

**Supplementary Table 1.** Information on measurements of metabolites included in the BIOCRATES AbsoluteIDQ™ p180 kit in the total dataset and in each sub-study, and whether the metabolite was included for the current analysis.

| Total dataset (n=2,974) |                                  |              |                          |               |                    |                            |                                     |                       | Hepatobiliary cancer controls (n=327) |                                     | Colorectal cancer controls (n=491) |                                     | Prostate cancer controls (n=1,521) |                                     | Kidney cancer controls (n=635) |                                     |
|-------------------------|----------------------------------|--------------|--------------------------|---------------|--------------------|----------------------------|-------------------------------------|-----------------------|---------------------------------------|-------------------------------------|------------------------------------|-------------------------------------|------------------------------------|-------------------------------------|--------------------------------|-------------------------------------|
|                         |                                  |              |                          |               |                    |                            |                                     |                       | Detected                              | Total                               | Detected                           | Total                               | Detected                           | Total                               | Detected                       | Total                               |
| Metabolite class        | Biochemical name                 | Abbreviation | Detected in ≥1 sub-study | Perc. missing | Perc. <LOD or <LOQ | Perc. above quantification | Total perc. missing /outside limits | Included for analysis | Detected                              | Total perc. missing /outside limits | Detected                           | Total perc. missing /outside limits | Detected                           | Total perc. missing /outside limits | Detected                       | Total perc. missing /outside limits |
| Acylcarnitines          | Carnitine                        | C0           | Yes                      | 0.0           | 0.0                | 0.0                        | 0.0                                 | Yes                   | Yes                                   | 0.0                                 | Yes                                | 0.0                                 | Yes                                | 0.0                                 | Yes                            | 0.0                                 |
| Acylcarnitines          | Acetylcarnitine                  | C2           | Yes                      | 0.0           | 0.3                | 0.0                        | 0.3                                 | Yes                   | Yes                                   | 0.0                                 | Yes                                | 0.0                                 | Yes                                | 0.7                                 | Yes                            | 0.0                                 |
| Acylcarnitines          | Propionylcarnitine               | C3           | Yes                      | 1.3           | 6.0                | 0.0                        | 7.3                                 | Yes                   | Yes                                   | 11.9                                | Yes                                | 0.0                                 | Yes                                | 9.1                                 | Yes                            | 6.3                                 |
| Acylcarnitines          | Propenoylcarnitine               | C3:1         | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Hydroxypropionaylcarnitine       | C3-OH        | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Butyrylcarnitine                 | C4           | Yes                      | 1.3           | 10.0               | 0.0                        | 11.3                                | Yes                   | Yes                                   | 11.9                                | Yes                                | 0.2                                 | Yes                                | 14.3                                | Yes                            | 12.3                                |
| Acylcarnitines          | Butenylcarnitine                 | C4:1         | Yes                      | 81.6          | 15.8               | 0.0                        | 97.4                                | No                    | No                                    | 100.0                               | No                                 | 100.0                               | Yes                                | 95.0                                | No                             | 100.0                               |
| Acylcarnitines          | Hydroxybutyrylcarnitine          | C4-OH        | Yes                      | 34.1          | 33.4               | 0.0                        | 67.5                                | No                    | Yes                                   | 46.8                                | Yes                                | 63.1                                | Yes                                | 91.0                                | Yes                            | 24.9                                |
|                         |                                  | (C3-DC)      |                          |               |                    |                            |                                     |                       |                                       |                                     |                                    |                                     |                                    |                                     |                                |                                     |
| Acylcarnitines          | Valerylcarnitine                 | C5           | Yes                      | 1.3           | 14.8               | 0.0                        | 16.1                                | Yes                   | Yes                                   | 11.9                                | Yes                                | 9.6                                 | Yes                                | 20.9                                | Yes                            | 11.8                                |
| Acylcarnitines          | Tiglylcarnitine                  | C5:1         | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Glutaryl carnitine               | C5-DC        | Yes                      | 62.1          | 20.2               | 0.0                        | 82.3                                | No                    | No                                    | 100.0                               | Yes                                | 44.4                                | No                                 | 100.0                               | Yes                            | 60.3                                |
|                         |                                  | (C6-OH)      |                          |               |                    |                            |                                     |                       |                                       |                                     |                                    |                                     |                                    |                                     |                                |                                     |
| Acylcarnitines          | Glutaconyl carnitine             | C5-1-Dc      | Yes                      | 91.8          | 6.6                | 0.0                        | 98.4                                | No                    | Yes                                   | 85.9                                | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Methylglutaryl carnitine         | C5-M-Dc      | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Hydroxyvalerylcarnitine          | C5-OH        | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
|                         |                                  | (C3-DC-M)    |                          |               |                    |                            |                                     |                       |                                       |                                     |                                    |                                     |                                    |                                     |                                |                                     |
| Acylcarnitines          | Hexanoylcarnitine                | C6 (C4:1-DC) | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Hexenoylcarnitine                | C6:1         | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Pimelylcarnitine                 | C7-Dc        | Yes                      | 69.0          | 27.0               | 0.0                        | 96.0                                | No                    | Yes                                   | 78.6                                | No                                 | 100.0                               | No                                 | 100.0                               | Yes                            | 92.1                                |
| Acylcarnitines          | Octanoylcarnitine                | C8           | Yes                      | 62.1          | 36.7               | 0.0                        | 98.8                                | No                    | No                                    | 100.0                               | Yes                                | 98.2                                | No                                 | 100.0                               | Yes                            | 95.8                                |
| Acylcarnitines          | Nonaylcarnitine                  | C9           | Yes                      | 78.7          | 14.4               | 0.0                        | 93.1                                | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | Yes                            | 67.4                                |
| Acylcarnitines          | Decanoylcarnitine                | C10          | Yes                      | 52.5          | 27.1               | 0.0                        | 79.6                                | No                    | Yes                                   | 48.6                                | Yes                                | 82.5                                | No                                 | 100.0                               | Yes                            | 44.3                                |
| Acylcarnitines          | Decenoylcarnitine                | C10:1        | Yes                      | 1.3           | 42.4               | 0.0                        | 43.7                                | No                    | Yes                                   | 34.5                                | Yes                                | 22.8                                | Yes                                | 38.1                                | Yes                            | 78.0                                |
| Acylcarnitines          | Decadienyl carnitine             | C10:2        | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Dodecanoylcarnitine              | C12          | Yes                      | 19.7          | 44.5               | 0.0                        | 64.2                                | No                    | Yes                                   | 64.5                                | Yes                                | 42.8                                | Yes                                | 70.8                                | Yes                            | 65.0                                |
| Acylcarnitines          | Dodecenoylcarnitine              | C12:1        | Yes                      | 22.7          | 25.4               | 0.0                        | 48.1                                | No                    | Yes                                   | 76.1                                | Yes                                | 12.4                                | Yes                                | 31.9                                | No                             | 100.0                               |
| Acylcarnitines          | Dodecanedioyl carnitine          | C12-DC       | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Tetradecanoylcarnitine           | C14          | Yes                      | 83.5          | 10.4               | 0.0                        | 93.9                                | No                    | No                                    | 100.0                               | Yes                                | 63.1                                | No                                 | 100.0                               | No                             | 100.0                               |
| Acylcarnitines          | Tetradecenoylcarnitine           | C14:1        | Yes                      | 1.3           | 6.0                | 0.0                        | 7.3                                 | Yes                   | Yes                                   | 12.5                                | Yes                                | 0.0                                 | Yes                                | 7.0                                 | Yes                            | 11.0                                |
| Acylcarnitines          | Hydroxytetradecenoyl carnitine   | C14:1-OH     | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
|                         |                                  |              |                          |               |                    |                            |                                     |                       |                                       |                                     |                                    |                                     |                                    |                                     |                                |                                     |
| Acylcarnitines          | Tetradecadienyl carnitine        | C14:2        | Yes                      | 1.3           | 44.0               | 0.0                        | 45.3                                | No                    | Yes                                   | 48.6                                | Yes                                | 28.3                                | Yes                                | 47.0                                | Yes                            | 52.8                                |
| Acylcarnitines          | Hydroxytetradecadienyl carnitine | C14:2-OH     | No                       | 100.0         | 0.0                | 0.0                        | 100.0                               | No                    | No                                    | 100.0                               | No                                 | 100.0                               | No                                 | 100.0                               | No                             | 100.0                               |
|                         |                                  |              |                          |               |                    |                            |                                     |                       |                                       |                                     |                                    |                                     |                                    |                                     |                                |                                     |
| Acylcarnitines          | Hexadecanoylcarnitine            | C16          | Yes                      | 1.3           | 2.4                | 0.0                        | 3.7                                 | Yes                   | Yes                                   | 13.1                                | Yes                                | 0.0                                 | Yes                                | 0.3                                 | Yes                            | 9.9                                 |
| Acylcarnitines          | Hexadecenoylcarnitine            | C16:1        | Yes                      | 52.5          | 38.7               | 0.0                        | 91.2                                | No                    | Yes                                   | 67.3                                | Yes                                | 92.7                                | No                                 | 100.0                               | Yes                            | 81.3                                |
| Acylcarnitines          | Hydroxyhexadecenoylcarnitine     | C16:1-OH     | Yes                      | 83.5          | 14.1               | 0.0                        | 97.6                                | No                    | No                                    | 100.0                               | Yes                                | 85.1                                | No                                 | 100.0                               | No                             | 100.0                               |

|                 |                                |            |     |       |      |      |       |     |     |       |     |       |     |       |     |       |
|-----------------|--------------------------------|------------|-----|-------|------|------|-------|-----|-----|-------|-----|-------|-----|-------|-----|-------|
| Acylcarnitines  | Hexadecadienylcarnitine        | C16:2      | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Acylcarnitines  | Hydroxyhexadecadienylcarnitine | C16:2-OH   | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Acylcarnitines  | Hydroxyhexadecanoylcarnitine   | C16-OH     | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Acylcarnitines  | Octadecanoylcarnitine          | C18        | Yes | 1.3   | 10.4 | 0.0  | 11.7  | Yes | Yes | 21.4  | Yes | 7.9   | Yes | 9.4   | Yes | 15.3  |
| Acylcarnitines  | Octadecenoylcarnitine          | C18:1      | Yes | 1.3   | 1.3  | 0.0  | 2.6   | Yes | Yes | 11.9  | Yes | 0.0   | Yes | 0.1   | Yes | 6.1   |
| Acylcarnitines  | Hydroxyoctadecenoylcarnitine   | C18:1-OH   | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Acylcarnitines  | Octadecadienylcarnitine        | C18:2      | Yes | 1.3   | 7.9  | 0.0  | 9.2   | Yes | Yes | 39.7  | Yes | 0.4   | Yes | 2.7   | Yes | 16.1  |
| Amino acids     | Alanine                        | Ala        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Arginine                       | Arg        | Yes | 0.1   | 0.4  | 0.0  | 0.5   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.5   | Yes | 1.1   |
| Amino acids     | Asparagine                     | Asn        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Aspartate                      | Asp        | Yes | 0.1   | 25.4 | 0.0  | 25.5  | No  | Yes | 0.3   | Yes | 30.8  | Yes | 25.4  | Yes | 34.3  |
| Amino acids     | Citrulline                     | Cit        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Glutamine                      | Gln        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Glutamate                      | Glu        | Yes | 0.1   | 0.03 | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.2   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Glycine                        | Gly        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Histidine                      | His        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Isoleucine                     | Ile        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Leucine                        | Leu        | Yes | 0.1   | 0.1  | 0.03 | 0.2   | Yes | Yes | 0.3   | Yes | 0.4   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Lysine                         | Lys        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Methionine                     | Met        | Yes | 0.1   | 0.03 | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.5   |
| Amino acids     | Ornithine                      | Orn        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Phenylalanine                  | Phe        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Proline                        | Pro        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Serine                         | Ser        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Threonine                      | Thr        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Tryptophan                     | Trp        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Tyrosine                       | Tyr        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | Valine                         | Val        | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Amino acids     | t4-hydroxyproline              | t4-OH-Pro  | Yes | 11.1  | 0.0  | 0.0  | 11.1  | Yes | No  | 100.0 | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Biogenic amines | Acetylornithine                | Ac-Orn     | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Biogenic amines | alpha-Amino adipic acid        | alpha-AAA  | Yes | 32.8  | 38.5 | 0.0  | 71.3  | No  | Yes | 0.6   | Yes | 79.0  | Yes | 89.0  | Yes | 59.2  |
| Biogenic amines | Carnosine                      | Carnosine  | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Biogenic amines | Creatinine                     | Creatinine | Yes | 0.1   | 0.0  | 0.0  | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Biogenic amines | Histamine                      | Histamine  | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Biogenic amines | Kynurenine                     | Kynurenine | Yes | 0.1   | 0.2  | 0.0  | 0.3   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.2   | Yes | 0.9   |
| Biogenic amines | Methioninesulfoxide            | Met-SO     | Yes | 89.0  | 8.6  | 0.0  | 97.6  | No  | Yes | 78.6  | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Biogenic amines | Nitrotyrosine                  | Nitro-Tyr  | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Biogenic amines | Phenylethylamine               | PEA        | No  | 100.0 | 0.0  | 0.0  | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Biogenic amines | Putrescine                     | Putrescine | Yes | 62.2  | 27.8 | 0.0  | 90.0  | No  | No  | 100.0 | Yes | 77.0  | No  | 100.0 | Yes | 71.0  |
| Biogenic amines | Sarcosine                      | Sarcosine  | Yes | 11.1  | 16.3 | 0.0  | 27.4  | No  | No  | 100.0 | Yes | 20.2  | Yes | 15.2  | Yes | 24.9  |
| Biogenic amines | Serotonin                      | Serotonin  | Yes | 51.2  | 32.8 | 0.0  | 84.0  | No  | Yes | 3.1   | Yes | 86.6  | No  | 100.0 | Yes | 85.2  |
| Biogenic amines | Spermidine                     | Spermidine | Yes | 51.6  | 43.5 | 0.0  | 95.1  | No  | Yes | 79.3  | Yes | 92.7  | No  | 100.0 | Yes | 93.2  |
| Biogenic amines | Spermine                       | Spermine   | Yes | 51.6  | 45.3 | 0.0  | 96.9  | No  | Yes | 80.8  | Yes | 97.0  | No  | 100.0 | Yes | 97.6  |
| Biogenic amines | Taurine                        | Taurine    | Yes | 0.1   | 0.0  | 0.9  | 1.0   | Yes | Yes | 8.3   | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   |
| Biogenic amines | Total dimethylarginine         | Total DMA  | Yes | 89.0  | 9.5  | 0.0  | 98.5  | No  | Yes | 85.9  | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Biogenic amines | Asymmetric dimethylarginine    | ADMA       | Yes | 2.9   | 3.6  | 0.0  | 6.5   | Yes | Yes | 32.4  | Yes | 1.0   | Yes | 4.4   | Yes | 2.5   |
| Biogenic amines | Symmetric dimethylarginine     | SDMA       | Yes | 29.5  | 0.0  | 0.0  | 29.5  | No  | No  | 100.0 | Yes | 0.0   | Yes | 36.0  | Yes | 0.3   |
| Glycerophospho- | Lysophosphatidylcholine (acyl) | lysoPC a   | Yes | 89.0  | 9.9  | 0.0  | 98.9  | No  | Yes | 90.2  | No  | 100.0 | No  | 100.0 | No  | 100.0 |

|                       |                                      |                |     |       |     |     |       |     |     |       |     |       |     |       |     |       |       |
|-----------------------|--------------------------------------|----------------|-----|-------|-----|-----|-------|-----|-----|-------|-----|-------|-----|-------|-----|-------|-------|
| lipids                | C14:0                                | C14:0          |     |       |     |     |       |     |     |       |     |       |     |       |     |       |       |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C16:0 | lysoPC a C16:0 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C16:1 | lysoPC a C16:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C17:0 | lysoPC a C17:0 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C18:0 | lysoPC a C18:0 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C18:1 | lysoPC a C18:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C18:2 | lysoPC a C18:2 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C20:3 | lysoPC a C20:3 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C20:4 | lysoPC a C20:4 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C24:0 | lysoPC a C24:0 | Yes | 89.0  | 0.6 | 0.0 | 89.6  | No  | Yes | 5.5   | No  | 100.0 | No  | 100.0 | No  | 100.0 | 100.0 |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C26:0 | lysoPC a C26:0 | No  | 100.0 | 0.0 | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 | 100.0 |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C26:1 | lysoPC a C26:1 | No  | 100.0 | 0.0 | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 | 100.0 |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C28:0 | lysoPC a C28:0 | Yes | 90.3  | 2.1 | 0.0 | 92.4  | No  | Yes | 31.2  | No  | 100.0 | No  | 100.0 | No  | 100.0 | 100.0 |
| Glycerophospho-lipids | Lysophosphatidylcholine (acyl) C28:1 | lysoPC a C28:1 | Yes | 57.2  | 0.0 | 0.0 | 57.2  | No  | Yes | 0.0   | Yes | 0.0   | Yes | 70.2  | No  | 100.0 | 100.0 |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C24:0    | PC aa C24:0    | Yes | 89.0  | 6.0 | 0.0 | 95.0  | No  | Yes | 54.4  | No  | 100.0 | No  | 100.0 | No  | 100.0 | 100.0 |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C26:0    | PC aa C26:0    | No  | 100.0 | 0.0 | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 | 100.0 |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C28:1    | PC aa C28:1    | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C30:0    | PC aa C30:0    | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C30:2    | PC aa C30:2    | No  | 100.0 | 0.0 | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 | 100.0 |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C32:0    | PC aa C32:0    | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C32:1    | PC aa C32:1    | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C32:2    | PC aa C32:2    | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C32:3    | PC aa C32:3    | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C34:1    | PC aa C34:1    | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C34:2    | PC aa C34:2    | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | 0.0   |

|                       |                                   |             |     |       |      |     |       |     |     |       |     |       |     |       |     |       |
|-----------------------|-----------------------------------|-------------|-----|-------|------|-----|-------|-----|-----|-------|-----|-------|-----|-------|-----|-------|
|                       |                                   |             |     |       |      |     |       |     |     |       |     |       |     |       |     |       |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C34:3 | PC aa C34:3 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C34:4 | PC aa C34:4 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C36:0 | PC aa C36:0 | Yes | 0.0   | 0.3  | 0.0 | 0.3   | Yes | Yes | 2.1   | Yes | 0.0   | Yes | 0.0   | Yes | 0.2   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C36:1 | PC aa C36:1 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C36:2 | PC aa C36:2 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C36:3 | PC aa C36:3 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C36:4 | PC aa C36:4 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C36:5 | PC aa C36:5 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C36:6 | PC aa C36:6 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C38:0 | PC aa C38:0 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C38:1 | PC aa C38:1 | No  | 100.0 | 0.0  | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C38:3 | PC aa C38:3 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C38:4 | PC aa C38:4 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C38:5 | PC aa C38:5 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C38:6 | PC aa C38:6 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C40:1 | PC aa C40:1 | Yes | 35.9  | 38.1 | 0.0 | 74.0  | No  | Yes | 25.1  | Yes | 66.6  | Yes | 92.7  | Yes | 60.3  |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C40:2 | PC aa C40:2 | Yes | 3.1   | 0.0  | 0.0 | 3.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 6.1   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C40:3 | PC aa C40:3 | Yes | 3.1   | 0.0  | 0.0 | 3.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 6.1   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C40:4 | PC aa C40:4 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C40:5 | PC aa C40:5 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C40:6 | PC aa C40:6 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C42:0 | PC aa C42:0 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C42:1 | PC aa C42:1 | Yes | 0.0   | 0.0  | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C42:2 | PC aa C42:2 | Yes | 0.0   | 0.1  | 0.0 | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.3   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (diacyl) C42:4 | PC aa C42:4 | Yes | 3.1   | 0.0  | 0.0 | 3.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 6.1   | Yes | 0.0   |

|                       |  |             |     |       |     |     |       |     |     |       |     |       |     |       |     |       |  |
|-----------------------|--|-------------|-----|-------|-----|-----|-------|-----|-----|-------|-----|-------|-----|-------|-----|-------|--|
| lipids                | C42:4                                  |             |     |       |     |     |       |     |     |       |     |       |     |       |     |       |  |
| Glycerophospho-lipids | Phosphatidylcholine (diacyl) C42:5     | PC aa C42:5 | Yes | 3.1   | 0.0 | 0.0 | 3.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 6.1   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (diacyl) C42:6     | PC aa C42:6 | Yes | 3.1   | 4.5 | 0.0 | 7.6   | Yes | Yes | 19.0  | Yes | 2.7   | Yes | 8.7   | Yes | 3.2   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C30:0 | PC ae C30:0 | Yes | 3.1   | 0.5 | 0.0 | 3.6   | Yes | Yes | 0.0   | Yes | 0.4   | Yes | 7.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C30:1 | PC ae C30:1 | No  | 100.0 | 0.0 | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C30:2 | PC ae C30:2 | Yes | 3.1   | 0.0 | 0.0 | 3.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 6.1   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C32:1 | PC ae C32:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C32:2 | PC ae C32:2 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C34:0 | PC ae C34:0 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C34:1 | PC ae C34:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C34:2 | PC ae C34:2 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C34:3 | PC ae C34:3 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C36:0 | PC ae C36:0 | Yes | 3.1   | 0.0 | 0.0 | 3.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 6.1   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C36:1 | PC ae C36:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C36:2 | PC ae C36:2 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C36:3 | PC ae C36:3 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C36:4 | PC ae C36:4 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C36:5 | PC ae C36:5 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C38:0 | PC ae C38:0 | Yes | 18.4  | 0.0 | 0.0 | 18.4  | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 36.0  | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C38:1 | PC ae C38:1 | No  | 100.0 | 0.0 | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C38:2 | PC ae C38:2 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C38:3 | PC ae C38:3 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C38:4 | PC ae C38:4 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C38:5 | PC ae C38:5 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |
| Glycerophospho-lipids | Phosphatidylcholine (acyl-alkyl) C38:6 | PC ae C38:6 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |  |

|                       |                                       |               |     |       |     |     |       |     |     |       |     |       |     |       |     |       |
|-----------------------|---------------------------------------|---------------|-----|-------|-----|-----|-------|-----|-----|-------|-----|-------|-----|-------|-----|-------|
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C40:1 | PC ae C40:1   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C40:2 | PC ae C40:2   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C40:3 | PC ae C40:3   | Yes | 3.1   | 0.0 | 0.0 | 3.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 6.1   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C40:4 | PC ae C40:4   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C40:5 | PC ae C40:5   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C40:6 | PC ae C40:6   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C42:0 | PC ae C42:0   | No  | 100.0 | 0.0 | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C42:1 | PC ae C42:1   | Yes | 2.1   | 0.7 | 0.0 | 2.8   | Yes | Yes | 0.0   | Yes | 0.4   | Yes | 4.6   | Yes | 1.6   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C42:2 | PC ae C42:2   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C42:3 | PC ae C42:3   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C42:4 | PC ae C42:4   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C42:5 | PC ae C42:5   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C44:3 | PC ae C44:3   | Yes | 34.8  | 0.3 | 0.0 | 35.1  | No  | Yes | 0.0   | Yes | 0.8   | Yes | 68.4  | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C44:4 | PC ae C44:4   | Yes | 0.0   | 0.1 | 0.0 | 0.1   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.1   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C44:5 | PC ae C44:5   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Glycerophospho-lipids | Phospatidylcholine (acyl-alkyl) C44:6 | PC ae C44:6   | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Hydroxysphingomyeline C14:1           | SM (OH) C14:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Hydroxysphingomyeline C16:1           | SM (OH) C16:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Hydroxysphingomyeline C22:1           | SM (OH) C22:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Hydroxysphingomyeline C22:2           | SM (OH) C22:2 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Hydroxysphingomyeline C24:1           | SM (OH) C24:1 | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Sphingomyeline C16:0                  | SM C16:0      | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Sphingomyeline C16:1                  | SM C16:1      | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Sphingomyeline C18:0                  | SM C18:0      | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Sphingomyeline C18:1                  | SM C18:1      | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Sphingomyeline C20:2                  | SM C20:2      | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |
| Sphingolipids         | Sphingomyeline C22:3                  | SM C22:3      | No  | 100.0 | 0.0 | 0.0 | 100.0 | No  | No  | 100.0 | No  | 100.0 | No  | 100.0 | No  | 100.0 |
| Sphingolipids         | Sphingomyeline C24:0                  | SM C24:0      | Yes | 0.0   | 0.0 | 0.0 | 0.0   | Yes | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   | Yes | 0.0   |

|               |                      |          |     |      |     |     |      |     |     |     |     |     |     |       |     |     |
|---------------|----------------------|----------|-----|------|-----|-----|------|-----|-----|-----|-----|-----|-----|-------|-----|-----|
| Sphingolipids | Sphingomyeline C24:1 | SM C24:1 | Yes | 0.0  | 0.0 | 0.0 | 0.0  | Yes | Yes | 0.0 | Yes | 0.0 | Yes | 0.0   | Yes | 0.0 |
| Sphingolipids | Sphingomyeline C26:0 | SM C26:0 | Yes | 51.1 | 0.0 | 0.0 | 51.1 | No  | Yes | 0.0 | Yes | 0.0 | Yes | 100.0 | Yes | 0.0 |
| Sphingolipids | Sphingomyeline C26:1 | SM C26:1 | Yes | 32.8 | 0.0 | 0.0 | 32.8 | No  | Yes | 0.0 | Yes | 0.0 | Yes | 64.0  | Yes | 0.0 |
| Hexoses       | Hexoses              | H1       | Yes | 0.0  | 2.6 | 0.0 | 2.6  | Yes | Yes | 0.0 | Yes | 2.7 | Yes | 3.0   | No  | 3.0 |
| Total number  |                      | 186      | 157 |      |     |     |      | 123 | 147 |     | 147 |     | 138 |       | 144 |     |

Abbreviations: LOD, limit of detection; LOQ, limit of quantification; n, number; perc., percentage.

