Published in final edited form as:

Int J Obes (Lond). 2017 July ; 41(7): 1018–1026. doi:10.1038/ijo.2017.44.

Infant adiposity following a randomised controlled trial of a behavioural intervention in obese pregnancy

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Conflict of interests

All authors have no financial relationships relevant to this article to disclose.

Clinical Trial Registry Name and Registration Number

The UPBEAT trial is registered with Current Controlled Trials, ISRCTN89971375.

Contributors' Statement Page

Dr Nashita Patel, Mr Paul Seed, Dr Dharmintra Pasupathy and Professor Lucilla Poston conceptualized and designed the study, drafted and carried out the initial analyses, critically reviewed the manuscript, and approved the final manuscript as submitted.

Dr Louise Hayes, Ms Julia Levin, Dr Sara White and Ms Angela Flynn carried out the initial dietary and physical activity analyses.

All these authors critically reviewed and approved the final manuscript as submitted.

Dr Annette Briley, Dr Eugene Oteng-Ntim, Professor Stephen Robson, Professor Scott M Nelson, Ms Claire Singh designed the data collection instruments, and coordinated and supervised data collection, critically reviewed the manuscript and approved the final manuscript as submitted.

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Abstract

Objective—Randomised controlled trials are required to address causality in the reported associations between maternal influences and offspring adiposity. The aim of this study was to determine whether an antenatal lifestyle intervention in obese pregnant women associated with improved maternal diet and reduced gestational weight gain leads to a reduction in infant adiposity and sustained improvements in maternal lifestyle behaviours at 6 months postpartum.

Subjects and Methods—We conducted a planned postnatal follow up of a randomised controlled trial (UPBEAT) of a complex behavioural intervention targeting maternal diet (glycemic load and saturated fat intake) and physical activity in 1555 obese pregnant women. The main outcome measure was infant adiposity, assessed by subscapular and triceps skinfold thicknesses. Maternal diet and physical activity, indices of the familial lifestyle environment, were assessed by questionnaire.

Results—698 (45.9%) infants (342 intervention, 356 standard antenatal care) were followed up at mean age 5.92 months. There was no difference in triceps skinfold thickness z-scores between the intervention vs. standard care arms (difference -0.14 SD, 95% CI -0.38 to 0.10, $p=0.246$), but subscapular skinfold thickness z-score was 0.26 SD (-0.49 to -0.02; $p=0.03$) lower in the intervention arm. Maternal dietary glycemic load (-35.34; -48.0 to -22.67; $p<0.001$) and saturated fat intake (-1.93% energy; -2.64 to -1.22; $p<0.001$) were reduced in the intervention arm at 6 months postpartum. Causal mediation analysis suggested that lower infant subscapular skinfold thickness was mediated by changes in antenatal maternal diet and gestational weight gain rather than postnatal diet.

Conclusion—This study provides evidence from follow-up of a randomised controlled trial that a maternal behavioural intervention in obese pregnant women has the potential to reduce infant adiposity and to produce a sustained improvement in maternal diet at 6 months postpartum.

Introduction

The high prevalence of childhood obesity is a major health concern, with 27.3% of children estimated to be overweight or obese in the USA¹. A combination of antenatal and postnatal exposures including environmental factors have been implicated in the development of childhood obesity^{2,3}, which has been shown to track into adulthood¹. Observational studies suggest that manipulation of maternal metabolism through diet and/or physical activity in the antenatal period has the potential to reduce childhood obesity^{2,4} and this has been unequivocally achieved in pregnant obese experimental animals and their offspring⁵. These observations have led to a consensus that obesity is in part ‘programmed’ *in-utero*, in keeping with the ‘developmental programming’ hypothesis⁵. Recent analyses using Mendelian randomisation methods have provided evidence for a causal relationship between maternal pregnancy body mass index (BMI) and glucose with birth weight⁶, but any lasting causal effect on later infant adiposity is unknown. Well-designed randomized controlled trials in pregnant women and their offspring are required to infer causality through minimising selection bias and confounding^{5,7}.

