Supplement Material

Supplement Text 1: Cord blood metabolic profile methods

Cord blood candidate biochemical markers

Biochemical candidate markers associated with insulin resistance and neonatal growth were measured in plasma cord samples. These included; C-peptide assessed by Electrochemiluminescence immunoassay using Roche Cobas c311 (CV low 6.2%, high 5.1%); Insulin by Electrochemiluminescence immunoassay using Roche Cobas c411 (CV low 7.8%, high 5.4%); glucose by enzymatic, hexokinase using Roche Cobas c311; adiponectin by enzyme linked immunosorbent assay using R&D systems (CV intra 5.4%, inter 12.0%); leptin by enzyme linked immunosorbent assay using R&D systems (CV intra 2.0%, inter 9.3%); IGF-1 and II were assessed by enzyme linked immunosorbent assay using Roche Cobas c311(CV inter 7.2%, intra 6.6%), respectively. Lipids including HDL, LDL and triglycerides were assessed using homogeneous enzymatic colorimetric using Roche Cobas c311 (CV low 1.8%, high 1.1%).

Cord blood metabolomic analyses

Analysis was performed at LMU Munich. Amino acids, non-esterified fatty acids, carboxylic acids, acylcarnitines and phospholipids were measured in the cord plasma samples (n=607).

50 µL of plasma were thawed and diluted with 450 µl methanol, containing internal standards representing different groups of metabolites. After centrifugation (4000rpm, 10min, room temperature), supernatants were divided according to the following methods:

Amino acids

100 µL of the supernatant were prepared using derivatisation as previously reported (1). The supernatant was mixed with 50µl butanolic HCl for 15 min at 600 rpm at 60°C. After evaporation, the residue was solved in 50ml flow solution. AA butylester were determined by ion-pair liquid chromatography coupled to mass spectrometry detection (LC-MS/MS). 10 µL of the prepared sample were injected into the HPLC system (HPLC 1100, Agilent, Waldbronn, Germany) and chromatographic separation was performed with an XBridge C18 column (Waters GmbH, Eschborn, Germany). MS detection was performed with an API 2000 triple quadrupole instrument (Sciex, Darmstadt, Germany) with an APCI source operating in positive ion ionization mode. Data acquisition on the mass spectrometer was controlled by Analyst 1.6.2 software (AB Sciex, Darmstadt, Germany). Data handling and quantification were also performed with Analyst 1.6.2 software (AB Sciex, Darmstadt, Germany).

Non-esterified fatty acids

100 µl of the supernatant were analysed as previously reported (2).The supernatant was mixed for 20 min at 600rpm at room temperature and transferred for LC-MS/ MS analysis. An UPLC diphenyl column (Pursuit UPS Diphenyl, Varian, Darmstadt, Germany) was used for chromatographic separation with an Agilent 1200 SL series HPLC system (Waldbronn, Germany). The injection volume was set to 10 µL with an eluent flow rate of 700 mL/min. A hybrid triple quadrupole mass spectrometer (4000 QTRAP, Sciex, Darmstadt, Germany) operating in negative ESI mode was coupled to the HPLC system for identification of NEFA. With the analytical method applied, fatty acids (FA) are separated according to chain length and number of double bonds, but not according to position of double bonds. NEFA are mentioned as CX:Y. In this nomenclature, X is the length of the carbon chain, Y is the number of double bonds. NEFA sub-groups according to level of saturation were created and the constituents summed.

Carboxylic acids

Metabolites of the TCA cycle and keto-acids were measured by a modified LC-MS/MS method based on previously published methods [Luo 2007, Birkler 2010]. In detail, 100 µL of the supernatant were evaporated to dryness and re-suspended in 50 µL water. Fife µL of the extracted samples were injected to an Agilent 1200 HPLC and molecular species were separated on a Kinetex F5 core-shell HPLC column, 150 x 2.1 mm, 2.6 µm particle size (Phenomenex, Aschaffenburg, Germany). The mobile phase A was water with 1% formic acid and mobile phase B was composed of methanol/ isopropanol (50:50) with 1% formic acid. The gradient elution at a flow rate of 200 µL/ min was from 1% B to 85% B within 9 minutes and turned back to initial conditions of 1%B within 1 minute. Re-equilibration was held for 5 minutes at 1% B. The triple quadrupole mass spectrometer (AB Sciex API4000; Applied Biosystems, Darmstadt, Germany) was operated in negative scheduled multiple reaction monitoring mode using electrospray ionization (ESI).

Phospholipids

Flow-injection mass spectrometry (FIA-MS/MS) was used to analyse polar lipids. 30 µL of the centrifuged supernatant was mixed with 500 µl methanol (containing 1µM ammonium acetate) for 20 min at 600 rpm and then used for FIA-MS/MS analysis. Samples were analysed with a triple quadrupole mass spectrometer (QTRAP4000, Sciex, Darmstadt, Germany) with an electrospray ionization (ESI) source, which was used in both positive and negative mode. The MS was coupled to a LC system (Agilent, Waldbronn, Germany). MS/MS analysis was run in Multiple Reaction Monitoring (MRM) mode. Analyst 1.6.2 software, followed by in-house processing with the statistical program R (R Project for Statistical Computing, http://www.r-project.org/) was used to post-process the entire analytical process.

The analysis comprised diacyl-phosphatidylcholines (PCaa), acyl-alkyl-phosphatidylcholines (plasmalogens, PCae), sphingomyelins (SM), lyso-phosphatidylcholines (lyso-PC) and sum of hexoses which is further mentioned as glucose presenting more than 80% of this value. As a point to note, the analytical technique applied here is not capable of determining the position of the double bonds and the distribution of carbon atoms between fatty acid side chains. The polar lipids are mentioned as CX:Y. In this nomenclature, X is the length of the carbon chain, Y is the number of double bonds, "a" indicates that the acyl chain is bound via an ester bond to the backbone, while "e" means binding by an ether bond.

Acylcarnitines

Flow-injection mass spectrometry (FIA-MS/MS) was used to analyse acylcarnitines (Carn). 100 µL of the centrifuged supernatant was were mixed for 20 min at 600 rpm and then used for FIA-MS/MS analysis. Samples were analysed with a triple quadrupole mass spectrometer (QTRAP4000, Sciex, Darmstadt, Germany) with an electrospray ionization (ESI) source, which was used in both positive and negative mode. The MS was coupled to a LC system (Agilent, Waldbronn, Germany). MS/MS analysis was run in Multiple Reaction Monitoring (MRM) mode. Analyst 1.6.2 software, followed by in-house processing with the statistical program R (R Project for Statistical Computing, http://www.r-project.org/) was used to post-process the entire analytical process.

As a point to note, the analytical technique applied here is not capable of determining the position of the double bonds and the distribution of carbon atoms between fatty acid side chains. The polar lipids are mentioned as CX:Y. In this nomenclature, X is the length of the carbon chain, Y is the number of double bonds, "a" indicates that the acyl chain is bound via an ester bond to the backbone, while "e" means binding by an ether bond.

Supplement Text 2: Confounder selection

Confounders were selected based on a-priori knowledge and were selected for the following reasons, as summarised in Supplement Table 1.1

Variables	Reason
Maternal	
UPBEAT Intervention	The intervention was associated with a reduction in maternal gestational weight gain, measures of adiposity and improvements in maternal antenatal diet and physical activity (3). In the offspring, the intervention was associated with a reduction in cord insulin and a measure of central adiposity at 6 months of age.
BMI	Increasing maternal BMI is associated with raised cord lipid, inflammation markers and markers associated with insulin resistance as well as a determinants of neonatal body composition (4, 5).
Parity	Increasing maternal parity has been shown to be associated with increasing neonatal adiposity as shown in a rural Indian population (6).
Ethnicity	Maternal ethnicity is differentially associated with neonatal adiposity, for example offspring born to black ethnic groups have reduced birthweight in comparison to those from white ethnic groups (7, 8).
Socioeconomic status	Socioeconomic deprivation is associated with reduced educational attainment and poor maternal lifestyle behaviours which are known determinants of neonatal adiposity (9).
Smoker in early pregnancy	Smoking in pregnancy has been associated with intrauterine growth restriction associated with adverse metabolic adaptation in the fetal metabolic profile as measured in the cord blood (10).
Gestational weight gain	Multiple observational studies have demonstrated a linear association between gestational weight gain and neonatal adiposity (11). Gestational weight gain is thought to have a linear relationship with cord adipokines and markers of insulin resistance (12).
Gestational diabetes	Maternal glycaemia has recently shown to be causal in determining neonatal anthropometry. Furthermore, pathway analysis has identified maternal glucose to be key in determining neonatal anthropometry mediated by fetal metabolic profile at birth (13).
Neonate	
Sex	Offspring sex has shown to have a differential influence on cord biomarkers of inflammation and adipokines. Females have also shown to have significantly more adipose tissue in comparison to male offspring (14).
Gestation at delivery	Preterm delivery has been associated with reduced birthweight, length and measures of adiposity in comparison to infants born at term. More recently the metabolic profile at birth in preterm neonates significantly differs in comparison to offspring born at term (15).
Infant	
Mode of early life feeding	Breastfeeding has been demonstrated to be protective against childhood obesity in early life in comparison to offspring formula fed (16).

Supplement Table 1.1: A-priori reasoning for selection of maternal, neonatal and infant confounders.

Based on the selection above and using a directed acyclic graph (Figure 1.1), the following confounders were selected to provide minimal sufficient adjustment to assess the influence of the fetal metabolic profile on neonatal anthropometry;

Neonatal anthropometry Model 1: *Fetal confounders*- offspring sex, gestation at delivery, randomisation to UPBEAT intervention

Neonatal anthropometry; Model 2: *Maternal & Fetal confounders*- Maternal parity, ethnicity, smoker in early pregnancy, gestational diabetes, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention

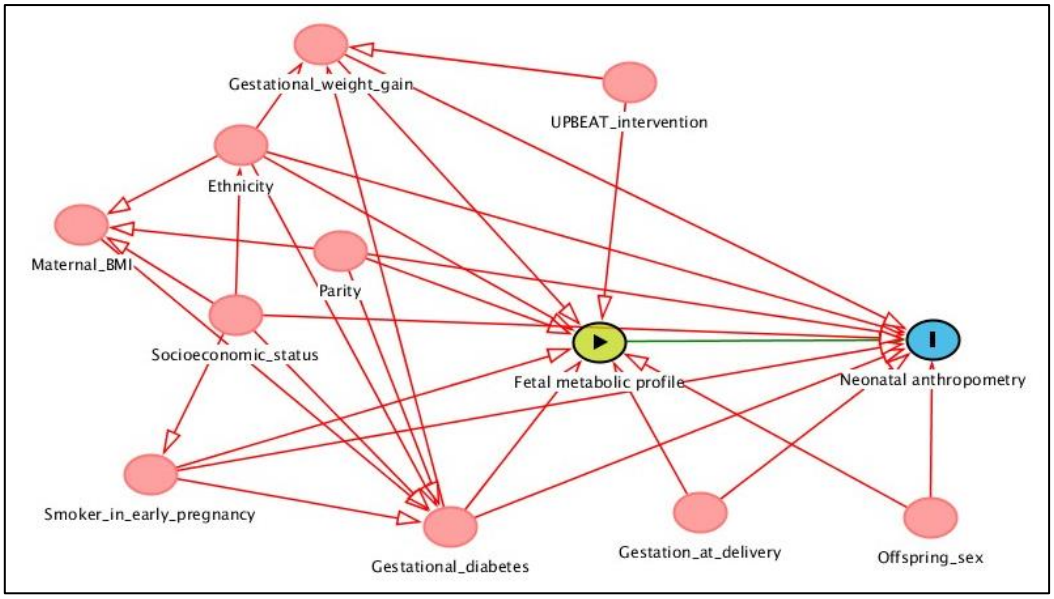


Figure 1a: Directed acyclic graph to demonstrate inter-relationships between variables potentially confounding the relationship between fetal biochemical profile and neonatal anthropometry.

Based on the selection above (Table 1.1) and using a directed acyclic graph (Figure 1.2), the following confounders were selected to provide minimal sufficient adjustment to assess the influence of the fetal metabolic profile on neonatal anthropometry;

Infant at age 6 months: *Maternal & Fetal confounders*- Maternal parity, ethnicity, smoker in early pregnancy, gestational diabetes, gestational weight gain, mode of early life feeding, randomisation to UPBEAT Intervention (Figure 1.2)

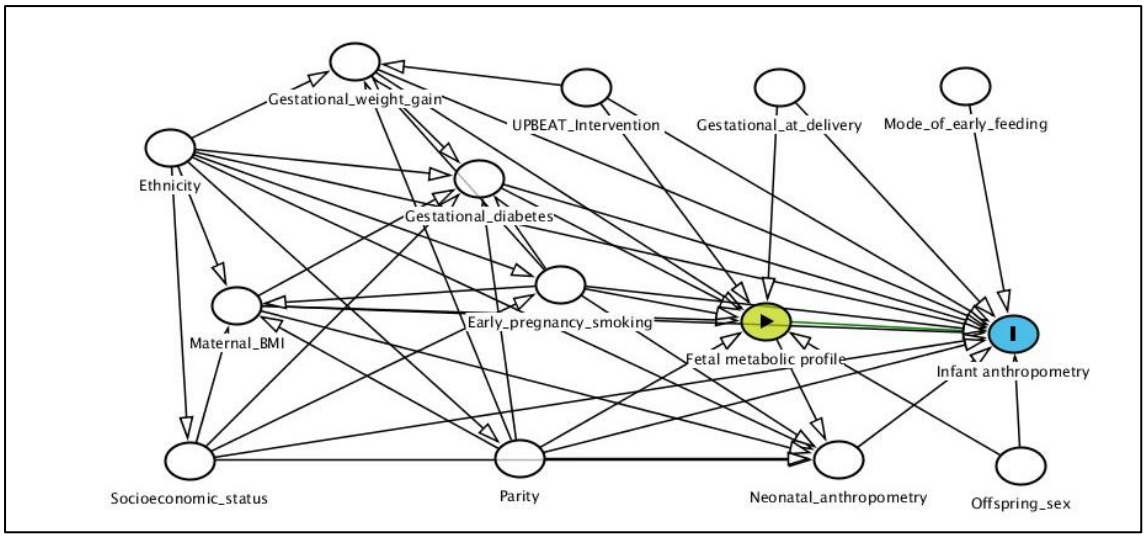
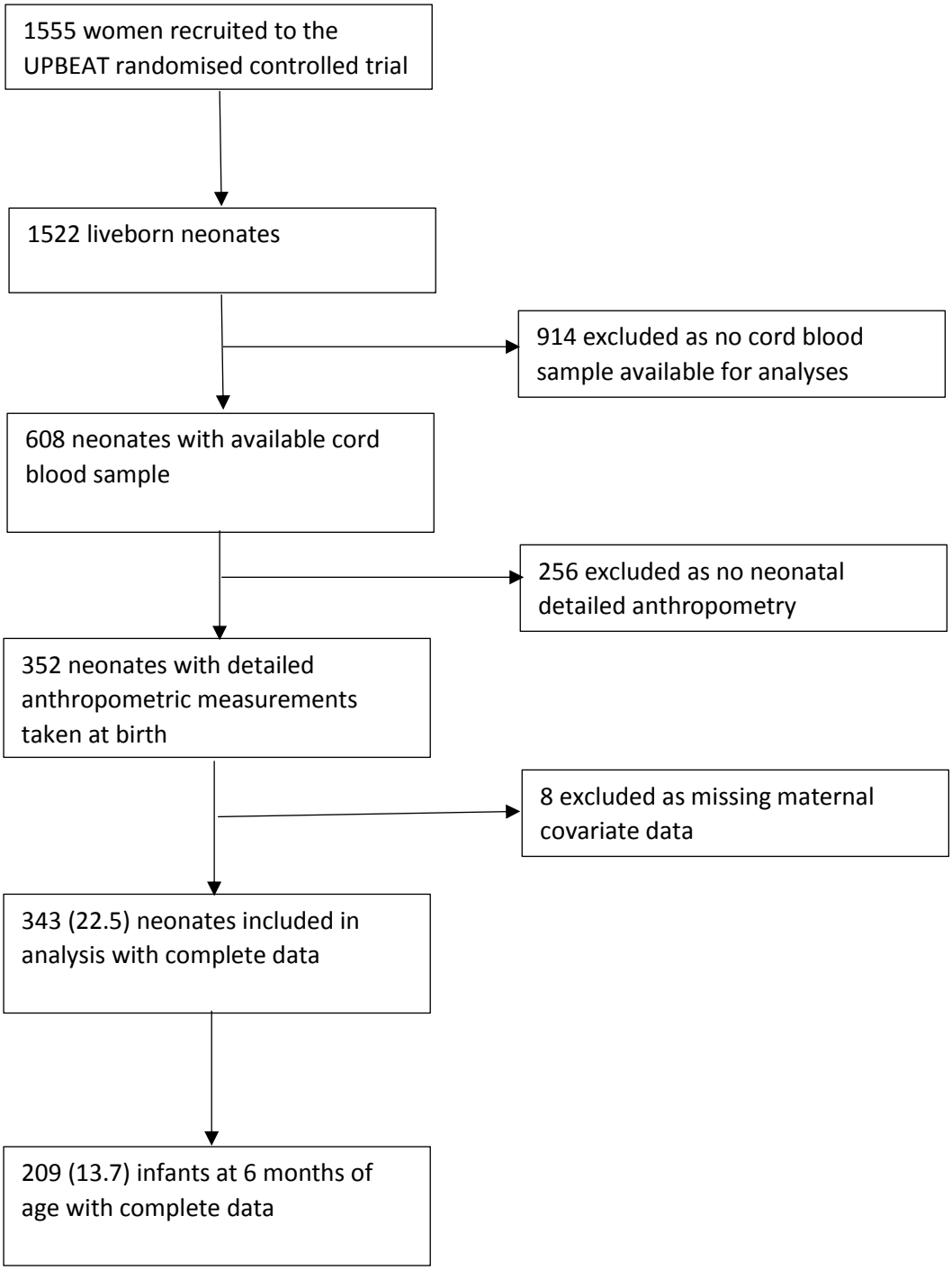


