**Title: Modifiable early life exposures associated with adiposity and obesity in 3-year old children born to mothers with obesity.**

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**Abbreviations**:

BIA: bio-electrical impedance analysis

BMI: body mass index

CEBQ: Childhood Eating Behaviour Questionnaire

GWG: Gestational weight gain

IOTF: International Obesity Task Force

NAM: National Academy of Medicine

RR: Relative risk

SD: Standard deviation

SWS: Southampton Women’s Survey

UPBEAT: UK Pregnancy Better Eating and Activity Trial

WH: weight-for-height

WHO: World Health Organisation

**Abstract:**

**Background**: Children born to mothers with obesity are at increased risk of obesity. Influences underlying this predisposition include in-utero exposures, genetic predisposition and a shared family environment. Effective intervention strategies are needed to prevent obesity in these high-risk children; this requires evaluation of modifiable pregnancy and early-life risk factors.

**Objectives**: To assess the individual and cumulative contributions of maternal and early-life modifiable exposures on childhood adiposity and obesity outcomes in 3-year-old children born to women with obesity.

**Methods**: We used adjusted regression to assess the individual and cumulative contributions of six exposures (early pregnancy BMI, excessive gestational weight gain, mode of infant feeding and three measures of childhood eating habits (food responsiveness, slowness in eating and a processed/snacking dietary pattern score)) on body composition in 495 three-year-old children. Outcomes included BMI z-score, arm circumference and overweight/obesity (BMI≥25.0kg/m2).

**Results**: While the UPBEAT intervention did not influence adiposity outcomes in 3-year-old children, the six modifiable exposures combined incrementally to increase childhood adiposity and obesity. For each additional exposure, children had a higher BMI z-score (β=0.35SD (95% confidence interval: 0.23, 0.47)), arm circumference (β=0.59cm (0.40, 0.79)) and risk of overweight/obesity (relative risk 1.49 (1.26, 1.77)). Compared to no exposures, children with four or more exposures had a higher BMI z-score (1.11SD (0.65, 1.58)), arm circumference (2.15cm (1.41, 2.89)) and risk of overweight/obesity (3.01 (1.67, 5.41)) (all p<0.001).

**Conclusion**: Our findings suggest that complex interventions targeting preconception, pregnancy, perinatal and early childhood exposures offer a potential strategy for prevention of pre-school obesity.

**Introduction**:

In parallel with the global obesity epidemic, childhood obesity is increasing worldwide 1. Between 2000 and 2013 the number of children with overweight and obesity rose from 32 to 42 million 2, with global prevalence expected to reach 70 million by 2025 3. The immediate effects of childhood obesity include health complications, such as behavioural disorders, fatty liver disease and asthma 4,5. Childhood or early-life obesity is known to track across the lifecourse 6 increasing the risk of cardiovascular disease 7 and type 2 diabetes 8 in the longer term. Prevention of childhood obesity is a worldwide public health priority 3. In the UK a quarter of children enter primary school with overweight or obesity 9, the highest prevalence being amongst ethnic minorities and those living in disadvantaged areas 10.

Environmental and lifestyle factors are widely implicated in the rising prevalence of childhood obesity, including interactions with hereditary predisposition. A substantial body of evidence suggests a key role for the environment in the earliest stages of life. Experimental animal studies 11, observational cohorts 12 and some randomised controlled trials 13 suggest that adverse *in-utero* exposures, including maternal obesity 14 or excessive gestational weight gain (GWG) 15, may contribute to offspring obesity, which can persist into later life 16. Nutritional exposures and behaviours in infancy and early childhood are also increasingly recognised to be influential 17. These include, short or no breastfeeding duration 18,19, and the development of eating habits and behaviours, such as responsiveness to food 20, high intake of energy dense foods and a higher rate of food consumption 21. Longitudinal analyses suggest that once established, these eating habits and behaviours persist into adulthood 22. Therefore, effective strategies implemented during these windows of vulnerability are needed to stem the rising trend of childhood obesity.

