

SUPPLEMENTAL MATERIAL

Article title: Using lipid profiling to better characterize metabolic differences in *apolipoprotein E (APOE)* genotype among community-dwelling older Black men

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Supplemental Table 1a. Prevalence of *APOE* genotype among n=292 Health ABC Black men with metabolomics

	Black men with metabolomics data (n=292)
<i>APOE</i> genotypes:	
ε2,ε2	3 (1%)
ε2,ε3	55 (19%)
ε2,ε4	14 (5%)
ε3,ε3	137 (47%)
ε3,ε4	74 (25%)
ε4,ε4	9 (3%)
<i>APOE</i> genotype categories:	
ε2 carrier (ε2,ε2 or ε2,ε3)	58 (20%)
ε3 homozygote (ε3,ε3)	137 (47%)
ε4 carrier (ε3,ε4 or ε4,ε4)	83 (28%)
ε2,ε4 carrier	14 (5%)

Supplemental Table 1b. Prevalence of *APOE* genotype among all Health ABC participants by race and gender

	All Health ABC participants with <i>APOE</i> genotype				Overall p-value Pairwise comparisons
	Black men (n=515)	Black women (n=683)	White men (n=897)	White women (n=814)	
<i>APOE</i> genotypes:					p<.0001 -----
ε2,ε2	5 (1%)	8 (1%)	8 (0.9%)	5 (0.6%)	
ε2,ε3	98 (19%)	85 (12%)	114 (13%)	98 (12%)	BM>WW,BW,WM
ε2,ε4	23 (4%)	33 (5%)	17 (2%)	11 (1%)	BW,BM>WM,WW
ε3,ε3	242 (47%)	328 (48%)	558 (62%)	523 (64%)	BM,BW<WM,WW
ε3,ε4	133 (26%)	203 (30%)	185 (21%)	168 (21%)	BW,BM>WM,WW
ε4,ε4	14 (3%)	26 (4%)	15 (2%)	9 (1%)	BW>WM,WW; BM>WW
<i>APOE</i> genotype categories:					p<.0001
ε2 carrier (ε2,ε2 or ε2,ε3)	103 (20%)	93 (14%)	122 (14%)	103 (13%)	BM>WW,BW,WM
ε3 homozygote (ε3,ε3)	242 (47%)	328 (48%)	558 (62%)	523 (64%)	BM,BW<WM,WW
ε4 carrier (ε3,ε4 or ε4,ε4)	147 (29%)	229 (34%)	200 (22%)	177 (22%)	BW,BM>WM,WW
ε2,ε4 carrier	23 (4%)	33 (5%)	17 (2%)	11 (1%)	BW,BM>WM,WW

BM=Black men; BW=Black women; WM=White men; WW=White women.

Supplemental Table 2. Information on platform and categorization of the 350 metabolites available among the N=319 Health ABC Black men, and which metabolites were considered for this report

Considered for this report	<u>189 total metabolites detected using lipid profiling method</u>	<u>68 total metabolites detected using negative ion mode polar metabolite profiling method</u>	<u>93 total metabolites detected using positive ion mode, polar metabolite profiling method</u>
Yes	<p>The following 189 metabolites were considered for this analysis:</p> <ul style="list-style-type: none"> • 56 TAG • 23 PC • 15 DAG • 13 CE • 13 PE plasmalogen • 13 PC plasmalogen • 12 PE • 11 SM • 10 LPC • 6 LPE • 5 PI • 4 Ceramide (d18:1) • 4 MAG • 2 PS plasmalogen • 1 PS • 1 Sphingosine 	<p>The following 8 metabolites were considered for this analysis:</p> <ul style="list-style-type: none"> • 5 bile acids: <ul style="list-style-type: none"> ➢ Glycocholate, cholate, chenodeoxycholate, glycodeoxycholate, taurodeoxycholate • 2 fatty acids: <ul style="list-style-type: none"> ➢ Adipate, 3-methyladipate • 1 glycerophosphates <ul style="list-style-type: none"> ➢ Alpha-glycerophosphate 	<p>The following 32 metabolites were considered for this analysis:</p> <ul style="list-style-type: none"> • 28 acylcarnitines: <ul style="list-style-type: none"> ➢ C10 carnitine; C10:2 carnitine; C12 carnitine; C12:1 carnitine; C14 carnitine; C14:1 carnitine; C14:2 carnitine; C16 carnitine; C18 carnitine; C18:1 carnitine; C18:2 carnitine; C2 carnitine; C20 carnitine; C20:4 carnitine; C26 carnitine; C3 carnitine; C4 carnitine; C5 carnitine; C5:1 carnitine; C6 carnitine; C8 carnitine; C16-OH carnitine; C18:1-OH carnitine; C3-DC-CH3 carnitine; C4-OH carnitine; C5-DC carnitine; C7 carnitine; C9 carnitine; • Free carnitine • 1 glycerophosphocholine: <ul style="list-style-type: none"> ➢ Alpha-glycerophosphocholine • 2 fatty acids: <ul style="list-style-type: none"> ➢ Butyrobetaine; mevalonic acid
No	0 metabolites	<p>The following 60 metabolites were excluded from this analysis:</p> <ul style="list-style-type: none"> • PEP; quinolinate; sorbitol; sucrose; 4-hydroxymandelate; ADP; benzoate; gentisate; hippurate; homogentisate; hydroxyphenylacetate; salicylurate; AMP; cAMP; GDP; GMP; IMP; inosine; UDP; UDP-galactose; uridine; 2-aminoadipate; 2-hydroxyglutarate; aconitate; alpha-hydroxybutyrate; alpha-ketoglutarate; beta-hydroxybutyrate; citrate; cystathionine; fumarate; glutathione oxidized; indoxylsulfate; isocitrate; lactate; malate; methylmalonate; oxalate; phosphocreatine; propionate; pyruvate; 2-phosphoglycerate; 6-phosphogluconate; glucose; glucuronate; hexose monophosphate; inositol; lactose; MDA; pantothenate; kynurenine; succinate; 4-pyridoxate; adenine; hypoxanthine; indole-3-propionate; orotate; uracil; xanthurenate; urate; xanthine. 	<p>The following 61 metabolites were excluded from this analysis:</p> <ul style="list-style-type: none"> • Serotonin; creatinine; 3-hydroxyanthranilic acid; anthranilic acid; thyroxine; adenosine; xanthosine; 5-aminolevulinic acid; acetylglycine; adma; alanine; aminoisobutyric acid; anserine; arginine; asparagine; beta-alanine; betaine; citrulline; creatine; dimethylglycine; GABA; glutamate; glutamine; glycine; histidine; homocysteine; hydroxyproline; isoleucine; leucine; lysine; methionine; methionine sulfoxide; N-carbamoyl-beta-alanine; nmma; ornithine; pipercolic acid; proline; pyroglutamic acid; sarcosine; sdma; serine; taurine; threonine; tyrosine; valine; phenylalanine; phosphoethanolamine; trimethylamine-N-oxide; 1-methylnicotinamide; 5-hydroxytryptophan; allantoin; cytosine; kynurenic acid; niacinamide; tryptophan; cotinine; 1-methylhistamine; acetylcholine; choline; histamine; putrescine.