Figure 1b: Directed acyclic graph to demonstrate inter-relationships between variables potentially confounding the relationship between fetal biochemical profile and infant anthropometry at 6 months of age.



Supplement Figure 2: Flow diagram of participants included within the analyses

		Included within analysis (n=343)/ (n=247)	Excluded from analysis (n=1211)	p-value
		Mean (SD)/ Median (IQR)/ N (%)	Mean (SD)/ Median (IQR)/ N (%)	
Maternal				
Age (years)		31.0 (27.0, 35.0)	30.0 (26.0, 35.0)	0.109
BMI (Kg/ m2)		35.6 (33.0, 38.9)	34.9 (32.7, 38.5)	0.150
Ethnicity	Asian	19 (5.5)	76 (6.3)	0.616
	Black	63 (18.4)	338 (27.9)	0.001
	Other	15 (4.4)	70 (5.8)	0.315
	White	246 (71.7)	727 (60.0)	<0.001
Multiparous		165 (48.1)	715 (59.0)	0.001
Smoker in early pregnancy		19 (5.5)	89 (7.3)	0.249
Socioeconomic deprivation		295 (86.5)	1085 (89.9)	0.102
Gestational weight gain (kg)		7.48 (4.07)	7.51 (4.74)	0.891
Gestational diabetes		111 (32.4)	269 (27.3)	0.070
Neonate				
Mode of delivery	Emergency c-section	78 (22.7)	171 (14.5)	0.159
	Operative vaginal	44 (12.8)	134 (11.4)	<0.001
	Elective c-section	83 (24.2)	212 (18.0)	0.010
	Vaginal	138 (40.2)	660 (56.1)	<0.001
Gestation at delivery (weeks)		39.9 (38.7, 40.9)	39.9 (38.7, 40.9)	<0.001
Birthweight (grams)		3555.0 (3210.0, 3827.0)	3435.0 (3090.0, 3780.0)	<0.001
Skinfold thickness subscapular (mm)		5.78 (1.42)	5.39 (1.43)	0.004
Skinfold thickness triceps (mm)		5.34 (1.45)	5.24 (1.61)	0.494
Sum of skinfold thicknesses (mm)		11.12 (2.59)	10.51 (2.70)	0.018
Midarm circumference (cm)		11.58 (0.97)	11.34 (1.24)	0.009
Abdominal circumference (cm)		32.63 (2.05)	32.28 (2.08)	0.061
Infant at 6 months				
Weight for age z-score		0.29 (1.01)	0.24 (1.15)	0.564
Length for age z-score		0.44 (1.85)	0.59 (1.84)	0.317
BMI for age z-score		0.10 (1.84)	-0.09 (1.80)	0.208
Arm circumference z-score		1.25 (1.47)	1.04 (1.76)	0.109
Triceps SFT z-score		0.29 (1.51)	0.09 (1.48	0.098
Subscapular SFT z-score		0.30 (1.45)	0.17 (1.32)	0.304

Supplement Table 2: Differences in maternal and neonatal demographic, clinical and anthropometric characteristics between mother-offspring pairs included and excluded within the analysis.

Abbreviations; BMI- Body Mass Index.

Cord blood biochemical profile	**N**	**Concentrations (Median/ IQR)**
Candidate cord blood biomarkers		
c-peptide (ng/ml)	574	1.3 (0.9,1.7)
Insulin (U/ml)	576	6.4 (3.8,10.1)
Glucose (mmol/l)	576	3.4 (2.4,4.2)
Triglycerides (mmol/l)	516	0.3 (0.3,0.5)
Cholesterol (mmol/l)	546	1.4 (1.1,1.7)
HDL (mmol/l)	577	41.0 (29.0,62.0)
IGF I (ng/ml)	577	45.0 (32.0,58.0)
IGF II (ng/ml)	577	496.0 (441.0,558.0)
Leptin (ng/ml)	577	14.5 (8.0,24.0)
Adiponectin (ng/ml)	577	31.5 (23.3,39.5)
IL-6 (pg/ml)	577	4.0 (2.0,8.9)
TNF-alpha (pg/ml)	577	139.0 (87.0,197.0)
Metabolites (*µmol/l l)*		
lyso.PC.a.C14.0	364	1.4 (1.1,1.8)
lyso.PC.a.C16.0	607	50.6 (39.8,61.4)
lyso.PC.a.C16.1	526	4.3 (3.1,5.4)
lyso.PC.a.C18.0	607	9.0 (6.8,11.1)
lyso.PC.a.C18.1	526	10.4 (8.1,13.6)
lyso.PC.a.C18.2	607	11.9 (8.7,15.6)
lyso.PC.a.C18.3	360	0.3 (0.2,0.4)
lyso.PC.a.C20.3	526	3.0 (2.2,4.0)
lyso.PC.a.C20.4	607	13.7 (10.3,18.7)
lyso.PC.a.C20.5	324	0.3 (0.2,0.4)
lyso.PC.a.C22.5	400	0.4 (0.3,0.7)
lyso.PC.a.C22.6	607	2.3 (1.6,3.1)
lyso.PC.e.C18.0	321	0.6 (0.4,0.8)
PC.aa.C30.0	522	2.8 (2.1,3.6)
PC.aa.C30.2	313	0.4 (0.3,0.6)
PC.aa.C32.0	526	16.3 (13.1,21.0)
PC.aa.C32.1	525	13.7 (10.4,18.4)
PC.aa.C32.2	342	0.7 (0.4,1.1)
PC.aa.C34.1	607	126.7 (99.5,161.3)
PC.aa.C34.2	607	70.9 (55.8,87.8)
PC.aa.C34.3	442	3.3 (2.6,4.1)
PC.aa.C34.4	440	0.5 (0.4,0.6)
PC.aa.C36.0	520	1.8 (1.2,2.5)
PC.aa.C36.1	525	22.0 (17.9,27.5)
PC.aa.C36.2	445	42.4 (33.8,52.1)
PC.aa.C36.3	607	57.1 (46.7,71.1)
PC.aa.C36.4	607	123.6 (98.3,152.8)
PC.aa.C36.5	445	3.9 (3.0,5.0)
PC.aa.C38.0	523	1.2 (1.0,1.7)
PC.aa.C38.3	525	35.3 (28.1,42.9)
PC.aa.C38.4	526	96.7 (76.6,119.9)
PC.aa.C38.5	445	20.9 (16.5,26.3)
PC.aa.C38.6	526	58.6 (44.7,75.9)
PC.aa.C40.4	441	3.2 (2.5,4.0)
PC.aa.C40.5	524	6.4 (4.4,8.4)
PC.aa.C40.6	526	27.0 (20.0,36.9)
PC.aa.C42.0	520	0.5 (0.3,0.7)

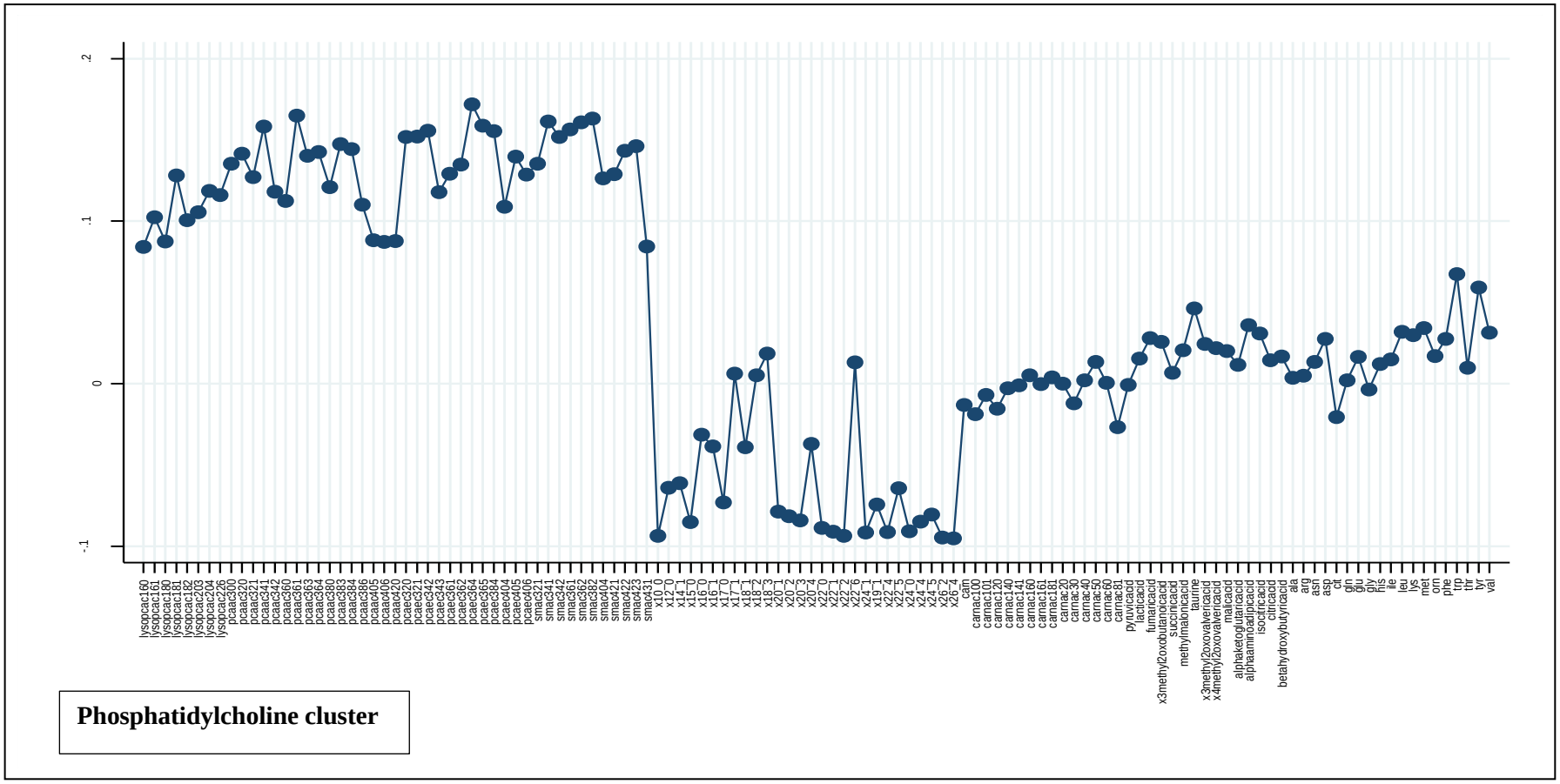
PC.aa.C43.6	318	0.8 (0.6,1.1)
PC.aa.C44.12	441	0.5 (0.4,0.6)
PC.ae.C32.0	525	2.5 (2.0,3.2)
PC.ae.C32.1	525	2.9 (2.3,3.7)
PC.ae.C32.2	443	0.8 (0.5,1.1)
PC.ae.C34.0	403	1.3 (1.0,1.7)
PC.ae.C34.1	483	4.5 (3.7,5.8)
PC.ae.C34.2	523	2.8 (2.1,3.5)
PC.ae.C34.3	524	1.0 (0.7,1.2)
PC.ae.C36.1	523	2.7 (2.2,3.3)
PC.ae.C36.2	521	2.4 (1.9,2.9)
PC.ae.C36.3	445	1.6 (1.2,2.1)
PC.ae.C36.4	606	7.0 (5.4,8.6)
PC.ae.C36.5	526	5.5 (4.2,7.0)
PC.ae.C38.0	482	1.1 (0.8,1.4)
PC.ae.C38.3	442	2.4 (1.8,3.0)
PC.ae.C38.4	526	7.4 (5.8,9.0)
PC.ae.C38.5	445	6.0 (4.8,7.5)
PC.ae.C38.6	443	2.8 (2.1,3.5)
PC.ae.C40.0	484	6.4 (4.9,7.9)
PC.ae.C40.1	403	1.0 (0.5,1.4)
PC.ae.C40.4	521	1.7 (1.3,2.2)
PC.ae.C40.5	604	1.7 (1.3,2.3)
PC.ae.C40.6	524	2.2 (1.7,2.8)
PC.ae.C42.2	322	0.3 (0.2,0.4)
PC.ae.C42.5	402	1.0 (0.8,1.4)
PC.ae.C42.6	440	0.6 (0.4,0.9)
SM.a.C32.1	525	2.7 (2.1,3.5)
SM.a.C33.1	439	1.8 (1.4,2.3)
SM.a.C34.0	443	3.4 (2.7,4.2)
SM.a.C34.1	607	60.8 (47.2,80.5)
SM.a.C34.2	525	9.7 (7.6,12.3)
SM.a.C35.1	364	1.5 (1.2,2.0)
SM.a.C36.1	526	18.3 (14.3,22.4)
SM.a.C36.2	606	12.1 (8.9,15.4)
SM.a.C38.1	324	15.6 (11.9,31.6)
SM.a.C38.2	523	14.2 (11.7,17.6)
SM.a.C39.1	477	1.3 (1.0,1.7)
SM.a.C40.2	483	18.5 (14.0,26.5)
SM.a.C40.4	520	2.0 (1.4,2.9)
SM.a.C41.1	364	3.9 (3.1,4.8)
SM.a.C41.2	445	2.7 (2.1,3.4)
SM.a.C42.1	425	23.9 (19.3,28.7)
SM.a.C42.2	605	31.7 (25.8,38.7)
SM.a.C42.3	605	19.1 (15.5,24.4)
SM.a.C42.6	359	3.6 (2.6,4.7)
SM.a.C43.1	520	1.1 (0.8,1.4)
SM.a.C44.1	305	0.6 (0.1,1.8)
SM.a.C41.0	401	0.7 (0.4,1.7)
SM.a.C47.5	481	0.0 (0.0,0.0)
SM.a.C47.6	314	0.0 (0.0,0.0)
NEFA 10_0	526	0.9 (0.5,1.3)
NEFA 12_0	605	1.9 (1.2,2.8)
NEFA 14_1	524	1.1 (0.5,1.7)

