

# **SUPPLEMENTAL MATERIAL**

1

## 2 **Data S1. Supplemental Methods**

### 3 **Subjects and clinical measurements**

4 The Finnish hyperlipidemia families included in this study (74 families,  $n = 1,445$  individuals with  
5 LDL-C and TG measurements) were identified as part of The European Multicenter Study on Familial  
6 Dyslipidemias in Patients with Premature Coronary Heart Disease (EUFAM) as reported previously.<sup>1,2</sup>  
7 The probands had premature CAD and high levels of total cholesterol, TGs, or both ( $\geq 90^{\text{th}}$  Finnish age-  
8 and sex-specific population percentile), or low HDL-C levels ( $\leq 10^{\text{th}}$  percentile). Initial recruitment  
9 aimed to identify families with Familial Combined Hyperlipidemia (elevation of TC and/or TGs in at  
10 least two family members including the proband) or families with aggregation of low HDL-C. To  
11 exclude families with classic familial hypercholesterolemia (FH), probands were screened with an in-  
12 house functional low-density lipoprotein receptor (LDLR) test similar to a test developed by Cuthbert  
13 and colleagues; further ascertainment of these families not pursued.<sup>3</sup> Founder mutations in LDLR have  
14 been estimated to explain most (approximately 80%) of FH cases in Finland.<sup>4</sup> Genotyping and  
15 imputation did not identify such FH mutations in the members of the remaining families.<sup>5</sup>

16 For the present study, designation of “high LDL-C with family history” or “high TGs with  
17 family history” was made if at least two first-degree relatives of each other had LDL-C or TG levels,  
18 respectively, that were  $> 90^{\text{th}}$  age- and sex-specific Finnish 1997 population percentiles (Supplemental  
19 Table 1). All other relatives meeting the same lipid criteria within the pedigrees were also classified as  
20 affected by the same type of hyperlipidemia with family history. A pedigree was designated as being  
21 characterized by both types of hyperlipidemias if the criteria for both designations were simultaneously  
22 fulfilled (Supplemental Figure 1). Individuals with known diabetes, hepatic or renal disease, hypo- or  
23 hyperthyroidism, pregnancy, or malignancies did not contribute to establishing family history of  
24 hyperlipidemia and were excluded from all analyses.

Samples from the Finnish National FINRISK study were used as a Finnish population-based comparison group. The National FINRISK Study is a population survey conducted every 5 years since 1972.<sup>2</sup> Collections from the 1992, 1997, 2002, 2007, and 2012 surveys are stored in the National Institute for Health and Welfare (THL) biobank. All available individuals from the 1992-2002 surveys ( $n = 19,644$  individuals) without CAD at baseline and who passed exclusion criteria were used to study the incidence of coronary artery disease associated with hyperlipidemias, and samples from the FINRISK 2012 cohort underwent lipidomic profiling ( $n = 1,141$  individuals, 897 of whom passed exclusion criteria). Individuals with known diabetes, pregnancy or cancer were excluded from the analyses. Individuals in all FINRISK cohorts were classified as being affected or unaffected by high LDL-C and high TGs based on the same lipid thresholds as in the EUFAM study.

For the EUFAM families, venous serum samples were obtained after an overnight fast and measurements were obtained as described.<sup>5</sup> Participants in the FINRISK population study were advised to fast for four hours before the examination and avoid heavy meals earlier during the day, and measurements were obtained from plasma samples as described.<sup>2</sup> In addition to those with chronic diseases and pregnancy, individuals known to use lipid-lowering or estrogen medication were excluded from the lipidomic analyses.

## **Registry data**

Tracking of incident CAD and CVD diagnoses was based on the National Finnish Hospital Discharge Register and the National Causes-of-Death Register, whose diagnoses have been previously validated.<sup>6</sup>

<sup>7</sup> The endpoint of incident CHD was defined as the first occurrence of fatal or nonfatal myocardial infarction (International Classification of Diseases [ICD]-10 codes I20.0 or I21-22, ICD-9 codes 410 or 411.0, or ICD-8 codes 410 or 411.0 for hospital discharge; or ICD-10 I21-25, I46, R96, or R98, ICD-9 410-414 or 798 [excluding 7980A], or ICD-8 410-414 or 798 for main cause-of-death) or cardiac revascularization (percutaneous transluminal angioplasty or coronary artery bypass graft surgery). Similar to a previous study, the endpoint of incident CVD additionally included stroke (ICD-10 codes I61 or I63-64 [excluding code I63.6 corresponding to subarachnoid hemorrhage]; ICD-9 codes 431,

433.0, 433.1, 433.9, 434.0, 434.1, 434.9, or 436; or ICD-8 codes 431 [excluding codes 431.01 and 431.91 of the Finnish adaptation of ICD-8], 433, 434, or 436 for hospital discharge or main cause-of-death).<sup>8</sup>

#### **Lipidomics measurements**

Lipidomics measurements were performed for the EUFAM family samples in two batches (228 and 322 individuals), and for the FINRISK population samples in a single batch. Plasma and serum lipids were extracted with methyl tert-butyl ether/methanol (7:2, V:V) as in Matyash et al.<sup>9</sup> Plasma was diluted 50-fold with 150 mM ammonium bicarbonate (in water). For lipid extraction, an equivalent of 1  $\mu$ L of undiluted plasma was used. Internal standards were pre-mixed with the organic solvents mixture. The internal standard mixture contained: cholesterol D6, cholesteryl ester 20:0, ceramide 18:1;2/17:0, diacylglyceride 17:0/17:0, phosphatidylcholine 17:0/17:0, phosphatidylethanolamine 17:0/17:0, lysophosphatidylcholine 12:0, lysophosphatidylethanolamine 17:1, triacylglyceride 17:0/17:0/17:0 and sphingomyelin 18:1;2/12:0. After extraction, the organic phase was transferred to an infusion plate and dried in a speed vacuum concentrator. Dried extract was re-suspended in 7.5 mM ammonium acetate in chloroform/methanol/propanol (1:2:4, vol/vol/vol). All liquid handling steps were performed using Hamilton Robotics STARlet robotic platform with the Anti Droplet Control feature for organic solvents pipetting.

Samples were analyzed by direct infusion in a QExactive mass spectrometer (Thermo Scientific) equipped with a TriVersa NanoMate ion source (Advion Biosciences). Samples were analyzed in both positive and negative ion modes with a resolution of  $R_{m/z=200}=280000$  for MS and  $R_{m/z=200}=17500$  for MSMS experiments, in a single acquisition. MSMS was triggered by an inclusion list encompassing corresponding MS mass ranges scanned in 1 Da increments. Both MS and MSMS data were combined to monitor CE, DAG and TAG ions as ammonium adducts; PC, PC O-, as acetate adducts; and PE, PE O- and PI as deprotonated anions. MS only was used to monitor LPE as deprotonated anion; Cer, SM and LPC as acetate adducts and cholesterol as ammonium adduct.

1 Data were analyzed with in-house developed lipid identification software based on  
2 LipidXplorer.<sup>10, 11</sup> Data post-processing and normalization were performed using an in-house developed  
3 data management system. Only lipid identifications with a signal-to-noise ratio >5, and a signal intensity  
4 5-fold higher than in corresponding blank samples were considered for further data analysis.  
5 Reproducibility was assessed by the inclusion of reference plasma samples (8 reference samples for  
6 EUFAM and 3 reference samples for FINRISK) per 96 well plate. Data were corrected for batch and  
7 drift effects. Median coefficient of variation was <10% across all batches.

8 A total of 230 lipid species were successfully detected in both the EUFAM and FINRISK 2012  
9 cohorts, with detection rates (proportion of samples with successful quantification) between 9.7-100%.  
10 Among these, 151 species were detected in at least 80% of both EUFAM and FINRISK samples and  
11 were included in the subsequent analyses. The median absolute concentrations of the analyzed lipid  
12 species are presented separately for the family and population cohorts in Supplemental Table 5.  
13 SwissLipids names and ID codes are presented for each of the 151 lipid species in Supplemental Table  
14 6.<sup>12</sup> Right-skewed lipidomics measures (skewness > 1 in the FINRISK population cohort) were natural  
15 logarithm transformed prior to analyses. Values were then normalized using mean and standard  
16 deviation values derived from the FINRISK population cohort. Additionally, we calculated weighted  
17 class-specific saturation averages for each subject using the following formula:  $1 * p_1 + 2 * p_2 + \dots + n * p_n$   
18 (where  $p_n$  = the concentration of lipid species with  $n$  double bonds divided by the total concentration of  
19 all species belonging to the class).

## 20 **Genotyping and imputation**

21 To assess the association of known genetic lipid loci with the circulating lipid species, we genotyped  
22 and imputed the EUFAM and FINRISK samples using several arrays: the HumanCoreExome BeadChip,  
23 the Human610-Quad BeadChip, the Affymetrix6.0, and the Infinium HumanOmniExpress (Illumina  
24 Inc., San Diego, CA, USA). Genotype calls were generated together with other available data sets using  
25 zCall at the Institute for Molecular Medicine Finland (FIMM). After quality control, the samples were  
26 phased using SHAPEIT (version 2)<sup>13</sup> and imputed with IMPUTE (version 2.3.1)<sup>14</sup>. We used a combined

reference panel based on 1000 Genomes Phase I integrated haplotypes produced using SHAPEIT (version 2) release on June 2014 and an in-house reference panel from 1941 whole genome sequenced Finnish individuals from the FINRISK and Health 2000 population cohorts.<sup>15</sup> We successfully genotyped or imputed 87 lead variants associated with LDL-C and 74 lead variants associated with TGs in published genome-wide association studies.<sup>16-18</sup>

## Statistical analyses

To assess the risk of incident coronary artery disease associated with the hyperlipidemias, we used Cox proportional hazards models stratified by sex and excluding individuals with prevalent CAD to estimate hazard ratios (HR) for incident CAD events. We confirmed the validity of Cox proportional hazards assumptions using the *cox.zph* function in R.

We used linear mixed models to estimate the association between lipidomic parameters (concentrations of lipid species or weighted saturation averages) and the other parameter of interest (hyperlipidemia status, continuous lipid measurement, or genotype) as implemented in MMM (version 1.01).<sup>19</sup> Transformed lipid species values (or weighted saturation averages) were used as the outcomes, and hyperlipidemia status, age, age<sup>2</sup>, and sex were used as fixed effect covariates. We first assessed both cohorts (the EUFAM family cohort and the FINRISK population cohort) separately, and then together by including an interaction term between cohort and hyperlipidemia status. We examined the independent effects of LDL-C and TG levels by using transformed lipid species as the outcomes and LDL-C, log(TGs), age, age<sup>2</sup>, and sex as fixed effect covariates. Because the lipid species had been quantified in two batches for the EUFAM cohort, we performed all EUFAM analyses separately for both batches, and combined the results using fixed effects inverse-variance weighted meta-analysis as implemented in the R package ‘metafor’. P-values were calculated using Wald test.

# 1 Supplemental References

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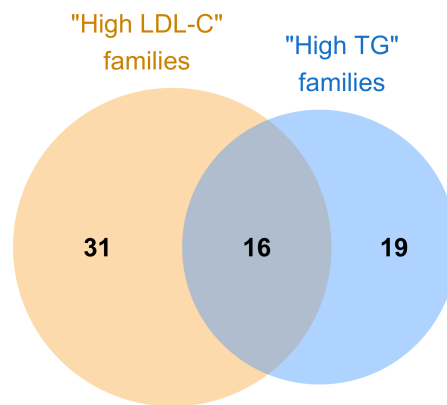
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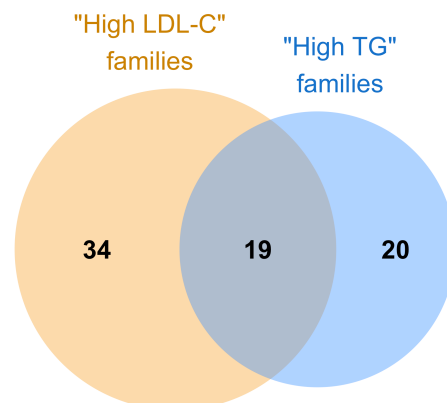
## 1 Supplemental Figures

### 2 Figure S1. Overlap of families with family histories of high LDL-C and high TGs.

#### A. Families included in the analysis of incident CAD risk



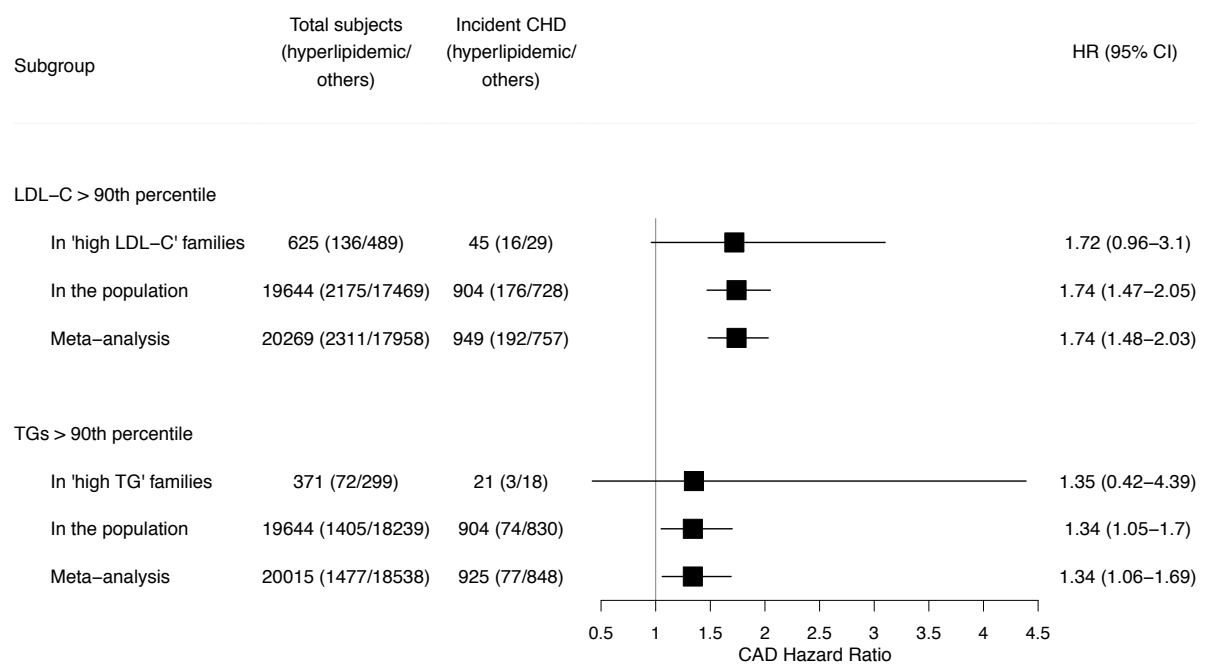
#### B. Families included in the analysis of detailed lipidomic profiles



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4 Designation of high LDL-C with family history or high TGs with family history was made if at least  
5 two first-degree relatives of each other had LDL-C or TG levels, respectively, that were  $\geq 90^{\text{th}}$  age- and  
6 sex-specific Finnish 1997 population percentiles. A pedigree was designated as being affected by both  
7 high LDL-C with family history and high TGs with family history if the criteria for both designations  
8 were simultaneously fulfilled. The diagrams are presented separately for the set of families included in  
9 the analysis of incident CAD risk and B) the families included in the analysis of detailed lipidomic  
10 profiles. *LDL-C* = low-density lipoprotein cholesterol, *TG* = triglyceride.

