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# Greater maternal weight gain during pregnancy predicts a large but lean fetal phenotype: a prospective cohort study

**Short title:** Weight gain & fetal phenotype

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## Abstract

**Objective:** To describe the fetal phenotype *in utero* and its associations with maternal pre-pregnancy weight and gestational weight gain.

**Methods:** This prospective longitudinal cohort included 179 Australian women with singleton pregnancies. Serial ultrasound measurements were performed at 19, 25, 30 and 36 (± 1) weeks gestation and maternal anthropometry were collected concurrently. The ultrasound scans included the standard fetal biometry of head circumference, biparietal diameter, abdominal circumference, and femur length, and body composition at the abdomen and mid-thigh, including fat and lean mass cross-sectional areas. Maternal gestational weight gain was compared to current clinical guidelines.

**Results:** The participants had an average of 3.7 ±0.8 scans and birth data were available for 165 neonates. Fifty five per cent of the cohort gained weight in excess of current recommendations, according to pre-pregnancy body mass index (BMI). Maternal gestational weight positively predicted fetal abdominal circumference (*P* .029) and lean abdominal mass area (*P* .046) in linear mixed model regression analysis, adjusted for known and potential confounders. At any pre-pregnancy BMI gaining weight above the current recommendations resulted in a larger fetus according to standard biometry, because of significantly larger lean muscle mass at the abdomen (*P* .024) and not due to an increase in fat mass (*P* .463).

**Conclusions:** We have demonstrated the importance of maternal weight gain, independent of pre-pregnancy BMI, to support the growth of a large but lean fetus. Prenatal counselling should focus on achieving a healthy BMI prior to conception so that gestational weight gain restrictions can be minimised.

**Keywords:** fetus, growth, pregnancy, ultrasound, weight gain

## *Introduction*

Maternal nutritional and metabolic factors which affect fetal growth and birth weight are of particular interest, as these may offer valuable intervention points for preventative programming of the offspring's adult health.(1-3) The Barker hypothesis and accompanying evidence has supported an inverse association between birth weight and lifetime risk for type 2 diabetes,(4) coronary heart disease(5, 6) and stroke.(6) Contrary to this, a recent meta-analysis by Harder *et al*(7) showed that infants at both the lowest and highest end of the birth weight spectrum were at an increased risk of type 2 diabetes in adulthood. The lowest odds ratio (0.55) for type 2 diabetes was at a birth weight of 3.5 to 4.0 kg.(7) Extending this work, Whincup *et al*(4) have systematically reviewed the literature, and have applied exclusions for macrosomia and maternal diabetes. The inverse association between birth weight and type 2 diabetes was appreciably strengthened with the exclusion of macrosomia and maternal diabetes.(4) It is likely that these exclusion criteria would have removed the infants of a disproportionate fat mass, as well as of a high birth weight.(8)

It is remarkable that long term health outcomes are, at least in part, predicted by the size of the newborn given that birth weight is only a snapshot of the fetal growth trajectory. Recent studies have recognised the need to extend beyond this single marker and adopt a more sophisticated approach to describing fetal and infant growth.(9, 10) This includes differentiating lean from fat mass. Intrauterine measures of adiposity are far less common than postnatal studies(11-13) but can be done using magnetic resonance imaging(14) or ultrasound technology.(15, 16)

Longitudinal data reporting concurrent changes in maternal body weight during pregnancy and the pattern of fetal growth *in utero* have not been previously described in the obstetrics literature. The aims of our study were to test maternal pre-pregnancy weight and gestational weight gain as the predictors of intrauterine fetal growth and body composition outcomes, including fat and lean mass areas.

## *Methods*

The data were collected as part of the Women and Their Children's Health (WATCH) study; a prospective longitudinal cohort spanning pregnancy and early childhood. Ethics approval was obtained from the Hunter New England Human Research Ethics Committee. Participants were recruited at the antenatal clinic of the John Hunter Hospital, Newcastle, Australia. Sixty-one per cent of those approached to participate in the WATCH study provided written informed consent and attended one or more study visits.(17) Pregnancy data collection occurred from July 2006 to June 2008. There were no exclusion criteria for the WATCH cohort, however, the current analyses excludes data from twin pregnancies and repeat participants.

The study visits, which included serial ultrasound scans, were scheduled for approximately 19 (fetal anomaly scan), 25, 30 and 36 (±1) weeks gestation. The ultrasound scans were performed by a team of clinical Obstetricians and Sonographers. Naegele's Rule(18) was used to calculate the estimated date of delivery (EDD) unless: (i) menstrual dates were unknown or unreliable; or (ii) in the first trimester (~6 to 13 weeks) the scan EDD was >4 days different to that of the menstrual EDD; or (iii) in the second trimester (13 to 20 weeks) the scan EDD was >7 days different to that of the menstrual EDD. Ultrasounds were performed using an Acuson Aspen (AspenUltrasound, Oceanside, California, USA) or Voluson 730 Pro (GE Healthcare, Giles, Buckinghamshire, UK) with a curvilinear array transducer. Each ultrasound included the standard fetal biometric measures of biparietal diameter, head circumference, abdominal circumference and femur length. Fetal body composition measurements of fat and lean muscle mass areas ($cm^2$) at the abdomen and mid-thigh were collected on cross-sectional images. The abdominal fat and lean mass imaging was performed at the level of the standard abdominal circumference measurement with the transducer rotated 90$^{o}$. The total area of the fetal abdomen was calculated (A1); then the lean abdominal area, which excluded the hyperechoic subcutaneous fat layer, was calculated (A2). The fetal abdominal fat area was: A1-A2 cms$^{2}$. The measurements of the fetal mid-thigh fat and lean mass were taken following the measurement of the femur length, over the mid-point of the femur with the transducer rotated 90$^{o}$.(15, 16) The total cross-sectional area of the fetal mid-thigh (T1) was calculated; then the cross-sectional area of the hypoechoic fetal mid-thigh muscle was calculated (T2). The fetal mid-thigh fat area was: T1-T2 cms$^{2}$.(16)

Maternal anthropometry was collected by an Accredited Practising Dietitian with Level One Anthropometry certification from the International Society for the Advancement of Kinanthropometry.(19) Maternal weight, without shoes or overclothes, was measured at each study visit using the same set of annually calibrated A&D FV-150K electronic weighing scales (A&D Mercury Pty Ltd, Thebarton, South Australia). Pre-pregnancy weight was self-reported at the first antenatal clinic visit; usually at 14 weeks gestation, otherwise at the first study visit. Standing height, without shoes, was measured to the nearest millimetre on two separate occasions, using the same wall-mounted Seca stadiometer (Seca Deutschland, Hamburg, Germany). The readings were averaged, unless the measures differed by more than 1.5%, where a third measure was taken and the median value used.