**Supplementary Table 2.** Participant characteristics by sub-study (nested case-control study the controls were derived from) and in the total dataset

|   | Colorectal cancer<br>controls<br>(n=491, 16.5%) | Kidney cancer<br>controls<br>(n=635, 21.4%) | Hepatobiliary cancer<br>controls<br>(n=327, 11.0%) | Prostate cancer<br>controls<br>(n=1,521, 51.1%) | Total dataset<br>(n=2,974, 100%) |
|---|---|---|--|---|----------------------------------|
| Age, mean (SD)  | 56.5 (8.0)                                      | 55.9 (8.3)                                  | 59.6 (7.4)   | 59.7 (7.0)                                      | 58.3 (7.7)                       |
| Sex, n (%)  |   |   |  |   |                                  |
| Men   | 188 (38.3)                                      | 337 (53.1)                                  | 185 (56.6)   | 1,521 (100.0)                                   | 2,231 (75.0)                     |
| Women   | 303 (61.7)                                      | 298 (46.9)                                  | 142 (43.4)   | 0 (0.0)   | 743 (25.0)                       |
| Education level, n (%) <sup>a</sup>   |   |   |  |   |                                  |
| None/primary  | 262 (54.4)                                      | 271 (44.2)                                  | 152 (47.8)   | 614 (42.6)                                      | 1,299 (1,299)                    |
| Secondary   | 65 (13.5)                                       | 90 (14.7)                                   | 37 (11.6)  | 161 (11.2)                                      | 353 (353)                        |
| Technical/professional  | 81 (16.8)                                       | 135 (22.0)                                  | 74 (23.3)  | 359 (24.9)                                      | 649 (649)                        |
| University or higher  | 74 (15.4)                                       | 117 (19.1)                                  | 55 (17.3)  | 306 (21.3)                                      | 552 (552)                        |
| Alcohol intake in men (g/day), median (5 <sup>th</sup> , 95 <sup>th</sup> perc)                                   | 18.5 (0.1, 60.8)                                | 15.5 (0.0, 73.9)                            | 12.8 (0.1, 57.1)                                   | 13.2 (0.0, 63.4)                                | 13.7 (0.0, 64.0)                 |
| Alcohol intake in women (g/day), median (5 <sup>th</sup> , 95 <sup>th</sup> perc)                                 | 2.0 (0.0, 25.3)                                 | 3.3 (0.0, 29.5)                             | 3.3 (0.0, 24.7)                                    | NA NA   | 2.8 (0.0, 25.7)                  |
| Categories of alcohol intake, n (%)   |   |   |  |   |                                  |
| Non-drinkers (<0.1 g/day)   | 97 (19.8)                                       | 85 (13.4)                                   | 40 (12.2)  | 123 (8.1)                                       | 345 (11.6)                       |
| Light drinkers (0.1-4.9 g/day)  | 136 (27.7)                                      | 184 (29.0)                                  | 97 (29.7)  | 309 (20.3)                                      | 726 (24.4)                       |
| Moderate drinkers (5-39.9 g/day)  | 216 (44.0)                                      | 300 (47.2)                                  | 163 (49.9)   | 842 (55.4)                                      | 1,521 (51.1)                     |
| Heavy drinkers (≥40 g/day)  | 42 (8.6)  | 66 (10.4)                                   | 27 (8.3)   | 247 (16.2)                                      | 382 (12.8)                       |
| Body mass index (kg/m <sup>2</sup> ), mean (SD)   | 26.6 (3.7)                                      | 26.7 (4.0)                                  | 27.1 (4.1)   | 26.9 (3.5)                                      | 26.8 (26.8)                      |
| Physical activity, n (%) <sup>b</sup>   |   |   |  |   |                                  |
| Inactive  | 154 (31.4)                                      | 171 (27.1)                                  | 108 (33.2)   | 390 (26.2)                                      | 823 (823)                        |
| Moderately inactive   | 193 (39.4)                                      | 195 (31.0)                                  | 103 (31.7)   | 489 (32.9)                                      | 980 (980)                        |
| Moderately active   | 80 (16.3)                                       | 147 (23.3)                                  | 61 (18.8)  | 332 (22.3)                                      | 620 (620)                        |
| Active  | 63 (12.9)                                       | 117 (18.6)                                  | 53 (16.3)  | 277 (18.6)                                      | 510 (510)                        |
| Smoking status, n (%) <sup>c</sup>  |   |   |  |   |                                  |
| Current smoker  | 92 (18.9)                                       | 131 (20.9)                                  | 68 (21.2)  | 373 (24.9)                                      | 664 (22.7)                       |
| Former smoker   | 136 (27.9)                                      | 210 (33.5)                                  | 105 (32.7)   | 678 (45.3)                                      | 1,129 (38.5)                     |
| Never smoker  | 260 (53.3)                                      | 286 (45.6)                                  | 148 (46.1)   | 445 (29.8)                                      | 1,139 (38.9)                     |
| Meat intake (g/day), median (5 <sup>th</sup> , 95 <sup>th</sup> perc)   | 104.4 (32.9, 198.7)                             | 101.7 (30.2, 234.3)                         | 101.1 (35.4, 209.2)                                | 111.0 (36.2, 232.5)                             | 106.6 (32.9, 222.9)              |
| Fish intake (g/day), median (5 <sup>th</sup> , 95 <sup>th</sup> perc)   | 27.1 (1.6, 110.4)                               | 26.3 (3.0, 110.9)                           | 28.6 (3.8, 93.1)                                   | 30.4 (2.5, 119.8)                               | 28.8 (2.5, 113.2)                |
| Energy intake (kcal/day), median (5 <sup>th</sup> , 95 <sup>th</sup> perc)  | 2120.1 (1292.2, 3355.0)                         | 2037.3 (1304.3, 3413.5)                     | 2094.8 (1290.7, 3334.1)                            | 2300.0 (1390.6, 3555.7)                         | 2188.3 (1327.7, 3480.4)          |
| Fasting status, n (%) <sup>d</sup>  |   |   |  |   |                                  |
| ≥6 hours  | 375 (76.4)                                      | 223 (35.5)                                  | 86 (30.8)  | 482 (32.1)                                      | 1,166 (40.2)                     |
| 3-5.9 hours   | 92 (18.7)                                       | 121 (19.3)                                  | 59 (21.2)  | 292 (19.5)                                      | 564 (19.5)                       |
| <3 hours  | 24 (4.9)  | 284 (45.2)                                  | 134 (48.0)   | 727 (48.4)                                      | 1,169 (40.3)                     |
| Time between blood collection and metabolomics analysis (years), median (5 <sup>th</sup> , 95 <sup>th</sup> perc) | 21.1 (18.2, 22.8)                               | 21.0 (18.2, 23.2)                           | 17.3 (14.6, 20.0)                                  | 20.7 (18.3, 22.9)                               | 20.6 (16.9, 22.9)                |
| Country, n (%)  |   |   |  |   |                                  |
| Denmark   | 0 (0.0)   | 0 (0.0)                                     | 51 (15.6)  | 0 (0.0)   | 51 (1.7)                         |
| France  | 24 (4.9)  | 16 (2.5)                                    | 0 (0.0)  | 0 (0.0)   | 40 (1.3)                         |
| Germany   | 41 (8.4)  | 153 (24.1)                                  | 63 (19.3)  | 347 (22.8)                                      | 604 (20.3)                       |
| Greece  | 23 (4.7)  | 28 (4.4)                                    | 31 (9.5)   | 36 (2.4)  | 118 (4.0)                        |
| Italy   | 204 (41.6)                                      | 129 (20.3)                                  | 52 (15.9)  | 273 (18.0)                                      | 658 (22.1)                       |
| Norway  | 0 (0.0)   | 14 (2.2)                                    | 0 (0.0)  | 0 (0.0)   | 14 (0.5)                         |
| Spain   | 114 (23.2)                                      | 123 (19.4)                                  | 31 (9.5)   | 303 (19.9)                                      | 571 (19.2)                       |
| Sweden  | 0 (0.0)   | 0 (0.0)                                     | 48 (14.7)  | 0 (0.0)   | 48 (1.6)                         |



|                 |          |            |           |            |            |
|-----------------|----------|------------|-----------|------------|------------|
| The Netherlands | 40 (8.2) | 68 (10.7)  | 16 (4.9)  | 72 (4.7)   | 196 (6.6)  |
| United Kingdom  | 45 (9.2) | 104 (16.4) | 35 (10.7) | 490 (32.2) | 674 (22.7) |

Abbreviations: n, number; NA, not applicable (no women among prostate cancer controls), perc, percentile; SD, standard deviation.

<sup>a</sup> Data missing for 121 participants (99 men and 22 women).

<sup>b</sup> Cambridge physical activity index: cross-classification of the level of occupational activity with cycling and sports activities and recreational activities(1); data missing for 41 participants (36 men and 5 women)

<sup>c</sup> Data missing for 42 participants (3 from colorectal cancer, 8 from kidney cancer, 6 from hepatobiliary cancer, and 25 from prostate cancer case-control study).

<sup>d</sup> Data missing for 75 participants (24 from colorectal cancer [4.9%], 7 from kidney cancer [1.1%], 48 from hepatobiliary cancer [14.7], and 20 from prostate cancer case-control study [1.3%]).

| <b>Supplementary Table 3.</b> Summary statistics of untransformed concentrations (µM) of metabolites included in the current analysis (n=123) |       |          |          |        |          |           |       |         |
|---|-------|----------|----------|--------|----------|-----------|-------|---------|
|   | n     | Mean     | SD       | Median | 5th perc | 95th perc | Min   | Max     |
| <b>Acylcarnitines</b>   |       |          |          |        |          |           |       |         |
| Acylcarnitine C0  | 2,974 | 32.73461 | 7.389134 | 32.1   | 22.2     | 45.9      | 8.38  | 69.985  |
| Acylcarnitine C14:1   | 2,935 | 0.060699 | 0.030026 | 0.055  | 0.027    | 0.111     | 0.008 | 0.391   |
| Acylcarnitine C16   | 2,935 | 0.099341 | 0.036127 | 0.093  | 0.057    | 0.157     | 0.031 | 0.499   |
| Acylcarnitine C18   | 2,935 | 0.049809 | 0.018678 | 0.047  | 0.025    | 0.084     | 0.012 | 0.278   |
| Acylcarnitine C18:1   | 2,935 | 0.115449 | 0.056586 | 0.101  | 0.06     | 0.216     | 0.026 | 0.615   |
| Acylcarnitine C18:2   | 2,935 | 0.052078 | 0.035809 | 0.043  | 0.021    | 0.113     | 0.006 | 0.448   |
| Acylcarnitine C2  | 2,974 | 5.16648  | 1.914669 | 4.79   | 2.87     | 8.82      | 1.58  | 19.792  |
| Acylcarnitine C3  | 2,935 | 0.351729 | 0.117688 | 0.333  | 0.203    | 0.579     | 0.086 | 0.996   |
| Acylcarnitine C4  | 2,790 | 0.209533 | 0.100354 | 0.187  | 0.113    | 0.375     | 0.05  | 2.11    |
| Acylcarnitine C5  | 2,756 | 0.145771 | 0.051897 | 0.141  | 0.061    | 0.232     | 0.029 | 0.528   |
| <b>Amino acids</b>  |       |          |          |        |          |           |       |         |
| Alanine   | 2,972 | 346.0491 | 92.84259 | 333.5  | 217      | 517       | 136   | 776     |
| Arginine  | 2,972 | 59.87138 | 29.16129 | 56.1   | 17.8     | 115       | 2.5   | 249     |
| Asparagine  | 2,972 | 42.23913 | 11.1565  | 39.9   | 29.2     | 62.5      | 17.2  | 122     |
| Citrulline  | 2,972 | 30.58997 | 9.411851 | 29.2   | 18.3     | 47.4      | 6.21  | 131     |
| Glutamine   | 2,972 | 595.7638 | 94.65734 | 594    | 445      | 754       | 271   | 985     |
| Glutamate   | 2,972 | 61.75424 | 43.80076 | 49.95  | 21.9     | 144       | 5     | 513     |
| Glycine   | 2,972 | 196.9827 | 65.91607 | 181    | 124      | 335       | 86.5  | 632     |
| Histidine   | 2,972 | 72.4718  | 13.63417 | 70.2   | 54.8     | 97.6      | 31.8  | 173     |
| Isoleucine  | 2,972 | 70.21726 | 22.61768 | 66.05  | 42.9     | 112       | 23.5  | 267.1   |
| Leucine   | 2,971 | 130.3946 | 37.09274 | 123    | 82.4     | 199       | 25    | 383     |
| Lysine  | 2,972 | 190.1272 | 44.11736 | 185    | 128      | 267       | 67.5  | 424     |
| Methionine  | 2,972 | 20.34027 | 6.056021 | 19.3   | 12.9     | 31.5      | 2.5   | 69.3    |
| Ornithine   | 2,972 | 86.15192 | 32.37985 | 80.25  | 46.7     | 149       | 23.9  | 319     |
| Phenylalanine   | 2,972 | 59.42937 | 13.428   | 56.8   | 42.6     | 85.1      | 28.5  | 155     |
| Proline   | 2,972 | 188.2811 | 59.69239 | 179    | 109      | 298       | 57    | 646     |
| Serine  | 2,972 | 92.26396 | 28.44239 | 86.95  | 59.4     | 146       | 33.8  | 329     |
| Threonine   | 2,972 | 109.053  | 27.08418 | 106    | 72       | 157       | 40.8  | 254     |
| Tryptophan  | 2,972 | 54.13321 | 11.2671  | 52.8   | 38.1     | 73.9      | 21    | 114     |
| Tyrosine  | 2,972 | 64.9753  | 16.65244 | 62.5   | 42.9     | 96.2      | 20.8  | 181     |
| Valine  | 2,972 | 210.035  | 46.20568 | 205    | 145      | 293       | 100   | 450     |
| t4-hydroxyproline   | 2,645 | 9.042219 | 4.810462 | 7.84   | 4.19     | 17.9      | 2.43  | 62.9    |
| <b>Biogenic amines</b>  |       |          |          |        |          |           |       |         |
| ADMA  | 2,888 | 0.400684 | 0.109534 | 0.393  | 0.258    | 0.589     | 0.125 | 0.951   |
| Creatine  | 2,972 | 67.89186 | 18.30918 | 66.55  | 44.7     | 94.8      | 29.5  | 513     |
| Kynurenine  | 2,972 | 2.217786 | 0.671095 | 2.095  | 1.37     | 3.44      | 0.5   | 6.99    |
| Taurine   | 2,972 | 57.2146  | 30.62363 | 48     | 30.1     | 120       | 19.6  | 200     |
| <b>Glycerophospholipids</b>   |       |          |          |        |          |           |       |         |
| LysoPC a C16:0  | 2,974 | 110.6712 | 37.07529 | 102    | 68.8     | 187.694   | 45.8  | 321.972 |
| LysoPC a C16:1  | 2,974 | 3.202193 | 1.318059 | 2.95   | 1.64     | 5.621     | 0.9   | 18.14   |
| LysoPC a C17:0  | 2,974 | 2.174364 | 0.948001 | 1.98   | 1.08     | 4.062     | 0.549 | 7.285   |
| LysoPC a C18:0  | 2,974 | 35.91004 | 14.50811 | 32.05  | 20.7     | 66.8      | 9.74  | 146.171 |
| LysoPC a C18:1  | 2,974 | 24.52513 | 9.907317 | 22.4   | 13       | 43.2      | 7.51  | 94.262  |
| LysoPC a C18:2  | 2,974 | 34.70049 | 14.16139 | 31.9   | 17.9     | 60.828    | 7.49  | 129.118 |
| LysoPC a C20:3  | 2,974 | 2.456442 | 0.974579 | 2.27   | 1.24     | 4.35      | 0.413 | 9.243   |
| LysoPC a C20:4  | 2,974 | 6.606712 | 2.508269 | 6.18   | 3.41     | 11.377    | 1.89  | 21.659  |

|             |       |          |          |         |         |        |         |         |
|-------------|-------|----------|----------|---------|---------|--------|---------|---------|
| PC aa C28:1 | 2,974 | 2.48236  | 0.807288 | 2.36    | 1.38    | 3.97   | 0.573   | 7.74    |
| PC aa C30:0 | 2,974 | 3.471262 | 1.396116 | 3.225   | 1.71    | 6.16   | 0.903   | 12.604  |
| PC aa C32:0 | 2,974 | 19.52583 | 4.882344 | 19      | 12.5    | 28.5   | 8.17    | 42.8    |
| PC aa C32:1 | 2,974 | 23.27354 | 13.97404 | 20.1    | 7.93    | 50.1   | 3.49    | 123     |
| PC aa C32:2 | 2,974 | 5.912849 | 2.318035 | 5.62    | 2.64    | 10.2   | 0.333   | 16.1    |
| PC aa C32:3 | 2,974 | 0.773056 | 0.246226 | 0.727   | 0.452   | 1.24   | 0.299   | 2.24    |
| PC aa C34:1 | 2,974 | 251.3815 | 80.18321 | 236     | 150     | 402    | 76.5    | 716     |
| PC aa C34:2 | 2,974 | 468.2106 | 165.9334 | 493.5   | 212.683 | 719    | 147.605 | 957     |
| PC aa C34:3 | 2,974 | 20.58805 | 7.311645 | 19.4    | 10.7    | 33.614 | 4.77    | 67.909  |
| PC aa C34:4 | 2,974 | 2.345382 | 0.87204  | 2.2     | 1.17    | 4.01   | 0.224   | 7.415   |
| PC aa C36:0 | 2,974 | 2.741276 | 1.151084 | 2.57    | 1.25    | 4.68   | 0.101   | 12.7    |
| PC aa C36:1 | 2,974 | 52.63843 | 16.50842 | 49.9    | 31      | 83.508 | 16.3    | 150.315 |
| PC aa C36:2 | 2,974 | 274.449  | 67.76033 | 271     | 177     | 391    | 78.6    | 537     |
| PC aa C36:3 | 2,974 | 159.0656 | 37.48239 | 156     | 105     | 225    | 42.1    | 336     |
| PC aa C36:4 | 2,974 | 206.3662 | 56.28536 | 197     | 130     | 311    | 58.2    | 519     |
| PC aa C36:5 | 2,974 | 30.82985 | 19.38193 | 26.0705 | 11.5    | 68.636 | 3.58    | 240     |
| PC aa C36:6 | 2,974 | 1.266968 | 0.563601 | 1.16    | 0.59    | 2.316  | 0.193   | 6.52    |
| PC aa C38:0 | 2,974 | 2.997285 | 0.986715 | 2.83    | 1.72    | 4.8    | 1       | 8.669   |
| PC aa C38:3 | 2,974 | 46.52686 | 13.09129 | 44.8    | 28.2    | 70.913 | 14.6    | 112.289 |
| PC aa C38:4 | 2,974 | 99.32027 | 27.23202 | 96.1    | 60.7    | 149    | 21.4    | 236     |
| PC aa C38:5 | 2,974 | 51.2289  | 14.55407 | 49.2    | 31.2    | 77.6   | 17.6    | 150     |
| PC aa C38:6 | 2,974 | 88.55192 | 28.45438 | 84.2    | 49.9    | 142    | 24      | 230.756 |
| PC aa C40:2 | 2,881 | 0.276511 | 0.110369 | 0.257   | 0.169   | 0.457  | 0.119   | 3.02    |
| PC aa C40:3 | 2,881 | 0.461409 | 0.169306 | 0.422   | 0.281   | 0.77   | 0.139   | 2.74    |
| PC aa C40:4 | 2,974 | 2.654658 | 0.813049 | 2.528   | 1.59    | 4.1    | 0.529   | 8.959   |
| PC aa C40:5 | 2,974 | 6.590204 | 2.266583 | 6.23    | 3.58    | 10.642 | 2.19    | 30.1    |
| PC aa C40:6 | 2,974 | 26.02427 | 9.140255 | 24.8    | 13.9    | 42.9   | 6.8     | 89.466  |
| PC aa C42:0 | 2,974 | 0.376757 | 0.156556 | 0.341   | 0.19    | 0.679  | 0.123   | 1.469   |
| PC aa C42:1 | 2,974 | 0.190883 | 0.079939 | 0.174   | 0.098   | 0.348  | 0.059   | 0.722   |
| PC aa C42:2 | 2,974 | 0.169405 | 0.063685 | 0.158   | 0.097   | 0.284  | 0.039   | 0.749   |
| PC aa C42:4 | 2,881 | 0.108635 | 0.034551 | 0.102   | 0.065   | 0.172  | 0.026   | 0.527   |
| PC aa C42:5 | 2,881 | 0.234329 | 0.091164 | 0.215   | 0.128   | 0.407  | 0.066   | 1.09    |
| PC aa C42:6 | 2,881 | 0.365058 | 0.137807 | 0.337   | 0.208   | 0.632  | 0.092   | 1.472   |
| PC ae C30:0 | 2,881 | 0.298554 | 0.104036 | 0.284   | 0.157   | 0.489  | 0.05    | 0.961   |
| PC ae C30:2 | 2,881 | 0.080207 | 0.03334  | 0.074   | 0.042   | 0.141  | 0.023   | 0.461   |
| PC ae C32:1 | 2,974 | 3.675022 | 0.910912 | 3.59    | 2.37    | 5.283  | 1.36    | 9.031   |
| PC ae C32:2 | 2,974 | 1.049277 | 0.266466 | 1.0205  | 0.665   | 1.53   | 0.396   | 2.382   |
| PC ae C34:0 | 2,974 | 2.005947 | 0.639761 | 1.92    | 1.15    | 3.17   | 0.587   | 6.23    |
| PC ae C34:1 | 2,974 | 12.69445 | 3.334533 | 12.3    | 7.98    | 18.7   | 4.68    | 28.9    |
| PC ae C34:2 | 2,974 | 15.37617 | 4.099373 | 14.954  | 9.5     | 22.9   | 5.36    | 39.151  |
| PC ae C34:3 | 2,974 | 10.26412 | 3.081846 | 9.8725  | 5.93    | 15.9   | 3.47    | 29.731  |
| PC ae C36:0 | 2,881 | 0.971688 | 0.308394 | 0.917   | 0.587   | 1.501  | 0.346   | 3.86    |
| PC ae C36:1 | 2,974 | 9.70715  | 3.086505 | 9.27    | 5.78    | 14.957 | 3.45    | 72.3    |
| PC ae C36:2 | 2,974 | 17.87198 | 4.853692 | 17.249  | 10.9    | 26.3   | 6.2     | 45.4    |
| PC ae C36:3 | 2,974 | 9.347051 | 2.313299 | 9.11    | 6.05    | 13.5   | 3.44    | 22.635  |
| PC ae C36:4 | 2,974 | 19.44095 | 5.55142  | 18.7    | 11.9    | 29.4   | 7.33    | 50.556  |
| PC ae C36:5 | 2,974 | 13.52497 | 3.936125 | 13.1    | 7.93    | 20.6   | 4.62    | 31.4    |
| PC ae C38:0 | 2,427 | 2.371954 | 0.827715 | 2.22    | 1.35    | 3.91   | 0.776   | 6.41    |
| PC ae C38:2 | 2,974 | 2.28626  | 0.768703 | 2.17    | 1.43    | 3.46   | 0.948   | 25.1    |

