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SUPPLEMENTARY MATERIAL

The effect of a lifestyle intervention in obese pregnant women on change in gestational metabolic profiles: findings from the UK Pregnancies Better Eating and Activity Trial (UPBEAT) RCT. Harriet Mills, Nashita Patel, Sara L White, Dharmintra Pasupathy, Annette Briley, Diana L Santos Ferreira, Paul Seed, Scott M. Nelson, Naveed Sattar, Kate Tilling, Lucilla Poston, Debbie A Lawlor, On behalf of the UPBEAT Consortium.

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Box S1

Nuclear Magnetic Resonance (NMR) Spectroscopy Methods

The NMR spectroscopy methodology is summarised in **Figure S1** below and the metabolites that were quantified, together with the units in which they are quantified, are shown **Table S2**. This approach uses three molecular windows, (two that were applied to native serum and one to serum lipid extracts requiring minimal preparation) to quantify the 158 metabolic traits. The NMR-based metabolite quantification is achieved through measurements of three molecular windows from each serum sample.[1, 2] Two of the spectra (LIPO and LMWM windows) are acquired from native serum and one spectrum from serum lipid extracts (LIPID window). The NMR spectra are measured using Bruker AVANCE III spectrometer operating at 500 or 600 MHz. Measurements of native serum samples and serum lipid extracts are conducted at 37°C and 22°C, respectively.

The LIPO window represents a standard spectrum of human serum displaying broad overlapping resonances arising from lipid molecules in various lipoprotein particles. The LIPO data are recorded using 8 transients acquired using a NOESY-presat pulse sequence with mixing time of 10ms and water peak suppression. The LMWM window includes signals from various low-molecular-weight molecules. The LMWM spectrum is recorded using a relaxation-filtered pulse sequence that suppresses most of the broad macromolecule and lipid signals to enhance detection of small solutes. Specifically, a Carr-Purcell-Meiboom-Gill (CPMG) pulse sequence with a 78ms T_2 -filter and fixed echo delay of 403 μ s is applied using 24 transients. The LIPID window of the serum extracts is acquired with a standard 1D spectrum using 32 transients.

QC and outputs

The NMR spectra were analysed for absolute metabolite quantification (molar concentration) in an automated fashion.[2] For each metabolite a ridge regression model was applied for quantification in order to overcome the problems of heavily overlapping spectral data. In the case of the lipoprotein lipid data, quantification models were calibrated using high performance liquid chromatography methods, and individually cross-validated against NMR-independent lipid data. Low-molecular-weight metabolites, as well as lipid extract measures, were quantified as mmol/l based on regression modelling calibrated against a set of manually fitted metabolite measures. The calibration data are quantified based on iterative line-shape fitting analysis using PERCH NMR software (PERCH Solutions Ltd., Kuopio, Finland). Absolute quantification cannot be directly established for the lipid extract measures due to experimental variation in the lipid extraction protocol. Therefore, serum extract metabolites are scaled via the total cholesterol as quantified from the native serum LIPO spectrum.

Statistical Methods

Data preparation prior to modelling repeatedly assessed metabolic trait measurements

Gestation week of clinic attendance was centred by subtracting 16-weeks from all values. 16-weeks was chosen as the nearest 4-week multiple to the average time of the first clinic (17.0-weeks). For some results absolute (total) change between 16- and 36-weeks are used; for others the rate of change per 4 weeks of gestation are used by dividing the time unit in the multilevel models by 4.

In order to ensure model convergence the data were scaled such that for each metabolite, if 25% were less than 0.5 every response was multiplied by a factor of 10 until this was not the case. Model results were then rescaled to their original units for presentation. The only

metabolic trait for which this was not done was cholesterol esters in IDL, as this trait did not converge properly in the multilevel model when scaled in this way, but did converge when it was not scaled.

Modelling repeat metabolic profile data

Data were modelled using a multilevel model[3, 4] with fixed effects for BMI, ethnicity, parity, age group, clinic centre, time-point (centered on gestational age) and the interaction of randomised group (intervention vs control) and time-point, and with random intercepts and random slopes for the individual participants. We restricted the time frame to between 16 and 36 weeks of gestation so that we were not predicting beyond available data. Therefore, the intercept represents the concentration of a metabolic trait at 16-weeks and the slope the rate of change in the concentration of a trait per week of gestation between 16 and 36 weeks (divided by 4 in all analyses to give a rate of change per 4-weeks of gestation). In all analyses we controlled for the minimising variables used in randomization (BMI, ethnicity, parity, age and clinic centre).[5] An interaction term between time (gestational weeks) and randomised arm (control or intervention) was also included.

We present exact p-values for all results but focus our discussion of the magnitudes of point estimates (i.e. pregnancy change in metabolites or effect of the intervention) and their precision (i.e. 95% confidence intervals) as recommended by the American Statistics Society and others.[6-8] We explore the role of chance by providing exact p-values after controlling the false discovery rate using the method of Benjamini and Hochberg to deal with multiple testing.[9]

Metabolic profile change in obese pregnant women

We estimated the absolute mean difference in each metabolite between 16- and 36-weeks by subtracting the predicted (from the multi-level model) value at 16-weeks from that at 36-weeks for each woman in the control group. These results are presented in standard deviation (SD) units, to aid comparison of results with those from other studies. In these analyses the magnitude of the SD for each metabolite was that from levels at 16-weeks. Thus, if the SD for one metabolite at 16 weeks is 0.5mmol/l, we divided levels at 36-weeks for that metabolite by 0.5mmol/l. We also present the mean absolute differences in the original units of measure for each metabolite (mostly mmol/l). These absolute difference results are presented in Table S3 below.

The full model results (mean intercept and mean slope per 4-weeks) for each metabolite in their original units are also presented for all 1158 women included in analyses. As the model includes a term for the randomised arm for each woman, these can be interpreted as the mean level of each metabolite at 16-weeks, and its change per 4-weeks of gestation between 16- and 36-weeks having adjusted for any effect of the intervention. The slope is therefore an indication of mean rate of change in metabolites in obese women in general (i.e. without any intervention effect). These results are presented in Table S4 below.

Effect of a lifestyle intervention that changed diet and physical activity in obese pregnant women on change in their metabolic profiles

In the multi-level model described above the interaction term between intervention group and gestation weeks represents the mean difference in the rate of change (slope) for each metabolic measure between 16- and 36-weeks between women in the intervention and control groups. It therefore provides the effect of the intervention on rate of change in metabolites. In the main analyses we express this in SD units per 4-weeks (using the SD value of the control

group), for ease of interpretation and to enable effects of the intervention to be compared across different metabolic measures. We also present the difference in mean rate of change in original units (mostly mmol/l per 4-weeks). These results are presented in Table S5 below.

Additional sensitivity analyses

Our main analyses assume that change in metabolic trait concentrations across the three measurements are linear (i.e. the change between the first (16 weeks) and second (28 weeks) measurement is consistent with that between the second (28 weeks) and third (36 weeks) for each trait). To test this assumption we modified the multilevel model to include a knot point at the second clinic, giving two slopes (differences in metabolic trait concentration) for the periods time periods before and after the second clinic assessment – i.e. comparing the difference in rate of change for each metabolite between intervention and control group in SD per 4-weeks between 16- and 28-weeks to that between 28- and 36-weeks. The model had similar fixed and random effects to the main analyses. The two separate slopes over the two time periods of change (16- to 28-weeks and 28- to 36-weeks) came from two fixed effects time periods (instead of one) and two fixed effects interaction terms for treatment with these two time periods.

Assumptions of the multilevel linear spline model

Due to the nature of the data collection, we cannot explore the pattern of change between the three timepoints, as the data in the intervening periods is sparse (see Figure S2 below). Specifically, we had to use linear spline methods and could not explore smoothing methods, or use fractional polynomials [3, 4] to determine the exact shape of metabolic trait change over pregnancy. The linear spline method we have had to use assumes the model residuals are approximately Normally distributed, which may not be the case with our data. However, there is evidence that estimates of population average change, such as those we present here are robust to non-Normality in the residuals (for example see reference [10]) and we have further explored this using generalised estimating equations with robust standard errors (as described in the main paper).

We conducted the following additional sensitivity analyses to explore how robust our results were to heteroskedasticity, skewed distributions and outliers:

1. Multilevel model using SD as the scale comparison. The parameter estimate should be unbiased but the standard errors may be affected by non-normality of the measures.
2. Multilevel model using IQR as the scale comparison. This analysis should be robust to non-normality in the original measure, and the parameter estimate should be unbiased but the standard errors may be affected by non-normality of the measures.
3. A paired t-test (final measure–first measure), using bootstrapping to obtain standard errors, and with the SD of the first measure (in the control group) used as the scale comparison. This analysis should be robust to non-normality in the differences (via bootstrapping). Furthermore, when removing outliers (see below) bootstrapping will ensure that the standard error is correct.[11]
4. A paired t-test (final measure–first measure), using bootstrapping to obtain standard errors, and with the IQR used as the scale comparison rather than the SD. This analysis should be robust to non-normality in the original measure (using the IQR rather than the SD), and also robust to non-normality in the differences (via bootstrapping). Furthermore, when removing outliers (see below) bootstrapping will ensure that the standard error is correct.
5. A paired t-test (final measure–first measure), using bootstrapping to obtain standard errors, and with the Median Absolute Deviation (MAD) used as the scale comparison

rather than the SD or IQR, as one reviewer[11] suggested this was a more robust measure of deviation, though in our analyses the correlation between the MAD and SD was > 0.98 across all metabolites and the two gave virtually identical results.

Repeated 1-5 above but first removing all outliers (top and bottom) at each timepoint and by treatment group. We initially removed the top and bottom 1% in these analyses having considered the following: (i) it is important to only remove measures that are highly likely to be erroneous and not true values that are markedly different to the mean for the study population, as the latter may introduce selection bias; (ii) in this study we were exploring a binary exposure (randomisation to intervention or standard treatment) and would not expect a high proportion of erroneous results at the extremes to influence our findings; and (iii) when we used the MAD*3.5 threshold for defining outliers as suggested by Ramsey and Ramsey,[12] for all of metabolites $<1\%$ were above this threshold (see final spreadsheet in Supplementary File 2). However, one of the reviewers[11] preferred that we use the MAD-median rule applied to our data, which, gave a threshold of MAD*2.24. For the vast majority of metabolites this also resulted in fewer than 1% at top and bottom being removed.

Results across these 10-sensitivity analyses (the listed 5, with and without removal of the top and bottom MAD*2.24 defined outliers) were very similar with correlations between each other and with the main results all > 0.9 . Removal of outliers did not notably alter any results.

Additionally, we undertook four further sensitivity analyses; median quantile regression and 75th centile quantile regression, both with and without outliers removed based on the MAD*2.24 rule. The overall pattern of results were similar to those of the main analyses and all other sensitivity analyses, with some evidence of larger differences in the upper quartile of metabolites than around the middle 50% (see Supplementary File 2).

All results for these sensitivity analyses are shown in Supplementary File 2. **Table S6** below shows correlation coefficients between the main analyses and sensitivity analyses (these are all ≥ 0.9).

Multilevel models of change over time allow all participants with at least one measure to be included in analyses under the assumption that data are missing at random. The statistical term ‘missing at random (MAR)’ differs from missing completely at random (MCAR) in that it does not mean missingness is independent of all other characteristics. It means that conditional on the covariables included in the model (here age, parity, ethnicity, BMI and study centre) and the observed repeat measurements, the missing repeat measurements are not systematically different to those observed. This means that the effect of the intervention in those with some missing metabolic profile data is the same as in those with complete data at all three-time points conditional on the covariables included in the model. The MAR assumption would also be necessary if we restricted analyses to only those with all three repeat measurements (i.e. a complete case analysis). Whilst we cannot directly assess this assumption we feel that it is unlikely to be violated given most women had all three repeats, with just 16% having only one measure and that loss to follow-up in the trial was minimal and similar in both arms. The standard errors, and hence 95% confidence intervals, in these models take account of the greater random error of predicted levels at any time in those with just one or two of the repeat measurements.

Statistical Code for all analyses presented in this paper can be found alongside a pre-peer review, pre-print version of the paper at <http://biorxiv.org/content/early/2017/04/10/125740>

Supplementary Tables

Table S1: Participant characteristics (extended from Main Text Table 1)

	Participants with at least one metabolic profile analysed during pregnancy (analysis sample for this study). N = 1158*		All participants in the six centres with blood sampling (eligible sample for this study). N = 1194*		Participants in all eight samples who were included in the original RCT (irrespective of whether blood samples were collected at their centre) N = 1554*	
	Control N = 577	Intervention N = 581	Control N = 593	Intervention N = 601	Control N = 771	Intervention N = 783
BMI (N (%))						
30 to 34.9 kg/m ²	273 (47.3)	287 (49.4)	279 (47%)	296 (49.3%)	374 (48.5)	391 (49.9)
35 to 39.9 kg/m ²	203 (35.2)	177 (30.5)	209 (35.2%)	185 (30.8%)	262 (34.0)	246 (31.4)
≥40 kg/m ²	101 (17.5)	117 (20.1)	105 (17.7%)	120 (20%)	135 (17.5)	146 (18.6)
Ethnicity (N (%))						
White	389 (67.4)	384 (66.1)	396 (66.8%)	397 (66.1%)	483 (62.6)	490 (62.6)
Asian	38 (6.6)	43 (7.4)	43 (7.3%)	45 (7.5%)	48 (6.2)	47 (6.0)
Black	120 (20.8)	127 (21.9)	123 (20.7%)	130 (21.6%)	199 (25.8)	202 (25.8)
Other	30 (5.2)	27 (4.6)	31 (5.2%)	29 (4.8%)	41 (5.3)	44 (5.6)
Parity (N (%))						
Primiparous	260 (45.1)	257 (44.2)	266 (44.9%)	265 (44.1%)	338 (43.8)	336 (42.9)
Multiparous	317 (54.9)	324 (55.8)	327 (55.1%)	336 (55.9%)	433 (56.2)	447 (57.1)
Age (N (%))						
<25 years	97 (16.8)	85 (14.6)	100 (16.9%)	90 (15%)	125 (17.3)	116 (15.7)
25 to 29 years	141 (24.4)	165 (28.4)	147 (24.8%)	169 (28.1%)	199 (27.6)	215 (29.1)
30 to 34 years	187 (32.4)	174 (29.9)	188 (31.7%)	182 (30.3%)	192 (26.6)	205 (27.8)
≥35 years	152 (26.3)	157 (27)	158 (26.6%)	160 (26.6%)	206 (28.5)	202 (27.4)
Centre (N (%))						
Bradford	19 (3.3)	22 (3.8)	25 (4.2%)	28 (4.7%)	25 (3.2)	28 (3.6)
Glasgow	130 (22.5)	132 (22.7)	131 (22.1%)	134 (22.3%)	131 (17.0)	134 (17.1)
Manchester	67 (11.6)	67 (11.5)	70 (11.8%)	69 (11.5%)	70 (9.1)	69 (8.8)
Newcastle	120 (20.8)	116 (20)	122 (20.6%)	120 (20%)	122 (15.8)	120 (15.3)
Sunderland	0	0	0	0	41 (5.3)	43 (5.5)
St George's, London	53 (9.2)	55 (9.5)	54 (9.1%)	57 (9.5%)	54 (7.0)	57 (7.3)
St Thomas's, London	188 (32.6)	189 (32.5)	191 (32.2%)	193 (32.1%)	191 (24.8)	193 (24.6)
King's College Hospital, London	0	0	0	0	137 (17.8)	139 (17.8)

Table 1: continued

First clinic						
N (%)	538 (93.2)	545 (93.8)	593 (100.0)	601 (100.0)	771 (100.0)	783 (100.0)
Median (IQR) gestation (weeks)	17 (16.1, 17.9)	17 (16.1, 18.0)	17.0 (16.1, 17.9)	17.0 (16.1, 18.0)	17 (16.1, 18.0)	17.0 (16.1, 18.0)
Second clinic						
N (%)	500 (86.7)	477 (82.1)	591 (99.7)	598 (99.5)	768 (99.6)	780 (99.6)
Median (IQR) gestation (weeks)	27.7 (27.3, 28.1)	27.7 (27.3, 28.1)	27.7 (27.3, 28.3)	27.7 (27.3, 28.1)	27.7 (27.3, 28.3)	27.7 (27.3, 28.3)
Third clinic						
N (%)	407 (70.5)	374 (64.4)	524 (88.4)	485 (80.7)	662 (85.9)	630 (80.5)
Median (IQR) gestation (weeks)	34.7 (34.3, 35.1)	34.6 (34.3, 35.1)	34.7 (34.3, 35.3)	34.7 (34.3, 35.3)	34.8 (34.3, 35.3)	34.7 (34.3, 35.4)

*The 1158 participants whose results are in the first two columns are a subgroup of the 1194 whose results are presented in the middle two columns who are in turn a subgroup of the 1554 whose results are in the final two columns.

