**Supplemental Figures and Tables accompanying manuscript *Herzog et al. 2020 Metabolic effects of gastric bypass surgery - is it all about calories?***

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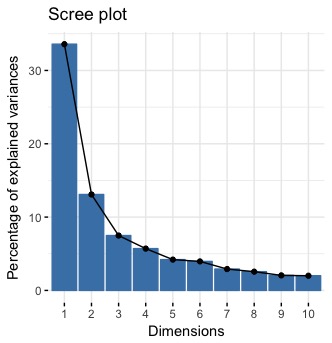
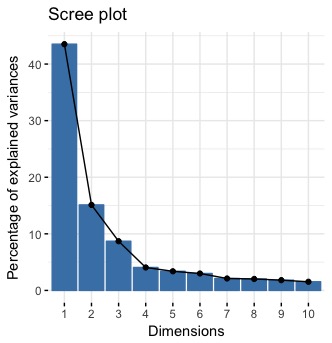
**Figure S1.** Changes in weight of individual participants over the study period.

**Macintosh HD:Users:katharina.herzog:Documents:PROJECT GASTRO Metabolomics diet vs RYGB:20191218 Figure S1.pdf**

Line plot depicting weight loss (in kg) by individual study participant at different time points of the study. VLCD, very low-calorie diet, RYGB (6w), 6 week after gastric bypass surgery.

**Figure S2A.** Assessment of principal component analysis by eigenvalues (scree plot).

**Metabolomics data Lipidomics data**

****

Scree plot of principal component analysis conducted on metabolomics data (left panel) and lipidomics data (right panel) derived from fasting plasma samples. Boxes depict eigenvalues of the first 10 principal components as boxplots shown as the percentage of variances explained by each principal component.

**Figure S2B.** Assessment of principal component analysis by coefficients of metabolites and lipids (loadings plot).

Metabolomics data Lipidomics data

Macintosh HD:Users:katharina.herzog:Documents:PROJECT GASTRO Metabolomics diet vs RYGB:20200325 PCA loading plot Barplot PC2 LIPIDS.pdf**Macintosh HD:Users:katharina.herzog:Documents:PROJECT GASTRO Metabolomics diet vs RYGB:20200325 PCA loading plot Barplot PC2.pdf**

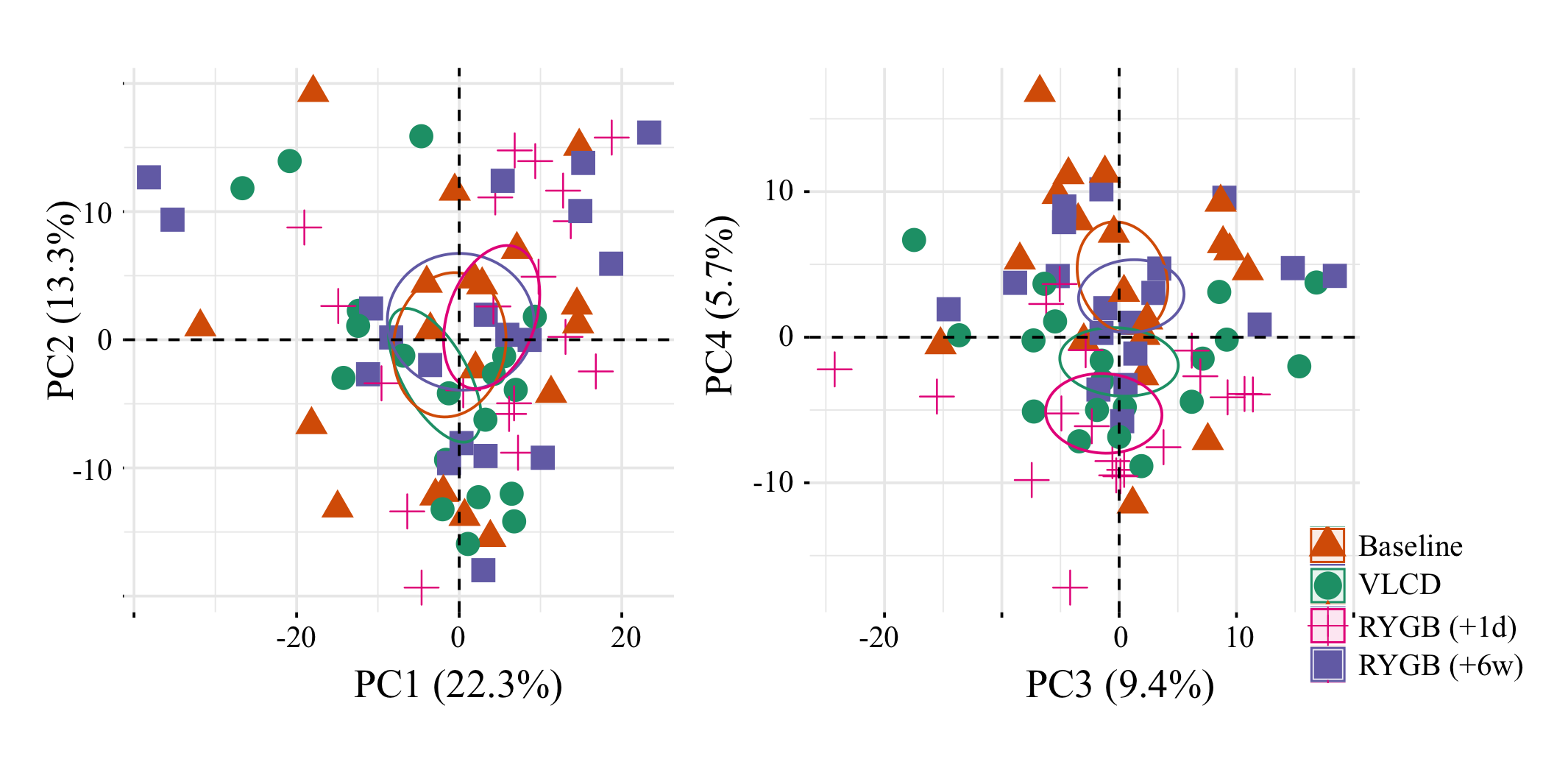
Loading plot of principal component analysis conducted on metabolomics data (left panel) and lipidomics data (right panel) derived from fasting plasma samples. Boxes depict the coefficients for each variable for the second principal component.

Macintosh HD:Users:katharina.herzog:Documents:PROJECT GASTRO Metabolomics diet vs RYGB:20190912 Figure S2.pdf**Figure S3.** Heatmap and box-and-whisker plots displaying significantly changed metabolites as determined by linear mixed-effect models.

Enlargement of Figure 2A with indication of individual metabolites (displayed on the left panel). See corresponding legend of Figure 2A for details.

**Figure S4.** Principal component analysis using untargeted data: (A) score plot and (B) assessment by eigenvalues, and (C) evaluation of scores.

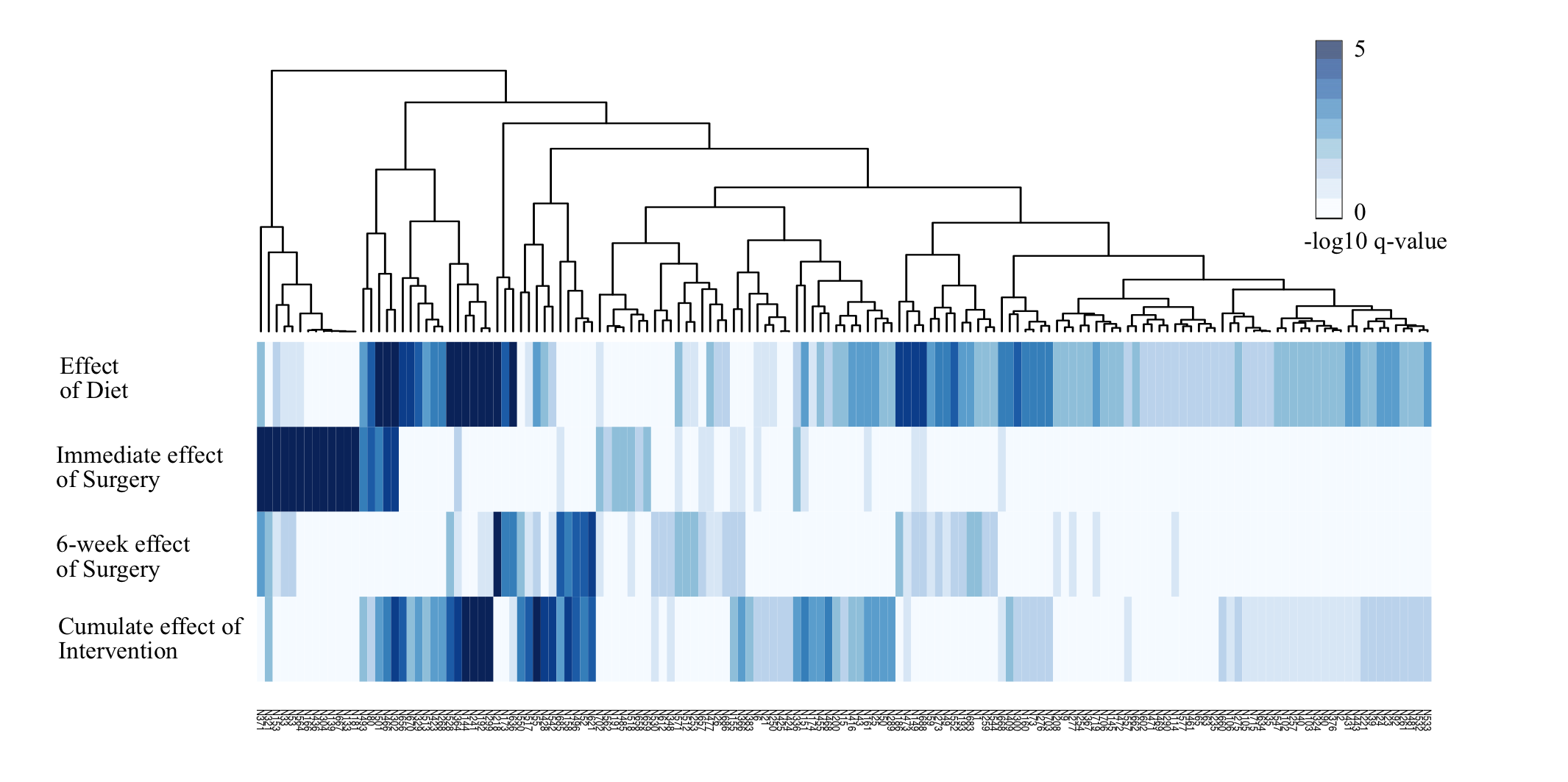
Features were extracted in data generated in positive ESI mode for the pooled metabolite extracts. 820 features remained after filtering for S/N>10, >2 isotopes and gaussian peak shape (manual investigation). Next, these features were extracted from all samples. Features found in <15% of samples were excluded and peaks manually re-integrated, leaving a total of 719 features in the data. These data were subsequently processed and analysed as outlined for the identified metabolites.

**A Scree plot B PCA score plots**

**Macintosh HD:Users:katharina.herzog:Documents:PROJECT GASTRO Metabolomics diet vs RYGB:20200406 PCA screeplot UNtargeted data.eps**

Principal component analysis (PCA) conducted on untargeted data derived from fasting plasma samples. (A) Scree plot PCA; boxes depict eigenvalues of the first 10 principal components (PCs) as boxplots shown as the percentage of variances explained by each principal component. (B) Score scatter plot of PCA are shown; PC1 vs. PC2 (left panel) and PC3 vs. PC4 (right panel), and the percentage of explained variance by the components is indicated in parentheses. Ellipses show the 95% confidence regions of the indicated study occasions. Fasting plasma samples obtained at baseline (-4w) are depicted as orange triangles, samples obtained after the VLCD (-1d) are depicted as green circles, samples obtained immediately after surgery (+1d) are depicted as pink crosses, and samples obtained after at 6-week recovery period (+6w) are depicted as purple squares.

**Figure S5.** Heatmap displaying significantly changed metabolites as determined by linear mixed-effect models using untargeted data.



Metabolites as determined using untargeted metabolomics data with significant differences in response to the very low-calorie diet, the immediate effect of Roux-en-Y gastric bypass surgery, the 6-week effect of surgery, and the cumulative effect of the intervention as determined by linear mixed-effect models (LMMs) are displayed in a heatmap. Colour intensity reflects the –log10 q-values of the LMMs.

**Table S1.** Anthropometric and clinical data of the study population for the different study occasions.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Whole cohort** | | | | **Normoglycaemic patients** | | | | **T2D patients** | | | |
|  | Baseline | VLCD | RYGB (+1d) | RYGB (+6w) | Baseline | VLCD | RYGB (+1d) | RYGB (+6w) | Baseline | VLCD | RYGB (+1d) | RYGB (+6w) |
| **N** | 19 | - | - | - | 9 | - | - | - | 10 | - | - | - |
| **Age** (Yr) # | 43.1 ± 6.3 | - | - | - | 40.4± 4.8 | - | - | - | 45.4 ± 6.6 | - | - | - |
| **Diabetes duration** (Yr) § | - | - | - | - | - | - | - | - | 2.0 (2.8) | - | - | - |
| **HbA1c** (mmol/mol) § | 41.0 (14.5) | - | - | - | 37.0 (2.0) \*\* | - | - | - | 51.0 (9.8) \*\* | - | - | - |
| **HbA1c** (%) § | 5.9 (3.5) |  |  |  | 5.5 (2.3) \*\* |  |  |  | 6.8 (3.1) \*\* |  |  |  |
| **Body weight** (kg) # | 112.8 ± 11.9 | 104.9 ± 10.9 | - | 94.3 ± 10.9 | 114.2 ± 10.4 | 106.5 ± 9.1 | - | 95.1 ± 10.0 | 111.6 ± 12.9 | 103.4 ± 12.2 | - | 93.7 ± 11.6 |
| **BMI** (kg/m2) # | 39.8 ± 3.3 | 37.0 ± 3.0 | - | 33.3 ± 3.1 | 40.2 ± 3.3 | 37.5 ± 3.0 | - | 33.5 ± 3.2 | 39.4 ± 3.3 | 36.5 ± 2.9 | - | 33.1 ± 3.0 |
| **Weight loss** (kg) § | - | 8.0 (3.0) | - | 10.3 (5.2) | - | 7.0 (3.6) | - | 10.3 (5.3) | - | 8.1 (2.1) | - | 10.6 (6.0) |
| **Fasting GIP** (pg) § | 175.4 (100.5) | 165.6 (66.2) | 104.2 (61.3) | 128.7 (72.9) | 184.9 (118.1) | 188.8 (85.1) | 99.6 (39.8) | 90.1 (72.9) | 158.1 (63.3) | 143.4 (75.3) | 107.2 (61.4) | 135.0 (81.9) |
| **Fasting GLP-1** (pM) § | 3.6 (1.2) | 3.6 (0.7) | 3.9 (11.2) | 4.8 (7.4) | 3.8 (1.6) | 3.6 (0.5) | 4.1 (14.3) | 4.2 (1.5) \* | 3.5 (0.2) | 3.6 (0.8) | 3.6 (1.9) | 11.1 (13.8) \* |
| **Fasting glucose** (mmol/L) § | 5.1 (1.3) | 5.8 (3.8) | 6.1 (3.0) | 6.1 (2.7) | 5.1 (1.0) | 6.7 (3.9) | 6.3 (3.1) | 6.0 (1.5) | 5.5 (2.7) | 5.7 (3.2) | 6.0 (2.4) | 6.8 (3.9) |
| **Fasting insulin** (uIU/mL) § | 18.3 (8.6) | 12.9 (4.8) | 15.6 (4.7) | 12.8 (5.9) | 18.3 (6.4) | 13.8 (7.2) | 15.3 (10.2) | 14.8 (7.0) | 18.0 (9.2) | 12.9 (3.8) | 18.0 (4.4) | 12.0 (4.5) |
| **HOMA-IR** § | 4.8 (2.9) | 3.5 (1.9) | 4.8 (2.2) | 4.9 (6.9) | 4.6 (1.6) | 3.6 (2.0) | 5.5 (2.4) | 4.0 (2.4) | 5.5 (3.2) | 3.1 (1.8) | 3.9 (1.9) | 6.0 (9.0) |
| **HOMA-B** § | 12.5 (10.1) | 5.3 (7.8) | 7.3 (8.2) | 8.2 (9.4) | 15.1 (13.7) | 6.7 (8.2) | 7.8 (10.9) | 11.2 (10.7) | 7.6 (10.2) | 4.8 (6.3) | 6.5 (4.9) | 4.1 (9.1) |

# mean ± SD; § median, IQR; \* and \*\*, p-value < 0.05 (\*) and < 0.01 (\*\*), respectively, estimating the difference between normoglycaemic and T2d patients as determined by Wilcoxon Rank Sum Test; BMI, body mass index; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide 1; HbA1c, haemoglobin A1c; HOMA-IR, homeostatic model assessment of insulin resistance; HOMA-B, homeostatic model assessment beta-cell function; RYGB (1d), Roux-en-Y gastric bypass surgery after Day 1; RYGB (6w), 6-weeks after surgery; VLCD, very low-calorie diet.

**Table S2.** Medications in T2D patients.

|  |  |
| --- | --- |
| **N** | **T2D treatment** |
| 2 | Dietary intervention only |
| 1 | Dietary intervention, insulin at times |
| 3 | Metformin only |
| 1 | Metformin, Insulin |
| 1 | Metformin, Glibenklamid |
| 1 | Insulin only |
| 1 | Insulin, Novorapid, Insulatard |

Overview of prescribed diabetes medications among T2D patients (N= 10). After surgery, none of the study participants obtained pharmacological treatment for diabetes. One individual was prescribed metformin again four years after surgery.

**Table S3.** Assessment of changes in anthropometric and clinical data elicited by VLCD, RYGB and the combined intervention.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Weight** | **BMI** | **Glucose** | **Insulin** | **HbA1c** | **GIP #** | **GLP-1 #** | **HOMA-IR #** | **HOMA-B #** | **Matsuda** | **Disposition index** |
| **VLCD vs. Baseline** | <0.0001 | <0.0001 | 0.1873 | 0.4149 | 1.0000 | 0.9979 | 0.9999 | 0.9783 | 0.0271 | 0.2160 | 0.9991 |
| **RYGB (1d) vs. VLCD** | 1.0000 | 1.0000 | 0.9923 | 0.9906 | 1.0000 | 0.0070 | 0.0850 | 0.9031 | 0.8106 | 0.0469 | 0.9979 |
| **RYGB (6w) vs. VLCD** | <0.0001 | <0.0001 | 0.4950 | 0.9586 | 1.0000 | 0.0057 | 0.9935 | 0.9979 | 0.3550 | 0.1541 | 0.7049 |
| **RYGB (6w) vs. Baseline** | <0.0001 | <0.0001 | 0.9719 | 0.8206 | 1.0000 | 0.0021 | 0.9986 | 0.9989 | 0.7573 | 0.9998 | 0.5555 |
| **T2D vs. ND** | 0.9754 | 0.9577 | 0.9916 | 0.9976 | <0.0001 | 0.2567 | 0.9885 | 1.0000 | 0.9844 | 0.9998 | 0.9871 |
|  |  |  |  |  |  |  |  |  |  |  |  |

Variation between individual participants was acknowledged by using linear mixed-effect models; differences in values are presented as p-value after adjustment for the multiple comparisons. BMI, body mass index; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide 1; HbA1c, haemoglobin A1c; HOMA-IR, homeostatic model assessment of insulin resistance; HOMA-B, homeostatic model assessment beta-cell function; #, log-2 transformed values were used for calculations (data were non-normal distributed); RYGB (1d), Roux-en-Y gastric bypass surgery after Day 1; RYGB (6w), 6-weeks after surgery; VLCD, very low-calorie diet.

**Table S4A.** Identification levels of detected metabolites.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metabolite** | **ID level** | **Metabolite** | **ID level** | **Metabolite** | **ID level** | **Metabolite** | **ID level** | |
| 1-Methyl-adenosine | 2b | Carnitine C4:0 | 2a | LPC 17:0 | 2a | PC 32:1 | 2a |
| 1-Methylhistidine | 2b | Carnitine C5:0 | 2a | LPC 18:0 | 2a | PC 34:1 | 2a |
| 2-Hydroxycinnamic acid | 2b | Carnitine C6:0 | 2a | LPC 18:1 | 2a | PC 34:2 | 2a |
| 3-Hydroxybutyrate | 1 | Carnitine C8:0 | 2a | LPC 18:2 | 2a | PC 36:2 | 2a |
| 5-Oxoproline | 2b | Carnitine C8:1 | 2a | LPC 19:0 | 2a | PC 36:3 | 2a |
| Acetylalanine | 2b | Citric acid | 2b | LPC 20:1 | 2a | PC 36:4 | 2a |
| Alanine | 1 | Creatine | 2b | LPC 20:2 | 2a | PC 38:5 | 2a |
| Arginine | 1 | Cystine | 1 | LPC 20:3 | 2a | PC 38:6 | 2a |
| Asparagine | 1 | Dihydroorotic acid | 2b | LPC 20:4 | 2a | PC 40:7 | 2a |
| Aspartic acid | 1 | Gluconic acid | 2b | LPC 20:5 | 2a | PC 40:8 | 2a |
| Caffeine | 1 | Glucosamine-6-phosphate | 2b | LPC 22:5 | 2a | Phenylalanine | 1 |
| Carnitine | 2b | Glutamic acid | 1 | LPC 22:6 | 2a | Proline | 1 |
| Carnitine C10:0 | 2a | Glutamine | 1 | LPE 16:0 | 2a | Serine | 1 |
| Carnitine C10:1 | 2a | Glyceric acid | 2b | LPE 18:0 | 2a | SM 32:1 | 2a |
| Carnitine C10:2 | 2a | Hippuric acid | 2b | LPE 18:1 | 2a | SM 32:2 | 2a |
| Carnitine C12:0 | 2a | Histidine | 1 | LPE 18:2 | 2a | SM 33:1 | 2a |
| Carnitine C12:1 | 2a | Hydroxyproline | 2b | LPE 20:0 | 2a | SM 34:1 | 2a |
| Carnitine C14:0 | 2a | Hypoxanthine | 2b | LPE 20:4 | 2a | SM 34:2 | 2a |
| Carnitine C14:1 | 2a | Indole | 2b | LPE 20:5 | 2a | SM 35:2 | 2a |
| Carnitine C14:2 | 2a | Kynurenine | 1 | LPE 22:6 | 2a | SM 36:2 | 2a |
| Carnitine C16:0 | 2a | Lactic acid | 2b | Lysine | 1 | Taurine | 2b |
| Carnitine C18:0 | 2a | Leucine-Isoleucine | 1 | Malic acid | 2b | Transcinnamic acid | 2b |
| Carnitine C18:1 | 2a | LPC 14:0 | 2a | Methionine | 1 | Tryptophan | 1 |
| Carnitine C18:2 | 2a | LPC 15:0 | 2a | Mevalonic acid | 2b | Tyrosine | 1 |
| Carnitine C2:0 | 2a | LPC 16:0 | 2a | Orotic acid | 2b | Uric acid | 2b |
| Carnitine C3:0 | 2a | LPC 16:1 | 2a | Paraxanthine | 1 | Valine | 1 |

|  |
| --- |
| Level of identificating according to the Metabolomics Standards Initiative (Sumner et al, Metabolomics, 3, 2007) |
| Level 1: Identified based on retention time and MS/MS spectrum of standard. |
| Level 2a: Putatively identified based MS/MS spectrum and structure-retention correlation (physicochemical properties) |
| Level 2b: Putatively identified based on MS/MS spectrum database searches (Metlin) |

**Table S4B.** Identification levels of detected lipids.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Lipid** | **ID level** | **Lipid** | **ID level** | **Lipid** | **ID level** |
| CE16.0\* | 2a | PC38.3\* | 2a | SM42.2\* | 2a |
| CE18.1\* | 2a | PC38.4\* | 2a | SM42.3\* | 2a |
| CE18.2\* | 2a | PC38.5\* | 2a | SM43.1\* | 2a |
| CE18.3\* | 2a | PC38.6\* | 2a | SM43.2\* | 2a |
| CE20.4\* | 2a | PC40.4\* | 2a | SM44.2\* | 2a |
| LPC16.0\* | 2a | PC40.5\* | 2a | TG48.1\* | 2a |
| LPC16.1\* | 2a | PC40.6\* | 2a | TG48.2\* | 2a |
| LPC18.0\* | 2a | SM32.1\* | 2a | TG50.0\* | 2a |
| LPC18.1\* | 2a | SM32.2\* | 2a | TG50.1\* | 2a |
| LPC18.2\* | 2a | SM33.1\* | 2a | TG50.2\* | 2a |
| LPC20.3\* | 2a | SM34.1\* | 2a | TG50.3\* | 2a |
| LPC20.4\* | 2a | SM34.2\* | 2a | TG50.4\* | 2a |
| LPC22.6\* | 2a | SM35.1\* | 2a | TG52.1\* | 2a |
| PC32.0\* | 2a | SM36.0\* | 2a | TG52.2\* | 2a |
| PC32.1\* | 2a | SM36.1\* | 2a | TG52.3\* | 2a |
| PC32.2\* | 2a | SM36.2\* | 2a | TG52.4\* | 2a |
| PC34.0\* | 2a | SM38.1\* | 2a | TG52.5\* | 2a |
| PC34.1\* | 2a | SM38.2\* | 2a | TG54.3\* | 2a |
| PC34.2\* | 2a | SM39.1\* | 2a | TG54.4\* | 2a |
| PC34.3\* | 2a | SM40.0\* | 2a | TG54.5\* | 2a |
| PC36.1\* | 2a | SM40.1\* | 2a | TG54.6\* | 2a |
| PC36.2\* | 2a | SM40.2\* | 2a | TG56.6\* | 2a |
| PC36.3\* | 2a | SM41.1\* | 2a |  |  |
| PC36.4\* | 2a | SM41.2\* | 2a |  |  |
| PC36.5\* | 2a | SM42.1\* | 2a |  |  |

|  |
| --- |
| Level of identificating according to the Metabolomics Standards Initiative (Sumner et al, Metabolomics, 3, 2007) |
| Level 1: Identified based on retention time and MS/MS spectrum of standard. |
| Level 2a: Putatively identified based MS/MS spectrum and structure-retention correlation (physicochemical properties) |
| Level 2b: Putatively identified based on MS/MS spectrum database searches (Metlin) |

**Table S5.** Evaluation of principal component scores as determined by PCA analysis.

**A.** PCA using metabolomics data **B.** PCA using lipidomics data

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **DIFF** | **LWR** | **UPR** | **P** |
| Baseline-VLCD | -5.27 | -6.99 | -3.54 | <0.0001 |
| RYGB (6w)-VLCD | -2.24 | -3.97 | -0.52 | 0.0056 |
| RYGB (1d)-VLCD | 3.18 | 1.46 | 4.90 | <0.0001 |
| RYGB (6w)-Baseline | 3.03 | 1.32 | 4.73 | 0.0001 |
| RYGB (1d)-Baseline | 8.45 | 6.75 | 10.15 | <0.0001 |
| RYGB (1d)- RYGB (6w) | 5.42 | 3.72 | 7.13 | <0.0001 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **DIFF** | **LWR** | **UPR** | **P** |
| Baseline- VLCD | -5.72 | -7.66 | -3.77 | <0.0001 |
| RYGB (6w)- VLCD | -1.05 | -2.99 | 0.90 | 0.4945 |
| RYGB (1d)- VLCD | 0.48 | -1.44 | 2.39 | 0.9142 |
| RYGB (6w)-Baseline | 4.67 | 2.70 | 6.64 | <0.0001 |
| RYGB (1d)-Baseline | 6.19 | 4.25 | 8.14 | <0.0001 |
| RYGB (1d)- RYGB (6w) | 1.52 | -0.42 | 3.47 | 0.1769 |

Analysis Of Variance (ANOVA) models were fitted using scores along principal component 2 for principal component analysis using (A) metabolomics data and (B) lipidomics data, followed by post-hoc analysis testing using Tukey Honest Significant Differences. DIFF, the difference in the observed means; LWR, lower end point of the interval; UPR, upper end point; P, p-value after adjustment for the multiple comparisons; RYGB (1d), Roux-en-Y gastric bypass surgery after Day 1; RYGB (6w), 6-weeks after surgery; VLCD, very low-calorie diet.

