Metabolomic profiles of childhood obesity

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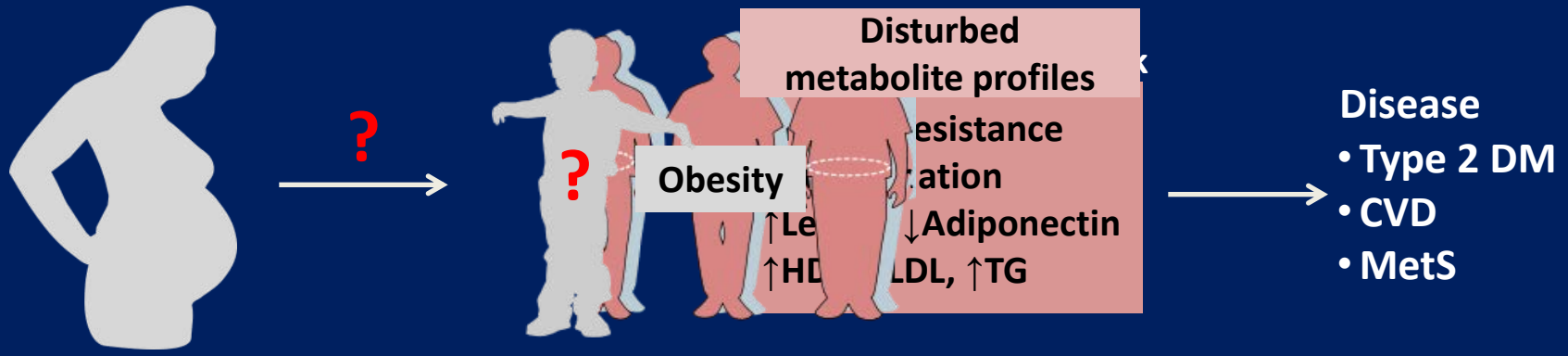
Background