N: number; IQR: Interquartile range

Table S2: NMR metabolic measures

Molecular class	Lipid, lipoprotein or metabolite name	Units*
Extremely large VLDL	Concentration of chylomicrons and extremely large VLDL particles	mol/l
	Total lipids in chylomicrons and extremely large VLDL	mmol/l
	Phospholipids in chylomicrons and extremely large VLDL	mmol/l
	Total cholesterol in chylomicrons and extremely large VLDL	mmol/l
	Free cholesterol in chylomicrons and extremely large VLDL	mmol/l
	Triglycerides in chylomicrons and extremely large VLDL	mmol/l
Very large VLDL	Concentration of very large VLDL particles	mol/l
	Total lipids in very large VLDL	mmol/l
	Phospholipids in very large VLDL	mmol/l
	Total cholesterol in very large VLDL	mmol/l
	Cholesterol esters in very large VLDL	mmol/l
	Free cholesterol in very large VLDL	mmol/l
	Triglycerides in very large VLDL	mmol/l
Large VLDL	Concentration of large VLDL particles	mol/l
	Total lipids in large VLDL	mmol/l
	Phospholipids in large VLDL	mmol/l
	Total cholesterol in large VLDL	mmol/l
	Cholesterol esters in large VLDL	mmol/l
	Free cholesterol in large VLDL	mmol/l
	Triglycerides in large VLDL	mmol/l
Medium VLDL	Concentration of large VLDL particles	mol/l
	Total lipids in small VLDL	mmol/l
	Phospholipids in small VLDL	mmol/l
	Total cholesterol in small VLDL	mmol/l
	Cholesterol esters in small VLDL	mmol/l
	Free cholesterol in small VLDL	mmol/l
	Triglycerides in small VLDL	mmol/l
Small VLDL	Concentration of very small VLDL particles	mol/l
	Total lipids in very small VLDL	mmol/l
	Phospholipids in very small VLDL	mmol/l
	Total cholesterol in very small VLDL	mmol/l
	Cholesterol esters in very small VLDL	mmol/l
	Free cholesterol in very small VLDL	mmol/l
	Triglycerides in very small VLDL	mmol/l
IDI	Concentration of IDL particles	mol/l
	Total lipids in IDL	mmol/l
	Phospholipids in IDL	mmol/l
	Total cholesterol in IDL	mmol/l
	Cholesterol esters in IDL	mmol/l
	Free cholesterol in IDL	mmol/l
	Triglycerides in IDL	mmol/l
Large LDL	Concentration of large LDL particles	mol/l
	Total lipids in large LDL	mmol/l
	Phospholipids in large LDL	mmol/l
	Total cholesterol in large LDL	mmol/l
	Cholesterol esters in large LDL	mmol/l
	Free cholesterol in large LDL	mmol/l
	Triglycerides in large LDL	mmol/l

Table S2: NMR metabolic profiles continued

Molecular class	Lipid, lipoprotein or metabolite name	Units*
Medium LDL	Concentration of medium LDL particles	mol/l
	Total lipids in medium LDL	mmol/l
	Phospholipids in medium LDL	mmol/l
	Total cholesterol in medium LDL	mmol/l
	Cholesterol esters in medium LDL	mmol/l
	Free cholesterol in medium LDL	mmol/l
	Triglycerides in medium LDL	mmol/l
Small LDL	Concentration of small LDL particles	mol/l
	Total lipids in small LDL	mmol/l
	Phospholipids in small LDL	mmol/l
	Total cholesterol in small LDL	mmol/l
	Cholesterol esters in small LDL	mmol/l
	Free cholesterol in small LDL	mmol/l
	Triglycerides in small LDL	mmol/l
Very large HDL	Concentration of very large HDL particles	mol/l
	Total lipids in very large HDL	mmol/l
	Phospholipids in very large HDL	mmol/l
	Total cholesterol in very large HDL	mmol/l
	Cholesterol esters in very large HDL	mmol/l
	Free cholesterol in very large HDL	mmol/l
	Triglycerides in very large HDL	mmol/l
Large HDL	Concentration of large HDL particles	mol/l
	Total lipids in large HDL	mmol/l
	Phospholipids in large HDL	mmol/l
	Total cholesterol in large HDL	mmol/l
	Cholesterol esters in large HDL	mmol/l
	Free cholesterol in large HDL	mmol/l
	Triglycerides in large HDL	mmol/l
Medium HDL	Concentration of medium HDL particles	mol/l
	Total lipids in medium HDL	mmol/l
	Phospholipids in medium HDL	mmol/l
	Total cholesterol in medium HDL	mmol/l
	Cholesterol esters in medium HDL	mmol/l
	Free cholesterol in medium HDL	mmol/l
	Triglycerides in medium HDL	mmol/l
Small HDL	Concentration of small HDL particles	mol/l
	Total lipids in small HDL	mmol/l
	Phospholipids in small HDL	mmol/l
	Total cholesterol in small HDL	mmol/l
	Cholesterol esters in small HDL	mmol/l
	Free cholesterol in small HDL	mmol/l
	Triglycerides in small HDL	mmol/l
Lipoprotein particle size	Mean diameter for VLDL particles	nm
	Mean diameter for LDL particles	nm
	Mean diameter for HDL particles	nm

Table S2: NMR metabolic profiles continued

Molecular class	Lipid, lipoprotein or metabolite name	Units*
Cholesterol concentrations	Total cholesterol	mmol/l
	Total cholesterol in VLDL	mmol/l
	Remnant cholesterol (non-HDL and non-LDL cholesterol)	mmol/l
	Total cholesterol in LDL	mmol/l
	Total cholesterol in HDL	mmol/l
	Total cholesterol in HDL2	mmol/l
	Total cholesterol in HDL3	mmol/l
	Esterified cholesterol	mmol/l
	Free cholesterol	mmol/l
Glycerides and phospholipid concentrations (and one ratio)	Total triglycerides	mmol/l
	Triglycerides in VLDL	mmol/l
	Triglycerides in LDL	mmol/l
	Triglycerides in HDL	mmol/l
	Total phosphoglycerides	mmol/l
	Ratio of triglycerides to phosphoglycerides	
	Phosphatidylcholine and other cholines	mmol/l
	Sphingomyelins	mmol/l
	Total cholines	mmol/l
Apolipoprotein concentrations (and one ratio)	Apolipoprotein A-1	g/l
	Apolipoprotein B	g/l
	Ratio of apolipoprotein B to apolipoprotein A-1	
Fatty acid concentrations	Total fatty acids	mmol/l
	Estimated degree of saturation	
	22:6, docosahexaenoic acid	mmol/l
	18:2 linoleic acid	mmol/l
	Omega-3 fatty acids	mmol/l
	Omega-6 fatty acids	mmol/l
	Polyunsaturated fatty acids	mmol/l
	Monounsaturated fatty acids; 16:1, 18:1	mmol/l
	Saturated fatty acids	mmol/l
Fatty acid ratios	Ratio of 22:6, docosahexaenoic acid to total fatty acids	%
	Ratio of 18:2 linoleic acid to total fatty acids	%
	Ratio of omega-3 fatty acids to total fatty acids	%
	Ratio of omega-6 fatty acids to total fatty acids	%
	Ratio of polyunsaturated fatty acids to total fatty acids	%
	Ratio of monounsaturated fatty acids to total fatty acids	%
	Ratio of saturated fatty acids to total fatty acids	%
Glycolysis related metabolite	Glucose	mmol/l
	Lactate	mmol/l
	Pyruvate	mmol/l
	Citrate	mmol/l
	Glycerol	mmol/l

Table S2: NMR metabolic profiles continued

Molecular class	Lipid, lipoprotein or metabolite name	Units*
Amino acid concentrations	Alanine	mmol/l
	Glutamine	mmol/l
	Glycine	mmol/l
	Histidine	mmol/l
	branched Isoleucine	mmol/l
	branched Leucine	mmol/l
	branched Valine	mmol/l
	aromatic Phenylalanine	mmol/l
aromatic Tyrosine	mmol/l	
Ketone body concentrations	Acetate	mmol/l
	Acetoacetate	mmol/l
	3-hydroxybutyrate	mmol/l
Fluid balance marker	Albumin	mmol/l
	Creatinine	mmol/l
Inflammation marker	Glycoprotein acetyls, mainly a1-acid glycoprotein	mmol/l

* These are the units used throughout the paper for each of the metabolic measures, unless we state that we are presenting results in standard deviation (SD) units. Where we present results that are the mean (in control participants) at 16-weeks these are the units. Where we present change in metabolic marker (between 16- to 36-weeks) or difference in change of metabolic markers the units are those listed in the table above per one week of gestational age.

VLDL: very low density lipoprotein; LDL: low density lipoprotein; IDL: intermediate density lipoprotein; HDL: high density lipoprotein

Table S3: Absolute difference between 16- and 36-weeks of gestation for each metabolic trait in obese pregnant women who were randomised to the control arm of the UPBEAT RCT (N = 577). NOTE: ONLY THE FINAL COLUMN OF RESULTS HAS CHANGED. The whole table is replaced because the statistical package produces the whole table

	Mean absolute difference between 16 and 36 weeks of gestation in original units* (95% CI)	Mean absolute difference between 16 and 36 weeks of gestational age in SD units ^S
Extremely large VLDL		
Concentration of chylomicrons and extremely large VLDL particles (mol/l)	1.1434x10 ⁻¹⁰ (1.1003x10 ⁻¹⁰ , 1.1864x10 ⁻¹⁰)	1.4744 (1.3386, 1.6101)
Total lipids in chylomicrons and extremely large VLDL (mmol/l)	0.0253 (0.0243, 0.0262)	1.5209 (1.3852, 1.6567)
Phospholipids in chylomicrons and extremely large VLDL (mmol/l)	0.0038 (0.0037, 0.0039)	1.7572 (1.6199, 1.8946)
Total cholesterol in chylomicrons and extremely large VLDL (mmol/l)	0.0058 (0.0056, 0.0059)	1.9934 (1.8573, 2.1295)
Cholesterol esters in chylomicrons and extremely large VLDL (mmol/l)	0.0031 (0.0030, 0.0032)	1.9763 (1.8428, 2.1099)
Free cholesterol in chylomicrons and extremely large VLDL (mmol/l)	0.0026 (0.0026, 0.0027)	1.8955 (1.7569, 2.0341)
Triglycerides in chylomicrons and extremely large VLDL (mmol/l)	0.0157 (0.0150, 0.0163)	1.3390 (1.2028, 1.4753)
Very large VLDL		
Concentration of very large VLDL particles (mol/l)	8.5288x10 ⁻¹⁰ (8.2336x10 ⁻¹⁰ , 8.8240x10 ⁻¹⁰)	1.8215 (1.6907, 1.9523)
Total lipids in very large VLDL (mmol/l)	0.0834 (0.0805, 0.0862)	1.8329 (1.7022, 1.9636)
Phospholipids in very large VLDL (mmol/l)	0.0147 (0.0142, 0.0152)	1.9244 (1.7932, 2.0556)
Total cholesterol in very large VLDL (mmol/l)	0.0164 (0.0159, 0.0169)	1.8729 (1.7442, 2.0016)
Cholesterol esters in very large VLDL (mmol/l)	0.0084 (0.0081, 0.0086)	1.7910 (1.6643, 1.9177)
Free cholesterol in very large VLDL (mmol/l)	0.0080 (0.0078, 0.0083)	1.9491 (1.8180, 2.0803)
Triglycerides in very large VLDL (mmol/l)	0.0523 (0.0504, 0.0542)	1.7856 (1.6544, 1.9168)

Table S3: continued

Large VLDL		
Concentration of large VLDL particles (mol/l)	5.2624x10 ⁻⁹ (5.0853x10 ⁻⁹ , 5.4396x10 ⁻⁹)	1.9810 (1.8515, 2.1106)
Total lipids in large VLDL (mmol/l)	0.3066 (0.2964, 0.3168)	1.9925 (1.8630, 2.1220)
Phospholipids in large VLDL (mmol/l)	0.0588 (0.0569, 0.0607)	2.1000 (1.9692, 2.2308)
Total cholesterol in large VLDL (mmol/l)	0.0688 (0.0667, 0.0710)	2.0026 (1.8759, 2.1293)
Cholesterol esters in large VLDL (mmol/l)	0.0310 (0.0300, 0.0319)	1.8446 (1.7224, 1.9668)
Free cholesterol in large VLDL (mmol/l)	0.0379 (0.0367, 0.0391)	2.1227 (1.9906, 2.2549)
Triglycerides in large VLDL (mmol/l)	0.1790 (0.1727, 0.1852)	1.9476 (1.8173, 2.0779)
Medium VLDL		
Concentration of medium VLDL particles (mol/l)	1.4126x10 ⁻⁸ (1.3685x10 ⁻⁸ , 1.4566x10 ⁻⁸)	2.0533 (1.9282, 2.1784)
Total lipids in medium VLDL (mmol/l)	0.4744 (0.4598, 0.4889)	2.0810 (1.9556, 2.2063)
Phospholipids in medium VLDL (mmol/l)	0.0946 (0.0917, 0.0974)	2.1388 (2.0131, 2.2644)
Total cholesterol in medium VLDL (mmol/l)	0.1270 (0.1234, 0.1306)	2.2276 (2.1005, 2.3546)
Cholesterol esters in medium VLDL (mmol/l)	0.0619 (0.0601, 0.0637)	2.1050 (1.9786, 2.2314)
Free cholesterol in medium VLDL (mmol/l)	0.0651 (0.0632, 0.0670)	2.2462 (2.1169, 2.3756)
Triglycerides in medium VLDL (mmol/l)	0.2528 (0.2444, 0.2612)	1.9532 (1.8282, 2.0781)
Small VLDL		
Concentration of small VLDL particles (mol/l)	1.9052x10 ⁻⁸ (1.8499x10 ⁻⁸ , 1.9605x10 ⁻⁸)	2.3518 (2.2210, 2.4827)
Total lipids in small VLDL (mmol/l)	0.3694 (0.3587, 0.3801)	2.3770 (2.2453, 2.5087)
Phospholipids in small VLDL (mmol/l)	0.0777 (0.0754, 0.0799)	2.3103 (2.1823, 2.4383)
Total cholesterol in small VLDL (mmol/l)	0.1224 (0.1185, 0.1263)	2.2717 (2.1356, 2.4078)
Cholesterol esters in small VLDL (mmol/l)	0.0672 (0.0648, 0.0697)	1.9488 (1.8153, 2.0822)
Free cholesterol in small VLDL (mmol/l)	0.0552 (0.0536, 0.0568)	2.5385 (2.4013, 2.6757)
Triglycerides in small VLDL (mmol/l)	0.1692 (0.1640, 0.1744)	2.2049 (2.0758, 2.3339)