We undertook an RCT, the UK Pregnancies Better Eating and Activity Trial (UPBEAT) of a dietary and physical activity intervention in 1555 obese pregnant women⁸. Women were randomised to standard antenatal care or standard antenatal care with an intense behavioural intervention that focussed on improving insulin sensitivity through reducing dietary glycemic load and saturated fat intake⁸. Although the intervention did not reduce gestational diabetes (GDM) or large for gestational age delivery, the primary outcomes, there were significant improvements in maternal antenatal diet (maternal glycaemic load/day at 28 weeks' gestation, mean difference -21, SD -26 to -16, $p < 0.0001$), a reduction in maternal anthropometric measures of body fat assessed by sum of skinfold thicknesses (-3.2mm, -5.6 to -0.8, $p = 0.008$), lower total gestational weight gain (GWG) (-0.55kg, -1.08 to -0.02, $p = 0.041$), and a modest improvement in physical activity at 28 weeks' gestation (295 min/week, 108 to 485, $p = 0.0015$)⁸, all of which have been implicated in childhood obesity.

To examine the hypothesis that the lifestyle intervention might reduce the influence of maternal obesity on offspring adiposity, our principal aim was to assess whether the UPBEAT intervention was associated with a reduction in measures of childhood adiposity at 6 months of age, a pre-defined hypothesis within the trial protocol⁹. We also examined whether the pregnancy intervention had lasting effects on maternal diet and physical activity, and on known postnatal determinants of infant adiposity, including breastfeeding.

Patients and Methods

Study design and setting

Between July 2010 and May 2015, we conducted a planned follow up at 6 months postpartum of mothers and their offspring who had participated in the UPBEAT RCT in eight inner-city NHS Trust Hospitals in the UK. The study design and protocol⁹ were approved by the NHS Research Ethics Committee (UK Integrated Research Application System; reference 09/H0802/5).

Participants and consent

1555 women were recruited to the UPBEAT trial (16 years of age; pre-pregnancy BMI ≥ 30 kg/m²). Exclusion criteria included pre-existing disease and multiple pregnancy⁹. Following informed consent for themselves and follow up of their infants at 6 months postpartum, the participants were randomised to the intervention or standard antenatal care at 15⁺⁰-18⁺⁶ weeks' gestation. For the purposes of this follow up study, women (but not their children), were excluded if pregnant at 6 months postpartum. If a participant had withdrawn from the trial but was willing to take part ($n=2$), written consent was obtained at the 6 month visit. Infants were excluded if aged ≥ 4 months or ≥ 8 months of age at this visit. Comparison of demographic details at trial entry was made between women who declined to participate and those who took part.

Outcomes

Infant anthropometry—The principal outcome of interest was infant adiposity assessed by measurement of infant skinfold thicknesses (triceps and subscapular, measured in triplicate by trained research staff using infant skinfold callipers). Subsidiary infant

outcomes of infant adiposity included sum of skinfold thickness (calculated by addition), estimated total body fat (calculated by applying validated equations specific for infant sex¹⁰), weight (using a calibrated scale⁹), abdominal and upper mid-arm circumferences. For these measures, when reference World Health Organization population data were available, z-scores were calculated¹¹, including adjustment for infant age, sex and length. These standards are applicable to infant growth regardless of ethnicity, socioeconomic status and mode of feeding¹¹. Z-scores were calculated for infant subscapular, triceps skinfold thickness, weight, BMI and arm circumference but not for sum of skinfold thicknesses. Occipitofrontal circumference, and crown-rump length and crown-heel length obtained with a calibrated infantometer, were also measured.

Duration of breastfeeding, weaning history, measures of appetite, infant sleeping patterns, physical activity, healthcare resource use and childcare⁹ were pre-specified outcomes. These were evaluated using the Infant Feeding and Growth Questionnaire¹², the Child Eating and Behaviour Questionnaire¹³, the BISQ (Brief Infant Sleep Questionnaire)¹⁴, the Infant Behaviour Questionnaire (for child physical activity)¹⁵ and questionnaires ascertaining infant health, medical resource use and early care and education, respectively.

Maternal dietary and physical activity analysis—Maternal diet at 6 months postpartum was assessed using the same semi-quantitative food frequency questionnaire (FFQ) and analysed as previously reported for the mothers during their pregnancy⁸. Data was analysed only in questionnaires which were fully completed for both maternal diet and physical activity. Those with incomplete/missing dietary data were excluded (65.8%). There was no missing physical activity data. The main outcomes of interest were maternal dietary glycaemic load, saturated fat intake and energy intake. Other outcomes included glycaemic index (GI), glycaemic load (GL), protein and fibre intake. Physical Activity was assessed, as it had been in pregnancy, using the International Physical Activity Questionnaire (IPAQ) and summarised as metabolic equivalents (METs) of energy expenditure¹⁶.