Supplemental Table 3. Mean (standard deviation) of 222 metabolites by APOE among Health ABC Black men, organized by significance

Mean (standard error)	APOE genotype categories				Overall p-value**
	$\epsilon 2$ carrier (n=58)	$\epsilon 3$ homozygous (n=137)	$\epsilon 4$ carrier (n=83)	$\epsilon 2\epsilon 4$ carriers (n=14)	
Metabolites:					
Monoacylglycerol (MAG):					
C16:1 MAG	0.06 (0.13)	-0.09 (0.09)	0.04 (0.11)	0.36 (0.27)	0.0002
C14:1 MAG	-0.32 (0.11)	0.13 (0.09)	0.06 (0.11)	-0.25 (0.22)	0.004
C22:1 MAG	-0.26 (0.13)	0.18 (0.08)	-0.09 (0.11)	-0.15 (0.26)	0.01
C18:0 MAG	-0.06 (0.12)	0.09 (0.09)	-0.06 (0.09)	-0.24 (0.31)	0.47
Cholesteryl ester (CE):					
C18:2 CE	-0.39 (0.13)	0.10 (0.08)	0.12 (0.11)	-0.12 (0.26)	0.003
C16:0 CE	-0.35 (0.13)	0.04 (0.08)	0.21 (0.11)	-0.15 (0.26)	0.004
C20:3 CE	-0.36 (0.13)	0.16 (0.08)	0.03 (0.11)	-0.20 (0.26)	0.004
C20:4 CE	-0.32 (0.13)	0.09 (0.08)	0.09 (0.11)	-0.10 (0.27)	0.02
C22:6 CE	-0.30 (0.13)	0.08 (0.08)	0.13 (0.11)	-0.28 (0.26)	0.02
C22:5 CE	-0.29 (0.13)	0.05 (0.08)	0.12 (0.11)	-0.009 (0.27)	0.04
C18:1 CE	-0.28 (0.13)	0.05 (0.08)	0.13 (0.11)	-0.11 (0.27)	0.05
C22:4 CE	-0.24 (0.13)	0.10 (0.09)	-0.02 (0.11)	0.11 (0.27)	0.10
C18:3 CE	-0.21 (0.13)	0.08 (0.08)	-0.06 (0.11)	0.40 (0.27)	0.16
C20:5 CE	-0.20 (0.13)	0.03 (0.09)	0.04 (0.11)	0.27 (0.27)	0.27
C16:1 CE	-0.08 (0.13)	0.04 (0.09)	0.005 (0.11)	-0.11 (0.27)	0.73
C18:0 CE	0.03 (0.13)	-0.03 (0.09)	0.05 (0.11)	-0.14 (0.27)	0.86
Triacylglycerol (TAG) that consist mostly of polyunsaturated fatty acids:					
C58:11 TAG	0.27 (0.13)	-0.05 (0.08)	-0.17 (0.11)	0.39 (0.26)	0.03
C52:7 TAG	0.27 (0.13)	-0.05 (0.08)	-0.15 (0.11)	0.23 (0.27)	0.04
C58:9 TAG	0.28 (0.13)	-0.05 (0.08)	-0.13 (0.11)	0.13 (0.27)	0.04
C58:10 TAG	0.27 (0.13)	-0.05 (0.08)	-0.15 (0.11)	0.25 (0.27)	0.04
C56:9 TAG	0.27 (0.13)	-0.04 (0.08)	-0.16 (0.11)	0.25 (0.27)	0.04
C56:7 TAG	0.29 (0.13)	-0.05 (0.08)	-0.11 (0.11)	-0.02 (0.27)	0.05
C56:10 TAG	0.25 (0.13)	-0.06 (0.08)	-0.15 (0.11)	0.38 (0.27)	0.06
C54:8 TAG	0.24 (0.13)	-0.03 (0.08)	-0.16 (0.11)	0.25 (0.27)	0.06
C54:6 TAG	0.25 (0.13)	-0.04 (0.09)	-0.12 (0.11)	0.06 (0.27)	0.08
C50:6 TAG	0.25 (0.13)	-0.05 (0.09)	-0.12 (0.11)	0.15 (0.27)	0.09
C58:8 TAG	0.25 (0.13)	-0.06 (0.09)	-0.10 (0.11)	0.11 (0.27)	0.09
C54:7 TAG	0.22 (0.13)	-0.03 (0.09)	-0.14 (0.11)	0.18 (0.27)	0.11
C56:8 TAG	0.22 (0.13)	-0.03 (0.09)	-0.12 (0.11)	0.08 (0.27)	0.15
C48:5 TAG	0.20 (0.13)	-0.06 (0.09)	-0.04 (0.11)	-0.04 (0.27)	0.24
C46:4 TAG	0.17 (0.13)	-0.04 (0.09)	-0.04 (0.11)	-0.05 (0.27)	0.37
C50:5 TAG	0.14 (0.13)	-0.02 (0.09)	-0.08 (0.11)	0.09 (0.27)	0.41
C58:7 TAG	0.11 (0.13)	-0.03 (0.09)	-0.06 (0.11)	0.15 (0.27)	0.59
C48:4 TAG	0.07 (0.13)	-0.02 (0.09)	-0.007 (0.11)	-0.04 (0.27)	0.83
Triacylglycerol (TAG) that do <i>not</i> consist mostly of polyunsaturated fatty acids:					
C56:6 TAG	0.25 (0.13)	-0.04 (0.09)	-0.12 (0.11)	0.07 (0.27)	0.08
C52:6 TAG	0.19 (0.13)	-0.03 (0.09)	-0.11 (0.11)	0.14 (0.27)	0.21
C56:1 TAG	0.14 (0.13)	0.02 (0.09)	-0.14 (0.11)	0.02 (0.27)	0.22
C52:5 TAG	0.13 (0.12)	0.005 (0.09)	-0.10 (0.11)	0.04 (0.28)	0.32
C54:5 TAG	0.13 (0.14)	0.02 (0.09)	-0.11 (0.09)	-0.08 (0.31)	0.33
C56:5 TAG	0.18 (0.13)	-0.04 (0.09)	-0.03 (0.11)	-0.2 (0.27)	0.36
C58:6 TAG	0.15 (0.12)	-0.02 (0.08)	-0.07 (0.12)	-0.04 (0.27)	0.39
C56:4 TAG	0.14 (0.13)	0.02 (0.09)	-0.09 (0.11)	-0.22 (0.27)	0.39
C46:1 TAG	-0.10 (0.13)	-0.01 (0.09)	0.12 (0.11)	-0.12 (0.27)	0.41
C52:4 TAG	0.10 (0.13)	0.03 (0.09)	-0.09 (0.09)	-0.17 (0.27)	0.43
C46:0 TAG	-0.10 (0.13)	-0.0021 (0.09)	0.10 (0.11)	-0.18 (0.27)	0.49
C44:0 TAG	-0.09 (0.13)	0.005 (0.09)	0.10 (0.11)	-0.26 (0.27)	0.54
C56:2 TAG	0.10 (0.13)	0.00003 (0.09)	-0.07 (0.11)	0.01 (0.27)	0.56
C52:0 TAG	0.12 (0.13)	-0.02 (0.09)	-0.03 (0.11)	-0.12 (0.27)	0.58
C48:2 TAG	-0.10 (0.15)	0.005 (0.08)	0.08 (0.11)	-0.12 (0.26)	0.61
C54:4 TAG	0.08 (0.13)	0.03 (0.09)	-0.08 (0.11)	-0.09 (0.27)	0.62
C48:1 TAG	-0.10 (0.15)	0.01 (0.08)	0.08 (0.11)	-0.19 (0.26)	0.63
C46:2 TAG	-0.08 (0.13)	0.001 (0.09)	0.08 (0.11)	-0.11 (0.27)	0.64
C56:3 TAG	0.09 (0.13)	0.0001 (0.09)	-0.06 (0.11)	-0.02 (0.27)	0.65
C54:1 TAG	0.11 (0.13)	-0.02 (0.09)	-0.03 (0.11)	-0.05 (0.27)	0.66
C44:1 TAG	-0.05 (0.13)	-0.02 (0.09)	0.09 (0.11)	-0.14 (0.27)	0.66

