**Supplementary Table 1. Mediation tests for all metabolic markers with fish consumption analysed as a dichotomous variable (less than two serves per week as reference group)**

|  |  |  |  |
| --- | --- | --- | --- |
| Metabolic marker | Step 2a,b | Step 3d | Step 4f |
| **Fishc > Metabolite** | **Metabolite > Depressione** | **Indirect****effect** | **Mediation****(%)** |
| Docosahexaenoic acid (mmol/l) | 0.025 | \*\*\*\* | -3.9 | \* | -0.024 | 16.6 |
| Omega-3 fatty acids (mmol/l) | 0.036 | \*\*\*\* | -2.0 | # | -0.018 | 12.5 |
| Estimated degree of unsaturation | 0.018 | \*\*\*\* | -2.4 |   | -0.010 | 7.0 |
| Glucose (mmol/l) | -0.072 |  | 0.39 | \*\* | -0.009 | 6.3 |
| Omega-3 to Omega-6 ratio | 0.00 | \*\*\*\* | -5.1 |   | -0.009 | 6.0 |
| Ratio of docosahexaenoic acid to total fatty acids (%) | 0.24 | \*\*\*\* | -0.26 |   | -0.008 | 5.9 |
| Pyruvate (mmol/l) | 0.00 | \* | 4.5 |   | -0.008 | 5.5 |
| Free cholesterol to total lipids ratio in small VLDL (%) | 0.22 |  | -0.1 | \* | -0.007 | 5.3 |
| Phospholipids to total lipids ratio in small VLDL (%) | 0.88 | \* | -0.03 |   | -0.006 | 4.6 |
| Polyunsaturated fatty acids (mmol/l) | 0.093 |  | -0.23 |   | -0.006 | 4.2 |
| Total cholesterol in small HDL (mmol/l) | 0.014 |  | -1.2 | # | -0.005 | 3.8 |
| Non-DHA omega-3 fatty acids (omega-3-DHA) (mmol/l) | 0.011 | \* | -1.8 |   | -0.005 | 3.6 |
| Total lipids in small HDL (mmol/l) | 0.021 |  | -0.76 | # | -0.005 | 3.5 |
| Cholesterol esters in small HDL (mmol/l) | 0.012 |  | -1.3 |   | -0.005 | 3.4 |
| Concentration of small HDL particles (mmol/l) | 0.00 |  | -1.70E+05 | # | -0.005 | 3.4 |
| Triglycerides to total lipids ratio in small VLDL (%) | -0.51 |  | 0.03 | \* | -0.005 | 3.3 |
| Triglycerides to total lipids ratio in very large VLDL (%) | -1.2 |  | 0.01 | # | -0.004 | 3.2 |
| Free cholesterol in small HDL (mmol/l) | 0.00 |  | -8.9 | \* | -0.004 | 3.0 |
| Ratio of omega-3 fatty acids to total fatty acids (%) | 0.34 | \*\*\*\* | -0.11 |   | -0.004 | 2.8 |
| Omega-6 fatty acids (mmol/l) | 0.057 |  | -0.23 |   | -0.004 | 2.7 |
| Total cholines (mmol/l) | 0.036 |  | -0.35 |   | -0.004 | 2.6 |
| Apolipoprotein A-I (g/l) | 0.054 | \* | -0.29 |   | -0.004 | 2.5 |
| Phosphatidylcholine and other cholines (mmol/l) | 0.033 |  | -0.35 |   | -0.003 | 2.4 |
| Glycoprotein acetyls, mainly a1-acid glycoprotein (mmol/l) | -0.024 |  | 0.47 |   | -0.003 | 2.3 |
| Mean diameter for VLDL particles (nm) | -0.22 | \* | 0.07 |   | -0.003 | 2.2 |
| Total phosphoglycerides (mmol/l) | 0.031 |  | -0.33 |   | -0.003 | 2.1 |
| Phospholipids in small HDL (mmol/l) | 0.00 |  | -1.1 |   | -0.003 | 2.1 |
| Triglycerides to total lipids ratio in chylomicrons and extremely large VLDL (%) | -1.2 |  | 0.00 |   | -0.003 | 2.0 |
| Ratio of conjugated linoleic acid to total fatty acids (%) | -0.028 | \* | 0.45 |   | -0.003 | 2.0 |
| Total cholesterol to total lipids ratio in small HDL (%) | 0.36 |  | -0.03 |   | -0.003 | 2.0 |
| 18:2, linoleic acid (mmol/l) | 0.053 |  | -0.20 |   | -0.003 | 2.0 |
| Phospholipids to total lipids ratio in medium VLDL (%) | 1.1 |  | 0.00 |   | -0.002 | 1.9 |
| Acetate (mmol/l) | 0.00 |  | -14 | \* | -0.003 | 1.9 |
| Phospholipids to total lipids ratio in small HDL (%) | -0.19 |  | 0.04 | # | -0.002 | 1.8 |
| Triglycerides to total lipids ratio in large VLDL (%) | -1.9 |  | 0.00 |   | -0.002 | 1.6 |
| Cholesterol esters to total lipids ratio in very large HDL (%) | -1 |  | 0.00 |   | -0.002 | 1.6 |
| Ratio of diacylglycerol to triglycerides (%) | 0.00 |  | 7.1 |   | -0.002 | 1.5 |
| Phospholipids to total lipids ratio in IDL (%) | 0.53 |  | -0.02 |   | -0.002 | 1.5 |
| Phospholipids in medium HDL (mmol/l) | 0.023 | \* | -0.39 |   | -0.002 | 1.4 |
| Phospholipids in chylomicrons and extremely large VLDL (mmol/l) | 0.00 |  | 89 |   | -0.002 | 1.3 |
| Total cholesterol to total lipids ratio in very large HDL (%) | -1.1 |  | 0.00 |   | -0.002 | 1.3 |
| Cholesterol esters to total lipids ratio in small HDL (%) | 0.41 |  | -0.01 |   | -0.002 | 1.1 |
| Triglycerides in chylomicrons and extremely large VLDL (mmol/l) | 0.00 |  | 9.4 |   | -0.001 | 1.1 |
| Total lipids in chylomicrons and extremely large VLDL (mmol/l) | 0.00 |  | 6.5 |   | -0.001 | 1.0 |
| Cholesterol esters to total lipids ratio in chylomicrons and extremely large VLDL (%) | -0.41 |  | 0.01 |   | -0.001 | 1.0 |
| Sphingomyelins (mmol/l) | 0.00 |  | -1.1 |   | -0.001 | 1.0 |
| Free cholesterol to total lipids ratio in large VLDL (%) | 0.41 |  | 0.00 |   | -0.001 | 0.9 |
| Free cholesterol in medium HDL (mmol/l) | 0.00 | \* | -1.2 |   | -0.001 | 0.9 |
| Total cholesterol in HDL3 (mmol/l) | 0.00 |  | -3.8 |   | -0.001 | 0.9 |
| Histidine (mmol/l) | 0.00 |  | -10 |   | -0.001 | 0.8 |
| Phospholipids to total lipids ratio in chylomicrons and extremely large VLDL (%) | 2.4 |  | 0.00 |   | -0.001 | 0.8 |
| Isoleucine (mmol/l) | 0.00 |  | 5.5 |   | -0.001 | 0.8 |
| Glycerol (mmol/l) | 0.00 |  | 1.5 |   | -0.001 | 0.8 |
| Cholesterol esters to total lipids ratio in very large VLDL (%) | -0.58 |  | 0.00 |   | -0.001 | 0.8 |
| Free cholesterol to total lipids ratio in medium HDL (%) | 0.17 |  | -0.03 |   | -0.001 | 0.7 |