Statistical analyses

A complete-case analysis was undertaken for all participating mothers and infants. Treatment effects for continuous outcomes were expressed as differences in means obtained from multivariable linear regression, and binary endpoints as risk ratios with 95% confidence intervals (95%CI) obtained using binomial regression. For both we adjusted for minimisation variables (maternal BMI at trial enrolment, parity and ethnicity) and infant sex and age at follow up. We evaluated the number of intervention contact sessions during pregnancy on measures of infant adiposity.

Although loss to follow-up was similar in both of the trial arms, we assessed the possibility that loss to follow-up resulted in selection bias using three complementary methods (further details in Supplementary Text 1). All sets of analyses were pre-planned sensitivity analyses. First, we used Little's chi-squared covariate-dependent missing (CDM) test to explore evidence of data being missing not at random (MNAR), i.e. examining the possibility that in those who were lost to follow-up the effect of the intervention on outcomes differed from those who did attend the follow-up¹⁷. This was done for both offspring and maternal

outcomes. Second, for the primary offspring outcomes only (subscapular and triceps skinfold thicknesses), we generated several simulation datasets, over a range of scenarios regarding missing data in both arms of the study that were informed by predictors of loss to follow-up (maternal BMI, parity and ethnicity)¹⁸. The scenarios selected aimed to cover a range of plausible situations that could result in bias under the assumption of data being missing at random (MAR). Thirdly, for the primary infant outcomes we used multivariate imputation chained equations to impute missing data for infant adiposity. Data were imputed to create 50 datasets using 10 burn-in iterations for live-born infants using the following in the multivariate equations: maternal trial entry BMI, age, ethnicity, parity, early pregnancy smoking status, randomisation allocation, measures of maternal anthropometry including GWG, maternal diet and physical activity at 27-28⁺⁶, 34⁺⁰-36⁺⁰ weeks' and 6 months postpartum (glycaemic load, glycaemic index, saturated fat, carbohydrate, protein, energy intake), gestation at delivery, infant sex, age at follow up, mode and duration of early feeding, sleep, child health and infant inpatient admissions. The multivariate imputations assume MAR and can also increase statistical power and so allow us to explore whether loss to follow-up might have resulted in type-2 statistical errors. Full details of all of these sensitivity analyses are provided in Supplementary Text 1. Analyses were performed using Stata version 14.0.

Results

Participants

Of the 1555 participants randomised to UPBEAT at 15⁺⁰-18⁺⁶ week's gestation between July 2010 and May 2015 and with a live born infant, 1522 were approached at this time. Of these 1522, 720 (47.3%) infants and 707 (46.5%) mothers took part in this study. Thirteen mothers were excluded as they were pregnant at time of study, and 22 infants were excluded because the follow up appointment was held 4 months or 8 months postpartum (Figure 1). In comparison to those who did not take part, mothers who attended the 6 month visit were on average 1.3 years older, more likely to be Caucasian, nulliparous, to have had GDM in the index pregnancy (28.2% vs. 23.3%; $p=0.041$), and were less likely to be current smokers (Supplementary Table 1a, Supplementary Text 1). There were no differences in maternal early pregnancy BMI and sum of skinfold thicknesses between women who participated in the 6 month follow-up visit compared to those who did not.

Women in the intervention arm demonstrated reduced GWG as previously reported⁸. The infants who attended the 6 month appointment had a longer gestational age at delivery (by 2 days), were 67g heavier, and more likely to have been breastfed at birth than those that did not attend (Supplementary Table 1b).

There was no difference between mean maternal BMI between the intervention and standard care groups at trial entry (36.17 vs. 36.31 kg/m², respectively) or at 6 months postpartum (36.26 vs. 36.45 kg/m², respectively). The incidence of maternal smoking at 15⁺⁰-18⁺⁶ weeks' gestation was higher in the standard antenatal care arm in comparison to the intervention arm (5.6% vs. 2.0%)(Table 1). There were no differences in all other demographic and clinical variables between the two study arms (Table 1).

