

Prediagnostic plasma metabolite concentrations and liver cancer risk: a population-based study of Chinese men

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Supplementary Tables

Supplementary Table ST1 List of the metabolites quantitated by the UPLC-MS/MS (Metabo-Profile, Shanghai, China)

Metabolites	Classes	HMDB	KEGG	CV of pooled QC samples ^a	
				Average intra-batch CV	Inter-batch CV
2-Hydroxyglutaric acid	Amino acids	HMDB0000606	C01087	22.39	26.33
2-Phenylglycine	Amino acids	HMDB0002210	NA	12.90	22.81
5-Aminolevulinic acid	Amino acids	HMDB0001149	C00430	20.66	20.26
Alanine	Amino acids	HMDB0000161	C00041	4.32	4.10
alpha-Aminobutyric acid	Amino acids	HMDB0000452	C02356	6.14	6.02
Arginine	Amino acids	HMDB0000517	C00062	9.78	9.13
Asparagine	Amino acids	HMDB0000168	C00152	5.52	5.21
Aspartic acid	Amino acids	HMDB0000191	C00049	9.03	8.62
beta-Alanine	Amino acids	HMDB0000056	C00099	15.01	17.45
Citrulline	Amino acids	HMDB0000904	C00327	7.41	7.30
Creatine	Amino acids	HMDB0000064	C00300	5.87	6.25
Dimethylglycine	Amino acids	HMDB0000092	C01026	7.56	7.10
GABA	Amino acids	HMDB0000112	C00334	16.48	16.02
Glutamic acid	Amino acids	HMDB0000148	C00025	4.90	4.84
Glutamine	Amino acids	HMDB0000641	C00064	5.31	5.20
Glycine	Amino acids	HMDB0000123	C00037	3.79	3.73
Hippuric acid	Amino acids	HMDB0000714	C01586	7.50	7.48
Histidine	Amino acids	HMDB0000177	C00135	7.58	7.11
Homoserine	Amino acids	HMDB0000719	C00263	13.03	12.71
Isoleucine	Amino acids	HMDB0000172	C00407	8.53	9.73
Leucine	Amino acids	HMDB0000687	C00123	4.50	4.68
Lysine	Amino acids	HMDB0000182	C00047	7.47	7.47
Methionine	Amino acids	HMDB0000696	C00073	5.96	6.15
Methylcysteine	Amino acids	HMDB0002108	NA	6.65	6.95
N-Acetylglycine	Amino acids	HMDB0000532	NA	7.20	6.94
N-Acetyls erine	Amino acids	HMDB0002931	NA	8.71	8.32

Metabolites	Classes	HMDB	KEGG	CV of pooled QC samples ^a	
				Average intra-batch CV	Inter-batch CV
N-Phenylacetylglutamine	Amino acids	HMDB0006344	C04148	7.61	7.57
Norvaline	Amino acids	HMDB0013716	C01799	5.74	5.54
Ornithine	Amino acids	HMDB0000214	C00077	9.74	9.52
Phenylalanine	Amino acids	HMDB0000159	C00079	6.82	6.67
Pipecolic acid	Amino acids	HMDB0000716	C00408	6.66	6.94
Proline	Amino acids	HMDB0000162	C00148	9.78	9.15
Pyroglutamic acid	Amino acids	HMDB0000267	C01879	6.71	6.77
Sarcosine	Amino acids	HMDB0000271	C00213	12.09	11.44
Selenomethionine	Amino acids	HMDB0003966	C05335	6.53	7.17
Serine	Amino acids	HMDB0000187	C00065	5.21	4.91
Threonine	Amino acids	HMDB0000167	C00188	6.41	6.12
Tryptophan	Amino acids	HMDB0000929	C00078	8.24	7.69
Tyrosine	Amino acids	HMDB0000158	C00082	3.56	3.65
Valine	Amino acids	HMDB0000883	C00183	6.05	5.74
ortho-Hydroxyphenylacetic acid	Benzenoids	HMDB0000669	C05852	14.79	15.05
Phenylacetic acid	Benzenoids	HMDB0000209	C07086	15.67	14.87
Phenylpyruvic acid	Benzenoids	HMDB0000205	C00166	14.20	15.77
4-Hydroxybenzoic acid	Benzoic acids	HMDB0000500	C00156	21.05	21.64
m-Aminobenzoic acid	Benzoic acids	HMDB0001891	NA	28.48	29.31
m-Hydroxyhippuric acid	Benzoic acids	HMDB0006116	NA	13.64	13.90
Phthalic acid	Benzoic acids	HMDB0002107	C01606	15.12	14.79
7-DHCA	Bile acids	NA	C13154	26.20	25.48
apoCA	Bile acids	NA	NA	25.89	25.59
beta-HDCA	Bile acids	HMDB0000664	NA	13.88	13.77
CA	Bile acids	HMDB0000619	C00695	10.03	11.11
CDCA	Bile acids	HMDB0000518	C02528	8.64	8.20
DCA	Bile acids	HMDB0000626	C04483	11.77	10.91
GCA	Bile acids	HMDB0000138	C01921	7.45	7.12
GCDCA	Bile acids	HMDB0000637	C05466	5.86	5.98

Metabolites	Classes	HMDB	KEGG	CV of pooled QC samples ^a	
				Average intra-batch CV	Inter-batch CV
GDCA	Bile acids	HMDB0000631	C05464	8.47	8.16
GHCA	Bile acids	HMDB0240607	NA	19.29	19.71
GLCA	Bile acids	HMDB0000698	C15557	11.96	11.85
GLCA-3S	Bile acids	HMDB0002639	C11301	14.96	15.96
GUDCA	Bile acids	HMDB0000708	NA	9.94	10.38
HCA	Bile acids	HMDB0000760	NA	15.29	15.13
HDCA	Bile acids	HMDB0000733	NA	26.60	26.50
LCA	Bile acids	HMDB0000761	C03990	19.32	20.92
TCA	Bile acids	HMDB0000036	C05122	8.53	8.19
TCDCA	Bile acids	HMDB0000951	C05465	6.74	6.43
TDCA	Bile acids	HMDB0000896	C05463	10.88	10.35
UCA	Bile acids	HMDB0000917	C17644	11.14	12.77
D-Xylulose	Carbohydrates	HMDB0001644	C00310	14.78	14.28
Fructose	Carbohydrates	HMDB0000660	C02336	4.50	4.50
Galactonic acid	Carbohydrates	HMDB0000565	C00880	19.84	19.96
Gluconolactone	Carbohydrates	HMDB0000150	C00198	10.03	9.51
Glucose	Carbohydrates	HMDB0000122	C00221	3.18	2.98
Glutaconic acid	Carbohydrates	HMDB0000620	C02214	13.68	12.80
Glyceric acid	Carbohydrates	HMDB0000139	C00258	5.99	6.11
Maltose/Lactose	Carbohydrates	NA	NA	14.56	14.21
N-Acetylneuraminic acid	Carbohydrates	HMDB0000230	C19910	8.12	7.87
Rhamnose	Carbohydrates	HMDB0000849	C00507	27.87	28.97
Tartaric acid	Carbohydrates	HMDB0000956	C00898	8.18	7.87
Threonic acid	Carbohydrates	HMDB0000943	C01620	9.30	9.21
Trehalose	Carbohydrates	HMDB0000975	C01083	4.61	4.50
Xylose	Carbohydrates	HMDB0000098	C00181	20.24	20.00
2-Methylbutyrylcarnitine	Carnitines	HMDB0000378	NA	6.79	7.02
3-Hydroxyisovalerylcarnitine	Carnitines	HMDB0061189	NA	10.77	13.45
Acetylcarnitine	Carnitines	HMDB0000201	C02571	9.26	8.71

Metabolites	Classes	HMDB	KEGG	CV of pooled QC samples ^a	
				Average intra-batch CV	Inter-batch CV
Adipoylcarnitine	Carnitines	HMDB0061677	NA	9.65	13.85
Carnitine	Carnitines	HMDB0000062	C00318	3.46	3.38
Decanoylcarnitine	Carnitines	HMDB0000651	NA	5.70	5.63
Glutaryl carnitine	Carnitines	HMDB0013130	NA	5.07	5.36
Hexanylcarnitine	Carnitines	HMDB0000705	NA	9.41	11.04
Isovelarylcarnitine	Carnitines	HMDB0000688	NA	6.80	6.95
Lauroyl carnitine	Carnitines	HMDB0002250	NA	4.89	4.69
Linoleyl carnitine	Carnitines	HMDB0006469	NA	6.00	5.75
Malonylcarnitine	Carnitines	HMDB0002095	NA	26.43	27.05
Myristoylcarnitine	Carnitines	HMDB0005066	NA	5.78	6.59
Octanoylcarnitine	Carnitines	HMDB0000791	C02838	3.35	3.20
Oleylcarnitine	Carnitines	HMDB0005065	NA	5.82	5.72
Palmitoylcarnitine	Carnitines	HMDB0000222	C02990	6.73	6.68
Propionyl carnitine	Carnitines	HMDB0000824	C03017	8.27	8.90
Stearyl carnitine	Carnitines	HMDB0000848	NA	20.80	20.19
10Z-Heptadecenoic acid	Fatty acids	HMDB0060038	NA	29.62	28.46
12-Hydroxystearic acid	Fatty acids	HMDB0061706	NA	5.12	5.03
2-Hydroxy-3-methylbutyric acid	Fatty acids	HMDB0000407	NA	27.69	29.48
2,2-Dimethyladipic acid	Fatty acids	NA	NA	8.74	8.61
3-Methyladipic acid	Fatty acids	HMDB0000555	NA	28.86	28.99
5-Dodecenoic acid	Fatty acids	HMDB0000529	NA	5.98	6.15
8,11,14-Eicosatrienoic acid	Fatty acids	HMDB0002925	C03242	13.51	13.25
Adrenic acid	Fatty acids	HMDB0002226	C16527	28.95	28.54
alpha-Linolenic acid	Fatty acids	HMDB0001388	C06427	8.66	11.15
Arachidonic acid	Fatty acids	HMDB0001043	C00219	9.15	9.32
Decanoic acid	Fatty acids	HMDB0000511	C01571	12.16	11.48
DHA	Fatty acids	HMDB0002183	C06429	14.54	16.37
Dodecanoic acid	Fatty acids	HMDB0000638	C02679	8.40	8.15
DPA _n -3	Fatty acids	HMDB0006528	C16513	16.85	17.53

Metabolites	Classes	HMDB	KEGG	CV of pooled QC samples ^a	
				Average intra-batch CV	Inter-batch CV
DPAn-6	Fatty acids	HMDB0001976	NA	23.94	23.94
EPA	Fatty acids	HMDB0001999	C06428	11.05	11.84
gamma-Linolenic acid	Fatty acids	HMDB0003073	C06426	9.52	9.06
Heptadecanoic acid	Fatty acids	HMDB0002259	NA	27.21	29.36
Heptanoic acid	Fatty acids	HMDB0000666	C17714	10.67	11.34
Linoleic acid	Fatty acids	HMDB0000673	C01595	5.71	5.81
Methylglutaric acid	Fatty acids	HMDB0000752	NA	18.23	20.79
Methylmalonic acid	Fatty acids	HMDB0000202	C02170	8.71	8.75
Myristelaidic acid	Fatty acids	HMDB0062248	NA	9.06	10.26
Myristic acid	Fatty acids	HMDB0000806	C06424	14.65	15.30
Myristoleic acid	Fatty acids	HMDB0002000	C08322	7.06	8.66
Nonanoic acid	Fatty acids	HMDB0000847	C01601	28.81	27.93
Octanoic acid	Fatty acids	HMDB0000482	C06423	7.07	7.22
Oleic acid	Fatty acids	HMDB0000207	C00712	15.47	15.90
Palmitic acid	Fatty acids	HMDB0000220	C00249	13.63	13.11
Palmitoleic acid	Fatty acids	HMDB0003229	C08362	15.78	16.16
Pentadecanoic acid	Fatty acids	HMDB0000826	C16537	20.04	19.30
Ricinoleic acid	Fatty acids	HMDB0034297	C08365	7.55	8.66
Undecylenic acid	Fatty acids	HMDB0033724	C13910	6.69	6.55
3-Indolepropionic acid	Indoles	HMDB0002302	NA	6.60	6.61
Indoleacetic acid	Indoles	HMDB0000197	C00954	9.02	8.93
AMP	Nucleotides	HMDB0000045	C00020	10.93	10.40
2-Furoic acid	Organic acids	HMDB0000617	C01546	24.84	25.19
2-Hydroxybutyric acid	Organic acids	HMDB0000008	C05984	6.34	7.03
3-Hydroxybutyric acid	Organic acids	HMDB0000357	C01089	8.14	8.70
3-Methyl-2-oxovaleric acid	Organic acids	HMDB0000491	C03465	4.92	5.09
Aconitic acid	Organic acids	HMDB0000958	C02341	8.46	8.59
Adipic acid	Organic acids	HMDB0000448	C06104	24.46	22.72
alpha-Hydroxyisobutyric acid	Organic acids	HMDB0000729	NA	13.86	13.50

Metabolites	Classes	HMDB	KEGG	CV of pooled QC samples ^a	
				Average intra-batch CV	Inter-batch CV
alpha-Ketoisovaleric acid	Organic acids	HMDB0000019	C00141	8.83	8.46
Azelaic acid	Organic acids	HMDB0000784	C08261	10.42	10.59
Benzoic acid	Organic acids	HMDB0001870	C00180	6.11	6.98
Citramalic acid	Organic acids	HMDB0000426	C00815	8.72	8.94
Citric acid	Organic acids	HMDB0000094	C00158	2.64	2.47
Erythronic acid	Organic acids	HMDB0000613	NA	5.78	5.69
Fumaric acid	Organic acids	HMDB0000134	C00122	25.87	25.82
Glutaric acid	Organic acids	HMDB0000661	C00489	18.19	20.51
Glycolic acid	Organic acids	HMDB0000115	C00160	8.96	8.51
Guanidoacetic acid	Organic acids	HMDB0000128	C00581	10.34	10.32
Isocitric acid	Organic acids	HMDB0000193	C00311	7.54	7.38
Ketoleucine	Organic acids	HMDB0000695	C00233	4.19	4.11
Lactic acid	Organic acids	HMDB0000190	C00186	4.04	3.91
Maleic acid	Organic acids	HMDB0000176	C01384	23.45	25.32
Malic acid	Organic acids	HMDB0000156	C00149	8.44	8.43
Malonic acid	Organic acids	HMDB0000691	C00383	26.46	25.63
Methylsuccinic acid	Organic acids	HMDB0001844	NA	17.58	16.93
Oxalic acid	Organic acids	HMDB0002329	C00209	7.60	9.38
Oxoadipic acid	Organic acids	HMDB0000225	C00322	28.05	29.04
Oxoglutaric acid	Organic acids	HMDB0000208	C00026	9.09	8.54
Petroselinic acid	Organic acids	HMDB0002080	C08363	13.68	14.35
Pimelic acid	Organic acids	HMDB0000857	C02656	25.52	27.61
Pyruvic acid	Organic acids	HMDB0000243	C00022	11.97	11.15
Succinic acid	Organic acids	HMDB0000254	C00042	8.15	8.33
4-Hydroxyphenylpyruvic acid	Phenols	HMDB0000707	C01179	15.17	14.83
Homovanillic acid	Phenols	HMDB0000118	C05582	9.38	9.43
p-Hydroxyphenylacetic acid	Phenols	HMDB0000020	C00642	23.62	26.31
2-Phenylpropionate	Phenylpropanoic acids	HMDB0011743	NA	6.03	5.82
3-Hydroxyphenylhydracrylic acid	Phenylpropanoic acids	HMDB0002643	NA	16.45	17.77

Metabolites	Classes	HMDB	KEGG	CV of pooled QC samples ^a	
				Average intra-batch CV	Inter-batch CV
Hydrocinnamic acid	Phenylpropanoic acids	HMDB0000764	C05629	12.00	11.14
Hydroxyphenyllactic acid	Phenylpropanoic acids	HMDB0000755	C03672	11.69	11.21
Phenyllactic acid	Phenylpropanoic acids	HMDB0000779	C01479	17.97	17.59
N-Methylnicotinamide	Pyridines	HMDB0003152	NA	10.21	9.92
3-Hydroxyisovaleric acid	SCFAs	HMDB0000754	NA	12.83	13.94
Acetic acid	SCFAs	HMDB0000042	C00033	8.42	8.45
Butyric acid	SCFAs	HMDB0000039	C00246	12.05	11.61
Caproic acid	SCFAs	HMDB0000535	C01585	7.19	6.81
Ethylmethylacetic acid	SCFAs	HMDB0002176	C18319	7.62	8.02
Formic acid	SCFAs	HMDB0000142	C00058	15.91	15.73
Isobutyric acid	SCFAs	HMDB0001873	C02632	15.54	17.16
Isocaproic acid	SCFAs	HMDB0000689	NA	17.25	20.51
Isovaleric acid	SCFAs	HMDB0000718	C08262	8.87	8.47
Pentanoic acid	SCFAs	HMDB0000892	C00803	15.47	14.96
Propanoic acid	SCFAs	HMDB0000237	C00163	10.52	10.57

^a CV: coefficient of variation; QC: quality control.