| Phospholipids to total lipids ratio in medium HDL (%) | 0.33 |  | 0.00 |   | -0.001 | 0.6 |
| Phospholipids to total lipids ratio in very large VLDL (%) | 0.45 |  | 0.00 |   | -0.001 | 0.5 |
| Alanine (mmol/l) | 0.00 |  | -0.75 |   | -0.001 | 0.4 |
| Ratio of saturated fatty acids to total fatty acids (%) | 0.043 |  | -0.05 |   | -0.001 | 0.4 |
| Free cholesterol in chylomicrons and extremely large VLDL (mmol/l) | 0.00 |  | 37 |   | 0.000 | 0.3 |
| Total cholesterol to total lipids ratio in very small VLDL (%) | -0.81 |  | 0.00 |   | 0.000 | 0.3 |
| Concentration of medium HDL particles (mmol/l) | 0.00 | \* | -3.70E+04 |   | 0.000 | 0.2 |
| Esterified cholesterol (mmol/l) | 0.00 |  | -0.21 |   | 0.000 | 0.2 |
| Saturated fatty acids (mmol/l) | 0.00 |  | -0.20 |   | 0.000 | 0.2 |
| Serum total cholesterol (mmol/l) | 0.00 |  | -0.14 |   | 0.000 | 0.2 |
| Acetoacetate (mmol/l) | 0.00 |  | -0.52 |   | 0.000 | 0.2 |
| 3-hydroxybutyrate (mmol/l) | 0.00 |  | -0.23 |   | 0.000 | 0.2 |
| Creatinine (mmol/l) | 0.00 |  | 6.1 |   | 0.000 | 0.2 |
| Total cholesterol to total lipids ratio in IDL (%) | -0.4 |  | 0.00 |   | 0.000 | 0.2 |
| Triglycerides to total lipids ratio in IDL (%) | -0.13 |  | 0.00 |   | 0.000 | 0.2 |
| Glutamine (mmol/l) | 0.00 |  | 1.7 |   | 0.000 | 0.2 |
| Total lipids in medium HDL (mmol/l) | 0.059 | \* | -0.08 |   | 0.000 | 0.1 |
| Triglycerides in large HDL (mmol/l) | 0.00 |  | -5.0 |   | 0.000 | 0.1 |
| Phospholipids to total lipids ratio in large LDL (%) | 0.058 |  | -0.01 |   | 0.000 | 0.1 |
| Triglycerides to total lipids ratio in medium LDL (%) | 0.041 |  | -0.02 |   | 0.000 | 0.1 |
| Phospholipids to total lipids ratio in medium LDL (%) | -0.13 |  | 0.00 |   | 0.000 | 0.1 |
| Phospholipids to total lipids ratio in small LDL (%) | -0.054 |  | 0.00 |   | 0.000 | 0.1 |
| Triglycerides in very large VLDL (mmol/l) | 0.00 |  | 1.3 |   | 0.000 | 0.1 |
| Cholesterol esters to total lipids ratio in very small VLDL (%) | -1.1 |  | 0.00 |   | 0.000 | 0.1 |
| Total cholesterol in chylomicrons and extremely large VLDL (mmol/l) | 0.00 |  | 13 |   | 0.000 | 0.1 |
| Total cholesterol to total lipids ratio in large LDL (%) | 0.02 |  | 0.00 |   | 0.000 | 0.0 |
| Leucine (mmol/l) | 0.00 |  | 3.2 |   | 0.000 | 0.0 |
| Tyrosine (mmol/l) | 0.00 |  | 0.84 |   | 0.000 | 0.0 |
| Cholesterol esters to total lipids ratio in large LDL (%) | -0.034 |  | 0.00 |   | 0.000 | 0.0 |
| Lactate (mmol/l) | -0.03 |  | 0.01 |   | 0.000 | 0.0 |
| Valine (mmol/l) | 0.00 |  | 0.29 |   | 0.000 | 0.0 |
| Total cholesterol to total lipids ratio in very large VLDL (%) | -0.62 |  | 0.00 |   | 0.000 | 0.0 |
| Cholesterol esters in chylomicrons and extremely large VLDL (mmol/l) | 0.00 |  | 16 |   | 0.000 | 0.0 |
| Conjugated linoleic acid (mmol/l) | 0.00 |  | 0.70 |   | 0.000 | 0.0 |
| Triglycerides in large VLDL (mmol/l) | 0.00 |  | 0.14 |   | 0.000 | 0.0 |
| Total fatty acids (mmol/l) | 0.00 |  | -0.07 |   | 0.000 | 0.0 |
| Triglycerides in medium LDL (mmol/l) | 0.00 |  | -3.8 |   | 0.000 | 0.0 |
| Cholesterol esters in small LDL (mmol/l) | 0.00 |  | -0.64 |   | 0.000 | 0.0 |
| Concentration of very large VLDL particles (mmol/l) | 0.00 |  | 4.70E+07 |   | 0.000 | 0.0 |
| Free cholesterol (mmol/l) | 0.00 |  | -0.39 |   | 0.000 | 0.0 |
| Free cholesterol to total lipids ratio in very large VLDL (%) | -0.04 |  | 0.00 |   | 0.000 | 0.0 |
| Triglycerides to total lipids ratio in large LDL (%) | -0.077 |  | 0.00 |   | 0.000 | -0.1 |
| Free cholesterol to total lipids ratio in medium LDL (%) | -0.086 |  | 0.00 |   | 0.000 | -0.1 |
| Total cholesterol in small LDL (mmol/l) | 0.00 |  | -0.76 |   | 0.000 | -0.1 |
| Triglycerides in small LDL (mmol/l) | 0.00 |  | -4.7 |   | 0.000 | -0.1 |
| Total lipids in small LDL (mmol/l) | 0.00 |  | -0.64 |   | 0.000 | -0.1 |
| Concentration of small LDL particles (mmol/l) | 0.00 |  | -1.70E+06 |   | 0.000 | -0.1 |
| Cholesterol esters to total lipids ratio in IDL (%) | -0.65 |  | 0.00 |   | 0.000 | -0.1 |
| Total lipids in very large VLDL (mmol/l) | 0.00 |  | 0.38 |   | 0.000 | -0.1 |
| Cholesterol esters in very large VLDL (mmol/l) | 0.00 |  | 1.9 |   | 0.000 | -0.1 |
| Total cholesterol in HDL (mmol/l) | 0.084 | \* | -0.05 |   | 0.000 | -0.1 |
| Total cholesterol to total lipids ratio in medium LDL (%) | 0.093 |  | 0.00 |   | 0.000 | -0.1 |
| Triglycerides to total lipids ratio in medium VLDL (%) | 0.13 |  | 0.00 |   | 0.000 | -0.1 |
| Cholesterol esters to total lipids ratio in medium LDL (%) | 0.18 |  | 0.00 |   | 0.000 | -0.2 |
| Total cholesterol to total lipids ratio in small LDL (%) | 0.096 |  | 0.00 |   | 0.000 | -0.2 |
| Tyrosine to Large Neutral Amino Acid ratio | 0.00 |  | 1.7 |   | 0.000 | -0.2 |
| Estimated description of fatty acid chain length, not actual carbon number | 0.00 |  | -0.59 | \* | 0.000 | -0.2 |
| Concentration of large VLDL particles (mmol/l) | 0.00 |  | -3.40E+06 |   | 0.000 | -0.2 |
| Phospholipids in small LDL (mmol/l) | 0.00 |  | -3.7 |   | 0.000 | -0.2 |
| Triglycerides to total lipids ratio in small LDL (%) | -0.042 |  | -0.03 |   | 0.000 | -0.3 |