**Table 6A.** Linear-mixed-effect models fitted to metabolomics data between study occasions (fasting plasma samples).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 1**  **(adjusted for age)** | | | | **Model 2**  **(adj. for age and weight loss)** | | | | **Model 3**  **(adj. for age and insulin)** | | | | **Direction (Mean, SD)** | | | |
|  | **Effect VLCD** | **RYGB (1d)** | **RYGB (6w)** | **Cum.**  **effect** | **Effect VLCD** | **RYGB (1d)** | **RYGB (6w)** | **Cum.**  **effect** | **Effect VLCD** | **RYGB (1d)** | **RYGB (6w)** | **Cum.**  **effect** | **Effect of VLCD** | **RYGB**  **(1d)** | **RYGB (6w)** | **Cum. effect** |
| **1-Methyl-adenosine** | 0.348 | 0.995 | 0.944 | 0.782 | 0.301 | 0.884 | 0.999 | 0.635 | 0.363 | 0.994 | 0.945 | 0.788 | 0.24 ± 0.49 | -0.29 ± 0.62 | -0.19 ± 0.5 | 0.05 ± 0.48 |
| **1-Methylhistidine** | 0.089 | 0.782 | 0.029 | 0.991 | 0.344 | 0.908 | 0.066 | 1.000 | 0.078 | 0.763 | 0.031 | 0.997 | -0.77 ± 1.92 | -0.07 ± 1.83 | 0.75 ± 1.97 | -0.02 ± 0.65 |
| **2-Hydroxy-**  **cinnamic acid** | 0.649 | 0.132 | 0.261 | 0.958 | 0.737 | 0.602 | 0.443 | 1.000 | 0.738 | 0.122 | 0.268 | 0.931 | -0.01 ± 0.46 | 0.13 ± 0.35 | -0.33 ± 0.34 | -0.34 ± 0.5 |
| **3-Hydroxybutyrate** | 0.000 | 0.000 | 0.000 | 0.392 | 0.000 | 0.006 | 0.000 | 0.979 | 0.000 | 0.000 | 0.000 | 0.493 | 1.25 ± 0.63 | 0.77 ± 0.51 | -1.08 ± 0.56 | 0.17 ± 0.73 |
| **5-Oxoproline** | 0.995 | 0.703 | 0.234 | 0.112 | 1.000 | 0.814 | 0.380 | 0.756 | 0.999 | 0.684 | 0.234 | 0.151 | 0.24 ± 1.04 | 0.07 ± 1.21 | 0.48 ± 1.08 | 0.73 ± 0.87 |
| **Acetylalanine** | 0.404 | 0.135 | 0.057 | 0.839 | 0.838 | 0.279 | 0.070 | 0.886 | 0.307 | 0.158 | 0.054 | 0.916 | -0.46 ± 0.74 | -0.6 ± 0.62 | 0.63 ± 0.76 | 0.17 ± 0.68 |
| **Alanine** | 0.319 | 0.324 | 0.632 | 0.981 | 0.693 | 0.697 | 0.662 | 1.000 | 0.297 | 0.315 | 0.632 | 0.972 | -0.56 ± 1.59 | 0.37 ± 1.83 | 0.17 ± 1.66 | -0.38 ± 0.74 |
| **Arginine** | 0.033 | 0.044 | 0.063 | 0.999 | 0.602 | 0.648 | 0.040 | 0.957 | 0.027 | 0.042 | 0.067 | 0.995 | -0.52 ± 1.38 | 0.39 ± 1.35 | 0.56 ± 1.33 | 0.04 ± 0.45 |
| **Asparagine** | 0.256 | 0.016 | 0.246 | 1.000 | 0.780 | 0.292 | 0.237 | 0.993 | 0.197 | 0.014 | 0.247 | 1.000 | -0.33 ± 1.43 | 0.62 ± 1.5 | 0.28 ± 1.48 | -0.05 ± 0.32 |
| **Aspartic acid** | 0.984 | 0.940 | 0.734 | 0.419 | 0.984 | 0.612 | 0.976 | 1.000 | 0.986 | 0.941 | 0.738 | 0.444 | -0.06 ± 1.51 | 0.06 ± 1.21 | -0.12 ± 1.44 | -0.18 ± 1.33 |
| **Caffeine** | 1.000 | 0.000 | 0.485 | 0.594 | 0.998 | 0.001 | 0.659 | 0.979 | 0.999 | 0.000 | 0.490 | 0.686 | -0.42 ± 2.29 | -3.34 ± 2.45 | -1.29 ± 2.52 | -1.71 ± 2.66 |
| **Carnitine** | 0.587 | 0.000 | 0.420 | 0.017 | 0.995 | 0.002 | 0.759 | 0.845 | 0.505 | 0.000 | 0.442 | 0.014 | -0.15 ± 0.2 | 0.66 ± 0.36 | -0.07 ± 0.29 | -0.22 ± 0.26 |
| **Carnitine C10:0** | 0.000 | 0.000 | 0.974 | 0.000 | 0.006 | 0.020 | 0.980 | 0.112 | 0.000 | 0.000 | 0.981 | 0.001 | 0.88 ± 1.07 | -1.28 ± 0.69 | -0.2 ± 0.72 | 0.68 ± 1.09 |
| **Carnitine C10:1** | 0.000 | 0.000 | 0.323 | 0.001 | 0.000 | 0.002 | 0.509 | 0.106 | 0.000 | 0.000 | 0.358 | 0.004 | 0.74 ± 0.87 | -1.09 ± 0.49 | -0.32 ± 0.56 | 0.42 ± 0.8 |
| **Carnitine C10:2** | 0.092 | 0.002 | 0.802 | 0.593 | 0.456 | 0.079 | 0.822 | 0.959 | 0.090 | 0.001 | 0.800 | 0.570 | 0.17 ± 0.52 | -0.63 ± 0.48 | -0.22 ± 0.46 | -0.05 ± 0.63 |
| **Carnitine C12:0** | 0.000 | 0.002 | 0.455 | 0.004 | 0.003 | 0.055 | 0.584 | 0.243 | 0.000 | 0.004 | 0.481 | 0.024 | 0.91 ± 0.96 | -1.04 ± 0.65 | -0.53 ± 0.65 | 0.38 ± 0.96 |
| **Carnitine C12:1** | 0.000 | 0.020 | 0.101 | 0.003 | 0.000 | 0.094 | 0.262 | 0.109 | 0.000 | 0.036 | 0.110 | 0.015 | 1.14 ± 1.14 | -0.77 ± 0.7 | -0.64 ± 0.64 | 0.5 ± 0.98 |
| **Carnitine C14:0** | 0.000 | 0.321 | 0.026 | 0.008 | 0.000 | 0.499 | 0.085 | 0.194 | 0.000 | 0.434 | 0.023 | 0.038 | 0.88 ± 0.72 | -0.46 ± 0.48 | -0.66 ± 0.47 | 0.23 ± 0.72 |
| **Carnitine C14:1** | 0.000 | 0.083 | 0.266 | 0.000 | 0.000 | 0.399 | 0.354 | 0.095 | 0.000 | 0.151 | 0.286 | 0.001 | 1.34 ± 1.03 | -0.64 ± 0.59 | -0.62 ± 0.62 | 0.72 ± 0.9 |
| **Carnitine C14:2** | 0.000 | 0.077 | 0.142 | 0.004 | 0.001 | 0.390 | 0.213 | 0.317 | 0.000 | 0.145 | 0.173 | 0.034 | 1.04 ± 0.97 | -0.58 ± 0.64 | -0.55 ± 0.6 | 0.49 ± 0.8 |
| **Carnitine C16:0** | 0.000 | 0.999 | 0.188 | 0.000 | 0.000 | 0.975 | 0.400 | 0.013 | 0.000 | 1.000 | 0.193 | 0.000 | 0.8 ± 0.6 | -0.14 ± 0.42 | -0.41 ± 0.43 | 0.38 ± 0.6 |
| **Carnitine C18:0** | 0.001 | 0.994 | 0.756 | 0.055 | 0.023 | 0.964 | 0.912 | 0.305 | 0.012 | 1.000 | 0.772 | 0.196 | 0.36 ± 0.56 | -0.11 ± 0.36 | -0.18 ± 0.42 | 0.18 ± 0.53 |
| **Carnitine C18:1** | 0.000 | 0.860 | 0.247 | 0.000 | 0.000 | 0.963 | 0.327 | 0.003 | 0.000 | 0.951 | 0.276 | 0.000 | 1.1 ± 0.65 | -0.22 ± 0.41 | -0.42 ± 0.47 | 0.68 ± 0.58 |
| **Carnitine C18:2** | 0.000 | 0.487 | 0.012 | 0.001 | 0.000 | 0.629 | 0.046 | 0.077 | 0.000 | 0.671 | 0.019 | 0.008 | 0.78 ± 0.55 | -0.27 ± 0.41 | -0.5 ± 0.47 | 0.28 ± 0.47 |
| **Carnitine C2:0** | 0.000 | 0.003 | 0.001 | 0.848 | 0.022 | 0.021 | 0.001 | 1.000 | 0.000 | 0.002 | 0.001 | 0.970 | 0.89 ± 0.48 | 0.63 ± 0.46 | -0.66 ± 0.48 | 0.23 ± 0.53 |
| **Carnitine C3:0** | 0.999 | 0.999 | 0.004 | 0.008 | 0.885 | 0.975 | 0.043 | 0.820 | 1.000 | 0.999 | 0.004 | 0.007 | -0.2 ± 0.51 | 0.12 ± 0.5 | -0.33 ± 0.53 | -0.52 ± 0.57 |
| **Carnitine C4:0** | 0.223 | 0.935 | 0.738 | 0.890 | 0.975 | 0.584 | 0.446 | 0.979 | 0.416 | 0.886 | 0.748 | 0.978 | 0.24 ± 0.64 | 0 ± 0.54 | -0.22 ± 0.55 | 0.02 ± 0.73 |
| **Carnitine C5:0** | 0.673 | 0.773 | 0.004 | 0.144 | 0.856 | 0.944 | 0.015 | 0.739 | 0.773 | 0.748 | 0.004 | 0.123 | 0.18 ± 0.65 | 0.3 ± 0.69 | -0.8 ± 0.63 | -0.61 ± 0.73 |
| **Carnitine C6:0** | 0.000 | 0.332 | 0.030 | 0.012 | 0.000 | 0.643 | 0.074 | 0.349 | 0.000 | 0.431 | 0.038 | 0.044 | 0.84 ± 0.82 | -0.34 ± 0.65 | -0.51 ± 0.44 | 0.33 ± 0.68 |
| **Carnitine C8:0** | 0.000 | 0.000 | 0.706 | 0.001 | 0.004 | 0.022 | 0.754 | 0.207 | 0.000 | 0.000 | 0.731 | 0.006 | 0.84 ± 1.01 | -1.12 ± 0.63 | -0.29 ± 0.65 | 0.55 ± 0.95 |
| **Carnitine C8:1** | 0.247 | 0.006 | 0.996 | 0.118 | 0.742 | 0.187 | 1.000 | 0.819 | 0.221 | 0.006 | 0.996 | 0.106 | 0.05 ± 0.8 | -0.75 ± 0.49 | -0.07 ± 0.55 | -0.02 ± 0.85 |
| **Citric acid** | 0.081 | 1.000 | 0.985 | 0.232 | 0.400 | 1.000 | 0.985 | 0.805 | 0.121 | 1.000 | 0.987 | 0.300 | 0.59 ± 0.99 | -0.23 ± 0.73 | -0.31 ± 0.81 | 0.27 ± 0.98 |
| **Creatine** | 0.004 | 0.012 | 0.608 | 0.166 | 0.145 | 0.239 | 0.573 | 0.866 | 0.003 | 0.011 | 0.605 | 0.147 | -1.13 ± 1.6 | 1 ± 1.68 | 0.4 ± 1.63 | -0.73 ± 0.78 |
| **Cystine** | 0.284 | 0.456 | 0.939 | 0.717 | 0.569 | 0.709 | 0.962 | 0.931 | 0.340 | 0.480 | 0.942 | 0.770 | -0.49 ± 2.01 | 0.22 ± 1.9 | 0.19 ± 1.74 | -0.3 ± 0.83 |
| **Dihydroorotic acid** | 1.000 | 0.803 | 0.533 | 0.657 | 1.000 | 0.912 | 0.641 | 0.954 | 0.999 | 0.795 | 0.539 | 0.716 | -0.15 ± 1.65 | 0.09 ± 1.12 | 0.14 ± 1.42 | -0.01 ± 1.22 |
| **Gluconic acid** | 0.993 | 0.779 | 0.793 | 0.544 | 0.856 | 0.990 | 0.999 | 0.969 | 0.983 | 0.754 | 0.795 | 0.489 | 0.02 ± 1.36 | 0.19 ± 1.55 | -0.8 ± 2.05 | -0.78 ± 1.73 |
| **Glucosamine-**  **6-phosphate** | 0.270 | 0.378 | 0.035 | 0.869 | 0.564 | 0.660 | 0.068 | 0.982 | 0.269 | 0.378 | 0.036 | 0.889 | -0.3 ± 2.04 | -0.14 ± 2.32 | 0.46 ± 2.17 | 0.16 ± 0.6 |
| **Glutamic acid** | 0.878 | 0.966 | 0.787 | 1.000 | 0.996 | 1.000 | 0.738 | 0.989 | 0.917 | 0.973 | 0.795 | 0.999 | -0.23 ± 1.52 | -0.04 ± 1.93 | 0.06 ± 1.52 | -0.17 ± 0.85 |
| **Glutamine** | 0.268 | 0.092 | 0.147 | 0.997 | 0.671 | 0.435 | 0.187 | 0.996 | 0.223 | 0.086 | 0.149 | 1.000 | -0.36 ± 1.8 | 0.45 ± 1.89 | 0.44 ± 1.86 | 0.08 ± 0.32 |
| **Glyceric acid** | 0.021 | 0.000 | 0.645 | 0.396 | 0.031 | 0.002 | 0.929 | 0.325 | 0.021 | 0.000 | 0.644 | 0.377 | 0.7 ± 0.71 | -1.02 ± 0.68 | -0.49 ± 0.56 | 0.2 ± 0.93 |
| **Hippuric acid** | 0.974 | 0.013 | 0.885 | 0.556 | 1.000 | 0.303 | 0.972 | 0.994 | 0.960 | 0.013 | 0.890 | 0.525 | -0.55 ± 1.49 | -1.18 ± 0.8 | 0.79 ± 1.13 | 0.24 ± 1.28 |
| **Histidine** | 0.032 | 0.128 | 0.077 | 0.996 | 0.372 | 0.617 | 0.083 | 1.000 | 0.032 | 0.127 | 0.080 | 0.994 | -0.61 ± 1.72 | 0.32 ± 1.75 | 0.5 ± 1.67 | -0.11 ± 0.33 |
| **Hydroxyproline** | 0.926 | 0.908 | 0.997 | 0.988 | 0.992 | 0.942 | 0.995 | 1.000 | 0.972 | 0.880 | 0.998 | 0.998 | 0.29 ± 1.14 | 0.16 ± 0.94 | -0.28 ± 1.28 | 0.01 ± 1.42 |
| **Hypoxanthine** | 0.993 | 0.006 | 0.992 | 1.000 | 0.971 | 0.197 | 1.000 | 0.996 | 1.000 | 0.006 | 0.994 | 0.999 | 0.07 ± 0.77 | 1.68 ± 1.86 | 0.1 ± 1.55 | 0.17 ± 1.3 |
| **Indole** | 0.670 | 0.370 | 0.149 | 0.839 | 0.795 | 0.777 | 0.267 | 0.994 | 0.662 | 0.386 | 0.152 | 0.863 | 0.09 ± 0.47 | 0.03 ± 0.44 | -0.39 ± 0.55 | -0.3 ± 0.61 |
| **Kynurenine** | 0.598 | 0.176 | 0.009 | 0.296 | 0.564 | 0.255 | 0.057 | 0.986 | 0.653 | 0.190 | 0.010 | 0.299 | 0.14 ± 0.4 | -0.43 ± 0.34 | -0.38 ± 0.4 | -0.24 ± 0.4 |
| **Lactic acid** | 0.829 | 0.997 | 0.496 | 0.979 | 0.929 | 0.998 | 0.615 | 0.999 | 0.850 | 0.998 | 0.503 | 0.978 | -0.03 ± 0.48 | -0.07 ± 0.32 | -0.22 ± 0.32 | -0.25 ± 0.42 |
| **Leucine-Isoleucine** | 0.022 | 0.999 | 0.107 | 0.966 | 0.102 | 0.990 | 0.224 | 0.957 | 0.041 | 1.000 | 0.109 | 0.991 | 0.17 ± 0.27 | -0.04 ± 0.39 | -0.24 ± 0.27 | -0.07 ± 0.27 |
| **LPC 14:0** | 0.001 | 0.259 | 1.000 | 0.002 | 0.170 | 0.284 | 0.987 | 0.559 | 0.002 | 0.266 | 1.000 | 0.003 | -1.04 ± 0.76 | -0.61 ± 0.48 | 0.11 ± 0.64 | -0.93 ± 0.8 |
| **LPC 15:0** | 1.000 | 0.529 | 0.933 | 0.865 | 1.000 | 0.649 | 0.980 | 0.999 | 0.997 | 0.571 | 0.937 | 0.815 | -0.22 ± 0.57 | -0.46 ± 0.48 | -0.06 ± 0.61 | -0.28 ± 0.65 |
| **LPC 16:0** | 0.040 | 0.534 | 0.357 | 0.815 | 0.243 | 0.796 | 0.442 | 0.972 | 0.085 | 0.605 | 0.379 | 0.917 | 0.11 ± 0.26 | -0.17 ± 0.23 | -0.12 ± 0.25 | -0.01 ± 0.23 |
| **LPC 16:1** | 0.960 | 0.762 | 0.774 | 0.988 | 0.947 | 0.813 | 0.895 | 1.000 | 0.988 | 0.802 | 0.783 | 0.968 | -0.13 ± 0.74 | -0.39 ± 0.49 | -0.19 ± 0.64 | -0.32 ± 0.76 |
| **LPC 17:0** | 0.999 | 0.822 | 1.000 | 1.000 | 0.991 | 0.851 | 1.000 | 0.994 | 1.000 | 0.903 | 1.000 | 0.999 | -0.13 ± 0.61 | -0.42 ± 0.51 | 0.03 ± 0.59 | -0.1 ± 0.68 |
| **LPC 18:0** | 0.606 | 0.392 | 0.995 | 0.824 | 0.904 | 0.627 | 0.992 | 0.993 | 0.434 | 0.476 | 0.994 | 0.673 | -0.49 ± 0.73 | -0.54 ± 0.54 | 0.12 ± 0.61 | -0.37 ± 0.69 |
| **LPC 18:1** | 0.812 | 0.947 | 0.899 | 0.302 | 0.999 | 1.000 | 0.986 | 0.985 | 0.974 | 0.982 | 0.893 | 0.580 | 0 ± 0.52 | -0.26 ± 0.46 | 0.06 ± 0.53 | 0.06 ± 0.57 |
| **LPC 18:2** | 0.951 | 0.739 | 0.979 | 1.000 | 0.987 | 0.912 | 0.984 | 1.000 | 0.984 | 0.787 | 0.982 | 1.000 | -0.1 ± 0.53 | -0.42 ± 0.56 | -0.17 ± 0.59 | -0.27 ± 0.68 |
| **LPC 19:0** | 0.971 | 0.999 | 0.837 | 0.993 | 0.990 | 1.000 | 0.883 | 1.000 | 0.960 | 0.999 | 0.836 | 0.997 | -0.39 ± 0.74 | 0.01 ± 0.61 | 0.33 ± 0.71 | -0.06 ± 0.83 |
| **LPC 20:1** | 0.902 | 0.690 | 0.478 | 0.106 | 0.999 | 0.976 | 0.695 | 0.843 | 0.986 | 0.782 | 0.483 | 0.232 | -0.08 ± 0.44 | -0.22 ± 0.56 | 0.21 ± 0.5 | 0.13 ± 0.58 |
| **LPC 20:2** | 0.581 | 0.996 | 0.996 | 0.371 | 0.963 | 0.964 | 1.000 | 0.978 | 0.412 | 0.999 | 0.997 | 0.241 | -0.3 ± 0.49 | -0.05 ± 0.34 | 0.04 ± 0.41 | -0.26 ± 0.48 |
| **LPC 20:3** | 0.834 | 0.976 | 1.000 | 0.905 | 1.000 | 0.765 | 0.969 | 0.994 | 0.806 | 0.981 | 1.000 | 0.883 | -0.49 ± 0.84 | -0.42 ± 0.65 | -0.11 ± 0.83 | -0.6 ± 0.96 |
| **LPC 20:4** | 0.001 | 0.999 | 0.999 | 0.003 | 0.088 | 0.995 | 0.997 | 0.364 | 0.002 | 0.999 | 0.999 | 0.004 | 0.56 ± 0.63 | -0.16 ± 0.66 | -0.27 ± 0.68 | 0.29 ± 0.83 |
| **LPC 20:5** | 0.778 | 0.996 | 0.781 | 1.000 | 0.998 | 0.999 | 0.662 | 0.977 | 0.791 | 0.996 | 0.785 | 1.000 | -0.67 ± 0.88 | -0.13 ± 0.61 | -0.02 ± 0.92 | -0.68 ± 1.19 |
| **LPC 22:5** | 0.630 | 1.000 | 1.000 | 0.569 | 0.807 | 0.999 | 1.000 | 0.871 | 0.772 | 1.000 | 1.000 | 0.708 | 0.13 ± 0.78 | -0.24 ± 0.64 | -0.12 ± 0.84 | 0.01 ± 0.85 |
| **LPC 22:6** | 0.018 | 0.999 | 0.995 | 0.006 | 0.117 | 0.995 | 0.989 | 0.184 | 0.031 | 1.000 | 0.995 | 0.010 | 0.44 ± 0.68 | -0.3 ± 0.66 | -0.18 ± 0.73 | 0.25 ± 0.87 |
| **LPE 16:0** | 0.058 | 0.716 | 0.785 | 0.002 | 0.585 | 0.659 | 0.942 | 0.500 | 0.056 | 0.744 | 0.792 | 0.002 | 0.18 ± 0.53 | 0.1 ± 0.39 | 0.03 ± 0.48 | 0.21 ± 0.54 |
| **LPE 18:0** | 1.000 | 0.520 | 0.932 | 0.860 | 1.000 | 0.647 | 0.979 | 0.999 | 0.997 | 0.562 | 0.937 | 0.808 | -0.22 ± 0.56 | -0.46 ± 0.48 | -0.06 ± 0.61 | -0.28 ± 0.65 |
| **LPE 18:1** | 0.791 | 0.999 | 0.981 | 0.977 | 0.684 | 0.996 | 1.000 | 0.883 | 0.718 | 1.000 | 0.980 | 0.951 | -0.31 ± 0.46 | -0.08 ± 0.35 | 0.03 ± 0.39 | -0.28 ± 0.53 |
| **LPE 18:2** | 0.527 | 0.986 | 0.999 | 0.686 | 0.660 | 1.000 | 1.000 | 0.843 | 0.550 | 0.987 | 0.999 | 0.702 | -0.48 ± 0.6 | -0.17 ± 0.42 | -0.01 ± 0.51 | -0.49 ± 0.68 |
| **LPE 20:0** | 0.998 | 0.826 | 1.000 | 0.991 | 0.994 | 0.877 | 0.999 | 0.988 | 1.000 | 0.904 | 1.000 | 1.000 | -0.12 ± 0.59 | -0.36 ± 0.45 | 0.05 ± 0.53 | -0.07 ± 0.64 |
| **LPE 20:4** | 0.000 | 0.905 | 0.980 | 0.002 | 0.129 | 0.644 | 0.863 | 0.675 | 0.000 | 0.912 | 0.980 | 0.002 | 0.32 ± 0.51 | 0.06 ± 0.38 | -0.13 ± 0.39 | 0.19 ± 0.46 |
| **LPE 20:5** | 0.032 | 0.998 | 0.470 | 0.669 | 0.519 | 0.998 | 0.375 | 1.000 | 0.045 | 0.998 | 0.479 | 0.715 | -0.92 ± 0.8 | -0.04 ± 0.42 | 0.15 ± 0.66 | -0.77 ± 0.89 |
| **LPE 22:6** | 0.001 | 0.119 | 0.992 | 0.000 | 0.094 | 0.281 | 0.999 | 0.215 | 0.001 | 0.137 | 0.993 | 0.000 | 0.3 ± 0.53 | 0.29 ± 0.37 | -0.08 ± 0.43 | 0.22 ± 0.58 |
| **Lysine** | 0.122 | 0.041 | 0.237 | 0.997 | 0.600 | 0.399 | 0.224 | 1.000 | 0.106 | 0.039 | 0.237 | 0.992 | -0.46 ± 1.51 | 0.47 ± 1.66 | 0.28 ± 1.56 | -0.18 ± 0.39 |
| **Malic acid** | 0.362 | 0.745 | 0.662 | 0.985 | 0.639 | 0.886 | 0.739 | 0.997 | 0.431 | 0.770 | 0.670 | 0.993 | 0.38 ± 1.04 | -0.23 ± 0.87 | -0.29 ± 0.81 | 0.09 ± 0.83 |
| **Methionine** | 0.020 | 0.000 | 0.638 | 0.397 | 0.013 | 0.042 | 0.972 | 0.179 | 0.036 | 0.000 | 0.650 | 0.497 | 0.16 ± 0.47 | 0.53 ± 0.33 | -0.25 ± 0.4 | -0.09 ± 0.44 |
| **Mevalonic acid** | 0.768 | 0.845 | 1.000 | 0.830 | 0.663 | 0.999 | 1.000 | 0.751 | 0.864 | 0.808 | 1.000 | 0.906 | 0.14 ± 0.61 | 0.11 ± 0.46 | -0.03 ± 0.54 | 0.11 ± 0.58 |
| **Orotic acid** | 0.275 | 0.969 | 0.012 | 0.671 | 0.376 | 0.919 | 0.052 | 0.998 | 0.224 | 0.958 | 0.013 | 0.771 | -0.82 ± 1.53 | 0.01 ± 1 | 1.12 ± 1.57 | 0.3 ± 1.23 |
| **Paraxanthine** | 0.637 | 0.006 | 0.105 | 0.789 | 0.481 | 0.020 | 0.342 | 1.000 | 0.540 | 0.005 | 0.106 | 0.882 | 0.24 ± 2.02 | -1.9 ± 1.91 | -1.5 ± 2.22 | -1.25 ± 1.96 |
| **PC 32:1** | 0.366 | 0.852 | 0.913 | 0.069 | 1.000 | 0.987 | 1.000 | 1.000 | 0.381 | 0.852 | 0.916 | 0.078 | -0.47 ± 0.69 | 0 ± 0.35 | -0.15 ± 0.57 | -0.63 ± 0.7 |
| **PC 34:1** | 0.335 | 0.413 | 0.999 | 0.231 | 0.193 | 0.997 | 0.941 | 0.199 | 0.513 | 0.357 | 0.999 | 0.370 | 0.12 ± 0.45 | 0.07 ± 0.34 | -0.07 ± 0.45 | 0.04 ± 0.5 |
| **PC 34:2** | 0.292 | 0.998 | 0.352 | 1.000 | 0.149 | 0.765 | 0.804 | 0.756 | 0.470 | 1.000 | 0.363 | 1.000 | 0.08 ± 0.34 | -0.13 ± 0.27 | -0.22 ± 0.34 | -0.14 ± 0.38 |
| **PC 36:2** | 0.406 | 0.471 | 0.963 | 0.801 | 1.000 | 0.164 | 0.685 | 0.953 | 0.316 | 0.529 | 0.960 | 0.706 | -0.45 ± 0.61 | -0.44 ± 0.4 | 0.07 ± 0.55 | -0.38 ± 0.54 |
| **PC 36:3** | 0.412 | 0.891 | 0.970 | 0.786 | 0.912 | 0.842 | 0.926 | 1.000 | 0.329 | 0.919 | 0.967 | 0.699 | -0.32 ± 0.47 | -0.26 ± 0.31 | 0.06 ± 0.39 | -0.26 ± 0.43 |
| **PC 36:4** | 0.000 | 0.959 | 0.421 | 0.002 | 0.003 | 0.966 | 0.456 | 0.290 | 0.000 | 0.953 | 0.427 | 0.003 | 0.36 ± 0.4 | -0.01 ± 0.27 | -0.23 ± 0.25 | 0.14 ± 0.38 |
| **PC 38:5** | 0.968 | 0.999 | 0.960 | 0.689 | 0.994 | 1.000 | 0.977 | 0.961 | 0.989 | 1.000 | 0.959 | 0.784 | -0.16 ± 0.62 | -0.16 ± 0.29 | 0.03 ± 0.48 | -0.13 ± 0.6 |
| **PC 38:6** | 0.001 | 1.000 | 0.995 | 0.002 | 0.005 | 0.934 | 1.000 | 0.041 | 0.001 | 1.000 | 0.996 | 0.005 | 0.5 ± 0.63 | -0.16 ± 0.43 | -0.16 ± 0.48 | 0.34 ± 0.66 |
| **PC 40:7** | 0.080 | 1.000 | 0.999 | 0.042 | 0.334 | 1.000 | 0.999 | 0.465 | 0.097 | 1.000 | 0.999 | 0.051 | 0.18 ± 0.48 | -0.11 ± 0.36 | -0.08 ± 0.44 | 0.1 ± 0.52 |
| **PC 40:8** | 0.498 | 0.540 | 0.294 | 0.996 | 0.912 | 0.927 | 0.288 | 0.977 | 0.481 | 0.534 | 0.299 | 0.998 | -0.33 ± 0.49 | 0.36 ± 0.49 | 0.24 ± 0.51 | -0.08 ± 0.54 |
| **Phenylalanine** | 0.247 | 0.000 | 0.037 | 0.902 | 0.410 | 0.004 | 0.108 | 1.000 | 0.344 | 0.000 | 0.038 | 0.840 | 0.05 ± 0.4 | 0.55 ± 0.34 | -0.39 ± 0.35 | -0.34 ± 0.46 |
| **Proline** | 0.203 | 0.018 | 0.166 | 1.000 | 0.367 | 0.099 | 0.340 | 0.998 | 0.277 | 0.022 | 0.174 | 0.999 | 0.03 ± 0.27 | -0.3 ± 0.36 | -0.16 ± 0.19 | -0.13 ± 0.27 |
| **Serine** | 0.125 | 0.659 | 0.972 | 0.030 | 0.148 | 0.510 | 0.878 | 0.123 | 0.232 | 0.730 | 0.971 | 0.066 | 0.4 ± 0.71 | -0.34 ± 0.46 | 0.01 ± 0.54 | 0.41 ± 0.63 |
| **SM 32:1** | 1.000 | 0.998 | 0.486 | 0.511 | 0.719 | 0.845 | 0.944 | 0.982 | 0.992 | 0.988 | 0.508 | 0.284 | -0.17 ± 0.58 | -0.2 ± 0.49 | -0.28 ± 0.46 | -0.44 ± 0.58 |
| **SM 32:2** | 0.702 | 0.997 | 0.989 | 0.408 | 1.000 | 0.906 | 0.999 | 0.998 | 0.458 | 0.987 | 0.991 | 0.227 | -0.29 ± 0.53 | -0.19 ± 0.45 | -0.12 ± 0.51 | -0.41 ± 0.58 |
| **SM 33:1** | 0.054 | 0.450 | 1.000 | 0.047 | 0.066 | 0.994 | 0.982 | 0.120 | 0.157 | 0.387 | 1.000 | 0.129 | 0.29 ± 0.36 | 0 ± 0.55 | -0.14 ± 0.42 | 0.14 ± 0.51 |
| **SM 34:1** | 0.168 | 0.302 | 0.789 | 0.009 | 0.138 | 0.978 | 0.558 | 0.056 | 0.352 | 0.247 | 0.778 | 0.031 | 0.3 ± 0.7 | 0.04 ± 0.88 | 0 ± 0.62 | 0.3 ± 0.8 |
| **SM 34:2** | 0.026 | 0.996 | 0.955 | 0.140 | 0.007 | 0.791 | 1.000 | 0.042 | 0.102 | 0.983 | 0.963 | 0.342 | 0.28 ± 0.49 | -0.16 ± 0.45 | -0.19 ± 0.43 | 0.1 ± 0.52 |
| **SM 35:2** | 0.003 | 1.000 | 0.972 | 0.000 | 0.008 | 0.932 | 0.801 | 0.010 | 0.006 | 1.000 | 0.972 | 0.001 | 0.26 ± 0.34 | -0.1 ± 0.35 | 0.01 ± 0.34 | 0.27 ± 0.39 |
| **SM 36:2** | 0.000 | 0.692 | 1.000 | 0.000 | 0.000 | 0.996 | 0.946 | 0.002 | 0.001 | 0.599 | 1.000 | 0.001 | 0.65 ± 0.71 | 0.02 ± 0.57 | -0.17 ± 0.6 | 0.48 ± 0.67 |
| **Taurine** | 1.000 | 0.154 | 0.078 | 0.059 | 0.917 | 0.881 | 0.047 | 0.127 | 0.990 | 0.093 | 0.067 | 0.185 | -0.01 ± 0.43 | 0.45 ± 0.98 | 0.34 ± 0.47 | 0.33 ± 0.58 |
| **Transcinnamic acid** | 0.082 | 0.000 | 0.010 | 0.926 | 0.255 | 0.004 | 0.036 | 1.000 | 0.140 | 0.000 | 0.010 | 0.863 | 0.08 ± 0.42 | 0.51 ± 0.28 | -0.37 ± 0.3 | -0.29 ± 0.39 |
| **Tryptophan** | 0.738 | 0.228 | 0.140 | 0.766 | 0.724 | 0.785 | 0.318 | 0.999 | 0.747 | 0.236 | 0.143 | 0.781 | 0.06 ± 0.47 | 0.04 ± 0.44 | -0.35 ± 0.49 | -0.3 ± 0.56 |
| **Tyrosine** | 0.730 | 0.123 | 0.306 | 0.949 | 0.717 | 0.674 | 0.546 | 1.000 | 0.791 | 0.120 | 0.314 | 0.933 | -0.02 ± 0.44 | 0.12 ± 0.33 | -0.3 ± 0.32 | -0.32 ± 0.47 |
| **Uric acid** | 0.104 | 0.491 | 0.494 | 0.895 | 0.647 | 0.943 | 0.437 | 1.000 | 0.148 | 0.526 | 0.509 | 0.931 | 0.39 ± 0.57 | -0.44 ± 0.59 | -0.49 ± 0.63 | -0.09 ± 0.76 |
| **Valine** | 0.610 | 0.944 | 0.003 | 0.141 | 0.370 | 0.660 | 0.039 | 0.997 | 0.537 | 0.929 | 0.003 | 0.222 | -0.13 ± 0.3 | 0.01 ± 0.29 | 0.28 ± 0.48 | 0.14 ± 0.34 |

Model 1, fitted models were adjusted for age; Model 2, models were adjusted for age and weight loss; Model 3, models were adjusted for age and levels of fasting insulin. VLCD, very low-calorie diet; RYGB (1d), immediate effect of gastric bypass surgery; RYGB (6w), 6-week effect of gastric bypass surgery; Cum. Effect, cumulative effect of the intervention.