Table S3: continued

Very small VLDL		
Concentration of very small VLDL particles (mol/l)	1.8605x10 ⁻⁸ (1.7963x10 ⁻⁸ , 1.9247x10 ⁻⁸)	2.2794 (2.1422, 2.4166)
Total lipids in very small VLDL (mmol/l)	0.2258 (0.2177, 0.2338)	2.1825 (2.0466, 2.3184)
Phospholipids in very small VLDL (mmol/l)	0.0638 (0.0612, 0.0664)	1.8884 (1.7570, 2.0198)
Total cholesterol in very small VLDL (mmol/l)	0.0845 (0.0809, 0.0881)	1.6930 (1.5632, 1.8227)
Cholesterol esters in very small VLDL (mmol/l)	0.0490 (0.0467, 0.0512)	1.5036 (1.3759, 1.6312)
Free cholesterol in very small VLDL (mmol/l)	0.0355 (0.0340, 0.0369)	1.9718 (1.8349, 2.1087)
Triglycerides in very small VLDL (mmol/l)	0.0775 (0.0751, 0.0799)	2.6855 (2.5380, 2.8330)
IDL		
Concentration of IDL particles (mol/l)	3.8023x10 ⁻⁸ (3.6572x10 ⁻⁸ , 3.9474x10 ⁻⁸)	1.7353 (1.6148, 1.8558)
Total lipids in IDL (mmol/l)	0.3651 (0.3506, 0.3796)	1.6281 (1.5094, 1.7467)
Phospholipids in IDL (mmol/l)	0.0761 (0.0725, 0.0798)	1.3530 (1.2370, 1.4689)
Total cholesterol in IDL (mmol/l)	0.2056 (0.1966, 0.2146)	1.3939 (1.2797, 1.5081)
Cholesterol esters in IDL (mmol/l)	0.1525 (0.1463, 0.1588)	1.4720 (1.3576, 1.5865)
Free cholesterol in IDL (mmol/l)	0.0531 (0.0503, 0.0559)	1.1812 (1.0678, 1.2946)
Triglycerides in IDL (mmol/l)	0.0833 (0.0806, 0.0859)	2.8347 (2.6825, 2.9870)
Large LDL		
Concentration of large LDL particles (mol/l)	6.3247x10 ⁻⁸ (6.0733x10 ⁻⁸ , 6.5762x10 ⁻⁸)	1.6580 (1.5392, 1.7769)
Total lipids in large LDL (mmol/l)	0.4301 (0.4124, 0.4479)	1.5768 (1.4593, 1.6943)
Phospholipids in large LDL (mmol/l)	0.0808 (0.0774, 0.0843)	1.4571 (1.3421, 1.5722)
Total cholesterol in large LDL (mmol/l)	0.2782 (0.2656, 0.2908)	1.4009 (1.2864, 1.5154)
Cholesterol esters in large LDL (mmol/l)	0.2182 (0.2087, 0.2277)	1.4597 (1.3448, 1.5747)
Free cholesterol in large LDL (mmol/l)	0.0600 (0.0569, 0.0631)	1.2054 (1.0923, 1.3186)
Triglycerides in large LDL (mmol/l)	0.0711 (0.0690, 0.0732)	2.7454 (2.6016, 2.8893)

Table S3: continued

Medium LDL		
Concentration of medium LDL particles (mol/l)	5.4777x10 ⁻⁸ (5.2623x10 ⁻⁸ , 5.6932x10 ⁻⁸)	1.6759 (1.5578, 1.7941)
Total lipids in medium LDL (mmol/l)	0.2677 (0.2570, 0.2785)	1.6221 (1.5051, 1.7392)
Phospholipids in medium LDL (mmol/l)	0.0562 (0.0543, 0.0582)	1.7851 (1.6702, 1.9000)
Total cholesterol in medium LDL (mmol/l)	0.1768 (0.1688, 0.1848)	1.4073 (1.2929, 1.5218)
Cholesterol esters in medium LDL (mmol/l)	0.1417 (0.1351, 0.1483)	1.3726 (1.2578, 1.4875)
Free cholesterol in medium LDL (mmol/l)	0.0351 (0.0337, 0.0365)	1.5349 (1.4224, 1.6473)
Triglycerides in medium LDL (mmol/l)	0.0347 (0.0337, 0.0357)	2.7407 (2.5984, 2.8831)
Small LDL		
Concentration of small LDL particles (mol/l)	6.0152x10 ⁻⁸ (5.7904x10 ⁻⁸ , 6.2400x10 ⁻⁸)	1.6958 (1.5801, 1.8115)
Total lipids in small LDL (mmol/l)	0.1629 (0.1566, 0.1691)	1.6348 (1.5200, 1.7496)
Phospholipids in small LDL (mmol/l)	0.0368 (0.0357, 0.0379)	1.8173 (1.7069, 1.9276)
Total cholesterol in small LDL (mmol/l)	0.1036 (0.0988, 0.1083)	1.3643 (1.2513, 1.4773)
Cholesterol esters in small LDL (mmol/l)	0.0817 (0.0778, 0.0857)	1.3012 (1.1879, 1.4144)
Free cholesterol in small LDL (mmol/l)	0.0218 (0.0211, 0.0226)	1.5944 (1.4836, 1.7053)
Triglycerides in small LDL (mmol/l)	0.0226 (0.0220, 0.0232)	2.8622 (2.7234, 3.0009)
Very large HDL		
Concentration of very large HDL particles (mol/l)	7.9744x10 ⁻⁸ (7.6882x10 ⁻⁸ , 8.2605x10 ⁻⁸)	0.4226 (0.3545, 0.4906)
Total lipids in very large HDL (mmol/l)	0.0778 (0.0749, 0.0808)	0.4068 (0.3384, 0.4752)
Phospholipids in very large HDL (mmol/l)	0.0240 (0.0227, 0.0252)	0.2372 (0.1692, 0.3052)
Total cholesterol in very large HDL (mmol/l)	0.0385 (0.0369, 0.0401)	0.4448 (0.3733, 0.5162)
Cholesterol esters in very large HDL (mmol/l)	0.0285 (0.0273, 0.0297)	0.4683 (0.3970, 0.5396)
Free cholesterol in very large HDL (mmol/l)	0.0100 (0.0095, 0.0104)	0.3850 (0.3122, 0.4577)
Triglycerides in very large HDL (mmol/l)	0.0152 (0.0149, 0.0155)	2.0577 (1.9505, 2.1650)

Table S3: continued

Large HDL		
Concentration of large HDL particles (mol/l)	1.0288x10 ⁻⁸ (1.5883x10 ⁻⁹ , 1.8988x10 ⁻⁸)	0.0250 (-0.0529, 0.1030)
Total lipids in large HDL (mmol/l)	-0.0024 (-0.0079, 0.0031)	-0.0073 (-0.0849, 0.0702)
Phospholipids in large HDL (mmol/l)	-0.0096 (-0.0121, -0.0071)	-0.0791 (-0.1615, 0.0033)
Total cholesterol in large HDL (mmol/l)	-0.0142 (-0.0170, -0.0113)	-0.0948 (-0.1694, -0.0203)
Cholesterol esters in large HDL (mmol/l)	-0.0091 (-0.0113, -0.0069)	-0.0798 (-0.1549, -0.0048)
Free cholesterol in large HDL (mmol/l)	-0.0051 (-0.0057, -0.0044)	-0.1428 (-0.2160, -0.0695)
Triglycerides in large HDL (mmol/l)	0.0213 (0.0208, 0.0217)	1.4396 (1.3464, 1.5327)
Medium HDL		
Concentration of medium HDL particles (mol/l)	-1.7335x10 ⁻⁷ (-1.8439x10 ⁻⁷ , -1.6231x10 ⁻⁷)	-0.5444 (-0.6467, -0.4420)
Total lipids in medium HDL (mmol/l)	-0.0826 (-0.0874, -0.0777)	-0.6007 (-0.7040, -0.4974)
Phospholipids in medium HDL (mmol/l)	-0.0184 (-0.0204, -0.0163)	-0.2986 (-0.4004, -0.1967)
Total cholesterol in medium HDL (mmol/l)	-0.0769 (-0.0799, -0.0739)	-1.0402 (-1.1484, -0.9319)
Cholesterol esters in medium HDL (mmol/l)	-0.0682 (-0.0707, -0.0657)	-1.1619 (-1.2712, -1.0527)
Free cholesterol in medium HDL (mmol/l)	-0.0086 (-0.0092, -0.0081)	-0.5468 (-0.6521, -0.4414)
Triglycerides in medium HDL (mmol/l)	0.0126 (0.0124, 0.0129)	1.2199 (1.1251, 1.3147)
Small HDL		
Concentration of small HDL particles (mol/l)	-1.9756x10 ⁻⁹ (-1.4709x10 ⁻⁸ , 1.0758x10 ⁻⁸)	-0.0017 (-0.0880, 0.0846)
Total lipids in small HDL (mmol/l)	-0.0057 (-0.0086, -0.0028)	-0.0531 (-0.1412, 0.0350)
Phospholipids in small HDL (mmol/l)	-0.0324 (-0.0349, -0.0298)	-0.4458 (-0.5332, -0.3584)
Total cholesterol in small HDL (mmol/l)	0.0035 (0.0016, 0.0054)	0.0707 (-0.0361, 0.1775)
Cholesterol esters in small HDL (mmol/l)	0.0044 (0.0024, 0.0064)	0.0937 (-0.0150, 0.2023)
Free cholesterol in small HDL (mmol/l)	-0.0010 (-0.0014, -0.0007)	-0.0884 (-0.1822, 0.0054)
Triglycerides in small HDL (mmol/l)	0.0236 (0.0231, 0.0242)	2.1177 (2.0032, 2.2322)

Table S3: continued

Lipoprotein particle size		
Mean diameter for VLDL particles (nm)	0.9280 (0.9079, 0.9481)	0.8301 (0.7538, 0.9064)
Mean diameter for LDL particles (nm)	-0.0224 (-0.0229, -0.0218)	-0.3429 (-0.4197, -0.2660)
Mean diameter for HDL particles (nm)	0.0193 (0.0165, 0.0222)	0.1039 (0.0386, 0.1691)
Cholesterol		
Serum total cholesterol (mmol/l)	1.1410 (1.1005, 1.1815)	1.5301 (1.4169, 1.6433)
Total cholesterol in VLDL (mmol/l)	0.4257 (0.4140, 0.4375)	2.3951 (2.2656, 2.5245)
Remnant cholesterol (non-HDL, non-LDL -cholesterol) (mmol/l)	0.6311 (0.6117, 0.6504)	2.1657 (2.0402, 2.2912)
Total cholesterol in LDL (mmol/l)	0.5585 (0.5332, 0.5838)	1.3984 (1.2842, 1.5126)
Total cholesterol in HDL (mmol/l)	-0.0495 (-0.0558, -0.0432)	-0.1836 (-0.2713, -0.0958)
Total cholesterol in HDL2 (mmol/l)	-0.0933 (-0.0994, -0.0873)	-0.3804 (-0.4696, -0.2912)
Total cholesterol in HDL3 (mmol/l)	0.0436 (0.0427, 0.0445)	1.4894 (1.3966, 1.5823)
Esterified cholesterol (mmol/l)	0.7862 (0.7591, 0.8134)	1.3998 (1.2973, 1.5022)
Free cholesterol (mmol/l)	0.3427 (0.3306, 0.3547)	1.4004 (1.2667, 1.5342)
Glycerides and phospholipids		
Serum total triglycerides (mmol/l)	1.0325 (1.0030, 1.0621)	2.4433 (2.3118, 2.5749)
Triglycerides in VLDL (mmol/l)	0.7475 (0.7238, 0.7712)	2.0889 (1.9625, 2.2154)
Triglycerides in LDL (mmol/l)	0.1284 (0.1247, 0.1321)	2.7944 (2.6514, 2.9375)
Triglycerides in HDL (mmol/l)	0.0726 (0.0711, 0.0740)	2.2624 (2.1419, 2.3829)
Total phosphoglycerides (mmol/l)	0.4613 (0.4535, 0.4691)	1.5492 (1.4272, 1.6711)
Ratio of triglycerides to phosphoglycerides (mmol/l)	0.2263 (0.2214, 0.2312)	1.4034 (1.3131, 1.4936)
Phosphatidylcholine and other cholines (mmol/l)	0.4833 (0.4742, 0.4924)	1.6998 (1.5741, 1.8255)
Sphingomyelins (mmol/l)	0.0411 (0.0388, 0.0434)	0.5664 (0.4357, 0.6970)
Total cholines (mmol/l)	0.4688 (0.4592, 0.4783)	1.4979 (1.3543, 1.6414)
Apolipoproteins		
Apolipoprotein A-I (g/l)	0.0886 (0.0850, 0.0921)	0.5564 (0.4660, 0.6468)
Apolipoprotein B (g/l)	0.3360 (0.3260, 0.3460)	2.2789 (2.1537, 2.4041)
Apolipoproteins ratio		

Ratio of apolipoprotein B to apolipoprotein A-I	0.1627 (0.1574, 0.1680)	1.9077 (1.7944, 2.0209)
Fatty acids		
Total fatty acids (mmol/l)	3.8748 (3.7979, 3.9517)	1.9642 (1.8277, 2.1006)
Estimated degree of unsaturation	-0.0371 (-0.0376, -0.0366)	-0.8438 (-0.9304, -0.7571)
22:6, docosahexaenoic acid (mmol/l)	0.0137 (0.0130, 0.0143)	0.2957 (0.1934, 0.3981)
18:2, linoleic acid (mmol/l)	0.9050 (0.8813, 0.9288)	1.5801 (1.4440, 1.7161)
Omega-3 fatty acids (mmol/l)	0.0907 (0.0889, 0.0924)	0.6754 (0.5763, 0.7744)
Omega-6 fatty acids (mmol/l)	0.8278 (0.8035, 0.8521)	1.3989 (1.2596, 1.5382)
Polyunsaturated fatty acids (mmol/l)	0.9185 (0.8924, 0.9447)	1.3271 (1.1918, 1.4623)
Monounsaturated fatty acids; 16:1, 18:1 (mmol/l)	1.4682 (1.4409, 1.4956)	2.0734 (1.9541, 2.1927)
Saturated fatty acids (mmol/l)	1.4802 (1.4515, 1.5089)	1.9564 (1.8160, 2.0968)
Fatty acid ratios		
Ratio of 22:6 docosahexaenoic acid to total fatty acids (%)	-0.3120 (-0.3277, -0.2963)	-0.7954 (-0.8618, -0.7289)
Ratio of 18:2 linoleic acid to total fatty acids (%)	-0.4925 (-0.5183, -0.4668)	-0.1792 (-0.2577, -0.1008)
Ratio of omega-3 fatty acids to total fatty acids (%)	-0.5671 (-0.5824, -0.5519)	-0.7898 (-0.8608, -0.7187)
Ratio of omega-6 fatty acids to total fatty acids (%)	-2.0000 (-2.0344, -1.9657)	-0.8198 (-0.9013, -0.7382)
Ratio of polyunsaturated fatty acids to total fatty acids (%)	-2.5647 (-2.6054, -2.5240)	-0.9330 (-1.0110, -0.8549)
Ratio of monounsaturated fatty acids to total fatty acids (%)	2.1382 (2.0245, 2.2519)	0.6084 (0.5437, 0.6732)
Ratio of saturated fatty acids to total fatty acids (%)	0.2234 (0.2111, 0.2357)	0.1714 (0.0729, 0.2699)
Glycolysis related metabolites		
Glucose (mmol/l)	0.3700 (0.3506, 0.3894)	0.5445 (0.4015, 0.6875)
Lactate (mmol/l)	0.1899 (0.1757, 0.2041)	0.3612 (0.2668, 0.4555)
Pyruvate (mmol/l)	0.0248 (0.0241, 0.0255)	0.5726 (0.4623, 0.6828)
Citrate (mmol/l)	0.0180 (0.0174, 0.0186)	1.0796 (0.9674, 1.1917)
Glycerol (mmol/l)	-0.0055 (-0.0060, -0.0051)	-0.1979 (-0.2940, -0.1019)
Amino acids		
Alanine (mmol/l)	0.0329 (0.0322, 0.0335)	0.8250 (0.7138, 0.9362)