Supplementary Table ST2 Distributions and comparisons of plasma metabolite concentrations ($\mu\text{mol/L}$) in cases and controls

Metabolites	Classes	Cases		Controls		Ratio of Geometric means (95% CI)
		Geometric mean	Geometric SD	Geometric mean	Geometric SD	
2-Hydroxyglutaric acid	Amino acids	0.525	1.864	0.466	1.971	1.13 (0.84, 1.51)
2-Phenylglycine	Amino acids	0.243	1.748	0.255	1.472	0.95 (0.74, 1.22)
5-Aminolevulinic acid	Amino acids	1.946	1.589	2.061	1.515	0.94 (0.74, 1.20)
Alanine	Amino acids	483.553	1.242	494.79	1.242	0.98 (0.81, 1.18)
Arginine	Amino acids	106.483	1.346	101.648	1.424	1.05 (0.85, 1.30)
Asparagine	Amino acids	75.799	1.322	70.495	1.254	1.08 (0.88, 1.31)
Aspartic acid	Amino acids	6.465	1.452	6.325	1.404	1.02 (0.82, 1.27)
Citrulline	Amino acids	58.188	1.357	51.559	1.389	1.13 (0.91, 1.40)
Creatine	Amino acids	27.818	1.606	35.892	1.522	0.78 (0.61, 0.99)
Dimethylglycine	Amino acids	8.273	1.404	6.994	1.336	1.18 (0.96, 1.46)
GABA	Amino acids	0.348	1.388	0.329	1.435	1.06 (0.85, 1.32)
Glutamic acid	Amino acids	23.923	1.479	23.573	1.383	1.01 (0.81, 1.27)
Glutamine	Amino acids	1355.254	1.598	1424.88	1.183	0.95 (0.77, 1.18)
Glycine	Amino acids	296.077	1.276	293.465	1.28	1.01 (0.83, 1.23)
Hippuric acid	Amino acids	1.686	2.795	1.702	2.962	0.99 (0.64, 1.55)
Histidine	Amino acids	88.517	1.204	84.043	1.178	1.05 (0.88, 1.27)
Homoserine	Amino acids	16.081	1.359	14.43	1.358	1.11 (0.90, 1.37)
Isoleucine	Amino acids	61.281	1.422	65.023	1.413	0.94 (0.76, 1.17)
Leucine	Amino acids	169.412	1.33	181.903	1.302	0.93 (0.76, 1.14)
Lysine	Amino acids	364.986	1.27	387.926	1.25	0.94 (0.77, 1.14)
Methionine	Amino acids	38.058	1.377	32.008	1.309	1.19 (0.97, 1.46)
Methylcysteine	Amino acids	7.764	1.555	8.086	1.541	0.96 (0.76, 1.22)
N-Acetylglycine	Amino acids	6.769	1.255	7.244	1.276	0.93 (0.77, 1.14)
N-Acetylserine	Amino acids	2.927	1.24	2.842	1.219	1.03 (0.85, 1.25)
N-Phenylacetylglutamine	Amino acids	1.877	2.328	1.835	2.407	1.02 (0.71, 1.48)
Norvaline	Amino acids	36.161	1.078	36.094	1.076	1.00 (0.85, 1.18)
Ornithine	Amino acids	149.868	1.399	139.791	1.35	1.07 (0.87, 1.33)
Phenylalanine	Amino acids	68.33	1.291	62.718	1.184	1.09 (0.90, 1.32)

Metabolites	Classes	Cases		Controls		Ratio of Geometric means (95% CI)
		Geometric mean	Geometric SD	Geometric mean	Geometric SD	
Pipecolic acid	Amino acids	4.563	1.533	4.075	1.476	1.12 (0.89, 1.41)
Proline	Amino acids	244.646	1.3	239.932	1.382	1.02 (0.83, 1.25)
Pyroglutamic acid	Amino acids	22.886	1.504	21.965	1.395	1.04 (0.83, 1.30)
Sarcosine	Amino acids	14.999	1.334	14.555	1.278	1.03 (0.84, 1.26)
Selenomethionine	Amino acids	92.706	1.405	91.315	1.393	1.02 (0.82, 1.26)
Serine	Amino acids	145.564	1.311	133.501	1.259	1.09 (0.89, 1.33)
Threonine	Amino acids	122.002	1.304	111.069	1.265	1.10 (0.90, 1.34)
Tryptophan	Amino acids	119.51	1.245	112.503	1.227	1.06 (0.88, 1.29)
Tyrosine	Amino acids	115.713	1.38	89.015	1.267	1.30 (1.06, 1.60)
Valine	Amino acids	210.806	1.236	219.813	1.221	0.96 (0.79, 1.16)
alpha-Aminobutyric acid	Amino acids	4.618	1.344	4.767	1.3	0.97 (0.79, 1.19)
beta-Alanine	Amino acids	3.337	2.44	3.446	2.09	0.97 (0.68, 1.38)
Phenylacetic acid	Benzenoids	6.482	2.383	4.843	2.488	1.34 (0.92, 1.95)
Phenylpyruvic acid	Benzenoids	0.361	1.949	0.317	1.729	1.14 (0.86, 1.51)
ortho-Hydroxyphenylacetic acid	Benzenoids	0.229	1.588	0.245	1.529	0.93 (0.73, 1.19)
4-Hydroxybenzoic acid	Benzoic acids	0.177	1.282	0.171	1.241	1.03 (0.85, 1.25)
Phthalic acid	Benzoic acids	0.724	1.461	0.757	1.427	0.96 (0.77, 1.20)
m-Aminobenzoic acid	Benzoic acids	4.248	1.775	4.423	1.703	0.96 (0.73, 1.26)
m-Hydroxyhippuric acid	Benzoic acids	0.107	1.387	0.108	1.428	0.99 (0.80, 1.23)
7-DHCA	Bile acids	0.062	2.052	0.058	1.94	1.07 (0.79, 1.46)
CA	Bile acids	0.056	3.146	0.042	3.161	1.33 (0.82, 2.17)
CDCA	Bile acids	0.8	3.272	0.625	3.596	1.28 (0.75, 2.18)
DCA	Bile acids	0.455	2.404	0.483	2.542	0.94 (0.64, 1.38)
GCA	Bile acids	1.746	3.81	0.534	3	3.27 (1.93, 5.56)
GCDCA	Bile acids	9.771	3.009	3.679	2.281	2.66 (1.76, 4.01)
GDCA	Bile acids	0.793	7.788	0.472	6.34	1.68 (0.56, 5.02)
GHCA	Bile acids	0.068	2.269	0.044	1.737	1.57 (1.15, 2.14)
GLCA	Bile acids	0.224	1.865	0.196	1.624	1.14 (0.87, 1.50)
GLCA-3S	Bile acids	0.477	3.381	0.358	3.339	1.33 (0.79, 2.24)

Metabolites	Classes	Cases		Controls		Ratio of Geometric means (95% CI)
		Geometric mean	Geometric SD	Geometric mean	Geometric SD	
GDCA	Bile acids	0.668	3.132	0.432	2.62	1.54 (0.99, 2.41)
HCA	Bile acids	0.155	1.496	0.134	1.319	1.16 (0.93, 1.44)
HDCA	Bile acids	0.159	2.1	0.168	2.444	0.94 (0.66, 1.34)
LCA	Bile acids	0.034	2.086	0.029	1.677	1.19 (0.89, 1.59)
TCA	Bile acids	0.193	5.22	0.042	3.167	4.63 (2.38, 9.02)
TCDCA	Bile acids	1.023	4.626	0.215	2.811	4.75 (2.63, 8.58)
TDCA	Bile acids	0.218	3.278	0.102	2.383	2.13 (1.37, 3.31)
UCA	Bile acids	0.096	1.401	0.093	1.372	1.04 (0.84, 1.29)
apoCA	Bile acids	0.736	1.33	0.76	1.349	0.97 (0.79, 1.19)
beta-HDCA	Bile acids	0.128	3.422	0.125	2.988	1.03 (0.62, 1.68)
D-Xylulose	Carbohydrates	1.839	1.398	1.611	1.297	1.14 (0.93, 1.41)
Fructose	Carbohydrates	0.548	2.64	0.435	2.156	1.26 (0.87, 1.83)
Galactonic acid	Carbohydrates	0.196	1.694	0.188	1.544	1.04 (0.81, 1.34)
Gluconolactone	Carbohydrates	4.291	1.459	4.272	1.398	1.00 (0.81, 1.25)
Glucose	Carbohydrates	8054.545	1.446	7385.193	1.357	1.09 (0.88, 1.35)
Glutaconic acid	Carbohydrates	6.53	1.56	6.571	1.502	0.99 (0.78, 1.26)
Glyceric acid	Carbohydrates	5.885	1.632	5.805	1.599	1.01 (0.79, 1.30)
Maltose/Lactose	Carbohydrates	2.159	2.018	2.455	1.905	0.88 (0.65, 1.19)
N-Acetylneuraminic acid	Carbohydrates	1.016	1.305	1.081	1.268	0.94 (0.77, 1.15)
Rhamnose	Carbohydrates	2.407	1.959	1.639	2.182	1.47 (1.07, 2.02)
Tartaric acid	Carbohydrates	0.828	1.759	0.856	1.915	0.97 (0.73, 1.29)
Threonic acid	Carbohydrates	2.401	1.964	2.591	1.779	0.93 (0.69, 1.24)
Trehalose	Carbohydrates	12.846	1.103	13.112	1.081	0.98 (0.83, 1.16)
Xylose	Carbohydrates	4.364	1.582	4.048	1.622	1.08 (0.84, 1.38)
2-Methylbutyrylcarnitine	Carnitines	0.053	1.524	0.054	1.472	0.99 (0.79, 1.25)
3-Hydroxyisovaleryl carnitine	Carnitines	0.082	1.456	0.088	1.341	0.93 (0.75, 1.16)
Acetylcarnitine	Carnitines	6.062	1.496	5.728	1.397	1.06 (0.85, 1.32)
Adipoylcarnitine	Carnitines	0.028	1.374	0.027	1.418	1.05 (0.85, 1.31)
Carnitine	Carnitines	28.373	1.233	27.561	1.222	1.03 (0.85, 1.24)

Metabolites	Classes	Cases		Controls		Ratio of Geometric means (95% CI)
		Geometric mean	Geometric SD	Geometric mean	Geometric SD	
Decanoylcarnitine	Carnitines	0.187	1.881	0.181	1.802	1.03 (0.77, 1.37)
Glutarylcarnitine	Carnitines	0.087	1.258	0.083	1.235	1.05 (0.87, 1.27)
Hexanoylcarnitine	Carnitines	0.035	2.352	0.034	2.1	1.00 (0.71, 1.42)
Isovelarylcarnitine	Carnitines	0.068	1.548	0.072	1.506	0.94 (0.75, 1.19)
Lauroylcarnitine	Carnitines	0.078	2.17	0.07	2.389	1.12 (0.79, 1.60)
Linoleylcarnitine	Carnitines	0.298	1.574	0.289	1.548	1.03 (0.81, 1.31)
Malonylcarnitine	Carnitines	0.162	2.723	0.168	2.285	0.96 (0.65, 1.42)
Myristoylcarnitine	Carnitines	0.066	1.393	0.059	1.504	1.12 (0.90, 1.40)
Octanoylcarnitine	Carnitines	0.069	1.875	0.067	1.782	1.04 (0.78, 1.38)
Oleylcarnitine	Carnitines	0.157	1.535	0.142	1.602	1.11 (0.87, 1.41)
Palmitoylcarnitine	Carnitines	0.17	1.471	0.159	1.537	1.07 (0.85, 1.35)
Propionylcarnitine	Carnitines	0.802	1.394	0.79	1.362	1.01 (0.82, 1.26)
Stearylcarnitine	Carnitines	0.19	1.66	0.17	1.829	1.12 (0.85, 1.47)
10Z-Heptadecenoic acid	Fatty acids	0.105	2.514	0.092	2.472	1.15 (0.78, 1.69)
12-Hydroxystearic acid	Fatty acids	0.306	1.3	0.321	1.351	0.95 (0.78, 1.17)
2,2-Dimethyladipic acid	Fatty acids	0.491	3.959	0.523	3.881	0.94 (0.51, 1.72)
2-Hydroxy-3-methylbutyric acid	Fatty acids	29.129	1.972	25.024	1.784	1.16 (0.87, 1.56)
3-Methyladipic acid	Fatty acids	0.482	3.008	0.517	3.499	0.93 (0.56, 1.54)
5-Dodecenoic acid	Fatty acids	0.205	2.13	0.182	2.019	1.13 (0.82, 1.56)
8,11,14-Eicosatrienoic acid	Fatty acids	0.297	2.15	0.32	1.777	0.93 (0.69, 1.26)
Adrenic acid	Fatty acids	0.372	1.98	0.369	1.961	1.01 (0.74, 1.37)
Arachidonic acid	Fatty acids	1.533	1.772	1.857	1.528	0.83 (0.64, 1.07)
DHA	Fatty acids	1.593	2.105	1.788	1.784	0.89 (0.66, 1.20)
DPA _n -3	Fatty acids	0.296	2.156	0.327	1.789	0.91 (0.67, 1.23)
DPA _n -6	Fatty acids	0.209	2.383	0.227	1.876	0.92 (0.66, 1.28)
Decanoic acid	Fatty acids	1.135	2.511	0.917	2.374	1.24 (0.85, 1.80)
Dodecanoic acid	Fatty acids	0.545	3.227	0.536	2.808	1.02 (0.64, 1.62)
EPA	Fatty acids	0.304	2.496	0.373	2.314	0.82 (0.56, 1.18)
Heptadecanoic acid	Fatty acids	0.574	1.649	0.613	1.53	0.94 (0.73, 1.20)

Metabolites	Classes	Cases		Controls		Ratio of Geometric means (95% CI)
		Geometric mean	Geometric SD	Geometric mean	Geometric SD	
Heptanoic acid	Fatty acids	14.953	1.324	15.064	1.36	0.99 (0.81, 1.22)
Linoleic acid	Fatty acids	131.024	1.906	141.922	1.796	0.92 (0.69, 1.23)
Methylglutaric acid	Fatty acids	0.475	1.73	0.461	1.693	1.03 (0.79, 1.34)
Methylmalonic acid	Fatty acids	6.146	1.765	5.696	1.691	1.08 (0.83, 1.41)
Myristelaidic acid	Fatty acids	0.209	3.112	0.174	5.009	1.20 (0.63, 2.29)
Myristic acid	Fatty acids	5.677	1.486	5.51	1.462	1.03 (0.82, 1.29)
Myristoleic acid	Fatty acids	0.121	2.255	0.105	2.031	1.16 (0.83, 1.61)
Nonanoic acid	Fatty acids	0.783	2.668	0.768	2.774	1.02 (0.67, 1.55)
Octanoic acid	Fatty acids	25.127	1.415	24.051	1.339	1.04 (0.84, 1.29)
Oleic acid	Fatty acids	58.751	2.036	60.075	1.921	0.98 (0.72, 1.33)
Palmitic acid	Fatty acids	536.736	1.265	543.352	1.24	0.99 (0.81, 1.20)
Palmitoleic acid	Fatty acids	5.638	2.589	4.734	2.46	1.19 (0.81, 1.76)
Pentadecanoic acid	Fatty acids	0.299	1.659	0.295	1.54	1.01 (0.79, 1.30)
Ricinoleic acid	Fatty acids	0.085	1.685	0.082	1.746	1.04 (0.80, 1.35)
Undecylenic acid	Fatty acids	0.55	2.698	0.52	2.449	1.06 (0.71, 1.57)
alpha-Linolenic acid	Fatty acids	6.661	2.47	7.308	2.308	0.91 (0.63, 1.32)
gamma-Linolenic acid	Fatty acids	0.255	2.446	0.309	2.099	0.83 (0.58, 1.17)
3-Indolepropionic acid	Indoles	0.481	3.884	0.412	4.836	1.17 (0.59, 2.30)
Indoleacetic acid	Indoles	1.817	2.194	1.88	2.123	0.97 (0.69, 1.35)
AMP	Nucleotides	241.836	3.423	362.214	2.942	0.67 (0.41, 1.09)
2-Furoic acid	Organic acids	0.83	2.058	0.677	1.884	1.23 (0.90, 1.66)
2-Hydroxybutyric acid	Organic acids	37.953	1.72	37.491	1.632	1.01 (0.78, 1.31)
3-Hydroxybutyric acid	Organic acids	86.997	2.265	95.243	2.145	0.91 (0.65, 1.28)
3-Methyl-2-oxovaleric acid	Organic acids	36.443	1.354	38.324	1.325	0.95 (0.77, 1.17)
Aconitic acid	Organic acids	204.07	1.301	177.99	1.275	1.15 (0.94, 1.40)
Adipic acid	Organic acids	0.792	2.25	0.808	2.081	0.98 (0.70, 1.37)
Azelaic acid	Organic acids	0.332	1.669	0.334	1.662	0.99 (0.77, 1.28)
Benzoic acid	Organic acids	10.917	1.157	10.517	1.106	1.04 (0.87, 1.24)
Citramalic acid	Organic acids	0.504	1.694	0.465	1.737	1.08 (0.83, 1.41)

Metabolites	Classes	Cases		Controls		Ratio of Geometric means (95% CI)
		Geometric mean	Geometric SD	Geometric mean	Geometric SD	
Citric acid	Organic acids	174.09	1.276	148.801	1.239	1.17 (0.96, 1.42)
Erythronic acid	Organic acids	2.821	1.689	2.967	1.572	0.95 (0.74, 1.22)
Fumaric acid	Organic acids	0.144	2.038	0.14	1.961	1.03 (0.75, 1.40)
Glutaric acid	Organic acids	0.506	6.374	0.289	6.331	1.75 (0.66, 4.67)
Glycolic acid	Organic acids	11.291	1.34	9.964	1.278	1.13 (0.93, 1.39)
Guanidoacetic acid	Organic acids	5.402	1.394	5.068	1.292	1.07 (0.87, 1.31)
Isocitric acid	Organic acids	7.224	1.418	5.683	1.372	1.27 (1.02, 1.58)
Ketoleucine	Organic acids	68.527	1.386	73.339	1.337	0.93 (0.76, 1.15)
Lactic acid	Organic acids	2922.131	1.332	3093.084	1.33	0.94 (0.77, 1.16)
Maleic acid	Organic acids	1.201	1.847	1.2	1.679	1.00 (0.76, 1.31)
Malic acid	Organic acids	5.227	1.517	4.632	1.603	1.13 (0.89, 1.44)
Malonic acid	Organic acids	1.015	2.243	1.05	2.265	0.97 (0.68, 1.37)
Methylsuccinic acid	Organic acids	0.902	3.282	0.526	4.38	1.71 (0.94, 3.12)
Oxalic acid	Organic acids	76.363	1.706	79.74	1.644	0.96 (0.74, 1.24)
Oxoadipic acid	Organic acids	0.195	1.811	0.168	1.813	1.16 (0.88, 1.54)
Oxoglutaric acid	Organic acids	15.592	1.864	13.697	1.472	1.14 (0.88, 1.48)
Petroselinic acid	Organic acids	1.074	1.943	1.086	1.844	0.99 (0.74, 1.32)
Pimelic acid	Organic acids	0.593	2.728	0.654	2.734	0.91 (0.60, 1.38)
Pyruvic acid	Organic acids	940.278	2.01	1047.463	1.663	0.90 (0.68, 1.19)
Succinic acid	Organic acids	6.467	1.528	6.034	1.456	1.07 (0.85, 1.35)
alpha-Hydroxyisobutyric acid	Organic acids	1.224	2.328	1.288	1.985	0.95 (0.68, 1.33)
alpha-Ketoisovaleric acid	Organic acids	11.345	1.606	12.279	1.252	0.92 (0.74, 1.15)
4-Hydroxyphenylpyruvic acid	Phenols	0.744	2.118	0.664	2.276	1.12 (0.80, 1.57)
Homovanillic acid	Phenols	1.738	1.55	1.26	1.367	1.38 (1.10, 1.73)
p-Hydroxyphenylacetic acid	Phenols	0.847	3.382	0.907	3.21	0.93 (0.56, 1.55)
2-Phenylpropionate	Phenylpropanoic acids	0.145	2.952	0.109	3.051	1.34 (0.84, 2.13)
3-Hydroxyphenylhydracrylic acid	Phenylpropanoic acids	0.368	2.611	0.392	2.904	0.94 (0.61, 1.44)
Hydrocinnamic acid	Phenylpropanoic acids	0.504	2.704	0.39	3.01	1.29 (0.83, 2.01)
Hydroxyphenyllactic acid	Phenylpropanoic acids	1.719	1.686	1.238	1.483	1.39 (1.09, 1.77)

Metabolites	Classes	Cases		Controls		Ratio of Geometric means (95% CI)
		Geometric mean	Geometric SD	Geometric mean	Geometric SD	
Phenyllactic acid	Phenylpropanoic acids	0.409	1.894	0.329	1.68	1.24 (0.94, 1.64)
N-Methylnicotinamide	Pyridines	6.755	2.255	5.027	2.426	1.34 (0.94, 1.93)
3-Hydroxyisovaleric acid	SCFAs	0.828	1.574	0.847	1.357	0.98 (0.78, 1.23)
Acetic acid	SCFAs	34.282	1.858	34.948	1.997	0.98 (0.73, 1.32)
Butyric acid	SCFAs	1.411	1.541	1.255	1.556	1.12 (0.89, 1.43)
Caproic acid	SCFAs	1.581	1.406	1.5	1.355	1.05 (0.85, 1.30)
Ethylmethylacetic acid	SCFAs	0.48	1.543	0.439	1.57	1.09 (0.86, 1.39)
Formic acid	SCFAs	46.623	1.489	42.475	1.499	1.10 (0.87, 1.38)
Isobutyric acid	SCFAs	1.611	1.474	1.52	1.355	1.06 (0.85, 1.32)
Isocaproic acid	SCFAs	1.294	1.494	1.326	1.545	0.98 (0.77, 1.23)
Isovaleric acid	SCFAs	0.483	2.118	0.444	1.703	1.09 (0.81, 1.47)
Pentanoic acid	SCFAs	0.502	1.671	0.474	1.788	1.06 (0.81, 1.38)
Propanoic acid	SCFAs	4.94	1.291	4.552	1.26	1.09 (0.89, 1.32)

Supplementary Table ST3 Association between all quantitated metabolites and liver cancer risk (Model 1)^a