**Table 6B.** Linear-mixed-effect models fitted to lipidomics data between study occasions (fasting plasma samples).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 1**  **(adjusted for age)** | | | | **Model 2**  **(adj. for age and weight loss)** | | | | **Model 3**  **(adj. for age and insulin)** | | | | **Direction (Mean, SD)** | | | |
|  | **Effect of VLCD** | **RYGB (1d)** | **RYGB (6w)** | **Cum. effect** | **Effect of VLCD** | **RYGB (1d)** | **RYGB (6w)** | **Cum. effect** | **Effect of VLCD** | **RYGB (1d)** | **RYGB (6w)** | **Cum. effect** | **Effect of VLCD** | **RYGB (1d)** | **RYGB (6w)** | **Cum. effect** |
| **CE16.0\*** | 0.999 | 0.859 | 0.965 | 0.893 | 0.976 | 0.803 | 0.916 | 0.862 | 0.999 | 0.857 | 0.966 | 0.889 | 0.71 ± 3.14 | 0.3 ± 1.38 | 0.32 ± 3.07 | 1.19 ± 4.35 |
| **CE18.1\*** | 0.983 | 1.000 | 0.896 | 0.608 | 0.895 | 0.994 | 0.784 | 0.640 | 1.000 | 0.997 | 0.890 | 0.859 | 1.09 ± 3.99 | -0.05 ± 0.4 | 1 ± 3.95 | 2 ± 5.23 |
| **CE18.2\*** | 0.715 | 0.532 | 0.831 | 0.999 | 0.482 | 0.360 | 0.986 | 0.853 | 0.722 | 0.536 | 0.833 | 0.999 | 1.02 ± 4.16 | -0.43 ± 1.12 | 0.78 ± 4.3 | 1.71 ± 5.51 |
| **CE18.3\*** | 0.001 | 0.930 | 0.794 | 0.022 | 0.001 | 0.492 | 0.993 | 0.027 | 0.001 | 0.919 | 0.792 | 0.019 | -0.3 ± 3.81 | 0.5 ± 1.47 | 0.62 ± 3.02 | 0.35 ± 4.57 |
| **CE20.4\*** | 0.059 | 0.945 | 1.000 | 0.061 | 0.195 | 0.928 | 1.000 | 0.362 | 0.152 | 0.977 | 1.000 | 0.144 | 1.25 ± 2.81 | 0.03 ± 0.98 | 0.55 ± 3.27 | 1.81 ± 4.24 |
| **LPC16.0\*** | 0.109 | 0.186 | 0.388 | 0.953 | 0.263 | 0.354 | 0.592 | 0.947 | 0.080 | 0.165 | 0.381 | 0.908 | 1.34 ± 5.02 | -0.27 ± 0.59 | 0.92 ± 5.11 | 2.17 ± 6.83 |
| **LPC16.1\*** | 0.982 | 0.320 | 0.488 | 0.807 | 0.903 | 0.363 | 0.761 | 1.000 | 0.970 | 0.308 | 0.488 | 0.861 | 0.65 ± 3.74 | -0.53 ± 1.08 | 0.43 ± 3.63 | 0.88 ± 4.62 |
| **LPC18.0\*** | 1.000 | 0.014 | 0.875 | 0.904 | 0.991 | 0.073 | 0.969 | 1.000 | 1.000 | 0.014 | 0.872 | 0.942 | 0.85 ± 4.87 | -0.79 ± 1.03 | 0.91 ± 4.79 | 1.62 ± 6.34 |
| **LPC18.1\*** | 0.936 | 0.420 | 0.995 | 0.775 | 0.979 | 0.726 | 0.996 | 0.963 | 0.967 | 0.462 | 0.995 | 0.843 | 1 ± 4.59 | -0.26 ± 0.75 | 1.11 ± 4.48 | 1.99 ± 6.02 |
| **LPC18.2\*** | 0.985 | 0.439 | 0.853 | 0.988 | 0.903 | 0.442 | 0.974 | 0.997 | 0.985 | 0.446 | 0.855 | 0.990 | 0.85 ± 4.65 | -0.41 ± 0.96 | 0.77 ± 4.61 | 1.51 ± 6.18 |
| **LPC20.3\*** | 0.932 | 0.884 | 0.925 | 0.510 | 0.968 | 0.983 | 1.000 | 0.988 | 0.915 | 0.877 | 0.929 | 0.492 | 0.18 ± 3.79 | 0.08 ± 1.27 | 0.64 ± 3.61 | 0.73 ± 4.92 |
| **LPC20.4\*** | 0.000 | 0.986 | 0.948 | 0.004 | 0.009 | 0.965 | 0.986 | 0.118 | 0.000 | 0.983 | 0.947 | 0.004 | 2.08 ± 3.96 | -0.11 ± 1.45 | 0.42 ± 4.34 | 2.5 ± 5.83 |
| **LPC22.6\*** | 0.102 | 0.983 | 0.994 | 0.231 | 0.163 | 0.887 | 1.000 | 0.388 | 0.186 | 0.992 | 0.995 | 0.351 | 1.11 ± 3.02 | -0.1 ± 1.07 | 0.64 ± 3.58 | 1.68 ± 4.62 |
| **PC32.0\*** | 0.001 | 0.934 | 1.000 | 0.001 | 0.002 | 0.551 | 0.977 | 0.010 | 0.001 | 0.910 | 1.000 | 0.000 | 1.24 ± 4.1 | 0.01 ± 0.51 | 0.85 ± 4.2 | 2.04 ± 5.7 |
| **PC32.1\*** | 0.001 | 1.000 | 0.999 | 0.000 | 0.771 | 0.376 | 0.887 | 0.996 | 0.002 | 1.000 | 0.999 | 0.001 | -0.51 ± 4.72 | -0.09 ± 0.8 | 0.78 ± 3.69 | 0.2 ± 5.42 |
| **PC32.2\*** | 0.020 | 0.295 | 0.611 | 0.000 | 0.460 | 0.333 | 0.862 | 0.332 | 0.036 | 0.285 | 0.612 | 0.000 | -1.26 ± 4.85 | -1.88 ± 2.21 | 0.37 ± 3.55 | -1.32 ± 4.04 |
| **PC34.0\*** | 1.000 | 0.948 | 0.827 | 0.863 | 0.994 | 0.864 | 0.728 | 0.815 | 1.000 | 0.945 | 0.832 | 0.856 | 0.39 ± 3.83 | -0.25 ± 1.37 | 1.06 ± 3.75 | 1.24 ± 4.89 |
| **PC34.1\*** | 0.775 | 0.934 | 0.935 | 0.995 | 0.686 | 1.000 | 0.995 | 0.930 | 0.785 | 0.939 | 0.936 | 0.995 | 1.23 ± 5.1 | 0.13 ± 0.19 | 1.04 ± 5.04 | 2.22 ± 6.91 |
| **PC34.2\*** | 0.374 | 0.599 | 0.003 | 0.321 | 0.046 | 0.086 | 0.107 | 0.944 | 0.188 | 0.478 | 0.002 | 0.532 | 1.24 ± 5.21 | -0.05 ± 0.15 | 0.96 ± 5.19 | 2.16 ± 7.11 |
| **PC34.3\*** | 0.051 | 0.843 | 0.999 | 0.025 | 0.823 | 0.477 | 0.997 | 0.967 | 0.087 | 0.822 | 0.999 | 0.043 | -0.34 ± 5.13 | -0.32 ± 1.17 | 0.86 ± 4.37 | 0.29 ± 5.9 |
| **PC36.1\*** | 0.016 | 0.253 | 0.744 | 0.268 | 0.465 | 0.267 | 0.586 | 0.993 | 0.021 | 0.260 | 0.750 | 0.300 | 0.12 ± 5.24 | -0.46 ± 0.68 | 1.35 ± 4.57 | 1.37 ± 6.41 |
| **PC36.2\*** | 0.742 | 0.003 | 1.000 | 0.626 | 1.000 | 0.006 | 0.991 | 0.995 | 0.764 | 0.004 | 1.000 | 0.651 | 0.85 ± 5.31 | -0.54 ± 0.51 | 1.16 ± 5.08 | 1.93 ± 6.95 |
| **PC36.3\*** | 0.205 | 0.093 | 0.890 | 0.024 | 0.966 | 0.076 | 0.998 | 0.959 | 0.261 | 0.093 | 0.891 | 0.036 | 0.89 ± 5.24 | -0.26 ± 0.29 | 1.09 ± 4.99 | 1.9 ± 6.82 |
| **PC36.4\*** | 0.000 | 0.956 | 0.058 | 0.000 | 0.000 | 0.897 | 0.063 | 0.248 | 0.000 | 0.981 | 0.054 | 0.000 | 1.49 ± 4.95 | 0.05 ± 0.08 | 0.95 ± 5.04 | 2.43 ± 6.85 |
| **PC36.5\*** | 0.963 | 0.968 | 0.999 | 0.886 | 0.995 | 0.693 | 0.998 | 0.989 | 0.994 | 0.948 | 0.999 | 0.960 | 0.71 ± 5.04 | -0.08 ± 0.49 | 0.79 ± 4.59 | 1.45 ± 6.44 |
| **PC38.3\*** | 0.005 | 0.127 | 1.000 | 0.003 | 0.611 | 0.048 | 0.978 | 0.933 | 0.010 | 0.122 | 1.000 | 0.006 | 0.26 ± 5.16 | -0.51 ± 0.54 | 1.06 ± 4.68 | 1.21 ± 6.42 |
| **PC38.4\*** | 0.015 | 0.679 | 0.942 | 0.108 | 0.186 | 0.889 | 0.959 | 0.663 | 0.004 | 0.561 | 0.929 | 0.042 | 1.29 ± 4.7 | -0.14 ± 0.14 | 0.93 ± 4.67 | 2.21 ± 6.32 |
| **PC38.5\*** | 0.734 | 0.806 | 0.993 | 0.927 | 1.000 | 0.470 | 0.878 | 0.976 | 0.854 | 0.770 | 0.994 | 0.973 | 0.46 ± 4.62 | -0.21 ± 0.24 | 0.99 ± 4.16 | 1.37 ± 5.74 |
| **PC38.6\*** | 0.000 | 0.701 | 0.682 | 0.000 | 0.000 | 0.465 | 0.947 | 0.004 | 0.000 | 0.666 | 0.677 | 0.000 | 1.68 ± 4.84 | -0.08 ± 0.3 | 0.97 ± 5.07 | 2.58 ± 6.75 |
| **PC40.4\*** | 0.634 | 0.613 | 0.998 | 0.450 | 0.883 | 0.834 | 0.999 | 0.904 | 0.716 | 0.598 | 0.998 | 0.531 | 0.35 ± 4.18 | -0.5 ± 1.13 | 0.67 ± 3.94 | 0.74 ± 5.27 |
| **PC40.5\*** | 0.215 | 1.000 | 0.751 | 0.870 | 0.785 | 0.994 | 0.684 | 1.000 | 0.272 | 1.000 | 0.760 | 0.905 | 0.15 ± 3.89 | -0.01 ± 0.94 | 0.96 ± 3.45 | 0.9 ± 4.82 |
| **PC40.6\*** | 0.019 | 0.118 | 0.993 | 0.058 | 0.021 | 0.076 | 1.000 | 0.088 | 0.013 | 0.101 | 0.992 | 0.041 | 1.34 ± 4.55 | -0.3 ± 0.46 | 0.84 ± 4.62 | 2.08 ± 6.11 |
| **SM32.1\*** | 0.957 | 0.280 | 0.170 | 0.511 | 0.402 | 0.068 | 0.677 | 0.974 | 0.963 | 0.291 | 0.176 | 0.529 | 0.95 ± 4.51 | -0.41 ± 0.87 | 0.41 ± 4.6 | 1.25 ± 6.15 |
| **SM32.2\*** | 0.969 | 0.823 | 0.666 | 0.297 | 0.911 | 0.263 | 0.992 | 0.994 | 0.941 | 0.851 | 0.673 | 0.255 | 0.37 ± 3.57 | -0.13 ± 0.92 | 0.44 ± 3.32 | 0.7 ± 4.51 |
| **SM33.1\*** | 0.008 | 0.354 | 0.282 | 0.594 | 0.007 | 0.132 | 0.768 | 0.249 | 0.014 | 0.383 | 0.295 | 0.658 | 1.38 ± 3.88 | -0.25 ± 0.68 | 0.58 ± 4.27 | 1.87 ± 5.6 |
| **SM34.1\*** | 0.186 | 0.588 | 0.926 | 0.027 | 0.074 | 0.223 | 0.611 | 0.037 | 0.327 | 0.664 | 0.925 | 0.065 | 1.25 ± 4.93 | -0.11 ± 0.31 | 1.17 ± 4.9 | 2.35 ± 6.67 |
| **SM34.2\*** | 0.018 | 0.699 | 0.685 | 0.336 | 0.004 | 0.152 | 0.997 | 0.068 | 0.023 | 0.709 | 0.691 | 0.364 | 1.52 ± 4.57 | -0.18 ± 0.7 | 0.67 ± 4.8 | 2.09 ± 6.36 |
| **SM35.1\*** | 0.007 | 0.949 | 1.000 | 0.003 | 0.368 | 1.000 | 0.999 | 0.684 | 0.012 | 0.961 | 1.000 | 0.007 | 2.15 ± 2.94 | -0.26 ± 1.78 | 0.31 ± 3.56 | 2.51 ± 4.48 |
| **SM36.0\*** | 0.000 | 0.952 | 0.001 | 0.000 | 0.000 | 0.599 | 0.024 | 0.001 | 0.000 | 0.938 | 0.001 | 0.000 | 3.1 ± 2.76 | -0.11 ± 0.67 | -0.63 ± 4.1 | 2.51 ± 4.96 |
| **SM36.1\*** | 0.000 | 0.995 | 0.981 | 0.000 | 0.000 | 0.778 | 0.996 | 0.001 | 0.000 | 0.994 | 0.982 | 0.000 | 1.7 ± 3.94 | 0.08 ± 0.33 | 0.76 ± 4.26 | 2.41 ± 5.67 |
| **SM36.2\*** | 0.002 | 0.999 | 1.000 | 0.004 | 0.000 | 0.286 | 0.882 | 0.001 | 0.009 | 1.000 | 1.000 | 0.015 | 1.4 ± 3.81 | -0.02 ± 0.24 | 0.87 ± 3.93 | 2.19 ± 5.25 |
| **SM38.1\*** | 1.000 | 0.915 | 0.762 | 0.764 | 0.751 | 0.393 | 0.997 | 0.947 | 1.000 | 0.910 | 0.764 | 0.814 | 0.84 ± 4.4 | -0.13 ± 0.46 | 0.7 ± 4.29 | 1.49 ± 5.93 |
| **SM38.2\*** | 0.079 | 0.489 | 1.000 | 0.082 | 0.008 | 0.059 | 0.858 | 0.014 | 0.075 | 0.475 | 1.000 | 0.078 | 1.17 ± 3.71 | -0.18 ± 0.51 | 0.79 ± 3.67 | 1.87 ± 4.88 |
| **SM39.1\*** | 0.998 | 0.406 | 0.121 | 0.058 | 0.763 | 0.076 | 0.632 | 1.000 | 0.999 | 0.407 | 0.125 | 0.075 | 0.56 ± 4.27 | -0.5 ± 0.99 | 0.13 ± 4.26 | 0.64 ± 5.79 |
| **SM40.0\*** | 1.000 | 0.822 | 0.969 | 0.985 | 0.999 | 0.885 | 0.990 | 1.000 | 0.997 | 0.777 | 0.966 | 0.998 | 0.57 ± 4.24 | -0.14 ± 1.69 | -0.06 ± 3.37 | 0.23 ± 4.68 |
| **SM40.1\*** | 0.700 | 0.569 | 0.266 | 0.012 | 1.000 | 0.211 | 0.763 | 0.982 | 0.755 | 0.565 | 0.271 | 0.018 | 0.81 ± 4.87 | -0.17 ± 0.42 | 0.74 ± 4.66 | 1.5 ± 6.45 |
| **SM40.2\*** | 1.000 | 0.926 | 0.967 | 0.986 | 0.257 | 0.098 | 0.974 | 0.290 | 1.000 | 0.934 | 0.969 | 0.982 | 1.13 ± 4.61 | -0.22 ± 0.94 | 0.67 ± 4.7 | 1.76 ± 6.28 |
| **SM41.1\*** | 1.000 | 0.412 | 0.014 | 0.012 | 0.755 | 0.122 | 0.175 | 0.992 | 1.000 | 0.415 | 0.015 | 0.018 | 0.85 ± 4.62 | -0.31 ± 0.72 | 0.36 ± 4.6 | 1.15 ± 6.28 |
| **SM41.2\*** | 0.650 | 0.475 | 0.730 | 1.000 | 0.191 | 0.128 | 0.996 | 0.548 | 0.742 | 0.512 | 0.739 | 1.000 | 1.14 ± 4.43 | -0.35 ± 0.98 | 0.58 ± 4.58 | 1.63 ± 6.09 |
| **SM42.1\*** | 1.000 | 0.491 | 0.205 | 0.268 | 0.799 | 0.222 | 0.650 | 1.000 | 1.000 | 0.499 | 0.211 | 0.301 | 0.95 ± 4.78 | -0.25 ± 0.63 | 0.6 ± 4.71 | 1.5 ± 6.45 |
| **SM42.2\*** | 0.001 | 0.691 | 0.987 | 0.003 | 0.002 | 0.378 | 1.000 | 0.026 | 0.001 | 0.710 | 0.987 | 0.005 | 1.46 ± 4.97 | -0.09 ± 0.33 | 1.06 ± 5.02 | 2.45 ± 6.77 |
| **SM42.3\*** | 0.000 | 0.990 | 0.978 | 0.000 | 0.000 | 0.822 | 1.000 | 0.003 | 0.000 | 0.995 | 0.981 | 0.000 | 1.98 ± 4.43 | -0.05 ± 0.46 | 0.89 ± 4.78 | 2.79 ± 6.22 |
| **SM43.1\*** | 1.000 | 0.838 | 0.238 | 0.188 | 0.964 | 0.587 | 0.586 | 0.995 | 1.000 | 0.843 | 0.243 | 0.204 | 0.54 ± 3.14 | -0.49 ± 1.19 | -0.13 ± 3.16 | 0.56 ± 4.57 |
| **SM43.2\*** | 0.009 | 0.656 | 0.998 | 0.023 | 0.001 | 0.083 | 0.950 | 0.005 | 0.015 | 0.679 | 0.998 | 0.033 | 2.14 ± 3.38 | -0.54 ± 1.34 | 0.39 ± 3.76 | 2.42 ± 4.73 |
| **SM44.2\*** | 0.852 | 0.997 | 1.000 | 0.830 | 0.975 | 1.000 | 1.000 | 0.991 | 0.849 | 0.997 | 1.000 | 0.827 | 1.12 ± 3.11 | -0.16 ± 1.76 | 0.73 ± 3.47 | 1.44 ± 3.96 |
| **TG48.1\*** | 0.000 | 0.294 | 1.000 | 0.000 | 0.006 | 0.323 | 0.998 | 0.082 | 0.000 | 0.289 | 1.000 | 0.000 | -1.2 ± 5.17 | -0.41 ± 0.76 | 0.87 ± 3.49 | -0.38 ± 5.49 |
| **TG48.2\*** | 0.004 | 0.065 | 1.000 | 0.004 | 0.541 | 0.039 | 0.966 | 0.922 | 0.010 | 0.064 | 1.000 | 0.010 | -0.59 ± 5.31 | -0.73 ± 0.87 | 0.9 ± 3.8 | 0.16 ± 5.54 |
| **TG50.0\*** | 0.041 | 0.999 | 0.652 | 0.000 | 0.246 | 0.999 | 0.696 | 0.133 | 0.074 | 1.000 | 0.659 | 0.001 | -0.78 ± 4.78 | 0.28 ± 0.94 | 0.16 ± 2.95 | -0.43 ± 5.39 |
| **TG50.1\*** | 0.775 | 0.995 | 0.161 | 0.008 | 1.000 | 0.751 | 0.553 | 0.923 | 0.929 | 0.986 | 0.159 | 0.026 | 0.77 ± 4.98 | 0.02 ± 0.29 | 0.73 ± 4.63 | 1.45 ± 6.55 |
| **TG50.2\*** | 0.740 | 0.505 | 0.727 | 0.113 | 0.991 | 0.122 | 0.997 | 1.000 | 0.846 | 0.482 | 0.728 | 0.183 | 0.76 ± 5.15 | -0.17 ± 0.34 | 0.91 ± 4.69 | 1.58 ± 6.56 |
| **TG50.3\*** | 0.863 | 0.242 | 0.702 | 0.174 | 0.971 | 0.054 | 0.995 | 0.999 | 0.943 | 0.224 | 0.702 | 0.277 | 0.59 ± 5.07 | -0.34 ± 0.62 | 0.83 ± 4.49 | 1.3 ± 6.22 |
| **TG50.4\*** | 0.306 | 0.035 | 0.696 | 0.015 | 0.991 | 0.032 | 0.971 | 0.948 | 0.467 | 0.032 | 0.697 | 0.037 | -0.55 ± 5.32 | -1.48 ± 1.89 | 0.5 ± 4.17 | -0.41 ± 5.17 |
| **TG52.1\*** | 0.360 | 0.986 | 1.000 | 0.342 | 0.599 | 1.000 | 1.000 | 0.740 | 0.527 | 0.976 | 1.000 | 0.494 | 0.42 ± 5.08 | 0 ± 0.67 | 0.66 ± 4.18 | 1.03 ± 6.22 |
| **TG52.2\*** | 0.003 | 0.695 | 0.641 | 0.146 | 0.019 | 0.565 | 0.899 | 0.295 | 0.004 | 0.687 | 0.645 | 0.146 | 1.41 ± 5.2 | -0.06 ± 0.2 | 1.06 ± 5.16 | 2.42 ± 7.03 |
| **TG52.3\*** | 0.002 | 0.501 | 0.208 | 0.477 | 0.006 | 0.267 | 0.605 | 0.305 | 0.002 | 0.477 | 0.211 | 0.422 | 1.43 ± 5.16 | -0.1 ± 0.28 | 1 ± 5.18 | 2.38 ± 7.03 |
| **TG52.4\*** | 0.754 | 0.276 | 0.251 | 0.902 | 0.420 | 0.158 | 0.661 | 0.980 | 0.600 | 0.235 | 0.248 | 0.975 | 1.13 ± 5.15 | -0.25 ± 0.56 | 0.86 ± 5.01 | 1.89 ± 6.82 |
| **TG52.5\*** | 0.538 | 0.243 | 0.770 | 0.066 | 0.996 | 0.202 | 0.971 | 0.964 | 0.778 | 0.192 | 0.756 | 0.157 | 0.41 ± 5.06 | -0.45 ± 0.81 | 0.84 ± 4.47 | 1.07 ± 6.08 |
| **TG54.3\*** | 0.013 | 0.820 | 0.915 | 0.001 | 0.627 | 1.000 | 1.000 | 0.735 | 0.023 | 0.845 | 0.913 | 0.001 | 1.41 ± 4.8 | -0.1 ± 0.24 | 1.09 ± 4.61 | 2.4 ± 6.25 |
| **TG54.4\*** | 0.011 | 0.720 | 0.911 | 0.107 | 0.293 | 0.985 | 0.854 | 0.869 | 0.015 | 0.727 | 0.912 | 0.122 | 1.39 ± 4.85 | -0.13 ± 0.38 | 0.96 ± 4.69 | 2.25 ± 6.38 |
| **TG54.5\*** | 0.398 | 0.750 | 0.949 | 0.823 | 0.349 | 0.590 | 0.999 | 0.687 | 0.270 | 0.689 | 0.944 | 0.687 | 1.24 ± 5.03 | -0.22 ± 0.76 | 0.8 ± 4.82 | 1.92 ± 6.6 |
| **TG54.6\*** | 0.897 | 0.696 | 0.834 | 1.000 | 0.592 | 0.420 | 0.991 | 0.900 | 0.671 | 0.576 | 0.807 | 0.999 | 0.87 ± 5.03 | -0.36 ± 0.8 | 0.69 ± 4.8 | 1.43 ± 6.4 |
| **TG56.6\*** | 0.000 | 0.999 | 0.951 | 0.005 | 0.012 | 0.979 | 0.993 | 0.138 | 0.000 | 0.998 | 0.950 | 0.005 | 1.64 ± 4.5 | -0.02 ± 0.52 | 0.77 ± 4.57 | 2.3 ± 6.13 |

Model 1, fitted models were adjusted for age; Model 2, models were adjusted for age and weight loss; Model 3, models were adjusted for age and levels of fasting insulin. VLCD, very low-calorie diet; RYGB (1d), immediate effect of gastric bypass surgery; RYGB (6w), 6-week effect of gastric bypass surgery; Cum. Effect, cumulative effect of the intervention.

**Table 7A.** Assessment of difference in metabolomics data between normoglycaemic and T2D patients (fasting plasma samples).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Occasion:**  **Baseline** | | **Occasion:**  **Diet** | | **Occasion:**  **Surgery** | | **Occasion:**  **Recovery** | | **Effect of VLCD** | | **RYGB (1d)** | | **RYGB (6w)** | | **Cum. effect** | |
|  | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* |
| **1-Methyl-adenosine** | 0.7486 | 0.8110 | 0.5594 | 0.8853 | 0.0698 | 0.4405 | 0.2190 | 0.7918 | 0.3900 | 0.5557 | 0.1906 | 0.7259 | 0.6220 | 0.9770 | 0.1390 | 0.2891 |
| **1-Methylhistidine** | 0.5655 | 0.6673 | 0.3207 | 0.7678 | 0.7052 | 0.8492 | 0.5305 | 0.9309 | 0.4818 | 0.6263 | 0.2416 | 0.7259 | 0.2576 | 0.9770 | 0.3153 | 0.4431 |
| **2-Hydroxycinnamic acid** | 0.0457 | 0.2617 | 0.7964 | 0.9622 | 0.1096 | 0.4515 | 0.3893 | 0.7918 | 0.1146 | 0.3971 | 0.0773 | 0.7259 | 0.3445 | 0.9770 | 0.0154 | 0.0890 |
| **3-Hydroxybutyrate** | 0.0814 | 0.2867 | 0.6312 | 0.9513 | 0.5775 | 0.7722 | 0.6268 | 0.9822 | 0.2501 | 0.4920 | 0.4030 | 0.7259 | 0.9993 | 0.9993 | 0.3139 | 0.4431 |
| **5-Oxoproline** | 0.7039 | 0.7803 | 0.4697 | 0.8279 | 0.3977 | 0.6267 | 0.6875 | 0.9822 | 0.6449 | 0.7621 | 0.3704 | 0.7259 | 0.6490 | 0.9770 | 0.9524 | 0.9710 |
| **Acetylalanine** | 0.7052 | 0.7803 | 0.9725 | 0.9918 | 0.6891 | 0.8432 | 0.9520 | 0.9948 | 0.7820 | 0.8447 | 0.7696 | 0.9136 | 0.9394 | 0.9770 | 0.7084 | 0.7596 |
| **Alanine** | 0.2085 | 0.4577 | 0.3400 | 0.7678 | 0.9544 | 0.9828 | 0.9492 | 0.9948 | 0.6053 | 0.7280 | 0.3944 | 0.7259 | 0.3957 | 0.9770 | 0.2084 | 0.3674 |
| **Arginine** | 0.8926 | 0.9284 | 0.2398 | 0.7678 | 0.4948 | 0.7147 | 0.2299 | 0.7918 | 0.2774 | 0.4920 | 0.1649 | 0.7259 | 0.4585 | 0.9770 | 0.4218 | 0.5314 |
| **Asparagine** | 0.5505 | 0.6581 | 0.3045 | 0.7678 | 0.6669 | 0.8356 | 0.9089 | 0.9948 | 0.4035 | 0.5596 | 0.2676 | 0.7259 | 0.3330 | 0.9770 | 0.5676 | 0.6347 |
| **Aspartic acid** | 0.0873 | 0.2929 | 0.2611 | 0.7678 | 0.8136 | 0.8907 | 0.8790 | 0.9948 | 0.7246 | 0.8103 | 0.3042 | 0.7259 | 0.3546 | 0.9770 | 0.1555 | 0.2993 |
| **Caffeine** | 0.3022 | 0.5119 | 0.9918 | 0.9918 | 0.0545 | 0.4405 | 0.9233 | 0.9948 | 0.5016 | 0.6361 | 0.1050 | 0.7259 | 0.9320 | 0.9770 | 0.5354 | 0.6187 |
| **Carnitine** | 0.2122 | 0.4577 | 0.2667 | 0.7678 | 0.2189 | 0.5276 | 0.0135 | 0.7551 | 0.9560 | 0.9653 | 0.9187 | 0.9651 | 0.1255 | 0.9770 | 0.2506 | 0.4049 |
| **Carnitine C10:0** | 0.5711 | 0.6673 | 0.0555 | 0.7678 | 0.0324 | 0.4405 | 0.1176 | 0.7918 | 0.1245 | 0.3971 | 0.8587 | 0.9305 | 0.8614 | 0.9770 | 0.0990 | 0.2336 |
| **Carnitine C10:1** | 0.3937 | 0.5459 | 0.0525 | 0.7678 | 0.0569 | 0.4405 | 0.2532 | 0.7918 | 0.0628 | 0.3482 | 0.7866 | 0.9136 | 0.7056 | 0.9770 | 0.1081 | 0.2404 |
| **Carnitine C10:2** | 0.4923 | 0.6235 | 0.1743 | 0.7678 | 0.2181 | 0.5276 | 0.2486 | 0.7918 | 0.0620 | 0.3482 | 0.8015 | 0.9160 | 0.7742 | 0.9770 | 0.1117 | 0.2420 |
| **Carnitine C12:0** | 0.3593 | 0.5189 | 0.2742 | 0.7678 | 0.0999 | 0.4515 | 0.1439 | 0.7918 | 0.1113 | 0.3971 | 0.6645 | 0.9102 | 0.4515 | 0.9770 | 0.0323 | 0.1345 |
| **Carnitine C12:1** | 0.3695 | 0.5194 | 0.1237 | 0.7678 | 0.2661 | 0.5276 | 0.2573 | 0.7918 | 0.0674 | 0.3482 | 0.7906 | 0.9136 | 0.8956 | 0.9770 | 0.0872 | 0.2313 |
| **Carnitine C14:0** | 0.1110 | 0.3298 | 0.6905 | 0.9622 | 0.2493 | 0.5276 | 0.2939 | 0.7918 | 0.0365 | 0.3482 | 0.5211 | 0.8088 | 0.4139 | 0.9770 | 0.0142 | 0.0875 |
| **Carnitine C14:1** | 0.3642 | 0.5189 | 0.3807 | 0.7918 | 0.4942 | 0.7147 | 0.1603 | 0.7918 | 0.1271 | 0.3971 | 0.9408 | 0.9735 | 0.4870 | 0.9770 | 0.0509 | 0.1721 |
| **Carnitine C14:2** | 0.3361 | 0.5189 | 0.2659 | 0.7678 | 0.5194 | 0.7300 | 0.3843 | 0.7918 | 0.0933 | 0.3971 | 0.7885 | 0.9136 | 0.8854 | 0.9770 | 0.0991 | 0.2336 |
| **Carnitine C16:0** | 0.0201 | 0.2093 | 0.4675 | 0.8279 | 0.1520 | 0.4515 | 0.2177 | 0.7918 | 0.0132 | 0.3482 | 0.4227 | 0.7327 | 0.4728 | 0.9770 | 0.0031 | 0.0704 |
| **Carnitine C18:0** | 0.0579 | 0.2617 | 0.9581 | 0.9918 | 0.7189 | 0.8492 | 0.9692 | 0.9948 | 0.1439 | 0.3971 | 0.6067 | 0.8630 | 0.9914 | 0.9993 | 0.0556 | 0.1753 |
| **Carnitine C18:1** | 0.0350 | 0.2277 | 0.4135 | 0.7964 | 0.2740 | 0.5276 | 0.1060 | 0.7918 | 0.0200 | 0.3482 | 0.6140 | 0.8630 | 0.4300 | 0.9770 | 0.0034 | 0.0704 |
| **Carnitine C18:2** | 0.0038 | 0.1318 | 0.7412 | 0.9622 | 0.5179 | 0.7300 | 0.6074 | 0.9822 | 0.0197 | 0.3482 | 0.7642 | 0.9136 | 0.8675 | 0.9770 | 0.0057 | 0.0792 |
| **Carnitine C2:0** | 0.4752 | 0.6102 | 0.4960 | 0.8598 | 0.8863 | 0.9406 | 0.1920 | 0.7918 | 0.8895 | 0.9199 | 0.7173 | 0.9136 | 0.5370 | 0.9770 | 0.7062 | 0.7596 |
| **Carnitine C3:0** | 0.0132 | 0.2093 | 0.8794 | 0.9918 | 0.2830 | 0.5312 | 0.0368 | 0.7918 | 0.1896 | 0.4286 | 0.4979 | 0.7947 | 0.0208 | 0.9770 | 0.8070 | 0.8518 |
| **Carnitine C4:0** | 0.0663 | 0.2653 | 0.2672 | 0.7678 | 0.9987 | 0.9987 | 0.2154 | 0.7918 | 0.4158 | 0.5690 | 0.2513 | 0.7259 | 0.8489 | 0.9770 | 0.4231 | 0.5314 |
| **Carnitine C5:0** | 0.4282 | 0.5709 | 0.9432 | 0.9918 | 0.7801 | 0.8723 | 0.9099 | 0.9948 | 0.6090 | 0.7280 | 0.8340 | 0.9305 | 0.9715 | 0.9905 | 0.5541 | 0.6333 |
| **Carnitine C6:0** | 0.3509 | 0.5189 | 0.0749 | 0.7678 | 0.2446 | 0.5276 | 0.3502 | 0.7918 | 0.0363 | 0.3482 | 0.7726 | 0.9136 | 0.5627 | 0.9770 | 0.0781 | 0.2137 |
| **Carnitine C8:0** | 0.5981 | 0.6761 | 0.0873 | 0.7678 | 0.0767 | 0.4405 | 0.1995 | 0.7918 | 0.1419 | 0.3971 | 0.9553 | 0.9741 | 0.9273 | 0.9770 | 0.1423 | 0.2901 |
| **Carnitine C8:1** | 0.0633 | 0.2635 | 0.8142 | 0.9622 | 0.9754 | 0.9946 | 0.5383 | 0.9309 | 0.1722 | 0.4286 | 0.8589 | 0.9305 | 0.3864 | 0.9770 | 0.0113 | 0.0870 |
| **Citric acid** | 0.9748 | 0.9922 | 0.3617 | 0.7678 | 0.0805 | 0.4405 | 0.0710 | 0.7918 | 0.4295 | 0.5802 | 0.4732 | 0.7906 | 0.4061 | 0.9770 | 0.1687 | 0.3133 |
| **Creatine** | 0.1031 | 0.3298 | 0.1598 | 0.7678 | 0.2462 | 0.5276 | 0.0145 | 0.7551 | 0.3792 | 0.5557 | 0.4561 | 0.7776 | 0.6799 | 0.9770 | 0.2187 | 0.3750 |
| **Cystine** | 0.4708 | 0.6102 | 0.5618 | 0.8853 | 0.1149 | 0.4515 | 0.5337 | 0.9309 | 0.4006 | 0.5596 | 0.3440 | 0.7259 | 0.7263 | 0.9770 | 0.3091 | 0.4431 |
| **Dihydroorotic acid** | 0.1398 | 0.3817 | 0.3163 | 0.7678 | 0.9093 | 0.9496 | 0.5007 | 0.9309 | 0.8473 | 0.8901 | 0.2984 | 0.7259 | 0.2152 | 0.9770 | 0.0514 | 0.1721 |
| **Gluconic acid** | 0.5039 | 0.6235 | 0.9268 | 0.9918 | 0.1823 | 0.4921 | 0.3594 | 0.7918 | 0.5275 | 0.6610 | 0.3562 | 0.7259 | 0.5483 | 0.9770 | 0.9217 | 0.9491 |
| **Glucosamine-6-phosphate** | 0.3058 | 0.5119 | 0.1281 | 0.7678 | 0.3065 | 0.5312 | 0.2945 | 0.7918 | 0.1874 | 0.4286 | 0.1109 | 0.7259 | 0.0899 | 0.9770 | 0.0383 | 0.1475 |
| **Glutamic acid** | 0.2253 | 0.4595 | 0.3133 | 0.7678 | 0.6777 | 0.8391 | 0.9923 | 0.9948 | 0.6819 | 0.7880 | 0.5476 | 0.8175 | 0.2805 | 0.9770 | 0.2857 | 0.4331 |
| **Glutamine** | 0.5793 | 0.6678 | 0.3144 | 0.7678 | 0.2694 | 0.5276 | 0.9178 | 0.9948 | 0.3586 | 0.5452 | 0.2448 | 0.7259 | 0.3075 | 0.9770 | 0.4343 | 0.5314 |
| **Glyceric acid** | 0.5843 | 0.6678 | 0.6858 | 0.9622 | 0.5374 | 0.7452 | 0.3815 | 0.7918 | 0.8934 | 0.9199 | 0.9454 | 0.9735 | 0.2487 | 0.9770 | 0.4023 | 0.5314 |
| **Hippuric acid** | 0.1667 | 0.3939 | 0.1876 | 0.7678 | 0.1514 | 0.4515 | 0.6853 | 0.9822 | 0.0684 | 0.3482 | 0.7816 | 0.9136 | 0.1105 | 0.9770 | 0.4069 | 0.5314 |
| **Histidine** | 0.4983 | 0.6235 | 0.2180 | 0.7678 | 0.8297 | 0.8989 | 0.3502 | 0.7918 | 0.2791 | 0.4920 | 0.2008 | 0.7259 | 0.3157 | 0.9770 | 0.8108 | 0.8518 |
| **Hydroxyproline** | 0.5096 | 0.6235 | 0.5604 | 0.8853 | 0.9986 | 0.9987 | 0.9726 | 0.9948 | 0.9894 | 0.9894 | 0.5043 | 0.7947 | 0.6239 | 0.9770 | 0.5755 | 0.6368 |
| **Hypoxanthine** | 0.4123 | 0.5620 | 0.2635 | 0.7678 | 0.2608 | 0.5276 | 0.9331 | 0.9948 | 0.7456 | 0.8249 | 0.8792 | 0.9427 | 0.4156 | 0.9770 | 0.6479 | 0.7093 |
| **Indole** | 0.0625 | 0.2635 | 0.7506 | 0.9622 | 0.0220 | 0.4405 | 0.9947 | 0.9948 | 0.2894 | 0.4935 | 0.0223 | 0.7259 | 0.8538 | 0.9770 | 0.2873 | 0.4331 |
| **Kynurenine** | 0.3301 | 0.5189 | 0.2358 | 0.7678 | 0.0181 | 0.4405 | 0.3659 | 0.7918 | 0.7878 | 0.8447 | 0.1203 | 0.7259 | 0.7579 | 0.9770 | 0.9966 | 0.9966 |
| **Lactic acid** | 0.0330 | 0.2277 | 0.4249 | 0.8035 | 0.6508 | 0.8254 | 0.6591 | 0.9822 | 0.2331 | 0.4848 | 0.7436 | 0.9136 | 0.7210 | 0.9770 | 0.1087 | 0.2404 |
| **Leucine-Isoleucine** | 0.0377 | 0.2305 | 0.3226 | 0.7678 | 0.4251 | 0.6502 | 0.6162 | 0.9822 | 0.0268 | 0.3482 | 0.8906 | 0.9451 | 0.6685 | 0.9770 | 0.0654 | 0.1999 |
| **LPC 14:0** | 0.2448 | 0.4714 | 0.3256 | 0.7678 | 0.0255 | 0.4405 | 0.8539 | 0.9948 | 0.1389 | 0.3971 | 0.1133 | 0.7259 | 0.6500 | 0.9770 | 0.2199 | 0.3750 |
| **LPC 15:0** | 0.3496 | 0.5189 | 0.3485 | 0.7678 | 0.0511 | 0.4405 | 0.9948 | 0.9948 | 0.2723 | 0.4920 | 0.2257 | 0.7259 | 0.6486 | 0.9770 | 0.4969 | 0.6006 |
| **LPC 16:0** | 0.0559 | 0.2617 | 0.3977 | 0.7943 | 0.1266 | 0.4515 | 0.9898 | 0.9948 | 0.0694 | 0.3482 | 0.3633 | 0.7259 | 0.7419 | 0.9770 | 0.1011 | 0.2336 |
| **LPC 16:1** | 0.4377 | 0.5762 | 0.1259 | 0.7678 | 0.0465 | 0.4405 | 0.5229 | 0.9309 | 0.1753 | 0.4286 | 0.3382 | 0.7259 | 0.7803 | 0.9770 | 0.2403 | 0.4032 |
| **LPC 17:0** | 0.1642 | 0.3939 | 0.8513 | 0.9837 | 0.1484 | 0.4515 | 0.6853 | 0.9822 | 0.3144 | 0.5172 | 0.1399 | 0.7259 | 0.7613 | 0.9770 | 0.4325 | 0.5314 |
| **LPC 18:0** | 0.1557 | 0.3939 | 0.9596 | 0.9918 | 0.2001 | 0.5075 | 0.7469 | 0.9948 | 0.3165 | 0.5172 | 0.1932 | 0.7259 | 0.7604 | 0.9770 | 0.4089 | 0.5314 |
| **LPC 18:1** | 0.2201 | 0.4577 | 0.6567 | 0.9620 | 0.1463 | 0.4515 | 0.3321 | 0.7918 | 0.2611 | 0.4920 | 0.3253 | 0.7259 | 0.5374 | 0.9770 | 0.0890 | 0.2313 |
| **LPC 18:2** | 0.1395 | 0.3817 | 0.3247 | 0.7678 | 0.0698 | 0.4405 | 0.2522 | 0.7918 | 0.1424 | 0.3971 | 0.2727 | 0.7259 | 0.6610 | 0.9770 | 0.0951 | 0.2336 |
| **LPC 19:0** | 0.3101 | 0.5119 | 0.4617 | 0.8279 | 0.3886 | 0.6217 | 0.9389 | 0.9948 | 0.2308 | 0.4848 | 0.8176 | 0.9243 | 0.6442 | 0.9770 | 0.4279 | 0.5314 |
| **LPC 20:1** | 0.1096 | 0.3298 | 0.2180 | 0.7678 | 0.5890 | 0.7754 | 0.2556 | 0.7918 | 0.0703 | 0.3482 | 0.9932 | 0.9963 | 0.6089 | 0.9770 | 0.0488 | 0.1721 |
| **LPC 20:2** | 0.7477 | 0.8110 | 0.1206 | 0.7678 | 0.1841 | 0.4921 | 0.6594 | 0.9822 | 0.4728 | 0.6224 | 0.9963 | 0.9963 | 0.3981 | 0.9770 | 0.9698 | 0.9792 |
| **LPC 20:3** | 0.2770 | 0.5119 | 0.8826 | 0.9918 | 0.1300 | 0.4515 | 0.3418 | 0.7918 | 0.3523 | 0.5452 | 0.2438 | 0.7259 | 0.4789 | 0.9770 | 0.0683 | 0.2013 |
| **LPC 20:4** | 0.0220 | 0.2093 | 0.8063 | 0.9622 | 0.3344 | 0.5521 | 0.1617 | 0.7918 | 0.0654 | 0.3482 | 0.3502 | 0.7259 | 0.1932 | 0.9770 | 0.0010 | 0.0334 |
| **LPC 20:5** | 0.0282 | 0.2257 | 0.6206 | 0.9492 | 0.3057 | 0.5312 | 0.2320 | 0.7918 | 0.0635 | 0.3482 | 0.2183 | 0.7259 | 0.1612 | 0.9770 | 0.0058 | 0.0792 |
| **LPC 22:5** | 0.2166 | 0.4577 | 0.9863 | 0.9918 | 0.2284 | 0.5276 | 0.3959 | 0.7918 | 0.3617 | 0.5452 | 0.2853 | 0.7259 | 0.5037 | 0.9770 | 0.0246 | 0.1116 |
| **LPC 22:6** | 0.0154 | 0.2093 | 0.2574 | 0.7678 | 0.3177 | 0.5416 | 0.3469 | 0.7918 | 0.1227 | 0.3971 | 0.1895 | 0.7259 | 0.1390 | 0.9770 | 0.0117 | 0.0870 |
| **LPE 16:0** | 0.0063 | 0.1420 | 0.3606 | 0.7678 | 0.9131 | 0.9496 | 0.6980 | 0.9822 | 0.0924 | 0.3971 | 0.3964 | 0.7259 | 0.3690 | 0.9770 | 0.0097 | 0.0870 |
| **LPE 18:0** | 0.3638 | 0.5189 | 0.3445 | 0.7678 | 0.0542 | 0.4405 | 0.9851 | 0.9948 | 0.2777 | 0.4920 | 0.2319 | 0.7259 | 0.6402 | 0.9770 | 0.5173 | 0.6045 |
| **LPE 18:1** | 0.2403 | 0.4714 | 0.4451 | 0.8266 | 0.2923 | 0.5312 | 0.3384 | 0.7918 | 0.2010 | 0.4448 | 0.6957 | 0.9136 | 0.7022 | 0.9770 | 0.1322 | 0.2806 |
| **LPE 18:2** | 0.4161 | 0.5620 | 0.2997 | 0.7678 | 0.1158 | 0.4515 | 0.2218 | 0.7918 | 0.2290 | 0.4848 | 0.5665 | 0.8298 | 0.6877 | 0.9770 | 0.1577 | 0.2993 |
| **LPE 20:0** | 0.1468 | 0.3817 | 0.7632 | 0.9622 | 0.2356 | 0.5276 | 0.7376 | 0.9948 | 0.3183 | 0.5172 | 0.2012 | 0.7259 | 0.8732 | 0.9770 | 0.3300 | 0.4577 |
| **LPE 20:4** | 0.0350 | 0.2277 | 0.4048 | 0.7943 | 0.2879 | 0.5312 | 0.1819 | 0.7918 | 0.0379 | 0.3482 | 0.6651 | 0.9102 | 0.5837 | 0.9770 | 0.0068 | 0.0792 |
| **LPE 20:5** | 0.1444 | 0.3817 | 0.5492 | 0.8853 | 0.1893 | 0.4921 | 0.1833 | 0.7918 | 0.0888 | 0.3971 | 0.4118 | 0.7259 | 0.2422 | 0.9770 | 0.0143 | 0.0875 |
| **LPE 22:6** | 0.0068 | 0.1420 | 0.2214 | 0.7678 | 0.7726 | 0.8723 | 0.5327 | 0.9309 | 0.0405 | 0.3482 | 0.5774 | 0.8340 | 0.2054 | 0.9770 | 0.0168 | 0.0912 |
| **Lysine** | 0.3280 | 0.5189 | 0.2193 | 0.7678 | 0.6108 | 0.7941 | 0.6989 | 0.9822 | 0.3286 | 0.5178 | 0.2368 | 0.7259 | 0.2971 | 0.9770 | 0.5093 | 0.6019 |
| **Malic acid** | 0.7896 | 0.8379 | 0.7684 | 0.9622 | 0.8061 | 0.8907 | 0.9621 | 0.9948 | 0.6775 | 0.7880 | 0.7546 | 0.9136 | 0.8097 | 0.9770 | 0.8528 | 0.8869 |
| **Methionine** | 0.0221 | 0.2093 | 0.9887 | 0.9918 | 0.1382 | 0.4515 | 0.2840 | 0.7918 | 0.0651 | 0.3482 | 0.3109 | 0.7259 | 0.3049 | 0.9770 | 0.0079 | 0.0821 |
| **Mevalonic acid** | 0.9208 | 0.9481 | 0.6094 | 0.9460 | 0.2469 | 0.5276 | 0.5460 | 0.9309 | 0.5769 | 0.7059 | 0.6779 | 0.9136 | 0.9142 | 0.9770 | 0.5603 | 0.6333 |
| **Orotic acid** | 0.3046 | 0.5119 | 0.1446 | 0.7678 | 0.4917 | 0.7147 | 0.8073 | 0.9948 | 0.9390 | 0.9574 | 0.3749 | 0.7259 | 0.4488 | 0.9770 | 0.5024 | 0.6006 |
| **Paraxanthine** | 0.8864 | 0.9284 | 0.1645 | 0.7678 | 0.6379 | 0.8191 | 0.2603 | 0.7918 | 0.2647 | 0.4920 | 0.3871 | 0.7259 | 0.8387 | 0.9770 | 0.4103 | 0.5314 |
| **PC 32:1** | 0.3550 | 0.5189 | 0.9230 | 0.9918 | 0.1054 | 0.4515 | 0.9122 | 0.9948 | 0.3879 | 0.5557 | 0.0754 | 0.7259 | 0.9651 | 0.9905 | 0.2706 | 0.4264 |
| **PC 34:1** | 0.0813 | 0.2867 | 0.2169 | 0.7678 | 0.3255 | 0.5460 | 0.7690 | 0.9948 | 0.1871 | 0.4286 | 0.1407 | 0.7259 | 0.3640 | 0.9770 | 0.0175 | 0.0912 |
| **PC 34:2** | 0.0827 | 0.2867 | 0.7901 | 0.9622 | 0.2989 | 0.5312 | 0.8946 | 0.9948 | 0.1831 | 0.4286 | 0.3095 | 0.7259 | 0.7335 | 0.9770 | 0.1474 | 0.2947 |
| **PC 36:2** | 0.0482 | 0.2617 | 0.5489 | 0.8853 | 0.3522 | 0.5723 | 0.8162 | 0.9948 | 0.3242 | 0.5178 | 0.1156 | 0.7259 | 0.7922 | 0.9770 | 0.1924 | 0.3510 |
| **PC 36:3** | 0.1609 | 0.3939 | 0.3949 | 0.7943 | 0.4039 | 0.6269 | 0.6420 | 0.9822 | 0.4914 | 0.6309 | 0.1513 | 0.7259 | 0.8057 | 0.9770 | 0.2530 | 0.4049 |
| **PC 36:4** | 0.0015 | 0.1318 | 0.1541 | 0.7678 | 0.8724 | 0.9353 | 0.8915 | 0.9948 | 0.0121 | 0.3482 | 0.4805 | 0.7906 | 0.4852 | 0.9770 | 0.0006 | 0.0334 |
| **PC 38:5** | 0.0259 | 0.2243 | 0.1783 | 0.7678 | 0.4796 | 0.7147 | 0.9644 | 0.9948 | 0.1192 | 0.3971 | 0.1320 | 0.7259 | 0.5577 | 0.9770 | 0.0069 | 0.0792 |
| **PC 38:6** | 0.0184 | 0.2093 | 0.0109 | 0.7678 | 0.7527 | 0.8698 | 0.6008 | 0.9822 | 0.1280 | 0.3971 | 0.2432 | 0.7259 | 0.4358 | 0.9770 | 0.0529 | 0.1721 |
| **PC 40:7** | 0.0030 | 0.1318 | 0.0307 | 0.7678 | 0.7720 | 0.8723 | 0.6476 | 0.9822 | 0.1737 | 0.4286 | 0.3034 | 0.7259 | 0.3112 | 0.9770 | 0.0009 | 0.0334 |
| **PC 40:8** | 0.9922 | 0.9922 | 0.7205 | 0.9622 | 0.7228 | 0.8492 | 0.1759 | 0.7918 | 0.7827 | 0.8447 | 0.5441 | 0.8175 | 0.4537 | 0.9770 | 0.2853 | 0.4331 |
| **Phenylalanine** | 0.0579 | 0.2617 | 0.5273 | 0.8853 | 0.0879 | 0.4515 | 0.1883 | 0.7918 | 0.0490 | 0.3482 | 0.4081 | 0.7259 | 0.4521 | 0.9770 | 0.0104 | 0.0870 |
| **Proline** | 0.3232 | 0.5189 | 0.0199 | 0.7678 | 0.2673 | 0.5276 | 0.5242 | 0.9309 | 0.0045 | 0.3482 | 0.8582 | 0.9305 | 0.1520 | 0.9770 | 0.1583 | 0.2993 |
| **Serine** | 0.7882 | 0.8379 | 0.8253 | 0.9644 | 0.1865 | 0.4921 | 0.2593 | 0.7918 | 0.6971 | 0.7881 | 0.5502 | 0.8175 | 0.3498 | 0.9770 | 0.3084 | 0.4431 |
| **SM 32:1** | 0.1962 | 0.4435 | 0.8047 | 0.9622 | 0.0766 | 0.4405 | 0.9564 | 0.9948 | 0.2849 | 0.4935 | 0.1383 | 0.7259 | 0.9004 | 0.9770 | 0.2514 | 0.4049 |
| **SM 32:2** | 0.5350 | 0.6469 | 0.9352 | 0.9918 | 0.0569 | 0.4405 | 0.8291 | 0.9948 | 0.5571 | 0.6897 | 0.0762 | 0.7259 | 0.7459 | 0.9770 | 0.3822 | 0.5230 |
| **SM 33:1** | 0.2435 | 0.4714 | 0.7602 | 0.9622 | 0.1487 | 0.4515 | 0.3140 | 0.7918 | 0.3901 | 0.5557 | 0.1474 | 0.7259 | 0.2723 | 0.9770 | 0.0477 | 0.1721 |
| **SM 34:1** | 0.2717 | 0.5119 | 0.9810 | 0.9918 | 0.0495 | 0.4405 | 0.1364 | 0.7918 | 0.1888 | 0.4286 | 0.1115 | 0.7259 | 0.0852 | 0.9770 | 0.0265 | 0.1149 |
| **SM 34:2** | 0.2947 | 0.5119 | 0.7407 | 0.9622 | 0.0409 | 0.4405 | 0.3741 | 0.7918 | 0.2505 | 0.4920 | 0.1520 | 0.7259 | 0.4197 | 0.9770 | 0.0933 | 0.2336 |
| **SM 35:2** | 0.2976 | 0.5119 | 0.2659 | 0.7678 | 0.0738 | 0.4405 | 0.2335 | 0.7918 | 0.1451 | 0.3971 | 0.3159 | 0.7259 | 0.5461 | 0.9770 | 0.0708 | 0.2013 |
| **SM 36:2** | 0.1050 | 0.3298 | 0.7022 | 0.9622 | 0.1706 | 0.4921 | 0.4792 | 0.9309 | 0.1211 | 0.3971 | 0.1935 | 0.7259 | 0.3061 | 0.9770 | 0.0343 | 0.1372 |
| **Taurine** | 0.1883 | 0.4352 | 0.2401 | 0.7678 | 0.7267 | 0.8492 | 0.2540 | 0.7918 | 0.8034 | 0.8526 | 0.7786 | 0.9136 | 0.1147 | 0.9770 | 0.0247 | 0.1116 |
| **Transcinnamic acid** | 0.1366 | 0.3817 | 0.2521 | 0.7678 | 0.1290 | 0.4515 | 0.1219 | 0.7918 | 0.0583 | 0.3482 | 0.7131 | 0.9136 | 0.6560 | 0.9770 | 0.0228 | 0.1116 |
| **Tryptophan** | 0.0733 | 0.2823 | 0.7932 | 0.9622 | 0.0147 | 0.4405 | 0.9436 | 0.9948 | 0.2606 | 0.4920 | 0.0154 | 0.7259 | 0.9243 | 0.9770 | 0.3058 | 0.4431 |
| **Tyrosine** | 0.0562 | 0.2617 | 0.9629 | 0.9918 | 0.0944 | 0.4515 | 0.2947 | 0.7918 | 0.1145 | 0.3971 | 0.0509 | 0.7259 | 0.3202 | 0.9770 | 0.0140 | 0.0875 |
| **Uric acid** | 0.3012 | 0.5119 | 0.7855 | 0.9622 | 0.5792 | 0.7722 | 0.3919 | 0.7918 | 0.4590 | 0.6120 | 0.4865 | 0.7906 | 0.3304 | 0.9770 | 0.0716 | 0.2013 |
| **Valine** | 0.9840 | 0.9922 | 0.6449 | 0.9581 | 0.5659 | 0.7722 | 0.2088 | 0.7918 | 0.6896 | 0.7881 | 0.2757 | 0.7259 | 0.1346 | 0.9770 | 0.2005 | 0.3594 |

