

Supplementary Data 1 - Bootstrapping analysis

for: Sex and APOE $\epsilon 4$ genotype modify the Alzheimer's disease serum metabolome

Matthias Arnold, Kwangsik Nho, Alexandra Kueider-Paisley, Tyler Massaro, Kevin Huynh, Barbara Brauner, Siamak MahmoudianDehkordi, Gregory Louie, M. Arthur Moseley, J. Will Thompson, Lisa St John Williams, Jessica D. Tenenbaum, Colette Blach, Rui Chang, Roberta D. Brinton, Rebecca Baillie, Xianlin Han, John Q. Trojanowski, Leslie M. Shaw, Ralph Martins, Michael W. Weiner, Eugenia Trushina, Jon B. Toledo, Peter J. Meikle, David A. Bennett, Jan Krumsiek, P. Murali Doraiswamy, Andrew J. Saykin, Rima Kaddurah-Daouk, and Gabi Kastenmüller for the Alzheimer's Disease Neuroimaging Initiative and the Alzheimer's Disease Metabolomics Consortium

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β_0 : original beta (as reported in manuscript); P_0 : original P-value; bias (β_0): bias of the original beta as determined by 1000 bootstraps; β_{boot} : histogram of β -estimates across 1000 bootstraps, with β_0 indicated as dashed line and 95% bootstrap-t confidence intervals given by grey lines; P_N : P-value of the Shapiro-Wilk test for normality; $\mu(\beta)_{boot}$: mean β across the 1000 bootstraps; $\mu(SE)_{boot}$: mean of the standard error of β across the 1000 bootstraps; P_{boot} : two-tailed P-value of the standard normal distribution for $-\text{abs}(\mu(\beta)_{boot} / \mu(SE)_{boot})$; % $P_{bonf.sign.}$: fraction of bootstraps yielding a Bonferroni-significant P-value ($P \leq 9.09 \times 10^{-4}$); % $P_{nom.sign.}$: fraction of bootstraps yielding a nominally significant P-value ($P \leq 0.05$); $\Delta \text{Sex} / \Delta \text{APOE } \epsilon 4 \pm$: statistics for heterogeneity (P_{boot} : two-tailed P-value of the standard normal distribution for the mean heterogeneity estimate; % $P_{nom.sign.}$: fraction of bootstraps yielding a nominally significant P-value; I^2_{boot} : I^2 calculated for the mean heterogeneity estimate; % $I^2_{boot} = 0$: fraction of bootstraps yielding an I^2 estimate of exactly zero)

Sex-stratified analysis

Pathological CSF $A\beta_{1-42}$

metabolite	statistic	pooled	males	females
	β_0	0.283	0.282	0.299
	P_0	0.000258	0.00596	0.0133
	bias (β_0)	0.00486	0.00453	0.0105
PC ae C44:6	β_{boot}			
	$\mu(\beta)_{boot}$	0.288	0.286	0.309
	$\mu(SE)_{boot}$	0.0783	0.104	0.123
	P_{boot}	0.000233	0.006	0.012
	% $P_{bonf.sign.}$	63.9	27.5	20
	% $P_{nom.sign.}$	95.6	79.4	71
Δ Sex	P_{boot}		% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
	0.891		4.8	0 (68)

metabolite	statistic	pooled	males	females
	β_0	0.265	0.274	0.255
	P_0	0.000457	0.00629	0.0307
	bias (β_0)	0.00664	0.00383	0.0136
PC ae C44:4	β_{boot}			
	$\mu(\beta)_{boot}$	0.272	0.277	0.269
	$\mu(SE)_{boot}$	0.0765	0.102	0.121
	P_{boot}	0.000378	0.00638	0.0259
	% $P_{bonf.sign.}$	60.8	25	11.2
	% $P_{nom.sign.}$	94.8	78.6	62.3
Δ Sex	P_{boot}		% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
	0.955		4.7	0 (70)

metabolite	statistic	pooled	males	females	
	β_0	0.26	0.294	0.214	
	P_0	0.000523	0.00326	0.0638	
	bias (β_0)	0.00113	0.00458	0.000925	
PC ae C44:5	β_{boot}				
	$\mu(\beta)_{boot}$	0.261	0.299	0.215	
	$\mu(SE)_{boot}$	0.0758	0.102	0.118	
	P_{boot}	0.000567	0.00337	0.0672	
	% $P_{bonf.sign.}$	55.4	34.4	5	
	% $P_{nom.sign.}$	93.4	85.6	46.5	
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)	
		0.591	8.8	0 (64)	

