

ONLINE SUPPLEMENTAL MATERIAL

**An amino acid signature associated with obesity predicts 2-year risk of
hypertriglyceridemia in school-age children**

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Supplemental Table 1. Abbreviations and internal standard used for measured analytes by FIA-MS/MS

Analyte	Name	Internal Standard
Ala	Alanine	$^2\text{H}_4\text{-Ala}$
Arg	Arginine	$^2\text{H}_4, ^{13}\text{C-Arg}$
Cit	Citrulline	$^2\text{H}_2\text{-Cit}$
Gly	Glycine	$^2\text{N}_2, ^{13}\text{C-Gly}$
Leu/Ileu	Leucine/Isoleucine	$^2\text{H}_3\text{-Leu}$
Met	Methionine	$^2\text{H}_3\text{-Met}$
Orn	Ornithine	$^2\text{H}_6\text{-Orn}$
Phe	Phenylalanine	$^{13}\text{C}_6\text{-Phe}$
Pro	Proline	$^{13}\text{C}_5\text{-Pro}$
Tyr	Tyrosine	$^{13}\text{C}_5\text{-Tyr}$
Val	Valine	$^2\text{H}_8\text{-Val}$
C0	Free carnitine	$^2\text{H}_9\text{-C0}$
C2	Acetyl carnitine	$^2\text{H}_3\text{-C2}$
C3	Propionyl carnitine	$^2\text{H}_3\text{-C3}$
C3DC/C4OH	Malonyl/3-hydroxy-buteryl carnitine	$^2\text{H}_3\text{-C4}$
C4	Butyryl carnitine	$^2\text{H}_3\text{-C4}$
C4DC/C5OH	Methylmalonyl/3-hydroxy-isovaleryl carnitine	$^2\text{H}_3\text{-C5}$
C5	Isovaleryl carnitine	$^2\text{H}_9\text{-C5}$
C5:1	Tiglyl carnitine	$^2\text{H}_9\text{-C5}$
C5DC/C6OH	Glutaryl/3-Hydroxy-hexanoyl carnitine	$^2\text{H}_6\text{-C5DC}$
C6	Hexanoyl carnitine	$^2\text{H}_3\text{-C6}$
C6DC	Adipyl carnitine	$^2\text{H}_6\text{-C5DC}$
C8	Octanoyl carnitine	$^2\text{H}_3\text{-C8}$
C8:1	Octenoyl carnitine	$^2\text{H}_3\text{-C8}$
C10	Decanoyl carnitine	$^2\text{H}_3\text{-C10}$
C10:1	Decenoyl carnitine	$^2\text{H}_3\text{-C10}$
C10:2	Decadienoyl carnitine	$^2\text{H}_3\text{-C10}$
C12	Dodecanoyl carnitine	$^2\text{H}_3\text{-C12}$
C12:1	Dodecenoyl carnitine	$^2\text{H}_3\text{-C12}$
C14	Tetradecanoyl (Myristoyl) carnitine	$^2\text{H}_3\text{-C14}$
C14:1	Tetradecenoyl carnitine	$^2\text{H}_3\text{-C14}$
C14:2	Tetradecadienoyl carnitine	$^2\text{H}_3\text{-C14}$
C14OH	3-Hydroxy-tetradecanoyl carnitine	$^2\text{H}_3\text{-C14}$
C16	Hexadecanoyl (Palmitoyl) carnitine	$^2\text{H}_3\text{-C16}$
C16:1	Hexadecenoyl carnitine	$^2\text{H}_3\text{-C16}$
C16OH	3-Hydroxy-hexadecanoyl carnitine	$^2\text{H}_3\text{-C16}$

Supplemental Table 2. Characteristics of normal-weight and obese children from the case-control study.

