Electronic supplementary material

ESM Table 1: Effect estimates for anthropometric and metabolic outcomes in offspring born to mothers with type 1 diabetes and fathers with type 1 diabetes compared to those of parents without type 1 diabetes in the TEENDIAB and BABYDIAB/BABYDIET cohort.

Outcomes	**TEENDIAB** **Reference: No parental type 1 diabetes (N=104)**		**BABYDIAB/BABYDIET** **Reference: No parental type 1 diabetes (N=56)**	
	Maternal type 1 diabetes (n=250)	Paternal type 1 diabetes (n=249)	Maternal type 1 diabetes (n=1243)	Paternal type 1 diabetes (n=826)
	Estimates (95% CI)	Estimates (95% CI)	Estimates (95% CI)	Estimates (95% CI)
Absolute change in SD scores				
Height SDS	0.04 (-0.18, 0.27)	0.16 (-0.06, 0.38)	0.09 (-0.16, 0.33)	0.16 (-0.09, 0.40)
Weight SDS	0.33 (0.10, 0.57)*	0.16 (-0.07, 0.40)	0.26 (0.04, 0.49)*	0.21 (-0.02, 0.44)
BMI SDS	0.43 (0.18, 0.67)**	0.11 (-0.13, 0.35)	0.28 (0.05, 0.52)*	0.15 (-0.08, 0.39)
Waist circumference SDS	0.26 (0.01, 0.52)*	0.04 (-0.21, 0.29)	-	-
Subscapular skinfold SDS	0.28 (0.05, 0.51)*	0.16 (-0.06, 0.39)	-	-
Triceps skinfold SDS	0.17 (-0.09, 0.43)	0.04 (-0.22, 0.30)	-	-
SBP SDS	0.18 (-0.05, 0.41)	0.06 (-0.16, 0.29)	-	-
DBP SDS	0.29 (0.07, 0.51)*	0.21 (-0.01, 0.43)	-	-
HDL-cholesterol SDS	0.16 (-0.16, 0.48)	0.17 (-0.14, 0.49)	-	-
LDL-cholesterol SDS	0.12 (-0.15, 0.39)	0.04 (-0.23, 0.31)	-	-
Triacylglycerol SDS	0.11 (-0.09, 0.31)	0.03 (-0.17, 0.24)	-	-
Cholesterol SDS	0.16 (-0.09, 0.42)	0.11 (-0.15, 0.36)	-	-
Percent change in metabolic outcomes				
Fasting glucose	2.78 (0.74, 4.85)*	1.53 (-0.49, 3.58)	-	-
Fasting insulin	15.63 (4.57, 27.85)**	10.54 (-0.04, 22.24)	-	-
Fasting C-peptide	10.93 (2.29, 20.29)*	8.25 (-0.16, 17.37)	-	-
HOMA-IR	16.39 (4.77, 29.31)**	10.13 (-0.89, 22.36)	-	-
OR				
Overweight	3.10 (1.30, 7.42)*	1.60 (0.65, 3.90)	3.23 (1.55, 6.73)**	2.30 (1.10, 4.82)*
Abdominal obesity	2.34 (1.05, 5.22)*	1.34 (0.59, 3.06)	-	-
Metabolic risk	1.66 (1.07, 2.56)*	1.20 (0.77, 1.85)	-	-

Adjusted for age, sex (except for overweight, abdominal obesity, metabolic risk and SDS outcomes), Tanner's staging, maternal smoking and additionally socioeconomic status only in TEENDIAB study. *$p < 0.05$; ** $p < 0.01$

ESM Table 2: Effect estimates for anthropometric and metabolic outcomes in offspring born to a mother with compared to without type 1 diabetes in the TEENDIAB cohort after adjustment for dietary inflammatory index (DII, model 3a) and energy residuals (model 3b).

