

Supplementary Online Content

Schjeide BMM, Schnack C, Lambert JC, Lill CM, Kirchheiner J, Tumani H, Otto M, Tanzi RE, Lehrach H, Amouyel P, von Arnim CAF, Bertram L. The role of clusterin, complement receptor 1, and phosphatidylinositol binding clathrin assembly protein in Alzheimer disease risk and cerebrospinal fluid biomarker levels. *Arch Gen Psychiatry*. 2011;68(2):207-213.

eFigure 1. Supplementary figure 1

eFigure 2. Supplementary figure 2

eFigure 3. Supplementary figure 3

eFigure 4. Supplementary figure 4

eTable 1. Demographic characteristics

eTable 2. Sample-specific effect sizes and random effects meta-analyses of the family-based data sets

This supplementary material has been provided by the authors to give readers additional information about their work.

Legend to eFigures 1-3. AlzGene-style forest plots of random-effects, allele-based meta-analyses of the lead signals in *CLU* (rs11136000; eFigure1), *CR1* (rs6656401; eFigure 2) and *PICALM* (rs541458; eFigure 3) analyzed in this study. Meta-analyses are based on allelic crude ORs combined via random-effects models. Data not generated in "Current study" was taken from the AlzGene database (www.alzgene.org). Note that confidence intervals (CIs) for "This study" are different from those depicted in Table 2 of the main text where they were calculated as 90% CIs. The summary OR and CIs across "All studies" are identical to those in Table 2. # Violation from HWE in controls ($P \leq 0.05$). † Data not provided in original publication.

Legend to eFigure 4. Box plot of the distribution of absolute CSF A β 42 levels across ϵ 3/3, ϵ 3/4, and ϵ 4/4 genotypes at *APOE* in the combined case-control dataset from Germany. Horizontal lines represent median values, boxes are 25-75% ranges and whiskers extend to 1x the interquartile range; values outside this range are depicted as circles. As can be seen, CSF A β 42 levels decrease with increasing numbers of ϵ 4 (=risk) allele.

eTable 1. Demographic characteristics of the populations studied. Median fam size = median number of subjects per family with DNA available for association testing; SD = standard deviation. AAO = age at onset; AAE = age at last examination; AD = Alzheimer disease; CAG = Consortium on Alzheimer's Genetics; CSF = cerebrospinal fluid; DX = diagnosis; NCRAD = National Cell Repository for Alzheimer Disease; NIA = National Institute on Aging; NIMH = National Institute of Mental Health. While individuals with "DX unknown" were not included in the association analyses on AD risk, they were included in