	Normal-weight			Obese			P value
	311/295			305/209			
	Percentile			Percentile			
	Median	25	75	Median	25	75	
Clinical							
Age (years)	9.9	8.3	11.3	10.1	8.6	11.5	0.137
Body weight (kg)	30	25	37	51	41	60	4.0x10⁻¹²⁵
Height (cm)	135	125	146	143	133	151	1.4x10⁻¹⁵
BMI (kg/m ²)	16.4	15.6	17.4	24.6	22.9	26.7	6.0x10⁻¹⁸³
BMI percentile	47.6	30.0	59.6	97.4	96.2	98.5	2.6x10⁻¹⁸³
BMI z score	-0.06	-0.52	0.24	1.94	1.77	2.17	2.7x10⁻¹⁸³
Fat mass (% of BW)	25.3	21.9	29.35	45.25	41.78	48.8	1.5x10⁻¹⁷⁰
Lean mass (% of BW)	74.7	70.7	78.1	54.8	51.2	58.2	1.5x10⁻¹⁷⁰
Systolic blood pressure percentile	32.5	14.5	55.2	58.0	34.6	81.5	2.0x10⁻³²
Diastolic blood pressure percentile	63.7	42.7	81.3	67.7	46.0	85.7	0.006
Biochemical							
Glucose (mg/dL)	89	85	95	91	86.75	96	0.001
Insulin (μ U/mL)	4.4	3.0	6.3	10.6	6.8	15.5	7.5x10⁻⁸¹
CRP (mg/dL)	0.027	0.01	0.076	0.202	0.092	0.389	6.5x10⁻⁶⁹
HOMA-IR	0.97	0.66	1.45	2.34	1.52	3.47	1.4x10⁻⁷⁸
Creatinine (mg/dL)	0.46	0.39	0.54	0.49	0.43	0.57	1.1x10⁻⁵
Uric acid (mg/dL)	4.5	4	5.2	5.5	4.7	6.3	7.4x10⁻⁴²
Lipids							
Triacylglycerol (mg/dL)	74	54	103	129	94	175	4.9x10⁻⁶⁶
Total cholesterol (mg/dL)	166	147	182	177	155	197	1.4x10⁻⁹
HDL-cholesterol (mg/dL)	51	45	59	41	35	47	2.9x10⁻⁵⁴
LDL-cholesterol (mg/dL)	97	82	111	106	91	121	1.2x10⁻⁹
Apo-B	71	61	82	82	71	95	2.0x10⁻²⁰
Liver enzymes							
AST (U/L)	29	25	33	30	25	36	0.007
ALT (U/L)	18	15	21	26	20	38	5.1x10⁻⁶¹
GGT (UL)	13	11	16	19	15	22	2.7x10⁻⁶¹

Significant P-values are shown in bold

Supplemental Table 3. Association of principal components with biochemical parameters in normal-weight and obese children.