Outcomes	Model 1		Model 2		Model 3a		Model 3b	
	n	Estimates (95% CI)	n	Estimates (95% CI)	n	Estimates (95% CI)	n	Estimates (95% CI)
Absolute change in SD scores								
Height SDS	330	-0.26 (-0.48, -0.04)*	292	-0.25 (-0.49, -0.02)*	292	-0.27 (-0.50, -0.04)*	292	-0.29 (-0.52, -0.06)*
Weight SDS	330	0.14 (-0.07, 0.36)	292	0.14 (-0.08, 0.37)	292	0.14 (-0.08, 0.37)	292	0.12 (-0.11, 0.34)
BMI SDS	330	0.39 (0.17, 0.62)**	292	0.40 (0.17, 0.63)**	292	0.41 (0.17, 0.64)**	292	0.38 (0.15, 0.62)**
Waist circumference SDS	134	0.04 (-0.31, 0.38)	119	0.04 (-0.31, 0.40)	119	0.04 (-0.32, 0.39)	119	0.02 (-0.33, 0.38)
Subscapular skinfold SDS	315	0.22 (0.03, 0.43)*	282	0.20 (-0.01, 0.42)	282	0.20 (-0.01, 0.42)	282	0.21 (-0.01, 0.42)
Triceps skinfold SDS	316	0.25 (0.03, 0.47)*	282	0.19 (-0.04, 0.42)	282	0.20 (-0.03, 0.44)	282	0.20 (-0.03, 0.44)
SBP SDS	320	0.19 (-0.09, 0.47)	284	0.25 (-0.05, 0.56)	284	0.25 (-0.06, 0.57)	284	0.26 (-0.05, 0.57)
DBP SDS	320	0.26 (0.00, 0.52)	284	0.28 (-0.01, 0.56)	284	0.28 (-0.01, 0.56)	284	0.27 (-0.02, 0.55)
HDL-cholesterol SDS	324	0.15 (-0.14, 0.44)	288	0.20 (-0.10, 0.51)	288	0.21 (-0.09, 0.51)	288	0.20 (-0.12, 0.53)
LDL-cholesterol SDS	324	0.11 (-0.14, 0.35)	288	0.13 (-0.13, 0.39)	288	0.13 (-0.13, 0.39)	288	0.13 (-0.13, 0.39)
Triglyceride SDS	324	0.03 (-0.16, 0.22)	288	0.09 (-0.11, 0.29)	288	0.09 (-0.12, 0.29)	288	0.08 (-0.12, 0.28)
Cholesterol SDS	324	0.15 (-0.08, 0.38)	288	0.19 (-0.05, 0.43)	288	0.19 (-0.05, 0.43)	288	0.19 (-0.05, 0.42)
Percent change in metabolic outcomes								
Fasting glucose	320	1.37 (-0.59, 3.37)	284	2.40 (0.42, 4.42)*	284	2.39 (0.40, 4.41)*	284	2.03 (0.08, 4.01)*
Fasting insulin	321	3.90 (-9.23, 18.93)	285	10.70 (-3.18, 26.57)	285	10.35 (-3.52, 26.22)	285	9.79 (-4.06, 25.63)
Fasting C-peptide	142	0.38 (-12.33, 14.92)	132	1.70 (-11.10, 16.35)	132	0.05 (-12.51, 14.42)	132	-0.71 (-13.31, 13.73)
HOMA-IR	317	3.77 (-9.91, 19.52)	281	11.63 (-2.81, 28.21)	281	11.25 (-3.17, 27.82)	281	10.50 (-3.85, 26.99)
OR								
Overweight	330	1.90 (0.87, 4.14)	292	1.94 (0.82, 4.60)	292	2.06 (0.86, 4.93)	292	1.89 (0.80, 4.50)
Abdominal obesity	155	0.75 (0.22, 2.62)	139	1.35 (0.33, 5.56)	139	1.34 (0.32, 5.64)	139	1.35 (0.33, 5.56)
Metabolic risk (Cut-off 1.5 SD)	330	1.51 (0.96, 2.36)	292	1.37 (0.84, 2.23)	292	1.40 (0.86, 2.29)	292	1.36 (0.83, 2.22)

