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Antenatal dietary and lifestyle advice for women who are overweight or obese and the effect on fetal growth and adiposity: the LIMIT randomised trial

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Abstract

Objective—To report the influence of maternal overweight and obesity on fetal growth and adiposity and effects of an antenatal dietary and lifestyle intervention among these women on measures of fetal growth and adiposity as secondary outcomes of the LIMIT Trial.

Design—Randomised controlled trial.

Setting—Public maternity hospitals in metropolitan Adelaide, South Australia.

Population—Pregnant women with a BMI $\geq 25\text{kg/m}^2$, and singleton gestation between 10⁺⁰–20⁺⁰ weeks.

Methods—Women were randomised to Lifestyle Advice or continued Standard Care and offered two research ultrasound scans at 28 and 36 weeks gestation.

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Disclosure of Interests

The authors have no competing interests to declare. The ICMJE disclosure forms are available as online supporting information.

Author Contributions

Each author fulfils the requirements for authorship. All authors, RMG, LNY, ARD, CAC and JMD have been involved equally in the study concept and design of the trial, supervision of conduct of the trial, the acquisition of data, the analysis and interpretation of data, critical revision of the manuscript for important intellectual content, and provides approval of the final submitted version. RMG and LNY were responsible for conducting the statistical analyses. RMG drafted the manuscript, had full access to all of the study data, and takes responsibility for the integrity of the data, and the accuracy of the data analysis.

Ethics Approvals

Ethics approval was provided by the Women's and Children's Local Health Network Human Research and Ethics Committee at the Women's and Children's Hospital, REC numbers 1839 (main study) and 2051 (ancillary studies including ultrasound) (1st of August 2006 (main study) 11th January 2009 (ancillary studies)), the Central Northern Adelaide Health Service Ethics of Human Research Committee (Lyell McEwin Hospital) REC number 2008033 (15th of April 2008) and the Flinders Clinical Research Ethics Committee (Flinders Medical Centre) REC number 128 (8th of July 2008).

Main Outcome Measures—Ultrasound measures of fetal growth and adiposity.

Results—For each fetal body composition parameter, mean Z-scores were substantially higher when compared with population standards. Fetuses of women receiving Lifestyle Advice demonstrated significantly greater mean mid thigh fat mass, when compared with fetuses of women receiving Standard Care (Adjusted Difference in Means 0.17; 95% Confidence Intervals (CI) 0.02 to 0.32; $p=0.0245$). While subscapular fat mass increased between 28 and 36 weeks gestation in fetuses in both treatment groups, the rate of adipose tissue deposition slowed among fetuses of women receiving Lifestyle Advice, when compared with fetuses of women receiving Standard Care ($p=0.0160$). No other significant differences were observed.

Conclusions—These findings provide the first evidence of changes to fetal growth following an antenatal dietary and lifestyle intervention among women who are overweight or obese.

Keywords

fetal ultrasound; fetal growth; fetal body composition; overweight and obesity; lifestyle intervention

Introduction

Overweight and obesity represents a considerable challenge for pregnancy care, with data indicating approximately 50% of women enter pregnancy with a BMI above 25kg/m².^(ref. 1) The risks during pregnancy and childbirth associated with increasing maternal BMI are well documented, including risk of their infant born large for gestational age or macrosomic.^{2, 3} There have been few reports to date on the effects of maternal overweight and obesity on measures of fetal growth.

Techniques to measure body composition (lean and fat mass) have the potential to provide more useful information than weight and height alone. Studies in the newborn have suggested that infants of overweight and obese women had significantly greater percentage of fat mass and total fat mass, and significantly less fat free mass.⁴ This increase in fat mass may be an important mediator of later health.