Previous studies addressing the early-life determinants of childhood obesity have generally focused on children born to women of heterogeneous BMI23,24,17 in cohorts which frequently have a small proportion of women with clinical obesity (BMI≥30kg/m2) yet children of women with obesity are those at greatest risk. In accord with the WHO ECHO report 3 recommending that effective public health strategies to prevent childhood obesity be tailored to high-risk women and their families, we have attempted to identify modifiable risk factors in a cohort confined to children born to women with obesity. Maternal BMI was distributed across the WHO categories (I, II and III) and the women were ethnically diverse and of a predominantly social deprived backgrounds. In a follow-up study of the UK Pregnancies Better Eating and Activity Trial (UPBEAT) 25 we examined the association between six modifiable early-life exposures and their cumulative contribution on nine measures of offspring adiposity and obesity outcomes at 3 years of age. These exposures comprised early pregnancy BMI (WHO obesity categories I, II and III), GWG, mode of infant feeding, and childhood eating habits (food responsiveness, slowness in eating and a processed/snacking dietary pattern score) at 3-years of age.

**Methods**:

*Setting*

UPBEAT, a multi-centre randomised controlled trial, investigated the effect of an intense 8-week diet and physical activity intervention in 1555 pregnant women with obesity (BMI≥30kg/m2) 25. Participants were randomised to the intervention or to standard antenatal care and were from UK inner-city settings of ethnic diversity and from predominantly socioeconomically deprived backgrounds. Details of the intervention inclusion and exclusion criteria have been published previously 26. Research Ethics Committee approval was obtained in all participating centres, UK Integrated Research Application System; reference 09/H0802/5 (South East London Research Ethics Committee). All participants provided written informed consent. The intervention had no effect on the primary outcomes, the incidence of maternal gestational diabetes and large-for-gestational-age infants. However, improvements were observed in several secondary maternal outcomes, including a reduction in total GWG 25.

*3-year post-delivery follow-up*

Between August 2014 and October 2017 participants in the UPBEAT study were invited to attend a 3-year post-delivery visit with their children. Of the 1555 women originally recruited, 514 mother-children dyads took part in the 3-year visit (Figure 1). The study design and protocol were approved by the NHS Research Ethics Committee (UK Integrated Research Application System; reference 13/LO/1108). The children were included in this analysis if they had 1) attended the follow-up visit at 3-years of age and 2) had body composition variables recorded during the 3-year visit. Children were excluded if they were suffering from severe illness (n=4) or if born before 34 weeks’ gestation (n=5).

*Exposures variables*

For the purpose of this study we addressed relationships between maternal and early life (nutritional) exposures and measures of childhood adiposity and obesity. Maternal and infant exposures were selected based on previous literature. Maternal exposures were defined as: 1) early pregnancy BMI (30.0–34.9kg/m2 vs ≥35.0kg/m2; WHO classification, I vs II and III, 27) measured at trial baseline (15+0-18+6 weeks’ gestation). Height and weight were used to calculate BMI (kg/m2); height was measured to the nearest 0.1cm with a portable stadiometer (Harpenden; CMS Weighing Equipment Ltd.). Weight was measured to the nearest 0.1kg with calibrated electronic scales (Seca), after removal of shoes and heavy clothing or jewellery; 2) GWG categorised using the National Academy of Medicine (NAM) guidelines 28 (inadequate: <5kg vs adequate: 5-9kg vs excessive >9kg). GWG was calculated using estimated weight before pregnancy by the difference in the mother’s weight measured at baseline minus 1.25kg and weight recorded at 34+0-36+6 weeks gestation, and 3) mode of infant feeding recorded on hospital discharge as exclusively breastfeeding, exclusively formula feeding or partial breastfeeding (defined as any breast feeding). The nutritional exposures were recorded at 3-years of age and included 1) a ‘processed/snacking’ dietary pattern score, 2) child’s food responsiveness and 3) slowness in eating. The data collection and methodology of these dietary variables has been published previously 29. In brief, dietary patterns were derived using factor analysis of a culturally appropriate 85-item food frequency questionnaire. Eating behaviours were assessed using the validated Childhood Eating Behaviour Questionnaire (CEBQ) 30, consisting of 35 items, divided into 8 eating behaviours. Slowness in eating and food responsiveness, were selected for analysis; as being most amenable to intervention 31, Furthermore, we reported strong associations between these two eating behaviours and adiposity and obesity in the 3-year old UPBEAT children 29.

**Child Outcomes**

*Body composition and measures of obesity*

Body composition was assessed by sum of skinfold thicknesses using children’s Holtain skinfold callipers (calculated by addition of triceps, biceps, suprailiac, subscapular and abdominal skinfold thicknesses), mid-upper arm and waist circumferences and body fat percentage assessed by ImpediMed Imp SFB7 bioelectrical impedance analysis (BIA). Weight to the nearest 0.1kg (using calibrated scales) and height (using the Leicester height measurer) to the nearest 0.1cm were used to derive the WHO z-scores 32 and to define childhood overweight by International Obesity Task Force (IOTF) sex-specific centiles (boys overweight = 90.5th centile and girls overweight = 89.3th centile) 33.

