

Supplementary Table #1. Concentrations of log(phospholipids) by cognitive status in standard deviation units, Atherosclerosis Risk in Communities (ARIC) Study, 2011 to 2013

	Normal (n = 144)	MCI (n = 137)	Dementia (n = 102)
Asymmetric dimethylarginine (ADMA)	-5.1 (1.0)	-4.6 (0.9)	-5.0 (1.2)
Hydroxybutyryl-L-carnitine [C4-OH (C3-DC)]	-7.3 (1.0)	-7.1 (0.9)	-7.0 (1.1)
LysoPC a C16:1	2.4 (1.1)	2.6 (0.9)	2.6 (1.0)
Octadecanoyl-L-carnitine (C18)	-12.1 (1.0)	-12.0 (1.0)	-11.8 (1.0)
PC aa C36:5	6.2 (1.0)	5.9 (1.0)	5.8 (1.0)
PC aa C36:6	-0.1 (1.0)	-0.3 (1.0)	-0.5 (1.0)
PC aa C38:1	-0.4 (0.9)	-0.7 (1.1)	-0.7 (1.1)
PC aa C40:2	-5.1 (1.0)	-5.4 (0.9)	-5.0 (1.1)
SM C26:0	-7.3 (1.0)	-7.5 (1.1)	-7.6 (1.0)
SM (OH) C22:1	8.6 (0.9)	8.3 (0.9)	8.1 (1.2)
SM (OH) C22:2	7.4 (1.0)	7.0 (1.0)	7.1 (1.0)
SM (OH) C24:1	-0.6 (1.0)	-0.9 (1.0)	-1.0 (1.1)
Total phospholipids			
PC aa	37 (0.9)	37 (1.0)	38 (1.1)
PC ae	25 (0.9)	25 (1.0)	25 (1.0)
SM	24 (0.9)	23 (0.9)	23 (1.1)
SM (OH)	13 (0.9)	13 (1.0)	13 (1.1)
LysoPC a	20 (1.0)	20 (1.0)	20 (1.0)

Values correspond to mean (SD) of the log transformed and standardized concentrations of the phospholipid

Supplement Table 2. Linear regression of phospholipids (log-transformed per 1-SD difference) with grip strength, Atherosclerosis Risk in Communities (ARIC) Study, 2011 to 2013

Phospholipid	Model	n	β (95% CI)	p-value
Asymmetric dimethylarginine (ADMA)	Model 1	380	-0.97 (-1.74, -0.19)	0.02
	Model 2	380	-0.94 (-1.68, -0.20)	0.01
Hydroxybutyryl-L-carnitine [C4-OH (C3-DC)]	Model 1	379	-0.15 (-0.89, 0.59)	0.69
	Model 2	379	0.15 (-0.55, 0.85)	0.67
LysoPC a C16:1	Model 1	380	0.52 (-0.31, 1.35)	0.22
	Model 2	380	0.07 (-0.87, 1.02)	0.15
Octadecanoyl-L-carnitine (C18)	Model 1	369	-0.46 (-1.20, 0.28)	0.22
	Model 2	369	-0.32 (-1.10, 0.46)	0.42
PC aa C36:5	Model 1	380	0.96 (0.20, 1.72)	0.01
	Model 2	380	0.51 (-0.33, 1.36)	0.24
PC aa C36:6	Model 1	380	1.27 (0.49, 2.06)	0.002
	Model 2	380	0.83 (-0.10, 1.75)	0.08
PC aa C38:1	Model 1	380	-0.13 (-0.87, 0.62)	0.73
	Model 2	380	-0.30 (-0.97, 0.38)	0.50
PC aa C40:2	Model 1	380	0.07 (-0.69, 0.83)	0.86
	Model 2	380	-0.19 (-0.97, 0.59)	0.63
SM C26:0	Model 1	380	0.37 (-0.35, 1.08)	0.31
	Model 2	380	0.15 (-0.55, 0.85)	0.67
SM (OH) C22:1	Model 1	380	0.98 (0.23, 1.74)	0.01
	Model 2	380	0.89 (0.00, 1.78)	0.05
SM (OH) C22:2	Model 1	380	1.13 (0.32, 1.94)	0.006
	Model 2	380	1.05 (0.06, 2.05)	0.04
SM (OH) C24:1	Model 1	380	1.06 (0.34, 1.79)	0.004
	Model 2	380	0.86 (0.10, 1.61)	0.03

