

Supplementary Methods – Quantification of LPIs, fatty acids, and acylcarnitines using LC-MS/MS and GC-MS/MS

Chemicals and reagents

Methanol, formic acid, ammonium formate, and most standards including α -lysophosphatidylinositol (LPI) sodium salt (LPI 16:0, 58%), *myo*-inositol, myristic acid, palmitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid, α -linolenic acid, gondoic acid, arachidonic acid, eicosapentaenoic acid, docosahexaenoic acid, carnitine hydrochloride, acetylcarnitine hydrochloride, propionylcarnitine, butyrylcarnitine, octanoylcarnitine, and palmitoylcarnitine were purchased from Sigma-Aldrich. Isotopically labeled acylcarnitine mix standard (NSK-B) and 6-¹³C-glucose (CLM-481) was purchased from Cambridge Isotope Laboratories. 12,13-dihydroxy-octadecenoic acid-d₄ (12,13-DiHOME-d₄) and 12,13-epoxy-octadecenoic acid-d₄ (12,13-EpOME-d₄) were purchased from Cayman Chemical. Acetonitrile (mass grade) was purchased from Merck. Distilled water was purified "in-house" using a Milli-Q purification system (Bedford, MA, USA).

Serum collection and preparation

Antecubital venous blood samples (20 ml) were taken from consenting participants in the morning; fasting was not required before blood collection. After collection, blood samples were immediately placed on ice for transportation and were processed within 6 h to obtain serum samples, which were subsequently stored at -80°C. Serum samples used for the current study were allowed to thaw at 4°C overnight. Thawed serum samples (50 μ L) were diluted with 50 μ L of distilled water. The mixture was treated with 500 μ L of ice-cold methanol (isotope labeled acylcarnitine mix standard, 12,13-EpOME-d₄, and 12,13-DiHOME-d₄ as internal standards) for protein precipitation. After centrifugation at 20,817 g for 15 min at 4°C, the supernatant fraction was filtered by Thermo Scientific™ national 750 μ L micro-centrifugal filters (PTFE membrane, 0.2 μ m pore size, non-sterile). The filtrate was direct-injected for quantitative analyses of LPIs, fatty acids, and acylcarnitines. Quality control (QC) was prepared by spiking certain amount native and labeled standards into a pooled plasma from all participants, and six QCs were analyzed along with the samples in each batch to ensure the reliability of the method and the instrument stability.

LC-MS/MS analysis

The quantitative analyses of LPIs, fatty acids, and acylcarnitines were performed on an Agilent 1200 HPLC system coupled to a 6410 Triple Quadrupole (QQQ) mass spectrometer equipped with an electrospray ionization source. The metabolites were separated by using an Acquity UPLC BEH C18 column (2.1 mm \times 100 mm, 1.7 μ m, Waters). The mobile phases A (water/acetonitrile [30/70, v/v] with 0.1% formic acid and 10 mmol/L ammonium formate) and B (acetonitrile/isopropanol [90/10, v/v]) were employed for LPIs and fatty acids analyses. The gradient program was: 0-1 min, 0% B; 1-11 min, 0-100% B; 11-16 min, 100% B; 16-16.5 min, 100-0% B. For acylcarnitine analysis, the mobile phases A (water with 10 mmol/L ammonium formate and 0.1% formic acid) and B (acetonitrile/isopropanol [90/10, v/v]) were employed. The gradient program was: 0-1 min, 1%B; 1-2 min, 1-90% B; 2-6 min, 90% B; 6-11 min, 90-100% B; 11-16 min, 100% B; 16-16.5 min, 100-1% B. The flow rate was set at 0.3 mL/min. The column temperature and injection volume were set at 40°C and 10 μ L, respectively. The LPIs and fatty acids were analyzed in negative ion mode, whereas acylcarnitines were detected in positive ion mode. The mass spectrum was acquired in the multiple reaction monitoring (MRM) mode with a capillary voltage of 3500 V, gas temperature of 350°C, gas flow of 12 L/min and nebulizer nitrogen gas flow rate of 30 psi. The retention time, MRM transition, fragmentor voltage and collision energy (CE) were shown in **Supplementary Table S1**.

GC-MS/MS analysis

The quantitative analysis of inositol was performed on an Agilent 7890 GC system coupled to a 7000B QQQ mass detector equipped with a chemical ionization (CI) source. A J&W HP-5MS-23 column (60 m \times 0.25 mm \times 0.25 μ m, USA) was used for sample separation. The injection volume was 1 μ L in pulsed splitless mode. The flow rate of the carrier gas, helium, was 2 mL/min. The GC oven temperature was started at 120 °C for 1 min and raised from 120 °C to 200 °C at 25 °C/min, then raised to 217 °C at 1.5 °C/min, followed by raising from 217 °C to 300 °C at 25 °C/min and maintained at 300 °C for 5 min. Mass spectrum was acquired in positive MRM mode with the parameters as follow: methane was used as reactant gas, and gas flow was set at 20%, ion source temperature was 250 °C. The optimized parameters on MRM transition and CE are shown in **Supplementary Table S1**.

Method validation

Both LC-MS/MS and GC-MS/MS methods were validated for linearity, recovery, accuracy, and precision, according to Food and Drug Administration (FDA) guideline for biological method as our previous published report (1). The

limit of detection (LOD) was calculated based on the signal-to-noise ratio at 3. The calibration curves were constructed from three replicate measurements of six concentrations of each standard. A linear regression with $r^2 > 0.995$ was obtained in all relevant ranges. Recoveries were evaluated by spiking defined amounts of deuterated internal standards into aliquots of unprocessed serum and calculated by comparing peak areas from serum against mean peak areas of three equal amounts of unprocessed compounds in pure solvent. The recoveries generally ranged from 72.1% to 120.5% for all compounds. For intra-batch and inter-batch precision and accuracy, the relative standard deviation (RSD) values ranged from 0.05% to 19.27% and 0.15% to 18.50%, respectively.

Data analysis

All metabolites were quantified by normalizing to their corresponding internal standards described in **Supplemental Table S1**. The normalization for metabolite_{*i*} of sample_{*j*} and internal standards_{*k*} was performed by using the following equation (1):

$$\text{metabolite}_{ij, \text{normalized}} = \text{metabolite}_{ij, \text{raw}} / \text{internal standards}_k \times \text{concentration internal standards} \quad (1)$$

Reference:

1. Xu YJ, Ho WE, Xu F, Wen T, Ong CN. Exploratory investigation reveals parallel alteration of plasma fatty acids and eicosanoids in coronary artery disease patients. *Prostaglandins Other Lipid Mediat* 2013;106:29-36.