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	<i>P</i> _{non-linear} ^b	FDR _{non-linear} ^b	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^c	S value
2-Hydroxyglutaric acid	Amino acids	Ref.	1.16 (0.74, 1.80)	1.03 (0.64, 1.67)	1.37 (0.88, 2.14)	3.7E-01	5.2E-01	1.28 (1.06, 1.55)	1.2E-02	2.6E-02	1.0E+00	6.43
2-Phenylglycine	Amino acids	Ref.	0.63 (0.39, 1.02)	0.65 (0.41, 1.04)	0.63 (0.40, 0.99)	5.2E-02	2.0E-01	0.85 (0.67, 1.09)	2.0E-01	2.8E-01	1.0E+00	2.31
5-Aminolevulinic acid	Amino acids	Ref.	0.65 (0.42, 1.00)	0.84 (0.54, 1.31)	0.56 (0.34, 0.93)	1.9E-01	4.1E-01	0.77 (0.58, 1.02)	6.4E-02	1.1E-01	1.0E+00	3.97
Alanine	Amino acids	Ref.	0.93 (0.59, 1.45)	0.77 (0.49, 1.20)	0.80 (0.51, 1.27)	9.5E-01	9.8E-01	0.70 (0.42, 1.17)	1.7E-01	2.5E-01	1.0E+00	2.55
alpha-Aminobutyric acid	Amino acids	Ref.	0.94 (0.61, 1.43)	0.56 (0.36, 0.87)	0.76 (0.49, 1.18)	3.4E-02	1.7E-01	0.76 (0.52, 1.11)	1.6E-01	2.3E-01	1.0E+00	2.69
Arginine	Amino acids	Ref.	1.66 (1.02, 2.69)	1.86 (1.12, 3.09)	1.79 (1.05, 3.07)	2.6E-01	4.8E-01	1.45 (1.00, 2.12)	5.2E-02	9.4E-02	1.0E+00	4.27
Asparagine	Amino acids	Ref.	0.98 (0.60, 1.62)	1.27 (0.79, 2.04)	2.05 (1.27, 3.31)	8.7E-03	8.1E-02	2.42 (1.51, 3.89)	2.6E-04	1.2E-03	4.8E-02	11.92
Aspartic acid	Amino acids	Ref.	0.83 (0.52, 1.31)	0.88 (0.55, 1.39)	0.94 (0.57, 1.54)	2.5E-01	4.8E-01	1.16 (0.83, 1.64)	3.8E-01	4.9E-01	1.0E+00	1.40
beta-Alanine	Amino acids	Ref.	0.79 (0.49, 1.25)	1.11 (0.72, 1.72)	0.88 (0.55, 1.39)	1.1E-01	3.3E-01	0.97 (0.85, 1.10)	6.1E-01	7.0E-01	1.0E+00	0.71
Citrulline	Amino acids	Ref.	1.25 (0.74, 2.12)	2.71 (1.65, 4.45)	3.12 (1.86, 5.22)	9.6E-01	9.8E-01	2.62 (1.76, 3.92)	2.4E-06	1.8E-05	4.5E-04	18.67
Creatine	Amino acids	Ref.	0.42 (0.26, 0.65)	0.27 (0.17, 0.44)	0.23 (0.14, 0.38)	7.2E-03	7.9E-02	0.41 (0.31, 0.54)	2.4E-10	3.4E-09	4.4E-08	31.96
Dimethylglycine	Amino acids	Ref.	1.71 (0.99, 2.96)	1.81 (1.05, 3.10)	4.57 (2.74, 7.64)	2.9E-01	4.8E-01	3.38 (2.25, 5.07)	4.2E-09	4.9E-08	7.9E-07	27.82
GABA	Amino acids	Ref.	0.68 (0.42, 1.10)	0.85 (0.52, 1.39)	1.57 (1.00, 2.45)	6.7E-01	7.7E-01	1.43 (1.02, 2.01)	3.8E-02	7.5E-02	1.0E+00	4.73
Glutamic acid	Amino acids	Ref.	1.03 (0.65, 1.61)	0.76 (0.47, 1.24)	0.91 (0.57, 1.45)	7.3E-03	7.9E-02	1.10 (0.79, 1.51)	5.7E-01	6.7E-01	1.0E+00	0.80
Glutamine	Amino acids	Ref.	0.47 (0.29, 0.75)	0.71 (0.45, 1.11)	1.02 (0.66, 1.56)	1.7E-06	1.1E-04	0.71 (0.49, 1.05)	8.4E-02	1.4E-01	1.0E+00	3.58
Glycine	Amino acids	Ref.	0.86 (0.55, 1.33)	0.98 (0.63, 1.53)	1.17 (0.77, 1.80)	9.5E-01	9.8E-01	1.10 (0.72, 1.70)	6.5E-01	7.4E-01	1.0E+00	0.62
Hippuric acid	Amino acids	Ref.	1.30 (0.84, 2.02)	0.84 (0.53, 1.33)	1.03 (0.64, 1.64)	3.0E-01	4.8E-01	0.99 (0.90, 1.10)	9.1E-01	9.2E-01	1.0E+00	0.14
Histidine	Amino acids	Ref.	1.43 (0.89, 2.30)	1.52 (0.94, 2.44)	1.90 (1.22, 2.96)	9.4E-01	9.8E-01	3.06 (1.61, 5.80)	6.3E-04	2.6E-03	1.2E-01	10.62
Homoserine	Amino acids	Ref.	1.24 (0.78, 1.96)	1.75 (1.10, 2.79)	2.37 (1.46, 3.87)	8.6E-02	2.7E-01	2.52 (1.67, 3.80)	1.1E-05	6.5E-05	2.0E-03	16.54
Isoleucine	Amino acids	Ref.	0.69 (0.44, 1.08)	0.83 (0.53, 1.30)	0.48 (0.29, 0.78)	7.6E-01	8.2E-01	0.67 (0.47, 0.94)	2.0E-02	4.3E-02	1.0E+00	5.63
Leucine	Amino acids	Ref.	0.64 (0.41, 1.00)	0.62 (0.39, 0.97)	0.51 (0.32, 0.81)	2.6E-01	4.8E-01	0.53 (0.35, 0.79)	1.7E-03	5.5E-03	3.2E-01	9.18
Lysine	Amino acids	Ref.	1.05 (0.69, 1.61)	0.47 (0.29, 0.76)	0.56 (0.35, 0.90)	6.8E-01	7.8E-01	0.41 (0.24, 0.68)	6.1E-04	2.6E-03	1.1E-01	10.68
Methionine	Amino acids	Ref.	1.20 (0.69, 2.07)	1.77 (1.05, 2.98)	3.57 (2.17, 5.85)	2.8E-01	4.8E-01	3.83 (2.50, 5.85)	5.5E-10	7.3E-09	1.0E-07	30.76
Methylcysteine	Amino acids	Ref.	0.92 (0.58, 1.44)	0.77 (0.48, 1.24)	0.81 (0.50, 1.32)	3.9E-01	5.4E-01	0.84 (0.64, 1.10)	2.0E-01	2.8E-01	1.0E+00	2.34
N-Acetylglycine	Amino acids	Ref.	0.50 (0.32, 0.79)	0.51 (0.33, 0.78)	0.48 (0.31, 0.73)	1.5E-01	3.6E-01	0.45 (0.28, 0.72)	8.2E-04	3.1E-03	1.5E-01	10.24
N-Acetylserine	Amino acids	Ref.	0.84 (0.54, 1.32)	0.87 (0.54, 1.39)	1.57 (0.98, 2.53)	2.1E-01	4.4E-01	1.78 (1.00, 3.18)	5.0E-02	9.2E-02	1.0E+00	4.32
N-Phenylacetylglutamine	Amino acids	Ref.	1.13 (0.71, 1.78)	1.05 (0.67, 1.65)	1.17 (0.75, 1.84)	5.9E-01	7.1E-01	1.02 (0.90, 1.16)	7.3E-01	7.9E-01	1.0E+00	0.46
Norvaline	Amino acids	Ref.	0.78 (0.47, 1.30)	1.07 (0.63, 1.82)	1.10 (0.62, 1.98)	5.3E-01	6.5E-01	1.54 (0.22, 10.82)	6.7E-01	7.5E-01	1.0E+00	0.59

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	$P_{\text{non-linear}}^b$	FDR _{non-linear}^b}	OR _{doubling} (95% CI)	P value	FDR	P_{Bon}^c	S value
Ornithine	Amino acids	Ref.	0.93 (0.58, 1.51)	1.42 (0.88, 2.30)	1.70 (1.06, 2.73)	4.3E-01	5.7E-01	1.69 (1.17, 2.44)	5.2E-03	1.4E-02	9.7E-01	7.59
Phenylalanine	Amino acids	Ref.	1.12 (0.68, 1.85)	1.66 (1.00, 2.75)	3.27 (1.96, 5.43)	2.6E-02	1.6E-01	5.70 (2.88, 11.26)	5.5E-07	5.1E-06	1.0E-04	20.79
Pipecolic acid	Amino acids	Ref.	1.69 (1.02, 2.79)	2.72 (1.62, 4.55)	2.93 (1.76, 4.88)	4.1E-02	1.9E-01	1.67 (1.25, 2.23)	5.5E-04	2.5E-03	1.0E-01	10.82
Proline	Amino acids	Ref.	1.37 (0.88, 2.14)	1.68 (1.05, 2.69)	1.30 (0.81, 2.09)	1.4E-03	2.7E-02	1.18 (0.81, 1.73)	3.8E-01	4.9E-01	1.0E+00	1.38
Pyroglutamic acid	Amino acids	Ref.	1.23 (0.81, 1.88)	0.65 (0.40, 1.06)	1.21 (0.76, 1.91)	2.6E-02	1.6E-01	1.26 (0.93, 1.72)	1.4E-01	2.1E-01	1.0E+00	2.84
Sarcosine	Amino acids	Ref.	0.75 (0.47, 1.20)	0.95 (0.61, 1.46)	1.44 (0.91, 2.27)	7.6E-03	7.9E-02	1.37 (0.90, 2.08)	1.5E-01	2.2E-01	1.0E+00	2.78
Selenomethionine	Amino acids	Ref.	1.13 (0.61, 2.12)	1.00 (0.51, 1.96)	1.33 (0.72, 2.44)	3.2E-01	5.0E-01	1.21 (0.76, 1.93)	4.1E-01	5.2E-01	1.0E+00	1.27
Serine	Amino acids	Ref.	0.92 (0.57, 1.48)	1.30 (0.81, 2.11)	2.21 (1.43, 3.42)	8.5E-03	8.1E-02	2.56 (1.63, 4.01)	4.5E-05	2.6E-04	8.4E-03	14.44
Threonine	Amino acids	Ref.	1.33 (0.82, 2.15)	1.43 (0.87, 2.35)	2.68 (1.66, 4.35)	1.5E-01	3.6E-01	3.12 (1.92, 5.07)	4.6E-06	3.2E-05	8.6E-04	17.72
Tryptophan	Amino acids	Ref.	0.84 (0.50, 1.39)	1.51 (0.93, 2.45)	1.88 (1.20, 2.96)	2.6E-01	4.8E-01	2.71 (1.57, 4.67)	3.5E-04	1.6E-03	6.5E-02	11.49
Tyrosine	Amino acids	Ref.	1.31 (0.65, 2.62)	2.54 (1.36, 4.74)	9.32 (4.98, 17.46)	6.0E-02	2.2E-01	13.42 (7.35, 24.49)	2.7E-17	1.8E-15	5.0E-15	55.04
Valine	Amino acids	Ref.	0.91 (0.60, 1.39)	0.34 (0.20, 0.56)	0.67 (0.43, 1.04)	4.3E-01	5.7E-01	0.51 (0.30, 0.86)	1.2E-02	2.8E-02	1.0E+00	6.33
ortho-Hydroxyphenylacetic acid	Benzenoids	Ref.	0.76 (0.49, 1.20)	0.59 (0.37, 0.95)	0.53 (0.32, 0.86)	5.8E-01	7.0E-01	0.74 (0.55, 0.98)	3.7E-02	7.4E-02	1.0E+00	4.77
Phenylacetic acid	Benzenoids	Ref.	1.86 (1.10, 3.16)	2.73 (1.67, 4.48)	2.91 (1.74, 4.89)	4.1E-01	5.6E-01	1.30 (1.14, 1.49)	6.9E-05	3.9E-04	1.3E-02	13.81
Phenylpyruvic acid	Benzenoids	Ref.	1.18 (0.75, 1.85)	1.25 (0.75, 2.07)	1.83 (1.13, 2.95)	1.6E-04	4.3E-03	1.29 (1.06, 1.58)	1.2E-02	2.6E-02	1.0E+00	6.42
4-Hydroxybenzoic acid	Benzoic acids	Ref.	0.56 (0.35, 0.91)	0.58 (0.36, 0.94)	1.17 (0.76, 1.80)	1.5E-01	3.6E-01	1.52 (0.94, 2.44)	8.5E-02	1.4E-01	1.0E+00	3.55
m-Aminobenzoic acid	Benzoic acids	Ref.	1.09 (0.70, 1.69)	0.77 (0.47, 1.26)	0.84 (0.53, 1.33)	4.4E-01	5.8E-01	0.90 (0.73, 1.11)	3.3E-01	4.5E-01	1.0E+00	1.60
m-Hydroxyhippuric acid	Benzoic acids	Ref.	0.86 (0.48, 1.52)	0.73 (0.44, 1.23)	0.97 (0.59, 1.58)	9.9E-01	9.9E-01	0.95 (0.68, 1.31)	7.3E-01	7.9E-01	1.0E+00	0.45
Phthalic acid	Benzoic acids	Ref.	0.84 (0.52, 1.35)	0.75 (0.46, 1.22)	0.66 (0.40, 1.08)	4.8E-01	6.2E-01	0.77 (0.56, 1.07)	1.2E-01	1.9E-01	1.0E+00	3.09
7-DHCA	Bile acids	Ref.	1.22 (0.65, 2.32)	1.67 (0.86, 3.26)	1.84 (1.02, 3.32)	3.1E-01	5.0E-01	1.19 (0.97, 1.46)	1.0E-01	1.7E-01	1.0E+00	3.25
apoCA	Bile acids	Ref.	0.70 (0.42, 1.15)	0.91 (0.55, 1.49)	0.72 (0.43, 1.19)	9.9E-01	9.9E-01	0.73 (0.48, 1.10)	1.3E-01	2.0E-01	1.0E+00	2.96
beta-HDCA	Bile acids	Ref.	0.98 (0.61, 1.57)	0.97 (0.60, 1.57)	1.21 (0.76, 1.91)	1.8E-01	4.0E-01	1.01 (0.92, 1.12)	7.8E-01	8.2E-01	1.0E+00	0.36
CA	Bile acids	Ref.	2.24 (1.30, 3.87)	2.99 (1.68, 5.33)	2.76 (1.58, 4.82)	4.6E-02	2.0E-01	1.21 (1.08, 1.35)	7.6E-04	2.9E-03	1.4E-01	10.36
CDCA	Bile acids	Ref.	1.30 (0.82, 2.07)	1.47 (0.92, 2.35)	1.91 (1.18, 3.09)	1.1E-01	3.1E-01	1.14 (1.03, 1.25)	8.0E-03	2.0E-02	1.0E+00	6.97
DCA	Bile acids	Ref.	0.86 (0.56, 1.33)	0.95 (0.62, 1.47)	0.80 (0.51, 1.25)	5.0E-01	6.4E-01	0.95 (0.84, 1.07)	4.0E-01	5.0E-01	1.0E+00	1.33
GCA	Bile acids	Ref.	2.48 (1.21, 5.10)	4.11 (1.95, 8.64)	13.00 (6.39, 26.45)	8.0E-01	8.5E-01	1.86 (1.61, 2.15)	3.9E-17	1.8E-15	7.2E-15	54.52
GCDCA	Bile acids	Ref.	1.98 (0.93, 4.23)	5.16 (2.53, 10.53)	13.16 (6.50, 26.65)	4.4E-01	5.8E-01	2.15 (1.80, 2.56)	3.2E-17	1.8E-15	6.0E-15	54.79
GDCA	Bile acids	Ref.	0.75 (0.45, 1.23)	1.12 (0.69, 1.82)	2.46 (1.55, 3.92)	1.8E-06	1.1E-04	1.11 (1.05, 1.19)	9.4E-04	3.4E-03	1.7E-01	10.06
GHCA	Bile acids	Ref.	1.54 (0.79, 3.00)	3.23 (1.56, 6.68)	5.82 (3.01, 11.24)	5.1E-01	6.4E-01	2.52 (1.92, 3.31)	2.9E-11	4.5E-10	5.4E-09	35.01