**Figure S 2. Risk of incident CAD in hyperlipidemias with family history and population-ascertained hyperlipidemias, adjusted by lipid lowering medication usage and smoking.**

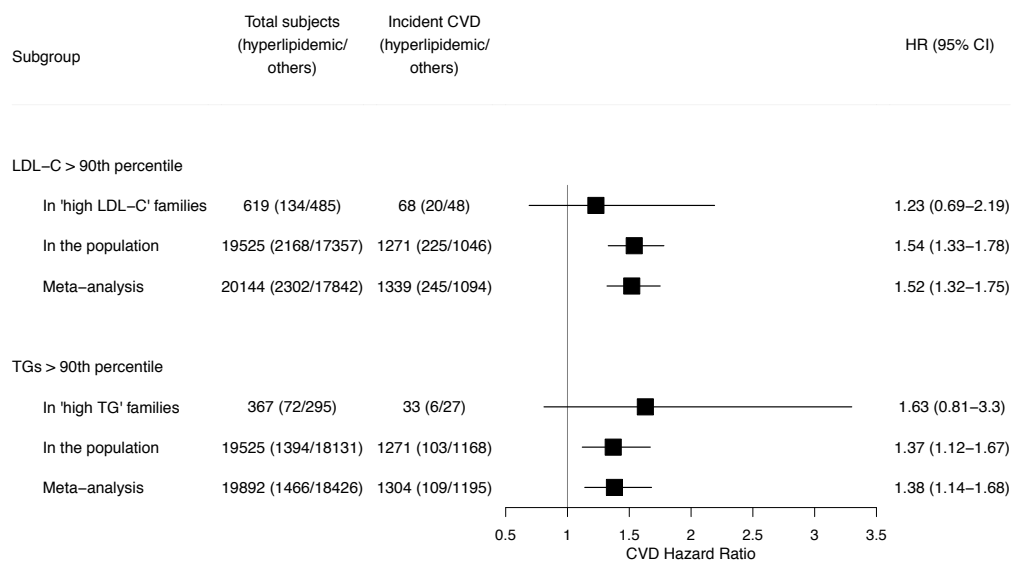


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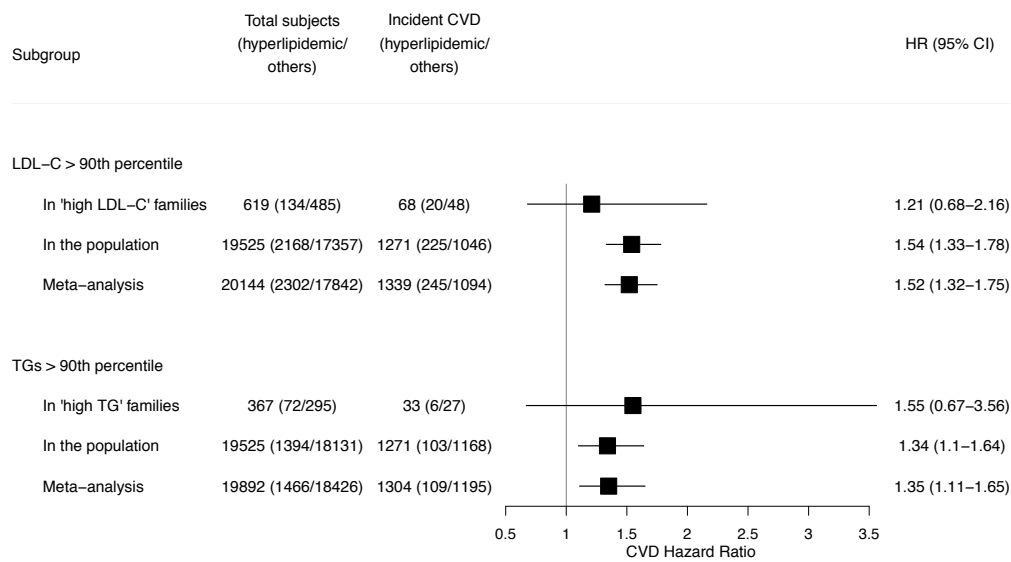
5    The risk of incident coronary artery disease (CAD) was estimated with Cox proportional hazards models  
6    similarly to Figure 1. Smoking and use of lipid lowering medication at baseline were included as  
7    additional covariates.

8

**Figure S3. A. Risk of incident CVD in hyperlipidemias with family history and population-ascertained hyperlipidemias**

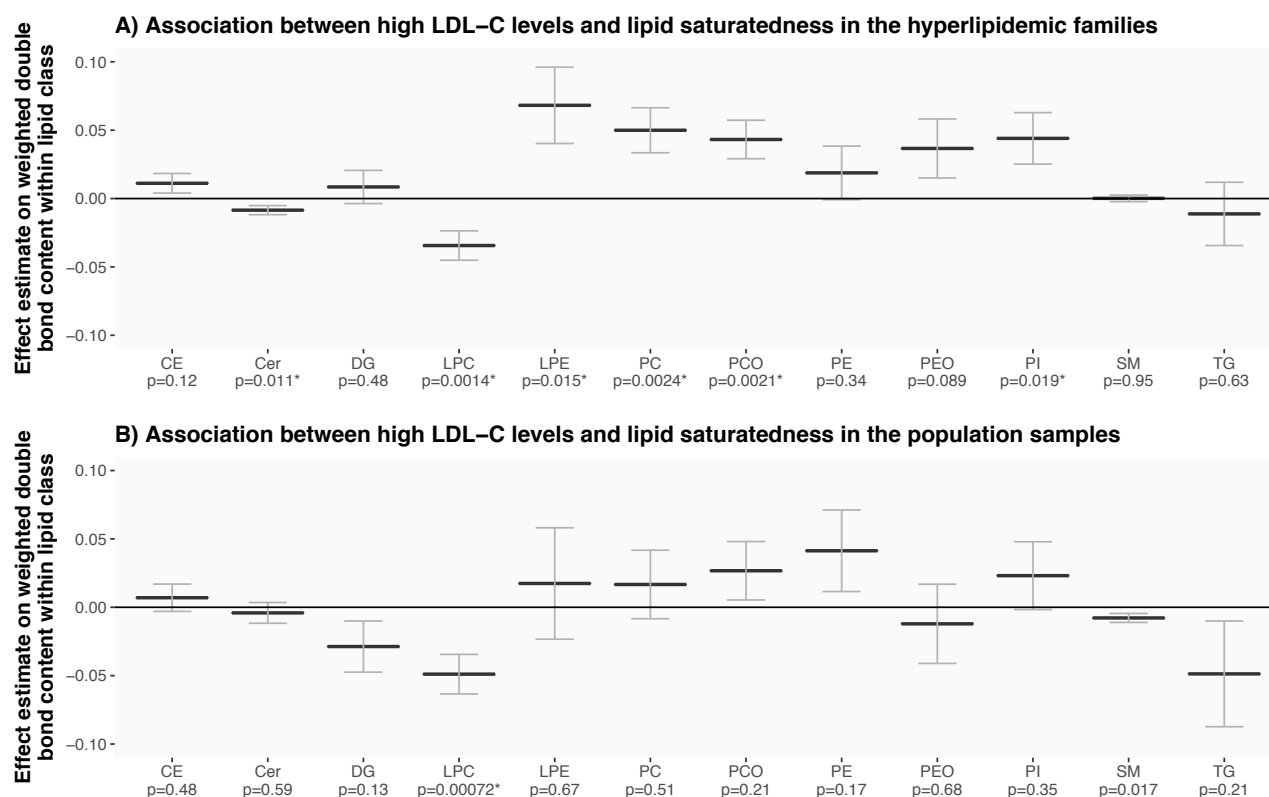


**B. Risk of incident CVD in hyperlipidemias with family history and population-ascertained hyperlipidemias, adjusted for lipid lowering medication usage and smoking.**



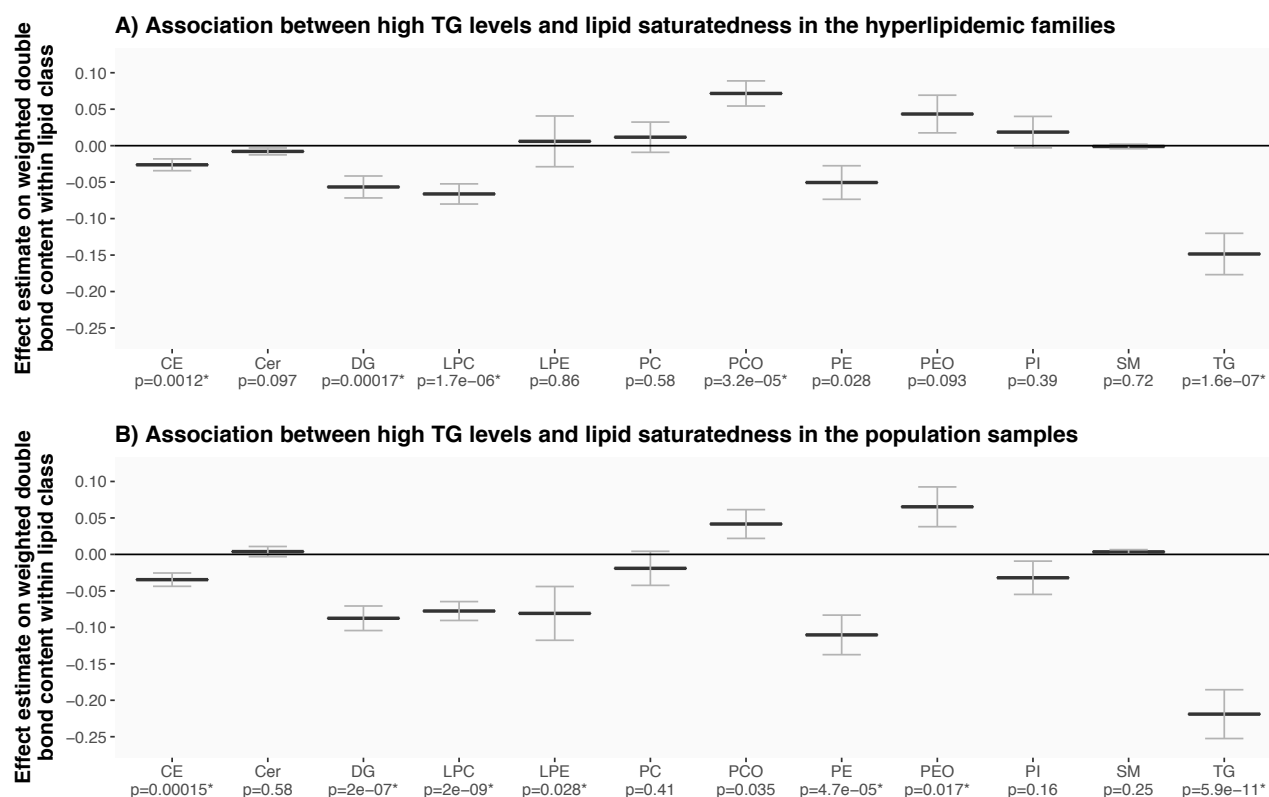
Panel A: The risk of incident cardiovascular disease (CVD) was estimated with Cox proportional hazards models similarly to Figure 1. Panel B: Smoking and use of lipid lowering medication at baseline were included as additional covariates.

**Figure S4. Association of high LDL-C status and weighted saturation averages within each class.**



The associations were estimated separately A) in “high LDL-C” families (total  $n = 463$  individuals) and B) in the population samples (total  $n = 897$  individuals). Negative effect estimates correspond to increased average saturation, and positive effect estimates correspond to decreased average saturation (increased unsaturation). Statistically significant effects at 5% FDR are marked with an asterisk (\*). *Cer* = ceramide, *DG* = diacylglyceride, *FDR* = false detection rate, *LDL-C* = low-density lipoprotein cholesterol, *LPC* = lysophosphatidylcholine, *LPE* = lysophosphatidylethanolamine, *PC* = phosphatidylcholine, *PCO* = phosphatidylcholine-ether, *PE* = phosphatidylethanolamine, *PEO* = phosphatidylethanolamine-ether, *PI* = phosphatidylinositol, *CE* = cholesteryl ester; *SM* = sphingomyelin, *ST* = sterol, *TG* = triacylglyceride.

**Figure S5. Association of high TG status and weighted saturation averages within each class.**



The associations were estimated separately A) in “high TG” families (total  $n = 287$  individuals) and B) in the population (total  $n = 897$  individuals). Negative effect estimates correspond to increased average saturation, and positive effect estimates correspond to decreased average saturation (increased unsaturation). Statistically significant effects at 5% FDR are marked with an asterisk (\*). *Cer* = ceramide, *DG* = diacylglyceride, *FDR* = false detection rate, *LDL-C* = low-density lipoprotein cholesterol, *LPC* = lysophosphatidylcholine, *LPE* = lysophosphatidylethanolamine, *PC* = phosphatidylcholine, *PCO* = phosphatidylcholine-ether, *PE* = phosphatidylethanolamine, *PEO* = phosphatidylethanolamine-ether, *PI* = phosphatidylinositol, *CE* = cholesteryl ester; *SM* = sphingomyelin, *ST* = sterol, *TG* = triacylglyceride.

## Supplemental Tables

**Table S1. Sex- and age-specific 90<sup>th</sup> population percentiles for LDL-C and TGs based on the FINRISK 1997 cohort.**

Sex	Age	90 <sup>th</sup> percentile for LDL-C (mmol/l)	90 <sup>th</sup> percentile for TGs (mmol/l)
Male	25	4,25	2,27
	30	4,27	2,79
	35	4,51	2,98
	40	4,76	3,36
	45	4,79	3,40
	50	4,86	2,90
	55	4,79	3,09
	60	4,76	3,01
Female	25	3,93	1,56
	30	3,86	1,75
	35	4,03	1,68
	40	4,18	1,88
	45	4,59	1,93
	50	4,65	2,33
	55	5,09	2,49
	60	5,12	2,70

Individuals with known diabetes, pregnancy or cancer were excluded prior to estimation of 90<sup>th</sup> percentile values. *LDL-C* = low-density lipoprotein cholesterol, *TGs* = triglycerides.

Table S2. Clinical and metabolic characteristics of the study individuals included in the analyses of incident CAD risk.