metabolite	statistic	pooled	males	females	
	β_0	0.207	0.372	0.0699	
	P_0	0.00672	0.000883	0.517	
	bias (β_0)	0.00311	0.00544	0.00391	
Threonine	β_{boot}				
	$\mu(\beta)_{boot}$	0.21	0.377	0.0738	
	$\mu(SE)_{boot}$	0.077	0.114	0.11	
	P_{boot}	0.00642	0.000892	0.502	
	% $P_{bonf.sign.}$	27.1	50.9	0.3	
	% $P_{nom.sign.}$	79.1	92.2	9.6	
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)	
		0.0553	47.8	47.8 (19)	

metabolite	statistic	pooled	males	females
	β_0	-0.134	0.0319	-0.299
	P_0	0.105	0.78	0.015
	bias (β_0)	-0.00348	-0.00022	-0.00717
Valine	β_{boot}			
	$\mu(\beta)_{boot}$	-0.137	0.0317	-0.306
	$\mu(SE)_{boot}$	0.0833	0.116	0.125
	P_{boot}	0.0995	0.785	0.0144
	% $P_{bonf.sign.}$	4.3	0	19.9
	% $P_{nom.sign.}$	39.8	5	70.3
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0483	49.9	49.4 (18)

CSF p-tau

metabolite	statistic	pooled	males	females
	β_0	0.0839	0.0141	0.144
	P_0	0.00458	0.734	0.000607
	bias (β_0)	0.000206	-0.00031	0.000518
C10	β_{boot}			
	$\mu(\beta)_{boot}$	0.0841	0.0138	0.144
	$\mu(SE)_{boot}$	0.0295	0.0416	0.0417
	P_{boot}	0.00438	0.74	0.000545
	% $P_{bonf.sign.}$	33.7	0.2	54.8
	% $P_{nom.sign.}$	80.1	8.9	92.5
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0267	59.6	54.9 (12)

metabolite	statistic	pooled	males	females
	β_0	0.103	0.0116	0.205
	P_0	0.0235	0.852	0.00227
	bias (β_0)	-0.000864	0.00161	-0.00285
C5-DC (C6-OH)	β_{boot}			
	$\mu(\beta)_{boot}$	0.102	0.0132	0.202
	$\mu(SE)_{boot}$	0.0454	0.0626	0.0668
	P_{boot}	0.0248	0.832	0.00253
	% $P_{bonf.sign.}$	13.4	0.1	36.6
	% $P_{nom.sign.}$	63.1	4.7	86.3
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0392	53.9	51.5 (15)

metabolite	statistic	pooled	males	females
	β_0	0.0644	0.00316	0.127
	P_0	0.0342	0.939	0.00511
	bias (β_0)	-0.000902	-0.000382	-0.00103
C8	β_{boot}			
	$\mu(\beta)_{boot}$	0.0635	0.00278	0.126
	$\mu(SE)_{boot}$	0.0305	0.0412	0.0453
	P_{boot}	0.037	0.946	0.00548
	% $P_{bonf.sign.}$	10.8	0.2	27.6
	% $P_{nom.sign.}$	55.7	5.6	81.1
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0441	53.1	50.3 (14)

metabolite	statistic	pooled	males	females
	β_0	0.0557	0.129	-0.0228
	P_0	0.0865	0.0048	0.618
	bias (β_0)	0.000661	0.00102	0.000452
PC ae C36:2	β_{boot}			
	$\mu(\beta)_{boot}$	0.0563	0.13	-0.0223
	$\mu(SE)_{boot}$	0.0325	0.0458	0.0457
	P_{boot}	0.0828	0.00439	0.625
	% $P_{bonf.sign.}$	5	31.4	0
	% $P_{nom.sign.}$	40.5	82.4	6.2
	Δ Sex	P_{boot}		% $P_{nom.sign.}$
	0.0182		68.2	57.6 (7.9)

metabolite	statistic	pooled	males	females
	β_0	-0.0338	0.0325	-0.105
	P_0	0.272	0.439	0.0197
	bias (β_0)	0.000196	-0.00113	0.00152
Histidine	β_{boot}			
	$\mu(\beta)_{boot}$	-0.0336	0.0314	-0.103
	$\mu(SE)_{boot}$	0.0308	0.0422	0.0449
	P_{boot}	0.276	0.456	0.0212
	% $P_{bonf.sign.}$	1.7	0.1	17.8
	% $P_{nom.sign.}$	20.4	10.2	63.1
	Δ Sex	P_{boot}		% $P_{nom.sign.}$
	0.0285		60.1	54.3 (11)