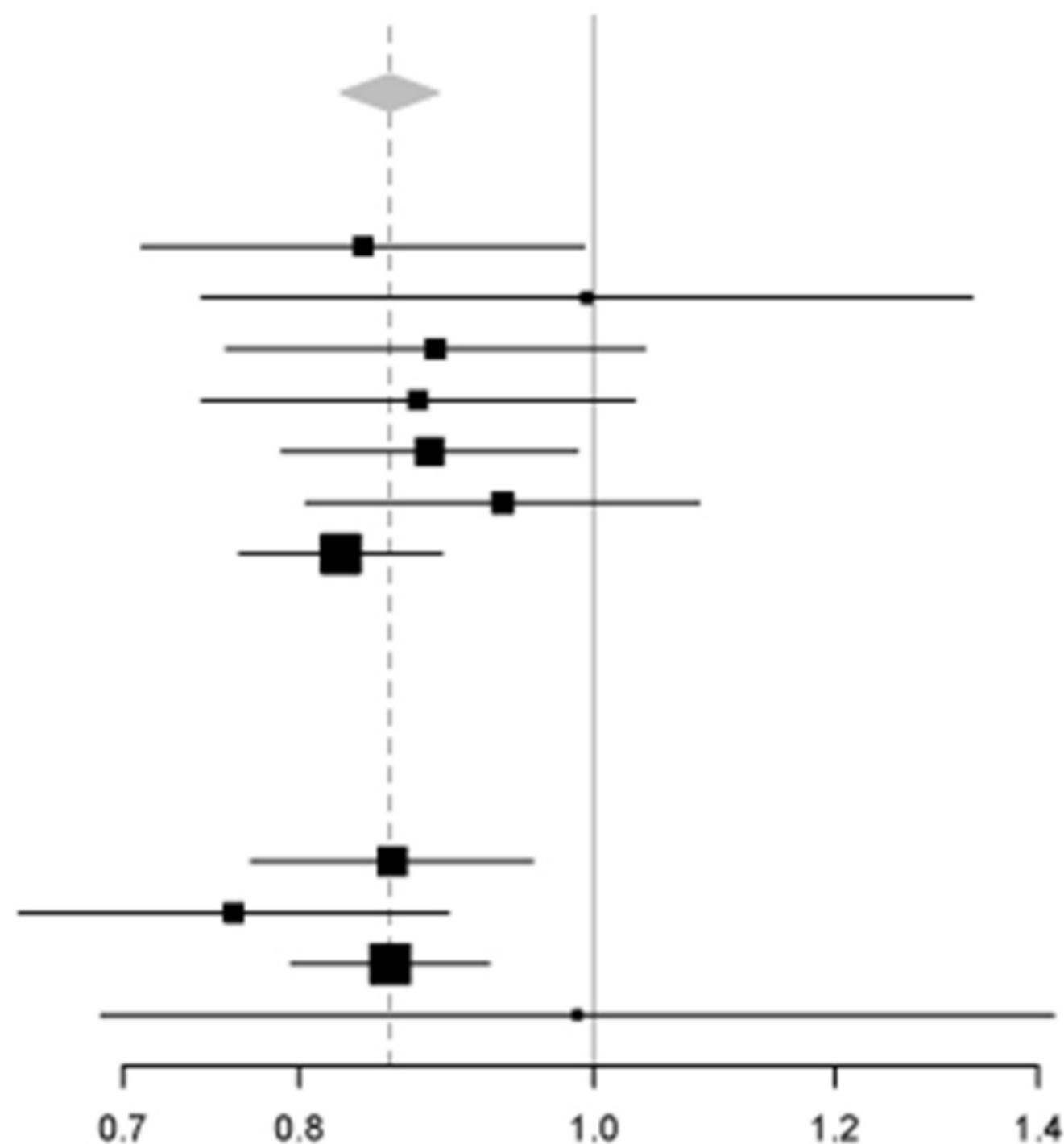
tests of Mendelian transmission (family-samples) and for the quantification of CSF biomarker levels irrespective of affection status.

eTable 2. Sample-specific effect sizes and random effects meta-analyses of the family-based datasets. Sample-specific odds ratios (ORs) and 95% confidence intervals (CIs) were calculated via logistic regression stratified by family. CAG = Consortium on Alzheimer's Genetics; Chr = chromosome; Meta-analysis = combining sample-specific results using random effects models; NCRAD = National Cell Repository for Alzheimer Disease; NIA = National Institute on Aging; NIMH = National Institute of Mental Health; SNP = single-nucleotide polymorphism. Note that the ORs and CIs derived from the meta-analysis are similar, but not identical, to the corresponding values from Table 1 for which all family samples were pooled prior to analyses. MAF = minor allele frequency. I^2 = measure of between-study heterogeneity which is calculated based on the Q-statistic: $I^2 = 100 \times ((Q-d.f.)/Q)$. I^2 values below 25% are considered to display no significant between-study heterogeneity.

Supplementary figure 1.