Model 1: Crude model ; Model 2: adjusted for age, sex (except for overweight, abdominal obesity, metabolic risk and SDS outcomes), Tanner's staging, socioeconomic status and maternal smoking; Model 3a: Model 2 + DII; Model 3b: Model 2+ energy residuals

*$p < 0.05$; **$p < 0.01$

n, no of participants

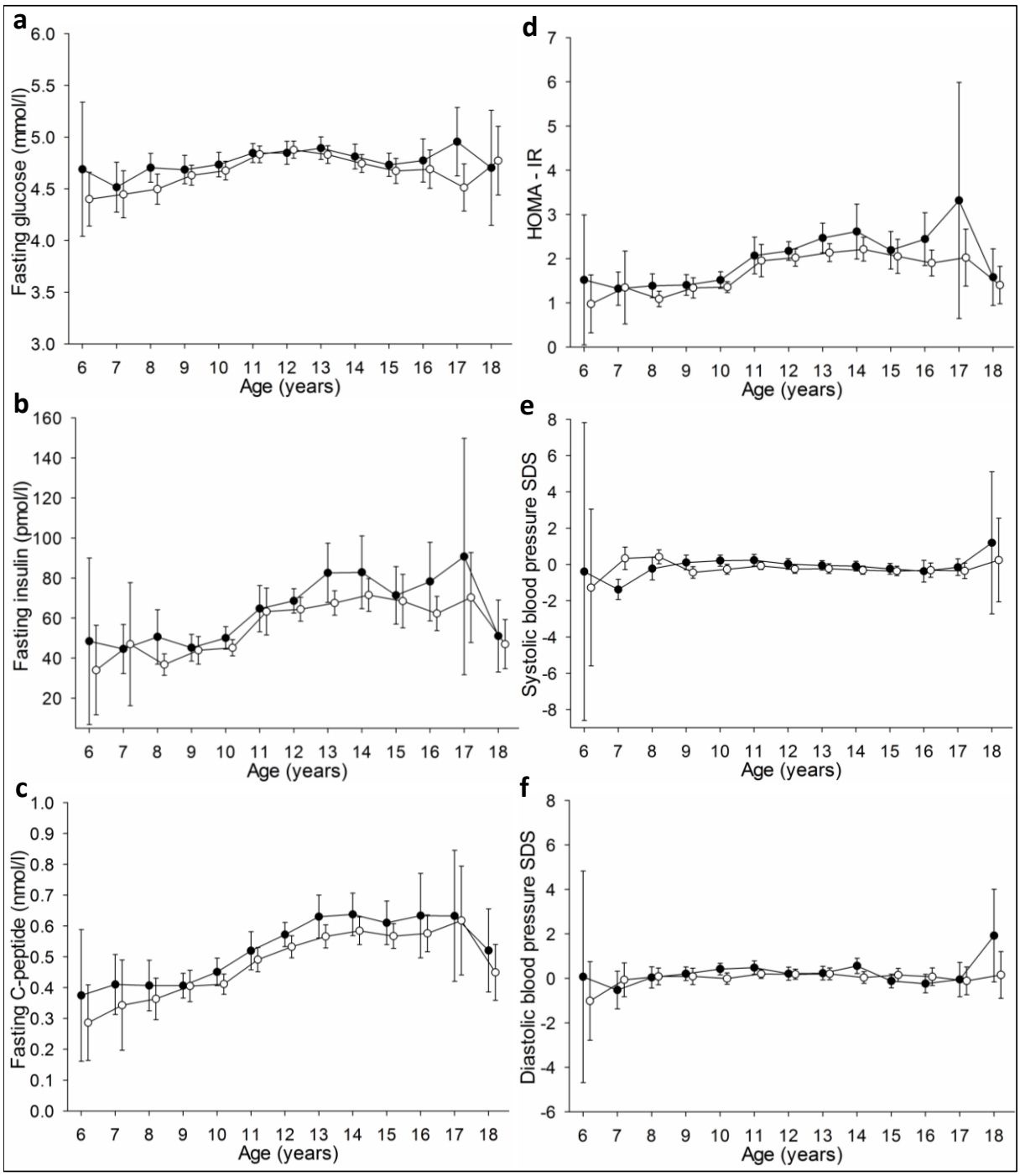
ESM Table 3: Description of the principal components (PC) significantly associated with overweight and its metabolites with higher loading values