The role of metabolomics



Research aims

Aim 1

Obese vs. lean → **Difference in metabolite profiles?**

Aim 2

Metabolite profiles → **Classic biomarkers**

HOMA-IR ● leptin, adiponectin
triglycerides ● CRP, IL-6

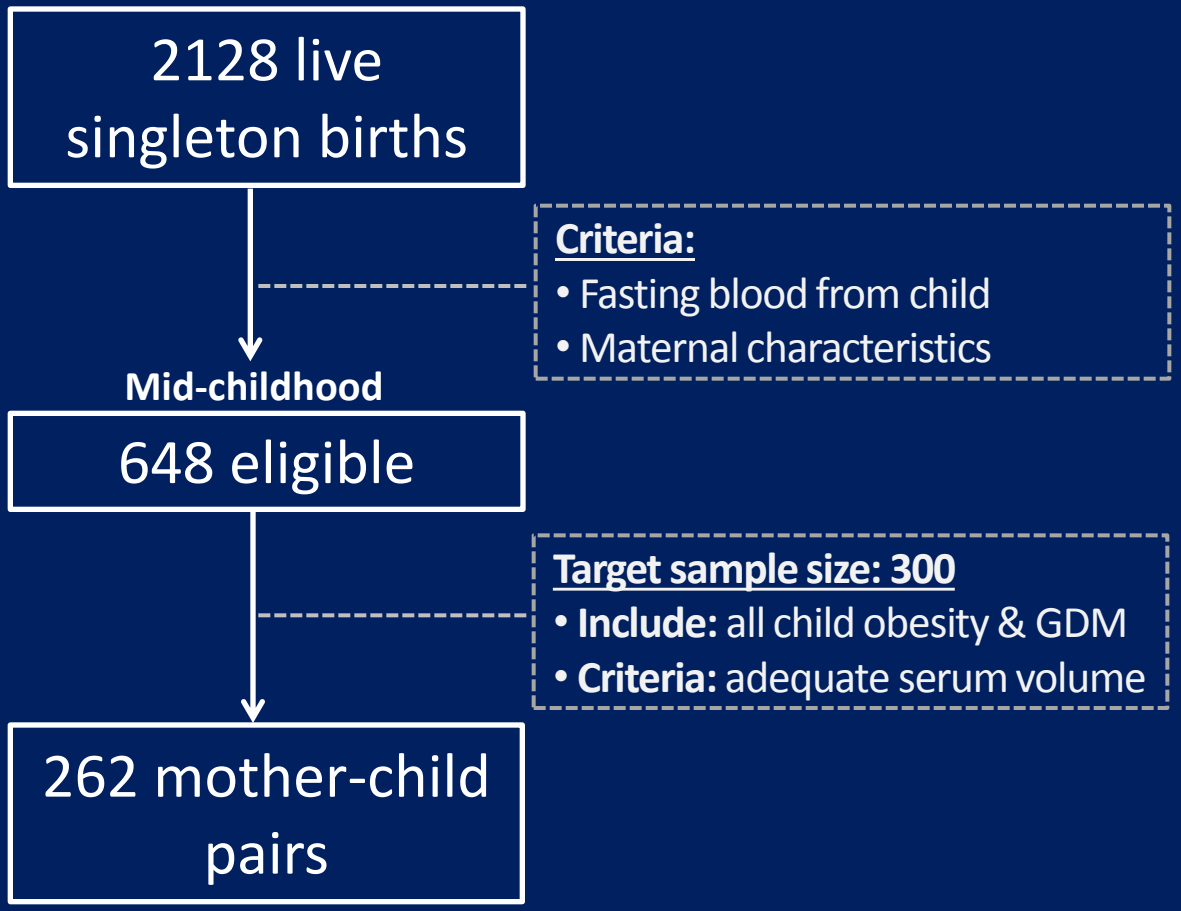
Aim 3

Maternal peripartum characteristics → **Child metabolite profile**

obesity ● excessive GWG
gestational diabetes

Study population

PROJECT Viva | *A Study of Health for the Next Generation*

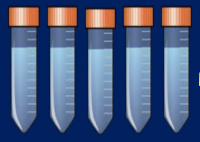


Study population

Characteristics of 262 Project Viva mother-child pairs

	Mean ± SD or % (N)
Child	
Child's age (years)	8.0 ± 0.9
Female	50% (131)
Obesity (BMI ≥95th percentile)	32.1% (84)
Race/ethnicity	
White	56.3% (147)
African American	24.1% (63)
Hispanic	6.9 %(18)
Mother	
Mother's age at enrollment (years)	32.0 ± 5.8
Pre-pregnancy obesity (BMI >30 kg/m^2)	22.5% (59)
Excessive gestational weight gain	58.8% (154)
Gestational diabetes	8.4% (22)

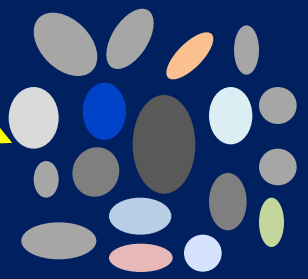
Methods



Serum
(*n* = 262)

Step 1:
Untargeted metabolomic profiling
345 metabolites

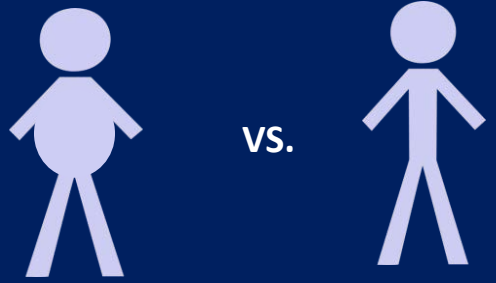
Step 2:
Principal components analysis (PCA)



18 factors

Step 3:
Compare factor scores

Obese (BMI≥95th %ile) vs. Lean (BMI<85th %ile)