Glutamine (mmol/l)	-0.0030 (-0.0036, -0.0023)	-0.0686 (-0.1589, 0.0218)
Glycine (mmol/l)	0.0093 (0.0089, 0.0096)	0.3764 (0.2871, 0.4656)
Histidine (mmol/l)	0.0014 (0.0014, 0.0015)	0.1996 (0.0925, 0.3066)
Amino acids - branched chain		
Isoleucine (mmol/l)	0.0037 (0.0032, 0.0042)	0.2880 (0.1863, 0.3897)
Leucine (mmol/l)	1.3926x10 ⁻⁵ (-0.0003, 0.0003)	0.0059 (-0.0895, 0.1013)
Valine (mmol/l)	-0.0207 (-0.0218, -0.0196)	-0.6803 (-0.7740, -0.5866)
Amino acids - aromatic		
Phenylalanine (mmol/l)	0.0058 (0.0057, 0.0059)	0.5802 (0.4807, 0.6797)
Tyrosine (mmol/l)	-0.0013 (-0.0014, -0.0012)	-0.1398 (-0.2356, -0.0441)
Ketone bodies		
Acetate (mmol/l)	0.0007 (0.0007, 0.0008)	0.1013 (-0.0371, 0.2398)
Acetoacetate (mmol/l)	0.0017 (0.0012, 0.0021)	0.1424 (0.0378, 0.2470)
3-hydroxybutyrate (mmol/l)	0.0216 (0.0185, 0.0248)	0.3319 (0.2354, 0.4285)
Fluid balance		
Creatinine (mmol/l)	0.0011 (0.0011, 0.0012)	0.1847 (0.0758, 0.2936)
Albumin (mmol/l)	-0.0029 (-0.0029, -0.0028)	-0.8731 (-0.9871, -0.7591)
Inflammation		
Glycoprotein acetyls, mainly a1-acid glycoprotein (mmol/l)	0.2370 (0.2333, 0.2406)	1.7367 (1.6290, 1.8444)

* Total difference in each trait between 16 and 36 weeks in original units as given in first column

§ Total difference in each trait between 16 and 36 weeks in SD units; for these analyses the SD for each trait at 16 weeks was used

VLDL: very low density lipoprotein; LDL: low density lipoprotein; IDL: intermediate density lipoprotein; HDL: high density lipoprotein

All results are adjusted for the following baseline (recruitment / 16 weeks) characteristics: Age, Parity, Ethnicity, BMI and clinical centre.

Table S4: Mean concentration at 16-weeks of gestation and mean rate of change concentration per 4 weeks of gestational age between 16- and 36-weeks of gestation for each metabolic trait in obese pregnant women in the UPBEAT RCT (N = 115).

	Mean concentration at 16-weeks (95%CI)*	Mean change in concentration per 4 weeks gestational age (95%CI)*
Extremely large VLDL		
Concentration of chylomicrons and extremely large VLDL particles (mol/l)	9.633x10 ⁻¹¹ (6.954x10 ⁻¹¹ , 1.231x10 ⁻¹⁰)	2.283x10 ⁻¹¹ (2.072x10 ⁻¹¹ , 2.493x10 ⁻¹¹)
Total lipids in chylomicrons and extremely large VLDL (mmol/l)	0.021 (0.015, 0.027)	0.005 (0.005, 0.005)
Phospholipids in chylomicrons and extremely large VLDL (mmol/l)	0.003 (0.002, 0.003)	7.630x10 ⁻⁴ (7.033x10 ⁻⁴ , 8.227x10 ⁻⁴)
Total cholesterol in chylomicrons and extremely large VLDL (mmol/l)	0.004 (0.003, 0.005)	0.001 (0.001, 0.001)
Cholesterol esters in chylomicrons and extremely large VLDL (mmol/l)	0.002 (0.002, 0.003)	6.248x10 ⁻⁴ (5.825x10 ⁻⁴ , 6.671x10 ⁻⁴)
Free cholesterol in chylomicrons and extremely large VLDL (mmol/l)	0.002 (0.001, 0.002)	5.268x10 ⁻⁴ (4.882x10 ⁻⁴ , 5.654x10 ⁻⁴)
Triglycerides in chylomicrons and extremely large VLDL (mmol/l)	0.014 (0.010, 0.018)	0.003 (0.003, 0.003)
Very large VLDL		
Concentration of very large VLDL particles (mol/l)	6.901x10 ⁻¹⁰ (5.279x10 ⁻¹⁰ , 8.524x10 ⁻¹⁰)	1.702x10 ⁻¹⁰ (1.580x10 ⁻¹⁰ , 1.824x10 ⁻¹⁰)
Total lipids in very large VLDL (mmol/l)	0.067 (0.051, 0.083)	0.017 (0.015, 0.018)
Phospholipids in very large VLDL (mmol/l)	0.011 (0.008, 0.013)	0.003 (0.003, 0.003)
Total cholesterol in very large VLDL (mmol/l)	0.013 (0.010, 0.016)	0.003 (0.003, 0.004)
Cholesterol esters in very large VLDL (mmol/l)	0.007 (0.006, 0.009)	0.002 (0.002, 0.002)
Free cholesterol in very large VLDL (mmol/l)	0.006 (0.004, 0.007)	0.002 (0.001, 0.002)
Triglycerides in very large VLDL (mmol/l)	0.043 (0.033, 0.053)	0.010 (0.010, 0.011)

Table S4: continued

	Mean concentration at 16-weeks (95%CI)*	Change in mean concentration per 4 weeks gestational age (95%CI)*
Large VLDL		
Concentration of large VLDL particles (mol/l)	4.702x10 ⁻⁹ (3.788x10 ⁻⁹ , 5.617x10 ⁻⁹)	1.050x10 ⁻⁹ (9.812x10 ⁻¹⁰ , 1.119x10 ⁻⁹)
Total lipids in large VLDL (mmol/l)	0.271 (0.218, 0.324)	0.061 (0.057, 0.065)
Phospholipids in large VLDL (mmol/l)	0.049 (0.039, 0.059)	0.012 (0.011, 0.012)
Total cholesterol in large VLDL (mmol/l)	0.060 (0.048, 0.072)	0.014 (0.013, 0.015)
Cholesterol esters in large VLDL (mmol/l)	0.032 (0.026, 0.038)	0.006 (0.006, 0.007)
Free cholesterol in large VLDL (mmol/l)	0.028 (0.021, 0.034)	0.008 (0.007, 0.008)
Triglycerides in large VLDL (mmol/l)	0.162 (0.131, 0.194)	0.036 (0.033, 0.038)
Medium VLDL		
Concentration of medium VLDL particles (mol/l)	1.648x10 ⁻⁸ (1.415x10 ⁻⁸ , 1.881x10 ⁻⁸)	2.819x10 ⁻⁹ (2.647x10 ⁻⁹ , 2.991x10 ⁻⁹)
Total lipids in medium VLDL (mmol/l)	0.550 (0.472, 0.627)	0.095 (0.089, 0.100)
Phospholipids in medium VLDL (mmol/l)	0.110 (0.095, 0.125)	0.019 (0.018, 0.020)
Total cholesterol in medium VLDL (mmol/l)	0.149 (0.129, 0.169)	0.025 (0.024, 0.027)
Cholesterol esters in medium VLDL (mmol/l)	0.085 (0.074, 0.095)	0.012 (0.012, 0.013)
Free cholesterol in medium VLDL (mmol/l)	0.064 (0.054, 0.074)	0.013 (0.012, 0.014)
Triglycerides in medium VLDL (mmol/l)	0.291 (0.248, 0.335)	0.050 (0.047, 0.054)
Small VLDL		
Concentration of small VLDL particles (mol/l)	2.838x10 ⁻⁸ (2.557x10 ⁻⁸ , 3.120x10 ⁻⁸)	3.813x10 ⁻⁹ (3.600x10 ⁻⁹ , 4.026x10 ⁻⁹)
Total lipids in small VLDL (mmol/l)	0.559 (0.505, 0.613)	0.074 (0.070, 0.078)
Phospholipids in small VLDL (mmol/l)	0.131 (0.120, 0.143)	0.016 (0.015, 0.016)
Total cholesterol in small VLDL (mmol/l)	0.205 (0.186, 0.224)	0.025 (0.023, 0.026)
Cholesterol esters in small VLDL (mmol/l)	0.124 (0.112, 0.137)	0.013 (0.013, 0.014)
Free cholesterol in small VLDL (mmol/l)	0.081 (0.073, 0.088)	0.011 (0.010, 0.012)
Triglycerides in small VLDL (mmol/l)	0.222 (0.196, 0.249)	0.034 (0.032, 0.036)

Table S4: continued

	Mean concentration at 16-weeks (95%CI)*	Change in mean concentration per 4 weeks gestational age (95%CI)*
Very small VLDL		
Concentration of very small VLDL particles (mol/l)	3.608x10 ⁻⁸ (3.318x10 ⁻⁸ , 3.897x10 ⁻⁸)	3.735x10 ⁻⁹ (3.510x10 ⁻⁹ , 3.960x10 ⁻⁹)
Total lipids in very small VLDL (mmol/l)	0.456 (0.419, 0.493)	0.045 (0.043, 0.048)
Phospholipids in very small VLDL (mmol/l)	0.129 (0.117, 0.141)	0.013 (0.012, 0.014)
Total cholesterol in very small VLDL (mmol/l)	0.224 (0.207, 0.242)	0.017 (0.016, 0.018)
Cholesterol esters in very small VLDL (mmol/l)	0.153 (0.142, 0.165)	0.010 (0.009, 0.011)
Free cholesterol in very small VLDL (mmol/l)	0.071 (0.065, 0.077)	0.007 (0.007, 0.008)
Triglycerides in very small VLDL (mmol/l)	0.103 (0.092, 0.113)	0.016 (0.015, 0.016)
IDL		
Concentration of IDL particles (mol/l)	9.478x10 ⁻⁸ (8.690x10 ⁻⁸ , 1.027x10 ⁻⁷)	7.630x10 ⁻⁹ (7.099x10 ⁻⁹ , 8.161x10 ⁻⁹)
Total lipids in IDL (mmol/l)	0.955 (0.874, 1.036)	0.073 (0.068, 0.079)
Phospholipids in IDL (mmol/l)	0.254 (0.234, 0.274)	0.015 (0.014, 0.017)
Total cholesterol in IDL (mmol/l)	0.594 (0.541, 0.647)	0.041 (0.038, 0.045)
Cholesterol esters in IDL (mmol/l)	0.426 (0.388, 0.463)	0.031 (0.028, 0.033)
Free cholesterol in IDL (mmol/l)	0.168 (0.152, 0.184)	0.011 (0.010, 0.012)
Triglycerides in IDL (mmol/l)	0.107 (0.097, 0.118)	0.017 (0.016, 0.018)
Large LDL		
Concentration of large LDL particles (mol/l)	1.526x10 ⁻⁷ (1.390x10 ⁻⁷ , 1.663x10 ⁻⁷)	1.269x10 ⁻⁸ (1.178x10 ⁻⁸ , 1.360x10 ⁻⁸)
Total lipids in large LDL (mmol/l)	1.082 (0.985, 1.180)	0.086 (0.080, 0.093)
Phospholipids in large LDL (mmol/l)	0.279 (0.259, 0.299)	0.016 (0.015, 0.017)
Total cholesterol in large LDL (mmol/l)	0.707 (0.636, 0.778)	0.056 (0.051, 0.060)
Cholesterol esters in large LDL (mmol/l)	0.500 (0.447, 0.553)	0.044 (0.040, 0.047)
Free cholesterol in large LDL (mmol/l)	0.207 (0.189, 0.225)	0.012 (0.011, 0.013)
Triglycerides in large LDL (mmol/l)	0.096 (0.086, 0.105)	0.014 (0.014, 0.015)

Table S4: continued

	Mean concentration at 16-weeks (95%CI)	Change in mean concentration per 4 weeks gestational age (95%CI)
Medium LDL		
Concentration of medium LDL particles (mol/l)	1.185x10 ⁻⁷ (1.069x10 ⁻⁷ , 1.301x10 ⁻⁷)	1.099x10 ⁻⁸ (1.021x10 ⁻⁸ , 1.177x10 ⁻⁸)
Total lipids in medium LDL (mmol/l)	0.602 (0.544, 0.661)	0.054 (0.050, 0.058)
Phospholipids in medium LDL (mmol/l)	0.171 (0.160, 0.183)	0.011 (0.011, 0.012)
Total cholesterol in medium LDL (mmol/l)	0.384 (0.339, 0.428)	0.035 (0.033, 0.038)
Cholesterol esters in medium LDL (mmol/l)	0.264 (0.227, 0.300)	0.028 (0.026, 0.031)
Free cholesterol in medium LDL (mmol/l)	0.120 (0.112, 0.128)	0.007 (0.007, 0.008)
Triglycerides in medium LDL (mmol/l)	0.047 (0.042, 0.051)	0.007 (0.007, 0.007)
Small LDL		
Concentration of small LDL particles (mol/l)	1.405x10 ⁻⁷ (1.278x10 ⁻⁷ , 1.531x10 ⁻⁷)	1.207x10 ⁻⁸ (1.124x10 ⁻⁸ , 1.289x10 ⁻⁸)
Total lipids in small LDL (mmol/l)	0.393 (0.357, 0.428)	0.033 (0.030, 0.035)
Phospholipids in small LDL (mmol/l)	0.128 (0.121, 0.136)	0.007 (0.007, 0.008)
Total cholesterol in small LDL (mmol/l)	0.235 (0.208, 0.261)	0.021 (0.019, 0.023)
Cholesterol esters in small LDL (mmol/l)	0.163 (0.140, 0.185)	0.016 (0.015, 0.018)
Free cholesterol in small LDL (mmol/l)	0.072 (0.067, 0.077)	0.004 (0.004, 0.005)
Triglycerides in small LDL (mmol/l)	0.030 (0.027, 0.033)	0.005 (0.004, 0.005)
Very large HDL		
Concentration of very large HDL particles (mol/l)	6.020x10 ⁻⁷ (5.372x10 ⁻⁷ , 6.669x10 ⁻⁷)	1.599x10 ⁻⁸ (1.341x10 ⁻⁸ , 1.858x10 ⁻⁸)
Total lipids in very large HDL (mmol/l)	0.608 (0.542, 0.674)	0.016 (0.013, 0.018)
Phospholipids in very large HDL (mmol/l)	0.309 (0.275, 0.344)	0.005 (0.003, 0.006)
Total cholesterol in very large HDL (mmol/l)	0.277 (0.248, 0.307)	0.008 (0.006, 0.009)
Cholesterol esters in very large HDL (mmol/l)	0.200 (0.179, 0.221)	0.006 (0.005, 0.007)
Free cholesterol in very large HDL (mmol/l)	0.077 (0.068, 0.086)	0.002 (0.002, 0.002)
Triglycerides in very large HDL (mmol/l)	0.021 (0.018, 0.024)	0.003 (0.003, 0.003)