Clinical					Normal-weight					Obese				
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	0.87	3.84	0.0001	0.0010	-0.12	-0.66	0.51	0.68	0.02	1.07	0.29	0.48		
PC2	5.08	14.64	1.6x10 ⁻⁴⁴	1.12x10 ⁻⁴²	0.86	2.51	0.01	0.048	0.04	1.46	0.15	0.30		
PC3	0.87	1.83	0.07	0.17	0.49	1.15	0.25	0.44	0.04	1.44	0.15	0.31		
PC4	0.11	0.20	0.83	0.90	0.28	0.62	0.54	0.69	0.00	-0.06	0.96	0.98		
PC5	-3.37	-5.79	9.4x10 ⁻⁹	2.2x10 ⁻⁷	-0.51	-1.20	0.23	0.42	0.05	0.99	0.32	0.51		
PC6	-1.54	-2.08	0.04	0.11	-0.50	-0.79	0.43	0.62	-0.04	-0.90	0.37	0.56		
Body fat %					Normal-weight					Obese				
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	0.48	5.35	1.1x10 ⁻⁷	2.2x10 ⁻⁶	0.14	2.17	0.03	0.10	0.11	1.72	0.09	0.21		
PC2	1.87	13.32	1.3x10 ⁻³⁷	2.7x10 ⁻³⁵	0.25	1.98	0.05	0.14	0.01	1.10	0.92	0.97		
PC3	0.29	1.52	0.13	0.28	-0.06	-0.37	0.71	0.83	0.05	0.39	0.70	0.82		
PC4	0.17	0.79	0.42	0.61	0.51	3.12	0.002	0.01	-0.14	-0.97	0.33	0.53		
PC5	-1.48	-6.39	2.5x10 ⁻¹⁰	7.6x10 ⁻⁹	-0.33	-2.21	0.03	0.09	-0.18	-0.88	0.38	0.57		
PC6	-0.39	-1.30	0.19	0.37	0.42	1.81	0.07	0.18	-0.18	-0.89	0.37	0.57		
Systolic blood					Normal-weight					Obese				
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	-0.02	-1.20	0.23	0.42	-0.08	-2.97	0.003	0.02	0.04	1.46	0.15	0.30		
PC2	0.08	2.57	0.01	0.04	0.05	1.02	0.31	0.50	0.10	2.21	0.03	0.09		
PC3	0.20	5.22	2.2x10 ⁻⁷	4.1x10 ⁻⁶	0.28	4.46	9.9x10 ⁻⁶	0.0001	0.13	2.69	0.01	0.03		
PC4	-0.12	-2.89	0.004	0.02	-0.22	-3.64	0.0003	0.002	-0.02	-0.41	0.68	0.81		
PC5	-0.01	-0.24	0.81	0.89	0.03	0.36	0.72	0.83	-0.07	-0.85	0.39	0.59		
PC6	-0.10	-1.81	0.07	0.18	-0.23	-2.72	0.007	0.03	0.05	0.65	0.51	0.68		
Diastolic blood					Normal-weight					Obese				
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	-1.76	-0.08	0.94	0.97	-63.92	-2.13	0.03	0.10	77.71	2.28	0.02	0.08		
PC2	78.70	1.98	0.047	0.14	87.07	1.61	0.11	0.24	38.25	0.64	0.52	0.68		
PC3	115.50	2.44	0.01	0.06	152.03	2.06	0.04	0.12	72.85	1.17	0.24	0.43		
PC4	36.66	0.72	0.47	0.64	26.29	0.37	0.71	0.83	61.75	0.86	0.39	0.59		
PC5	-38.21	-0.57	0.57	0.72	-88.68	-1.04	0.30	0.49	90.13	0.78	0.44	0.62		
PC6	66.49	0.97	0.33	0.53	8.40	0.09	0.93	0.97	169.89	1.75	0.08	0.20		
Biochemical					Normal-weight					Obese				
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	-0.0003	-0.38	0.70	0.83	-0.0011	-1.00	0.32	0.51	0.0005	0.51	0.61	0.76		
PC2	0.0063	4.91	1.0x10 ⁻⁶	1.9x10 ⁻⁵	0.0070	3.69	0.0002	0.002	0.0064	3.71	0.0002	0.002		
PC3	-0.0006	-0.41	0.68	0.81	-0.0014	-0.53	0.60	0.74	0.0001	0.07	0.94	0.97		
PC4	0.0020	1.24	0.22	0.41	0.0017	0.68	0.50	0.67	0.0023	1.07	0.29	0.48		
PC5	-0.0042	-1.92	0.06	0.15	-0.0058	-1.93	0.05	0.15	-0.0040	-1.17	0.24	0.43		
PC6	-0.0012	-0.54	0.59	0.74	0.0010	0.28	0.78	0.87	-0.0034	-1.19	0.24	0.42		
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	-0.013	-2.55	0.01	0.04	-0.022	-3.00	0.002	0.01	-0.011	-1.60	0.11	0.25		
PC2	0.088	9.77	1.4x10 ⁻²¹	7.9x10 ⁻²⁰	0.097	7.31	1.2x10 ⁻¹²	4.7x10 ⁻¹¹	0.076	6.47	2.4x10 ⁻¹⁰	7.6x10 ⁻⁹		
PC3	0.003	0.24	0.81	0.89	-0.001	-0.04	0.97	0.98	-0.006	-0.46	0.65	0.79		
PC4	0.037	3.20	0.001	0.008	0.072	4.11	4.6x10 ⁻⁵	0.0004	0.014	0.95	0.34	0.53		
PC5	-0.013	-0.76	0.45	0.62	-0.006	-0.24	0.81	0.89	-0.030	-1.25	0.21	0.40		
PC6	-0.028	-1.76	0.08	0.19	-0.036	-1.51	0.13	0.28	-0.015	-0.77	0.44	0.62		
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	0.013	1.09	0.27	0.47	-0.012	-0.62	0.54	0.69	0.017	1.20	0.23	0.42		
PC2	0.032	1.54	0.12	0.27	0.031	0.88	0.38	0.57	0.010	0.40	0.69	0.82		
PC3	0.008	0.35	0.73	0.84	-0.014	-0.32	0.75	0.86	0.009	0.35	0.73	0.84		
PC4	-0.070	-2.67	0.01	0.034	-0.079	-1.69	0.09	0.22	-0.048	-1.63	0.10	0.24		
PC5	0.072	1.74	0.08	0.20	0.087	1.36	0.17	0.34	0.059	1.21	0.23	0.42		
PC6	-0.063	-1.80	0.07	0.18	-0.119	-1.98	0.05	0.14	-0.032	-0.81	0.42	0.61		
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	-0.014	-2.53	0.01	0.045	-0.023	-2.99	0.002	0.015	-0.012	-1.61	0.11	0.24		
PC2	0.094	10.02	1.5x10 ⁻²²	1.5x10 ⁻²⁰	0.103	7.39	5.7x10 ⁻¹³	3.0x10 ⁻¹¹	0.081	6.74	1.6x10 ⁻¹¹	1.7x10 ⁻⁹		
PC3	0.001	0.11	0.91	0.97	-0.004	-0.23	0.82	0.89	-0.006	-0.46	0.65	0.79		
PC4	0.040	3.31	0.0009	0.006	0.076	4.09	5.1x10 ⁻⁵	0.0005	0.017	1.09	0.28	0.47		
PC5	-0.018	-0.95	0.34	0.53	-0.011	-0.42	0.68	0.81	-0.033	-1.34	0.18	0.35		
PC6	-0.027	-1.65	0.10	0.23	-0.032	-1.27	0.20	0.39	-0.017	-0.83	0.41	0.60		
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	-0.0019	-3.34	8.6x10 ⁻⁴	0.005	-0.0018	-2.36	0.02	0.07	-0.0017	-1.98	0.049	0.14		
PC2	0.0003	0.26	0.79	0.88	-0.0011	-0.77	0.44	0.62	0.0011	0.77	0.44	0.62		
PC3	0.0056	4.69	3.1x10 ⁻⁶	4.6x10 ⁻⁵	0.0055	2.89	0.004	0.02	0.0052	3.43	0.0006	0.005		
PC4	-0.0037	-2.92	0.003	0.018	-0.0057	-3.14	0.002	0.01	-0.0018	-1.04	0.30	0.49		
PC5	-0.0013	-0.76	0.45	0.62	-0.0037	-1.69	0.09	0.22	0.0033	1.16	0.25	0.43		
PC6	-0.0005	-0.27	0.79	0.88	-0.0024	-0.96	0.34	0.53	0.0027	1.11	0.27	0.46		
3MI percentile	All individuals				β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted										
PC1	0.0030	4.79	1.9x10 ⁻⁶	3.1x10 ⁻⁵	0.0041	4.82	1.9x10 ⁻⁶	3.1x10 ⁻⁵	0.0013	1.43	0.15	0.31		
PC2	-0.0035	-3.16	0.002	0.009	-0.0056	-3.69	0.0002	0.002	-0.0021	-1.33	0.19	0.36		
PC3	0.0048	3.58	0.0004	0.003	0.0065	3.12	0.002	0.01	0.0027	1.63	0.10	0.24		
PC4	-0.0066	-4.68	3.2x10 ⁻⁶	4.6x10 ⁻⁵	-0.0084	-4.20	3.1x10 ⁻⁵	0.0003	-0.0053	-2.76	0.006	0.028		
PC5	0.0023	1.21	0.23	0.42	-0.0001	-0.04	0.97	0.98	0.0052	1.67	0.10	0.22		
PC6	0.0066	3.43	0.0006	0.004	0.0086	3.14	0.002	0.01	0.0061	2.36	0.019	0.07		