PC significant for overweight	Metabolites with absolute loading values greater than 0.40	Eigen value	Variance explained (%)
PC3 (Lipids: Androgenic, pregnenolone and progestin steroids)	Andro steroid monosulfate (2) Androsterone sulfate Androstenediol (3beta,17beta) disulfate (1) Androstenediol (3beta,17beta) disulfate (2) Epiandrosterone sulfate 5alpha-androstan-3beta,17beta-diol disulfate Dehydroisoandrosterone sulfate (DHEA-S) Thromboxane B2 21-hydroxypregnenolone disulfate Pregnenolone sulfate 5alpha-pregnan-3beta,20alpha-diol disulfate Pregn steroid monosulfate Pregnen-diol disulfate	16.50	3.74%
PC5 (Amino acid: BCAA, lysine, phenyalanine, tryptophan, tyrosine metabolism, urea cycle, acetylated peptides)	Creatine 2-methylbutyrylcarnitine C5 Valine Isobutyrylcarnitne C4 Leucine Isovalerylcarnitine C5 Isoleucine N6-acetyllysine Urea N1-Methyl-4-pyridone-3-carboxamide N1-Methyl-2-pyridone-5-carboxamide Propionylcarnitine C3 Gamma-glutamylvaline Gamma-glutamylphenylalanine Gamma-glutamylleucine Gamma-glutamylisoleucine	10.53	2.39%
PC13 (Amino acid, lipid, acetylated peptides and xenobiotics)	3-indoxyl sulfate Glycolithocholate sulfate Phenylacetylcarnitine Phenylacetylglutamine 4-methylcatechol sulfate P-cresol sulfate 3-phenylpropionate hydrocinnamate	5.75	1.30%