metabolite	statistic	pooled	males	females
	β_0	0.0336	0.107	-0.0524
	P_0	0.284	0.0166	0.232
	bias (β_0)	-0.000114	-0.000374	-9.01E-05
Asparagine	β_{boot}			
	$\mu(\beta)_{boot}$	0.0335	0.107	-0.0525
	$\mu(SE)_{boot}$	0.0314	0.0446	0.0439
	P_{boot}	0.286	0.017	0.231
	% $P_{bonf.sign.}$	1.1	17	1.5
	% $P_{nom.sign.}$	19.7	66.2	21.5
	Δ Sex	P_{boot}		% $P_{nom.sign.}$
	0.011		71.5	60.7 (5.1)

metabolite	statistic	pooled	males	females
	β_0	0.032	0.0909	-0.0389
	P_0	0.31	0.0336	0.399
	bias (β_0)	0.000366	0.00102	-0.000497
SM (OH) C16:1	β_{boot}			
	$\mu(\beta)_{boot}$	0.0323	0.092	-0.0394
	$\mu(SE)_{boot}$	0.0315	0.0428	0.0461
	P_{boot}	0.304	0.0315	0.393
	% $P_{bonf.sign.}$	0.7	11.7	0.8
	% $P_{nom.sign.}$	18.4	59.2	11
	Δ Sex	P_{boot}		% $P_{nom.sign.}$
	0.0365		57.2	52.2 (14)

metabolite	statistic	pooled	males	females	
	β_0	0.0296	0.104	-0.0256	
	P_0	0.35	0.0394	0.523	
	bias (β_0)	-0.00114	-0.0019	-0.0013	
Glycine	β_{boot}				
	$\mu(\beta)_{boot}$	0.0285	0.102	-0.0269	
	$\mu(SE)_{boot}$	0.0317	0.0506	0.0402	
	P_{boot}	0.369	0.0428	0.503	
	% $P_{bonf.sign.}$	1	10.5	0.7	
	% $P_{nom.sign.}$	16.5	52.7	12.2	
	Δ Sex	P_{boot}		% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0447		50.6	50.2 (18)

metabolite	statistic	pooled	males	females	
	β_0	0.028	0.0883	-0.0413	
	P_0	0.368	0.0417	0.351	
	bias (β_0)	0.000567	0.00219	-0.00172	
PC ae C36:1	β_{boot}				
	$\mu(\beta)_{boot}$	0.0285	0.0905	-0.043	
	$\mu(SE)_{boot}$	0.0311	0.0434	0.0444	
	P_{boot}	0.359	0.0369	0.333	
	% $P_{bonf.sign.}$	1.4	12.2	1.2	
	% $P_{nom.sign.}$	15.4	54.3	16.8	
	Δ Sex	P_{boot}		% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0314		58.3	53.5 (13)

metabolite	statistic	pooled	males	females
	β_0	0.0155	-0.054	0.0885
	P_0	0.585	0.167	0.0302
	bias (β_0)	0.00164	0.00196	0.00204
C2	β_{boot}			
	$\mu(\beta)_{boot}$	0.0171	-0.0521	0.0906
	$\mu(SE)_{boot}$	0.0284	0.0391	0.0408
	P_{boot}	0.546	0.183	0.0265
	% $P_{bonf.sign.}$	0.5	2.6	11.4
	% $P_{nom.sign.}$	9	28	60.7
	Δ Sex	P_{boot}		% $P_{nom.sign.}$
	0.0116		70.6	60.4 (5.4)

FDG-PET

metabolite	statistic	pooled	males	females
	β_0	-0.127	-0.14	-0.11
	P_0	2.32E-05	0.000631	0.015
	bias (β_0)	-0.00013	0.000483	-0.00101
PC aa C32:1	β_{boot}			
	$\mu(\beta)_{boot}$	-0.127	-0.139	-0.111
	$\mu(SE)_{boot}$	0.0299	0.0407	0.0449
	P_{boot}	2.08E-05	0.000621	0.0138
	% $P_{bonf.sign.}$	83.5	54.9	17.9
	% $P_{nom.sign.}$	99.2	93.8	69.6
	Δ Sex	P_{boot}		% $P_{nom.sign.}$
	0.636		5.8	0 (63)