Lipids						Normal-weight						Obese								
Triacylglycerol	All individuals					β	t	P value	Adjusted	P	β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted	P															
PC1	-0.008	-2.05	0.04		0.12	-0.025	-4.69	3.5x10⁻⁶		4.8x10⁻⁵	0.007	1.21	0.23		0.42	0.062	6.33	5.5x10⁻¹⁰		1.6x10⁻⁸
PC2	0.067	10.15	3.4x10⁻²³		4.5x10⁻²¹	0.071	7.75	1.1x10⁻¹⁴		2.0x10⁻¹²	0.006	0.60	0.55		0.70	-0.013	-0.96	0.34		0.53
PC3	0.001	0.15	0.88		0.95	0.072	5.90	6.1x10⁻⁹		1.5x10⁻⁷	-0.006	-0.47	0.64		0.78	-0.009	-0.61	0.54		0.70
PC4	0.030	3.38	0.0008		0.005	-0.045	-2.28	0.02		0.02	-0.045	-2.28	0.02		0.08	-0.031	-1.86	0.06		0.17
PC5	-0.022	-1.91	0.06		0.15	-0.045	-2.61	0.009		0.04										
PC6	-0.038	-3.17	0.001		0.009															
Total cholesterol						Normal-weight						Obese								
PC1	All individuals					β	t	P value	Adjusted	P	β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted	P															
PC1	0.0013	0.85	0.40		0.59	0.0002	0.12	0.91		0.96	0.0024	1.02	0.31		0.50	0.0066	1.80	0.07		0.18
PC2	0.0073	2.76	0.006		0.028	0.0141	2.84	0.005		0.02	0.0025	0.59	0.55		0.71	0.0010	0.21	0.83		0.90
PC3	0.0069	2.15	0.03		0.10	-0.0021	-0.37	0.71		0.83	-0.0054	-0.69	0.49		0.66	-0.0022	-0.04	0.97		0.98
PC4	0.0002	0.05	0.96		0.98	-0.0039	-0.59	0.56		0.71	-0.0007	-0.10	0.92		0.97	0.0002	0.05	0.96		0.98
PC5	-0.0038	-0.84	0.40		0.59	0.0011	0.66	0.51		0.68	-0.0015	-0.80	0.42		0.61	-0.0019	-0.63	0.53		0.69
PC6	-0.0020	-0.43	0.66		0.80	0.0086	2.14	0.03		0.10	0.0026	0.78	0.44		0.62	0.0010	0.26	0.80		0.88
DL-cholesterol						Normal-weight						Obese								
PC1	All individuals					β	t	P value	Adjusted	P	β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted	P															
PC1	-0.0004	-0.33	0.74		0.85	0.0011	0.66	0.51		0.68	-0.0015	-0.80	0.42		0.61	-0.0019	-0.63	0.53		0.69
PC2	-0.0042	-1.96	0.05		0.14	0.0086	2.14	0.03		0.10	0.0026	0.78	0.44		0.62	0.0010	0.26	0.80		0.88
PC3	0.0038	1.48	0.14		0.29	-0.0086	-1.85	0.06		0.17	0.0022	0.37	0.71		0.83	-0.0086	-1.85	0.06		0.17
PC4	0.0040	1.45	0.15		0.30	0.0003	0.05	0.96		0.98	0.0106	2.09	0.04		0.11	0.0010	0.26	0.80		0.88
PC5	-0.0024	-0.67	0.50		0.67	0.0003	0.05	0.96		0.98	0.0106	2.09	0.04		0.11	-0.0086	-1.85	0.06		0.17
PC6	0.0064	1.74	0.08		0.20	0.0003	0.05	0.96		0.98	0.0106	2.09	0.04		0.11	0.0003	0.05	0.96		0.98
DL-cholesterol						Normal-weight						Obese								
PC1	All individuals					β	t	P value	Adjusted	P	β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted	P															
PC1	0.0152	1.40	0.16		0.32	0.0145	1.04	0.30		0.49	0.0137	0.78	0.44		0.62	0.0029	0.11	0.91		0.97
PC2	0.0026	0.13	0.89		0.95	0.0029	0.11	0.91		0.97	-0.0008	-0.03	0.98		0.98	0.0936	2.74	0.006		0.029
PC3	0.0395	1.79	0.07		0.18	0.0936	2.74	0.006		0.029	0.0084	0.29	0.77		0.87	-0.0612	-1.84	0.07		0.17
PC4	-0.0456	-1.91	0.06		0.15	-0.0612	-1.84	0.07		0.17	-0.0237	-0.68	0.50		0.67	0.0394	0.99	0.32		0.51
PC5	0.0316	1.01	0.31		0.51	0.0394	0.99	0.32		0.51	0.0249	0.45	0.65		0.79	-0.0125	-0.28	0.78		0.87
PC6	-0.0152	-0.47	0.64		0.78	-0.0125	-0.28	0.78		0.87	-0.0203	-0.44	0.66		0.80	-0.0125	-0.28	0.78		0.87