As an extension of many studies into neonatal body composition, Bernstein and others developed ultrasound techniques to characterise fetal body composition.^{5, 6} Fetal body composition measures that have been most frequently examined to date include subscapular fat mass (SSFm), abdominal wall fat mass (fetal abdominal fat layer) (AFM), mid thigh total mass (MTM), mid thigh lean mass (MTLM) and mid thigh fat mass (MTFM).⁵⁻⁹

Normal ranges have been published from the prospective study of 218 healthy Italian women by Larciprete and colleagues.¹⁰ However there is little information available regarding the effect of maternal BMI on fetal body composition, with only one recent prospective study describing fetal body composition amongst women of all BMI categories.¹¹ To date, the literature has been largely confined to women diagnosed with gestational and pre-existing diabetes,^{12, 13} although there is some limited data available to suggest that increasing maternal BMI impacts fetal growth from as early as 24 weeks gestation.^{11, 14, 15}

We have previously reported the findings of the LIMIT Randomised Trial which indicated provision of an antenatal dietary and lifestyle intervention to women who are overweight or obese showed an 18% relative risk reduction in the chance their infant would have a birth weight above 4kg.¹⁶ We report, for the first time, ultrasound measures of fetal growth and adiposity on women who participated in the LIMIT Trial. A secondary aim of this study was to assess the interobserver variability of measures of fetal body composition.

Methods

Eligibility

The protocol¹⁷ and findings^{16, 18, 19} of the LIMIT randomised trial have been published previously. We conducted a multi-centre randomised trial, in which women with a singleton pregnancy at 10⁺⁰ and 20⁺⁰ weeks gestation, and BMI ≥ 25 kg/m² were included. Women were enrolled from the three public maternity units across metropolitan Adelaide (Women's and Children's Hospital, Lyell McEwin Hospital, and Flinders Medical Centre). Exclusion criteria included multiple pregnancy, or type 1 or 2 diabetes diagnosed prior to pregnancy. Ethics approval to conduct the trial was provided by each hospital review board, and women provided written informed consent to participate.

Randomisation

At the time of presenting for their initial booking antenatal visit, all women had their height and weight measured, and BMI calculated. Women were randomised to either 'Lifestyle Advice' or 'Standard Care', by telephoning the central randomisation service, which used a computer-generated schedule, with balanced variable blocks. Stratification occurred for parity (0 versus 1/more), BMI at antenatal booking (25–29.9 kg/m² versus ≥ 30 kg/m²), and collaborating centre.

Intervention

Women who were randomised to Lifestyle Advice participated in a comprehensive dietary and lifestyle intervention during their pregnancy that included a combination of dietary, exercise and behavioural strategies, delivered by a research dietician and trained research assistants.¹⁷ The dietary advice was consistent with current Australian standards,²⁰ to maintain a balance of carbohydrates, fat and protein, to reduce intake of foods high in refined carbohydrates and saturated fats, while increasing intake of fibre, and recommended to consume two servings of fruit, five servings of vegetables, and three servings of dairy each day.²⁰ Women were encouraged to increase their physical activity, in particular walking and incidental activity.²¹ Tailoring of the intervention was informed by stage theories of health decision making.²²

Women who were randomised to receive Standard Care continued their pregnancy care according to local hospital guidelines, which did not include the provision of information related to diet, exercise, or gestational weight gain.

Sonography

All women participating in the trial were offered a research ultrasound scan at both 28 (range 26⁺⁰ to 29⁺⁶) and 36 (range 34⁺⁰ to 37⁺⁶) weeks gestation to obtain measures of fetal growth and body composition. An accurate assessment of gestational age and expected date of confinement was obtained using early pregnancy ultrasound and menstrual period dating. All research ultrasounds were performed by five medical practitioners with specialist or subspecialist level training in obstetric ultrasound, with training and supervision by the main study sonographer. Scans were performed in the majority of cases using a Medison Accuvix V20 Ultrasound System (Samsung Medison Co., Ltd.) with a small proportion being undertaken by miscellaneous machines in clinical use at each of the sites where women were attending for their clinical care. Low frequency, high penetration ultrasound probes were used as is appropriate for this population.

All measurements and calculations for biometry were obtained prospectively in real time and sonographers were blinded to treatment allocation.

