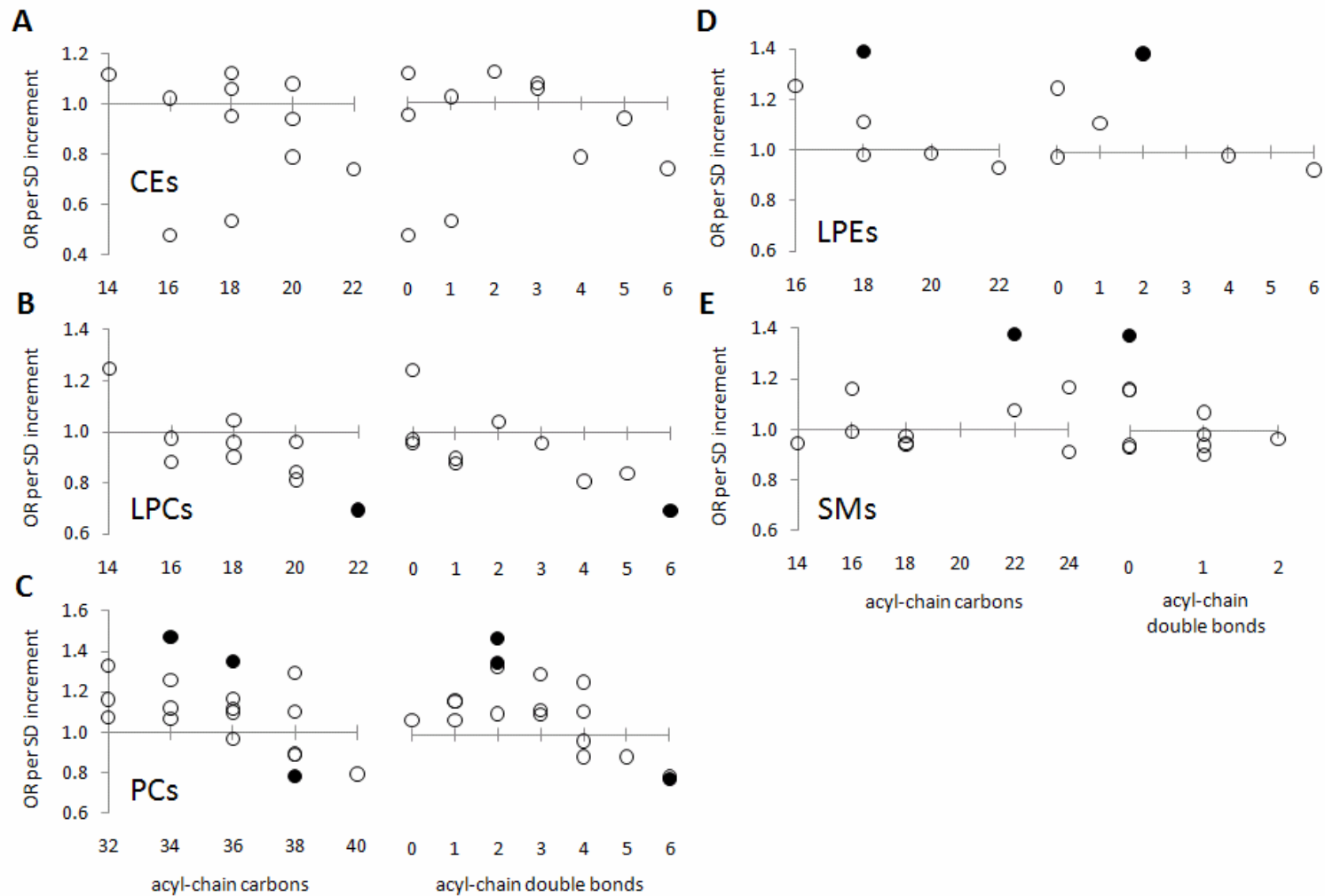
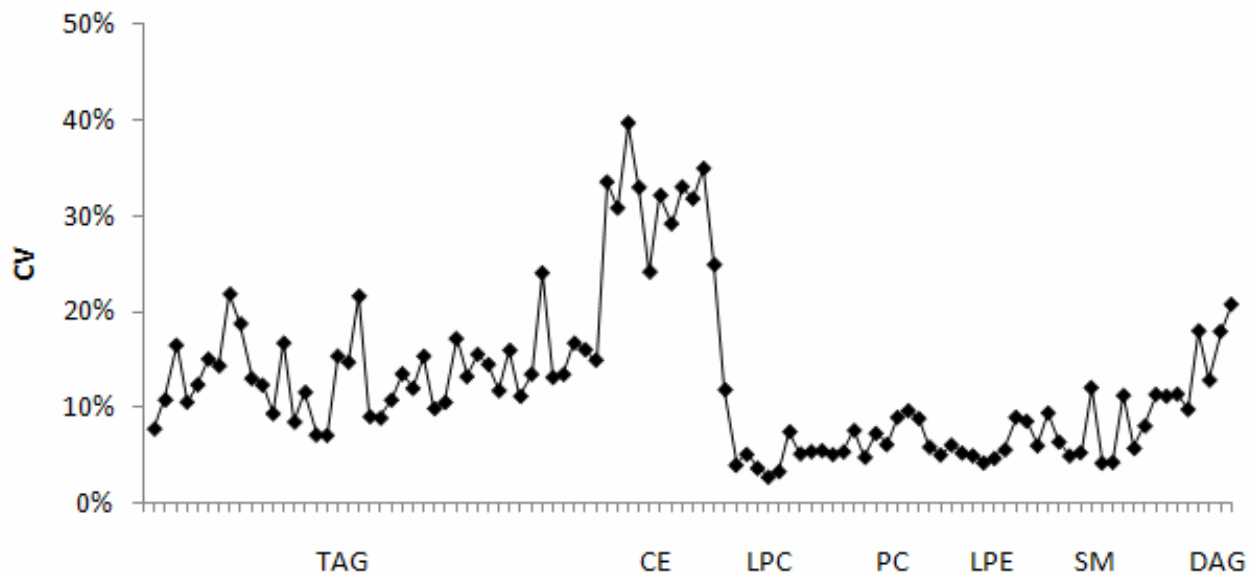