NEFA 15_0	587	0.3 (0.1,0.5)
NEFA 15_1	371	0.0 (0.0,0.0)
NEFA 16_0	607	61.8 (42.9,85.4)
NEFA 16_1	607	4.2 (2.7,6.9)
NEFA 17_0	607	2.0 (1.5,2.5)
NEFA 17_1	526	0.5 (0.4,0.8)
NEFA 18_1	607	51.3 (35.2,73.4)
NEFA 18_2	524	16.4 (10.8,25.8)
NEFA 18_3	583	1.1 (0.7,1.9)
NEFA 20_0	481	0.4 (0.3,0.5)
NEFA 20_1	604	0.6 (0.4,0.9)
NEFA 20_2	526	0.7 (0.5,0.9)
NEFA 20_3	607	1.5 (1.1,2.2)
NEFA 20_4	606	2.3 (1.6,3.6)
NEFA 22_0	526	0.2 (0.1,0.2)
NEFA 22_1	597	0.1 (0.1,0.2)
NEFA 22_2	596	0.1 (0.1,0.1)
NEFA 22_6	521	3.2 (2.2,4.6)
NEFA 24_1	598	0.4 (0.3,0.6)
NEFA 19_0	441	0.4 (0.3,0.5)
NEFA 19_1	523	0.3 (0.2,0.4)
NEFA 20_5	451	0.1 (0.0,0.2)
NEFA 22_3	402	0.3 (0.2,0.4)
NEFA 22_4	599	0.7 (0.5,1.0)
NEFA 22_5	599	0.6 (0.4,0.9)
NEFA 24_0	517	0.2 (0.1,0.2)
NEFA 24_2	323	0.1 (0.1,0.2)
NEFA 24_4	601	0.2 (0.2,0.3)
NEFA 24_5	524	0.2 (0.1,0.2)
NEFA 24_6	402	0.0 (0.0,0.1)
NEFA 26_0	356	0.0 (0.0,0.1)
NEFA 26_1	479	0.1 (0.1,0.1)
NEFA 26_2	517	0.1 (0.1,0.1)
NEFA 26_3	440	0.1 (0.1,0.1)
NEFA 26_4	519	0.2 (0.1,0.2)
NEFA 26_6	359	0.1 (0.1,0.1)
Carn	525	17.3 (14.3,21.6)
Carn.a.C10.0	525	0.1 (0.1,0.1)
Carn.a.C10.1	525	0.1 (0.1,0.2)
Carn.a.C12.0	524	0.1 (0.0,0.1)
Carn.a.C12.1	442	0.1 (0.1,0.2)
Carn.a.C14.0	606	0.1 (0.0,0.1)
Carn.a.C14.1	525	0.1 (0.1,0.1)
Carn.a.C15.0	401	0.0 (0.0,0.0)
Carn.a.C16.0	602	0.1 (0.1,0.2)
Carn.a.C16.1	605	0.1 (0.1,0.1)
Carn.a.C18.0	442	0.0 (0.0,0.0)
Carn.a.C18.1	604	0.1 (0.1,0.2)
Carn.a.C18.2	357	0.1 (0.1,0.3)
Carn.a.C2.0	525	5.1 (3.9,7.0)
Carn.a.C20.0	397	0.0 (0.0,0.0)
Carn.a.C20.4	304	0.0 (0.0,0.0)
Carn.a.C3.0	605	0.4 (0.3,0.6)
Carn.a.C3.0.DC	444	0.3 (0.2,0.9)

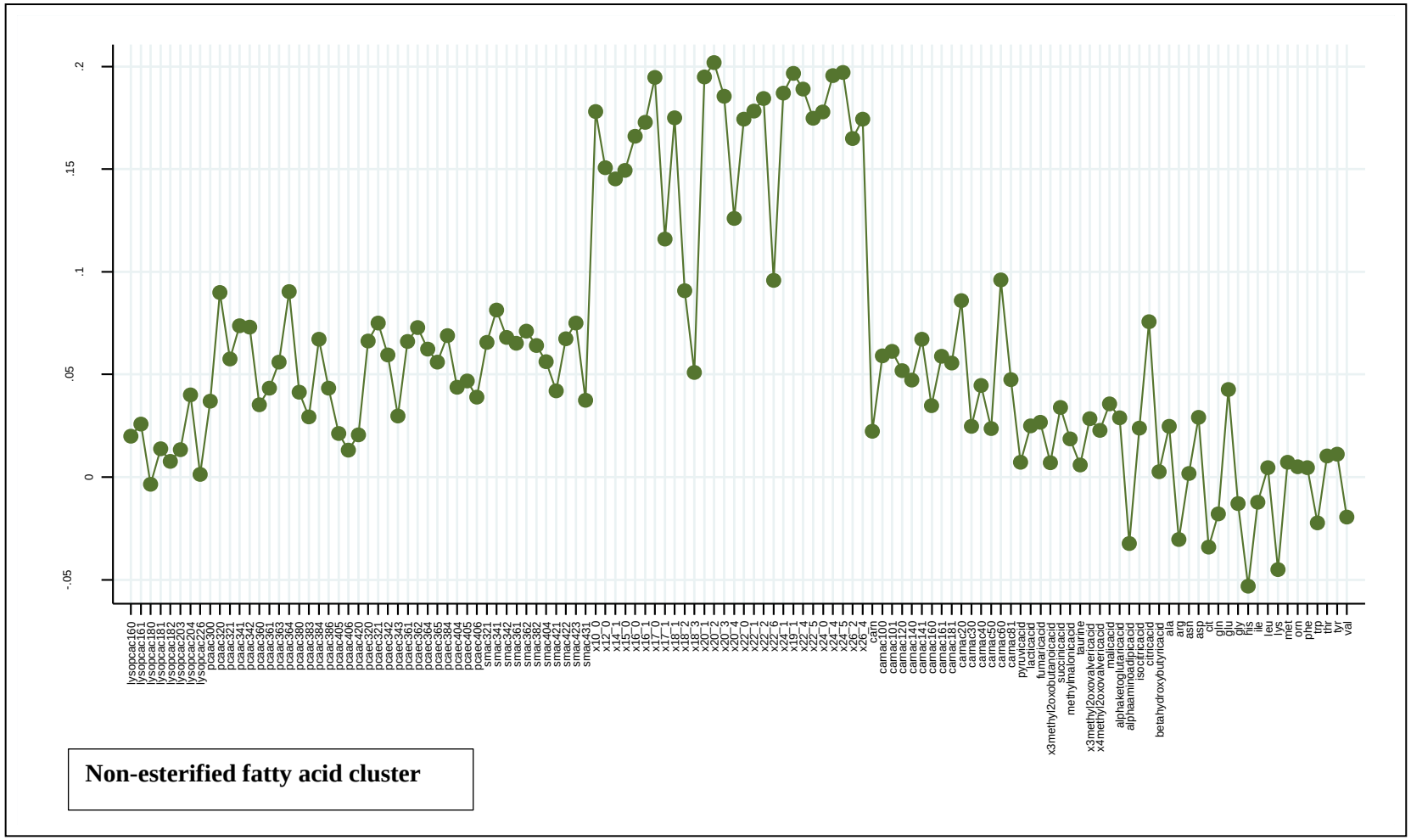
Carn.a.C4.0	605	0.2 (0.1,0.2)
Carn.a.C4.0.DC	442	0.0 (0.0,0.0)
Carn.a.C5.0	606	0.1 (0.1,0.2)
Carn.a.C6.0	606	0.1 (0.1,0.1)
Carn.a.C8.0	444	0.1 (0.1,0.1)
Carn.a.C8.1	526	0.1 (0.1,0.1)
Carn.a.C9.0	441	0.0 (0.0,0.0)
Pyruvic.acid	605	15.5 (11.2,22.5)
Lactic.acid	605	27.7 (20.1,41.2)
Fumaric.acid	605	47.3 (36.2,64.4)
X3.Methyl.2.oxobutanoic.acid	606	240.5 (115.0,466.0)
Succinic.acid	606	5600.0 (3210.0,10200.0)
Methyl.Malonic.acid	605	1.6 (1.2,2.3)
Taurine	605	6.5 (4.9,9.5)
X3.Methyl.2.oxovalveric.acid	603	0.3 (0.3,0.4)
X4.Methyl.2.oxovalveric.acid	605	121.0 (86.8,173.0)
Malic.acid	604	7.1 (5.4,10.7)
Alpha.Ketoglutaric.acid	605	4.3 (3.0,6.2)
Alpha.Aminoadipic.acid	604	0.7 (0.5,0.9)
Isocitric.acid	604	21.2 (17.4,25.5)
Citric.acid	604	114.0 (96.5,133.0)
Beta.Hydroxybutyric.acid	524	138.0 (63.5,240.0)
Ala	605	454.0 (367.0,555.0)
Arg	606	36.0 (21.5,52.1)
Asn	605	41.5 (33.2,52.6)
Asp	605	13.8 (9.0,22.1)
Cit	606	13.8 (10.7,17.3)
Gln	605	400.0 (322.0,497.0)
Glu	601	106.0 (78.1,149.0)
Gly	604	276.5 (231.0,327.0)
His	603	154.0 (125.0,188.0)
Ile	602	61.3 (50.0,77.1)
Leu	606	107.5 (92.3,128.0)
Lys	606	230.0 (193.0,288.0)
Met	606	28.3 (23.4,35.4)
Orn	511	108.0 (85.0,132.0)
Phe	606	82.8 (70.3,96.7)
Pro	485	186.0 (156.0,243.0)
Trp	605	49.2 (40.3,59.9)
Ser	484	98.0 (79.5,123.0)
Thr	562	202.5 (162.0,253.0)
Tyr	606	58.8 (49.3,73.2)
Val	606	204.0 (176.0,250.0)
Cys	483	14.0 (11.4,17.2)

Supplement Table 3: Summary statistics of the cord blood metabolic profile including candidate biomarkers and metabolome from obese pregnant women included in the UPBEAT trial (n=607)

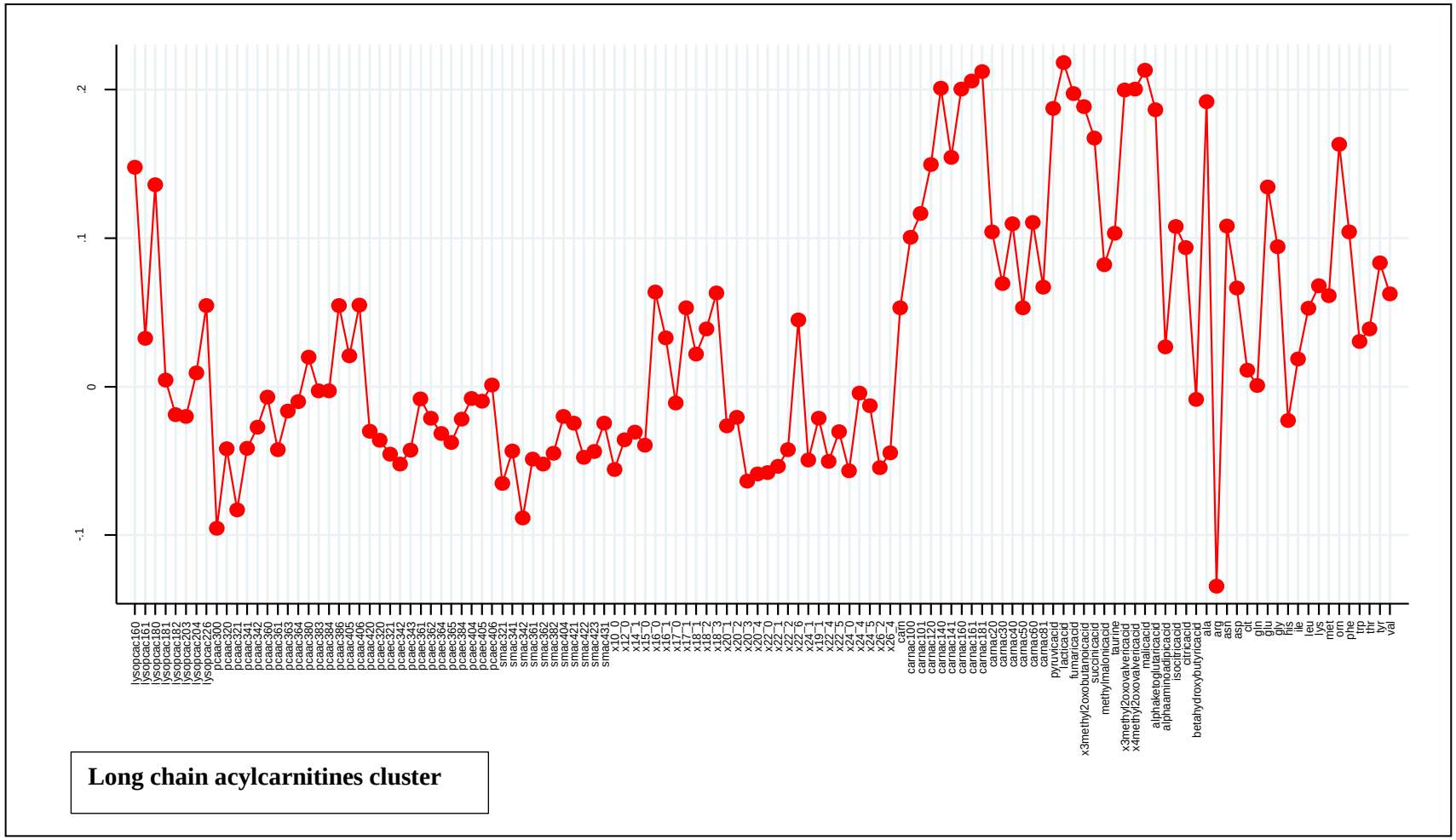
Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins; TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V- 3methyl2oxovalvericacid; X40B-4methyl2oxovalvericacid.