	EUFAM (n = 755)							FINRISK (n = 19,644)							Effect of "high LDL-C" status in EUFAM vs. FINRISK	Effect of "high TG" status in EUFAM vs. FINRISK
	High LDL-C families (n = 47)				High TG families (n = 35)											
	All	Affected by High LDL-C	Unaffected by High LDL-C	p-value	Affected by High TGs	Unaffected by High TGs	p-value	All	Affected by High LDL-C	Unaffected by High LDL-C	p-value	Affected by High TGs	Unaffected by High TGs	p-value		
n (male/female)	755 (347/408)	136 (67/69)	489 (228/261)		72 (23/49)	299 (137/162)		19,644 (9,026/10,618)	2,175 (1,102/1,073)	17,469 (7,924/9,545)		1,405 (581/824)	18,239 (8,445/9,794)			
Age (years)	40.0 ± 13.9	43.7 ± 12.4	39.2 ± 14.0	0.0014	37.1 ± 14.1	40.6 ± 14.1	0.07	46.1 ± 12.8	46.7 ± 12.3	46.0 ± 12.9	0.017	44.4 ± 12.6	46.2 ± 12.8	7.6e-07	0.0047	0.37
BMI (kg/m2)	25.5 ± 5.0	26.5 ± 4.7	25.2 ± 4.9	0.03	27.3 ± 4.5	25.4 ± 4.8	7e-07	26.1 ± 5.3	27.0 ± 5.1	25.9 ± 5.3	1.2e-26	28.5 ± 5.9	25.9 ± 5.2	5.5e-144	0.63	0.56
LDL-C (mmol/l)	3.6 ± 1.0	5.1 ± 0.7	3.2 ± 0.8	3.9e-135	3.7 ± 1.0	3.4 ± 1.0	1.2e-05	3.5 ± 1.0	5.1 ± 0.7	3.3 ± 0.8	<5e-324	3.6 ± 1.0	3.5 ± 0.9	1.8e-11	0.026	0.033
TGs (mmol/l)	1.4 ± 0.9	1.7 ± 1.0	1.3 ± 0.7	2.2e-10	2.8 ± 1.4	1.2 ± 0.6	6.1e-87	1.3 ± 0.8	1.6 ± 0.9	1.3 ± 0.7	1.8e-86	3.0 ± 1.2	1.2 ± 0.7	<5e-324	0.15	0.32
TC (mmol/l)	5.6 ± 1.2	7.1 ± 0.9	5.2 ± 0.9	6.6e-106	6.1 ± 1.1	5.3 ± 1.1	7.3e-15	5.5 ± 1.1	7.2 ± 0.8	5.3 ± 0.9	<5e-324	6.1 ± 1.1	5.5 ± 1.0	3.2e-155	0.079	0.21
HDL-C (mmol/l)	1.4 ± 0.4	1.3 ± 0.4	1.4 ± 0.4	0.0013	1.2 ± 0.4	1.4 ± 0.4	3.8e-08	1.5 ± 0.4	1.4 ± 0.4	1.5 ± 0.4	2.3e-10	1.2 ± 0.4	1.5 ± 0.4	9.3e-178	0.22	0.99

Values are presented as mean ± interquantile range for TGs, BMI, and waist circumference, and mean ± standard deviation for all other variables. A subset of the families fulfilled criteria for both “high LDL-C with family history” and “high TGs with family history” and were thus included in both analysis groups (Supplemental Figure 1.A.). P-values for between-group comparisons were calculated using Wald test by a linear mixed model correcting for genetic sample relatedness. Sex and age were used as other fixed effect covariates in addition to the group variable except when age was used as the outcome. *BMI* = *Body Mass Index*, *HDL-C* = *high-density lipoprotein cholesterol*, *LDL-C* = *low-density lipoprotein cholesterol*, *TGs* = *triglycerides*, *TC* = *total cholesterol*.



**Table S3. Risk of incident CAD or CVD in hyperlipidemias with family history and population-ascertained hyperlipidemias.**

Outcome	Hyperlipidemia type	Covariates	HR in hyperlipidemic families	HR in the population	p-value for between-cohort difference	Meta-analysis HR
CAD	High LDL-C	None	1.71 (0.94-3.10)	1.74 (1.48-2.05)	0.84	1.74 (1.48-2.04)
		Lipid-lowering therapy + Smoking	1.72 (0.96-3.10)	1.74 (1.47-2.05)	0.73	1.74 (1.48-2.03)
		Lipid-lowering therapy + Smoking + BMI	1.83 (1.02-3.30)	1.76 (1.49-2.07)	0.92	1.76 (1.50-2.07)
	High TGs	None	1.35 (0.52-3.51)	1.38 (1.09-1.75)	0.82	1.38 (1.09-1.74)
		Lipid-lowering therapy + Smoking	1.35 (0.42-4.39)	1.34 (1.05-1.70)	0.59	1.34 (1.06-1.69)
		Lipid-lowering therapy + Smoking + BMI	1.67 (0.60-4.65)	1.16 (0.91-1.48)	0.75	1.18 (0.93-1.50)
CVD	High LDL-C	None	1.23 (0.69-2.19)	1.54 (1.33-1.78)	0.45	1.52 (1.32-1.75)
		Lipid-lowering therapy + Smoking	1.21 (0.68-2.16)	1.54 (1.33-1.78)	0.42	1.52 (1.32-1.75)
		Lipid-lowering therapy + Smoking + BMI	1.33 (0.74-2.38)	1.54 (1.33-1.79)	0.59	1.53 (1.33-1.76)
	High TGs	None	1.63 (0.81-3.30)	1.37 (1.12-1.67)	0.74	1.38 (1.14-1.68)
		Lipid-lowering therapy + Smoking	1.55 (0.67-3.56)	1.34 (1.10-1.64)	0.98	1.35 (1.11-1.65)
		Lipid-lowering therapy + Smoking + BMI	1.98 (0.98-3.98)	1.17 (0.95-1.45)	0.81	1.23 (1.00-1.50)

The risk of incident CAD or CVD was estimated with Cox proportional hazards models similarly to Figure 1. Additional models included adjustment for selected covariates.

Table S4. Clinical and metabolic characteristics of the study individuals included in the analyses of circulating lipidomics profiles.

	EUFAM ( <i>n</i> = 550)							FINRISK ( <i>n</i> = 897)							Effect of "high LDL-C" status in EUFAM vs. FINRISK	Effect of "high TG" status in EUFAM vs. FINRISK		
	High LDL-C families ( <i>n</i> = 53)				High TG families ( <i>n</i> = 39)													
	All	Affected by High LDL-C	Unaffected by High LDL-C	<i>p</i> -value	Affected by High TGs	Unaffected by High TGs	<i>p</i> -value	All	Affected by High LDL-C	Unaffected by High LDL-C	<i>p</i> -value	Affected by High TGs	Unaffected by High TGs	<i>p</i> -value			<i>p</i> -value	<i>p</i> -value
n (male/female)	550 (276/274)	105 (54/51)	358 (178/180)		64 (30/34)	223 (108/115)		897 (399/498)	56 (27/29)	841 (372/469)		65 (34/31)	832 (365/467)					
Age (years)	39.5 ± 14.0	41.8 ± 13.7	39.2 ± 14.0	0.11	40.3 ± 13.3	39.0 ± 14.5	0.63	48.3 ± 13.7	49.0 ± 15.4	48.2 ± 13.6	0.61	44.6 ± 12.2	48.6 ± 13.8	0.0054	0.36	0.039		
BMI (kg/m2)	25.6 ± 4.3	26.1 ± 4.2	25.3 ± 4.0	0.00054	28.1 ± 7.7	25.5 ± 3.4	0.051	26.0 ± 5.4	27.9 ± 6.2	25.9 ± 5.3	0.0051	29.1 ± 6.1	25.7 ± 5.3	1.6e-10	0.41	0.46		
Waist circumference (cm)	86.9 ± 12.8	88.4 ± 11.0	85.7 ± 11.0	0.0034	92.5 ± 19.0	88.0 ± 15.0	0.011	89.3 ± 19.0	95.1 ± 16.1	88.9 ± 19.0	0.0014	99.1 ± 16.0	88.6 ± 18.4	2.5e-13	0.38	0.23		
LDL-C (mmol/l)	3.6 ± 1.1	5.2 ± 0.8	3.2 ± 0.8	3.7e-120	3.9 ± 1.3	3.5 ± 1.1	4.2e-05	3.3 ± 0.9	5.3 ± 1.1	3.2 ± 0.7	8.8e-113	3.5 ± 1.4	3.3 ± 0.9	0.081	0.0019	0.38		
TGs (mmol/l)	1.5 ± 0.9	1.8 ± 1.1	1.4 ± 0.7	2e-06	3.6 ± 1.8	1.2 ± 0.6	3.4e-94	1.3 ± 0.7	1.6 ± 1.0	1.3 ± 0.7	0.00074	3.5 ± 1.9	1.1 ± 0.6	8.9e-117	0.52	0.11		
TC (mmol/l)	5.6 ± 1.2	7.0 ± 1.0	5.2 ± 1.0	1.3e-75	6.6 ± 1.4	5.3 ± 1.1	1.9e-21	5.4 ± 1.1	7.5 ± 1.2	5.3 ± 0.9	2e-85	6.3 ± 1.5	5.3 ± 1.0	1.9e-15	0.00044	0.48		
HDL-C (mmol/l)	1.3 ± 0.4	1.2 ± 0.3	1.4 ± 0.4	0.00095	1.0 ± 0.3	1.3 ± 0.4	5.4e-12	1.5 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	0.5	1.2 ± 0.3	1.5 ± 0.4	3.6e-09	0.2	0.97		

Values are presented as mean ± interquantile range for TGs and BMI, and mean ± standard deviation for all other variables. A subset of the families fulfilled criteria for both “high LDL-C with family history” and “high TGs with family history” and were thus included in both analysis groups (Supplemental Figure 1.B.). P-values for between-group comparisons were calculated using Wald test by a linear mixed model correcting for genetic sample relatedness. Sex and age were used as other fixed effect covariates in addition to the group variable except when age was used as the outcome. *BMI = Body Mass Index, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TGs = triglycerides, TC = total cholesterol, WC = waist circumference.*

**Table S5. Median concentrations of the 151 lipid species in the family and population cohorts.**

Species	Median concentration (pmols/mcL) in the hyperlipidemic families	Median concentration (pmols/mcL) in the population	Species	Median concentration (pmols/mcL) in the hyperlipidemic families	Median concentration (pmols/mcL) in the population	Species	Median concentration (pmols/mcL) in the hyperlipidemic families	Median concentration (pmols/mcL) in the population
Cholesterol	1900 ± 580	1600 ± 530	PC(16:0;0_18:3;0)	10 ± 5.6	8.8 ± 5.4	PCO(18:2;0/18:1;0)	0.44 ± 0.29	0.46 ± 0.28
CE(14:0;0)	35 ± 21	28 ± 16	PC(16:0;0_20:1;0)	1.1 ± 0.61	1.1 ± 0.57	PCO(18:2;0/18:2;0)	2.4 ± 1.1	2.4 ± 1.2
CE(15:0;0)	8.8 ± 5.1	8 ± 3.7	PC(16:0;0_20:2;0)	9 ± 4.3	7.9 ± 3.4	SM(32:1;2)	7.9 ± 3	7.7 ± 2.9
CE(16:0;0)	430 ± 170	370 ± 120	PC(16:0;0_20:3;0)	63 ± 34	53 ± 33	SM(34:0;2)	1.7 ± 0.84	1.8 ± 0.72
CE(16:1;0)	190 ± 120	150 ± 100	PC(16:0;0_20:4;0)	140 ± 63	130 ± 68	SM(34:1;2)	75 ± 25	69 ± 20
CE(17:0;0)	7.6 ± 3.8	6.2 ± 2.7	PC(16:0;0_20:5;0)	30 ± 25	33 ± 29	SM(34:2;2)	9.6 ± 3.2	9.2 ± 2.9
CE(17:1;0)	16 ± 8.2	12 ± 5.7	PC(16:0;0_22:4;0)	5.5 ± 2.3	4.6 ± 2.2	SM(36:1;2)	14 ± 4.9	12 ± 4.2
CE(18:0;0)	21 ± 11	16 ± 8.1	PC(16:0;0_22:5;0)	21 ± 9.4	21 ± 11	SM(36:2;2)	6.5 ± 2.5	5.9 ± 2.1
CE(18:1;0)	910 ± 350	770 ± 290	PC(16:0;0_22:6;0)	88 ± 56	82 ± 49	SM(38:1;2)	9.7 ± 3.4	9.5 ± 3.2
CE(18:2;0)	2700 ± 1000	2200 ± 710	PC(16:1;0_18:1;0)	8.1 ± 4.4	7.1 ± 3.5	SM(38:2;2)	3.8 ± 1.4	3.7 ± 1.3
CE(18:3;0)	110 ± 55	88 ± 48	PC(16:1;0_18:2;0)	6.5 ± 3.5	5.7 ± 2.9	SM(40:1;2)	16 ± 6.3	16 ± 5.1
CE(19:1;0)	1.9 ± 0.87	1.8 ± 0.84	PC(17:0;0_18:2;0)	33 ± 15	30 ± 13	SM(40:2;2)	15 ± 5	15 ± 5
CE(20:2;0)	2.6 ± 1.2	2.3 ± 1.2	PC(17:0;0_20:3;0)	7.2 ± 4.3	5.6 ± 3.1	SM(42:2;2)	38 ± 14	36 ± 12
CE(20:3;0)	39 ± 19	30 ± 14	PC(17:0;0_20:4;0)	13 ± 5.9	11 ± 5	Cer(40:1;2)	0.75 ± 0.34	0.66 ± 0.3
CE(20:4;0)	320 ± 140	270 ± 120	PC(18:0;0_18:1;0)	31 ± 16	27 ± 14	Cer(40:2;2)	0.21 ± 0.1	0.17 ± 0.09
CE(20:5;0)	82 ± 74	82 ± 73	PC(18:0;0_18:2;0)	200 ± 81	190 ± 71	Cer(42:1;2)	2 ± 0.93	1.8 ± 0.79
CE(22:6;0)	38 ± 25	34 ± 22	PC(18:0;0_18:3;0)	3.2 ± 2.2	3.3 ± 2.1	Cer(42:2;2)	1.4 ± 0.62	1.2 ± 0.55
DG(16:0;0_18:1;0)	5 ± 4.4	3.1 ± 2.8	PC(18:0;0_20:2;0)	4.1 ± 2.1	3.5 ± 1.6	PI(16:0;0_18:1;0)	1.8 ± 1.3	1.6 ± 1
DG(18:1;0_18:1;0)	7.9 ± 6.6	5.2 ± 4.2	PC(18:0;0_20:3;0)	29 ± 16	25 ± 14	PI(16:0;0_18:2;0)	1.2 ± 0.7	1.2 ± 0.69
DG(18:1;0_18:2;0)	6.6 ± 5	4.6 ± 3	PC(18:0;0_20:4;0)	61 ± 31	58 ± 25	PI(16:0;0_20:4;0)	1.8 ± 0.99	1.7 ± 1
TG(48:0;0)	5.2 ± 8.2	4.6 ± 7.7	PC(18:0;0_20:5;0)	9.9 ± 8.4	12 ± 13	PI(18:0;0_18:1;0)	2.3 ± 1.3	2.1 ± 1.1
TG(48:1;0)	29 ± 38	20 ± 27	PC(18:0;0_22:5;0)	7.1 ± 3.9	6.3 ± 2.9	PI(18:0;0_18:2;0)	4 ± 2	4.1 ± 2.1
TG(48:2;0)	24 ± 28	17 ± 20	PC(18:0;0_22:6;0)	27 ± 18	24 ± 13	PI(18:0;0_20:3;0)	2.6 ± 1.4	2.5 ± 1.3
TG(50:1;0)	66 ± 71	43 ± 53	PC(18:1;0_18:1;0)	23 ± 11	21 ± 8.7	PI(18:0;0_20:4;0)	18 ± 7.8	18 ± 6.6
TG(50:2;0)	110 ± 100	74 ± 75	PC(18:1;0_18:2;0)	62 ± 29	53 ± 23	PI(18:1;0_18:1;0)	0.82 ± 0.51	0.78 ± 0.51
TG(50:3;0)	51 ± 50	36 ± 32	PC(18:1;0_20:3;0)	9.7 ± 5.4	8.5 ± 4.1	PI(18:1;0_18:2;0)	0.66 ± 0.42	0.6 ± 0.27
TG(50:4;0)	15 ± 14	11 ± 9.8	PC(18:1;0_20:4;0)	17 ± 7.1	16 ± 6.9	PI(18:2;0_18:2;0)	0.95 ± 0.49	0.83 ± 0.52
TG(51:2;0)	10 ± 9	7 ± 5.9	PC(18:2;0_18:2;0)	26 ± 14	23 ± 12	PE(16:0;0_18:2;0)	1.6 ± 1.6	1.5 ± 1.3
TG(51:3;0)	6.4 ± 5.3	4.7 ± 3.5	PC(18:2;0_20:4;0)	11 ± 4.3	9.9 ± 4.4	PE(18:0;0_18:2;0)	4.1 ± 3.2	3.5 ± 2.6
TG(52:2;0)	240 ± 210	160 ± 140	PCO(16:0;0/16:0;0)	0.83 ± 0.45	0.64 ± 0.37	PE(18:0;0_20:4;0)	5.4 ± 3.8	4.8 ± 3.1
TG(52:3;0)	240 ± 200	160 ± 130	PCO(16:0;0/16:1;0)	0.7 ± 0.43	0.67 ± 0.57	PE(18:1;0_18:1;0)	0.48 ± 0.43	0.62 ± 0.76
TG(52:4;0)	99 ± 86	75 ± 58	PCO(16:0;0/18:1;0)	1.7 ± 0.7	1.6 ± 0.56	PEO(16:1;0/18:2;0)	1.3 ± 0.75	1.1 ± 0.61
TG(52:5;0)	26 ± 24	21 ± 16	PCO(16:0;0/18:2;0)	3.5 ± 1.6	3.4 ± 1.5	PEO(16:1;0/20:4;0)	3.7 ± 2.3	3.4 ± 2
TG(54:3;0)	64 ± 52	46 ± 37	PCO(16:0;0/20:3;0)	0.83 ± 0.57	0.95 ± 0.47	PEO(18:1;0/18:2;0)	2.3 ± 1.4	1.8 ± 1.1
TG(54:4;0)	60 ± 48	46 ± 35	PCO(16:0;0/20:4;0)	5.5 ± 2.9	5.1 ± 2.4	PEO(18:2;0/18:2;0)	1.6 ± 0.86	1.6 ± 0.82
TG(54:5;0)	43 ± 37	34 ± 27	PCO(16:1;0/16:0;0)	1.9 ± 0.77	1.8 ± 0.79	PEO(18:2;0/20:4;0)	5.7 ± 3.2	5.8 ± 2.9
TG(54:6;0)	25 ± 23	22 ± 17	PCO(16:1;0/18:1;0)	0.32 ± 0.18	0.35 ± 0.22	LPE(16:0;0)	0.56 ± 0.25	0.51 ± 0.22
TG(56:4;0)	3.8 ± 2.8	3 ± 2.1	PCO(16:1;0/18:2;0)	5.3 ± 2.6	5.2 ± 2.3	LPE(18:1;0)	0.52 ± 0.29	0.56 ± 0.37
TG(56:5;0)	10 ± 7	7.7 ± 5.1	PCO(16:1;0/20:3;0)	0.6 ± 0.29	0.57 ± 0.46	LPE(18:2;0)	1 ± 0.56	1.2 ± 0.72
TG(56:6;0)	18 ± 13	15 ± 10	PCO(17:0;0/17:1;0)	0.087 ± 0.047	0.076 ± 0.044	LPE(20:4;0)	0.71 ± 0.33	0.76 ± 0.31
TG(56:7;0)	25 ± 23	22 ± 19	PCO(18:0;0/14:0;0)	2.1 ± 0.74	1.9 ± 0.48	LPE(22:6;0)	0.7 ± 0.35	0.78 ± 0.35
PC(14:0;0_16:0;0)	2.8 ± 2	2.4 ± 1.6	PCO(18:0;0/18:2;0)	0.77 ± 0.44	0.71 ± 0.33	LPC(14:0;0)	1.1 ± 0.58	0.88 ± 0.4
PC(14:0;0_18:1;0)	3.5 ± 2.6	2.9 ± 1.9	PCO(18:0;0/20:4;0)	3.4 ± 1.6	3 ± 1.2	LPC(16:0;0)	72 ± 25	56 ± 17
PC(14:0;0_18:2;0)	3.8 ± 2.3	3.4 ± 1.7	PCO(18:1;0/16:0;0)	0.93 ± 0.37	0.87 ± 0.31	LPC(16:1;0)	1.8 ± 0.83	1.4 ± 0.66
PC(15:0;0_18:2;0)	47 ± 20	44 ± 16	PCO(18:1;0/18:1;0)	0.18 ± 0.099	0.14 ± 0.079	LPC(18:0;0)	18 ± 8.3	14 ± 5.6
PC(16:0;0_16:0;0)	9.6 ± 3.7	9.1 ± 3.4	PCO(18:1;0/18:2;0)	2.2 ± 1.1	2 ± 0.92	LPC(18:1;0)	14 ± 7.4	12 ± 5.2
PC(16:0;0_16:1;0)	12 ± 8.7	9.6 ± 7.6	PCO(18:1;0/20:3;0)	1.2 ± 0.62	0.9 ± 0.48	LPC(18:2;0)	17 ± 11	18 ± 11
PC(16:0;0_17:1;0)	20 ± 12	18 ± 11	PCO(18:1;0/20:4;0)	8.5 ± 2.8	7.6 ± 2.9	LPC(20:3;0)	1 ± 0.53	1 ± 0.5
PC(16:0;0_18:0;0)	30 ± 10	25 ± 10	PCO(18:2;0/16:0;0)	1.2 ± 0.48	1.1 ± 0.44	LPC(20:4;0)	3 ± 1.6	2.8 ± 1.4
PC(16:0;0_18:1;0)	240 ± 110	210 ± 96	PCO(18:2;0/18:0;0)	0.17 ± 0.099	0.16 ± 0.072	LPC(22:6;0)	1.1 ± 0.66	1.2 ± 0.63
PC(16:0;0_18:2;0)	480 ± 180	440 ± 150						