| Phospholipids to total lipids ratio in large HDL (%) | -0.18 |  | 0.00 |   | 0.000 | -0.3 |
| Total lipids in large VLDL (mmol/l) | 0.00 |  | -0.11 |   | 0.000 | -0.3 |
| Free cholesterol to total lipids ratio in chylomicrons and extremely large VLDL (%) | 0.00 |  | 0.00 |   | 0.000 | -0.3 |
| Total cholesterol in very large VLDL (mmol/l) | 0.00 |  | -0.55 |   | 0.000 | -0.3 |
| Free cholesterol in very large HDL (mmol/l) | 0.00 |  | 0.82 |   | 0.001 | -0.4 |
| Total cholesterol to total lipids ratio in chylomicrons and extremely large VLDL (%) | -0.55 |  | 0.00 |   | 0.001 | -0.4 |
| Phospholipids in large VLDL (mmol/l) | 0.00 |  | -1.5 |   | 0.001 | -0.4 |
| Cholesterol esters in medium LDL (mmol/l) | 0.00 |  | -0.77 |   | 0.001 | -0.4 |
| Free cholesterol to total lipids ratio in very large HDL (%) | -0.12 |  | -0.01 |   | 0.001 | -0.5 |
| Free cholesterol to total lipids ratio in large LDL (%) | 0.053 |  | 0.03 |   | 0.001 | -0.5 |
| Free cholesterol in very large VLDL (mmol/l) | 0.00 |  | -3.3 |   | 0.001 | -0.5 |
| Phospholipids in very large VLDL (mmol/l) | 0.00 |  | -2.3 |   | 0.001 | -0.5 |
| Free cholesterol to total lipids ratio in large HDL (%) | 0.23 |  | 0.00 |   | 0.001 | -0.6 |
| Cholesterol esters to total lipids ratio in small LDL (%) | 0.21 |  | 0.01 |   | 0.001 | -0.6 |
| Cholesterol esters in large VLDL (mmol/l) | 0.00 |  | -3.5 |   | 0.001 | -0.6 |
| Total cholesterol in medium LDL (mmol/l) | 0.00 |  | -0.72 |   | 0.001 | -0.7 |
| Total cholesterol in large VLDL (mmol/l) | 0.00 |  | -2.1 |   | 0.001 | -0.7 |
| Free cholesterol in large VLDL (mmol/l) | 0.00 |  | -4.4 |   | 0.001 | -0.7 |
| Triglycerides in LDL (mmol/l) | 0.00 |  | -1.1 |   | 0.001 | -0.7 |
| Total cholesterol in very large HDL (mmol/l) | 0.00 |  | 0.66 |   | 0.001 | -0.7 |
| Cholesterol esters in very large HDL (mmol/l) | 0.00 |  | 1.1 |   | 0.001 | -0.7 |
| Cholesterol esters to total lipids ratio in large HDL (%) | 0.17 |  | 0.02 |   | 0.001 | -0.8 |
| Total lipids in medium LDL (mmol/l) | 0.00 |  | -0.59 |   | 0.001 | -0.8 |
| Concentration of medium LDL particles (mmol/l) | 0.00 |  | -3.00E+06 |   | 0.001 | -0.8 |
| Triglycerides in very large HDL (mmol/l) | 0.00 |  | -9.6 |   | 0.001 | -0.9 |
| Triglycerides in very small VLDL (mmol/l) | 0.00 |  | -0.62 |   | 0.001 | -0.9 |
| Total cholesterol to total lipids ratio in large VLDL (%) | -0.52 |  | 0.00 |   | 0.001 | -0.9 |
| Triglycerides in medium VLDL (mmol/l) | -0.011 |  | -0.18 |   | 0.001 | -0.9 |
| Total cholesterol in HDL2 (mmol/l) | 0.085 | \* | -0.02 |   | 0.001 | -0.9 |
| Phospholipids in large HDL (mmol/l) | 0.033 | \* | 0.00 |   | 0.001 | -0.9 |
| Triglycerides in VLDL (mmol/l) | -0.035 |  | -0.07 |   | 0.001 | -1.0 |
| Phospholipids to total lipids ratio in very large HDL (%) | 1 |  | 0.00 |   | 0.001 | -1.0 |
| Free cholesterol in small LDL (mmol/l) | 0.00 |  | -7.1 |   | 0.001 | -1.1 |
| Free cholesterol to total lipids ratio in very small VLDL (%) | 0.28 |  | 0.02 |   | 0.002 | -1.2 |
| Total cholesterol in LDL (mmol/l) | -0.022 |  | -0.23 |   | 0.002 | -1.2 |
| Total cholesterol to total lipids ratio in large HDL (%) | 0.4 |  | 0.01 |   | 0.002 | -1.2 |
| Total lipids in very large HDL (mmol/l) | 0.016 |  | 0.27 |   | 0.002 | -1.2 |
| Concentration of very large HDL particles (mmol/l) | 0.00 |  | 2.80E+05 |   | 0.002 | -1.3 |
| Triglycerides in large LDL (mmol/l) | 0.00 |  | -2.1 |   | 0.002 | -1.3 |
| Albumin (signal area) | 0.00 |  | 5.9 |   | 0.002 | -1.3 |
| Glycine (mmol/l) | 0.00 |  | -0.44 |   | 0.002 | -1.5 |
| Total cholesterol to total lipids ratio in small VLDL (%) | -0.37 |  | -0.01 |   | 0.002 | -1.5 |
| Triglycerides in small VLDL (mmol/l) | -0.012 |  | -0.36 |   | 0.002 | -1.6 |
| Triglycerides in IDL (mmol/l) | 0.00 |  | -1.4 |   | 0.002 | -1.6 |
| Free cholesterol to total lipids ratio in small LDL (%) | -0.11 |  | -0.05 |   | 0.002 | -1.6 |
| Cholesterol esters to total lipids ratio in small VLDL (%) | -0.6 |  | 0.00 |   | 0.002 | -1.6 |
| Diacylglycerol (mmol/l) | 0.00 |  | -4.7 |   | 0.003 | -1.7 |
| Phospholipids in very large HDL (mmol/l) | 0.012 |  | 0.48 |   | 0.003 | -1.8 |
| Total cholesterol in medium HDL (mmol/l) | 0.037 | \* | 0.06 |   | 0.002 | -1.8 |
| Concentration of medium VLDL particles (mmol/l) | 0.00 |  | -7.50E+06 |   | 0.002 | -1.8 |
| Phospholipids in medium LDL (mmol/l) | 0.00 |  | -3.8 |   | 0.003 | -1.8 |
| Citrate (mmol/l) | 0.00 |  | -4.8 |   | 0.003 | -1.8 |
| Concentration of large HDL particles (mmol/l) | 0.00 | \* | 3.10E+04 |   | 0.002 | -1.8 |
| Phospholipids in very small VLDL (mmol/l) | 0.00 |  | -1.6 |   | 0.003 | -1.9 |
| Phospholipids to total lipids ratio in large VLDL (%) | -0.57 |  | -0.01 |   | 0.003 | -1.9 |
| Free cholesterol in medium LDL (mmol/l) | 0.00 |  | -5.0 |   | 0.003 | -1.9 |
| Total lipids in medium VLDL (mmol/l) | -0.024 |  | -0.25 |   | 0.003 | -2.0 |
| Serum total triglycerides (mmol/l) | -0.045 |  | -0.15 |   | 0.003 | -2.0 |
| Total lipids in large HDL (mmol/l) | 0.067 | \* | 0.06 |   | 0.003 | -2.0 |
| Triglycerides in medium HDL (mmol/l) | 0.00 |  | -5.5 |   | 0.003 | -2.1 |
| Cholesterol esters in large LDL (mmol/l) | -0.012 |  | -0.68 |   | 0.003 | -2.1 |