Infant anthropometry

Three hundred and fifty six infants in the standard antenatal care arm and 342 infants in the intervention arm (mean age 5.82 months) had anthropometric measurements at age 6 months. There was no statistical difference in triceps skinfold thickness in the intervention vs. the standard care arm (difference -0.14 SD, 95% CI -0.38 to 0.10), $p=0.246$), but subscapular skinfold thickness z-score was -0.26 SD (-0.49 to -0.02; $p=0.031$) lower in the intervention arm (Table 2). Infants in the intervention arm had a 5% lower subscapular skinfold thickness (-0.38mm; -0.70 to -0.06; $p=0.021$), compared to infants in the standard antenatal care arm (Table 2). The infant sum of skinfold thickness was 0.63mm lower in the intervention arm, but did not reach statistical significance ($p=0.058$) in comparison to the standard antenatal care arm (Table 2). There were no differences in BMI z-score and abdominal circumference (Table 2) or in other anthropometric measures between the two arms (Supplementary Table 2).

Maternal smoking status at trial entry did not influence the difference in subscapular skinfold thickness between the two arms (Supplementary Table 3). Undertaking sensitivity analyses for deviation from the missing at random assumption, significant differences in infant subscapular skinfold thickness (mm) were found within a range of -0.35 to -0.38mm dependent on the assumption of missingness taken (Supplementary Text 1 and Supplementary Table 4). Similar results to the complete-case analysis were also observed for infant triceps skinfold thickness (Supplementary Table 5).

There was no difference in infant feeding between the two trial arms, nor appetite and satiety responsiveness and infant childcare. Infants were exclusively breastfed, on average for 82.7 (SD 65.3) days and total number of hours spent sleeping were similar between arms (Supplementary Table 7). There was an increase in infant inpatient nights in the intervention arm, attributable to 1 infant requiring long-term hospital admission due a ventricular septal defect repair (Supplementary Table 7). We observed no differences in infant use of medications (Supplementary Table 6) or in cause of hospital inpatient admissions, except for gastrointestinal related disorders, which were lower in the intervention arm (Supplementary Table 8). There was no association between the number of antenatal contact sessions with the health trainer and measures of infant anthropometry (Supplementary Table 9).

No interactions were observed between randomisation allocation and infant sex (Supplementary Table 10), but there was a significant interaction of breast feeding (< 3mths/ 3mths) with the intervention; triceps skin fold thickness was lower in infants of mothers in the intervention arm who breastfed < 3 months vs those in the standard care arm -0.90mm (-1.59 to -0.21); $p=0.011$; Wald interaction test; $p=0.016$) (Figure 3). Similar patterns of differences of effect by breastfeeding for sum of skinfold thicknesses, estimated total body fat and arm circumference did not achieve statistical significance (p -values for interactions all > 0.05) (Supplementary Table 11).

Maternal diet and physical activity

In those women who provided complete dietary data GI, GL, saturated fat and total energy intake were reduced in the mothers in the intervention arm in comparison to standard care,

as well as a significant reduction in total fat and protein intakes (Figure 2 & Table 3). When the under-reporters (calorie intake) were included in sensitivity analyses, there were no differences in the effect size estimates of dietary variables. Furthermore we found no difference in maternal characteristics (including maternal age, BMI and socioeconomic deprivation status) between those under-reporting and those not under-reporting calorie intake. There was no effect of the intervention on maternal physical activity (Table 3).

Causal analysis suggested direct effects of the intervention associated reduction in maternal early GWG (between 15-18⁺⁶ and 27-28⁺⁶ weeks' gestation) ($p=0.015$), late GWG (between 27-28⁺⁶ and 34-36 weeks' gestation) ($p=0.009$), total GWG ($p=0.014$) and maternal dietary saturated fat intake at 27-28⁺⁶ week's gestation ($p=0.016$) in relation to infant subscapular skinfold thickness at age 6 months (Supplementary Figure 1). In contrast, there was no suggested effect of postnatal maternal diet on the observed differences in infant subscapular skinfold measurements (Supplementary Figure 2). As there was no effect of the intervention on maternal physical activity, there was no rationale for exploring a causal mediating impact of maternal physical activity on offspring adiposity.