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	$P_{\text{non-linear}}^b$	FDR _{non-linear}^b}	OR _{doubling} (95% CI)	P value	FDR	P_{Bon}^c	S value
GLCA	Bile acids	Ref.	1.09 (0.68, 1.76)	1.42 (0.85, 2.37)	1.53 (0.95, 2.47)	1.7E-01	3.9E-01	1.39 (1.12, 1.72)	2.4E-03	7.4E-03	4.5E-01	8.70
GLCA-3S	Bile acids	Ref.	1.14 (0.71, 1.82)	1.28 (0.79, 2.06)	1.93 (1.22, 3.08)	1.4E-01	3.6E-01	1.19 (1.07, 1.31)	1.3E-03	4.3E-03	2.4E-01	9.61
GUDCA	Bile acids	Ref.	1.35 (0.83, 2.22)	1.41 (0.85, 2.32)	2.57 (1.61, 4.11)	5.3E-02	2.0E-01	1.31 (1.18, 1.47)	1.3E-06	1.0E-05	2.5E-04	19.50
HCA	Bile acids	Ref.	1.78 (0.97, 3.25)	1.87 (0.98, 3.57)	3.64 (2.02, 6.54)	4.8E-01	6.2E-01	3.02 (1.96, 4.64)	4.9E-07	4.8E-06	9.2E-05	20.95
HDCA	Bile acids	Ref.	1.00 (0.64, 1.56)	0.82 (0.49, 1.37)	0.80 (0.50, 1.28)	4.3E-03	6.1E-02	0.94 (0.82, 1.07)	3.4E-01	4.5E-01	1.0E+00	1.56
LCA	Bile acids	Ref.	1.09 (0.64, 1.84)	0.92 (0.50, 1.68)	2.17 (1.34, 3.54)	9.1E-05	2.8E-03	1.44 (1.17, 1.78)	5.8E-04	2.5E-03	1.1E-01	10.75
TCA	Bile acids	Ref.	2.59 (1.14, 5.92)	3.56 (1.59, 7.98)	19.83 (8.96, 43.88)	2.9E-01	4.8E-01	1.92 (1.64, 2.24)	2.6E-16	9.8E-15	4.9E-14	51.75
TCDCa	Bile acids	Ref.	2.58 (1.07, 6.20)	3.79 (1.66, 8.62)	23.38 (10.22, 53.49)	3.8E-01	5.4E-01	2.20 (1.84, 2.63)	5.7E-18	1.1E-15	1.1E-15	57.27
TDCA	Bile acids	Ref.	1.63 (0.91, 2.93)	1.67 (0.91, 3.04)	6.11 (3.49, 10.68)	1.7E-01	3.9E-01	1.71 (1.48, 1.98)	5.1E-13	9.5E-12	9.5E-11	40.84
UCA	Bile acids	Ref.	1.38 (0.71, 2.68)	1.54 (0.74, 3.22)	1.59 (0.80, 3.13)	1.7E-01	3.9E-01	1.36 (0.92, 1.99)	1.2E-01	1.9E-01	1.0E+00	3.06
D-Xylulose	Carbohydrates	Ref.	1.50 (0.89, 2.55)	1.78 (1.06, 2.98)	3.63 (2.12, 6.21)	6.0E-01	7.1E-01	3.69 (2.31, 5.91)	5.3E-08	5.8E-07	9.9E-06	24.16
Fructose	Carbohydrates	Ref.	1.15 (0.71, 1.87)	1.34 (0.81, 2.23)	1.87 (1.15, 3.06)	1.5E-01	3.6E-01	1.30 (1.12, 1.51)	5.1E-04	2.3E-03	9.4E-02	10.95
Galactonic acid	Carbohydrates	Ref.	0.83 (0.50, 1.36)	0.88 (0.55, 1.38)	0.90 (0.57, 1.43)	2.0E-01	4.2E-01	1.15 (0.91, 1.46)	2.5E-01	3.5E-01	1.0E+00	1.99
Gluconolactone	Carbohydrates	Ref.	0.60 (0.38, 0.93)	0.69 (0.44, 1.09)	0.94 (0.59, 1.50)	2.8E-02	1.6E-01	1.03 (0.74, 1.43)	8.6E-01	8.8E-01	1.0E+00	0.21
Glucose	Carbohydrates	Ref.	0.75 (0.45, 1.24)	0.97 (0.60, 1.56)	1.70 (1.11, 2.61)	7.4E-01	8.1E-01	1.68 (1.21, 2.34)	1.9E-03	6.1E-03	3.6E-01	9.00
Glutaconic acid	Carbohydrates	Ref.	1.01 (0.61, 1.65)	1.01 (0.61, 1.68)	0.85 (0.52, 1.41)	2.6E-01	4.8E-01	0.97 (0.72, 1.30)	8.2E-01	8.5E-01	1.0E+00	0.28
Glyceric acid	Carbohydrates	Ref.	0.84 (0.54, 1.31)	1.00 (0.64, 1.56)	1.03 (0.66, 1.63)	2.2E-01	4.5E-01	1.05 (0.83, 1.33)	7.0E-01	7.7E-01	1.0E+00	0.52
Maltose/Lactose	Carbohydrates	Ref.	0.56 (0.35, 0.91)	0.71 (0.45, 1.13)	0.48 (0.29, 0.79)	4.4E-01	5.8E-01	0.78 (0.64, 0.94)	7.9E-03	2.0E-02	1.0E+00	6.99
N-Acetylneuraminic acid	Carbohydrates	Ref.	0.64 (0.40, 1.03)	0.51 (0.32, 0.82)	0.43 (0.27, 0.70)	2.8E-03	4.3E-02	0.46 (0.29, 0.75)	1.5E-03	5.1E-03	2.9E-01	9.34
Rhamnose	Carbohydrates	Ref.	1.11 (0.63, 1.98)	1.98 (1.11, 3.53)	5.09 (2.91, 8.89)	3.0E-01	4.8E-01	2.05 (1.63, 2.58)	8.5E-10	1.1E-08	1.6E-07	30.13
Tartaric acid	Carbohydrates	Ref.	0.81 (0.46, 1.42)	1.06 (0.60, 1.87)	0.98 (0.57, 1.70)	3.3E-01	5.0E-01	0.93 (0.78, 1.13)	4.7E-01	5.7E-01	1.0E+00	1.08
Threonic acid	Carbohydrates	Ref.	0.69 (0.45, 1.06)	0.49 (0.31, 0.79)	0.89 (0.58, 1.37)	6.2E-02	2.2E-01	0.87 (0.74, 1.04)	1.3E-01	2.0E-01	1.0E+00	2.98
Trehalose	Carbohydrates	Ref.	0.68 (0.42, 1.08)	0.52 (0.31, 0.87)	0.41 (0.23, 0.74)	7.0E-01	7.8E-01	0.04 (0.01, 0.25)	6.7E-04	2.6E-03	1.2E-01	10.55
Xylose	Carbohydrates	Ref.	1.51 (0.93, 2.45)	1.91 (1.15, 3.17)	1.69 (1.03, 2.78)	2.9E-02	1.6E-01	1.32 (1.02, 1.69)	3.2E-02	6.7E-02	1.0E+00	4.96
2-Methylbutyrylcarnitine	Carnitines	Ref.	1.04 (0.67, 1.62)	0.71 (0.45, 1.13)	1.02 (0.67, 1.56)	2.7E-01	4.8E-01	0.96 (0.74, 1.24)	7.6E-01	8.1E-01	1.0E+00	0.40
3-Hydroxyisovalerylcarnitine	Carnitines	Ref.	0.94 (0.57, 1.56)	0.44 (0.25, 0.77)	0.60 (0.37, 1.00)	2.8E-01	4.8E-01	0.54 (0.35, 0.83)	4.6E-03	1.4E-02	8.6E-01	7.75
Acetylcarnitine	Carnitines	Ref.	0.82 (0.52, 1.30)	0.99 (0.63, 1.56)	1.26 (0.82, 1.93)	1.8E-02	1.5E-01	1.35 (1.00, 1.82)	5.0E-02	9.2E-02	1.0E+00	4.34
Adipoylcarnitine	Carnitines	Ref.	0.93 (0.56, 1.55)	1.32 (0.79, 2.23)	1.19 (0.76, 1.88)	1.3E-01	3.4E-01	1.42 (1.00, 2.01)	5.3E-02	9.6E-02	1.0E+00	4.24
Carnitine	Carnitines	Ref.	1.21 (0.78, 1.87)	1.63 (1.04, 2.53)	1.34 (0.85, 2.10)	5.7E-01	6.9E-01	1.64 (0.96, 2.79)	7.2E-02	1.2E-01	1.0E+00	3.80

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	$P_{\text{non-linear}}^b$	FDR _{non-linear}^b}	OR _{doubling} (95% CI)	P value	FDR	P_{Bon}^c	S value
Decanoylcarnitine	Carnitines	Ref.	0.67 (0.42, 1.06)	0.78 (0.49, 1.23)	1.32 (0.83, 2.12)	6.3E-02	2.2E-01	1.07 (0.88, 1.31)	4.8E-01	5.8E-01	1.0E+00	1.05
Glutaryl carnitine	Carnitines	Ref.	1.31 (0.84, 2.04)	1.43 (0.90, 2.28)	1.99 (1.26, 3.13)	6.9E-01	7.8E-01	2.03 (1.23, 3.37)	5.8E-03	1.6E-02	1.0E+00	7.42
Hexanoylcarnitine	Carnitines	Ref.	0.91 (0.55, 1.50)	1.02 (0.62, 1.67)	1.41 (0.88, 2.27)	4.9E-02	2.0E-01	1.01 (0.86, 1.17)	9.4E-01	9.4E-01	1.0E+00	0.09
Isovalerylcarnitine	Carnitines	Ref.	0.94 (0.60, 1.47)	0.88 (0.56, 1.39)	0.55 (0.34, 0.88)	9.9E-01	9.9E-01	0.80 (0.62, 1.03)	8.4E-02	1.4E-01	1.0E+00	3.57
Lauroyl carnitine	Carnitines	Ref.	1.01 (0.62, 1.64)	1.23 (0.75, 2.02)	1.83 (1.10, 3.04)	7.3E-02	2.4E-01	1.19 (1.01, 1.41)	3.9E-02	7.6E-02	1.0E+00	4.69
Linoleyl carnitine	Carnitines	Ref.	1.03 (0.66, 1.60)	0.93 (0.59, 1.48)	1.19 (0.74, 1.92)	2.6E-01	4.8E-01	1.15 (0.87, 1.50)	3.2E-01	4.4E-01	1.0E+00	1.63
Malonylcarnitine	Carnitines	Ref.	0.70 (0.42, 1.15)	0.69 (0.42, 1.11)	0.97 (0.62, 1.51)	2.0E-01	4.2E-01	0.96 (0.84, 1.09)	5.5E-01	6.5E-01	1.0E+00	0.86
Myristoylcarnitine	Carnitines	Ref.	0.72 (0.42, 1.25)	1.76 (0.99, 3.11)	2.57 (1.55, 4.26)	4.8E-02	2.0E-01	2.30 (1.52, 3.48)	8.2E-05	4.5E-04	1.5E-02	13.57
Octanoylcarnitine	Carnitines	Ref.	0.69 (0.44, 1.08)	0.94 (0.61, 1.45)	1.23 (0.78, 1.93)	8.2E-02	2.6E-01	1.09 (0.90, 1.33)	3.7E-01	4.9E-01	1.0E+00	1.42
Oleylcarnitine	Carnitines	Ref.	0.81 (0.50, 1.31)	1.17 (0.73, 1.89)	1.71 (1.08, 2.71)	2.8E-02	1.6E-01	1.47 (1.11, 1.95)	6.5E-03	1.7E-02	1.0E+00	7.26
Palmitoylcarnitine	Carnitines	Ref.	0.87 (0.54, 1.39)	0.90 (0.57, 1.43)	1.88 (1.19, 2.98)	2.1E-02	1.6E-01	1.37 (1.02, 1.85)	3.9E-02	7.6E-02	1.0E+00	4.68
Propionyl carnitine	Carnitines	Ref.	1.14 (0.74, 1.76)	0.98 (0.63, 1.52)	1.28 (0.80, 2.02)	2.9E-01	4.8E-01	1.12 (0.78, 1.60)	5.3E-01	6.3E-01	1.0E+00	0.91
Stearyl carnitine	Carnitines	Ref.	0.91 (0.57, 1.46)	1.07 (0.68, 1.69)	1.66 (1.05, 2.62)	7.1E-01	7.9E-01	1.32 (1.07, 1.63)	1.0E-02	2.5E-02	1.0E+00	6.59
10Z-Heptadecenoic acid	Fatty acids	Ref.	1.18 (0.74, 1.87)	1.13 (0.71, 1.79)	1.53 (0.96, 2.44)	2.6E-01	4.8E-01	1.15 (1.01, 1.31)	3.6E-02	7.4E-02	1.0E+00	4.79
12-Hydroxystearic acid	Fatty acids	Ref.	0.74 (0.47, 1.18)	0.59 (0.35, 0.99)	0.52 (0.30, 0.90)	6.3E-01	7.4E-01	0.53 (0.32, 0.87)	1.2E-02	2.6E-02	1.0E+00	6.42
2-Hydroxy-3-methylbutyric acid	Fatty acids	Ref.	1.28 (0.81, 2.01)	1.18 (0.74, 1.87)	1.55 (0.98, 2.45)	2.2E-01	4.5E-01	1.34 (1.11, 1.61)	2.1E-03	6.5E-03	3.9E-01	8.91
2,2-Dimethyladipic acid	Fatty acids	Ref.	1.06 (0.68, 1.64)	0.58 (0.34, 0.99)	0.90 (0.53, 1.53)	6.3E-01	7.4E-01	0.97 (0.89, 1.06)	5.1E-01	6.1E-01	1.0E+00	0.96
3-Methyladipic acid	Fatty acids	Ref.	1.12 (0.71, 1.76)	0.90 (0.55, 1.46)	0.72 (0.45, 1.16)	1.3E-02	1.2E-01	0.95 (0.85, 1.06)	3.7E-01	4.9E-01	1.0E+00	1.45
5-Dodecenoic acid	Fatty acids	Ref.	0.77 (0.47, 1.28)	1.12 (0.68, 1.85)	1.70 (1.05, 2.74)	4.8E-02	2.0E-01	1.26 (1.05, 1.51)	1.3E-02	2.9E-02	1.0E+00	6.24
8,11,14-Eicosatrienoic acid	Fatty acids	Ref.	0.62 (0.40, 0.95)	0.77 (0.50, 1.17)	0.71 (0.46, 1.11)	2.3E-02	1.6E-01	0.89 (0.76, 1.05)	1.7E-01	2.6E-01	1.0E+00	2.52
Adrenic acid	Fatty acids	Ref.	1.23 (0.80, 1.89)	1.06 (0.65, 1.71)	1.02 (0.63, 1.65)	9.4E-01	9.8E-01	1.01 (0.85, 1.21)	8.8E-01	9.0E-01	1.0E+00	0.18
alpha-Linolenic acid	Fatty acids	Ref.	0.84 (0.55, 1.29)	0.85 (0.54, 1.34)	0.77 (0.49, 1.20)	3.6E-01	5.2E-01	0.91 (0.80, 1.04)	1.6E-01	2.4E-01	1.0E+00	2.63
Arachidonic acid	Fatty acids	Ref.	0.45 (0.29, 0.70)	0.39 (0.24, 0.63)	0.37 (0.23, 0.60)	1.3E-03	2.7E-02	0.49 (0.37, 0.65)	6.0E-07	5.3E-06	1.1E-04	20.67
Decanoic acid	Fatty acids	Ref.	0.98 (0.59, 1.64)	1.70 (1.02, 2.83)	2.05 (1.26, 3.33)	6.9E-01	7.8E-01	1.30 (1.12, 1.51)	6.2E-04	2.6E-03	1.2E-01	10.65
DHA	Fatty acids	Ref.	0.78 (0.50, 1.21)	0.72 (0.45, 1.14)	0.69 (0.42, 1.12)	4.1E-02	1.9E-01	0.79 (0.66, 0.96)	1.6E-02	3.4E-02	1.0E+00	5.98
Dodecanoic acid	Fatty acids	Ref.	1.04 (0.66, 1.63)	1.27 (0.80, 2.00)	1.16 (0.73, 1.86)	5.3E-01	6.5E-01	1.01 (0.91, 1.12)	8.2E-01	8.5E-01	1.0E+00	0.28
DPAn-3	Fatty acids	Ref.	0.79 (0.50, 1.25)	0.71 (0.44, 1.13)	0.71 (0.44, 1.15)	4.8E-03	6.4E-02	0.83 (0.70, 0.99)	4.3E-02	8.3E-02	1.0E+00	4.53
DPAn-6	Fatty acids	Ref.	1.24 (0.79, 1.94)	0.95 (0.59, 1.53)	0.90 (0.57, 1.40)	2.3E-01	4.5E-01	0.88 (0.75, 1.03)	1.2E-01	1.9E-01	1.0E+00	3.03
EPA	Fatty acids	Ref.	0.68 (0.43, 1.07)	0.57 (0.35, 0.94)	0.43 (0.26, 0.71)	7.8E-01	8.3E-01	0.75 (0.63, 0.89)	9.4E-04	3.4E-03	1.8E-01	10.05

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	$P_{\text{non-linear}}^b$	FDR _{non-linear}^b}	OR _{doubling} (95% CI)	P value	FDR	P_{Bon}^c	S value
gamma-Linolenic acid	Fatty acids	Ref.	0.90 (0.58, 1.40)	0.75 (0.48, 1.17)	0.58 (0.36, 0.93)	1.5E-01	3.6E-01	0.81 (0.70, 0.93)	3.4E-03	1.0E-02	6.2E-01	8.22
Heptadecanoic acid	Fatty acids	Ref.	0.80 (0.50, 1.29)	0.88 (0.56, 1.38)	0.67 (0.40, 1.10)	2.9E-01	4.8E-01	0.76 (0.59, 1.00)	4.7E-02	8.8E-02	1.0E+00	4.42
Heptanoic acid	Fatty acids	Ref.	1.33 (0.85, 2.10)	1.20 (0.69, 2.10)	0.80 (0.44, 1.44)	3.2E-01	5.0E-01	0.91 (0.57, 1.44)	6.9E-01	7.6E-01	1.0E+00	0.54
Linoleic acid	Fatty acids	Ref.	0.75 (0.50, 1.14)	0.68 (0.44, 1.05)	0.71 (0.45, 1.12)	1.8E-01	4.0E-01	0.85 (0.71, 1.02)	8.8E-02	1.5E-01	1.0E+00	3.51
Methylglutaric acid	Fatty acids	Ref.	1.20 (0.69, 2.06)	1.65 (0.90, 3.02)	1.31 (0.76, 2.26)	3.9E-01	5.4E-01	1.09 (0.87, 1.37)	4.6E-01	5.6E-01	1.0E+00	1.11
Methylmalonic acid	Fatty acids	Ref.	0.88 (0.54, 1.44)	0.98 (0.59, 1.64)	1.37 (0.81, 2.32)	6.9E-03	7.9E-02	1.31 (1.01, 1.71)	4.3E-02	8.2E-02	1.0E+00	4.55
Myristelaidic acid	Fatty acids	Ref.	0.80 (0.48, 1.32)	0.94 (0.54, 1.64)	1.32 (0.79, 2.22)	6.6E-01	7.7E-01	1.10 (0.99, 1.21)	6.4E-02	1.1E-01	1.0E+00	3.98
Myristic acid	Fatty acids	Ref.	1.07 (0.68, 1.70)	1.34 (0.82, 2.19)	1.17 (0.69, 2.00)	9.7E-01	9.9E-01	1.26 (0.88, 1.80)	2.1E-01	2.9E-01	1.0E+00	2.26
Myristoleic acid	Fatty acids	Ref.	0.91 (0.57, 1.46)	1.07 (0.63, 1.81)	1.64 (1.01, 2.66)	2.7E-02	1.6E-01	1.26 (1.07, 1.49)	6.3E-03	1.6E-02	1.0E+00	7.32
Nonanoic acid	Fatty acids	Ref.	0.94 (0.58, 1.52)	0.84 (0.51, 1.37)	0.98 (0.59, 1.65)	9.5E-01	9.8E-01	1.02 (0.89, 1.16)	7.7E-01	8.1E-01	1.0E+00	0.38
Octanoic acid	Fatty acids	Ref.	0.81 (0.50, 1.29)	0.88 (0.54, 1.41)	1.14 (0.71, 1.84)	1.4E-01	3.6E-01	1.43 (0.98, 2.08)	6.1E-02	1.1E-01	1.0E+00	4.03
Oleic acid	Fatty acids	Ref.	0.98 (0.64, 1.50)	0.89 (0.59, 1.35)	0.89 (0.56, 1.41)	2.9E-01	4.8E-01	0.96 (0.82, 1.14)	6.6E-01	7.5E-01	1.0E+00	0.59
Palmitic acid	Fatty acids	Ref.	0.74 (0.47, 1.17)	0.88 (0.55, 1.43)	0.71 (0.42, 1.20)	5.2E-01	6.5E-01	0.77 (0.42, 1.40)	3.9E-01	4.9E-01	1.0E+00	1.37
Palmitoleic acid	Fatty acids	Ref.	0.80 (0.50, 1.28)	1.06 (0.68, 1.65)	1.45 (0.91, 2.30)	3.1E-01	4.9E-01	1.18 (1.04, 1.34)	1.1E-02	2.6E-02	1.0E+00	6.46
Pentadecanoic acid	Fatty acids	Ref.	0.92 (0.60, 1.40)	0.90 (0.57, 1.42)	1.01 (0.63, 1.61)	6.1E-02	2.2E-01	1.06 (0.81, 1.38)	6.8E-01	7.6E-01	1.0E+00	0.55
Ricinoleic acid	Fatty acids	Ref.	0.50 (0.30, 0.82)	0.81 (0.48, 1.38)	1.06 (0.67, 1.66)	5.3E-01	6.5E-01	1.11 (0.89, 1.38)	3.4E-01	4.5E-01	1.0E+00	1.56
Undecylenic acid	Fatty acids	Ref.	1.12 (0.70, 1.79)	1.18 (0.73, 1.91)	1.39 (0.87, 2.22)	4.2E-02	1.9E-01	1.05 (0.93, 1.20)	4.1E-01	5.2E-01	1.0E+00	1.28
3-Indolepropionic acid	Indoles	Ref.	1.03 (0.65, 1.63)	1.28 (0.83, 1.98)	1.14 (0.73, 1.78)	4.8E-01	6.2E-01	1.05 (0.98, 1.13)	1.9E-01	2.8E-01	1.0E+00	2.36
Indoleacetic acid	Indoles	Ref.	1.06 (0.69, 1.62)	0.68 (0.42, 1.10)	0.81 (0.52, 1.25)	3.4E-01	5.1E-01	0.96 (0.83, 1.11)	5.7E-01	6.7E-01	1.0E+00	0.80
AMP	Nucleotides	Ref.	0.51 (0.33, 0.79)	0.30 (0.18, 0.49)	0.25 (0.15, 0.42)	4.3E-02	1.9E-01	0.71 (0.61, 0.82)	5.4E-06	3.6E-05	1.0E-03	17.49
2-Furoic acid	Organic acids	Ref.	3.53 (1.95, 6.38)	2.83 (1.55, 5.20)	3.37 (1.89, 6.01)	2.8E-01	4.8E-01	1.44 (1.20, 1.74)	1.2E-04	6.4E-04	2.3E-02	12.98
2-Hydroxybutyric acid	Organic acids	Ref.	0.69 (0.44, 1.06)	0.88 (0.56, 1.36)	0.92 (0.60, 1.40)	1.3E-01	3.6E-01	1.03 (0.84, 1.27)	7.6E-01	8.1E-01	1.0E+00	0.39
3-Hydroxybutyric acid	Organic acids	Ref.	0.75 (0.49, 1.14)	0.48 (0.30, 0.77)	0.67 (0.42, 1.07)	4.3E-02	1.9E-01	0.89 (0.77, 1.03)	1.3E-01	2.0E-01	1.0E+00	2.98
3-Methyl-2-oxovaleric acid	Organic acids	Ref.	0.91 (0.59, 1.40)	0.49 (0.29, 0.81)	0.60 (0.38, 0.96)	3.6E-01	5.2E-01	0.63 (0.42, 0.93)	2.2E-02	4.5E-02	1.0E+00	5.54
Aconitic acid	Organic acids	Ref.	1.86 (0.99, 3.50)	4.31 (2.29, 8.10)	5.83 (3.06, 11.11)	5.7E-01	6.9E-01	9.37 (4.91, 17.88)	1.1E-11	1.9E-10	2.0E-09	36.41
Adipic acid	Organic acids	Ref.	0.84 (0.53, 1.33)	1.01 (0.64, 1.60)	0.94 (0.58, 1.55)	7.1E-01	7.9E-01	0.97 (0.84, 1.13)	7.2E-01	7.8E-01	1.0E+00	0.48
alpha-Hydroxyisobutyric acid	Organic acids	Ref.	0.67 (0.43, 1.04)	0.69 (0.44, 1.09)	1.09 (0.70, 1.69)	5.5E-02	2.1E-01	0.93 (0.80, 1.09)	3.7E-01	4.9E-01	1.0E+00	1.43
alpha-Ketoisovaleric acid	Organic acids	Ref.	1.01 (0.66, 1.55)	0.81 (0.52, 1.26)	0.79 (0.50, 1.24)	2.6E-02	1.6E-01	0.63 (0.44, 0.90)	1.1E-02	2.6E-02	1.0E+00	6.48
Azelaic acid	Organic acids	Ref.	1.08 (0.69, 1.68)	0.85 (0.52, 1.37)	0.97 (0.61, 1.55)	6.8E-01	7.8E-01	0.97 (0.78, 1.22)	8.3E-01	8.5E-01	1.0E+00	0.28