Table S1. Optimized multiple reaction monitoring (MRM) conditions for determination of 61 metabolites

Metabolite	Platform	R.T. (min)	Transition ion (m/z)	Fragmentor voltage (V)	CE (eV)	Internal standard	Calibration curve
<i>Inositol and lysophosphatidylinositols</i>							
<i>myo</i> -Inositol	GC-MS/MS	19.46	265.0 → 221.0	-	10	6- ¹³ C-Glucose	<i>myo</i> -Inositol
Lysophosphatidylinositol (LPI) (16:0)	LC-MS/MS, neg	10.83	571.3 → 241.2	135	35	12,13-DiHOME-d ₄	LPI (16:0)
LPI (16:1)	LC-MS/MS, neg	9.87	569.3 → 241.2	135	35	12,13-DiHOME-d ₄	LPI (16:0)
LPI (18:0)	LC-MS/MS, neg	12.14	599.3 → 241.2	135	35	12,13-DiHOME-d ₄	LPI (16:0)
LPI (18:1)	LC-MS/MS, neg	11.14	597.3 → 241.2	135	35	12,13-DiHOME-d ₄	LPI (16:0)
LPI (18:2)	LC-MS/MS, neg	10.31	595.3 → 241.2	135	35	12,13-DiHOME-d ₄	LPI (16:0)
LPI (20:4)	LC-MS/MS, neg	10.33	619.2 → 241.2	135	35	12,13-DiHOME-d ₄	LPI (16:0)
LPI (22:6)	LC-MS/MS, neg	10.28	643.3 → 241.2	135	35	12,13-DiHOME-d ₄	LPI (16:0)
<i>Fatty acids</i>							
Lauric acid (12:0)	LC-MS/MS, neg	12.10	199.1 → 199.1	110	-	12,13-EpOME-d ₄	Myristic acid
Myristic acid (14:0)	LC-MS/MS, neg	13.46	227.2 → 227.2	110	-	12,13-EpOME-d ₄	Myristic acid
Palmitic acid (16:0)	LC-MS/MS, neg	14.59	255.2 → 255.2	110	-	12,13-EpOME-d ₄	Palmitic acid
Palmitoleic acid (16:1n-7)	LC-MS/MS, neg	13.62	253.2 → 253.2	110	-	12,13-EpOME-d ₄	Palmitoleic acid
Stearic acid (18:0)	LC-MS/MS, neg	15.69	283.3 → 283.3	110	-	12,13-EpOME-d ₄	Stearic acid
Oleic acid (18:1n-9)	LC-MS/MS, neg	14.69	281.3 → 281.3	110	-	12,13-EpOME-d ₄	Oleic acid
Linoleic acid (18:2n-6)	LC-MS/MS, neg	13.87	279.2 → 279.2	110	-	12,13-EpOME-d ₄	Linoleic acid
α-Linolenic acid (18:3n-3)	LC-MS/MS, neg	13.14	277.2 → 277.2	110	-	12,13-EpOME-d ₄	α-Linolenic acid
γ-Linolenic acid (18:3n-6)	LC-MS/MS, neg	13.24	277.2 → 277.2	110	-	12,13-EpOME-d ₄	α-Linolenic acid
Gondoic acid (20:1n-11)	LC-MS/MS, neg	15.70	309.3 → 309.3	110	-	12,13-EpOME-d ₄	Gondoic acid
Eicosadienoic acid (20:2n-6)	LC-MS/MS, neg	14.83	307.3 → 307.3	110	-	12,13-EpOME-d ₄	Arachidonic acid
Dihomo-γ-linolenic acid (20:3n-6)	LC-MS/MS, neg	14.14	305.2 → 305.2	110	-	12,13-EpOME-d ₄	Arachidonic acid
Mead acid (20:3n-9)	LC-MS/MS, neg	14.39	305.2 → 305.2	110	-	12,13-EpOME-d ₄	Arachidonic acid
Arachidonic acid (20:4n-6)	LC-MS/MS, neg	13.67	303.2 → 259.3	110	5	12,13-EpOME-d ₄	Arachidonic acid
Eicosapentaenoic acid (EPA) (20:5n-3)	LC-MS/MS, neg	13.00	301.2 → 257.2	110	5	12,13-EpOME-d ₄	EPA
Adrenic acid (22:4n-6)	LC-MS/MS, neg	14.41	331.2 → 331.2	110	-	12,13-EpOME-d ₄	Arachidonic acid
Clupanodonic acid (22:5n-3)	LC-MS/MS, neg	13.79	329.2 → 329.2	110	-	12,13-EpOME-d ₄	Arachidonic acid

Osbond acid (22:5n-6)	LC-MS/MS, neg	14.06	329.2 -> 329.2	110	-	12,13-EpOME-d ₄	Arachidonic acid
Docosahexaenoic acid (DHA) (22:6n-3)	LC-MS/MS, neg	13.45	327.2 -> 283.2	110	5	12,13-EpOME-d ₄	DHA
<i>Carnitine and acylcarnitines</i>							
L-Carnitine	LC-MS/MS, pos	1.00	162.1 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -carnitine
Acetylcarnitine (C2)	LC-MS/MS, pos	1.06	204.1 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C2 carnitine
Propionylcarnitine (C3)	LC-MS/MS, pos	1.05	218.2 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C3 carnitine
Butyrylcarnitine (C4)	LC-MS/MS, pos	4.71	232.2 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C4 carnitine
3-Hydroxybutyrylcarnitine(C4OH)	LC-MS/MS, pos	1.06	248.2 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C3 carnitine
Valerylcarnitine (C5)	LC-MS/MS, pos	4.82	246.2 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C5 carnitine
3-Hydroxyisovalerylcarnitine (C5OH)	LC-MS/MS, pos	1.06	262.2 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C3 carnitine
Hexanoylcarnitine (C6)	LC-MS/MS, pos	4.94	260.2 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C5 carnitine
3-Hydroxyhexanoylcarnitine (C6OH)	LC-MS/MS, pos	4.74	276.2 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C4 carnitine
Octanoylcarnitine (C8)	LC-MS/MS, pos	5.22	288.3 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C8 carnitine
3-Hydroxyoctanoylcarnitine (C8OH)	LC-MS/MS, pos	4.95	304.3 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C8 carnitine
Decanoylcarnitine (C10)	LC-MS/MS, pos	5.60	316.3 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C8 carnitine
3-Hydroxydecanoylcarnitine (C10OH)	LC-MS/MS, pos	5.22	332.3 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C8 carnitine
9-Decenoylcarnitine (C10:1)	LC-MS/MS, pos	5.41	314.3 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C8 carnitine
Dodecanoylcarnitine (C12)	LC-MS/MS, pos	6.09	344.3 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C8 carnitine
3-Hydroxydodecanoylcarnitine (C12OH)	LC-MS/MS, pos	5.60	360.3 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C8 carnitine
2-Dodecenoylcarnitine (C12:1)	LC-MS/MS, pos	5.80	342.3 -> 85.0	135	20	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C8 carnitine
Tetradecanoylcarnitine (C14)	LC-MS/MS, pos	6.76	372.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
3-Hydroxytetradecanoylcarnitine(C14OH)	LC-MS/MS, pos	6.10	388.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
2-Tetradecenoylcarnitine (C14:1)	LC-MS/MS, pos	6.34	370.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
Hexadecanoylcarnitine (C16)	LC-MS/MS, pos	7.72	400.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C16 carnitine
3-Hydroxyhexadecanoylcarnitine (C16OH)	LC-MS/MS, pos	6.77	416.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
9-Hexadecenoylcarnitine (C16:1)	LC-MS/MS, pos	6.98	398.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
3-Hydroxy-9-hexadecenoylcarnitine (C16:1OH)	LC-MS/MS, pos	6.33	414.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
9,12-Hexadecadienoylcarnitine (C16:2)	LC-MS/MS, pos	6.50	396.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
Octadecanoylcarnitine (C18)	LC-MS/MS, pos	8.96	428.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C16 carnitine