Table S4: continued

	Mean concentration at 16- weeks (95%CI)	Change in mean concentration per 4 weeks gestational age (95%CI)
Large HDL		
Concentration of large HDL particles (mol/l)	1.643x10 ⁻⁶ (1.497x10 ⁻⁶ , 1.790x10 ⁻⁶)	2.113x10 ⁻⁹ (-4.657x10 ⁻⁹ , 8.883x10 ⁻⁹)
Total lipids in large HDL (mmol/l)	1.034 (0.941, 1.128)	-4.406x10 ⁻⁴ (-0.005, 0.004)
Phospholipids in large HDL (mmol/l)	0.498 (0.458, 0.538)	-0.002 (-0.004, 6.452x10 ⁻⁵)
Total cholesterol in large HDL (mmol/l)	0.495 (0.445, 0.545)	-0.003 (-0.005, -6.039x10 ⁻⁴)
Cholesterol esters in large HDL (mmol/l)	0.387 (0.349, 0.425)	-0.002 (-0.003, -1.133x10 ⁻⁴)
Free cholesterol in large HDL (mmol/l)	0.108 (0.096, 0.120)	-0.001 (-0.002, -4.887x10 ⁻⁴)
Triglycerides in large HDL (mmol/l)	0.040 (0.035, 0.045)	0.004 (0.004, 0.005)
Medium HDL		
Concentration of medium HDL particles (mol/l)	2.283x10 ⁻⁶ (2.173x10 ⁻⁶ , 2.393x10 ⁻⁶)	-3.467x10 ⁻⁸ (-4.120x10 ⁻⁸ , -2.815x10 ⁻⁸)
Total lipids in medium HDL (mmol/l)	0.968 (0.921, 1.016)	-0.017 (-0.019, -0.014)
Phospholipids in medium HDL (mmol/l)	0.453 (0.432, 0.474)	-0.004 (-0.005, -0.002)
Total cholesterol in medium HDL (mmol/l)	0.468 (0.441, 0.494)	-0.015 (-0.017, -0.014)
Cholesterol esters in medium HDL (mmol/l)	0.377 (0.356, 0.398)	-0.014 (-0.015, -0.012)
Free cholesterol in medium HDL (mmol/l)	0.090 (0.085, 0.096)	-0.002 (-0.002, -0.001)
Triglycerides in medium HDL (mmol/l)	0.045 (0.042, 0.049)	0.003 (0.002, 0.003)

Table S4: continued

	Mean concentration at 16-weeks (95%CI)*	Change in mean concentration per 4 weeks gestational age (95%CI)*
Small HDL		
Concentration of small HDL particles (mol/l)	5.042x10 ⁻⁶ (4.893x10 ⁻⁶ , 5.191x10 ⁻⁶)	-2.350x10 ⁻¹⁰ (-8.239x10 ⁻⁹ , 7.769x10 ⁻⁹)
Total lipids in small HDL (mmol/l)	1.119 (1.086, 1.151)	-0.001 (-0.003, 6.969x10 ⁻⁴)
Phospholipids in small HDL (mmol/l)	0.611 (0.586, 0.636)	-0.007 (-0.008, -0.005)
Total cholesterol in small HDL (mmol/l)	0.452 (0.436, 0.467)	7.082x10 ⁻⁴ (-3.675x10 ⁻⁴ , 0.002)
Cholesterol esters in small HDL (mmol/l)	0.335 (0.320, 0.350)	8.876x10 ⁻⁴ (-1.397x10 ⁻⁴ , 0.002)
Free cholesterol in small HDL (mmol/l)	0.115 (0.111, 0.119)	-2.085x10 ⁻⁴ (-4.291x10 ⁻⁴ , 1.220x10 ⁻⁵)
Triglycerides in small HDL (mmol/l)	0.048 (0.044, 0.052)	0.005 (0.004, 0.005)
Lipoprotein particle size		
Mean diameter for VLDL particles (nm)	36.822 (36.484, 37.160)	0.186 (0.169, 0.204)
Mean diameter for LDL particles (nm)	23.599 (23.579, 23.619)	-0.004 (-0.005, -0.003)
Mean diameter for HDL particles	10.158 (10.096, 10.221)	0.004 (0.001, 0.006)
Cholesterol		
Serum total cholesterol (mmol/l)	4.222 (3.951, 4.492)	0.229 (0.212, 0.246)
Total cholesterol in VLDL (mmol/l)	0.657 (0.594, 0.720)	0.085 (0.081, 0.090)
Remnant cholesterol (non-HDL, non-LDL -cholesterol) (mmol/l)	1.252 (1.147, 1.357)	0.126 (0.119, 0.134)
Total cholesterol in LDL (mmol/l)	1.326 (1.184, 1.468)	0.112 (0.103, 0.121)
Total cholesterol in HDL (mmol/l)	1.691 (1.598, 1.783)	-0.010 (-0.015, -0.005)
Total cholesterol in HDL2 (mmol/l)	1.160 (1.075, 1.246)	-0.019 (-0.023, -0.014)
Total cholesterol in HDL3 (mmol/l)	0.527 (0.518, 0.537)	0.009 (0.008, 0.009)
Esterified cholesterol (mmol/l)	2.814 (2.607, 3.021)	0.158 (0.145, 0.172)
Free cholesterol (mmol/l)	1.308 (1.216, 1.400)	0.069 (0.062, 0.076)

Table S4: continued

	Mean concentration at 16-weeks (95%CI)*	Change in mean concentration per 4 weeks gestational age (95%CI)*
Glycerides and phospholipids		
Serum total triglycerides (mmol/l)	1.273 (1.125, 1.421)	0.206 (0.195, 0.218)
Triglycerides in VLDL (mmol/l)	0.838 (0.716, 0.959)	0.149 (0.140, 0.158)
Triglycerides in LDL (mmol/l)	0.172 (0.155, 0.189)	0.026 (0.024, 0.027)
Triglycerides in HDL (mmol/l)	0.153 (0.141, 0.165)	0.015 (0.014, 0.015)
Total phosphoglycerides (mmol/l)	2.239 (2.133, 2.345)	0.093 (0.085, 0.100)
Ratio of triglycerides to phosphoglycerides	0.651 (0.597, 0.704)	0.045 (0.042, 0.048)
Phosphatidylcholine and other cholines (mmol/l)	2.052 (1.947, 2.157)	0.097 (0.090, 0.104)
Sphingomyelins (mmol/l)	0.396 (0.369, 0.422)	0.008 (0.006, 0.010)
Total cholines (mmol/l)	2.529 (2.410, 2.648)	0.094 (0.085, 0.103)
Apolipoproteins		
Apolipoprotein A-I (g/l)	1.662 (1.606, 1.717)	0.018 (0.015, 0.021)
Apolipoprotein B (g/l)	0.794 (0.741, 0.846)	0.067 (0.064, 0.071)
Apolipoprotein Ratio		
Ratio of apolipoprotein B to apolipoprotein A-I	0.493 (0.463, 0.522)	0.032 (0.031, 0.034)
Fatty acids		
Total fatty acids (mmol/l)	12.627 (11.894, 13.359)	0.777 (0.723, 0.831)
Estimated degree of unsaturation	1.118 (1.105, 1.131)	-0.007 (-0.008, -0.007)
22:6, docosahexaenoic acid (mmol/l)	0.211 (0.196, 0.225)	0.003 (0.002, 0.004)
18:2, linoleic acid (mmol/l)	3.462 (3.250, 3.673)	0.182 (0.166, 0.197)
Omega-3 fatty acids (mmol/l)	0.594 (0.549, 0.639)	0.018 (0.015, 0.021)
Omega-6 fatty acids (mmol/l)	3.913 (3.688, 4.138)	0.166 (0.150, 0.183)
Polyunsaturated fatty acids (mmol/l)	4.511 (4.251, 4.770)	0.184 (0.166, 0.203)
Monounsaturated fatty acids; 16:1, 18:1 (mmol/l)	3.558 (3.318, 3.798)	0.294 (0.277, 0.311)
Saturated fatty acids (mmol/l)	4.590 (4.313, 4.866)	0.297 (0.276, 0.318)

Table S4: continued

	Mean concentration at 16-weeks (95%CI)*	Change in mean concentration per 4 weeks gestational age (95%CI)*
Fatty acid ratios		
Ratio of 22:6 docosahexaenoic acid to total fatty acids (%)	1.672 (1.595, 1.748)	-0.061 (-0.067, -0.056)
Ratio of 18:2 linoleic acid to total fatty acids (%)	27.209 (26.460, 27.959)	-0.099 (-0.143, -0.056)
Ratio of omega-3 fatty acids to total fatty acids (%)	4.663 (4.464, 4.863)	-0.113 (-0.123, -0.103)
Ratio of omega-6 fatty acids to total fatty acids (%)	30.969 (30.261, 31.678)	-0.400 (-0.440, -0.360)
Ratio of polyunsaturated fatty acids to total fatty acids (%)	35.670 (34.897, 36.443)	-0.513 (-0.556, -0.470)
Ratio of monounsaturated fatty acids to total fatty acids (%)	27.690 (27.069, 28.310)	0.436 (0.390, 0.482)
Ratio of saturated fatty acids to total fatty acids (%)	36.555 (36.180, 36.931)	0.045 (0.018, 0.072)
Glycolysis related metabolites		
Glucose (mmol/l)	3.764 (3.551, 3.977)	0.074 (0.054, 0.093)
Lactate (mmol/l)	1.061 (0.937, 1.185)	0.039 (0.029, 0.049)
Pyruvate (mmol/l)	0.088 (0.077, 0.099)	0.005 (0.004, 0.006)
Citrate (mmol/l)	0.109 (0.104, 0.114)	0.004 (0.003, 0.004)
Glycerol (mmol/l)	0.064 (0.058, 0.070)	-0.001 (-0.001, -5.240x10 ⁻⁴)
Amino acids		
Alanine (mmol/l)	0.378 (0.366, 0.390)	0.007 (0.006, 0.007)
Glutamine (mmol/l)	0.407 (0.395, 0.420)	-6.445x10 ⁻⁴ (-0.002, 2.203x10 ⁻⁴)
Glycine (mmol/l)	0.206 (0.198, 0.214)	0.002 (0.001, 0.002)
Histidine (mmol/l)	0.064 (0.062, 0.066)	2.780x10 ⁻⁴ (1.281x10 ⁻⁴ , 4.278x10 ⁻⁴)
Amino acids - branched chain		
Isoleucine (mmol/l)	0.047 (0.043, 0.050)	7.648x10 ⁻⁴ (4.956x10 ⁻⁴ , 0.001)
Leucine (mmol/l)	0.062 (0.058, 0.065)	2.006x10 ⁻⁵ (-2.551x10 ⁻⁴ , 2.952x10 ⁻⁴)
Valine (mmol/l)	0.131 (0.123, 0.138)	-0.004 (-0.005, -0.004)

Table S4: continued

	Mean concentration at 16-weeks (95%CI)*	Change in mean concentration per 4 weeks gestational age (95%CI)*
Amino acids - aromatic		
Phenylalanine (mmol/l)	0.072 (0.069, 0.075)	0.001 (9.617×10^{-4} , 0.001)
Tyrosine (mmol/l)	0.038 (0.036, 0.040)	-2.555×10^{-4} (-4.270×10^{-4} , -8.403×10^{-5})
Ketone bodies		
Acetate (mmol/l)	0.041 (0.039, 0.044)	1.444×10^{-4} (-5.902×10^{-5} , 3.477×10^{-4})
Acetoacetate (mmol/l)	0.021 (0.018, 0.024)	3.697×10^{-4} (9.760×10^{-5} , 6.419×10^{-4})
3-hydroxybutyrate (mmol/l)	0.078 (0.062, 0.093)	0.005 (0.003, 0.006)
Fluid balance		
Creatinine (mmol/l)	0.036 (0.034, 0.038)	2.231×10^{-4} (9.232×10^{-5} , 3.539×10^{-4})
Albumin (mmol/l)	0.084 (0.083, 0.085)	-5.740×10^{-4} (-6.492×10^{-4} , -4.988×10^{-4})
Inflammation		
Glycoprotein acetyls, mainly a1-acid glycoprotein (mmol/l)	1.540 (1.495, 1.585)	0.047 (0.044, 0.050)

* Units for each metabolic measure are provided in column one with the metabolic measure name. The results for mean levels are 16-weeks of gestation are these units; results for the change between 16 and 36 weeks are these units per 4 week of gestation.

VLDL: very low density lipoprotein; LDL: low density lipoprotein; IDL: intermediate density lipoprotein; HDL: high density lipoprotein

All results are adjusted for the following baseline (recruitment / 16 weeks) characteristics: Age, Parity, Ethnicity, BMI and clinical centre.

Table S5: Effect of the UPBEAT diet and physical activity lifestyle intervention on metabolic profiles: difference in mean rate of change in metabolic traits (original units) comparing women receiving intervention to the control group. N = 1158

	Difference in mean rate of change in traits per 4 weeks of gestation between 16 and 36 weeks between women receiving intervention and control group (reference)	p-value
Extremely large VLDL		
Concentration of chylomicrons and extremely large VLDL particles (mol/l)	-5.430x10 ⁻¹² (-8.323x10 ⁻¹² , -2.537x10 ⁻¹²)	2.48x10 ⁻⁴
Total lipids in chylomicrons and extremely large VLDL (mmol/l)	-0.001 (-0.002, -5.322x10 ⁻⁴)	2.87x10 ⁻⁴
Phospholipids in chylomicrons and extremely large VLDL (mmol/l)	-1.457x10 ⁻⁴ (-2.287x10 ⁻⁴ , -6.274x10 ⁻⁵)	6.06x10 ⁻⁴
Total cholesterol in chylomicrons and extremely large VLDL (mmol/l)	-1.623x10 ⁻⁴ (-2.725x10 ⁻⁴ , -5.212x10 ⁻⁵)	0.004
Cholesterol esters in chylomicrons and extremely large VLDL (mmol/l)	-6.952x10 ⁻⁵ (-1.289x10 ⁻⁴ , -1.015x10 ⁻⁵)	0.022
Free cholesterol in chylomicrons and extremely large VLDL (mmol/l)	-9.276x10 ⁻⁵ (-1.468x10 ⁻⁴ , -3.868x10 ⁻⁵)	8.08x10 ⁻⁴
Triglycerides in chylomicrons and extremely large VLDL (mmol/l)	-8.450x10 ⁻⁴ (-0.001, -4.077x10 ⁻⁴)	1.62x10 ⁻⁴
Very large VLDL		
Concentration of very large VLDL particles (mol/l)	-2.919x10 ⁻¹¹ (-4.656x10 ⁻¹¹ , -1.183x10 ⁻¹¹)	0.001
Total lipids in very large VLDL (mmol/l)	-0.003 (-0.005, -0.001)	0.001
Phospholipids in very large VLDL (mmol/l)	-4.618x10 ⁻⁴ (-7.453x10 ⁻⁴ , -1.782x10 ⁻⁴)	0.001
Total cholesterol in very large VLDL (mmol/l)	-4.869x10 ⁻⁴ (-8.058x10 ⁻⁴ , -1.681x10 ⁻⁴)	0.003
Cholesterol esters in very large VLDL (mmol/l)	-2.409x10 ⁻⁴ (-4.085x10 ⁻⁴ , -7.328x10 ⁻⁵)	0.005
Free cholesterol in very large VLDL (mmol/l)	-2.459x10 ⁻⁴ (-3.986x10 ⁻⁴ , -9.316x10 ⁻⁵)	0.002
Triglycerides in very large VLDL (mmol/l)	-0.002 (-0.003, -7.781x10 ⁻⁴)	8.16x10 ⁻⁴
Large VLDL		
Concentration of large VLDL particles (mol/l)	-1.436x10 ⁻¹⁰ (-2.419x10 ⁻¹⁰ , -4.524x10 ⁻¹¹)	0.004
Total lipids in large VLDL (mmol/l)	-0.008 (-0.014, -0.003)	0.005
Phospholipids in large VLDL (mmol/l)	-0.001 (-0.003, -4.202x10 ⁻⁴)	0.006
Total cholesterol in large VLDL (mmol/l)	-0.002 (-0.003, -3.658x10 ⁻⁴)	0.011
Cholesterol esters in large VLDL (mmol/l)	-6.322x10 ⁻⁴ (-0.001, -4.684x10 ⁻⁵)	0.035
Free cholesterol in large VLDL (mmol/l)	-9.788x10 ⁻⁴ (-0.002, -3.053x10 ⁻⁴)	0.004
Triglycerides in large VLDL (mmol/l)	-0.005 (-0.009, -0.002)	0.003