| Free cholesterol to total lipids ratio in IDL (%) | 0.25 |  | 0.02 |   | 0.003 | -2.2 |
| Cholesterol esters to total lipids ratio in large VLDL (%) | -0.93 |  | 0.00 |   | 0.003 | -2.3 |
| Total cholesterol in large LDL (mmol/l) | -0.017 |  | -0.55 |   | 0.003 | -2.3 |
| Free cholesterol in large HDL (mmol/l) | 0.00 | \* | 0.67 |   | 0.003 | -2.4 |
| Concentration of very small VLDL particles (mmol/l) | 0.00 |  | -4.90E+06 |   | 0.003 | -2.5 |
| Free cholesterol to total lipids ratio in medium VLDL (%) | -0.61 |  | -0.02 |   | 0.003 | -2.6 |
| Triglycerides in HDL (mmol/l) | 0.00 |  | -3.0 |   | 0.004 | -2.6 |
| Cholesterol esters in medium HDL (mmol/l) | 0.031 | \* | 0.17 |   | 0.004 | -2.6 |
| Total lipids in large LDL (mmol/l) | -0.025 |  | -0.43 |   | 0.004 | -2.7 |
| Concentration of large LDL particles (mmol/l) | 0.00 |  | -3.00E+06 |   | 0.004 | -2.7 |
| Total lipids in very small VLDL (mmol/l) | -0.023 |  | -0.41 |   | 0.004 | -2.7 |
| Triglycerides to total lipids ratio in very large HDL (%) | -0.21 |  | -0.05 |   | 0.004 | -2.8 |
| Free cholesterol in medium VLDL (mmol/l) | 0.00 |  | -2.9 |   | 0.004 | -2.8 |
| Free cholesterol in IDL (mmol/l) | 0.00 |  | -2.4 |   | 0.004 | -2.8 |
| Free cholesterol in very small VLDL (mmol/l) | 0.00 |  | -2.8 |   | 0.004 | -2.9 |
| Free cholesterol in large LDL (mmol/l) | 0.00 |  | -2.6 |   | 0.004 | -2.9 |
| Cholesterol esters in medium VLDL (mmol/l) | 0.00 |  | -2.2 |   | 0.004 | -3.0 |
| Cholesterol esters in IDL (mmol/l) | -0.017 |  | -0.73 |   | 0.004 | -3.1 |
| Total cholesterol in medium VLDL (mmol/l) | 0.00 |  | -1.3 |   | 0.004 | -3.1 |
| Phospholipids in medium VLDL (mmol/l) | 0.00 |  | -2.0 |   | 0.004 | -3.2 |
| Total cholesterol in IDL (mmol/l) | -0.021 |  | -0.58 |   | 0.004 | -3.2 |
| Mean diameter for HDL particles (nm) | 0.024 |  | 0.51 |   | 0.005 | -3.3 |
| Triglycerides to total lipids ratio in very small VLDL (%) | 0.73 |  | 0.02 | # | 0.005 | -3.3 |
| Cholesterol esters in very small VLDL (mmol/l) | 0.00 |  | -1.1 |   | 0.005 | -3.3 |
| Triglycerides to total lipids ratio in medium HDL (%) | -0.22 |  | -0.06 |   | 0.005 | -3.4 |
| Apolipoprotein B (g/l) | -0.027 |  | -0.48 |   | 0.005 | -3.4 |
| Ratio of monounsaturated fatty acids to total fatty acids (%) | -0.95 | \*\*\* | 0.00 |   | 0.005 | -3.4 |
| Total cholesterol in large HDL (mmol/l) | 0.033 | \* | 0.30 |   | 0.005 | -3.4 |
| Total lipids in IDL (mmol/l) | -0.032 |  | -0.43 |   | 0.005 | -3.4 |
| Ratio of apolipoprotein B to apolipoprotein A-I (%) | -0.025 | \* | -0.43 |   | 0.005 | -3.5 |
| Phospholipids in large LDL (mmol/l) | 0.00 |  | -2.5 |   | 0.005 | -3.5 |
| Concentration of IDL particles (mmol/l) | 0.00 |  | -4.30E+06 |   | 0.005 | -3.5 |
| Total cholesterol in very small VLDL (mmol/l) | -0.014 |  | -0.88 |   | 0.005 | -3.5 |
| Concentration of small VLDL particles (mmol/l) | 0.00 |  | -6.90E+06 |   | 0.005 | -3.5 |
| Cholesterol esters in large HDL (mmol/l) | 0.025 | \* | 0.45 |   | 0.005 | -3.6 |
| Triglycerides to total lipids ratio in large HDL (%) | -0.2 |  | -0.07 |   | 0.005 | -3.6 |
| Monounsaturated fatty acids; 16:1, 18:1 (mmol/l) | -0.097 |  | -0.15 |   | 0.005 | -3.6 |
| Total lipids in small VLDL (mmol/l) | -0.034 |  | -0.39 |   | 0.005 | -3.8 |
| Cholesterol esters to total lipids ratio in medium VLDL (%) | -1.4 |  | 0.00 |   | 0.005 | -3.8 |
| Phospholipids in IDL (mmol/l) | 0.00 |  | -2.4 |   | 0.005 | -3.9 |
| Phospholipids to total lipids ratio in very small VLDL (%) | 1.4 | \* | 0.00 |   | 0.006 | -4.1 |
| Remnant cholesterol (non-HDL, non-LDL -cholesterol) (mmol/l) | -0.06 |  | -0.26 |   | 0.006 | -4.1 |
| Total cholesterol to total lipids ratio in medium VLDL (%) | -2 |  | 0.00 |   | 0.005 | -4.1 |
| Phenylalanine (mmol/l) | 0.00 |  | -9.8 |   | 0.006 | -4.1 |
| Mean diameter for LDL particles (nm) | -0.047 |  | -0.33 |   | 0.006 | -4.4 |
| Phospholipids in small VLDL (mmol/l) | 0.00 |  | -2.3 |   | 0.006 | -4.5 |
| Total cholesterol in VLDL (mmol/l) | -0.034 |  | -0.49 |   | 0.006 | -4.6 |
| Ratio of triglycerides to phosphoglycerides (%) | -0.019 |  | -1.0 |   | 0.007 | -4.8 |
| Ratio of omega-6 fatty acids to total fatty acids (%) | 0.57 | \* | 0.03 |   | 0.007 | -4.9 |
| Cholesterol esters in small VLDL (mmol/l) | 0.00 |  | -1.9 |   | 0.007 | -4.9 |
| Free cholesterol to total lipids ratio in small HDL (%) | -0.051 |  | -0.36 | \*\*\* | 0.007 | -4.9 |
| Free cholesterol in small VLDL (mmol/l) | 0.00 |  | -3.4 |   | 0.007 | -5.0 |
| Total cholesterol in small VLDL (mmol/l) | -0.015 |  | -1.3 |   | 0.007 | -5.3 |
| Ratio of 18:2 linoleic acid to total fatty acids (%) | 0.53 | \* | 0.04 |   | 0.008 | -5.4 |
| Total cholesterol to total lipids ratio in medium HDL (%) | 1.2 | \* | 0.02 |   | 0.008 | -6.0 |
| Triglycerides in small HDL (mmol/l) | 0.00 |  | -14 | \* | 0.009 | -6.2 |
| Triglycerides to total lipids ratio in small HDL (%) | -0.17 |  | -0.15 | # | 0.009 | -6.6 |
| Ratio of polyunsaturated fatty acids to total fatty acids (%) | 0.91 | \*\*\* | 0.02 |   | 0.010 | -7.0 |
| Cholesterol esters to total lipids ratio in medium HDL (%) | 1 | \* | 0.03 |   | 0.010 | -7.6 |