metabolite	statistic	pooled	males	females
	β_0	-0.111	-0.0974	-0.141
	P_0	0.000227	0.018	0.00184
	bias (β_0)	-0.00105	-0.00203	-0.000168
PC ae C44:4	β_{boot}			
	$\mu(\beta)_{boot}$	-0.112	-0.0994	-0.141
	$\mu(SE)_{boot}$	0.0301	0.0411	0.0451
	P_{boot}	0.000189	0.0155	0.00174
	% $P_{bonf.sign.}$	67.5	17.6	41.6
	% $P_{nom.sign.}$	96.8	69.9	89.3
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
	0.492	10	0 (61)	

metabolite	statistic	pooled	males	females
	β_0	-0.105	-0.112	-0.111
	P_0	0.000407	0.0058	0.013
	bias (β_0)	-0.0012	-0.00169	-0.000339
PC ae C44:5	β_{boot}			
	$\mu(\beta)_{boot}$	-0.106	-0.114	-0.111
	$\mu(SE)_{boot}$	0.0296	0.0405	0.0444
	P_{boot}	0.000335	0.005	0.0125
	% $P_{bonf.sign.}$	62.3	29	19.1
	% $P_{nom.sign.}$	96.8	82.4	71.7
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
	0.967	2.7	0 (71)	

metabolite	statistic	pooled	males	females
	β_0	-0.107	-0.125	-0.0906
	P_0	0.000685	0.00567	0.0425
	bias (β_0)	-0.00132	0.000661	-0.00381
PC aa C32:0	β_{boot}			
	$\mu(\beta)_{boot}$	-0.109	-0.125	-0.0944
	$\mu(SE)_{boot}$	0.0315	0.0451	0.0446
	P_{boot}	0.000563	0.00577	0.0342
	% $P_{bonf.sign.}$	54.6	26.1	10.3
	% $P_{nom.sign.}$	94.8	82	56
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.635	5.2	0 (65)

metabolite	statistic	pooled	males	females
	β_0	-0.103	-0.103	-0.112
	P_0	0.000856	0.0158	0.0133
	bias (β_0)	-0.00249	-0.00367	-0.00161
PC ae C42:4	β_{boot}			
	$\mu(\beta)_{boot}$	-0.105	-0.106	-0.114
	$\mu(SE)_{boot}$	0.0308	0.0425	0.0454
	P_{boot}	0.000623	0.0122	0.012
	% $P_{bonf.sign.}$	53.2	20.5	19.2
	% $P_{nom.sign.}$	93.4	69.3	72.4
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.902	4.5	0 (69)

metabolite	statistic	pooled	males	females
	β_0	-0.103	-0.165	-0.0285
	P_0	0.000909	9.64E-05	0.538
	bias (β_0)	-2.19E-05	-0.000244	0.000573
C16:1	β_{boot}			
	$\mu(\beta)_{boot}$	-0.103	-0.165	-0.0279
	$\mu(SE)_{boot}$	0.0309	0.0419	0.0463
	P_{boot}	0.000879	8.44E-05	0.546
	% $P_{bonf.sign.}$	49.9	72.4	0.3
	% $P_{nom.sign.}$	92.6	98.2	11.6
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0284	57.5	54.4 (14)

metabolite	statistic	pooled	males	females
	β_0	-0.0529	-0.119	0.016
	P_0	0.0782	0.00434	0.715
	bias (β_0)	0.000617	0.00174	-0.000552
PC ae C40:2	β_{boot}			
	$\mu(\beta)_{boot}$	-0.0523	-0.117	0.0154
	$\mu(SE)_{boot}$	0.0301	0.0417	0.0438
	P_{boot}	0.0818	0.00485	0.725
	% $P_{bonf.sign.}$	5	29	0
	% $P_{nom.sign.}$	40.1	82	5.8
	Δ Sex	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0279	58.5	54.5 (9.6)

metabolite	statistic	pooled	males	females
	β_0	-0.0234	0.0591	-0.118
	P_0	0.451	0.177	0.00818
	bias (β_0)	-0.00143	-0.00103	-0.00162
Proline	β_{boot}			
	$\mu(\beta)_{boot}$	-0.0248	0.0581	-0.119
	$\mu(SE)_{boot}$	0.031	0.0437	0.0443
	P_{boot}	0.424	0.184	0.00709
	% $P_{bonf.sign.}$	0.3	1.7	24.9
	% $P_{nom.sign.}$	10.7	25.5	78.9
	Δ Sex	P_{boot}		% $P_{nom.sign.}$
	0.00432		80.4	65 (1.9)