Discussion

This study has addressed the effect of a pregnancy lifestyle behavioural intervention in obese women on offspring adiposity and maternal diet and physical activity at 6 months postpartum. We have found, to our knowledge for the first time, that a dietary and physical activity intervention in pregnant women with obesity was associated with a reduction in a measure of offspring adiposity, and that changes in maternal diet during pregnancy persisted into the postnatal period. Further analyses suggested that the effect of the intervention on offspring adiposity was independently mediated by the observed reduction in maternal gestational weight gain, dietary fat and energy intake in pregnancy and therefore an expectation that lifestyle interventions have the potential to reduce offspring adiposity. Subscapular skinfold thickness, in comparison to the other anthropometric measurements assessed, is recognised as an accurate index of central adiposity, with a generally lower measurement error than triceps skinfold thickness^{19,20}. In children and adults, subscapular skinfold thickness has been related to impaired glucose metabolism, and in adolescents to increased serum cholesterol concentration^{21, 22}. It is plausible, therefore that the maternal dietary and weight changes resulting from the intervention may influence infant body composition towards a healthier metabolic profile^{22–24}.

Although the magnitude of difference in this measure of adiposity (subscapular skinfold thickness) between intervention and controls arms was modest (5%), it reflected a 0.26 reduction in z-score, which incorporated adjustment for infant sex, age and length to allow comparisons to a reference population. Indications from mother-child cohorts, including the USA Project Viva study, suggest that even modest differences in body composition at age 6 months may be amplified as the child grows older, and that this may be apparent as early as 3 years²⁵. The Bogalusa Heart Study observed that greater offspring childhood subscapular skinfold thickness related to parental type 2 diabetes was associated with a subsequent adverse metabolic profile in early adulthood²². Any persistent influence of the intervention on childhood obesity will only be revealed as the children grow up, but an abundance of

evidence suggests that increased adiposity tracks from infancy, through childhood to adulthood¹.

We are aware of only two relevant similar studies. The first, the Lifestyle in Pregnancy study (LIP)²⁶, assessed body composition in older infants (2.8 years) of obese mothers (n=157) who had been randomised to an antenatal lifestyle intervention with the primary aim of reducing gestational weight gain. No change in infant total fat mass, as assessed by DEXA scan, was observed²⁷. However, it was not reported whether this intervention modified specific components of maternal antenatal diet or body composition, although a reduction in median gestational weight gain was observed. Secondly, a recent RCT of a low glycaemic diet, but in women of heterogeneous BMI, despite a difference in reduction of thigh circumference found no difference in infant body composition at 6 months of age between intervention and control arms^{28, 29}. The difference between these studies and UPBEAT may relate to the greater intensity of the UPBEAT intervention, involving 8 contact sessions with health trainers, at weekly intervals⁸.

There remains a paucity of data regarding the long-term efficacy of lifestyle interventions in obese pregnant women⁵. Our study has shown that dietary advice focussing on reduction of maternal insulin resistance, as a component of a complex intervention, can have a prolonged effect which may have potential to improve long term health as well as familial nutritional environment^{12, 30, 31}. We did not, however, find any differences between groups in maternal BMI or measures of adiposity at 6 months postpartum. A sustained effect of any maternal dietary intervention on maternal dietary intake postpartum has to our knowledge not been reported previously. In contrast, in the LIMIT trial, follow up of 50.5% of participants, reported no difference in maternal dietary composition at 4 months postpartum³², also by self-report. The lower magnitude of intervention effects on maternal dietary variables compared with UPBEAT may explain these differences.

Using the method of causal mediation analysis, we found evidence that the lower dietary saturated fat and energy intake at 28 weeks' gestation induced by the UPBEAT intervention, rather than the change in glycemic load, was associated with the reduction in infant subscapular skinfold thickness at 6 months of age. The reduction in gestational weight gain irrespective of timing and total gestational weight gain were also directly associated with the observed difference. These observations would concur with several reports describing associations between maternal gestational weight gain or diet and offspring adiposity^{4, 33, 34}. Antenatal interventions shown to improve maternal diet and subsequently reduce GWG may therefore be pragmatic and effective measures to reduce early infant adiposity.

The observation that exclusive breastfeeding for more than 3 months may interact with the maternal intervention to reduce offspring triceps skinfold thickness provides some evidence that breast feeding may compound the benefits of the maternal intervention, although caution should be exercised in over-interpretation as the study was not powered to test interactions such as these. The role of other intrauterine exposures remains to be elucidated; whilst we previously reported no differences in fasting lipids, c-peptide and insulin at 28 weeks' gestation between randomisation arms⁸, ongoing biochemical and metabolomic analyses in maternal and cord blood may provide insight into mechanistic pathways.