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	$P_{\text{non-linear}}^b$	FDR _{non-linear}^b}	OR _{doubling} (95% CI)	P value	FDR	P_{Bon}^c	S value
Benzoic acid	Organic acids	Ref.	1.20 (0.72, 2.02)	1.37 (0.80, 2.36)	1.94 (1.12, 3.34)	2.8E-01	4.8E-01	10.74 (3.21, 35.89)	1.2E-04	6.2E-04	2.2E-02	13.08
Citramalic acid	Organic acids	Ref.	0.98 (0.61, 1.58)	0.96 (0.61, 1.52)	1.06 (0.67, 1.67)	3.9E-01	5.4E-01	1.23 (0.99, 1.53)	5.7E-02	1.0E-01	1.0E+00	4.12
Citric acid	Organic acids	Ref.	1.78 (1.01, 3.16)	2.05 (1.12, 3.77)	8.17 (4.41, 15.13)	1.3E-01	3.5E-01	17.34 (8.36, 35.98)	1.9E-14	4.3E-13	3.4E-12	45.62
Erythronic acid	Organic acids	Ref.	0.78 (0.51, 1.20)	0.49 (0.31, 0.79)	0.89 (0.58, 1.37)	2.3E-02	1.6E-01	0.86 (0.69, 1.08)	1.9E-01	2.7E-01	1.0E+00	2.43
Fumaric acid	Organic acids	Ref.	0.98 (0.62, 1.56)	1.00 (0.62, 1.63)	1.45 (0.91, 2.30)	3.2E-02	1.7E-01	1.05 (0.88, 1.24)	6.0E-01	7.0E-01	1.0E+00	0.73
Glutaric acid	Organic acids	Ref.	1.01 (0.56, 1.80)	1.06 (0.60, 1.87)	3.31 (2.01, 5.47)	4.3E-07	8.1E-05	1.13 (1.06, 1.20)	2.4E-04	1.2E-03	4.4E-02	12.03
Glycolic acid	Organic acids	Ref.	1.50 (0.89, 2.53)	1.89 (1.11, 3.20)	3.30 (2.00, 5.46)	2.7E-01	4.8E-01	3.89 (2.38, 6.37)	6.3E-08	6.5E-07	1.2E-05	23.91
Guanidoacetic acid	Organic acids	Ref.	1.38 (0.88, 2.14)	0.82 (0.50, 1.34)	1.54 (0.98, 2.40)	1.4E-02	1.2E-01	1.76 (1.19, 2.62)	5.0E-03	1.4E-02	9.4E-01	7.63
Isocitric acid	Organic acids	Ref.	1.87 (0.98, 3.56)	3.00 (1.64, 5.47)	9.32 (4.86, 17.87)	7.5E-01	8.2E-01	6.64 (4.12, 10.68)	6.8E-15	1.8E-13	1.3E-12	47.06
Ketoleucine	Organic acids	Ref.	0.74 (0.48, 1.13)	0.49 (0.31, 0.78)	0.55 (0.35, 0.86)	1.2E-01	3.3E-01	0.58 (0.40, 0.85)	4.7E-03	1.4E-02	8.8E-01	7.72
Lactic acid	Organic acids	Ref.	0.88 (0.59, 1.33)	0.39 (0.24, 0.64)	0.53 (0.33, 0.86)	7.9E-01	8.4E-01	0.55 (0.36, 0.84)	6.0E-03	1.6E-02	1.0E+00	7.39
Maleic acid	Organic acids	Ref.	0.82 (0.50, 1.33)	1.02 (0.63, 1.64)	1.15 (0.72, 1.84)	1.4E-01	3.6E-01	1.00 (0.82, 1.22)	9.9E-01	9.9E-01	1.0E+00	0.01
Malic acid	Organic acids	Ref.	1.54 (0.93, 2.56)	1.58 (0.93, 2.66)	3.89 (2.27, 6.68)	4.9E-02	2.0E-01	1.82 (1.33, 2.48)	1.5E-04	7.8E-04	2.9E-02	12.66
Malonic acid	Organic acids	Ref.	0.68 (0.42, 1.09)	1.09 (0.69, 1.72)	1.07 (0.68, 1.69)	3.2E-01	5.0E-01	0.97 (0.85, 1.10)	6.1E-01	7.0E-01	1.0E+00	0.71
Methylsuccinic acid	Organic acids	Ref.	1.44 (0.82, 2.54)	1.86 (1.07, 3.24)	4.61 (2.65, 8.00)	8.2E-05	2.8E-03	1.40 (1.22, 1.60)	1.1E-06	9.2E-06	2.1E-04	19.74
Oxalic acid	Organic acids	Ref.	0.94 (0.60, 1.46)	0.82 (0.51, 1.32)	0.96 (0.60, 1.54)	3.6E-01	5.2E-01	0.88 (0.70, 1.10)	2.5E-01	3.5E-01	1.0E+00	1.98
Oxoadipic acid	Organic acids	Ref.	0.80 (0.44, 1.46)	1.53 (0.87, 2.68)	2.49 (1.48, 4.20)	8.5E-02	2.7E-01	1.46 (1.16, 1.83)	1.2E-03	4.2E-03	2.2E-01	9.69
Oxoglutaric acid	Organic acids	Ref.	1.13 (0.69, 1.86)	1.58 (0.97, 2.58)	3.91 (2.30, 6.63)	3.3E-05	1.5E-03	1.49 (1.17, 1.89)	1.1E-03	3.8E-03	2.0E-01	9.84
Petroselinic acid	Organic acids	Ref.	0.89 (0.58, 1.35)	0.95 (0.63, 1.43)	0.89 (0.56, 1.40)	2.4E-01	4.6E-01	0.98 (0.82, 1.17)	8.1E-01	8.4E-01	1.0E+00	0.31
Pimelic acid	Organic acids	Ref.	0.49 (0.29, 0.81)	0.50 (0.29, 0.86)	0.67 (0.42, 1.06)	3.4E-01	5.1E-01	0.93 (0.83, 1.04)	2.0E-01	2.8E-01	1.0E+00	2.31
Pyruvic acid	Organic acids	Ref.	0.88 (0.57, 1.37)	1.03 (0.67, 1.59)	0.79 (0.49, 1.28)	1.5E-01	3.6E-01	0.79 (0.65, 0.96)	2.0E-02	4.3E-02	1.0E+00	5.64
Succinic acid	Organic acids	Ref.	0.84 (0.50, 1.42)	0.85 (0.50, 1.46)	1.43 (0.82, 2.48)	3.2E-02	1.7E-01	1.69 (1.16, 2.45)	5.8E-03	1.6E-02	1.0E+00	7.43
4-Hydroxyphenylpyruvic acid	Phenols	Ref.	0.86 (0.54, 1.37)	1.03 (0.64, 1.65)	1.85 (1.17, 2.95)	6.6E-04	1.5E-02	1.19 (1.00, 1.40)	4.7E-02	8.8E-02	1.0E+00	4.42
Homovanillic acid	Phenols	Ref.	2.33 (1.23, 4.42)	4.42 (2.21, 8.84)	10.88 (5.59, 21.16)	4.3E-01	5.7E-01	6.34 (4.06, 9.90)	4.6E-16	1.4E-14	8.6E-14	50.95
p-Hydroxyphenylacetic acid	Phenols	Ref.	1.20 (0.77, 1.85)	0.81 (0.51, 1.29)	0.97 (0.62, 1.52)	7.7E-01	8.3E-01	0.96 (0.88, 1.06)	4.5E-01	5.6E-01	1.0E+00	1.15
2-Phenylpropionate	Phenylpropanoic acids	Ref.	1.81 (1.07, 3.04)	1.83 (1.11, 3.03)	2.24 (1.39, 3.61)	2.3E-01	4.5E-01	1.17 (1.06, 1.29)	1.6E-03	5.3E-03	3.0E-01	9.27
3-Hydroxyphenylhydraacrylic acid	Phenylpropanoic acids	Ref.	0.86 (0.52, 1.42)	0.75 (0.44, 1.27)	0.80 (0.50, 1.30)	1.2E-01	3.3E-01	0.95 (0.84, 1.07)	3.8E-01	4.9E-01	1.0E+00	1.38
Hydrocinnamic acid	Phenylpropanoic acids	Ref.	0.85 (0.51, 1.44)	1.57 (0.98, 2.50)	1.49 (0.97, 2.30)	3.7E-01	5.2E-01	1.16 (1.05, 1.29)	4.3E-03	1.3E-02	8.0E-01	7.87
Hydroxyphenyllactic acid	Phenylpropanoic acids	Ref.	0.97 (0.53, 1.77)	1.85 (1.05, 3.29)	5.85 (3.30, 10.37)	1.8E-03	3.0E-02	3.42 (2.48, 4.71)	6.1E-14	1.3E-12	1.1E-11	43.90

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	$P_{\text{non-linear}}^b$	FDR _{non-linear}^b}	OR _{doubling} (95% CI)	P value	FDR	P_{Bon}^c	S value
Phenyllactic acid	Phenylpropanoic acids	Ref.	0.92 (0.55, 1.55)	1.02 (0.60, 1.71)	2.23 (1.41, 3.54)	2.1E-01	4.4E-01	1.71 (1.35, 2.16)	6.9E-06	4.4E-05	1.3E-03	17.15
N-Methylnicotinamide	Pyridines	Ref.	1.37 (0.81, 2.31)	2.85 (1.78, 4.55)	2.19 (1.34, 3.56)	9.4E-02	2.8E-01	1.34 (1.17, 1.53)	2.6E-05	1.6E-04	4.9E-03	15.21
3-Hydroxyisovaleric acid	SCFAs	Ref.	0.68 (0.43, 1.07)	0.92 (0.59, 1.43)	0.84 (0.55, 1.29)	2.3E-02	1.6E-01	0.89 (0.67, 1.20)	4.5E-01	5.6E-01	1.0E+00	1.14
Acetic acid	SCFAs	Ref.	1.04 (0.65, 1.67)	1.30 (0.79, 2.12)	1.11 (0.69, 1.78)	9.0E-02	2.7E-01	0.97 (0.82, 1.14)	7.0E-01	7.7E-01	1.0E+00	0.50
Butyric acid	SCFAs	Ref.	2.51 (1.37, 4.61)	3.47 (1.69, 7.13)	3.80 (1.75, 8.25)	5.4E-01	6.6E-01	3.21 (1.96, 5.25)	3.5E-06	2.5E-05	6.6E-04	18.11
Caproic acid	SCFAs	Ref.	0.97 (0.61, 1.55)	1.22 (0.72, 2.09)	1.94 (1.06, 3.54)	6.6E-02	2.2E-01	1.87 (1.16, 3.03)	1.0E-02	2.5E-02	1.0E+00	6.62
Ethylmethylacetic acid	SCFAs	Ref.	1.23 (0.77, 1.96)	1.46 (0.86, 2.48)	1.58 (0.92, 2.70)	3.5E-01	5.2E-01	1.50 (1.11, 2.01)	8.1E-03	2.0E-02	1.0E+00	6.94
Formic acid	SCFAs	Ref.	1.43 (0.86, 2.37)	2.14 (1.31, 3.51)	2.44 (1.41, 4.22)	3.4E-01	5.1E-01	1.74 (1.25, 2.42)	1.1E-03	3.8E-03	2.0E-01	9.87
Isobutyric acid	SCFAs	Ref.	0.62 (0.38, 1.02)	1.40 (0.83, 2.36)	1.14 (0.65, 1.99)	1.1E-01	3.3E-01	1.69 (1.13, 2.54)	1.1E-02	2.6E-02	1.0E+00	6.51
Isocaproic acid	SCFAs	Ref.	1.07 (0.67, 1.71)	0.95 (0.60, 1.51)	0.89 (0.56, 1.42)	2.5E-01	4.8E-01	0.91 (0.70, 1.17)	4.6E-01	5.6E-01	1.0E+00	1.12
Isovaleric acid	SCFAs	Ref.	0.85 (0.54, 1.34)	0.84 (0.53, 1.34)	0.93 (0.59, 1.49)	6.8E-02	2.3E-01	1.15 (0.97, 1.37)	1.0E-01	1.7E-01	1.0E+00	3.27
Pentanoic acid	SCFAs	Ref.	1.18 (0.76, 1.84)	0.95 (0.58, 1.54)	1.28 (0.78, 2.08)	2.2E-01	4.5E-01	1.15 (0.94, 1.42)	1.8E-01	2.6E-01	1.0E+00	2.49
Propanoic acid	SCFAs	Ref.	1.22 (0.73, 2.03)	1.87 (1.11, 3.18)	3.13 (1.74, 5.65)	7.7E-01	8.3E-01	5.33 (2.74, 10.37)	8.7E-07	7.4E-06	1.6E-04	20.13

a Conditioned on matching factors.

b Log₂-transformed metabolite concentrations was fitted with a 3-knots restricted cubic spline (10th, 50th, and 90th percentile).

c Bonferroni corrected P values.

Supplementary Table ST4 Association between all quantitated metabolites and liver cancer risk (Model 2)^a

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	<i>P</i> _{non-linear} ^b	FDR _{non-linear} ^b	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^c	S value
2-Hydroxyglutaric acid	Amino acids	Ref.	1.57 (0.68, 3.64)	1.49 (0.62, 3.59)	1.42 (0.61, 3.31)	3.4E-01	6.8E-01	1.24 (0.87, 1.77)	2.4E-01	4.4E-01	1.0E+00	2.04
2-Phenylglycine	Amino acids	Ref.	0.32 (0.14, 0.73)	0.83 (0.38, 1.84)	0.78 (0.36, 1.71)	2.4E-03	1.2E-01	0.80 (0.54, 1.17)	2.5E-01	4.4E-01	1.0E+00	2.02
5-Aminolevulinic acid	Amino acids	Ref.	0.58 (0.27, 1.21)	0.93 (0.44, 1.94)	0.45 (0.19, 1.06)	1.8E-01	5.6E-01	0.75 (0.47, 1.20)	2.2E-01	4.2E-01	1.0E+00	2.16
Alanine	Amino acids	Ref.	0.59 (0.26, 1.38)	0.53 (0.23, 1.18)	0.55 (0.26, 1.19)	2.5E-01	6.2E-01	0.36 (0.15, 0.90)	2.9E-02	1.2E-01	1.0E+00	5.13
alpha-Aminobutyric acid	Amino acids	Ref.	0.78 (0.38, 1.60)	0.44 (0.21, 0.93)	0.76 (0.34, 1.68)	3.8E-02	3.5E-01	0.70 (0.36, 1.38)	3.0E-01	5.1E-01	1.0E+00	1.71
Arginine	Amino acids	Ref.	2.88 (1.15, 7.26)	3.12 (1.20, 8.13)	1.91 (0.74, 4.92)	3.4E-02	3.5E-01	0.97 (0.50, 1.90)	9.4E-01	9.6E-01	1.0E+00	0.10
Asparagine	Amino acids	Ref.	1.25 (0.56, 2.77)	1.12 (0.50, 2.51)	1.15 (0.48, 2.71)	5.4E-01	7.6E-01	1.14 (0.48, 2.71)	7.7E-01	9.1E-01	1.0E+00	0.37
Aspartic acid	Amino acids	Ref.	1.09 (0.52, 2.28)	1.23 (0.58, 2.62)	1.74 (0.74, 4.12)	3.8E-01	7.0E-01	1.93 (1.03, 3.62)	4.0E-02	1.4E-01	1.0E+00	4.66
beta-Alanine	Amino acids	Ref.	0.51 (0.24, 1.08)	0.61 (0.27, 1.37)	0.44 (0.19, 1.00)	2.5E-01	6.2E-01	0.70 (0.54, 0.90)	4.8E-03	3.6E-02	9.0E-01	7.69
Citrulline	Amino acids	Ref.	1.13 (0.45, 2.81)	1.93 (0.81, 4.61)	2.00 (0.81, 4.93)	7.3E-01	8.5E-01	1.61 (0.85, 3.04)	1.4E-01	2.9E-01	1.0E+00	2.83
Creatine	Amino acids	Ref.	0.61 (0.30, 1.24)	0.30 (0.13, 0.67)	0.46 (0.20, 1.06)	3.5E-02	3.5E-01	0.52 (0.33, 0.81)	4.3E-03	3.5E-02	8.0E-01	7.86
Dimethylglycine	Amino acids	Ref.	0.93 (0.39, 2.23)	1.52 (0.61, 3.77)	2.84 (1.27, 6.37)	1.9E-01	5.6E-01	2.24 (1.19, 4.22)	1.3E-02	6.6E-02	1.0E+00	6.29
GABA	Amino acids	Ref.	0.36 (0.15, 0.87)	0.43 (0.17, 1.04)	0.89 (0.40, 1.99)	5.9E-01	8.2E-01	1.13 (0.65, 1.98)	6.7E-01	8.1E-01	1.0E+00	0.59
Glutamic acid	Amino acids	Ref.	2.36 (1.02, 5.44)	1.88 (0.79, 4.46)	2.28 (0.92, 5.62)	5.3E-01	7.5E-01	1.78 (0.92, 3.43)	8.6E-02	2.4E-01	1.0E+00	3.53
Glutamine	Amino acids	Ref.	0.22 (0.09, 0.50)	0.32 (0.14, 0.72)	0.48 (0.21, 1.07)	1.3E-02	2.4E-01	0.47 (0.20, 1.09)	7.8E-02	2.2E-01	1.0E+00	3.69
Glycine	Amino acids	Ref.	0.64 (0.31, 1.32)	0.51 (0.23, 1.15)	0.71 (0.33, 1.54)	1.3E-01	5.2E-01	0.64 (0.29, 1.41)	2.7E-01	4.6E-01	1.0E+00	1.91
Hippuric acid	Amino acids	Ref.	1.32 (0.64, 2.70)	0.90 (0.41, 1.99)	0.61 (0.27, 1.37)	1.5E-01	5.2E-01	0.89 (0.74, 1.07)	2.2E-01	4.2E-01	1.0E+00	2.17
Histidine	Amino acids	Ref.	0.66 (0.30, 1.48)	0.75 (0.33, 1.69)	0.63 (0.29, 1.37)	7.7E-01	8.6E-01	1.04 (0.37, 2.92)	9.4E-01	9.6E-01	1.0E+00	0.08
Homoserine	Amino acids	Ref.	1.13 (0.52, 2.44)	1.46 (0.65, 3.29)	1.08 (0.46, 2.56)	6.6E-01	8.5E-01	1.49 (0.75, 2.96)	2.5E-01	4.4E-01	1.0E+00	1.99
Isoleucine	Amino acids	Ref.	0.93 (0.42, 2.06)	1.01 (0.45, 2.25)	0.50 (0.20, 1.24)	2.4E-01	6.2E-01	0.57 (0.31, 1.07)	7.9E-02	2.2E-01	1.0E+00	3.65
Leucine	Amino acids	Ref.	0.57 (0.26, 1.28)	0.73 (0.32, 1.67)	0.49 (0.21, 1.12)	5.1E-01	7.4E-01	0.50 (0.24, 1.05)	6.9E-02	2.0E-01	1.0E+00	3.86
Lysine	Amino acids	Ref.	0.56 (0.25, 1.26)	0.16 (0.06, 0.42)	0.32 (0.14, 0.76)	2.0E-01	5.9E-01	0.16 (0.06, 0.41)	1.6E-04	3.3E-03	3.0E-02	12.62
Methionine	Amino acids	Ref.	1.25 (0.54, 2.88)	1.57 (0.68, 3.60)	1.58 (0.72, 3.44)	7.0E-01	8.5E-01	1.42 (0.74, 2.73)	3.0E-01	5.0E-01	1.0E+00	1.76
Methylcysteine	Amino acids	Ref.	0.60 (0.28, 1.32)	0.55 (0.25, 1.23)	0.65 (0.28, 1.51)	5.1E-01	7.4E-01	0.79 (0.48, 1.30)	3.6E-01	5.5E-01	1.0E+00	1.48
N-Acetylglycine	Amino acids	Ref.	0.42 (0.20, 0.90)	0.44 (0.21, 0.92)	0.75 (0.36, 1.56)	1.4E-01	5.2E-01	0.76 (0.35, 1.66)	4.9E-01	6.6E-01	1.0E+00	1.01
N-Acetylserine	Amino acids	Ref.	1.52 (0.69, 3.36)	1.41 (0.63, 3.15)	2.84 (1.20, 6.74)	7.3E-01	8.5E-01	2.17 (0.84, 5.63)	1.1E-01	2.6E-01	1.0E+00	3.17
N-Phenylacetylglutamine	Amino acids	Ref.	0.79 (0.36, 1.78)	0.56 (0.25, 1.25)	1.58 (0.72, 3.47)	3.7E-01	7.0E-01	1.04 (0.84, 1.29)	7.2E-01	8.7E-01	1.0E+00	0.47
Norvaline	Amino acids	Ref.	1.29 (0.53, 3.15)	1.82 (0.68, 4.92)	1.06 (0.37, 2.98)	1.4E-01	5.2E-01	1.62 (0.06, 42.13)	7.7E-01	9.1E-01	1.0E+00	0.37