P a, p-value as estimated by unequal variances t-test; P b, p-value as estimated by unequal variances t-test adjusted for multiple testing according to the false discovery rate method. VLCD, very low-calorie diet; RYGB (1d), immediate effect of gastric bypass surgery; RYGB (6w), 6-week effect of gastric bypass surgery; Cum. Effect, cumulative effect of the intervention.

**Table 7B.** Assessment of difference in lipidomics data between normoglycaemic and T2D patients (fasting plasma samples).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Occasion:**  **Baseline** | | **Occasion:**  **Diet** | | **Occasion:**  **Surgery** | | **Occasion:**  **Recovery** | | **Effect of VLCD** | | **RYGB (1d)** | | **RYGB (6w)** | | **Cum. effect** | |
|  | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* |
| **CE16.0\*** | 0.6435 | 0.8643 | 0.9757 | 0.9902 | 0.5929 | 0.9814 | 0.6670 | 0.9880 | 0.8904 | 0.9516 | 0.7437 | 0.9486 | 0.7101 | 0.9741 | 0.4165 | 0.7119 |
| **CE18.1\*** | 0.0721 | 0.6002 | 0.1568 | 0.7456 | 0.0272 | 0.9814 | 0.1361 | 0.9721 | 0.5432 | 0.7375 | 0.4590 | 0.9486 | 0.8496 | 0.9741 | 0.5836 | 0.7640 |
| **CE18.2\*** | 0.1702 | 0.6002 | 0.3046 | 0.7847 | 0.8151 | 0.9814 | 0.9484 | 0.9880 | 0.0882 | 0.7105 | 0.6315 | 0.9486 | 0.6132 | 0.9741 | 0.6150 | 0.7769 |
| **CE18.3\*** | 0.0396 | 0.6002 | 0.5549 | 0.9303 | 0.1610 | 0.9814 | 0.2632 | 0.9721 | 0.0614 | 0.7105 | 0.7425 | 0.9486 | 0.3233 | 0.9741 | 0.4609 | 0.7119 |
| **CE20.4\*** | 0.8181 | 0.9368 | 0.2284 | 0.7830 | 0.9838 | 0.9838 | 0.0149 | 0.6686 | 0.2938 | 0.7105 | 0.3490 | 0.9486 | 0.5610 | 0.9741 | 0.0430 | 0.5169 |
| **LPC16.0\*** | 0.2546 | 0.6547 | 0.0766 | 0.7007 | 0.8703 | 0.9814 | 0.5589 | 0.9721 | 0.0322 | 0.7105 | 0.5397 | 0.9486 | 0.5755 | 0.9741 | 0.1783 | 0.6777 |
| **LPC16.1\*** | 0.6482 | 0.8643 | 0.0798 | 0.7007 | 0.4271 | 0.9814 | 0.6846 | 0.9880 | 0.3693 | 0.7105 | 0.5375 | 0.9486 | 0.4743 | 0.9741 | 0.9042 | 0.9515 |
| **LPC18.0\*** | 0.2251 | 0.6484 | 0.3409 | 0.7847 | 0.8929 | 0.9814 | 0.9605 | 0.9880 | 0.1076 | 0.7105 | 0.6341 | 0.9486 | 0.5869 | 0.9741 | 0.4429 | 0.7119 |
| **LPC18.1\*** | 0.5700 | 0.8643 | 0.2053 | 0.7766 | 0.8984 | 0.9814 | 0.4738 | 0.9721 | 0.2277 | 0.7105 | 0.5725 | 0.9486 | 0.9354 | 0.9741 | 0.3187 | 0.6777 |
| **LPC18.2\*** | 0.4125 | 0.7657 | 0.1018 | 0.7007 | 0.4817 | 0.9814 | 0.3838 | 0.9721 | 0.0683 | 0.7105 | 0.7570 | 0.9486 | 0.8979 | 0.9741 | 0.2586 | 0.6777 |
| **LPC20.3\*** | 0.4663 | 0.7994 | 0.4742 | 0.8985 | 0.2428 | 0.9814 | 0.9514 | 0.9880 | 0.4014 | 0.7105 | 0.4144 | 0.9486 | 0.5561 | 0.9741 | 0.5264 | 0.7180 |
| **LPC20.4\*** | 0.0503 | 0.6002 | 0.5059 | 0.9204 | 0.9526 | 0.9814 | 0.1359 | 0.9721 | 0.0332 | 0.7105 | 0.7049 | 0.9486 | 0.4749 | 0.9741 | 0.0171 | 0.5169 |
| **LPC22.6\*** | 0.0666 | 0.6002 | 0.8960 | 0.9902 | 0.8631 | 0.9814 | 0.6947 | 0.9880 | 0.2273 | 0.7105 | 0.8250 | 0.9486 | 0.9606 | 0.9741 | 0.2029 | 0.6777 |
| **PC32.0\*** | 0.1857 | 0.6002 | 0.0333 | 0.7007 | 0.6368 | 0.9814 | 0.0323 | 0.6686 | 0.0094 | 0.6788 | 0.3775 | 0.9486 | 0.2901 | 0.9741 | 0.0046 | 0.3318 |
| **PC32.1\*** | 0.1922 | 0.6002 | 0.3705 | 0.7847 | 0.2119 | 0.9814 | 0.6753 | 0.9880 | 0.9977 | 0.9977 | 0.7318 | 0.9486 | 0.8271 | 0.9741 | 0.7638 | 0.8483 |
| **PC32.2\*** | 0.5758 | 0.8643 | 0.6678 | 0.9427 | 0.1628 | 0.9814 | 0.2965 | 0.9721 | 0.6342 | 0.7942 | 0.2584 | 0.9486 | 0.2342 | 0.9741 | 0.4653 | 0.7119 |
| **PC34.0\*** | 0.1678 | 0.6002 | 0.4600 | 0.8951 | 0.8284 | 0.9814 | 0.3456 | 0.9721 | 0.1297 | 0.7105 | 0.7634 | 0.9486 | 0.6755 | 0.9741 | 0.1128 | 0.6777 |
| **PC34.1\*** | 0.7360 | 0.9297 | 0.9178 | 0.9902 | 0.4029 | 0.9814 | 0.7673 | 0.9880 | 0.9318 | 0.9516 | 0.3951 | 0.9486 | 0.7114 | 0.9741 | 0.3708 | 0.6777 |
| **PC34.2\*** | 0.5646 | 0.8643 | 0.5556 | 0.9303 | 0.8459 | 0.9814 | 0.9937 | 0.9973 | 0.5294 | 0.7375 | 0.2920 | 0.9486 | 0.7620 | 0.9741 | 0.6662 | 0.7818 |
| **PC34.3\*** | 0.5593 | 0.8643 | 0.2157 | 0.7766 | 0.5854 | 0.9814 | 0.5638 | 0.9721 | 0.5461 | 0.7375 | 0.7306 | 0.9486 | 0.8778 | 0.9741 | 0.6761 | 0.7818 |
| **PC36.1\*** | 0.5452 | 0.8643 | 0.6389 | 0.9427 | 0.4418 | 0.9814 | 0.7805 | 0.9880 | 0.9258 | 0.9516 | 0.5425 | 0.9486 | 0.9252 | 0.9741 | 0.7955 | 0.8678 |
| **PC36.2\*** | 0.3366 | 0.6996 | 0.5754 | 0.9415 | 0.8249 | 0.9814 | 0.8950 | 0.9880 | 0.4046 | 0.7105 | 0.5054 | 0.9486 | 0.8213 | 0.9741 | 0.5042 | 0.7119 |
| **PC36.3\*** | 0.6306 | 0.8643 | 0.3115 | 0.7847 | 0.7008 | 0.9814 | 0.8806 | 0.9880 | 0.9086 | 0.9516 | 0.7498 | 0.9486 | 0.6464 | 0.9741 | 0.8356 | 0.8980 |
| **PC36.4\*** | 0.0733 | 0.6002 | 0.6474 | 0.9427 | 0.5657 | 0.9814 | 0.7751 | 0.9880 | 0.2270 | 0.7105 | 0.8432 | 0.9486 | 0.5179 | 0.9741 | 0.0556 | 0.5169 |
| **PC36.5\*** | 0.1436 | 0.6002 | 0.9663 | 0.9902 | 0.7403 | 0.9814 | 0.5239 | 0.9721 | 0.2573 | 0.7105 | 0.6100 | 0.9486 | 0.7054 | 0.9741 | 0.1143 | 0.6777 |
| **PC38.3\*** | 0.8977 | 0.9368 | 0.8466 | 0.9675 | 0.9785 | 0.9838 | 0.9973 | 0.9973 | 0.9323 | 0.9516 | 0.8333 | 0.9486 | 0.8420 | 0.9741 | 0.9452 | 0.9585 |
| **PC38.4\*** | 0.1207 | 0.6002 | 0.3369 | 0.7847 | 0.4445 | 0.9814 | 0.7658 | 0.9880 | 0.4234 | 0.7112 | 0.9194 | 0.9825 | 0.5326 | 0.9741 | 0.1779 | 0.6777 |
| **PC38.5\*** | 0.2533 | 0.6547 | 0.6558 | 0.9427 | 0.7124 | 0.9814 | 0.5467 | 0.9721 | 0.2998 | 0.7105 | 0.9663 | 0.9825 | 0.9316 | 0.9741 | 0.1979 | 0.6777 |
| **PC38.6\*** | 0.1054 | 0.6002 | 0.3372 | 0.7847 | 0.2254 | 0.9814 | 0.8813 | 0.9880 | 0.1678 | 0.7105 | 0.3973 | 0.9486 | 0.7431 | 0.9741 | 0.1952 | 0.6777 |
| **PC40.4\*** | 0.9558 | 0.9809 | 0.9610 | 0.9902 | 0.7870 | 0.9814 | 0.7527 | 0.9880 | 0.7971 | 0.8967 | 0.7978 | 0.9486 | 0.7757 | 0.9741 | 0.6538 | 0.7818 |
| **PC40.5\*** | 0.6619 | 0.8665 | 0.7659 | 0.9675 | 0.6999 | 0.9814 | 0.5203 | 0.9721 | 0.4862 | 0.7375 | 0.9864 | 0.9864 | 0.5180 | 0.9741 | 0.6841 | 0.7818 |
| **PC40.6\*** | 0.1201 | 0.6002 | 0.0897 | 0.7007 | 0.1588 | 0.9814 | 0.8135 | 0.9880 | 0.5253 | 0.7375 | 0.6068 | 0.9486 | 0.4729 | 0.9741 | 0.3274 | 0.6777 |
| **SM32.1\*** | 0.5913 | 0.8643 | 0.1495 | 0.7456 | 0.8574 | 0.9814 | 0.5254 | 0.9721 | 0.2018 | 0.7105 | 0.6081 | 0.9486 | 0.8931 | 0.9741 | 0.2821 | 0.6777 |
| **SM32.2\*** | 0.8584 | 0.9368 | 0.2729 | 0.7847 | 0.9305 | 0.9814 | 0.8249 | 0.9880 | 0.5135 | 0.7375 | 0.4577 | 0.9486 | 0.5488 | 0.9741 | 0.9251 | 0.9515 |
| **SM33.1\*** | 0.8430 | 0.9368 | 0.1008 | 0.7007 | 0.7328 | 0.9814 | 0.3636 | 0.9721 | 0.2588 | 0.7105 | 0.5609 | 0.9486 | 0.9285 | 0.9741 | 0.3105 | 0.6777 |
| **SM34.1\*** | 0.8019 | 0.9368 | 0.0486 | 0.7007 | 0.2473 | 0.9814 | 0.1297 | 0.9721 | 0.2750 | 0.7105 | 0.5797 | 0.9486 | 0.7828 | 0.9741 | 0.2320 | 0.6777 |
| **SM34.2\*** | 0.5814 | 0.8643 | 0.1657 | 0.7456 | 0.8152 | 0.9814 | 0.2612 | 0.9721 | 0.1923 | 0.7105 | 0.5809 | 0.9486 | 0.6943 | 0.9741 | 0.1495 | 0.6777 |
| **SM35.1\*** | 0.8260 | 0.9368 | 0.6532 | 0.9427 | 0.9541 | 0.9814 | 0.0266 | 0.6686 | 0.7665 | 0.8760 | 0.7820 | 0.9486 | 0.2295 | 0.9741 | 0.0561 | 0.5169 |
| **SM36.0\*** | 0.1295 | 0.6002 | 0.1991 | 0.7766 | 0.4989 | 0.9814 | 0.1408 | 0.9721 | 0.0937 | 0.7105 | 0.6261 | 0.9486 | 0.6034 | 0.9741 | 0.0574 | 0.5169 |
| **SM36.1\*** | 0.7135 | 0.9174 | 0.2605 | 0.7847 | 0.1868 | 0.9814 | 0.1290 | 0.9721 | 0.6423 | 0.7942 | 0.8973 | 0.9788 | 0.4381 | 0.9741 | 0.3664 | 0.6777 |
| **SM36.2\*** | 0.2746 | 0.6589 | 0.3633 | 0.7847 | 0.5012 | 0.9814 | 0.3837 | 0.9721 | 0.9384 | 0.9516 | 0.7742 | 0.9486 | 0.9846 | 0.9846 | 0.9209 | 0.9515 |
| **SM38.1\*** | 0.3086 | 0.6841 | 0.8459 | 0.9675 | 0.9387 | 0.9814 | 0.5615 | 0.9721 | 0.4670 | 0.7375 | 0.9430 | 0.9825 | 0.7398 | 0.9741 | 0.2256 | 0.6777 |
| **SM38.2\*** | 0.3595 | 0.6996 | 0.0944 | 0.7007 | 0.4900 | 0.9814 | 0.1629 | 0.9721 | 0.6619 | 0.7942 | 0.5327 | 0.9486 | 0.8548 | 0.9741 | 0.4897 | 0.7119 |
| **SM39.1\*** | 0.2718 | 0.6589 | 0.8339 | 0.9675 | 0.8971 | 0.9814 | 0.8559 | 0.9880 | 0.3457 | 0.7105 | 0.7919 | 0.9486 | 0.9380 | 0.9741 | 0.3765 | 0.6777 |
| **SM40.0\*** | 0.4147 | 0.7657 | 0.1071 | 0.7007 | 0.6496 | 0.9814 | 0.0371 | 0.6686 | 0.5363 | 0.7375 | 0.4388 | 0.9486 | 0.5844 | 0.9741 | 0.2402 | 0.6777 |
| **SM40.1\*** | 0.6137 | 0.8643 | 0.6875 | 0.9483 | 0.9126 | 0.9814 | 0.7925 | 0.9880 | 0.5700 | 0.7461 | 0.6599 | 0.9486 | 0.9412 | 0.9741 | 0.5285 | 0.7180 |
| **SM40.2\*** | 0.8590 | 0.9368 | 0.6130 | 0.9427 | 0.7707 | 0.9814 | 0.4244 | 0.9721 | 0.6294 | 0.7942 | 0.9590 | 0.9825 | 0.4446 | 0.9741 | 0.5042 | 0.7119 |
| **SM41.1\*** | 0.7667 | 0.9368 | 0.3586 | 0.7847 | 0.8644 | 0.9814 | 0.7849 | 0.9880 | 0.4248 | 0.7112 | 0.6877 | 0.9486 | 0.6437 | 0.9741 | 0.6452 | 0.7818 |
| **SM41.2\*** | 0.7792 | 0.9368 | 0.1960 | 0.7766 | 0.8596 | 0.9814 | 0.2929 | 0.9721 | 0.3097 | 0.7105 | 0.6159 | 0.9486 | 0.8280 | 0.9741 | 0.2347 | 0.6777 |
| **SM42.1\*** | 0.8227 | 0.9368 | 0.3876 | 0.7974 | 0.8656 | 0.9814 | 0.5671 | 0.9721 | 0.4632 | 0.7375 | 0.6822 | 0.9486 | 0.9291 | 0.9741 | 0.4921 | 0.7119 |
| **SM42.2\*** | 0.9814 | 0.9814 | 0.0915 | 0.7007 | 0.4213 | 0.9814 | 0.1389 | 0.9721 | 0.2889 | 0.7105 | 0.6596 | 0.9486 | 0.7263 | 0.9741 | 0.1473 | 0.6777 |
| **SM42.3\*** | 0.9673 | 0.9809 | 0.2555 | 0.7847 | 0.3345 | 0.9814 | 0.1731 | 0.9721 | 0.5019 | 0.7375 | 0.8121 | 0.9486 | 0.5874 | 0.9741 | 0.3183 | 0.6777 |
| **SM43.1\*** | 0.6044 | 0.8643 | 0.2678 | 0.7847 | 0.3675 | 0.9814 | 0.8908 | 0.9880 | 0.8966 | 0.9516 | 0.8700 | 0.9637 | 0.5143 | 0.9741 | 0.7658 | 0.8483 |
| **SM43.2\*** | 0.8861 | 0.9368 | 0.1574 | 0.7456 | 0.7422 | 0.9814 | 0.3815 | 0.9721 | 0.5531 | 0.7375 | 0.5637 | 0.9486 | 0.8930 | 0.9741 | 0.3448 | 0.6777 |
| **SM44.2\*** | 0.3587 | 0.6996 | 0.2907 | 0.7847 | 0.3281 | 0.9814 | 0.3605 | 0.9721 | 0.7535 | 0.8750 | 0.9689 | 0.9825 | 0.8700 | 0.9741 | 0.6794 | 0.7818 |
| **TG48.1\*** | 0.3521 | 0.6996 | 0.6395 | 0.9427 | 0.8225 | 0.9814 | 0.8156 | 0.9880 | 0.3144 | 0.7105 | 0.4224 | 0.9486 | 0.6872 | 0.9741 | 0.6004 | 0.7719 |
| **TG48.2\*** | 0.3018 | 0.6841 | 0.6981 | 0.9483 | 0.7468 | 0.9814 | 0.8545 | 0.9880 | 0.3700 | 0.7105 | 0.4192 | 0.9486 | 0.7548 | 0.9741 | 0.4306 | 0.7119 |
| **TG50.0\*** | 0.0859 | 0.6002 | 0.8300 | 0.9675 | 0.4438 | 0.9814 | 0.3492 | 0.9721 | 0.2637 | 0.7105 | 0.5288 | 0.9486 | 0.7572 | 0.9741 | 0.3346 | 0.6777 |
| **TG50.1\*** | 0.2001 | 0.6002 | 0.9902 | 0.9902 | 0.5879 | 0.9814 | 0.9581 | 0.9880 | 0.2076 | 0.7105 | 0.4869 | 0.9486 | 0.9500 | 0.9741 | 0.1440 | 0.6777 |
| **TG50.2\*** | 0.3136 | 0.6841 | 0.8330 | 0.9675 | 0.7153 | 0.9814 | 0.7948 | 0.9880 | 0.3955 | 0.7105 | 0.4752 | 0.9486 | 0.7748 | 0.9741 | 0.4260 | 0.7119 |
| **TG50.3\*** | 0.2458 | 0.6547 | 0.7474 | 0.9675 | 0.6663 | 0.9814 | 0.6316 | 0.9880 | 0.3579 | 0.7105 | 0.4187 | 0.9486 | 0.5949 | 0.9741 | 0.5017 | 0.7119 |
| **TG50.4\*** | 0.4595 | 0.7994 | 0.3998 | 0.7995 | 0.8810 | 0.9814 | 0.6941 | 0.9880 | 0.3625 | 0.7105 | 0.6820 | 0.9486 | 0.4548 | 0.9741 | 0.9636 | 0.9636 |
| **TG52.1\*** | 0.0683 | 0.6002 | 0.0991 | 0.7007 | 0.1077 | 0.9814 | 0.5595 | 0.9721 | 0.7155 | 0.8446 | 0.4670 | 0.9486 | 0.4644 | 0.9741 | 0.1132 | 0.6777 |
| **TG52.2\*** | 0.1628 | 0.6002 | 0.5126 | 0.9204 | 0.2347 | 0.9814 | 0.4687 | 0.9721 | 0.3672 | 0.7105 | 0.4014 | 0.9486 | 0.9348 | 0.9741 | 0.2564 | 0.6777 |
| **TG52.3\*** | 0.1259 | 0.6002 | 0.7777 | 0.9675 | 0.2763 | 0.9814 | 0.3907 | 0.9721 | 0.2047 | 0.7105 | 0.3535 | 0.9486 | 0.5899 | 0.9741 | 0.3401 | 0.6777 |
| **TG52.4\*** | 0.0913 | 0.6002 | 0.9893 | 0.9902 | 0.3597 | 0.9814 | 0.3871 | 0.9721 | 0.2168 | 0.7105 | 0.3678 | 0.9486 | 0.4973 | 0.9741 | 0.3443 | 0.6777 |
| **TG52.5\*** | 0.1768 | 0.6002 | 0.9175 | 0.9902 | 0.6686 | 0.9814 | 0.4738 | 0.9721 | 0.3849 | 0.7105 | 0.6131 | 0.9486 | 0.5445 | 0.9741 | 0.5657 | 0.7543 |
| **TG54.3\*** | 0.8775 | 0.9368 | 0.5241 | 0.9204 | 0.8252 | 0.9814 | 0.1981 | 0.9721 | 0.6553 | 0.7942 | 0.6695 | 0.9486 | 0.5034 | 0.9741 | 0.3550 | 0.6777 |
| **TG54.4\*** | 0.4370 | 0.7867 | 0.1303 | 0.7456 | 0.6463 | 0.9814 | 0.3462 | 0.9721 | 0.1486 | 0.7105 | 0.5962 | 0.9486 | 0.8656 | 0.9741 | 0.2030 | 0.6777 |
| **TG54.5\*** | 0.1257 | 0.6002 | 0.7802 | 0.9675 | 0.7924 | 0.9814 | 0.3752 | 0.9721 | 0.1533 | 0.7105 | 0.6371 | 0.9486 | 0.5692 | 0.9741 | 0.0332 | 0.5169 |
| **TG54.6\*** | 0.0872 | 0.6002 | 0.7579 | 0.9675 | 0.7834 | 0.9814 | 0.9130 | 0.9880 | 0.1738 | 0.7105 | 0.4221 | 0.9486 | 0.8499 | 0.9741 | 0.1381 | 0.6777 |
| **TG56.6\*** | 0.1639 | 0.6002 | 0.9487 | 0.9902 | 0.8114 | 0.9814 | 0.4250 | 0.9721 | 0.2903 | 0.7105 | 0.7792 | 0.9486 | 0.5015 | 0.9741 | 0.0432 | 0.5169 |

P a, p-value as estimated by unequal variances t-test; P b, p-value as estimated by unequal variances t-test adjusted for multiple testing according to the false discovery rate method. VLCD, very low-calorie diet; RYGB (1d), immediate effect of gastric bypass surgery; RYGB (6w), 6-week effect of gastric bypass surgery; Cum. Effect, cumulative effect of the intervention.

**Figure S8.** Evaluation of principal component scores using untargeted data.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **DIFF** | **LWR** | **UPR** | **P** |
| Baseline-VLCD | 5.80 | 1.37 | 10.22 | 0.0052 |
| RYGB (6w)-VLCD | 4.51 | 0.09 | 8.94 | 0.0439 |
| RYGB (1d)-VLCD | -3.54 | -7.96 | 0.89 | 0.1627 |
| RYGB (6w)-Baseline | -1.28 | -5.71 | 3.14 | 0.8708 |
| RYGB (1d)-Baseline | -9.33 | -13.76 | -4.91 | <0.0001 |
| RYGB (1d)- RYGB (6w) | -8.05 | -12.48 | -3.62 | 0.0001 |

Analysis Of Variance (ANOVA) models were fitted using scores along principal component 4 for principal component analysis using untargeted data, followed by post-hoc analysis testing using Tukey Honest Significant Differences. DIFF, the difference in the observed means; LWR, lower end point of the interval; UPR, upper end point; P, p-value after adjustment for the multiple comparisons; RYGB (1d), Roux-en-Y gastric bypass surgery after Day 1; RYGB (6w), 6-weeks after surgery; VLCD, very low-calorie diet.