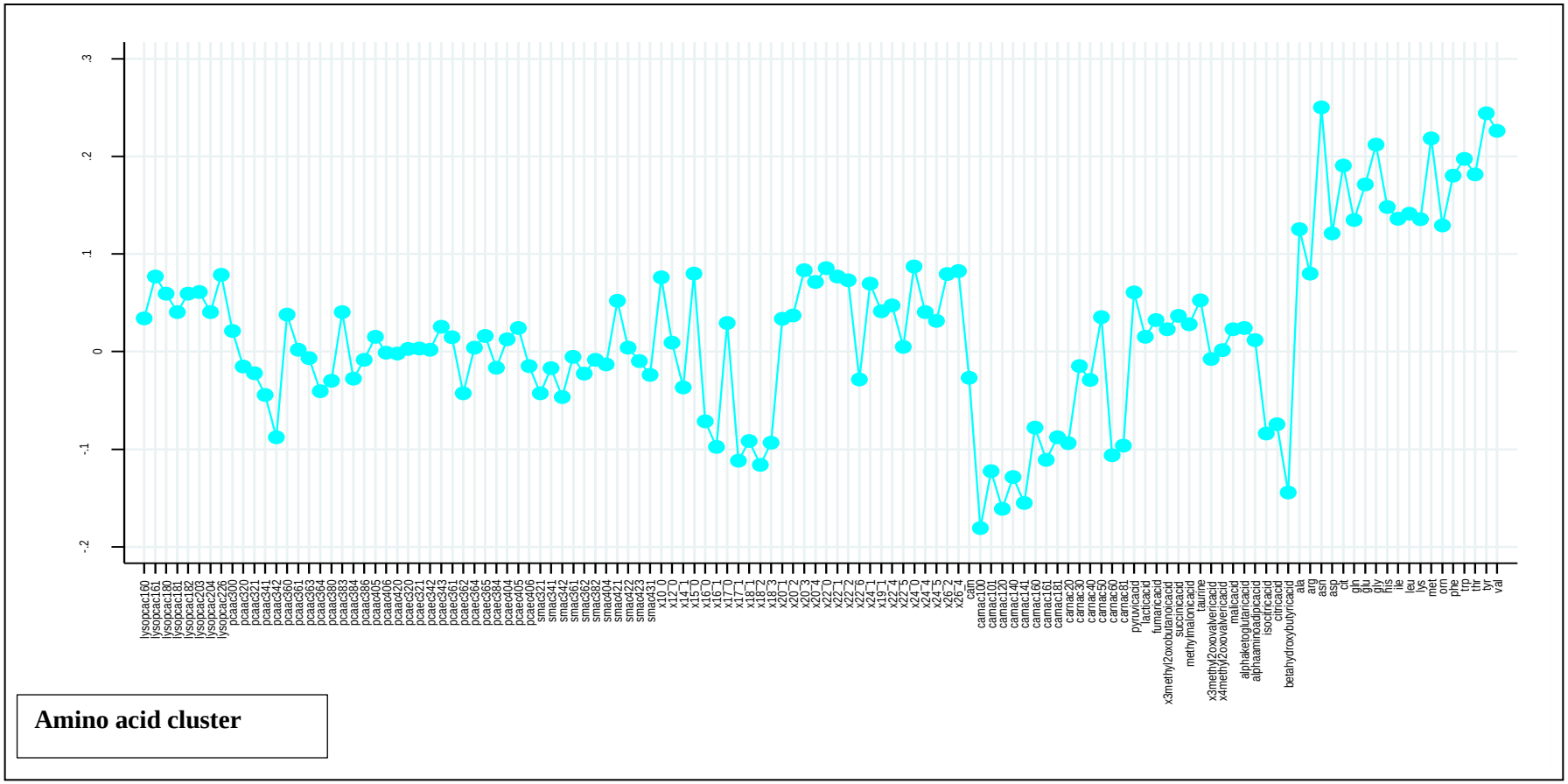
Supplement Figure 3a: Graphical representation of phosphatidylcholine cluster derived from principal component analysis of the cord blood metabolomic profile from infants born to obese pregnant women (N=609).



Supplement Figure 3b: Graphical representation of non-esterified fatty acid cluster derived from principal component analysis of the cord blood metabolomic profile from infants born to obese pregnant women (N=609).



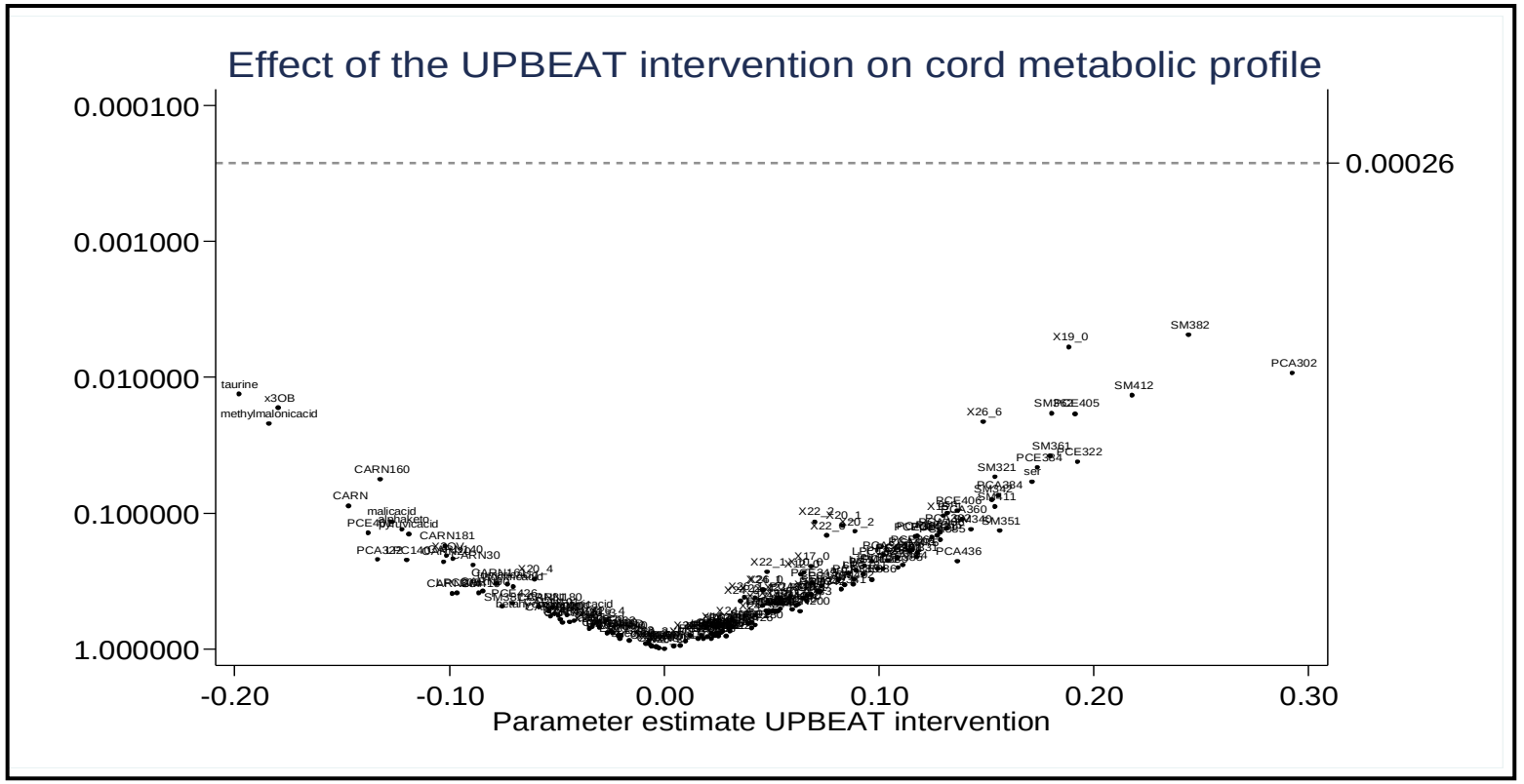
Supplement Figure 3c: Graphical representation of long chain acylcarnitines and tricarboxylic acid cycle associated metabolites cluster derived from principal component analysis of the cord blood metabolomic profile from infants born to obese pregnant women (N=609).



Supplement Figure 3d: Graphical representation of amino acids metabolite cluster derived from principal component analysis of the cord blood metabolomic profile from infants born to obese pregnant women (N=609).

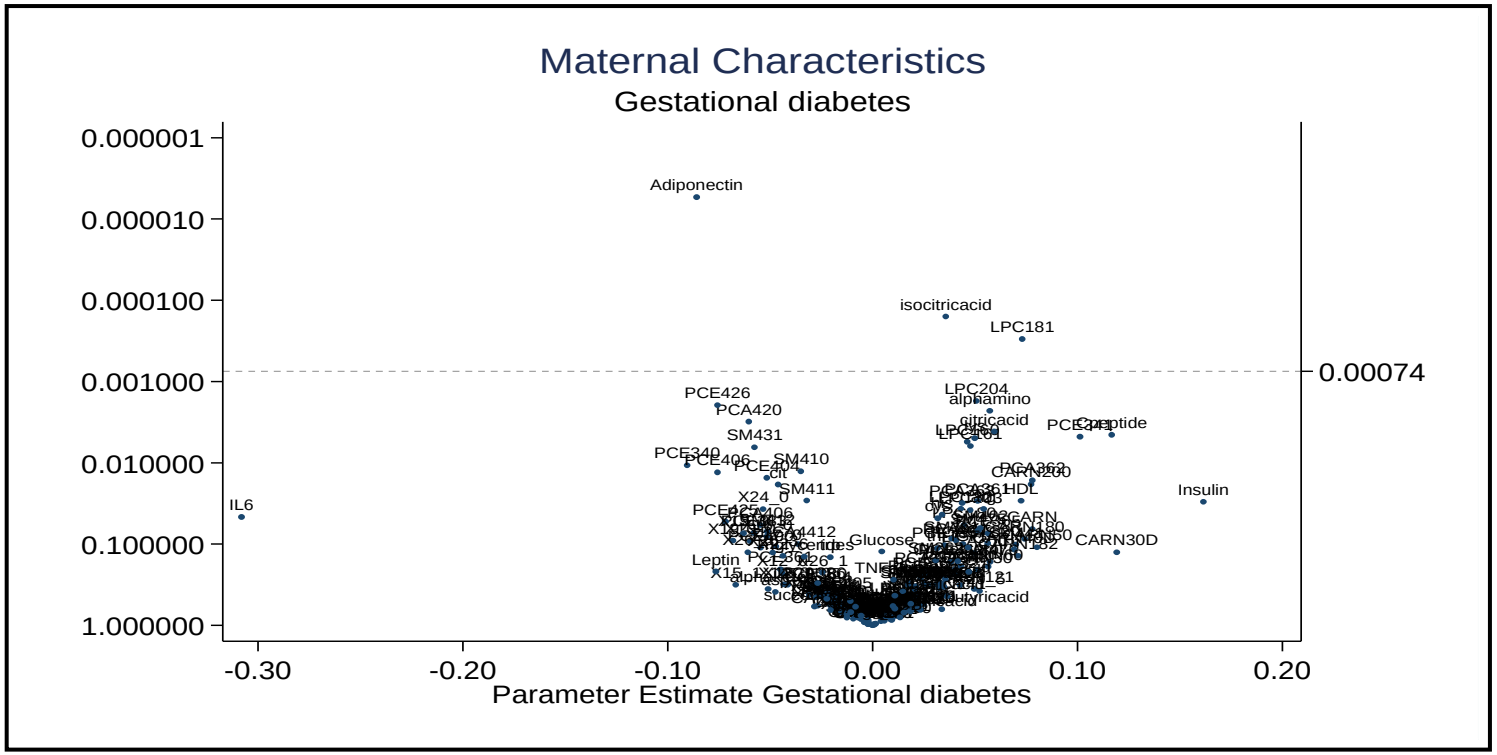
	Included N=607	Excluded N=947	Comparison (95% CI)	p-value
Maternal age	30.97 (5.39)	30.17 (5.58)	0.81 (0.25 to 1.36)	0.005
Multiparity	318 (52.4%)	562 (59.3%)	0.75 (0.61 to 0.93)	0.007
BMI (kg/m^2)	36.52 (4.93)	36.15 (4.66)	0.37 (-0.12 to 0.86)	0.138
Socioeconomic deprivation	341 (80.0%)	N=822; 666 (80.6%)	0.96 (0.72 to 1.29)	0.806
White ethnicity	433 (71.6)	524 (57.3)	1.25 (1.16 to 1.35)	<0.001
Black ethnicity	116 (19.1%)	272 (29.8%)	0.56 (0.43 to 0.71)	<0.001
Asian ethnicity	29 (4.8%)	62/ (6.8%)	0.69 (0.44 to 1.08)	0.107
Other ethnicity	28 (4.6%)	56 (6.1%)	0.74 (0.46 to 1.18)	0.205
Smoker in early pregnancy	33 (6.4)	66(7.2)	0.88 (0.58 to 1.33)	0.545

Supplement Table 4: Baseline differences in maternal baseline demographic characteristics of those included versus those excluded in the analyses to assess the effect of the UPBEAT intervention on the cord blood metabolic profile.



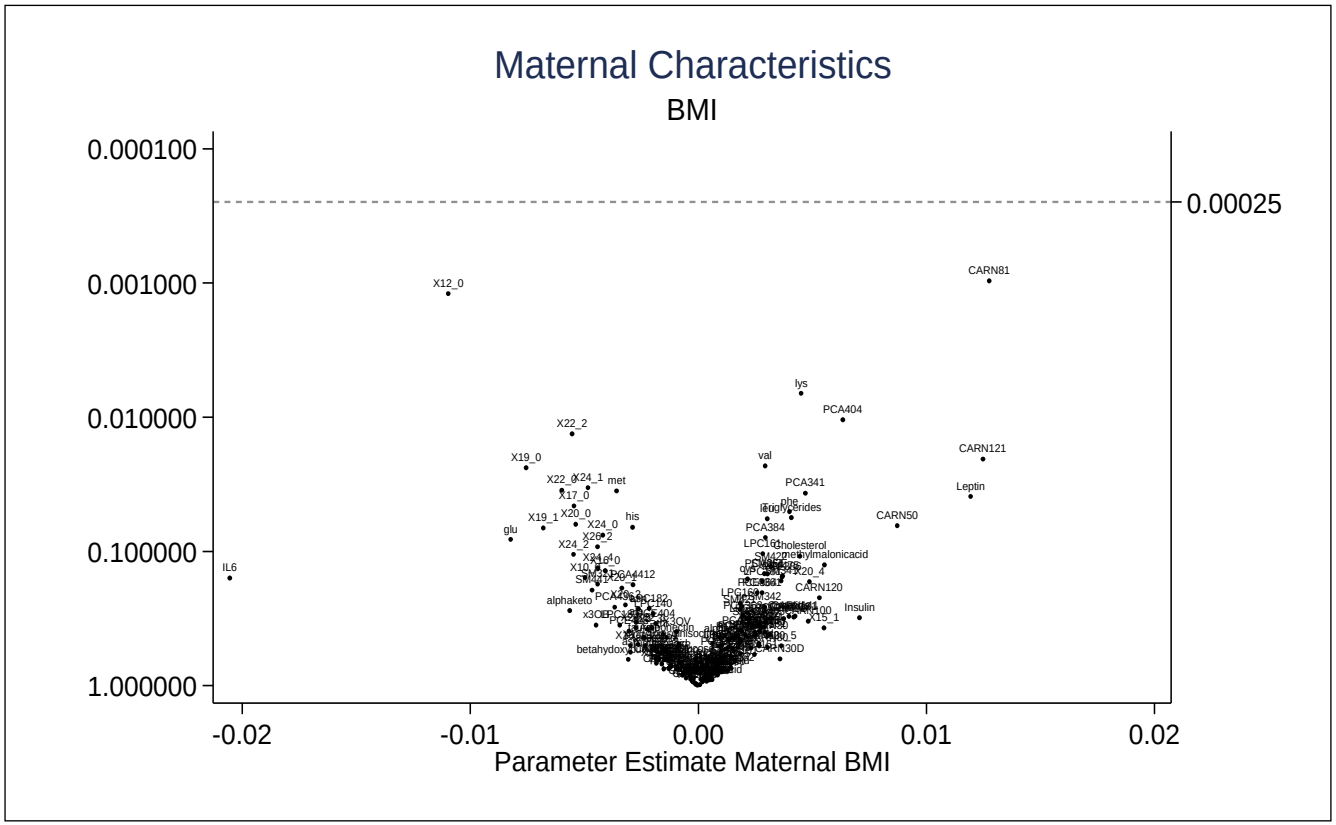
Supplement Figure 4: Effect of the UPBEAT intervention on the cord blood metabolic profile in infants born to obese pregnant women (n=607).