*Statistical analysis*

We have previously reported that the UPBEAT intervention did not affect any measure of adiposity/obesity in the 3-year old children 34, therefore, the data was treated as a cohort. Demographic results were expressed as mean ± standard deviation (SD), median and interquartile range or percent and number as appropriate. Children’s sum of skinfolds was positively skewed and log-transformed for analysis. Depending on the outcome of interest, adjusted linear or logistic regression was used. Poisson regression with robust variance were used to estimate the relative risk of child overweight. All outcomes were adjusted for maternal age, parity, ethnicity, smoking status at baseline, years spent in full time education, randomisation arm and gestational age at delivery. Additional adjustments were made for child age at follow-up (months) and infant sex when indicated. Using regression analyses, the first objective was to assess the relationship between the individual maternal exposures (early pregnancy BMI, excessive GWG and mode of infant feeding on hospital discharge) and measures of childhood adiposity and obesity outcomes. The second objective was to address the incremental impact of the exposure variables on childhood outcomes, using three composite models were created: i) maternal exposures (BMI, GWG and mode of feeding on hospital discharge), ii) child nutritional exposures (processed/snacking dietary pattern score, food responsiveness and slowness in eating) and iii) the combined contribution of all six exposures. To create the composite models, binary variables were derived for each exposure (BMI: 30.0–34.9kg/m2=0, ≥35.0kg/m2=1; inadequate/adequate GWG=0, excessive GWG=1 and exclusively breastfeeding=0, partial breastfeeding or formula feeding=1). As the nutritional exposures are continuous variables, with no published reference guidelines to dichotomise the variables, we categorised a high (=1) association as mean ±1 SD, with the remainder categorised as normal/low (=0); food responsiveness and the dietary pattern scores are positively associated with measures of adiposity, therefore the high categories were defined as mean + 1 SD, as slowness in eating in negatively associated with measures of adiposity the high category was defined as mean – 1 SD. Each child was assigned a score for the three models, the maternal model ranged from 0-3, the nutritional model ranged from 0-2, as categorises 2 and 3 were combined. For the combined model and overall score was calculated ranging from 0 to 6 (0 was the reference group for all models). Using adjusted regression, the association with childhood outcomes were examined on a continuous and categorical scale. All data was analysed using Stata software, version 15.0 (StataCorp, College Station, Texas).

**Results***:*

Five hundred and fourteen (33%) of the 1555 women from UPBEAT agreed to participate and attended the follow-up appointments 3 years after delivery. Of those who attended the follow-up visit 5 children were born <34 weeks gestation, 4 were suffering from major ill health and 10 provided no outcome data for this analysis. The study population therefore comprised of 495 children (Figure 1). The average age of the mothers at trial baseline was 31.2 years, 49% were nulliparous, 68% were White and the median early-pregnancy BMI was 34.7kg/m2 (32.5 – 37.9). The average GWG was 7.5 (4.3) kg and using the NAM guidelines for GWG, 28%, 35% and 37% of women were categorised as having inadequate, adequate and excessive GWG, respectively. 63% of mothers were exclusively breast feeding on hospital discharge. For the children, the average age at follow-up was 42 (3.4) months, the BMI z-score was 0.88 (1.0) and 35% were classified as having overweight/obesity according to the IOTF criteria (Table 1).

Maternal Exposures

*Maternal BMI*

When compared to obesity class I, maternal pre-pregnancy BMI≥35kg/m2 was associated with higher child arm (0.56cm; 0.24 to 0.88, p<0.001) and waist circumferences (0.88cm; 0.13 to 1.64, p=0.02); BMI (0.34; 0.15 to 0.53); weight-for-age (0.33; 0.15 to 0.52) and weight-for-height (0.37; 0.20 to 0.55) z-scores (all p<0.001). The relative risk of child overweight/obesity was 1.36 (1.06 to 1.74, p=0.01) for maternal BMI ≥35kg/m2 (Supplementary Table 1).

*Gestational weight gain*

Excessive GWG (>9kg) was associated with higher child BMI (0.24; 0.002 to 0.47, p=0.04), weight-for-age (0.25; 0.17 to 0.49, p=0.03) and height-for-age z-scores (0.28; 0.49 to 0.53, p=0.01) (Supplementary Table 2).