|                      |       |          |          |         |       |         |       |         |
|----------------------|-------|----------|----------|---------|-------|---------|-------|---------|
| PC ae C38:3          | 2,974 | 4.21808  | 1.156773 | 4.08    | 2.62  | 6.12    | 1.71  | 22.7    |
| PC ae C38:4          | 2,974 | 12.90652 | 3.18535  | 12.543  | 8.41  | 18.4    | 4.84  | 38.1    |
| PC ae C38:5          | 2,974 | 17.72872 | 4.2043   | 17.3    | 11.7  | 25.3    | 7.71  | 41.8    |
| PC ae C38:6          | 2,974 | 8.03502  | 2.288435 | 7.71    | 4.9   | 12.1    | 3.03  | 23.514  |
| PC ae C40:1          | 2,974 | 1.195129 | 0.31475  | 1.16    | 0.77  | 1.736   | 0.409 | 4.62    |
| PC ae C40:2          | 2,974 | 1.541132 | 0.464061 | 1.47    | 0.921 | 2.38    | 0.539 | 6.01    |
| PC ae C40:3          | 2,881 | 0.818917 | 0.245829 | 0.789   | 0.537 | 1.2     | 0.363 | 7.84    |
| PC ae C40:4          | 2,974 | 1.951638 | 0.437764 | 1.91    | 1.35  | 2.73    | 0.762 | 7.17    |
| PC ae C40:5          | 2,974 | 3.010946 | 0.696726 | 2.937   | 2.06  | 4.232   | 1.39  | 8.294   |
| PC ae C40:6          | 2,974 | 4.359259 | 1.206708 | 4.18    | 2.71  | 6.523   | 1.79  | 11.744  |
| PC ae C42:1          | 2,913 | 0.308291 | 0.079129 | 0.298   | 0.213 | 0.436   | 0.078 | 1.88    |
| PC ae C42:2          | 2,974 | 0.414051 | 0.11783  | 0.395   | 0.258 | 0.633   | 0.168 | 1.55    |
| PC ae C42:3          | 2,974 | 0.5581   | 0.158788 | 0.539   | 0.339 | 0.846   | 0.205 | 1.76    |
| PC ae C42:4          | 2,974 | 0.560443 | 0.160301 | 0.537   | 0.345 | 0.85    | 0.212 | 1.811   |
| PC ae C42:5          | 2,974 | 1.475112 | 0.34811  | 1.43    | 0.996 | 2.09    | 0.665 | 3.878   |
| PC ae C44:4          | 2,974 | 0.2082   | 0.073364 | 0.193   | 0.116 | 0.352   | 0.039 | 0.709   |
| PC ae C44:5          | 2,974 | 0.867868 | 0.324382 | 0.803   | 0.474 | 1.481   | 0.238 | 2.917   |
| PC ae C44:6          | 2,974 | 0.709821 | 0.24342  | 0.669   | 0.402 | 1.153   | 0.249 | 2.316   |
| <b>Sphingolipids</b> |       |          |          |         |       |         |       |         |
| SM C16:0             | 2,974 | 78.57645 | 25.29808 | 71.1    | 48.8  | 129.135 | 23.8  | 181.565 |
| SM C16:1             | 2,974 | 11.11282 | 4.202389 | 9.72    | 6.58  | 19.562  | 3.58  | 33.319  |
| SM C18:0             | 2,974 | 14.52333 | 6.613006 | 12.2585 | 7.62  | 28.555  | 3.72  | 48.362  |
| SM C18:1             | 2,974 | 7.102597 | 3.262151 | 5.97    | 3.69  | 13.8    | 2.15  | 26.78   |
| SM C20:2             | 2,974 | 0.3769   | 0.292159 | 0.294   | 0.11  | 0.924   | 0.036 | 4.03    |
| SM C24:0             | 2,974 | 9.350157 | 4.563673 | 7.525   | 4.69  | 18.3    | 2.47  | 34.6    |
| SM C24:1             | 2,974 | 19.9373  | 10.00519 | 15.9    | 9.58  | 39.55   | 4.97  | 71.3    |
| SM(OH) C14:1         | 2,974 | 4.542725 | 1.863094 | 4.08    | 2.34  | 8.249   | 1.13  | 14.151  |
| SM(OH) C16:1         | 2,974 | 2.299296 | 1.053568 | 1.97    | 1.14  | 4.47    | 0.552 | 7.327   |
| SM(OH) C22:1         | 2,974 | 6.851216 | 3.262027 | 5.59    | 3.39  | 13.592  | 1.46  | 20.798  |
| SM(OH) C22:2         | 2,974 | 5.240825 | 2.565633 | 4.33    | 2.58  | 10.412  | 1.44  | 16.456  |
| SM(OH) C24:1         | 2,974 | 0.553493 | 0.311254 | 0.43    | 0.236 | 1.19    | 0.09  | 1.86    |
| <b>Hexoses</b>       |       |          |          |         |       |         |       |         |
| Hexoses              | 2,974 | 4113.384 | 1542.154 | 4004.5  | 2178  | 6124    | 750   | 20297   |

Abbreviations: min, minimum; max, maximum; n, number; perc, percentile; SD, standard deviation.

For an explanation of abbreviated metabolite names, see Supplementary Table 1.

| <b>Supplementary Table 4.</b> Results of discovery and replication analysis on associations of alcohol intake with concentrations of metabolites included in the current analysis (n=123) <sup>a</sup> |   |       |      |          |                             |                |   |       |      |          |                                    |                |
|--|---|-------|------|----------|-----------------------------|----------------|---|-------|------|----------|------------------------------------|----------------|
| Metabolite   | Discovery analysis (n=1,983) <sup>b</sup> |       |      |          |                             |                | Replication analysis (n=991) <sup>b</sup> |       |      |          |                                    |                |
|  | n   | β     | SE   | p-value  | FDR<br>q-value <sup>c</sup> | R <sup>2</sup> | n   | β     | SE   | p-value  | Bonf.-adj.<br>p-value <sup>d</sup> | R <sup>2</sup> |
| <b>Acylcarnitines</b>  |   |       |      |          |                             |                |   |       |      |          |                                    |                |
| Acylcarnitine C0   | 1,983                                     | 0.05  | 0.02 | 0.003939 | <b>0.008354</b>             | 0.06           | 991                                       | 0.02  | 0.02 | 0.474501 | 1                                  | 0.07           |
| Acylcarnitine C14:1  | 1,956                                     | 0.05  | 0.02 | 0.002151 | <b>0.004725</b>             | 0.09           | 979                                       | 0.08  | 0.02 | 0.000653 | <b>0.047001</b>                    | 0.14           |
| Acylcarnitine C16  | 1,956                                     | 0.11  | 0.02 | <1E-12   | <b>&lt;1E-12</b>            | 0.15           | 979                                       | 0.13  | 0.02 | 4.38E-09 | <b>3.15E-07</b>                    | 0.20           |
| Acylcarnitine C18  | 1,956                                     | 0.06  | 0.02 | 0.000534 | <b>0.001289</b>             | 0.09           | 979                                       | 0.03  | 0.02 | 0.192015 | 1                                  | 0.11           |
| Acylcarnitine C18:1  | 1,956                                     | 0.06  | 0.02 | 0.000236 | <b>0.000617</b>             | 0.16           | 979                                       | 0.08  | 0.02 | 0.000669 | <b>0.048198</b>                    | 0.25           |
| Acylcarnitine C18:2  | 1,956                                     | 0.00  | 0.02 | 0.892851 | 0.914111                    | 0.18           | NA  |       |      |          |                                    |                |
| Acylcarnitine C2   | 1,983                                     | 0.07  | 0.02 | 5.9E-05  | <b>0.000191</b>             | 0.10           | 991                                       | 0.06  | 0.03 | 0.013201 | 0.950489                           | 0.13           |
| Acylcarnitine C3   | 1,956                                     | -0.05 | 0.02 | 0.005628 | <b>0.011348</b>             | 0.06           | 979                                       | -0.06 | 0.02 | 0.02248  | 1                                  | 0.12           |
| Acylcarnitine C4   | 1,852                                     | -0.03 | 0.02 | 0.119927 | 0.175608                    | 0.04           | NA  |       |      |          |                                    |                |
| Acylcarnitine C5   | 1,828                                     | 0.01  | 0.02 | 0.41167  | 0.506354                    | 0.04           | NA  |       |      |          |                                    |                |
| <b>Amino acids</b>   |   |       |      |          |                             |                |   |       |      |          |                                    |                |
| Alanine  | 1,983                                     | -0.02 | 0.02 | 0.16263  | 0.229925                    | 0.11           | NA  |       |      |          |                                    |                |
| Arginine   | 1,983                                     | -0.05 | 0.01 | 0.000173 | <b>0.000506</b>             | 0.19           | 989                                       | -0.07 | 0.02 | 0.00155  | 0.11157                            | 0.23           |
| Asparagine   | 1,983                                     | 0.02  | 0.02 | 0.209993 | 0.28699                     | 0.13           | NA  |       |      |          |                                    |                |
| Citrulline   | 1,983                                     | -0.10 | 0.02 | 8.2E-10  | <b>5.93E-09</b>             | 0.11           | 989                                       | -0.10 | 0.02 | 1.24E-05 | <b>0.00089</b>                     | 0.16           |
| Glutamine  | 1,983                                     | -0.01 | 0.02 | 0.452687 | 0.551292                    | 0.05           | NA  |       |      |          |                                    |                |
| Glutamate  | 1,983                                     | 0.04  | 0.01 | 0.001849 | <b>0.004135</b>             | 0.26           | 989                                       | 0.04  | 0.02 | 0.059717 | 1                                  | 0.26           |
| Glycine  | 1,983                                     | -0.02 | 0.01 | 0.270663 | 0.346787                    | 0.11           | NA  |       |      |          |                                    |                |
| Histidine  | 1,983                                     | 0.02  | 0.01 | 0.256257 | 0.335315                    | 0.08           | NA  |       |      |          |                                    |                |
| Isoleucine   | 1,983                                     | 0.00  | 0.02 | 0.798684 | 0.854245                    | 0.08           | NA  |       |      |          |                                    |                |
| Leucine  | 1,982                                     | 0.00  | 0.02 | 0.97628  | 0.97628                     | 0.08           | NA  |       |      |          |                                    |                |
| Lysine   | 1,983                                     | 0.01  | 0.02 | 0.600089 | 0.689822                    | 0.06           | NA  |       |      |          |                                    |                |
| Methionine   | 1,983                                     | 0.02  | 0.02 | 0.218007 | 0.291467                    | 0.08           | NA  |       |      |          |                                    |                |
| Ornithine  | 1,983                                     | -0.01 | 0.02 | 0.327788 | 0.415648                    | 0.17           | NA  |       |      |          |                                    |                |
| Phenylalanine  | 1,983                                     | -0.01 | 0.01 | 0.675429 | 0.755252                    | 0.10           | NA  |       |      |          |                                    |                |
| Proline  | 1,983                                     | -0.02 | 0.02 | 0.153941 | 0.220172                    | 0.10           | NA  |       |      |          |                                    |                |
| Serine   | 1,983                                     | -0.03 | 0.01 | 0.049036 | 0.079361                    | 0.10           | NA  |       |      |          |                                    |                |
| Threonine  | 1,983                                     | 0.03  | 0.02 | 0.123534 | 0.178761                    | 0.09           | NA  |       |      |          |                                    |                |
| Tryptophan   | 1,983                                     | 0.01  | 0.02 | 0.722739 | 0.786698                    | 0.06           | NA  |       |      |          |                                    |                |
| Tyrosine   | 1,983                                     | 0.06  | 0.02 | 0.000135 | <b>0.000416</b>             | 0.11           | 989                                       | 0.05  | 0.02 | 0.027538 | 1                                  | 0.12           |
| Valine   | 1,983                                     | -0.01 | 0.02 | 0.516758 | 0.617099                    | 0.08           | NA  |       |      |          |                                    |                |
| t4-hydroxyproline  | 1,774                                     | 0.03  | 0.02 | 0.058478 | 0.091048                    | 0.12           | NA  |       |      |          |                                    |                |
| <b>Biogenic amines</b>   |   |       |      |          |                             |                |   |       |      |          |                                    |                |
| ADMA   | 1,930                                     | -0.02 | 0.02 | 0.229624 | 0.303697                    | 0.04           | NA  |       |      |          |                                    |                |
| Creatine   | 1,983                                     | 0.01  | 0.01 | 0.527088 | 0.623383                    | 0.04           | NA  |       |      |          |                                    |                |
| Kynurenine   | 1,983                                     | -0.04 | 0.02 | 0.017437 | <b>0.03064</b>              | 0.10           | 989                                       | -0.05 | 0.02 | 0.019566 | 1                                  | 0.13           |
| Taurine  | 1,983                                     | 0.03  | 0.01 | 0.018218 | <b>0.031561</b>             | 0.32           | 989                                       | 0.03  | 0.02 | 0.098293 | 1                                  | 0.31           |
| <b>Glycerophospholipids</b>  |   |       |      |          |                             |                |   |       |      |          |                                    |                |
| LysoPC a C16:0   | 1,983                                     | 0.09  | 0.01 | 1.8E-10  | <b>1.48E-09</b>             | 0.16           | 991                                       | 0.08  | 0.02 | 6.38E-05 | <b>0.004596</b>                    | 0.13           |
| LysoPC a C16:1   | 1,983                                     | 0.11  | 0.02 | <1E-12   | <b>&lt;1E-12</b>            | 0.14           | 991                                       | 0.12  | 0.02 | 2.47E-08 | <b>1.78E-06</b>                    | 0.14           |
| LysoPC a C17:0   | 1,983                                     | -0.09 | 0.01 | 1E-10    | <b>9.46E-10</b>             | 0.19           | 991                                       | -0.11 | 0.02 | 2E-07    | <b>1.44E-05</b>                    | 0.17           |
| LysoPC a C18:0   | 1,983                                     | -0.01 | 0.01 | 0.266416 | 0.344939                    | 0.14           | NA  |       |      |          |                                    |                |
| LysoPC a C18:1   | 1,983                                     | 0.05  | 0.01 | 0.000221 | <b>0.000605</b>             | 0.15           | 991                                       | 0.05  | 0.02 | 0.024597 | 1                                  | 0.15           |

|                |       |       |      |          |                  |      |     |       |      |          |                  |      |
|----------------|-------|-------|------|----------|------------------|------|-----|-------|------|----------|------------------|------|
| LysoPC a C18:2 | 1,983 | 0.01  | 0.02 | 0.558303 | 0.647842         | 0.14 | NA  |       |      |          |                  |      |
| LysoPC a C20:3 | 1,983 | 0.04  | 0.02 | 0.007569 | <b>0.014778</b>  | 0.08 | 991 | 0.06  | 0.02 | 0.003616 | 0.260342         | 0.10 |
| LysoPC a C20:4 | 1,983 | 0.06  | 0.02 | 3.46E-05 | <b>0.000122</b>  | 0.10 | 991 | 0.08  | 0.02 | 0.000119 | <b>0.008543</b>  | 0.12 |
| PC aa C28:1    | 1,983 | 0.03  | 0.01 | 0.014347 | <b>0.025951</b>  | 0.17 | 991 | 0.01  | 0.02 | 0.460948 | 1                | 0.16 |
| PC aa C30:0    | 1,983 | 0.10  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 991 | 0.12  | 0.02 | 4.29E-08 | <b>3.09E-06</b>  | 0.22 |
| PC aa C32:0    | 1,983 | 0.12  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.11 | 991 | 0.13  | 0.02 | 5.3E-10  | <b>3.82E-08</b>  | 0.15 |
| PC aa C32:1    | 1,983 | 0.20  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.25 | 991 | 0.22  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.28 |
| PC aa C32:2    | 1,983 | 0.07  | 0.02 | 7.27E-06 | <b>2.98E-05</b>  | 0.13 | 991 | 0.10  | 0.02 | 1.62E-05 | <b>0.001163</b>  | 0.18 |
| PC aa C32:3    | 1,983 | -0.04 | 0.01 | 0.002701 | <b>0.005827</b>  | 0.20 | 991 | -0.08 | 0.02 | 4.83E-05 | <b>0.003481</b>  | 0.22 |
| PC aa C34:1    | 1,983 | 0.17  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 991 | 0.14  | 0.02 | 2E-11    | <b>1.44E-09</b>  | 0.13 |
| PC aa C34:2    | 1,983 | 0.03  | 0.01 | 3.46E-06 | <b>1.47E-05</b>  | 0.04 | 991 | 0.03  | 0.01 | 0.008202 | 0.590576         | 0.04 |
| PC aa C34:3    | 1,983 | 0.07  | 0.01 | 3.98E-07 | <b>2.13E-06</b>  | 0.24 | 991 | 0.08  | 0.02 | 4.71E-05 | <b>0.003392</b>  | 0.28 |
| PC aa C34:4    | 1,983 | 0.11  | 0.02 | 1.5E-10  | <b>1.32E-09</b>  | 0.12 | 991 | 0.13  | 0.02 | 1.87E-08 | <b>1.34E-06</b>  | 0.17 |
| PC aa C36:0    | 1,983 | 0.05  | 0.01 | 0.000227 | <b>0.000607</b>  | 0.16 | 991 | 0.04  | 0.02 | 0.044044 | 1                | 0.18 |
| PC aa C36:1    | 1,983 | 0.10  | 0.02 | 1.67E-09 | <b>1.14E-08</b>  | 0.05 | 991 | 0.08  | 0.02 | 0.000812 | 0.058493         | 0.06 |
| PC aa C36:2    | 1,983 | 0.00  | 0.01 | 0.875533 | 0.907071         | 0.03 | NA  |       |      |          |                  |      |
| PC aa C36:3    | 1,983 | 0.03  | 0.02 | 0.074809 | 0.115019         | 0.05 | NA  |       |      |          |                  |      |
| PC aa C36:4    | 1,983 | 0.14  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.11 | 991 | 0.15  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.17 |
| PC aa C36:5    | 1,983 | 0.16  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 991 | 0.17  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.23 |
| PC aa C36:6    | 1,983 | 0.11  | 0.02 | 2.1E-10  | <b>1.61E-09</b>  | 0.15 | 991 | 0.10  | 0.02 | 6.15E-06 | <b>0.000443</b>  | 0.18 |
| PC aa C38:0    | 1,983 | 0.00  | 0.01 | 0.827574 | 0.877514         | 0.25 | NA  |       |      |          |                  |      |
| PC aa C38:3    | 1,983 | 0.00  | 0.02 | 0.755364 | 0.814998         | 0.13 | NA  |       |      |          |                  |      |
| PC aa C38:4    | 1,983 | 0.03  | 0.02 | 0.056358 | 0.088872         | 0.10 | NA  |       |      |          |                  |      |
| PC aa C38:5    | 1,983 | 0.09  | 0.02 | 1.92E-07 | <b>1.12E-06</b>  | 0.10 | 991 | 0.11  | 0.02 | 6.34E-06 | <b>0.000456</b>  | 0.12 |
| PC aa C38:6    | 1,983 | 0.12  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 991 | 0.09  | 0.02 | 7.82E-05 | <b>0.005632</b>  | 0.21 |
| PC aa C40:2    | 1,922 | -0.03 | 0.02 | 0.105692 | 0.158538         | 0.14 | NA  |       |      |          |                  |      |
| PC aa C40:3    | 1,922 | 0.00  | 0.02 | 0.899248 | 0.914111         | 0.12 | NA  |       |      |          |                  |      |
| PC aa C40:4    | 1,983 | 0.03  | 0.02 | 0.0503   | 0.080349         | 0.10 | NA  |       |      |          |                  |      |
| PC aa C40:5    | 1,983 | 0.03  | 0.02 | 0.039237 | 0.064349         | 0.15 | NA  |       |      |          |                  |      |
| PC aa C40:6    | 1,983 | 0.03  | 0.02 | 0.029924 | 0.050419         | 0.15 | NA  |       |      |          |                  |      |
| PC aa C42:0    | 1,983 | -0.05 | 0.01 | 7.08E-05 | <b>0.000223</b>  | 0.17 | 991 | -0.03 | 0.02 | 0.058689 | 1                | 0.16 |
| PC aa C42:1    | 1,983 | -0.03 | 0.01 | 0.006508 | <b>0.012911</b>  | 0.17 | 991 | -0.02 | 0.02 | 0.301232 | 1                | 0.16 |
| PC aa C42:2    | 1,983 | 0.05  | 0.01 | 0.000875 | <b>0.002031</b>  | 0.24 | 991 | 0.05  | 0.02 | 0.01158  | 0.83377          | 0.26 |
| PC aa C42:4    | 1,922 | -0.01 | 0.01 | 0.629828 | 0.710723         | 0.04 | NA  |       |      |          |                  |      |
| PC aa C42:5    | 1,922 | 0.01  | 0.01 | 0.499936 | 0.602864         | 0.15 | NA  |       |      |          |                  |      |
| PC aa C42:6    | 1,922 | 0.00  | 0.01 | 0.868533 | 0.907071         | 0.08 | NA  |       |      |          |                  |      |
| PC ae C30:0    | 1,922 | 0.00  | 0.01 | 0.877573 | 0.907071         | 0.18 | NA  |       |      |          |                  |      |
| PC ae C30:2    | 1,922 | -0.05 | 0.01 | 4.96E-05 | <b>0.000165</b>  | 0.11 | 959 | -0.07 | 0.02 | 4.36E-05 | <b>0.003142</b>  | 0.12 |
| PC ae C32:1    | 1,983 | 0.06  | 0.02 | 1.81E-05 | <b>6.75E-05</b>  | 0.07 | 991 | 0.08  | 0.02 | 0.000208 | <b>0.014996</b>  | 0.12 |
| PC ae C32:2    | 1,983 | 0.06  | 0.02 | 0.000367 | <b>0.000921</b>  | 0.07 | 991 | 0.05  | 0.02 | 0.035601 | 1                | 0.08 |
| PC ae C34:0    | 1,983 | 0.04  | 0.02 | 0.013391 | <b>0.024583</b>  | 0.09 | 991 | 0.02  | 0.02 | 0.464805 | 1                | 0.12 |
| PC ae C34:1    | 1,983 | 0.01  | 0.02 | 0.612845 | 0.697962         | 0.08 | NA  |       |      |          |                  |      |
| PC ae C34:2    | 1,983 | -0.04 | 0.02 | 0.004067 | <b>0.008478</b>  | 0.08 | 991 | -0.05 | 0.02 | 0.021188 | 1                | 0.10 |
| PC ae C34:3    | 1,983 | 0.06  | 0.02 | 0.000527 | <b>0.001289</b>  | 0.09 | 991 | 0.04  | 0.02 | 0.062088 | 1                | 0.08 |
| PC ae C36:0    | 1,922 | 0.16  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.13 | 959 | 0.15  | 0.02 | 9E-11    | <b>6.48E-09</b>  | 0.12 |
| PC ae C36:1    | 1,983 | 0.00  | 0.02 | 0.940879 | 0.948592         | 0.06 | NA  |       |      |          |                  |      |
| PC ae C36:2    | 1,983 | -0.11 | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 991 | -0.14 | 0.02 | 1.32E-09 | <b>9.5E-08</b>   | 0.14 |
| PC ae C36:3    | 1,983 | -0.04 | 0.02 | 0.023764 | <b>0.040596</b>  | 0.06 | 991 | -0.05 | 0.02 | 0.033217 | 1                | 0.06 |
| PC ae C36:4    | 1,983 | 0.04  | 0.01 | 0.010777 | <b>0.020084</b>  | 0.15 | 991 | 0.05  | 0.02 | 0.032606 | 1                | 0.19 |