Abbreviations: DHA, docosahexaenoic acid; HDL, high-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein.

aMediation steps proposed by Baron and Kenny.1

bStep 2: Effect size of association between fish consumption (independent variable) and metabolic marker (dependant variable). The reported values are beta-coefficients.

cFish consumption treated as a dichotomous variable, comparing women who ate fish at least two times per week (n=325) at baseline compared with women who consumed fish lessthan two times per week (n=221).

dStep 3: Effect size of association between metabolic marker (independent variable) and new episodes of depression during the five-year period (dependant variable). The reported values are beta-coefficients.

e98 participants had a new depressive episode during the five-year follow-up and 448 did not.

fStep 4: Proportion of total effect mediated by metabolic marker when included as a covariate in a model with fish consumption (independent variable) and depression (dependant variable), estimated using the binary\_mediation STATA command.

#P<0.1, \*P<0.05, \*\*P<0.01, \*\*\*P<0.001, \*\*\*\*P<0.0001

**Supplementary Table 2. Mediation tests for all metabolic markers with fish consumption analysed as a continuous variable (serves per week)**

|  |  |  |  |
| --- | --- | --- | --- |
| Metabolic marker | Step 2a,b | Step 3 a,d | Step 4 a,f |
| **Fishc > Metabolite** | **Metabolite > Depressione** | **Indirect****effect** | **Mediation****(%)** |
| Docosahexaenoic acid (mmol/l) | 0.0046 | \*\*\*\* | -3.9 | \* | -0.024 | 25.3 |
| Omega-3 fatty acids (mmol/l) | 0.0083 | \*\*\*\* | -2.0 | # | -0.021 | 22.4 |
| Omega-3 to Omega-6 ratio | 0.0027 | \*\*\*\* | -0.027 |  | -0.015 | 15.4 |
| Ratio of docosahexaenoic acid to total fatty acids (%) | 0.058 | \*\*\*\* | -5.1 |  | -0.015 | 15.3 |
| Estimated degree of unsaturation | 0.0049 | \*\*\*\* | -2.4 |  | -0.014 | 14.7 |
| Non-DHA omega-3 fatty acids (omega-3-DHA) (mmol/l) | 0.0036 | \*\*\*\* | -0.10 |  | -0.008 | 8.6 |
| Ratio of omega-3 fatty acids to total fatty acids (%) | 0.11 | \*\* | -0.23 |  | -0.008 | 8.4 |
| Phospholipids to total lipids ratio in small VLDL (%) | 0.15 | \*\*\*\* | -1.3 |  | -0.006 | 6.0 |
| Triglycerides to total lipids ratio in very large VLDL (%) | -0.32 |  | -0.046 | # | -0.005 | 5.9 |
| Estimated description of fatty acid chain length, not actual carbon number | 0.006 |  | -0.29 | \* | -0.005 | 5.3 |
| Ratio of conjugated linoleic acid to total fatty acids (%) | -0.011 |  | -1.1 |  | -0.005 | 5.2 |
| Acetate (mmol/l) | 0.000 |  | -0.26 | \* | -0.004 | 4.7 |
| Phospholipids to total lipids ratio in medium VLDL (%) | 0.38 | \* | -8.9 |  | -0.004 | 4.5 |
| Free cholesterol to total lipids ratio in small LDL (%) | 0.036 |  | -1.8 |  | -0.003 | 2.9 |
| Phospholipids to total lipids ratio in IDL (%) | 0.12 |  | -0.21 |  | -0.002 | 2.6 |
| Free cholesterol to total lipids ratio in small VLDL (%) | 0.01 |  | -0.11 | \* | -0.002 | 1.8 |
| Apolipoprotein A-I (g/l) | 0.004 |  | -0.23 |  | -0.002 | 1.7 |
| Phospholipids in medium HDL (mmol/l) | 0.002 |  | -3.8 |  | -0.001 | 1.2 |
| Free cholesterol in medium HDL (mmol/l) | 0.001 |  | -10 |  | -0.001 | 1.1 |
| Phospholipids to total lipids ratio in chylomicrons and extremely large VLDL (%) | 0.25 |  | -0.016 |  | -0.001 | 0.9 |
| Free cholesterol to total lipids ratio in medium HDL (%) | 0.021 |  | -0.029 |  | -0.001 | 0.9 |
| Phospholipids to total lipids ratio in medium HDL (%) | 0.051 |  | -0.39 |  | -0.001 | 0.8 |
| Free cholesterol to total lipids ratio in very large HDL (%) | 0.043 |  | -0.35 |  | -0.001 | 0.7 |
| Concentration of medium HDL particles (mmol/l) | 0.000 |  | -1.2 |  | -0.001 | 0.7 |
| Cholesterol esters to total lipids ratio in large VLDL (%) | 0.055 |  | -0.76 |  | -0.001 | 0.6 |
| Total lipids in medium HDL (mmol/l) | 0.0065 |  | -1.70E+05 |  | -0.001 | 0.6 |
| 3-hydroxybutyrate (mmol/l) | 0.0028 |  | -1.1 |  | -0.001 | 0.5 |
| Total cholesterol in HDL (mmol/l) | 0.01 |  | -0.20 |  | -0.001 | 0.5 |
| Free cholesterol to total lipids ratio in very large VLDL (%) | 0.16 |  | -0.35 |  | 0.000 | 0.5 |
| Glucose (mmol/l) | -0.001 | \*\*\*\* | 0.00 | \*\* | 0.000 | 0.5 |
| Free cholesterol to total lipids ratio in small HDL (%) | 0.00054 |  | -1.2 | \*\*\* | 0.000 | 0.4 |
| Acetoacetate (mmol/l) | 0.0014 |  | -0.076 |  | 0.000 | 0.3 |
| Pyruvate (mmol/l) | -0.001 | \*\* | -0.64 |  | -0.006 | 6.7 |
| Triglycerides to total lipids ratio in small VLDL (%) | -0.13 |  | -0.14 | \* | -0.006 | 6.1 |
| Glycoprotein acetyls, mainly a1-acid glycoprotein (mmol/l) | -0.0053 |  | -3.4 |  | -0.004 | 3.7 |
| Mean diameter for VLDL particles (nm) | -0.038 |  | -0.39 |  | -0.003 | 3.4 |
| Ratio of diacylglycerol to triglycerides (%) | -0.000 | \* | -6.90E+06 |  | -0.003 | 2.7 |
| Triglycerides to total lipids ratio in large VLDL (%) | -0.43 |  | -2.3 |  | -0.002 | 2.1 |
| Isoleucine (mmol/l) | -0.000 |  | -0.36 |  | -0.002 | 1.7 |
| Cholesterol esters to total lipids ratio in small LDL (%) | -0.11 |  | -0.15 |  | -0.002 | 1.7 |
| Cholesterol esters to total lipids ratio in chylomicrons and extremely large VLDL (%) | -0.081 |  | -0.49 |  | -0.001 | 1.5 |
| Glycerol (mmol/l) | -0.001 |  | -0.07 |  | -0.001 | 1.2 |
| Cholesterol esters to total lipids ratio in very large HDL (%) | -0.081 |  | -0.053 |  | -0.001 | 0.8 |
| Creatinine (mmol/l) | -0.000 |  | -0.55 |  | -0.001 | 0.5 |
| Free cholesterol to total lipids ratio in very small VLDL (%) | -0.022 |  | -3.3 |  | 0.000 | 0.5 |
| Total cholesterol to total lipids ratio in small LDL (%) | -0.078 |  | -2.3 |  | 0.000 | 0.4 |
| Total cholesterol to total lipids ratio in very large HDL (%) | -0.038 |  | -0.88 |  | 0.000 | 0.4 |