3-Hydroxyoctadecanoylcarnitine (C18OH)	LC-MS/MS, pos	7.78	444.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C16 carnitine
Oleylcarnitine (C18:1)	LC-MS/MS, pos	7.91	426.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C16 carnitine
3-Hydroxy-9-octadecenoylcarnitine (C18:1OH)	LC-MS/MS, pos	7.01	442.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C16 carnitine
Linoleylcarnitine(C18:2)	LC-MS/MS, pos	7.18	424.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C16 carnitine
3-Hydroxy-9,12-octadecenoylcarnitine (C18:2OH)	LC-MS/MS, pos	6.49	440.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
C20:4-carnitine	LC-MS/MS, pos	7.11	448.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₃ -C16 carnitine
C20:5-carnitine	LC-MS/MS, pos	6.66	446.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine
C22:6-carnitine	LC-MS/MS, pos	6.99	472.4 -> 85.0	135	25	¹³ C ₆ , ¹⁵ N-Leucine	D ₉ -C14 carnitine

- Not applicable

Table S2. Metabolite concentrations (μM , Mean \pm SD) in controls stratified by fasting status, The Singapore Chinese Health Study

Metabolite	Non-fasting (n =228)	Fasting (n = 76)	<i>P</i> ^a
<i>Inositol and lysophosphatidylinositols</i>			
<i>myo</i> -Inositol	27.44 \pm 9.12	27.54 \pm 11.91	0.948
Lysophosphatidylinositol (LPI) (16:0)	0.28 \pm 0.11	0.27 \pm 0.10	0.316
LPI (16:1)	0.08 \pm 0.04	0.09 \pm 0.04	0.684
LPI (18:0)	1.19 \pm 0.32	1.12 \pm 0.29	0.095
LPI (18:1)	0.51 \pm 0.18	0.51 \pm 0.20	0.994
LPI (18:2)	0.47 \pm 0.16	0.46 \pm 0.13	0.621
LPI (20:4)	0.40 \pm 0.11	0.42 \pm 0.11	0.322
LPI (22:6)	0.06 \pm 0.02	0.06 \pm 0.02	0.692
<i>Fatty acids</i>			
Lauric acid (12:0)	5.90 \pm 4.81	4.94 \pm 2.15	0.018
Myristic acid (14:0)	7.44 \pm 4.06	8.93 \pm 2.84	0.001
Palmitic acid (16:0)	63.09 \pm 48.73	104.06 \pm 45.58	<0.001
Palmitoleic acid (16:1n-7)	11.47 \pm 10.88	21.85 \pm 11.37	<0.001
Stearic acid (18:0)	14.37 \pm 8.80	19.12 \pm 6.45	<0.001
Oleic acid (18:1n-9)	65.3 \pm 54.42	114.31 \pm 53.70	<0.001
Linoleic acid (18:2n-6)	40.91 \pm 29.62	63.29 \pm 28.85	<0.001
α -Linolenic acid (18:3n-3)	3.36 \pm 1.29	3.91 \pm 1.26	0.001
γ -Linolenic acid (18:3n-6)	2.47 \pm 0.55	2.66 \pm 0.61	0.022
Gondoic acid (20:1n-11)	0.71 \pm 0.55	1.11 \pm 0.52	<0.001
Eicosadienoic acid (20:2n-6)	6.14 \pm 3.45	9.63 \pm 3.71	<0.001
Dihomo- γ -linolenic acid (20:3n-6)	7.36 \pm 3.50	10.22 \pm 4.08	<0.001
Mead acid (20:3n-9)	1.41 \pm 0.86	2.15 \pm 1.14	<0.001
Arachidonic acid (20:4n-6)	4.81 \pm 1.99	6.29 \pm 2.45	<0.001
Eicosapentaenoic acid (EPA) (20:5n-3)	0.85 \pm 0.44	0.95 \pm 0.49	0.113
Adrenic acid (22:4n-6)	3.00 \pm 1.66	4.47 \pm 2.04	<0.001
Clupanodonic acid (22:5n-3)	8.04 \pm 5.67	12.11 \pm 6.35	<0.001
Osbond acid (22:5n-6)	5.37 \pm 3.01	8.29 \pm 3.79	<0.001
Docosahexaenoic acid (DHA) (22:6n-3)	21.87 \pm 11.66	29.55 \pm 13.69	<0.001
<i>Carnitine and acylcarnitines</i>			
L-Carnitine	31.88 \pm 6.22	32.00 \pm 6.21	0.886
Acetylcarnitine (C2)	4.78 \pm 1.48	5.75 \pm 2.07	<0.001
Propionylcarnitine (C3)	0.44 \pm 0.15	0.38 \pm 0.11	<0.001
Butyrylcarnitine (C4)	0.33 \pm 0.07	0.32 \pm 0.07	0.115
3-Hydroxybutyrylcarnitine(C4OH)	0.04 \pm 0.01	0.05 \pm 0.02	0.007
Valerylcarnitine (C5)	0.21 \pm 0.03	0.20 \pm 0.03	0.063
3-Hydroxyisovalerylcarnitine (C5OH)	0.05 \pm 0.01	0.05 \pm 0.01	0.943
Hexanoylcarnitine (C6)	0.20 \pm 0.03	0.24 \pm 0.05	<0.001
3-Hydroxyhexanoylcarnitine (C6OH)	0.13 \pm 0.00	0.13 \pm 0.00	0.018
Octanoylcarnitine (C8)	0.12 \pm 0.06	0.22 \pm 0.11	<0.001