CLU (rs11136000): T vs. C

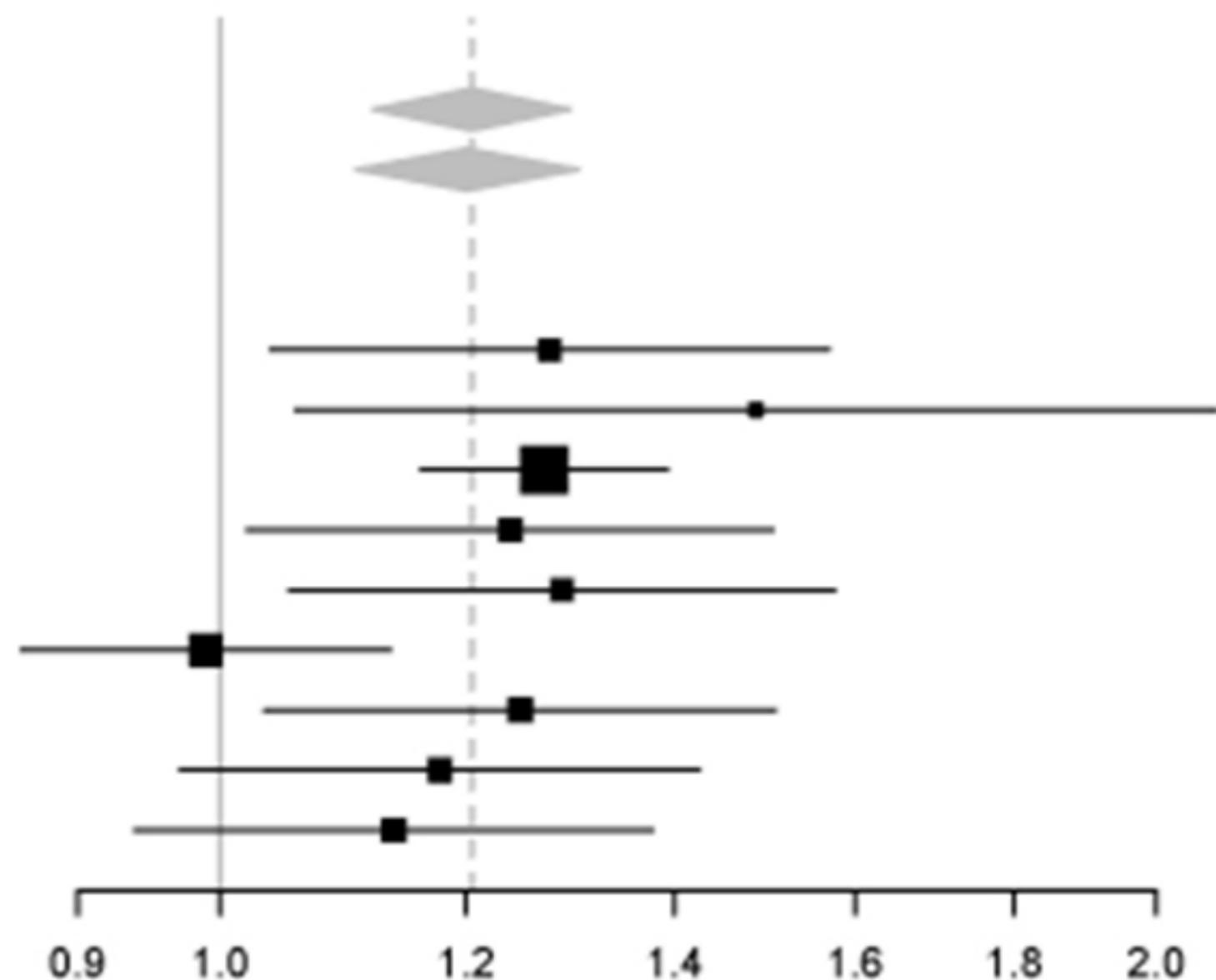
	OR	95% CI	I ²
All studies	0.86	[0.83,0.89]	0
Study specific ORs			
Current study, USA (FBAT) [C]	0.84	[0.71,0.99]	
Current study, Germany [C]	0.99	[0.74,1.33]	
Lambert, 2009, Belgium (Stage 2) [C]	0.89	[0.76,1.04]	
Lambert, 2009, Finland (Stage 2) [C]	0.88	[0.74,1.03]	
Lambert, 2009, Italy (Stage 2) [C]	0.88	[0.79,0.99]	
Lambert, 2009, Spain (Stage 2) [C]	0.93	[0.80,1.08]	
Lambert, 2009, France (Stage 1) [C]	0.83	[0.76,0.89]	
Harold, 2009, Belgium [C] ‡	–	–	
Harold, 2009, UK, Ireland (Stage 2) [C] †	–	–	
Harold, 2009, UK-ART (Stage 2) [C] †	–	–	
Harold, 2009, Germany (Stage 2) [C] †	–	–	
Harold, 2009, Greece (Stage 2) [C] †	–	–	
Harold, 2009, USA (Stage 1) [C]	0.86	[0.77,0.95]	
Harold, 2009, Germany (Stage 1) [C]	0.76	[0.65,0.90]	
Harold, 2009, UK, Ireland (Stage 1) [C]	0.86	[0.80,0.92]	
Giedraitis, 2009 [C]	0.99	[0.69,1.42]	



Supplementary figure 2.