**Table S6. SwissLipids names and ID codes for the 151 lipid species included in the analyses of circulating lipidomic profiles.**

Species	SwissLipids Name	SwissLipids ID	Species	SwissLipids Name	SwissLipids ID
Cholesterol	cholesterol	SLM:000000287	PC(18:1;0_20:3;0)	Phosphatidylcholine (18:1_20:3)	SLM:000063992
CE(14:0;0)	Sterol ester (27:1/14:0)	SLM:000500342	PC(18:1;0_20:4;0)	Phosphatidylcholine (18:1_20:4)	SLM:000063993
CE(15:0;0)	Sterol ester (27:1/15:0)	SLM:000500343	PC(18:2;0_18:2;0)	Phosphatidylcholine (18:2_18:2)	SLM:000064033
CE(16:0;0)	Sterol ester (27:1/16:0)	SLM:000500346	PC(18:2;0_20:4;0)	Phosphatidylcholine (18:2_20:4)	SLM:000064041
CE(16:1;0)	Sterol ester (27:1/16:1)	SLM:000500345	PCO(16:0;0/16:0;0)	Phosphatidylcholine (O-16:0_16:0)	SLM:000065919
CE(17:0;0)	Sterol ester (27:1/17:0)	SLM:000500347	PCO(16:0;0/16:1;0)	Phosphatidylcholine (O-16:0_16:1)	SLM:000065920
CE(17:1;0)	Sterol ester (27:1/17:1)	n/a	PCO(16:0;0/18:1;0)	Phosphatidylcholine (O-16:0_18:1)	SLM:000065924
CE(18:0;0)	Sterol ester (27:1/18:0)	SLM:000500352	PCO(16:0;0/18:2;0)	Phosphatidylcholine (O-16:0_18:2)	SLM:000065925
CE(18:1;0)	Sterol ester (27:1/18:1)	SLM:000500351	PCO(16:0;0/20:3;0)	Phosphatidylcholine (O-16:0_20:3)	SLM:000065932
CE(18:2;0)	Sterol ester (27:1/18:2)	SLM:000500350	PCO(16:0;0/20:4;0)	Phosphatidylcholine (O-16:0_20:4)	SLM:000065933
CE(18:3;0)	Sterol ester (27:1/18:3)	SLM:000500349	PCO(16:1;0/16:0;0)	Phosphatidylcholine (O-16:1_16:0)	SLM:000065984
CE(19:1;0)	Sterol ester (27:1/19:1)	n/a	PCO(16:1;0/18:1;0)	Phosphatidylcholine (O-16:1_18:1)	SLM:000065989
CE(20:2;0)	Sterol ester (27:1/20:2)	SLM:000500357	PCO(16:1;0/18:2;0)	Phosphatidylcholine (O-16:1_18:2)	SLM:000065990
CE(20:3;0)	Sterol ester (27:1/20:3)	SLM:000500356	PCO(16:1;0/20:3;0)	Phosphatidylcholine (O-16:1_20:3)	SLM:000065997
CE(20:4;0)	Sterol ester (27:1/20:4)	SLM:000500355	PCO(17:0;0/17:1;0)	Phosphatidylcholine (O-17:0_17:1)	n/a
CE(20:5;0)	Sterol ester (27:1/20:5)	SLM:000500354	PCO(18:0;0/14:0;0)	Phosphatidylcholine (O-18:0_14:0)	SLM:000066176
CE(22:6;0)	Sterol ester (27:1/22:6)	SLM:000500361	PCO(18:0;0/18:2;0)	Phosphatidylcholine (O-18:0_18:2)	SLM:000066185
DG(16:0;0_18:1;0)	Diacylglycerol (16:0_18:1)	SLM:000308862	PCO(18:0;0/20:4;0)	Phosphatidylcholine (O-18:0_20:4)	SLM:000066193
DG(18:1;0_18:1;0)	Diacylglycerol (18:1_18:1)	SLM:000309012	PCO(18:1;0/16:0;0)	Phosphatidylcholine (O-18:1_16:0)	SLM:000066244
DG(18:1;0_18:2;0)	Diacylglycerol (18:1_18:2)	SLM:000309013	PCO(18:1;0/18:1;0)	Phosphatidylcholine (O-18:1_18:1)	SLM:000066249
TG(48:0;0)	Triacylglycerol (48:0)	SLM:000308257	PCO(18:1;0/18:2;0)	Phosphatidylcholine (O-18:1_18:2)	SLM:000066250
TG(48:1;0)	Triacylglycerol (48:1)	SLM:000308258	PCO(18:1;0/20:3;0)	Phosphatidylcholine (O-18:1_20:3)	SLM:000066257
TG(48:2;0)	Triacylglycerol (48:2)	SLM:000308259	PCO(18:1;0/20:4;0)	Phosphatidylcholine (O-18:1_20:4)	SLM:000066258
TG(50:1;0)	Triacylglycerol (50:1)	SLM:000308276	PCO(18:2;0/16:0;0)	Phosphatidylcholine (O-18:2_16:0)	SLM:000066309
TG(50:2;0)	Triacylglycerol (50:2)	SLM:000308277	PCO(18:2;0/18:0;0)	Phosphatidylcholine (O-18:2_18:0)	SLM:000066313
TG(50:3;0)	Triacylglycerol (50:3)	SLM:000308278	PCO(18:2;0/18:1;0)	Phosphatidylcholine (O-18:2_18:1)	SLM:000066314
TG(50:4;0)	Triacylglycerol (50:4)	SLM:000308279	PCO(18:2;0/18:2;0)	Phosphatidylcholine (O-18:2_18:2)	SLM:000066315
TG(51:2;0)	Triacylglycerol (51:2)	SLM:000308287	SM(32:1;2)	Sphingomyelin (d32:1)	SLM:000390695
TG(51:3;0)	Triacylglycerol (51:3)	SLM:000308288	SM(34:0;2)	Sphingomyelin (d34:0)	SLM:000390716
TG(52:2;0)	Triacylglycerol (52:2)	SLM:000308298	SM(34:1;2)	Sphingomyelin (d34:1)	SLM:000390714
TG(52:3;0)	Triacylglycerol (52:3)	SLM:000308299	SM(34:2;2)	Sphingomyelin (d34:2)	SLM:000390712
TG(52:4;0)	Triacylglycerol (52:4)	SLM:000308300	SM(36:1;2)	Sphingomyelin (d36:1)	SLM:000390739
TG(52:5;0)	Triacylglycerol (52:5)	SLM:000308301	SM(36:2;2)	Sphingomyelin (d36:2)	SLM:000390737
TG(54:3;0)	Triacylglycerol (54:3)	SLM:000308323	SM(38:1;2)	Sphingomyelin (d38:1)	SLM:000390767
TG(54:4;0)	Triacylglycerol (54:4)	SLM:000308324	SM(38:2;2)	Sphingomyelin (d38:2)	SLM:000390765
TG(54:5;0)	Triacylglycerol (54:5)	SLM:000308325	SM(40:1;2)	Sphingomyelin (d40:1)	SLM:000390797
TG(54:6;0)	Triacylglycerol (54:6)	SLM:000308326	SM(40:2;2)	Sphingomyelin (d40:2)	SLM:000390795
TG(56:4;0)	Triacylglycerol (56:4)	SLM:000308350	SM(42:2;2)	Sphingomyelin (d42:2)	SLM:000390823