Parameter effect estimates of the UPBEAT intervention and significance level following adjustment for false discovery rate using Benjamin & Hochberg procedure. Statistical significance p<0.00026. Adjustment was made for maternal ethnicity, age, pre-pregnancy BMI and ethnicity; minimisation variables used in the randomisation procedure. Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins. TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V-- x4methyl2oxovalvericacid. NEFAs are described using the nomenclature CX:Y, where X is the length of the carbon chain, Y is the number of double bonds, OH in the formula means the molecule contains a hydroxyl-group.



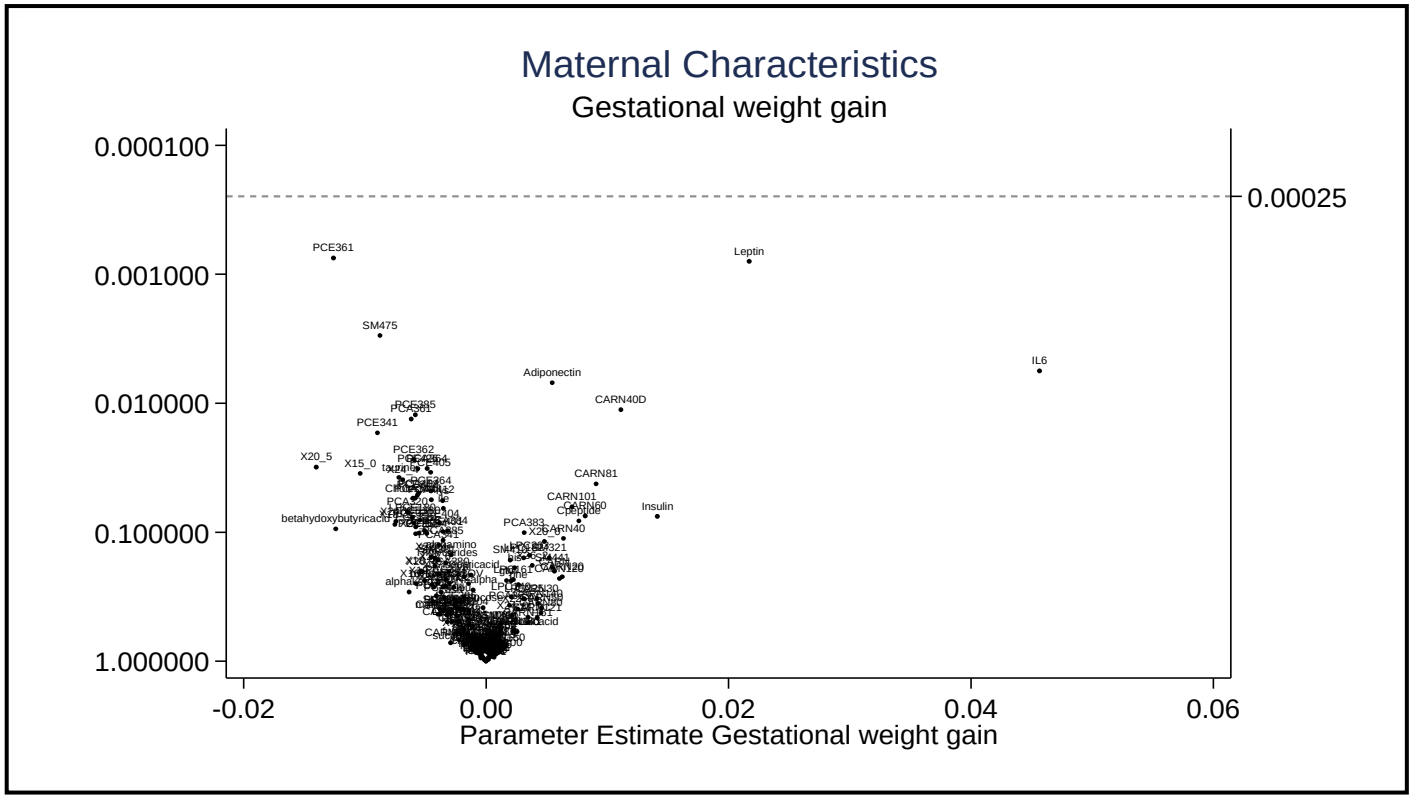
Supplement Figure 5: Volcano plot demonstrating the association of maternal gestational diabetes with cord blood metabolic profile in infants born to obese pregnant women (n=607).

Parameter estimates are graphically represented for each biochemical variable in relation to maternal clinical characteristics following adjustment using a false discovery rate (Benjamin & Hochberg procedure) (17). Statistical significance p<0.00074. Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins. TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V-- x4methyl2oxovalvericacid. NEFAs are described using the nomenclature CX:Y, where X is the length of the carbon chain, Y is the number of double bonds, OH in the formula means the molecule contains a hydroxyl-group.



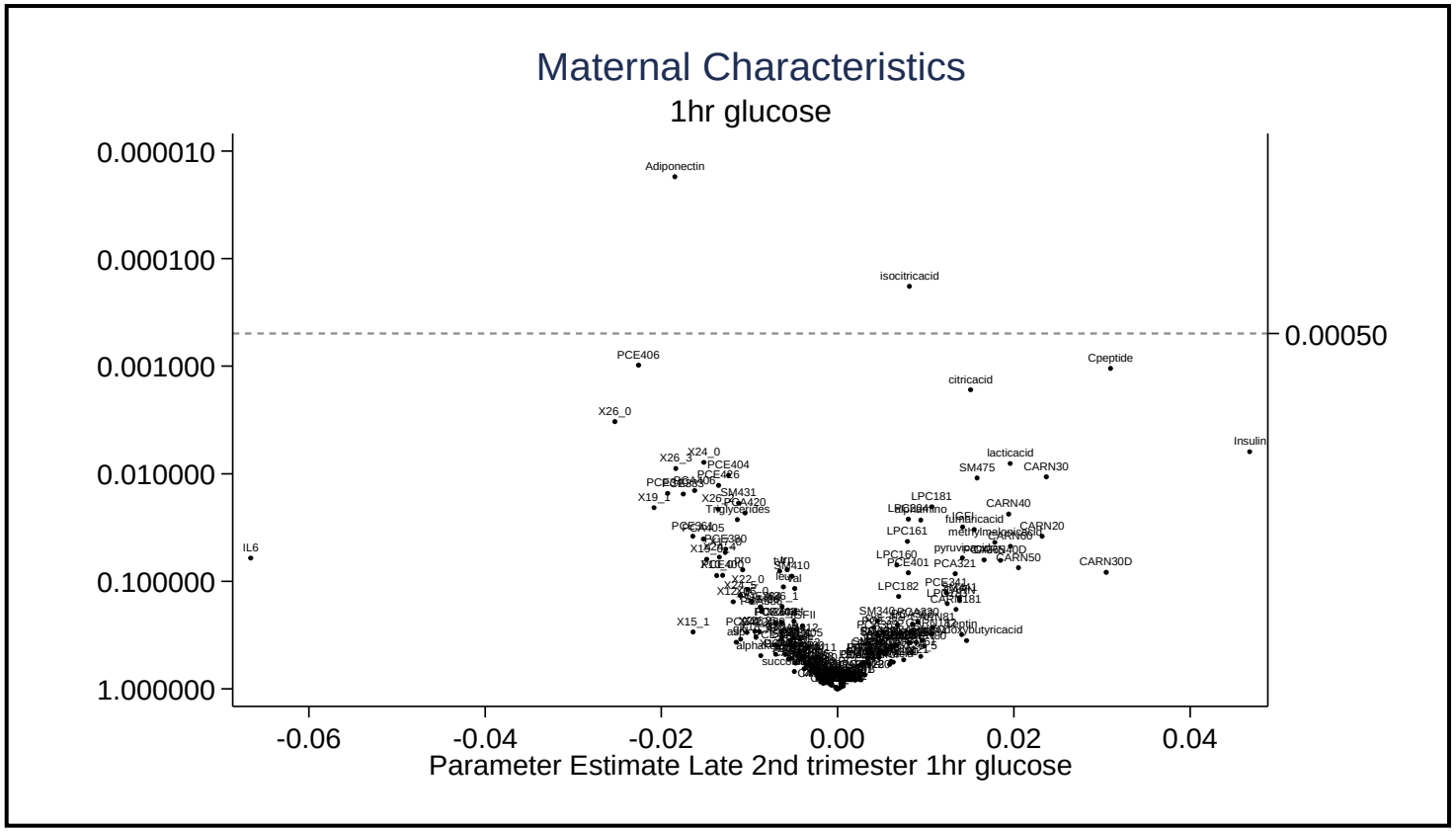
Supplement Figure 6: Volcano plot demonstrating the association of maternal pre-pregnancy BMI with cord blood metabolic profile in infants born to obese pregnant women (n=607).

Parameter estimates are graphically represented for each biochemical variable in relation to maternal clinical characteristics following adjustment using a false discovery rate (Benjamin & Hochberg procedure) (17).Statistical significance p<0.00025. Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins. TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V-- x4methyl2oxovalvericacid. NEFAs are described using the nomenclature CX:Y, where X is the length of the carbon chain, Y is the number of double bonds, OH in the formula means the molecule contains a hydroxyl-group.



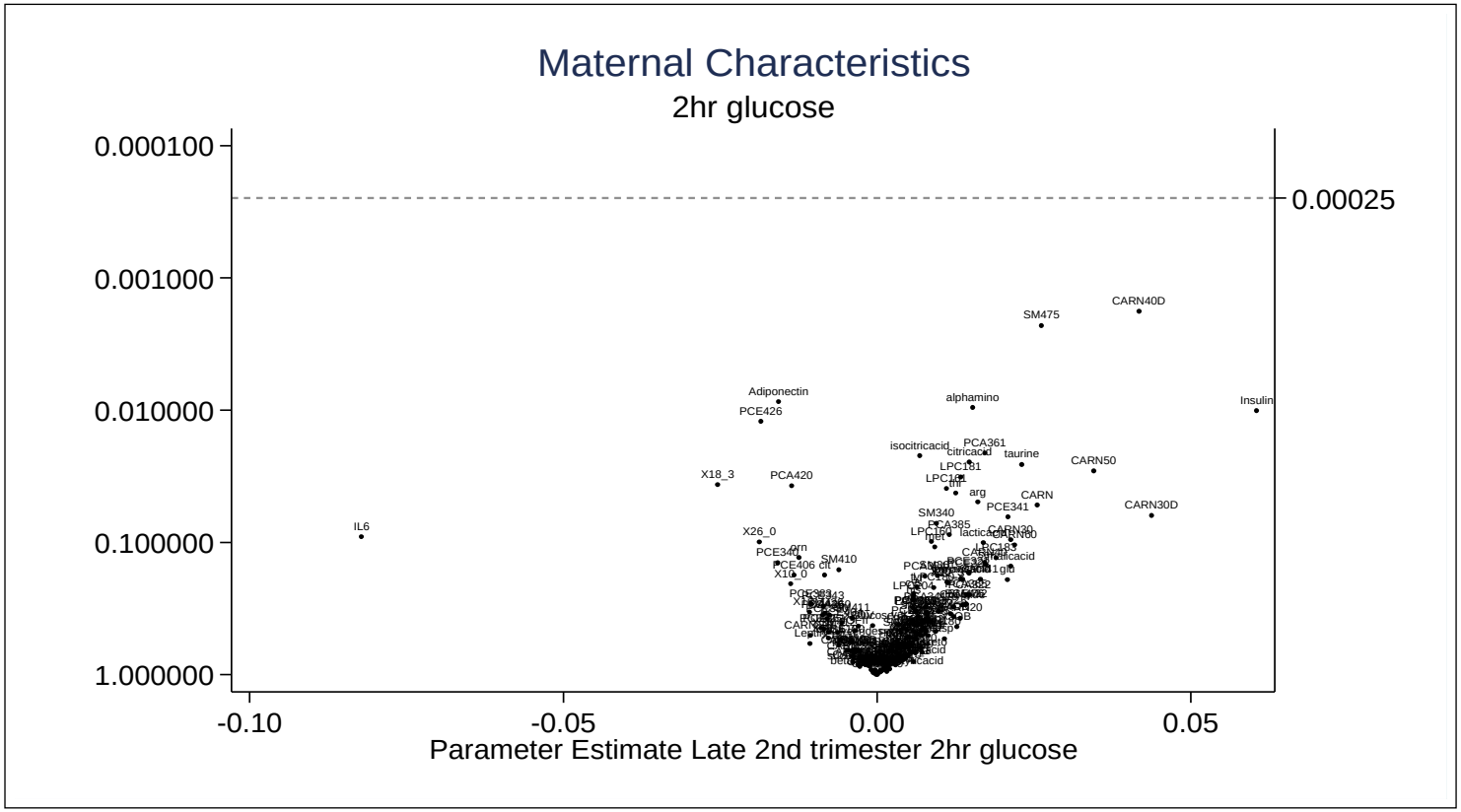
Supplement Figure 7: Volcano plot demonstrating the association of maternal gestational weight gain with cord blood metabolic profile in infants born to obese pregnant women (n=607).

Parameter estimates are graphically represented for each biochemical variable in relation to maternal clinical characteristics following adjustment using a false discovery rate (Benjamin & Hochberg procedure) (17). Statistical significance p<0.00025. Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins. TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V-- x4methyl2oxovalvericacid. NEFAs are described using the nomenclature CX:Y, where X is the length of the carbon chain, Y is the number of double bonds, OH in the formula means the molecule contains a hydroxyl-group.



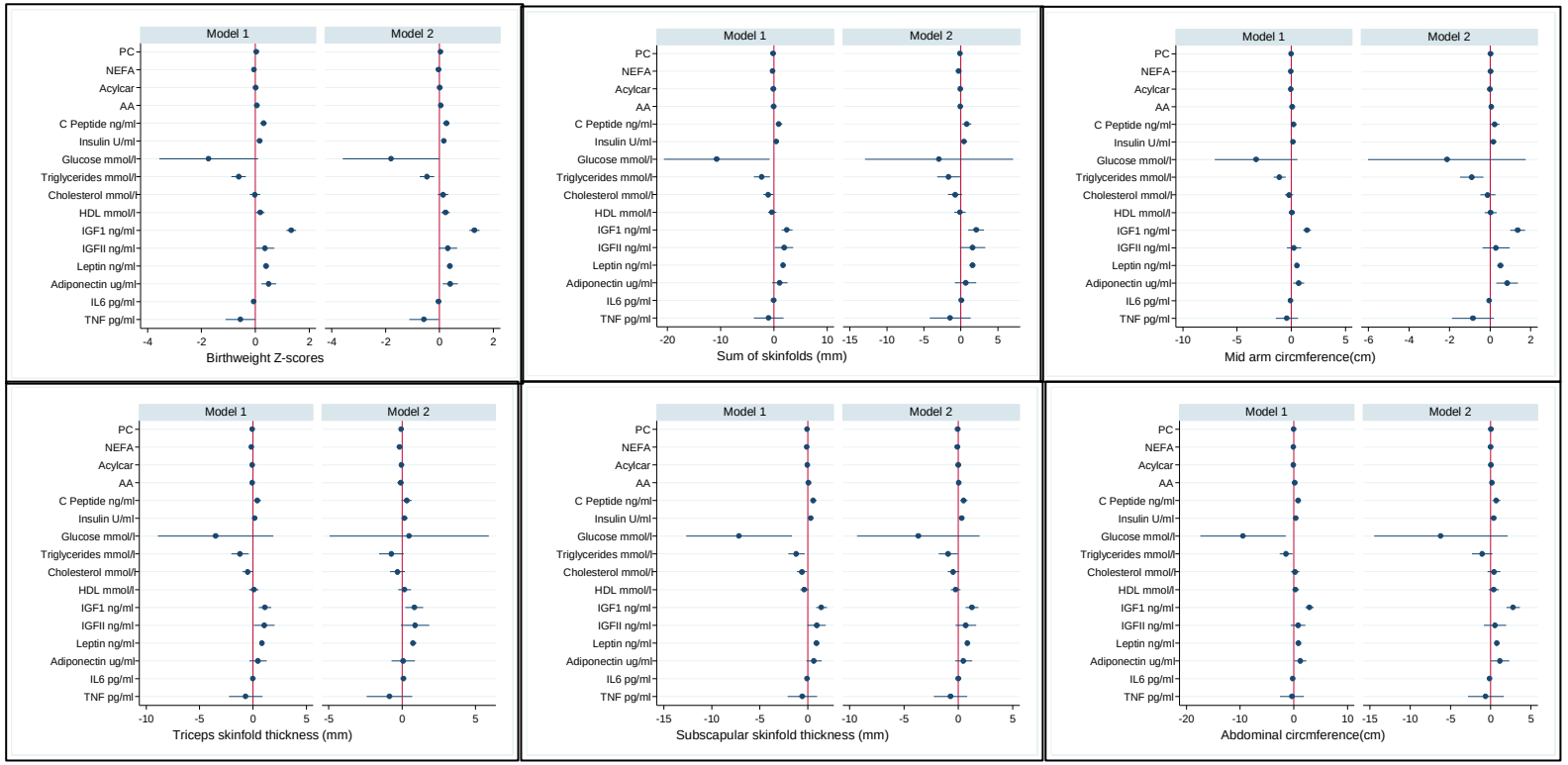
Supplement Figure 8: Volcano plot demonstrating the association of maternal glucose at 1 hour at the time of the oral glucose tolerance test with cord blood metabolic profile in infants born to obese pregnant women (n=607).