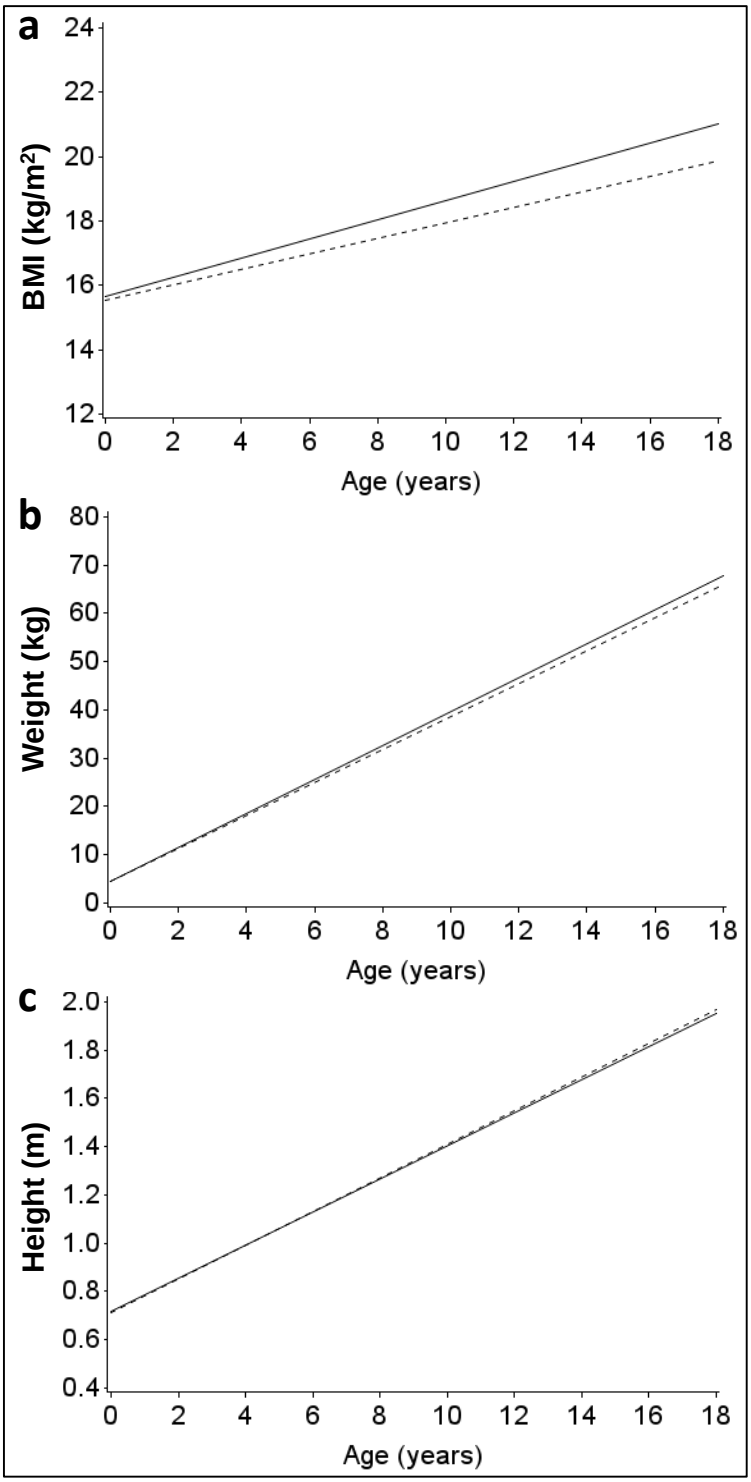
ESM Table 4: Percent change in metabolomics outcomes in offspring of type 1 diabetic mothers compared to offspring of non-diabetic mothers

Outcomes	**Adjusted analysis* (N=485)**	
	% change (95% CI)	***p* value**
Amino acid		
alanine	2.35 (-1.88; 6.76)	0.28
valine	-1.15 (-3.32; 1.06)	0.30
kynurenate	0.04 (-4.48; 4.77)	0.99
tyrosine	1.06 (-1.92; 4.12)	0.49
Lipid		
androsterone sulfate	-4.2 (-17.74; 11.57)	0.58
androstenediol (3β.17β) disulfate (1)*	-4.34 (-16.53; 9.62)	0.52
epiandrosterone sulfate	-5.38 (-18.34; 9.63)	0.46
5α-androstan-3β.17β-diol disulfate	7.56 (-4.26; 20.83)	0.22
dehydroisoandrosterone sulfate (DHEA-S)	-5.86 (-16.65; 6.31)	0.33
carnitine	1.41 (-1.18; 4.06)	0.29
thromboxane B2	-4.77 (-15.04; 6.74)	0.40
butyrylcarnitine (C4)	-0.96 (-8.4; 7.09)	0.81
2-aminoheptanoate	1.24 (-4.56; 7.38)	0.68
glycerol	3.32 (-1.8; 8.72)	0.21
stearidonate (18:4n3)	-0.25 (-7.18; 7.2)	0.95
Cofactors and Vitamins		
N1-Methyl-4-pyridone-3-carboxamide	-2.59 (-9.04; 4.32)	0.45
Nucleotide		
urate	0.68 (-2.22; 3.66)	0.65
Peptide		
gamma-glutamyltyrosine	2.11 (-2.2; 6.61)	0.34
Xenobiotic		
piperine	-2.99 (-18.83; 15.94)	0.74