3-Hydroxyoctanoylcarnitine (C8OH)	0.05 ± 0.02	0.06 ± 0.02	<0.001
Decanoylcarnitine (C10)	0.02 ± 0.12	0.39 ± 0.21	<0.001
3-Hydroxydecanoylcarnitine (C10OH)	0.04 ± 0.01	0.05 ± 0.02	<0.001
9-Decenoylcarnitine (C10:1)	0.15 ± 0.07	0.22 ± 0.09	<0.001
Dodecanoylcarnitine (C12)	0.09 ± 0.04	0.13 ± 0.06	<0.001
3-Hydroxydodecanoylcarnitine (C12OH)	0.02 ± 0.00	0.03 ± 0.00	<0.001
2-Dodecenoylcarnitine (C12:1)	0.09 ± 0.04	0.14 ± 0.06	<0.001
Tetradecanoylcarnitine (C14)	0.04 ± 0.01	0.05 ± 0.01	<0.001
3-Hydroxytetradecanoylcarnitine(C14OH)	0.01 ± 0.00	0.01 ± 0.00	<0.001
2-Tetradecenoylcarnitine (C14:1)	0.07 ± 0.04	0.12 ± 0.06	<0.001
Hexadecanoylcarnitine (C16)	0.27 ± 0.04	0.30 ± 0.04	<0.001
3-Hydroxyhexadecanoylcarnitine (C16OH)	0.01 ± 0.00	0.01 ± 0.00	<0.001
9-Hexadecenoylcarnitine (C16:1)	0.04 ± 0.01	0.05 ± 0.02	<0.001
3-Hydroxy-9-hexadecenoylcarnitine (C16:1OH)	0.01 ± 0.00	0.01 ± 0.00	<0.001
9,12-Hexadecadienoylcarnitine (C16:2)	0.01 ± 0.00	0.02 ± 0.00	<0.001
Octadecanoylcarnitine (C18)	0.18 ± 0.01	0.19 ± 0.01	0.009
3-Hydroxyoctadecanoylcarnitine (C18OH)	0.15 ± 0.00	0.15 ± 0.00	0.027
Oleylcarnitine (C18:1)	0.27 ± 0.04	0.31 ± 0.06	<0.001
3-Hydroxy-9-octadecenoylcarnitine (C18:1OH)	0.15 ± 0.00	0.15 ± 0.00	<0.001
Linoleylcarnitine(C18:2)	0.20 ± 0.02	0.21 ± 0.02	0.001
3-Hydroxy-9,12-octadecenoylcarnitine (C18:2OH)	0.01 ± 0.00	0.01 ± 0.00	<0.001
C20:4-carnitine	0.15 ± 0.00	0.15 ± 0.00	0.005
C20:5-carnitine	0.01 ± 0.00	0.01 ± 0.00	0.001
C22:6-carnitine	0.01 ± 0.00	0.01 ± 0.00	<0.001

^a *P* values were calculated by the Student *t* test.

Table S3. The associations between 61 measured metabolites and risk of type 2 diabetes, The Singapore Chinese Health Study ^a

Metabolite	Groups	OR across tertiles				OR per SD increment			
		T1	T2, OR (95% CI)	T3, OR (95% CI)	P for trend	FDR	OR (95% CI)	P	FDR
<i>Inositol and lysophosphatidylinositols</i>									
<i>myo</i> -Inositol	Prevalent type 2 diabetes	1.00	0.86 (0.43, 1.74)	0.27 (0.12, 0.65)	0.003	0.016	0.38 (0.23, 0.61)	<0.001	0.003
	Incident type 2 diabetes	1.00	0.41 (0.18, 0.92)	0.40 (0.16, 0.98)	0.038	0.136	0.73 (0.51, 1.05)	0.089	0.249
Lysophosphatidylinositol (16:0)	Prevalent type 2 diabetes	1.00	1.69 (0.81, 3.54)	2.02 (0.94, 4.37)	0.041	0.089	1.20 (0.88, 1.64)	0.257	0.306
	Incident type 2 diabetes	1.00	0.80 (0.39, 1.63)	1.24 (0.58, 2.65)	0.693	0.798	1.51 (1.02, 2.24)	0.041	0.142
Lysophosphatidylinositol (16:1)	Prevalent type 2 diabetes	1.00	1.35 (0.51, 3.57)	2.53 (1.05, 6.06)	0.016	0.041	1.24 (0.87, 1.78)	0.228	0.278
	Incident type 2 diabetes	1.00	1.70 (0.43, 6.75)	5.33 (1.53, 18.59)	0.016	0.104	1.96 (1.15, 3.34)	0.013	0.085
Lysophosphatidylinositol (18:0)	Prevalent type 2 diabetes	1.00	1.84 (0.76, 4.46)	2.99 (1.05, 8.52)	0.053	0.095	1.51 (0.95, 2.39)	0.079	0.142
	Incident type 2 diabetes	1.00	1.19 (0.53, 2.68)	3.24 (1.29, 8.10)	0.008	0.104	1.97 (1.24, 3.12)	0.004	0.081
Lysophosphatidylinositol (18:1)	Prevalent type 2 diabetes	1.00	1.45 (0.70, 2.99)	1.84 (0.91, 3.70)	0.065	0.110	1.23 (0.93, 1.64)	0.142	0.201
	Incident type 2 diabetes	1.00	0.86 (0.42, 1.77)	1.01 (0.49, 2.08)	0.855	0.893	1.06 (0.75, 1.50)	0.732	0.812
Lysophosphatidylinositol (18:2)	Prevalent type 2 diabetes	1.00	2.32 (1.07, 5.01)	2.78 (1.29, 5.98)	0.007	0.024	1.30 (0.98, 1.71)	0.066	0.126
	Incident type 2 diabetes	1.00	1.52 (0.66, 3.51)	2.04 (0.88, 4.72)	0.140	0.275	1.26 (0.91, 1.74)	0.168	0.342
Lysophosphatidylinositol (20:4)	Prevalent type 2 diabetes	1.00	1.83 (0.75, 4.48)	4.05 (1.71, 9.57)	0.001	0.009	2.36 (1.57, 3.55)	<0.001	0.003
	Incident type 2 diabetes	1.00	1.15 (0.59, 2.23)	1.13 (0.50, 2.57)	0.773	0.842	1.32 (0.90, 1.96)	0.157	0.330
Lysophosphatidylinositol (22:6)	Prevalent type 2 diabetes	1.00	1.86 (0.85, 4.09)	2.02 (0.82, 4.97)	0.044	0.093	1.30 (0.93, 1.83)	0.129	0.192
	Incident type 2 diabetes	1.00	0.51 (0.23, 1.13)	0.83 (0.36, 1.92)	0.765	0.842	0.98 (0.68, 1.41)	0.913	0.916
<i>Fatty acids</i>									
Lauric acid (C12:0)	Prevalent type 2 diabetes	1.00	0.85 (0.41, 1.77)	2.28 (0.95, 5.47)	0.269	0.346	0.99 (0.73, 1.35)	0.966	0.966
	Incident type 2 diabetes	1.00	0.88 (0.44, 1.75)	1.31 (0.63, 2.72)	0.601	0.748	1.15 (0.86, 1.52)	0.344	0.456
Myristic acid (C14:0)	Prevalent type 2 diabetes	1.00	0.90 (0.35, 2.28)	3.15 (1.38, 7.20)	0.007	0.024	2.04 (1.37, 3.04)	<0.001	0.003
	Incident type 2 diabetes	1.00	1.10 (0.58, 2.08)	2.10 (1.07, 4.13)	0.067	0.178	1.72 (1.25, 2.37)	0.001	0.031
Palmitic acid (C16:0)	Prevalent type 2 diabetes	1.00	2.76 (1.11, 6.86)	6.45 (2.52, 16.51)	0.001	0.009	2.18 (1.50, 3.17)	<0.001	0.003
	Incident type 2 diabetes	1.00	1.62 (0.81, 3.23)	2.79 (1.33, 5.86)	0.014	0.104	1.48 (1.10, 1.99)	0.010	0.085
Palmitoleic acid (C16:1n-7)	Prevalent type 2 diabetes	1.00	4.43 (1.75, 11.26)	7.70 (2.69, 22.02)	0.002	0.014	1.90 (1.29, 2.81)	0.001	0.003
	Incident type 2 diabetes	1.00	1.20 (0.58, 2.48)	2.32 (1.19, 4.55)	0.026	0.118	1.44 (1.08, 1.92)	0.013	0.085
Stearic acid (C18:0)	Prevalent type 2 diabetes	1.00	2.98 (1.25, 7.13)	4.74 (2.06, 10.88)	0.002	0.014	2.13 (1.45, 3.12)	<0.001	0.003