*Mode of infant feeding*

Compared to exclusive breastfeeding, formula feeding on hospital discharge was associated with higher child logged sum of skinfolds (0.29; 0.003 to 0.57, p=0.04), arm circumference, (0.51cm; 0.06 to 0.96, p=0.02), BMI z-score (0.35; 0.09 to 0.62, p=0.01), weight-for-height z-score (0.31; 0.05 to 0.57, p=0.01) and increased risk of overweight/obesity (RR 1.50; 1.11 to 2.04, p=0.008). Compared to exclusively breastfeeding at hospital discharge there were no associations between partial breastfeeding and any childhood outcome (Supplementary Table 3).

*Combined contribution of maternal exposures*

A score, from zero to three, based on three maternal exposures was generated for each child. 23% of the children had no exposures, 41% had one exposure, 30% had two exposures and 6% had three (Table 2). Child BMI z-score, weight-for-height (WH) z-score, arm circumference and overweight/obesity were included in the combined model analyses as these were most frequently associated with maternal risk factors. On a continuous scale, for each additional maternal exposure, child WH and BMI z-scores increased by 0.25 SD (0.13 to 0.36, p<0.001) and 0.23 SD (0.12 to 0.36, p<0.001), respectively. For overweight/obesity, the relative risk increased by 1.24 (1.07 to 1.44, p=0.004), and arm circumference by 0.35cm (0.16 to 0.55, p<0.001). Compared to children with no exposures, for those with three exposures WH and BMI z-scores increased by 0.78 (0.33 to 1.23) and 0.79 (0.31 to 1.27, p<0.0001), respectively (Table 2). Similarly, the risk of overweight/obesity increased by 1.71 (1.04 to 2.80, p=0.03) and arm circumference by 1.04cm (0.25 to 1.82, p=0.01) (Table 2).

*Combined contribution of childhood dietary exposures analysis*

For the dietary exposures (range 0-3), categorises 2 and 3 were combined. 58% of children had no exposures, 31% had one exposure, 11% had two or more exposures (Table 3). On a continuous scale, for each additional dietary exposure children had an increase in WH and BMI z-scores of 0.28 SD (0.15 to 0.341 p<0.001) and 0.29 SD (0.15 to 0.43, p<0.001), respectively. For overweight/obesity, there was an increase in relative risk of 1.37 (1.18 to 1.60, p<0.001), and for arm circumference an increase of 0.44cm (0.21 to 0.68, p<0.001). Compared to children with no exposures, children with two or more exposures had an increase of 0.56 (0.27 to 0.86) and 0.60 (0.30 to 0.90) for WH and BMI z-scores (both p<0.001), respectively (Table 3). There was a 1.81 (1.32 to 2.50, p<0.001) increase in the risk for overweight/obesity and an increase of 0.90cm (0.38 to 1.43, p=0.001) in arm circumference (Table 3).

*Combined contribution of maternal and nutritional exposures*

For the final model, the maternal and childhood dietary exposures were combined. The total score ranged from 0-5 (no child was assigned all 6 risk factors). The children were subdivided into groups with 0 exposures (15%), 1 exposure (29%) 2-3 exposures (49%) 4-5 exposures (7%), Table 4. Compared to children with no exposures, children with four or more had an increase in WH and BMI z-scores of 1.08 (0.64 to 1.51) and 1.11 (0.65 to 1.58) (both p<0.0001), respectively (Figure 2, Table 4). There was an increase in the relative risk for overweight/obesity of 3.01 (1.67 to 5.41, p<0.0001) and in arm circumference of 2.15cm (1.41 to 2.89, p=0.001) (Figure 3, Table 4).

*Sensitivity analyses*

As the risk factors are associated and may be a result of maternal obesity, we completed an additional analysis to examine the relationship between the offspring outcomes and the combined exposures with maternal BMI as a covariate, rather than an exposure. These results show that the significant incremental increase in childhood adiposity and obesity remained with the 5 risk factors. Furthermore, our decision to exclude infants born <34 weeks gestation may have resulted in collider bias as prematurity may be a mediator between gestational weight gain and childhood obesity. However, inclusion of all infants did not change the final results.