Parameter estimates are graphically represented for each biochemical variable in relation to maternal clinical characteristics following adjustment using a false discovery rate (Benjamin & Hochberg procedure) (17). Statistical significance p<0.005. Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins. TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V-- x4methyl2oxovalvericacid. NEFAs are described using the nomenclature CX:Y, where X is the length of the carbon chain, Y is the number of double bonds, OH in the formula means the molecule contains a hydroxyl-group.



Supplement Figure 9: Volcano plot demonstrating the association of maternal glucose at 2 hours at the time of the oral glucose tolerance test with cord blood metabolic profile in infants born to obese pregnant women (n=607).

Parameter estimates are graphically represented for each biochemical variable in relation to maternal clinical characteristics following adjustment using a false discovery rate (Benjamin & Hochberg procedure) (17). Statistical significance p<0.0025. Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins. TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V-- x4methyl2oxovalvericacid. NEFAs are described using the nomenclature CX:Y, where X is the length of the carbon chain, Y is the number of double bonds, OH in the formula means the molecule contains a hydroxyl-group.



Supplement Figure 10: Associations of the cord blood metabolic profile with neonatal anthropometry in infants born to obese pregnant women (n=344)

Regression coefficients graphically presented with corresponding 95% confidence intervals. Model 1: Adjustment made for offspring sex, gestation at delivery and randomisation to the UPBEAT intervention. Model 2: Adjustment made for maternal parity, ethnicity, and smoker in early pregnancy, gestational diabetes, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention. Abbreviations; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IGFII- Insulin growth factor II; IL6-Interleukin 6; MUAC-Mid upper arm circumference; SDS- Standard deviation scores; SFT- skinfold thickness; TNFalpha- Tumour Necrosis Factor alpha.

	Weight z-scores (n=247)	**Length z-score (n=238)**	**BMI z-score (n=238)**	**MUAC z-score (n=246)**	**Triceps SFT z-score (n=242)**	**Subscapular SFT z-score (n=209)**
	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)	Coef (95% CI)
PCA-Phosphatidylcholines	0.05 (0.00 to 0.10) *	0.07 (0.01 to 0.13) *	0.01 (-0.04 to 0.07)	0.04 (0.00 to 0.08)	0.05 (-0.02 to 0.13)	-0.03 (-0.11 to 0.05)
PCA-NEFA	-0.03 (-0.09 to 0.04)	-0.02 (-0.10 to 0.06)	-0.02 (-0.09 to 0.05)	-0.05 (-0.10 to 0.01)	-0.04 (-0.15 to 0.08)	0.01 (-0.11 to 0.14)
Cpeptide (log_2) ng/ml	0.00 (-0.023 to 0.23)	-0.18 (-0.59 to 0.24)	0.14 (-0.30 to 0.58)	0.08 (-0.32 to 0.49)	0.32 (-0.03 to 0.67)	0.21 (-0.13 to 0.56)
Insulin (log_2) U/ml	0.07 (-0.05 to 0.20)	-0.10 (-0.33 to 0.13)	0.19 (-0.06 to 0.43)	0.06 (-0.16 to 0.28)	-0.01 (-0.20 to 0.19)	0.02 (-0.18 to 0.22)
Glucose (log_2) mmol/l	-0.80 (-4.29 to 2.69)	0.28 (-6.16 to 6.71)	-1.64 (-8.38 to 5.10)	1.19 (-4.95 to 7.32)	1.35 (-4.13 to 6.82)	-0.49 (-6.13 to 5.15)
Triglycerides mmol/l	-0.30 (-0.83 to 0.24)	0.37 (-0.64 to 1.38)	-0.89 (-1.95 to 0.18)	-1.05 (-2.01 to -0.08) *	-0.39 (-1.22 to 0.44)	-0.34 (-1.20 to 0.53)
HDL mmol/l	0.18 (-0.10 to 0.47)	0.20 (-0.32 to 0.72)	0.07 (-0.48 to 0.61)	0.35 (-0.15 to 0.85)	0.26 (-0.18 to 0.69)	0.20 (-0.23 to 0.63)
IGFI (log_2) ng/ml	0.45 (0.11 to 0.79) *	-0.12 (-0.75 to 0.51)	0.87 (0.22 to 1.53)	0.64 (0.04 to 1.24) *	-0.04 (-0.59 to 0.50)	0.07 (-0.46 to 0.61)
Leptin (log_2) ng/ml	-0.05 (-0.21 to 0.10)	0.09 (-0.19 to 0.37)	-0.21 (-0.50 to 0.08)	-0.27 (-0.53 to 0.00) *	0.00 (-0.23 to 0.24)	0.12 (-0.11 to 0.35)
Adiponectin (log_2) up/ml	0.82 (0.30 to 1.33) **	0.98 (0.05 to 1.92) *	0.18 (-0.81 to 1.17)	0.34 (-0.56 to 1.24)	0.72 (-0.07 to 1.52)	1.00 (0.20 to 1.80) *
IL6 (log_2) pg/ml	-0.03 (-0.09 to 0.04)	0.06 (-0.05 to 0.18)	-0.09 (-0.21 to 0.03)	-0.09 (-0.19 to 0.02)	-0.05 (-0.14 to 0.04)	-0.09 (-0.18 to 0.00)
TNF alpha (log_2) pg/ml	-0.20 (-1.22 to 0.81)	1.51 (-0.33 to 3.35)	-1.99 (-3.92 to -0.06) *	-0.46 (-2.23 to 1.31)	-0.58 (-2.13 to 0.97)	0.90 (-0.63 to 2.43)

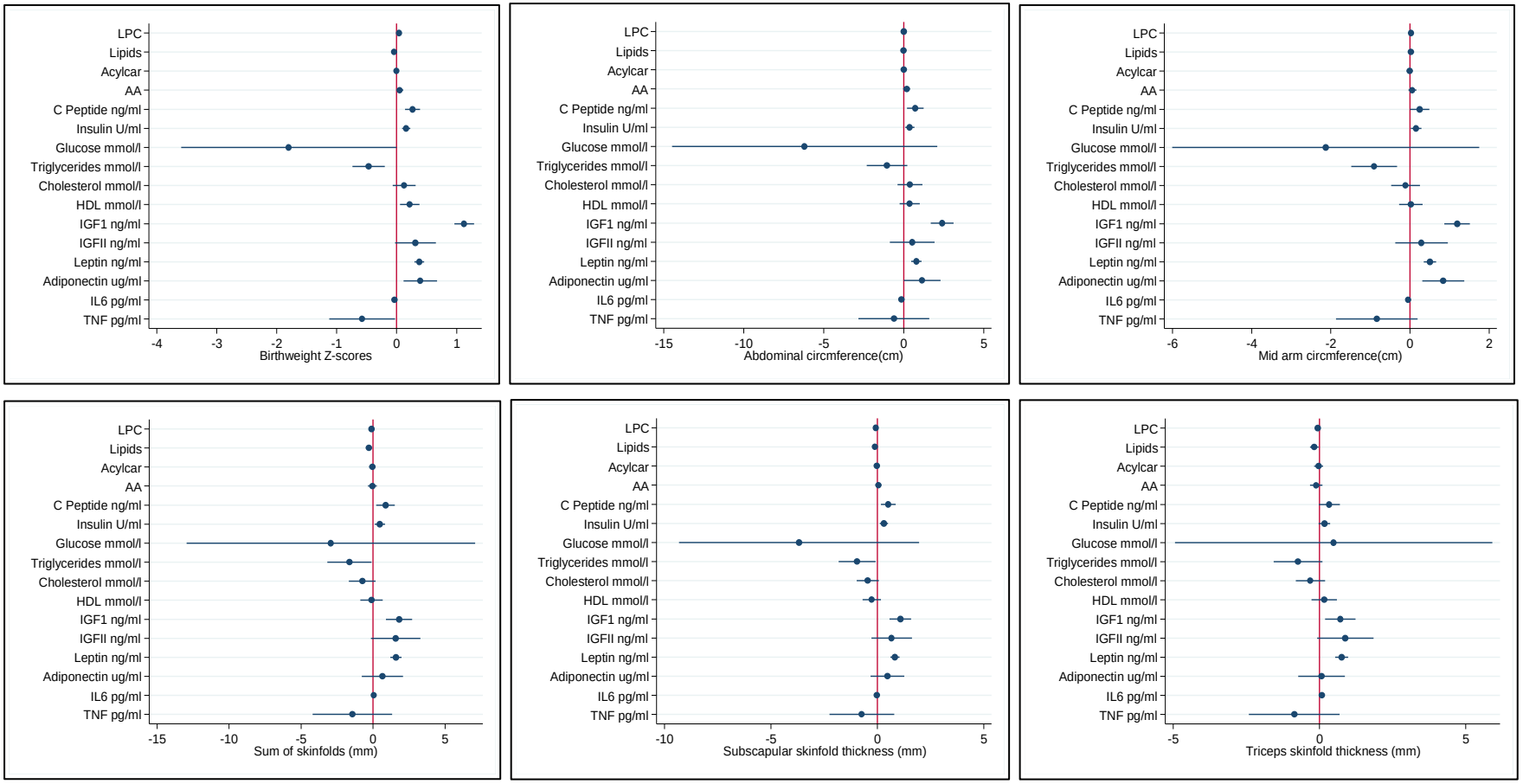
Supplement Table 5: Associations between candidate biomarkers and metabolite clusters from cord blood samples with infant anthropometry at 6 months; data from the UPBEAT study (n=209).

*Regression coefficients with corresponding 95% confidence intervals presented are adjusted for maternal parity, ethnicity, smoker in early pregnancy, gestational diabetes, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention and mode of early life feeding. Abbreviations; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IL6-Interleukin 6; MUAC-Mid upper arm circumference; NEFA-non-esterified fatty acids; SDS- Standard deviation scores; SFT- skinfold thickness; TNFalpha- Tumour Necrosis Factor alpha. *p<0.05; ** p<0.001.*

	Catch up growth (n=246) ^	**Catch down growth(n=246) ^^**
	Odds ratio (95% CI)	Odds ratio (95% CI)
PCA-Phosphatidylcholines	1.35 (1.04 to 1.75) *	1.03 (0.86 to 1.22)
PCA-NEFAs	1.34 (0.93 to 1.93)	1.07 (0.82 to 1.39)
Cpeptide (log_2) ng/ml	0.50 (0.24 to 1.05)	1.22 (0.58 to 2.58)
Insulin (log_2) U/ml	0.72 (0.48 to 1.06)	1.10 (0.74 to 1.65)
Glucose (log_2) mmol/l	0.04 (0.00 to 55.03)	0.00 (0.00 to 14.21)
Triglycerides mmol/l	1.48 (0.29 to 7.62)	0.54 (0.10 to 3.06)
HDL mmol/l	2.21 (0.93 to 5.26)	1.59 (0.67 to 3.76)
IGFI (log_2) ng/ml	0.40 (0.14 to 1.16)	5.00 (1.62 to 15.21) *
Leptin (log_2) ng/ml	0.30 (0.17 to 0.52) **	2.26 (1.37 to 3.75) **
Adiponectin (log_2) ug/ml	0.20 (0.04 to 1.06)	1.32 (0.27 to 6.89)
IL6 (log_2) pg/ml	0.94 (0.78 to 1.13)	0.95 (0.79 to 1.14)
TNF alpha (log_2) pg/ml	1.44 (0.06 to 35.12)	0.20 (0.01 to 5.10)

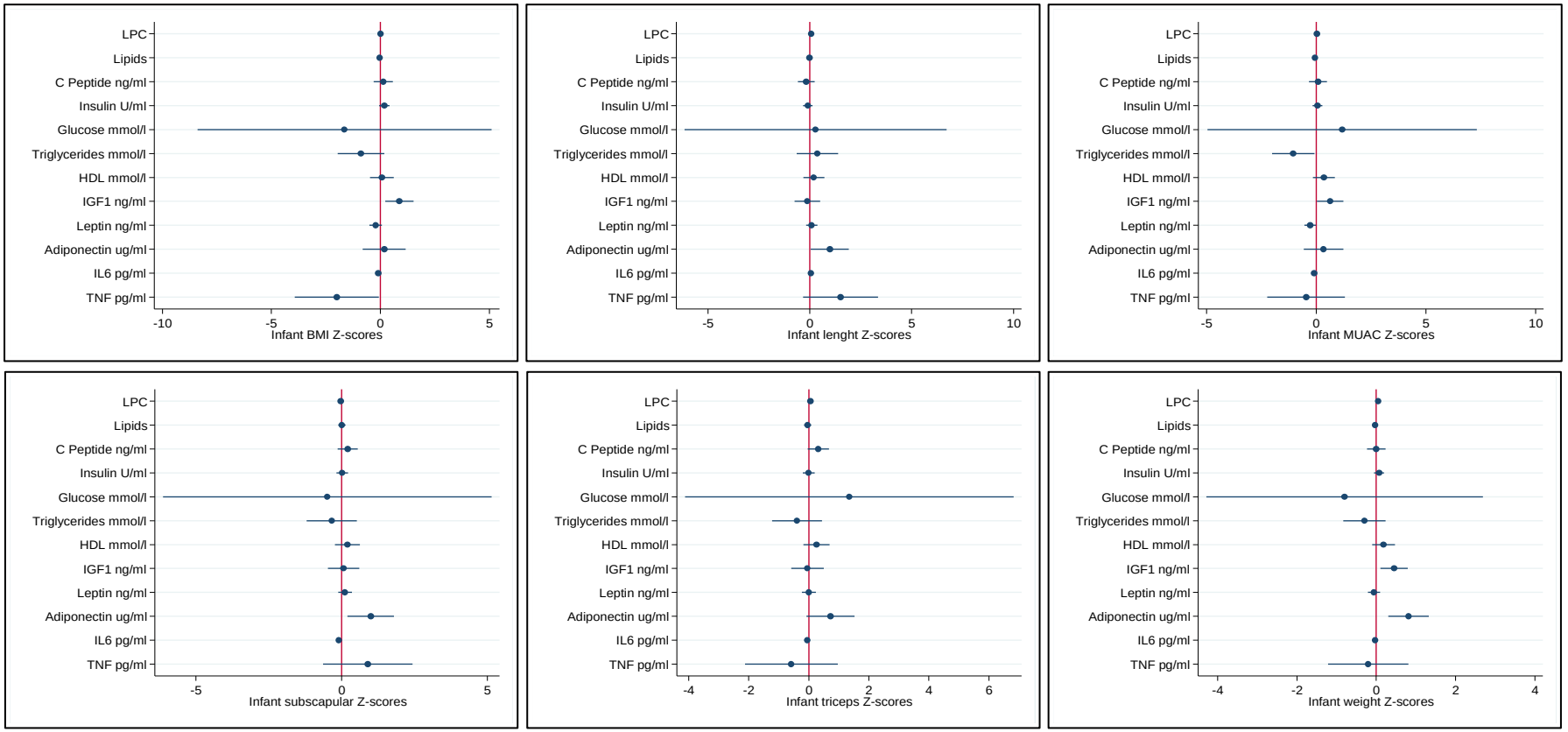
Supplement Table 6: Associations between candidate biomarkers and metabolite clusters from cord blood samples and early infant growth velocities; data from the UPBEAT study (n=246).