| Total cholesterol to total lipids ratio in very small VLDL (%) | -0.13 |  | -1.1 |  | 0.000 | 0.4 |
| Triglycerides to total lipids ratio in IDL  | -0.04 |  | -2.8 |  | 0.000 | 0.4 |
| Total cholesterol to total lipids ratio in large LDL (%) | -0.038 |  | -0.41 |  | 0.000 | 0.4 |
| Cholesterol esters to total lipids ratio in large LDL (%) | -0.073 |  | -4.90E+06 |  | 0.000 | 0.4 |
| Leucine (mmol/l) | -0.000 |  | 7.1 |  | 0.000 | 0.4 |
| Total cholesterol to total lipids ratio in medium LDL (%) | -0.064 |  | 1.7 |  | 0.000 | 0.4 |
| Cholesterol esters to total lipids ratio in medium LDL (%) | -0.11 |  | 1.5 |  | 0.000 | 0.3 |
| Total cholesterol to total lipids ratio in IDL (%) | -0.077 |  | 0.47 |  | 0.000 | 0.3 |
| Cholesterol esters to total lipids ratio in very small VLDL (%) | -0.11 |  | 0.04 |  | 0.000 | 0.2 |
| Triglycerides in very large VLDL (mmol/l) | -0.000 |  | 0.00 |  | 0.000 | 0.1 |
| Concentration of very large VLDL particles (mmol/l) | -0.000 |  | 0.00 |  | 0.000 | 0.1 |
| Triglycerides to total lipids ratio in very small VLDL (%) | -0.0048 |  | 4.5 | # | 0.000 | 0.1 |
| Polyunsaturated fatty acids (mmol/l) | 0.00022 | \* | -3.70E+04 |  | 0.000 | 0.1 |
| Phospholipids to total lipids ratio in large LDL (%) | 0.06 |  | -14 |  | 0.000 | 0.1 |
| Phospholipids to total lipids ratio in very large VLDL (%) | 0.017 |  | -0.072 |  | 0.000 | 0.1 |
| Cholesterol esters in large VLDL (mmol/l) | 0.000 |  | -0.33 |  | 0.000 | 0.1 |
| Total lipids in very large VLDL (mmol/l) | -0.000 |  | 0.00 |  | 0.000 | 0.0 |
| Cholesterol esters to total lipids ratio in IDL (%) | -0.13 |  | 0.011 |  | 0.000 | 0.0 |
| Triglycerides in large VLDL (mmol/l) | -0.001 |  | 0.013 |  | 0.000 | 0.0 |
| Lactate (mmol/l) | 0.0013 |  | 37 |  | 0.000 | 0.0 |
| Alanine (mmol/l) | -0.000 |  | 6.5 |  | 0.000 | 0.0 |
| Free cholesterol in very large VLDL (mmol/l) | -0.000 |  | 0.00 |  | 0.000 | 0.0 |
| Cholesterol esters in very large VLDL (mmol/l) | 0.000 |  | 9.4 |  | 0.000 | 0.0 |
| Triglycerides to total lipids ratio in medium LDL (%) | 0.001 |  | 0.00 |  | 0.000 | 0.0 |
| Total cholesterol in very large VLDL (mmol/l) | 0.000 |  | -0.054 |  | 0.000 | 0.0 |
| Total cholesterol in HDL2 (mmol/l) | 0.012 |  | -14 |  | 0.000 | -0.1 |
| Phospholipids in small HDL (mmol/l) | -0.000 |  | 0.39 |  | 0.000 | -0.1 |
| Tyrosine (mmol/l) | 0.000 |  | 0.011 |  | 0.000 | -0.1 |
| Free cholesterol in chylomicrons and extremely large VLDL (mmol/l) | 0.000 |  | 0.018 |  | 0.000 | -0.1 |
| Phospholipids in very large VLDL (mmol/l) | -0.000 |  | 0.00 |  | 0.000 | -0.1 |
| Concentration of large VLDL particles (mmol/l) | -0.000 |  | 0.033 |  | 0.000 | -0.1 |
| Valine (mmol/l) | 0.000 |  | 3.2 |  | 0.000 | -0.2 |
| Total lipids in large VLDL (mmol/l) | -0.001 |  | 0.00 |  | 0.000 | -0.2 |
| Total cholesterol in chylomicrons and extremely large VLDL (mmol/l) | 0.000 |  | 0.00 |  | 0.000 | -0.2 |
| Cholesterol esters in chylomicrons and extremely large VLDL (mmol/l) | 0.000 |  | 0.00 |  | 0.000 | -0.2 |
| Total cholesterol in large VLDL (mmol/l) | -0.000 |  | 0.00 |  | 0.000 | -0.2 |
| Free cholesterol to total lipids ratio in medium LDL (%) | 0.044 |  | -0.43 |  | 0.000 | -0.2 |
| Phospholipids in large HDL (mmol/l) | 0.0042 |  | -4.30E+06 |  | 0.000 | -0.2 |
| Triglycerides to total lipids ratio in large LDL (%) | -0.022 |  | 0.011 |  | 0.000 | -0.3 |
| Phospholipids to total lipids ratio in very large HDL (%) | 0.067 |  | 0.84 |  | 0.000 | -0.3 |
| Total cholesterol to total lipids ratio in small VLDL (%) | -0.014 |  | -0.069 |  | 0.000 | -0.4 |
| Phospholipids in large VLDL (mmol/l) | -0.001 |  | 1.7 |  | 0.000 | -0.4 |
| Cholesterol esters to total lipids ratio in small VLDL (%) | -0.024 |  | 0.66 |  | 0.000 | -0.4 |
| Conjugated linoleic acid (mmol/l) | -0.0013 |  | 1.1 |  | 0.000 | -0.5 |
| Total cholesterol to total lipids ratio in very large VLDL (%) | 0.22 | \*\*\* | 0.82 |  | 0.001 | -0.6 |
| Free cholesterol to total lipids ratio in large HDL (%) | 0.052 |  | 0.27 |  | 0.001 | -0.6 |
| Tyrosine to Large Neutral Amino Acid ratio | 0.001 |  | 2.80E+05 |  | 0.001 | -0.6 |
| Triglycerides to total lipids ratio in medium VLDL (%) | 0.16 |  | 0.015 |  | 0.001 | -0.7 |
| Free cholesterol in large VLDL (mmol/l) | -0.001 |  | 4.70E+07 |  | 0.001 | -0.7 |
| Sphingomyelins (mmol/l) | -0.001 |  | -4.8 |  | 0.001 | -0.7 |
| Cholesterol esters to total lipids ratio in medium VLDL (%) | -0.048 |  | -0.39 |  | 0.001 | -0.8 |
| Cholesterol esters to total lipids ratio in very large VLDL (%) | 0.057 |  | -1.4 |  | 0.001 | -0.8 |
| Phospholipids to total lipids ratio in large HDL (%) | -0.075 |  | 0.00 |  | 0.001 | -0.8 |
| Glycine (mmol/l) | -0.0011 |  | -0.55 |  | 0.001 | -0.9 |
| Free cholesterol in very large HDL (mmol/l) | 0.001 |  | -0.68 |  | 0.001 | -1.0 |
| Total cholesterol in medium HDL (mmol/l) | 0.0051 |  | -2.1 |  | 0.001 | -1.0 |
| Total cholesterol to total lipids ratio in large VLDL (%) | -0.1 |  | -9.8 |  | 0.001 | -1.0 |
| Total cholines (mmol/l) | -0.002 |  | -0.15 |  | 0.001 | -1.1 |
| Total lipids in chylomicrons and extremely large VLDL (mmol/l) | 0.000 |  | 0.00 |  | 0.001 | -1.1 |
| Phospholipids to total lipids ratio in medium LDL (%) | 0.063 |  | -2.1 |  | 0.001 | -1.1 |
| Cholesterol esters to total lipids ratio in small HDL (%) | -0.047 |  | -3.5 |  | 0.001 | -1.1 |
| Concentration of large HDL particles (mmol/l) | 0.000 |  | -4.4 |  | 0.001 | -1.2 |
| Triglycerides in chylomicrons and extremely large VLDL (mmol/l) | 0.000 |  | -0.11 |  | 0.001 | -1.3 |
| Phosphatidylcholine and other cholines (mmo/l) | -0.0023 |  | -1.0 |  | 0.001 | -1.3 |
| Glutamine (mmol/l) | 0.00047 |  | 0.03 |  | 0.001 | -1.3 |
| Total phosphoglycerides (mmol/l) | -0.0025 |  | 0.30 |  | 0.001 | -1.3 |
| Total lipids in large HDL (mmol/l) | 0.01 |  | -1.5 |  | 0.001 | -1.4 |
