tau	Plasma	111+222	357	0.027	0.035	4.33E-01
FHS_C2	Tau	Plasma	1XY+2XY	448	0.053	0.032	1.01E-01
FHS_C2	Tau	Plasma	100+200	118	Reference		
FHS_C3	Tau	Plasma	111+222	511	0.037	0.029	2.03E-01
FHS_C3	Tau	Plasma	1XY+2XY	614	0.041	0.028	1.39E-01
FHS_C3	Tau	Plasma	100+200	128	Reference		
<i>Meta</i>	Tau	Plasma	111+222	1033	0.033	0.021	1.25E-01
<i>Meta</i>	Tau	Plasma	1XY+2XY	1280	0.047	0.021	2.27E-02
<i>Meta</i>	Tau	Plasma	100+200	289	Reference		

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Supplementary Table 7. Comparative analysis of the associations of the selected compound genotypes with Alzheimer's disease (AD) A β 42 and tau biomarkers with carriers of the ϵ 2 allele excluded.

Study	Biomarker	Source	Genotype	N	Beta	SE	P value
ADNI-1	A β 42	CSF	111+222	97	-0.060	0.082	4.67E-01
ADNI-1	A β 42	CSF	1XY+2XY	134	-0.099	0.078	2.06E-01
ADNI-1	A β 42	CSF	100+200	31	Reference		
ADNI-2/GO	A β 42	CSF	111+222	75	-0.054	0.094	5.67E-01
ADNI-2/GO	A β 42	CSF	1XY+2XY	102	-0.091	0.096	3.46E-01
ADNI-2/GO	A β 42	CSF	100+200	25	Reference		
<i>Meta</i>	A β 42	CSF	111+222	172	-0.057	0.062	3.54E-01
<i>Meta</i>	A β 42	CSF	1XY+2XY	236	-0.096	0.061	1.14E-01
<i>Meta</i>	A β 42	CSF	100+200	56	Reference		
ADNI-1	A β 42	Plasma	111+222	187	-1.291	1.661	4.38E-01
ADNI-1	A β 42	Plasma	1XY+2XY	241	-1.261	1.685	4.55E-01
ADNI-1	A β 42	Plasma	100+200	50	Reference		
FHS_C1	A β 42	Plasma	111+222	43	0.658	2.716	8.09E-01
FHS_C1	A β 42	Plasma	1XY+2XY	70	0.840	2.261	7.11E-01
FHS_C1	A β 42	Plasma	100+200	21	Reference		
FHS_C2	A β 42	Plasma	111+222	362	0.334	1.035	7.47E-01
FHS_C2	A β 42	Plasma	1XY+2XY	465	-0.067	0.981	9.46E-01
FHS_C2	A β 42	Plasma	100+200	116	Reference		
FHS_C3	A β 42	Plasma	111+222	460	0.870	1.068	4.16E-01
FHS_C3	A β 42	Plasma	1XY+2XY	561	1.088	1.063	3.06E-01
FHS_C3	A β 42	Plasma	100+200	113	Reference		
ARIC	A β 42	Plasma	111+222	273	2.587	1.474	8.02E-02
ARIC	A β 42	Plasma	1XY+2XY	338	2.458	1.476	9.66E-02

ARIC	A β 42	Plasma	100+200	59	Reference		
Meta	A β 42	Plasma	111+222	1325	0.682	0.601	2.57E-01
Meta	A β 42	Plasma	1XY+2XY	1675	0.594	0.584	3.09E-01
Meta	A β 42	Plasma	100+200	359	Reference		
ADNI-1	Tau	CSF	111+222	100	0.036	0.071	6.16E-01
ADNI-1	Tau	CSF	1XY+2XY	137	0.023	0.065	7.22E-01
ADNI-1	Tau	CSF	100+200	30	Reference		
ADNI-2/GO	Tau	CSF	111+222	82	0.116	0.092	2.11E-01
ADNI-2/GO	Tau	CSF	1XY+2XY	109	0.128	0.094	1.79E-01
ADNI-2/GO	Tau	CSF	100+200	26	Reference		
Meta	Tau	CSF	111+222	182	0.066	0.056	2.43E-01
Meta	Tau	CSF	1XY+2XY	246	0.057	0.054	2.89E-01
Meta	Tau	CSF	100+200	56	Reference		
ADNI-1	Tau	Plasma	111+222	150	0.033	0.085	6.99E-01
ADNI-1	Tau	Plasma	1XY+2XY	197	0.067	0.099	4.97E-01
ADNI-1	Tau	Plasma	100+200	38	Reference		
FHS_C1	Tau	Plasma	111+222	8	0.079	0.299	7.98E-01
FHS_C1	Tau	Plasma	1XY+2XY	13	0.001	0.259	9.97E-01
FHS_C1	Tau	Plasma	100+200	5	Reference		
FHS_C2	Tau	Plasma	111+222	329	0.022	0.037	5.49E-01
FHS_C2	Tau	Plasma	1XY+2XY	417	0.050	0.034	1.46E-01
FHS_C2	Tau	Plasma	100+200	104	Reference		
FHS_C3	Tau	Plasma	111+222	459	0.031	0.029	2.93E-01
FHS_C3	Tau	Plasma	1XY+2XY	560	0.038	0.028	1.84E-01
FHS_C3	Tau	Plasma	100+200	113	Reference		
Meta	Tau	Plasma	111+222	946	0.028	0.022	2.03E-01
Meta	Tau	Plasma	1XY+2XY	1187	0.044	0.021	4.06E-02
Meta	Tau	Plasma	100+200	260	Reference		

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