**Discussion**:

This study reports several important findings that inform the established relationship between maternal obesity and childhood obesity risk. First, we have demonstrated strong associations between maternal early-pregnancy BMI, excessive GWG, mode of infant feeding and measures of adiposity and obesity in 3-year old children born to mothers with obesity. These relationships provide the first demonstration that these maternal exposures, previously implicated in children from weight heterogenous mothers 24,35, also apply to children of mothers with obesity and are likely to contribute to their high risk of obesity. Next, we found that eating behaviours and dietary intake in the children combined incrementally to increase obesity risk. We also observed positive, additive associations between each of the maternal and nutritional exposures and childhood adiposity and obesity, suggesting that each of these modifiable factors are potential targets for intervention.

In agreement with a meta-analysis of children aged 1-18 years 12, and our previous study in 6-year old children from the SCOPE cohort 14, we confirmed that maternal early-pregnancy BMI was strongly associated with childhood adiposity and obesity in 3-year olds; 35% of the children studied were overweight or had obesity. Similar relationships have been widely described in animal models of maternal obesity in which maternal metabolic disturbances have been implicated in offspring obesity through persistent developmental changes in the fetus 36. In common with others, we showed excessive maternal GWG to be a risk factor for offspring obesity 37,38. A recent meta-analysis of 37 cohorts has assessed the separate and combined association of maternal BMI and GWG with the risk of overweight/obesity throughout childhood, and in common with this study pre-pregnancy BMI was found to be a greater determinant of childhood overweight/obesity than GWG. This meta-analysis also identified the strongest association with maternal BMI and GWG to be in late childhood (10-18 years). Translating this to the UPBEAT children might suggest that more that the current 35% will be overweight or have obesity in later childhood and adolescence.

Formula feeding on hospital discharge (within 72hrs of delivery) was independently associated with increased rates of obesity and adiposity compared to breastfed children. We have already shown in this cohort that adiposity in 6-month infants was associated with formula feeding 39 and now report that this persists until early childhood. This aligns with previous studies in children of weight heterogenous women, including the CHOP RCT which attributed higher adiposity rates in formula-fed children compared to breast fed children to the higher protein content of formula milk 40. Our data also concord with the recent WHO European Childhood Obesity Surveillance Initiative from 22 European countries which concluded that formula feeding from birth was associated with the highest rates of obesity in older children (6-9 years) born to women of heterogeneous BMI 41. Whilst the benefits of any breastfeeding on prevention of childhood obesity remain equivocal 42,43 our findings support initiation of breastfeeding at birth to reduce obesity in pre-school children born to women with obesity. Importantly, we report for the first time that maternal BMI, GWG and neonatal feeding combine independently to increase the risk of obesity in these children.

Several reports suggest independent relationships between eating behaviours 44,20 or dietary intake 45,46 and childhood body composition. To our knowledge no previous study has assessed the combined impact of these nutritional exposures on childhood outcomes. We recently reported the associations between dietary patterns, eating behaviours and body composition/adiposity in 3 year old children from the same cohort 29. In the present study, analysing the exposures on a continuous scale, we have found positive independent relationships between the high ‘processed/snacking’ dietary pattern, food responsiveness and overweight/obesity. Conversely, we found a negative relationship between slowness in eating and childhood adiposity and obesity. This added information confirms a robust association between these exposures and childhood adiposity and obesity. Whilst eating behaviours have been repeatedly causally associated with obesity, we are aware of one report which infers bi-directionality of effect 44. However, in that study the association was stronger between eating behaviours and obesity compared with the reverse.

Finally, evaluating the combined contribution of all maternal and postnatal exposures on childhood outcomes, compared to children with no exposures, the relative risk of overweight/obesity was over 3-times higher for children with 4 or more exposures. Three previous mother-child cohorts, The Southampton Women’s Survey (SWS) 24, Project Viva 23 and Growing Up in Singapore Towards healthy Outcomes (GUSTO) 35 have similarly reported that maternal variables summate to increase childhood obesity risk. SWS and Project Viva combined GWG, smoking in pregnancy and short breastfeeding duration in the risk factor model, with SWS also including maternal BMI and vitamin D status, and Project Viva adding reduced infant sleep as additional exposures. GUSTO combined maternal and paternal overweight, GWG, raised fasting plasma glucose during pregnancy, short breastfeeding duration, and early introduction of solid foods. Although the exposures in our study differ, altogether these cohorts present strong evidence for a cumulative effect of multiple risk factors on the development of childhood obesity. A limitation of the previous investigations was inclusion of women with a predominantly healthy BMI, recruitment being undertaken prior to the present obesity ‘pandemic’. Given that children of women with obesity are most at risk of developing obesity, this study adds to the literature by demonstrating for the first-time cumulative risk of early-life exposures in this high-risk group. The importance lies in the translational potential for combined interventions from preconception to postpartum to reduce childhood obesity in children born to mothers with a BMI < 30kg/m2.