Model 1: Linear regression adjusted for age, sex, race, center, dementia status and mini-mental state examination

Model 2: Model 1 with additional adjustment for educational level, smoking and drinking status, APOE genotype, body mass index, physical activity, coronary artery disease, stroke, heart failure, diabetes mellitus, total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, high sensitive C-reactive protein (hsCRP), systolic blood pressure, use of antihypertensive medications, use of lipid lowering medications, depressive symptoms, executive function score, bodily pain score, prevalent coronary heart disease, stroke, and heart failure weighted by selection probabilities.

Supplement Table 3. Linear regression of phospholipids (log-transformed per 1-SD difference) with short physical performance battery summary score, Atherosclerosis Risk in Communities (ARIC) Study, 2011 to 2013

Phospholipid	Model	n	β (95% CI)	p-value
Asymmetric dimethylarginine (ADMA)	Model 1	382	-0.11 (-0.38, 0.16)	0.42
	Model 2	382	0.01 (-0.23, 0.25)	0.92
Hydroxybutyryl-L-carnitine [C4-OH (C3-DC)]	Model 1	381	-0.16 (-0.41, 0.10)	0.22
	Model 2	381	-0.01 (-0.24, 0.21)	0.91
LysoPC a C16:1	Model 1	382	-0.10 (-0.38, 0.18)	0.49
	Model 2	382	-0.35 (-0.62, -0.08)	0.01
Octadecanoyl-L-carnitine (C18)	Model 1	371	-0.25 (-0.50, 0.00)	0.05
	Model 2	371	-0.15 (-0.40, 0.08)	0.19
PC aa C36:5	Model 1	382	0.42 (0.15, 0.68)	0.002
	Model 2	382	0.22 (-0.04, 0.48)	0.09
PC aa C36:6	Model 1	382	0.51 (0.24, 0.78)	0.0002
	Model 2	382	0.28 (-0.01, 0.56)	0.06
PC aa C38:1	Model 1	382	0.17 (-0.09, 0.43)	0.20
	Model 2	382	0.09 (-0.18, 0.37)	0.51
PC aa C40:2	Model 1	382	0.09 (-0.17, 0.35)	0.50
	Model 2	382	-0.05 (-0.31, 0.20)	0.70
SM C26:0	Model 1	382	0.11 (-0.14, 0.36)	0.38
	Model 2	382	0.03 (-0.20, 0.26)	0.79
SM (OH) C22:1	Model 1	382	0.42 (0.16, 0.68)	0.002
	Model 2	382	0.61 (0.34, 0.88)	<0.0001
SM (OH) C22:2	Model 1	382	0.33 (0.05, 0.61)	0.02
	Model 2	382	0.32 (0.02, 0.62)	0.03
SM (OH) C24:1	Model 1	382	0.43 (0.18, 0.68)	0.0007
	Model 2	382	0.41 (0.19, 0.63)	0.0003

Model 1: Linear regression adjusted for age, sex, race, center, dementia status and mini-mental state examination

Model 2: Model 1 with additional adjustment for educational level, smoking and drinking status, APOE genotype, body mass index, physical activity, coronary artery disease, stroke, heart failure, diabetes mellitus, total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, high sensitive C-reactive protein (hsCRP), systolic blood pressure, use of antihypertensive medications, use of lipid lowering medications, depressive symptoms, executive function score, bodily pain score, prevalent coronary heart disease, stroke, and heart failure weighted by selection probabilities.