| Triglycerides to total lipids ratio in small LDL (%) | -0.031 |  | -0.23 |  | 0.001 | -1.4 |
| Triglycerides in medium VLDL (mmol/l) | -0.003 |  | -1.1 |  | 0.001 | -1.4 |
| 18:2, linoleic acid (mmol/l) | -0.0047 |  | -5.5 |  | 0.001 | -1.5 |
| Histidine (mmol/l) | -0.000 |  | 0.45 |  | 0.002 | -1.6 |
| Albumin (signal area) | 0.001 |  | -0.72 |  | 0.002 | -1.7 |
| Total cholesterol to total lipids ratio in chylomicrons and extremely large VLDL (%) | -0.33 |  | 0.67 |  | 0.002 | -1.8 |
| Cholesterol esters in medium HDL (mmol/l) | 0.0045 |  | -0.77 |  | 0.002 | -1.8 |
| Phospholipids to total lipids ratio in very small VLDL (%) | 0.11 |  | 0.00 |  | 0.002 | -1.9 |
| Concentration of very large HDL particles (mmol/l) | 0.000 |  | -0.59 |  | 0.002 | -1.9 |
| Total lipids in very large HDL (mmol/l) | 0.0039 |  | -3.00E+06 |  | 0.002 | -2.0 |
| Free cholesterol to total lipids ratio in large VLDL (%) | -0.16 |  | -0.015 |  | 0.002 | -2.0 |
| Total cholesterol to total lipids ratio in small HDL (%) | -0.046 |  | -0.76 |  | 0.002 | -2.0 |
| Total cholesterol in very large HDL (mmol/l) | 0.0017 |  | -0.053 |  | 0.002 | -2.1 |
| Phospholipids in very large HDL (mmol/l) | 0.0023 |  | -0.64 |  | 0.002 | -2.1 |
| Free cholesterol in large HDL (mmol/l) | 0.0014 |  | -1.70E+06 |  | 0.002 | -2.1 |
| Phospholipids to total lipids ratio in small LDL (%) | 0.11 | \* | 0.060 |  | 0.002 | -2.1 |
| Triglycerides in VLDL (mmol/l) | -0.011 | \* | 3.10E+04 |  | 0.002 | -2.2 |
| Cholesterol esters in medium VLDL (mmol/l) | -0.001 |  | -3.7 |  | 0.002 | -2.2 |
| Total cholesterol to total lipids ratio in medium VLDL (%) | -0.17 |  | -4.7 |  | 0.002 | -2.2 |
| Ratio of saturated fatty acids to total fatty acids (%) | -0.029 |  | -0.026 |  | 0.002 | -2.3 |
| Cholesterol esters in very large HDL (mmol/l) | 0.0012 |  | 0.00 |  | 0.002 | -2.4 |
| Free cholesterol to total lipids ratio in IDL (%) | 0.049 |  | -0.013 |  | 0.002 | -2.5 |
| Triglycerides in large HDL (mmol/l) | -0.001 |  | -9.6 |  | 0.002 | -2.6 |
| Triglycerides in very large HDL (mmol/l) | -0.000 |  | 0.00 |  | 0.002 | -2.6 |
| Concentration of medium VLDL particles (mmol/l) | -0.000 | \* | 0.037 |  | 0.002 | -2.7 |
| Cholesterol esters in small HDL (mmol/l) | -0.0013 |  | 0.064 |  | 0.003 | -2.8 |
| Total lipids in medium VLDL (mmol/l) | -0.0056 |  | -1.6 |  | 0.003 | -2.9 |
| Free cholesterol to total lipids ratio in large LDL (%) | 0.035 |  | 0.17 |  | 0.003 | -2.9 |
| Ratio of monounsaturated fatty acids to total fatty acids (%) | -0.18 | \* | 0.020 |  | 0.003 | -2.9 |
| Cholesterol esters in small LDL (mmol/l) | -0.0023 |  | -0.62 |  | 0.003 | -3.0 |
| Omega-6 fatty acids (mmol/l) | -0.0081 | \*\* | 0.00 |  | 0.003 | -3.0 |
| Total lipids in small HDL (mmol/l) | -0.0025 |  | 0.017 | # | 0.003 | -3.2 |
| Total cholesterol in small HDL (mmol/l) | -0.0016 |  | 0.027 | # | 0.003 | -3.3 |
| Concentration of small HDL particles (mmol/l) | -0.000 |  | -0.43 | # | 0.003 | -3.4 |
| Free cholesterol to total lipids ratio in medium VLDL (%) | -0.12 |  | 0.00 |  | 0.003 | -3.4 |
| Total cholesterol in medium VLDL (mmol/l) | -0.0013 |  | 0.00 |  | 0.003 | -3.4 |
| Total cholesterol in large HDL (mmol/l) | 0.0061 |  | 6.1 |  | 0.003 | -3.6 |
| Cholesterol esters in very small VLDL (mmol/l) | -0.0018 |  | 0.00 |  | 0.003 | -3.8 |
| Citrate (mmol/l) | -0.000 |  | 0.00 |  | 0.004 | -3.9 |
| Triglycerides in small VLDL (mmol/l) | -0.0046 |  | -7.50E+06 |  | 0.004 | -4.0 |
| Total cholesterol in small LDL (mmol/l) | -0.0028 |  | 5.5 |  | 0.004 | -4.1 |
| Cholesterol esters in large HDL (mmol/l) | 0.0046 |  | 0.00 |  | 0.004 | -4.1 |
| Triglycerides in very small VLDL (mmol/l) | -0.0028 | \*\* | 0.00 |  | 0.004 | -4.1 |
| Diacylglycerol (mmol/l) | -0.000 | \*\* | 0.45 |  | 0.004 | -4.2 |
| Free cholesterol in small HDL (mmol/l) | -0.000 | \* | 0.067 | \* | 0.004 | -4.2 |
| Free cholesterol to total lipids ratio in chylomicrons and extremely large VLDL (%) | -0.25 |  | -0.59 |  | 0.004 | -4.4 |
| Total cholesterol to total lipids ratio in large HDL (%) | 0.2 | \* | -0.36 |  | 0.004 | -4.4 |
| Triglycerides in small LDL (mmol/l) | -0.001 |  | 0.028 |  | 0.004 | -4.5 |
| Free cholesterol in medium VLDL (mmol/l) | -0.0008 |  | 0.00 |  | 0.004 | -4.6 |
| Concentration of small LDL particles (mmol/l) | -0.000 |  | 0.012 |  | 0.004 | -4.8 |
| Phospholipids in small LDL (mmol/l) | -0.001 |  | 0.00 |  | 0.004 | -4.8 |
| Total lipids in small LDL (mmol/l) | -0.004 |  | 0.00 |  | 0.004 | -4.8 |
| Phospholipids in medium VLDL (mmol/l) | -0.0013 |  | 0.29 |  | 0.004 | -4.9 |
| Triglycerides to total lipids ratio in medium HDL (%) | -0.05 |  | 0.00 |  | 0.005 | -5.1 |
| Cholesterol esters to total lipids ratio in large HDL (%) | 0.15 |  | 5.9 |  | 0.005 | -5.1 |
| Ratio of apolipoprotein B to apolipoprotein A-I (%) | -0.0059 |  | 0.51 |  | 0.005 | -5.2 |
| Free cholesterol (mmol/l) | -0.008 |  | 1.3 |  | 0.005 | -5.4 |
| Total cholesterol in very small VLDL (mmol/l) | -0.0033 |  | 0.00 |  | 0.005 | -5.5 |
| Ratio of omega-6 fatty acids to total fatty acids (%) | 0.1 | \* | 0.024 |  | 0.005 | -5.6 |
| Triglycerides to total lipids ratio in chylomicrons and extremely large VLDL (%) | 0.42 | \* | 0.00 |  | 0.005 | -5.8 |
| Triglycerides in medium LDL (mmol/l) | -0.001 |  | 0.00 |  | 0.005 | -5.8 |
| Mean diameter for HDL particles (nm) | 0.0063 |  | 13 |  | 0.005 | -5.8 |
| Esterified cholesterol (mmol/l) | -0.017 |  | 0.48 |  | 0.006 | -5.9 |
| Ratio of 18:2 linoleic acid to total fatty acids (%) | 0.094 |  | 16 |  | 0.006 | -6.0 |
| Serum total cholesterol (mmol/l) | -0.025 |  | 89 |  | 0.006 | -6.1 |
| Mean diameter for LDL particles (nm) | -0.01 |  | 0.70 |  | 0.006 | -6.2 |
| Serum total triglycerides (mmol/l) | -0.019 |  | 0.00 |  | 0.006 | -6.2 |