*Strengths and Limitations*

Strengths of the study include the rich UPBEAT dataset which provided comprehensive information including multiple indicators of childhood body composition and adiposity. The mother-child dyads were ethnically diverse and predominantly from low socioeconomic backgrounds, a population with a high-risk of obesity 47. To our knowledge, the UPBEAT cohort is unique in the size of the cohort of women with pre-pregnancy obesity and with detail of *in-utero*, early postnatal and dietary exposures and multiple health outcomes, with a focus on measures of childhood adiposity, enabling adjustment for recognised confounding factors. Very few previous studies have focused on children of this age, yet pre-school adiposity tracks into adulthood 6. The main limitation is the observational study design, which is subject to residual confounding and potential overestimation of reported effects. The measures of adiposity and obesity, although detailed, have limitations; BMI is an indirect measure of fat mass, and the BIA method has not been validated against dual-energy x-ray absorptiometry, the gold standard for adiposity measurement 48. Attrition of the study population may have resulted in selection bias. However, the UPBEAT population studied at the 3-year visit were a representative sample of the main UPBEAT cohort34. Furthermore, while the findings are generalisable for clinical practice amongst women with obesity, they are not directly generalisable to the general population.

In conclusion, we identified exposures in pregnancy and early childhood that result in a cumulative increase in the risk of obesity in 3-year-old children born to mothers with obesity. Interventions to reduce childhood obesity have to date predominantly focused on a single age group and have shown little benefit 49,50.Our study suggests that prevention of pre-school obesity is likely to be better achieved through complex interventions beginning pre-conceptionally and continuing postpartum These should encompass pre-conceptual care, weight management in pregnancy, breastfeeding support as well as dietary advice for pre-schoolers. We await with interest the results of the HELTI cohort which, uniquely, has adopted this approach 51.

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**Author’ contributions to the manuscript**: KVD, MOK, KMG and LP conceptualised and designed the study, drafted and carried out the initial analyses, critically reviewed the manuscript, and approved the final manuscript as submitted. PTS provided statistical support and advice, critically reviewed the manuscript and approved the final submitted version. ALB and ACF designed the data collection instruments, and coordinated and supervised data collection, critically reviewed the manuscript and approved the final manuscript as submitted. KVD wrote the first draft of the paper and coordinated updates following input from co-authors. All other authors critically reviewed the first and subsequent drafts. All authors approved the final version.

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1555 obese pregnant women randomised

1 excluded after trial enrolment

1522 (98.1%) infants with known birthweight

8 lost to follow up

6 withdrew permission to use data

8 miscarriage

6 fetal death in utero

4 terminations

514 (35.2%) children followed up at 3 years

* 10 partial participation

503 not responded to follow up contact

422 refused follow up

82 did not attend follow-up

1 cot death (2.5 months)

495 children included in the analysis

* 5 children born ≤ 34 weeks gestation
* 4 major health problems
* 10 children excluded for not providing outcome data

Figure 1: Consort diagram of participants enrolled in the UPBEAT trial at 3 years after delivery