We evaluated the maternal characteristics, pregnancy outcomes and birth outcomes of the cohort, according to whether women completed the study (‘main cohort’), withdrew prior to the 36 week study visit (‘withdrew’) or delivered before 37 completed weeks of gestation (‘preterm delivery’). Data on pregnancy and birth outcomes were extracted from the ObstetriX database, the major repository in New South Wales, Australia for recording antenatal information and birth outcomes(20). Statistical comparisons between the groups were undertaken and then cohort characteristics were described as a whole (‘all women’).

***Statistical Analyses***

Statistical analyses were performed using the statistical software package Intercooled Stata, version 11 (StataCorp LP, College Station, Texas, USA). Data were tested for normality. The maternal weight variables were significantly skewed, as were the fetal abdominal fat, lean abdominal mass, mid-thigh fat and mid-thigh lean mass variables. Rather than using transformations (log etc.) to normalise data that were being analysed as continuous, the bootstrap technique was applied(21), using 1000 repetitions. Bootstrapping was not used in any of the categorical data analyses.

Analysis of variance, $\chi^2$, Kruskal-Wallis and Wilcoxon rank-sum tests were performed to compare the maternal characteristics, pregnancy outcomes and birth outcomes for the sub-groups of women (main, withdrew and preterm) before merging the data for all women. Fetal biometry and body composition data from 19 to 36 (±1) weeks gestation were summarised for the cohort into 5$^{th}$, 50$^{th}$ and 95$^{th}$ percentile charts. Pairwise correlations, with Bonferroni correction for multiple comparisons, were performed to assess the relationship between intrauterine body composition from 36 weeks gestation and neonatal birth weight and Ponderal Index (kg/m$^3$).

Linear mixed-models were performed using the paired longitudinal maternal and fetal data, with adjustment for maternal height, gestational age, fetal sex, smoking, parity, diabetes, and relative socioeconomic disadvantage from postcode. Linear mixed-models adjust for the estimated errors associated with repeated measures on an individual and can handle missing data. Maternal pre-pregnancy weight and gestational weight were used as the predictors of the intrauterine fetal size and body composition measurements. A multiplicative interaction term was applied for pre-pregnancy and gestational weight.

Weight gain categories were determined for women based on their pre-pregnancy body mass index ((BMI) kg/m$^2$) and the Institute of Medicine's 2009 *Weight Gain During Pregnancy* recommendations.(22) Appropriate weight gain at 36 weeks gestation (when our final weight measure was collected) was calculated from the Institute of Medicine's guidelines, (22) taking into account a 0.5 to 2.0 kg increase in weight during the first trimester for all women, and then a combined second and third trimester range of weekly weight gain based on pre-pregnancy BMI. Women were classified as 'below', 'within' and 'above' the recommended weight gain ranges for their pre-pregnancy BMI category.

Analysis of covariance (ANCOVA) models, adjusted for pre-pregnancy BMI, gestational age, fetal sex, smoking, parity, diabetes, and relative socioeconomic disadvantage from postcode, were used to determine whether weight gain category predicted the size and body composition of the fetus at 36 weeks gestation. A post hoc power analysis using the observed mean and standard deviation of the fetal abdominal fat at 36 weeks gestation demonstrated that this study had 82% power to detect a 10% difference between the 'within' and 'above' recommended weight gain categories. Power calculations were based on a two-sample t test for unequal variance using a two-sided significance level of 0.05 (PS Power and Sample Size, version 3.0.14, Vanderbilt University, Nashville, Tennessee, USA).

## Results

A total of 179 different women having a singleton pregnancy were included in the current analyses. Recruitment, withdrawals and study visit attendance are documented in Figure 1. The maternal characteristics, pregnancy outcomes and birth outcomes of our cohort are described in Table 1, according to whether women completed the study ('main cohort'), withdrew prior to the 36 week study visit ('withdrew') or delivered before 37 completed weeks of gestation ('preterm delivery'). There were few differences between the groups, hence all available data have been included in the analyses for all 179 women. Overall, the female offspring were significantly smaller than males at birth according to weight, length and head circumference.

The fetal growth trajectories over gestation within our cohort have been summarised into 5$^{th}$, 50$^{th}$ and 95$^{th}$ percentiles in Figure 2. The standard fetal biometric measures of head circumference, biparietal diameter and femur length are curvilinear, with growth slowing slightly towards the end of gestation. The increase in fetal abdominal circumference to 36 weeks gestation is linear. The fetal body composition markers at the abdomen and mid-thigh demonstrate an exponential rise to up 36 weeks gestation. At 36 weeks gestation there is on average only 1cm$^2$ less fat at the mid-thigh compared to the lean muscle area at this site.

After Bonferroni correction, moderate positive correlations were observed for the fetal body composition variables (measured after 36 weeks gestation) and neonatal birth weight (all $P$<.05), except for the abdominal fat area ($P$=.91) (Figure 3). The abdominal total, lean and fat areas were more strongly associated with neonatal Ponderal Index than the mid-thigh measurements. Overall, the fetal body composition variables were not as strongly correlated with neonatal Ponderal Index compared to birth weight.

The statistically significant associations of maternal pre-pregnancy weight and gestational weight (maternal weight at each study visit) as the predictors of fetal size and body composition *in utero* based on mixed-model regression analysis are shown in Table 2. Neither pre-pregnancy weight nor gestational weight was associated with the other markers of fetal size or body composition, including fetal adiposity. Interestingly, pre-pregnancy weight was inversely predictive of the fetal abdominal circumference and lean mass area, while gestational weight was positively predictive of both fetal abdominal measures. Within the same mixed-models there were significant differences between fetal size and body composition according to fetal sex. The female fetuses had smaller head circumference (coefficient (CE) -6.27; 95% confidence interval (CI) -8.63, -3.92), biparietal diameter (CE - 1.95; 95% CI -2.73, -1.17) and smaller abdominal circumference (in Table 2) compared to male fetuses. There were no significant differences in femur length (CE -0.37; 95% CI -0.95, 0.21), abdominal fat (CE -0.29; 95% CI -0.59, 0.01) and thigh fat areas (CE -0.06; 95% CI -0.30, 0.18) according to fetal sex. However, female fetuses had smaller abdominal lean muscle areas (Table 2) and mid-thigh muscle areas (CE -0.43; 95% CI -0.62, -0.23), compared to male fetuses.