Outcome measures

Biometry—Standard biometric parameters were obtained utilising standardised procedures and anatomical views, including biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL).²³ Estimated fetal weight (EFW) was calculated using the Hadlock C formula.²⁴

Fetal body composition – establishment of technique—In the initial phase of the study, two research sonographers established a technique for measuring fetal body composition based on the methods described by Gardeil, Larciprete and Bernstein (Bernstein et al 1997; Gardeil et al 1999; Larciprete et al 2003), which took place over a 3 month period. After establishment of appropriate technique, a process of inter-observer variability testing was undertaken. All measurements on individual women were performed on the same day using the same ultrasound equipment by two research sonographers blinded to the other's measurements and results. Two sonographers measured SSFM, AFM, MTTM, MTFM and MTLM at 28 weeks' (49 women) or 36 weeks' (28 women) gestation. Thigh measures (MTTM and MTLM) were made once for each woman by each sonographer and SSFM and AFM were made at least twice by each sonographer for each woman. Subsequent to the initial phase as described above, all sonographers were trained in the measurement of fetal body composition by the main study sonographer.

Mid-thigh total, lean and fat mass—Measurements were obtained according to previously described techniques.^{5, 10, 25} A longitudinal view of the femur was obtained and the midpoint identified with an angle of 0 degrees to the transducer. The transducer was then rotated through 90 degrees to obtain a cross sectional view of the mid thigh (Figure S1). Mid thigh fat mass (MTFM) was measured by taking the total cross sectional limb area (mid thigh total mass or MTTM) and subtracting the mid thigh lean mass (MTLM) consisting of the central lean area comprising muscle and bone. Two observations were made using separate images. Two measurements were obtained, and the mean value of each set of observations used in the analysis.

The inter-observer variability of the fetal anthropometry was assessed on 49 women at 28 weeks gestation and 27 women at 36 weeks gestation. Two observers, blinded to the others measurements, repeated each anthropometric measurement on the same day using the same equipment.

Anterior abdominal wall thickness/abdominal fat mass (AFM)—Fetal abdominal fat mass (AFM) was measured using previously described techniques,^{6, 10} at the level of the abdominal circumference, between the fetal mid-axillary lines and anterior to the margins of the ribs. Subcutaneous fat was identified as the echogenic envelope surrounding the abdomen and most clearly identified anteriorly, and measured in millimetres on the anterior abdominal wall, using magnification (Figure S2). Four measurements were obtained from 1 or 2 separate images, and the mean used in the analysis.

Subscapular fat mass (SSFM)—Subscapular fat mass was obtained using previously described techniques.¹⁰ A sagittal view of the fetal trunk was evaluated longitudinally, to view the entire longitudinal section of the scapula between the skin surface and the subcutaneous tissue at the interface with the super-spinous and infra-spinous muscles. The measurement was taken at the end of the bone, taking the shoulder skin width (Figure S3). Two measurements were made and the mean value used in the analysis.

Statistical Analysis

Inter-observer variability was tested by calculating the intra-class correlation (Shrout et al 1979). For the variables MTTM, MTLM, MTFM where each woman was measured once by each sonographer a variance component model was used with women and sonographers fitted as random effects. For the variables SSFM and AFM, where each woman was measured more than once by each sonographer, the variance component model also included a random effect for the interaction between woman and sonographer. The intra-class correlation was defined as the correlation between measurements taken from the same woman by different sonographers/observers.

Baseline characteristics of women included in the analysis were compared descriptively between treatment groups. Normally distributed continuous variables were reported as means and standard deviations. Continuous variables, which were not normally distributed, were reported as medians and interquartile ranges. Categorical variables were reported as the number and percentage. Z-scores were calculated for each fetal growth measurement utilising ultrasound growth charts in clinical use.²³ Analyses were performed on the available data with women included in the treatment group allocated at randomisation. Fetal biometry and adiposity outcomes were analysed using linear mixed effects models including treatment group, time and their interaction, with adjustment made for the stratification variables center, parity and BMI, as well as maternal age, smoking status and socioeconomic status as fixed effects. A random subject effect was included in the model to allow for correlation between outcomes measured on the same subject at the different time points. Post hoc tests were performed to assess the effect of treatment group at each time point. Where the treatment by time interaction was not significant, it was removed from the model and the main effect of treatment group was estimated. Growth velocities were calculated as

the change in measurements between the ultrasounds divided by the number of days between the ultrasounds and analysed using linear regression models. Statistical significance was assessed at the 2-sided $p < 0.05$ level and no adjustment was made for multiple comparisons. All analyses were performed using SAS v9.3 (Cary, NC, USA).