A limitation of our study was the follow up of only 47.3% of those infants eligible from the original RCT8, but this was similar to the rate of follow up of recently published RCTs in pregnant women^{27, 28, 35}. Due to the stringent inclusion of only complete dietary questionnaires, maternal dietary data was calculated only for 34.2% of the mothers. The dietary data was by self report but compared favourably to a more rigorous method (triple pass 24hr recall) as assessed in the pilot trial³⁶. Strengths of the study include the prospective collection of in-depth data addressing familial and individual determinants of infant adiposity, and of maternal *in-utero* exposures. The richness of data in the UPBEAT study can be considered both a strength and limitation. Whilst providing comprehensive information relevant to developmental origins of early infant obesity, and assessment of mediation effects, limits are imposed on interpretation of secondary analyses in the context of multiple testing.

In conclusion, this study provides evidence of the potential for targeted intervention in obese women to improve health for the mother and her offspring. Pregnancy, as demonstrated in this study, appears to be a pragmatic ‘teachable’ moment for initiating long-term healthier dietary behaviours in the mother and reducing a physiologically relevant measure of adiposity in the offspring.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We are particularly grateful to the women and children who participated in UPBEAT. We would like to acknowledge Jennie Louise PhD (Senior Statistician at the University of Adelaide) for her statistical advice, and all the UPBEAT staff.

Funding source.

This work was supported by the European Union's 7th Framework Programme (FP7/2007–2013), project EarlyNutrition under grant agreement no. 289346 and the National Institute for Health Research (NIHR) (UK) Programme Grants for Applied Research Programme (RP-0407-10452). The views expressed in this paper are those of the authors and not necessarily those of the National Health Service, the NIHR or the Department of Health or any other listed funders. Support was also provided from the Biomedical Research Centre at Guy's and St.Thomas' NHS Foundation Trust and King's College London, the Chief Scientist Office Scotland, Guy's and St Thomas' Charity and Tommy's Charity (Registered charity no. 1060508). The funders had no role in study design, data collection, data analysis, data interpretation or writing of the final report. The corresponding author had access to all the data in the study and had final responsibility for the decision to submit for publication. Professor Godfrey is supported by the National Institute for Health Research through the NIHR Southampton Biomedical Research Centre. Professor Lawlor's contribution to this paper is supported by a grant from the European Research Council (ObesityDevelop; grant number 669545) the MRC Integrative Epidemiology Unit (MC_UU_1201/5) and Professor Lawlor and Professor Poston are National Institute of Health Research Senior Investigators. Mr Seed is funded by Tommy's Charity and by CLAHRC South London (NIHR).

Abbreviations

BISQ	Brief Infant Sleep Questionnaire
BMI	Body Mass Index
CDM	Covariate-dependent Missing

FFQ	Food Frequency Questionnaire
GDM	Gestational Diabetes
GI	Glycaemic Index
GL	Glycaemic Load
GWG	Gestational Weight Gain
IPAQ	International Physical Activity Questionnaire
MET	Metabolic Equivalent of Energy Expenditure
MAR	Missing at Random
MNAR	Missing not at Random
UPBEAT	UK Pregnancies Better Eating and Activity Trial

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Figure 1. Consort diagram of participants enrolled in the UPBEAT trial at 6 months postpartum

Figure 2. Maternal Glycaemic load (a), Saturated fat (b) and Energy intake (c) at 6 months postpartum by randomisation allocation.

Abbreviations: %E- Percentage energy; kcal/day- kilocalorie per day. Arithmetic mean with standard error plotted at each gestation (weeks), showing nutritional consumption per day.

Figure 3. Relationship between duration of exclusive breast feeding and anthropometry measured at 6 months postpartum in 698 infants from the UPBEAT trial.

Effect estimates/ mean differences plotted with 95% confidence intervals.

For triceps skinfold thickness (n=627), sum of skinfold thickness (n=547), total body fat (n=547) and upper mid-arm circumference (n=676). *Significant Wald test for interaction $p < 0.05$

Table 1
Maternal and Infant demographics by randomisation allocation at 6 month postpartum visit.