| Cholesterol esters in medium LDL (mmol/l) | -0.0043 | \* | 0.018 |  | 0.006 | -6.3 |
| Triglycerides in medium HDL (mmol/l) | -0.001 |  | 0.00 |  | 0.006 | -6.4 |
| Phospholipids to total lipids ratio in small HDL (%) | 0.095 | \* | -0.48 | # | 0.006 | -6.7 |
| Triglycerides to total lipids ratio in large HDL (%) | -0.054 |  | -4.7 |  | 0.006 | -6.7 |
| Concentration of very small VLDL particles (mmol/l) | -0.000 |  | -0.44 |  | 0.006 | -6.8 |
| Free cholesterol in small LDL (mmol/l) | -0.001 |  | -3.0 |  | 0.006 | -6.9 |
| Triglycerides in LDL (mmol/l) | -0.0034 |  | -0.58 |  | 0.006 | -6.9 |
| Total lipids in very small VLDL (mmol/l) | -0.0086 | \* | -0.73 |  | 0.006 | -6.9 |
| Cholesterol esters in small VLDL (mmol/l) | -0.002 |  | 0.14 |  | 0.006 | -6.9 |
| Total fatty acids (mmol/l) | -0.06 | \* | -2.4 |  | 0.007 | -7.1 |
| Phospholipids to total lipids ratio in large VLDL (%) | -0.37 |  | -2.4 |  | 0.009 | -7.3 |
| Total cholesterol in medium LDL (mmol/l) | -0.0055 |  | -2.6 |  | 0.007 | -7.4 |
| Phospholipids in very small VLDL (mmol/l) | -0.0025 | \* | -0.43 |  | 0.007 | -7.5 |
| Cholesterol esters in IDL (mmol/l) | -0.0056 |  | 1.9 |  | 0.007 | -7.5 |
| Total cholesterol in VLDL (mmol/l) | -0.0083 | \* | 0.38 |  | 0.007 | -7.5 |
| Concentration of small VLDL particles (mmol/l) | -0.000 | \* | -3.00E+06 |  | 0.007 | -7.6 |
| Total cholesterol in LDL (mmol/l) | -0.019 |  | -2.5 |  | 0.007 | -7.6 |
| Remnant cholesterol (non-HDL, non-LDL -cholesterol) (mmol/l) | -0.017 | \* | 0.00 |  | 0.008 | -7.8 |
| Triglycerides in IDL (mmol/l) | -0.0028 | \* | 0.00 |  | 0.007 | -7.9 |
| Total cholesterol to total lipids ratio in medium HDL (%) | 0.25 | \* | -3.40E+06 |  | 0.007 | -7.9 |
| Triglycerides in large LDL (mmol/l) | -0.0021 | \* | -0.014 |  | 0.007 | -8.0 |
| Free cholesterol in very small VLDL (mmol/l) | -0.0015 | \* | -0.33 |  | 0.007 | -8.0 |
| Total lipids in small VLDL (mmol/l) | -0.011 | \* | -0.056 |  | 0.008 | -8.3 |
| Ratio of triglycerides to phosphoglycerides (%) | -0.005 | \*\* | -5.0 |  | 0.008 | -8.7 |
| Saturated fatty acids (mmol/l) | -0.026 |  | -3.8 |  | 0.008 | -8.7 |
| Monounsaturated fatty acids; 16:1, 18:1 (mmol/l) | -0.034 |  | -1.3 |  | 0.008 | -8.7 |
| Total cholesterol in IDL (mmol/l) | -0.0081 | \* | 0.00 |  | 0.008 | -8.8 |
| Total lipids in medium LDL (mmol/l) | -0.008 | \* | -2.2 |  | 0.008 | -8.8 |
| Concentration of medium LDL particles (mmol/l) | -0.000 | \* | 0.00 |  | 0.008 | -8.8 |
| Total cholesterol in HDL3 (mmol/l) | -0.0014 | \* | -2.9 |  | 0.009 | -8.9 |
| Apolipoprotein B (g/l) | -0.0099 |  | -0.25 |  | 0.009 | -8.9 |
| Total cholesterol in small VLDL (mmol/l) | -0.0038 | \*\* | -2.0 |  | 0.008 | -9.2 |
| Phenylalanine (mmol/l) | -0.001 |  | -0.019 |  | 0.009 | -9.5 |
| Cholesterol esters in large LDL (mmol/l) | -0.0075 | \* | -0.18 |  | 0.009 | -9.6 |
| Ratio of polyunsaturated fatty acids to total fatty acids (%) | 0.21 | \* | -0.15 |  | 0.009 | -9.6 |
| Total cholesterol in large LDL (mmol/l) | -0.010 | \*\*\*\* | -0.26 |  | 0.009 | -10.4 |
| Triglycerides in HDL (mmol/l) | -0.0019 | \* | 0.00 |  | 0.009 | -10.4 |
| Free cholesterol in medium LDL (mmol/l) | -0.0012 | \* | -0.52 |  | 0.010 | -10.7 |
| Phospholipids in small VLDL (mmol/l) | -0.0025 | \* | -7.1 |  | 0.010 | -11.0 |
| Cholesterol esters to total lipids ratio in medium HDL (%) | 0.23 | \*\* | -1.3 |  | 0.010 | -11.1 |
| Free cholesterol in IDL (mmol/l) | -0.0025 | \* | -0.75 |  | 0.010 | -11.1 |
| Total lipids in IDL (mmol/l) | -0.015 | \* | -0.23 |  | 0.011 | -11.2 |
| Free cholesterol in small VLDL (mmol/l) | -0.0018 | \* | -0.016 |  | 0.010 | -11.4 |
| Phospholipids in medium LDL (mmol/l) | -0.0016 | \* | -5.0 |  | 0.010 | -11.4 |
| Concentration of IDL particles (mmol/l) | -0.000 | \* | -0.011 |  | 0.011 | -11.6 |
| Total lipids in large LDL (mmol/l) | -0.016 | \* | 0.00 |  | 0.011 | -12.4 |
| Triglycerides to total lipids ratio in very large HDL (%) | -0.13 | \* | -0.20 |  | 0.011 | -12.5 |
| Free cholesterol in large LDL (mmol/l) | -0.0026 | \* | 0.00 |  | 0.011 | -12.6 |
| Concentration of large LDL particles (mmol/l) | -0.000 | \* | -3.8 |  | 0.011 | -12.7 |
| Triglycerides to total lipids ratio in small HDL (%) | -0.049 | \*\* | -0.015 | # | 0.012 | -13.3 |
| Phospholipids in large LDL (mmol/l) | -0.0033 | \* | 0.00 |  | 0.014 | -15.0 |
| Phospholipids in IDL (mmol/l) | -0.0037 | \* | -0.025 |  | 0.014 | -16.1 |
| Triglycerides in small HDL (mmol/l) | -0.001 | \*\* | -0.014 | \* | 0.019 | -21.3 |
| Phospholipids in chylomicrons and extremely large VLDL (mmol/l) | 0.000 | \*\* | -1.9 |  | ---g | ---g |

Abbreviations: DHA, docosahexaenoic acid; HDL, high-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein.

aMediation steps proposed by Baron and Kenny.1

bStep 2: Effect size of association between fish consumption (independent variable) and metabolic marker (dependant variable). The reported values are beta-coefficients.

cFish consumption treated as a continuous variable (serves/week).

dStep 3: Effect size of association between metabolic marker (independent variable) and new episodes of depression during the five-year period (dependant variable). The reported values are beta-coefficients.

e98 participants had a new depressive episode during the five-year follow-up and 448 did not.

fStep 4: Proportion of total effect mediated by metabolic marker when included as a covariate in a model with fish consumption (independent variable) and depression (dependant variable), estimated using the binary\_mediation STATA command.

gModel failed to converge.

#P<0.1, \*P<0.05, \*\*P<0.01, \*\*\*P<0.001, \*\*\*\*P<0.0001.

**Reference**

1. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol.* 1986;51(6):1173-1182.