APOE $\epsilon 4$ status-stratified analyses

Pathological CSF $A\beta_{1-42}$

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	0.283	0.63	0.158
	P_0	0.000258	2.5E-05	0.0796
	bias (β_0)	0.00486	0.00984	0.00611
PC ae C44:6	β_{boot}			
	$\mu(\beta)_{boot}$	0.288	0.64	0.164
	$\mu(SE)_{boot}$	0.0783	0.153	0.0914
	P_{boot}	0.000233	2.85E-05	0.0724
	% $P_{bonf.sign.}$	63.9	81.4	5
	% $P_{nom.sign.}$	95.6	99.6	44
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}		% $P_{nom.sign.}$
	0.00791		76.1	62.3 (4)

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	0.265	0.565	0.139
	P_0	0.000457	0.00013	0.113
	bias (β_0)	0.00664	0.011	0.00656
PC ae C44:4	β_{boot}			
	$\mu(\beta)_{boot}$	0.272	0.577	0.146
	$\mu(SE)_{boot}$	0.0765	0.151	0.0893
	P_{boot}	0.000378	0.000137	0.102
	% $P_{bonf.sign.}$	60.8	69.9	3.4
	% $P_{nom.sign.}$	94.8	98.1	37.3
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}		% $P_{nom.sign.}$
	0.0148		67.2	59 (6.1)

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	0.26	0.609	0.129
	P_0	0.000523	2.64E-05	0.137
	bias (β_0)	0.00113	0.00849	0.000964
PC ae C44:5	β_{boot}			
	$\mu(\beta)_{boot}$	0.261	0.618	0.13
	$\mu(SE)_{boot}$	0.0758	0.148	0.0884
	P_{boot}	0.000567	3.18E-05	0.14
	% $P_{bonf.sign.}$	55.4	82	2.9
	% $P_{nom.sign.}$	93.4	99.5	31.1
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}		% $P_{nom.sign.}$
	0.00504		81.7	64.3 (1.9)

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$	
	β_0	0.242	0.564	0.114	
	P_0	0.00198	0.000132	0.215	
	bias (β_0)	0.000364	0.00878	-0.00137	
PC ae C42:4					
	$\mu(\beta)_{boot}$	0.242	0.573	0.113	
	$\mu(SE)_{boot}$	0.0788	0.151	0.0931	
	P_{boot}	0.00214	0.000147	0.227	
	% $P_{bonf.sign.}$	38.5	70	1.6	
	% $P_{nom.sign.}$	88.3	98.1	22.8	
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)	
		0.00975	74.9	61.3 (3.9)	

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$	
	β_0	-0.0755	0.176	-0.202	
	P_0	0.352	0.215	0.044	
	bias (β_0)	-0.0019	-0.00185	-0.00142	
Proline					
	$\mu(\beta)_{boot}$	-0.0774	0.174	-0.203	
	$\mu(SE)_{boot}$	0.0819	0.145	0.102	
	P_{boot}	0.345	0.231	0.0455	
	% $P_{bonf.sign.}$	0.7	1.9	7.3	
	% $P_{nom.sign.}$	14.7	21.9	51.1	
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)	
		0.0341	57.3	52.8 (12)	

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	0.0603	0.363	-0.102
	P_0	0.46	0.0183	0.305
	bias (β_0)	0.000846	0.0135	-0.00342
Glycine	β_{boot}			
	$\mu(\beta)_{boot}$	0.0612	0.376	-0.106
	$\mu(SE)_{boot}$	0.0823	0.157	0.101
	P_{boot}	0.457	0.0164	0.296
	% $P_{bonf.sign.}$	0.3	15.7	1.1
	% $P_{nom.sign.}$	12.5	69.2	20.4
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0104	72.8	61 (6.8)

FDG-PET

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	-0.127	-0.0873	-0.162
	P_0	2.32E-05	0.0535	0.000134
	bias (β_0)	-0.00013	-0.00142	0.000826
PC aa C32:1	β_{boot}			
	$\mu(\beta)_{boot}$	-0.127	-0.0887	-0.161
	$\mu(SE)_{boot}$	0.0299	0.0452	0.0421
	P_{boot}	2.08E-05	0.0495	0.000131
	% $P_{bonf.sign.}$	83.5	9.5	70.7
	% $P_{nom.sign.}$	99.2	50.3	97.5
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.241	19.2	14.8 (42)

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	-0.111	-0.115	-0.114
	P_0	0.000227	0.0139	0.00634
	bias (β_0)	-0.00105	-0.000257	-0.00172
PC ae C44:4	β_{boot}			
	$\mu(\beta)_{boot}$	-0.112	-0.115	-0.115
	$\mu(SE)_{boot}$	0.0301	0.0466	0.0415
	P_{boot}	0.000189	0.0134	0.00549
	% $P_{bonf.sign.}$	67.5	20.6	26.3
	% $P_{nom.sign.}$	96.8	70.1	81
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
	1	4.6	0 (70)	