|                      |       |       |      |          |                 |      |     |       |      |          |                 |      |
|----------------------|-------|-------|------|----------|-----------------|------|-----|-------|------|----------|-----------------|------|
| PC ae C36:5          | 1,983 | 0.10  | 0.02 | 1E-11    | <b>1.02E-10</b> | 0.15 | 991 | 0.13  | 0.02 | 5.31E-09 | <b>3.82E-07</b> | 0.18 |
| PC ae C38:0          | 1,616 | 0.09  | 0.02 | 8.47E-07 | <b>4.34E-06</b> | 0.17 | 811 | 0.05  | 0.02 | 0.049169 | 1               | 0.22 |
| PC ae C38:2          | 1,983 | -0.07 | 0.01 | 1.21E-05 | <b>4.65E-05</b> | 0.06 | 991 | -0.05 | 0.02 | 0.014344 | 1               | 0.09 |
| PC ae C38:3          | 1,983 | -0.09 | 0.02 | 5.86E-09 | <b>3.79E-08</b> | 0.08 | 991 | -0.09 | 0.02 | 8.22E-05 | <b>0.005921</b> | 0.11 |
| PC ae C38:4          | 1,983 | -0.05 | 0.02 | 0.001614 | <b>0.003677</b> | 0.11 | 991 | -0.05 | 0.02 | 0.061835 | 1               | 0.14 |
| PC ae C38:5          | 1,983 | 0.02  | 0.02 | 0.213677 | 0.288816        | 0.12 | NA  |       |      |          |                 |      |
| PC ae C38:6          | 1,983 | 0.05  | 0.02 | 0.000744 | <b>0.001759</b> | 0.17 | 991 | 0.06  | 0.02 | 0.011821 | 0.851126        | 0.18 |
| PC ae C40:1          | 1,983 | 0.07  | 0.02 | 4.05E-05 | <b>0.000138</b> | 0.09 | 991 | 0.05  | 0.02 | 0.043308 | 1               | 0.08 |
| PC ae C40:2          | 1,983 | 0.01  | 0.01 | 0.721044 | 0.786698        | 0.12 | NA  |       |      |          |                 |      |
| PC ae C40:3          | 1,922 | -0.05 | 0.01 | 0.000163 | <b>0.000489</b> | 0.10 | 959 | -0.06 | 0.02 | 0.00777  | 0.559431        | 0.12 |
| PC ae C40:4          | 1,983 | -0.08 | 0.02 | 2.17E-06 | <b>9.9E-06</b>  | 0.08 | 991 | -0.05 | 0.03 | 0.039047 | 1               | 0.09 |
| PC ae C40:5          | 1,983 | -0.03 | 0.02 | 0.030533 | 0.050751        | 0.08 | NA  |       |      |          |                 |      |
| PC ae C40:6          | 1,983 | -0.06 | 0.02 | 0.000284 | <b>0.000727</b> | 0.17 | 991 | -0.08 | 0.02 | 0.000539 | <b>0.038842</b> | 0.19 |
| PC ae C42:1          | 1,938 | 0.01  | 0.02 | 0.557053 | 0.647842        | 0.04 | NA  |       |      |          |                 |      |
| PC ae C42:2          | 1,983 | 0.02  | 0.02 | 0.118477 | 0.175574        | 0.10 | NA  |       |      |          |                 |      |
| PC ae C42:3          | 1,983 | 0.02  | 0.01 | 0.084541 | 0.128377        | 0.14 | NA  |       |      |          |                 |      |
| PC ae C42:4          | 1,983 | -0.06 | 0.02 | 0.000204 | <b>0.000584</b> | 0.11 | 991 | -0.04 | 0.02 | 0.094471 | 1               | 0.12 |
| PC ae C42:5          | 1,983 | -0.06 | 0.02 | 0.000217 | <b>0.000605</b> | 0.08 | 991 | -0.03 | 0.02 | 0.181366 | 1               | 0.07 |
| PC ae C44:4          | 1,983 | -0.02 | 0.01 | 0.181462 | 0.250785        | 0.06 | NA  |       |      |          |                 |      |
| PC ae C44:5          | 1,983 | -0.01 | 0.01 | 0.399652 | 0.496538        | 0.10 | NA  |       |      |          |                 |      |
| PC ae C44:6          | 1,983 | -0.04 | 0.01 | 0.007742 | <b>0.01488</b>  | 0.09 | 991 | 0.00  | 0.02 | 0.979539 | 1               | 0.07 |
| <b>Sphingolipids</b> |       |       |      |          |                 |      |     |       |      |          |                 |      |
| SM C16:0             | 1,983 | 0.01  | 0.01 | 0.36541  | 0.458627        | 0.05 | NA  |       |      |          |                 |      |
| SM C16:1             | 1,983 | 0.02  | 0.01 | 0.014882 | <b>0.026528</b> | 0.07 | 991 | 0.00  | 0.01 | 0.761088 | 1               | 0.07 |
| SM C18:0             | 1,983 | 0.04  | 0.01 | 1.07E-05 | <b>4.25E-05</b> | 0.07 | 991 | 0.00  | 0.01 | 0.737895 | 1               | 0.09 |
| SM C18:1             | 1,983 | 0.01  | 0.01 | 0.178527 | 0.249532        | 0.05 | NA  |       |      |          |                 |      |
| SM C20:2             | 1,983 | -0.06 | 0.01 | 1.43E-06 | <b>6.75E-06</b> | 0.26 | 991 | -0.08 | 0.02 | 4.84E-07 | <b>3.48E-05</b> | 0.30 |
| SM C24:0             | 1,983 | 0.04  | 0.01 | 1.27E-06 | <b>6.26E-06</b> | 0.05 | 991 | 0.05  | 0.01 | 2.68E-05 | <b>0.00193</b>  | 0.08 |
| SM C24:1             | 1,983 | 0.03  | 0.01 | 2.8E-05  | <b>0.000101</b> | 0.08 | 991 | 0.04  | 0.01 | 0.000521 | <b>0.037513</b> | 0.14 |
| SM(OH) C14:1         | 1,983 | -0.06 | 0.01 | 3.89E-07 | <b>2.13E-06</b> | 0.14 | 991 | -0.08 | 0.02 | 2.35E-06 | <b>0.000169</b> | 0.16 |
| SM(OH) C16:1         | 1,983 | -0.05 | 0.01 | 2.55E-06 | <b>1.12E-05</b> | 0.07 | 991 | -0.08 | 0.02 | 2.12E-07 | <b>1.53E-05</b> | 0.11 |
| SM(OH) C22:1         | 1,983 | -0.03 | 0.01 | 0.004525 | <b>0.009275</b> | 0.05 | 991 | -0.02 | 0.01 | 0.101529 | 1               | 0.07 |
| SM(OH) C22:2         | 1,983 | -0.05 | 0.01 | 1.34E-07 | <b>8.25E-07</b> | 0.09 | 991 | -0.05 | 0.01 | 2.25E-05 | <b>0.001621</b> | 0.10 |
| SM(OH) C24:1         | 1,983 | 0.00  | 0.01 | 0.694071 | 0.769106        | 0.05 | NA  |       |      |          |                 |      |
| <b>Hexoses</b>       |       |       |      |          |                 |      |     |       |      |          |                 |      |
| Hexoses              | 1,983 | -0.04 | 0.02 | 0.008591 | <b>0.016256</b> | 0.16 | 991 | -0.02 | 0.02 | 0.346628 | 1               | 0.24 |

Abbreviations:  $\beta$ , unstandardized regression coefficient derived from multivariable linear models; Bonf.-adj. p-value, Bonferroni-adjusted p-value ; NA, not applicable (metabolites that were not significant in the discovery analysis were not taken forward to the replication analysis); SE, standard error.

For an explanation of abbreviated metabolite names, see Supplementary Table 1.

<sup>a</sup> Analyzed with multivariable linear regression analyses analyzing associations of alcohol consumption (ln-transformed alcohol intake + 1) as main independent variable and as dependent variables the residuals obtained from linear mixed models with Z-standardized ln-transformed metabolite concentrations as dependent variables, sex as independent variable, and random intercepts for analytical batches nested within studies. Adjusted for: sex; age (y; continuous), body mass index (kg/m<sup>2</sup>; continuous), self-reported physical activity levels (Cambridge physical activity index(1): inactive, moderately inactive, moderately active, active, unknown), fasting status ( $\geq 6$  hours, 3-5.9 hours,  $< 3$  hours, unknown), meat intake (g/day; continuous), fish intake (g/day; continuous), energy intake (kcal/day; continuous), country, and smoking status (current, former, never, unknown).

<sup>b</sup> The discovery and replication set were taken as random samples without replacement of 66.7% and 33.3% of the total dataset, respectively.

<sup>c</sup> The analysis in the discovery set was adjusted for multiple testing using the false discovery rate (FDR) method. Statistically significant associations (FDR q-value $<0.05$ ) are depicted in bold.

<sup>d</sup> The analysis in the replication set was adjusted for multiple testing using Bonferroni correction. Statistically significant associations (Bonferroni-adjusted p-value $<0.05$ ) are depicted in bold.

**Supplementary Table 5.** Comparison of results of sex-stratified discovery analysis on associations of alcohol intake with concentrations of included metabolites (n=123) with results obtained in the total discovery set and results of statistical interaction analysis for sex<sup>a</sup>

| Metabolite                  | Total group (n=1,756) |       |      |          |                          |                | Men (n=1,378) |       |      |          |                          |                | Women (n=378) |       |      |          |                          |                | Interaction analysis <sup>b</sup> |
|-----------------------------|-----------------------|-------|------|----------|--------------------------|----------------|---------------|-------|------|----------|--------------------------|----------------|---------------|-------|------|----------|--------------------------|----------------|-----------------------------------|
|                             | n                     | B     | SE   | p-value  | FDR q-value <sup>c</sup> | R <sup>2</sup> | N             | β     | SE   | p-value  | FDR q-value <sup>c</sup> | R <sup>2</sup> | N             | β     | SE   | p-value  | FDR q-value <sup>b</sup> | R <sup>2</sup> | FDR q-value <sup>c</sup>          |
| <b>Acylcarnitines</b>       |                       |       |      |          |                          |                |               |       |      |          |                          |                |               |       |      |          |                          |                |                                   |
| Acylcarnitine C0            | 1,983                 | 0.05  | 0.02 | 0.003939 | <b>0.008354</b>          | 0.06           | 1,497         | 0.06  | 0.02 | 0.000871 | <b>0.002379</b>          | 0.06           | 486           | 0.00  | 0.04 | 0.967893 | 0.977559                 | 0.14           | 0.196795                          |
| Acylcarnitine C14:1         | 1,956                 | 0.05  | 0.02 | 0.002151 | <b>0.004725</b>          | 0.09           | 1,482         | 0.06  | 0.02 | 0.001833 | <b>0.004336</b>          | 0.09           | 474           | 0.01  | 0.04 | 0.738715 | 0.842254                 | 0.15           | 0.474573                          |
| Acylcarnitine C16           | 1,956                 | 0.11  | 0.02 | <1E-12   | <b>&lt;1E-12</b>         | 0.15           | 1,482         | 0.12  | 0.02 | <1E-12   | <b>&lt;1E-12</b>         | 0.13           | 474           | 0.07  | 0.03 | 0.036787 | 0.17403                  | 0.25           | 0.392036                          |
| Acylcarnitine C18           | 1,956                 | 0.06  | 0.02 | 0.000534 | <b>0.001289</b>          | 0.09           | 1,482         | 0.05  | 0.02 | 0.002657 | <b>0.005837</b>          | 0.07           | 474           | 0.05  | 0.04 | 0.255448 | 0.476062                 | 0.16           | 0.702646                          |
| Acylcarnitine C18:1         | 1,956                 | 0.06  | 0.02 | 0.000236 | <b>0.000617</b>          | 0.16           | 1,482         | 0.06  | 0.02 | 0.001242 | <b>0.003183</b>          | 0.15           | 474           | 0.02  | 0.03 | 0.508463 | 0.687092                 | 0.27           | 0.942879                          |
| Acylcarnitine C18:2         | 1,956                 | 0.00  | 0.02 | 0.892851 | 0.914111                 | 0.18           | 1,482         | 0.00  | 0.02 | 0.891534 | 0.937254                 | 0.15           | 474           | -0.03 | 0.03 | 0.305858 | 0.537437                 | 0.33           | 0.392036                          |
| Acylcarnitine C2            | 1,983                 | 0.07  | 0.02 | 5.9E-05  | <b>0.000191</b>          | 0.10           | 1,497         | 0.07  | 0.02 | 5.45E-05 | <b>0.000186</b>          | 0.09           | 486           | 0.05  | 0.04 | 0.217508 | 0.438582                 | 0.19           | 0.592031                          |
| Acylcarnitine C3            | 1,956                 | -0.05 | 0.02 | 0.005628 | <b>0.011348</b>          | 0.06           | 1,482         | -0.04 | 0.02 | 0.028891 | 0.051501                 | 0.06           | 474           | -0.07 | 0.04 | 0.076491 | 0.232922                 | 0.15           | 0.459804                          |
| Acylcarnitine C4            | 1,852                 | -0.03 | 0.02 | 0.119927 | 0.175608                 | 0.04           | 1,378         | -0.02 | 0.02 | 0.211669 | 0.29071                  | 0.04           | 474           | -0.01 | 0.04 | 0.888349 | 0.933906                 | 0.11           | 0.695685                          |
| Acylcarnitine C5            | 1,828                 | 0.01  | 0.02 | 0.41167  | 0.506354                 | 0.04           | 1,354         | 0.01  | 0.02 | 0.621033 | 0.713897                 | 0.05           | 474           | 0.01  | 0.04 | 0.802835 | 0.881685                 | 0.09           | 0.609073                          |
| <b>Amino acids</b>          |                       |       |      |          |                          |                |               |       |      |          |                          |                |               |       |      |          |                          |                |                                   |
| Alanine                     | 1,983                 | -0.02 | 0.02 | 0.16263  | 0.229925                 | 0.11           | 1,497         | -0.01 | 0.02 | 0.514048 | 0.626019                 | 0.11           | 486           | -0.08 | 0.04 | 0.032798 | 0.17403                  | 0.15           | 0.453176                          |
| Arginine                    | 1,983                 | -0.05 | 0.01 | 0.000173 | <b>0.000506</b>          | 0.19           | 1,497         | -0.05 | 0.02 | 0.002054 | <b>0.004714</b>          | 0.13           | 486           | -0.04 | 0.03 | 0.128381 | 0.322262                 | 0.39           | 0.840132                          |
| Asparagine                  | 1,983                 | 0.02  | 0.02 | 0.209993 | 0.28699                  | 0.13           | 1,497         | 0.02  | 0.02 | 0.295165 | 0.390379                 | 0.12           | 486           | 0.00  | 0.03 | 0.969612 | 0.977559                 | 0.21           | 0.850574                          |
| Citrulline                  | 1,983                 | -0.10 | 0.02 | 8.2E-10  | <b>5.93E-09</b>          | 0.11           | 1,497         | -0.11 | 0.02 | 1.2E-09  | <b>9.22E-09</b>          | 0.11           | 486           | -0.07 | 0.04 | 0.047813 | 0.177204                 | 0.14           | 0.702646                          |
| Glutamine                   | 1,983                 | -0.01 | 0.02 | 0.452687 | 0.551292                 | 0.05           | 1,497         | -0.01 | 0.02 | 0.641384 | 0.730465                 | 0.05           | 486           | -0.02 | 0.04 | 0.690128 | 0.81621                  | 0.11           | 0.859952                          |
| Glutamate                   | 1,983                 | 0.04  | 0.01 | 0.001849 | <b>0.004135</b>          | 0.26           | 1,497         | 0.04  | 0.02 | 0.00597  | <b>0.012239</b>          | 0.20           | 486           | -0.01 | 0.03 | 0.777842 | 0.869768                 | 0.47           | 0.394299                          |
| Glycine                     | 1,983                 | -0.02 | 0.01 | 0.270663 | 0.346787                 | 0.11           | 1,497         | -0.01 | 0.01 | 0.467161 | 0.580412                 | 0.12           | 486           | -0.04 | 0.04 | 0.292812 | 0.521969                 | 0.13           | 0.548849                          |
| Histidine                   | 1,983                 | 0.02  | 0.01 | 0.256257 | 0.335315                 | 0.08           | 1,497         | 0.03  | 0.02 | 0.114683 | 0.167928                 | 0.08           | 486           | -0.04 | 0.03 | 0.253023 | 0.476062                 | 0.16           | 0.338359                          |
| Isoleucine                  | 1,983                 | 0.00  | 0.02 | 0.798684 | 0.854245                 | 0.08           | 1,497         | 0.00  | 0.02 | 0.860703 | 0.928653                 | 0.09           | 486           | -0.04 | 0.04 | 0.269377 | 0.494528                 | 0.14           | 0.4572                            |
| Leucine                     | 1,982                 | 0.00  | 0.02 | 0.97628  | 0.97628                  | 0.08           | 1,496         | 0.01  | 0.02 | 0.550486 | 0.639862                 | 0.09           | 486           | -0.05 | 0.04 | 0.195468 | 0.414526                 | 0.11           | 0.392036                          |
| Lysine                      | 1,983                 | 0.01  | 0.02 | 0.600089 | 0.689822                 | 0.06           | 1,497         | 0.02  | 0.02 | 0.336802 | 0.436071                 | 0.07           | 486           | -0.03 | 0.04 | 0.376601 | 0.6095                   | 0.08           | 0.453176                          |
| Methionine                  | 1,983                 | 0.02  | 0.02 | 0.218007 | 0.291467                 | 0.08           | 1,497         | 0.03  | 0.02 | 0.082273 | 0.126495                 | 0.08           | 486           | -0.02 | 0.03 | 0.496148 | 0.685687                 | 0.12           | 0.378752                          |
| Ornithine                   | 1,983                 | -0.01 | 0.02 | 0.327788 | 0.415648                 | 0.17           | 1,497         | -0.02 | 0.02 | 0.163855 | 0.231658                 | 0.16           | 486           | -0.02 | 0.03 | 0.630818 | 0.784524                 | 0.27           | 0.803036                          |
| Phenylalanine               | 1,983                 | -0.01 | 0.01 | 0.675429 | 0.755252                 | 0.10           | 1,497         | 0.00  | 0.02 | 0.912747 | 0.943427                 | 0.10           | 486           | -0.07 | 0.03 | 0.046638 | 0.177204                 | 0.16           | 0.392036                          |
| Proline                     | 1,983                 | -0.02 | 0.02 | 0.153941 | 0.220172                 | 0.10           | 1,497         | -0.02 | 0.02 | 0.311322 | 0.407368                 | 0.10           | 486           | -0.05 | 0.04 | 0.223843 | 0.439219                 | 0.15           | 0.628543                          |
| Serine                      | 1,983                 | -0.03 | 0.01 | 0.049036 | 0.079361                 | 0.10           | 1,497         | -0.02 | 0.02 | 0.167136 | 0.233611                 | 0.10           | 486           | -0.06 | 0.03 | 0.048983 | 0.177204                 | 0.17           | 0.427211                          |
| Threonine                   | 1,983                 | 0.03  | 0.02 | 0.123534 | 0.178761                 | 0.09           | 1,497         | 0.03  | 0.02 | 0.111257 | 0.164874                 | 0.09           | 486           | 0.02  | 0.04 | 0.655986 | 0.794669                 | 0.16           | 0.800906                          |
| Tryptophan                  | 1,983                 | 0.01  | 0.02 | 0.722739 | 0.786698                 | 0.06           | 1,497         | 0.01  | 0.02 | 0.397324 | 0.498682                 | 0.08           | 486           | -0.06 | 0.04 | 0.107264 | 0.293188                 | 0.08           | 0.378752                          |
| Tyrosine                    | 1,983                 | 0.06  | 0.02 | 0.000135 | <b>0.000416</b>          | 0.11           | 1,497         | 0.07  | 0.02 | 0.000131 | <b>0.000423</b>          | 0.12           | 486           | 0.01  | 0.04 | 0.720306 | 0.842254                 | 0.14           | 0.392036                          |
| Valine                      | 1,983                 | -0.01 | 0.02 | 0.516758 | 0.617099                 | 0.08           | 1,497         | 0.01  | 0.02 | 0.696935 | 0.765384                 | 0.09           | 486           | -0.08 | 0.04 | 0.040912 | 0.177204                 | 0.11           | 0.211397                          |
| t4-hydroxyproline           | 1,774                 | 0.03  | 0.02 | 0.058478 | 0.091048                 | 0.12           | 1,383         | 0.03  | 0.02 | 0.212714 | 0.29071                  | 0.13           | 391           | 0.07  | 0.04 | 0.073523 | 0.232922                 | 0.10           | 0.628543                          |
| <b>Biogenic amines</b>      |                       |       |      |          |                          |                |               |       |      |          |                          |                |               |       |      |          |                          |                |                                   |
| ADMA                        | 1,930                 | -0.02 | 0.02 | 0.229624 | 0.303697                 | 0.04           | 1,467         | -0.03 | 0.02 | 0.102514 | 0.15377                  | 0.03           | 463           | 0.02  | 0.04 | 0.631446 | 0.784524                 | 0.14           | 0.605156                          |
| Creatine                    | 1,983                 | 0.01  | 0.01 | 0.527088 | 0.623383                 | 0.04           | 1,497         | 0.00  | 0.02 | 0.885936 | 0.937254                 | 0.05           | 486           | 0.03  | 0.04 | 0.457913 | 0.662628                 | 0.07           | 0.394299                          |
| Kynurenine                  | 1,983                 | -0.04 | 0.02 | 0.017437 | <b>0.03064</b>           | 0.10           | 1,497         | -0.03 | 0.02 | 0.074583 | 0.117612                 | 0.10           | 486           | -0.06 | 0.04 | 0.095175 | 0.27064                  | 0.14           | 0.628543                          |
| Taurine                     | 1,983                 | 0.03  | 0.01 | 0.018218 | <b>0.031561</b>          | 0.32           | 1,497         | 0.03  | 0.01 | 0.041361 | 0.068749                 | 0.27           | 486           | 0.00  | 0.03 | 0.865606 | 0.925822                 | 0.48           | 0.550657                          |
| <b>Glycerophospholipids</b> |                       |       |      |          |                          |                |               |       |      |          |                          |                |               |       |      |          |                          |                |                                   |
| LysoPC a C16:0              | 1,983                 | 0.09  | 0.01 | 1.8E-10  | <b>1.48E-09</b>          | 0.16           | 1,497         | 0.10  | 0.02 | 1E-10    | <b>8.79E-10</b>          | 0.14           | 486           | 0.02  | 0.03 | 0.480863 | 0.672116                 | 0.30           | 0.098905                          |
| LysoPC a C16:1              | 1,983                 | 0.11  | 0.02 | <1E-12   | <b>&lt;1E-12</b>         | 0.14           | 1,497         | 0.13  | 0.02 | <1E-12   | <b>&lt;1E-12</b>         | 0.11           | 486           | 0.02  | 0.03 | 0.625131 | 0.784524                 | 0.33           | <b>0.0462</b>                     |
| LysoPC a C17:0              | 1,983                 | -0.09 | 0.01 | 1E-10    | <b>9.46E-10</b>          | 0.19           | 1,497         | -0.09 | 0.02 | 2.7E-09  | <b>1.95E-08</b>          | 0.19           | 486           | -0.09 | 0.03 | 0.002835 | <b>0.04981</b>           | 0.27           | 0.981878                          |