Table S5: continued

Medium VLDL		
Concentration of medium VLDL particles (mol/l)	-2.706x10 ⁻¹⁰ (-5.176x10 ⁻¹⁰ , -2.363x10 ⁻¹¹)	0.032
Total lipids in medium VLDL (mmol/l)	-0.009 (-0.017, -5.203x10 ⁻⁴)	0.037
Phospholipids in medium VLDL (mmol/l)	-0.002 (-0.003, 2.571x10 ⁻⁵)	0.054
Total cholesterol in medium VLDL (mmol/l)	-0.001 (-0.004, 6.072x10 ⁻⁴)	0.165
Cholesterol esters in medium VLDL (mmol/l)	-3.934x10 ⁻⁴ (-0.001, 6.747x10 ⁻⁴)	0.471
Free cholesterol in medium VLDL (mmol/l)	-0.001 (-0.002, -5.763x10 ⁻⁶)	0.049
Triglycerides in medium VLDL (mmol/l)	-0.006 (-0.010, -0.001)	0.016
Small VLDL		
Concentration of small VLDL particles (mmol/l)	-8.340x10 ⁻¹¹ (-3.894x10 ⁻¹⁰ , 2.226x10 ⁻¹⁰)	0.593
Total lipids in small VLDL (mmol/l)	-0.001 (-0.007, 0.005)	0.702
Phospholipids in small VLDL (mmol/l)	-2.123x10 ⁻⁴ (-0.001, 0.001)	0.738
Total cholesterol in small VLDL (mmol/l)	8.711x10 ⁻⁴ (-0.001, 0.003)	0.421
Cholesterol esters in small VLDL (mmol/l)	9.298x10 ⁻⁴ (-4.024x10 ⁻⁴ , 0.002)	0.172
Free cholesterol in small VLDL (mmol/l)	-5.333x10 ⁻⁵ (-9.154x10 ⁻⁴ , 8.087x10 ⁻⁴)	0.904
Triglycerides in small VLDL (mmol/l)	-0.002 (-0.005, 0.001)	0.215
Very small VLDL		
Concentration of very small VLDL particles (mmol/l)	2.266x10 ⁻¹⁰ (-9.757x10 ⁻¹¹ , 5.508x10 ⁻¹⁰)	0.171
Total lipids in very small VLDL (mmol/l)	0.003 (-9.195x10 ⁻⁴ , 0.007)	0.13
Phospholipids in very small VLDL (mmol/l)	0.001 (-3.358x10 ⁻⁵ , 0.003)	0.057
Total cholesterol in very small VLDL (mmol/l)	0.002 (-2.896x10 ⁻⁵ , 0.004)	0.054
Cholesterol esters in very small VLDL (mmol/l)	0.001 (-7.809x10 ⁻⁵ , 0.002)	0.067
Free cholesterol in very small VLDL (mmol/l)	7.239x10 ⁻⁴ (1.017x10 ⁻⁵ , 0.001)	0.047
Triglycerides in very small VLDL (mmol/l)	6.178x10 ⁻⁵ (-0.001, 0.001)	0.922

Table S5: continued

IDL		
Concentration of IDL particles (mmol/l)	5.615x10 ⁻¹⁰ (-2.024x10 ⁻¹⁰ , 1.325x10 ⁻⁹)	0.15
Total lipids in IDL (mmol/l)	0.006 (-0.002, 0.014)	0.132
Phospholipids in IDL (mmol/l)	0.002 (-1.812x10 ⁻⁴ , 0.004)	0.077
Total cholesterol in IDL (mmol/l)	0.004 (-0.001, 0.009)	0.133
Cholesterol esters in IDL (mmol/l)	0.002 (-0.001, 0.006)	0.216
Free cholesterol in IDL (mmol/l)	0.002 (9.352x10 ⁻⁵ , 0.003)	0.037
Triglycerides in IDL (mmol/l)	4.641x10 ⁻⁴ (-8.328x10 ⁻⁴ , 0.002)	0.483
Large LDL		
Concentration of large LDL particles (mol/l)	9.960x10 ⁻¹⁰ (-3.150x10 ⁻¹⁰ , 2.307x10 ⁻⁹)	0.137
Total lipids in large LDL (mmol/l)	0.007 (-0.002, 0.017)	0.121
Phospholipids in large LDL (mmol/l)	0.001 (-4.370x10 ⁻⁴ , 0.003)	0.135
Total cholesterol in large LDL (mmol/l)	0.006 (-0.001, 0.012)	0.098
Cholesterol esters in large LDL (mmol/l)	0.004 (-0.001, 0.009)	0.121
Free cholesterol in large LDL (mmol/l)	0.002 (-1.379x10 ⁻⁵ , 0.003)	0.052
Triglycerides in large LDL (mmol/l)	3.603x10 ⁻⁴ (-7.183x10 ⁻⁴ , 0.001)	0.513
Medium LDL		
Concentration of medium LDL particles (mol/l)	8.685x10 ⁻¹⁰ (-2.488x10 ⁻¹⁰ , 1.986x10 ⁻⁹)	0.128
Total lipids in medium LDL (mmol/l)	0.004 (-0.001, 0.010)	0.121
Phospholipids in medium LDL (mmol/l)	4.492x10 ⁻⁴ (-5.950x10 ⁻⁴ , 0.001)	0.399
Total cholesterol in medium LDL (mmol/l)	0.004 (-3.480x10 ⁻⁴ , 0.008)	0.073
Cholesterol esters in medium LDL (mmol/l)	0.003 (-1.232x10 ⁻⁴ , 0.007)	0.059
Free cholesterol in medium LDL (mmol/l)	5.072x10 ⁻⁴ (-2.358x10 ⁻⁴ , 0.001)	0.181
Triglycerides in medium LDL (mmol/l)	1.647x10 ⁻⁴ (-3.576x10 ⁻⁴ , 6.870x10 ⁻⁴)	0.537
Small LDL		
Concentration of small LDL particles (mol/l)	8.393x10 ⁻¹⁰ (-3.470x10 ⁻¹⁰ , 2.025x10 ⁻⁹)	0.166
Total lipids in small LDL (mmol/l)	0.002 (-8.675x10 ⁻⁴ , 0.006)	0.149
Phospholipids in small LDL (mmol/l)	1.340x10 ⁻⁴ (-5.082x10 ⁻⁴ , 7.762x10 ⁻⁴)	0.683
Total cholesterol in small LDL (mmol/l)	0.002 (-1.279x10 ⁻⁴ , 0.005)	0.063
Cholesterol esters in small LDL (mmol/l)	0.002 (3.884x10 ⁻⁵ , 0.004)	0.046
Free cholesterol in small LDL (mmol/l)	2.574x10 ⁻⁴ (-1.803x10 ⁻⁴ , 6.951x10 ⁻⁴)	0.249
Triglycerides in small LDL (mmol/l)	-5.176x10 ⁻⁵ (-3.683x10 ⁻⁴ , 2.648x10 ⁻⁴)	0.749

Table S5: continued

Very large HDL		
Concentration of very large HDL particles (mol/l)	-1.228x10 ⁻⁹ (-4.887x10 ⁻⁹ , 2.432x10 ⁻⁹)	0.511
Total lipids in very large HDL (mmol/l)	-0.001 (-0.005, 0.002)	0.491
Phospholipids in very large HDL (mmol/l)	5.000x10 ⁻⁵ (-0.002, 0.002)	0.96
Total cholesterol in very large HDL (mmol/l)	-0.001 (-0.003, 6.460x10 ⁻⁴)	0.215
Cholesterol esters in very large HDL (mmol/l)	-8.292x10 ⁻⁴ (-0.002, 4.028x10 ⁻⁴)	0.187
Free cholesterol in very large HDL (mmol/l)	-2.818x10 ⁻⁴ (-8.186x10 ⁻⁴ , 2.550x10 ⁻⁴)	0.304
Triglycerides in very large HDL (mmol/l)	-2.479x10 ⁻⁴ (-4.714x10 ⁻⁴ , -2.436x10 ⁻⁵)	0.03
Large HDL		
Concentration of large HDL particles (mol/l)	-1.478x10 ⁻⁹ (-1.098x10 ⁻⁸ , 8.028x10 ⁻⁹)	0.761
Total lipids in large HDL (mmol/l)	-8.993x10 ⁻⁴ (-0.007, 0.005)	0.771
Phospholipids in large HDL (mmol/l)	-1.159x10 ⁻⁴ (-0.003, 0.003)	0.934
Total cholesterol in large HDL (mmol/l)	-6.220x10 ⁻⁴ (-0.004, 0.002)	0.695
Cholesterol esters in large HDL (mmol/l)	-5.784x10 ⁻⁴ (-0.003, 0.002)	0.634
Free cholesterol in large HDL (mmol/l)	-4.172x10 ⁻⁵ (-7.685x10 ⁻⁴ , 6.851x10 ⁻⁴)	0.91
Triglycerides in large HDL (mmol/l)	-1.699x10 ⁻⁴ (-5.560x10 ⁻⁴ , 2.162x10 ⁻⁴)	0.389
Medium HDL		
Concentration of medium HDL particles (mol/l)	-3.573x10 ⁻⁹ (-1.261x10 ⁻⁸ , 5.468x10 ⁻⁹)	0.439
Total lipids in medium HDL (mmol/l)	-0.001 (-0.005, 0.003)	0.481
Phospholipids in medium HDL (mmol/l)	-7.396x10 ⁻⁴ (-0.002, 9.798x10 ⁻⁴)	0.399
Total cholesterol in medium HDL (mmol/l)	-5.119x10 ⁻⁴ (-0.003, 0.002)	0.657
Cholesterol esters in medium HDL (mmol/l)	-4.907x10 ⁻⁴ (-0.002, 0.001)	0.598
Free cholesterol in medium HDL (mmol/l)	-2.018x10 ⁻⁵ (-4.787x10 ⁻⁴ , 4.383x10 ⁻⁴)	0.931
Triglycerides in medium HDL (mmol/l)	-1.433x10 ⁻⁴ (-4.170x10 ⁻⁴ , 1.305x10 ⁻⁴)	0.305

Table S5: continued

Small HDL		
Concentration of small HDL particles (mol/l)	-3.956x10 ⁻⁹ (-1.489x10 ⁻⁸ , 6.978x10 ⁻⁹)	0.478
Total lipids in small HDL (mmol/l)	-6.961x10 ⁻⁴ (-0.003, 0.002)	0.578
Phospholipids in small HDL (mmol/l)	-0.002 (-0.004, -1.363x10 ⁻⁴)	0.035
Total cholesterol in small HDL (mmol/l)	0.002 (1.270x10 ⁻⁴ , 0.003)	0.033
Cholesterol esters in small HDL (mmol/l)	0.002 (5.153x10 ⁻⁴ , 0.003)	0.008
Free cholesterol in small HDL (mmol/l)	-3.001x10 ⁻⁴ (-6.091x10 ⁻⁴ , 8.987x10 ⁻⁶)	0.057
Triglycerides in small HDL (mmol/l)	-2.744x10 ⁻⁴ (-6.414x10 ⁻⁴ , 9.250x10 ⁻⁵)	0.143
Lipoprotein particle size		
Mean diameter for VLDL particles (nm)	-0.031 (-0.054, -0.008)	0.008
Mean diameter for LDL particles (nm)	1.061x10 ⁻⁴ (-0.001, 0.001)	0.873
Mean diameter for HDL particles (nm)	-3.594x10 ⁻⁵ (-0.004, 0.003)	0.984
Cholesterol		
Serum total cholesterol (mol/l)	0.014 (-0.010, 0.039)	0.245
Total cholesterol in VLDL (mmol/l)	-0.001 (-0.008, 0.006)	0.76
Remnant cholesterol (non-HDL, non-LDL -cholesterol) (mmol/l)	0.003 (-0.008, 0.013)	0.621
Total cholesterol in LDL (mmol/l)	0.012 (-0.001, 0.025)	0.082
Total cholesterol in HDL (mmol/l)	-4.998x10 ⁻⁴ (-0.007, 0.006)	0.882
Total cholesterol in HDL2 (mmol/l)	-3.999x10 ⁻⁴ (-0.007, 0.006)	0.899
Total cholesterol in HDL3 (mmol/l)	-8.860x10 ⁻⁵ (-8.504x10 ⁻⁴ , 6.732x10 ⁻⁴)	0.82
Esterified cholesterol (mmol/l)	0.008 (-0.011, 0.028)	0.387
Free cholesterol (mmol/l)	0.003 (-0.006, 0.013)	0.466
Glycerides and phospholipids		
Serum total triglycerides (mol/l)	-0.015 (-0.031, 8.645x10 ⁻⁴)	0.064
Triglycerides in VLDL (mmol/l)	-0.015 (-0.028, -0.002)	0.022
Triglycerides in LDL (mmol/l)	4.618x10 ⁻⁴ (-0.001, 0.002)	0.635
Triglycerides in HDL (mmol/l)	-8.483x10 ⁻⁴ (-0.002, 2.444x10 ⁻⁴)	0.128
Total phosphoglycerides (mmol/l)	-0.003 (-0.013, 0.007)	0.569
Ratio of triglycerides to phosphoglycerides	-0.005 (-0.009, -6.198x10 ⁻⁴)	0.024
Phosphatidylcholine and other cholines (mmol/l)	-0.001 (-0.011, 0.009)	0.809
Sphingomyelins (mmol/l)	7.135x10 ⁻⁴ (-0.002, 0.003)	0.586
Total cholines (mmol/l)	-9.504x10 ⁻⁴ (-0.013, 0.011)	0.875
Apolipoproteins		
Apolipoprotein A-I (g/l)	-0.001 (-0.005, 0.003)	0.558
Apolipoprotein B (g/l)	6.907x10 ⁻⁴ (-0.005, 0.006)	0.8
Apolipoproteins ratio		
Ratio of apolipoprotein B to apolipoprotein A-I	7.824x10 ⁻⁴ (-0.002, 0.004)	0.582