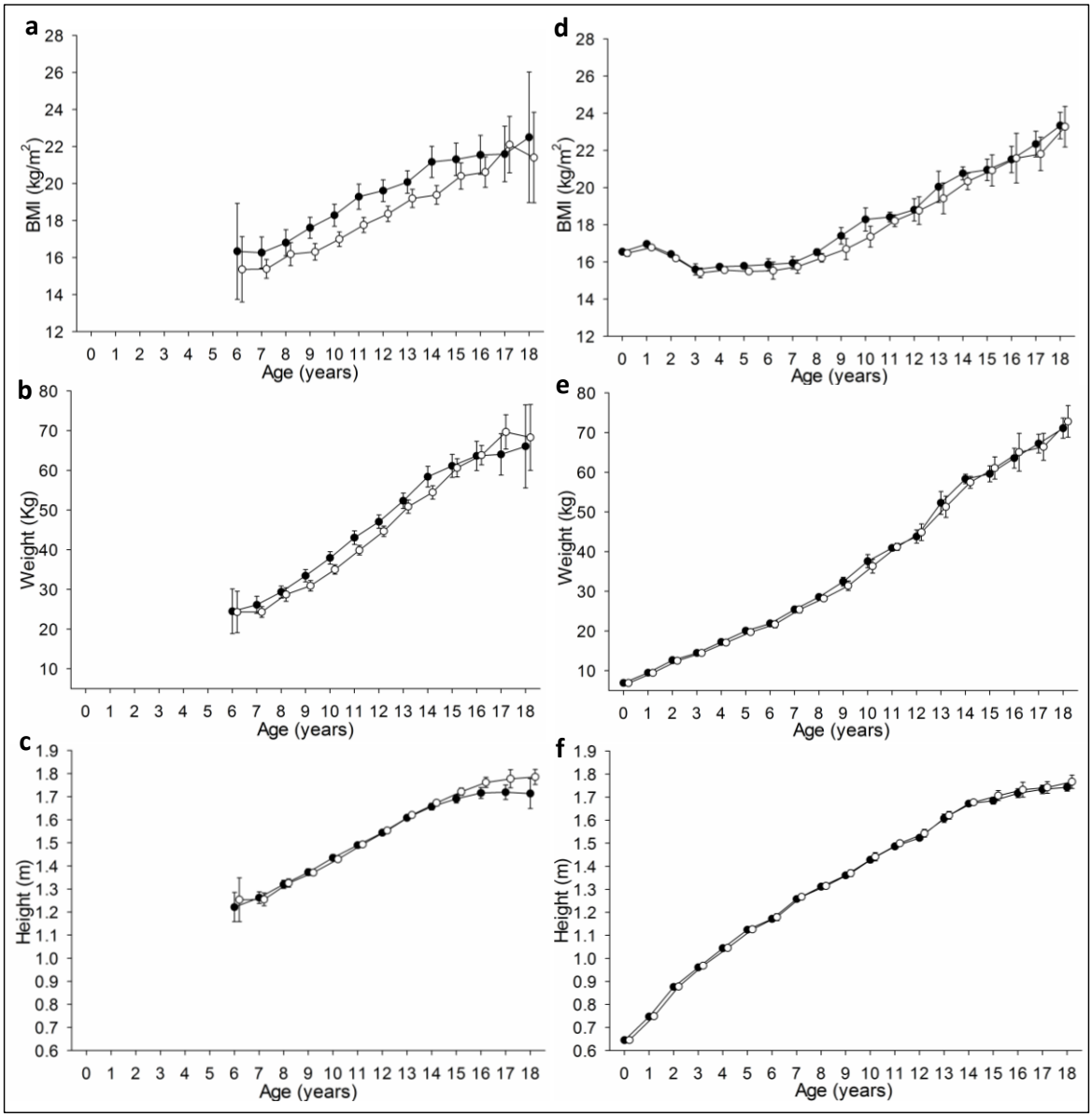
*Adjusted for age and sex



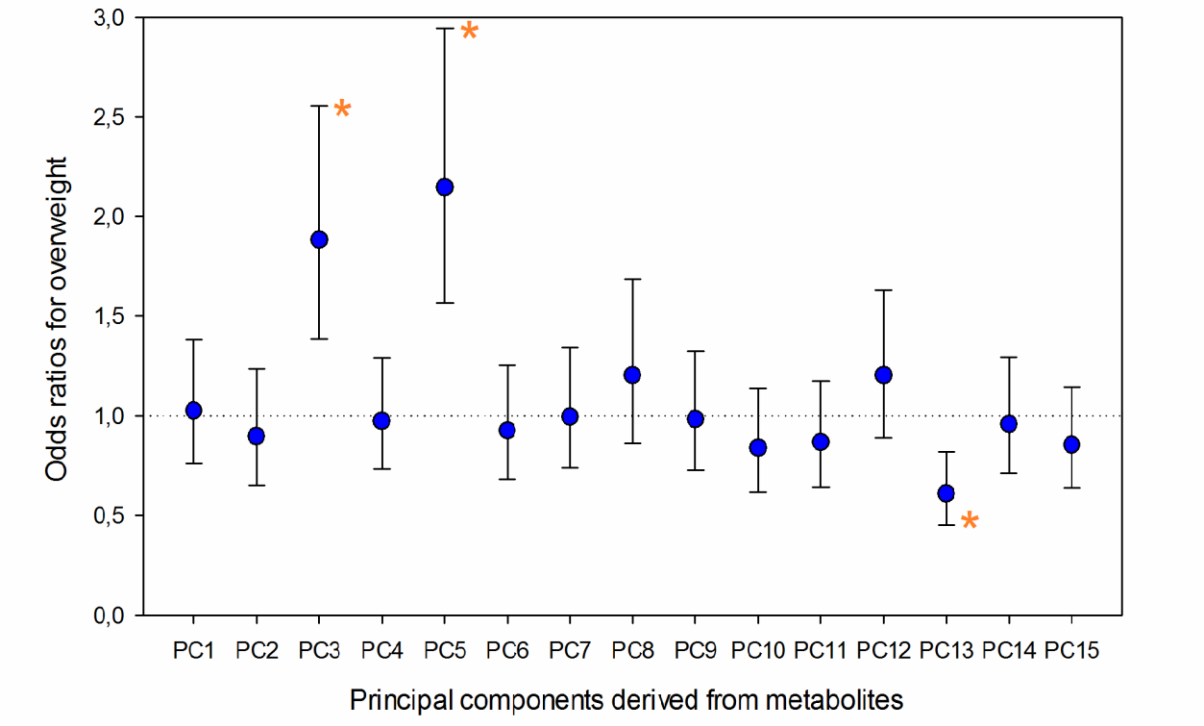
ESM Fig 1: Mean and 95% CI of **a)** fasting glucose, **b)** fasting insulin, **c)** fasting C-peptide, **d)** homeostasis model assessment of insulin resistance (HOMA-IR), **e)** systolic blood pressure standard deviation scores (SDS), and **f)** diastolic blood pressure SDS stratified by age and maternal type 1 diabetes (black circles: offspring of type 1 diabetic mothers; white circles: offspring of non-diabetic mothers) in the TEENDIAB cohort.