TG(56:5;0)	Triacylglycerol (56:5)	SLM:000308351	Cer(40:1;2)	Ceramide (d40:1)	SLM:000391319
TG(56:6;0)	Triacylglycerol (56:6)	SLM:000308352	Cer(40:2;2)	Ceramide (d40:2)	SLM:000391317
TG(56:7;0)	Triacylglycerol (56:7)	SLM:000308353	Cer(42:1;2)	Ceramide (d42:1)	SLM:000391346
PC(14:0;0_16:0;0)	Phosphatidylcholine (14:0_16:0)	SLM:000063559	Cer(42:2;2)	Ceramide (d42:2)	SLM:000391345
PC(14:0;0_18:1;0)	Phosphatidylcholine (14:0_18:1)	SLM:000063564	PI(16:0;0_18:1;0)	Phosphatidylinositol (16:0_18:1)	SLM:000073801
PC(14:0;0_18:2;0)	Phosphatidylcholine (14:0_18:2)	SLM:000063565	PI(16:0;0_18:2;0)	Phosphatidylinositol (16:0_18:2)	SLM:000073802
PC(15:0;0_18:2;0)	Phosphatidylcholine (15:0_18:2)	SLM:000063676	PI(16:0;0_20:4;0)	Phosphatidylinositol (16:0_20:4)	SLM:000073810
PC(16:0;0_16:0;0)	Phosphatidylcholine (16:0_16:0)	SLM:000063724	PI(18:0;0_18:1;0)	Phosphatidylinositol (18:0_18:1)	SLM:000074007
PC(16:0;0_16:1;0)	Phosphatidylcholine (16:0_16:1)	SLM:000063725	PI(18:0;0_18:2;0)	Phosphatidylinositol (18:0_18:2)	SLM:000074008
PC(16:0;0_17:1;0)	Phosphatidylcholine (16:0_17:1)	n/a	PI(18:0;0_20:3;0)	Phosphatidylinositol (18:0_20:3)	SLM:000074015
PC(16:0;0_18:0;0)	Phosphatidylcholine (16:0_18:0)	SLM:000063728	PI(18:0;0_20:4;0)	Phosphatidylinositol (18:0_20:4)	SLM:000074016
PC(16:0;0_18:1;0)	Phosphatidylcholine (16:0_18:1)	SLM:000063729	PI(18:1;0_18:1;0)	Phosphatidylinositol (18:1_18:1)	SLM:000074056
PC(16:0;0_18:2;0)	Phosphatidylcholine (16:0_18:2)	SLM:000063730	PI(18:1;0_18:2;0)	Phosphatidylinositol (18:1_18:2)	SLM:000074057
PC(16:0;0_18:3;0)	Phosphatidylcholine (16:0_18:3)	SLM:000063731	PI(18:2;0_18:2;0)	Phosphatidylinositol (18:2_18:2)	SLM:000074105
PC(16:0;0_20:1;0)	Phosphatidylcholine (16:0_20:1)	SLM:000063735	PE(16:0;0_18:2;0)	Phosphatidylethanolamine (16:0_18:2)	SLM:000067694
PC(16:0;0_20:2;0)	Phosphatidylcholine (16:0_20:2)	SLM:000063736	PE(18:0;0_18:2;0)	Phosphatidylethanolamine (18:0_18:2)	SLM:000067900
PC(16:0;0_20:3;0)	Phosphatidylcholine (16:0_20:3)	SLM:000063737	PE(18:0;0_20:4;0)	Phosphatidylethanolamine (18:0_20:4)	SLM:000067908
PC(16:0;0_20:4;0)	Phosphatidylcholine (16:0_20:4)	SLM:000063738	PE(18:1;0_18:1;0)	Phosphatidylethanolamine (18:1_18:1)	SLM:000067948
PC(16:0;0_20:5;0)	Phosphatidylcholine (16:0_20:5)	SLM:000063739	PEO(16:1;0/18:2;0)	Phosphatidylethanolamine (O-16:1_18:2)	SLM:000069954
PC(16:0;0_22:4;0)	Phosphatidylcholine (16:0_22:4)	SLM:000063745	PEO(16:1;0/20:4;0)	Phosphatidylethanolamine (O-16:1_20:4)	SLM:000069962
PC(16:0;0_22:5;0)	Phosphatidylcholine (16:0_22:5)	SLM:000063746	PEO(18:1;0/18:2;0)	Phosphatidylethanolamine (O-18:1_18:2)	SLM:000070214
PC(16:0;0_22:6;0)	Phosphatidylcholine (16:0_22:6)	SLM:000063747	PEO(18:2;0/18:2;0)	Phosphatidylethanolamine (O-18:2_18:2)	SLM:000070279
PC(16:1;0_18:1;0)	Phosphatidylcholine (16:1_18:1)	SLM:000063782	PEO(18:2;0/20:4;0)	Phosphatidylethanolamine (O-18:2_20:4)	SLM:000070287
PC(16:1;0_18:2;0)	Phosphatidylcholine (16:1_18:2)	SLM:000063783	LPE(16:0;0)	Phosphatidylethanolamine (16:0_0:0)	SLM:000067687
PC(17:0;0_18:2;0)	Phosphatidylcholine (17:0_18:2)	SLM:000063886	LPE(18:1;0)	Phosphatidylethanolamine (18:1_0:0)	SLM:000067947
PC(17:0;0_20:3;0)	Phosphatidylcholine (17:0_20:3)	SLM:000063893	LPE(18:2;0)	Phosphatidylethanolamine (18:2_0:0)	SLM:000067996
PC(17:0;0_20:4;0)	Phosphatidylcholine (17:0_20:4)	SLM:000063894	LPE(20:4;0)	Phosphatidylethanolamine (20:4_0:0)	SLM:000068352
PC(18:0;0_18:1;0)	Phosphatidylcholine (18:0_18:1)	SLM:000063935	LPE(22:6;0)	Phosphatidylethanolamine (22:6_0:0)	SLM:000068676
PC(18:0;0_18:2;0)	Phosphatidylcholine (18:0_18:2)	SLM:000063936	LPC(14:0;0)	Phosphatidylcholine (14:0_0:0)	SLM:000063555
PC(18:0;0_18:3;0)	Phosphatidylcholine (18:0_18:3)	SLM:000063937	LPC(16:0;0)	Phosphatidylcholine (16:0_0:0)	SLM:000063723
PC(18:0;0_20:2;0)	Phosphatidylcholine (18:0_20:2)	SLM:000063942	LPC(16:1;0)	Phosphatidylcholine (16:1_0:0)	SLM:000063777
PC(18:0;0_20:3;0)	Phosphatidylcholine (18:0_20:3)	SLM:000063943	LPC(18:0;0)	Phosphatidylcholine (18:0_0:0)	SLM:000063933
PC(18:0;0_20:4;0)	Phosphatidylcholine (18:0_20:4)	SLM:000063944	LPC(18:1;0)	Phosphatidylcholine (18:1_0:0)	SLM:000063983
PC(18:0;0_20:5;0)	Phosphatidylcholine (18:0_20:5)	SLM:000063945	LPC(18:2;0)	Phosphatidylcholine (18:2_0:0)	SLM:000064032
PC(18:0;0_22:5;0)	Phosphatidylcholine (18:0_22:5)	SLM:000063952	LPC(20:3;0)	Phosphatidylcholine (20:3_0:0)	SLM:000064347
PC(18:0;0_22:6;0)	Phosphatidylcholine (18:0_22:6)	SLM:000063953	LPC(20:4;0)	Phosphatidylcholine (20:4_0:0)	SLM:000064388
PC(18:1;0_18:1;0)	Phosphatidylcholine (18:1_18:1)	SLM:000063984	LPC(22:6;0)	Phosphatidylcholine (22:6_0:0)	SLM:000064712
PC(18:1;0_18:2;0)	Phosphatidylcholine (18:1_18:2)	SLM:000063985			

Table S7. Effect estimates in SD units (± SE) and p-values from linear mixed models for each lipid species.

Class	Species	Effect of high LDL-C affection in "high LDL-C" families		Effect of high LDL-C affection in FINRISK		Effect of high TG affection in "high TG" families		Effect of high TG affection in FINRISK		Independent association with LDL-C in EUFAM		Independent association with LDL-C in FINRISK		Independent association with TG in EUFAM		Independent association with TG in FINRISK	
			p-value		p-value		p-value		p-value		p-value		p-value		p-value		p-value
ST	Cholesterol	0.83 ± 0.093	5.4e-19*	0.93 ± 0.14	7.1e-11*	1 ± 0.12	1.3e-18*	0.99 ± 0.13	1.4e-13*	0.33 ± 0.029	4.2e-31*	0.39 ± 0.034	7.7e-30*	0.32 ± 0.029	3.3e-27*	0.25 ± 0.032	1.3e-14*
CE	CE(14;0;0)	0.64 ± 0.099	1.3e-10*	0.99 ± 0.14	2.1e-12*	0.75 ± 0.12	9.5e-10*	1 ± 0.13	7.5e-15*	0.24 ± 0.033	2.7e-13*	0.34 ± 0.033	1.4e-24*	0.31 ± 0.034	1e-19*	0.33 ± 0.031	1.9e-26*
	CE(15;0;0)	0.49 ± 0.1	1.1e-06*	0.84 ± 0.14	4.1e-09*	0.42 ± 0.13	0.0013*	0.26 ± 0.13	0.051	0.28 ± 0.036	8.7e-15*	0.32 ± 0.036	1.3e-18*	0.088 ± 0.037	0.017*	0.064 ± 0.034	0.061
	CE(16;0;0)	0.71 ± 0.078	7.3e-20*	1 ± 0.14	6.5e-14*	0.81 ± 0.11	1.4e-13*	0.75 ± 0.13	5e-09*	0.31 ± 0.027	7.1e-32*	0.42 ± 0.033	1.6e-37*	0.26 ± 0.027	1e-21*	0.2 ± 0.031	7.9e-11*
	CE(16;1;0)	0.44 ± 0.1	2.3e-05*	0.2 ± 0.14	0.15	0.92 ± 0.13	4.4e-13*	0.65 ± 0.13	6.3e-07*	0.16 ± 0.035	8.5e-06*	0.14 ± 0.036	0.00011*	0.37 ± 0.036	9.1e-25*	0.26 ± 0.034	1.6e-14*
	CE(17;0;0)	0.61 ± 0.097	4.6e-10*	0.85 ± 0.14	4.2e-09*	0.38 ± 0.12	0.0021*	0.24 ± 0.14	0.073	0.3 ± 0.035	3.4e-17*	0.34 ± 0.037	2.2e-20*	0.079 ± 0.036	0.03*	0.022 ± 0.035	0.53
	CE(17;1;0)	0.62 ± 0.098	2.9e-10*	1.1 ± 0.14	6.2e-16*	0.67 ± 0.13	1e-07*	0.79 ± 0.13	1.7e-09*	0.28 ± 0.034	1.2e-16*	0.41 ± 0.033	1.1e-35*	0.22 ± 0.035	2.1e-10*	0.24 ± 0.031	1.8e-14*
	CE(18;0;0)	0.75 ± 0.099	2.3e-14*	1.3 ± 0.14	6.8e-21*	0.95 ± 0.13	3.1e-13*	0.75 ± 0.13	1.1e-08*	0.32 ± 0.032	1.8e-23*	0.46 ± 0.033	4.4e-45*	0.31 ± 0.032	7.4e-22*	0.21 ± 0.031	5.2e-12*
	CE(18;1;0)	0.63 ± 0.089	1.6e-12*	1 ± 0.14	3.2e-14*	0.77 ± 0.12	3e-11*	0.71 ± 0.13	6.1e-08*	0.28 ± 0.031	1.2e-19*	0.41 ± 0.033	2.3e-35*	0.26 ± 0.031	1.7e-16*	0.19 ± 0.032	2.1e-09*
	CE(18;2;0)	0.63 ± 0.078	3.6e-16*	0.99 ± 0.14	1.4e-12*	0.45 ± 0.11	2.6e-05*	0.35 ± 0.13	0.008*	0.34 ± 0.027	3.7e-35*	0.43 ± 0.034	5.3e-36*	0.076 ± 0.028	0.0068*	0.046 ± 0.033	0.17
	CE(18;3;0)	0.48 ± 0.09	9.6e-08*	0.76 ± 0.15	4.5e-07*	0.74 ± 0.11	4.6e-11*	1 ± 0.13	3.8e-15*	0.2 ± 0.031	8.1e-11*	0.3 ± 0.035	3.1e-17*	0.28 ± 0.031	1.6e-19*	0.35 ± 0.032	1.2e-26*
	CE(19;1;0)	0.69 ± 0.11	9e-11*	0.92 ± 0.15	2.4e-10*	0.39 ± 0.15	0.01*	0.37 ± 0.15	0.013*	0.36 ± 0.041	1.1e-18*	0.36 ± 0.038	1.7e-21*	-0.0066 ± 0.047	0.89	-0.046 ± 0.038	0.22
	CE(20;2;0)	0.5 ± 0.1	8.2e-07*	0.76 ± 0.15	3.1e-07*	0.18 ± 0.14	0.22	-0.086 ± 0.15	0.57	0.34 ± 0.038	4.3e-19*	0.36 ± 0.038	6.5e-21*	-0.044 ± 0.042	0.3	-0.21 ± 0.038	1.6e-08*
	CE(20;3;0)	0.63 ± 0.093	1.2e-11*	0.94 ± 0.14	5.7e-11*	0.98 ± 0.13	1.4e-13*	0.91 ± 0.13	3.9e-12*	0.29 ± 0.031	5.3e-21*	0.38 ± 0.033	7.4e-31*	0.33 ± 0.031	7.2e-27*	0.34 ± 0.031	7.7e-28*
	CE(20;4;0)	0.62 ± 0.088	1.7e-12*	0.92 ± 0.14	3.9e-11*	0.65 ± 0.13	5.4e-07*	0.49 ± 0.13	0.00022*	0.32 ± 0.032	2.1e-23*	0.42 ± 0.034	6.9e-35*	0.16 ± 0.032	3.3e-07*	0.15 ± 0.032	2.8e-06*
	CE(20;5;0)	0.54 ± 0.092	3.8e-09*	0.55 ± 0.14	8.2e-05*	0.37 ± 0.12	0.0015*	0.27 ± 0.13	0.037*	0.26 ± 0.034	5.6e-15*	0.25 ± 0.036	5.2e-12*	0.12 ± 0.034	0.00044*	0.062 ± 0.034	0.066
	CE(22;6;0)	0.6 ± 0.088	1.2e-11*	0.58 ± 0.14	6e-05*	0.34 ± 0.11	0.0032*	0.17 ± 0.13	0.21	0.3 ± 0.033	1.7e-20*	0.25 ± 0.037	2.9e-11*	0.068 ± 0.033	0.038	0.03 ± 0.035	0.39
DG	DG(16;0;0_18;1;0)	0.31 ± 0.1	0.0023*	0.29 ± 0.14	0.041	1.5 ± 0.11	2.5e-42*	1.8 ± 0.12	6e-55*	-0.06 ± 0.021	0.0043*	-0.027 ± 0.024	0.27	0.75 ± 0.022	6e-255*	0.79 ± 0.023	6.8e-246*
	DG(18;1;0_18;1;0)	0.38 ± 0.1	0.00015*	0.33 ± 0.14	0.021	1.6 ± 0.12	3.7e-41*	1.7 ± 0.12	1.8e-47*	-0.026 ± 0.021	0.23	-0.014 ± 0.024	0.54	0.77 ± 0.022	1.8e-267*	0.78 ± 0.022	1.9e-260*
	DG(18;1;0_18;2;0)	0.43 ± 0.1	2.2e-05*	0.21 ± 0.14	0.14	1.5 ± 0.11	2.4e-38*	1.8 ± 0.12	3.9e-52*	0.0094 ± 0.024	0.7	-0.035 ± 0.024	0.14	0.72 ± 0.024	9e-194*	0.79 ± 0.023	7e-269*
TG	TG(48;0;0)	0.26 ± 0.1	0.01*	0.25 ± 0.15	0.096	1.3 ± 0.12	1.4e-30*	1.7 ± 0.12	7.8e-47*	-0.074 ± 0.026	0.0047*	-0.04 ± 0.027	0.15	0.68 ± 0.027	7.8e-144*	0.74 ± 0.026	3.7e-175*
	TG(48;1;0)	0.29 ± 0.1	0.0057*	0.26 ± 0.15	0.072	1.4 ± 0.12	3.2e-34*	1.8 ± 0.12	1.4e-53*	-0.055 ± 0.024	0.024*	-0.025 ± 0.022	0.27	0.74 ± 0.025	1.1e-190*	0.83 ± 0.021	<5e-324*
	TG(48;2;0)	0.28 ± 0.11	0.0088*	0.26 ± 0.16	0.094	1.5 ± 0.12	3.5e-36*	1.9 ± 0.12	4.4e-56*	-0.06 ± 0.025	0.014*	-0.044 ± 0.022	0.043	0.77 ± 0.025	2.1e-200*	0.86 ± 0.02	<5e-324*
	TG(50;1;0)	0.32 ± 0.1	0.0013*	0.26 ± 0.15	0.076	1.5 ± 0.11	1.4e-39*	1.7 ± 0.12	2.5e-46*	-0.06 ± 0.021	0.0043*	-0.011 ± 0.026	0.67	0.76 ± 0.022	1.4e-266*	0.76 ± 0.024	1.3e-218*