Women who were underweight before pregnancy gained the greatest amount of weight up to 36 (±1) weeks gestation (Table 3). With each ascent in BMI category a lower median weight gain was observed. Underweight and overweight women gained on average more than the Institute of Medicine 2009 guidelines recommend,(22) and normal weight and obese women gained weight at close to the upper recommended limit. Overall, 54% of the women measured at 36 weeks had increased their weight beyond the recommended weight gain according to their pre-pregnancy BMI.

Within the normal range pre-pregnancy BMI category, gaining weight above the Institute of Medicine 2009 recommendations was associated with a larger fetal abdominal circumference made up of both abdominal fat and lean areas, compared to those gaining within the recommendations for the same pre-pregnancy BMI (Table 4). However, when all pre-pregnancy BMI categories were combined and only the 'below', 'within' and 'above' recommended gestational weight gain categories were used to predict the fetal size and body composition outcomes (Table 5), greater weight gain was positively predictive of biparietal diameter, abdominal circumference and the abdominal lean muscle area, as well as birth weight and length. Overall, greater maternal weight gain did not predict a greater accretion of fat at the fetal abdomen or mid-thigh fat areas, nor the mid-thigh lean muscle area after adjusting for pre-pregnancy BMI, gestational age, fetal sex, smoking, parity, diabetes, and socio-economic status from postcode. \

## Discussion

This study is the first report of longitudinal changes in fetal growth and body composition, from ultrasound scans, and their relationship with maternal pre-pregnancy weight and weight gain throughout gestation. We have shown that more than half the women in our study were gaining in excess of the current weight gain recommendations, stratified by pre-pregnancy BMI. In our longitudinal mixed-models the fetal abdominal circumference *in utero*, particularly the lean abdominal area, was positively predicted by maternal gestational weight and not pre-pregnancy weight. Gaining weight at or above the current recommendations for pregnancy resulted in a larger but relatively leaner fetal phenotype. Our study confirms the report by others, that males and females have similar fat masses, although males tend carry greater lean mass.(23)

Bernstein *et al*(15) have previously established the use of ultrasound scans to collect body composition data on fetuses at the mid-upper arm and mid-thigh from 19 to 40 weeks gestation. Body composition data from standardised cross-sectional images were validated in 25 subjects who had neonatal anthropometry (skinfolds) collected within 24 hours of delivery.(15) There was a strong positive correlation between the intrauterine femoral lean area and estimated neonatal lean mass (r 0.70, $P$<.001), and a moderate correlation between the femoral fat area and neonatal fat mass (r 0.63, $P$<.001).(15) The fetal mid-thigh areas proved to be the stronger predictors of birth weight and neonatal body composition compared to the mid-upper arm.(15) Total abdominal area but not abdominal fat and lean mass areas were reported by Bernstein *et al*.(15) However, many others have quantified subcutaneous abdominal fat thickness *in utero*, which appears as a well-delineated echogenic layer on the same ultrasound section as the fetal abdominal circumference measurement.(16, 24-26)

The current Institute of Medicine weight gain recommendations advise women with a lower pre-pregnancy BMI to gain a greater amount during pregnancy, and those in the high BMI categories to limit weight gain. In 2007, Cedergren(27) published modelling of the optimal gestational weight gain range based on pre-pregnancy BMI for 268,648 singleton pregnancies delivered in Sweden. At an overweight pre-pregnancy BMI (25-29.99 kg/m$^2$) the optimal gestational weight gain was 0 to 9 kg, and at an obese pre-pregnancy BMI (≥30 kg/m$^2$) the optimal gestational weight gain was only 0 to 6 kg. The estimated cumulative total of the compartmental (fetus, tissue, blood and fluid) weight increases during pregnancy, even when no maternal fat is gained, is 9.2 kg at term.(28) Hence, an energy intake during pregnancy which utilises maternal energy stores to support the fetal demands was associated with more favourable birth outcomes for overweight and obese women.(27) Cedergren acknowledged that any longer-term effects based on maternal weight gain were not considered for either the mother or offspring.(27)

Weight is often cited as an indicator of maternal nutritional status but also as a proxy for the intrauterine nutritional environment experienced by the fetus. It has been proposed that the intrauterine nutritional cues a fetus receives serves to forecast that of the extrauterine environment, and growth and body composition may be adapted in an effort to optimise the chance of survival.(29) Some studies have, rather simplistically, reported a positive association between birth weight and adult BMI.(10) However, more recent reviews that consider adult body composition rather than just BMI have shown that birth weight is positively correlated with later lean mass, but not body fat.(10, 30)

The ‘thin-fat phenotype’, is characterised by a low BMI with a disproportionately high fat mass. Asian Indians, compared to other ethnic groups such as white Caucasians and African Americans, display this thin-fat phenotype from birth.(31) Indians carry little weight-for-height (or length), which is comprised of a greater proportion of fat, especially at the abdomen, and a lower proportion of lean muscle.(31) It has been suggested that it is this phenotype which accounts for the increased prevalence of insulin resistance in the Indian population.(32) Optimising fetal body composition *in utero* may serve as a primary health target for adult diseases like type 2 diabetes and coronary heart disease.

We have relied on self-reported data as the baseline measure of maternal weight and for the calculation of pre-pregnancy BMI. A study by Stevens-Simon *et al*(33) specifically assessed the relationship between self-reported and documented pre-pregnancy weights, finding they are highly correlated (r 0.96, $P<.001$). In this study, 93 subjects were asked to recall their pre-pregnant weight at 14.4 ±5.1 weeks gestation,(33) which was almost identical to our study. Medical and school records were reviewed for measurements collected by health professionals in the six months before conception, up to two weeks after conception.(33) The calculated difference in self-reported and documented weights according to weight category (under, average, or over-weight) were not significantly different and averaged -1.3 ±5.0 kg.(33) Overweight females were identified as the most likely group to underreport their pre-pregnant weight.(33) This study, along with others,(34, 35) suggests it is valid to use self-reported weight in lieu of a direct measure, though we acknowledge that this may introduce some bias, particularly for those at high body weights.