			Intervention (n=342)	Control (n= 356)
			Mean (SD)/N(%)	Mean (SD)/N(%)
Maternal demographics				
Pre-pregnancy				
Maternal age (years)		N=342	31.30 (5.04)	N=356 31.00 (5.58)
Maternal ethnicity	Asian	N=342	14 (4.1)	N=356 11 (3.1)
	Black		62 (18.1)	72 (20.2)
	Other		19 (5.6)	22 (6.2)
	White		247 (72.2)	251 (70.5)
Multiparous		N=342	169 (49.4)	N=356 174 (48.9)
Index of multiple deprivation quintiles *	1 (least deprived)	N=341	15 (4.4)	N=355 19 (5.4)
	2		29 (8.5)	19 (5.4)
	3		35 (10.3)	38 (10.7)
	4		119 (34.9)	136 (38.3)
	5 (most deprived)		143 (41.9)	143 (40.3)
Family history	GDM	N=333	10 (3.0)	N=344 11 (3.2)
	PET	N=333	40 (12.0)	N=344 33 (9.6)
	T2DM	N=341	86 (25.2)	N=356 70 (19.7)
15-18 weeks' gestation				
Current smoker [^]		N=342	7 (2.0)	N=356 20 (5.6)
Maternal anthropometry	Maternal BMI (kg/m ²)	N=342	36.17 (4.98)	N=356 36.31 (4.69)
	Systolic blood pressure (mmHg)	N=340	117.90 (11.15)	N=352 119.32 (11.00)
	Sum of skin folds (cm) [‡]	N=337	124.34 (28.46)	N=354 122.18 (25.06)
Maternal Antenatal and postpartum history				
Gestational diabetes ^{**}		N=336	97 (28.9)	N=346 93 (26.9)
Pre-eclampsia [∞]		N=340	11 (3.2)	N=353 11 (3.1)
Gestational weight gain between 15-18 weeks' gestation to 34-36 weeks' gestation		N=320	5.85 (4.75)	N=332 6.62 (4.56)
Total gestational weight gain from pre-pregnancy weight [¶]		N=320	6.92 (4.65)	N=332 7.83 (4.41)
Maternal 6 month postpartum BMI (kg/m ²)		N=345	36.26 (5.14)	N=355 36.45 (5.41)
Change in maternal weight from 15-18 weeks to 6 months postpartum (kg)		N=344	-0.37 (7.41)	N=355 0.36 (6.71)
Infant demographics				
Infant age at 6 months follow up (months)		N=342	5.80 (0.65)	N=356 5.85 (0.72)
Gestation at birth (weeks)		N=342	39.73 (1.54)	N=356 39.55 (2.29)

		Intervention (n=342)		Control (n= 356)	
		Mean (SD)/N(%)		Mean (SD)/N(%)	
Birthweight (gm)		N=342	3479.23 (529.40)	N=356	3436.55 (604.09)
Large for Gestational Age >90 th (customised) [‡]		N=342	30 (8.8)	N=356	27 (7.6)
Neonatal feeding history at 72 hrs	Artificial feeding	N=341	63 (18.5)	N=354	78 (22.0)
	Breast feeding	N=341	213 (62.5)	N=354	216 (61.0)
	Partially breastfeeding	N=341	65 (19.1)	N=354	132 (37.1)

[^] Maternal current smoking at 15-18 weeks' gestation (pre-intervention) was significantly different between intervention and control groups (p=0.02).

^{*} IMD quintiles are calculated for the region of residence, by fifths of the population. UK wide-scores were developed by reconciling Scottish data to English norms.

^{**} Gestational diabetes diagnosis by International Association of Diabetes in Pregnancy Study Group criteria at 27⁺⁰ to 28⁺⁶ weeks' gestation.

[‡] Calculated by the addition of biceps, triceps, suprailiac and subscapular skinfold measurements each measured in triplicate.

[∞] Pre-eclampsia defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or both, on at least two occasions 4 hours apart, with proteinuria ≥300 mg/24 hours.

[¶] Gestational weight gain calculated using estimated weight before pregnancy according to the Institute of Medicine Weight Management in Pregnancy Guidelines.

[‡] Customised birthweight centile calculated adjusting for maternal height and weight, ethnic origin, parity and sex of the infant.