PC	TG(50;2;0)	0.34 ± 0.1	0.0011*	0.31 ± 0.15	0.039	1.6 ± 0.12	1.5e-45*	1.8 ± 0.12	6.3e-49*	-0.058 ± 0.02	0.0033*	0.00052 ± 0.024	0.98	0.82 ± 0.02	<5e-324*	0.8 ± 0.022	2.5e-277*
	TG(50;3;0)	0.36 ± 0.11	0.00054*	0.25 ± 0.15	0.084	1.6 ± 0.12	4e-45*	1.8 ± 0.12	3e-51*	-0.042 ± 0.02	0.04	-0.03 ± 0.022	0.17	0.83 ± 0.021	<5e-324*	0.82 ± 0.021	<5e-324*
	TG(50;4;0)	0.34 ± 0.11	0.0016*	0.21 ± 0.15	0.16	1.5 ± 0.12	1.4e-39*	1.9 ± 0.12	2.3e-56*	-0.038 ± 0.022	0.083	-0.075 ± 0.022	0.00048*	0.81 ± 0.023	1.1e-283*	0.85 ± 0.02	<5e-324*
	TG(51;2;0)	0.38 ± 0.1	0.00026*	0.32 ± 0.15	0.028	1.5 ± 0.11	5.4e-41*	1.8 ± 0.12	4.5e-53*	-0.018 ± 0.023	0.42	0.0012 ± 0.019	0.95	0.77 ± 0.023	4.3e-244*	0.87 ± 0.019	<5e-324*
	TG(51;3;0)	0.44 ± 0.11	3.5e-05*	0.39 ± 0.15	0.012*	1.5 ± 0.12	1.4e-40*	1.8 ± 0.12	6.2e-53*	0.0087 ± 0.022	0.7	-0.016 ± 0.021	0.44	0.78 ± 0.022	9.7e-264*	0.86 ± 0.019	<5e-324*
	TG(52;2;0)	0.37 ± 0.1	2e-04*	0.12 ± 0.14	0.4	1.6 ± 0.11	1.8e-49*	1.4 ± 0.12	8.7e-32*	-0.031 ± 0.018	0.086	-0.0023 ± 0.029	0.94	0.8 ± 0.019	<5e-324*	0.66 ± 0.028	1.9e-124*
	TG(52;3;0)	0.42 ± 0.1	4.1e-05*	0.16 ± 0.15	0.28	1.6 ± 0.12	8.2e-44*	1.5 ± 0.12	2.4e-36*	-0.0075 ± 0.021	0.72	-0.04 ± 0.029	0.16	0.79 ± 0.022	2.1e-289*	0.67 ± 0.027	2.9e-137*
	TG(52;4;0)	0.4 ± 0.1	8.5e-05*	0.25 ± 0.15	0.093	1.5 ± 0.12	5.8e-38*	1.5 ± 0.12	2.2e-34*	0.0019 ± 0.024	0.94	-0.0072 ± 0.028	0.8	0.76 ± 0.024	3.4e-217*	0.69 ± 0.027	9.5e-147*
	TG(52;5;0)	0.39 ± 0.1	2e-04*	0.2 ± 0.15	0.17	1.5 ± 0.12	2.6e-36*	1.8 ± 0.12	1.4e-52*	-0.0045 ± 0.024	0.85	-0.066 ± 0.023	0.0047*	0.76 ± 0.024	5.5e-215*	0.81 ± 0.022	5.8e-298*
	TG(54;3;0)	0.33 ± 0.099	0.00072*	0.15 ± 0.15	0.32	1.5 ± 0.12	1.4e-36*	1.4 ± 0.13	2.8e-27*	-0.037 ± 0.023	0.11	-0.032 ± 0.031	0.29	0.73 ± 0.024	6e-207*	0.62 ± 0.029	5.8e-102*
	TG(54;4;0)	0.34 ± 0.1	0.00067*	0.068 ± 0.15	0.64	1.4 ± 0.12	2.4e-32*	1.4 ± 0.12	2.3e-28*	-0.027 ± 0.026	0.3	-0.076 ± 0.03	0.012*	0.7 ± 0.027	8.5e-153*	0.62 ± 0.028	7.6e-108*
	TG(54;5;0)	0.35 ± 0.1	0.00046*	0.19 ± 0.15	0.19	1.4 ± 0.11	1.2e-35*	1.6 ± 0.12	4.7e-42*	-0.021 ± 0.025	0.41	-0.076 ± 0.029	0.0082*	0.72 ± 0.025	1.2e-175*	0.68 ± 0.027	1.4e-141*
	TG(54;6;0)	0.4 ± 0.099	6.6e-05*	0.24 ± 0.14	0.094	1.4 ± 0.11	2.3e-35*	1.7 ± 0.12	2.2e-48*	-0.0034 ± 0.024	0.89	-0.08 ± 0.026	0.0025*	0.71 ± 0.024	1.8e-185*	0.71 ± 0.025	5e-181*
	TG(56;4;0)	0.33 ± 0.11	0.0029*	0.012 ± 0.15	0.94	1.5 ± 0.11	6.3e-43*	1.8 ± 0.12	2.1e-49*	-0.028 ± 0.024	0.26	-0.12 ± 0.025	7.3e-07*	0.74 ± 0.024	1.5e-216*	0.81 ± 0.024	1.5e-245*
	TG(56;5;0)	0.4 ± 0.098	5.2e-05*	0.26 ± 0.15	0.082	1.5 ± 0.1	3.9e-46*	1.8 ± 0.12	2.2e-49*	0.017 ± 0.023	0.45	-0.015 ± 0.024	0.52	0.7 ± 0.023	2.7e-212*	0.8 ± 0.023	2.1e-269*
	TG(56;6;0)	0.43 ± 0.096	6.2e-06*	0.43 ± 0.14	0.0027*	1.4 ± 0.1	3.3e-42*	1.7 ± 0.12	1.7e-46*	0.027 ± 0.022	0.23	0.045 ± 0.026	0.079	0.69 ± 0.022	1.6e-208*	0.71 ± 0.024	8.7e-191*
	TG(56;7;0)	0.46 ± 0.096	1.3e-06*	0.36 ± 0.14	0.014*	1.3 ± 0.11	3.8e-31*	1.4 ± 0.12	4.8e-30*	0.061 ± 0.025	0.016*	0.072 ± 0.03	0.016*	0.61 ± 0.026	9.6e-122*	0.58 ± 0.028	8.6e-91*
	PC(14;0;0_16;0;0)	0.26 ± 0.11	0.019*	0.19 ± 0.14	0.18	0.58 ± 0.13	4.2e-06*	0.85 ± 0.13	4.7e-11*	0.029 ± 0.039	0.46	0.0087 ± 0.036	0.81	0.29 ± 0.039	7.2e-14*	0.32 ± 0.034	1.3e-21*
	PC(14;0;0_18;1;0)	0.13 ± 0.11	0.23	0.079 ± 0.15	0.59	0.61 ± 0.12	6e-07*	0.95 ± 0.13	5e-13*	-0.034 ± 0.037	0.35	0.0035 ± 0.035	0.92	0.37 ± 0.036	6.8e-24*	0.39 ± 0.034	6.4e-31*
	PC(14;0;0_18;2;0)	0.11 ± 0.1	0.26	0.15 ± 0.16	0.33	0.56 ± 0.11	3e-07*	0.98 ± 0.14	5.3e-13*	0.00082 ± 0.034	0.98	0.0067 ± 0.039	0.86	0.28 ± 0.034	7.6e-16*	0.37 ± 0.035	3.9e-25*
	PC(15;0;0_18;2;0)	0.22 ± 0.1	0.033*	0.24 ± 0.16	0.13	0.51 ± 0.12	2.1e-05*	0.83 ± 0.15	2.2e-08*	0.0014 ± 0.038	0.97	-0.0068 ± 0.04	0.86	0.27 ± 0.04	1.8e-11*	0.26 ± 0.038	8.2e-12*
	PC(16;0;0_16;0;0)	0.3 ± 0.086	0.00052*	0.48 ± 0.14	0.00089*	0.63 ± 0.1	8.2e-10*	0.65 ± 0.13	6.9e-07*	0.053 ± 0.031	0.092	0.09 ± 0.037	0.015*	0.22 ± 0.033	1.6e-11*	0.16 ± 0.035	6.7e-06*
	PC(16;0;0_16;1;0)	0.13 ± 0.11	0.25	0.082 ± 0.15	0.57	0.95 ± 0.12	2.2e-14*	1.1 ± 0.13	1.3e-17*	-0.048 ± 0.037	0.19	-0.035 ± 0.035	0.31	0.41 ± 0.037	1.1e-29*	0.42 ± 0.033	2.7e-37*
	PC(16;0;0_17;1;0)	0.027 ± 0.09	0.77	0.075 ± 0.16	0.63	0.52 ± 0.11	3e-06*	0.4 ± 0.14	0.0039*	-0.023 ± 0.033	0.48	-0.022 ± 0.039	0.58	0.26 ± 0.033	1.2e-14*	0.23 ± 0.037	5.9e-10*
	PC(16;0;0_18;0;0)	0.32 ± 0.089	3e-04*	0.12 ± 0.15	0.44	0.5 ± 0.11	8.7e-06*	0.49 ± 0.14	0.00036*	0.13 ± 0.032	1e-04*	0.033 ± 0.039	0.4	0.19 ± 0.033	1.1e-08*	0.15 ± 0.037	4.4e-05*
	PC(16;0;0_18;1;0)	0.23 ± 0.1	0.026*	0.16 ± 0.14	0.28	0.93 ± 0.11	1.2e-16*	1 ± 0.13	1.1e-15*	-0.015 ± 0.035	0.67	0.028 ± 0.035	0.43	0.39 ± 0.035	9.2e-28*	0.38 ± 0.034	2.3e-29*
	PC(16;0;0_18;2;0)	0.3 ± 0.095	0.0013*	0.082 ± 0.15	0.58	0.77 ± 0.11	5e-12*	0.73 ± 0.13	4.2e-08*	0.058 ± 0.034	0.082	0.00071 ± 0.037	0.98	0.3 ± 0.034	5.1e-18*	0.25 ± 0.035	1.8e-12*
	PC(16;0;0_18;3;0)	0.19 ± 0.11	0.083	-3e-04 ± 0.15	1	0.68 ± 0.13	1.8e-07*	1 ± 0.13	8.5e-15*	0.006 ± 0.038	0.87	-0.048 ± 0.035	0.17	0.36 ± 0.038	1.4e-21*	0.41 ± 0.033	4.3e-34*
	PC(16;0;0_20;1;0)	0.32 ± 0.1	0.0025*	0.45 ± 0.15	0.0028*	0.58 ± 0.12	3.4e-06*	0.82 ± 0.14	2.7e-09*	0.11 ± 0.038	0.0035*	0.054 ± 0.038	0.16	0.18 ± 0.038	4e-06*	0.24 ± 0.036	2.3e-11*
	PC(16;0;0_20;2;0)	0.42 ± 0.1	2.7e-05*	0.13 ± 0.15	0.37	0.91 ± 0.12	1.5e-13*	0.79 ± 0.14	6.1e-09*	0.1 ± 0.033	0.002*	0.051 ± 0.037	0.17	0.39 ± 0.034	2.4e-30*	0.32 ± 0.035	6.8e-20*

	PC(16:0;0_20:3;0)	0.39 ± 0.1	9.5e-05*	0.13 ± 0.15	0.37	1.2 ± 0.13	3.2e-21*	1.2 ± 0.13	8e-21*	0.027 ± 0.031	0.39	0.023 ± 0.033	0.49	0.53 ± 0.032	7.3e-61*	0.5 ± 0.032	1.3e-56*
	PC(16:0;0_20:4;0)	0.25 ± 0.092	0.0079*	0.21 ± 0.15	0.15	0.9 ± 0.12	2.1e-13*	0.77 ± 0.13	7.1e-09*	0.0024 ± 0.033	0.94	0.068 ± 0.036	0.059	0.37 ± 0.033	2.3e-29*	0.33 ± 0.034	2.2e-21*
	PC(16:0;0_20:5;0)	0.31 ± 0.1	0.0024*	0.36 ± 0.14	0.011*	0.49 ± 0.12	4e-05*	0.48 ± 0.13	0.00019*	0.067 ± 0.036	0.061	0.08 ± 0.037	0.029*	0.26 ± 0.036	6.5e-13*	0.12 ± 0.035	0.00034*
	PC(16:0;0_22:4;0)	0.24 ± 0.098	0.016*	0.24 ± 0.16	0.14	0.69 ± 0.13	5e-08*	0.95 ± 0.14	3.1e-12*	0.031 ± 0.035	0.37	0.083 ± 0.039	0.031*	0.27 ± 0.036	2.5e-14*	0.33 ± 0.036	1.3e-19*
	PC(16:0;0_22:5;0)	0.4 ± 0.1	6.1e-05*	0.28 ± 0.14	0.049	0.68 ± 0.12	2.5e-08*	0.67 ± 0.13	2.6e-07*	0.11 ± 0.035	0.0015*	0.055 ± 0.037	0.14	0.3 ± 0.035	1.3e-17*	0.24 ± 0.035	1.3e-11*
	PC(16:0;0_22:6;0)	0.45 ± 0.095	1.8e-06*	0.28 ± 0.14	0.05	0.58 ± 0.12	1.2e-06*	0.42 ± 0.13	0.00099*	0.13 ± 0.034	8.5e-05*	0.067 ± 0.036	0.066	0.24 ± 0.034	1.8e-12*	0.14 ± 0.035	6.3e-05*
	PC(16:1;0_18:1;0)	0.083 ± 0.11	0.43	-0.025 ± 0.15	0.86	0.62 ± 0.12	2.4e-07*	0.6 ± 0.13	4.4e-06*	-0.059 ± 0.037	0.11	-0.035 ± 0.037	0.34	0.32 ± 0.037	5.3e-18*	0.29 ± 0.035	5.2e-17*
	PC(16:1;0_18:2;0)	0.09 ± 0.1	0.38	-0.15 ± 0.15	0.3	0.53 ± 0.12	7.5e-06*	0.75 ± 0.13	1.6e-08*	-0.0016 ± 0.037	0.96	-0.1 ± 0.036	0.0047*	0.25 ± 0.037	7.8e-12*	0.29 ± 0.034	8.7e-18*
	PC(17:0;0_18:2;0)	0.37 ± 0.096	0.00014*	0.36 ± 0.15	0.017*	0.56 ± 0.13	8.4e-06*	0.33 ± 0.14	0.017*	0.075 ± 0.036	0.037	0.059 ± 0.039	0.13	0.24 ± 0.037	7.4e-11*	0.13 ± 0.037	0.00027*
	PC(17:0;0_20:3;0)	0.4 ± 0.11	0.00046*	0.33 ± 0.15	0.029	0.44 ± 0.13	0.00086*	0.59 ± 0.14	1.9e-05*	0.12 ± 0.04	0.0017*	0.082 ± 0.038	0.032*	0.27 ± 0.039	3.3e-12*	0.25 ± 0.036	2.8e-12*
	PC(17:0;0_20:4;0)	0.27 ± 0.1	0.0066*	0.38 ± 0.15	0.011*	0.5 ± 0.13	7.7e-05*	0.58 ± 0.14	2.1e-05*	0.026 ± 0.037	0.48	0.15 ± 0.038	0.00011*	0.28 ± 0.037	9.8e-15*	0.24 ± 0.036	2.2e-11*
	PC(18:0;0_18:1;0)	0.3 ± 0.099	0.0025*	0.4 ± 0.15	0.0058*	0.68 ± 0.13	1.2e-07*	0.63 ± 0.13	1.7e-06*	0.066 ± 0.038	0.081	0.12 ± 0.037	0.0015*	0.3 ± 0.038	2.5e-15*	0.24 ± 0.035	2.3e-12*
	PC(18:0;0_18:2;0)	0.44 ± 0.092	2e-06*	0.29 ± 0.15	0.045	0.75 ± 0.11	2.1e-11*	0.71 ± 0.13	8.7e-08*	0.14 ± 0.033	4e-05*	0.09 ± 0.037	0.016*	0.27 ± 0.033	2.6e-16*	0.21 ± 0.036	2.2e-09*
	PC(18:0;0_18:3;0)	0.21 ± 0.094	0.028*	0.17 ± 0.16	0.28	0.56 ± 0.12	1e-06*	1 ± 0.14	7.5e-14*	0.047 ± 0.033	0.15	0.014 ± 0.038	0.71	0.3 ± 0.034	5.5e-19*	0.35 ± 0.035	7.6e-24*
	PC(18:0;0_20:2;0)	0.47 ± 0.1	3.2e-06*	0.38 ± 0.15	0.011*	0.71 ± 0.12	2.5e-09*	0.67 ± 0.14	2.5e-06*	0.15 ± 0.034	8.8e-06*	0.088 ± 0.039	0.022*	0.29 ± 0.034	3.1e-17*	0.22 ± 0.038	6.4e-09*
	PC(18:0;0_20:3;0)	0.48 ± 0.098	1.1e-06*	0.31 ± 0.15	0.033	1.3 ± 0.13	1.3e-22*	1.3 ± 0.13	2.4e-26*	0.1 ± 0.03	0.00056*	0.081 ± 0.033	0.013*	0.54 ± 0.03	6.7e-70*	0.53 ± 0.031	1.5e-66*
	PC(18:0;0_20:4;0)	0.42 ± 0.085	5.6e-07*	0.46 ± 0.15	0.0016*	0.88 ± 0.12	3.6e-13*	0.76 ± 0.13	1e-08*	0.11 ± 0.03	0.00019*	0.15 ± 0.036	2.4e-05*	0.33 ± 0.031	5e-27*	0.29 ± 0.034	6.5e-17*
	PC(18:0;0_20:5;0)	0.39 ± 0.1	0.00011*	0.24 ± 0.14	0.098	0.44 ± 0.13	0.00058*	0.48 ± 0.13	0.00028*	0.12 ± 0.036	0.00097*	0.11 ± 0.037	0.002*	0.23 ± 0.036	1.5e-10*	0.12 ± 0.035	0.00074*
	PC(18:0;0_22:5;0)	0.45 ± 0.09	6.9e-07*	0.34 ± 0.15	0.019	0.76 ± 0.12	5.4e-11*	1.1 ± 0.13	4.3e-17*	0.15 ± 0.03	1e-06*	0.088 ± 0.036	0.013*	0.32 ± 0.031	1.3e-24*	0.36 ± 0.034	1.2e-26*
	PC(18:0;0_22:6;0)	0.54 ± 0.091	3.5e-09*	0.45 ± 0.14	0.0017*	0.67 ± 0.11	2.3e-09*	0.83 ± 0.13	2.7e-10*	0.17 ± 0.032	7.4e-08*	0.12 ± 0.036	0.001*	0.27 ± 0.032	3.9e-17*	0.23 ± 0.035	1e-11*
	PC(18:1;0_18:1;0)	0.065 ± 0.1	0.52	0.12 ± 0.15	0.4	0.23 ± 0.12	0.064	0.52 ± 0.13	9.7e-05*	-0.045 ± 0.036	0.22	-0.0037 ± 0.038	0.92	0.19 ± 0.037	4.6e-07*	0.18 ± 0.036	8.7e-07*
	PC(18:1;0_18:2;0)	0.19 ± 0.099	0.052	0.059 ± 0.15	0.69	0.37 ± 0.12	0.0018*	0.32 ± 0.13	0.017*	0.031 ± 0.036	0.39	-0.033 ± 0.038	0.39	0.16 ± 0.037	1.2e-05*	0.1 ± 0.036	0.0051*
	PC(18:1;0_20:3;0)	0.36 ± 0.1	0.00032*	0.099 ± 0.15	0.5	0.84 ± 0.12	4.1e-12*	0.73 ± 0.13	4.5e-08*	0.072 ± 0.033	0.029*	0.041 ± 0.036	0.26	0.37 ± 0.034	5.3e-28*	0.38 ± 0.034	4.7e-28*
	PC(18:1;0_20:4;0)	0.24 ± 0.089	0.0069*	0.25 ± 0.15	0.089	0.59 ± 0.12	6.7e-07*	0.56 ± 0.13	3.7e-05*	0.029 ± 0.032	0.37	0.072 ± 0.038	0.058	0.27 ± 0.033	1.9e-16*	0.21 ± 0.036	2.5e-09*
	PC(18:2;0_18:2;0)	0.11 ± 0.1	0.28	0.059 ± 0.15	0.69	0.15 ± 0.12	0.23	0.22 ± 0.14	0.11	0.038 ± 0.038	0.32	-0.034 ± 0.038	0.38	0.025 ± 0.039	0.53	0.045 ± 0.036	0.22
	PC(18:2;0_20:4;0)	0.43 ± 0.11	7.6e-05*	0.05 ± 0.16	0.75	0.54 ± 0.14	0.00014*	0.38 ± 0.15	0.0084*	0.11 ± 0.039	0.0073*	0.0077 ± 0.04	0.85	0.19 ± 0.041	2.4e-06*	0.13 ± 0.038	0.00099*
PCO	PCO(16:0;0/16:0;0)	0.31 ± 0.097	0.0012*	0.35 ± 0.15	0.019	0.46 ± 0.13	0.00031*	0.34 ± 0.14	0.014*	0.083 ± 0.037	0.026*	0.083 ± 0.039	0.032*	0.18 ± 0.037	1e-06*	0.038 ± 0.037	0.31
	PCO(16:0;0/16:1;0)	-0.00036 ± 0.11	1	0.19 ± 0.15	0.22	0.26 ± 0.13	0.05	0.57 ± 0.14	4.3e-05*	-0.049 ± 0.04	0.23	0.0052 ± 0.039	0.9	0.12 ± 0.041	0.0043*	0.16 ± 0.037	1.1e-05*
	PCO(16:0;0/18:1;0)	0.051 ± 0.089	0.56	0.29 ± 0.15	0.049	-0.18 ± 0.11	0.082	-0.16 ± 0.14	0.24	0.031 ± 0.032	0.32	0.07 ± 0.038	0.065	-0.17 ± 0.033	2.9e-07*	-0.21 ± 0.036	2.6e-09*
	PCO(16:0;0/18:2;0)	0.23 ± 0.1	0.024*	0.2 ± 0.15	0.17	-0.14 ± 0.12	0.25	-0.28 ± 0.14	0.038*	0.14 ± 0.038	0.00014*	0.086 ± 0.038	0.024*	-0.16 ± 0.038	3.3e-05*	-0.21 ± 0.036	6.7e-09*