Supplement Table 4. Linear regression of phospholipids (log-transformed per 1-SD difference) with four meter walk speed (in m/s), Atherosclerosis Risk in Communities (ARIC) Study, 2011 to 2013

Phospholipid	Model	n	β (95% CI)	p-value
Asymmetric dimethylarginine (ADMA)	Model 1	377	-0.006 (-0.029, 0.017)	0.62
	Model 2	377	0.006 (-0.015, 0.027)	0.57
Hydroxybutyryl-L-carnitine [C4-OH (C3-DC)]	Model 1	376	-0.013 (-0.035, 0.008)	0.23
	Model 2	376	0.001 (-0.020, 0.022)	0.91
LysoPC a C16:1	Model 1	377	0.001 (-0.023, 0.025)	0.93
	Model 2	377	-0.025 (-0.047, -0.002)	0.04
Octadecanoyl-L-carnitine (C18)	Model 1	366	-0.020 (-0.041, 0.001)	0.06
	Model 2	366	-0.020 (-0.039, -0.001)	0.04
PC aa C36:5	Model 1	377	0.031 (0.009, 0.053)	0.006
	Model 2	377	0.010 (-0.012, 0.032)	0.35
PC aa C36:6	Model 1	377	0.039 (0.016, 0.062)	0.0008
	Model 2	377	0.016 (-0.008, 0.039)	0.19
PC aa C38:1	Model 1	377	0.013 (-0.009, 0.035)	0.25
	Model 2	377	0.005 (-0.014, 0.024)	0.50
PC aa C40:2	Model 1	377	0.013 (-0.009, 0.035)	0.23
	Model 2	377	-0.005 (-0.029, 0.018)	0.66
SM C26:0	Model 1	377	0.013 (-0.007, 0.034)	0.20
	Model 2	377	0.003 (-0.018, 0.023)	0.79
SM (OH) C22:1	Model 1	377	0.029 (0.007, 0.051)	0.01
	Model 2	377	0.035 (0.013, 0.056)	0.002
SM (OH) C22:2	Model 1	377	0.027 (0.003, 0.050)	0.03
	Model 2	377	0.018 (-0.005, 0.042)	0.12
SM (OH) C24:1	Model 1	377	0.035 (0.014, 0.056)	0.001
	Model 2	377	0.028 (0.008, 0.047)	0.005

Model 1: Linear regression adjusted for age, sex, race, center, dementia status and mini-mental state examination

Model 2: Model 1 with additional adjustment for educational level, smoking and drinking status, APOE genotype, body mass index, physical activity, coronary artery disease, stroke, heart failure, diabetes mellitus, total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, high sensitive C-reactive protein (hsCRP), systolic blood pressure, use of antihypertensive medications, use of lipid lowering medications, depressive symptoms, executive function score, bodily pain score, prevalent coronary heart disease, stroke, and heart failure weighted by selection probabilities.

Supplement Table 5. Partial correlation coefficient between phospholipid totals (log-transformed per 1-SD difference) and physical performance measurements, Atherosclerosis Risk in Communities (ARIC) Study, 2011 to 2013

Physical Performance	Total Phospholipid	partial r2	p-value
Grip Strength			
	PC aa	0.078	0.15
	PC ae	0.078	0.15
	SM	0.101	0.06
	SM (OH)	0.137	0.01
	LysoPC a	0.035	0.52
SPPB Score			
	PC aa	0.015	0.78
	PC ae	0.004	0.95
	SM	0.059	0.27
	SM (OH)	0.162	0.002
	LysoPC a	-0.098	0.07
4-Meter walk speed			
	PC aa	-0.006	0.91
	PC ae	0.027	0.62
	SM	0.049	0.37
	SM (OH)	0.114	0.03
	LysoPC a	-0.088	0.10

Partial correlation coefficient controlled for age, sex, race, center, MMSE, dementia status, Model 2: Model 1 with additional adjustment for educational level, smoking and drinking status, APOE genotype, body mass index, physical activity, coronary artery disease, stroke, heart failure, diabetes mellitus, total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, high sensitive C-reactive protein (hsCRP), systolic blood pressure, use of antihypertensive medications, use of lipid lowering medications, depressive symptoms, executive function score, bodily pain score, prevalent coronary heart disease, stroke, and heart failure weighted by selection probabilities.