Mean (standard error)	APOE genotype categories				Overall p-value**
	$\epsilon 2$ carrier (n=58)	$\epsilon 3$ homozygous (n=137)	$\epsilon 4$ carrier (n=83)	$\epsilon 2\epsilon 4$ carriers (n=14)	
Metabolites:					
C52:3 TAG	-0.05 (0.13)	0.05 (0.09)	-0.01 (0.11)	-0.18 (0.27)	0.80
C50:4 TAG	0.06 (0.13)	0.008 (0.09)	-0.05 (0.11)	-0.03 (0.27)	0.80
C42:0 TAG	-0.03 (0.13)	-0.008 (0.09)	0.06 (0.11)	-0.15 (0.27)	0.84
C52:2 TAG	-0.04 (0.13)	0.04 (0.09)	0.01 (0.11)	-0.26 (0.27)	0.89
C48:3 TAG	-0.03 (0.13)	-0.006 (0.09)	0.04 (0.11)	-0.07 (0.27)	0.89
C44:2 TAG	-0.006 (0.13)	-0.01 (0.09)	0.04 (0.11)	-0.11 (0.27)	0.93
C48:0 TAG	-0.03 (0.13)	0.03 (0.09)	0.008 (0.11)	-0.16 (0.27)	0.93
C46:3 TAG	0.03 (0.13)	-0.02 (0.09)	0.02 (0.11)	-0.11 (0.27)	0.94
C50:2 TAG	0.04 (0.13)	0.0001 (0.09)	-0.009 (0.11)	-0.12 (0.27)	0.95
C54:2 TAG	0.04 (0.13)	-0.0003 (0.09)	-0.005 (0.11)	-0.13 (0.27)	0.96
C50:1 TAG	-0.02 (0.15)	0.02 (0.08)	0.006 (0.11)	-0.16 (0.32)	0.97
C50:3 TAG	-0.01 (0.13)	0.02 (0.09)	-0.008 (0.11)	-0.09 (0.27)	0.97
C50:0 TAG	0.03 (0.13)	0.01 (0.09)	-0.007 (0.11)	-0.21 (0.27)	0.98
C52:1 TAG	0.001 (0.13)	0.02 (0.09)	0.0006 (0.11)	-0.21 (0.27)	0.99
C54:3 TAG	-0.003 (0.13)	0.009 (0.09)	0.009 (0.11)	-0.12 (0.27)	0.997
Phosphatidylethanolamine (PE) plasmalogen:					
C36:4 PE plasmalogen	0.29 (0.13)	0.005 (0.08)	-0.22 (0.11)	0.09 (0.26)	0.01
C36:2 PE plasmalogen	0.30 (0.13)	-0.04 (0.08)	-0.18 (0.11)	0.20 (0.26)	0.02
C36:3 PE plasmalogen	0.25 (0.13)	-0.007 (0.08)	-0.21 (0.11)	0.27 (0.26)	0.03
C38:5 PE plasmalogen	0.28 (0.13)	-0.05 (0.08)	-0.14 (0.11)	0.15 (0.27)	0.04
C34:3 PE plasmalogen	0.20 (0.13)	-0.0004 (0.09)	-0.18 (0.11)	0.27 (0.27)	0.09
C38:6 PE plasmalogen	0.21 (0.13)	-0.04 (0.09)	-0.12 (0.11)	0.17 (0.27)	0.14
C36:5 PE plasmalogen	0.19 (0.13)	-0.04 (0.09)	-0.09 (0.11)	0.16 (0.27)	0.23
C38:3 PE plasmalogen	0.04 (0.12)	0.05 (0.08)	-0.15 (0.13)	0.23 (0.22)	0.43
C40:7 PE plasmalogen	0.06 (0.13)	0.02 (0.09)	-0.11 (0.11)	0.12 (0.27)	0.54
C34:2 PE plasmalogen	0.07 (0.13)	-0.01 (0.09)	-0.08 (0.11)	0.31 (0.27)	0.69
C38:7 PE plasmalogen	0.04 (0.13)	0.03 (0.09)	-0.08 (0.11)	-0.003 (0.27)	0.69
C42:11 PE plasmalogen	0.01 (0.13)	0.01 (0.09)	-0.06 (0.11)	0.16 (0.27)	0.87