***n* = 84** ***n* = 150**

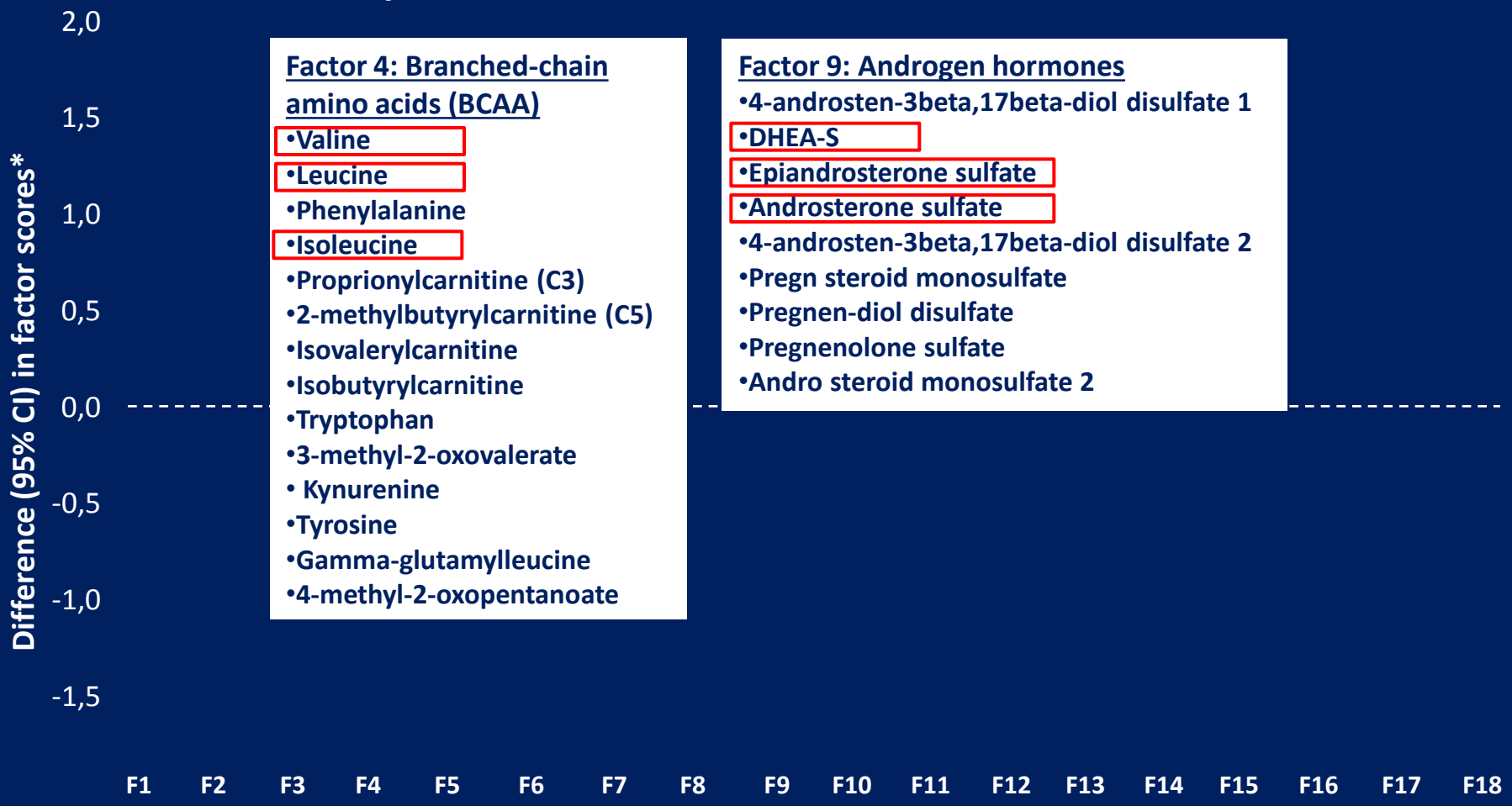
Step 4:
Multivariable linear regression

Metabolite factors scores → **Classic biomarkers**

Maternal peripartum characteristics → **Metabolite factor scores**

Results

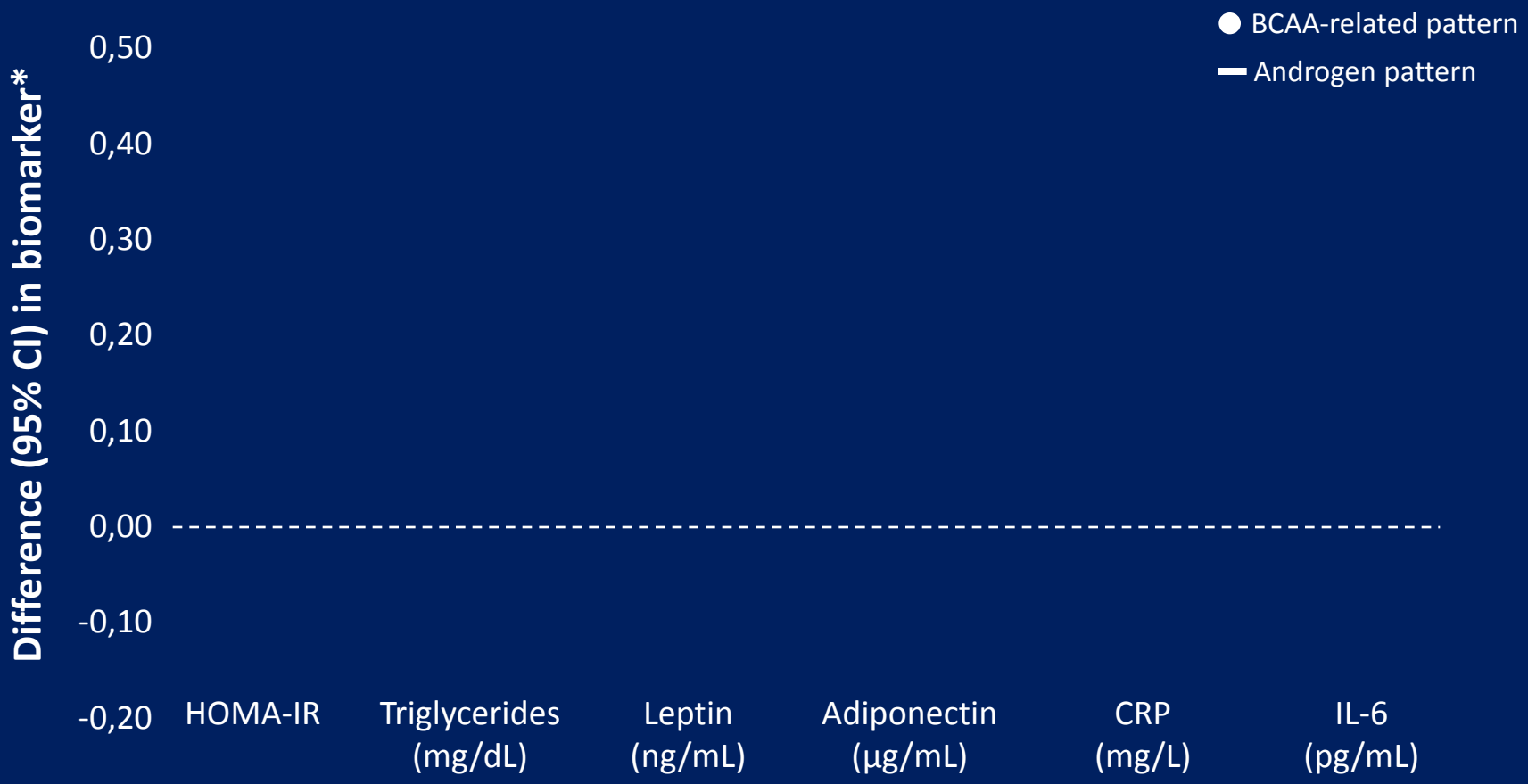
Aim 1: Comparison of factor scores between obese & lean children



*Estimates are adjusted for child's sex, age, and race/ethnicity; 95% CIs reflect Bonferroni's correction.

Results

Aim 2: Associations of BCAA & androgen metabolite patterns with cardiometabolic risk biomarkers



*Adjusted for maternal education and child age, sex, race/ethnicity, and fast-food intake.
All biomarkers are ln-transformed.