Apo B						Normal-weight						Obese								
PC1	All individuals					β	t	P value	Adjusted	P	β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted	P															
PC1	-0.0037	-1.67	0.10		0.22	-0.0098	-2.74	0.006		0.029	-0.0008	-0.27	0.79		0.88	0.0085	1.33	0.18		0.36
PC2	0.0042	1.06	0.29		0.49	0.0085	1.33	0.18		0.36	0.0004	0.07	0.94		0.97	0.0126	1.58	0.11		0.25
PC3	0.0041	0.92	0.36		0.55	0.0126	1.58	0.11		0.25	-0.0002	-0.04	0.97		0.98	0.0036	0.41	0.68		0.81
PC4	0.0001	0.02	0.99		0.99	0.0036	0.41	0.68		0.81	-0.0002	-0.04	0.97		0.98	0.0111	0.95	0.34		0.53
PC5	0.0088	1.14	0.25		0.44	0.0111	0.95	0.34		0.53	0.0071	0.69	0.49		0.66	-0.0085	-0.76	0.44		0.62
PC6	0.0006	0.08	0.93		0.97	-0.0085	-0.76	0.44		0.62	0.0063	0.74	0.46		0.63					
Liver enzymes						Normal-weight						Obese								
AST	All individuals					β	t	P value	Adjusted	P	β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted	P															
PC1	-0.0007	-3.66	0.0002		0.002	-0.0004	-1.79	0.07		0.18	-0.0008	-2.61	0.009		0.04	0.0013	0.85	0.40		0.59
PC2	0.0007	2.12	0.03		0.10	0.0013	3.43	0.0006		0.004	0.0002	0.39	0.70		0.82	0.0003	0.47	0.64		0.78
PC3	-0.0013	-3.17	0.001		0.009	0.0003	0.47	0.64		0.78	-0.0021	-3.71	0.0002		0.002	-0.0003	-0.57	0.57		0.72
PC4	-0.0009	-2.20	0.03		0.09	-0.0003	-0.57	0.57		0.72	-0.0015	-2.28	0.02		0.08	0.0004	0.59	0.56		0.71
PC5	0.0002	0.30	0.77		0.87	0.0004	0.59	0.56		0.71	0.0001	0.07	0.94		0.97	-0.0014	-1.99	0.047		0.14
PC6	-0.0014	-2.39	0.02		0.06	-0.0014	-1.99	0.047		0.14	-0.0012	-1.32	0.19		0.37					
ALT						Normal-weight						Obese								
PC1	All individuals					β	t	P value	Adjusted	P	β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted	P															
PC1	-0.0005	-3.30	0.0009		0.006	-0.0002	-1.16	0.25		0.44	-0.0005	-2.54	0.01		0.05	0.0011	3.38	0.0007		0.005
PC2	0.0002	0.94	0.35		0.54	0.0000	0.08	0.93		0.97	-0.0004	-1.08	0.28		0.48	0.0000	0.08	0.93		0.97
PC3	-0.0005	-1.51	0.13		0.28	0.0001	0.24	0.81		0.89	-0.0006	-1.53	0.13		0.28	0.0001	0.24	0.81		0.89
PC4	0.0001	0.29	0.77		0.87	0.0003	0.51	0.61		0.76	0.0001	0.14	0.89		0.95	-0.0001	-0.16	0.76		0.76
PC5	0.0001	0.28	0.78		0.87	-0.0005	-0.76	0.45		0.62	-0.0001	-0.16	0.87		0.93	0.0009	1.50	0.13		0.28
PC6	0.0002	0.53	0.60		0.74	0.0009	1.50	0.13		0.28	0.0009	1.50	0.13		0.28					
GGT						Normal-weight						Obese								
PC1	All individuals					β	t	P value	Adjusted	P	β	t	P value	Adjusted	P	β	t	P value	Adjusted	P
	β	t	P value	Adjusted	P															
PC1	-0.0009	-2.67	0.008		0.03	0.0011	2.49	0.01		0.05	-0.0016	-3.18	0.002		0.009	-0.0005	-0.70	0.48		0.66
PC2	-0.0003	-0.50	0.61		0.76	-0.0005	-0.70	0.48		0.66	-0.0009	-0.97	0.33		0.53	-0.0021	-2.14	0.03		0.10
PC3	-0.0032	-4.58	5.1x10⁻⁶		6.6x10⁻⁵	0.0009	0.95	0.34		0.53	-0.0039	-4.17	3.6x10⁻⁵		3.9x10⁻⁴	0.0003	0.28	0.78		0.87
PC4	0.0001	0.19	0.85		0.92	0.0023	2.04	0.04		0.12	-0.0005	-0.29	0.77		0.87	0.0003	0.28	0.78		0.87
PC5	0.0001	0.09	0.93		0.97	0.0008	0.56	0.58		0.72	-0.0007	-0.46	0.65		0.79	0.0001	0.09	0.93		0.97
PC6	-0.0006	-0.63	0.53		0.69	0.0008	0.56	0.58		0.72	-0.0007	-0.46	0.65		0.79					