C44:13 PE plasmalogen	-0.03 (0.13)	0.03 (0.09)	-0.04 (0.11)	0.06 (0.27)	0.88
Lysophosphatidylethanolamine (LPE):					
C22:6 LPE	-0.12 (0.15)	-0.08 (0.09)	0.19 (0.09)	0.21 (0.23)	0.06
C16:0 LPE	0.16 (0.13)	-0.17 (0.08)	0.10 (0.11)	0.40 (0.26)	0.06
C18:0 LPE	0.13 (0.13)	-0.16 (0.08)	0.10 (0.11)	0.45 (0.26)	0.07
C20:4 LPE	0.06 (0.13)	-0.14 (0.08)	0.12 (0.11)	0.42 (0.27)	0.13
C18:1 LPE	0.06 (0.13)	-0.09 (0.09)	0.04 (0.11)	0.36 (0.27)	0.51
C18:2 LPE	0.04 (0.13)	-0.09 (0.09)	0.05 (0.11)	0.40 (0.27)	0.51
Phosphatidylserine (PS) plasmalogen:					
C36:2 PS plasmalogen	-0.17 (0.13)	0.11 (0.09)	-0.06 (0.11)	0.002 (0.27)	0.17
C36:1 PS plasmalogen	-0.19 (0.13)	0.07 (0.09)	-0.007 (0.11)	0.20 (0.27)	0.25
Sphingomyelin (SM):					
C24:0 SM	-0.30 (0.13)	0.12 (0.08)	0.001 (0.11)	0.06 (0.27)	0.03
C22:0 SM	-0.24 (0.13)	0.10 (0.09)	0.02 (0.11)	-0.07 (0.27)	0.09
C20:0 SM	-0.24 (0.13)	0.07 (0.09)	0.04 (0.11)	0.10 (0.27)	0.12
C22:1 SM	-0.21 (0.13)	0.06 (0.09)	0.05 (0.11)	0.01 (0.27)	0.20
C18:0 SM	-0.18 (0.13)	-0.003 (0.09)	0.11 (0.11)	0.12 (0.27)	0.25
C14:0 SM	-0.19 (0.13)	0.06 (0.09)	0.02 (0.11)	0.08 (0.27)	0.26
C16:1 SM	-0.17 (0.13)	0.04 (0.09)	-0.003 (0.11)	0.29 (0.27)	0.39
C24:1 SM	-0.14 (0.13)	0.03 (0.09)	0.04 (0.11)	0.05 (0.27)	0.49
C16:0 SM	-0.13 (0.13)	0.03 (0.09)	-0.003 (0.11)	0.26 (0.27)	0.62
C18:1 SM	-0.09 (0.13)	-0.01 (0.09)	0.07 (0.11)	0.04 (0.27)	0.64
C18:2 SM	0.0003 (0.13)	0.02 (0.09)	-0.006 (0.11)	-0.13 (0.27)	0.99
Phosphorylcholine (PC) plasmalogen:					
C36:3 PC plasmalogen	0.11 (0.13)	0.05 (0.08)	-0.22 (0.11)	0.33 (0.27)	0.08
C40:7 PC plasmalogen	0.06 (0.13)	0.06 (0.09)	-0.19 (0.11)	0.25 (0.27)	0.16
C36:2 PC plasmalogen	0.08 (0.13)	0.05 (0.09)	-0.18 (0.11)	0.26 (0.27)	0.19
C38:6 PC plasmalogen	0.08 (0.13)	0.04 (0.09)	-0.18 (0.11)	0.32 (0.27)	0.22
C34:3 PC plasmalogen	0.009 (0.13)	0.06 (0.09)	-0.16 (0.11)	0.36 (0.27)	0.28
C38:7 PC plasmalogen	-0.01 (0.13)	0.06 (0.09)	-0.13 (0.11)	0.22 (0.27)	0.37
C34:2 PC plasmalogen	-0.009 (0.13)	0.04 (0.09)	-0.14 (0.11)	0.43 (0.27)	0.43
C36:5 PC plasmalogen-B	0.10 (0.13)	-0.02 (0.09)	-0.11 (0.11)	0.47 (0.27)	0.49
C36:4 PC plasmalogen	0.11 (0.13)	-0.05 (0.09)	-0.07 (0.11)	0.41 (0.27)	0.51
C38:4 PC plasmalogen	0.10 (0.13)	-0.006 (0.09)	-0.09 (0.11)	0.23 (0.27)	0.54