**Table S9A.** Assessment of associations and correlation analyses between metabolites and clinical parameters.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Glucose** | | | **Insulin** | | | **GIP** | | | **GLP-1** | | | **HOMA-IR** | | | **HOMA-B** | | | **HbA1c** | | | **Matsuda** | | |
|  | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P |
|  | coef |  |  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  |
| 1-Methylhistidine | -0.124 | -0.035 | 0.606 | -0.107 | -0.048 | 0.606 | -0.231 | -0.117 | 0.606 | 0.045 | 0.051 | 0.671 | 0.008 | 0.021 | 1.000 | -0.012 | -0.008 | 1.000 | 0.111 | 0.022 | 0.606 | 0.092 | 0.038 | 0.606 |
| 3-Hydroxybutyrate | 0.178 | 0.068 | 0.345 | -0.129 | -0.070 | 0.616 | -0.328 | -0.176 | 0.099 | 0.191 | 0.152 | 0.345 | -0.152 | -0.106 | 0.567 | -0.046 | -0.043 | 0.907 | 0.087 | 0.023 | 0.616 | 0.018 | 0.005 | 1.000 |
| Arginine | -0.116 | -0.033 | 0.787 | -0.143 | -0.089 | 0.709 | -0.247 | -0.173 | 0.252 | 0.134 | 0.129 | 0.589 | 0.014 | 0.065 | 0.803 | -0.006 | -0.031 | 0.988 | 0.030 | 0.024 | 0.779 | 0.091 | 0.037 | 0.803 |
| Asparagine | -0.085 | -0.028 | 0.756 | -0.159 | -0.102 | 0.562 | -0.397 | -0.270 | 0.004 | 0.064 | 0.092 | 0.688 | -0.047 | -0.005 | 1.000 | -0.007 | -0.017 | 1.000 | 0.116 | 0.040 | 0.475 | 0.083 | 0.044 | 0.756 |
| Caffeine | 0.125 | 0.014 | 0.919 | 0.202 | 0.039 | 0.385 | 0.178 | 0.040 | 0.384 | -0.267 | -0.081 | 0.053 | 0.000 | -0.009 | 1.000 | 0.032 | 0.010 | 1.000 | 0.096 | 0.006 | 1.000 | 0.010 | 0.001 | 1.000 |
| Carnitine | 0.068 | 0.033 | 0.975 | -0.094 | -0.145 | 0.917 | -0.088 | -0.105 | 0.975 | 0.269 | 0.555 | 0.047 | 0.000 | -0.034 | 0.975 | -0.053 | -0.054 | 0.975 | 0.146 | 0.050 | 0.917 | -0.066 | -0.043 | 0.975 |
| Carnitine C10:0 | -0.006 | -0.003 | 1.000 | -0.405 | -0.212 | 0.004 | -0.004 | -0.001 | 1.000 | 0.008 | 0.004 | 1.000 | -0.094 | -0.073 | 0.671 | -0.224 | -0.166 | 0.133 | -0.121 | -0.025 | 0.480 | 0.342 | 0.148 | 0.013 |
| Carnitine C10:1 | -0.026 | -0.005 | 0.983 | -0.394 | -0.248 | 0.004 | -0.042 | -0.030 | 0.958 | 0.017 | 0.021 | 0.983 | -0.073 | -0.048 | 0.958 | -0.213 | -0.203 | 0.190 | -0.128 | -0.026 | 0.687 | 0.406 | 0.211 | 0.004 |
| Carnitine C10:2 | -0.023 | -0.025 | 0.957 | -0.108 | -0.110 | 0.927 | 0.093 | 0.079 | 0.957 | -0.087 | -0.058 | 0.957 | 0.068 | 0.089 | 0.957 | -0.016 | -0.007 | 1.000 | -0.066 | -0.030 | 0.957 | 0.139 | 0.131 | 0.535 |
| Carnitine C12:0 | 0.073 | 0.020 | 1.000 | -0.401 | -0.264 | 0.004 | 0.012 | -0.002 | 1.000 | -0.032 | 0.002 | 1.000 | -0.077 | -0.079 | 0.876 | -0.245 | -0.214 | 0.153 | 0.014 | -0.003 | 1.000 | 0.309 | 0.178 | 0.013 |
| Carnitine C12:1 | 0.051 | 0.014 | 0.919 | -0.390 | -0.229 | 0.006 | -0.081 | -0.054 | 0.869 | 0.021 | 0.045 | 0.919 | -0.058 | -0.043 | 0.919 | -0.178 | -0.140 | 0.361 | -0.030 | -0.010 | 0.919 | 0.353 | 0.179 | 0.006 |
| Carnitine C14:0 | 0.242 | 0.114 | 0.210 | -0.417 | -0.383 | 0.002 | -0.140 | -0.131 | 0.392 | -0.049 | 0.012 | 1.000 | -0.057 | -0.086 | 0.747 | -0.292 | -0.345 | 0.082 | 0.115 | 0.025 | 0.747 | 0.279 | 0.236 | 0.023 |
| Carnitine C14:1 | 0.075 | 0.020 | 0.923 | -0.482 | -0.302 | 0.000 | -0.161 | -0.098 | 0.492 | 0.054 | 0.069 | 0.738 | -0.100 | -0.097 | 0.655 | -0.274 | -0.229 | 0.082 | 0.011 | -0.004 | 1.000 | 0.348 | 0.190 | 0.006 |
| Carnitine C14:2 | 0.039 | 0.015 | 1.000 | -0.462 | -0.310 | 0.001 | -0.146 | -0.104 | 0.550 | 0.064 | 0.083 | 0.828 | -0.125 | -0.105 | 0.770 | -0.228 | -0.220 | 0.165 | -0.003 | 0.001 | 1.000 | 0.392 | 0.222 | 0.002 |
| Carnitine C16:0 | 0.338 | 0.212 | 0.020 | -0.367 | -0.412 | 0.010 | -0.194 | -0.165 | 0.570 | 0.060 | 0.065 | 0.953 | -0.057 | -0.135 | 0.723 | -0.326 | -0.491 | 0.022 | 0.047 | 0.004 | 1.000 | 0.177 | 0.169 | 0.349 |
| Carnitine C18:0 | 0.420 | 0.298 | 0.001 | -0.458 | -0.576 | 0.000 | -0.185 | -0.157 | 0.544 | 0.039 | 0.013 | 1.000 | -0.043 | -0.141 | 0.643 | -0.469 | -0.808 | 0.000 | 0.129 | 0.043 | 0.603 | 0.190 | 0.199 | 0.221 |
| Carnitine C18:1 | 0.208 | 0.106 | 0.281 | -0.401 | -0.389 | 0.003 | -0.222 | -0.165 | 0.298 | 0.090 | 0.092 | 0.662 | -0.088 | -0.161 | 0.496 | -0.322 | -0.416 | 0.038 | -0.020 | -0.021 | 0.690 | 0.234 | 0.192 | 0.118 |
| Carnitine C18:2 | 0.116 | 0.073 | 0.690 | -0.379 | -0.440 | 0.007 | -0.202 | -0.199 | 0.417 | 0.092 | 0.159 | 0.690 | -0.131 | -0.224 | 0.611 | -0.338 | -0.547 | 0.021 | -0.008 | -0.010 | 1.000 | 0.272 | 0.270 | 0.059 |
| Carnitine C2:0 | 0.064 | 0.022 | 0.941 | -0.269 | -0.209 | 0.145 | -0.285 | -0.197 | 0.155 | 0.256 | 0.279 | 0.141 | -0.134 | -0.152 | 0.400 | -0.101 | -0.090 | 0.733 | 0.056 | 0.007 | 0.943 | 0.159 | 0.111 | 0.319 |
| Carnitine C3:0 | 0.154 | 0.062 | 1.000 | 0.021 | -0.006 | 1.000 | 0.043 | 0.044 | 1.000 | 0.131 | 0.342 | 0.420 | 0.078 | 0.050 | 1.000 | -0.087 | -0.062 | 1.000 | 0.101 | -0.001 | 1.000 | -0.065 | 0.007 | 1.000 |
| Carnitine C5:0 | 0.058 | 0.003 | 1.000 | 0.011 | -0.004 | 1.000 | 0.048 | 0.034 | 1.000 | 0.090 | 0.158 | 1.000 | -0.063 | -0.103 | 1.000 | -0.054 | -0.017 | 1.000 | -0.026 | -0.030 | 1.000 | 0.011 | 0.041 | 1.000 |
| Carnitine C6:0 | 0.164 | 0.068 | 0.385 | -0.411 | -0.293 | 0.003 | -0.120 | -0.077 | 0.549 | 0.090 | 0.097 | 0.549 | -0.088 | -0.087 | 0.611 | -0.289 | -0.290 | 0.050 | -0.065 | -0.020 | 0.628 | 0.321 | 0.193 | 0.020 |
| Carnitine C8:0 | -0.003 | -0.004 | 0.998 | -0.419 | -0.231 | 0.004 | -0.034 | -0.021 | 0.894 | 0.021 | 0.026 | 0.894 | -0.103 | -0.081 | 0.628 | -0.250 | -0.192 | 0.099 | -0.107 | -0.025 | 0.557 | 0.370 | 0.172 | 0.004 |
| Carnitine C8:1 | 0.126 | 0.024 | 0.863 | 0.157 | 0.106 | 0.652 | 0.204 | 0.131 | 0.573 | -0.208 | -0.135 | 0.652 | 0.131 | 0.090 | 0.810 | 0.031 | 0.097 | 0.810 | 0.116 | 0.005 | 1.000 | -0.097 | -0.016 | 0.979 |
| Creatine | -0.020 | -0.010 | 1.000 | -0.028 | -0.015 | 1.000 | -0.255 | -0.131 | 0.142 | 0.105 | 0.099 | 0.462 | -0.028 | -0.016 | 1.000 | -0.019 | -0.006 | 1.000 | 0.214 | 0.039 | 0.223 | -0.117 | -0.041 | 0.821 |
| Glucosamine-6-phosphate | -0.068 | -0.021 | 0.963 | -0.040 | -0.019 | 1.000 | -0.159 | -0.080 | 0.878 | -0.003 | 0.014 | 1.000 | 0.049 | 0.041 | 1.000 | -0.008 | -0.002 | 1.000 | 0.102 | 0.019 | 0.906 | -0.032 | -0.010 | 1.000 |
| Glyceric acid | -0.031 | -0.024 | 0.985 | -0.038 | -0.039 | 0.985 | -0.008 | 0.008 | 1.000 | -0.214 | -0.247 | 0.328 | -0.093 | -0.140 | 0.700 | -0.009 | -0.002 | 1.000 | 0.130 | 0.034 | 0.700 | 0.206 | 0.149 | 0.328 |
| Hippuric acid | -0.036 | -0.019 | 0.721 | 0.104 | 0.040 | 0.698 | 0.099 | 0.047 | 0.698 | -0.112 | -0.078 | 0.660 | 0.108 | 0.040 | 0.724 | 0.074 | 0.056 | 0.698 | -0.041 | -0.013 | 0.698 | 0.092 | 0.041 | 0.698 |
| Histidine | -0.118 | -0.035 | 0.893 | -0.047 | -0.021 | 0.972 | -0.284 | -0.172 | 0.221 | 0.067 | 0.071 | 0.893 | 0.020 | 0.053 | 0.972 | 0.046 | 0.029 | 0.972 | 0.106 | 0.034 | 0.652 | 0.071 | 0.029 | 0.972 |
| Hypoxanthine | -0.028 | -0.007 | 0.995 | -0.191 | -0.075 | 0.238 | -0.265 | -0.107 | 0.124 | 0.202 | 0.134 | 0.124 | -0.100 | -0.043 | 0.693 | -0.039 | -0.019 | 0.995 | -0.206 | -0.031 | 0.207 | 0.103 | 0.039 | 0.536 |
| Kynurenine | 0.216 | 0.174 | 0.151 | 0.047 | 0.064 | 0.921 | 0.211 | 0.283 | 0.155 | -0.191 | -0.334 | 0.182 | -0.023 | -0.029 | 1.000 | -0.050 | -0.103 | 0.910 | -0.268 | -0.120 | 0.097 | -0.003 | -0.017 | 1.000 |
| Leucine-Isoleucine | 0.175 | 0.260 | 0.367 | -0.121 | -0.232 | 1.000 | -0.085 | -0.158 | 1.000 | 0.013 | 0.036 | 1.000 | 0.031 | 0.182 | 1.000 | -0.003 | -0.058 | 1.000 | -0.023 | 0.013 | 1.000 | 0.050 | 0.055 | 1.000 |
| LPC 14:0 | 0.127 | 0.063 | 0.517 | 0.139 | 0.109 | 0.517 | 0.250 | 0.141 | 0.383 | -0.256 | -0.201 | 0.374 | 0.182 | 0.226 | 0.374 | 0.039 | 0.034 | 1.000 | -0.018 | 0.003 | 1.000 | -0.106 | -0.064 | 0.726 |
| LPC 16:0 | 0.255 | 0.489 | 0.080 | -0.133 | -0.374 | 0.709 | -0.005 | -0.013 | 1.000 | -0.033 | -0.038 | 1.000 | 0.118 | 0.604 | 0.626 | -0.293 | -1.286 | 0.064 | 0.032 | 0.060 | 0.866 | 0.130 | 0.311 | 0.709 |
| LPC 20:4 | 0.156 | 0.091 | 0.595 | -0.057 | -0.045 | 0.929 | -0.150 | -0.146 | 0.595 | 0.057 | 0.102 | 0.929 | 0.008 | 0.043 | 0.929 | -0.160 | -0.214 | 0.595 | 0.001 | 0.008 | 0.938 | 0.056 | 0.042 | 0.929 |
| LPC 22:6 | 0.240 | 0.127 | 0.415 | -0.123 | -0.124 | 0.663 | -0.124 | -0.109 | 0.699 | 0.013 | 0.043 | 0.902 | 0.024 | 0.014 | 1.000 | -0.148 | -0.182 | 0.663 | 0.173 | 0.052 | 0.648 | 0.064 | 0.066 | 0.774 |
| LPE 16:0 | 0.123 | 0.078 | 0.682 | 0.068 | 0.073 | 0.874 | -0.191 | -0.204 | 0.682 | 0.098 | 0.148 | 0.682 | 0.142 | 0.199 | 0.682 | 0.044 | 0.115 | 0.868 | 0.152 | 0.052 | 0.682 | -0.007 | 0.009 | 1.000 |
| LPE 20:4 | 0.254 | 0.233 | 0.258 | 0.060 | 0.089 | 0.993 | 0.000 | 0.034 | 0.993 | 0.059 | 0.079 | 0.993 | 0.130 | 0.263 | 0.945 | -0.127 | -0.271 | 0.945 | -0.035 | -0.019 | 0.993 | -0.068 | -0.092 | 0.993 |
| LPE 20:5 | 0.191 | 0.095 | 0.376 | 0.147 | 0.122 | 0.376 | 0.343 | 0.231 | 0.185 | -0.203 | -0.166 | 0.376 | 0.127 | 0.171 | 0.376 | -0.026 | -0.030 | 0.902 | -0.045 | -0.009 | 0.902 | -0.204 | -0.130 | 0.376 |
| LPE 22:6 | 0.327 | 0.217 | 0.098 | 0.023 | 0.006 | 1.000 | -0.177 | -0.193 | 0.467 | 0.098 | 0.202 | 0.499 | 0.167 | 0.220 | 0.499 | -0.055 | -0.039 | 1.000 | 0.319 | 0.118 | 0.098 | -0.162 | -0.128 | 0.499 |
| Lysine | -0.015 | 0.006 | 1.000 | -0.076 | -0.043 | 1.000 | -0.291 | -0.203 | 0.176 | 0.030 | 0.053 | 1.000 | -0.020 | 0.028 | 1.000 | 0.000 | -0.015 | 1.000 | 0.138 | 0.049 | 0.348 | 0.000 | -0.009 | 1.000 |
| Methionine | 0.208 | 0.171 | 0.339 | -0.036 | -0.039 | 1.000 | -0.162 | -0.199 | 0.645 | 0.112 | 0.236 | 0.668 | 0.026 | 0.088 | 1.000 | -0.131 | -0.246 | 0.695 | 0.077 | 0.044 | 0.857 | -0.106 | -0.112 | 0.857 |
| Orotic acid | 0.114 | 0.022 | 0.874 | -0.122 | -0.069 | 0.745 | -0.105 | -0.061 | 0.745 | -0.057 | -0.021 | 0.968 | 0.156 | 0.084 | 0.745 | -0.116 | -0.063 | 0.864 | 0.283 | 0.042 | 0.607 | -0.068 | -0.013 | 0.968 |
| Paraxanthine | 0.030 | 0.009 | 1.000 | 0.169 | 0.053 | 0.463 | 0.235 | 0.065 | 0.309 | -0.316 | -0.128 | 0.028 | -0.013 | 0.002 | 1.000 | 0.077 | 0.026 | 1.000 | -0.032 | 0.000 | 1.000 | 0.002 | -0.004 | 1.000 |
| PC 36:4 | 0.235 | 0.176 | 0.733 | -0.010 | -0.073 | 1.000 | -0.088 | -0.190 | 0.733 | 0.026 | 0.262 | 0.733 | 0.078 | 0.056 | 1.000 | -0.222 | -0.453 | 0.733 | 0.221 | 0.080 | 0.733 | -0.084 | -0.008 | 1.000 |
| PC 38:6 | 0.297 | 0.153 | 0.172 | -0.223 | -0.306 | 0.104 | -0.243 | -0.255 | 0.172 | 0.026 | 0.115 | 0.679 | 0.091 | 0.022 | 0.983 | -0.218 | -0.275 | 0.318 | 0.395 | 0.122 | 0.086 | 0.085 | 0.156 | 0.318 |
| PC 40:7 | 0.370 | 0.260 | 0.072 | 0.007 | -0.046 | 0.866 | -0.036 | -0.086 | 0.789 | -0.067 | 0.055 | 0.866 | 0.218 | 0.322 | 0.345 | -0.310 | -0.555 | 0.115 | 0.286 | 0.089 | 0.322 | -0.158 | -0.082 | 0.789 |
| Phenylalanine | 0.165 | 0.143 | 0.729 | 0.036 | 0.062 | 0.879 | -0.030 | -0.079 | 0.879 | 0.055 | 0.209 | 0.871 | -0.046 | -0.017 | 1.000 | -0.034 | -0.060 | 0.890 | 0.026 | 0.020 | 0.879 | -0.167 | -0.177 | 0.777 |
| Proline | 0.088 | 0.124 | 0.719 | -0.097 | -0.160 | 0.719 | 0.200 | 0.338 | 0.719 | -0.097 | -0.220 | 0.719 | 0.110 | 0.359 | 0.719 | -0.012 | -0.063 | 0.910 | -0.078 | -0.034 | 0.744 | 0.098 | 0.128 | 0.719 |
| Serine | -0.002 | 0.012 | 0.995 | -0.233 | -0.256 | 0.334 | -0.162 | -0.156 | 0.520 | -0.011 | -0.054 | 0.953 | -0.036 | -0.039 | 0.983 | -0.255 | -0.438 | 0.216 | -0.075 | -0.021 | 0.951 | 0.056 | 0.033 | 0.953 |
| SM 33:1 | 0.070 | 0.045 | 0.877 | -0.349 | -0.375 | 0.042 | -0.185 | -0.195 | 0.520 | 0.054 | 0.118 | 0.877 | -0.062 | -0.074 | 0.877 | -0.164 | -0.253 | 0.563 | -0.019 | -0.006 | 1.000 | 0.270 | 0.248 | 0.112 |
| SM 34:1 | 0.028 | 0.010 | 1.000 | -0.269 | -0.203 | 0.486 | -0.010 | -0.006 | 1.000 | 0.058 | 0.072 | 0.927 | -0.014 | -0.015 | 1.000 | -0.104 | -0.107 | 0.927 | -0.109 | -0.033 | 0.927 | 0.169 | 0.110 | 0.841 |
| SM 34:2 | 0.081 | 0.043 | 0.793 | -0.361 | -0.441 | 0.026 | 0.063 | 0.094 | 0.793 | 0.046 | 0.099 | 0.793 | -0.059 | -0.127 | 0.793 | -0.237 | -0.381 | 0.263 | -0.145 | -0.080 | 0.340 | 0.219 | 0.236 | 0.217 |
| SM 35:2 | 0.095 | 0.062 | 0.886 | -0.234 | -0.377 | 0.317 | -0.071 | -0.094 | 0.886 | 0.036 | 0.106 | 0.886 | 0.016 | -0.020 | 1.000 | -0.137 | -0.256 | 0.714 | -0.120 | -0.096 | 0.439 | 0.139 | 0.209 | 0.441 |
| SM 36:2 | 0.156 | 0.055 | 0.895 | -0.297 | -0.283 | 0.116 | -0.038 | -0.021 | 1.000 | 0.068 | 0.117 | 0.895 | 0.043 | -0.006 | 1.000 | -0.209 | -0.221 | 0.781 | 0.077 | 0.000 | 1.000 | 0.077 | 0.091 | 0.895 |
| Transcinnamic acid | 0.132 | 0.142 | 0.778 | 0.014 | 0.046 | 0.953 | -0.010 | -0.064 | 0.953 | 0.080 | 0.276 | 0.799 | -0.089 | -0.072 | 0.953 | -0.048 | -0.114 | 0.953 | 0.006 | 0.023 | 0.953 | -0.163 | -0.205 | 0.778 |
| Valine | -0.074 | -0.092 | 0.679 | -0.145 | -0.239 | 0.679 | -0.047 | -0.177 | 0.679 | -0.071 | -0.015 | 1.000 | -0.103 | -0.212 | 0.679 | -0.301 | -0.673 | 0.094 | -0.022 | -0.025 | 0.884 | 0.071 | 0.132 | 0.679 |

Associations between metabolites and clinical parameters were assessed by linear models using empirical Bayes statistics for differential expression. Only metabolites that were shown to be significantly different between two occasions (as described in detail in Fig. 2) are included in the table; clinical parameters were pooled between occasions and determined at time = 0 min. Models were adjusted for age and body mass index (BMI). Corr.coef., Pearson correlation coefficient as estimated for pairwise complete observations; FC, standardised regression coefficient representing the log-fold-change (standardised beta), P, p-value as estimated by unequal variances t-test adjusted for multiple testing according to the false discovery rate method.

**Table S9B.** Assessment of associations and correlation analyses between lipids and clinical parameters.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Glucose** | | | **Insulin** | | | **GIP** | | | **GLP-1** | | | **HOMA-IR** | | | **HOMA-B** | | | **HbA1c** | | | **Matsuda** | | |
|  | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P | corr. | FC | P |
|  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  | coef. |  |  |
| CE18.3 | 0.157 | 0.058 | 0.376 | 0.035 | 0.033 | 0.914 | 0.182 | 0.094 | 0.376 | 0.006 | -0.006 | 1.000 | -0.266 | -0.140 | 0.376 | 0.201 | 0.120 | 0.376 | -0.054 | 0.007 | 0.947 | -0.041 | -0.044 | 0.721 |
| LPC18.0 | 0.134 | 0.048 | 0.802 | 0.121 | 0.076 | 0.898 | 0.144 | 0.109 | 0.802 | -0.179 | -0.160 | 0.802 | 0.225 | 0.190 | 0.802 | -0.055 | -0.040 | 0.922 | -0.005 | -0.011 | 0.922 | 0.014 | 0.015 | 0.922 |
| LPC20.4 | -0.061 | -0.021 | 1.000 | -0.011 | -0.013 | 1.000 | -0.050 | -0.019 | 1.000 | 0.074 | 0.043 | 1.000 | 0.127 | 0.053 | 1.000 | -0.158 | -0.086 | 1.000 | 0.009 | -0.008 | 1.000 | -0.010 | 0.005 | 1.000 |
| PC32.0 | 0.089 | 0.037 | 0.990 | 0.046 | 0.024 | 0.990 | 0.026 | 0.048 | 0.990 | -0.137 | -0.216 | 0.662 | 0.208 | 0.273 | 0.662 | -0.110 | -0.140 | 0.990 | -0.110 | -0.103 | 0.353 | -0.080 | -0.041 | 0.990 |
| PC32.1 | 0.252 | 0.067 | 0.111 | 0.242 | 0.124 | 0.111 | 0.261 | 0.117 | 0.118 | -0.119 | -0.056 | 0.547 | 0.204 | 0.167 | 0.111 | 0.150 | 0.095 | 0.398 | -0.138 | -0.018 | 0.502 | -0.252 | -0.106 | 0.111 |
| PC32.2 | 0.189 | 0.028 | 0.269 | 0.212 | 0.057 | 0.269 | 0.230 | 0.056 | 0.269 | -0.110 | -0.034 | 0.867 | 0.176 | 0.072 | 0.269 | 0.078 | 0.022 | 0.867 | 0.029 | 0.006 | 0.867 | -0.058 | -0.016 | 0.867 |
| PC34.2 | 0.031 | 0.105 | 0.680 | 0.023 | 0.092 | 0.808 | 0.215 | 0.501 | 0.212 | -0.072 | -0.314 | 0.597 | 0.051 | 0.321 | 0.597 | -0.125 | -0.489 | 0.422 | -0.005 | 0.058 | 0.720 | 0.033 | -0.049 | 0.878 |
| PC34.3 | 0.136 | 0.033 | 0.434 | 0.238 | 0.103 | 0.338 | 0.242 | 0.102 | 0.338 | -0.166 | -0.086 | 0.426 | 0.145 | 0.094 | 0.426 | 0.150 | 0.085 | 0.434 | -0.075 | -0.009 | 0.732 | -0.129 | -0.048 | 0.434 |
| PC36.1 | 0.342 | 0.090 | 0.091 | 0.108 | 0.054 | 0.700 | 0.211 | 0.115 | 0.247 | -0.434 | -0.281 | 0.014 | 0.252 | 0.176 | 0.198 | -0.063 | -0.012 | 1.000 | 0.087 | -0.002 | 1.000 | -0.129 | -0.033 | 0.819 |
| PC36.2 | 0.210 | 0.114 | 0.236 | 0.059 | 0.053 | 0.970 | 0.230 | 0.236 | 0.206 | -0.340 | -0.427 | 0.023 | 0.178 | 0.228 | 0.373 | -0.066 | -0.084 | 0.970 | -0.029 | -0.016 | 0.970 | 0.019 | 0.014 | 1.000 |
| PC36.3 | 0.181 | 0.156 | 0.239 | 0.175 | 0.268 | 0.255 | 0.333 | 0.483 | 0.064 | -0.193 | -0.356 | 0.239 | 0.222 | 0.509 | 0.093 | 0.095 | 0.163 | 0.745 | -0.103 | -0.036 | 0.745 | -0.094 | -0.141 | 0.534 |
| PC36.4 | 0.107 | 0.078 | 0.881 | 0.110 | 0.189 | 0.881 | 0.023 | 0.069 | 1.000 | 0.012 | 0.094 | 1.000 | 0.116 | 0.142 | 0.961 | -0.206 | -0.546 | 0.724 | 0.192 | 0.081 | 0.881 | -0.186 | -0.250 | 0.881 |
| PC38.3 | 0.279 | 0.106 | 0.088 | 0.251 | 0.190 | 0.092 | 0.267 | 0.183 | 0.092 | -0.183 | -0.137 | 0.432 | 0.250 | 0.275 | 0.088 | 0.120 | 0.128 | 0.543 | -0.038 | -0.009 | 0.980 | -0.159 | -0.094 | 0.430 |
| PC38.4 | 0.235 | 0.145 | 0.390 | 0.219 | 0.331 | 0.390 | 0.128 | 0.217 | 0.451 | -0.080 | -0.038 | 1.000 | 0.233 | 0.337 | 0.390 | -0.249 | -0.467 | 0.390 | 0.148 | -0.003 | 1.000 | -0.239 | -0.215 | 0.390 |
| PC38.6 | 0.104 | 0.029 | 1.000 | -0.029 | -0.141 | 0.963 | -0.124 | -0.174 | 0.963 | -0.001 | 0.028 | 1.000 | 0.154 | 0.055 | 1.000 | -0.234 | -0.382 | 0.498 | 0.322 | 0.090 | 0.498 | -0.062 | 0.032 | 1.000 |
| PC40.6 | 0.268 | 0.104 | 0.355 | 0.081 | 0.029 | 1.000 | -0.005 | -0.013 | 1.000 | -0.129 | -0.099 | 0.903 | 0.251 | 0.191 | 0.498 | -0.233 | -0.243 | 0.369 | 0.363 | 0.072 | 0.355 | -0.154 | -0.039 | 1.000 |
| SM33.1 | 0.047 | 0.025 | 0.888 | -0.231 | -0.224 | 0.256 | -0.066 | -0.053 | 0.888 | -0.139 | -0.176 | 0.465 | 0.034 | 0.027 | 0.945 | -0.219 | -0.280 | 0.271 | -0.031 | -0.016 | 0.888 | 0.218 | 0.165 | 0.271 |
| SM34.1 | -0.012 | 0.018 | 0.949 | -0.385 | -0.572 | 0.009 | 0.115 | 0.205 | 0.386 | -0.134 | -0.325 | 0.243 | 0.032 | 0.100 | 0.796 | -0.257 | -0.573 | 0.067 | -0.227 | -0.108 | 0.201 | 0.218 | 0.226 | 0.240 |
| SM34.2 | -0.002 | -0.016 | 0.918 | -0.240 | -0.215 | 0.290 | 0.065 | 0.053 | 0.897 | -0.078 | -0.062 | 0.897 | 0.040 | 0.015 | 0.988 | -0.235 | -0.250 | 0.301 | -0.062 | -0.035 | 0.642 | 0.146 | 0.116 | 0.395 |
| SM35.1 | -0.086 | -0.015 | 0.798 | -0.149 | -0.067 | 0.367 | -0.085 | -0.018 | 0.952 | -0.109 | -0.079 | 0.367 | -0.150 | -0.105 | 0.262 | -0.040 | -0.019 | 0.953 | 0.019 | -0.003 | 0.977 | 0.140 | 0.045 | 0.442 |
| SM36.0 | -0.115 | -0.028 | 1.000 | -0.060 | -0.026 | 1.000 | -0.122 | -0.048 | 1.000 | 0.043 | 0.025 | 1.000 | -0.010 | -0.013 | 1.000 | -0.088 | -0.042 | 1.000 | 0.036 | 0.002 | 1.000 | 0.016 | 0.009 | 1.000 |
| SM36.1 | -0.079 | -0.042 | 0.844 | -0.238 | -0.221 | 0.265 | 0.020 | 0.026 | 0.959 | 0.057 | 0.056 | 0.865 | 0.055 | 0.036 | 0.959 | -0.146 | -0.166 | 0.633 | -0.134 | -0.054 | 0.480 | 0.041 | 0.037 | 0.865 |
| SM36.2 | -0.124 | -0.058 | 0.471 | -0.373 | -0.364 | 0.009 | 0.086 | 0.113 | 0.471 | -0.010 | -0.062 | 0.793 | 0.017 | -0.033 | 0.927 | -0.195 | -0.241 | 0.275 | -0.075 | -0.039 | 0.471 | 0.151 | 0.114 | 0.402 |
| SM40.1 | 0.256 | 0.164 | 0.221 | 0.109 | 0.135 | 0.604 | 0.224 | 0.237 | 0.294 | -0.182 | -0.246 | 0.346 | 0.086 | 0.202 | 0.541 | -0.024 | -0.062 | 0.811 | 0.002 | 0.019 | 0.788 | -0.028 | -0.054 | 0.788 |
| SM41.1 | 0.165 | 0.071 | 0.490 | 0.088 | 0.071 | 0.928 | 0.198 | 0.142 | 0.490 | -0.158 | -0.144 | 0.490 | 0.009 | 0.041 | 1.000 | 0.011 | -0.002 | 1.000 | -0.037 | -0.001 | 1.000 | 0.032 | 0.005 | 1.000 |
| SM42.2 | -0.020 | -0.005 | 1.000 | -0.149 | -0.298 | 0.436 | 0.037 | 0.133 | 0.786 | -0.015 | -0.140 | 0.786 | 0.114 | 0.168 | 0.786 | -0.126 | -0.288 | 0.572 | -0.109 | -0.096 | 0.436 | 0.119 | 0.167 | 0.572 |
| SM42.3 | -0.195 | -0.099 | 0.266 | -0.352 | -0.332 | 0.017 | -0.087 | -0.054 | 0.712 | 0.116 | 0.099 | 0.585 | 0.029 | -0.030 | 0.894 | -0.191 | -0.210 | 0.279 | -0.087 | -0.048 | 0.304 | 0.243 | 0.185 | 0.147 |
| SM43.2 | 0.033 | 0.010 | 0.785 | -0.169 | -0.061 | 0.541 | -0.119 | -0.037 | 0.633 | 0.079 | 0.024 | 0.785 | 0.126 | 0.059 | 0.541 | -0.135 | -0.068 | 0.541 | 0.126 | 0.016 | 0.541 | 0.177 | 0.047 | 0.541 |
| TG48.1 | 0.374 | 0.068 | 0.021 | 0.357 | 0.129 | 0.021 | 0.312 | 0.108 | 0.044 | -0.322 | -0.127 | 0.046 | 0.260 | 0.121 | 0.077 | 0.032 | 0.028 | 0.884 | 0.122 | 0.011 | 0.741 | -0.297 | -0.078 | 0.060 |
| TG48.2 | 0.281 | 0.052 | 0.089 | 0.352 | 0.137 | 0.029 | 0.318 | 0.120 | 0.043 | -0.229 | -0.091 | 0.233 | 0.315 | 0.162 | 0.042 | 0.046 | 0.040 | 0.665 | 0.083 | 0.005 | 0.841 | -0.272 | -0.077 | 0.089 |
| TG50.0 | 0.355 | 0.060 | 0.025 | 0.433 | 0.149 | 0.003 | 0.264 | 0.089 | 0.086 | -0.159 | -0.050 | 0.575 | 0.303 | 0.131 | 0.042 | 0.033 | 0.033 | 0.786 | 0.251 | 0.024 | 0.194 | -0.420 | -0.108 | 0.004 |
| TG50.1 | 0.355 | 0.177 | 0.029 | 0.391 | 0.404 | 0.012 | 0.283 | 0.290 | 0.059 | -0.191 | -0.189 | 0.438 | 0.246 | 0.303 | 0.169 | -0.012 | 0.038 | 0.939 | 0.155 | 0.032 | 0.753 | -0.383 | -0.288 | 0.013 |
| TG50.4 | 0.201 | 0.029 | 0.319 | 0.318 | 0.097 | 0.033 | 0.303 | 0.084 | 0.064 | -0.208 | -0.061 | 0.334 | 0.267 | 0.117 | 0.048 | 0.066 | 0.031 | 0.790 | -0.036 | -0.004 | 1.000 | -0.243 | -0.056 | 0.125 |
| TG52.2 | 0.089 | 0.048 | 0.878 | 0.098 | 0.132 | 0.766 | 0.133 | 0.295 | 0.434 | -0.037 | -0.063 | 0.953 | 0.310 | 0.654 | 0.258 | -0.165 | -0.344 | 0.536 | 0.277 | 0.126 | 0.351 | -0.194 | -0.240 | 0.434 |
| TG52.3 | 0.047 | 0.010 | 1.000 | 0.103 | 0.135 | 0.748 | 0.106 | 0.201 | 0.674 | -0.029 | -0.041 | 1.000 | 0.239 | 0.443 | 0.619 | -0.150 | -0.283 | 0.674 | 0.233 | 0.096 | 0.619 | -0.155 | -0.169 | 0.674 |
| TG54.3 | -0.069 | -0.088 | 0.452 | -0.096 | -0.194 | 0.437 | 0.231 | 0.374 | 0.194 | -0.137 | -0.255 | 0.437 | 0.207 | 0.250 | 0.437 | -0.142 | -0.205 | 0.487 | -0.067 | -0.095 | 0.371 | -0.035 | 0.013 | 1.000 |
| TG54.4 | -0.041 | -0.049 | 0.869 | -0.031 | -0.067 | 0.895 | 0.234 | 0.323 | 0.447 | -0.162 | -0.259 | 0.505 | 0.184 | 0.253 | 0.505 | -0.157 | -0.244 | 0.505 | -0.061 | -0.059 | 0.505 | -0.040 | -0.014 | 0.989 |
| TG56.6 | 0.131 | 0.027 | 1.000 | 0.045 | 0.017 | 1.000 | 0.039 | 0.017 | 1.000 | -0.070 | -0.008 | 1.000 | 0.237 | 0.214 | 1.000 | -0.156 | -0.131 | 1.000 | 0.157 | 0.016 | 1.000 | -0.183 | -0.082 | 1.000 |

Associations between metabolites and clinical parameters were assessed by linear models using empirical Bayes statistics for differential expression. Only metabolites that were shown to be significantly different between two occasions (as described in detail in Fig. 2) are included in the table; clinical parameters were pooled between occasions and determined at time = 0 min. Models were adjusted for age and body mass index (BMI). Corr.coef., Pearson correlation coefficient as estimated for pairwise complete observations; FC, standardised regression coefficient representing the log-fold-change (standardised beta), P, p-value as estimated by unequal variances t-test adjusted for multiple testing according to the false discovery rate method.