The data supports that at any maternal pre-pregnancy BMI some weight gain is appropriate, with the aim of optimising fetal body composition. Weight gain above the current Institute of Medicine guidelines resulted in a larger fetus at birth according to birth weight and length. However, late in pregnancy, only increases in the abdominal lean mass and subsequent increases in abdominal circumference were predicted by greater maternal weight gain, not increases in fat mass. The benefits of increasing birth weight and lean mass need to be carefully evaluated against the difficulties associated with delivering a larger fetus. Furthermore, the maternal outcomes related to excessive weight gain in pregnancy must also be considered, as there is evidence that high weight gain during pregnancy is associated with retention of excess weight at one and 15 years after the birth.(36) Prenatal counselling should therefore focus on achieving a healthy BMI prior to conception, thereby reducing the need for lower gestational weight gain targets due to maternal overweight and obesity.

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## *Figure Legends*

**Figure 1:** Recruitment, withdrawals and participant attendance for the Women and their Children's Health (WATCH) Study of intrauterine growth and body composition (N=179), Newcastle, Australia.

*Stillborn at 21 weeks gestation; withdrawn after visit 1. All other preterm deliveries are not withdrawals, but did not attend further pregnancy study visits.

**Figure 2:** Intrauterine percentiles ($5^{th}$, $50^{th}$ and $95^{th}$) for markers of fetal size and fetal body composition at the abdomen and mid-thigh from 19 ±1 to 36 ±1 weeks gestation, determined by serial ultrasound scans (up to four) in the Women and their Children's Health (WATCH) Study (N=179).

The solid lines show the $50^{th}$ percentiles, while the dotted lines show the $5^{th}$ and $95^{th}$ percentiles for the pooled data.

**Figure 3:** Pairwise correlation coefficients for the fetal body composition markers, at the abdomen and mid-thigh after 36 weeks gestation, with neonatal birth weight (a) and Ponderal Index (b) (n=71).

*$P<.05$, after Bonferonni correction.

**Table 1:** Maternal characteristics, pregnancy outcomes and birth outcomes for participants in the Women and their Children's Health Study of intrauterine growth and body composition (N=179).

| Characteristic | Main cohort (n=151) | Withdrew (n=12) | Preterm delivery (n=16) | All women (N=179) |
|---|---|---|---|---|
| Age (y), mean ±SD | 28.8 ±5.5 | 26.6 ±6.4 | 29.0 ±7.3 | 28.7 ±5.7 |
| Number of ultrasound scans, mean ±SD | 3.9 ±0.3 | 1.2 ±0.4 | 3.3 ±0.9 | 3.7 ±0.8 |
| Country of birth[*] | | | | |
| *Australia*, n (%) | 142 (94.0) | 12 (100) | 15 (93.8) | 169 (94.4) |
| *Other*, n (%) | 9 (6.0) | 0 | 1 (6.3) | 10 (5.6) |
| Aboriginal (not Torres Strait Islander), n (%) | 5 (3.3) | 0 | 0 | 5 (2.8) |
| Married or defacto relationship, n (%) | 131 (86.8) | 7 (58.3)[†] | 13 (81.3) | 151 (84.4) |
| Smoked during pregnancy, n (%) | 16 (10.6) | 2 (16.7) | 2 (12.5) | 20 (11.2) |
| Maternal education level ≥ yr 12 Higher School Certificate[‡], n (%) | 102 (71.8) n=142 | 3 (75.0) n=4 | 9 (64.3) n=14 | 114 (71.3) n=160 |
| Relative disadvantage and lack of advantage based on postcode (IRSAD decile ≤5)[§], n (%) | 47 (31.1) | 5 (41.7) | 5 (31.3) | 57 (31.8) |
| Pre-pregnancy weight (kg), median [IQR] | 65.0 [21.0] | 77.0 [28.0] | 60.5 [19.0] | 65.0 [21.0] |
| Height (cm), median [IQR] | 164.2 [8.9] | 166.4 [10.5] | 162.0 [9.4] | 164.2 [9.1] |
| Pre-pregnancy BMI (kg/m$^2$), median [IQR] | 24.4 [8.0] | 27.7 [9.3] | 23.1 [6.9] | 24.4 [7.8] |
| Nulliparous, n (%) | 64 (42.4) | 4 (33.3) | 9 (56.3) | 77 (43.0) |
| Gestational age at birth (wk), median [IQR] | 39.6 [1.8] | 40.3 [3.4] | 35.7 [3.5][ǁ] | 39.4 [2.0] |
| Hypertension | | | | |
| *Gestational*, n (%) | 7 (4.6) | 0 | 0 | 7 (3.9) |
| *Pre-eclampsia*, n (%) | 2 (1.3) | 1 (8.3) | 0 | 3 (1.7) |
| Diabetes | | | | |
| *Gestational*, n (%) | 5 (3.3) | 0 | 2 (12.5) | 7 (3.9) |

| Characteristic | Main cohort (n=151) | Withdrew (n=12) | Preterm delivery (n=16) | All women (N=179) |
|---|---|---|---|---|
| *Pre-existing*, n (%) | 1 (0.7) | 0 | 0 | 1 (0.6%) |
| Fetal Sex | | | | |
| *Female*, n (%) | 75 (49.7) | 7 (58.3) | 9 (56.3) | 91 (50.8) |
| *Male*, n (%) | 76 (50.3) | 5 (41.7) | 7 (42.8) | 88 (49.2) |
| Birth weight (g) | | [¶] | | |
| *Female*, median [IQR] | 3460 [610] n=74 | | 2000 [810][‖] n=9 | 3400 [820][**] n=83 |
| *Male*, median [IQR] | 3663 [780] n=74 | | 2700 [1100][‖] n=7 | 3600 [840] n=81 |
| Birth length | | [¶] | | |
| *Female*, median [IQR] | 51 [3.5] n=71 | | 48 [10.8][‖] n=4 | 51 [3][**] n=75 |
| *Male*, median [IQR] | 52 [4] n=72 | | 47.5 [12.5][‖] n=4 | 51.3 [4] n=76 |
| Head circumference | | [¶] | | |
| *Female*, median [IQR] | 34.5 [2] n=73 | | 30.7 [4.5][‖] n=6 | 34 [2][**] n=79 |
| *Male*, median [IQR] | 35 [2] n=74 | | 32 [1][‖] n=7 | 35 [2] n=81 |
| Mode of birth | n=149 | [¶] | n=16 | n=165 |
| *Vaginal*, n (%) | 120 (79.5) | | 11 (68.8) | 131 (79.4) |
| *Caesarean section*, n (%) | 29 (19.5) | | 5 (31.3) | 34 (20.6) |

BMI, body mass index; IRSAD, index of relative socio-economic advantage and disadvantage.