|                |       |       |      |          |                  |      |       |       |      |          |                  |      |     |       |      |          |                 |      |                 |
|----------------|-------|-------|------|----------|------------------|------|-------|-------|------|----------|------------------|------|-----|-------|------|----------|-----------------|------|-----------------|
| LysoPC a C18:0 | 1,983 | -0.01 | 0.01 | 0.266416 | 0.344939         | 0.14 | 1,497 | 0.00  | 0.01 | 0.889911 | 0.937254         | 0.14 | 486 | -0.07 | 0.03 | 0.03423  | 0.17403         | 0.25 | <b>0.0462</b>   |
| LysoPC a C18:1 | 1,983 | 0.05  | 0.01 | 0.000221 | <b>0.000605</b>  | 0.15 | 1,497 | 0.07  | 0.02 | 3.66E-05 | <b>0.000136</b>  | 0.16 | 486 | -0.02 | 0.03 | 0.506347 | 0.687092        | 0.21 | 0.145357        |
| LysoPC a C18:2 | 1,983 | 0.01  | 0.02 | 0.558303 | 0.647842         | 0.14 | 1,497 | 0.02  | 0.02 | 0.363746 | 0.466049         | 0.15 | 486 | -0.03 | 0.03 | 0.4548   | 0.662628        | 0.19 | 0.378752        |
| LysoPC a C20:3 | 1,983 | 0.04  | 0.02 | 0.007569 | <b>0.014778</b>  | 0.08 | 1,497 | 0.06  | 0.02 | 0.000431 | <b>0.001325</b>  | 0.10 | 486 | -0.05 | 0.03 | 0.143782 | 0.3401          | 0.16 | <b>0.0462</b>   |
| LysoPC a C20:4 | 1,983 | 0.06  | 0.02 | 3.46E-05 | <b>0.000122</b>  | 0.10 | 1,497 | 0.09  | 0.02 | 1.44E-07 | <b>8.06E-07</b>  | 0.14 | 486 | -0.04 | 0.03 | 0.224966 | 0.439219        | 0.09 | <b>0.018324</b> |
| PC aa C28:1    | 1,983 | 0.03  | 0.01 | 0.014347 | <b>0.025951</b>  | 0.17 | 1,497 | 0.04  | 0.02 | 0.014447 | <b>0.027338</b>  | 0.15 | 486 | 0.00  | 0.03 | 0.928075 | 0.959271        | 0.28 | 0.392036        |
| PC aa C30:0    | 1,983 | 0.10  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 1,497 | 0.11  | 0.02 | 1E-10    | <b>8.79E-10</b>  | 0.17 | 486 | 0.05  | 0.03 | 0.085363 | 0.249992        | 0.26 | 0.392036        |
| PC aa C32:0    | 1,983 | 0.12  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.11 | 1,497 | 0.13  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.10 | 486 | 0.08  | 0.03 | 0.00424  | 0.057952        | 0.19 | 0.471988        |
| PC aa C32:1    | 1,983 | 0.20  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.25 | 1,497 | 0.21  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.24 | 486 | 0.12  | 0.03 | 0.00016  | <b>0.009828</b> | 0.32 | 0.145357        |
| PC aa C32:2    | 1,983 | 0.07  | 0.02 | 7.27E-06 | <b>2.98E-05</b>  | 0.13 | 1,497 | 0.08  | 0.02 | 5.69E-06 | <b>2.42E-05</b>  | 0.14 | 486 | 0.01  | 0.04 | 0.734098 | 0.842254        | 0.17 | 0.162393        |
| PC aa C32:3    | 1,983 | -0.04 | 0.01 | 0.002701 | <b>0.005827</b>  | 0.20 | 1,497 | -0.04 | 0.02 | 0.005086 | <b>0.010604</b>  | 0.17 | 486 | -0.05 | 0.03 | 0.077641 | 0.232922        | 0.35 | 0.694067        |
| PC aa C34:1    | 1,983 | 0.17  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 1,497 | 0.19  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 486 | 0.08  | 0.03 | 0.00768  | 0.072662        | 0.18 | <b>0.042409</b> |
| PC aa C34:2    | 1,983 | 0.03  | 0.01 | 3.46E-06 | <b>1.47E-05</b>  | 0.04 | 1,497 | 0.04  | 0.01 | 1.21E-06 | <b>6.48E-06</b>  | 0.05 | 486 | 0.01  | 0.01 | 0.553253 | 0.723937        | 0.07 | 0.127192        |
| PC aa C34:3    | 1,983 | 0.07  | 0.01 | 3.98E-07 | <b>2.13E-06</b>  | 0.24 | 1,497 | 0.08  | 0.02 | 2.24E-06 | <b>1.15E-05</b>  | 0.22 | 486 | 0.03  | 0.03 | 0.4207   | 0.63105         | 0.35 | 0.207953        |
| PC aa C34:4    | 1,983 | 0.11  | 0.02 | 1.5E-10  | <b>1.32E-09</b>  | 0.12 | 1,497 | 0.13  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.14 | 486 | 0.01  | 0.04 | 0.73954  | 0.842254        | 0.16 | <b>0.04154</b>  |
| PC aa C36:0    | 1,983 | 0.05  | 0.01 | 0.000227 | <b>0.000607</b>  | 0.16 | 1,497 | 0.05  | 0.01 | 0.001759 | <b>0.004242</b>  | 0.15 | 486 | 0.06  | 0.03 | 0.036293 | 0.17403         | 0.27 | 0.911148        |
| PC aa C36:1    | 1,983 | 0.10  | 0.02 | 1.67E-09 | <b>1.14E-08</b>  | 0.05 | 1,497 | 0.12  | 0.02 | 4E-10    | <b>3.28E-09</b>  | 0.06 | 486 | 0.02  | 0.04 | 0.577745 | 0.740236        | 0.10 | 0.098905        |
| PC aa C36:2    | 1,983 | 0.00  | 0.01 | 0.875533 | 0.907071         | 0.03 | 1,497 | 0.01  | 0.01 | 0.513982 | 0.626019         | 0.03 | 486 | -0.02 | 0.03 | 0.426885 | 0.632613        | 0.08 | 0.251914        |
| PC aa C36:3    | 1,983 | 0.03  | 0.02 | 0.074809 | 0.115019         | 0.05 | 1,497 | 0.04  | 0.02 | 0.026737 | <b>0.048362</b>  | 0.05 | 486 | -0.03 | 0.03 | 0.392161 | 0.618409        | 0.12 | 0.187222        |
| PC aa C36:4    | 1,983 | 0.14  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.11 | 1,497 | 0.16  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.14 | 486 | 0.05  | 0.03 | 0.137856 | 0.332477        | 0.13 | <b>0.018324</b> |
| PC aa C36:5    | 1,983 | 0.16  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 1,497 | 0.17  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.17 | 486 | 0.10  | 0.03 | 0.002469 | <b>0.04981</b>  | 0.27 | 0.474573        |
| PC aa C36:6    | 1,983 | 0.11  | 0.02 | 2.1E-10  | <b>1.61E-09</b>  | 0.15 | 1,497 | 0.11  | 0.02 | 5.4E-09  | <b>3.69E-08</b>  | 0.14 | 486 | 0.06  | 0.03 | 0.096814 | 0.27064         | 0.23 | 0.392036        |
| PC aa C38:0    | 1,983 | 0.00  | 0.01 | 0.827574 | 0.877514         | 0.25 | 1,497 | 0.00  | 0.02 | 0.909485 | 0.943427         | 0.24 | 486 | -0.01 | 0.03 | 0.788294 | 0.873515        | 0.39 | 0.803036        |
| PC aa C38:3    | 1,983 | 0.00  | 0.02 | 0.755364 | 0.814998         | 0.13 | 1,497 | 0.01  | 0.02 | 0.688023 | 0.765384         | 0.12 | 486 | -0.06 | 0.04 | 0.068242 | 0.232922        | 0.25 | 0.145357        |
| PC aa C38:4    | 1,983 | 0.03  | 0.02 | 0.056358 | 0.088872         | 0.10 | 1,497 | 0.06  | 0.02 | 0.002069 | <b>0.004714</b>  | 0.11 | 486 | -0.06 | 0.04 | 0.076921 | 0.232922        | 0.16 | <b>0.018324</b> |
| PC aa C38:5    | 1,983 | 0.09  | 0.02 | 1.92E-07 | <b>1.12E-06</b>  | 0.10 | 1,497 | 0.11  | 0.02 | 1.6E-08  | <b>1.04E-07</b>  | 0.11 | 486 | -0.01 | 0.04 | 0.81269  | 0.88461         | 0.16 | 0.063778        |
| PC aa C38:6    | 1,983 | 0.12  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 1,497 | 0.13  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.17 | 486 | 0.09  | 0.03 | 0.006257 | 0.068576        | 0.28 | 0.4572          |
| PC aa C40:2    | 1,922 | -0.03 | 0.02 | 0.105692 | 0.158538         | 0.14 | 1,436 | -0.03 | 0.02 | 0.087664 | 0.13312          | 0.13 | 486 | -0.03 | 0.03 | 0.404987 | 0.622667        | 0.24 | 0.989802        |
| PC aa C40:3    | 1,922 | 0.00  | 0.02 | 0.899248 | 0.914111         | 0.12 | 1,436 | 0.00  | 0.02 | 0.980177 | 0.983765         | 0.10 | 486 | -0.05 | 0.03 | 0.119314 | 0.305742        | 0.25 | 0.507345        |
| PC aa C40:4    | 1,983 | 0.03  | 0.02 | 0.0503   | 0.080349         | 0.10 | 1,497 | 0.06  | 0.02 | 0.001171 | <b>0.003065</b>  | 0.11 | 486 | -0.07 | 0.04 | 0.045489 | 0.177204        | 0.21 | <b>0.018324</b> |
| PC aa C40:5    | 1,983 | 0.03  | 0.02 | 0.039237 | 0.064349         | 0.15 | 1,497 | 0.05  | 0.02 | 0.002341 | <b>0.005235</b>  | 0.16 | 486 | -0.06 | 0.03 | 0.07217  | 0.232922        | 0.24 | <b>0.018324</b> |
| PC aa C40:6    | 1,983 | 0.03  | 0.02 | 0.029924 | 0.050419         | 0.15 | 1,497 | 0.04  | 0.02 | 0.019052 | <b>0.035505</b>  | 0.14 | 486 | 0.00  | 0.03 | 0.964774 | 0.977559        | 0.24 | 0.302384        |
| PC aa C42:0    | 1,983 | -0.05 | 0.01 | 7.08E-05 | <b>0.000223</b>  | 0.17 | 1,497 | -0.04 | 0.01 | 0.000971 | <b>0.002597</b>  | 0.16 | 486 | -0.06 | 0.02 | 0.013227 | 0.101681        | 0.28 | 0.719524        |
| PC aa C42:1    | 1,983 | -0.03 | 0.01 | 0.006508 | <b>0.012911</b>  | 0.17 | 1,497 | -0.03 | 0.01 | 0.064633 | 0.104604         | 0.16 | 486 | -0.06 | 0.02 | 0.009759 | 0.084396        | 0.30 | 0.251914        |
| PC aa C42:2    | 1,983 | 0.05  | 0.01 | 0.000875 | <b>0.002031</b>  | 0.24 | 1,497 | 0.05  | 0.02 | 0.003369 | <b>0.007269</b>  | 0.22 | 486 | 0.04  | 0.03 | 0.18723  | 0.414526        | 0.36 | 0.628543        |
| PC aa C42:4    | 1,922 | -0.01 | 0.01 | 0.629828 | 0.710723         | 0.04 | 1,436 | 0.01  | 0.02 | 0.526042 | 0.634345         | 0.04 | 486 | -0.06 | 0.03 | 0.044275 | 0.177204        | 0.08 | 0.134127        |
| PC aa C42:5    | 1,922 | 0.01  | 0.01 | 0.499936 | 0.602864         | 0.15 | 1,436 | 0.01  | 0.02 | 0.542748 | 0.639862         | 0.13 | 486 | -0.03 | 0.03 | 0.389592 | 0.618409        | 0.27 | 0.679339        |
| PC aa C42:6    | 1,922 | 0.00  | 0.01 | 0.868533 | 0.907071         | 0.08 | 1,436 | 0.01  | 0.02 | 0.683511 | 0.765384         | 0.08 | 486 | -0.04 | 0.03 | 0.194471 | 0.414526        | 0.16 | 0.362465        |
| PC ae C30:0    | 1,922 | 0.00  | 0.01 | 0.877573 | 0.907071         | 0.18 | 1,436 | 0.00  | 0.02 | 0.928044 | 0.951246         | 0.17 | 486 | 0.01  | 0.03 | 0.853675 | 0.92107         | 0.27 | 0.82908         |
| PC ae C30:2    | 1,922 | -0.05 | 0.01 | 4.96E-05 | <b>0.000165</b>  | 0.11 | 1,436 | -0.06 | 0.01 | 2.72E-05 | <b>0.000105</b>  | 0.10 | 486 | -0.02 | 0.02 | 0.412759 | 0.626781        | 0.19 | 0.702646        |
| PC ae C32:1    | 1,983 | 0.06  | 0.02 | 1.81E-05 | <b>6.75E-05</b>  | 0.07 | 1,497 | 0.06  | 0.02 | 0.000294 | <b>0.000928</b>  | 0.06 | 486 | 0.05  | 0.03 | 0.112697 | 0.301341        | 0.14 | 0.85351         |
| PC ae C32:2    | 1,983 | 0.06  | 0.02 | 0.000367 | <b>0.000921</b>  | 0.07 | 1,497 | 0.05  | 0.02 | 0.007897 | <b>0.015924</b>  | 0.06 | 486 | 0.06  | 0.03 | 0.046568 | 0.177204        | 0.17 | 0.989802        |
| PC ae C34:0    | 1,983 | 0.04  | 0.02 | 0.013391 | <b>0.024583</b>  | 0.09 | 1,497 | 0.03  | 0.02 | 0.068193 | 0.108931         | 0.08 | 486 | 0.05  | 0.03 | 0.133745 | 0.329012        | 0.16 | 0.803036        |
| PC ae C34:1    | 1,983 | 0.01  | 0.02 | 0.612845 | 0.697962         | 0.08 | 1,497 | 0.01  | 0.02 | 0.543822 | 0.639862         | 0.07 | 486 | -0.02 | 0.03 | 0.525433 | 0.694928        | 0.18 | 0.923927        |
| PC ae C34:2    | 1,983 | -0.04 | 0.02 | 0.004067 | <b>0.008478</b>  | 0.08 | 1,497 | -0.05 | 0.02 | 0.004524 | <b>0.009594</b>  | 0.09 | 486 | -0.02 | 0.03 | 0.513922 | 0.687092        | 0.10 | 0.984001        |
| PC ae C34:3    | 1,983 | 0.06  | 0.02 | 0.000527 | <b>0.001289</b>  | 0.09 | 1,497 | 0.06  | 0.02 | 0.000738 | <b>0.002112</b>  | 0.10 | 486 | 0.03  | 0.03 | 0.35019  | 0.590494        | 0.15 | 0.308286        |
| PC ae C36:0    | 1,922 | 0.16  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.13 | 1,436 | 0.16  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.11 | 486 | 0.16  | 0.03 | 3.52E-07 | <b>4.33E-05</b> | 0.22 | 0.989802        |
| PC ae C36:1    | 1,983 | 0.00  | 0.02 | 0.940879 | 0.948592         | 0.06 | 1,497 | 0.00  | 0.02 | 0.983765 | 0.983765         | 0.05 | 486 | -0.02 | 0.03 | 0.576932 | 0.740236        | 0.16 | 0.861659        |
| PC ae C36:2    | 1,983 | -0.11 | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 1,497 | -0.13 | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.13 | 486 | -0.07 | 0.03 | 0.051579 | 0.181262        | 0.15 | 0.394299        |

|                      |       |       |      |          |                 |      |       |       |      |          |                  |      |     |       |      |          |                 |      |               |
|----------------------|-------|-------|------|----------|-----------------|------|-------|-------|------|----------|------------------|------|-----|-------|------|----------|-----------------|------|---------------|
| PC ae C36:3          | 1,983 | -0.04 | 0.02 | 0.023764 | <b>0.040596</b> | 0.06 | 1,497 | -0.04 | 0.02 | 0.033095 | 0.058153         | 0.07 | 486 | -0.03 | 0.03 | 0.355256 | 0.590494        | 0.09 | 0.803036      |
| PC ae C36:4          | 1,983 | 0.04  | 0.01 | 0.010777 | <b>0.020084</b> | 0.15 | 1,497 | 0.05  | 0.02 | 0.001594 | <b>0.003921</b>  | 0.17 | 486 | 0.00  | 0.03 | 0.981032 | 0.981032        | 0.16 | 0.207953      |
| PC ae C36:5          | 1,983 | 0.10  | 0.02 | 1E-11    | <b>1.02E-10</b> | 0.15 | 1,497 | 0.12  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.17 | 486 | 0.04  | 0.03 | 0.198911 | 0.414678        | 0.13 | <b>0.0462</b> |
| PC ae C38:0          | 1,616 | 0.09  | 0.02 | 8.47E-07 | <b>4.34E-06</b> | 0.17 | 1,130 | 0.09  | 0.02 | 1.03E-05 | <b>4.21E-05</b>  | 0.15 | 486 | 0.03  | 0.03 | 0.287731 | 0.520454        | 0.31 | 0.308286      |
| PC ae C38:2          | 1,983 | -0.07 | 0.01 | 1.21E-05 | <b>4.65E-05</b> | 0.06 | 1,497 | -0.08 | 0.02 | 1.41E-05 | <b>5.59E-05</b>  | 0.06 | 486 | -0.04 | 0.03 | 0.171414 | 0.393153        | 0.11 | 0.705171      |
| PC ae C38:3          | 1,983 | -0.09 | 0.02 | 5.86E-09 | <b>3.79E-08</b> | 0.08 | 1,497 | -0.09 | 0.02 | 6.83E-08 | <b>4E-07</b>     | 0.07 | 486 | -0.09 | 0.03 | 0.005427 | 0.066758        | 0.16 | 0.944055      |
| PC ae C38:4          | 1,983 | -0.05 | 0.02 | 0.001614 | <b>0.003677</b> | 0.11 | 1,497 | -0.04 | 0.02 | 0.025237 | <b>0.04633</b>   | 0.11 | 486 | -0.08 | 0.03 | 0.016027 | 0.110172        | 0.16 | 0.4572        |
| PC ae C38:5          | 1,983 | 0.02  | 0.02 | 0.213677 | 0.288816        | 0.12 | 1,497 | 0.04  | 0.02 | 0.038506 | 0.064879         | 0.12 | 486 | -0.03 | 0.03 | 0.335917 | 0.581941        | 0.14 | 0.308286      |
| PC ae C38:6          | 1,983 | 0.05  | 0.02 | 0.000744 | <b>0.001759</b> | 0.17 | 1,497 | 0.06  | 0.02 | 0.000717 | <b>0.0021</b>    | 0.16 | 486 | 0.02  | 0.03 | 0.479871 | 0.672116        | 0.24 | 0.378752      |
| PC ae C40:1          | 1,983 | 0.07  | 0.02 | 4.05E-05 | <b>0.000138</b> | 0.09 | 1,497 | 0.08  | 0.02 | 4.6E-05  | <b>0.000166</b>  | 0.09 | 486 | 0.03  | 0.03 | 0.35212  | 0.590494        | 0.16 | 0.230262      |
| PC ae C40:2          | 1,983 | 0.01  | 0.01 | 0.721044 | 0.786698        | 0.12 | 1,497 | 0.00  | 0.02 | 0.942795 | 0.958378         | 0.09 | 486 | 0.01  | 0.03 | 0.747041 | 0.842991        | 0.25 | 0.705171      |
| PC ae C40:3          | 1,922 | -0.05 | 0.01 | 0.000163 | <b>0.000489</b> | 0.10 | 1,436 | -0.05 | 0.02 | 0.001368 | <b>0.003435</b>  | 0.11 | 486 | -0.07 | 0.03 | 0.010292 | 0.084396        | 0.16 | 0.803036      |
| PC ae C40:4          | 1,983 | -0.08 | 0.02 | 2.17E-06 | <b>9.9E-06</b>  | 0.08 | 1,497 | -0.06 | 0.02 | 0.000619 | <b>0.001856</b>  | 0.08 | 486 | -0.13 | 0.04 | 0.000443 | <b>0.01816</b>  | 0.13 | 0.378752      |
| PC ae C40:5          | 1,983 | -0.03 | 0.02 | 0.030533 | 0.050751        | 0.08 | 1,497 | -0.03 | 0.02 | 0.141617 | 0.202546         | 0.08 | 486 | -0.07 | 0.03 | 0.046623 | 0.177204        | 0.16 | 0.709057      |
| PC ae C40:6          | 1,983 | -0.06 | 0.02 | 0.000284 | <b>0.000727</b> | 0.17 | 1,497 | -0.06 | 0.02 | 0.000845 | <b>0.002361</b>  | 0.15 | 486 | -0.05 | 0.03 | 0.116999 | 0.305742        | 0.29 | 0.989802      |
| PC ae C42:1          | 1,938 | 0.01  | 0.02 | 0.557053 | 0.647842        | 0.04 | 1,452 | 0.02  | 0.02 | 0.287403 | 0.384245         | 0.05 | 486 | -0.03 | 0.04 | 0.400005 | 0.622667        | 0.11 | 0.211397      |
| PC ae C42:2          | 1,983 | 0.02  | 0.02 | 0.118477 | 0.175574        | 0.10 | 1,497 | 0.03  | 0.02 | 0.082209 | 0.126495         | 0.10 | 486 | -0.01 | 0.03 | 0.658403 | 0.794669        | 0.16 | 0.394299      |
| PC ae C42:3          | 1,983 | 0.02  | 0.01 | 0.084541 | 0.128377        | 0.14 | 1,497 | 0.03  | 0.02 | 0.03721  | 0.063568         | 0.13 | 486 | -0.02 | 0.03 | 0.473695 | 0.672116        | 0.24 | 0.378752      |
| PC ae C42:4          | 1,983 | -0.06 | 0.02 | 0.000204 | <b>0.000584</b> | 0.11 | 1,497 | -0.05 | 0.02 | 0.009529 | <b>0.018605</b>  | 0.12 | 486 | -0.10 | 0.03 | 0.00142  | <b>0.04366</b>  | 0.14 | 0.444066      |
| PC ae C42:5          | 1,983 | -0.06 | 0.02 | 0.000217 | <b>0.000605</b> | 0.08 | 1,497 | -0.05 | 0.02 | 0.008104 | <b>0.016078</b>  | 0.08 | 486 | -0.11 | 0.03 | 0.001956 | <b>0.048114</b> | 0.17 | 0.581284      |
| PC ae C44:4          | 1,983 | -0.02 | 0.01 | 0.181462 | 0.250785        | 0.06 | 1,497 | -0.01 | 0.01 | 0.691974 | 0.765384         | 0.06 | 486 | -0.06 | 0.03 | 0.020246 | 0.118586        | 0.13 | 0.427211      |
| PC ae C44:5          | 1,983 | -0.01 | 0.01 | 0.399652 | 0.496538        | 0.10 | 1,497 | 0.00  | 0.02 | 0.820449 | 0.893055         | 0.09 | 486 | -0.07 | 0.03 | 0.016733 | 0.110172        | 0.19 | 0.392036      |
| PC ae C44:6          | 1,983 | -0.04 | 0.01 | 0.007742 | <b>0.01488</b>  | 0.09 | 1,497 | -0.02 | 0.02 | 0.136503 | 0.197527         | 0.10 | 486 | -0.09 | 0.03 | 0.003635 | 0.055888        | 0.12 | 0.308286      |
| <b>Sphingolipids</b> |       |       |      |          |                 |      |       |       |      |          |                  |      |     |       |      |          |                 |      |               |
| SM C16:0             | 1,983 | 0.01  | 0.01 | 0.36541  | 0.458627        | 0.05 | 1,497 | 0.01  | 0.01 | 0.256339 | 0.34648          | 0.06 | 486 | -0.01 | 0.02 | 0.665454 | 0.794669        | 0.10 | 0.628543      |
| SM C16:1             | 1,983 | 0.02  | 0.01 | 0.014882 | <b>0.026528</b> | 0.07 | 1,497 | 0.02  | 0.01 | 0.036575 | 0.063363         | 0.05 | 486 | 0.03  | 0.02 | 0.207867 | 0.426127        | 0.16 | 0.928366      |
| SM C18:0             | 1,983 | 0.04  | 0.01 | 1.07E-05 | <b>4.25E-05</b> | 0.07 | 1,497 | 0.04  | 0.01 | 6.43E-05 | <b>0.000214</b>  | 0.07 | 486 | 0.03  | 0.02 | 0.190824 | 0.414526        | 0.16 | 0.803036      |
| SM C18:1             | 1,983 | 0.01  | 0.01 | 0.178527 | 0.249532        | 0.05 | 1,497 | 0.01  | 0.01 | 0.374309 | 0.47464          | 0.04 | 486 | 0.03  | 0.02 | 0.232678 | 0.447179        | 0.13 | 0.742517      |
| SM C20:2             | 1,983 | -0.06 | 0.01 | 1.43E-06 | <b>6.75E-06</b> | 0.26 | 1,497 | -0.07 | 0.01 | 3.97E-06 | <b>1.81E-05</b>  | 0.22 | 486 | -0.06 | 0.02 | 0.00669  | 0.068576        | 0.47 | 0.989802      |
| SM C24:0             | 1,983 | 0.04  | 0.01 | 1.27E-06 | <b>6.26E-06</b> | 0.05 | 1,497 | 0.05  | 0.01 | 5.06E-08 | <b>3.11E-07</b>  | 0.08 | 486 | 0.00  | 0.02 | 0.87462  | 0.927399        | 0.10 | 0.055943      |
| SM C24:1             | 1,983 | 0.03  | 0.01 | 2.8E-05  | <b>0.000101</b> | 0.08 | 1,497 | 0.04  | 0.01 | 4.71E-05 | <b>0.000166</b>  | 0.08 | 486 | 0.02  | 0.02 | 0.369723 | 0.606346        | 0.18 | 0.679339      |
| SM(OH) C14:1         | 1,983 | -0.06 | 0.01 | 3.89E-07 | <b>2.13E-06</b> | 0.14 | 1,497 | -0.06 | 0.01 | 4.72E-06 | <b>2.07E-05</b>  | 0.13 | 486 | -0.06 | 0.02 | 0.021886 | 0.122363        | 0.21 | 0.972987      |
| SM(OH) C16:1         | 1,983 | -0.05 | 0.01 | 2.55E-06 | <b>1.12E-05</b> | 0.07 | 1,497 | -0.06 | 0.01 | 3.94E-06 | <b>1.81E-05</b>  | 0.06 | 486 | -0.03 | 0.02 | 0.172604 | 0.393153        | 0.14 | 0.476525      |
| SM(OH) C22:1         | 1,983 | -0.03 | 0.01 | 0.004525 | <b>0.009275</b> | 0.05 | 1,497 | -0.02 | 0.01 | 0.052577 | 0.086227         | 0.05 | 486 | -0.05 | 0.02 | 0.017018 | 0.110172        | 0.12 | 0.54816       |
| SM(OH) C22:2         | 1,983 | -0.05 | 0.01 | 1.34E-07 | <b>8.25E-07</b> | 0.09 | 1,497 | -0.05 | 0.01 | 2.84E-06 | <b>1.39E-05</b>  | 0.09 | 486 | -0.04 | 0.02 | 0.019293 | 0.118586        | 0.14 | 0.969953      |
| SM(OH) C24:1         | 1,983 | 0.00  | 0.01 | 0.694071 | 0.769106        | 0.05 | 1,497 | 0.01  | 0.01 | 0.551426 | 0.639862         | 0.06 | 486 | -0.01 | 0.02 | 0.65952  | 0.794669        | 0.12 | 0.803036      |
| <b>Hexoses</b>       |       |       |      |          |                 |      |       |       |      |          |                  |      |     |       |      |          |                 |      |               |
| Hexoses              | 1,983 | -0.04 | 0.02 | 0.008591 | <b>0.016256</b> | 0.16 | 1,497 | -0.05 | 0.02 | 0.010598 | <b>0.020368</b>  | 0.14 | 486 | 0.00  | 0.03 | 0.916543 | 0.95538         | 0.27 | 0.427211      |

Abbreviations:  $\beta$ , unstandardized regression coefficient derived from multivariable linear models; SE, standard error.