CR1 (rs6656401): A vs. G

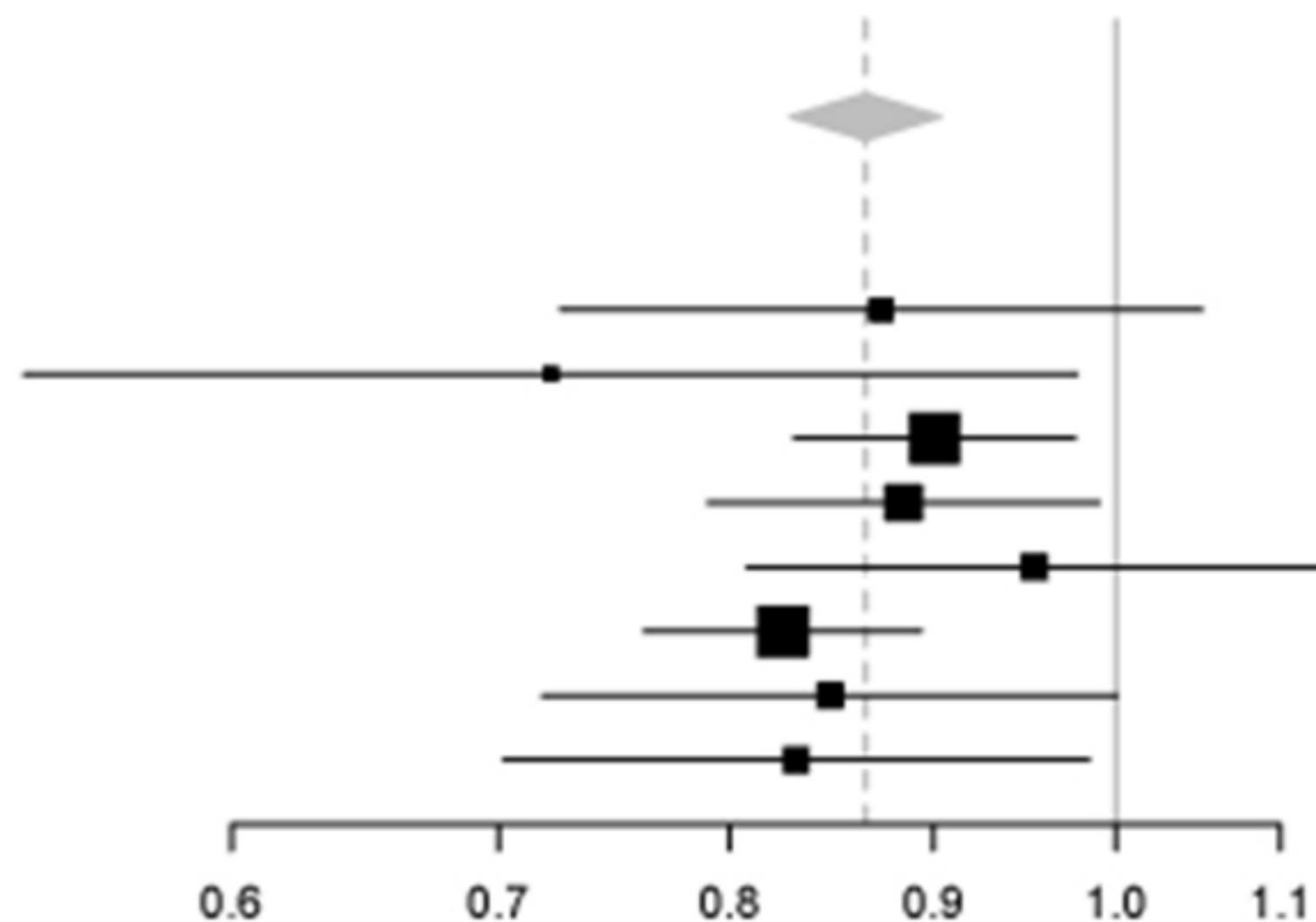
	OR	95% CI	I ²
All studies	1.20	[1.12,1.30]	36
All excl HWE violations	1.20	[1.11,1.30]	44
Study specific ORs			
Current study, USA (FBAT) [C]	1.28	[1.04,1.57]	
Current study, Germany [C]	1.49	[1.06,2.09]	
Lambert, 2009, France (Stage 1) [C]	1.27	[1.16,1.39]	
Lambert, 2009, Belgium (Stage 2) [C]	1.24	[1.02,1.51]	
Lambert, 2009, Finland (Stage 2) [C]	1.29	[1.05,1.58]	
Lambert, 2009, Italy (Stage 2) [C]	0.99	[0.86,1.13]	
Lambert, 2009, Spain (Stage 2) [C] #	1.25	[1.03,1.51]	
Li, 2008 [C]	1.18	[0.97,1.43]	
Reiman, 2007 [C]	1.14	[0.94,1.38]	