The beta value is given for the Box-Cox transformed variables. Insulin, CRP, ApoB, glucose, TG, total cholesterol and HOMA-IR were log-transformed. Creatinine and fat mass were square root-transformed. Other variables were transformed according to the following λ factors: $\lambda=2$ for diastolic blood pressure percentile, $\lambda=1$ for ALT, $\lambda=-0.5$ for GGT and AST, and $\lambda=0.25$ for uric acid and HDL cholesterol. The multivariate model was adjusted by gender, age and BMI percentile. P-values were corrected by Fdr and significant values are shown in bold. Significant P-values are shown in bold.

Supplemental Table 4. Characteristics of the cross-sectional study of Mexican children.

	All subjects (554)		
	M/F (278/276)		
		Percentile	
	Median	25	75
Clinical			
Age (years)	10.0	8.4	11.5
Body weight (kg)	36.0	27.3	45.0
Height (cm)	138.2	127.4	147.3
BMI (kg/m ²)	19.0	16.9	21.1
BMI percentile	81.3	60.1	90.9
BMI z score	0.89	0.22	1.34
Fat mass (% of BW)	33.8	25.1	40.4
Lean mass (% of BW)	66.2	59.5	74.9
Systolic blood pressure percentile	38.0	21.4	58.3
Diastolic blood pressure percentile	75.5	59.7	86.0
Biochemical			
Glucose (mg/dL)	91	86	96
Insulin (μ U/mL)	5.7	4	8.8
CRP (mg/dL)	0.03	0.01	0.10
HOMA-IR	1.28	0.87	1.97
Creatinine (mg/dL)	0.47	0.41	0.54
Uric acid (mg/dL)	4.7	4.1	5.6
Lipids			
Triacylglycerol (mg/dL)	86	61	121
Total cholesterol (mg/dL)	166	148	187
HDL-cholesterol (mg/dL)	49	41	57
LDL-cholesterol (mg/dL)	98	83	113
Liver enzymes			
AST (U/L)	30	26	34
ALT (U/L)	19	16	24
GGT (UL)	14	12	17

Supplemental Table 5. Effect of PC2-Z on metabolic traits in the cross-sectional study of Mexican children.

	All subjects (554) M/F (278/276)			
	β	t	P value	Adjusted P
Clinical				
BMI percentile	0.899	3.089	0.002	0.011
Fat mass (% of BW)	0.388	4.089	5.0x10⁻⁵	0.0006
Systolic blood pressure percentile	-0.004	-0.219	0.827	0.879
Diastolic blood pressure percentile	-1.096	-0.049	0.961	0.980
Biochemical				
Glucose (mg/dL)	-0.002	-2.022	0.044	0.104
Insulin (μ U/mL)	0.014	2.698	0.007	0.036
CRP (mg/dL)	-0.025	-2.485	0.014	0.057
HOMA-IR	0.013	2.334	0.020	0.066
Creatinine (mg/dL)	0.000	-0.634	0.526	0.711
Uric acid (mg/dL)	0.001	1.936	0.053	0.116
Lipids				
Triacylglycerol (mg/dL)	0.017	4.324	1.8x10⁻⁵	0.0003
Total cholesterol (mg/dL)	0.002	1.429	0.153	0.240
HDL-cholesterol (mg/dL)	-0.005	-2.589	0.010	0.045
LDL-cholesterol (mg/dL)	0.013	1.159	0.247	0.363
Liver enzymes				
AST (U/L)	0.000	-2.313	0.021	0.066
ALT (U/L)	0.000	-2.233	0.026	0.076
GGT (U/L)	-0.001	-4.937	1.1x10⁻⁶	4.9x10⁻⁵