Data are presented as: mean ±standard deviation (SD); n (%); or, median [interquartile range (IQR)].

[*]Other countries include: England n=4, Belgium n=1, Canada n=1, Malaysia n=1, New Zealand n=1, Papua New Guinea n=1, and USA n=1.

[†]Women who withdrew from the study were less likely to be married or in a defacto relationship ($\chi^2$, *P*=.03).

[‡]Self-reported using a socioeconomic questionnaire issued at visit 1; 89% completed and returned.

[§]Pink B. An introduction to Socio-Economic Indexes for Areas (SEIFA). Australian Bureau of Statistics. Commonwealth of Australia; 2006.

[‖]Gestational age at birth was lower in the preterm group (Kruskal-Wallis *P*<.01). Preterm infants (female and male) were significantly smaller at birth according to birth weight, length, and head circumference (Wilcoxon rank-sum tests <P.01).

[¶]Birth weight, length, head circumference and mode of birth were not recorded for the women who withdrew from the study prior to delivery.

[**]Female infants were significantly smaller at birth than males according to birth weight (*P*<.01), length (*P*=.02), and head circumference (*P*<.01); Wilcoxon rank-sum tests.

**Table 2:** Significant associations of maternal pre-pregnancy weight and gestational weight as the predictors fetal size and body composition *in utero*, determined via serial ultrasound scans from 19 ±1 to 36 ±1 weeks gestation (N=179), based on mixed-model regression analysis.

| | Fetal growth and body composition outcomes | | | | | |
|---|---|---|---|---|---|---|
| | Abdominal circumference (mm) | | | Abdominal lean mass area ($cm^2$) | | |
| **Maternal predictors** | **Coefficient** | **95% Confidence Interval** | ***P*** | **Coefficient** | **95% Confidence Interval** | ***P*** |
| Pre-pregnancy weight (kg) | -0.407 | -0.826, 0.012 | .057 | -0.151 | -0.307, 0.005 | .058 |
| Height (cm) | 0.062 | -0.183, 0.308 | .621 | -0.019 | -0.088, 0.050 | .583 |
| Gestational weight (kg) | 0.405 | 0.042, 0.768 | .029 | 0.133 | 0.003, 0.263 | .046 |
| Interaction term (pre-pregnancy * gestational weight) (kg) | <0.001 | -0.003, 0.004 | .598 | <0.001 | <-0.001, 0.001 | .215 |
| Gestation (weeks) | 10.844 | 10.661, 11.027 | <.001 | 3.269 | 3.172, 3.366 | <.001 |
| Fetal sex (0, male; 1, female) | -4.525 | -7.600, -1.450 | .004 | -1.886 | -2.627, -1.144 | <.001 |
| Smoker (0, yes; 1, no) | 3.964 | -1.141, 9.069 | .128 | 1.083 | -0.221, 2.387 | .104 |
| Parity | 0.761 | -0.577, 2.099 | .265 | 0.374 | -0.014, 0.761 | .059 |
| Diabetes (0, yes; 1, no) | 3.742 | -4.357, 11.842 | .365 | 0.962 | -1.610, 3.534 | .464 |
| Socioeconomic decile based on postcode (0, lowest, most disadvantaged; 10, highest, least disadvantaged) | -0.392 | -1.150, 0.366 | .311 | -0.257 | -0.454, -0.060 | .011 |
| Constant | -83.984 | -127.421, -40.548 | <.001 | -49.614 | -61.847, -37.381 | <.001 |

**Table 3:** Maternal weight change (in kg) from pre-pregnancy to 36 ±1 weeks gestation according to pre-pregnancy body mass index (BMI) category and compared to the Institute of Medicine (2009) *Weight Gain During Pregnancy* Guidelines*.

| BMI category† | Pre-pregnancy BMI ($kg/m^2$) | WATCH Cohort | | | Institute of Medicine, 2009 Recommendations | | Calculated recommended weight gain at 36 weeks gestation‡ (kg) |
|---|---|---|---|---|---|---|---|
| | | n=157 | Median [interquartile range] | Minimum, maximum | Total weight gain (kg) | Mean (range) weight gain for 2nd and 3rd trimester in kg/week | |
| Underweight | <18.5 | 8 | 20.6 [9.5] | 13.4, 44.8 | 12.5 - 18.0 | 0.51 (0.44 - 0.58) | 11.06 -15.92 |
| Normal range | 18.5 - 24.99 | 79 | 13.6 [6.5] | 5.4, 35.1 | 11.5 - 16.0 | 0.42 (0.35 - 0.50) | 8.90 - 14.0 |
| Overweight | 25 - 29.99 | 37 | 12.2 [7.2] | -2.5, 24.4 | 7.0 - 11.5 | 0.28 (0.23 - 0.33) | 6.02 - 9.92 |
| Obese | ≥30 | 33 | 8.2 [8.7] | -4.7, 21.1 | 5.0 - 9.0 | 0.22 (0.17 - 0.27) | 4.58 - 8.48 |

*Rasmussen KM, Yaktine AL, editors. Weight gain during pregnancy: reexamining the guidelines. Washington DC: Institute of Medicine, National Academy of Sciences; 2009

†World Health Organization (2010). The international classification of adult underweight, overweight and obesity according to BMI.

‡Calculations assume 0.5 - 2.0 kg weight gain in the first trimester for all pre-pregnancy BMI categories.