**Table 10A.** Linear-mixed-effect models fitted to metabolomics data between study occasions (mixed-meal test).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 1**  **(adjusted for age)** | | | | **Model 2**  **(adj. for age and weight loss)** | | | | **Model 3**  **(adj. for age and insulin)** | | | | **Direction (Mean, SD)** | | | |
|  | Effect VLCD | RYGB (1d) | RYGB (6w) | Cum.  effect | Effect VLCD | RYGB (1d) | RYGB (6w) | Cum.  effect | Effect VLCD | RYGB (1d) | RYGB (6w) | Cum.  effect | Effect  of VLCD | RYGB  (1d) | RYGB (6w) | Cum. effect |
| **1-Methyl-adenosine** | 0.607 | 0.995 | 0.876 | 0.986 | 0.768 | 0.993 | 0.899 | 0.988 | 0.605 | 0.999 | 0.960 | 0.952 | -19.35 ± 41.64 | 14.84 ± 47.47 | 11.7 ± 30.75 | -4.96 ± 32.08 |
| **1-Methyl-histidine** | 0.349 | 0.089 | 0.308 | 1.000 | 0.726 | 0.422 | 0.315 | 1.000 | 0.353 | 0.113 | 0.395 | 1.000 | 21.92 ± 125.05 | -28.14 ± 139.81 | -20.7 ± 130.64 | -0.73 ± 23.49 |
| **2-Hydroxy-cinnamic acid** | 0.028 | 0.953 | 0.138 | 0.960 | 0.092 | 1.000 | 0.201 | 0.882 | 0.029 | 1.000 | 0.029 | 1.000 | -14.74 ± 33.92 | 1.58 ± 34.74 | 26.08 ± 27.31 | 7.31 ± 33.53 |
| **3-Hydroxy-butyrate** | 0.394 | 0.455 | 1.000 | 0.288 | 0.086 | 1.000 | 0.972 | 0.066 | 0.414 | 0.600 | 1.000 | 0.519 | -44.88 ± 68.61 | -0.22 ± 101.16 | 15.68 ± 64.9 | -32.66 ± 30.22 |
| **5-Oxoproline** | 0.999 | 0.058 | 0.761 | 0.876 | 1.000 | 0.500 | 0.714 | 0.860 | 0.999 | 0.079 | 0.837 | 0.927 | 2.43 ± 67.23 | -19.68 ± 91.71 | -15.79 ± 65.55 | -13.26 ± 39.63 |
| **Acetylalanine** | 0.874 | 0.966 | 0.946 | 0.999 | 0.281 | 0.896 | 0.997 | 0.508 | 0.880 | 0.995 | 0.820 | 1.000 | -30.57 ± 101.31 | 16.16 ± 111.51 | 37.48 ± 88.79 | -2.25 ± 57.33 |
| **Alanine** | 0.866 | 0.042 | 0.744 | 0.999 | 0.953 | 0.258 | 0.759 | 1.000 | 0.862 | 0.079 | 0.908 | 1.000 | 10.84 ± 104.26 | -35.62 ± 139.83 | -7.82 ± 116.05 | -1.13 ± 47.32 |
| **Arginine** | 0.170 | 0.065 | 0.260 | 0.999 | 0.607 | 0.422 | 0.256 | 1.000 | 0.175 | 0.078 | 0.317 | 1.000 | 23.48 ± 107.48 | -27.43 ± 107.94 | -16.87 ± 106.75 | 1.39 ± 36.42 |
| **Asparagine** | 0.514 | 0.052 | 0.446 | 1.000 | 0.826 | 0.329 | 0.455 | 1.000 | 0.512 | 0.083 | 0.623 | 1.000 | 21.14 ± 102.77 | -35.26 ± 112.69 | -15.41 ± 107.22 | 2.62 ± 29.06 |
| **Aspartic acid** | 0.772 | 0.863 | 0.565 | 0.996 | 0.549 | 0.629 | 0.702 | 0.979 | 0.779 | 0.734 | 0.361 | 0.936 | -38.57 ± 183.21 | 23.47 ± 156.18 | 24.75 ± 164.55 | -18.44 ± 102.77 |
| **Caffeine** | 0.878 | 0.001 | 0.654 | 0.992 | 0.952 | 0.042 | 0.681 | 1.000 | 0.879 | 0.002 | 0.789 | 0.999 | -14.07 ± 56.08 | 105.53 ± 105.03 | 43.27 ± 112.89 | 29.46 ± 115.39 |
| **Carnitine** | 0.825 | 0.427 | 0.972 | 0.990 | 0.982 | 0.844 | 0.963 | 1.000 | 0.825 | 0.505 | 0.991 | 0.978 | -2.29 ± 17.97 | 5.85 ± 19.06 | 0.3 ± 14.11 | -1.84 ± 16.37 |
| **Carnitine C10:0** | 0.000 | 0.004 | 0.983 | 0.002 | 0.017 | 0.073 | 0.988 | 0.086 | 0.000 | 0.001 | 0.712 | 0.028 | -40.01 ± 75.48 | 60.16 ± 47.93 | -7.98 ± 51.1 | -52.78 ± 56.51 |
| **Carnitine C10:1** | 0.000 | 0.000 | 0.766 | 0.001 | 0.003 | 0.016 | 0.818 | 0.056 | 0.000 | 0.000 | 0.448 | 0.016 | -38.34 ± 64.25 | 55.09 ± 38.02 | -0.69 ± 44.2 | -42.25 ± 42.85 |
| **Carnitine C10:2** | 0.005 | 0.366 | 0.998 | 0.002 | 0.109 | 0.720 | 0.999 | 0.129 | 0.004 | 0.185 | 0.996 | 0.022 | -24.98 ± 47.79 | 27.15 ± 35.91 | -5.83 ± 34.57 | -32.42 ± 39.57 |
| **Carnitine C12:0** | 0.001 | 0.092 | 0.972 | 0.006 | 0.048 | 0.401 | 0.973 | 0.203 | 0.001 | 0.037 | 0.723 | 0.078 | -35.79 ± 71.84 | 44.59 ± 50.52 | -1.56 ± 41.57 | -45.17 ± 46.96 |
| **Carnitine C12:1** | 0.000 | 0.017 | 0.874 | 0.001 | 0.009 | 0.186 | 0.884 | 0.102 | 0.000 | 0.006 | 0.572 | 0.018 | -44.4 ± 66.2 | 45.32 ± 56.23 | 1.16 ± 45.27 | -47.39 ± 48.51 |
| **Carnitine C14:0** | 0.003 | 0.858 | 0.880 | 0.047 | 0.064 | 0.932 | 0.897 | 0.332 | 0.002 | 0.612 | 0.517 | 0.253 | -29.44 ± 53 | 20.4 ± 46.87 | 7.86 ± 32.83 | -26.85 ± 41.62 |
| **Carnitine C14:1** | 0.000 | 0.072 | 0.985 | 0.003 | 0.025 | 0.297 | 0.989 | 0.110 | 0.001 | 0.033 | 0.813 | 0.035 | -36.3 ± 57.51 | 40.59 ± 48.82 | -0.33 ± 33.92 | -42.14 ± 40.97 |
| **Carnitine C14:2** | 0.000 | 0.020 | 0.770 | 0.008 | 0.006 | 0.082 | 0.852 | 0.085 | 0.000 | 0.010 | 0.495 | 0.075 | -37.7 ± 59.04 | 45.69 ± 51.84 | -0.72 ± 39.13 | -42.46 ± 37.06 |
| **Carnitine C16:0** | 0.004 | 1.000 | 0.645 | 0.143 | 0.092 | 1.000 | 0.652 | 0.592 | 0.004 | 0.997 | 0.367 | 0.423 | -24.53 ± 45.45 | 6.47 ± 44.58 | 12.74 ± 33.24 | -16.64 ± 35.61 |
| **Carnitine C18:0** | 0.005 | 0.981 | 0.908 | 0.059 | 0.195 | 1.000 | 0.877 | 0.627 | 0.004 | 0.870 | 0.597 | 0.271 | -22 ± 41.03 | 7.65 ± 40.51 | 5.78 ± 35.61 | -21.14 ± 32.27 |
| **Carnitine C18:1** | 0.001 | 0.973 | 0.589 | 0.090 | 0.023 | 0.947 | 0.660 | 0.303 | 0.001 | 0.843 | 0.264 | 0.365 | -27.26 ± 46.39 | 11.35 ± 41.58 | 12.24 ± 34.09 | -20.26 ± 38.31 |
| **Carnitine C18:2** | 0.001 | 0.997 | 0.273 | 0.265 | 0.059 | 1.000 | 0.284 | 0.730 | 0.001 | 0.945 | 0.106 | 0.687 | -25.2 ± 41.31 | 5.33 ± 38.82 | 13.73 ± 38.34 | -14.98 ± 35.06 |
| **Carnitine C2:0** | 0.223 | 0.491 | 0.979 | 0.509 | 0.311 | 0.951 | 0.993 | 0.574 | 0.228 | 0.653 | 0.897 | 0.776 | 8.13 ± 22.92 | 11.48 ± 33.85 | -0.56 ± 18.36 | 7.46 ± 16.32 |
| **Carnitine C3:0** | 0.000 | 0.033 | 0.024 | 0.592 | 0.006 | 0.108 | 0.038 | 0.650 | 0.000 | 0.013 | 0.007 | 0.911 | -19.36 ± 24.05 | 20.26 ± 22.47 | 16.18 ± 22.94 | -0.42 ± 23.53 |
| **Carnitine C4:0** | 0.001 | 0.502 | 0.412 | 0.169 | 0.038 | 0.719 | 0.449 | 0.517 | 0.001 | 0.432 | 0.331 | 0.326 | -25.56 ± 46.31 | 30.93 ± 41.84 | 13.2 ± 33.68 | -11.57 ± 40.18 |
| **Carnitine C5:0** | 0.120 | 0.998 | 0.183 | 0.999 | 0.165 | 0.995 | 0.262 | 0.938 | 0.122 | 1.000 | 0.105 | 1.000 | -21.55 ± 45.04 | 3.87 ± 42.31 | 33.7 ± 39.02 | 5.56 ± 40.87 |
| **Carnitine C6:0** | 0.000 | 0.000 | 0.342 | 0.017 | 0.005 | 0.023 | 0.388 | 0.219 | 0.000 | 0.000 | 0.135 | 0.147 | -37.11 ± 52.88 | 49.23 ± 40.96 | 13.21 ± 35.9 | -25.73 ± 43.14 |
| **Carnitine C8:0** | 0.000 | 0.001 | 0.880 | 0.002 | 0.008 | 0.038 | 0.900 | 0.090 | 0.000 | 0.000 | 0.532 | 0.027 | -36.81 ± 71.1 | 54.41 ± 41.75 | -2.77 ± 50.55 | -41.11 ± 49.67 |
| **Carnitine C8:1** | 0.004 | 0.681 | 0.646 | 0.159 | 0.134 | 0.942 | 0.628 | 0.704 | 0.004 | 0.544 | 0.454 | 0.380 | -27.95 ± 33.17 | 16.94 ± 41.45 | 15.59 ± 31.56 | -12.32 ± 36.22 |
| **Citric acid** | 0.448 | 1.000 | 0.664 | 0.996 | 0.383 | 0.964 | 0.777 | 0.891 | 0.456 | 0.985 | 0.287 | 0.994 | -45.66 ± 134.59 | 14.58 ± 146.88 | 59.28 ± 121.84 | -0.66 ± 90.57 |
| **Creatine** | 0.570 | 0.068 | 0.909 | 0.964 | 0.834 | 0.345 | 0.914 | 0.994 | 0.568 | 0.102 | 0.966 | 0.931 | 17.44 ± 109.46 | -28.98 ± 124.9 | -1.53 ± 116.34 | 18.89 ± 41.92 |
| **Cystine** | 0.163 | 0.009 | 0.128 | 1.000 | 0.402 | 0.096 | 0.153 | 1.000 | 0.166 | 0.016 | 0.211 | 1.000 | 34.36 ± 115.57 | -46.51 ± 142.08 | -35.62 ± 119.98 | -6.39 ± 38.52 |
| **Dihydroorotic acid** | 0.998 | 0.626 | 0.884 | 0.968 | 1.000 | 0.965 | 0.847 | 0.933 | 0.998 | 0.612 | 0.866 | 0.956 | 2.66 ± 155.46 | -4.22 ± 114.71 | 18.07 ± 115.33 | 17.91 ± 103.63 |
| **Gluconic acid** | 0.742 | 0.339 | 0.536 | 0.997 | 0.875 | 0.615 | 0.568 | 1.000 | 0.735 | 0.480 | 0.774 | 1.000 | 16.37 ± 82.11 | -19.68 ± 107.26 | -9.77 ± 96.08 | 5.19 ± 43.7 |
| **Glucosamine-6-phosphate** | 0.146 | 0.041 | 0.284 | 0.996 | 0.658 | 0.424 | 0.258 | 1.000 | 0.147 | 0.070 | 0.457 | 0.977 | 33.36 ± 160.6 | -24.57 ± 179.32 | -25.35 ± 167.4 | 11.26 ± 57.24 |
| **Glutamic acid** | 0.992 | 0.306 | 0.792 | 0.955 | 0.998 | 0.651 | 0.800 | 0.990 | 0.992 | 0.407 | 0.913 | 0.992 | -4.19 ± 113.03 | -28.91 ± 140.47 | -6.45 ± 114.07 | -6.72 ± 68.42 |
| **Glutamine** | 0.420 | 0.026 | 0.321 | 1.000 | 0.764 | 0.240 | 0.332 | 1.000 | 0.419 | 0.042 | 0.467 | 1.000 | 25.72 ± 128.32 | -42.4 ± 144.49 | -27.77 ± 134.23 | -4.55 ± 26.09 |
| **Glyceric acid** | 0.852 | 1.000 | 0.896 | 1.000 | 0.312 | 0.760 | 0.983 | 0.618 | 0.858 | 1.000 | 0.836 | 1.000 | -29.74 ± 76.2 | 26.72 ± 99.97 | 32.43 ± 70.33 | -3.27 ± 50.81 |
| **Hippuric acid** | 0.583 | 0.959 | 0.997 | 0.773 | 0.893 | 0.997 | 0.996 | 0.976 | 0.586 | 0.976 | 1.000 | 0.744 | -10.98 ± 53.46 | 18.4 ± 59.35 | 7.44 ± 51.27 | -10.03 ± 37.91 |
| **Histidine** | 0.138 | 0.038 | 0.317 | 0.989 | 0.488 | 0.280 | 0.327 | 0.999 | 0.140 | 0.049 | 0.392 | 0.989 | 31.92 ± 119.7 | -35.08 ± 126.67 | -21.01 ± 118.99 | 7.17 ± 25.96 |
| **Hydroxyproline** | 0.181 | 0.806 | 0.951 | 0.532 | 0.460 | 0.960 | 0.960 | 0.810 | 0.180 | 0.939 | 0.763 | 0.860 | -41.13 ± 104.67 | -15.43 ± 100.15 | 2.36 ± 84.16 | -29.29 ± 82.12 |
| **Hypoxanthine** | 0.381 | 0.849 | 0.471 | 1.000 | 0.262 | 1.000 | 0.623 | 0.870 | 0.385 | 0.945 | 0.307 | 0.999 | -18.36 ± 99.47 | -23.71 ± 66.81 | 10.94 ± 138.99 | -3.34 ± 118.6 |
| **Indole** | 0.132 | 0.988 | 0.590 | 0.866 | 0.452 | 0.996 | 0.604 | 0.973 | 0.127 | 1.000 | 0.279 | 0.998 | -16.27 ± 41.16 | 5.43 ± 44.61 | 17.45 ± 37.22 | 0.7 ± 38.66 |
| **Kynurenine** | 0.158 | 0.987 | 0.964 | 0.454 | 0.289 | 1.000 | 0.982 | 0.594 | 0.151 | 1.000 | 0.701 | 0.867 | -16.41 ± 37.16 | -1.35 ± 34.35 | 6.43 ± 30.5 | -15.02 ± 30.89 |
| **Lactic acid** | 0.996 | 0.997 | 0.991 | 1.000 | 0.716 | 0.938 | 1.000 | 0.835 | 0.997 | 1.000 | 0.930 | 0.990 | -16.08 ± 79.42 | 21.02 ± 91.73 | 29.74 ± 72.76 | 6.98 ± 33.31 |
| **Leucine-Isoleucine** | 0.077 | 0.945 | 0.952 | 0.305 | 0.565 | 1.000 | 0.928 | 0.910 | 0.083 | 0.924 | 0.925 | 0.462 | -7.76 ± 28.57 | 1.79 ± 32.25 | 2.07 ± 23.35 | -8.6 ± 20.74 |
| **LPC 14:0** | 0.016 | 0.999 | 0.671 | 0.320 | 0.218 | 0.998 | 0.662 | 0.810 | 0.016 | 1.000 | 0.434 | 0.641 | -21.96 ± 38.26 | 7.5 ± 41.69 | 14 ± 32.79 | -9.1 ± 35.35 |
| **LPC 15:0** | 0.024 | 0.998 | 0.696 | 0.365 | 0.321 | 0.987 | 0.662 | 0.900 | 0.023 | 1.000 | 0.456 | 0.693 | -21.45 ± 39.78 | 3.58 ± 46.35 | 13.42 ± 35.66 | -9.29 ± 34.89 |
| **LPC 16:0** | 0.013 | 1.000 | 0.433 | 0.497 | 0.139 | 1.000 | 0.460 | 0.810 | 0.014 | 0.999 | 0.278 | 0.777 | -11.47 ± 18.29 | 2.62 ± 22.65 | 8.32 ± 15.53 | -4.67 ± 15.58 |
| **LPC 16:1** | 0.019 | 1.000 | 0.655 | 0.365 | 0.280 | 0.998 | 0.627 | 0.885 | 0.019 | 0.999 | 0.410 | 0.699 | -23.17 ± 47.62 | 5.58 ± 46.27 | 13.83 ± 37.49 | -13.61 ± 42.73 |
| **LPC 17:0** | 0.092 | 0.996 | 0.670 | 0.713 | 0.506 | 0.988 | 0.645 | 0.979 | 0.088 | 1.000 | 0.330 | 0.977 | -21.81 ± 41.95 | 5.07 ± 48.06 | 14.7 ± 38.81 | -10.48 ± 39.15 |
| **LPC 18:0** | 0.056 | 0.987 | 0.738 | 0.512 | 0.600 | 0.901 | 0.657 | 0.992 | 0.053 | 1.000 | 0.412 | 0.881 | -20.36 ± 41.57 | 2.72 ± 45.94 | 11.34 ± 33.94 | -10.02 ± 39.45 |
| **LPC 18:1** | 0.024 | 1.000 | 0.826 | 0.255 | 0.236 | 1.000 | 0.824 | 0.730 | 0.025 | 0.994 | 0.683 | 0.482 | -21.63 ± 40.84 | 5.78 ± 44.75 | 10.91 ± 31.71 | -14.51 ± 35.11 |
| **LPC 18:2** | 0.039 | 1.000 | 0.771 | 0.393 | 0.387 | 0.999 | 0.739 | 0.911 | 0.041 | 1.000 | 0.635 | 0.631 | -22.46 ± 42.04 | 6.57 ± 52.35 | 10.61 ± 37.32 | -14.9 ± 38.52 |
| **LPC 19:0** | 0.189 | 1.000 | 0.673 | 0.889 | 0.569 | 1.000 | 0.680 | 0.984 | 0.189 | 1.000 | 0.563 | 0.974 | -20.75 ± 68.37 | -0.5 ± 56.01 | 10.73 ± 77.56 | -11.34 ± 56.09 |
| **LPC 20:1** | 0.218 | 1.000 | 0.980 | 0.501 | 0.669 | 1.000 | 0.973 | 0.919 | 0.224 | 0.998 | 0.863 | 0.817 | -10.17 ± 29.13 | -2.42 ± 43.33 | 4.1 ± 25.81 | -6.33 ± 29.81 |
| **LPC 20:2** | 0.709 | 0.884 | 0.869 | 0.998 | 0.914 | 0.973 | 0.872 | 1.000 | 0.717 | 0.858 | 0.836 | 1.000 | -9.16 ± 33.98 | 1.88 ± 37.15 | 4.9 ± 40.68 | -10.45 ± 39.36 |
| **LPC 20:3** | 0.044 | 1.000 | 0.931 | 0.237 | 0.254 | 1.000 | 0.939 | 0.639 | 0.046 | 0.999 | 0.811 | 0.473 | -30.45 ± 60.31 | 8.95 ± 61.91 | 11.91 ± 48.52 | -21.84 ± 61.52 |
| **LPC 20:4** | 0.053 | 1.000 | 0.894 | 0.319 | 0.245 | 0.999 | 0.911 | 0.662 | 0.054 | 0.992 | 0.749 | 0.582 | -29.01 ± 55.15 | 10.34 ± 61.1 | 13.28 ± 46.65 | -19.24 ± 54.94 |
| **LPC 20:5** | 0.066 | 0.999 | 0.908 | 0.347 | 0.346 | 0.999 | 0.909 | 0.775 | 0.067 | 1.000 | 0.759 | 0.624 | -25.65 ± 54.63 | 5.07 ± 55.82 | 13.01 ± 42.35 | -15.56 ± 52.57 |
| **LPC 22:5** | 0.075 | 0.999 | 0.841 | 0.469 | 0.400 | 1.000 | 0.836 | 0.874 | 0.079 | 0.995 | 0.768 | 0.651 | -29.5 ± 55.66 | 7.88 ± 63.48 | 12.7 ± 48.4 | -17.81 ± 55.46 |
| **LPC 22:6** | 0.116 | 1.000 | 0.955 | 0.393 | 0.379 | 1.000 | 0.962 | 0.737 | 0.120 | 1.000 | 0.867 | 0.639 | -29.3 ± 53.84 | 9.31 ± 62.67 | 12.55 ± 48.49 | -17.77 ± 59.51 |
| **LPE 16:0** | 0.040 | 0.931 | 0.858 | 0.306 | 0.506 | 1.000 | 0.799 | 0.945 | 0.042 | 0.928 | 0.859 | 0.394 | -19.25 ± 35.38 | 5.32 ± 45.93 | 9.51 ± 33.65 | -13.17 ± 34.69 |
| **LPE 18:0** | 0.023 | 0.999 | 0.694 | 0.359 | 0.311 | 0.991 | 0.661 | 0.894 | 0.022 | 1.000 | 0.448 | 0.691 | -21.57 ± 39.62 | 3.78 ± 46.1 | 13.23 ± 35.38 | -9.5 ± 34.66 |
| **LPE 18:1** | 0.026 | 0.840 | 0.999 | 0.052 | 0.566 | 0.623 | 0.989 | 0.825 | 0.026 | 0.940 | 0.965 | 0.170 | -12.06 ± 34.01 | -4.52 ± 32.27 | 0.87 ± 24.38 | -15.15 ± 30.08 |
| **LPE 18:2** | 0.052 | 0.757 | 0.946 | 0.241 | 0.563 | 0.677 | 0.906 | 0.924 | 0.053 | 0.890 | 0.807 | 0.511 | -12.96 ± 35.73 | -6.01 ± 41.57 | 5.61 ± 28.03 | -9.7 ± 32.04 |
| **LPE 20:0** | 0.092 | 0.991 | 0.826 | 0.543 | 0.587 | 0.960 | 0.783 | 0.974 | 0.089 | 1.000 | 0.500 | 0.903 | -19.13 ± 40.59 | 1.93 ± 42.8 | 12.71 ± 33.6 | -9.64 ± 39.43 |
| **LPE 20:4** | 0.034 | 0.982 | 0.906 | 0.226 | 0.597 | 0.827 | 0.828 | 0.966 | 0.036 | 0.995 | 0.837 | 0.389 | -16.17 ± 31.2 | -3.91 ± 40.48 | 3.95 ± 26.31 | -12.24 ± 27.6 |
| **LPE 20:5** | 0.170 | 0.888 | 0.996 | 0.317 | 0.840 | 0.720 | 0.982 | 0.976 | 0.175 | 0.971 | 0.933 | 0.634 | -14.63 ± 39.79 | -6.54 ± 43.86 | 3.14 ± 30.25 | -12.92 ± 35.89 |
| **LPE 22:6** | 0.020 | 0.996 | 0.960 | 0.108 | 0.457 | 0.918 | 0.918 | 0.856 | 0.022 | 1.000 | 0.900 | 0.231 | -17.96 ± 33.81 | -3.53 ± 41.67 | 2.82 ± 26.38 | -17.28 ± 30.82 |
| **Lysine** | 0.302 | 0.037 | 0.531 | 0.993 | 0.817 | 0.407 | 0.490 | 1.000 | 0.304 | 0.057 | 0.676 | 0.980 | 23.9 ± 114.77 | -36.82 ± 126.63 | -12.06 ± 117.55 | 8.25 ± 36.95 |
| **Malic acid** | 0.589 | 0.967 | 0.714 | 1.000 | 0.423 | 0.999 | 0.831 | 0.890 | 0.596 | 0.995 | 0.528 | 1.000 | -36.42 ± 121.83 | 3.65 ± 114.48 | 40.17 ± 91.93 | -10.54 ± 71.63 |
| **Methionine** | 0.010 | 0.996 | 0.141 | 0.829 | 0.033 | 0.995 | 0.225 | 0.664 | 0.010 | 1.000 | 0.040 | 0.997 | -18.16 ± 36.89 | 0.14 ± 33.41 | 26.53 ± 26.9 | 4.42 ± 28.59 |
| **Mevalonic acid** | 0.824 | 0.859 | 0.905 | 1.000 | 0.426 | 0.998 | 0.977 | 0.748 | 0.831 | 0.926 | 0.824 | 1.000 | -20.92 ± 74.86 | 1.98 ± 79.1 | 26.36 ± 62.97 | -3.92 ± 48.81 |
| **Orotic acid** | 0.988 | 0.069 | 0.536 | 0.811 | 1.000 | 0.568 | 0.477 | 0.782 | 0.987 | 0.126 | 0.778 | 0.958 | 0.04 ± 56.82 | -12.57 ± 72.36 | -7.09 ± 63.49 | -8.15 ± 29.18 |
| **Paraxanthine** | 0.757 | 0.034 | 0.121 | 0.706 | 0.269 | 0.015 | 0.247 | 0.984 | 0.761 | 0.045 | 0.176 | 0.769 | -28.92 ± 67.16 | 120.04 ± 115.34 | 107.39 ± 121.33 | 79.79 ± 114.31 |
| **PC 32:1** | 0.001 | 0.999 | 0.753 | 0.045 | 0.139 | 0.998 | 0.684 | 0.677 | 0.001 | 0.982 | 0.515 | 0.172 | -22.12 ± 38.34 | 5.26 ± 38.66 | 10.6 ± 28.84 | -15.44 ± 36.9 |
| **PC 34:1** | 0.001 | 1.000 | 0.883 | 0.022 | 0.119 | 0.993 | 0.839 | 0.524 | 0.001 | 0.996 | 0.570 | 0.134 | -20.11 ± 39.17 | 2.8 ± 35.01 | 9.58 ± 26.22 | -15.29 ± 38.29 |
| **PC 34:2** | 0.010 | 1.000 | 0.896 | 0.102 | 0.301 | 0.996 | 0.848 | 0.784 | 0.007 | 0.947 | 0.399 | 0.514 | -15.29 ± 32.05 | 4.5 ± 25.15 | 8.73 ± 22.26 | -9.53 ± 32.21 |
| **PC 36:2** | 0.001 | 0.991 | 0.804 | 0.030 | 0.142 | 0.914 | 0.729 | 0.653 | 0.001 | 1.000 | 0.427 | 0.183 | -19.65 ± 38.42 | 0.8 ± 34.26 | 10.15 ± 27.13 | -13.17 ± 36.19 |
| **PC 36:3** | 0.002 | 0.994 | 0.990 | 0.010 | 0.178 | 0.943 | 0.975 | 0.463 | 0.002 | 1.000 | 0.810 | 0.081 | -14.14 ± 30.66 | 0.63 ± 26.01 | 6 ± 21.76 | -11.12 ± 30.39 |
| **PC 36:4** | 0.003 | 1.000 | 0.880 | 0.047 | 0.257 | 0.980 | 0.805 | 0.768 | 0.003 | 0.990 | 0.594 | 0.212 | -12.41 ± 29.13 | 2.95 ± 21.97 | 7.65 ± 19.58 | -8.19 ± 25.64 |
| **PC 38:5** | 0.002 | 0.994 | 0.812 | 0.054 | 0.306 | 0.816 | 0.691 | 0.878 | 0.002 | 1.000 | 0.562 | 0.206 | -17.28 ± 33.62 | 2.25 ± 33.49 | 11.56 ± 27.89 | -8.96 ± 33.23 |
| **PC 38:6** | 0.016 | 1.000 | 0.753 | 0.251 | 0.278 | 0.994 | 0.718 | 0.841 | 0.016 | 1.000 | 0.463 | 0.599 | -20.75 ± 46.17 | 3.4 ± 43.16 | 12.61 ± 30.49 | -12.6 ± 44.7 |
| **PC 40:7** | 0.001 | 1.000 | 0.903 | 0.013 | 0.093 | 0.995 | 0.866 | 0.440 | 0.001 | 0.993 | 0.565 | 0.102 | -20.55 ± 35.37 | 2.97 ± 33.83 | 8.92 ± 26.77 | -15.57 ± 34.85 |
| **PC 40:8** | 0.998 | 0.998 | 0.914 | 0.982 | 0.999 | 1.000 | 0.922 | 0.998 | 0.998 | 1.000 | 0.775 | 0.901 | -4.16 ± 25.67 | -11.14 ± 41.15 | 8.76 ± 30.48 | -3.61 ± 39.48 |
| **Phenylalanine** | 0.025 | 0.999 | 0.182 | 0.909 | 0.090 | 0.999 | 0.244 | 0.850 | 0.022 | 0.999 | 0.037 | 1.000 | -15.31 ± 36.87 | -3.36 ± 34.33 | 23.42 ± 31.55 | 4.83 ± 32.02 |
| **Proline** | 0.291 | 0.243 | 0.308 | 1.000 | 0.325 | 0.289 | 0.416 | 0.970 | 0.326 | 0.183 | 0.203 | 0.995 | -3.88 ± 16.65 | 3.7 ± 20.53 | 4.55 ± 17.37 | 0.48 ± 9.96 |
| **Serine** | 0.820 | 0.942 | 0.801 | 1.000 | 0.455 | 0.993 | 0.919 | 0.853 | 0.825 | 0.993 | 0.547 | 0.982 | -29.59 ± 80.36 | 12.65 ± 77.85 | 39.24 ± 66.2 | 1.48 ± 56.12 |
| **SM 32:1** | 0.036 | 0.975 | 0.849 | 0.298 | 0.634 | 0.787 | 0.748 | 0.988 | 0.034 | 1.000 | 0.543 | 0.684 | -21.32 ± 51.17 | 4.51 ± 47.44 | 14.67 ± 34.22 | -10.77 ± 50.93 |
| **SM 32:2** | 0.049 | 0.979 | 0.858 | 0.348 | 0.612 | 0.856 | 0.780 | 0.980 | 0.047 | 1.000 | 0.558 | 0.738 | -21.15 ± 43.56 | 5.02 ± 41.53 | 8.43 ± 32.8 | -14.43 ± 42.07 |
| **SM 33:1** | 0.015 | 0.966 | 0.826 | 0.186 | 0.500 | 0.764 | 0.719 | 0.964 | 0.015 | 0.998 | 0.574 | 0.477 | -22.43 ± 38.47 | 0.62 ± 40.8 | 15.09 ± 32.62 | -12.03 ± 44 |
| **SM 34:1** | 0.015 | 0.967 | 0.946 | 0.095 | 0.448 | 0.813 | 0.891 | 0.871 | 0.014 | 0.999 | 0.707 | 0.345 | -29.82 ± 68.84 | 1.75 ± 58.08 | 18.79 ± 47.12 | -21.27 ± 70.1 |
| **SM 34:2** | 0.015 | 0.999 | 0.891 | 0.140 | 0.448 | 0.926 | 0.815 | 0.913 | 0.015 | 1.000 | 0.648 | 0.408 | -24.18 ± 52.78 | 6.56 ± 49.36 | 13.93 ± 34.58 | -15.5 ± 48.64 |
| **SM 35:2** | 0.026 | 1.000 | 0.956 | 0.136 | 0.517 | 0.957 | 0.908 | 0.900 | 0.024 | 0.998 | 0.691 | 0.463 | -10.72 ± 28.15 | 2.98 ± 28.59 | 6.03 ± 22.45 | -7.31 ± 29.46 |
| **SM 36:2** | 0.007 | 1.000 | 0.893 | 0.079 | 0.347 | 0.936 | 0.818 | 0.845 | 0.006 | 1.000 | 0.622 | 0.296 | -26.37 ± 54.66 | 5.05 ± 49.94 | 15.58 ± 38.79 | -17.08 ± 56.42 |
| **Taurine** | 0.997 | 0.246 | 1.000 | 0.998 | 0.836 | 0.955 | 1.000 | 0.821 | 0.998 | 0.397 | 0.992 | 1.000 | -16.11 ± 67.29 | -10.01 ± 103.03 | 23.43 ± 68.74 | 5.63 ± 38.77 |
| **Trans-**  **cinnamic acid** | 0.014 | 0.999 | 0.081 | 0.964 | 0.151 | 0.999 | 0.097 | 0.987 | 0.015 | 0.921 | 0.011 | 0.999 | -15.3 ± 37.19 | -2.94 ± 34.52 | 20.83 ± 29.86 | 3.43 ± 26.21 |
| **Tryptophan** | 0.203 | 0.977 | 0.738 | 0.855 | 0.520 | 0.995 | 0.755 | 0.962 | 0.200 | 1.000 | 0.427 | 0.996 | -14.22 ± 43.06 | 5.11 ± 45.68 | 14.16 ± 34.74 | -2.04 ± 36.3 |
| **Tyrosine** | 0.027 | 0.962 | 0.112 | 0.976 | 0.096 | 1.000 | 0.167 | 0.912 | 0.029 | 1.000 | 0.021 | 0.999 | -13.65 ± 30.79 | 1.67 ± 34.53 | 25.18 ± 24.75 | 8.4 ± 29.65 |
| **Uric acid** | 0.098 | 0.584 | 0.535 | 0.845 | 0.179 | 0.564 | 0.633 | 0.776 | 0.099 | 0.429 | 0.330 | 0.984 | -28.41 ± 42.97 | 25.15 ± 43.1 | 23.95 ± 34.6 | -6.35 ± 55.64 |
| **Valine** | 0.166 | 1.000 | 0.868 | 0.658 | 0.226 | 0.994 | 0.928 | 0.615 | 0.158 | 0.999 | 0.501 | 0.971 | -7.49 ± 15.72 | 4.58 ± 21.17 | 3.03 ± 11.44 | -4.91 ± 11.74 |

Mixed-meal tests for each metabolite were estimated as the incremental area under the curve (iAUC) using the time points 0, 30, and 90 min. Model 1, fitted models were adjusted for age; Model 2, models were adjusted for age and weight loss; Model 3, models were adjusted for age and levels of fasting insulin. VLCD, very low-calorie diet; RYGB (1d), immediate effect of gastric bypass surgery; RYGB (6w), 6-week effect of gastric bypass surgery; Cum. Effect, cumulative effect of the intervention.