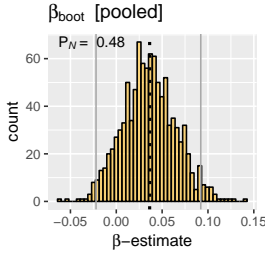
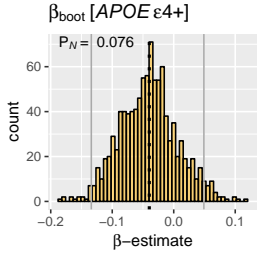
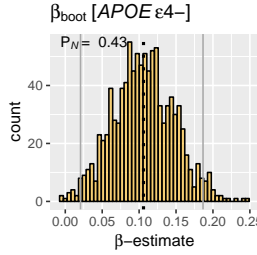
metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	-0.105	-0.122	-0.102
	P_0	0.000407	0.00834	0.013
	bias (β_0)	-0.0012	-0.00222	-0.000556
PC ae C44:5	β_{boot}			
	$\mu(\beta)_{boot}$	-0.106	-0.124	-0.102
	$\mu(SE)_{boot}$	0.0296	0.046	0.0408
	P_{boot}	0.000335	0.00712	0.0123
	% $P_{bonf.sign.}$	62.3	24.1	17.1
	% $P_{nom.sign.}$	96.8	76.8	73.6
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
	0.724	4.4	0 (69)	

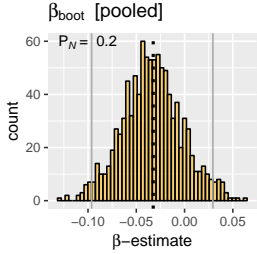
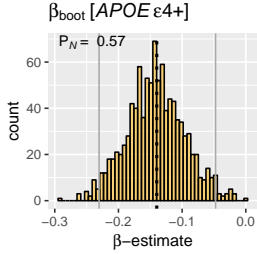
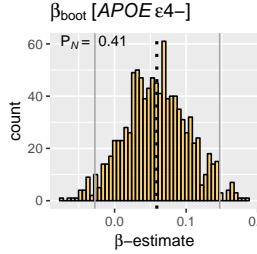
metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	-0.107	-0.135	-0.0823
	P_0	0.000685	0.00439	0.0658
	bias (β_0)	-0.00132	-0.00386	0.000352
PC aa C32:0	β_{boot}			
	$\mu(\beta)_{boot}$	-0.109	-0.139	-0.0819
	$\mu(SE)_{boot}$	0.0315	0.0474	0.0446
	P_{boot}	0.000563	0.0033	0.0664
	% $P_{bonf.sign.}$	54.6	34.2	5.3
	% $P_{nom.sign.}$	94.8	83.7	43.6
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
	0.378	14.1	0 (53)	

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	-0.103	-0.131	-0.0859
	P_0	0.000856	0.00579	0.0451
	bias (β_0)	-0.00249	-0.00038	-0.00426
PC ae C42:4	β_{boot}			
	$\mu(\beta)_{boot}$	-0.105	-0.131	-0.0901
	$\mu(SE)_{boot}$	0.0308	0.0472	0.0429
	P_{boot}	0.000623	0.00553	0.0355
	% $P_{bonf.sign.}$	53.2	29.4	9.1
	% $P_{nom.sign.}$	93.4	78.3	56.6
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
	0.522	9.5	0 (60)	

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$	
	β_0	-0.0573	0.0373	-0.135	
	P_0	0.0514	0.417	0.000717	
	bias (β_0)	-0.0007	-0.000221	-0.000571	
C10		β_{boot} [pooled]	β_{boot} [<i>APOE</i> $\epsilon 4+$]	β_{boot} [<i>APOE</i> $\epsilon 4-$]	
		$\mu(\beta)_{boot}$	-0.058	0.0371	-0.136
		$\mu(SE)_{boot}$	0.0294	0.0461	0.0399
	P_{boot}	0.0486	0.421	0.000655	
	% $P_{bonf.sign.}$	9.2	0	53.5	
	% $P_{nom.sign.}$	50.7	10.1	93.4	
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)	
		0.00447	83.1	64.8 (3.3)	