**Table 4:** Fetal size and body composition (median [interquartile range]) at 36 ±1 weeks gestation according to maternal weight gain below, within or above the Institute of Medicine's 2009[*] recommended target range for 36 weeks gestation[†] based on pre-pregnancy body mass index (BMI) category (n=157).

| **Pre-pregnancy BMI** | **Underweight n=8[‡]** | **Normal range n=79** | | | **Overweight n=37** | | | **Obese n=33** | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Weight Gain Category | Above n=7 | Below n=9 | Within n=33 | Above n=37 | Below n=7 | Within n=4 | Above n=26 | Below n=7 | Within n=11 | Above n=15 |
| *Markers of fetal size* | | | | | | | | | | |
| Head circumference (mm) | 320.0 [12.8] | 314.7 [12.9] | 324.4 [17.9][§] | 325.4 [12.4] | 322.4 [19.4] | 325.7 [9.9] | 322.7 [16.3] | 321.6 [14.6] | 325.8 [23.3] | 329.9 [16.6] |
| Biparietal diameter (mm) | 88.1 [5.5] | 86.2 [9.5] | 88.1 [4.5] | 90.0 [6.3] | 89.1 [3.9] | 89.3 [1.2] | 89.5 [3.0] | 87.0 [5.4] | 91.2 [5.5] | 91.7 [6.2] |
| Abdominal circumference (mm) | 315.1 [37.7] | 304.7 [14.9] | 330.1 [21.4][§] | 340 [21.4][\|\|] | 328.0 [25.9] | 330.5 [9.1] | 328.7 [18.4] | 328.9 [28.8] | 336.1 [29.6] | 337.3 [24.1] |
| Femur length (mm) | 67.3 [3.7] | 66.2 [4.1] | 69.1 [3.6] | 69.6 [4.6] | 70.3 [7.2] | 69.2 [2.3] | 70.0 [4.0] | 71.2 [4.2] | 70.0 [4.4] | 70.4 [6.0] |
| *Markers of fetal body composition* | | | | | | | | | | |
| Abdominal fat area ($cm^2$) | 15.1 [1.1] | 12.2 [2.5] | 15.3c [2.8][§] | 16.3 [4.1][\|\|] | 14.0 [7.8] | 18.4 [4.1] | 16.0 [5.3] | 17.6 [8.4] | 18.3 [4.6] | 16.1 [3.1] |
| Abdominal lean area ($cm^2$) | 63.9 [3.3] | 61.5d [7.9] | 69.0d [8.1][§] | 72.8 [10.7][\|\|] | 69.3 [13.1] | 70.8 [4.6] | 70.1 [9.0] | 66.5 [14.7] | 74.3 [15.4] | 75.4 [9.4] |
| Mid-thigh fat area ($cm^2$) | 8.6 [0.9] | 8.6 [2.8] | 9.5 [3.9] | 9.2 [2.9] | 7.4 [6.6] | 10.8 [4.9] | 8.9 [2.0] | 8.5 [4.7] | 9.7 [3.8] | 8.5 [5.0] |
| Mid-thigh lean area ($cm^2$) | 8.8 [4.7] | 9.0 [2.1] | 9.5 [2.9] | 10.1 [2.4] | 9.2 [4.7] | 10.4 [2.1] | 9.7 [3.3] | 9.3 [2.1] | 9.7 [2.3] | 10.8 [2.9] |

[*]Rasmussen KM, Yaktine AL, editors. Weight gain during pregnancy: reexamining the guidelines. Washington DC: Institute of Medicine, National Academy of Sciences; 2009.

[†]Recommended weight gain calculated at 36 weeks gestation assumes 0.5 - 2.0 kg weight gain in the first trimester for all pre-pregnancy BMI categories and then a weekly weight gain range for the second and third trimester based on pre-pregnancy BMI.

[‡]n=1 pre-pregnancy BMI category 'underweight' and was 'within' the recommended target weight gain; data not shown.

[§]Higher for women with a 'normal range' pre-pregnancy BMI gaining 'within' the recommendation compared to 'below', *P*<.05, Wilcoxon rank-sum tests.

[||]Higher for women with a 'normal range' pre-pregnancy BMI gaining 'above' the recommendation compared to 'within', *P*<.05, Wilcoxon rank-sum tests.

**Table 5:** Fetal size and body composition at 36 ±1 weeks gestation and at birth according to maternal weight gain below, within or above the Institute of Medicine's (IOM) 2009* recommended target range for pregnancy weight gain at 36 weeks gestation† (n=157).

| Weight Gain Category | Below n=23 | Within n=49 | Above n=85 | *P*‡ |
|---|---|---|---|---|
| | | Median [interquartile range] | | |
| *Markers of fetal size* | | | | |
| Head circumference (mm) | 320.3 [14.9] | 324.7 [18.7] | 325.4 [14.1] | .099 |
| Biparietal diameter (mm) | 88.7 [5.4] | 88.7 [4.3] | 89.8 [6.0] | .041 |
| Abdominal circumference (mm) | 319.0 [33.0] | 330.6 [18.0] | 332.2 [26.2] | .015 |
| Femur length (mm) | 68.2 [5.3] | 69.2 [3.7] | 69.6 [4.7] | .054 |
| *Markers of fetal body composition* | | | | |
| Abdominal fat area ($cm^2$) | 13.5 [6.9] | 15.4 [3.7] | 16.1 [3.8] | .463 |
| Abdominal lean area ($cm^2$) | 65.4 [13.4] | 69.4 [10.4] | 71.6 [11.8] | .024 |
| Mid-thigh fat area ($cm^2$) | 8.5 [3.0] | 9.5 [4.0] | 8.9 [2.2] | .372 |
| Mid-thigh lean area ($cm^2$) | 9.2 [2.5] | 9.7 [2.7] | 10.1 [2.9] | .728 |
| *Birth outcomes* | | | | |
| Weight (g) | 3120 [715] | 3475 [620] | 3673 [608] | <.001 |
| Length (cm) | 50.8 [2.5] | 51.0 [3.0] | 52.0 [3.0] | .034 |
| Head circumference (mm) | 34.0[2.0] | 34.5 [2.5] | 35.0 [2.0] | .085 |

*Rasmussen KM, Yaktine AL, editors. Weight gain during pregnancy: reexamining the guidelines. Washington DC: Institute of Medicine, National Academy of Sciences; 2009.

†Recommended weight gain calculated at 36 weeks gestation assumes 0.5 - 2.0 kg weight gain in the first trimester for all pre-pregnancy BMI categories and then a weekly weight gain range for the second and third trimester based on pre-pregnancy BMI.

‡Weight gain category (below, within, above) was used as the predictor of each of the fetal variables. Analysis of Covariance (ANCOVA) models have been adjusted for pre-pregnancy BMI, gestational age, fetal sex, smoking, parity, diabetes, and socio-economic status from postcode.

