Supplementary

The association between alcohol consumption and serum metabolites and the modifying effect of smoking

Table S1. Second order polynomial regression analysis of alcohol consumption and metabolite pattern scores in male participants

Metabolite pattern	Independent Variable[a]	β (CI)	p-Value
AAs, SUG, Acs	Alcohol consumption (12g/d)	-0.064 (-0.190 – 0.063)	0.322
	Alcohol consumption (12g/d) ^2	-0.000 (-0.000 – 0.000)	0.673
acyl-alkyl PCs	Alcohol consumption (12g/d)	0.018 (-0.041 – 0.078)	0.545
	Alcohol consumption (12g/d) ^2	-0.000 (-0.000 – 0.000)	0.990

Abbreviation: AAs, SUG, Acs, Amino acids, sugar and free and short chain acylcarnitines; acyl-alkyl PCs, Acyl-alkyl-phosphatidylcholine; CI, confidence interval; adjusted for: age, body shape, physical activity index, socioeconomic status, eggs, dairy products, fish, meat, antihypertensive, diuretic, lipidlower, antiphlogistika, antibiotics, nutritional supplement, cancer; [a] Alcohol consumption is defined as alcohol consumption during the 12 months prior to recruitment per 12g/d; Alcohol consumption (12g/d) ^2 is the transformed variable of alcohol consumption we used for the polynomial regression analysis

Table S2: Second order polynomial regression analysis of alcohol consumption and metabolite pattern scores in female participants

Metabolite pattern	Independent Variable[a]	β (CI)	p-Value
AAs, SUG, ACs	Alcohol consumption (12g/d)	-0.093 (-0.350 – 0.164)	0.479
	Alcohol consumption (12g/d) ^2	0.000 (-0.000 – 0.001)	0.745
ACs I	Alcohol consumption (12g/d)	0.067 (-0.151 – 0.285)	0.548
	Alcohol consumption (12g/d) ^2	-0.000 (-0.000 – 0.000)	0.661
ACs II	Alcohol consumption (12g/d)	-0.076 (-0.311 – 0.158)	0.523
	Alcohol consumption (12g/d) ^2	0.000 (-0.000 – 0.000)	0.872
ACs III	Alcohol consumption (12g/d)	-0.059 (-0.262 – 0.143)	0.567
	Alcohol consumption (12g/d) ^2	-0.000 (-0.000 – 0.000)	0.822
diacyl, acyl-alkyl, lysoPCs, SMs	Alcohol consumption (12g/d)	0.056 (-0.369 – 0.480)	0.797
	Alcohol consumption (12g/d) ^2	-0.000 (-0.001 – 0.001)	0.797
diacyl, acyl-alkyl PCs	Alcohol consumption (12g/d)	-0.072 (-0.350 – 0.207)	0.614
	Alcohol consumption (12g/d) ^2	-0.000 (-0.001 – 0.000)	0.763

adjusted for: age, body shape, physical activity index, socioeconomic status, eggs, dairy products, fish, meat, antihypertensive, diuretic, lipidlower, antiphlogistika, antibiotics, nutritional supplement, cancer, contraceptives and hormone replacement therapy; Abbreviation: AAs, SUG, Acs, Amino acids, sugar and free and short chain acylcarnitines; acyl-alkyl PCs, Acyl-alkyl-phosphatidylcholine; CI, confidence interval; [a] Alcohol consumption is defined as alcohol consumption during the 12 months prior to recruitment per 12g/d; Alcohol consumption (12g/d) ^2 is the transformed variable of alcohol consumption we used for the polynomial regression analysis;