|  |  |  |  |
| --- | --- | --- | --- |
| **Table 1: Maternal and offspring demographics of the analysed sample (n=495)** | | | |
| **Maternal demographics** |  | Mean (SD)/ Median (IQR)/N (%) | |
| **Pre-pregnancy** |
| Age (years) |  | | 31.2 (5.3) |
| Ethnicity | *White* | | 337 (68) |
|  | *Black* | | 114 (23) |
|  | *Asian* | | 20 (4) |
|  | *Other* | | 24 (5) |
| Years in full time education |  | | 15.1 (2.8) |
| Maternal BMI (kg/m2) | 34.7 (32.6 to 37.9) | | |
| Obesity class I (30.0-34.9 kg/m2)a |  | | 266 (53.7) |
| Obesity class II (35.0-39.9 kg/m2)a |  | | 143 (28.9) |
| Obesity class III (≥40.0 kg/m2)a |  | | 86 (17) |
| Nulliparous |  | | 244 (49) |
| Index of Multiple Deprivation Quintiles | *1 (least deprived)* | | 28 (6) |
| *2* | | 36 (7) |
| *3* | | 56 (11) |
|  | *4* | | 176 (35) |
|  | *5 (most deprived)* | | 196 (40) |
| **Maternal antenatal and neonatal demographics** | | |  |
| Mother assigned to UPBEAT intervention | | | 241 (49) |
| Gestational diabetes mellitus | | | 120 (26) |
| Gestational weight gain (kg) |  | | 7.5 (4.3) |
| Birthweight (g) |  | | 3499 (497) |
| Large for gestational age >90th centile b | | | 62 (12) |
| Small for gestational age <10th centile b | | | 35 (7) |
| **Child 3-year follow-up demographics** | | |  |
| Age (years) |  | | 3.5 (0.28) |
| Female |  | | 244 (49) |
| Mode of infant feeding at hospital discharge | *Breastfed* | | 312 (63) |
| *Formula fed* | | 96 (19) |
|  | *Mixed fed* | | 86 (18) |
| **World Health Organisation z-scores c** | | | |
| BMI-for-age (n=485) |  | | 0.88 (1.0) |
| Height-for-age (n=490) |  | | 0.38 (1.1) |
| Weight-for-age (n=490) |  | | 0.83 (1.0) |
| Weight-for-height (n=485) |  | | 0.90 (1.0) |
| **International Obesity Task Force BMI categorises d** | | | |
| Underweight | *< 18.5 kg/m2* | | 15 (3) |
| Healthy | *18.5-24.9 kg/m2* | | 292 (62) |
| Overweight | *25.0-29.9 kg/m2* | | 126 (27) |
| Obese | *30.0-34.9 kg/m2* | | 14 (3) |
| Morbidly obese | *≥35.0 kg/m2* | | 26 (5) |
| **Measures of adiposity** | | | |
| Sum of skinfolds (mm) (n=381) |  | | 41.3 (33.9 to 50.0) |
| Percentage body fat (%) (n=382) |  | | 22.4 (6.6) |
| Arm circumference (cm) (n=470) |  | | 17.8 (1.8) |
| Waist circumference (cm) (n=479) |  | | 53.3 (4.2) |
| Abbreviations: BMI: body mass index; cm: centimetre; g: grams; IQR: Interquartile range mm: millimetre; SD (Standard deviation; %: percent. a WHO BMI categories for adults. b Customised birthweight centile calculated by adjusting for maternal height, weight, ethnic origin, parity and infant sex; cZ-scores calculated using WHO Anthro (de Onis, 2006).d IOTF International gender specific cut-off as BMI references. | | | |

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| Table 2: Measures of childhood obesity according to number of maternal exposures | | | | | | | | | |
| Number of exposures | **Number (%)** | **WH Z-score a**  **Coefficient (95% CI)** | **P-value\*** | **BMI z-score a**  **Coefficient (95% CI)** | **P-value\*** | **Overweight/obesity**  **(BMI ≥25kg/m2) b**  **Relative risk (95% CI)** | **P-value\*** | **Arm circumference (cm) Coefficient (95% CI)** | **P-value\*** |
| 0 | 101 (23) | Ref |  | ref |  | ref |  | ref |  |
| 1 | 181 (41) | 0.14 (-0.10 to 0.39) | 0.25 | 0.14 (-0.12 to 0.40) | 0.30 | 1.04 (0.70 to 1.53) | 0.841 | 0.40 (-0.02 to 0.83) | 0.06 |
| 2 | 135 (30) | 0.45 (0.18 to 0.72) | 0.001 | 0.41 (0.13 to 0.69) | 0.004 | 1.49 (1.02 to 2.16) | 0.035 | 0.74 (0.28 to 1.19) | 0.002 |
| 3 | 26 (6) | 0.78 (0.33 to 1.23) | 0.001 | 0.79 (0.31 to 1.27) | 0.001 | 1.71 (1.04 to 2.80) | 0.033 | 1.04 (0.25 to 1.82) | 0.01 |
| Beta |  | 0.25 (0.13 to 0.36) | <0.0001 | 0.23 (0.12 to 0.36) | <0.0001 | 1.24 (1.07 to 1.44) | 0.004 | 0.35 (0.16 to 0.55) | <0.0001 |
| *Abbreviations: BMI: body mass index; CI: confidence intervals; cm: centimetres. a Z-scores calculated using WHO Anthro (de Onis, 2006). b IOTF International gender specific cut-off as BMI references. \* Adjusted for maternal age, parity, ethnicity, smoking status at baseline, years in full time education, randomisation arm, gestational age at delivery, child sex, age at follow up, processed/snacking diet score and weekly physical activity. BMI Z-score and IOTF category were not adjusted for child sex or age at follow-up.* | | | | | | | | | |