Results

Aim 3: Associations of maternal peripartum characteristics with offspring metabolite patterns

Conclusions

Aim 1

Childhood obesity → **↑ BCAA**, **↑ Androgen hormones**

Aim 2

↑ BCAA, **↑ Androgen hormones** → **Worse cardiometabolic profile**

Aim 3

Maternal obesity → **↑ BCAA in offspring**

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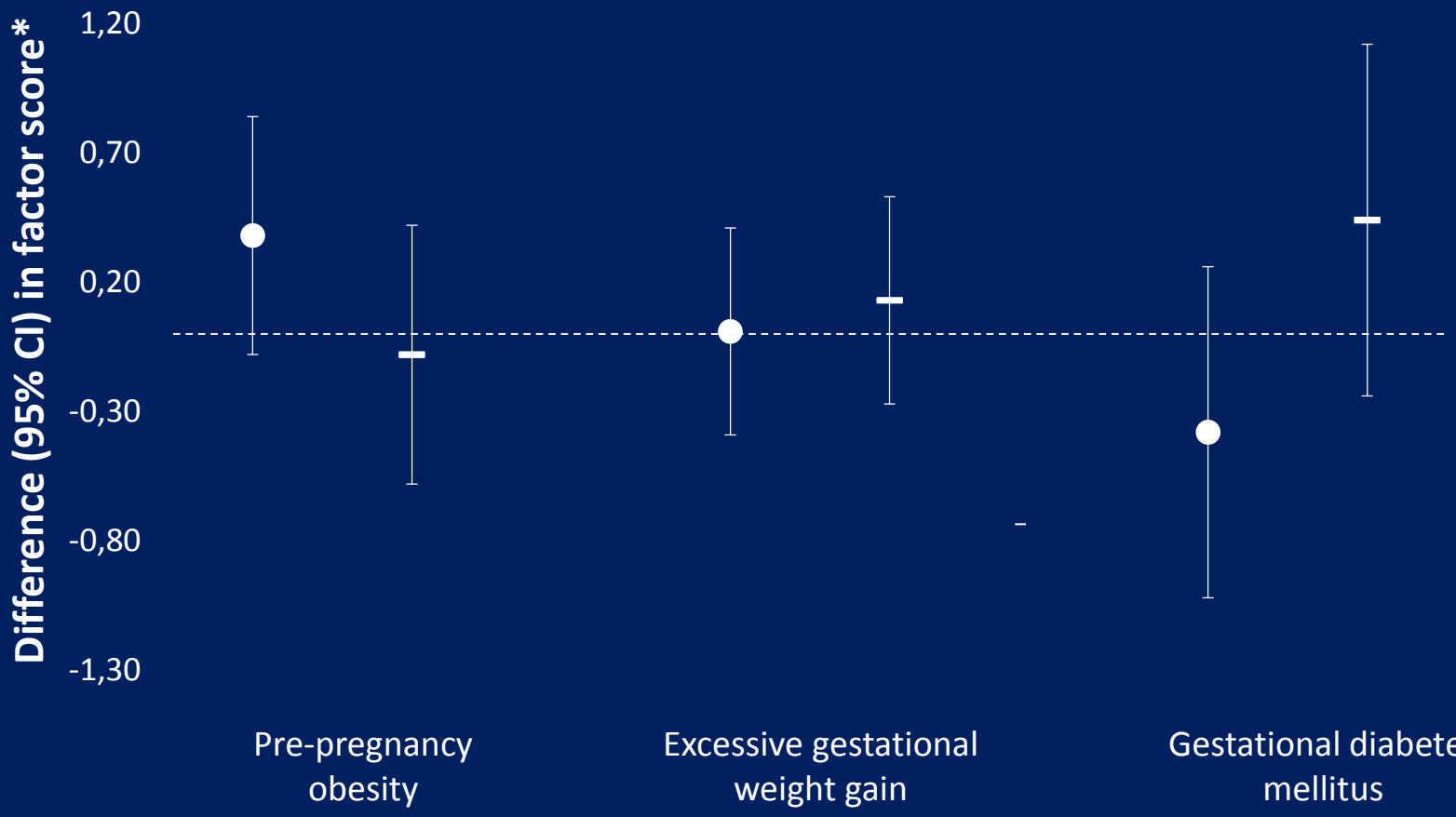
- The mothers and children of Project Viva.
- Past and present Project Viva staff.