Table S3. Summary of small polar metabolite patterns of male participants

Name metabolite pattern	Proportion of explained Variance in %	Number of metabolites	Metabolites (Loadings)	Stability in %
AAs, SUG, ACs	41.28	17	Acylcarnitines: C0(0.20), C3(0.20), Sugar: Hexose(0.23), Amino acids: Proline(0.23), Glycine(0.24), Serine(0.24), Threonine(0.24), Arginine(0.24), Tyrosine(0.24), Ornithine(0.25), Glutamine(0.25), Histidine(0.25), Methionine(0.25), Tryptophan(0.26), Phenylalanine(0.26), Valine(0.26), Leucine/Isoleucin(0.26)	86
ACs I	14.03	6	Acylcarnitines: C18:2(0.37), C18(0.39), C14:1(0.41), C2(0.42), C16(0.43), C18:1(0.43)	89
ACs II	9.51	4	Acylcarnitines: C16:2(0.47), C10(0.50), C14:2(0.51), C7-DC(0.51)	92

Abbrevation: AAs, SUG, ACs, Amino acids, sugar and free and short chain acylcarnitines; ACs I, Long and short chain acylcarnitines; ACs II, Medium and long chain acylcarnitines; Acylcarnitines are abbreviated as Cx:y, where x and y are the the cumulative number of carbon atoms and number of double bonds, respectively.

Table S4. Summary of lipid metabolite patterns of male participants

Name metabolite patterns	Proportion of explained Variance in %	Number of metabolites	Metabolites (Loadings)	Stability in %
diacyl PCs, acyl-alkyl PCs I	25.04	27	Phosphatidylcholine diacyl: C34:1(0.19), C34:2(0.19), C36:1(0.19), C36:2(0.19), C36:3(0.19), C36:4(0.19), C38:3(0.19), C38:4(0.19), C38:5(0.19), C40:4(0.19), C40:5(0.19), Phosphatidylcholine acyl-alkyl: C32:1(0.19), C34:1(0.19), C34:2(0.19), C34:3(0.19), C36:1(0.19), C36:2(0.19), C36:3(0.19), C38:2(0.19), C38:3(0.19), C38:4(0.19), C38:6(0.19), C40:3(0.19), C40:5(0.19), C36:4(0.20), C36:5(0.20), C38:5(0.20)	60
SMs	10.67	11	Hydroxysphingomyelin: C14:1(0.30), C16:1(0.30), C22:1(0.30), C22:2(0.30), C24:1(0.30), Sphingomyelin: C16:0(0.30), C16:1(0.30), C18:0(0.30), C18:1(0.30), C20:2 C24:0(0.30), C24:1(0.30)	87
lysoPCs	3.95	4	lysoPhosphatidylcholine acyl: C20:4(0.49), C18:1(0.50), C16:0(0.51), C18:0(0.51)	87
diacyl PCs	3	3	Phosphatidylcholine diacyl: C32:2(0.58), C34:3(0.58), C34:4(0.58)	54
diacyl PCs, acyl-alkyl PCs II	2.98	3	Phosphatidylcholine acyl-alkyl: C38:0(0.57), Phosphatidylcholine diacyl: C36:5(0.58), C36:6(0.58)	88
acyl-alkyl PCs	2.03	2	Phosphatidylcholine acyl-alkyl: C42:2(0.71), C42:3(0.71)	62

Abbreviations: acyl-alkyl PCs, Acyl-alkyl-phosphatidylcholine; diacyl PCs, Diacyl-phosphatidylcholines; diacyl PCs, acyl-alkyl PCs I, Diacyl-glycerophosphocholines and acyl-alkyl-phosphatidylcholine I; diacyl PCs, acyl-alkyl PCs II, Diacyl-phosphatidylcholines and acyl-alkyl-phosphatidylcholine II; lysoPCs, Lyso-phosphatidylcholines; SMs, Sphingomyelins; The lipids are abbreviated as Cx:y, where x and y are the the cumulative number of carbon atoms and number of double bonds, respectively.