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	<i>P</i> _{non-linear} ^b	FDR _{non-linear} ^b	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^c	S value
Ornithine	Amino acids	Ref.	0.61 (0.26, 1.45)	1.05 (0.48, 2.32)	0.91 (0.40, 2.10)	9.8E-01	9.8E-01	1.07 (0.56, 2.03)	8.4E-01	9.2E-01	1.0E+00	0.26
Phenylalanine	Amino acids	Ref.	1.11 (0.48, 2.58)	1.24 (0.53, 2.89)	1.41 (0.61, 3.25)	8.5E-01	9.1E-01	1.34 (0.45, 3.94)	6.0E-01	7.8E-01	1.0E+00	0.74
Pipecolic acid	Amino acids	Ref.	2.68 (1.12, 6.40)	2.92 (1.16, 7.37)	4.06 (1.63, 10.10)	4.2E-01	7.0E-01	2.04 (1.23, 3.39)	5.8E-03	4.1E-02	1.0E+00	7.43
Proline	Amino acids	Ref.	0.97 (0.43, 2.19)	2.62 (1.12, 6.18)	0.98 (0.41, 2.33)	2.5E-02	3.4E-01	0.95 (0.49, 1.84)	8.7E-01	9.4E-01	1.0E+00	0.20
Pyroglutamic acid	Amino acids	Ref.	2.16 (1.02, 4.60)	0.65 (0.26, 1.64)	3.38 (1.38, 8.30)	2.6E-01	6.2E-01	2.24 (1.19, 4.23)	1.2E-02	6.6E-02	1.0E+00	6.33
Sarcosine	Amino acids	Ref.	0.57 (0.25, 1.29)	0.63 (0.30, 1.32)	0.91 (0.41, 2.06)	3.9E-01	7.0E-01	0.83 (0.40, 1.71)	6.1E-01	7.8E-01	1.0E+00	0.72
Selenomethionine	Amino acids	Ref.	0.83 (0.24, 2.82)	0.54 (0.15, 1.97)	1.39 (0.41, 4.68)	5.2E-02	4.2E-01	1.56 (0.64, 3.84)	3.3E-01	5.2E-01	1.0E+00	1.60
Serine	Amino acids	Ref.	1.43 (0.68, 2.99)	1.30 (0.59, 2.88)	2.48 (1.11, 5.54)	1.5E-01	5.2E-01	1.89 (0.88, 4.04)	1.0E-01	2.5E-01	1.0E+00	3.30
Threonine	Amino acids	Ref.	1.02 (0.48, 2.20)	0.86 (0.38, 1.96)	1.10 (0.48, 2.56)	3.4E-01	6.8E-01	1.40 (0.61, 3.20)	4.3E-01	6.3E-01	1.0E+00	1.22
Tryptophan	Amino acids	Ref.	0.78 (0.36, 1.72)	0.89 (0.40, 1.96)	0.66 (0.31, 1.43)	4.2E-01	7.0E-01	0.61 (0.24, 1.56)	3.0E-01	5.1E-01	1.0E+00	1.72
Tyrosine	Amino acids	Ref.	1.08 (0.38, 3.05)	3.22 (1.14, 9.08)	5.38 (1.97, 14.70)	4.6E-01	7.4E-01	5.82 (2.38, 14.20)	1.1E-04	2.8E-03	2.0E-02	13.15
Valine	Amino acids	Ref.	1.33 (0.62, 2.86)	0.22 (0.08, 0.57)	0.78 (0.33, 1.83)	5.0E-01	7.4E-01	0.49 (0.19, 1.30)	1.5E-01	3.1E-01	1.0E+00	2.72
ortho-Hydroxyphenylacetic acid	Benzenoids	Ref.	0.69 (0.33, 1.45)	0.68 (0.32, 1.47)	0.57 (0.26, 1.24)	4.4E-01	7.1E-01	0.67 (0.45, 1.01)	5.7E-02	1.8E-01	1.0E+00	4.14
Phenylacetic acid	Benzenoids	Ref.	0.86 (0.37, 2.01)	1.35 (0.63, 2.93)	1.93 (0.84, 4.43)	4.1E-01	7.0E-01	1.16 (0.95, 1.42)	1.4E-01	2.9E-01	1.0E+00	2.87
Phenylpyruvic acid	Benzenoids	Ref.	1.48 (0.67, 3.27)	1.82 (0.76, 4.37)	1.09 (0.49, 2.41)	7.0E-02	4.7E-01	0.97 (0.72, 1.32)	8.6E-01	9.4E-01	1.0E+00	0.21
4-Hydroxybenzoic acid	Benzoic acids	Ref.	0.47 (0.20, 1.09)	0.77 (0.33, 1.80)	1.69 (0.78, 3.63)	9.0E-01	9.3E-01	2.18 (0.88, 5.39)	9.0E-02	2.4E-01	1.0E+00	3.47
m-Aminobenzoic acid	Benzoic acids	Ref.	1.41 (0.68, 2.94)	0.70 (0.30, 1.65)	0.84 (0.40, 1.77)	4.9E-01	7.4E-01	0.98 (0.71, 1.35)	9.0E-01	9.5E-01	1.0E+00	0.15
m-Hydroxyhippuric acid	Benzoic acids	Ref.	0.52 (0.17, 1.56)	0.72 (0.30, 1.75)	0.47 (0.19, 1.16)	2.6E-01	6.2E-01	0.68 (0.37, 1.26)	2.2E-01	4.2E-01	1.0E+00	2.20
Phthalic acid	Benzoic acids	Ref.	1.01 (0.46, 2.21)	1.06 (0.47, 2.39)	0.90 (0.38, 2.14)	8.7E-01	9.2E-01	0.93 (0.50, 1.73)	8.2E-01	9.2E-01	1.0E+00	0.29
7-DHCA	Bile acids	Ref.	1.22 (0.43, 3.52)	1.67 (0.57, 4.86)	2.32 (0.85, 6.34)	7.0E-01	8.5E-01	1.57 (1.03, 2.38)	3.5E-02	1.3E-01	1.0E+00	4.85
apoCA	Bile acids	Ref.	0.55 (0.24, 1.28)	1.08 (0.45, 2.57)	0.66 (0.28, 1.57)	9.5E-01	9.6E-01	0.65 (0.32, 1.33)	2.4E-01	4.4E-01	1.0E+00	2.06
beta-HDCA	Bile acids	Ref.	1.17 (0.52, 2.64)	0.93 (0.42, 2.08)	1.61 (0.72, 3.63)	1.5E-01	5.2E-01	1.10 (0.93, 1.31)	2.5E-01	4.4E-01	1.0E+00	2.02
CA	Bile acids	Ref.	2.16 (0.86, 5.40)	3.05 (1.16, 8.00)	2.71 (1.03, 7.13)	1.0E-01	5.2E-01	1.22 (1.01, 1.48)	4.1E-02	1.4E-01	1.0E+00	4.59
CDCA	Bile acids	Ref.	2.27 (0.99, 5.22)	1.81 (0.80, 4.08)	3.19 (1.34, 7.61)	7.9E-02	4.7E-01	1.20 (1.02, 1.43)	3.2E-02	1.2E-01	1.0E+00	4.97
DCA	Bile acids	Ref.	0.95 (0.41, 2.18)	0.75 (0.35, 1.59)	0.66 (0.29, 1.50)	7.4E-01	8.5E-01	0.84 (0.66, 1.06)	1.4E-01	3.0E-01	1.0E+00	2.80
GCA	Bile acids	Ref.	3.39 (1.15, 9.94)	5.15 (1.62, 16.41)	12.74 (4.17, 38.89)	2.5E-01	6.2E-01	1.66 (1.35, 2.04)	1.2E-06	7.5E-05	2.2E-04	19.66
GCDCA	Bile acids	Ref.	2.42 (0.77, 7.57)	5.25 (1.85, 14.86)	14.97 (4.92, 45.53)	7.5E-02	4.7E-01	2.03 (1.54, 2.68)	4.5E-07	4.2E-05	8.3E-05	21.09
GDCA	Bile acids	Ref.	0.51 (0.22, 1.22)	0.94 (0.40, 2.21)	1.53 (0.67, 3.47)	1.1E-01	5.2E-01	1.07 (0.96, 1.20)	2.0E-01	3.9E-01	1.0E+00	2.31
GHCA	Bile acids	Ref.	1.10 (0.38, 3.21)	2.67 (0.81, 8.85)	2.95 (0.98, 8.88)	2.9E-01	6.4E-01	1.81 (1.24, 2.66)	2.3E-03	2.2E-02	4.3E-01	8.74

Metabolite	Class	Categorical analysis						Continuous analysis					
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	<i>P</i> _{non-linear} ^b	FDR _{non-linear} ^b	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^c	S value	
GLCA	Bile acids	Ref.	0.72 (0.34, 1.56)	1.25 (0.55, 2.85)	0.78 (0.36, 1.69)	6.8E-01	8.5E-01	0.98 (0.69, 1.41)	9.3E-01	9.6E-01	1.0E+00	0.11	
GLCA-3S	Bile acids	Ref.	1.80 (0.76, 4.26)	1.37 (0.61, 3.05)	1.47 (0.65, 3.32)	7.2E-01	8.5E-01	1.07 (0.90, 1.28)	4.4E-01	6.3E-01	1.0E+00	1.18	
GUDCA	Bile acids	Ref.	1.25 (0.52, 2.99)	1.86 (0.73, 4.75)	3.53 (1.48, 8.45)	4.8E-01	7.4E-01	1.45 (1.20, 1.77)	1.7E-04	3.3E-03	3.3E-02	12.48	
HCA	Bile acids	Ref.	1.85 (0.73, 4.66)	1.45 (0.51, 4.07)	3.50 (1.36, 8.99)	1.3E-01	5.2E-01	2.54 (1.26, 5.10)	9.1E-03	5.8E-02	1.0E+00	6.78	
HDCA	Bile acids	Ref.	0.87 (0.39, 1.91)	0.65 (0.27, 1.56)	0.59 (0.25, 1.39)	4.6E-01	7.4E-01	0.77 (0.60, 0.99)	4.0E-02	1.4E-01	1.0E+00	4.63	
LCA	Bile acids	Ref.	0.61 (0.24, 1.52)	0.75 (0.28, 2.05)	1.39 (0.63, 3.06)	2.1E-02	3.3E-01	1.04 (0.79, 1.37)	7.9E-01	9.1E-01	1.0E+00	0.34	
TCA	Bile acids	Ref.	4.28 (1.33, 13.78)	2.63 (0.82, 8.45)	13.36 (4.35, 41.03)	3.3E-01	6.7E-01	1.59 (1.31, 1.93)	3.2E-06	1.2E-04	6.0E-04	18.25	
TCDCA	Bile acids	Ref.	2.94 (0.88, 9.82)	3.79 (1.26, 11.41)	19.06 (5.91, 61.49)	5.9E-01	8.2E-01	1.88 (1.48, 2.39)	2.3E-07	4.2E-05	4.3E-05	22.06	
TDCA	Bile acids	Ref.	2.25 (0.87, 5.82)	0.92 (0.33, 2.54)	4.95 (1.88, 13.01)	7.6E-01	8.5E-01	1.43 (1.14, 1.78)	1.7E-03	1.9E-02	3.2E-01	9.19	
UCA	Bile acids	Ref.	1.33 (0.41, 4.33)	1.23 (0.37, 4.06)	1.50 (0.49, 4.64)	7.2E-01	8.5E-01	1.57 (0.87, 2.84)	1.4E-01	2.9E-01	1.0E+00	2.87	
D-Xylulose	Carbohydrates	Ref.	2.35 (0.90, 6.15)	2.94 (1.09, 7.98)	3.61 (1.41, 9.26)	7.2E-01	8.5E-01	3.56 (1.61, 7.88)	1.7E-03	1.9E-02	3.2E-01	9.19	
Fructose	Carbohydrates	Ref.	1.36 (0.59, 3.11)	1.16 (0.49, 2.76)	2.34 (1.01, 5.44)	1.6E-01	5.2E-01	1.40 (1.10, 1.79)	6.4E-03	4.4E-02	1.0E+00	7.30	
Galactonic acid	Carbohydrates	Ref.	1.46 (0.64, 3.36)	0.94 (0.45, 1.99)	1.22 (0.54, 2.77)	4.9E-01	7.4E-01	1.02 (0.66, 1.59)	9.2E-01	9.6E-01	1.0E+00	0.12	
Gluconolactone	Carbohydrates	Ref.	0.64 (0.30, 1.39)	0.54 (0.24, 1.19)	1.67 (0.70, 4.03)	1.6E-01	5.2E-01	1.39 (0.73, 2.65)	3.2E-01	5.1E-01	1.0E+00	1.65	
Glucose	Carbohydrates	Ref.	1.41 (0.59, 3.39)	0.88 (0.40, 1.94)	1.67 (0.78, 3.58)	1.8E-01	5.6E-01	2.20 (1.16, 4.16)	1.5E-02	7.4E-02	1.0E+00	6.05	
Glutaconic acid	Carbohydrates	Ref.	1.33 (0.57, 3.11)	1.19 (0.50, 2.87)	0.81 (0.34, 1.98)	2.7E-01	6.2E-01	0.97 (0.55, 1.69)	9.0E-01	9.5E-01	1.0E+00	0.15	
Glyceric acid	Carbohydrates	Ref.	0.76 (0.34, 1.67)	1.09 (0.50, 2.37)	1.32 (0.59, 2.94)	3.9E-01	7.0E-01	1.17 (0.76, 1.80)	4.7E-01	6.5E-01	1.0E+00	1.10	
Maltose/Lactose	Carbohydrates	Ref.	0.41 (0.17, 0.97)	0.50 (0.20, 1.23)	0.36 (0.15, 0.89)	7.5E-01	8.5E-01	0.80 (0.59, 1.09)	1.6E-01	3.3E-01	1.0E+00	2.62	
N-Acetylneuraminic acid	Carbohydrates	Ref.	0.91 (0.40, 2.07)	0.53 (0.24, 1.17)	0.49 (0.21, 1.11)	3.0E-01	6.4E-01	0.54 (0.25, 1.18)	1.2E-01	2.7E-01	1.0E+00	3.03	
Rhamnose	Carbohydrates	Ref.	0.63 (0.25, 1.62)	1.48 (0.58, 3.77)	2.60 (1.03, 6.59)	7.4E-01	8.5E-01	1.63 (1.16, 2.28)	4.5E-03	3.5E-02	8.5E-01	7.78	
Tartaric acid	Carbohydrates	Ref.	0.82 (0.32, 2.06)	0.66 (0.25, 1.74)	0.80 (0.30, 2.13)	6.5E-01	8.5E-01	0.93 (0.70, 1.25)	6.4E-01	8.0E-01	1.0E+00	0.65	
Threonic acid	Carbohydrates	Ref.	0.73 (0.37, 1.46)	0.67 (0.31, 1.47)	1.02 (0.49, 2.15)	4.1E-01	7.0E-01	0.89 (0.66, 1.20)	4.3E-01	6.3E-01	1.0E+00	1.21	
Trehalose	Carbohydrates	Ref.	1.25 (0.55, 2.82)	0.97 (0.37, 2.53)	0.75 (0.28, 2.00)	4.1E-01	7.0E-01	0.19 (0.02, 2.14)	1.8E-01	3.6E-01	1.0E+00	2.48	
Xylose	Carbohydrates	Ref.	1.75 (0.75, 4.11)	1.90 (0.80, 4.52)	1.82 (0.78, 4.22)	2.9E-01	6.4E-01	1.42 (0.91, 2.23)	1.3E-01	2.8E-01	1.0E+00	2.98	
2-Methylbutyrylcarnitine	Carnitines	Ref.	1.18 (0.53, 2.59)	0.59 (0.24, 1.41)	0.84 (0.39, 1.81)	4.7E-01	7.4E-01	0.85 (0.55, 1.32)	4.7E-01	6.5E-01	1.0E+00	1.08	
3-Hydroxyisovalerylcarnitine	Carnitines	Ref.	1.19 (0.51, 2.79)	0.57 (0.22, 1.49)	0.63 (0.26, 1.53)	6.8E-01	8.5E-01	0.56 (0.30, 1.03)	6.4E-02	1.9E-01	1.0E+00	3.96	
Acetylcarnitine	Carnitines	Ref.	1.93 (0.85, 4.38)	2.17 (0.93, 5.11)	2.82 (1.26, 6.28)	4.8E-01	7.4E-01	2.55 (1.45, 4.49)	1.2E-03	1.6E-02	2.2E-01	9.73	
Adipoylcarnitine	Carnitines	Ref.	0.81 (0.33, 1.96)	1.33 (0.53, 3.33)	1.09 (0.50, 2.40)	7.0E-01	8.5E-01	1.28 (0.68, 2.41)	4.4E-01	6.3E-01	1.0E+00	1.19	
Carnitine	Carnitines	Ref.	1.25 (0.58, 2.69)	1.46 (0.69, 3.09)	0.86 (0.40, 1.85)	6.5E-01	8.5E-01	1.19 (0.47, 3.00)	7.1E-01	8.6E-01	1.0E+00	0.48	