*Odds ratio with corresponding 95% confidence intervals presented are adjusted for maternal parity, ethnicity, smoker in early pregnancy, gestational diabetes, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention and mode of early life feeding. Abbreviations; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IL6-Interleukin 6; MUAC-Mid upper arm circumference; NEFA-non-esterified fatty acids; SDS- Standard deviation scores; SFT- skinfold thickness; TNFalpha- Tumour Necrosis Factor alpha. *p<0.05; ** p<0.001. ^ Catch up growth defined as an increase ≥0.67SDs in weight-z-scores from birth to 6 months of age using the WHO reference population (18). ^^ Catch down growth defined as a decrease ≤0.67SDs in weight-z-scores from birth to 6 months of age using the WHO reference population (18)*



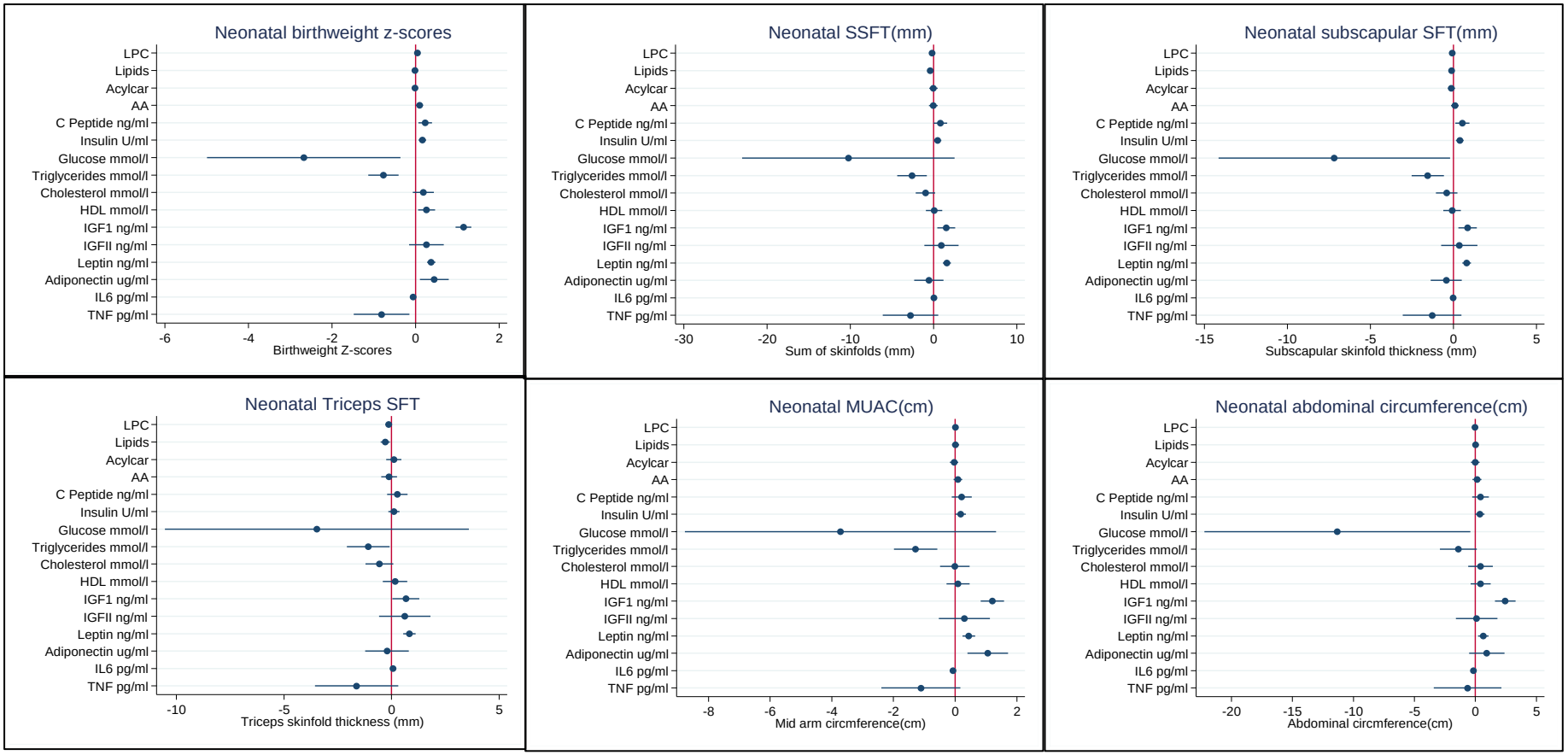
Supplement Figure 11: Sensitivity analyses following exclusion of offspring born <34 weeks' gestation demonstrating no differences in the associations between cord blood metabolic profile and neonatal anthropometry (excluded n= 36).

Regression coefficients graphically presented with corresponding 95% confidence intervals. Model 1: Adjustment made for offspring sex, gestation at delivery and randomisation to the UPBEAT intervention. Model 2: Adjustment made for maternal parity, ethnicity, and smoker in early pregnancy, gestational diabetes, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention. Abbreviations; AA-amino acids; Acylcar- Long chain acylcarnitines and TCA metabolites; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IGFII- Insulin growth factor II; IL6-Interleukin 6; MUAC-Mid upper arm circumference; NEFA-Non-esterified fatty acid; PC-phosphatidylcholine; SDS- Standard deviation scores; SFT- skinfold thickness; TNFalpha- Tumour Necrosis Factor alpha



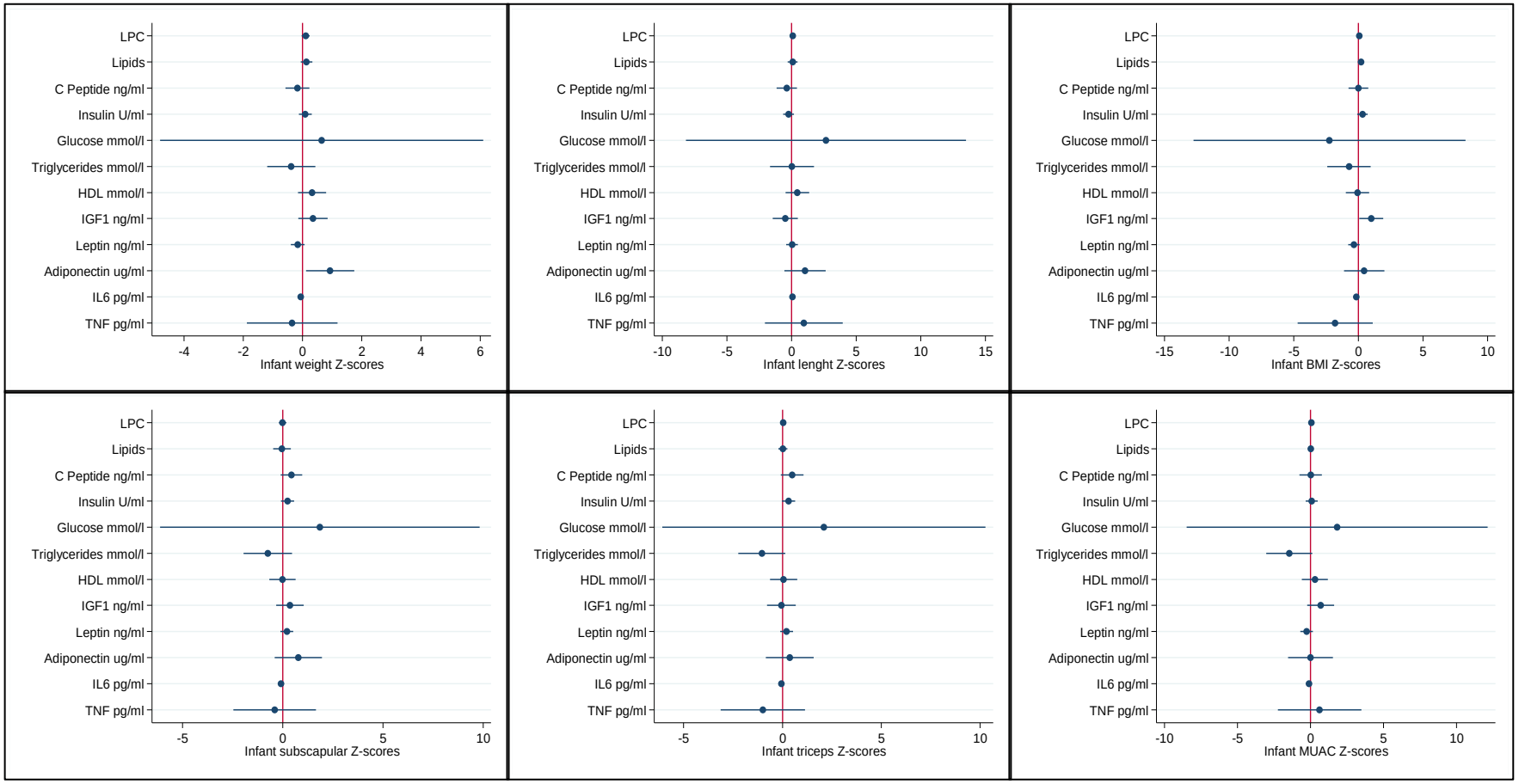
Supplement Figure 12: Sensitivity analyses following exclusion of offspring born <34 weeks' gestation demonstrating no differences in the associations between cord blood metabolic profile and infant anthropometry at 6 months of age (excluded n=36).

*Regression coefficients with corresponding 95% confidence intervals presented are adjusted for maternal parity, ethnicity, smoker in early pregnancy, gestational diabetes, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention and mode of early life feeding. Abbreviations; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IL6-Interleukin 6; MUAC-Mid upper arm circumference; NEFA-Non-esterified fatty acid; PC-phosphatidylcholine; SDS- Standard deviation scores; SFT- skinfold thickness; TNFalpha-Tumour Necrosis Factor alpha. *p<0.05; ** p<0.001.*



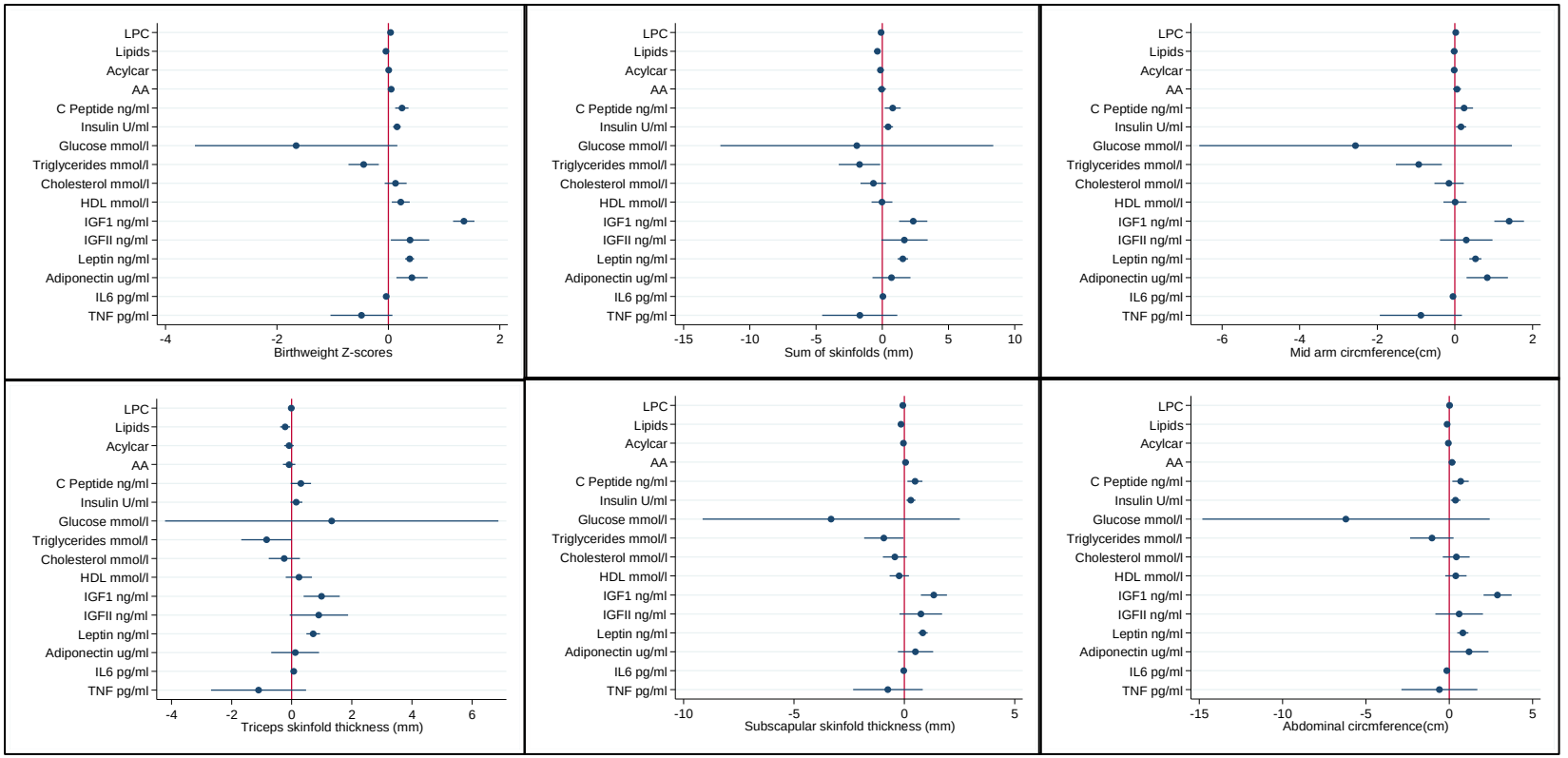
Supplement Figure 13: Sensitivity analyses of associations between cord blood metabolic profile and neonatal anthropometry, following exclusion of neonates exposed to gestational diabetes in-utero excluded n=111).