The sample size of 2180 women was pre-determined based on the primary outcome of the trial (large for gestational age infant) as reported previously.²⁹

Results

Between June 2008 and December 2011, 2212 women were recruited and randomised, with 1108 allocated to receive Lifestyle Advice, and 1104 Standard Care. Women who withdrew consent to use their data (10 women) or had a miscarriage, termination of pregnancy, or stillbirth (60 women), were excluded from the analyses. A total of 1733 women had an ultrasound at 28 weeks (844 Lifestyle Advice and 889 Standard Care) and 1713 at 36 (845 Lifestyle Advice and 868 Standard Care) weeks gestation (Figure 1). Baseline characteristics of the 1847 women who had an ultrasound at one or both time points were similar between treatment groups (Table 1).

For each biometry parameter, and at each time point assessed, the mean fetal Z-score of participants was positive, indicating infants in this study were larger on average compared with population standards. However, there were no statistically significant differences identified for any of the biometry parameters between the two treatment groups overall and there was no evidence to suggest the effect of treatment varied between the two ultrasounds (Table 2).

Fetal body composition measurements were collected for 49 women at 28 weeks' and 28 women at 36 weeks' gestation for the assessment of inter-observer variability. Intra-class correlation coefficients were calculated for the measures of fetal body composition (Table S1). At 28 and 36 weeks' gestation, moderate agreement (ICC 0.40–0.60) was demonstrated for the measures of SSFM, MTTM and MTFM, with fair agreement (ICC 0.20–0.40) for AFM and MTLM. (29)

For each fetal body composition parameter, and at each time point assessed, the mean measure of participants was substantially higher when compared with population standards. Independent of time, fetuses of women receiving Lifestyle Advice demonstrated significantly greater mean mid thigh fat mass, when compared with fetuses of women receiving Standard Care (Adjusted Difference in Means 0.17; 95% Confidence Intervals (CI) 0.02 to 0.32; $p = 0.0245$) (Table 3). While subscapular fat mass increased between 28 and 36 weeks gestation in fetuses in both treatment groups, the rate of adipose tissue deposition was slowed among fetuses of women receiving Lifestyle Advice, when compared with fetuses of women receiving Standard Care ($p = 0.0160$). No other statistically significant differences were identified for any of the body composition parameters between the two treatment groups (Table 3), or in fetal growth velocities (data not shown).

Discussion

Main findings

Our randomised trial is the largest reported to date evaluating the specific fetal ultrasound determined biometry and body composition effects of an antenatal lifestyle intervention for women who were overweight or obese during pregnancy. Our findings suggest that the intervention during pregnancy was associated with greater mean mid thigh fat mass and a slower rate of subscapular adipose tissue deposition among fetuses of women who received Lifestyle Advice. At each time point, and for each biometric and adiposity related measure, fetal Z-scores were above population means, regardless of treatment group allocation.

These findings are consistent with those reported by our group, in which overweight and obese women allocated to the intervention demonstrated improvements in their diet quality, with increased fruit and vegetable consumption and reduced percentage of energy derived from saturated fats,¹⁸ in addition to increased physical activity.¹⁸ These modest improvements in maternal diet quality and physical activity were associated with a reduction in the chance their baby's birth weight was above 4.0 or 4.5kg,^{16, 19} an effect independent of total caloric intake¹⁸ and gestational weight gain.¹⁶

Strengths

The study's strengths include the large sample size and participation rate in research scans where 86% of women had at least one scan. The scans were performed by qualified sonographers unaware of treatment allocation and supervised by a maternal fetal medicine specialist. All data were collected prospectively.