	Incident type 2 diabetes	1.00	1.68 (0.80, 3.50)	3.03 (1.37, 6.71)	0.011	0.104	1.59 (1.13, 2.23)	0.008	0.085	
Oleic acid (C18:1n-9)	Prevalent type 2 diabetes	1.00	2.38 (0.97, 5.85)	4.44 (1.82, 10.79)	0.009	0.026	1.93 (1.35, 2.76)	<0.001	0.003	
	Incident type 2 diabetes	1.00	1.93 (0.93, 4.00)	2.76 (1.32, 5.79)	0.017	0.104	1.38 (1.04, 1.84)	0.028	0.114	
Linoleic acid (C18:2n-6)	Prevalent type 2 diabetes	1.00	2.04 (0.91, 4.59)	4.61 (1.94, 10.98)	0.004	0.016	1.65 (1.19, 2.27)	0.002	0.006	
	Incident type 2 diabetes	1.00	1.48 (0.73, 3.00)	2.19 (1.11, 4.34)	0.047	0.159	1.39 (1.05, 1.85)	0.022	0.112	
α -Linolenic acid (C18:3n-3)	Prevalent type 2 diabetes	1.00	1.48 (0.67, 3.30)	3.20 (1.43, 7.15)	0.018	0.044	1.54 (1.11, 2.14)	0.009	0.022	
	Incident type 2 diabetes	1.00	1.39 (0.72, 2.67)	1.81 (0.88, 3.73)	0.190	0.305	1.28 (0.95, 1.73)	0.109	0.277	
γ -Linolenic acid (C18:3n-6)	Prevalent type 2 diabetes	1.00	5.91 (2.18, 15.99)	5.46 (1.85, 16.10)	0.012	0.032	2.07 (1.35, 3.17)	0.001	0.003	
	Incident type 2 diabetes	1.00	1.56 (0.69, 3.54)	2.21 (0.98, 5.00)	0.106	0.233	1.36 (0.98, 1.90)	0.064	0.195	
Gondoic acid (C20:1n-11)	Prevalent type 2 diabetes	1.00	1.23 (0.53, 2.84)	3.54 (1.57, 8.02)	0.008	0.026	2.20 (1.48, 3.28)	<0.001	0.003	
	Incident type 2 diabetes	1.00	1.34 (0.67, 2.68)	2.28 (1.07, 4.87)	0.054	0.165	1.41 (1.05, 1.90)	0.024	0.113	
Eicosadienoic acid (C20:2n-6)	Prevalent type 2 diabetes	1.00	3.33 (1.39, 8.00)	6.64 (2.72, 16.23)	<0.001	0.009	2.29 (1.55, 3.38)	<0.001	0.003	
	Incident type 2 diabetes	1.00	2.41 (1.13, 5.11)	3.11 (1.45, 6.68)	0.010	0.104	1.50 (1.12, 2.02)	0.006	0.085	
Dihomo-gamma-linolenic acid (C20:3n-6)	Prevalent type 2 diabetes	1.00	1.35 (0.57, 3.19)	5.02 (2.16, 11.69)	<0.001	0.009	2.20 (1.52, 3.20)	<0.001	0.003	
	Incident type 2 diabetes	1.00	1.56 (0.70, 3.50)	5.64 (2.38, 13.34)	<0.001	0.031	1.86 (1.34, 2.59)	<0.001	0.031	
Mead acid (C20:3n-9)	Prevalent type 2 diabetes	1.00	1.76 (0.75, 4.12)	3.14 (1.40, 7.02)	0.031	0.070	2.03 (1.40, 2.96)	<0.001	0.003	
	Incident type 2 diabetes	1.00	2.66 (1.13, 6.31)	4.91 (1.95, 12.32)	0.001	0.031	1.36 (1.02, 1.83)	0.039	0.142	
Arachidonic acid (C20:4n-6)	Prevalent type 2 diabetes	1.00	1.82 (0.77, 4.32)	3.86 (1.70, 8.75)	0.004	0.016	1.84 (1.31, 2.58)	<0.001	0.003	
	Incident type 2 diabetes	1.00	1.81 (0.86, 3.81)	2.21 (1.00, 4.86)	0.093	0.218	1.53 (1.09, 2.14)	0.014	0.085	
Eicosapentaenoic acid (EPA) (C20:5n-3)	Prevalent type 2 diabetes	1.00	3.96 (1.50, 10.48)	4.34 (1.76, 10.73)	0.009	0.026	1.61 (1.17, 2.23)	0.004	0.012	
	Incident type 2 diabetes	1.00	1.11 (0.50, 2.47)	1.22 (0.58, 2.58)	0.668	0.784	1.10 (0.82, 1.49)	0.520	0.622	
Adrenic acid (C22:4n-6)	Prevalent type 2 diabetes	1.00	3.14 (1.23, 8.02)	6.87 (2.69, 17.54)	<0.001	0.009	2.52 (1.66, 3.84)	<0.001	0.003	
	Incident type 2 diabetes	1.00	1.86 (0.82, 4.25)	3.41 (1.51, 7.70)	0.016	0.104	1.53 (1.11, 2.11)	0.010	0.085	
Clupanodonic acid (C22:5n-3)	Prevalent type 2 diabetes	1.00	1.66 (0.71, 3.92)	4.79 (2.00, 11.47)	0.001	0.009	2.16 (1.49, 3.12)	<0.001	0.003	
	Incident type 2 diabetes	1.00	1.13 (0.57, 2.25)	2.30 (1.15, 4.61)	0.032	0.130	1.32 (0.99, 1.75)	0.058	0.186	
Osbond acid (C22:5n-6)	Prevalent type 2 diabetes	1.00	1.51 (0.66, 3.44)	4.20 (1.85, 9.52)	0.003	0.016	2.41 (1.62, 3.57)	<0.001	0.003	
	Incident type 2 diabetes	1.00	0.73 (0.37, 1.46)	1.64 (0.81, 3.34)	0.279	0.414	1.43 (1.05, 1.94)	0.022	0.112	
Docosahexaenoic acid (DHA) (C22:6n-3)	Prevalent type 2 diabetes	1.00	2.30 (1.01, 5.21)	4.20 (1.83, 9.66)	0.004	0.016	1.98 (1.41, 2.78)	<0.001	0.003	
	Incident type 2 diabetes	1.00	0.84 (0.42, 1.68)	1.51 (0.74, 3.06)	0.396	0.525	1.22 (0.91, 1.62)	0.180	0.344	
<i>Carnitine and acylcarnitines</i>										
L-Carnitine	Prevalent type 2 diabetes	1.00	0.39 (0.19, 0.78)	0.17 (0.06, 0.44)	<0.001	0.009	0.57 (0.40, 0.81)	0.002	0.006	