Supplement Table 6. P-values for sex, age, and APOE interactions in the association of phospholipid totals (log-transformed per 1-SD difference) with physical performance measurements, Atherosclerosis Risk in Communities (ARIC) Study, 2011 to 2013

Physical Performance	Total Phospholipid	P for interaction		
		Sex	Age	APOE
Grip Strength				
	PC aa	0.12	0.56	0.60
	PC ae	0.16	0.49	0.28
	SM	0.28	0.75	0.06
	SM (OH)	0.15	0.27	0.04
	LysoPC a	0.13	0.51	0.58
SPPB Score				
	PC aa	0.91	0.16	0.31
	PC ae	1.00	0.41	0.51
	SM	0.26	0.49	0.40
	SM (OH)	0.72	0.66	0.17
	LysoPC a	0.47	0.11	0.71
4-Meter walk speed				
	PC aa	0.92	0.07	0.75
	PC ae	0.57	0.29	0.73
	SM	0.83	0.46	0.72
	SM (OH)	0.80	0.28	0.63
	LysoPC a	0.86	0.52	0.14

Model adjusted for age, sex, race, center, MMSE, dementia status, Model 2: Model 1 with additional adjustment for educational level, smoking and drinking status, APOE genotype, body mass index, physical activity, coronary artery disease, stroke, heart failure, diabetes mellitus, total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, high sensitive C-reactive protein (hsCRP), systolic blood pressure, use of antihypertensive medications, use of lipid lowering medications, depressive symptoms, executive function score, bodily pain score, prevalent coronary heart disease, stroke, and heart failure weighted by selection probabilities.

Supplement Table 7. Principal component analysis of concentrations of 12 plasma metabolites

	Rotated Factor Pattern				
	Factor1	Factor2	Factor3	Factor4	Factor5
logADMAsd	-0.10613	0.07334	0.01477	0.01696	0.94258
logC3_DC_C4_OHsd	-0.09888	-0.15889	0.3323	0.71869	0.1305
loglysoPC_a_C16_1sd	0.09934	0.74806	-0.21705	0.08656	0.25767
logC18sd	0.11519	0.15619	-0.2558	0.77398	-0.08522
logPC_aa_C36_5sd	0.18776	0.81986	0.35352	0.02096	-0.09351
logPC_aa_C36_6sd	0.26902	0.83561	0.3495	-0.10278	-0.04209
logPC_aa_C38_1sd	0.17738	0.12268	0.75807	0.00792	-0.12198
logPC_aa_C40_2sd	0.30752	0.15767	0.61282	-0.00185	0.18705
logSM_C26_0sd	0.78976	0.07797	0.04025	0.16356	-0.05339
logSM_OH_C22_1sd	0.87454	0.20528	0.17144	-0.06736	-0.06326
logSM_OH_C22_2sd	0.79307	0.21394	0.18234	-0.08078	-0.09186
logSM_OH_C24_1sd	0.90404	0.08474	0.20051	-0.00141	0.02964

Results from principal component analysis including the 12 phospholipids and selecting 5 factors (so all phospholipids are included in 1 factor).

These 5 factors account for 75% of the variance

Supplement Table 8. Linear regression of principal components (Factors 1-5) with physical performance measurements, Atherosclerosis Risk in Communities (ARIC) Study, 2011 to 2013. Coefficients correspond to difference in physical function measure per 1-SD increment in principal component

Physical Performance	Factor	Model	n	β (95% CI)	p-value
Grip Strength					
	Factor 1	Model 1	369	0.77 (0.01, 1.52)	0.05
		Model 2	369	0.63 (-0.21, 1.47)	0.14
	Factor 2	Model 1	369	0.91 (0.09, 1.73)	0.03
		Model 2	369	0.41 (-0.54, 1.36)	0.40
	Factor 3	Model 1	369	-0.10 (-0.87, 0.66)	0.79
		Model 2	369	-0.16 (-0.84, 0.51)	0.64
	Factor 4	Model 1	369	-0.52 (-1.26, 0.22)	0.17
		Model 2	369	-0.22 (-0.94, 0.49)	0.54
	Factor 5	Model 1	369	-0.85 (-1.65, -0.05)	0.04
		Model 2	369	-0.83 (-1.57, -0.08)	0.03
SPPB Score					
	Factor 1	Model 1	371	0.26 (0.00, 0.52)	0.05
		Model 2	371	0.32 (0.07, 0.57)	0.01
	Factor 2	Model 1	371	0.21 (-0.08, 0.49)	0.15
		Model 2	371	-0.11 (-0.38, 0.16)	0.41
	Factor 3	Model 1	371	0.21 (-0.05, 0.48)	0.12
		Model 2	371	0.15 (-0.10, 0.40)	0.24
	Factor 4	Model 1	371	-0.33 (-0.59, -0.08)	0.01
		Model 2	371	-0.18 (-0.42, 0.06)	0.15
	Factor 5	Model 1	371	-0.16 (-0.44, 0.12)	0.27
		Model 2	371	-0.06 (-0.31, 0.21)	0.69
4-Meter walk speed					
	Factor 1	Model 1	366	0.021 (0.000, 0.043)	0.05
		Model 2	366	0.020 (-0.001, 0.040)	0.06
	Factor 2	Model 1	366	0.016 (-0.007, 0.040)	0.17
		Model 2	366	-0.014 (-0.037, 0.009)	0.23
	Factor 3	Model 1	366	0.012 (-0.010, 0.035)	0.27
		Model 2	366	0.008 (-0.011, 0.028)	0.39
	Factor 4	Model 1	366	-0.027 (-0.048, -0.005)	0.01
		Model 2	366	-0.019 (-0.039, 0.003)	0.08
	Factor 5	Model 1	366	-0.004 (-0.027, 0.019)	0.71
		Model 2	366	0.005 (-0.016, 0.026)	0.65