Regression coefficients graphically presented with corresponding 95% confidence intervals. Model 1: Adjustment made for offspring sex, gestation at delivery and randomisation to the UPBEAT intervention. Model 2: Adjustment made for maternal parity, ethnicity, and smoker in early pregnancy, gestational diabetes, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention. Abbreviations; AA-amino acids; Acylcar- Long chain acylcarnitines and TCA metabolites; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IGFII- Insulin growth factor II; IL6-Interleukin 6; MUAC-Mid upper arm circumference; NEFA-Non-esterified fatty acid; PC-phosphatidylcholine; SDS- Standard deviation scores; SFT- skinfold thickness; TNFalpha- Tumour Necrosis Factor alpha



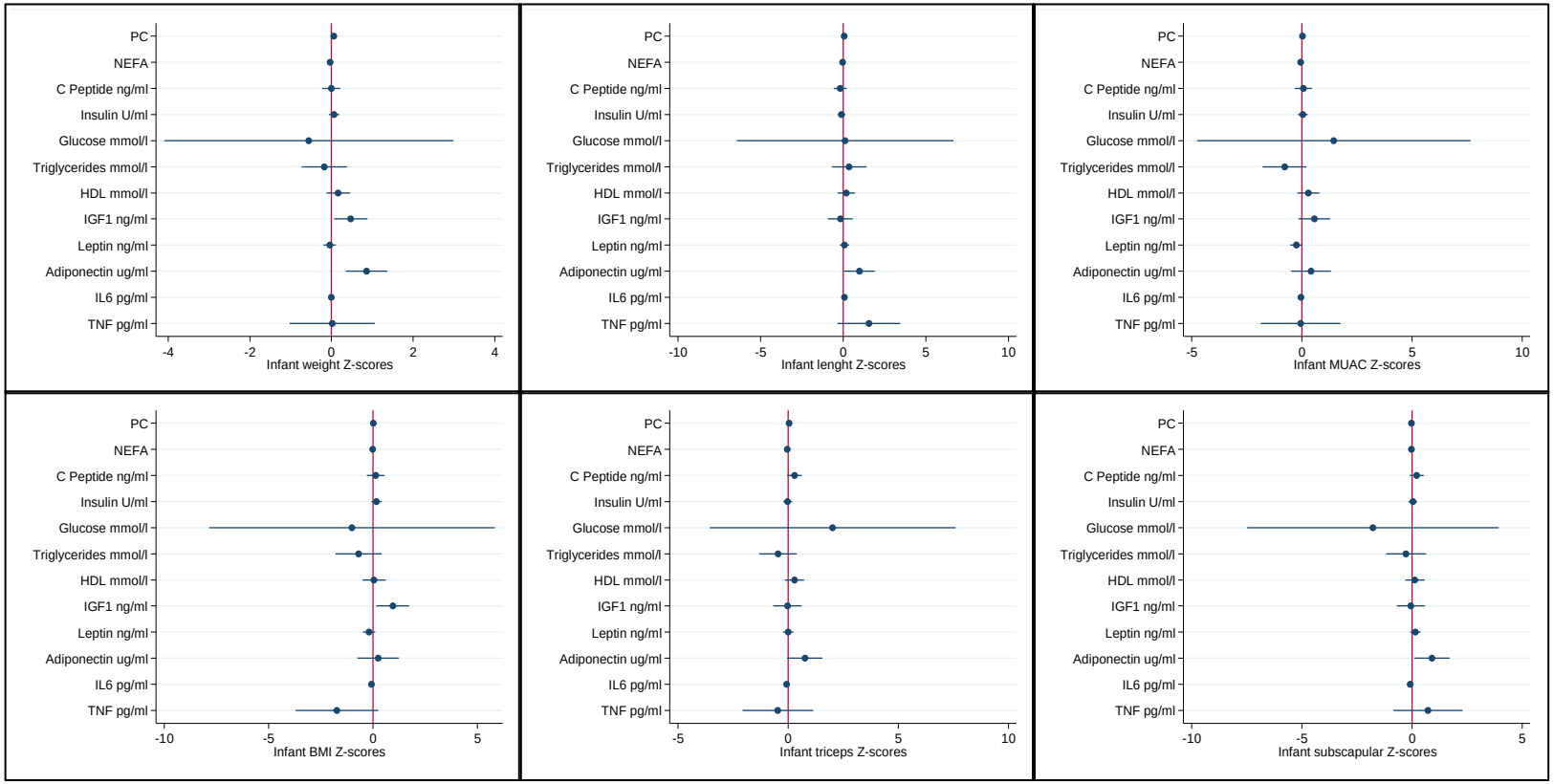
Supplement Figure 14: Sensitivity analyses of associations between cord blood metabolic profile and infant anthropometry, following exclusion of infants at 6 months exposed to gestational diabetes in-utero (excluded n=111).

*Regression coefficients with corresponding 95% confidence intervals presented are adjusted for maternal parity, ethnicity, smoker in early pregnancy, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention and mode of early life feeding. Abbreviations; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IL6-Interleukin 6; MUAC-Mid upper arm circumference; NEFA-Non-esterified fatty acid; PC-phosphatidylcholine; SDS- Standard deviation scores; SFT- skinfold thickness; TNFalpha- Tumour Necrosis Factor alpha. *p<0.05; ** p<0.001.*



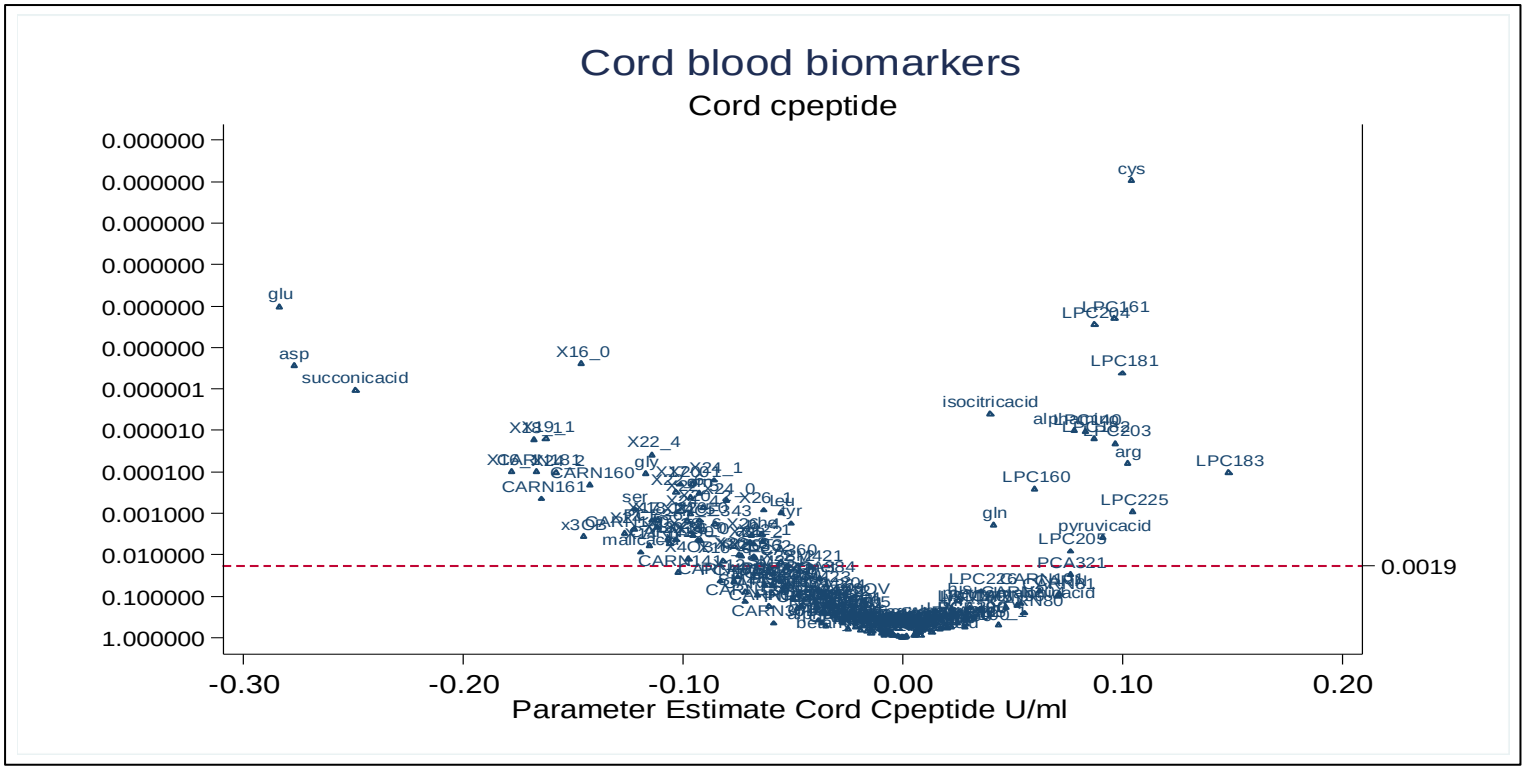
Supplement Figure 15: Sensitivity analyses of associations between cord blood metabolic profile and neonatal anthropometry, following further adjustment for mode of delivery.

Regression coefficients graphically presented with corresponding 95% confidence intervals. Adjustment made for maternal parity, ethnicity, and smoker in early pregnancy, gestational diabetes, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention and mode of delivery. Abbreviations; AA-amino acids cluster; Acylcar- Long chain acylcarnitines and TCA metabolites cluster; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IGFII- Insulin growth factor II; IL6-Interleukin 6; MUAC-Mid upper arm circumference; NEFA-Non-esterified fatty acid cluster; PC-phosphatidylcholine cluster; SDS- Standard deviation scores; SFT- skinfold thickness; TNFalpha- Tumour Necrosis Factor alpha



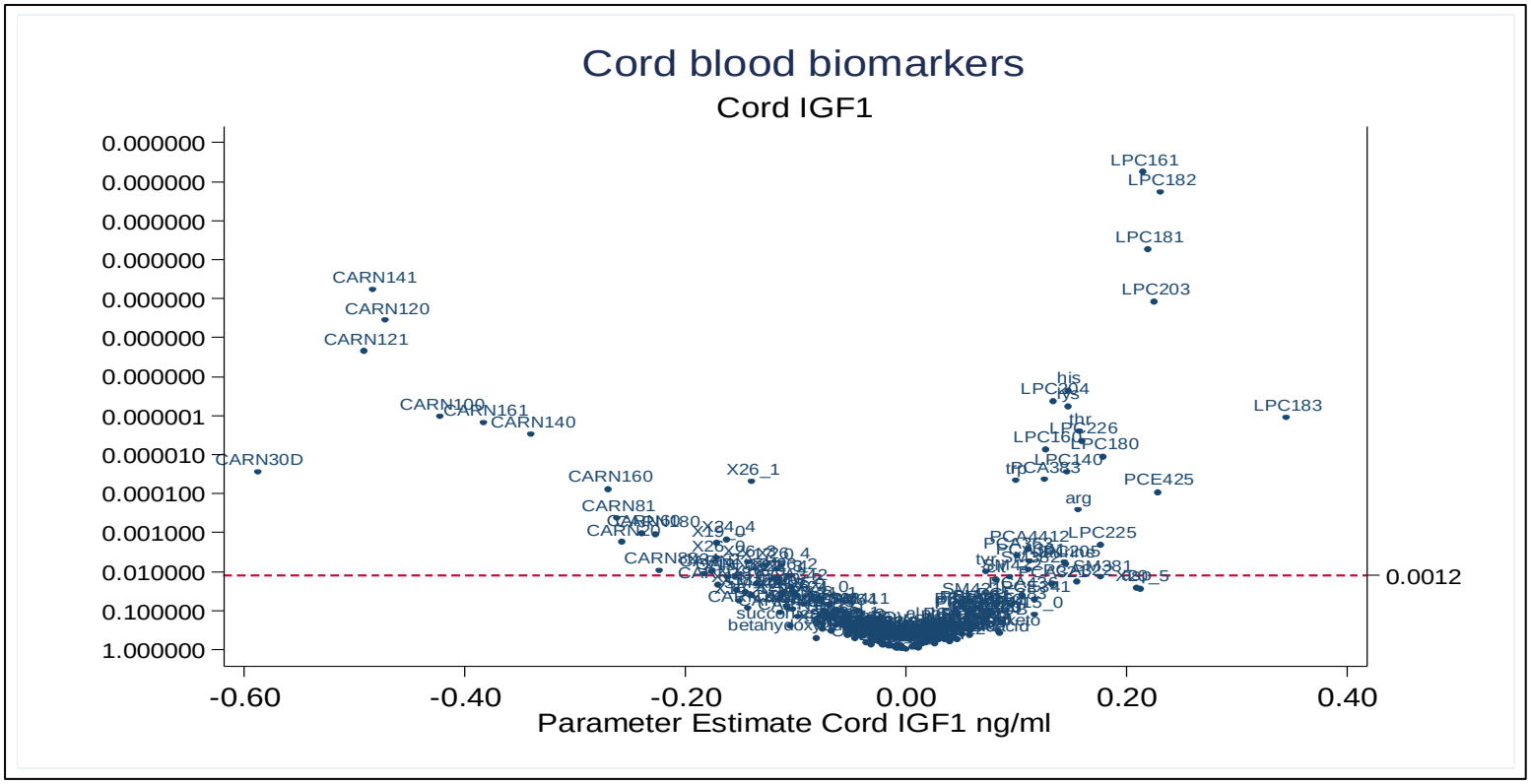
Supplement Figure 16: Sensitivity analyses of associations between cord blood metabolic profile and infant anthropometry, following adjustment for mode of delivery.

Regression coefficients with corresponding 95% confidence intervals presented are adjusted for maternal parity, ethnicity, smoker in early pregnancy, gestational weight gain, offspring sex, gestation at delivery, randomisation to UPBEAT Intervention, mode of early life feeding and mode of delivery. Abbreviations; HDL- High density lipoprotein; IGFI- Insulin growth factor I; IL6-Interleukin 6; MUAC-Mid upper arm circumference; NEFA-Non-esterified fatty acid cluster; PC-phosphatidylcholine cluster; TNFalpha- Tumour Necrosis Factor alpha.



Supplement Figure 17: Association of cord blood metabolomics profile with cord C-peptide in infants born to obese women; data from the UPBEAT study (n=343).

Parameter estimates are graphically represented for each biochemical variable in relation to cord blood C-peptide allowing correction for a false discovery rate (Benjamin & Hochberg procedure) (17). Adjustment made for randomisation to the UPBEAT intervention, offspring sex and gestation at delivery. Statistical significance p≤0.0019. Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins. TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V-- x4methyl2oxovalvericacid. NEFAs are described using the nomenclature CX:Y, where X is the length of the carbon chain, Y is the number of double bonds, OH in the formula means the molecule contains a hydroxyl-group



Supplement Figure 18: Association of cord blood metabolomics profile with cord IGF-1 in infants born to obese women; data from the UPBEAT study (n=343).

Parameter estimates are graphically represented for each biochemical variable in relation to cord blood IGF-1 allowing correction for a false discovery rate (Benjamin & Hochberg procedure) (17). Adjustment made for randomisation to the UPBEAT intervention, offspring sex and gestation at delivery. Statistical significance p≤0.0019. Abbreviations; CARN-Carnitines; HDL-High density lipoprotein; IGFI- Insulin growth factor I; IGF II- Insulin growth factor II; IL6- Interleukin 6; LPC- lysophosphatidylcholines; LPCE- lysophosphatidylethanolamine; PC-phosphatidylcholines; PCA- diacylphosphatidylcholines; PCE- acylalkylphosphatidylcholines; SM- sphingomyelins. TNFalpha- Tumor necrosis factor; X30B- x3methyl2oxobutanoicacid; X30V-- x4methyl2oxovalvericacid. NEFAs are described using the nomenclature CX:Y, where X is the length of the carbon chain, Y is the number of double bonds, OH in the formula means the molecule contains a hydroxyl-group.

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