	Incident type 2 diabetes	1.00	0.80 (0.39, 1.62)	0.51 (0.23, 1.15)	0.133	0.270	0.77 (0.54, 1.09)	0.135	0.317
Acetylcarnitine (C2)	Prevalent type 2 diabetes	1.00	1.19 (0.58, 2.42)	1.42 (0.65, 3.08)	0.712	0.749	1.05 (0.76, 1.46)	0.746	0.785
	Incident type 2 diabetes	1.00	1.47 (0.72, 3.01)	2.03 (1.03, 3.98)	0.061	0.177	1.09 (0.85, 1.40)	0.514	0.622
Propionylcarnitine (C3)	Prevalent type 2 diabetes	1.00	0.98 (0.50, 1.93)	0.60 (0.28, 1.29)	0.418	0.481	0.78 (0.56, 1.10)	0.156	0.216
	Incident type 2 diabetes	1.00	0.96 (0.46, 1.99)	1.19 (0.58, 2.47)	0.481	0.611	1.04 (0.75, 1.44)	0.796	0.867
Butyrylcarnitine (C4)	Prevalent type 2 diabetes	1.00	0.56 (0.26, 1.20)	0.60 (0.29, 1.23)	0.297	0.357	0.86 (0.63, 1.16)	0.308	0.348
	Incident type 2 diabetes	1.00	0.83 (0.42, 1.65)	1.26 (0.63, 2.53)	0.464	0.602	1.13 (0.81, 1.57)	0.466	0.580
3-Hydroxybutyrylcarnitine(C4OH)	Prevalent type 2 diabetes	1.00	1.33 (0.61, 2.91)	3.22 (1.48, 7.03)	0.011	0.031	1.46 (1.10, 1.95)	0.009	0.022
	Incident type 2 diabetes	1.00	3.82 (1.75, 8.30)	3.15 (1.45, 6.87)	0.017	0.104	1.14 (0.87, 1.49)	0.329	0.446
Valerylcarnitine (C5)	Prevalent type 2 diabetes	1.00	0.91 (0.39, 2.12)	1.57 (0.69, 3.53)	0.069	0.114	1.23 (0.88, 1.71)	0.220	0.274
	Incident type 2 diabetes	1.00	2.36 (1.14, 4.85)	1.70 (0.82, 3.53)	0.117	0.246	1.27 (0.89, 1.81)	0.189	0.344
3-Hydroxyisovalerylcarnitine (C5OH)	Prevalent type 2 diabetes	1.00	0.87 (0.43, 1.78)	2.04 (1.00, 4.17)	0.065	0.110	1.28 (0.94, 1.75)	0.117	0.183
	Incident type 2 diabetes	1.00	0.93 (0.46, 1.88)	1.13 (0.50, 2.53)	0.911	0.911	0.94 (0.73, 1.21)	0.630	0.725
Hexanoylcarnitine (C6)	Prevalent type 2 diabetes	1.00	1.39 (0.68, 2.83)	2.42 (1.12, 5.23)	0.140	0.203	1.24 (0.89, 1.72)	0.197	0.250
	Incident type 2 diabetes	1.00	1.73 (0.91, 3.29)	1.60 (0.79, 3.23)	0.332	0.460	1.17 (0.89, 1.54)	0.255	0.409
3-Hydroxyhexanoylcarnitine (C6OH)	Prevalent type 2 diabetes	1.00	1.04 (0.48, 2.24)	1.10 (0.54, 2.26)	0.880	0.880	1.09 (0.80, 1.48)	0.603	0.657
	Incident type 2 diabetes	1.00	1.41 (0.72, 2.74)	2.26 (1.13, 4.51)	0.034	0.130	1.14 (0.88, 1.49)	0.316	0.438
Octanoylcarnitine (C8)	Prevalent type 2 diabetes	1.00	1.63 (0.76, 3.49)	3.13 (1.37, 7.18)	0.050	0.095	1.23 (0.91, 1.68)	0.181	0.235
	Incident type 2 diabetes	1.00	1.42 (0.70, 2.90)	2.04 (1.03, 4.03)	0.091	0.218	1.14 (0.85, 1.52)	0.376	0.488
3-Hydroxyoctanoylcarnitine (C8OH)	Prevalent type 2 diabetes	1.00	1.51 (0.74, 3.09)	2.13 (1.01, 4.49)	0.253	0.346	1.30 (0.94, 1.80)	0.109	0.180
	Incident type 2 diabetes	1.00	1.48 (0.69, 3.20)	1.84 (0.91, 3.70)	0.173	0.293	1.23 (0.93, 1.63)	0.143	0.323
Decanoylcarnitine (C10)	Prevalent type 2 diabetes	1.00	1.59 (0.75, 3.33)	3.01 (1.33, 6.80)	0.052	0.095	1.24 (0.91, 1.68)	0.175	0.232
	Incident type 2 diabetes	1.00	1.85 (0.92, 3.72)	1.93 (0.97, 3.83)	0.153	0.288	1.17 (0.88, 1.55)	0.285	0.424
3-Hydroxydecanoylcarnitine (C10OH)	Prevalent type 2 diabetes	1.00	1.20 (0.59, 2.46)	2.19 (1.02, 4.71)	0.270	0.346	1.28 (0.94, 1.75)	0.122	0.186
	Incident type 2 diabetes	1.00	1.19 (0.58, 2.45)	1.66 (0.84, 3.27)	0.285	0.414	1.23 (0.93, 1.62)	0.149	0.325
9-Decenoylcarnitine (C10:1)	Prevalent type 2 diabetes	1.00	1.07 (0.54, 2.10)	1.86 (0.92, 3.78)	0.272	0.346	1.21 (0.92, 1.61)	0.175	0.232
	Incident type 2 diabetes	1.00	1.39 (0.70, 2.76)	1.37 (0.71, 2.66)	0.623	0.760	1.15 (0.88, 1.51)	0.303	0.436
Dodecanoylcarnitine (C12)	Prevalent type 2 diabetes	1.00	1.43 (0.70, 2.92)	2.86 (1.28, 6.41)	0.053	0.095	1.35 (0.97, 1.88)	0.074	0.137
	Incident type 2 diabetes	1.00	2.34 (1.10, 4.98)	2.31 (1.10, 4.84)	0.067	0.178	1.27 (0.96, 1.68)	0.094	0.249
3-Hydroxydodecanoylcarnitine (C12OH)	Prevalent type 2 diabetes	1.00	1.22 (0.58, 2.56)	2.56 (1.16, 5.63)	0.077	0.120	1.54 (1.12, 2.12)	0.008	0.021
	Incident type 2 diabetes	1.00	1.58 (0.79, 3.18)	2.23 (1.10, 4.54)	0.051	0.164	1.38 (1.04, 1.82)	0.026	0.113