Limitations

Fetal ultrasound assessment of weight and body composition has limitations including issues related to the accuracy in obtaining ultrasound measures in the setting of maternal obesity. While reported accuracy of fetal biometry and estimated weight is typically reported to be less than 10% depending upon gestation,²⁶ maternal obesity is a well recognised factor hampering accurate ultrasound visualization and assessment.^{27, 28} While ultrasound estimated fetal weight is reported to reflect actual birth weight with an error margin of $\pm 20\%$, across women of all BMI categories, performance is poorest among women who are the most obese,²⁹ and at extremes of fetal weight.³⁰

Whilst novel, the results we present are secondary outcomes of a larger trial that would not be considered statistically significant after adjustment for multiple comparisons. There remains a possibility that these findings are due to chance alone and should be replicated.

Interpretation

Our findings indicate that providing overweight and obese women with a dietary and lifestyle intervention was associated with a significant reduction in the rate of subscapular adipose tissue deposition. This intervention during pregnancy was also associated with greater fetal mean mid thigh fat mass, without differences in lean thigh mass, abdominal fat mass, or birth weight.^{16, 19}

The characteristic functional differences between adipocytes in the upper-body and lower-body have recently been described, and as such, the location of adipose tissue deposition may relate to differing associations with cardiovascular risk and type 2 diabetes mellitus, with upper-body and lower-body fat accumulation demonstrating opposing associations; lower-body fat having a protective role.³¹ A reduction in upper-body fat and an increase in lower-body fat as we have described in fetal life may therefore reflect a more favourable phenotype of adipose tissue distribution.

Cohort studies suggest that when compared with women of normal BMI, infants born to overweight or obese women have an increase in percentage of body fat and fat mass, despite minimal differences in birth weight.^{4, 32–34} Similarly, infants born to women with gestational diabetes have been shown to have an increase in the proportion of fat mass and a reduction in lean tissue mass at birth despite minimal differences in birth weight,^{35, 36} with evidence that differences in distribution of adipose tissue persist into early childhood.^{37, 38} Paretti et al have measured body composition of fetuses of women with normal BMI using ultrasound and found that fetuses of women with normal glucose tolerance have less subscapular adipose tissue compared with fetuses of women with mild glucose intolerance.³⁹ Importantly, none of these studies are directly comparable with the LIMIT randomised trial, and the data we present are therefore novel.

Overweight and obese women share a similar metabolic profile to women with gestational diabetes characterised by insulin resistance, hyperglycaemia, hyperlipidaemia, and low-grade chronic inflammation, which in turn has been documented to influence availability and transfer of nutrients to the fetus.⁴⁰ Whilst increasing maternal BMI is a well recognised risk factor for the development of gestational diabetes,^{2, 41, 42} increasing BMI with normal glucose tolerance does not preclude the existence of metabolic abnormalities associated with increased fetal growth.⁴⁰

While it has been suggested that assessment of fetal fat mass may be more sensitive to the effects of maternal overweight and obesity,⁴ there is little literature available evaluating the effect of maternal BMI on ultrasound measures of fetal body composition. While the ultrasonographic methodology is not directly comparable with our trial, Hure and colleagues,¹¹ in a prospective study did not identify an association between maternal BMI and measures of fetal lean mass.

To date, ultrasound assessment of fetal growth, particularly two-dimensional measures of skeletal growth have been poorly correlated with neonatal measures of body composition and body fat,^{43–45} regardless of whether the ultrasound biometry was obtained within 4 days^{43, 44} or more remote from birth.⁴⁵ In an attempt to refine this lack of association, some have advocated the use of three-dimensional ultrasound measures of fractional limb volume.^{43, 44} While these measures are more closely correlated with neonatal fat mass as determined by air displacement plethysmography⁴⁴ and skinfold thickness measurements,⁴³ tissue volumes are not routine in clinical practice and assessment of fetal growth.