**Figure**

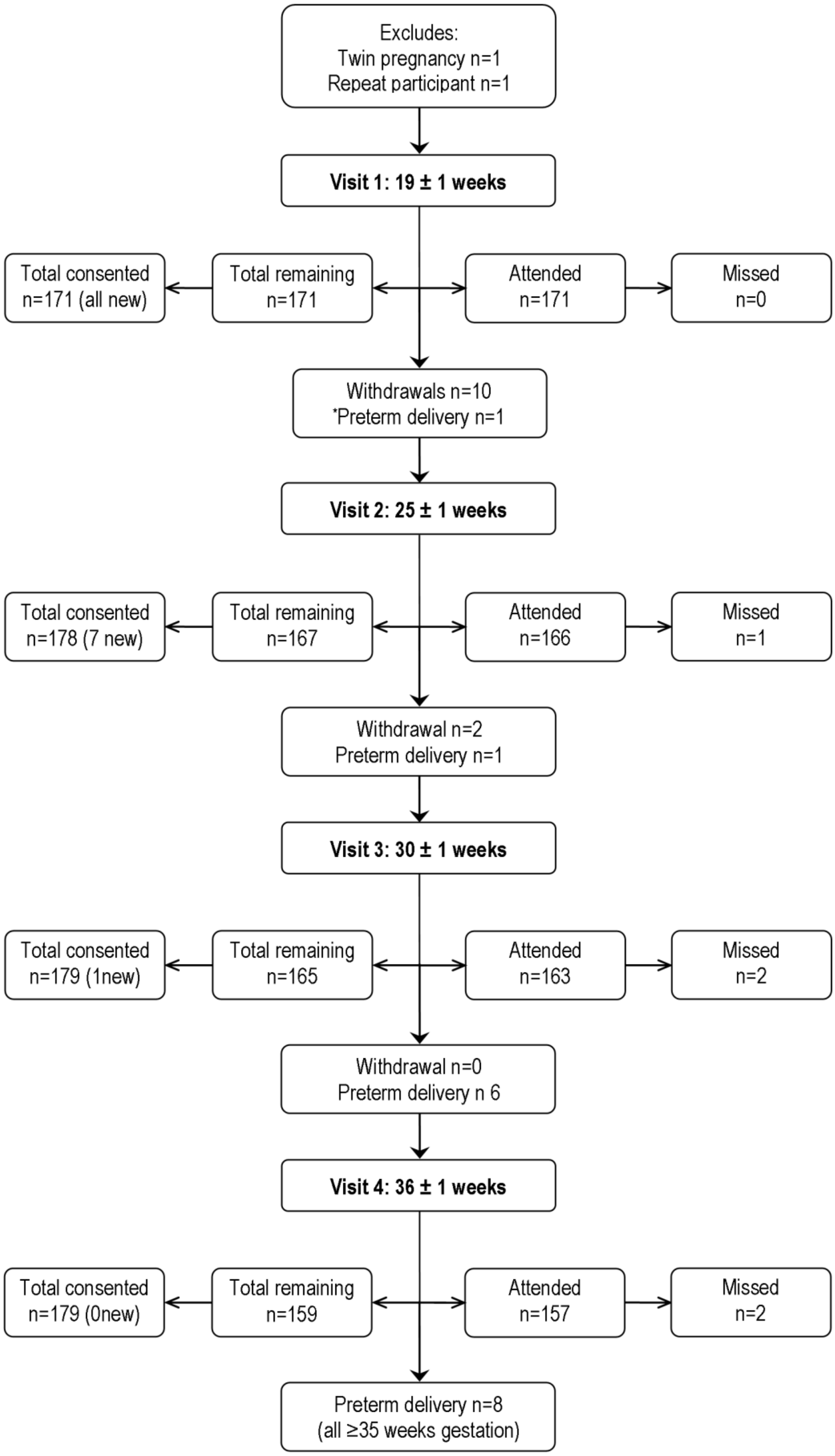



**Figure 1**

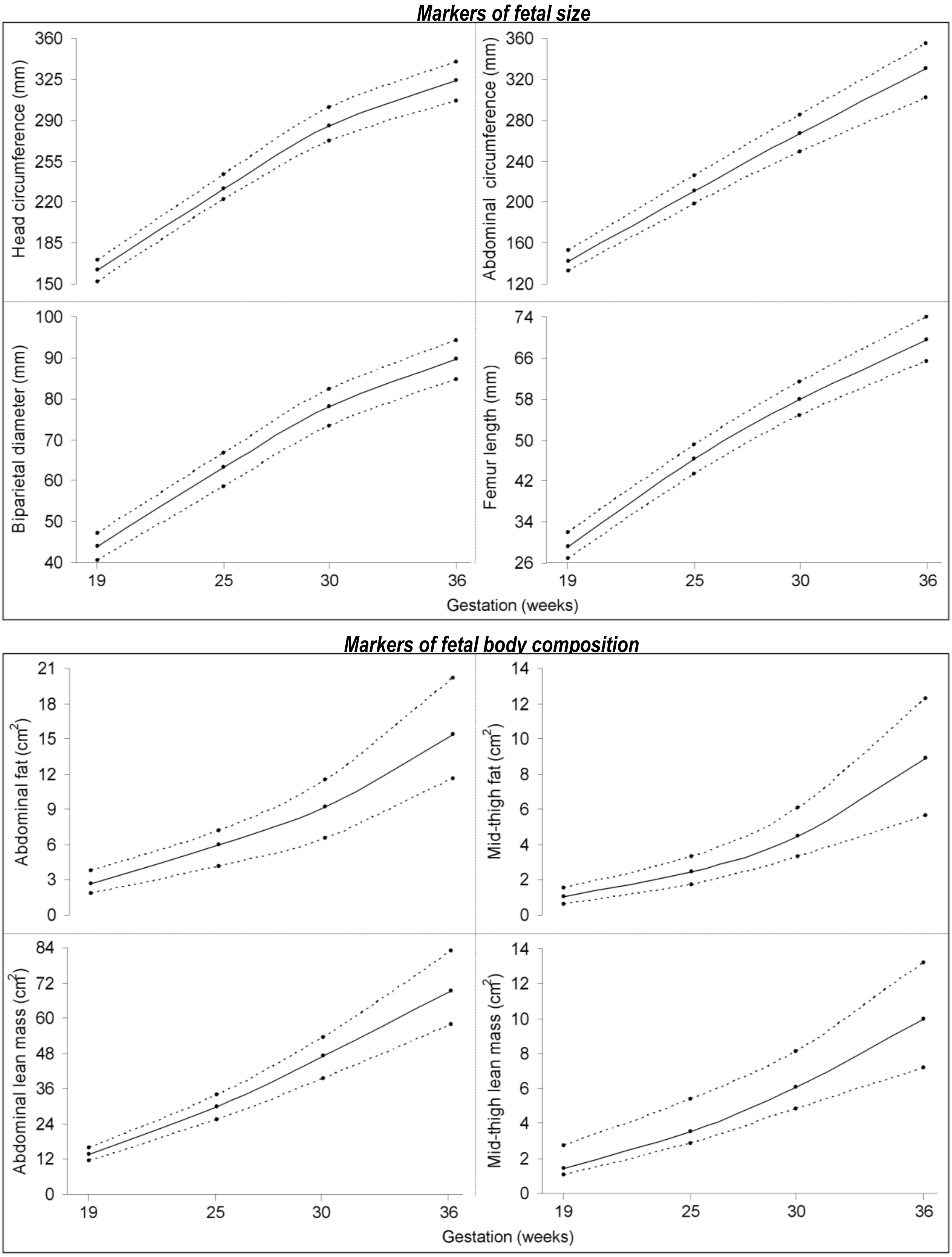
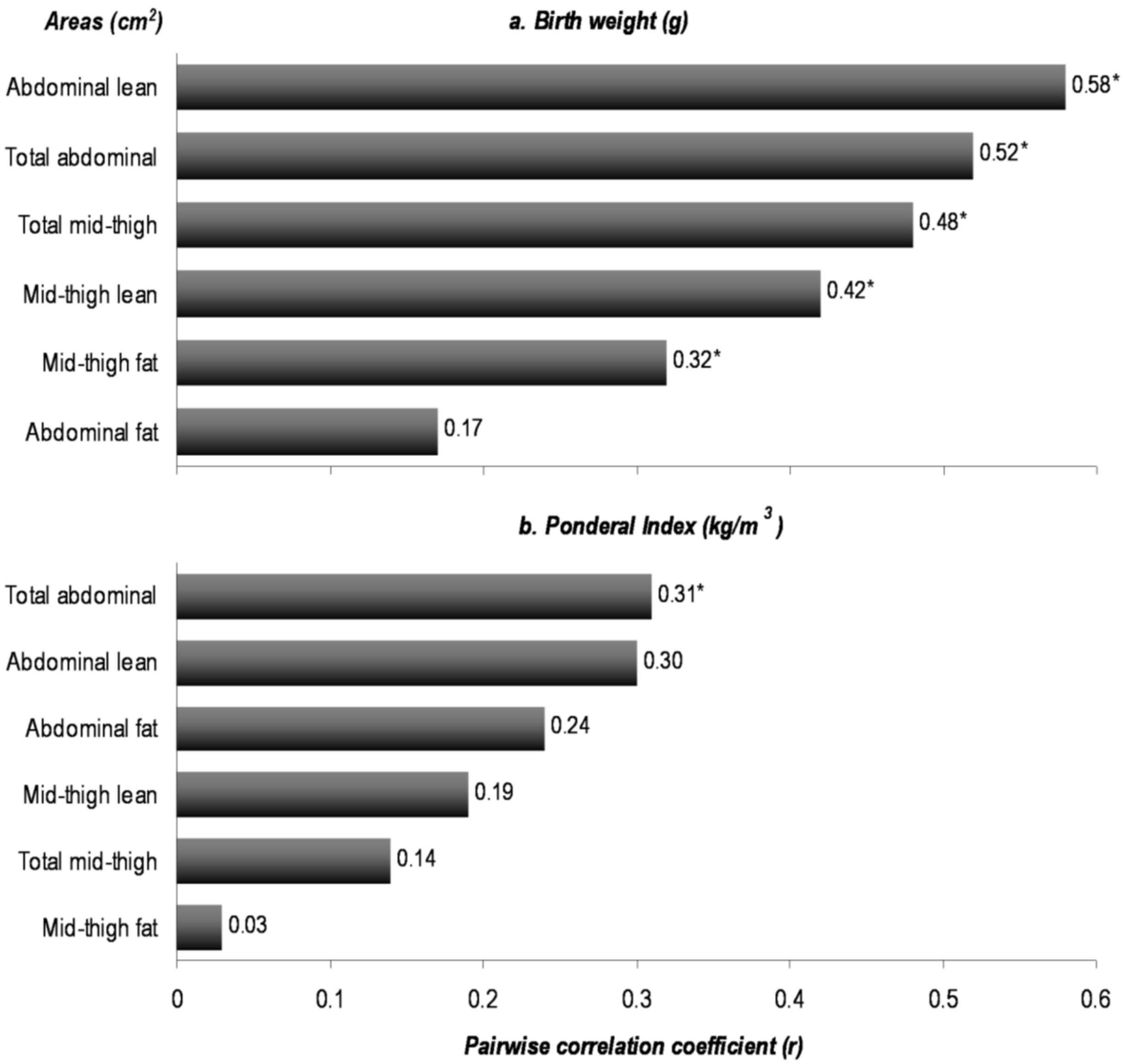

Markers of fetal size
Head circumference (mm)
Abdominal circumference (mm)
Biparietal diameter (mm)
Femur length (mm)
Gestation (weeks)
Markers of fetal body composition
Abdominal fat (cm2)
Mid-thigh fat (cm2)
Abdominal lean mass (cm2)
Mid-thigh lean mass (cm2)
Gestation (weeks)

**Figure 2**



Areas ($cm^2$)
a. Birth weight (g)
Abdominal lean
Total abdominal
Total mid-thigh
Mid-thigh lean
Mid-thigh fat
Abdominal fat
0.58*
0.52*
0.48*
0.42*
0.32*
0.17
b. Ponderal Index ($kg/m^3$)
Total abdominal
Abdominal lean
Abdominal fat
Mid-thigh lean
Total mid-thigh
Mid-thigh fat
0.31*
0.30
0.24
0.19
0.14
0.03
0
0.1
0.2
0.3
0.4
0.5
0.6
Pairwise correlation coefficient (r)


**Figure 3**