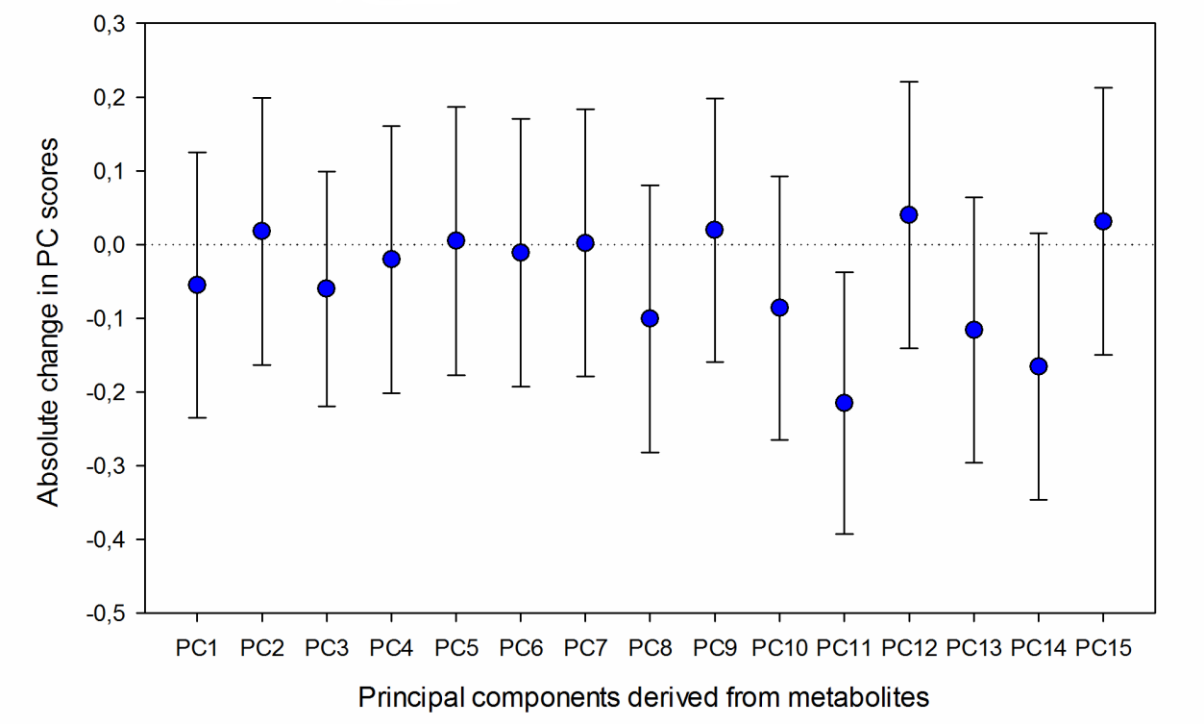
ESM Fig. 2: Trajectories of **a)** body mass index (BMI), **b)** weight and **c)** height by age and maternal diabetes status (solid lines: offspring of type 1 diabetic mothers; dashed lines: offspring of non-diabetic mothers) adjusted for age, sex, Tanner's staging and maternal smoking from the combined data of TEENDIAB and BABYDIAB/BABYDIET cohorts.



ESM Fig. 3: Mean and 95% CI for BMI **(a, d)**, weight **(b, e)** and height **(c, f)** stratified by age and maternal type 1 diabetes (black circles: offspring of type 1 diabetic mothers; white circles: offspring of non-diabetic mothers) in the TEENDIAB **(a-c)** and BABYDIAB/BABYDIET **(d-f)** cohorts.



ESM Fig. 4: Association between principal components (PC) of metabolites and overweight presented as OR (blue circles) with 95% CI (bars). *Significance after correction for multiple testing. After multiple testing correction, three principal components of metabolites were associated with offspring overweight.



ESM Fig. 5: Association between principal components (PC) of metabolites and maternal type 1 diabetes presented as absolute change in PC scores (blue circles) with 95% CI (bars). After multiple testing correction, no principal components of metabolites were associated with maternal type 1 diabetes.

ESM Fig. 6: Association between super and sub-pathways of metabolites and maternal type 1 diabetes

Pathways located to the right of the zero line indicate up-regulation, and left to the zero line down-regulation, in offspring of type 1 diabetic mothers. Pathways lying beyond the red dashed line indicate associations of $p<0.05$ without adjustment for multiple testing. However, after multiple testing correction, no super- and subpathways of metabolites were significantly associated with maternal type 1 diabetes. The numbers in brackets represent the number of metabolites in each super- or subpathway. Black squares, superpathway; grey squares, subpathway. SAM, S-Adenosyl methionine; TCA, tricarboxylic acid