2-Dodecenoylcarnitine (C12:1)	Prevalent type 2 diabetes	1.00	1.39 (0.65, 2.96)	2.12 (1.00, 4.47)	0.299	0.357	1.30 (0.94, 1.80)	0.115	0.183
	Incident type 2 diabetes	1.00	1.32 (0.67, 2.59)	1.78 (0.92, 3.42)	0.199	0.311	1.16 (0.89, 1.51)	0.266	0.416
Tetradecanoylcarnitine (C14)	Prevalent type 2 diabetes	1.00	1.16 (0.55, 2.43)	4.79 (1.99, 11.52)	0.005	0.019	1.54 (1.11, 2.15)	0.011	0.025
	Incident type 2 diabetes	1.00	2.54 (1.23, 5.23)	2.59 (1.27, 5.26)	0.027	0.118	1.35 (1.01, 1.79)	0.042	0.142
3-Hydroxytetradecanoylcarnitine(C14OH)	Prevalent type 2 diabetes	1.00	1.39 (0.62, 3.09)	3.30 (1.59, 6.85)	0.004	0.016	1.83 (1.29, 2.60)	0.001	0.003
	Incident type 2 diabetes	1.00	1.30 (0.64, 2.63)	2.08 (0.98, 4.40)	0.075	0.191	1.27 (0.96, 1.69)	0.092	0.249
2-Tetradecenoylcarnitine (C14:1)	Prevalent type 2 diabetes	1.00	2.70 (1.27, 5.71)	3.14 (1.33, 7.41)	0.075	0.120	1.40 (1.00, 1.96)	0.052	0.106
	Incident type 2 diabetes	1.00	1.32 (0.65, 2.67)	1.82 (0.92, 3.62)	0.188	0.305	1.20 (0.91, 1.58)	0.201	0.344
Hexadecanoylcarnitine (C16)	Prevalent type 2 diabetes	1.00	1.73 (0.87, 3.43)	2.02 (0.95, 4.29)	0.157	0.223	1.56 (1.10, 2.21)	0.013	0.028
	Incident type 2 diabetes	1.00	4.19 (1.71, 10.27)	3.92 (1.50, 10.28)	0.024	0.118	1.23 (0.88, 1.72)	0.227	0.374
3-Hydroxyhexadecanoylcarnitine (C16OH)	Prevalent type 2 diabetes	1.00	1.58 (0.80, 3.12)	2.80 (1.28, 6.09)	0.029	0.068	1.54 (1.10, 2.14)	0.011	0.025
	Incident type 2 diabetes	1.00	1.30 (0.70, 2.40)	1.89 (0.82, 4.35)	0.162	0.288	1.21 (0.91, 1.61)	0.192	0.344
9-Hexadecenoylcarnitine (C16:1)	Prevalent type 2 diabetes	1.00	2.12 (1.05, 4.29)	2.22 (1.00, 4.92)	0.289	0.357	1.38 (0.99, 1.92)	0.055	0.108
	Incident type 2 diabetes	1.00	1.62 (0.80, 3.28)	2.66 (1.28, 5.52)	0.021	0.116	1.20 (0.91, 1.58)	0.203	0.344
3-Hydroxy-9-hexadecenoylcarnitine (C16:1OH)	Prevalent type 2 diabetes	1.00	1.81 (0.85, 3.46)	2.67 (1.16, 6.16)	0.094	0.140	1.58 (1.13, 2.20)	0.007	0.019
	Incident type 2 diabetes	1.00	1.61 (0.84, 3.10)	1.73 (0.85, 3.50)	0.160	0.288	1.14 (0.88, 1.47)	0.307	0.436
9,12-Hexadecadienoylcarnitine (C16:2)	Prevalent type 2 diabetes	1.00	1.98 (1.01, 3.89)	2.72 (1.18, 6.26)	0.086	0.131	1.32 (0.96, 1.80)	0.088	0.153
	Incident type 2 diabetes	1.00	1.25 (0.63, 2.48)	1.57 (0.82, 2.98)	0.344	0.466	1.16 (0.88, 1.53)	0.284	0.424
Octadecanoylcarnitine (C18)	Prevalent type 2 diabetes	1.00	1.55 (0.79, 3.04)	1.76 (0.79, 3.94)	0.256	0.346	1.18 (0.85, 1.64)	0.324	0.359
	Incident type 2 diabetes	1.00	1.29 (0.65, 2.56)	1.07 (0.50, 2.31)	0.870	0.893	1.02 (0.74, 1.39)	0.916	0.916
3-Hydroxyoctadecanoylcarnitine (C18OH)	Prevalent type 2 diabetes	1.00	1.34 (0.67, 2.69)	0.95 (0.32, 2.87)	0.820	0.834	1.06 (0.78, 1.45)	0.698	0.747
	Incident type 2 diabetes	1.00	1.01 (0.53, 1.91)	0.85 (0.28, 2.59)	0.812	0.869	0.97 (0.71, 1.32)	0.855	0.884
Oleylcarnitine (C18:1)	Prevalent type 2 diabetes	1.00	2.55 (1.19, 5.44)	1.80 (0.79, 4.12)	0.519	0.586	1.31 (0.95, 1.82)	0.103	0.175
	Incident type 2 diabetes	1.00	2.53 (1.20, 5.33)	2.23 (1.02, 4.88)	0.107	0.233	1.06 (0.78, 1.43)	0.726	0.812
3-Hydroxy-9-octadecenoylcarnitine (C18:1OH)	Prevalent type 2 diabetes	1.00	1.85 (0.91, 3.80)	2.03 (0.79, 5.21)	0.544	0.603	1.29 (0.92, 1.81)	0.135	0.196
	Incident type 2 diabetes	1.00	2.36 (1.26, 4.44)	1.55 (0.67, 3.60)	0.165	0.288	1.25 (0.95, 1.65)	0.116	0.283
Linoleylcarnitine(C18:2)	Prevalent type 2 diabetes	1.00	0.96 (0.50, 1.85)	1.02 (0.52, 2.04)	0.642	0.687	0.98 (0.73, 1.30)	0.871	0.886
	Incident type 2 diabetes	1.00	2.23 (1.12, 4.43)	1.63 (0.73, 3.63)	0.249	0.380	1.03 (0.75, 1.42)	0.845	0.884
3-Hydroxy-9,12-octadecenoylcarnitine (C18:2OH)	Prevalent type 2 diabetes	1.00	1.88 (0.97, 3.64)	0.60 (0.11, 3.16)	0.808	0.834	1.19 (0.88, 1.60)	0.261	0.306
	Incident type 2 diabetes	1.00	1.58 (0.88, 2.83)	1.23 (0.26, 5.82)	0.326	0.460	1.20 (0.91, 1.58)	0.187	0.344
C20:4-carnitine	Prevalent type 2 diabetes	1.00	0.72 (0.34, 1.50)	0.97 (0.40, 2.34)	0.304	0.357	0.96 (0.71, 1.31)	0.819	0.847