For an explanation of abbreviated metabolite names, see Supplementary Table 1.

<sup>a</sup> Analyzed with multivariable linear regression analyses analyzing associations of alcohol consumption (ln-transformed alcohol intake + 1) as main independent variable and as dependent variables the residuals obtained from linear mixed models with Z-standardized ln-transformed metabolite concentrations as dependent variables, sex as independent variable, and random intercepts for analytical batches nested within studies. Adjusted for: sex (not in sex-stratified analysis); age (y; continuous), body mass index (kg/m<sup>2</sup>; continuous), self-reported physical activity levels (Cambridge physical activity index(1): inactive, moderately inactive, moderately active, active, unknown), fasting status ( $\geq 6$  hours, 3-5.9 hours, <3 hours, unknown), meat intake (g/day; continuous), fish intake (g/day; continuous), energy intake (kcal/day; continuous), country, and smoking status (current, former, never, unknown).

<sup>b</sup> Testing for statistical interaction was performed by including a product term for alcohol intake and sex and evaluating significance.

<sup>c</sup> The analysis in the discovery set was adjusted for multiple testing using the false discovery rate (FDR) method. Statistically significant associations (FDR q-value<0.05) are depicted in bold.

**Supplementary Table 6.** Comparison of results of discovery analysis on associations of alcohol intake with concentrations of included metabolites (n=123) in never smokers only with results obtained in the total discovery set and results of statistical interaction analysis for smoking status<sup>a</sup>

| Metabolite                  | Total group (n=1,756) |       |      |          |                          |                | Never smokers (n=639) |       |      |          |                          |                | Interaction analysis <sup>b</sup> | Interaction former vs never smokers <sup>b</sup> |      | Interaction current vs never smokers <sup>b</sup> |      |
|-----------------------------|-----------------------|-------|------|----------|--------------------------|----------------|-----------------------|-------|------|----------|--------------------------|----------------|-----------------------------------|--|------|---|------|
|                             | n                     | B     | SE   | p-value  | FDR q-value <sup>c</sup> | R <sup>2</sup> | n                     | β     | SE   | p-value  | FDR q-value <sup>c</sup> | R <sup>2</sup> | FDR q-value <sup>c</sup>          | B  | SE   | B   | SE   |
| <b>Acylcarnitines</b>       |                       |       |      |          |                          |                |                       |       |      |          |                          |                |                                   |  |      |   |      |
| Acylcarnitine C0            | 1,983                 | 0.05  | 0.02 | 0.003939 | <b>0.008354</b>          | 0.06           | 754                   | 0.03  | 0.03 | 0.210385 | 0.341715                 | 0.08           | 0.572879                          | 0.03   | 0.03 | 0.07  | 0.04 |
| Acylcarnitine C14:1         | 1,956                 | 0.05  | 0.02 | 0.002151 | <b>0.004725</b>          | 0.09           | 740                   | 0.03  | 0.03 | 0.357029 | 0.510634                 | 0.12           | 0.686143                          | 0.05   | 0.03 | 0.02  | 0.04 |
| Acylcarnitine C16           | 1,956                 | 0.11  | 0.02 | <1E-12   | <b>&lt;1E-12</b>         | 0.15           | 740                   | 0.09  | 0.03 | 0.000481 | 0.003946                 | 0.16           | 0.608217                          | 0.05   | 0.03 | 0.02  | 0.04 |
| Acylcarnitine C18           | 1,956                 | 0.06  | 0.02 | 0.000534 | <b>0.001289</b>          | 0.09           | 740                   | 0.08  | 0.03 | 0.003789 | 0.018853                 | 0.12           | 0.983917                          | -0.01  | 0.03 | 0.01  | 0.04 |
| Acylcarnitine C18:1         | 1,956                 | 0.06  | 0.02 | 0.000236 | <b>0.000617</b>          | 0.16           | 740                   | 0.08  | 0.03 | 0.001542 | 0.00998                  | 0.19           | 0.801755                          | -0.03  | 0.03 | -0.04   | 0.04 |
| Acylcarnitine C18:2         | 1,956                 | 0.00  | 0.02 | 0.892851 | 0.914111                 | 0.18           | 740                   | 0.01  | 0.03 | 0.791577 | 0.85407                  | 0.23           | 0.973462                          | 0.02   | 0.03 | 0.02  | 0.04 |
| Acylcarnitine C2            | 1,983                 | 0.07  | 0.02 | 5.9E-05  | <b>0.000191</b>          | 0.10           | 754                   | 0.02  | 0.03 | 0.532795 | 0.675607                 | 0.14           | 0.042838                          | 0.05   | 0.04 | 0.13  | 0.04 |
| Acylcarnitine C3            | 1,956                 | -0.05 | 0.02 | 0.005628 | <b>0.011348</b>          | 0.06           | 740                   | -0.01 | 0.03 | 0.652344 | 0.756965                 | 0.07           | 0.59968                           | -0.06  | 0.04 | 0.00  | 0.04 |
| Acylcarnitine C4            | 1,852                 | -0.03 | 0.02 | 0.119927 | 0.175608                 | 0.04           | 715                   | -0.04 | 0.03 | 0.182116 | 0.315497                 | 0.05           | 0.59968                           | 0.06   | 0.04 | 0.01  | 0.04 |
| Acylcarnitine C5            | 1,828                 | 0.01  | 0.02 | 0.41167  | 0.506354                 | 0.04           | 706                   | 0.01  | 0.03 | 0.772378 | 0.840731                 | 0.07           | 0.790111                          | 0.01   | 0.04 | 0.05  | 0.04 |
| <b>Amino acids</b>          |                       |       |      |          |                          |                |                       |       |      |          |                          |                |                                   |  |      |   |      |
| Alanine                     | 1,983                 | -0.02 | 0.02 | 0.16263  | 0.229925                 | 0.11           | 754                   | -0.04 | 0.03 | 0.166137 | 0.311701                 | 0.13           | 0.76721                           | 0.02   | 0.03 | 0.05  | 0.04 |
| Arginine                    | 1,983                 | -0.05 | 0.01 | 0.000173 | <b>0.000506</b>          | 0.19           | 754                   | -0.08 | 0.02 | 0.000863 | 0.006246                 | 0.25           | 0.345544                          | 0.06   | 0.03 | 0.01  | 0.03 |
| Asparagine                  | 1,983                 | 0.02  | 0.02 | 0.209993 | 0.28699                  | 0.13           | 754                   | 0.02  | 0.02 | 0.424187 | 0.579722                 | 0.17           | 0.998364                          | 0.00   | 0.03 | 0.00  | 0.04 |
| Citrulline                  | 1,983                 | -0.10 | 0.02 | 8.2E-10  | <b>5.93E-09</b>          | 0.11           | 754                   | -0.07 | 0.03 | 0.010058 | 0.042661                 | 0.12           | 0.801755                          | -0.01  | 0.03 | -0.04   | 0.04 |
| Glutamine                   | 1,983                 | -0.01 | 0.02 | 0.452687 | 0.551292                 | 0.05           | 754                   | -0.07 | 0.03 | 0.019617 | 0.06137                  | 0.09           | 0.551109                          | 0.07   | 0.04 | 0.04  | 0.04 |
| Glutamate                   | 1,983                 | 0.04  | 0.01 | 0.001849 | <b>0.004135</b>          | 0.26           | 754                   | 0.07  | 0.02 | 0.003832 | 0.018853                 | 0.34           | 0.59968                           | -0.03  | 0.03 | 0.03  | 0.03 |
| Glycine                     | 1,983                 | -0.02 | 0.01 | 0.270663 | 0.346787                 | 0.11           | 754                   | -0.02 | 0.03 | 0.376624 | 0.532469                 | 0.09           | 0.94797                           | 0.02   | 0.03 | 0.00  | 0.03 |
| Histidine                   | 1,983                 | 0.02  | 0.01 | 0.256257 | 0.335315                 | 0.08           | 754                   | -0.01 | 0.02 | 0.815245 | 0.871958                 | 0.12           | 0.676824                          | 0.05   | 0.03 | 0.02  | 0.04 |
| Isoleucine                  | 1,983                 | 0.00  | 0.02 | 0.798684 | 0.854245                 | 0.08           | 754                   | -0.02 | 0.03 | 0.444527 | 0.600844                 | 0.09           | 0.620042                          | -0.01  | 0.03 | 0.05  | 0.04 |
| Leucine                     | 1,982                 | 0.00  | 0.02 | 0.97628  | 0.97628                  | 0.08           | 754                   | -0.01 | 0.03 | 0.603252 | 0.72745                  | 0.08           | 0.962043                          | 0.01   | 0.03 | 0.03  | 0.04 |
| Lysine                      | 1,983                 | 0.01  | 0.02 | 0.600089 | 0.689822                 | 0.06           | 754                   | -0.01 | 0.03 | 0.6298   | 0.749217                 | 0.08           | 0.790111                          | 0.05   | 0.04 | 0.02  | 0.04 |
| Methionine                  | 1,983                 | 0.02  | 0.02 | 0.218007 | 0.291467                 | 0.08           | 754                   | -0.03 | 0.03 | 0.211141 | 0.341715                 | 0.10           | 0.345544                          | 0.08   | 0.03 | 0.07  | 0.04 |
| Ornithine                   | 1,983                 | -0.01 | 0.02 | 0.327788 | 0.415648                 | 0.17           | 754                   | 0.03  | 0.02 | 0.288723 | 0.434653                 | 0.21           | 0.59968                           | -0.06  | 0.03 | -0.03   | 0.04 |
| Phenylalanine               | 1,983                 | -0.01 | 0.01 | 0.675429 | 0.755252                 | 0.10           | 754                   | -0.03 | 0.02 | 0.169788 | 0.311701                 | 0.14           | 0.520145                          | 0.06   | 0.03 | 0.00  | 0.03 |
| Proline                     | 1,983                 | -0.02 | 0.02 | 0.153941 | 0.220172                 | 0.10           | 754                   | -0.04 | 0.03 | 0.206979 | 0.341715                 | 0.13           | 0.804924                          | 0.01   | 0.04 | 0.04  | 0.04 |
| Serine                      | 1,983                 | -0.03 | 0.01 | 0.049036 | 0.079361                 | 0.10           | 754                   | -0.05 | 0.02 | 0.020628 | 0.06137                  | 0.14           | 0.551109                          | 0.05   | 0.03 | 0.01  | 0.03 |
| Threonine                   | 1,983                 | 0.03  | 0.02 | 0.123534 | 0.178761                 | 0.09           | 754                   | -0.01 | 0.03 | 0.597345 | 0.72745                  | 0.14           | 0.620849                          | 0.04   | 0.04 | 0.06  | 0.04 |
| Tryptophan                  | 1,983                 | 0.01  | 0.02 | 0.722739 | 0.786698                 | 0.06           | 754                   | -0.04 | 0.03 | 0.166534 | 0.311701                 | 0.05           | 0.572879                          | 0.04   | 0.03 | 0.06  | 0.04 |
| Tyrosine                    | 1,983                 | 0.06  | 0.02 | 0.000135 | <b>0.000416</b>          | 0.11           | 754                   | 0.03  | 0.03 | 0.343318 | 0.502716                 | 0.11           | 0.509718                          | 0.04   | 0.03 | 0.08  | 0.04 |
| Valine                      | 1,983                 | -0.01 | 0.02 | 0.516758 | 0.617099                 | 0.08           | 754                   | -0.03 | 0.03 | 0.190793 | 0.321474                 | 0.09           | 0.892646                          | 0.02   | 0.03 | 0.03  | 0.04 |
| t4-hydroxyproline           | 1,774                 | 0.03  | 0.02 | 0.058478 | 0.091048                 | 0.12           | 657                   | 0.02  | 0.03 | 0.551174 | 0.684792                 | 0.14           | 0.616518                          | 0.03   | 0.04 | -0.04   | 0.04 |
| <b>Biogenic amines</b>      |                       |       |      |          |                          |                |                       |       |      |          |                          |                |                                   |  |      |   |      |
| ADMA                        | 1,930                 | -0.02 | 0.02 | 0.229624 | 0.303697                 | 0.04           | 735                   | 0.01  | 0.03 | 0.749998 | 0.823659                 | 0.11           | 0.520145                          | 0.02   | 0.04 | -0.06   | 0.04 |
| Creatine                    | 1,983                 | 0.01  | 0.01 | 0.527088 | 0.623383                 | 0.04           | 754                   | 0.00  | 0.02 | 0.952747 | 0.952747                 | 0.07           | 0.801755                          | -0.01  | 0.03 | 0.03  | 0.04 |
| Kynurenine                  | 1,983                 | -0.04 | 0.02 | 0.017437 | <b>0.03064</b>           | 0.10           | 754                   | -0.02 | 0.02 | 0.313557 | 0.464668                 | 0.11           | 0.801755                          | -0.01  | 0.03 | -0.04   | 0.04 |
| Taurine                     | 1,983                 | 0.03  | 0.01 | 0.018218 | <b>0.031561</b>          | 0.32           | 754                   | 0.04  | 0.02 | 0.039358 | 0.100855                 | 0.38           | 0.517739                          | -0.02  | 0.03 | 0.04  | 0.03 |
| <b>Glycerophospholipids</b> |                       |       |      |          |                          |                |                       |       |      |          |                          |                |                                   |  |      |   |      |
| LysoPC a C16:0              | 1,983                 | 0.09  | 0.01 | 1.8E-10  | <b>1.48E-09</b>          | 0.16           | 754                   | 0.08  | 0.02 | 0.000242 | 0.002711                 | 0.19           | 0.801755                          | 0.00   | 0.03 | 0.03  | 0.03 |
| LysoPC a C16:1              | 1,983                 | 0.11  | 0.02 | <1E-12   | <b>&lt;1E-12</b>         | 0.14           | 754                   | 0.06  | 0.02 | 0.013849 | 0.053232                 | 0.19           | 0.0108                            | 0.06   | 0.03 | 0.14  | 0.04 |
| LysoPC a C17:0              | 1,983                 | -0.09 | 0.01 | 1E-10    | <b>9.46E-10</b>          | 0.19           | 754                   | -0.03 | 0.02 | 0.17986  | 0.315497                 | 0.18           | 0.0108                            | -0.06  | 0.03 | -0.13   | 0.03 |