Supplementary Figure 1. Significant TAG predictors in FHS. Box and whisker plots for clinical laboratory measures (A), TAGs associated with increased risk of type 2 diabetes (B), and TAGs associated with decreased risk of type 2 diabetes in FHS (C). All data are unadjusted. The lines in the boxes indicate median levels; the lower and upper boundaries of the box represent the 25th and 75th percentiles respectively; the lower and upper whiskers represent the 5th and 95th percentiles respectively. The diamonds in the boxes indicate mean areas, and the corresponding percent difference between these means (case versus control) is shown in each figure.



Supplementary Figure 2. Lipid risk pattern following multivariable adjustment for non-TAG lipids. Conditional logistic regression models were fitted to assess the association between baseline lipid levels and future diabetes, adjusting for age, sex, BMI, fasting glucose, fasting insulin, total triglycerides, and HDL cholesterol. Odds ratio (OR) for future diabetes per standard deviation (SD) increment of each lipid is shown for **(A)** cholesterol esters (CEs), **(B)** lysophosphatidylcholines (LPCs), **(C)** phosphatidylcholines (PCs), **(D)** lysophosphatidylethanolamines (LPEs), and **(E)** sphingomyelins (SMs), organized along the x-axis based on total acyl chain carbon number (left panel) or double bond content (right panel). Solid circles, $p < 0.05$ for relating diabetes to lipid.



Supplementary Figure 3. Analytic performance of the lipid profiling platform. The CVs for each lipid analyte across a total of 29 pooled plasma samples are shown. Pooled plasma was profiled approximately every 30 samples in the overall experimental queue.