Metabolite	Class	Categorical analysis						Continuous analysis					
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	<i>P</i> _{non-linear} ^b	FDR _{non-linear} ^b	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^c	S value	
Decanoylcarnitine	Carnitines	Ref.	0.96 (0.42, 2.18)	1.03 (0.44, 2.42)	2.38 (1.00, 5.66)	1.7E-01	5.2E-01	1.45 (0.99, 2.13)	5.6E-02	1.8E-01	1.0E+00	4.17	
Glutaryl carnitine	Carnitines	Ref.	0.92 (0.43, 1.99)	0.80 (0.37, 1.73)	0.95 (0.43, 2.10)	4.9E-01	7.4E-01	0.93 (0.39, 2.21)	8.7E-01	9.4E-01	1.0E+00	0.20	
Hexanoylcarnitine	Carnitines	Ref.	0.75 (0.30, 1.86)	1.21 (0.49, 2.98)	2.52 (1.07, 5.92)	1.5E-02	2.6E-01	1.31 (1.00, 1.72)	4.8E-02	1.6E-01	1.0E+00	4.39	
Isovelarylcarnitine	Carnitines	Ref.	1.14 (0.52, 2.50)	0.86 (0.38, 1.95)	0.57 (0.25, 1.27)	7.6E-01	8.5E-01	0.79 (0.48, 1.28)	3.4E-01	5.3E-01	1.0E+00	1.58	
Lauroyl carnitine	Carnitines	Ref.	0.70 (0.27, 1.81)	0.99 (0.40, 2.45)	2.47 (1.00, 6.12)	7.2E-02	4.7E-01	1.27 (0.95, 1.70)	1.1E-01	2.6E-01	1.0E+00	3.23	
Linoleyl carnitine	Carnitines	Ref.	0.95 (0.43, 2.10)	1.01 (0.44, 2.35)	1.93 (0.76, 4.93)	1.6E-01	5.2E-01	1.44 (0.84, 2.47)	1.9E-01	3.7E-01	1.0E+00	2.41	
Malonylcarnitine	Carnitines	Ref.	0.45 (0.18, 1.12)	0.72 (0.31, 1.70)	0.56 (0.25, 1.25)	5.0E-01	7.4E-01	0.83 (0.65, 1.05)	1.2E-01	2.7E-01	1.0E+00	3.04	
Myristoylcarnitine	Carnitines	Ref.	1.13 (0.42, 3.05)	2.76 (0.94, 8.10)	4.11 (1.60, 10.60)	7.4E-01	8.5E-01	3.24 (1.56, 6.72)	1.6E-03	1.9E-02	3.0E-01	9.30	
Octanoylcarnitine	Carnitines	Ref.	0.58 (0.26, 1.27)	1.26 (0.56, 2.82)	1.76 (0.78, 3.99)	1.5E-01	5.2E-01	1.52 (1.04, 2.20)	2.9E-02	1.2E-01	1.0E+00	5.10	
Oleoylcarnitine	Carnitines	Ref.	0.84 (0.35, 2.04)	2.47 (0.95, 6.40)	4.14 (1.60, 10.69)	5.6E-03	1.3E-01	2.32 (1.30, 4.14)	4.5E-03	3.5E-02	8.3E-01	7.81	
Palmitoylcarnitine	Carnitines	Ref.	0.96 (0.41, 2.26)	1.88 (0.78, 4.51)	2.87 (1.17, 7.06)	9.5E-02	4.9E-01	1.76 (0.92, 3.38)	8.9E-02	2.4E-01	1.0E+00	3.49	
Propionyl carnitine	Carnitines	Ref.	1.56 (0.71, 3.40)	1.29 (0.59, 2.81)	1.35 (0.63, 2.90)	6.6E-01	8.5E-01	1.35 (0.74, 2.46)	3.2E-01	5.2E-01	1.0E+00	1.63	
Stearyl carnitine	Carnitines	Ref.	1.05 (0.46, 2.39)	1.60 (0.71, 3.60)	3.37 (1.43, 7.97)	2.7E-01	6.2E-01	1.94 (1.27, 2.97)	2.3E-03	2.2E-02	4.4E-01	8.74	
10Z-Heptadecenoic acid	Fatty acids	Ref.	1.46 (0.62, 3.44)	1.31 (0.58, 3.00)	3.35 (1.49, 7.51)	4.3E-01	7.1E-01	1.39 (1.12, 1.73)	3.1E-03	2.7E-02	5.7E-01	8.34	
12-Hydroxystearic acid	Fatty acids	Ref.	0.68 (0.32, 1.44)	0.46 (0.18, 1.18)	0.33 (0.13, 0.85)	3.8E-01	7.0E-01	0.41 (0.19, 0.86)	1.8E-02	8.2E-02	1.0E+00	5.79	
2-Hydroxy-3-methylbutyric acid	Fatty acids	Ref.	1.36 (0.58, 3.17)	0.71 (0.33, 1.53)	1.22 (0.55, 2.68)	2.4E-03	1.2E-01	1.44 (1.03, 2.01)	3.2E-02	1.2E-01	1.0E+00	4.97	
2,2-Dimethyladipic acid	Fatty acids	Ref.	0.89 (0.44, 1.83)	0.46 (0.20, 1.09)	0.93 (0.38, 2.27)	8.5E-01	9.1E-01	0.94 (0.80, 1.10)	4.1E-01	6.0E-01	1.0E+00	1.29	
3-Methyladipic acid	Fatty acids	Ref.	1.06 (0.47, 2.37)	0.71 (0.31, 1.63)	0.41 (0.18, 0.96)	4.6E-02	3.9E-01	0.89 (0.73, 1.09)	2.5E-01	4.4E-01	1.0E+00	2.01	
5-Dodecenoic acid	Fatty acids	Ref.	1.06 (0.44, 2.55)	1.23 (0.52, 2.92)	2.76 (1.19, 6.44)	3.9E-01	7.0E-01	1.53 (1.10, 2.13)	1.1E-02	6.1E-02	1.0E+00	6.55	
8,11,14-Eicosatrienoic acid	Fatty acids	Ref.	0.76 (0.35, 1.66)	0.97 (0.48, 1.99)	1.31 (0.62, 2.79)	3.4E-02	3.5E-01	1.14 (0.88, 1.47)	3.2E-01	5.1E-01	1.0E+00	1.66	
Adrenic acid	Fatty acids	Ref.	1.20 (0.57, 2.52)	1.68 (0.74, 3.83)	2.58 (1.07, 6.21)	3.8E-01	7.0E-01	1.43 (1.06, 1.92)	1.7E-02	8.1E-02	1.0E+00	5.85	
alpha-Linolenic acid	Fatty acids	Ref.	0.79 (0.38, 1.66)	1.72 (0.78, 3.82)	1.55 (0.70, 3.42)	8.5E-02	4.8E-01	1.11 (0.88, 1.40)	3.6E-01	5.6E-01	1.0E+00	1.46	
Arachidonic acid	Fatty acids	Ref.	0.44 (0.22, 0.90)	0.52 (0.23, 1.19)	0.66 (0.31, 1.45)	8.4E-05	1.6E-02	0.65 (0.42, 1.02)	5.9E-02	1.8E-01	1.0E+00	4.07	
Decanoic acid	Fatty acids	Ref.	0.81 (0.32, 2.04)	2.10 (0.81, 5.45)	2.47 (0.99, 6.17)	6.6E-01	8.5E-01	1.34 (1.02, 1.75)	3.5E-02	1.3E-01	1.0E+00	4.82	
DHA	Fatty acids	Ref.	0.80 (0.35, 1.83)	0.66 (0.29, 1.47)	0.77 (0.31, 1.92)	3.7E-03	1.2E-01	0.73 (0.53, 1.01)	5.8E-02	1.8E-01	1.0E+00	4.10	
Dodecanoic acid	Fatty acids	Ref.	1.38 (0.61, 3.10)	1.34 (0.61, 2.96)	0.99 (0.43, 2.29)	4.3E-01	7.1E-01	0.97 (0.81, 1.18)	7.8E-01	9.1E-01	1.0E+00	0.36	
DPA _n -3	Fatty acids	Ref.	0.92 (0.42, 2.01)	0.69 (0.32, 1.51)	1.31 (0.56, 3.06)	6.6E-03	1.4E-01	1.03 (0.76, 1.38)	8.5E-01	9.3E-01	1.0E+00	0.23	
DPA _n -6	Fatty acids	Ref.	1.15 (0.52, 2.52)	1.00 (0.45, 2.23)	1.60 (0.71, 3.60)	7.0E-02	4.7E-01	1.01 (0.77, 1.32)	9.7E-01	9.7E-01	1.0E+00	0.05	
EPA	Fatty acids	Ref.	1.42 (0.65, 3.12)	0.49 (0.20, 1.17)	0.63 (0.28, 1.42)	9.0E-01	9.3E-01	0.81 (0.64, 1.03)	8.9E-02	2.4E-01	1.0E+00	3.49	

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	<i>P</i> _{non-linear} ^b	FDR _{non-linear} ^b	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^c	S value
gamma-Linolenic acid	Fatty acids	Ref.	1.19 (0.56, 2.52)	1.22 (0.57, 2.60)	1.53 (0.67, 3.49)	3.6E-01	7.0E-01	1.06 (0.84, 1.34)	6.2E-01	7.8E-01	1.0E+00	0.69
Heptadecanoic acid	Fatty acids	Ref.	0.53 (0.23, 1.20)	0.76 (0.35, 1.66)	0.90 (0.38, 2.10)	1.5E-01	5.2E-01	0.94 (0.62, 1.44)	7.9E-01	9.1E-01	1.0E+00	0.34
Heptanoic acid	Fatty acids	Ref.	1.33 (0.61, 2.89)	0.96 (0.37, 2.50)	0.69 (0.25, 1.87)	7.6E-01	8.6E-01	0.71 (0.32, 1.56)	3.9E-01	5.9E-01	1.0E+00	1.34
Linoleic acid	Fatty acids	Ref.	0.68 (0.33, 1.39)	1.39 (0.65, 2.93)	1.22 (0.55, 2.71)	9.2E-02	4.9E-01	1.15 (0.83, 1.59)	3.9E-01	5.9E-01	1.0E+00	1.35
Methylglutaric acid	Fatty acids	Ref.	1.09 (0.41, 2.89)	1.64 (0.59, 4.58)	1.57 (0.58, 4.26)	7.9E-01	8.6E-01	0.95 (0.63, 1.43)	8.0E-01	9.2E-01	1.0E+00	0.31
Methylmalonic acid	Fatty acids	Ref.	1.17 (0.50, 2.73)	1.14 (0.45, 2.88)	1.43 (0.55, 3.71)	1.4E-01	5.2E-01	1.20 (0.75, 1.91)	4.5E-01	6.3E-01	1.0E+00	1.16
Myristelaidic acid	Fatty acids	Ref.	1.04 (0.41, 2.63)	2.33 (0.81, 6.71)	3.51 (1.30, 9.46)	9.6E-01	9.7E-01	1.32 (1.07, 1.63)	9.8E-03	6.1E-02	1.0E+00	6.67
Myristic acid	Fatty acids	Ref.	1.30 (0.59, 2.88)	1.50 (0.65, 3.47)	1.08 (0.43, 2.72)	9.7E-01	9.8E-01	1.14 (0.63, 2.05)	6.7E-01	8.1E-01	1.0E+00	0.58
Myristoleic acid	Fatty acids	Ref.	0.79 (0.37, 1.68)	1.50 (0.56, 4.00)	2.51 (1.04, 6.04)	3.6E-01	7.0E-01	1.43 (1.07, 1.91)	1.6E-02	7.4E-02	1.0E+00	6.00
Nonanoic acid	Fatty acids	Ref.	1.07 (0.47, 2.41)	0.57 (0.24, 1.35)	1.11 (0.44, 2.79)	3.1E-01	6.7E-01	0.91 (0.73, 1.13)	3.9E-01	5.9E-01	1.0E+00	1.36
Octanoic acid	Fatty acids	Ref.	0.62 (0.27, 1.44)	0.82 (0.33, 2.04)	1.43 (0.63, 3.24)	9.4E-01	9.6E-01	1.74 (0.88, 3.41)	1.1E-01	2.6E-01	1.0E+00	3.18
Oleic acid	Fatty acids	Ref.	1.00 (0.47, 2.11)	1.61 (0.76, 3.43)	1.89 (0.82, 4.36)	1.3E-01	5.2E-01	1.27 (0.94, 1.72)	1.2E-01	2.7E-01	1.0E+00	3.11
Palmitic acid	Fatty acids	Ref.	0.45 (0.21, 1.00)	0.65 (0.28, 1.51)	0.73 (0.31, 1.74)	6.4E-01	8.5E-01	1.04 (0.40, 2.67)	9.4E-01	9.6E-01	1.0E+00	0.09
Palmitoleic acid	Fatty acids	Ref.	0.56 (0.24, 1.34)	0.89 (0.40, 2.00)	2.24 (0.94, 5.33)	3.8E-01	7.0E-01	1.34 (1.06, 1.70)	1.6E-02	7.4E-02	1.0E+00	6.01
Pentadecanoic acid	Fatty acids	Ref.	0.88 (0.42, 1.83)	1.51 (0.69, 3.29)	1.07 (0.49, 2.38)	2.7E-01	6.2E-01	1.15 (0.76, 1.74)	5.1E-01	6.7E-01	1.0E+00	0.97
Ricinoleic acid	Fatty acids	Ref.	0.56 (0.24, 1.32)	1.95 (0.76, 5.02)	1.59 (0.72, 3.55)	6.4E-01	8.5E-01	1.25 (0.82, 1.91)	3.1E-01	5.1E-01	1.0E+00	1.70
Undecylenic acid	Fatty acids	Ref.	0.66 (0.31, 1.39)	0.72 (0.31, 1.66)	0.94 (0.42, 2.12)	1.5E-01	5.2E-01	0.98 (0.79, 1.20)	8.3E-01	9.2E-01	1.0E+00	0.28
3-Indolepropionic acid	Indoles	Ref.	0.77 (0.37, 1.58)	1.21 (0.59, 2.51)	0.96 (0.45, 2.04)	7.9E-01	8.6E-01	1.03 (0.91, 1.18)	6.2E-01	7.8E-01	1.0E+00	0.70
Indoleacetic acid	Indoles	Ref.	1.20 (0.58, 2.49)	0.53 (0.22, 1.29)	0.90 (0.41, 1.98)	3.3E-01	6.7E-01	1.02 (0.78, 1.32)	9.1E-01	9.5E-01	1.0E+00	0.13
AMP	Nucleotides	Ref.	0.55 (0.26, 1.16)	0.24 (0.10, 0.62)	0.37 (0.16, 0.86)	5.0E-01	7.4E-01	0.82 (0.66, 1.03)	9.4E-02	2.4E-01	1.0E+00	3.42
2-Furoic acid	Organic acids	Ref.	1.96 (0.84, 4.60)	1.57 (0.67, 3.66)	2.42 (0.97, 6.08)	7.3E-01	8.5E-01	1.51 (1.06, 2.16)	2.3E-02	1.0E-01	1.0E+00	5.45
2-Hydroxybutyric acid	Organic acids	Ref.	0.74 (0.34, 1.61)	1.28 (0.59, 2.76)	1.94 (0.95, 3.97)	3.3E-02	3.5E-01	1.40 (0.97, 2.00)	6.9E-02	2.0E-01	1.0E+00	3.86
3-Hydroxybutyric acid	Organic acids	Ref.	1.23 (0.56, 2.71)	0.96 (0.45, 2.08)	1.70 (0.73, 3.96)	2.2E-01	6.2E-01	1.23 (0.95, 1.59)	1.1E-01	2.6E-01	1.0E+00	3.19
3-Methyl-2-oxovaleric acid	Organic acids	Ref.	2.15 (0.97, 4.76)	0.84 (0.33, 2.11)	1.89 (0.83, 4.33)	2.4E-01	6.2E-01	1.40 (0.69, 2.84)	3.6E-01	5.5E-01	1.0E+00	1.49
Aconitic acid	Organic acids	Ref.	1.14 (0.40, 3.26)	3.53 (1.22, 10.22)	3.74 (1.26, 11.06)	7.6E-01	8.5E-01	6.89 (2.57, 18.43)	1.2E-04	2.8E-03	2.3E-02	13.01
Adipic acid	Organic acids	Ref.	0.67 (0.31, 1.47)	1.09 (0.50, 2.40)	0.80 (0.34, 1.89)	7.3E-01	8.5E-01	0.86 (0.66, 1.13)	2.9E-01	5.0E-01	1.0E+00	1.79
alpha-Hydroxyisobutyric acid	Organic acids	Ref.	0.62 (0.27, 1.38)	0.78 (0.36, 1.72)	1.25 (0.57, 2.73)	2.4E-01	6.2E-01	0.98 (0.74, 1.30)	8.9E-01	9.5E-01	1.0E+00	0.16
alpha-Ketoisovaleric acid	Organic acids	Ref.	1.66 (0.77, 3.58)	1.74 (0.81, 3.75)	1.64 (0.74, 3.60)	2.6E-02	3.4E-01	0.93 (0.53, 1.63)	8.0E-01	9.2E-01	1.0E+00	0.32
Azelaic acid	Organic acids	Ref.	0.96 (0.46, 2.02)	1.04 (0.47, 2.30)	1.26 (0.57, 2.80)	1.9E-01	5.6E-01	1.16 (0.80, 1.68)	4.4E-01	6.3E-01	1.0E+00	1.19