|                |       |       |      |          |                  |      |     |       |      |          |          |      |          |       |      |       |      |
|----------------|-------|-------|------|----------|------------------|------|-----|-------|------|----------|----------|------|----------|-------|------|-------|------|
| LysoPC a C18:0 | 1,983 | -0.01 | 0.01 | 0.266416 | 0.344939         | 0.14 | 754 | 0.00  | 0.02 | 0.898826 | 0.913682 | 0.16 | 0.899268 | 0.01  | 0.03 | -0.02 | 0.03 |
| LysoPC a C18:1 | 1,983 | 0.05  | 0.01 | 0.000221 | <b>0.000605</b>  | 0.15 | 754 | 0.04  | 0.02 | 0.10454  | 0.229614 | 0.15 | 0.899268 | 0.02  | 0.03 | 0.03  | 0.03 |
| LysoPC a C18:2 | 1,983 | 0.01  | 0.02 | 0.558303 | 0.647842         | 0.14 | 754 | -0.01 | 0.02 | 0.636598 | 0.749217 | 0.20 | 0.59968  | 0.05  | 0.03 | 0.05  | 0.04 |
| LysoPC a C20:3 | 1,983 | 0.04  | 0.02 | 0.007569 | <b>0.014778</b>  | 0.08 | 754 | 0.03  | 0.03 | 0.282719 | 0.434653 | 0.09 | 0.811707 | 0.02  | 0.03 | 0.04  | 0.04 |
| LysoPC a C20:4 | 1,983 | 0.06  | 0.02 | 3.46E-05 | <b>0.000122</b>  | 0.10 | 754 | 0.06  | 0.02 | 0.011069 | 0.045382 | 0.13 | 0.984326 | 0.01  | 0.03 | 0.01  | 0.04 |
| PC aa C28:1    | 1,983 | 0.03  | 0.01 | 0.014347 | <b>0.025951</b>  | 0.17 | 754 | 0.06  | 0.02 | 0.005485 | 0.02595  | 0.28 | 0.572879 | -0.03 | 0.03 | -0.06 | 0.03 |
| PC aa C30:0    | 1,983 | 0.10  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 754 | 0.07  | 0.02 | 0.001919 | 0.011805 | 0.26 | 0.899268 | 0.01  | 0.03 | 0.03  | 0.04 |
| PC aa C32:0    | 1,983 | 0.12  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.11 | 754 | 0.10  | 0.02 | 4.14E-05 | 0.000566 | 0.19 | 0.801755 | 0.00  | 0.03 | 0.04  | 0.04 |
| PC aa C32:1    | 1,983 | 0.20  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.25 | 754 | 0.13  | 0.02 | 1.51E-07 | 6.18E-06 | 0.30 | 0.021712 | 0.06  | 0.03 | 0.13  | 0.04 |
| PC aa C32:2    | 1,983 | 0.07  | 0.02 | 7.27E-06 | <b>2.98E-05</b>  | 0.13 | 754 | 0.03  | 0.03 | 0.258261 | 0.402103 | 0.16 | 0.203914 | 0.05  | 0.03 | 0.10  | 0.04 |
| PC aa C32:3    | 1,983 | -0.04 | 0.01 | 0.002701 | <b>0.005827</b>  | 0.20 | 754 | -0.03 | 0.02 | 0.136019 | 0.269844 | 0.24 | 0.976658 | -0.02 | 0.03 | -0.01 | 0.03 |
| PC aa C34:1    | 1,983 | 0.17  | 0.01 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 754 | 0.14  | 0.02 | 1.84E-08 | 1.13E-06 | 0.13 | 0.509718 | 0.00  | 0.03 | 0.07  | 0.04 |
| PC aa C34:2    | 1,983 | 0.03  | 0.01 | 3.46E-06 | <b>1.47E-05</b>  | 0.04 | 754 | 0.01  | 0.01 | 0.257175 | 0.402103 | 0.05 | 0.203914 | 0.03  | 0.02 | 0.04  | 0.02 |
| PC aa C34:3    | 1,983 | 0.07  | 0.01 | 3.98E-07 | <b>2.13E-06</b>  | 0.24 | 754 | 0.03  | 0.02 | 0.180403 | 0.315497 | 0.29 | 0.066999 | 0.05  | 0.03 | 0.11  | 0.03 |
| PC aa C34:4    | 1,983 | 0.11  | 0.02 | 1.5E-10  | <b>1.32E-09</b>  | 0.12 | 754 | 0.08  | 0.03 | 0.003013 | 0.016844 | 0.15 | 0.509718 | 0.01  | 0.04 | 0.07  | 0.04 |
| PC aa C36:0    | 1,983 | 0.05  | 0.01 | 0.000227 | <b>0.000607</b>  | 0.16 | 754 | 0.05  | 0.02 | 0.022733 | 0.063549 | 0.21 | 0.983917 | 0.01  | 0.03 | 0.01  | 0.03 |
| PC aa C36:1    | 1,983 | 0.10  | 0.02 | 1.67E-09 | <b>1.14E-08</b>  | 0.05 | 754 | 0.09  | 0.03 | 0.000989 | 0.00676  | 0.05 | 0.977406 | -0.01 | 0.04 | 0.01  | 0.04 |
| PC aa C36:2    | 1,983 | 0.00  | 0.01 | 0.875533 | 0.907071         | 0.03 | 754 | -0.02 | 0.02 | 0.417816 | 0.577431 | 0.04 | 0.501162 | 0.06  | 0.03 | 0.03  | 0.03 |
| PC aa C36:3    | 1,983 | 0.03  | 0.02 | 0.074809 | 0.115019         | 0.05 | 754 | 0.00  | 0.03 | 0.869043 | 0.905917 | 0.08 | 0.59968  | 0.04  | 0.03 | 0.06  | 0.04 |
| PC aa C36:4    | 1,983 | 0.14  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.11 | 754 | 0.12  | 0.02 | 3.75E-07 | 1.15E-05 | 0.15 | 0.620812 | 0.01  | 0.03 | 0.05  | 0.04 |
| PC aa C36:5    | 1,983 | 0.16  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 754 | 0.17  | 0.03 | 2.2E-09  | 2.71E-07 | 0.20 | 0.686143 | -0.05 | 0.04 | -0.01 | 0.04 |
| PC aa C36:6    | 1,983 | 0.11  | 0.02 | 2.1E-10  | <b>1.61E-09</b>  | 0.15 | 754 | 0.12  | 0.03 | 1.53E-05 | 0.000235 | 0.17 | 0.790111 | -0.04 | 0.04 | 0.01  | 0.04 |
| PC aa C38:0    | 1,983 | 0.00  | 0.01 | 0.827574 | 0.877514         | 0.25 | 754 | 0.02  | 0.02 | 0.477939 | 0.632113 | 0.30 | 0.801755 | -0.02 | 0.03 | -0.04 | 0.03 |
| PC aa C38:3    | 1,983 | 0.00  | 0.02 | 0.755364 | 0.814998         | 0.13 | 754 | -0.01 | 0.03 | 0.74278  | 0.823081 | 0.14 | 0.899268 | 0.01  | 0.03 | 0.03  | 0.04 |
| PC aa C38:4    | 1,983 | 0.03  | 0.02 | 0.056358 | 0.088872         | 0.10 | 754 | 0.03  | 0.03 | 0.289768 | 0.434653 | 0.12 | 0.983917 | 0.01  | 0.04 | 0.01  | 0.04 |
| PC aa C38:5    | 1,983 | 0.09  | 0.02 | 1.92E-07 | <b>1.12E-06</b>  | 0.10 | 754 | 0.10  | 0.03 | 0.000378 | 0.003572 | 0.12 | 0.801755 | -0.04 | 0.04 | 0.00  | 0.04 |
| PC aa C38:6    | 1,983 | 0.12  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 754 | 0.14  | 0.03 | 4.95E-07 | 1.22E-05 | 0.21 | 0.801755 | -0.03 | 0.03 | 0.02  | 0.04 |
| PC aa C40:2    | 1,922 | -0.03 | 0.02 | 0.105692 | 0.158538         | 0.14 | 734 | 0.00  | 0.03 | 0.883822 | 0.905917 | 0.19 | 0.891805 | -0.03 | 0.03 | -0.03 | 0.04 |
| PC aa C40:3    | 1,922 | 0.00  | 0.02 | 0.899248 | 0.914111         | 0.12 | 734 | 0.00  | 0.03 | 0.878653 | 0.905917 | 0.17 | 0.927214 | -0.01 | 0.03 | 0.02  | 0.04 |
| PC aa C40:4    | 1,983 | 0.03  | 0.02 | 0.0503   | 0.080349         | 0.10 | 754 | 0.00  | 0.03 | 0.874242 | 0.905917 | 0.16 | 0.509718 | 0.03  | 0.04 | 0.08  | 0.04 |
| PC aa C40:5    | 1,983 | 0.03  | 0.02 | 0.039237 | 0.064349         | 0.15 | 754 | 0.02  | 0.03 | 0.506941 | 0.656355 | 0.20 | 0.501162 | 0.00  | 0.03 | 0.07  | 0.04 |
| PC aa C40:6    | 1,983 | 0.03  | 0.02 | 0.029924 | 0.050419         | 0.15 | 754 | 0.04  | 0.03 | 0.131037 | 0.264222 | 0.17 | 0.801755 | -0.01 | 0.03 | 0.03  | 0.04 |
| PC aa C42:0    | 1,983 | -0.05 | 0.01 | 7.08E-05 | <b>0.000223</b>  | 0.17 | 754 | -0.05 | 0.02 | 0.006725 | 0.030638 | 0.19 | 0.983917 | 0.00  | 0.02 | -0.01 | 0.03 |
| PC aa C42:1    | 1,983 | -0.03 | 0.01 | 0.006508 | <b>0.012911</b>  | 0.17 | 754 | -0.05 | 0.02 | 0.017156 | 0.059504 | 0.20 | 0.962043 | 0.01  | 0.03 | 0.02  | 0.03 |
| PC aa C42:2    | 1,983 | 0.05  | 0.01 | 0.000875 | <b>0.002031</b>  | 0.24 | 754 | 0.05  | 0.02 | 0.03433  | 0.093834 | 0.30 | 0.998364 | 0.00  | 0.03 | 0.00  | 0.03 |
| PC aa C42:4    | 1,922 | -0.01 | 0.01 | 0.629828 | 0.710723         | 0.04 | 734 | 0.00  | 0.02 | 0.873776 | 0.905917 | 0.08 | 0.976658 | -0.02 | 0.03 | -0.01 | 0.03 |
| PC aa C42:5    | 1,922 | 0.01  | 0.01 | 0.499936 | 0.602864         | 0.15 | 734 | 0.01  | 0.02 | 0.662097 | 0.758164 | 0.20 | 0.529174 | -0.02 | 0.03 | 0.04  | 0.04 |
| PC aa C42:6    | 1,922 | 0.00  | 0.01 | 0.868533 | 0.907071         | 0.08 | 734 | 0.01  | 0.02 | 0.701766 | 0.784702 | 0.10 | 0.899268 | -0.02 | 0.03 | 0.01  | 0.03 |
| PC ae C30:0    | 1,922 | 0.00  | 0.01 | 0.877573 | 0.907071         | 0.18 | 734 | 0.01  | 0.02 | 0.665705 | 0.758164 | 0.26 | 0.59968  | -0.03 | 0.03 | -0.06 | 0.03 |
| PC ae C30:2    | 1,922 | -0.05 | 0.01 | 4.96E-05 | <b>0.000165</b>  | 0.11 | 734 | -0.03 | 0.02 | 0.083522 | 0.193834 | 0.15 | 0.572879 | -0.01 | 0.02 | -0.05 | 0.03 |
| PC ae C32:1    | 1,983 | 0.06  | 0.02 | 1.81E-05 | <b>6.75E-05</b>  | 0.07 | 754 | 0.05  | 0.02 | 0.068076 | 0.161026 | 0.12 | 0.966039 | 0.01  | 0.03 | 0.02  | 0.04 |
| PC ae C32:2    | 1,983 | 0.06  | 0.02 | 0.000367 | <b>0.000921</b>  | 0.07 | 754 | 0.06  | 0.03 | 0.017416 | 0.059504 | 0.12 | 0.977406 | -0.02 | 0.03 | -0.01 | 0.04 |
| PC ae C34:0    | 1,983 | 0.04  | 0.02 | 0.013391 | <b>0.024583</b>  | 0.09 | 754 | 0.06  | 0.03 | 0.019638 | 0.06137  | 0.16 | 0.501162 | -0.05 | 0.03 | -0.08 | 0.04 |
| PC ae C34:1    | 1,983 | 0.01  | 0.02 | 0.612845 | 0.697962         | 0.08 | 754 | 0.01  | 0.03 | 0.597487 | 0.72745  | 0.11 | 0.790842 | -0.02 | 0.03 | -0.05 | 0.04 |
| PC ae C34:2    | 1,983 | -0.04 | 0.02 | 0.004067 | <b>0.008478</b>  | 0.08 | 754 | -0.04 | 0.03 | 0.124872 | 0.255988 | 0.10 | 0.794049 | 0.01  | 0.03 | -0.03 | 0.04 |
| PC ae C34:3    | 1,983 | 0.06  | 0.02 | 0.000527 | <b>0.001289</b>  | 0.09 | 754 | 0.04  | 0.03 | 0.181238 | 0.315497 | 0.12 | 0.59968  | 0.06  | 0.03 | 0.04  | 0.04 |
| PC ae C36:0    | 1,922 | 0.16  | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.13 | 734 | 0.13  | 0.03 | 8.37E-07 | 1.72E-05 | 0.16 | 0.801755 | 0.03  | 0.03 | 0.04  | 0.04 |
| PC ae C36:1    | 1,983 | 0.00  | 0.02 | 0.940879 | 0.948592         | 0.06 | 754 | 0.04  | 0.03 | 0.08962  | 0.204135 | 0.11 | 0.171999 | -0.06 | 0.03 | -0.10 | 0.04 |
| PC ae C36:2    | 1,983 | -0.11 | 0.02 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 754 | -0.06 | 0.02 | 0.020501 | 0.06137  | 0.15 | 0.040198 | -0.04 | 0.03 | -0.12 | 0.04 |

|                      |       |       |      |          |                 |      |     |       |      |          |          |      |          |       |      |       |      |
|----------------------|-------|-------|------|----------|-----------------|------|-----|-------|------|----------|----------|------|----------|-------|------|-------|------|
| PC ae C36:3          | 1,983 | -0.04 | 0.02 | 0.023764 | <b>0.040596</b> | 0.06 | 754 | -0.04 | 0.03 | 0.114979 | 0.243836 | 0.07 | 0.891805 | 0.03  | 0.03 | 0.00  | 0.04 |
| PC ae C36:4          | 1,983 | 0.04  | 0.01 | 0.010777 | <b>0.020084</b> | 0.15 | 754 | 0.04  | 0.02 | 0.122414 | 0.255203 | 0.18 | 0.984326 | -0.01 | 0.03 | 0.00  | 0.04 |
| PC ae C36:5          | 1,983 | 0.10  | 0.02 | 1E-11    | <b>1.02E-10</b> | 0.15 | 754 | 0.10  | 0.03 | 7.57E-05 | 0.000931 | 0.19 | 0.977406 | 0.00  | 0.03 | 0.02  | 0.04 |
| PC ae C38:0          | 1,616 | 0.09  | 0.02 | 8.47E-07 | <b>4.34E-06</b> | 0.17 | 653 | 0.10  | 0.03 | 0.000772 | 0.005938 | 0.20 | 0.983917 | -0.01 | 0.04 | 0.01  | 0.04 |
| PC ae C38:2          | 1,983 | -0.07 | 0.01 | 1.21E-05 | <b>4.65E-05</b> | 0.06 | 754 | -0.05 | 0.02 | 0.060341 | 0.145529 | 0.09 | 0.49181  | 0.00  | 0.03 | -0.07 | 0.04 |
| PC ae C38:3          | 1,983 | -0.09 | 0.02 | 5.86E-09 | <b>3.79E-08</b> | 0.08 | 754 | -0.04 | 0.03 | 0.107934 | 0.232911 | 0.11 | 0.176035 | -0.06 | 0.03 | -0.10 | 0.04 |
| PC ae C38:4          | 1,983 | -0.05 | 0.02 | 0.001614 | <b>0.003677</b> | 0.11 | 754 | -0.01 | 0.03 | 0.683601 | 0.771403 | 0.14 | 0.295845 | -0.06 | 0.03 | -0.09 | 0.04 |
| PC ae C38:5          | 1,983 | 0.02  | 0.02 | 0.213677 | 0.288816        | 0.12 | 754 | 0.03  | 0.03 | 0.190163 | 0.321474 | 0.14 | 0.790111 | -0.03 | 0.03 | -0.05 | 0.04 |
| PC ae C38:6          | 1,983 | 0.05  | 0.02 | 0.000744 | <b>0.001759</b> | 0.17 | 754 | 0.08  | 0.03 | 0.003658 | 0.018853 | 0.21 | 0.801755 | -0.04 | 0.03 | -0.03 | 0.04 |
| PC ae C40:1          | 1,983 | 0.07  | 0.02 | 4.05E-05 | <b>0.000138</b> | 0.09 | 754 | 0.08  | 0.03 | 0.002424 | 0.0142   | 0.11 | 0.983917 | 0.01  | 0.04 | 0.00  | 0.04 |
| PC ae C40:2          | 1,983 | 0.01  | 0.01 | 0.721044 | 0.786698        | 0.12 | 754 | 0.06  | 0.02 | 0.012359 | 0.049037 | 0.18 | 0.012344 | -0.08 | 0.03 | -0.13 | 0.04 |
| PC ae C40:3          | 1,922 | -0.05 | 0.01 | 0.000163 | <b>0.000489</b> | 0.10 | 734 | -0.05 | 0.02 | 0.04763  | 0.119561 | 0.14 | 0.624792 | -0.01 | 0.03 | -0.05 | 0.03 |
| PC ae C40:4          | 1,983 | -0.08 | 0.02 | 2.17E-06 | <b>9.9E-06</b>  | 0.08 | 754 | -0.06 | 0.03 | 0.020237 | 0.06137  | 0.11 | 0.59968  | -0.03 | 0.03 | -0.06 | 0.04 |
| PC ae C40:5          | 1,983 | -0.03 | 0.02 | 0.030533 | 0.050751        | 0.08 | 754 | -0.02 | 0.03 | 0.502522 | 0.656355 | 0.12 | 0.520145 | -0.05 | 0.03 | -0.07 | 0.04 |
| PC ae C40:6          | 1,983 | -0.06 | 0.02 | 0.000284 | <b>0.000727</b> | 0.17 | 754 | 0.00  | 0.03 | 0.912514 | 0.919993 | 0.20 | 0.158904 | -0.07 | 0.03 | -0.10 | 0.04 |
| PC ae C42:1          | 1,938 | 0.01  | 0.02 | 0.557053 | 0.647842        | 0.04 | 741 | -0.02 | 0.03 | 0.454949 | 0.608246 | 0.06 | 0.509718 | 0.07  | 0.04 | 0.07  | 0.04 |
| PC ae C42:2          | 1,983 | 0.02  | 0.02 | 0.118477 | 0.175574        | 0.10 | 754 | 0.04  | 0.03 | 0.169513 | 0.311701 | 0.12 | 0.899268 | -0.02 | 0.03 | -0.03 | 0.04 |
| PC ae C42:3          | 1,983 | 0.02  | 0.01 | 0.084541 | 0.128377        | 0.14 | 754 | 0.03  | 0.02 | 0.249364 | 0.398335 | 0.17 | 0.983917 | -0.01 | 0.03 | -0.01 | 0.03 |
| PC ae C42:4          | 1,983 | -0.06 | 0.02 | 0.000204 | <b>0.000584</b> | 0.11 | 754 | -0.06 | 0.03 | 0.022107 | 0.063236 | 0.13 | 0.899268 | -0.01 | 0.03 | -0.03 | 0.04 |
| PC ae C42:5          | 1,983 | -0.06 | 0.02 | 0.000217 | <b>0.000605</b> | 0.08 | 754 | -0.06 | 0.03 | 0.035412 | 0.094688 | 0.10 | 0.608217 | -0.04 | 0.03 | -0.06 | 0.04 |
| PC ae C44:4          | 1,983 | -0.02 | 0.01 | 0.181462 | 0.250785        | 0.06 | 754 | -0.03 | 0.02 | 0.102852 | 0.229614 | 0.07 | 0.801755 | 0.01  | 0.03 | 0.03  | 0.03 |
| PC ae C44:5          | 1,983 | -0.01 | 0.01 | 0.399652 | 0.496538        | 0.10 | 754 | -0.02 | 0.02 | 0.350598 | 0.507336 | 0.09 | 0.801755 | -0.03 | 0.03 | -0.01 | 0.03 |
| PC ae C44:6          | 1,983 | -0.04 | 0.01 | 0.007742 | <b>0.01488</b>  | 0.09 | 754 | -0.06 | 0.02 | 0.016888 | 0.059504 | 0.10 | 0.966039 | -0.01 | 0.03 | 0.02  | 0.03 |
| <b>Sphingolipids</b> |       |       |      |          |                 |      |     |       |      |          |          |      |          |       |      |       |      |
| SM C16:0             | 1,983 | 0.01  | 0.01 | 0.36541  | 0.458627        | 0.05 | 754 | 0.03  | 0.02 | 0.056067 | 0.137924 | 0.07 | 0.501162 | -0.02 | 0.02 | -0.05 | 0.02 |
| SM C16:1             | 1,983 | 0.02  | 0.01 | 0.014882 | <b>0.026528</b> | 0.07 | 754 | 0.04  | 0.02 | 0.020955 | 0.06137  | 0.09 | 0.840841 | -0.02 | 0.02 | -0.02 | 0.02 |
| SM C18:0             | 1,983 | 0.04  | 0.01 | 1.07E-05 | <b>4.25E-05</b> | 0.07 | 754 | 0.07  | 0.02 | 1.26E-05 | 0.000221 | 0.14 | 0.501162 | -0.03 | 0.02 | -0.04 | 0.02 |
| SM C18:1             | 1,983 | 0.01  | 0.01 | 0.178527 | 0.249532        | 0.05 | 754 | 0.04  | 0.02 | 0.015016 | 0.055967 | 0.09 | 0.501162 | -0.04 | 0.02 | -0.05 | 0.02 |
| SM C20:2             | 1,983 | -0.06 | 0.01 | 1.43E-06 | <b>6.75E-06</b> | 0.26 | 754 | -0.04 | 0.02 | 0.036529 | 0.095597 | 0.32 | 0.801755 | -0.02 | 0.03 | -0.03 | 0.03 |
| SM C24:0             | 1,983 | 0.04  | 0.01 | 1.27E-06 | <b>6.26E-06</b> | 0.05 | 754 | 0.05  | 0.01 | 0.000408 | 0.003587 | 0.06 | 0.983917 | 0.00  | 0.02 | -0.01 | 0.02 |
| SM C24:1             | 1,983 | 0.03  | 0.01 | 2.8E-05  | <b>0.000101</b> | 0.08 | 754 | 0.05  | 0.01 | 0.000283 | 0.002904 | 0.10 | 0.608217 | -0.03 | 0.02 | -0.02 | 0.02 |
| SM(OH) C14:1         | 1,983 | -0.06 | 0.01 | 3.89E-07 | <b>2.13E-06</b> | 0.14 | 754 | -0.01 | 0.02 | 0.546985 | 0.684792 | 0.20 | 0.003291 | -0.05 | 0.02 | -0.12 | 0.03 |
| SM(OH) C16:1         | 1,983 | -0.05 | 0.01 | 2.55E-06 | <b>1.12E-05</b> | 0.07 | 754 | 0.01  | 0.02 | 0.639576 | 0.749217 | 0.11 | 4.36E-05 | -0.06 | 0.02 | -0.13 | 0.02 |
| SM(OH) C22:1         | 1,983 | -0.03 | 0.01 | 0.004525 | <b>0.009275</b> | 0.05 | 754 | 0.01  | 0.01 | 0.412677 | 0.57681  | 0.06 | 0.008559 | -0.04 | 0.02 | -0.09 | 0.02 |
| SM(OH) C22:2         | 1,983 | -0.05 | 0.01 | 1.34E-07 | <b>8.25E-07</b> | 0.09 | 754 | -0.01 | 0.01 | 0.528789 | 0.675607 | 0.09 | 0.008219 | -0.04 | 0.02 | -0.09 | 0.02 |
| SM(OH) C24:1         | 1,983 | 0.00  | 0.01 | 0.694071 | 0.769106        | 0.05 | 754 | 0.04  | 0.01 | 0.007398 | 0.0325   | 0.07 | 0.038822 | -0.05 | 0.02 | -0.07 | 0.02 |
| <b>Hexoses</b>       |       |       |      |          |                 |      |     |       |      |          |          |      |          |       |      |       |      |
| Hexoses              | 1,983 | -0.04 | 0.02 | 0.008591 | <b>0.016256</b> | 0.16 | 754 | -0.04 | 0.03 | 0.161336 | 0.311701 | 0.22 | 0.98062  | -0.02 | 0.03 | -0.01 | 0.04 |

Abbreviations:  $\beta$ , unstandardized regression coefficient derived from multivariable linear models; SE, standard error.

For an explanation of abbreviated metabolite names, see Supplementary Table 1.

<sup>a</sup> Analyzed with multivariable linear regression analyses analyzing associations of alcohol consumption (ln-transformed alcohol intake + 1) as main independent variable and as dependent variables the residuals obtained from linear mixed models with Z-standardized ln-transformed metabolite concentrations as dependent variables, sex as independent variable, and random intercepts for analytical batches nested within studies. Adjusted for: sex; age (y; continuous), body mass index (kg/m<sup>2</sup>; continuous), self-reported physical activity levels (Cambridge physical activity index(1): inactive, moderately inactive, moderately active, active, unknown), fasting status ( $\geq 6$  hours, 3-5.9 hours,  $< 3$  hours, unknown), meat intake (g/day; continuous), fish intake (g/day; continuous), energy intake (kcal/day; continuous), country, and smoking status (current, former, never, unknown; not in analysis in never smokers only).

<sup>b</sup> Testing for statistical interaction was performed by including product terms for alcohol intake and smoking status (former and current vs. never smokers) and evaluating overall significance of both product terms.

<sup>c</sup> The analysis in the discovery set was adjusted for multiple testing using the false discovery rate (FDR) method. Statistically significant associations (FDR q-value $<0.05$ ) are depicted in bold.

**Supplementary Table 7.** Results of discovery and replication analysis on associations of categories of alcohol intake (heavy vs. light) with concentrations of metabolites included in the current analysis (n=123)<sup>a</sup>