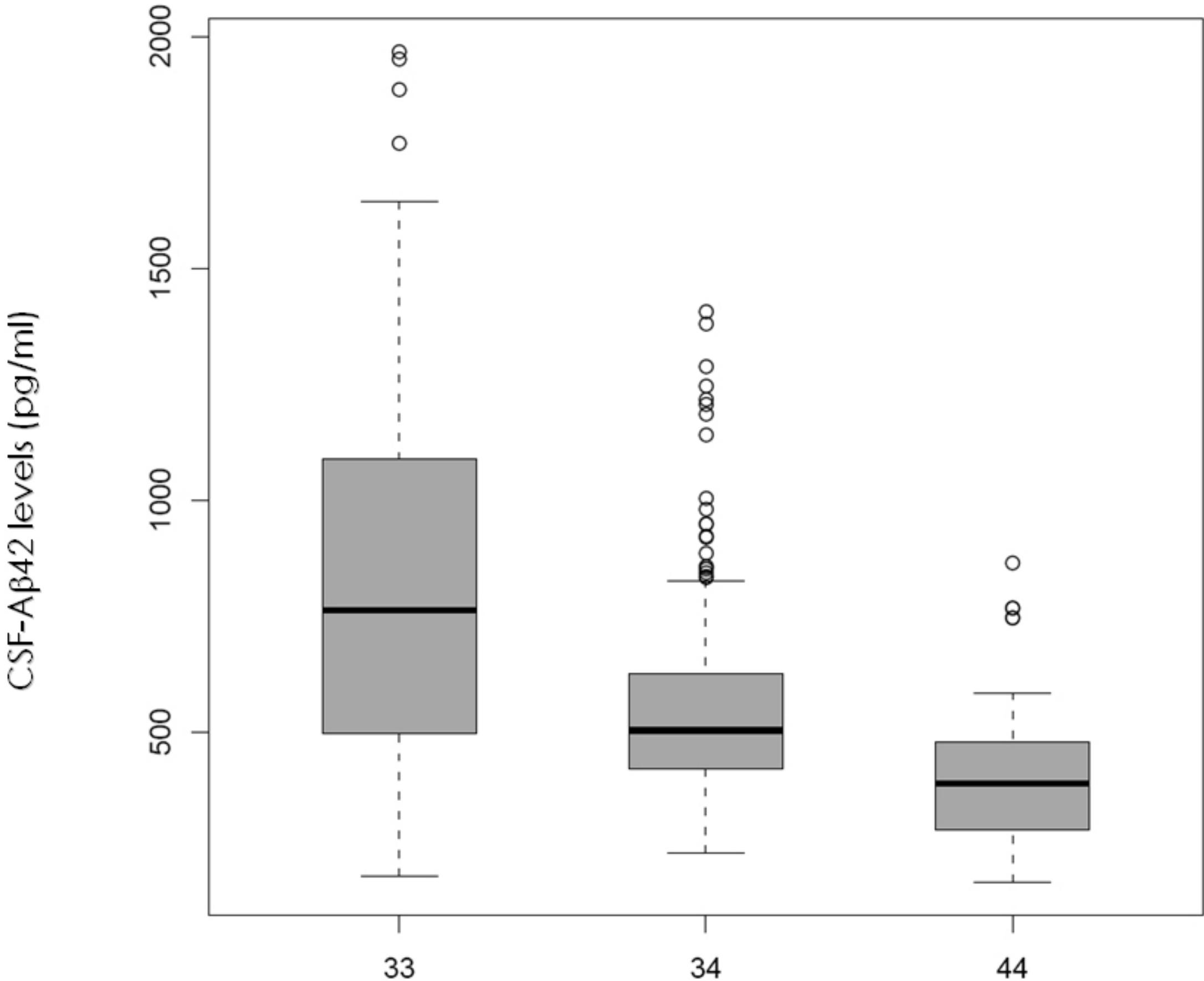
Supplementary figure 3.