Mean (standard error)	APOE genotype categories				Overall p-value**
	$\epsilon 2$ carrier (n=58)	$\epsilon 3$ homozygous (n=137)	$\epsilon 4$ carrier (n=83)	$\epsilon 2\epsilon 4$ carriers (n=14)	
Metabolites:					
C34:1 PC plasmalogen-A	-0.07 (0.13)	0.05 (0.09)	-0.09 (0.11)	0.38 (0.27)	0.56
C36:5 PC plasmalogen-A	0.08 (0.13)	-0.04 (0.09)	-0.06 (0.11)	0.37 (0.27)	0.69
C36:1 PC plasmalogen	0.001 (0.13)	0.02 (0.09)	-0.05 (0.11)	0.05 (0.27)	0.88
Phosphorylcholine (PC):					
C40:6 PC	-0.21 (0.13)	0.12 (0.09)	-0.06 (0.11)	0.07 (0.27)	0.10
C40:9 PC	-0.22 (0.13)	0.05 (0.09)	0.09 (0.11)	-0.07 (0.27)	0.15
C38:3 PC	-0.17 (0.13)	0.11 (0.09)	-0.08 (0.11)	0.10 (0.27)	0.17
C34:2 PC	-0.20 (0.13)	0.08 (0.09)	0.001 (0.11)	0.007 (0.27)	0.21
C38:6 PC	-0.20 (0.13)	0.04 (0.09)	0.08 (0.11)	-0.04 (0.27)	0.21
C30:0 PC	-0.20 (0.13)	0.04 (0.09)	0.08 (0.11)	-0.04 (0.27)	0.21
C36:2 PC	-0.13 (0.13)	0.08 (0.09)	-0.11 (0.11)	0.37 (0.27)	0.26
C34:0 PC	-0.15 (0.13)	-0.02 (0.09)	0.10 (0.11)	0.24 (0.27)	0.31
C38:2 PC	-0.15 (0.13)	0.08 (0.09)	-0.05 (0.11)	0.16 (0.27)	0.32
C32:2 PC	-0.17 (0.13)	0.05 (0.09)	0.02 (0.11)	0.09 (0.27)	0.38
C38:4 PC	-0.11 (0.13)	0.05 (0.09)	-0.08 (0.11)	0.44 (0.27)	0.46
C34:1 PC	-0.14 (0.13)	0.01 (0.09)	0.06 (0.11)	0.12 (0.27)	0.50
C36:3 PC	-0.10 (0.13)	0.06 (0.09)	-0.04 (0.11)	0.11 (0.27)	0.56
C34:3 PC	-0.11 (0.13)	0.05 (0.09)	-0.06 (0.11)	0.34 (0.27)	0.57
C32:0 PC	-0.13 (0.13)	0.03 (0.09)	0.003 (0.11)	0.27 (0.27)	0.59
C34:4 PC	-0.11 (0.13)	0.03 (0.09)	0.003 (0.11)	0.18 (0.27)	0.68
C36:0 PC	-0.05 (0.13)	-0.04 (0.09)	0.06 (0.11)	0.21 (0.27)	0.71
C40:10 PC	-0.10 (0.13)	0.03 (0.09)	-0.004 (0.11)	0.14 (0.27)	0.74
C36:1 PC	-0.09 (0.13)	0.02 (0.09)	-0.02 (0.11)	0.24 (0.27)	0.78
C30:1 PC	-0.09 (0.13)	0.01 (0.09)	0.02 (0.11)	0.12 (0.27)	0.79
C36:4 PC-B	-0.06 (0.10)	0.005 (0.09)	0.0009 (0.12)	0.18 (0.26)	0.89
C36:4 PC-A	-0.01 (0.13)	0.01 (0.09)	-0.04 (0.11)	0.18 (0.27)	0.93
C32:1 PC	-0.01 (0.13)	-0.0012 (0.09)	-0.006 (0.11)	0.09 (0.27)	0.998
Lysophosphatidylcholine (LPC):					
C20:4 LPC	0.12 (0.10)	-0.09 (0.09)	0.002 (0.11)	0.38 (0.25)	0.33
C16:0 LPC	0.03 (0.13)	-0.10 (0.09)	0.08 (0.11)	0.40 (0.27)	0.42