Table 2
Infant anthropometry by randomisation allocation at 6 months postpartum visit

	Intervention		Control		Mean Diff/ Risk Ratio* (95% CI)	p-value
	Mean (SD)		Mean (SD)			
Subscapular skinfold thickness z-scores**	N=267	0.08 (1.37)	N=280	0.36 (1.37)	-0.26 (-0.49 to -0.02)	0.031
Subscapular skinfold thickness (mm)	N=267	7.55 (1.86)	N=281	7.95 (2.03)	-0.38 (-0.70 to -0.06)	0.021
Triceps skinfold thickness z-scores**	N=296	0.10 (1.56)	N=298	0.24 (1.43)	-0.14 (-0.38 to 0.10)	0.246
Triceps skinfold thickness (mm)	N=307	9.69 (2.76)	N=320	9.87 (2.69)	-0.22 (-0.64 to 0.20)	0.305
Sum of skinfolds (mm)	N=267	17.08 (3.93)	N=280	17.71 (3.97)	-0.63 (-1.30 to 0.04)	0.058
BMI for age z-scores**	N=317	-0.07 (1.86)	N=320	0.04 (1.78)	-0.12 (-0.40 to 0.16)	0.393
Abdominal circumference (cm)	N=329	43.74 (4.73)	N=347	43.72 (6.27)	0.07 (-0.78 to 0.92)	0.872

* Treatment effect adjusted for minimisation variables of randomisation (maternal BMI, ethnicity and parity), infant age at 6 month follow up and infant sex.

** Z-scores calculated using WHO Anthro; version 3.2.2.

Table 3
Maternal dietary and physical activity data by randomisation allocation at 6 months postpartum

		Intervention		Standard care	Treatment effect*	P-value
		Mean (SD)/ N (%)		Mean (SD)/ N (%)	Mean Difference (95% CI)	
Maternal diet**						
Glycaemic Load per day	N=116	98.94 (32.80)	N=126	134.69 (62.68)	-35.34 (-48.00 to -22.67)	<0.001
Saturated fat (%E)	N=116	11.89 (2.61)	N=126	13.75 (2.85)	-1.93 (-2.64 to -1.22)	<0.001
Total energy (kcal/day)	N=116	1473.84 (596.60)	N=126	1831.21 (727.65)	-354.52 (-505.95 to -203.10)	<0.001
Glycaemic Index (0-100)	N=116	53.06 (4.06)	N=126	57.04 (3.74)	-3.94 (-4.93 to -2.94)	<0.001
Carbohydrate (%E)	N=116	47.69 (6.71)	N=126	48.03 (6.22)	-0.18 (-1.84 to 1.49)	0.835
Total fat (%E)	N=116	29.70 (4.94)	N=126	32.26 (4.75)	-2.65 (-3.91 to -1.38)	<0.001
Protein (%E)	N=116	22.57 (4.42)	N=126	19.82 (3.94)	2.70 (1.63 to 3.77)	<0.001
Fibre (g/day)	N=116	12.12 (4.36)	N=126	12.27 (6.81)	-0.12 (-1.57 to 1.33)	0.873
Maternal physical activity^						
		Median (IQR)		Median (IQR)	Median regression (95% CI)	
MET (min/week) [†]	N=349	2190 (1053, 4158)	N=358	2012 (990, 4088)	93.95 (-264.81 to 452.72)	0.607
MVPA (min/week)	N=349	120 (0, 360)	N=358	120 (0, 360)	10.43 (-39.31 to 60.18)	0.681
Walking (min/week)	N=349	420 (180, 840)	N=358	420 (180, 630)	0.00 (-68.88 to 68.88)	1.00

Abbreviations: CI- Confidence Intervals; %E- %Energy; g/day- grams per day; kcal/day- kilocalories per day; MET- Metabolic equivalent of task; MVPA- Moderate and Vigorous physical activity.

* Treatment effect adjusted for maternal trial entry BMI, parity and ethnicity.

** Maternal diet- Women with a reported energy 4.5 MJ/day or 20MJ/day at 15⁺⁰-18⁺⁶ weeks' gestation were excluded from the analyses of diet. Dietary intervention estimates were calculated using multiple regression and adjusted for maternal pre-pregnancy current smoking status.

^ Physical activity estimates were calculated using bootstrapped (1000 replications), median regression adjusting for maternal pre-pregnancy current smoking status.

[†] MET is defined as the energy expenditure ratio of activity to rest; 1 MET is approximately equal to an individual's resting energy expenditure.