	Incident type 2 diabetes	1.00	1.00 (0.55, 1.81)	0.80 (0.30, 2.13)	0.665	0.784	0.97 (0.70, 1.33)	0.829	0.884
C20:5-carnitine	Prevalent type 2 diabetes	1.00	1.77 (0.92, 3.43)	5.71 (1.05, 30.98)	0.049	0.095	1.40 (1.03, 1.91)	0.031	0.065
	Incident type 2 diabetes	1.00	1.09 (0.58, 2.08)	1.64 (0.41, 6.58)	0.746	0.842	1.14 (0.83, 1.56)	0.427	0.543
C22:6-carnitine	Prevalent type 2 diabetes	1.00	1.30 (0.69, 2.46)	1.74 (0.68, 4.45)	0.636	0.687	1.17 (0.88, 1.56)	0.289	0.333
	Incident type 2 diabetes	1.00	1.06 (0.57, 1.95)	1.25 (0.49, 3.21)	0.878	0.893	1.08 (0.81, 1.45)	0.607	0.712

^aOR (95% CI) and *p* values were calculated by conditional logistic regression after adjustment for BMI, history of hypertension, smoking, physical activity, fasting status, triglycerides, and HDL-cholesterol.

Table S4: Reclassification of incident type 2 diabetes cases and matched controls with no categories based on their serum metabolites, The Singapore Chinese Health Study ^a

Lysophosphatidylinositol (16:1)	All	Assigned to higher diabetes risk	Assigned to lower diabetes risk	NRI	
Expected number of event participants	160	84	76	Among event participants	4.5%
Expected number of non-event participants	160	54	106	Among non-event participants	32.8%
				Overall original (95% CI)	37.3% (12.5%, 62.1%)
Dihomo- γ -linolenic acid	All	Assigned to higher diabetes risk	Assigned to lower diabetes risk	NRI	
Expected number of event participants	160	84	76	Among event participants	5.0%
Expected number of non-event participants	160	53	107	Among non-event participants	33.8%
				Overall original (95% CI)	38.8% (16.8%, 60.8%)

^a Multivariate model adjusted for BMI, history of hypertension, smoking, physical activity, fasting status, triglycerides, and HDL-cholesterol.

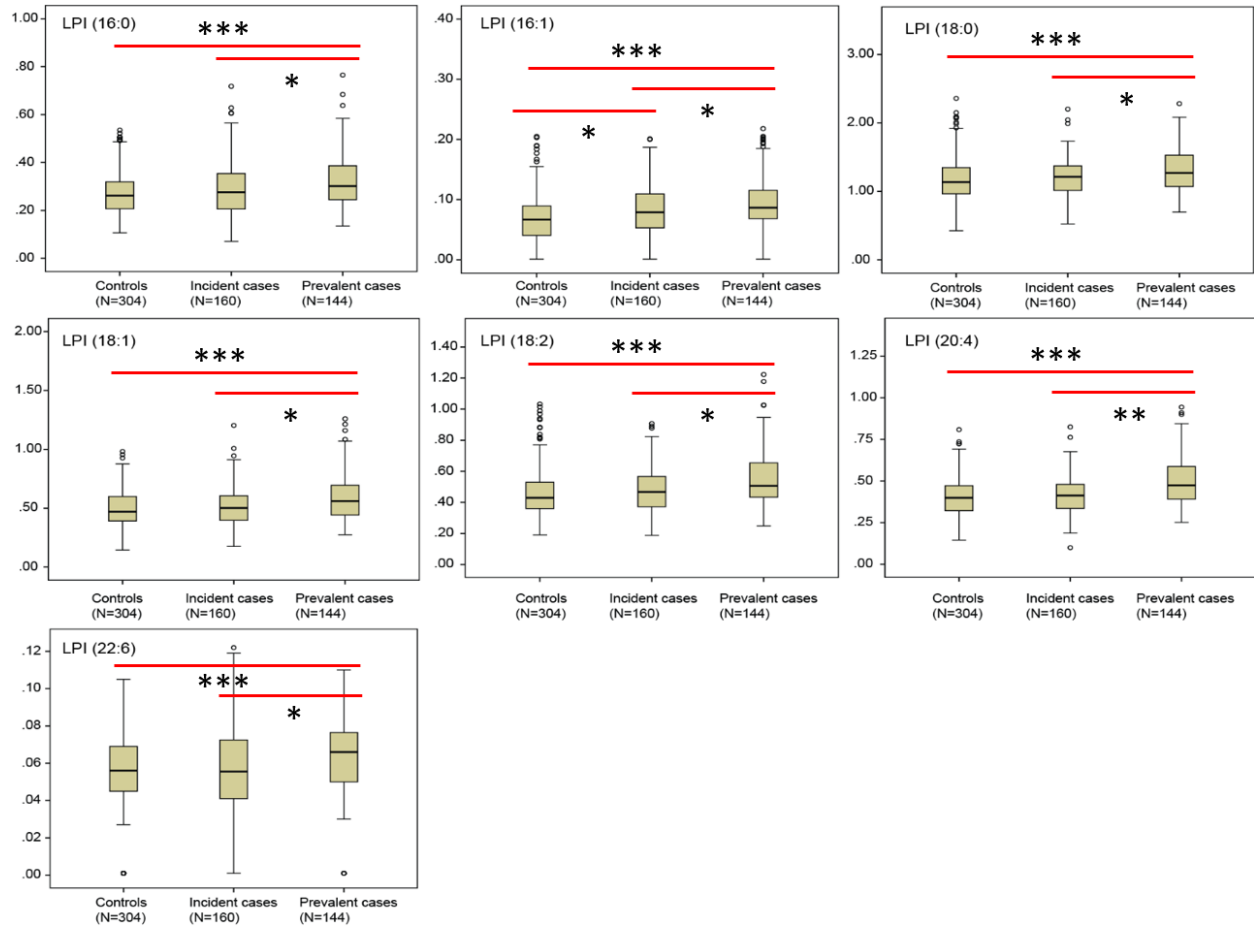


Figure S1. The expression of seven measured Isophosphatidylinositols (LPIs) in controls, incident and prevalent type 2 diabetes. The unit of Y-axis is μM . *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$ in one-way analysis of covariance (ANCOVA), adjusting for BMI, history of hypertension, smoking, physical activity, fasting status, triglycerides, and HDL-cholesterol.