The beta value is given for the Box-Cox transformed variables. Insulin, ApoB, glucose, TG, total cholesterol, HDL-cholesterol and HOMA-IR were log-transformed. Creatinine, systolic blood pressure percentile and LDL-cholesterol were square root-transformed. Other variables were transformed according to the following λ factors: $\lambda=2$ for diastolic blood pressure percentile, $\lambda=-1$ for ALT, $\lambda=-0.9$ for GGT, $\lambda=-0.5$ for AST, $\lambda=-0.25$ for CRP and $\lambda=0.25$ for uric acid. The association of hepatic enzymes and CRP with PC2-Z is positive, however due to the nature of the transformation ($\lambda=-x$) the β appears negative. The multivariate model was adjusted by gender, age and BMI percentile. Significant P-values are shown in bold.

Supplemental Table 6. Effect of PC2-Z on metabolic traits in the cross-sectional study of Mexican children stratified by weight status.

Clinical	Underweight (41)			Normal-weight (285)			Overweight (177)			Obese (51)		
	β	P value	Adjusted P	β	P value	Adjusted P	β	P value	Adjusted P	β	P value	Adjusted P
Fat mass (% of BW)	0.026	0.146	0.431	0.022	0.056	0.270	0.018	0.142	0.431	0.025	0.196	0.494
Systolic blood pressure percentile	0.066	0.246	0.519	-0.014	0.641	0.822	-0.019	0.589	0.813	-0.073	0.227	0.519
Diastolic blood pressure percentile	8.083	0.919	0.961	7.921	0.811	0.915	-35.957	0.424	0.740	8.408	0.917	0.961
Biochemical												
Glucose (mg/dL)	-0.001	0.706	0.842	-0.001	0.242	0.519	-0.002	0.165	0.449	-0.001	0.600	0.813
Insulin (μ U/mL)	-0.014	0.614	0.813	0.009	0.263	0.521	0.019	0.041	0.252	0.031	0.053	0.270
CRP (mg/dL)	-0.038	0.571	0.813	0.001	0.945	0.972	-0.054	0.002	0.064	-0.021	0.622	0.813
HOMA-IR	-0.016	0.604	0.813	0.006	0.424	0.740	0.018	0.048	0.270	0.030	0.063	0.285
Creatinine (mg/dL)	-0.001	0.596	0.813	0.000	0.804	0.915	-0.001	0.252	0.519	-0.001	0.673	0.832
Uric acid (mg/dL)	0.001	0.751	0.881	0.001	0.492	0.780	0.002	0.137	0.431	0.002	0.493	0.780
Lipids												
Triacylglycerol (mg/dL)	0.000	0.966	0.972	0.015	9.9×10^{-3}	0.096	0.023	6.7×10^{-3}	0.096	0.033	0.025	0.168
Total cholesterol (mg/dL)	0.004	0.493	0.780	0.000	0.865	0.949	0.005	0.144	0.431	-0.001	0.821	0.915
HDL-cholesterol (mg/dL)	0.002	0.706	0.842	-0.004	0.152	0.432	-0.007	0.080	0.334	-0.015	0.024	0.168
LDL-cholesterol (mg/dL)	0.026	0.444	0.755	0.001	0.972	0.972	0.032	0.176	0.461	-0.044	0.412	0.740
Liver enzymes												
AST (U/L)	0.000	0.414	0.740	0.000	0.661	0.832	0.000	0.268	0.521	-0.002	0.008	0.096
ALT (U/L)	0.000	0.911	0.961	0.000	0.214	0.519	0.000	0.518	0.782	-0.001	0.005	0.096
GGT (U/L)	-0.001	0.507	0.782	-0.001	0.009	0.096	-0.001	0.022	0.168	-0.002	0.000	0.023

The beta value is given for the Box-Cox transformed variables. Insulin, ApoB, glucose, TG, total cholesterol, HDL-cholesterol and HOMA-IR were log-transformed. Creatinine, systolic blood pressure percentile and LDL-cholesterol were square root-transformed. Other variables were transformed according to the following λ factors: $\lambda=2$ for diastolic blood pressure percentile, $\lambda=-1$ for ALT, $\lambda=-0.9$ for GGT, $\lambda=-0.5$ for AST, $\lambda=-0.25$ for CRP and $\lambda=0.25$ for uric acid. The association of hepatic enzymes and CRP with PC2-Z is positive, however due to the nature of the transformation ($\lambda=-x$) the β appears negative. The multivariate model was adjusted by gender, age and BMI percentile. Significant P-values are shown in bold.

Supplemental Table 7. Characteristics of Mexican children in the longitudinal cohort, at baseline and after 2 years.