| Metabolite                  | Discovery analysis (n=1,983) <sup>b</sup> |       |      |          |                             |                | Replication analysis (n=991) <sup>b</sup> |       |      |          |                                    |                |
|-----------------------------|---|-------|------|----------|-----------------------------|----------------|---|-------|------|----------|------------------------------------|----------------|
|                             | n   | β     | SE   | p-value  | FDR<br>q-value <sup>c</sup> | R <sup>2</sup> | n   | β     | SE   | p-value  | Bonf.-adj.<br>p-value <sup>d</sup> | R <sup>2</sup> |
| <b>Acylcarnitines</b>       |   |       |      |          |                             |                |   |       |      |          |                                    |                |
| Acylcarnitine C0            | 1,983                                     | 0.24  | 0.07 | 0.000934 | <b>0.002253</b>             | 0.06           | 991                                       | 0.14  | 0.11 | 0.194565 | 1                                  | 0.07           |
| Acylcarnitine C14:1         | 1,956                                     | 0.25  | 0.07 | 0.00036  | <b>0.001029</b>             | 0.09           | 979                                       | 0.30  | 0.10 | 0.002161 | 0.151261                           | 0.14           |
| Acylcarnitine C16           | 1,956                                     | 0.46  | 0.07 | <1E-12   | <b>&lt;1E-12</b>            | 0.15           | 979                                       | 0.32  | 0.09 | 0.000699 | <b>0.048941</b>                    | 0.19           |
| Acylcarnitine C18           | 1,956                                     | 0.25  | 0.07 | 0.000417 | <b>0.00109</b>              | 0.09           | 979                                       | 0.05  | 0.10 | 0.569899 | 1                                  | 0.11           |
| Acylcarnitine C18:1         | 1,956                                     | 0.29  | 0.07 | 2.09E-05 | <b>7.83E-05</b>             | 0.17           | 979                                       | 0.14  | 0.10 | 0.162496 | 1                                  | 0.24           |
| Acylcarnitine C18:2         | 1,956                                     | 0.10  | 0.07 | 0.158328 | 0.230313                    | 0.18           | NA  |       |      |          |                                    |                |
| Acylcarnitine C2            | 1,983                                     | 0.36  | 0.07 | 1.75E-06 | <b>8.26E-06</b>             | 0.10           | 991                                       | 0.27  | 0.11 | 0.012497 | 0.874795                           | 0.13           |
| Acylcarnitine C3            | 1,956                                     | -0.05 | 0.08 | 0.548656 | 0.648891                    | 0.07           | NA  |       |      |          |                                    |                |
| Acylcarnitine C4            | 1,852                                     | 0.07  | 0.07 | 0.373074 | 0.490008                    | 0.05           | NA  |       |      |          |                                    |                |
| Acylcarnitine C5            | 1,828                                     | 0.11  | 0.07 | 0.135205 | 0.205311                    | 0.04           | NA  |       |      |          |                                    |                |
| <b>Amino acids</b>          |   |       |      |          |                             |                |   |       |      |          |                                    |                |
| Alanine                     | 1,983                                     | -0.09 | 0.07 | 0.217054 | 0.303383                    | 0.11           | NA  |       |      |          |                                    |                |
| Arginine                    | 1,983                                     | -0.22 | 0.06 | 0.000171 | <b>0.000526</b>             | 0.20           | 989                                       | -0.16 | 0.09 | 0.08214  | 1                                  | 0.23           |
| Asparagine                  | 1,983                                     | 0.00  | 0.07 | 0.982346 | 0.990398                    | 0.13           | NA  |       |      |          |                                    |                |
| Citrulline                  | 1,983                                     | -0.30 | 0.07 | 1.98E-05 | <b>7.83E-05</b>             | 0.10           | 989                                       | -0.28 | 0.10 | 0.004686 | 0.327996                           | 0.15           |
| Glutamine                   | 1,983                                     | -0.12 | 0.08 | 0.100806 | 0.158964                    | 0.05           | NA  |       |      |          |                                    |                |
| Glutamate                   | 1,983                                     | 0.20  | 0.06 | 0.001334 | <b>0.003095</b>             | 0.26           | 989                                       | 0.08  | 0.09 | 0.377721 | 1                                  | 0.26           |
| Glycine                     | 1,983                                     | -0.12 | 0.06 | 0.048374 | 0.079333                    | 0.11           | NA  |       |      |          |                                    |                |
| Histidine                   | 1,983                                     | 0.05  | 0.07 | 0.480328 | 0.590804                    | 0.08           | NA  |       |      |          |                                    |                |
| Isoleucine                  | 1,983                                     | 0.03  | 0.07 | 0.724893 | 0.795585                    | 0.08           | NA  |       |      |          |                                    |                |
| Leucine                     | 1,982                                     | 0.03  | 0.07 | 0.652553 | 0.750132                    | 0.08           | NA  |       |      |          |                                    |                |
| Lysine                      | 1,983                                     | -0.02 | 0.07 | 0.798641 | 0.846835                    | 0.06           | NA  |       |      |          |                                    |                |
| Methionine                  | 1,983                                     | 0.06  | 0.07 | 0.374478 | 0.490008                    | 0.08           | NA  |       |      |          |                                    |                |
| Ornithine                   | 1,983                                     | -0.03 | 0.07 | 0.686945 | 0.771537                    | 0.17           | NA  |       |      |          |                                    |                |
| Phenylalanine               | 1,983                                     | 0.02  | 0.06 | 0.730903 | 0.795585                    | 0.10           | NA  |       |      |          |                                    |                |
| Proline                     | 1,983                                     | -0.06 | 0.08 | 0.437499 | 0.554767                    | 0.09           | NA  |       |      |          |                                    |                |
| Serine                      | 1,983                                     | -0.15 | 0.06 | 0.01538  | <b>0.029558</b>             | 0.11           | 989                                       | -0.31 | 0.08 | 0.000192 | <b>0.013473*</b>                   | 0.13           |
| Threonine                   | 1,983                                     | 0.00  | 0.07 | 0.994377 | 0.994377                    | 0.09           | NA  |       |      |          |                                    |                |
| Tryptophan                  | 1,983                                     | 0.02  | 0.07 | 0.743788 | 0.802508                    | 0.06           | NA  |       |      |          |                                    |                |
| Tyrosine                    | 1,983                                     | 0.22  | 0.07 | 0.001979 | <b>0.004346</b>             | 0.11           | 989                                       | 0.22  | 0.10 | 0.028657 | 1                                  | 0.12           |
| Valine                      | 1,983                                     | -0.01 | 0.07 | 0.912314 | 0.936033                    | 0.08           | NA  |       |      |          |                                    |                |
| t4-hydroxyproline           | 1,774                                     | 0.18  | 0.08 | 0.027244 | <b>0.047872</b>             | 0.12           | 871                                       | 0.24  | 0.11 | 0.031068 | 1                                  | 0.13           |
| <b>Biogenic amines</b>      |   |       |      |          |                             |                |   |       |      |          |                                    |                |
| ADMA                        | 1,930                                     | -0.07 | 0.07 | 0.317885 | 0.429669                    | 0.04           | NA  |       |      |          |                                    |                |
| Creatine                    | 1,983                                     | 0.05  | 0.07 | 0.444951 | 0.555297                    | 0.04           | NA  |       |      |          |                                    |                |
| Kynurenine                  | 1,983                                     | -0.03 | 0.07 | 0.689992 | 0.771537                    | 0.10           | NA  |       |      |          |                                    |                |
| Taurine                     | 1,983                                     | 0.08  | 0.05 | 0.161631 | 0.23117                     | 0.32           | NA  |       |      |          |                                    |                |
| <b>Glycerophospholipids</b> |   |       |      |          |                             |                |   |       |      |          |                                    |                |
| LysoPC a C16:0              | 1,983                                     | 0.36  | 0.06 | 4.3E-09  | <b>3.31E-08</b>             | 0.16           | 991                                       | 0.20  | 0.08 | 0.017818 | 1                                  | 0.13           |
| LysoPC a C16:1              | 1,983                                     | 0.52  | 0.07 | <1E-12   | <b>&lt;1E-12</b>            | 0.15           | 991                                       | 0.49  | 0.09 | 9.12E-08 | <b>6.38E-06</b>                    | 0.14           |
| LysoPC a C17:0              | 1,983                                     | -0.42 | 0.06 | <1E-12   | <b>&lt;1E-12</b>            | 0.20           | 991                                       | -0.57 | 0.09 | 1E-10    | <b>7E-09</b>                       | 0.19           |
| LysoPC a C18:0              | 1,983                                     | -0.04 | 0.06 | 0.503161 | 0.61276                     | 0.14           | NA  |       |      |          |                                    |                |

|                |       |       |      |          |                  |      |     |       |      |          |                  |      |
|----------------|-------|-------|------|----------|------------------|------|-----|-------|------|----------|------------------|------|
| LysoPC a C18:1 | 1,983 | 0.25  | 0.06 | 0.00011  | <b>0.000357</b>  | 0.15 | 991 | 0.19  | 0.09 | 0.035016 | 1                | 0.15 |
| LysoPC a C18:2 | 1,983 | -0.01 | 0.07 | 0.913203 | 0.936033         | 0.15 | NA  |       |      |          |                  |      |
| LysoPC a C20:3 | 1,983 | 0.18  | 0.07 | 0.008181 | <b>0.016497</b>  | 0.09 | 991 | 0.29  | 0.09 | 0.002295 | 0.160657         | 0.1  |
| LysoPC a C20:4 | 1,983 | 0.29  | 0.07 | 2.1E-05  | <b>7.83E-05</b>  | 0.11 | 991 | 0.29  | 0.09 | 0.000776 | 0.054329         | 0.12 |
| PC aa C28:1    | 1,983 | 0.07  | 0.06 | 0.242812 | 0.331843         | 0.17 | NA  |       |      |          |                  |      |
| PC aa C30:0    | 1,983 | 0.35  | 0.07 | 7.9E-08  | <b>4.63E-07</b>  | 0.18 | 991 | 0.48  | 0.09 | 2.1E-07  | <b>1.47E-05</b>  | 0.23 |
| PC aa C32:0    | 1,983 | 0.47  | 0.07 | <1E-12   | <b>&lt;1E-12</b> | 0.11 | 991 | 0.55  | 0.09 | 1.5E-09  | <b>1.05E-07</b>  | 0.16 |
| PC aa C32:1    | 1,983 | 0.82  | 0.07 | <1E-12   | <b>&lt;1E-12</b> | 0.25 | 991 | 0.93  | 0.10 | <1E-12   | <b>&lt;1E-12</b> | 0.28 |
| PC aa C32:2    | 1,983 | 0.26  | 0.07 | 0.000191 | <b>0.000573</b>  | 0.13 | 991 | 0.38  | 0.10 | 0.000121 | <b>0.008451</b>  | 0.18 |
| PC aa C32:3    | 1,983 | -0.20 | 0.06 | 0.000894 | <b>0.0022</b>    | 0.20 | 991 | -0.32 | 0.08 | 0.000177 | <b>0.012421</b>  | 0.22 |
| PC aa C34:1    | 1,983 | 0.69  | 0.07 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 991 | 0.61  | 0.09 | <1E-12   | <b>&lt;1E-12</b> | 0.14 |
| PC aa C34:2    | 1,983 | 0.15  | 0.03 | 2.52E-06 | <b>1.15E-05</b>  | 0.04 | 991 | 0.11  | 0.04 | 0.011269 | 0.788855         | 0.04 |
| PC aa C34:3    | 1,983 | 0.32  | 0.06 | 9.7E-07  | <b>4.77E-06</b>  | 0.24 | 991 | 0.40  | 0.09 | 4.8E-06  | <b>0.000336</b>  | 0.29 |
| PC aa C34:4    | 1,983 | 0.45  | 0.07 | 5E-10    | <b>4.73E-09</b>  | 0.13 | 991 | 0.55  | 0.10 | 9.67E-08 | <b>6.77E-06</b>  | 0.17 |
| PC aa C36:0    | 1,983 | 0.13  | 0.06 | 0.031656 | 0.054079         | 0.16 | NA  |       |      |          |                  |      |
| PC aa C36:1    | 1,983 | 0.45  | 0.07 | 1E-09    | <b>8.79E-09</b>  | 0.06 | 991 | 0.38  | 0.10 | 0.00019  | <b>0.013315*</b> | 0.06 |
| PC aa C36:2    | 1,983 | 0.07  | 0.06 | 0.21501  | 0.303383         | 0.03 | NA  |       |      |          |                  |      |
| PC aa C36:3    | 1,983 | 0.22  | 0.07 | 0.001966 | <b>0.004346</b>  | 0.06 | 991 | 0.24  | 0.10 | 0.01411  | 0.987668         | 0.1  |
| PC aa C36:4    | 1,983 | 0.63  | 0.07 | <1E-12   | <b>&lt;1E-12</b> | 0.13 | 991 | 0.66  | 0.09 | <1E-12   | <b>&lt;1E-12</b> | 0.18 |
| PC aa C36:5    | 1,983 | 0.56  | 0.07 | <1E-12   | <b>&lt;1E-12</b> | 0.18 | 991 | 0.55  | 0.10 | 7.49E-08 | <b>5.24E-06</b>  | 0.22 |
| PC aa C36:6    | 1,983 | 0.33  | 0.07 | 6.74E-06 | <b>2.86E-05</b>  | 0.14 | 991 | 0.31  | 0.10 | 0.001942 | 0.135946         | 0.18 |
| PC aa C38:0    | 1,983 | -0.12 | 0.06 | 0.062112 | 0.099217         | 0.26 | NA  |       |      |          |                  |      |
| PC aa C38:3    | 1,983 | 0.11  | 0.07 | 0.125489 | 0.192939         | 0.13 | NA  |       |      |          |                  |      |
| PC aa C38:4    | 1,983 | 0.30  | 0.07 | 4.93E-05 | <b>0.000178</b>  | 0.11 | 991 | 0.31  | 0.10 | 0.003632 | 0.254206         | 0.15 |
| PC aa C38:5    | 1,983 | 0.44  | 0.08 | 7E-09    | <b>4.53E-08</b>  | 0.11 | 991 | 0.47  | 0.11 | 1.15E-05 | <b>0.000805</b>  | 0.12 |
| PC aa C38:6    | 1,983 | 0.38  | 0.07 | 1.55E-07 | <b>8.67E-07</b>  | 0.18 | 991 | 0.25  | 0.10 | 0.014329 | 1                | 0.21 |
| PC aa C40:2    | 1,922 | -0.16 | 0.07 | 0.030152 | 0.052236         | 0.14 | NA  |       |      |          |                  |      |
| PC aa C40:3    | 1,922 | -0.03 | 0.07 | 0.639251 | 0.748837         | 0.12 | NA  |       |      |          |                  |      |
| PC aa C40:4    | 1,983 | 0.33  | 0.07 | 4.39E-06 | <b>1.93E-05</b>  | 0.12 | 991 | 0.44  | 0.11 | 4.31E-05 | <b>0.003019*</b> | 0.12 |
| PC aa C40:5    | 1,983 | 0.24  | 0.07 | 0.00041  | <b>0.00109</b>   | 0.16 | 991 | 0.35  | 0.10 | 0.000369 | <b>0.025824*</b> | 0.17 |
| PC aa C40:6    | 1,983 | 0.10  | 0.07 | 0.153283 | 0.227155         | 0.15 | NA  |       |      |          |                  |      |
| PC aa C42:0    | 1,983 | -0.23 | 0.05 | 1.1E-05  | <b>4.52E-05</b>  | 0.17 | 991 | -0.16 | 0.07 | 0.030369 | 1                | 0.16 |
| PC aa C42:1    | 1,983 | -0.14 | 0.05 | 0.006499 | <b>0.013324</b>  | 0.17 | 991 | -0.11 | 0.07 | 0.137027 | 1                | 0.17 |
| PC aa C42:2    | 1,983 | 0.16  | 0.06 | 0.009574 | <b>0.018994</b>  | 0.24 | 991 | 0.15  | 0.08 | 0.064457 | 1                | 0.26 |
| PC aa C42:4    | 1,922 | 0.09  | 0.06 | 0.159159 | 0.230313         | 0.04 | NA  |       |      |          |                  |      |
| PC aa C42:5    | 1,922 | -0.01 | 0.07 | 0.907776 | 0.936033         | 0.15 | NA  |       |      |          |                  |      |
| PC aa C42:6    | 1,922 | -0.02 | 0.06 | 0.727294 | 0.795585         | 0.08 | NA  |       |      |          |                  |      |
| PC ae C30:0    | 1,922 | -0.10 | 0.06 | 0.107673 | 0.167644         | 0.19 | NA  |       |      |          |                  |      |
| PC ae C30:2    | 1,922 | -0.28 | 0.05 | 4.39E-08 | <b>2.7E-07</b>   | 0.12 | 959 | -0.34 | 0.07 | 1.94E-06 | <b>0.000136</b>  | 0.13 |
| PC ae C32:1    | 1,983 | 0.20  | 0.07 | 0.002998 | <b>0.006469</b>  | 0.07 | 991 | 0.23  | 0.09 | 0.014133 | 0.989303         | 0.11 |
| PC ae C32:2    | 1,983 | 0.20  | 0.07 | 0.004681 | <b>0.009759</b>  | 0.07 | 991 | 0.06  | 0.09 | 0.503245 | 1                | 0.08 |
| PC ae C34:0    | 1,983 | 0.06  | 0.07 | 0.422491 | 0.541317         | 0.09 | NA  |       |      |          |                  |      |
| PC ae C34:1    | 1,983 | 0.01  | 0.07 | 0.84714  | 0.890583         | 0.08 | NA  |       |      |          |                  |      |
| PC ae C34:2    | 1,983 | -0.23 | 0.07 | 0.000858 | <b>0.002153</b>  | 0.08 | 991 | -0.25 | 0.10 | 0.009153 | 0.640682         | 0.1  |
| PC ae C34:3    | 1,983 | 0.15  | 0.07 | 0.040857 | 0.068841         | 0.09 | NA  |       |      |          |                  |      |
| PC ae C36:0    | 1,922 | 0.59  | 0.07 | <1E-12   | <b>&lt;1E-12</b> | 0.12 | 959 | 0.53  | 0.10 | 8.55E-08 | <b>5.98E-06</b>  | 0.12 |
| PC ae C36:1    | 1,983 | -0.04 | 0.07 | 0.538655 | 0.643249         | 0.07 | NA  |       |      |          |                  |      |
| PC ae C36:2    | 1,983 | -0.52 | 0.07 | <1E-12   | <b>&lt;1E-12</b> | 0.13 | 991 | -0.64 | 0.10 | 1E-10    | <b>7E-09</b>     | 0.14 |
| PC ae C36:3    | 1,983 | -0.17 | 0.07 | 0.0194   | <b>0.035616</b>  | 0.06 | 991 | -0.17 | 0.10 | 0.089515 | 1                | 0.06 |

|                      |       |       |      |          |                 |      |     |       |      |          |                 |      |
|----------------------|-------|-------|------|----------|-----------------|------|-----|-------|------|----------|-----------------|------|
| PC ae C36:4          | 1,983 | 0.17  | 0.07 | 0.011719 | <b>0.022879</b> | 0.16 | 991 | 0.27  | 0.09 | 0.004587 | 0.321122        | 0.2  |
| PC ae C36:5          | 1,983 | 0.42  | 0.07 | 5E-10    | <b>4.73E-09</b> | 0.15 | 991 | 0.47  | 0.09 | 5.6E-07  | <b>3.92E-05</b> | 0.18 |
| PC ae C38:0          | 1,616 | 0.27  | 0.08 | 0.000833 | <b>0.002134</b> | 0.17 | 811 | 0.16  | 0.10 | 0.118651 | 1               | 0.22 |
| PC ae C38:2          | 1,983 | -0.25 | 0.07 | 0.000162 | <b>0.00051</b>  | 0.06 | 991 | -0.17 | 0.09 | 0.07015  | 1               | 0.09 |
| PC ae C38:3          | 1,983 | -0.35 | 0.07 | 3.85E-07 | <b>1.97E-06</b> | 0.08 | 991 | -0.36 | 0.10 | 0.000374 | <b>0.026211</b> | 0.1  |
| PC ae C38:4          | 1,983 | -0.17 | 0.07 | 0.017794 | <b>0.033162</b> | 0.11 | 991 | -0.11 | 0.10 | 0.278653 | 1               | 0.14 |
| PC ae C38:5          | 1,983 | 0.10  | 0.07 | 0.142878 | 0.214317        | 0.12 | NA  |       |      |          |                 |      |
| PC ae C38:6          | 1,983 | 0.14  | 0.07 | 0.04153  | 0.069029        | 0.17 | NA  |       |      |          |                 |      |
| PC ae C40:1          | 1,983 | 0.29  | 0.07 | 7.94E-05 | <b>0.000277</b> | 0.09 | 991 | 0.20  | 0.10 | 0.045864 | 1               | 0.08 |
| PC ae C40:2          | 1,983 | -0.08 | 0.07 | 0.236843 | 0.327322        | 0.12 | NA  |       |      |          |                 |      |
| PC ae C40:3          | 1,922 | -0.25 | 0.06 | 8.6E-05  | <b>0.000286</b> | 0.10 | 959 | -0.25 | 0.10 | 0.009465 | 0.662555        | 0.12 |
| PC ae C40:4          | 1,983 | -0.25 | 0.07 | 0.000371 | <b>0.001036</b> | 0.08 | 991 | -0.11 | 0.11 | 0.31584  | 1               | 0.09 |
| PC ae C40:5          | 1,983 | -0.16 | 0.07 | 0.025056 | <b>0.044889</b> | 0.08 | 991 | -0.07 | 0.10 | 0.474978 | 1               | 0.06 |
| PC ae C40:6          | 1,983 | -0.35 | 0.07 | 3.22E-07 | <b>1.72E-06</b> | 0.18 | 991 | -0.40 | 0.10 | 7.4E-05  | <b>0.005178</b> | 0.2  |
| PC ae C42:1          | 1,938 | 0.17  | 0.08 | 0.025182 | <b>0.044889</b> | 0.05 | 975 | 0.25  | 0.10 | 0.01427  | 0.99891         | 0.05 |
| PC ae C42:2          | 1,983 | 0.06  | 0.07 | 0.396672 | 0.513586        | 0.10 | NA  |       |      |          |                 |      |
| PC ae C42:3          | 1,983 | 0.04  | 0.06 | 0.514523 | 0.620454        | 0.14 | NA  |       |      |          |                 |      |
| PC ae C42:4          | 1,983 | -0.24 | 0.07 | 0.000407 | <b>0.00109</b>  | 0.11 | 991 | -0.16 | 0.10 | 0.096208 | 1               | 0.12 |
| PC ae C42:5          | 1,983 | -0.23 | 0.07 | 0.001243 | <b>0.00294</b>  | 0.08 | 991 | -0.09 | 0.10 | 0.367984 | 1               | 0.07 |
| PC ae C44:4          | 1,983 | -0.02 | 0.06 | 0.662712 | 0.754755        | 0.06 | NA  |       |      |          |                 |      |
| PC ae C44:5          | 1,983 | -0.03 | 0.06 | 0.648538 | 0.750132        | 0.10 | NA  |       |      |          |                 |      |
| PC ae C44:6          | 1,983 | -0.16 | 0.06 | 0.015867 | <b>0.030026</b> | 0.09 | 991 | 0.01  | 0.09 | 0.92325  | 1               | 0.08 |
| <b>Sphingolipids</b> |       |       |      |          |                 |      |     |       |      |          |                 |      |
| SM C16:0             | 1,983 | 0.00  | 0.04 | 0.945382 | 0.961008        | 0.05 | NA  |       |      |          |                 |      |
| SM C16:1             | 1,983 | 0.04  | 0.04 | 0.3219   | 0.430366        | 0.07 | NA  |       |      |          |                 |      |
| SM C18:0             | 1,983 | 0.13  | 0.04 | 0.003071 | <b>0.006512</b> | 0.07 | 991 | -0.05 | 0.06 | 0.379058 | 1               | 0.09 |
| SM C18:1             | 1,983 | 0.01  | 0.04 | 0.772134 | 0.825848        | 0.05 | NA  |       |      |          |                 |      |
| SM C20:2             | 1,983 | -0.32 | 0.05 | 5.1E-09  | <b>3.69E-08</b> | 0.27 | 991 | -0.26 | 0.07 | 9.64E-05 | <b>0.006746</b> | 0.3  |
| SM C24:0             | 1,983 | 0.15  | 0.04 | 8.1E-05  | <b>0.000277</b> | 0.05 | 991 | 0.19  | 0.05 | 0.00031  | <b>0.021677</b> | 0.08 |
| SM C24:1             | 1,983 | 0.12  | 0.04 | 0.001739 | <b>0.00396</b>  | 0.08 | 991 | 0.17  | 0.05 | 0.000902 | 0.063164        | 0.14 |
| SM(OH) C14:1         | 1,983 | -0.30 | 0.05 | 5.5E-09  | <b>3.76E-08</b> | 0.15 | 991 | -0.35 | 0.07 | 9.23E-07 | <b>6.46E-05</b> | 0.16 |
| SM(OH) C16:1         | 1,983 | -0.27 | 0.05 | 4.2E-09  | <b>3.31E-08</b> | 0.08 | 991 | -0.38 | 0.06 | 3.3E-09  | <b>2.31E-07</b> | 0.12 |
| SM(OH) C22:1         | 1,983 | -0.15 | 0.04 | 0.000236 | <b>0.000693</b> | 0.05 | 991 | -0.14 | 0.05 | 0.008197 | 0.573816        | 0.07 |
| SM(OH) C22:2         | 1,983 | -0.25 | 0.04 | 2E-10    | <b>2.24E-09</b> | 0.10 | 991 | -0.25 | 0.05 | 4.58E-06 | <b>0.000321</b> | 0.11 |
| SM(OH) C24:1         | 1,983 | -0.03 | 0.04 | 0.446946 | 0.555297        | 0.05 | NA  |       |      |          |                 |      |
| <b>Hexoses</b>       |       |       |      |          |                 |      |     |       |      |          |                 |      |
| Hexoses              | 1,983 | -0.13 | 0.07 | 0.055507 | 0.089833        | 0.16 | NA  |       |      |          |                 |      |

Abbreviations:  $\beta$ , unstandardized regression coefficient derived from multivariable linear models; Bonf.-adj. p-value, Bonferroni-adjusted p-value; NA, not applicable (metabolites that were not significant in the discovery analysis were not taken forward to the replication analysis); SE, standard error.

For an explanation of abbreviated metabolite names, see Supplementary Table 1.

<sup>a</sup> Analyzed with multivariable linear regression analyses analyzing associations of heavy ( $\geq 40$  g/day) vs. light drinking (0.1-4.9 g/day) as independent variable and as dependent variables the residuals obtained from linear mixed models with Z-standardized ln-transformed metabolite concentrations as dependent variables, sex as independent variable, and random intercepts for analytical batches nested within studies. Adjusted for: sex; age (y; continuous), body mass index ( $\text{kg/m}^2$ ; continuous), self-reported physical activity levels (Cambridge physical activity index(1): inactive, moderately inactive, moderately active, active, unknown), fasting status ( $\geq 6$  hours, 3-5.9 hours,  $< 3$  hours, unknown), meat intake (g/day; continuous), fish intake (g/day; continuous), energy intake (kcal/day; continuous), country, and smoking status (current, former, never, unknown).

<sup>b</sup> The discovery and replication set were taken as random samples without replacement of 66.7% and 33.3% of the total dataset, respectively.

<sup>c</sup> The analysis in the discovery set was adjusted for multiple testing using the false discovery rate (FDR) method. Statistically significant associations (FDR q-value $< 0.05$ ) are depicted in bold.

<sup>d</sup> The analysis in the replication set was adjusted for multiple testing using Bonferroni correction. Statistically significant associations (Bonferroni-adjusted p-value $< 0.05$ ) are depicted in bold. Asterisk denotes that the metabolite was not identified in the main analysis with continuous ln-transformed alcohol intake.



## References

1. Wareham, N.J., R.W. Jakes, K.L. Rennie, J. Schuit, J. Mitchell, S. Hennings, and N.E. Day, *Validity and repeatability of a simple index derived from the short physical activity questionnaire used in the European Prospective Investigation into Cancer and Nutrition (EPIC) study*. Public Health Nutr, 2003. **6**(4): p. 407-13.