Few studies have reported ultrasound derived fetal growth parameters among women who are overweight or obese. The Dutch Generation R study reported estimated fetal weight Z-

scores obtained in mid-pregnancy (18–25 weeks gestation), and late pregnancy (after 25 weeks gestation), according to maternal BMI.¹⁴ While the characteristics of the women who participated in this study are not directly comparable with our trial population, fetuses of women in the highest BMI quintile ($>26.4\text{kg/m}^2$) had an EFW Z-score of 0.33,(ref.¹⁴) consistent with our observations. Furthermore, our findings indicate a contribution from both head and abdominal growth to the increase in fetal weight estimates. This is consistent with the findings of Schaefer-Gras and colleagues,⁴⁶ but in contrast to the pattern of fetal growth reported by others, particularly observed among women with gestational diabetes, where abdominal girth predominates.^{15, 47, 48} Importantly, the fetal growth charts in current clinical use²³ have been derived from cross sectional data obtained from women of unknown BMI categories.⁴⁹

Conclusions

The findings of our randomised trial provide the first evidence of changes to fetal growth following an antenatal dietary and lifestyle intervention among women who were overweight or obese. Specifically, we observed greater mean mid thigh fat mass and a slower rate of subscapular adipose tissue deposition among fetuses of women who received dietary and lifestyle advice during pregnancy. These effects appear to be mediated via changes in maternal diet quality¹⁸ and physical activity during pregnancy,¹⁸ independent of gestational weight gain.¹⁶ Replication of these findings is needed, as these were secondary trial outcomes. Ongoing follow-up of children born to women who participated in the LIMIT randomised trial, and correlation of ultrasound findings with neonatal and early childhood body composition measures remains a priority.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.

Flow of Participants

Legend: Flow of women eligible for inclusion in the analysis of ultrasound measurements and fetal growth and adiposity.

Table 1

Baseline characteristics of women included in the analysis

Characteristic	Lifestyle Advice n=935	Standard Care n=912	Total n=1847
Maternal Age (Years)*	29.3 (5.5)	29.6 (5.5)	29.5 (5.5)
Gestational Age at Entry (Weeks) ⁺	14.1 (12.0–17.0)	14.3 (12.0–17.1)	14.3 (12.0–17.0)
Body Mass Index (kg/m ²) ⁺	31.2 (28.1–35.9)	31.2 (27.8–35.8)	31.2 (28.0–35.9)
Body Mass Index Category [#]			
. BMI 25.0–29.9	382 (40.9)	377 (41.3)	759 (41.1)
. BMI 30.0–34.9	272 (29.1)	271 (29.7)	543 (29.4)
. BMI 35.0–39.9	180 (19.3)	153 (16.8)	333 (18.0)
. BMI ≥40.0	101 (10.8)	111 (12.2)	212 (11.5)
Public Patient [#]	917 (98.1)	890 (97.6)	1807 (97.8)
Weight (kg)*	88.8 (17.0)	88.6 (17.8)	88.7 (17.4)
Height (cm)*	164.9 (6.6)	164.7 (6.5)	164.8 (6.6)
Race [#]			
. Caucasian	845 (90.4)	836 (91.7)	1681 (91.0)
. Asian	21 (2.2)	25 (2.7)	46 (2.5)
. Indian/Pak/SriLank	33 (3.5)	27 (3.0)	60 (3.2)
. Other	32 (3.4)	24 (2.6)	56 (3.0)
Smoker [#]	128 (13.7)	101 (11.1)	229 (12.4)
Nulliparous [#]	378 (40.4)	369 (40.5)	747 (40.4)
Previous Preterm Birth [#]	47 (5.0)	49 (5.4)	96 (5.2)
Previous Pre-eclampsia [#]	42 (4.5)	48 (5.3)	90 (4.9)
Previous Stillbirth [#]	10 (1.1)	3 (0.3)	13 (0.7)
Previous Neonatal Death [#]	8 (0.9)	5 (0.5)	13 (0.7)
Previous Caesarean Section [#]	168 (18.0)	175 (19.2)	343 (18.6)
Family History of Diabetes [#]	240 (25.7)	248 (27.2)	488 (26.4)
Family History of Hypertension [#]	337 (36.0)	320 (35.1)	657 (35.6)
Family History of Heart Disease [#]	169 (18.1)	150 (16.4)	319 (17.3)
Index of Socio-economic Disadvantage [#]			
. Unknown	1 (0.1)	0 (0.0)	1 (0.1)
. Quintile 1 (Most Disadvantaged)	293 (31.3)	265 (29.1)	558 (30.2)
. Quintile 2	229 (24.5)	223 (24.5)	452 (24.5)
. Quintile 3	149 (15.9)	143 (15.7)	292 (15.8)
. Quintile 4	122 (13.0)	142 (15.6)	264 (14.3)
. Quintile 5 (Least Disadvantaged)	141 (15.1)	139 (15.2)	280 (15.2)

Women were included in the analysis if they had an ultrasound at 28 or 36 weeks or both.