C16:1 LPC	0.11 (0.13)	-0.09 (0.09)	0.01 (0.11)	0.32 (0.27)	0.44
C18:0 LPC	-0.001 (0.13)	-0.10 (0.08)	0.07 (0.11)	0.61 (0.27)	0.44
C18:1 LPC	0.05 (0.13)	-0.10 (0.09)	0.06 (0.11)	0.37 (0.27)	0.45
C20:3 LPC	0.003 (0.13)	-0.09 (0.09)	0.07 (0.11)	0.40 (0.27)	0.50
C18:2 LPC	0.09 (0.13)	-0.06 (0.09)	-0.02 (0.11)	0.35 (0.27)	0.62
C14:0 LPC	-0.09 (0.13)	-0.0003 (0.09)	0.05 (0.11)	0.10 (0.27)	0.71
C22:6 LPC	-0.02 (0.13)	-0.03 (0.09)	0.05 (0.11)	0.15 (0.27)	0.84
C20:5 LPC	0.05 (0.13)	-0.04 (0.09)	-0.03 (0.11)	0.32 (0.27)	0.85
Phosphatidylinositol (PI):					
C34:2 PI	-0.20 (0.13)	0.03 (0.09)	0.12 (0.11)	-0.21 (0.27)	0.16
C34:0 PI	-0.08 (0.13)	0.07 (0.09)	-0.11 (0.11)	0.26 (0.27)	0.37
C32:1 PI	-0.08 (0.13)	0.03 (0.09)	0.02 (0.11)	-0.10 (0.27)	0.78
C38:4 PI	-0.001 (0.13)	0.005 (0.09)	-0.05 (0.11)	0.27 (0.27)	0.91
C32:2 PI	-0.05 (0.13)	0.006 (0.09)	0.009 (0.11)	0.08 (0.27)	0.93
Acylcarnitines:					
C10:2 carnitine	0.10 (0.13)	0.08 (0.09)	-0.18 (0.11)	-0.17 (0.27)	0.12
C2 carnitine	0.05 (0.13)	0.06 (0.09)	-0.15 (0.11)	0.06 (0.27)	0.28
C14:2 carnitine	0.12 (0.13)	0.04 (0.09)	-0.13 (0.11)	-0.07 (0.27)	0.29
C5 carnitine	0.03 (0.13)	0.08 (0.09)	-0.12 (0.11)	-0.18 (0.27)	0.33
C6 carnitine	-0.0004 (0.13)	0.09 (0.09)	-0.12 (0.11)	-0.13 (0.27)	0.34
C26 carnitine	-0.13 (0.13)	0.07 (0.09)	-0.08 (0.11)	0.33 (0.27)	0.37
C18 carnitine	-0.12 (0.13)	-0.04 (0.09)	0.11 (0.11)	0.24 (0.27)	0.38
C3 carnitine	0.06 (0.16)	0.06 (0.07)	-0.13 (0.12)	-0.12 (0.20)	0.41
C4 carnitine	0.07 (0.13)	0.02 (0.09)	-0.12 (0.11)	0.20 (0.27)	0.45
C12:1 carnitine	0.11 (0.13)	0.03 (0.09)	-0.09 (0.11)	-0.20 (0.27)	0.46
C5:1 carnitine	-0.06 (0.13)	0.09 (0.09)	-0.04 (0.11)	-0.44 (0.27)	0.48
C16 carnitine	-0.09 (0.13)	-0.04 (0.09)	0.10 (0.11)	0.16 (0.27)	0.49
C16-OH carnitine	0.10 (0.13)	0.01 (0.09)	-0.10 (0.11)	0.06 (0.27)	0.49
C20:4 carnitine	-0.15 (0.13)	0.02 (0.09)	0.03 (0.11)	0.26 (0.27)	0.50
C18:1 carnitine	-0.13 (0.13)	0.004 (0.09)	0.06 (0.11)	0.13 (0.27)	0.52
C18:2 carnitine	-0.06 (0.13)	0.05 (0.09)	-0.06 (0.11)	0.12 (0.27)	0.66
C8 carnitine	0.09 (0.13)	0.04 (0.09)	-0.05 (0.11)	-0.45 (0.27)	0.67
C3-DC-CH3 carnitine	0.11 (0.13)	-0.003 (0.09)	-0.04 (0.11)	-0.20 (0.27)	0.69