Table S5. Summary of small polar metabolite patterns of female participants

Name metabolite patterns	Proportion of explained Variance in %	Number of metabolites	Metabolites (Loadings)	Stability in %
AAs, SUG, ACs	37.44	17	Acylcarnitines: C0(0.19), C3(0.19), Amino acids: Glycine(0.20), Threonine(0.23), Tyrosine(0.23), Ornithine(0.24), Proline(0.24), Serine(0.24), Arginine(0.25), Glutamine(0.26), Histidine(0.26), Methionine(0.26), Phenylalanine(0.27), Tryptophan(0.27), Valine(0.27), Leucine/Isoleucin(0.27), Sugar: Hexose(0.24),	89
ACs I	13.16	6	Acylcarnitines: C18(0.38), C18:2(0.38), C14:1(0.40), C2(0.42), C16(0.44), C18:1(0.44)	91
ACs II	9.44	4	Acylcarnitines: C16:2(0.48), C10(0.50), C14:2 (0.51), C7-DC(0.51)	81
ACs III	7	3	Acylcarnitines: C10(0.57), C3(0.58), C3-DC-M /C5-OH(0.58)	92

Abbrevation: AAs, SUG, ACs, Amino acids, sugar and free and short chain acylcarnitines; ACs I, Long and short chain acylcarnitines; ACs II, Medium and long chain acylcarnitines; ACs III, Short and medium chain acylcarnitines; acylcarnitines are abbreviated as Cx:y, where x and y are the the cumulative number of carbon atoms and number of double bonds, respectively.

Table S6. Summary of lipid metabolite patterns of female participants

Name metabolite patterns	Proportion of explained Variance in %	Number of metabolites	Metabolites (Loadings)	Stability in %
diacyl, acyl-alkyl, lysoPCs, SMs	57.9	73	Phosphatidylcholine diacyl: C 42:2(0.09), C30:0(0.10), C32:1(0.10), C36:0(0.10), C38:0(0.10), C42:5(0.10), C32:2(0.11), C34:3(0.11), C34:4(0.11), C36:5(0.11), C36:6(0.11), C40:2(0.11), C40:3(0.11), C40:5(0.11), C42:4(0.11), C28:1(0.12), C32:3(0.12), C34:1(0.12), C36:1(0.12), C36:3(0.12), C38:5(0.12), C38:6(0.12), C34:2(0.13), C36:2(0.13), C36:4(0.13), C38:3(0.13), C38:4(0.13), C40:4(0.13) Phosphatidylcholine acyl-alkyl: C40:1(0.10), C42:1(0.10), 38:0(0.11), C38:1(0.11), 32:1(0.12), C32:2(0.12), C34:0(0.12), C34:1(0.12), C34:2(0.12), C34:3(0.12), C36:1(0.12), C36:2(0.12), C36:3(0.12), C38:2(0.12), C38:3(0.12), C38:4(0.12), C38:6(0.12), C40:2(0.12), C40:3(0.12), C40:5(0.12), C40:6(0.12), C42:2(0.12), C42:3(0.12), C36:4(0.13), C36:5(0.13), C38:5(0.13) lysoPhosphatidylcholine: C16:0(0.11), C16:1(0.11), C17:0(0.11), C18:0(0.11), C18:1(0.11), C20:4(0.11), Sphingomyelin: C14:1(0.12), C16:1(0.12), C22:1(0.12), C22:2(0.12), C24:1(0.12), C26:0(0.10), C26:1(0.10), C16:0(0.12), C16:1(0.12), C18:0(0.12), C18:1(0.12), C24:0(0.12), C24:1(0.12)	44
diacyl, acyl-alkyl PCs	6.87	8	Phosphatidylcholine diacyl: C42:0(0.35), C42:1(0.35), Phosphatidylcholine acyl-alkyl: C42:4(0.33), C44:4(0.34), C40:4(0.35), C44:5(0.37), C44:6(0.37), C42:5(0.37)	72
acyl-alkyl, lysoPC	1.87	2	Phosphatidylcholine acyl-alkyl : C30:2(0.71), lysoPhosphatidylcholine: C28:1(0.71)	71

Abbreviations: acyl-alkyl, lysoPC, Acyl-alkyl- and lyso-phosphatidylcholine; diacyl, acyl-alkyl PCs, Diacyl- and acyl-alkyl-phosphatidylcholine; diacyl, acyl-alkyl, lysoPCs, SMs, Diacyl-, acyl-alkyl-, lyso- phosphatidylcholines and sphingomyelins; The lipids are abbreviated as Cx:y, where x and y are the the cumulative number of carbon atoms and number of double bonds, respectively.