SM	PCO(16:0;0/20:3;0)	0.45 ± 0.097	3e-06*	0.4 ± 0.15	0.008*	0.46 ± 0.13	0.00027*	0.36 ± 0.14	0.0081*	0.17 ± 0.036	3.3e-06*	0.23 ± 0.038	2.4e-09*	0.1 ± 0.036	0.0041*	0.12 ± 0.036	0.00096*
	PCO(16:0;0/20:4;0)	0.42 ± 0.1	4.6e-05*	0.43 ± 0.15	0.0032*	0.41 ± 0.14	0.0038*	0.26 ± 0.13	0.048	0.14 ± 0.038	0.00029*	0.22 ± 0.037	3.5e-09*	0.11 ± 0.039	0.0029*	0.0033 ± 0.035	0.93
	PCO(16:1;0/16:0;0)	0.11 ± 0.11	0.29	0.12 ± 0.15	0.44	-0.37 ± 0.12	0.0019*	-0.38 ± 0.14	0.007*	0.089 ± 0.038	0.018*	0.058 ± 0.039	0.13	-0.27 ± 0.038	1.3e-12*	-0.2 ± 0.037	5.5e-08*
	PCO(16:1;0/18:1;0)	-8e-04 ± 0.1	0.99	0.26 ± 0.15	0.072	-0.43 ± 0.12	0.00031*	-0.53 ± 0.13	7e-05*	0.076 ± 0.036	0.035	0.13 ± 0.036	0.00026*	-0.32 ± 0.037	1.1e-17*	-0.33 ± 0.034	2.5e-22*
	PCO(16:1;0/18:2;0)	0.12 ± 0.1	0.26	0.27 ± 0.15	0.071	-0.19 ± 0.12	0.1	-0.39 ± 0.14	0.0039*	0.12 ± 0.037	0.0011*	0.1 ± 0.037	0.0072*	-0.21 ± 0.038	2.4e-08*	-0.27 ± 0.035	5.3e-14*
	PCO(16:1;0/20:3;0)	0.33 ± 0.11	0.0034*	0.17 ± 0.16	0.27	0.26 ± 0.15	0.085	0.19 ± 0.15	0.21	0.15 ± 0.042	3e-04*	0.16 ± 0.041	7.4e-05*	0.0052 ± 0.043	0.9	0.0044 ± 0.039	0.91
	PCO(17:0;0/17:1;0)	0.12 ± 0.097	0.21	0.5 ± 0.15	0.0011*	0.16 ± 0.13	0.23	0.4 ± 0.14	0.004*	0.062 ± 0.038	0.097	0.12 ± 0.039	0.0013*	0.017 ± 0.038	0.66	0.11 ± 0.037	0.0019*
	PCO(18:0;0/14:0;0)	-0.24 ± 0.096	0.012*	-0.058 ± 0.15	0.7	-0.63 ± 0.12	3.7e-07*	-0.63 ± 0.14	3.8e-06*	-0.027 ± 0.033	0.41	0.07 ± 0.038	0.066	-0.33 ± 0.033	1.8e-23*	-0.25 ± 0.036	3e-12*
	PCO(18:0;0/18:2;0)	0.16 ± 0.096	0.11	0.24 ± 0.15	0.11	-0.28 ± 0.13	0.025*	-0.2 ± 0.16	0.21	0.1 ± 0.034	0.0026*	0.08 ± 0.039	0.039	-0.23 ± 0.038	1.3e-09*	-0.3 ± 0.039	1.6e-14*
	PCO(18:0;0/20:4;0)	0.35 ± 0.1	0.00047*	0.42 ± 0.15	0.0047*	0.063 ± 0.13	0.62	-0.015 ± 0.14	0.91	0.17 ± 0.037	6.7e-06*	0.18 ± 0.038	2.2e-06*	-0.13 ± 0.038	0.00041*	-0.16 ± 0.036	9.1e-06*
	PCO(18:1;0/16:0;0)	-0.0099 ± 0.097	0.92	0.2 ± 0.15	0.18	-0.25 ± 0.12	0.035*	-0.32 ± 0.14	0.018*	0.0093 ± 0.035	0.79	0.073 ± 0.037	0.051	-0.19 ± 0.035	1.1e-07*	-0.31 ± 0.035	2.5e-18*
	PCO(18:1;0/18:1;0)	-0.038 ± 0.1	0.71	0.046 ± 0.15	0.76	-0.51 ± 0.14	0.00022*	-0.038 ± 0.16	0.81	-0.021 ± 0.038	0.58	0.073 ± 0.039	0.061	-0.22 ± 0.041	1.2e-07*	-0.24 ± 0.04	1e-09*
	PCO(18:1;0/18:2;0)	0.16 ± 0.1	0.12	0.26 ± 0.15	0.085	-0.3 ± 0.13	0.022*	-0.44 ± 0.14	0.0014*	0.12 ± 0.038	0.0015*	0.13 ± 0.037	0.00062*	-0.21 ± 0.039	4e-08*	-0.29 ± 0.035	2e-16*
	PCO(18:1;0/20:3;0)	0.24 ± 0.092	0.0098*	0.036 ± 0.15	0.81	0.17 ± 0.12	0.17	0.0061 ± 0.14	0.97	0.065 ± 0.035	0.059	0.083 ± 0.039	0.034*	0.035 ± 0.036	0.33	-0.0088 ± 0.037	0.81
	PCO(18:1;0/20:4;0)	0.28 ± 0.11	0.011*	0.34 ± 0.15	0.024	0.14 ± 0.14	0.33	-0.032 ± 0.14	0.82	0.11 ± 0.04	0.0065*	0.16 ± 0.038	2.1e-05*	-0.019 ± 0.041	0.64	-0.15 ± 0.036	5.8e-05*
	PCO(18:2;0/16:0;0)	0.17 ± 0.11	0.12	0.3 ± 0.15	0.045	-0.041 ± 0.14	0.77	-0.29 ± 0.14	0.035*	0.058 ± 0.04	0.15	0.083 ± 0.038	0.028*	-0.046 ± 0.041	0.26	-0.22 ± 0.036	7.2e-10*
	PCO(18:2;0/18:0;0)	0.079 ± 0.097	0.41	0.26 ± 0.15	0.087	0.015 ± 0.14	0.91	-0.18 ± 0.16	0.28	0.059 ± 0.036	0.098	0.11 ± 0.04	0.0078*	-0.11 ± 0.04	0.0062*	-0.27 ± 0.04	1.2e-11*
	PCO(18:2;0/18:1;0)	0.12 ± 0.1	0.24	0.28 ± 0.15	0.065	-0.13 ± 0.13	0.3	-0.65 ± 0.13	1e-06*	0.074 ± 0.037	0.043	0.14 ± 0.037	1e-04*	-0.17 ± 0.037	4e-06*	-0.33 ± 0.035	8.5e-22*
	PCO(18:2;0/18:2;0)	0.13 ± 0.098	0.19	0.18 ± 0.15	0.23	-0.15 ± 0.12	0.21	-0.29 ± 0.14	0.032*	0.099 ± 0.035	0.0049*	0.12 ± 0.038	0.0024*	-0.17 ± 0.037	3.1e-06*	-0.22 ± 0.036	1.8e-09*
SM	SM(32:1;2)	0.52 ± 0.099	1.7e-07*	0.91 ± 0.14	5.6e-11*	0.44 ± 0.13	0.00058*	0.22 ± 0.13	0.082	0.26 ± 0.035	1.2e-13*	0.33 ± 0.035	1.8e-21*	0.097 ± 0.035	0.006*	0.038 ± 0.033	0.25
	SM(34:0;2)	0.55 ± 0.099	2.2e-08*	1 ± 0.14	3.6e-13*	0.18 ± 0.12	0.14	0.036 ± 0.13	0.79	0.28 ± 0.037	7.8e-15*	0.37 ± 0.035	1.3e-25*	-0.0017 ± 0.037	0.96	-0.17 ± 0.034	7.3e-07*
	SM(34:1;2)	0.56 ± 0.086	8.7e-11*	0.72 ± 0.14	1.8e-07*	0.15 ± 0.11	0.19	-0.036 ± 0.13	0.79	0.31 ± 0.031	2.7e-23*	0.33 ± 0.035	3.4e-21*	-0.098 ± 0.032	0.0023*	-0.11 ± 0.034	0.0013*
	SM(34:2;2)	0.43 ± 0.081	1.1e-07*	0.7 ± 0.14	2.8e-07*	0.44 ± 0.11	5e-05*	0.19 ± 0.13	0.13	0.23 ± 0.03	7.3e-15*	0.28 ± 0.035	6e-16*	0.087 ± 0.03	0.004*	0.0088 ± 0.033	0.79
	SM(36:1;2)	0.57 ± 0.084	1.2e-11*	0.94 ± 0.14	1.3e-11*	0.43 ± 0.13	0.00098*	0.35 ± 0.13	0.0079*	0.31 ± 0.031	4.2e-23*	0.39 ± 0.035	2.9e-29*	0.062 ± 0.032	0.053	0.039 ± 0.033	0.24
	SM(36:2;2)	0.41 ± 0.087	2.1e-06*	0.8 ± 0.14	3.2e-09*	0.36 ± 0.13	0.0053*	0.28 ± 0.13	0.026*	0.27 ± 0.032	6.8e-17*	0.33 ± 0.034	2.7e-22*	0.059 ± 0.032	0.068	-0.0013 ± 0.033	0.97
	SM(38:1;2)	0.64 ± 0.088	4.9e-13*	0.98 ± 0.14	4.5e-12*	0.47 ± 0.12	8.7e-05*	0.34 ± 0.13	0.011*	0.32 ± 0.031	1.8e-25*	0.38 ± 0.035	6.2e-27*	0.089 ± 0.032	0.0047*	0.051 ± 0.033	0.13
	SM(38:2;2)	0.43 ± 0.088	1.3e-06*	0.65 ± 0.14	1.8e-06*	0.28 ± 0.12	0.024*	0.048 ± 0.13	0.71	0.28 ± 0.032	4.7e-19*	0.29 ± 0.035	3.4e-17*	0.0082 ± 0.032	0.8	-0.066 ± 0.033	0.045
	SM(40:1;2)	0.65 ± 0.078	1.1e-16*	0.99 ± 0.14	2.6e-12*	0.49 ± 0.11	1.3e-05*	0.35 ± 0.13	0.0088*	0.32 ± 0.028	3e-31*	0.41 ± 0.035	2.7e-31*	0.1 ± 0.028	0.00035*	0.049 ± 0.033	0.14
	SM(40:2;2)	0.59 ± 0.086	8e-12*	0.85 ± 0.14	1.1e-09*	0.28 ± 0.12	0.014*	0.13 ± 0.13	0.32	0.33 ± 0.029	9.4e-30*	0.34 ± 0.035	4.8e-22*	0.00011 ± 0.03	1	-0.041 ± 0.033	0.22
	SM(42:2;2)	0.63 ± 0.087	6.9e-13*	0.66 ± 0.14	3e-06*	0.2 ± 0.12	0.092	0.14 ± 0.13	0.3	0.34 ± 0.032	5.5e-27*	0.3 ± 0.036	5.9e-17*	-0.04 ± 0.032	0.22	-0.039 ± 0.034	0.26