Model 1: Linear regression adjusted for age, sex, race, center, dementia status and mini-mental state examination

Model 2: Model 1 with additional adjustment for educational level, smoking and drinking status, APOE genotype, body mass index, physical activity, coronary artery disease, stroke, heart failure, diabetes mellitus, total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, high sensitive C-reactive protein (hsCRP), systolic blood pressure, use of antihypertensive medications, use of lipid lowering medications, depressive symptoms, executive function score, bodily pain score, prevalent coronary heart disease, stroke, and heart failure weighted by selection probabilities.

Supplement Table 9. Logistic regression of phospholipid totals (log-transformed per 1-SD difference) with low levels of physical performance measurements, Atherosclerosis Risk in Communities (ARIC) Study, 2011 to 2013

Physical Performance	Total Phospholipid	Model	n	OR (95% CI)	p-value
SPPB Score ≤6 (78 of 382, 20%)	PC aa	Model 1	382	0.93 (0.70, 1.24)	0.61
		Model 2	382	0.98 (0.52, 1.86)	0.96
	PC ae	Model 1	382	0.80 (0.60, 1.07)	0.14
		Model 2	382	0.77 (0.43, 1.36)	0.36
	SM	Model 1	382	0.86 (0.63, 1.16)	0.31
		Model 2	382	0.84 (0.48, 1.46)	0.54
	SM (OH)	Model 1	382	0.66 (0.49, 0.89)	0.007
		Model 2	382	0.50 (0.30, 0.83)	0.008
	LysoPC a	Model 1	382	1.09 (0.81, 1.46)	0.56
		Model 2	382	1.47 (1.04, 2.07)	0.03
4-Meter walk speed ≤0.6 m/s (48 of 377, 13%)	PC aa	Model 1	377	1.04 (0.74, 1.47)	0.83
		Model 2	377	1.10 (0.45, 2.70)	0.84
	PC ae	Model 1	377	0.93 (0.66, 1.31)	0.67
		Model 2	377	1.02 (0.45, 2.31)	0.96
	SM	Model 1	377	0.81 (0.56, 1.16)	0.25
		Model 2	377	0.53 (0.22, 1.29)	0.16
	SM (OH)	Model 1	377	0.70 (0.50, 1.00)	0.05
		Model 2	377	0.63 (0.33, 1.21)	0.16
	LysoPC a	Model 1	377	1.40 (0.98, 2.01)	0.06
		Model 2	377	2.10 (1.24, 3.56)	0.006

Model 1: Linear regression adjusted for age, sex, race, dementia status and mini-mental state examination

Model 2: Model 1 with additional adjustment for educational level, smoking and drinking status, APOE genotype, body mass index, physical activity, coronary artery disease, stroke, heart failure, diabetes mellitus, total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, high sensitive C-reactive protein (hsCRP), systolic blood pressure, use of antihypertensive medications, use of lipid lowering medications, depressive symptoms, executive function score, bodily pain score, prevalent coronary heart disease, stroke, and heart failure weighted by selection probabilities.