*
= mean and standard deviation;

⁺ = median and interquartile range;

[#] = number and %;

[^] = Socioeconomic index as measured by SEIFA (<http://www.abs.gov.au/websitedbs/censushome.nsf/home/seifa2011?opendocument&navpos=260>)

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TABLE 2

Effect of Treatment Group on Ultrasound Measurements of Fetal Biometry

Outcome	Time Point	Lifestyle Advice	Standard Care	Unadjusted Treatment Effect (95% CI)	Unadjusted P-value	Unadjusted Interaction P-value	Adjusted Treatment Effect (95% CI)	Adjusted P-value	Adjusted Interaction P-value
BPD Z-Score	28 Weeks	0.66 (1.49)	0.62 (1.45)	0.04 (-0.10, 0.17)	0.6152	0.6882	0.05 (-0.09, 0.19)	0.4837	0.8717
	36 Weeks	0.21 (1.12)	0.15 (1.15)	0.06 (-0.05, 0.17)	0.2732		0.06 (-0.05, 0.17)	0.2806	
	Total			0.05 (-0.05, 0.16)	0.3060		0.06 (-0.05, 0.16)	0.2805	
HC Z-Score	28 Weeks	0.77 (0.94)	0.76 (0.97)	0.01 (-0.08, 0.10)	0.8120	0.4427	0.02 (-0.07, 0.11)	0.7242	0.4398
	36 Weeks	0.67 (0.87)	0.62 (0.90)	0.05 (-0.04, 0.13)	0.2734		0.05 (-0.03, 0.14)	0.2143	
	Total			0.03 (-0.04, 0.10)	0.4067		0.04 (-0.04, 0.11)	0.3197	
AC Z-Score	28 Weeks	0.48 (1.02)	0.47 (0.99)	0.01 (-0.08, 0.11)	0.7662	0.5843	0.02 (-0.07, 0.11)	0.6646	0.7324
	36 Weeks	0.51 (1.02)	0.47 (1.07)	0.04 (-0.06, 0.14)	0.4269		0.04 (-0.06, 0.13)	0.4571	
	Total			0.03 (-0.06, 0.11)	0.5480		0.03 (-0.06, 0.11)	0.5081	
FL Z-Score	28 Weeks	0.23 (1.01)	0.22 (1.00)	0.00 (-0.10, 0.09)	0.9633	0.8432	0.00 (-0.09, 0.10)	0.9739	0.9449
	36 Weeks	0.16 (1.01)	0.15 (1.07)	0.01 (-0.09, 0.11)	0.8674		0.01 (-0.09, 0.10)	0.9155	
	Total			0.00 (-0.08, 0.08)	0.9474		0.00 (-0.08, 0.08)	0.9353	
EFW (g)	28 Weeks	1289.33 (237.12)	1272.12 (238.15)	17.53 (-4.85, 39.90)	0.1246	0.6775	21.24 (-1.25, 43.74)	0.0641	0.4544
	36 Weeks	2906.80 (401.72)	2894.41 (420.56)	9.50 (-29.46, 48.46)	0.6326		6.73 (-32.11, 45.57)	0.7340	
	Total			16.36 (-5.32, 38.05)	0.1391		19.01 (-2.70, 40.73)	0.0861	

Values are mean (SD) and treatment effects are differences in means from a linear mixed effects model.

Interaction p-values are for treatment by time point interaction. Interaction dropped from the model and main effect of treatment examined where interaction not significant.

Adjusted for centre, parity, BMI category, age, socioeconomic status quintile and smoking status.