Mean (standard error)	APOE genotype categories				Overall p-value**
	$\epsilon 2$ carrier (n=58)	$\epsilon 3$ homozygous (n=137)	$\epsilon 4$ carrier (n=83)	$\epsilon 2\epsilon 4$ carriers (n=14)	
Metabolites:					
C10 carnitine	0.09 (0.13)	0.04 (0.09)	-0.05 (0.11)	-0.42 (0.27)	0.71
C4-OH carnitine	0.08 (0.13)	0.009 (0.09)	-0.05 (0.11)	-0.12 (0.27)	0.73
C7 carnitine	0.03 (0.13)	0.05 (0.09)	-0.06 (0.11)	-0.28 (0.27)	0.73
C12 carnitine	0.04 (0.13)	0.04 (0.09)	-0.06 (0.11)	-0.20 (0.27)	0.74
C14:1 carnitine	0.06 (0.13)	0.02 (0.09)	-0.06 (0.11)	-0.05 (0.27)	0.75
C18:1-OH carnitine	-0.02 (0.13)	-0.04 (0.09)	0.06 (0.11)	0.12 (0.27)	0.79
C9 carnitine	0.05 (0.12)	0.04 (0.08)	-0.03 (0.13)	-0.41 (0.29)	0.86
C14 carnitine	-0.05 (0.13)	0.03 (0.09)	-0.01 (0.11)	0.03 (0.27)	0.87
C5-DC carnitine	0.02 (0.13)	0.01 (0.09)	-0.005 (0.11)	-0.16 (0.27)	0.99
Phosphatidylethanolamine (PE):					
C36:0 PE	-0.17 (0.13)	-0.006 (0.09)	0.13 (0.11)	-0.03 (0.27)	0.21
C34:0 PE	-0.14 (0.13)	0.03 (0.09)	0.10 (0.11)	-0.32 (0.27)	0.35
C36:4 PE	0.16 (0.13)	-0.05 (0.09)	-0.002 (0.11)	-0.13 (0.27)	0.38
C38:2 PE	-0.15 (0.13)	0.07 (0.09)	-0.01 (0.11)	0.02 (0.27)	0.39
C38:5 PE	0.15 (0.13)	-0.05 (0.09)	-0.04 (0.11)	0.06 (0.27)	0.43
C34:2 PE	0.11 (0.13)	0.04 (0.09)	-0.10 (0.11)	-0.24 (0.27)	0.45
C36:3 PE	0.12 (0.13)	-0.005 (0.09)	-0.07 (0.11)	0.006 (0.27)	0.53
C36:2 PE	0.07 (0.13)	0.02 (0.09)	-0.07 (0.11)	-0.07 (0.27)	0.71
C36:1 PE	0.08 (0.13)	-0.01 (0.09)	-0.04 (0.11)	0.05 (0.27)	0.76
C38:4 PE	0.08 (0.13)	-0.03 (0.09)	-0.01 (0.11)	0.03 (0.27)	0.76
C40:6 PE	-0.02 (0.13)	0.05 (0.09)	-0.02 (0.11)	-0.35 (0.27)	0.83
C38:6 PE	0.04 (0.13)	0.009 (0.09)	-0.01 (0.11)	-0.18 (0.27)	0.96
Bile acids:					
Glycodeoxycholate	-0.03 (0.13)	-0.007 (0.09)	0.12 (0.11)	-0.52 (0.27)	0.58
Chenodeoxycholate	0.07 (0.13)	-0.02 (0.09)	0.04 (0.11)	-0.32 (0.27)	0.83
Glycocholate	0.02 (0.13)	0.02 (0.09)	0.01 (0.11)	-0.31 (0.27)	0.998
Diacylglycerol (DAG):					
C38:5 DAG	0.26 (0.13)	-0.07 (0.09)	-0.09 (0.11)	0.14 (0.27)	0.06
C36:0 DAG	-0.09 (0.13)	0.12 (0.08)	-0.04 (0.11)	-0.52 (0.27)	0.31
C38:4 DAG	0.15 (0.13)	-0.006 (0.09)	-0.09 (0.11)	-0.02 (0.27)	0.37
C34:3 DAG	0.14 (0.13)	-0.0024 (0.09)	-0.08 (0.11)	-0.08 (0.27)	0.41
C36:4 DAG	0.11 (0.14)	0.02 (0.09)	-0.09 (0.09)	-0.12 (0.29)	0.47
C34:0 DAG	-0.007 (0.13)	0.07 (0.09)	-0.06 (0.11)	-0.27 (0.27)	0.62
C34:2 DAG	0.10 (0.13)	0.007 (0.09)	-0.04 (0.11)	-0.22 (0.27)	0.71
C32:2 DAG	0.05 (0.13)	0.03 (0.09)	-0.05 (0.11)	-0.16 (0.27)	0.82
C30:0 DAG	-0.01 (0.13)	-0.01 (0.09)	0.06 (0.11)	-0.18 (0.27)	0.87
C32:1 DAG	0.02 (0.13)	-0.02 (0.09)	0.04 (0.11)	-0.11 (0.27)	0.88
C36:3 DAG	0.05 (0.13)	0.01 (0.09)	-0.03 (0.11)	-0.14 (0.27)	0.88
C34:1 DAG	0.02 (0.13)	0.03 (0.09)	-0.03 (0.11)	-0.14 (0.27)	0.91
C36:2 DAG	-0.03 (0.13)	0.01 (0.09)	0.01 (0.11)	-0.09 (0.27)	0.96
C36:1 DAG	-0.008 (0.13)	0.02 (0.09)	-0.003 (0.11)	-0.10 (0.27)	0.98
C32:0 DAG	-0.006 (0.13)	0.01 (0.09)	0.007 (0.11)	-0.14 (0.27)	0.99
Ceramide:					
C24:1 Ceramide (d18:1)	0.21 (0.13)	-0.09 (0.09)	-0.02 (0.11)	0.13 (0.27)	0.16
C24:0 Ceramide (d18:1)	0.05 (0.13)	0.04 (0.09)	-0.10 (0.11)	-0.03 (0.27)	0.52
C16:0 Ceramide (d18:1)	-0.09 (0.13)	0.009 (0.09)	0.09 (0.11)	-0.21 (0.27)	0.57
C22:0 Ceramide (d18:1)	0.01 (0.13)	0.01 (0.09)	-0.03 (0.11)	-0.003 (0.27)	0.96
Extra metabolites***:					
Sphingosine	-0.23 (0.13)	0.18 (0.08)	-0.06 (0.11)	-0.49 (0.26)	0.02
Free carnitine	0.06 (0.13)	0.12 (0.08)	-0.23 (0.11)	-0.06 (0.27)	0.04
3-methyladipate	0.21 (0.16)	-0.03 (0.08)	-0.10 (0.11)	-0.006 (0.25)	0.28
Mevalonic acid	0.11 (0.13)	-0.09 (0.09)	0.07 (0.11)	-0.02 (0.27)	0.32
Alpha-glycerophosphocholine	0.13 (0.13)	-0.02 (0.09)	-0.08 (0.11)	0.12 (0.27)	0.48
Alpha-glycerophosphate	0.01 (0.13)	-0.02 (0.09)	0.06 (0.11)	-0.18 (0.27)	0.86
C34:0 PS	-0.09 (0.13)	-0.002 (0.09)	-0.02 (0.11)	0.47 (0.27)	0.87
Adipate	0.02 (0.13)	-0.02 (0.09)	0.03 (0.11)	-0.11 (0.27)	0.94