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$	
	β_0	-0.0505	0.0381	-0.138	
	P_0	0.0996	0.404	0.00158	
	bias (β_0)	-0.00134	-0.00293	7.96E-05	
C8		β_{boot} [pooled]	β_{boot} [<i>APOE</i> $\epsilon 4+$]	β_{boot} [<i>APOE</i> $\epsilon 4-$]	
		$\mu(\beta)_{boot}$	-0.0519	0.0351	-0.138
		$\mu(SE)_{boot}$	0.0306	0.0456	0.0435
	P_{boot}	0.0907	0.441	0.00154	
	% $P_{bonf.sign.}$	3.9	0.3	44.5	
	% $P_{nom.sign.}$	38.7	11.1	89.2	
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)	
		0.00602	79.1	63.6 (3.7)	

metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	0.0364	-0.0397	0.106
	P_0	0.249	0.408	0.0168
	bias (β_0)	-0.000386	-0.00077	8.57E-05
	β_{boot}			
Valine	$\mu(\beta)_{boot}$	0.036	-0.0405	0.106
	$\mu(SE)_{boot}$	0.0315	0.0479	0.0442
	P_{boot}	0.254	0.398	0.0165
	% $P_{bonf.sign.}$	1.1	0.5	16.5
	% $P_{nom.sign.}$	18.8	12.9	67.1
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	0.0245	% $P_{nom.sign.}$
			62.4	55.5 (10)

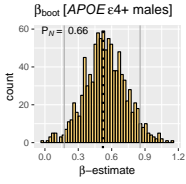
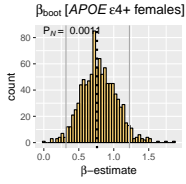
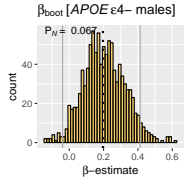
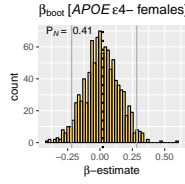
metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	-0.0325	-0.14	0.059
	P_0	0.3	0.00305	0.18
	bias (β_0)	-0.000904	-0.00172	-0.000546
	β_{boot}			
Glycine	$\mu(\beta)_{boot}$	-0.0334	-0.142	0.0585
	$\mu(SE)_{boot}$	0.0313	0.047	0.044
	P_{boot}	0.286	0.0026	0.184
	% $P_{bonf.sign.}$	1	37.3	2.6
	% $P_{nom.sign.}$	17.7	86.2	26.2
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	0.00187	% $P_{nom.sign.}$
			88.1	67.8 (1.9)

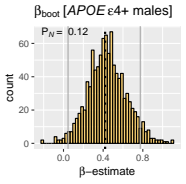
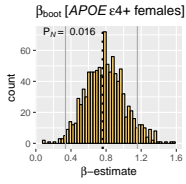
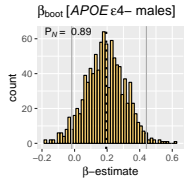
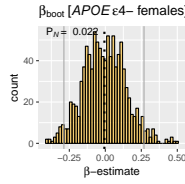
metabolite	statistic	pooled	<i>APOE</i> $\epsilon 4+$	<i>APOE</i> $\epsilon 4-$
	β_0	-0.0234	-0.1	0.0481
	P_0	0.451	0.0339	0.264
	bias (β_0)	-0.00143	-0.0019	-0.00158
Proline	β_{boot}			
	$\mu(\beta)_{boot}$	-0.0248	-0.102	0.0465
	$\mu(SE)_{boot}$	0.031	0.0473	0.0431
	P_{boot}	0.424	0.0303	0.28
	% $P_{bonf.sign.}$	0.3	12.7	0.7
	% $P_{nom.sign.}$	10.7	57.1	18.8
	Δ <i>APOE</i> $\epsilon 4\pm$	P_{boot}	% $P_{nom.sign.}$	I^2_{boot} (% $I^2_{boot} = 0$)
		0.0199	64	57.1 (8.4)

2-fold stratified analyses (sex * *APOE* $\epsilon 4$ status)

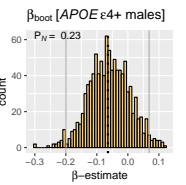
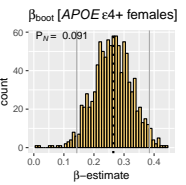
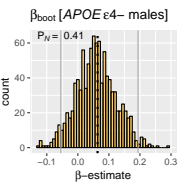
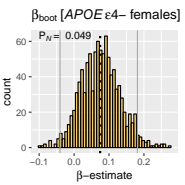
Pathological CSF $A\beta_{1-42}$

metabolite	statistic	<i>APOE</i> $\epsilon 4+$ males	<i>APOE</i> $\epsilon 4+$ females	<i>APOE</i> $\epsilon 4-$ males	<i>APOE</i> $\epsilon 4-$ females
	β_0	0.463	0.922	0.192	0.0998
	P_0	0.0168	0.00019	0.103	0.481
	bias (β_0)	0.0267	0.057	0.0054	-0.00329
PC ae C44:6	β_{boot}				
	$\mu(\beta)_{boot}$	0.49	0.979	0.197	0.0965
	$\mu(SE)_{boot}$	0.201	0.263	0.121	0.145
	P_{boot}	0.015	0.000204	0.103	0.505
	% $P_{bonf.sign.}$	16	68.8	4	0.1
	% $P_{nom.sign.}$	70	97.4	36.7	8.9