PICALM (rs541458): C vs. T

	OR	95% CI	I ²
All studies	0.87	[0.83,0.90]	0
Study specific ORs			
Current study, USA (FBAT) [C]	0.87	[0.73,1.05]	
Current study, Germany [C]	0.72	[0.53,0.98]	
Lambert, 2009 [C]	0.90	[0.83,0.98]	
Harold, 2009, USA (Stage 1) [C]	0.88	[0.79,0.99]	
Harold, 2009, Germany (Stage 1) [C]	0.95	[0.81,1.13]	
Harold, 2009, UK, Ireland (Stage 1) [C]	0.83	[0.76,0.89]	
Li, 2008 [C]	0.85	[0.72,1.00]	
Reiman, 2007 [C]	0.83	[0.70,0.98]	



Supplementary figure 4.



Supplementary Table 1. Demographic characteristics.

Sample	Family based				Case-control
	NIMH	NIA	NCRAD	CAG	Germany
# Families	405	333	331	176	-
Median fam size (range)	3 (2-28)	3 (2-9)	3 (2-10)	2 (2-5)	-
AD-cases	919	760	798	177	214
AAO (SD)	72.4 (8)	74.2 (7)	71.3 (8)	68.9 (9)	69.5 (10)
Women (%)	672 (73%)	483 (64%)	530 (66%)	105 (59%)	136 (64%)
CSF A β 42 (pg/ml)	-	-	-	-	444.6 (230)
CSF Tau (pg/ml)	-	-	-	-	583 (420)
Controls	384	284	293	214	211
AAE (SD)	73.3 (12)	73.4 (10)	71.2 (8)	72.1 (9)	62.1 (13)
Women (%)	222 (58%)	165 (58%)	162 (55%)	132 (62%)	103 (49%)
CSF A β 42 (pg/ml)	-	-	-	-	863.7 (371)
CSF Tau (pg/ml)	-	-	-	-	250.2 (190)
DX unknown	25	10	17	none	30

Supplementary Table 2. Sample-specific effect sizes and random effects meta-analyses of the family-based datasets.

Chr	Gene	SNP	Family sample	MAF	OR (CI)	I ²
1	<i>CR1</i>	rs6656401	NIMH	0.204	1.52 (1.05-2.17)	13.5
			NIA	0.216	1.41 (0.93-2.08)	
			NCRAD	0.202	1.15 (0.76-1.72)	
			CAG	0.203	0.87 (0.52-1.45)	
			Meta-analysis	-	1.25 (1.01-1.54)	
8	<i>CLU</i>	rs11136000	NIMH	0.352	0.88 (0.66-1.19)	0
			NIA	0.359	1.04 (0.74-1.47)	
			NCRAD	0.379	0.70 (0.51-0.97)	
			CAG	0.394	0.84 (0.56-1.25)	
			Meta-analysis	-	0.85 (0.72-1.01)	
8	<i>CLU</i>	rs2279590	NIMH	0.372	0.83 (0.62-1.1)	0
			NIA	0.368	1.05 (0.75-1.47)	
			NCRAD	0.393	0.71 (0.52-0.97)	
			CAG	0.406	0.85 (0.58-1.25)	
			Meta-analysis	-	0.84 (0.72-0.99)	
8	<i>CLU</i>	rs9331888	NIMH	0.325	0.97 (0.71-1.32)	0
			NIA	0.311	0.93 (0.67-1.3)	
			NCRAD	0.312	1.28 (0.9-1.81)	
			CAG	0.261	1.21 (0.76-1.95)	
			Meta-analysis	-	1.06 (0.89-1.27)	
11	<i>PICALM</i>	rs541458	NIMH	0.286	1.01 (0.73-1.38)	0
			NIA	0.304	0.86 (0.59-1.24)	
			NCRAD	0.279	0.68 (0.47-0.97)	
			CAG	0.273	0.95 (0.6-1.51)	
			Meta-analysis	-	0.86 (0.72-1.04)	