Supplementary Table 1: TAG correlations with HOMA-IR and total triglycerides in FHS

Lipid	Spearman correlation with HOMA-IR	P-value	Spearman correlation with total triglycerides	P-value
TAG 44:1	0.29	<0.0001	0.63	<0.0001
TAG 46:2	0.33	<0.0001	0.73	<0.0001
TAG 46:1	0.33	<0.0001	0.73	<0.0001
TAG 48:4	0.26	<0.0001	0.65	<0.0001
TAG 48:3	0.33	<0.0001	0.85	<0.0001
TAG 48:2	0.35	<0.0001	0.82	<0.0001
TAG 48:1	0.33	<0.0001	0.66	<0.0001
TAG 48:0	0.35	<0.0001	0.63	<0.0001
TAG 50:5	0.27	<0.0001	0.68	<0.0001
TAG 50:4	0.33	<0.0001	0.89	<0.0001
TAG 50:3	0.35	<0.0001	0.90	<0.0001
TAG 50:2	0.33	<0.0001	0.69	<0.0001
TAG 50:0	0.36	<0.0001	0.73	<0.0001
TAG 52:6	0.24	<0.0001	0.67	<0.0001
TAG 52:5	0.25	<0.0001	0.74	<0.0001
TAG 52:4	0.21	<0.0001	0.66	<0.0001
TAG 52:3	0.19	0.0002	0.51	<0.0001
TAG 52:2	0.29	<0.0001	0.76	<0.0001
TAG 52:1	0.37	<0.0001	0.84	<0.0001
TAG 54:10	0.26	<0.0001	0.62	<0.0001
TAG 54:9	0.26	<0.0001	0.72	<0.0001
TAG 54:8	0.15	0.0044	0.60	<0.0001
TAG 54:7	0.16	0.0015	0.57	<0.0001
TAG 54:6	0.17	0.0007	0.55	<0.0001
TAG 54:5	0.11	0.032	0.41	<0.0001
TAG 54:4	0.09	0.093	0.22	<0.0001
TAG 54:3	0.25	<0.0001	0.66	<0.0001
TAG 54:2	0.33	<0.0001	0.85	<0.0001
TAG 56:10	0.21	<0.0001	0.61	<0.0001
TAG 56:9	0.11	0.027	0.50	<0.0001
TAG 56:8	0.11	0.041	0.41	<0.0001
TAG 56:7	0.03	0.62	0.32	<0.0001
TAG 56:6	-0.07	0.2	0.10	0.045
TAG 56:5	0.07	0.16	0.39	<0.0001
TAG 56:4	0.16	0.0021	0.56	<0.0001
TAG 56:3	0.27	<0.0001	0.79	<0.0001
TAG 58:12	0.15	0.0029	0.46	<0.0001
TAG 58:11	0.12	0.019	0.44	<0.0001
TAG 58:10	0.10	0.058	0.40	<0.0001
TAG 58:9	0.01	0.78	0.22	<0.0001
TAG 58:8	-0.07	0.17	0.04	0.48
TAG 60:12	0.02	0.69	0.31	<0.0001

HOMA-IR: homeostasis model assessment of insulin resistance

Supplementary Table 2: Lipid levels and risk of future diabetes adjusted for parental history

Lipid	Baseline Model ^A		Baseline Model ^A + Parental History ^B	
	OR per SD	P-value	OR per SD	P-value
TAG 52:1	1.94	0.009	1.78	0.026
TAG 50:0	1.74	0.005	1.66	0.010
PC 34:2	1.47	0.021	1.50	0.019
TAG 48:1	1.47	0.026	1.41	0.048
TAG 46:1	1.44	0.043	1.36	0.097
TAG 48:0	1.41	0.042	1.40	0.046
TAG 44:1	1.41	0.036	1.32	0.092
LPE 18:2	1.39	0.016	1.38	0.018
SM 22:0	1.38	0.022	1.29	0.072
PC 36:2	1.35	0.039	1.32	0.059
TAG 58:10	0.67	0.006	0.68	0.010
LPC 22:6	0.69	0.006	0.69	0.007
TAG 56:9	0.70	0.017	0.71	0.024
TAG 60:12	0.74	0.022	0.75	0.030
PC 38:6	0.78	0.049	0.77	0.047
TAG 50:0+TAG 58:10^C	2.72	0.001	2.72	0.001

^AAdjusted for age, sex, BMI, fasting glucose, fasting insulin, triglycerides, and HDL cholesterol

^BParental history information missing in 57 participants

^CFor the combination of TAGs 50:0 and 58:10, values represent results for a weighted score comprised of coefficients for each TAG that were estimated from individually fitted models.