**Table 10B.** Linear-mixed-effect models fitted to lipidomics data between study occasions (mixed-meal test).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 1**  **(adjusted for age)** | | | | **Model 2**  **(adj. for age and weight loss)** | | | | **Model 3**  **(adj. for age and insulin)** | | | | **Direction (Mean, SD)** | | | |
|  | Effect of VLCD | RYGB (1d) | RYGB (6w) | Cum. effect | Effect of VLCD | RYGB (1d) | RYGB (6w) | Cum. effect | Effect of VLCD | RYGB (1d) | RYGB (6w) | Cum. effect | Effect of VLCD | RYGB (1d) | RYGB (6w) | Cum. effect |
| **CE16.0\*** | 1.000 | 0.994 | 0.642 | 0.762 | 0.931 | 0.996 | 0.762 | 1.000 | 1.000 | 0.999 | 0.531 | 0.647 | 21.21 ± 89.4 | -22.97 ± 102.39 | 25.98 ± 122.99 | 38.21 ± 107.71 |
| **CE18.1\*** | 0.885 | 0.999 | 0.843 | 0.323 | 0.332 | 0.603 | 0.638 | 0.091 | 0.888 | 0.956 | 0.997 | 0.758 | -9.04 ± 28.36 | 1.95 ± 31.38 | 0.53 ± 32.63 | -5.49 ± 26.79 |
| **CE18.2\*** | 0.811 | 0.988 | 0.920 | 0.999 | 0.960 | 0.999 | 0.917 | 1.000 | 0.793 | 1.000 | 0.999 | 0.925 | -21.04 ± 86.39 | 26.36 ± 111.66 | 20.63 ± 103.01 | 5.2 ± 102.91 |
| **CE18.3\*** | 0.141 | 1.000 | 1.000 | 0.177 | 0.629 | 0.998 | 1.000 | 0.782 | 0.145 | 1.000 | 1.000 | 0.203 | 39.28 ± 130.29 | -6.32 ± 139.56 | 21.25 ± 126.1 | 57.98 ± 105.24 |
| **CE20.4\*** | 0.818 | 0.378 | 0.998 | 0.653 | 0.642 | 0.333 | 0.988 | 0.541 | 0.822 | 0.396 | 0.999 | 0.718 | -15.36 ± 55.36 | 19.06 ± 79.63 | 3.55 ± 51.07 | -6.09 ± 61.09 |
| **LPC16.0\*** | 0.178 | 0.182 | 0.760 | 0.803 | 0.021 | 0.021 | 0.946 | 0.137 | 0.185 | 0.188 | 0.757 | 0.870 | -15.33 ± 24.66 | 15.19 ± 43.55 | 16.53 ± 35.37 | 1.99 ± 36.77 |
| **LPC16.1\*** | 0.502 | 0.442 | 0.630 | 1.000 | 0.058 | 0.049 | 0.877 | 0.329 | 0.511 | 0.441 | 0.633 | 1.000 | -21.04 ± 52.72 | 16.19 ± 83.53 | 30.18 ± 86.19 | 7.32 ± 85.92 |
| **LPC18.0\*** | 0.350 | 0.063 | 0.404 | 1.000 | 0.031 | 0.005 | 0.686 | 0.333 | 0.359 | 0.060 | 0.382 | 1.000 | -22.67 ± 37.26 | 36.48 ± 78.32 | 35.08 ± 65.3 | 12.34 ± 65.23 |
| **LPC18.1\*** | 0.404 | 0.321 | 0.965 | 0.782 | 0.061 | 0.047 | 1.000 | 0.150 | 0.412 | 0.328 | 0.960 | 0.849 | -14.35 ± 37.24 | 15.81 ± 61.2 | 16.73 ± 48.36 | 1.8 ± 52.77 |
| **LPC18.2\*** | 0.401 | 0.719 | 0.817 | 0.949 | 0.063 | 0.145 | 0.965 | 0.255 | 0.410 | 0.685 | 0.775 | 0.983 | -14.91 ± 46.06 | 13.46 ± 71.02 | 27.84 ± 67.9 | 9.83 ± 75.99 |
| **LPC20.3\*** | 0.904 | 0.950 | 0.644 | 0.985 | 0.569 | 0.994 | 0.811 | 0.962 | 0.906 | 0.971 | 0.614 | 0.971 | -4.54 ± 62.01 | -5.56 ± 133.18 | 41.54 ± 69.07 | 31.97 ± 83.75 |
| **LPC20.4\*** | 0.116 | 0.688 | 0.934 | 0.017 | 0.083 | 0.385 | 0.836 | 0.033 | 0.117 | 0.613 | 0.986 | 0.051 | -33.3 ± 99.75 | 17.32 ± 100.54 | 7.76 ± 100.63 | -30.9 ± 155.83 |
| **LPC22.6\*** | 0.801 | 0.991 | 0.865 | 1.000 | 0.581 | 0.840 | 0.942 | 0.907 | 0.801 | 0.997 | 0.941 | 0.998 | -8.86 ± 64.42 | 5.4 ± 94.64 | 18.85 ± 65.89 | 10.32 ± 64.52 |
| **PC32.0\*** | 0.166 | 0.598 | 0.999 | 0.252 | 0.083 | 0.271 | 1.000 | 0.134 | 0.173 | 0.544 | 0.993 | 0.414 | -14.15 ± 18.96 | 8.56 ± 42.58 | 9.25 ± 35.13 | -3.81 ± 37.63 |
| **PC32.1\*** | 0.818 | 0.998 | 0.992 | 0.574 | 0.442 | 0.762 | 0.952 | 0.296 | 0.824 | 0.974 | 1.000 | 0.871 | 15.21 ± 54.11 | 3.39 ± 48.77 | 10.76 ± 62.48 | 25.87 ± 70.1 |
| **PC32.2\*** | 0.799 | 0.852 | 0.271 | 0.877 | 0.117 | 0.138 | 0.523 | 0.731 | 0.803 | 0.649 | 0.102 | 0.568 | -38.98 ± 97.69 | 106.77 ± 186.94 | 80.54 ± 146.84 | 56.72 ± 150.27 |
| **PC34.0\*** | 0.644 | 0.685 | 0.975 | 0.928 | 0.364 | 0.390 | 0.997 | 0.593 | 0.652 | 0.589 | 0.912 | 0.991 | -26.09 ± 69.61 | 17.25 ± 128.98 | 34.53 ± 141.02 | 14.49 ± 136.35 |
| **PC34.1\*** | 0.333 | 0.725 | 0.998 | 0.201 | 0.425 | 0.706 | 0.993 | 0.377 | 0.341 | 0.625 | 1.000 | 0.406 | -6.2 ± 11.52 | 3.9 ± 17.65 | 3.65 ± 20.64 | -1.12 ± 23.2 |
| **PC34.2\*** | 0.372 | 0.821 | 0.998 | 0.534 | 0.401 | 0.725 | 1.000 | 0.556 | 0.378 | 0.692 | 0.961 | 0.817 | -5.44 ± 6.42 | 4.24 ± 12.56 | 4.81 ± 17.89 | 0.41 ± 18.22 |
| **PC34.3\*** | 0.958 | 0.614 | 0.740 | 0.981 | 0.478 | 0.212 | 0.903 | 0.879 | 0.961 | 0.518 | 0.605 | 0.923 | -14.05 ± 70.98 | 35.72 ± 114.18 | 51.55 ± 123.64 | 40.27 ± 127.32 |
| **PC36.1\*** | 0.919 | 0.981 | 0.636 | 0.190 | 0.975 | 0.997 | 0.645 | 0.656 | 0.923 | 0.997 | 0.862 | 0.432 | -27.78 ± 186.37 | 16.49 ± 59.04 | 35.69 ± 87.16 | 46.01 ± 165.4 |
| **PC36.2\*** | 0.450 | 0.188 | 0.815 | 0.968 | 0.125 | 0.052 | 0.952 | 0.414 | 0.455 | 0.116 | 0.602 | 1.000 | -12.14 ± 17.52 | 18.16 ± 37.35 | 16.47 ± 38.44 | 5.28 ± 41 |
| **PC36.3\*** | 0.788 | 0.244 | 0.355 | 0.942 | 0.140 | 0.027 | 0.616 | 0.719 | 0.794 | 0.156 | 0.203 | 0.779 | -4.33 ± 16.22 | 11.11 ± 23.26 | 14.05 ± 26.7 | 9.71 ± 31.69 |
| **PC36.4\*** | 0.027 | 0.949 | 0.778 | 0.001 | 0.352 | 0.999 | 0.831 | 0.156 | 0.028 | 0.958 | 0.799 | 0.001 | -5.3 ± 7.38 | -0.25 ± 8.7 | -0.09 ± 9.11 | -4.59 ± 12.1 |
| **PC36.5\*** | 0.655 | 0.202 | 0.961 | 0.953 | 0.235 | 0.069 | 0.997 | 0.444 | 0.664 | 0.158 | 0.889 | 0.995 | -8.02 ± 35.94 | 15 ± 44.49 | 17.59 ± 43.7 | 11.8 ± 57.79 |
| **PC38.3\*** | 0.980 | 0.224 | 0.238 | 0.528 | 0.343 | 0.032 | 0.452 | 0.969 | 0.982 | 0.164 | 0.158 | 0.381 | -1.33 ± 32.26 | 22.56 ± 43.56 | 30.16 ± 50.61 | 27.79 ± 63.18 |
| **PC38.4\*** | 0.109 | 0.138 | 0.999 | 0.179 | 0.231 | 0.265 | 1.000 | 0.373 | 0.114 | 0.122 | 0.993 | 0.318 | -4.86 ± 7.29 | 4.9 ± 14.77 | 3.86 ± 11.23 | -1.2 ± 11.24 |
| **PC38.5\*** | 0.351 | 0.312 | 0.972 | 0.707 | 0.927 | 0.910 | 0.941 | 0.999 | 0.359 | 0.239 | 0.897 | 0.899 | -8.79 ± 29.21 | 12.54 ± 26.39 | 5.31 ± 26.34 | 1.53 ± 34.23 |
| **PC38.6\*** | 0.015 | 0.159 | 0.994 | 0.004 | 0.015 | 0.089 | 0.956 | 0.011 | 0.015 | 0.117 | 1.000 | 0.021 | -14.15 ± 18.11 | 7.28 ± 25.26 | 2.46 ± 22.58 | -9.5 ± 27.87 |
| **PC40.4\*** | 0.906 | 0.475 | 0.917 | 1.000 | 0.470 | 0.197 | 0.984 | 0.766 | 0.908 | 0.515 | 0.940 | 1.000 | -5.77 ± 72.16 | 31.29 ± 94.63 | 35.87 ± 113.57 | 32.77 ± 114.63 |
| **PC40.5\*** | 0.712 | 0.995 | 0.998 | 0.539 | 0.970 | 0.985 | 1.000 | 0.957 | 0.710 | 0.989 | 0.992 | 0.495 | 49.61 ± 103.81 | 4.56 ± 90.8 | 16.85 ± 74.21 | 58.31 ± 133.32 |
| **PC40.6\*** | 0.096 | 0.086 | 0.994 | 0.214 | 0.026 | 0.023 | 1.000 | 0.060 | 0.097 | 0.049 | 0.924 | 0.492 | -16.28 ± 23.25 | 14.56 ± 38.04 | 9.9 ± 32.87 | -3.63 ± 36.53 |
| **SM32.1\*** | 0.308 | 0.282 | 0.457 | 0.999 | 0.041 | 0.037 | 0.719 | 0.366 | 0.316 | 0.227 | 0.357 | 1.000 | -21.55 ± 39.49 | 26.29 ± 68.71 | 36.75 ± 73.92 | 16.24 ± 78.33 |
| **SM32.2\*** | 0.844 | 0.758 | 0.278 | 0.844 | 0.084 | 0.063 | 0.560 | 0.624 | 0.848 | 0.773 | 0.330 | 0.867 | -6.76 ± 66.15 | 10.44 ± 85.87 | 48.21 ± 78.03 | 40.38 ± 83.28 |
| **SM33.1\*** | 0.163 | 0.366 | 0.901 | 0.602 | 0.054 | 0.115 | 0.983 | 0.201 | 0.169 | 0.298 | 0.800 | 0.812 | -24.52 ± 28.37 | 20.08 ± 61.54 | 19.86 ± 57.96 | -3.21 ± 56.95 |
| **SM34.1\*** | 0.250 | 0.591 | 1.000 | 0.334 | 0.240 | 0.463 | 1.000 | 0.335 | 0.255 | 0.460 | 0.981 | 0.618 | -12.07 ± 15.1 | 9.97 ± 34.23 | 8.95 ± 32.3 | -1.97 ± 35.24 |
| **SM34.2\*** | 0.212 | 0.473 | 0.996 | 0.375 | 0.055 | 0.125 | 1.000 | 0.101 | 0.219 | 0.392 | 0.972 | 0.604 | -24.02 ± 34.62 | 19.33 ± 65.7 | 17.55 ± 63.45 | -4.26 ± 69.33 |
| **SM35.1\*** | 0.560 | 0.237 | 0.833 | 0.100 | 0.943 | 0.775 | 0.881 | 0.724 | 0.563 | 0.290 | 0.823 | 0.120 | -40.52 ± 143.54 | 71.48 ± 171.45 | -26.58 ± 105.67 | -67.39 ± 161.51 |
| **SM36.0\*** | 0.003 | 0.750 | 0.965 | 0.000 | 0.355 | 1.000 | 0.994 | 0.321 | 0.003 | 0.846 | 0.911 | 0.000 | -48.63 ± 57.12 | 14.09 ± 61.7 | 9.95 ± 81.02 | -43.97 ± 90.25 |
| **SM36.1\*** | 0.048 | 1.000 | 0.747 | 0.001 | 0.645 | 0.978 | 0.850 | 0.353 | 0.048 | 0.993 | 0.958 | 0.011 | -14.65 ± 18.43 | 3.13 ± 24.83 | -1.96 ± 23.69 | -13.91 ± 29.38 |
| **SM36.2\*** | 0.957 | 0.990 | 0.870 | 0.490 | 0.959 | 0.984 | 0.852 | 0.726 | 0.960 | 0.966 | 0.972 | 0.731 | -3.3 ± 39.78 | 7.18 ± 22.55 | -8.5 ± 23.35 | -6.71 ± 34.81 |
| **SM38.1\*** | 0.482 | 0.711 | 0.969 | 0.840 | 0.258 | 0.390 | 0.996 | 0.485 | 0.491 | 0.625 | 0.907 | 0.956 | -14.06 ± 21.45 | 13.21 ± 49.07 | 14.92 ± 41.88 | 1.73 ± 46.16 |
| **SM38.2\*** | 0.152 | 0.436 | 0.978 | 0.397 | 0.081 | 0.202 | 0.999 | 0.200 | 0.154 | 0.296 | 0.856 | 0.725 | -16.61 ± 25.69 | 11.87 ± 44.19 | 8.54 ± 31.13 | -6.49 ± 35.8 |
| **SM39.1\*** | 0.289 | 0.473 | 0.421 | 0.999 | 0.136 | 0.215 | 0.604 | 0.719 | 0.298 | 0.411 | 0.349 | 1.000 | -24.59 ± 56.72 | 33.39 ± 90.22 | 47.11 ± 88.15 | 21.96 ± 89.53 |
| **SM40.0\*** | 0.971 | 0.709 | 0.985 | 1.000 | 1.000 | 0.773 | 0.977 | 0.999 | 0.970 | 0.634 | 0.999 | 0.996 | 13.75 ± 128.85 | 14.52 ± 124.39 | 10.52 ± 126.03 | 35.07 ± 118 |
| **SM40.1\*** | 0.588 | 0.600 | 0.566 | 1.000 | 0.155 | 0.159 | 0.789 | 0.633 | 0.597 | 0.538 | 0.487 | 0.999 | -10.53 ± 20.24 | 11.53 ± 40.61 | 18.49 ± 39.79 | 9.01 ± 43.34 |
| **SM40.2\*** | 0.581 | 0.846 | 0.930 | 0.954 | 0.164 | 0.296 | 0.993 | 0.380 | 0.590 | 0.795 | 0.874 | 0.991 | -19.72 ± 38.87 | 17.36 ± 53.11 | 21.4 ± 67.92 | 4.89 ± 58.09 |
| **SM41.1\*** | 0.331 | 0.505 | 0.208 | 0.999 | 0.044 | 0.074 | 0.414 | 0.570 | 0.340 | 0.467 | 0.194 | 0.992 | -18.32 ± 33.15 | 20.2 ± 58.58 | 32.56 ± 62.25 | 15.49 ± 66.67 |
| **SM41.2\*** | 0.195 | 0.196 | 0.914 | 0.635 | 0.065 | 0.065 | 0.987 | 0.221 | 0.201 | 0.162 | 0.836 | 0.820 | -24.4 ± 51.35 | 31.44 ± 86.82 | 27.38 ± 80.55 | 4.14 ± 81.65 |
| **SM42.1\*** | 0.072 | 0.087 | 0.085 | 1.000 | 0.027 | 0.033 | 0.178 | 0.674 | 0.076 | 0.092 | 0.102 | 1.000 | -29.69 ± 68.27 | 30.37 ± 73.83 | 38.45 ± 80.67 | 9.87 ± 60.53 |
| **SM42.2\*** | 0.130 | 0.288 | 1.000 | 0.165 | 0.025 | 0.055 | 0.998 | 0.035 | 0.135 | 0.234 | 0.995 | 0.334 | -13.1 ± 16.89 | 10.36 ± 29 | 6.75 ± 28.03 | -4.68 ± 29.69 |
| **SM42.3\*** | 0.083 | 0.563 | 0.971 | 0.017 | 0.042 | 0.230 | 0.882 | 0.019 | 0.086 | 0.466 | 0.998 | 0.063 | -21.51 ± 23.38 | 11.68 ± 45.48 | 5.15 ± 44.81 | -13.91 ± 44.64 |
| **SM43.1\*** | 0.840 | 0.987 | 0.022 | 0.223 | 0.293 | 0.499 | 0.058 | 1.000 | 0.841 | 0.994 | 0.049 | 0.343 | -24.98 ± 69.46 | 17.3 ± 132.48 | 95.26 ± 115.68 | 37.16 ± 140.56 |
| **SM43.2\*** | 0.281 | 0.601 | 1.000 | 0.224 | 0.050 | 0.121 | 0.978 | 0.042 | 0.282 | 0.501 | 1.000 | 0.432 | -65.6 ± 105.91 | 44.21 ± 101.81 | 37.09 ± 146.29 | -26.48 ± 193.92 |
| **SM44.2\*** | 0.891 | 0.610 | 0.996 | 0.980 | 0.445 | 0.253 | 1.000 | 0.563 | 0.896 | 0.515 | 0.969 | 0.999 | -27.59 ± 105.32 | 30.71 ± 161.84 | 2.33 ± 151.24 | 10.33 ± 114 |
| **TG48.1\*** | 0.641 | 0.730 | 0.157 | 0.004 | 0.967 | 0.753 | 0.204 | 0.302 | 0.610 | 0.479 | 0.044 | 0.001 | 31.61 ± 55.55 | 10.3 ± 49.7 | 29.07 ± 63.4 | 62.41 ± 87.42 |
| **TG48.2\*** | 0.991 | 0.234 | 0.065 | 0.168 | 0.576 | 0.076 | 0.143 | 1.000 | 0.992 | 0.253 | 0.089 | 0.210 | 3.41 ± 61.03 | 29.31 ± 45.29 | 44.87 ± 65.17 | 48.88 ± 86.05 |
| **TG50.0\*** | 0.514 | 0.932 | 0.671 | 0.042 | 0.549 | 0.864 | 0.609 | 0.173 | 0.512 | 0.972 | 0.567 | 0.034 | 41.33 ± 87.09 | -15.99 ± 63.34 | 32.65 ± 73.89 | 63.63 ± 107.52 |
| **TG50.1\*** | 0.939 | 0.879 | 0.444 | 0.870 | 0.681 | 0.605 | 0.594 | 0.999 | 0.943 | 0.781 | 0.305 | 0.714 | 0.68 ± 24.08 | 2.64 ± 19.24 | 9.99 ± 21.88 | 11.77 ± 29.74 |
| **TG50.2\*** | 0.875 | 0.433 | 0.676 | 0.995 | 0.461 | 0.193 | 0.841 | 0.906 | 0.880 | 0.389 | 0.606 | 0.979 | -2.48 ± 27.41 | 10.16 ± 21.03 | 12.44 ± 24.84 | 12.24 ± 35.7 |
| **TG50.3\*** | 0.759 | 0.250 | 0.699 | 1.000 | 0.221 | 0.057 | 0.891 | 0.651 | 0.766 | 0.229 | 0.647 | 0.999 | -4.99 ± 38.25 | 18.87 ± 36.74 | 20.21 ± 41.09 | 17.7 ± 53.59 |
| **TG50.4\*** | 0.982 | 0.074 | 0.140 | 0.355 | 0.978 | 0.257 | 0.171 | 0.868 | 0.982 | 0.119 | 0.269 | 0.551 | -10.39 ± 91.04 | 94.27 ± 118.08 | 66.41 ± 116.82 | 73.18 ± 112.02 |
| **TG52.1\*** | 0.990 | 0.825 | 1.000 | 0.987 | 1.000 | 0.721 | 1.000 | 0.999 | 0.989 | 0.723 | 0.996 | 0.924 | 6.4 ± 44.48 | 8.77 ± 41.33 | 9.41 ± 40.68 | 19.47 ± 59.36 |
| **TG52.2\*** | 0.086 | 0.217 | 0.959 | 0.015 | 0.100 | 0.189 | 0.900 | 0.050 | 0.091 | 0.201 | 0.988 | 0.040 | -7.36 ± 12.65 | 5.98 ± 12.52 | 2.07 ± 14.06 | -3.17 ± 17.81 |
| **TG52.3\*** | 0.072 | 0.246 | 1.000 | 0.051 | 0.082 | 0.195 | 0.996 | 0.089 | 0.076 | 0.250 | 1.000 | 0.093 | -9.55 ± 15.58 | 7.79 ± 18.87 | 4.24 ± 19.74 | -3.34 ± 24.21 |
| **TG52.4\*** | 0.287 | 0.315 | 0.981 | 0.589 | 0.075 | 0.082 | 1.000 | 0.166 | 0.295 | 0.297 | 0.964 | 0.728 | -9.65 ± 29.05 | 13.57 ± 36.26 | 11.55 ± 35.6 | 4.38 ± 42.95 |
| **TG52.5\*** | 0.920 | 0.652 | 0.998 | 0.985 | 0.225 | 0.104 | 1.000 | 0.277 | 0.924 | 0.576 | 0.982 | 0.999 | -4.13 ± 41.67 | 18.75 ± 43.79 | 16.63 ± 52.34 | 16.13 ± 66.14 |
| **TG54.3\*** | 0.066 | 0.680 | 0.499 | 0.000 | 0.051 | 0.362 | 0.352 | 0.004 | 0.070 | 0.677 | 0.596 | 0.001 | -12.25 ± 16.31 | 6.49 ± 13.86 | 0.67 ± 19.81 | -8.34 ± 24.19 |
| **TG54.4\*** | 0.054 | 0.780 | 0.997 | 0.024 | 0.036 | 0.387 | 0.971 | 0.029 | 0.057 | 0.764 | 1.000 | 0.050 | -14.65 ± 21.71 | 8.46 ± 27.1 | 5.77 ± 28.42 | -6.27 ± 35.19 |
| **TG54.5\*** | 0.342 | 0.880 | 0.996 | 0.187 | 0.229 | 0.591 | 0.974 | 0.170 | 0.349 | 0.779 | 1.000 | 0.415 | -16.78 ± 38.95 | 11.71 ± 58 | 10.75 ± 59.84 | -4.21 ± 70.44 |
| **TG54.6\*** | 0.967 | 0.786 | 0.960 | 1.000 | 0.693 | 0.481 | 0.993 | 0.891 | 0.969 | 0.740 | 0.923 | 0.999 | -6.47 ± 88.03 | 21.71 ± 80.3 | 17.35 ± 85.53 | 18.04 ± 89.6 |
| **TG56.6\*** | 0.082 | 0.601 | 0.848 | 0.005 | 0.069 | 0.347 | 0.720 | 0.018 | 0.085 | 0.645 | 0.854 | 0.009 | -18.18 ± 32.83 | 11.55 ± 38.97 | 4.04 ± 37.91 | -10.56 ± 49.35 |

Mixed-meal tests for each metabolite were estimated as the incremental area under the curve (iAUC) using the time points 0, 30, and 90 min. Model 1, fitted models were adjusted for age; Model 2, models were adjusted for age and weight loss; Model 3, models were adjusted for age and levels of fasting insulin. VLCD, very low-calorie diet; RYGB (1d), immediate effect of gastric bypass surgery; RYGB (6w), 6-week effect of gastric bypass surgery; Cum. Effect, cumulative effect of the intervention.