Table S5: continued

Fatty acids		
Total fatty acids (mmol/l)	-0.036 (-0.109, 0.038)	0.341
Estimated degree of unsaturation	0.001 (1.229x10 ⁻⁴ , 0.002)	0.028
22:6, docosahexaenoic acid (mmol/l)	3.139x10 ⁻⁴ (-9.443x10 ⁻⁴ , 0.002)	0.625
18:2, linoleic acid (mmol/l)	0.004 (-0.017, 0.025)	0.716
Omega-3 fatty acids (mmol/l)	-7.868x10 ⁻⁴ (-0.004, 0.003)	0.669
Omega-6 fatty acids (mmol/l)	0.004 (-0.019, 0.026)	0.735
Polyunsaturated fatty acids (mmol/l)	0.003 (-0.023, 0.029)	0.816
Monounsaturated fatty acids; 16:1, 18:1 (mmol/l)	-0.016 (-0.039, 0.008)	0.191
Saturated fatty acids	-0.021 (-0.050, 0.007)	0.14
Fatty acid ratios		
Ratio of 22:6 docosahexaenoic acid to total fatty acids (%)	0.005 (-0.001, 0.010)	0.111
Ratio of 18:2 linoleic acid to total fatty acids (%)	0.069 (0.013, 0.126)	0.017
Ratio of omega-3 fatty acids to total fatty acids (%)	0.003 (-0.010, 0.016)	0.623
Ratio of omega-6 fatty acids to total fatty acids (%)	0.077 (0.023, 0.131)	0.006
Ratio of polyunsaturated fatty acids to total fatty acids (%)	0.079 (0.020, 0.138)	0.008
Ratio of monounsaturated fatty acids to total fatty acids (%)	-0.025 (-0.073, 0.023)	0.311
Ratio of saturated fatty acids to total fatty acids (%)	-0.049 (-0.083, -0.015)	0.005
Glycolysis related metabolites		
Glucose (mmol/l)	-0.013 (-0.037, 0.010)	0.257
Lactate (mmol/l)	-0.017 (-0.027, -0.006)	0.003
Pyruvate (mmol/l)	-0.002 (-0.003, -6.028x10 ⁻⁴)	0.003
Citrate (mmol/l)	-1.962x10 ⁻⁴ (-6.819x10 ⁻⁴ , 2.896x10 ⁻⁴)	0.429
Glycerol (mmol/l)	-9.708x10 ⁻⁵ (-6.139x10 ⁻⁴ , 4.197x10 ⁻⁴)	0.713
Amino acids		
Alanine (mmol/l)	-0.001 (-0.002, -2.708x10 ⁻⁵)	0.045
Glutamine (mmol/l)	3.303x10 ⁻⁴ (-8.107x10 ⁻⁴ , 0.001)	0.571
Glycine (mmol/l)	-2.205x10 ⁻⁴ (-8.150x10 ⁻⁴ , 3.741x10 ⁻⁴)	0.468
Histidine (mmol/l)	3.324x10 ⁻⁶ (-1.746x10 ⁻⁴ , 1.813x10 ⁻⁴)	0.971
Amino acids - branched chain		
Isoleucine (mmol/l)	-2.696x10 ⁻⁴ (-5.843x10 ⁻⁴ , 4.512x10 ⁻⁵)	0.093
Leucine (mmol/l)	-7.271x10 ⁻⁵ (-3.835x10 ⁻⁴ , 2.381x10 ⁻⁴)	0.647
Valine (mmol/l)	1.108x10 ⁻⁴ (-4.927x10 ⁻⁴ , 7.143x10 ⁻⁴)	0.719
Amino acids - aromatic		
Phenylalanine (mmol/l)	5.374x10 ⁻⁵ (-2.019x10 ⁻⁴ , 3.094x10 ⁻⁴)	0.68
Tyrosine (mmol/l)	1.131x10 ⁻⁴ (-7.143x10 ⁻⁵ , 2.977x10 ⁻⁴)	0.23

Table S5: continued

Ketone bodies		
Acetate (mmol/l)	3.081x10 ⁻⁴ (7.541x10 ⁻⁵ , 5.408x10 ⁻⁴)	0.01
Acetoacetate (mmol/l)	-1.508x10 ⁻⁴ (-4.641x10 ⁻⁴ , 1.625x10 ⁻⁴)	0.346
3-hydroxybutyrate (mmol/l)	0.001 (-1.717x10 ⁻⁴ , 0.003)	0.084
Fluid balance		
Creatinine (mmol/l)	3.527x10 ⁻⁵ (-1.362x10 ⁻⁴ , 2.068x10 ⁻⁴)	0.687
Albumin (mmol/l)	-3.305x10 ⁻⁵ (-1.217x10 ⁻⁴ , 5.560x10 ⁻⁵)	0.465
Inflammation		
Glycoprotein acetyls, mainly a1-acid glycoprotein (mmo/l)	-0.003 (-0.007, 6.824x10 ⁻⁴)	0.105

Results are the difference in mean rate change of each trait in original units (see first column) per 4 weeks of gestation between 16 and 36 weeks.

VLDL: very low density lipoprotein; LDL: low density lipoprotein; IDL: intermediate density lipoprotein; HDL: high density lipoprotein

All results are adjusted for the following baseline (recruitment / 16 weeks) characteristics: Age, Parity, Ethnicity, BMI and clinical centre.

Table S6: Correlations between estimates of mean slope from different sensitivity analyses.

	Main Analyses	MLM SD	MLM SD no outliers	Paired-t SD	Paired-t SD no outliers	MLM IQR	MLM IQR no outliers	Paired-t IQR	Paired-t IQR no outliers	Paired-t MAD	Paired-t MAD no outliers
Main Analyses	1										
MLM SD	0.97	1									
MLM SD no outliers	0.97	0.99	1								
Paired-t SD	0.95	0.97	0.97	1							
Paired-t SD no outliers	0.93	0.97	0.97	0.98	1						
MLM IQR	0.97	1.00	0.99	0.97	0.96	1					
MLM IQR no outliers	0.96	0.99	1.00	0.98	0.97	0.99	1				
Paired-t IQR	0.94	0.95	0.96	0.99	0.98	0.97	0.96	1			
Paired-t IQR no outliers	0.93	0.95	0.97	0.98	1.00	0.96	0.97	0.98	1		
Paired-t MAD	0.93	0.95	0.95	0.99	0.97	0.96	0.96	1.00	0.98	1	
Paired-t MAD no outliers	0.90	0.90	0.92	0.93	0.94	0.90	0.92	0.93	0.94	0.93	1

Supplementary Figures

Figure S1: Stages and methods used for NMR platform metabolic measures (adapted from Wurtz et al.[13])

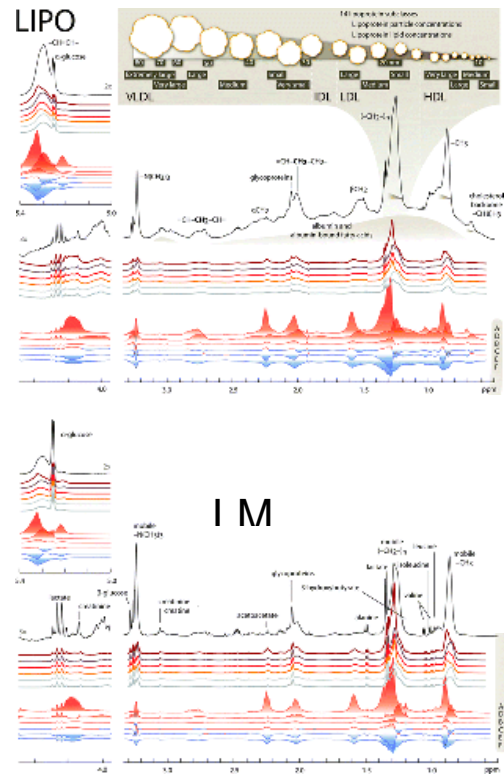
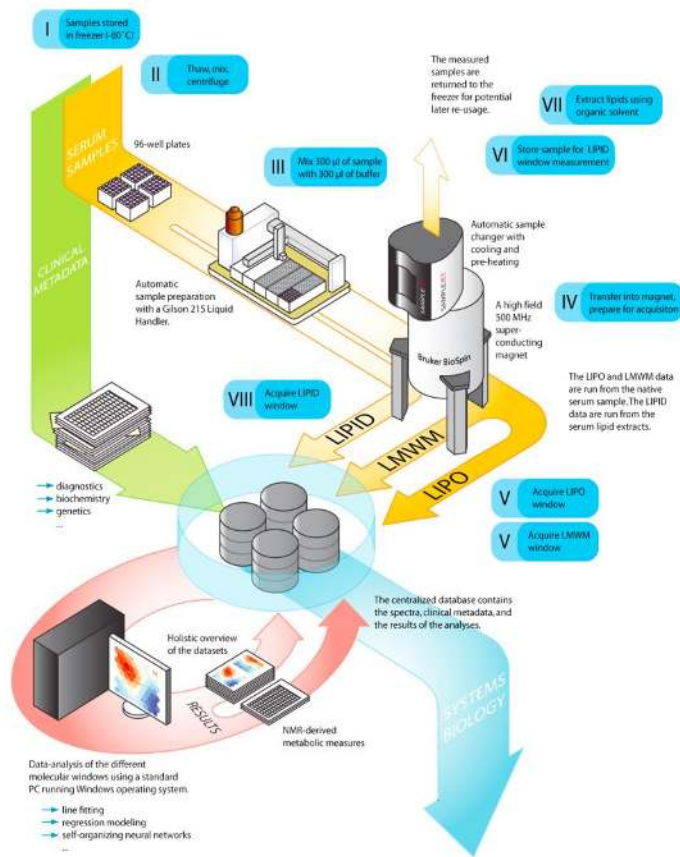


Figure S2: Illustration of the timing of metabolite measurements. This illustrates the wide gaps in time (gestational age) between measurements and therefore the inability to use smoothing/NON-linear models as we do not have any data between the three data collection points. For this reason we were only able to use linear spline models.

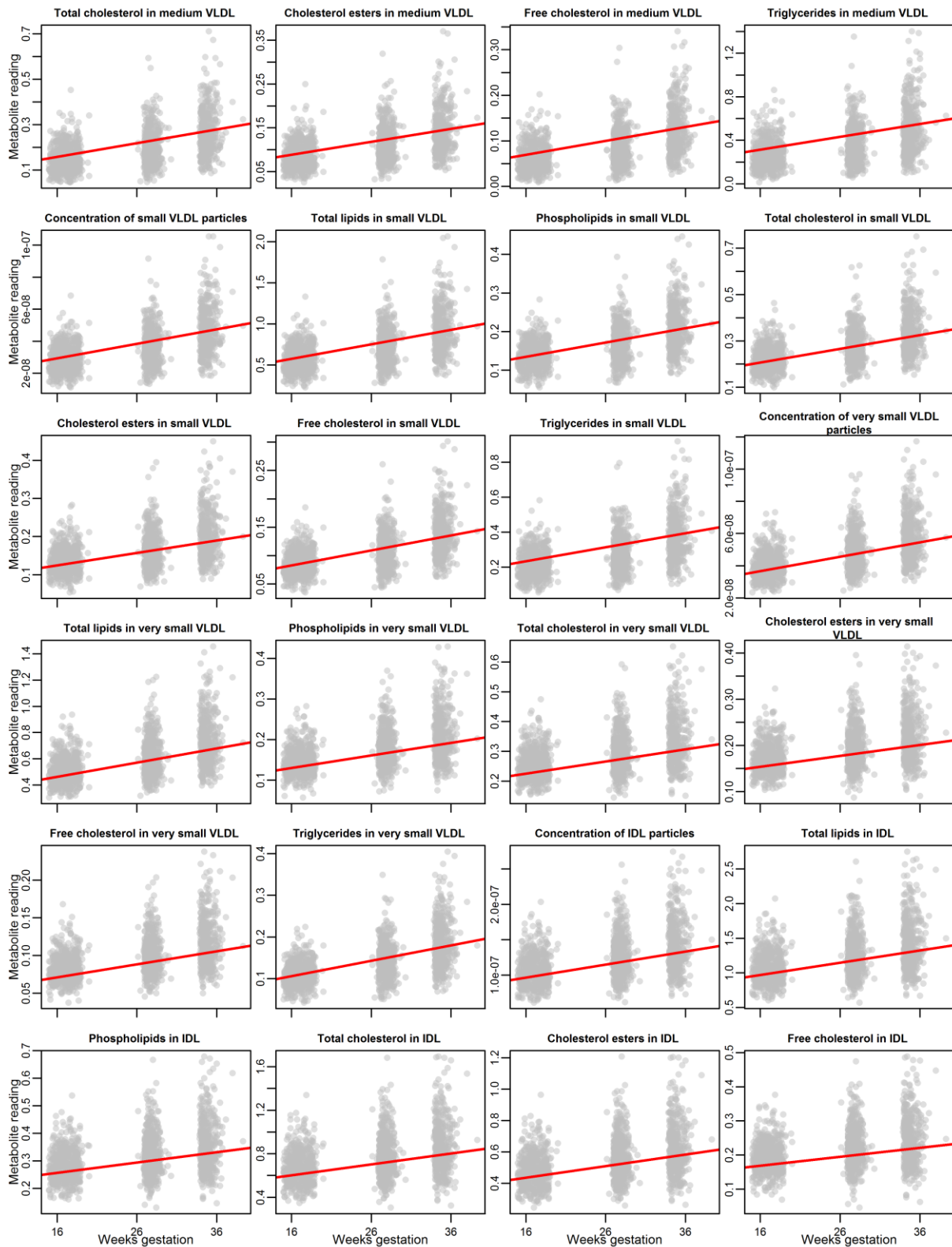
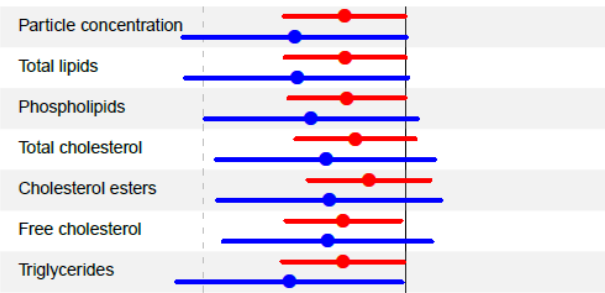
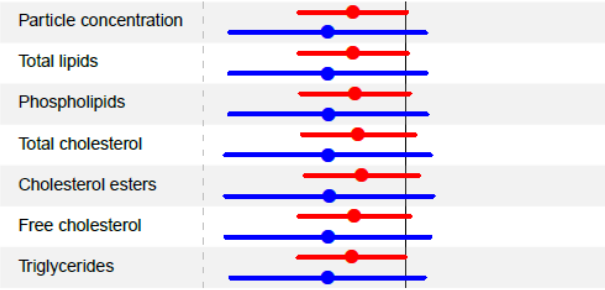


Figure S3: Comparison of the effect of the UPBEAT intervention between 16 and 28 weeks of gestation to that between 28 and 36 weeks of gestation. N = 1158.
Results in red are between 16 and 28 weeks and in blue between 28 and 36 weeks.