Cer	Cer(40:1;2)	0.49 ± 0.092	1.1e-07*	0.74 ± 0.14	2.2e-07*	0.97 ± 0.12	2.5e-16*	0.98 ± 0.13	2.2e-14*	0.2 ± 0.032	5.5e-10*	0.26 ± 0.035	4.5e-14*	0.34 ± 0.032	3.4e-27*	0.31 ± 0.033	6.8e-21*
	Cer(40:2;2)	0.31 ± 0.09	0.00054*	0.45 ± 0.15	0.003*	0.84 ± 0.11	1.1e-13*	0.7 ± 0.14	5.1e-07*	0.14 ± 0.031	1e-05*	0.11 ± 0.039	0.005*	0.3 ± 0.032	5.5e-22*	0.23 ± 0.037	7.5e-10*
	Cer(42:1;2)	0.44 ± 0.072	1.5e-09*	0.99 ± 0.14	6.8e-13*	0.87 ± 0.099	1e-18*	1.1 ± 0.13	4.8e-19*	0.19 ± 0.025	3e-14*	0.33 ± 0.033	1.5e-24*	0.26 ± 0.025	3e-24*	0.32 ± 0.031	7e-26*
	Cer(42:2;2)	0.35 ± 0.075	3.5e-06*	0.77 ± 0.14	2.7e-08*	0.9 ± 0.11	8.5e-16*	1.1 ± 0.12	2.4e-18*	0.15 ± 0.028	3.9e-08*	0.24 ± 0.033	5.5e-13*	0.3 ± 0.028	1.5e-25*	0.32 ± 0.032	1.8e-24*
PI	PI(16:0;0_18:1;0)	0.087 ± 0.11	0.45	0.35 ± 0.15	0.019	0.66 ± 0.13	3.8e-07*	0.77 ± 0.14	1.4e-08*	-0.046 ± 0.039	0.24	0.031 ± 0.038	0.41	0.34 ± 0.039	6.7e-18*	0.26 ± 0.036	8.9e-13*
	PI(16:0;0_18:2;0)	0.14 ± 0.11	0.19	-0.049 ± 0.14	0.73	0.75 ± 0.13	2.6e-09*	0.95 ± 0.13	1.2e-13*	-0.045 ± 0.035	0.2	-0.092 ± 0.035	0.0083*	0.41 ± 0.036	2e-30*	0.4 ± 0.033	3.1e-34*
	PI(16:0;0_20:4;0)	0.15 ± 0.12	0.19	-0.016 ± 0.16	0.92	0.79 ± 0.14	1e-08*	1.1 ± 0.13	2.2e-15*	-0.012 ± 0.039	0.75	-0.044 ± 0.036	0.22	0.42 ± 0.04	5.1e-26*	0.45 ± 0.035	4.9e-37*
	PI(18:0;0_18:1;0)	0.16 ± 0.11	0.13	0.27 ± 0.15	0.062	0.49 ± 0.13	0.00011*	0.79 ± 0.13	2.7e-09*	0.0087 ± 0.038	0.82	0.057 ± 0.037	0.12	0.29 ± 0.039	4.2e-14*	0.31 ± 0.035	3.1e-19*
	PI(18:0;0_18:2;0)	0.17 ± 0.1	0.09	0.059 ± 0.15	0.69	0.68 ± 0.12	3.4e-08*	0.72 ± 0.13	5.3e-08*	-0.031 ± 0.035	0.37	-0.042 ± 0.037	0.26	0.36 ± 0.036	9.5e-24*	0.24 ± 0.035	8.5e-12*
	PI(18:0;0_20:3;0)	0.31 ± 0.11	0.0031*	0.11 ± 0.15	0.44	0.89 ± 0.12	5e-13*	0.98 ± 0.13	5.7e-14*	0.019 ± 0.034	0.58	0.0082 ± 0.035	0.82	0.44 ± 0.034	2.6e-38*	0.41 ± 0.034	9e-35*
	PI(18:0;0_20:4;0)	0.36 ± 0.083	1.4e-05*	0.49 ± 0.14	0.00075*	0.84 ± 0.11	1.3e-14*	1.1 ± 0.13	5e-18*	0.071 ± 0.027	0.0086*	0.13 ± 0.035	0.00024*	0.38 ± 0.028	7.7e-44*	0.38 ± 0.033	1e-31*
	PI(18:1;0_18:1;0)	0.019 ± 0.1	0.85	-0.079 ± 0.15	0.59	0.09 ± 0.12	0.47	0.29 ± 0.14	0.034*	-0.017 ± 0.037	0.64	-0.069 ± 0.038	0.069	0.1 ± 0.038	0.0084*	0.16 ± 0.036	2.1e-05*
	PI(18:1;0_18:2;0)	-0.057 ± 0.086	0.51	-0.3 ± 0.15	0.045	0.28 ± 0.12	0.022*	0.45 ± 0.14	0.0012*	-0.1 ± 0.032	0.0014*	-0.15 ± 0.039	7.8e-05*	0.17 ± 0.034	3e-07*	0.15 ± 0.037	4.4e-05*
	PI(18:2;0_18:2;0)	0.035 ± 0.081	0.67	0.14 ± 0.16	0.38	-0.24 ± 0.11	0.024*	-0.19 ± 0.15	0.19	0.076 ± 0.032	0.019*	0.039 ± 0.04	0.33	-0.099 ± 0.033	0.0024*	-0.16 ± 0.039	4.1e-05*
	PE(16:0;0_18:2;0)	0.11 ± 0.11	0.32	-0.074 ± 0.16	0.64	0.95 ± 0.12	2.3e-14*	1.3 ± 0.13	5.7e-22*	-0.13 ± 0.034	0.00012*	-0.19 ± 0.034	3.1e-08*	0.51 ± 0.034	2.9e-51*	0.58 ± 0.032	2e-72*
	PE(18:0;0_18:2;0)	0.28 ± 0.11	0.0091*	0.0098 ± 0.15	0.95	1.3 ± 0.12	4.4e-25*	1.4 ± 0.13	2.5e-29*	-0.082 ± 0.03	0.0059*	-0.14 ± 0.031	2.9e-06*	0.64 ± 0.03	1.6e-101*	0.65 ± 0.029	2.8e-107*
PE	PE(18:0;0_20:4;0)	0.33 ± 0.1	0.0015*	0.12 ± 0.15	0.4	1.2 ± 0.12	4.3e-23*	1.3 ± 0.13	4.5e-23*	-0.047 ± 0.031	0.12	-0.072 ± 0.031	0.022*	0.58 ± 0.031	3.1e-79*	0.62 ± 0.03	3.1e-95*
	PE(18:1;0_18:1;0)	0.051 ± 0.11	0.63	-0.32 ± 0.16	0.039	0.79 ± 0.13	1.1e-09*	0.92 ± 0.14	5.8e-11*	-0.18 ± 0.035	3.3e-07*	-0.25 ± 0.036	1.1e-11*	0.5 ± 0.035	5.9e-46*	0.48 ± 0.035	8e-42*
	PEO(16:1;0/18:2;0)	0.19 ± 0.11	0.077	0.21 ± 0.15	0.16	0.091 ± 0.13	0.47	-0.026 ± 0.14	0.85	0.13 ± 0.039	0.0012*	0.13 ± 0.039	0.0011*	-0.04 ± 0.039	0.31	-0.058 ± 0.037	0.12
	PEO(16:1;0/20:4;0)	0.34 ± 0.11	0.0017*	0.19 ± 0.15	0.22	0.4 ± 0.13	0.0031*	0.31 ± 0.14	0.025*	0.14 ± 0.04	0.00029*	0.13 ± 0.039	0.001*	0.14 ± 0.04	0.00036*	0.073 ± 0.037	0.05
PEO	PEO(18:1;0/18:2;0)	0.19 ± 0.1	0.071	0.32 ± 0.15	0.027	-0.042 ± 0.12	0.73	-0.17 ± 0.14	0.22	0.12 ± 0.038	0.0018*	0.18 ± 0.038	1.5e-06*	-0.057 ± 0.038	0.14	-0.13 ± 0.036	0.00043*
	PEO(18:2;0/18:2;0)	0.23 ± 0.11	0.036	0.41 ± 0.15	0.007*	0.092 ± 0.14	0.52	-0.0042 ± 0.14	0.98	0.11 ± 0.04	0.0077*	0.18 ± 0.039	3.9e-06*	-0.035 ± 0.041	0.39	-0.063 ± 0.037	0.089
	PEO(18:2;0/20:4;0)	0.35 ± 0.1	0.00066*	0.39 ± 0.16	0.013*	0.19 ± 0.14	0.15	0.27 ± 0.14	0.064	0.15 ± 0.038	8.8e-05*	0.2 ± 0.04	4e-07*	0.073 ± 0.039	0.059	0.024 ± 0.037	0.52
LPE	LPE(16:0;0)	-0.16 ± 0.11	0.13	0.066 ± 0.15	0.66	0.2 ± 0.12	0.1	0.35 ± 0.14	0.01*	-0.1 ± 0.039	0.01*	-0.12 ± 0.038	0.0014*	0.089 ± 0.039	0.024*	0.19 ± 0.036	1e-07*
	LPE(18:1;0)	-0.26 ± 0.1	0.0094*	-0.15 ± 0.15	0.31	0.063 ± 0.13	0.62	0.46 ± 0.14	0.00063*	-0.12 ± 0.037	0.0014*	-0.18 ± 0.038	9.4e-07*	0.054 ± 0.038	0.15	0.25 ± 0.036	1.6e-12*
	LPE(18:2;0)	-0.23 ± 0.11	0.026*	-0.13 ± 0.15	0.39	0.058 ± 0.12	0.64	0.27 ± 0.14	0.044	-0.089 ± 0.039	0.022*	-0.16 ± 0.038	2.9e-05*	5.3e-06 ± 0.039	1	0.14 ± 0.036	5.9e-05*
	LPE(20:4;0)	-0.12 ± 0.1	0.23	-0.12 ± 0.15	0.42	0.093 ± 0.11	0.41	0.33 ± 0.14	0.016*	-0.085 ± 0.037	0.022*	-0.095 ± 0.038	0.013*	0.0044 ± 0.037	0.91	0.15 ± 0.036	2.9e-05*
	LPE(22:6;0)	0.013 ± 0.11	0.9	-0.046 ± 0.14	0.74	0.21 ± 0.12	0.089	0.12 ± 0.13	0.35	-0.026 ± 0.039	0.51	-0.047 ± 0.037	0.2	0.079 ± 0.04	0.045	0.03 ± 0.035	0.4
LPC	LPC(14:0;0)	-0.13 ± 0.11	0.23	-0.087 ± 0.15	0.57	0.37 ± 0.13	0.004*	0.7 ± 0.14	2.7e-07*	-0.062 ± 0.038	0.11	-0.11 ± 0.038	0.0033*	0.22 ± 0.039	2.6e-08*	0.33 ± 0.036	3.2e-20*
	LPC(16:0;0)	-0.098 ± 0.097	0.31	-0.00033 ± 0.14	1	0.12 ± 0.12	0.3	0.33 ± 0.13	0.013*	-0.044 ± 0.036	0.22	-0.084 ± 0.037	0.025*	0.022 ± 0.036	0.54	0.16 ± 0.035	4.2e-06*

LPC(16:1;0)	-0.27 ± 0.11	0.013*	-0.23 ± 0.15	0.13	0.31 ± 0.13	0.021*	0.5 ± 0.14	0.00026*	-0.13 ± 0.04	0.0011*	-0.14 ± 0.038	0.00017*	0.12 ± 0.041	0.0029*	0.25 ± 0.036	2.3e-12*
LPC(18:0;0)	0.16 ± 0.1	0.12	0.41 ± 0.15	0.0052*	0.048 ± 0.13	0.71	0.17 ± 0.13	0.2	0.085 ± 0.038	0.024*	0.09 ± 0.038	0.017*	-0.042 ± 0.038	0.26	0.066 ± 0.036	0.067
LPC(18:1;0)	-0.27 ± 0.1	0.0059*	-0.1 ± 0.15	0.49	-0.38 ± 0.12	0.0021*	-0.21 ± 0.14	0.13	-0.065 ± 0.036	0.069	-0.092 ± 0.038	0.016*	-0.22 ± 0.036	1.1e-09*	-0.077 ± 0.036	0.035*
LPC(18:2;0)	-0.24 ± 0.092	0.0086*	-0.1 ± 0.15	0.49	-0.47 ± 0.12	5.4e-05*	-0.29 ± 0.13	0.032*	-0.028 ± 0.031	0.38	-0.07 ± 0.038	0.064	-0.3 ± 0.032	5.8e-21*	-0.084 ± 0.036	0.02*
LPC(20:3;0)	-0.051 ± 0.11	0.64	-0.12 ± 0.15	0.43	0.2 ± 0.15	0.18	0.3 ± 0.13	0.024*	-0.025 ± 0.04	0.52	-0.091 ± 0.038	0.016*	-0.015 ± 0.04	0.71	0.22 ± 0.036	7.4e-10*
LPC(20:4;0)	-0.2 ± 0.096	0.04	-0.094 ± 0.14	0.51	-0.21 ± 0.12	0.074	-0.03 ± 0.13	0.82	-0.051 ± 0.034	0.14	-0.061 ± 0.037	0.11	-0.15 ± 0.035	1.4e-05*	0.0063 ± 0.035	0.86
LPC(22:6;0)	-0.033 ± 0.11	0.76	-0.068 ± 0.15	0.64	-0.19 ± 0.14	0.16	-0.22 ± 0.13	0.11	0.021 ± 0.04	0.6	-0.039 ± 0.038	0.3	-0.13 ± 0.04	0.00083*	-0.09 ± 0.036	0.012*

Effect estimates for having high LDL-C or TG values were derived from linear mixed models with the lipid species as outcomes, and hyperlipidemia status, age, age<sup>2</sup>, and sex as fixed effect covariates. The effect estimates were estimated separately in “high LDL-C” families for high LDL-C status (total  $n = 463$  individuals), in “high TG” families for high TG status (total  $n = 287$  individuals) and in the population for both high LDL-C and high TG status (total  $n = 897$  individuals). To estimate independent associations between the lipid species and LDL-C or TG levels, LDL-C,  $\log(TGs)$ , age, age<sup>2</sup>, and sex were used simultaneously as fixed effect covariates. This analysis was performed separately in the hyperlipidemic families (a);  $n = 550$  individuals) and the FINRISK population cohort (b);  $n = 897$  individuals). An empirical genetic correlation matrix between individuals was used as the covariance structure of a random effect in all models. Lipid species and continuous values of LDL-C and  $\log(TGs)$  were normalized based on mean and standard deviation values observed in the FINRISK population cohort. P-values were calculated using Wald test and statistical significance was evaluated using the Benjamini-Hochberg method at a 5% false discovery rate. Statistically significant effects are marked with an asterisk (\*). *Cer* = ceramide, *DG* = diacylglyceride, *LDL-C* = low-density lipoprotein cholesterol, *LPC* = lysophosphatidylcholine, *LPE* = lysophosphatidylethanolamine, *PC* = phosphatidylcholine, *PCO* = phosphatidylcholine-ether, *PE* = phosphatidylethanolamine, *PEO* = phosphatidylethanolamine-ether, *PI* = phosphatidylinositol, *CE* = cholesteryl ester; *SM* = sphingomyelin, *ST* = sterol, *TG* = triacylglyceride.