*Excluding n=14 participants with APOE genotype, $\epsilon 2\epsilon 4$.

**Overall p-value from ANOVA, adjusting for unequal variances when necessary (i.e., when p-value<0.10 from Levene's Test for Homogeneity of Variance)

***For lipid categories that did not contain enough metabolites for a factor analysis or if the first factor had an eigenvalue less than one, then we examined these metabolites individually.

Supplemental Table 4. Proportion of variance explained for each factor score

Factor scores:	Proportion of variance explained
Monoacylglycerol (MAG) score	2.0
Cholesteryl ester (CE) score	5.5
Triacylglycerol (TAG) that consist mostly of polyunsaturated fatty acids score	13.3
PE plasmalogen score	7.0
Lysophosphatidylethanolamine (LPE) score	3.7
PS plasmalogen score	1.3
Sphingomyelin (SM) score	6.7
PC plasmalogen score	6.8
Phosphorylcholine (PC) score	10.6
Lysophosphatidylcholine (LPC) score	6.3
Phosphatidylinositol (PI) score	0.7
Acylcarnitine score	10.4
Phosphatidylethanolamine (PE) score	6.7
Bile acid score	1.7
Diacylglycerol (DAG) score	9.9
Triacylglycerol (TAG) that do <i>not</i> consist mostly of polyunsaturated fatty acids score	21.4
Ceramide score	2.2