	All subjects T0 (301) M/F (137/164)			All subjects T1			P value
	Median	Percentile		Median	Percentile		
		25	75		25	75	
Clinical							
Age (years)	8.7	7.3	9.8	10.7	9.3	11.9	
Body weight (kg)	31	24	39	40	32	49	8.8x10⁻⁵⁰
Height (cm)	131	123	138	143	135	151	1.4x10⁻⁵⁰
BMI (kg/m ²)	17.6	15.9	20.7	19.5	17.0	22.8	9.1x10⁻³⁵
BMI percentile	77.8	47.2	95.0	80.6	47.9	94.5	0.632
BMI z score	0.76	-0.09	1.61	0.87	-0.05	1.59	0.789
Fat mass (% of BW)	31.0	24.4	38.2	35.6	26.6	41.6	4.6x10⁻¹⁸
Lean mass (% of BW)	69.0	61.8	75.7	64.4	58.4	73.4	1.7x10⁻¹⁸
Systolic blood pressure percentile	56	31	81	34	15	62	1.3x10⁻¹¹
Diastolic blood pressure percentile	64	45	82	63	43	85	0.846
Biochemical							
Glucose (mg/dL)	90	85	95	89	84	95	0.046
Insulin (μ U/mL)	5.0	3.0	7.8	6.4	4.2	10.0	1.9x10⁻¹⁰
CRP (mg/dL)	0.06	0.03	0.17	0.06	0.02	0.19	0.562
HOMA-IR	1.12	0.64	1.73	1.42	0.86	2.32	4.0x10⁻⁹
Creatinine (mg/dL)	0.80	0.40	1.00	0.48	0.43	0.54	8.4x10⁻¹³
Uric acid (mg/dL)	5.0	4.0	5.5	5.1	4.3	5.9	1.5x10⁻¹¹
Lipids							
Triacylglycerol (mg/dL)	92	59	131	94	61	133	0.543
Total cholesterol (mg/dL)	175	155	193	167	149	183	8.2x10⁻⁷
HDL-cholesterol (mg/dL)	48	40	57	47	40	56	0.02
LDL-cholesterol (mg/dL)	104	87	121	97	83	113	2.5x10⁻⁸
Apo-B	77	67	87	77	65	88	0.837
Liver enzymes							
AST (U/L)	29	26	34	29	24.5	33	0.049
ALT (U/L)	19	15	22	20	17	26.5	9.5x10⁻⁷
GGT (UL)	13	11	16	15	12	19	2.5x10⁻¹⁰

Significant P-values are shown in bold

Supplemental Table 8. Effect of baseline PC2-Z on future metabolic traits in Mexican children of the longitudinal cohort.

	All subjects T0 (301) M/F (137/164)			Adjusted <i>P</i>
	β	t	<i>P</i> value	
Clinical				
BMI percentile	2.377	4.640	5.3x10⁻⁶	5 x10⁻⁵
Fat mass (% of BW)	0.950	5.293	2.4x10⁻⁷	4.5x10⁻⁶
Systolic blood pressure percentile	0.058	1.377	0.170	0.248
Diastolic blood pressure percentile	0.804	1.888	0.060	0.127
Biochemical				
Glucose (mg/dL)	0.003	1.709	0.089	0.153
Insulin (μ U/mL)	0.026	2.245	0.026	0.081
CRP (mg/dL)	0.029	1.183	0.238	0.282
HOMA-IR	0.018	1.837	0.067	0.128
Creatinine (mg/dL)	-0.002	-1.242	0.215	0.273
Uric acid (mg/dL)	0.009	2.467	0.014	0.054
Lipids				
Triacylglycerol (mg/dL)	0.038	4.327	2.1x10⁻⁵	1.3x10⁻⁴
Total cholesterol (mg/dL)	0.007	2.144	0.033	0.089
HDL-cholesterol (mg/dL)	-0.006	-1.402	0.162	0.248
LDL-cholesterol (mg/dL)	0.150	0.316	0.752	0.752
Apo-B	0.000	-1.264	0.207	0.273
Liver enzymes				
AST (U/L)	0.008	1.987	0.048	0.114
ALT (U/L)	-0.001	-1.100	0.272	0.287
GGT (U/L)	-0.001	-1.143	0.254	0.284

The beta value is given for the Box-Cox transformed variables. CRP, insulin, glucose, TG, uric acid, TG, total cholesterol, HDL-cholesterol and AST were log-transformed. HOMA-IR and systolic blood pressure percentile were square root-transformed. Other variables were transformed according to the following λ factors: $\lambda=-0.5$ for ApoB, ALT and GGT. The remainder variables were normally distributed. The multivariate model was adjusted by gender, age and BMI percentile. Significant *P*-values are shown in bold.

Supplemental Table 9. Associations between baseline amino acids levels and hypertriglyceridemia

Amino acid	OR	95 % Confidence interval		P value
		Lower CI	Upper CI	
Arginine	1.73	0.97	3.14	0.0650
Leucine/Isoleucine	1.86	1.05	3.3	0.0300
Phenylalanine	2.12	1.21	3.81	0.0094
Tyrosine	1.37	0.82	2.31	0.2281
Valine	1.61	0.94	2.77	0.0778
Proline	0.976	0.59	1.62	0.9272

Regression adjusted for age, sex, sampling calendar year, baseline BMI percentile, HOMA and serum TG