Questions?

Associations of maternal peripartum characteristics with offspring metabolite patterns, accounting for child BMI



*Adjusted for maternal education and child age, sex, race/ethnicity, fast-food intake, and child's BMI z-score

Factor 4: Plasma metabolite concentrations of obese versus lean children

	Factor loading	Metabolite concentration z-score: Obese BMI ≥95th %ile *n* = 84	Metabolite concentration z-score: Lean BMI <85th %ile *n* = 150	*P*[b]
Factor 4: mean ± SD = 0.00 ± 1.52				
Valine	0.83	1.17 ± 0.30	-0.54 ±0.27	<0.0001
Leucine	0.76	1.38 ± 0.32	-0.37 ±0.29	<0.0001
Phenylalanine	0.72	1.23 ± 0.33	-0.27 ± 0.29	<0.0001
Isoleucine	0.71	1.18 ± 0.31	-0.37 ±0.27	<0.0001
Proprionylcarnitine (C3)	0.66	0.95 ± 0.29	-0.44 ±0.25	<0.0001
2-methylbutyrylcarnitine (C5)	0.63	0.80 ± 0.29	-0.03 ±0.26	0.0002
Isovalerylcarnitine	0.60	1.34 ± 0.30	-0.33 ±0.26	<0.0001
Isobutyrylcarnitine	0.56	1.19 ± 0.35	0.33 ± 0.31	0.001
Tryptophan	0.54	1.07 ± 0.33	0.21 ± 0.29	0.0007
3-methyl-2-oxovalerate	0.52	0.92 ± 0.30	-0.11 ± 0.26	<0.0001
Kynurenine	0.52	0.56 ± 0.32	-0.19 ± 0.28	0.002
Tyrosine	0.51	1.54 ± 0.28	0.04 ± 0.25	<0.0001
Gamma-glutamylleucine	0.51	0.53 ± 0.32	-0.23 ± 0.28	0.002
4-methyl-2-oxopentanoate	0.51	0.73 ± 0.30	-0.23 ± 0.26	<0.0001

a Estimates represent mean ± SE and are adjusted for child's sex, age, and race/ethnicity.

b From a t-test.

* Indicates tier 2 identification in which no commercially available authentic standards could be found, however annotated based on accurate mass, spectral and chromatographic similarity to tier 1 identified compounds.

Factor 9: Plasma metabolite concentrations of obese versus lean children

		Metabolite concentration z-score		
	Factor loading	**Obese** BMI ≥95th %ile *n* = 84	**Lean** BMI <85th %ile *n* = 150	***P**[b]*
Factor 9: mean ± SD: 0.00 ± 1.62				
4-androsten-3beta,17beta-diol disulfate 1*	0.86	0.61 ± 0.31	-0.49 ± 0.27	<0.0001
Dehydroepiandrosterone sulfate (DHEA-S)	0.84	0.45 ± 0.27	-0.41 ± 0.23	<0.0001
Epiandrosterone sulfate	0.79	0.14 ± 0.32	-0.70 ± 0.29	0.0007
Androsterone sulfate	0.79	0.30 ± 0.29	-0.38 ± 0.26	0.002
4-androsten-3beta,17beta-diol disulfate 2*	0.78	0.48 ± 0.35	-0.74 ± 0.31	<0.0001
Pregn steroid monosulfate*	0.76	0.70 ± 0.30	-0.22 ± 0.26	<0.0001
Pregnen-diol disulfate*	0.70	0.30 ± 0.30	-0.14 ± 0.26	0.05
Pregnenolone sulfate	0.65	0.71 ± 0.33	-0.09 ± 0.29	0.002
Andro steroid monosulfate 2*	0.61	0.41 ± 0.29	-0.46 ± 0.26	<0.0001

a Estimates represent mean ± SE and are adjusted for child's sex, age, and race/ethnicity.

b From the Wald chi-squared test.

* Indicates tier 2 identification in which no commercially available authentic standards could be found, however annotated based on accurate mass, spectral and chromatographic similarity to tier 1 identified compounds.