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| Table 3: Measures of childhood obesity according to number of dietary exposures | | | | | | | | | |
| Number of exposures | **Number (%)** | **WH Z-score a**  **Coefficient (95% CI)** | **P-value\*** | **BMI z-score a**  **Coefficient (95% CI)** | **P-value\*** | **Overweight/obesity**  **(BMI ≥25kg/m2) b**  **Relative risk (95% CI)** | **P-value\*** | **Arm circumference (cm) Coefficient (95% CI)** | **P-value\*** |
| 0 | 283 (58) | ref |  | ref |  | ref |  | ref |  |
| 1 | 149 (31) | 0.29 (0.09 to 0.50) | 0.004 | 0.27 (0.06 to 0.50) | 0.01 | 1.50 (1.14 to 1.97) | 0.003 | 0.43 (0.06 to 0.80) | 0.021 |
| 2+ | 53 (11) | 0.56 (0.27 to 0.86) | <0.001 | 0.60 (0.30 to 0.90) | <0.001 | 1.81 (1.32 to 2.50) | <0.001 | 0.90 (0.38 to 1.43) | 0.001 |
| Beta |  | 0.28 (0.15 to 0.41) | <0.001 | 0.29 (0.15 to 0.43) | <0.0001 | 1.37 (1.18 to 1.60) | <0.0001 | 0.44 (0.21 to 0.68) | <0.0001 |
| *Abbreviations: BMI: body mass index; CI: confidence intervals; cm: centimetres. a Z-scores calculated using WHO Anthro (de Onis, 2006). b IOTF International gender specific cut-off as BMI references. \* Adjusted for maternal age, parity, ethnicity, smoking status at baseline, years in full time education, randomisation arm, gestational age at delivery, child sex and age at follow up. BMI Z-score and IOTF category were not adjusted for child sex or age at follow-up. .* | | | | | | | | | |

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| Table 4: Measures of childhood obesity according to number of combined exposures | | | | | | | | | |
| Number of exposures | **N(%)** | **WH Z-score a**  **Coefficient (95% CI)** | **P-value\*** | **BMI z-score a**  **Coefficient (95% CI)** | **P-value\*** | **Overweight/**  **obesity (BMI ≥25kg/m2) b**  **RR (95% CI)** | **P-value\*** | **Arm circumference (cm) Coefficient (95% CI)** | **P-value\*** |
| 0 | 65 (15) | ref |  | ref |  | Ref |  | ref |  |
| 1 | 123 (29) | 0.19 (-0.09 to 0.49) | 0.17 | 0.20 (-0.10 to 0.51) | 0.19 | 1.35 (0.75 to 2.77) | 0.307 | 0.54 (0.04 to 1.04) | 0.03 |
| 2-3 | 212 (49) | 0.63 (0.36 to 0.91) | <0.001 | 0.61 (0.32 to 0.90) | <0.0001 | 2.25 (1.32 to 3.84) | 0.003 | 1.00 (0.54 to 1.48) | <0.0001 |
| 4+ | 30 (7) | 1.08 (0.64 to 1.51) | <0.0001 | 1.11 (0.65 to 1.58) | <0.0001 | 3.01 (1.67 to 5.41) | <0.0001 | 2.15 (1.41 to 2.89) | <0.0001 |
| Beta |  | 0.36 (0.24 to 0.47) | <0.0001 | 0.35 (0.23 to 0.47) | <0.0001 | 1.49 (1.26 to 1.77) | <0.0001 | 0.59 (0.40 to 0.79) | <0.0001 |
| *Abbreviations: BMI: body mass index; CI: confidence intervals; cm: centimetres, RR: relative risk. a Z-scores calculated using WHO Anthro (de Onis, 2006). b IOTF International gender specific cut-off as BMI references. \** *Adjusted for maternal age, parity, ethnicity, smoking status at baseline, years in full time education, randomisation arm, gestational age at delivery, child sex and age at follow up. BMI Z-score and IOTF category were not adjusted for* *child sex or age at follow-up.* | | | | | | | | | |





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