Metabolite	Class	Categorical analysis						Continuous analysis					
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	$P_{\text{non-linear}}^b$	FDR _{non-linear}^b}	OR _{doubling} (95% CI)	P value	FDR	P_{Bon}^c	S value	
Benzoic acid	Organic acids	Ref.	1.29 (0.57, 2.93)	0.87 (0.34, 2.21)	1.18 (0.47, 2.98)	2.3E-01	6.2E-01	7.30 (0.96, 55.32)	5.4E-02	1.7E-01	1.0E+00	4.20	
Citramalic acid	Organic acids	Ref.	0.48 (0.21, 1.13)	1.07 (0.48, 2.41)	0.82 (0.38, 1.76)	7.8E-01	8.6E-01	1.04 (0.73, 1.49)	8.3E-01	9.2E-01	1.0E+00	0.27	
Citric acid	Organic acids	Ref.	1.10 (0.43, 2.83)	1.70 (0.60, 4.80)	5.33 (1.94, 14.66)	2.5E-01	6.2E-01	12.86 (4.10, 40.30)	1.2E-05	3.6E-04	2.2E-03	16.37	
Erythronic acid	Organic acids	Ref.	1.09 (0.53, 2.21)	0.66 (0.31, 1.43)	0.95 (0.46, 1.98)	5.2E-01	7.4E-01	0.87 (0.59, 1.30)	5.1E-01	6.7E-01	1.0E+00	0.98	
Fumaric acid	Organic acids	Ref.	1.66 (0.76, 3.63)	1.80 (0.82, 3.99)	2.20 (0.95, 5.06)	4.7E-02	3.9E-01	1.12 (0.83, 1.52)	4.7E-01	6.5E-01	1.0E+00	1.09	
Glutaric acid	Organic acids	Ref.	1.21 (0.47, 3.13)	0.89 (0.37, 2.18)	3.05 (1.37, 6.80)	4.7E-03	1.2E-01	1.11 (1.00, 1.23)	5.1E-02	1.7E-01	1.0E+00	4.29	
Glycolic acid	Organic acids	Ref.	0.87 (0.36, 2.08)	1.26 (0.52, 3.04)	1.31 (0.58, 2.99)	6.8E-01	8.5E-01	2.42 (1.10, 5.33)	2.9E-02	1.2E-01	1.0E+00	5.13	
Guanidoacetic acid	Organic acids	Ref.	0.92 (0.42, 2.03)	0.47 (0.20, 1.09)	1.14 (0.53, 2.46)	5.4E-02	4.2E-01	1.28 (0.63, 2.57)	4.9E-01	6.6E-01	1.0E+00	1.02	
Isocitric acid	Organic acids	Ref.	2.36 (0.77, 7.24)	3.10 (1.11, 8.67)	9.22 (3.06, 27.83)	8.7E-01	9.2E-01	6.45 (2.98, 14.00)	2.3E-06	1.1E-04	4.4E-04	18.70	
Ketoleucine	Organic acids	Ref.	0.84 (0.39, 1.82)	0.91 (0.41, 2.00)	1.07 (0.49, 2.33)	1.4E-01	5.2E-01	1.01 (0.52, 1.97)	9.7E-01	9.7E-01	1.0E+00	0.04	
Lactic acid	Organic acids	Ref.	1.10 (0.55, 2.20)	0.42 (0.17, 1.02)	0.63 (0.27, 1.50)	8.8E-01	9.2E-01	0.81 (0.39, 1.66)	5.6E-01	7.3E-01	1.0E+00	0.83	
Maleic acid	Organic acids	Ref.	1.08 (0.48, 2.40)	1.39 (0.61, 3.17)	1.38 (0.64, 2.99)	3.2E-01	6.7E-01	1.15 (0.83, 1.59)	3.9E-01	5.9E-01	1.0E+00	1.34	
Malic acid	Organic acids	Ref.	1.27 (0.50, 3.24)	1.05 (0.42, 2.66)	4.33 (1.68, 11.15)	4.8E-01	7.4E-01	1.86 (1.15, 2.99)	1.1E-02	6.1E-02	1.0E+00	6.53	
Malonic acid	Organic acids	Ref.	0.59 (0.27, 1.28)	0.83 (0.38, 1.83)	0.99 (0.46, 2.14)	7.9E-01	8.6E-01	0.87 (0.70, 1.10)	2.5E-01	4.4E-01	1.0E+00	2.01	
Methylsuccinic acid	Organic acids	Ref.	0.93 (0.38, 2.28)	1.24 (0.51, 3.01)	2.32 (0.98, 5.52)	7.9E-02	4.7E-01	1.29 (1.06, 1.57)	1.1E-02	6.1E-02	1.0E+00	6.55	
Oxalic acid	Organic acids	Ref.	1.29 (0.60, 2.78)	1.13 (0.50, 2.58)	1.50 (0.61, 3.69)	2.5E-01	6.2E-01	0.95 (0.63, 1.43)	8.1E-01	9.2E-01	1.0E+00	0.31	
Oxoadipic acid	Organic acids	Ref.	0.67 (0.25, 1.78)	0.91 (0.38, 2.17)	1.30 (0.60, 2.83)	8.7E-01	9.2E-01	0.93 (0.67, 1.30)	6.7E-01	8.1E-01	1.0E+00	0.58	
Oxoglutaric acid	Organic acids	Ref.	1.41 (0.64, 3.08)	2.20 (0.99, 4.90)	4.67 (1.91, 11.40)	3.3E-03	1.2E-01	1.65 (1.11, 2.43)	1.2E-02	6.6E-02	1.0E+00	6.32	
Petroselinic acid	Organic acids	Ref.	0.72 (0.33, 1.55)	1.56 (0.75, 3.27)	1.81 (0.80, 4.10)	1.6E-01	5.2E-01	1.30 (0.95, 1.80)	1.1E-01	2.6E-01	1.0E+00	3.24	
Pimelic acid	Organic acids	Ref.	0.50 (0.21, 1.19)	0.34 (0.13, 0.88)	0.67 (0.30, 1.49)	4.0E-01	7.0E-01	0.97 (0.79, 1.19)	7.6E-01	9.0E-01	1.0E+00	0.40	
Pyruvic acid	Organic acids	Ref.	0.75 (0.36, 1.57)	1.01 (0.48, 2.12)	1.26 (0.54, 2.93)	3.8E-02	3.5E-01	0.90 (0.64, 1.26)	5.4E-01	7.1E-01	1.0E+00	0.88	
Succinic acid	Organic acids	Ref.	1.23 (0.50, 3.08)	0.90 (0.33, 2.43)	1.46 (0.52, 4.10)	9.5E-01	9.6E-01	1.71 (0.79, 3.70)	1.7E-01	3.4E-01	1.0E+00	2.56	
4-Hydroxyphenylpyruvic acid	Phenols	Ref.	0.94 (0.43, 2.09)	1.07 (0.47, 2.45)	1.00 (0.45, 2.21)	6.0E-01	8.2E-01	1.03 (0.78, 1.35)	8.5E-01	9.3E-01	1.0E+00	0.23	
Homovanillic acid	Phenols	Ref.	1.32 (0.54, 3.23)	1.88 (0.68, 5.21)	3.78 (1.48, 9.71)	1.9E-01	5.6E-01	3.19 (1.71, 5.98)	2.8E-04	4.8E-03	5.3E-02	11.78	
p-Hydroxyphenylacetic acid	Phenols	Ref.	1.74 (0.81, 3.76)	1.29 (0.57, 2.90)	1.62 (0.69, 3.82)	7.5E-01	8.5E-01	1.01 (0.85, 1.21)	8.9E-01	9.5E-01	1.0E+00	0.18	
2-Phenylpropionate	Phenylpropanoic acids	Ref.	2.75 (1.14, 6.61)	1.49 (0.67, 3.35)	1.68 (0.73, 3.87)	3.8E-01	7.0E-01	1.04 (0.87, 1.25)	6.7E-01	8.1E-01	1.0E+00	0.58	
3-Hydroxyphenylhydraacrylic acid	Phenylpropanoic acids	Ref.	0.72 (0.31, 1.70)	0.93 (0.37, 2.30)	0.44 (0.18, 1.11)	3.3E-01	6.7E-01	0.84 (0.67, 1.05)	1.3E-01	2.9E-01	1.0E+00	2.89	
Hydrocinnamic acid	Phenylpropanoic acids	Ref.	0.82 (0.33, 2.03)	1.18 (0.52, 2.70)	0.79 (0.33, 1.89)	2.7E-01	6.2E-01	1.05 (0.87, 1.25)	6.2E-01	7.8E-01	1.0E+00	0.69	
Hydroxyphenyllactic acid	Phenylpropanoic acids	Ref.	0.28 (0.10, 0.83)	0.75 (0.31, 1.85)	1.68 (0.69, 4.10)	4.6E-03	1.2E-01	2.11 (1.31, 3.41)	2.3E-03	2.2E-02	4.2E-01	8.79	

Metabolite	Class	Categorical analysis						Continuous analysis				
		Q1	OR _{Q2} (95% CI)	OR _{Q3} (95% CI)	OR _{Q4} (95% CI)	<i>P</i> _{non-linear} ^b	FDR _{non-linear} ^b	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^c	S value
Phenyllactic acid	Phenylpropanoic acids	Ref.	0.52 (0.22, 1.22)	0.77 (0.33, 1.80)	1.56 (0.69, 3.53)	1.6E-01	5.2E-01	1.53 (1.01, 2.30)	4.3E-02	1.5E-01	1.0E+00	4.53
N-Methylnicotinamide	Pyridines	Ref.	0.61 (0.27, 1.41)	1.64 (0.76, 3.51)	1.39 (0.65, 2.94)	5.2E-01	7.4E-01	1.26 (1.01, 1.56)	4.0E-02	1.4E-01	1.0E+00	4.65
3-Hydroxyisovaleric acid	SCFAs	Ref.	0.74 (0.35, 1.54)	0.74 (0.34, 1.57)	1.56 (0.70, 3.51)	1.4E-01	5.2E-01	1.20 (0.71, 2.04)	4.9E-01	6.6E-01	1.0E+00	1.02
Acetic acid	SCFAs	Ref.	1.38 (0.59, 3.21)	1.51 (0.64, 3.59)	2.14 (0.91, 5.04)	9.2E-02	4.9E-01	1.30 (0.96, 1.78)	9.5E-02	2.4E-01	1.0E+00	3.40
Butyric acid	SCFAs	Ref.	2.76 (1.03, 7.43)	6.79 (1.95, 23.66)	6.49 (1.59, 26.48)	8.0E-01	8.7E-01	4.17 (1.84, 9.46)	6.3E-04	9.8E-03	1.2E-01	10.63
Caproic acid	SCFAs	Ref.	0.99 (0.41, 2.39)	1.27 (0.48, 3.35)	1.82 (0.62, 5.32)	5.7E-01	8.0E-01	1.60 (0.66, 3.89)	3.0E-01	5.0E-01	1.0E+00	1.75
Ethylmethylacetic acid	SCFAs	Ref.	2.87 (1.13, 7.28)	2.87 (1.05, 7.85)	3.48 (1.24, 9.78)	6.1E-01	8.3E-01	2.10 (1.23, 3.60)	6.9E-03	4.6E-02	1.0E+00	7.19
Formic acid	SCFAs	Ref.	1.27 (0.54, 2.98)	1.59 (0.71, 3.55)	2.22 (0.89, 5.50)	8.6E-02	4.8E-01	1.57 (0.88, 2.78)	1.2E-01	2.8E-01	1.0E+00	3.01
Isobutyric acid	SCFAs	Ref.	0.38 (0.16, 0.89)	1.06 (0.45, 2.52)	0.61 (0.23, 1.64)	5.6E-02	4.2E-01	1.29 (0.62, 2.68)	4.9E-01	6.6E-01	1.0E+00	1.03
Isocaproic acid	SCFAs	Ref.	1.32 (0.57, 3.03)	0.78 (0.36, 1.69)	0.81 (0.37, 1.77)	3.2E-01	6.7E-01	0.71 (0.46, 1.10)	1.2E-01	2.7E-01	1.0E+00	3.05
Isovaleric acid	SCFAs	Ref.	0.79 (0.37, 1.72)	0.79 (0.35, 1.75)	1.76 (0.74, 4.14)	2.2E-01	6.2E-01	1.45 (1.04, 2.03)	3.0E-02	1.2E-01	1.0E+00	5.08
Pentanoic acid	SCFAs	Ref.	1.17 (0.50, 2.72)	1.06 (0.42, 2.70)	0.98 (0.39, 2.46)	2.9E-01	6.4E-01	0.99 (0.66, 1.48)	9.4E-01	9.6E-01	1.0E+00	0.08
Propanoic acid	SCFAs	Ref.	1.44 (0.58, 3.53)	3.47 (1.33, 9.01)	5.98 (2.01, 17.79)	1.2E-01	5.2E-01	6.80 (2.20, 21.05)	8.8E-04	1.3E-02	1.6E-01	10.15

a Conditioned on matching factors and adjusted for age, cigarette smoking, alcohol drinking, BMI, physical activity, CHFP score, medical history of hepatitis and cirrhosis, medical history of cholelithiasis and medical history of T2DM.

b Log₂-transformed metabolite concentrations was fitted with a 3-knots restricted cubic spline (10th, 50th, and 90th percentile).

c Bonferroni corrected *P* values.

Supplementary Table ST5 Association between selected metabolites and liver cancer risk after excluding participants with a follow-up time of less than 2 years

Metabolite	Class	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^b
beta-Alanine	Amino acids	0.85 (0.70, 1.04)	0.12	0.12	1.0
Creatine	Amino acids	0.53 (0.37, 0.75)	0.00033	0.00066	0.0093
Lysine	Amino acids	0.32 (0.16, 0.63)	0.00093	0.0017	0.026
Pipecolic acid	Amino acids	2.06 (1.40, 3.03)	0.00025	0.00054	0.0070
Tyrosine	Amino acids	4.37 (2.34, 8.16)	<0.0001	<0.0001	0.0001
GCA	Bile acids	1.54 (1.33, 1.79)	<0.0001	<0.0001	<0.0001
GCDCA	Bile acids	1.70 (1.42, 2.04)	<0.0001	<0.0001	<0.0001
GHCA	Bile acids	1.53 (1.18, 1.97)	0.0012	0.0020	0.032
GUDCA	Bile acids	1.25 (1.08, 1.44)	0.0023	0.0032	0.063
TCA	Bile acids	1.67 (1.42, 1.96)	<0.0001	<0.0001	<0.0001
TCDCA	Bile acids	1.69 (1.44, 1.98)	<0.0001	<0.0001	<0.0001
TDCA	Bile acids	1.41 (1.20, 1.66)	<0.0001	0.00011	0.001
D-Xylulose	Carbohydrates	2.28 (1.33, 3.90)	0.0026	0.0035	0.074
Fructose	Carbohydrates	1.27 (1.07, 1.50)	0.0057	0.0067	0.16
Rhamnose	Carbohydrates	1.57 (1.25, 1.97)	<0.0001	0.00028	0.0028
Acetylcarnitine	Carnitines	2.29 (1.47, 3.57)	0.00024	0.00054	0.0069
Myristoylcarnitine	Carnitines	2.30 (1.33, 3.98)	0.0030	0.0038	0.084
Oleylcarnitine	Carnitines	1.73 (1.18, 2.55)	0.0054	0.0066	0.15
Stearyl carnitine	Carnitines	1.55 (1.18, 2.06)	0.0020	0.0029	0.055
10Z-Heptadecenoic acid	Fatty acids	1.24 (1.04, 1.48)	0.019	0.020	0.53
Aconitic acid	Organic acids	2.76 (1.46, 5.24)	0.0018	0.0029	0.052
Citric acid	Organic acids	5.45 (2.63, 11.30)	<0.0001	<0.0001	0.00014
Isocitric acid	Organic acids	3.95 (2.41, 6.50)	<0.0001	<0.0001	<0.0001
Homovanillic acid	Phenols	3.03 (1.90, 4.84)	<0.0001	<0.0001	<0.0001
Hydroxyphenyllactic acid	Phenylpropanoic acids	2.00 (1.40, 2.86)	0.00015	0.00039	0.0043
Butyric acid	SCFAs	1.58 (1.10, 2.28)	0.013	0.015	0.38
Ethylmethylacetic acid	SCFAs	1.33 (0.93, 1.90)	0.12	0.12	1.0
Propanoic acid	SCFAs	2.83 (1.48, 5.42)	0.0016	0.0027	0.046

a Adjusted for age, cigarette smoking, alcohol drinking, BMI, physical activity, CHFP score, medical history of hepatitis and cirrhosis, medical history of cholelithiasis and medical history of T2DM.

b Bonferroni corrected *P* values.

Supplementary Table ST6 Association between plasma metabolite concentrations and liver cancer risk for participants without seropositive HBsAg or self-reported history of hepatobiliary diseases at blood collection

Metabolite	Class	OR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^b
beta-Alanine	Amino acids	0.82 (0.65, 1.04)	0.11	0.13	1.0
Creatine	Amino acids	0.75 (0.49, 1.15)	0.18	0.20	1.0
Lysine	Amino acids	0.58 (0.25, 1.32)	0.19	0.20	1.0
Pipecolic acid	Amino acids	1.72 (1.10, 2.69)	0.017	0.025	0.48
Tyrosine	Amino acids	3.87 (1.75, 8.57)	0.00085	0.0018	0.024
GCA	Bile acids	1.70 (1.38, 2.09)	<0.0001	<0.0001	<0.0001
GCDCA	Bile acids	1.85 (1.45, 2.38)	<0.0001	<0.0001	<0.0001
GHCA	Bile acids	1.66 (1.14, 2.42)	0.0085	0.013	0.24
GUDCA	Bile acids	1.22 (1.00, 1.48)	0.045	0.055	1.0
TCA	Bile acids	1.66 (1.34, 2.04)	<0.0001	<0.0001	<0.0001
TCDCA	Bile acids	1.60 (1.30, 1.98)	<0.0001	<0.0001	0.00029
TDCA	Bile acids	1.48 (1.18, 1.86)	0.00083	0.0018	0.023
D-Xylulose	Carbohydrates	2.24 (1.14, 4.40)	0.019	0.027	0.54
Fructose	Carbohydrates	1.27 (1.03, 1.55)	0.024	0.032	0.68
Rhamnose	Carbohydrates	1.75 (1.28, 2.39)	0.00043	0.0012	0.012
Acetylcarnitine	Carnitines	3.70 (2.03, 6.76)	<0.0001	<0.0001	0.00054
Myristoylcarnitine	Carnitines	3.42 (1.57, 7.44)	0.0019	0.0033	0.053
Oleylcarnitine	Carnitines	2.14 (1.30, 3.55)	0.0030	0.0049	0.083
Stearyl carnitine	Carnitines	1.87 (1.26, 2.76)	0.0018	0.0033	0.051
10Z-Heptadecenoic acid	Fatty acids	1.55 (1.21, 1.98)	0.00046	0.0012	0.013
Aconitic acid	Organic acids	6.28 (2.62, 15.04)	<0.0001	0.00013	0.0010
Citric acid	Organic acids	9.71 (3.66, 25.79)	<0.0001	<0.0001	0.00014
Isocitric acid	Organic acids	6.47 (3.26, 12.82)	<0.0001	<0.0001	<0.0001
Homovanillic acid	Phenols	3.23 (1.71, 6.09)	0.00030	0.00093	0.0084
Hydroxyphenyllactic acid	Phenylpropanoic acids	2.24 (1.37, 3.68)	0.0014	0.0028	0.039
Butyric acid	SCFAs	1.17 (0.75, 1.82)	0.48	0.48	1.0
Ethylmethylacetic acid	SCFAs	1.46 (0.92, 2.32)	0.11	0.13	1.0
Propanoic acid	SCFAs	2.43 (1.05, 5.61)	0.038	0.048	1.0

a Adjusted for age, cigarette smoking, alcohol drinking, BMI, physical activity, CHFP score, and history of T2DM.

b Bonferroni corrected *P* values.

Supplementary Table ST7 Association between plasma metabolite concentrations and liver cancer risk using Cox regression model

Metabolite	Class	HR _{doubling} (95% CI)	<i>P</i> value	FDR	<i>P</i> _{Bon} ^b
beta-Alanine	Amino acids	0.88 (0.80, 0.97)	0.010	0.049	1.0
Creatine	Amino acids	0.65 (0.54, 0.78)	<0.0001	<0.0001	0.00067
Lysine	Amino acids	0.46 (0.32, 0.65)	<0.0001	0.00024	0.0026
Pipecolic acid	Amino acids	1.24 (1.05, 1.45)	0.009	0.047	1.0
Tyrosine	Amino acids	2.42 (1.84, 3.20)	<0.0001	<0.0001	<0.0001
GCA	Bile acids	1.25 (1.17, 1.33)	<0.0001	<0.0001	<0.0001
GCDCA	Bile acids	1.30 (1.21, 1.40)	<0.0001	<0.0001	<0.0001
GHCA	Bile acids	1.25 (1.13, 1.38)	<0.0001	0.00020	0.0020
GUDCA	Bile acids	1.14 (1.06, 1.23)	0.00035	0.0035	0.066
TCA	Bile acids	1.25 (1.19, 1.32)	<0.0001	<0.0001	<0.0001
TCDCA	Bile acids	1.29 (1.22, 1.37)	<0.0001	<0.0001	<0.0001
TDCA	Bile acids	1.16 (1.08, 1.24)	<0.0001	0.00034	0.0044
D-Xylulose	Carbohydrates	1.65 (1.31, 2.09)	<0.0001	0.00036	0.0050
Fructose	Carbohydrates	1.15 (1.05, 1.25)	0.0017	0.012	0.31
Rhamnose	Carbohydrates	1.22 (1.08, 1.38)	0.0016	0.012	0.29
Acetylcarnitine	Carnitines	1.31 (1.05, 1.63)	0.016	0.063	1.0
Myristoylcarnitine	Carnitines	1.31 (1.05, 1.63)	0.015	0.063	1.0
Oleylcarnitine	Carnitines	1.27 (1.05, 1.53)	0.012	0.054	1.0
Stearyl carnitine	Carnitines	1.20 (1.04, 1.39)	0.012	0.053	1.0
10Z-Heptadecenoic acid	Fatty acids	1.07 (0.97, 1.17)	0.16	0.35	1.0
Aconitic acid	Organic acids	1.76 (1.28, 2.43)	0.00053	0.0049	0.098
Citric acid	Organic acids	2.22 (1.55, 3.19)	<0.0001	0.00024	0.0029
Isocitric acid	Organic acids	1.71 (1.36, 2.14)	<0.0001	<0.0001	0.00056
Homovanillic acid	Phenols	1.86 (1.53, 2.25)	<0.0001	<0.0001	<0.0001
Hydroxyphenyllactic acid	Phenylpropanoic acids	1.64 (1.38, 1.95)	<0.0001	<0.0001	<0.0001
Butyric acid	SCFAs	1.16 (0.96, 1.41)	0.12	0.29	1.0
Ethylmethylacetic acid	SCFAs	1.17 (0.99, 1.38)	0.072	0.22	1.0
Propanoic acid	SCFAs	1.47 (1.09, 1.98)	0.012	0.053	1.0

a Adjusted for age, cigarette smoking, alcohol drinking, BMI, physical activity, CHFP score, medical history of hepatitis and cirrhosis, medical history of cholelithiasis and medical history of T2DM.

b Bonferroni corrected *P* values.