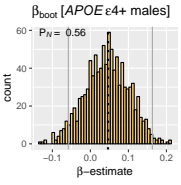
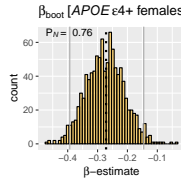
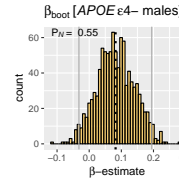
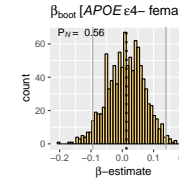
metabolite	statistic	<i>APOE</i> ϵ 4+ males	<i>APOE</i> ϵ 4+ females	<i>APOE</i> ϵ 4- males	<i>APOE</i> ϵ 4- females
	β_0	0.521	0.761	0.197	0.0223
	P_0	0.00617	0.000829	0.0879	0.87
	bias (β_0)	0.024	0.031	0.00801	-0.0084
PC ae C44:5	β_{boot}				
	$\mu(\beta)_{boot}$	0.545	0.792	0.205	0.0139
	$\mu(SE)_{boot}$	0.198	0.239	0.117	0.14
	P_{boot}	0.00579	0.000945	0.0815	0.921
	% $P_{bonf.sign.}$	25.7	50.3	5.1	0.1
	% $P_{nom.sign.}$	81.9	93.8	40.9	4.2

metabolite	statistic	<i>APOE</i> ϵ 4+ males	<i>APOE</i> ϵ 4+ females	<i>APOE</i> ϵ 4- males	<i>APOE</i> ϵ 4- females
	β_0	0.42	0.761	0.194	-0.00631
	P_0	0.0315	0.000865	0.106	0.965
	bias (β_0)	0.0212	0.0315	-0.0058	0.000854
PC ae C42:4	β_{boot}				
	$\mu(\beta)_{boot}$	0.441	0.793	0.189	-0.00546
	$\mu(SE)_{boot}$	0.202	0.241	0.123	0.149
	P_{boot}	0.0293	0.000977	0.124	0.971
	% $P_{bonf.sign.}$	9	50.9	2.2	0
	% $P_{nom.sign.}$	58.9	94.7	34.4	4.4

CSF p-tau

metabolite	statistic	<i>APOE</i> ϵ 4+ males	<i>APOE</i> ϵ 4+ females	<i>APOE</i> ϵ 4- males	<i>APOE</i> ϵ 4- females
	β_0	-0.0642	0.264	0.0635	0.0746
	P_0	0.324	0.000121	0.278	0.23
	bias (β_0)	0.00401	-0.00236	-0.00472	0.00132
C10	β_{boot}				
	$\mu(\beta)_{boot}$	-0.0602	0.262	0.0588	0.0759
	$\mu(SE)_{boot}$	0.0656	0.0682	0.0585	0.0623
	P_{boot}	0.359	0.000121	0.315	0.223
	% $P_{bonf.sign.}$	1.2	69.7	2	1.1
	% $P_{nom.sign.}$	14.7	97.5	19.7	19.3

FDG-PET

metabolite	statistic	<i>APOE</i> ϵ 4+ males	<i>APOE</i> ϵ 4+ females	<i>APOE</i> ϵ 4- males	<i>APOE</i> ϵ 4- females
	β_0	0.0464	-0.272	0.082	0.0132
	P_0	0.476	8.22E-05	0.185	0.829
	bias (β_0)	-0.00307	-0.00254	0.000889	-0.00121
Proline	β_{boot}				
	$\mu(\beta)_{boot}$	0.0433	-0.274	0.0829	0.012
	$\mu(SE)_{boot}$	0.0652	0.0683	0.0618	0.0615
	P_{boot}	0.506	6.04E-05	0.179	0.845
	% $P_{bonf.sign.}$	0	74.1	1.6	0.1
	% $P_{nom.sign.}$	7.7	98.1	25.7	4.3