**Table 11A.** Assessment of difference in metabolomics data between normoglycaemic and T2D patients (mixed-meal test).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Occasion:**  **Baseline** | | **Occasion:**  **Diet** | | **Occasion:**  **Surgery** | | **Occasion:**  **Recovery** | | **Effect of VLCD** | | **RYGB (1d)** | | **RYGB (6w)** | | **Cum. effect** | |
|  | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* |
| **1-Methyl-adenosine** | 0.705 | 0.884 | 0.738 | 0.992 | 0.491 | 0.751 | 0.373 | 0.608 | 0.926 | 0.964 | 0.448 | 0.923 | 0.375 | 0.965 | 0.236 | 0.327 |
| **1-Methylhistidine** | 0.829 | 0.922 | 0.242 | 0.992 | 0.438 | 0.743 | 0.656 | 0.769 | 0.264 | 0.489 | 0.132 | 0.923 | 0.225 | 0.965 | 0.606 | 0.675 |
| **2-Hydroxycinnamic acid** | 0.161 | 0.513 | 0.466 | 0.992 | 0.045 | 0.673 | 0.092 | 0.502 | 0.110 | 0.430 | 0.315 | 0.923 | 0.398 | 0.965 | 0.015 | 0.110 |
| **3-Hydroxybutyrate** | 0.337 | 0.631 | 0.373 | 0.992 | 0.227 | 0.673 | 0.331 | 0.578 | 0.539 | 0.650 | 0.164 | 0.923 | 0.188 | 0.965 | 0.140 | 0.221 |
| **5-Oxoproline** | 0.372 | 0.650 | 0.566 | 0.992 | 0.056 | 0.673 | 0.564 | 0.730 | 0.872 | 0.925 | 0.195 | 0.923 | 0.483 | 0.965 | 0.100 | 0.185 |
| **Acetylalanine** | 0.740 | 0.891 | 0.608 | 0.992 | 0.132 | 0.673 | 0.160 | 0.519 | 0.722 | 0.785 | 0.231 | 0.923 | 0.317 | 0.965 | 0.221 | 0.314 |
| **Alanine** | 0.600 | 0.843 | 0.446 | 0.992 | 0.107 | 0.673 | 0.330 | 0.578 | 0.532 | 0.650 | 0.217 | 0.923 | 0.350 | 0.965 | 0.157 | 0.242 |
| **Arginine** | 0.532 | 0.774 | 0.288 | 0.992 | 0.421 | 0.743 | 0.609 | 0.744 | 0.239 | 0.480 | 0.143 | 0.923 | 0.259 | 0.965 | 0.908 | 0.919 |
| **Asparagine** | 0.744 | 0.891 | 0.440 | 0.992 | 0.187 | 0.673 | 0.092 | 0.502 | 0.489 | 0.610 | 0.242 | 0.923 | 0.325 | 0.965 | 0.167 | 0.253 |
| **Aspartic acid** | 0.410 | 0.687 | 0.493 | 0.992 | 0.657 | 0.826 | 0.697 | 0.786 | 0.906 | 0.949 | 0.677 | 0.923 | 0.453 | 0.965 | 0.337 | 0.409 |
| **Caffeine** | 0.555 | 0.799 | 0.485 | 0.992 | 0.209 | 0.673 | 0.464 | 0.659 | 0.397 | 0.550 | 0.094 | 0.923 | 0.714 | 0.965 | 0.386 | 0.449 |
| **Carnitine** | 0.246 | 0.569 | 0.986 | 0.992 | 0.377 | 0.727 | 0.966 | 0.986 | 0.451 | 0.588 | 0.494 | 0.923 | 0.966 | 0.991 | 0.391 | 0.449 |
| **Carnitine C10:0** | 0.157 | 0.513 | 0.061 | 0.992 | 0.061 | 0.673 | 0.174 | 0.529 | 0.035 | 0.426 | 0.656 | 0.923 | 0.471 | 0.965 | 0.061 | 0.149 |
| **Carnitine C10:1** | 0.125 | 0.513 | 0.052 | 0.992 | 0.098 | 0.673 | 0.321 | 0.578 | 0.028 | 0.426 | 0.501 | 0.923 | 0.306 | 0.965 | 0.079 | 0.161 |
| **Carnitine C10:2** | 0.116 | 0.513 | 0.282 | 0.992 | 0.142 | 0.673 | 0.091 | 0.502 | 0.058 | 0.430 | 0.754 | 0.923 | 0.674 | 0.965 | 0.037 | 0.119 |
| **Carnitine C12:0** | 0.175 | 0.513 | 0.204 | 0.992 | 0.044 | 0.673 | 0.158 | 0.519 | 0.092 | 0.430 | 0.908 | 0.953 | 0.779 | 0.965 | 0.036 | 0.119 |
| **Carnitine C12:1** | 0.139 | 0.513 | 0.078 | 0.992 | 0.125 | 0.673 | 0.117 | 0.502 | 0.025 | 0.426 | 0.649 | 0.923 | 0.611 | 0.965 | 0.023 | 0.110 |
| **Carnitine C14:0** | 0.172 | 0.513 | 0.530 | 0.992 | 0.072 | 0.673 | 0.404 | 0.619 | 0.122 | 0.430 | 0.570 | 0.923 | 0.928 | 0.991 | 0.063 | 0.149 |
| **Carnitine C14:1** | 0.208 | 0.513 | 0.189 | 0.992 | 0.105 | 0.673 | 0.090 | 0.502 | 0.074 | 0.430 | 0.901 | 0.953 | 0.963 | 0.991 | 0.028 | 0.110 |
| **Carnitine C14:2** | 0.169 | 0.513 | 0.095 | 0.992 | 0.121 | 0.673 | 0.507 | 0.681 | 0.041 | 0.427 | 0.892 | 0.953 | 0.218 | 0.965 | 0.091 | 0.175 |
| **Carnitine C16:0** | 0.039 | 0.513 | 0.766 | 0.992 | 0.187 | 0.673 | 0.615 | 0.744 | 0.074 | 0.430 | 0.582 | 0.923 | 0.881 | 0.981 | 0.018 | 0.110 |
| **Carnitine C18:0** | 0.091 | 0.513 | 0.527 | 0.992 | 0.349 | 0.714 | 0.601 | 0.744 | 0.111 | 0.430 | 0.884 | 0.953 | 0.945 | 0.991 | 0.027 | 0.110 |
| **Carnitine C18:1** | 0.068 | 0.513 | 0.536 | 0.992 | 0.206 | 0.673 | 0.745 | 0.820 | 0.044 | 0.430 | 0.726 | 0.923 | 0.880 | 0.981 | 0.078 | 0.161 |
| **Carnitine C18:2** | 0.019 | 0.513 | 0.450 | 0.992 | 0.308 | 0.688 | 0.998 | 0.998 | 0.036 | 0.426 | 0.894 | 0.953 | 0.620 | 0.965 | 0.116 | 0.202 |
| **Carnitine C2:0** | 0.191 | 0.513 | 0.177 | 0.992 | 0.409 | 0.743 | 0.141 | 0.502 | 0.033 | 0.426 | 0.818 | 0.939 | 0.831 | 0.969 | 0.102 | 0.185 |
| **Carnitine C3:0** | 0.040 | 0.513 | 0.136 | 0.992 | 0.314 | 0.688 | 0.603 | 0.744 | 0.012 | 0.426 | 0.867 | 0.953 | 0.630 | 0.965 | 0.112 | 0.197 |
| **Carnitine C4:0** | 0.086 | 0.513 | 0.630 | 0.992 | 0.037 | 0.673 | 0.491 | 0.670 | 0.132 | 0.430 | 0.249 | 0.923 | 0.939 | 0.991 | 0.072 | 0.156 |
| **Carnitine C5:0** | 0.284 | 0.596 | 0.955 | 0.992 | 0.306 | 0.688 | 0.581 | 0.743 | 0.418 | 0.561 | 0.419 | 0.923 | 0.695 | 0.965 | 0.251 | 0.336 |
| **Carnitine C6:0** | 0.341 | 0.632 | 0.046 | 0.992 | 0.160 | 0.673 | 0.142 | 0.502 | 0.039 | 0.427 | 0.565 | 0.923 | 0.574 | 0.965 | 0.070 | 0.156 |
| **Carnitine C8:0** | 0.137 | 0.513 | 0.071 | 0.992 | 0.042 | 0.673 | 0.131 | 0.502 | 0.031 | 0.426 | 0.487 | 0.923 | 0.473 | 0.965 | 0.040 | 0.127 |
| **Carnitine C8:1** | 0.136 | 0.513 | 0.826 | 0.992 | 0.534 | 0.774 | 0.176 | 0.529 | 0.158 | 0.453 | 0.778 | 0.923 | 0.384 | 0.965 | 0.015 | 0.110 |
| **Citric acid** | 0.439 | 0.700 | 0.910 | 0.992 | 0.441 | 0.743 | 0.090 | 0.502 | 0.421 | 0.561 | 0.737 | 0.923 | 0.528 | 0.965 | 0.053 | 0.139 |
| **Creatine** | 0.980 | 0.980 | 0.364 | 0.992 | 0.239 | 0.673 | 0.835 | 0.888 | 0.363 | 0.532 | 0.145 | 0.923 | 0.361 | 0.965 | 0.799 | 0.833 |
| **Cystine** | 0.515 | 0.769 | 0.377 | 0.992 | 0.045 | 0.673 | 0.978 | 0.986 | 0.315 | 0.493 | 0.186 | 0.923 | 0.377 | 0.965 | 0.623 | 0.690 |
| **Dihydroorotic acid** | 0.258 | 0.585 | 0.300 | 0.992 | 0.252 | 0.673 | 0.180 | 0.529 | 0.950 | 0.978 | 0.138 | 0.923 | 0.126 | 0.965 | 0.101 | 0.185 |
| **Gluconic acid** | 0.931 | 0.973 | 0.435 | 0.992 | 0.526 | 0.774 | 0.109 | 0.502 | 0.469 | 0.594 | 0.377 | 0.923 | 0.246 | 0.965 | 0.386 | 0.449 |
| **Glucosamine-6-phosphate** | 0.961 | 0.973 | 0.193 | 0.992 | 0.064 | 0.673 | 0.823 | 0.885 | 0.182 | 0.453 | 0.076 | 0.923 | 0.206 | 0.965 | 0.819 | 0.843 |
| **Glutamic acid** | 0.875 | 0.962 | 0.590 | 0.992 | 0.299 | 0.688 | 0.063 | 0.502 | 0.537 | 0.650 | 0.440 | 0.923 | 0.258 | 0.965 | 0.126 | 0.211 |
| **Glutamine** | 0.641 | 0.860 | 0.369 | 0.992 | 0.163 | 0.673 | 0.695 | 0.786 | 0.404 | 0.551 | 0.165 | 0.923 | 0.351 | 0.965 | 0.376 | 0.447 |
| **Glyceric acid** | 0.942 | 0.973 | 0.550 | 0.992 | 0.116 | 0.673 | 0.208 | 0.529 | 0.558 | 0.668 | 0.226 | 0.923 | 0.245 | 0.965 | 0.312 | 0.392 |
| **Hippuric acid** | 0.156 | 0.513 | 0.598 | 0.992 | 0.468 | 0.748 | 0.358 | 0.599 | 0.193 | 0.453 | 0.742 | 0.923 | 0.782 | 0.965 | 0.077 | 0.161 |
| **Histidine** | 0.716 | 0.888 | 0.277 | 0.992 | 0.367 | 0.727 | 0.843 | 0.888 | 0.263 | 0.489 | 0.136 | 0.923 | 0.309 | 0.965 | 0.672 | 0.716 |
| **Hydroxyproline** | 0.639 | 0.860 | 0.422 | 0.992 | 0.126 | 0.673 | 0.274 | 0.567 | 0.319 | 0.493 | 0.487 | 0.923 | 0.873 | 0.981 | 0.243 | 0.331 |
| **Hypoxanthine** | 0.150 | 0.513 | 0.482 | 0.992 | 0.104 | 0.673 | 0.283 | 0.567 | 0.062 | 0.430 | 0.583 | 0.923 | 0.226 | 0.965 | 0.793 | 0.831 |
| **Indole** | 0.195 | 0.513 | 0.948 | 0.992 | 0.056 | 0.673 | 0.367 | 0.608 | 0.301 | 0.493 | 0.322 | 0.923 | 0.569 | 0.965 | 0.063 | 0.149 |
| **Kynurenine** | 0.193 | 0.513 | 0.920 | 0.992 | 0.525 | 0.774 | 0.842 | 0.888 | 0.319 | 0.493 | 0.631 | 0.923 | 0.816 | 0.965 | 0.139 | 0.221 |
| **Lactic acid** | 0.889 | 0.972 | 0.563 | 0.992 | 0.135 | 0.673 | 0.024 | 0.502 | 0.466 | 0.594 | 0.204 | 0.923 | 0.174 | 0.965 | 0.127 | 0.211 |
| **Leucine-Isoleucine** | 0.205 | 0.513 | 0.193 | 0.992 | 0.781 | 0.894 | 0.221 | 0.529 | 0.056 | 0.430 | 0.605 | 0.923 | 0.995 | 0.995 | 0.048 | 0.130 |
| **LPC 14:0** | 0.101 | 0.513 | 0.872 | 0.992 | 0.067 | 0.673 | 0.426 | 0.636 | 0.154 | 0.453 | 0.339 | 0.923 | 0.632 | 0.965 | 0.026 | 0.110 |
| **LPC 15:0** | 0.069 | 0.513 | 0.799 | 0.992 | 0.179 | 0.673 | 0.459 | 0.659 | 0.128 | 0.430 | 0.539 | 0.923 | 0.710 | 0.965 | 0.020 | 0.110 |
| **LPC 16:0** | 0.108 | 0.513 | 0.670 | 0.992 | 0.303 | 0.688 | 0.533 | 0.695 | 0.125 | 0.430 | 0.671 | 0.923 | 0.855 | 0.981 | 0.030 | 0.110 |
| **LPC 16:1** | 0.110 | 0.513 | 0.874 | 0.992 | 0.245 | 0.673 | 0.703 | 0.788 | 0.156 | 0.453 | 0.581 | 0.923 | 0.886 | 0.981 | 0.079 | 0.161 |
| **LPC 17:0** | 0.174 | 0.513 | 0.877 | 0.992 | 0.209 | 0.673 | 0.878 | 0.920 | 0.322 | 0.493 | 0.409 | 0.923 | 0.830 | 0.969 | 0.137 | 0.221 |
| **LPC 18:0** | 0.158 | 0.513 | 0.835 | 0.992 | 0.151 | 0.673 | 0.686 | 0.786 | 0.194 | 0.453 | 0.445 | 0.923 | 0.866 | 0.981 | 0.079 | 0.161 |
| **LPC 18:1** | 0.143 | 0.513 | 0.744 | 0.992 | 0.400 | 0.743 | 0.326 | 0.578 | 0.180 | 0.453 | 0.772 | 0.923 | 0.636 | 0.965 | 0.019 | 0.110 |
| **LPC 18:2** | 0.145 | 0.513 | 0.693 | 0.992 | 0.233 | 0.673 | 0.415 | 0.625 | 0.173 | 0.453 | 0.634 | 0.923 | 0.799 | 0.965 | 0.033 | 0.110 |
| **LPC 19:0** | 0.082 | 0.513 | 0.603 | 0.992 | 0.482 | 0.751 | 0.898 | 0.935 | 0.100 | 0.430 | 0.978 | 0.984 | 0.680 | 0.965 | 0.254 | 0.336 |
| **LPC 20:1** | 0.079 | 0.513 | 0.654 | 0.992 | 0.949 | 0.974 | 0.512 | 0.682 | 0.078 | 0.430 | 0.823 | 0.939 | 0.739 | 0.965 | 0.023 | 0.110 |
| **LPC 20:2** | 0.953 | 0.973 | 0.142 | 0.992 | 0.851 | 0.905 | 0.908 | 0.940 | 0.231 | 0.480 | 0.234 | 0.923 | 0.484 | 0.965 | 0.907 | 0.919 |
| **LPC 20:3** | 0.211 | 0.513 | 0.822 | 0.992 | 0.227 | 0.673 | 0.304 | 0.567 | 0.253 | 0.484 | 0.589 | 0.923 | 0.544 | 0.965 | 0.044 | 0.128 |
| **LPC 20:4** | 0.207 | 0.513 | 0.797 | 0.992 | 0.321 | 0.688 | 0.324 | 0.578 | 0.243 | 0.480 | 0.673 | 0.923 | 0.568 | 0.965 | 0.042 | 0.128 |
| **LPC 20:5** | 0.184 | 0.513 | 0.971 | 0.992 | 0.242 | 0.673 | 0.369 | 0.608 | 0.277 | 0.493 | 0.527 | 0.923 | 0.514 | 0.965 | 0.045 | 0.130 |
| **LPC 22:5** | 0.297 | 0.602 | 0.718 | 0.992 | 0.443 | 0.743 | 0.346 | 0.591 | 0.321 | 0.493 | 0.836 | 0.939 | 0.670 | 0.965 | 0.068 | 0.156 |
| **LPC 22:6** | 0.283 | 0.596 | 0.985 | 0.992 | 0.233 | 0.673 | 0.303 | 0.567 | 0.387 | 0.549 | 0.524 | 0.923 | 0.433 | 0.965 | 0.063 | 0.149 |
| **LPE 16:0** | 0.141 | 0.513 | 0.485 | 0.992 | 0.898 | 0.930 | 0.304 | 0.567 | 0.124 | 0.430 | 0.743 | 0.923 | 0.773 | 0.965 | 0.012 | 0.110 |
| **LPE 18:0** | 0.073 | 0.513 | 0.794 | 0.992 | 0.194 | 0.673 | 0.471 | 0.659 | 0.131 | 0.430 | 0.559 | 0.923 | 0.728 | 0.965 | 0.023 | 0.110 |
| **LPE 18:1** | 0.064 | 0.513 | 0.609 | 0.992 | 0.205 | 0.673 | 0.388 | 0.610 | 0.067 | 0.430 | 0.533 | 0.923 | 0.800 | 0.965 | 0.013 | 0.110 |
| **LPE 18:2** | 0.053 | 0.513 | 0.742 | 0.992 | 0.195 | 0.673 | 0.414 | 0.625 | 0.093 | 0.430 | 0.554 | 0.923 | 0.736 | 0.965 | 0.015 | 0.110 |
| **LPE 20:0** | 0.170 | 0.513 | 0.908 | 0.992 | 0.292 | 0.688 | 0.673 | 0.784 | 0.271 | 0.493 | 0.492 | 0.923 | 0.683 | 0.965 | 0.074 | 0.160 |
| **LPE 20:4** | 0.096 | 0.513 | 0.578 | 0.992 | 0.480 | 0.751 | 0.526 | 0.691 | 0.108 | 0.430 | 0.905 | 0.953 | 0.993 | 0.995 | 0.032 | 0.110 |
| **LPE 20:5** | 0.128 | 0.513 | 0.944 | 0.992 | 0.428 | 0.743 | 0.583 | 0.743 | 0.252 | 0.484 | 0.716 | 0.923 | 0.737 | 0.965 | 0.087 | 0.171 |
| **LPE 22:6** | 0.094 | 0.513 | 0.572 | 0.992 | 0.589 | 0.803 | 0.610 | 0.744 | 0.086 | 0.430 | 0.976 | 0.984 | 0.963 | 0.991 | 0.026 | 0.110 |
| **Lysine** | 0.898 | 0.973 | 0.332 | 0.992 | 0.200 | 0.673 | 0.654 | 0.769 | 0.326 | 0.494 | 0.188 | 0.923 | 0.320 | 0.965 | 0.805 | 0.834 |
| **Malic acid** | 0.765 | 0.897 | 0.856 | 0.992 | 0.243 | 0.673 | 0.738 | 0.817 | 0.962 | 0.978 | 0.421 | 0.923 | 0.767 | 0.965 | 0.667 | 0.716 |
| **Methionine** | 0.213 | 0.513 | 0.431 | 0.992 | 0.100 | 0.673 | 0.049 | 0.502 | 0.128 | 0.430 | 0.680 | 0.923 | 0.312 | 0.965 | 0.014 | 0.110 |
| **Mevalonic acid** | 0.684 | 0.877 | 0.818 | 0.992 | 0.087 | 0.673 | 0.282 | 0.567 | 0.950 | 0.978 | 0.284 | 0.923 | 0.467 | 0.965 | 0.270 | 0.349 |
| **Orotic acid** | 0.416 | 0.687 | 0.384 | 0.992 | 0.046 | 0.673 | 0.150 | 0.519 | 0.578 | 0.673 | 0.127 | 0.923 | 0.234 | 0.965 | 0.064 | 0.149 |
| **Paraxanthine** | 0.708 | 0.884 | 0.315 | 0.992 | 0.723 | 0.860 | 0.204 | 0.529 | 0.390 | 0.549 | 0.964 | 0.984 | 0.386 | 0.965 | 0.223 | 0.314 |
| **PC 32:1** | 0.086 | 0.513 | 0.542 | 0.992 | 0.260 | 0.673 | 0.226 | 0.529 | 0.057 | 0.430 | 0.772 | 0.923 | 0.752 | 0.965 | 0.031 | 0.110 |
| **PC 34:1** | 0.073 | 0.513 | 0.445 | 0.992 | 0.250 | 0.673 | 0.127 | 0.502 | 0.036 | 0.426 | 0.734 | 0.923 | 0.517 | 0.965 | 0.026 | 0.110 |
| **PC 34:2** | 0.143 | 0.513 | 0.969 | 0.992 | 0.409 | 0.743 | 0.286 | 0.567 | 0.172 | 0.453 | 0.594 | 0.923 | 0.403 | 0.965 | 0.052 | 0.139 |
| **PC 36:2** | 0.040 | 0.513 | 0.433 | 0.992 | 0.121 | 0.673 | 0.162 | 0.519 | 0.018 | 0.426 | 0.574 | 0.923 | 0.616 | 0.965 | 0.015 | 0.110 |
| **PC 36:3** | 0.039 | 0.513 | 0.515 | 0.992 | 0.155 | 0.673 | 0.088 | 0.502 | 0.029 | 0.426 | 0.588 | 0.923 | 0.365 | 0.965 | 0.006 | 0.110 |
| **PC 36:4** | 0.038 | 0.513 | 0.648 | 0.992 | 0.282 | 0.688 | 0.208 | 0.529 | 0.028 | 0.426 | 0.692 | 0.923 | 0.521 | 0.965 | 0.004 | 0.110 |
| **PC 38:5** | 0.018 | 0.513 | 0.575 | 0.992 | 0.132 | 0.673 | 0.208 | 0.529 | 0.019 | 0.426 | 0.506 | 0.923 | 0.517 | 0.965 | 0.002 | 0.110 |
| **PC 38:6** | 0.160 | 0.513 | 0.534 | 0.992 | 0.203 | 0.673 | 0.280 | 0.567 | 0.129 | 0.430 | 0.630 | 0.923 | 0.740 | 0.965 | 0.024 | 0.110 |
| **PC 40:7** | 0.036 | 0.513 | 0.404 | 0.992 | 0.185 | 0.673 | 0.157 | 0.519 | 0.018 | 0.426 | 0.726 | 0.923 | 0.571 | 0.965 | 0.008 | 0.110 |
| **PC 40:8** | 0.749 | 0.891 | 0.702 | 0.992 | 0.447 | 0.743 | 0.806 | 0.881 | 0.986 | 0.986 | 0.445 | 0.923 | 0.961 | 0.991 | 0.963 | 0.963 |
| **Phenylalanine** | 0.118 | 0.513 | 0.416 | 0.992 | 0.380 | 0.727 | 0.140 | 0.502 | 0.084 | 0.430 | 0.927 | 0.960 | 0.574 | 0.965 | 0.008 | 0.110 |
| **Proline** | 0.520 | 0.769 | 0.096 | 0.992 | 0.344 | 0.714 | 0.484 | 0.665 | 0.108 | 0.430 | 0.068 | 0.923 | 0.710 | 0.965 | 0.248 | 0.336 |
| **Serine** | 0.956 | 0.973 | 0.682 | 0.992 | 0.043 | 0.673 | 0.063 | 0.502 | 0.614 | 0.707 | 0.117 | 0.923 | 0.196 | 0.965 | 0.294 | 0.372 |
| **SM 32:1** | 0.138 | 0.513 | 0.965 | 0.992 | 0.088 | 0.673 | 0.287 | 0.567 | 0.183 | 0.453 | 0.302 | 0.923 | 0.459 | 0.965 | 0.032 | 0.110 |
| **SM 32:2** | 0.203 | 0.513 | 0.910 | 0.992 | 0.074 | 0.673 | 0.812 | 0.882 | 0.295 | 0.493 | 0.257 | 0.923 | 0.817 | 0.965 | 0.119 | 0.205 |
| **SM 33:1** | 0.108 | 0.513 | 0.889 | 0.992 | 0.260 | 0.673 | 0.127 | 0.502 | 0.138 | 0.442 | 0.448 | 0.923 | 0.351 | 0.965 | 0.017 | 0.110 |
| **SM 34:1** | 0.083 | 0.513 | 0.945 | 0.992 | 0.204 | 0.673 | 0.102 | 0.502 | 0.090 | 0.430 | 0.394 | 0.923 | 0.315 | 0.965 | 0.027 | 0.110 |
| **SM 34:2** | 0.137 | 0.513 | 0.918 | 0.992 | 0.161 | 0.673 | 0.229 | 0.529 | 0.162 | 0.453 | 0.434 | 0.923 | 0.436 | 0.965 | 0.030 | 0.110 |
| **SM 35:2** | 0.024 | 0.513 | 0.730 | 0.992 | 0.264 | 0.674 | 0.225 | 0.529 | 0.033 | 0.426 | 0.603 | 0.923 | 0.476 | 0.965 | 0.006 | 0.110 |
| **SM 36:2** | 0.080 | 0.513 | 0.685 | 0.992 | 0.182 | 0.673 | 0.114 | 0.502 | 0.071 | 0.430 | 0.542 | 0.923 | 0.412 | 0.965 | 0.013 | 0.110 |
| **Taurine** | 0.362 | 0.650 | 0.248 | 0.992 | 0.219 | 0.673 | 0.210 | 0.529 | 0.567 | 0.669 | 0.137 | 0.923 | 0.111 | 0.965 | 0.071 | 0.156 |
| **Transcinnamic acid** | 0.218 | 0.519 | 0.231 | 0.992 | 0.630 | 0.815 | 0.169 | 0.529 | 0.093 | 0.430 | 0.533 | 0.923 | 0.967 | 0.991 | 0.030 | 0.110 |
| **Tryptophan** | 0.263 | 0.585 | 0.810 | 0.992 | 0.028 | 0.673 | 0.380 | 0.608 | 0.322 | 0.493 | 0.300 | 0.923 | 0.697 | 0.965 | 0.096 | 0.182 |
| **Tyrosine** | 0.146 | 0.513 | 0.394 | 0.992 | 0.047 | 0.673 | 0.096 | 0.502 | 0.070 | 0.430 | 0.350 | 0.923 | 0.447 | 0.965 | 0.018 | 0.110 |
| **Uric acid** | 0.279 | 0.596 | 0.817 | 0.992 | 0.794 | 0.894 | 0.461 | 0.659 | 0.393 | 0.549 | 0.780 | 0.923 | 0.426 | 0.965 | 0.150 | 0.235 |
| **Valine** | 0.128 | 0.513 | 0.902 | 0.992 | 0.179 | 0.673 | 0.596 | 0.744 | 0.113 | 0.430 | 0.262 | 0.923 | 0.534 | 0.965 | 0.373 | 0.447 |

Mixed-meal tests for each metabolite were estimated as the incremental area under the curve (iAUC) using the time points 0, 30, and 90 min. P a, p-value as estimated by unequal variances t-test; P b, p-value as estimated by unequal variances t-test adjusted for multiple testing according to the false discovery rate method. VLCD, very low-calorie diet; RYGB (1d), immediate effect of gastric bypass surgery; RYGB (6w), 6-week effect of gastric bypass surgery; Cum. Effect, cumulative effect of the intervention.

**Table 11B.** Assessment of difference in lipidomics data between normoglycaemic and T2D patients (mixed-meal test).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Occasion:**  **Baseline** | | **Occasion:**  **Diet** | | **Occasion:**  **Surgery** | | **Occasion:**  **Recovery** | | **Effect of VLCD** | | **RYGB (1d)** | | **RYGB (6w)** | | **Cum. effect** | |
|  | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* | *P a* | *P b* |
| **CE16.0\*** | 0.042 | 0.513 | 0.623 | 0.992 | 0.974 | 0.974 | 0.379 | 0.608 | 0.181 | 0.453 | 0.697 | 0.923 | 0.420 | 0.965 | 0.793 | 0.831 |
| **CE18.1\*** | 0.781 | 0.898 | 0.771 | 0.992 | 0.859 | 0.905 | 0.038 | 0.502 | 0.961 | 0.978 | 0.959 | 0.984 | 0.182 | 0.965 | 0.212 | 0.306 |
| **CE18.2\*** | 0.368 | 0.650 | 0.852 | 0.992 | 0.545 | 0.774 | 0.980 | 0.986 | 0.795 | 0.848 | 0.696 | 0.923 | 0.912 | 0.991 | 0.658 | 0.714 |
| **CE18.3\*** | 0.084 | 0.513 | 0.745 | 0.992 | 0.335 | 0.711 | 0.470 | 0.659 | 0.198 | 0.453 | 0.835 | 0.939 | 0.525 | 0.965 | 0.320 | 0.397 |
| **CE20.4\*** | 0.320 | 0.626 | 0.977 | 0.992 | 0.273 | 0.687 | 0.301 | 0.567 | 0.566 | 0.669 | 0.362 | 0.923 | 0.401 | 0.965 | 0.047 | 0.130 |
| **LPC16.0\*** | 0.604 | 0.843 | 0.278 | 0.992 | 0.628 | 0.815 | 0.117 | 0.502 | 0.166 | 0.453 | 0.374 | 0.923 | 0.527 | 0.965 | 0.063 | 0.149 |
| **LPC16.1\*** | 0.937 | 0.973 | 0.153 | 0.992 | 0.560 | 0.789 | 0.355 | 0.599 | 0.448 | 0.588 | 0.255 | 0.923 | 0.969 | 0.991 | 0.383 | 0.449 |
| **LPC18.0\*** | 0.687 | 0.877 | 0.330 | 0.992 | 0.610 | 0.808 | 0.280 | 0.567 | 0.185 | 0.453 | 0.417 | 0.923 | 0.762 | 0.965 | 0.187 | 0.277 |
| **LPC18.1\*** | 0.502 | 0.768 | 0.437 | 0.992 | 0.454 | 0.743 | 0.133 | 0.502 | 0.232 | 0.480 | 0.394 | 0.923 | 0.451 | 0.965 | 0.063 | 0.149 |
| **LPC18.2\*** | 0.260 | 0.585 | 0.392 | 0.992 | 0.797 | 0.894 | 0.250 | 0.563 | 0.111 | 0.430 | 0.553 | 0.923 | 0.584 | 0.965 | 0.088 | 0.171 |
| **LPC20.3\*** | 0.435 | 0.700 | 0.311 | 0.992 | 0.319 | 0.688 | 0.524 | 0.691 | 0.224 | 0.480 | 0.569 | 0.923 | 0.849 | 0.981 | 0.236 | 0.327 |
| **LPC20.4\*** | 0.142 | 0.513 | 0.233 | 0.992 | 0.460 | 0.743 | 0.068 | 0.502 | 0.036 | 0.426 | 0.286 | 0.923 | 0.148 | 0.965 | 0.010 | 0.110 |
| **LPC22.6\*** | 0.977 | 0.980 | 0.315 | 0.992 | 0.580 | 0.797 | 0.342 | 0.591 | 0.322 | 0.493 | 0.833 | 0.939 | 0.940 | 0.991 | 0.258 | 0.337 |
| **PC32.0\*** | 0.149 | 0.513 | 0.673 | 0.992 | 0.519 | 0.774 | 0.143 | 0.502 | 0.160 | 0.453 | 0.541 | 0.923 | 0.330 | 0.965 | 0.023 | 0.110 |
| **PC32.1\*** | 0.959 | 0.973 | 0.714 | 0.992 | 0.603 | 0.808 | 0.606 | 0.744 | 0.419 | 0.561 | 0.513 | 0.923 | 0.666 | 0.965 | 0.507 | 0.573 |
| **PC32.2\*** | 0.770 | 0.897 | 0.999 | 0.999 | 0.069 | 0.673 | 0.974 | 0.986 | 0.974 | 0.980 | 0.219 | 0.923 | 0.959 | 0.991 | 0.638 | 0.701 |
| **PC34.0\*** | 0.354 | 0.642 | 0.346 | 0.992 | 0.484 | 0.751 | 0.273 | 0.567 | 0.179 | 0.453 | 0.326 | 0.923 | 0.639 | 0.965 | 0.131 | 0.215 |
| **PC34.1\*** | 0.290 | 0.599 | 0.784 | 0.992 | 0.422 | 0.743 | 0.128 | 0.502 | 0.267 | 0.490 | 0.544 | 0.923 | 0.282 | 0.965 | 0.023 | 0.110 |
| **PC34.2\*** | 0.212 | 0.513 | 0.887 | 0.992 | 0.817 | 0.902 | 0.295 | 0.567 | 0.305 | 0.493 | 0.978 | 0.984 | 0.360 | 0.965 | 0.086 | 0.171 |
| **PC34.3\*** | 0.817 | 0.922 | 0.913 | 0.992 | 0.663 | 0.826 | 0.313 | 0.575 | 0.782 | 0.840 | 0.764 | 0.923 | 0.494 | 0.965 | 0.253 | 0.336 |
| **PC36.1\*** | 0.387 | 0.669 | 0.357 | 0.992 | 0.490 | 0.751 | 0.304 | 0.567 | 0.744 | 0.803 | 0.910 | 0.953 | 0.724 | 0.965 | 0.576 | 0.646 |
| **PC36.2\*** | 0.467 | 0.725 | 0.732 | 0.992 | 0.653 | 0.826 | 0.274 | 0.567 | 0.336 | 0.506 | 0.653 | 0.923 | 0.453 | 0.965 | 0.126 | 0.211 |
| **PC36.3\*** | 0.920 | 0.973 | 0.338 | 0.992 | 0.803 | 0.894 | 0.385 | 0.610 | 0.390 | 0.549 | 0.483 | 0.923 | 0.795 | 0.965 | 0.328 | 0.403 |
| **PC36.4\*** | 0.337 | 0.631 | 0.410 | 0.992 | 0.372 | 0.727 | 0.041 | 0.502 | 0.194 | 0.453 | 0.315 | 0.923 | 0.189 | 0.965 | 0.032 | 0.110 |
| **PC36.5\*** | 0.673 | 0.877 | 0.306 | 0.992 | 0.292 | 0.688 | 0.066 | 0.502 | 0.258 | 0.488 | 0.218 | 0.923 | 0.301 | 0.965 | 0.047 | 0.130 |
| **PC38.3\*** | 0.920 | 0.973 | 0.386 | 0.992 | 0.769 | 0.894 | 0.430 | 0.636 | 0.466 | 0.594 | 0.517 | 0.923 | 0.791 | 0.965 | 0.389 | 0.449 |
| **PC38.4\*** | 0.108 | 0.513 | 0.294 | 0.992 | 0.460 | 0.743 | 0.039 | 0.502 | 0.084 | 0.430 | 0.317 | 0.923 | 0.236 | 0.965 | 0.002 | 0.110 |
| **PC38.5\*** | 0.331 | 0.631 | 0.556 | 0.992 | 0.611 | 0.808 | 0.399 | 0.619 | 0.197 | 0.453 | 0.511 | 0.923 | 0.797 | 0.965 | 0.208 | 0.303 |
| **PC38.6\*** | 0.460 | 0.722 | 0.201 | 0.992 | 0.311 | 0.688 | 0.035 | 0.502 | 0.127 | 0.430 | 0.183 | 0.923 | 0.319 | 0.965 | 0.016 | 0.110 |
| **PC40.4\*** | 0.519 | 0.769 | 0.493 | 0.992 | 0.681 | 0.826 | 0.261 | 0.567 | 0.320 | 0.493 | 0.499 | 0.923 | 0.593 | 0.965 | 0.159 | 0.244 |
| **PC40.5\*** | 0.403 | 0.687 | 0.608 | 0.992 | 0.385 | 0.728 | 0.947 | 0.975 | 0.572 | 0.671 | 0.781 | 0.923 | 0.620 | 0.965 | 0.334 | 0.408 |
| **PC40.6\*** | 0.642 | 0.860 | 0.314 | 0.992 | 0.362 | 0.727 | 0.057 | 0.502 | 0.241 | 0.480 | 0.276 | 0.923 | 0.380 | 0.965 | 0.025 | 0.110 |
| **SM32.1\*** | 0.558 | 0.799 | 0.265 | 0.992 | 0.831 | 0.904 | 0.227 | 0.529 | 0.158 | 0.453 | 0.456 | 0.923 | 0.652 | 0.965 | 0.107 | 0.189 |
| **SM32.2\*** | 0.812 | 0.922 | 0.414 | 0.992 | 0.676 | 0.826 | 0.216 | 0.529 | 0.373 | 0.543 | 0.427 | 0.923 | 0.782 | 0.965 | 0.181 | 0.270 |
| **SM33.1\*** | 0.441 | 0.700 | 0.494 | 0.992 | 0.743 | 0.878 | 0.219 | 0.529 | 0.246 | 0.482 | 0.576 | 0.923 | 0.529 | 0.965 | 0.096 | 0.182 |
| **SM34.1\*** | 0.206 | 0.513 | 0.958 | 0.992 | 0.576 | 0.797 | 0.186 | 0.529 | 0.293 | 0.493 | 0.730 | 0.923 | 0.294 | 0.965 | 0.048 | 0.130 |
| **SM34.2\*** | 0.410 | 0.687 | 0.543 | 0.992 | 0.662 | 0.826 | 0.138 | 0.502 | 0.242 | 0.480 | 0.557 | 0.923 | 0.361 | 0.965 | 0.055 | 0.143 |
| **SM35.1\*** | 0.811 | 0.922 | 0.710 | 0.992 | 0.545 | 0.774 | 0.074 | 0.502 | 0.630 | 0.717 | 0.483 | 0.923 | 0.332 | 0.965 | 0.202 | 0.296 |
| **SM36.0\*** | 0.114 | 0.513 | 0.522 | 0.992 | 0.607 | 0.808 | 0.078 | 0.502 | 0.098 | 0.430 | 0.526 | 0.923 | 0.241 | 0.965 | 0.042 | 0.128 |
| **SM36.1\*** | 0.201 | 0.513 | 0.830 | 0.992 | 0.656 | 0.826 | 0.225 | 0.529 | 0.305 | 0.493 | 0.685 | 0.923 | 0.235 | 0.965 | 0.151 | 0.235 |
| **SM36.2\*** | 0.749 | 0.891 | 0.875 | 0.992 | 0.519 | 0.774 | 0.644 | 0.766 | 0.646 | 0.723 | 0.644 | 0.923 | 0.812 | 0.965 | 0.672 | 0.716 |
| **SM38.1\*** | 0.428 | 0.698 | 0.944 | 0.992 | 0.855 | 0.905 | 0.242 | 0.553 | 0.441 | 0.583 | 0.887 | 0.953 | 0.361 | 0.965 | 0.097 | 0.182 |
| **SM38.2\*** | 0.833 | 0.922 | 0.096 | 0.992 | 0.960 | 0.974 | 0.099 | 0.502 | 0.320 | 0.493 | 0.528 | 0.923 | 0.657 | 0.965 | 0.181 | 0.270 |
| **SM39.1\*** | 0.280 | 0.596 | 0.300 | 0.992 | 0.820 | 0.902 | 0.306 | 0.567 | 0.141 | 0.443 | 0.756 | 0.923 | 0.697 | 0.965 | 0.132 | 0.216 |
| **SM40.0\*** | 0.345 | 0.632 | 0.708 | 0.992 | 0.346 | 0.714 | 0.049 | 0.502 | 0.693 | 0.767 | 0.364 | 0.923 | 0.250 | 0.965 | 0.648 | 0.709 |
| **SM40.1\*** | 0.646 | 0.860 | 0.631 | 0.992 | 0.792 | 0.894 | 0.405 | 0.619 | 0.401 | 0.551 | 0.687 | 0.923 | 0.680 | 0.965 | 0.242 | 0.331 |
| **SM40.2\*** | 0.947 | 0.973 | 0.970 | 0.992 | 0.878 | 0.914 | 0.187 | 0.529 | 0.903 | 0.949 | 0.901 | 0.953 | 0.373 | 0.965 | 0.105 | 0.189 |
| **SM41.1\*** | 0.618 | 0.852 | 0.278 | 0.992 | 0.784 | 0.894 | 0.496 | 0.672 | 0.217 | 0.480 | 0.680 | 0.923 | 0.983 | 0.994 | 0.287 | 0.369 |
| **SM41.2\*** | 0.302 | 0.604 | 0.223 | 0.992 | 0.787 | 0.894 | 0.113 | 0.502 | 0.097 | 0.430 | 0.424 | 0.923 | 0.529 | 0.965 | 0.043 | 0.128 |
| **SM42.1\*** | 0.653 | 0.860 | 0.247 | 0.992 | 0.835 | 0.904 | 0.448 | 0.657 | 0.108 | 0.430 | 0.229 | 0.923 | 0.566 | 0.965 | 0.258 | 0.337 |
| **SM42.2\*** | 0.678 | 0.877 | 0.418 | 0.992 | 0.674 | 0.826 | 0.064 | 0.502 | 0.320 | 0.493 | 0.486 | 0.923 | 0.321 | 0.965 | 0.029 | 0.110 |
| **SM42.3\*** | 0.292 | 0.599 | 0.737 | 0.992 | 0.578 | 0.797 | 0.071 | 0.502 | 0.287 | 0.493 | 0.619 | 0.923 | 0.222 | 0.965 | 0.020 | 0.110 |
| **SM43.1\*** | 0.531 | 0.774 | 0.159 | 0.992 | 0.367 | 0.727 | 0.824 | 0.885 | 0.477 | 0.600 | 0.995 | 0.995 | 0.481 | 0.965 | 0.702 | 0.744 |
| **SM43.2\*** | 0.754 | 0.891 | 0.645 | 0.992 | 0.534 | 0.774 | 0.096 | 0.502 | 0.632 | 0.717 | 0.475 | 0.923 | 0.175 | 0.965 | 0.041 | 0.128 |
| **SM44.2\*** | 0.753 | 0.891 | 0.462 | 0.992 | 0.692 | 0.834 | 0.617 | 0.744 | 0.515 | 0.634 | 0.515 | 0.923 | 0.809 | 0.965 | 0.508 | 0.573 |
| **TG48.1\*** | 0.962 | 0.973 | 0.281 | 0.992 | 0.422 | 0.743 | 0.683 | 0.786 | 0.638 | 0.720 | 0.249 | 0.923 | 0.394 | 0.965 | 0.951 | 0.956 |
| **TG48.2\*** | 0.620 | 0.852 | 0.538 | 0.992 | 0.545 | 0.774 | 0.621 | 0.744 | 0.515 | 0.634 | 0.483 | 0.923 | 0.980 | 0.994 | 0.343 | 0.413 |
| **TG50.0\*** | 0.826 | 0.922 | 0.706 | 0.992 | 0.282 | 0.688 | 0.737 | 0.817 | 0.708 | 0.779 | 0.831 | 0.939 | 0.788 | 0.965 | 0.830 | 0.849 |
| **TG50.1\*** | 0.418 | 0.687 | 0.545 | 0.992 | 0.443 | 0.743 | 0.696 | 0.786 | 0.297 | 0.493 | 0.466 | 0.923 | 0.964 | 0.991 | 0.290 | 0.370 |
| **TG50.2\*** | 0.701 | 0.884 | 0.441 | 0.992 | 0.864 | 0.905 | 0.199 | 0.529 | 0.456 | 0.590 | 0.564 | 0.923 | 0.551 | 0.965 | 0.126 | 0.211 |
| **TG50.3\*** | 0.602 | 0.843 | 0.439 | 0.992 | 0.843 | 0.904 | 0.117 | 0.502 | 0.361 | 0.532 | 0.555 | 0.923 | 0.450 | 0.965 | 0.072 | 0.156 |
| **TG50.4\*** | 0.741 | 0.891 | 0.905 | 0.992 | 0.615 | 0.808 | 0.478 | 0.662 | 0.719 | 0.785 | 0.771 | 0.923 | 0.886 | 0.981 | 0.315 | 0.393 |
| **TG52.1\*** | 0.777 | 0.898 | 0.593 | 0.992 | 0.249 | 0.673 | 0.456 | 0.659 | 0.972 | 0.980 | 0.585 | 0.923 | 0.437 | 0.965 | 0.414 | 0.473 |
| **TG52.2\*** | 0.506 | 0.768 | 0.579 | 0.992 | 0.258 | 0.673 | 0.027 | 0.502 | 0.376 | 0.543 | 0.366 | 0.923 | 0.147 | 0.965 | 0.004 | 0.110 |
| **TG52.3\*** | 0.373 | 0.650 | 0.500 | 0.992 | 0.420 | 0.743 | 0.054 | 0.502 | 0.227 | 0.480 | 0.419 | 0.923 | 0.269 | 0.965 | 0.007 | 0.110 |
| **TG52.4\*** | 0.332 | 0.631 | 0.442 | 0.992 | 0.721 | 0.860 | 0.076 | 0.502 | 0.184 | 0.453 | 0.521 | 0.923 | 0.400 | 0.965 | 0.019 | 0.110 |
| **TG52.5\*** | 0.469 | 0.725 | 0.847 | 0.992 | 0.974 | 0.974 | 0.119 | 0.502 | 0.362 | 0.532 | 0.915 | 0.953 | 0.261 | 0.965 | 0.064 | 0.149 |
| **TG54.3\*** | 0.655 | 0.860 | 0.899 | 0.992 | 0.837 | 0.904 | 0.009 | 0.502 | 0.583 | 0.675 | 0.838 | 0.939 | 0.040 | 0.965 | 0.010 | 0.110 |
| **TG54.4\*** | 0.313 | 0.618 | 0.592 | 0.992 | 0.763 | 0.894 | 0.032 | 0.502 | 0.237 | 0.480 | 0.911 | 0.953 | 0.209 | 0.965 | 0.005 | 0.110 |
| **TG54.5\*** | 0.231 | 0.542 | 0.639 | 0.992 | 0.972 | 0.974 | 0.023 | 0.502 | 0.233 | 0.480 | 0.814 | 0.939 | 0.174 | 0.965 | 0.003 | 0.110 |
| **TG54.6\*** | 0.914 | 0.973 | 0.533 | 0.992 | 0.958 | 0.974 | 0.224 | 0.529 | 0.649 | 0.723 | 0.700 | 0.923 | 0.788 | 0.965 | 0.220 | 0.314 |
| **TG56.6\*** | 0.281 | 0.596 | 0.626 | 0.992 | 0.671 | 0.826 | 0.013 | 0.502 | 0.231 | 0.480 | 0.614 | 0.923 | 0.092 | 0.965 | 0.005 | 0.110 |

Mixed-meal tests for each metabolite were estimated as the incremental area under the curve (iAUC) using the time points 0, 30, and 90 min. P a, p-value as estimated by unequal variances t-test; P b, p-value as estimated by unequal variances t-test adjusted for multiple testing according to the false discovery rate method. VLCD, very low-calorie diet; RYGB (1d), immediate effect of gastric bypass surgery; RYGB (6w), 6-week effect of gastric bypass surgery; Cum. Effect, cumulative effect of the intervention.