BPD=biparietal diameter; HC=head circumference; AC=abdominal circumference; FL=femur length; EFW=estimated fetal weight (Hadlock C Formula)

TABLE 3

Effect of Treatment Group on Ultrasound Measurements of Fetal Adiposity

Outcome	Time Point	Lifestyle Advice	Standard Care	Unadjusted Treatment Effect (95% CI)	Unadjusted P-value	Unadjusted Interaction P-value	Adjusted Treatment Effect (95% CI)	Adjusted P-value	Adjusted Interaction P-value
Total Thigh Area (cm ²)	28 Weeks	9.76 (2.02)	9.53 (1.97)	0.22 (-0.01, 0.45)	0.0614	0.7956	0.21 (-0.02, 0.45)	0.0726	0.8374
	36 Weeks#	20.52 (4.39)	20.22 (3.89)	0.29 (-0.23, 0.81)	0.2716		0.27 (-0.25, 0.79)	0.3117	
	Total			0.23 (0.00, 0.45)	0.0470		0.22 (-0.01, 0.45)	0.0574	
MTLM (cm ²)	28 Weeks	5.03 (1.10)	4.99 (1.06)	0.03 (-0.09, 0.16)	0.5864	0.3352	0.04 (-0.09, 0.16)	0.5612	0.4190
	36 Weeks	9.14 (2.14)	8.97 (1.93)	0.16 (-0.09, 0.42)	0.2058		0.15 (-0.11, 0.40)	0.2606	
	Total			0.05 (-0.07, 0.17)	0.3767		0.05 (-0.07, 0.17)	0.3798	
MTFM (cm ²)	28 Weeks	4.73 (1.34)	4.54 (1.24)	0.18 (0.03, 0.33)	0.0167	0.7821	0.17 (0.02, 0.32)	0.0241	0.8090
	36 Weeks	11.37 (3.16)	11.25 (2.87)	0.13 (-0.25, 0.51)	0.4960		0.13 (-0.25, 0.51)	0.5105	
	Total			0.18 (0.03, 0.33)	0.0172		0.17 (0.02, 0.32)	0.0245	
AFM (mm)	28 Weeks	3.54 (1.09)	3.52 (1.04)	0.02 (-0.10, 0.14)	0.7151	0.2144	0.04 (-0.08, 0.16)	0.5448	0.2206
	36 Weeks	5.59 (1.66)	5.71 (1.57)	-0.11 (-0.31, 0.09)	0.2778		-0.09 (-0.29, 0.10)	0.3488	
	Total			-0.01 (-0.12, 0.11)	0.9132		0.01 (-0.10, 0.12)	0.9048	
SSFm (mm)	28 Weeks	3.25 (0.95)	3.18 (0.89)	0.08 (-0.03, 0.19)	0.1472	0.0180	0.09 (-0.02, 0.20)	0.0924	0.0160
	36 Weeks	5.24 (1.32)	5.38 (1.41)	-0.14 (-0.31, 0.03)	0.0953		-0.14 (-0.31, 0.03)	0.1155	

Values are mean (SD) and treatment effects are differences in means from a linear mixed effects model.

Total Thigh Area, MTLM, MTFM: 28 weeks n(%) = 566(64) Lifestyle Advice; 568(67) Routine Care; 36 weeks n(%) = 490(57) Lifestyle Advice, 485(57) Routine Care

AFM: 28 weeks n(%) = 597 (67%) Lifestyle Advice, 591(70) Routine Care; 36 weeks n(%) = 516 (59.4) Lifestyle Advice, 504(60) Routine Care

SSFm: 28 weeks n(%) = 578(65) Lifestyle Advice, 565(67) Routine Care, 498(57) Lifestyle Advice, 507(60) Routine Care

Interaction p-values are for treatment by time point interaction. Interaction dropped from the model and main effect of treatment examined where interaction not significant.

Adjusted for centre, parity, BMI category, age, socioeconomic status quintile and smoking status.

MTLM=mid thigh lean mass; MTFM=mid thigh fat mass; AFM= abdominal fat mass; SSFM= subscapular fat mass