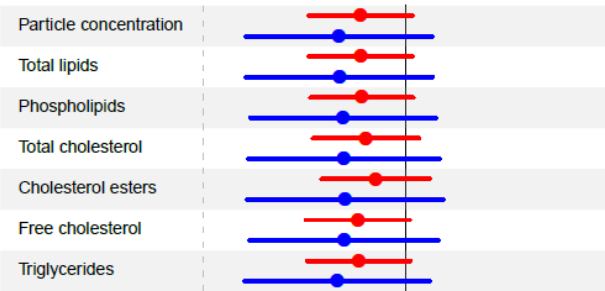
Extremely large VLDL



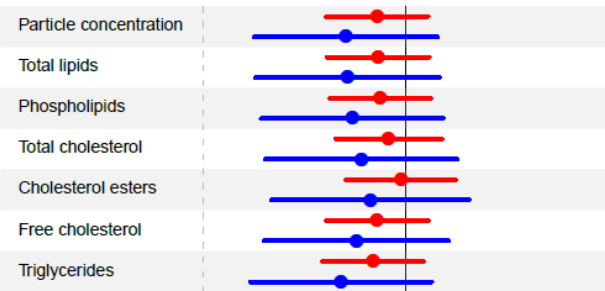
Very large VLDL



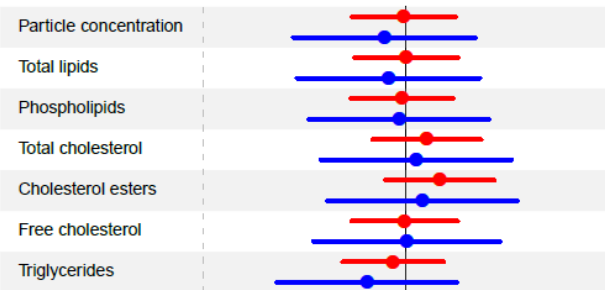
Large VLDL



Medium VLDL

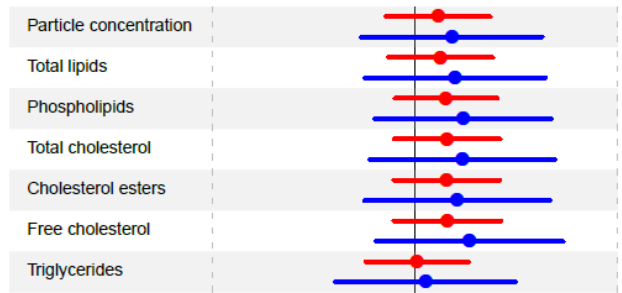


Small VLDL

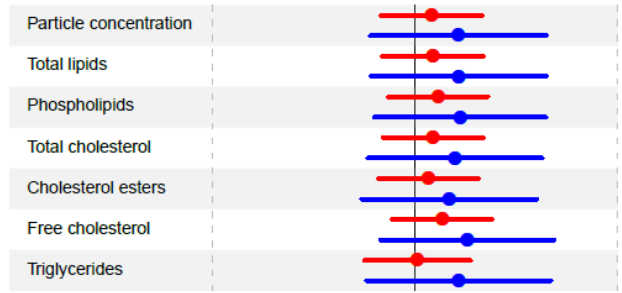


-0.1 0.0 0.1
Difference in mean change in outcome (SD units)

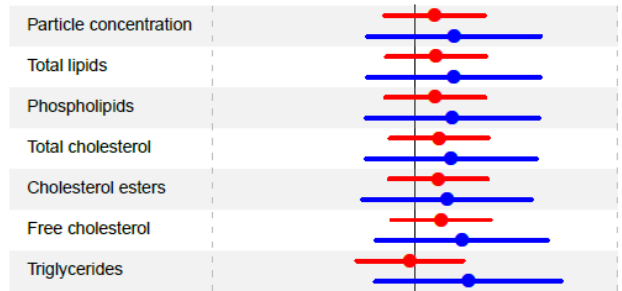
Very small VLDL



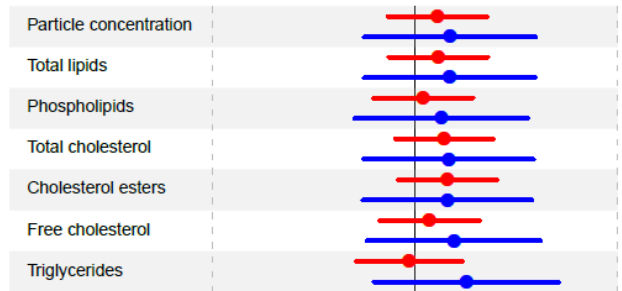
IDL



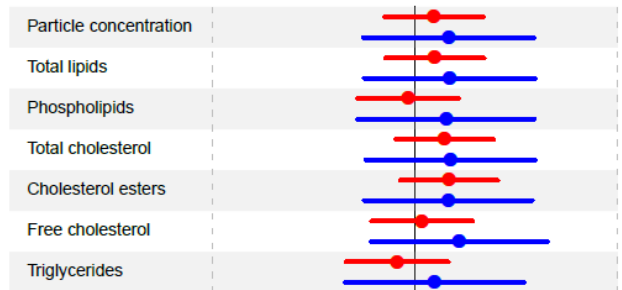
Large LDL



Medium LDL



Small LDL



-0.1 0.0 0.1
Difference in mean change in outcome (SD units)

Figure S3: Continued

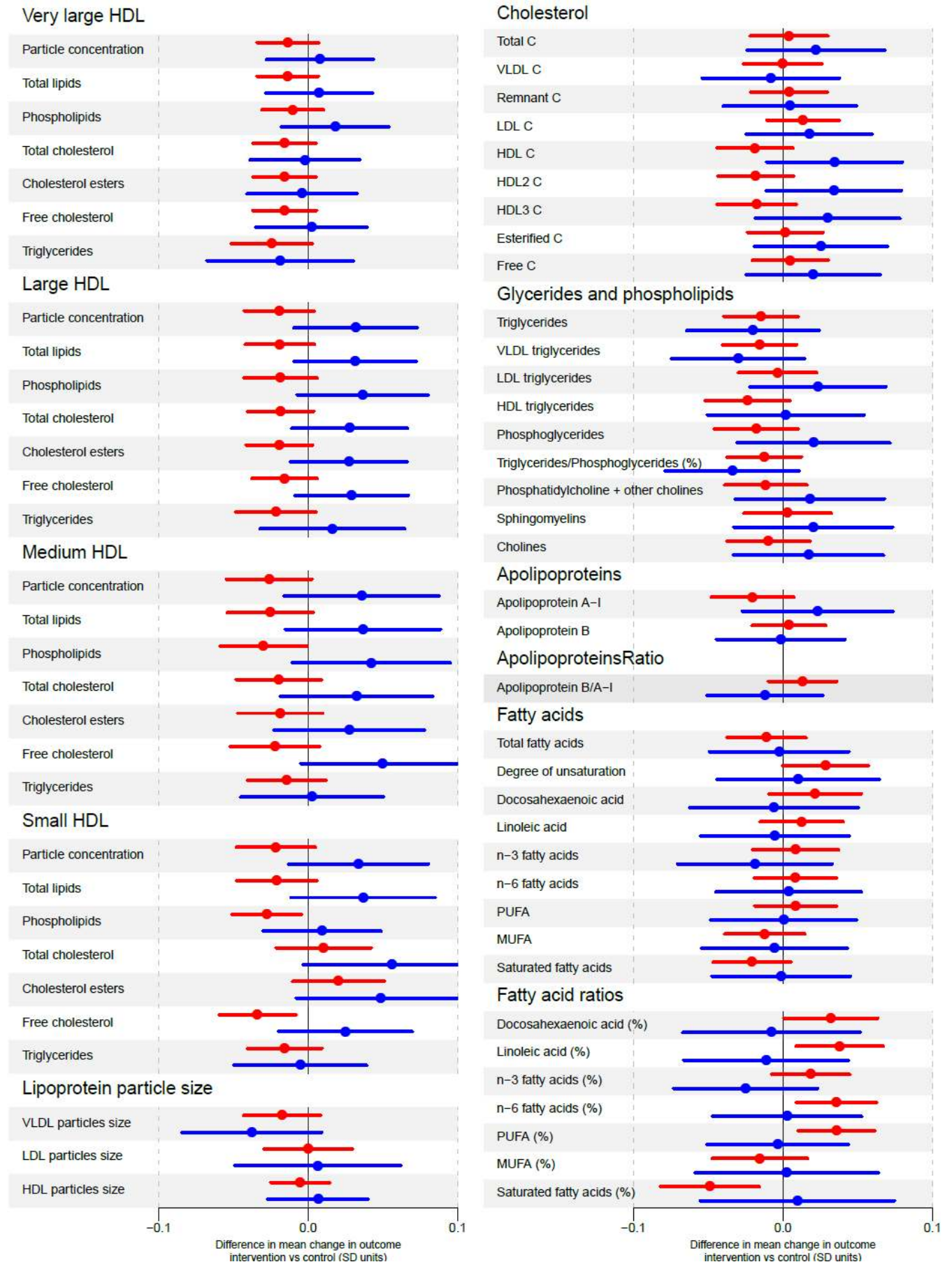
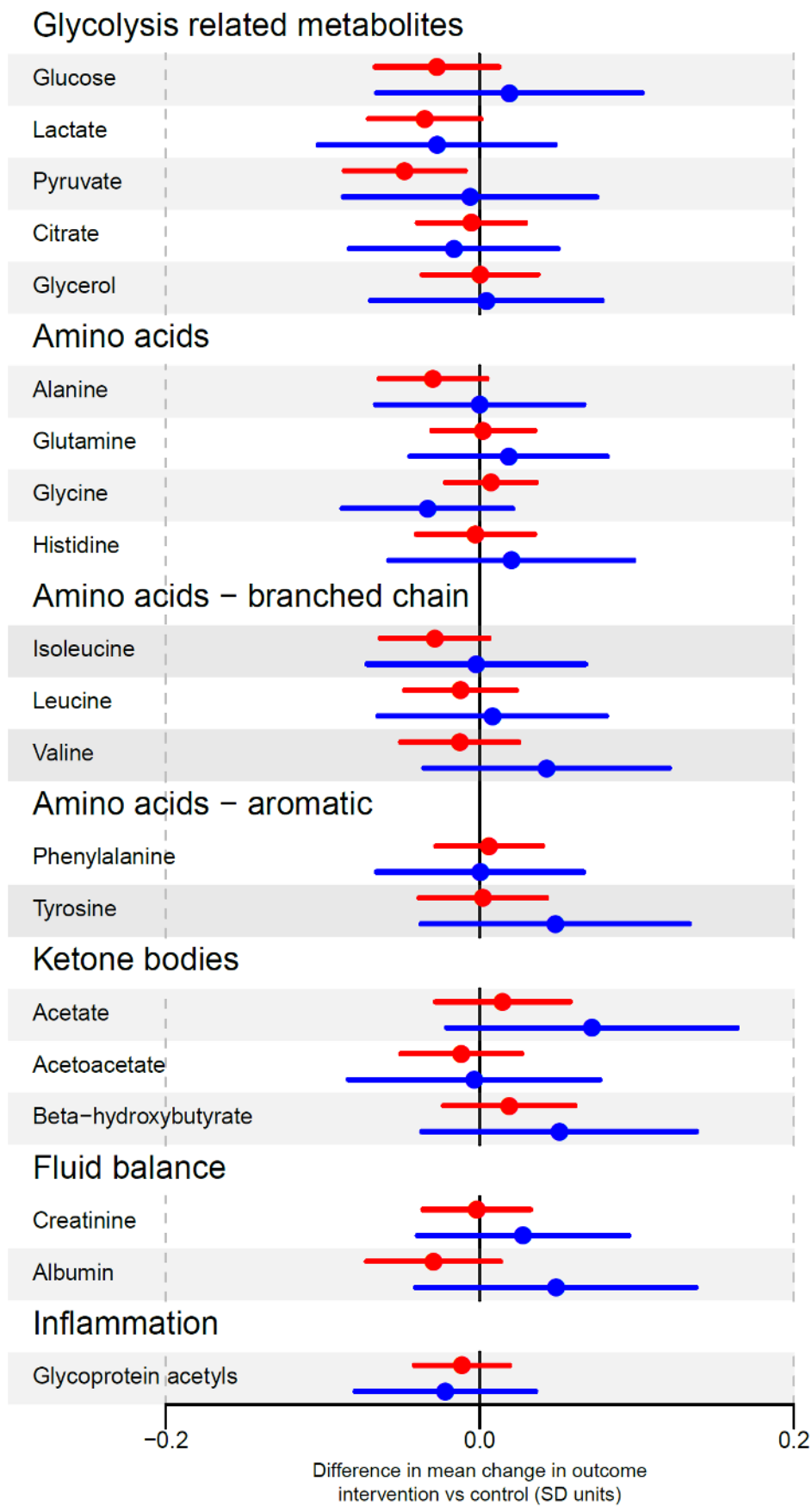


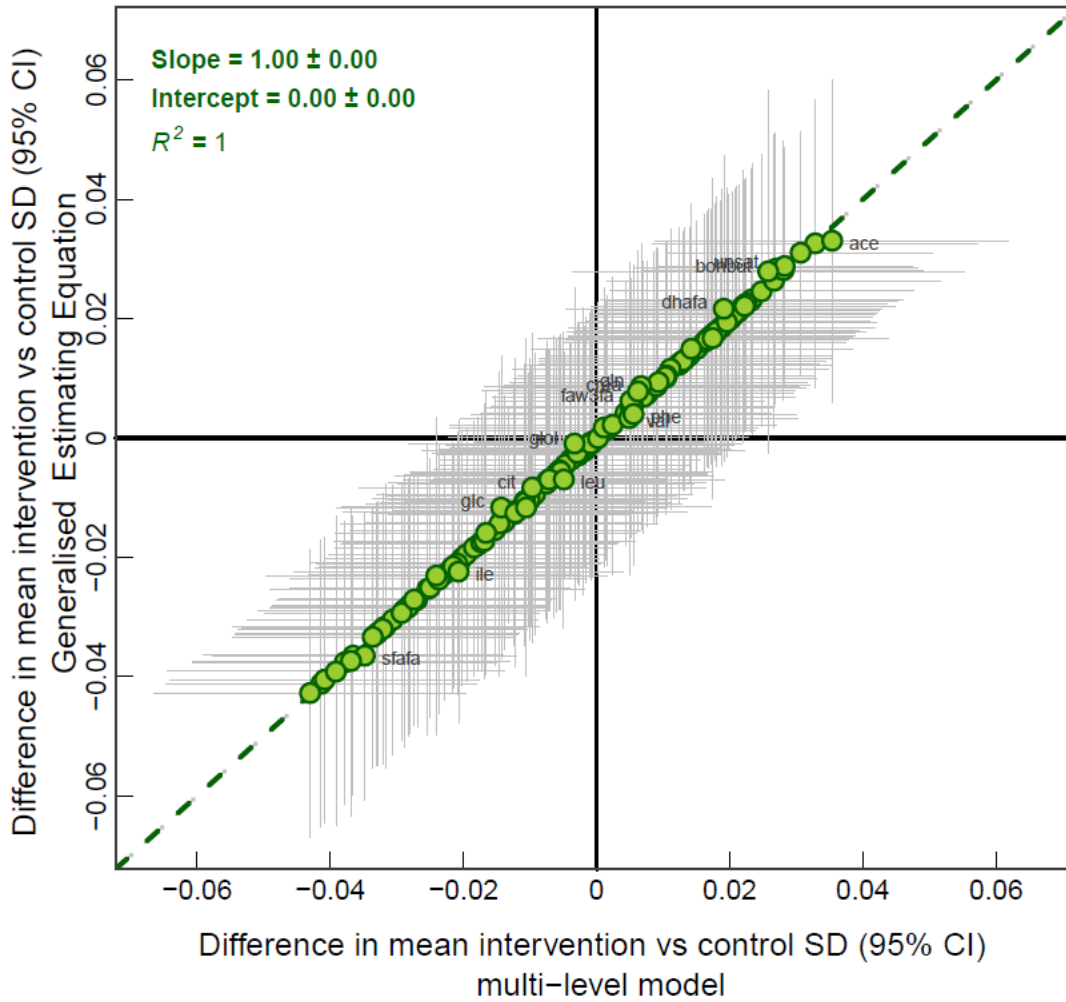
Figure S3: Continued



Footnote to Figure S3

All results are adjusted for the following baseline (recruitment / 16 weeks) characteristics: Age, Parity, Ethnicity, BMI and clinical centre.

Figure S4: Comparison of results from our main multilevel model analyses and sensitivity analyses using generalised estimating equations for the effect of the UPBEAT intervention on change in metabolites



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