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Second Trimester Estimated Fetal Weight and Fetal Weight Gain Predict Childhood Obesity

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Abstract

Objective—To determine the extent to which fetal weight during mid-pregnancy and fetal weight gain from mid-pregnancy to birth predict adiposity and blood pressure (BP) at age 3 years.

Study design—Among 438 children in the Project Viva cohort, we estimated fetal weight at 16–20 (median 18) weeks gestation using ultrasound biometry measures. We analyzed fetal weight gain as change in quartile of weight from the second trimester until birth, and we measured height, weight, subscapular and triceps skinfold thicknesses and BP at age 3.

Results—Mean (SD) estimated weight at 16–20 weeks was 234 (30) grams and birth weight was 3518 (420) grams. In adjusted models, weight estimated during the second trimester and at birth were associated with higher BMI z-scores at age 3 years (0.32 units [95% C.I. 0.04, 0.60] and 0.53 units [95% C.I. 0.24, 0.81] for the highest v. lowest quartile of weight). Infants with more rapid fetal weight gain and those who remained large from mid-pregnancy to birth had higher BMI z-scores (0.85 units [95% C.I. 0.30, 1.39] and 0.63 units [95% C.I. 0.17, 1.09], respectively) at age 3 than infants who remained small during fetal life. We did not find associations between our main predictors and sum or ratio of subscapular and triceps skinfold thicknesses or systolic BP.

Conclusion—More rapid fetal weight gain and persistently high fetal weight during the second half of gestation predicted higher BMI z-score at age 3 years. The rate of fetal weight gain throughout pregnancy may be important for future risk of adiposity in childhood.

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Keywords

childhood blood pressure; cohort

Human and animal studies suggest that developmental programming during critical periods of rapid growth, such as the prenatal period and infancy, influence the risk of cardiometabolic disease in later life. [1, 2] Although many studies show that faster weight gain in early infancy predicts higher body mass index (BMI), higher blood pressure (BP), and increased risk for poor metabolic outcomes childhood and adulthood, [3–6] there are few studies of prenatal period.

Examining *change* in fetal weight is important because a single measure of weight at birth is inadequate to represent intrauterine weight gain patterns. For instance, an infant born at the 90th percentile at birth may represent a fetus who was large throughout gestation or one who gained weight rapidly only in the last trimester. Few studies have explored associations of fetal weight gain and childhood outcomes. In one study of Dutch children, no association was found between fetal weight gain during the third trimester and abdominal adiposity at age 2 years. [13] This study only measured change in fetal weight from the third trimester until birth only. Measurements of fetal weight gain over both the second and third trimester, reflecting a longer period of fetal growth may be more informative. No associations between static measures of fetal weight or change in fetal weight from the second trimester until birth and childhood systolic BP were found among children in the same cohort.[14]

A better understanding of the association of fetal weight gain and childhood outcomes may enable us to identify risk factors for obesity and high BP in the earliest stages of life. The purpose of this study was to evaluate the extent to which estimated fetal weight in the second trimester and fetal weight gain from the second trimester until birth predict childhood obesity and BP. We hypothesized that more rapid fetal weight gain would be associated with higher BMI and BP in childhood as rapid weight gain in early infancy has similarly been associated with obesity and higher BP. [4, 5]

Methods

We studied participants in Project Viva, a prospective, observational, cohort study of gestational diet, pregnancy outcomes and offspring health.[15] Details of recruitment and retention procedures are available elsewhere. [15] All mothers provided written informed consent. The human subjects committees of Harvard Pilgrim Health Care, Brigham and Women's Hospital and Beth Israel Deaconess Medical Center approved the study protocols. Of the 2128 women who delivered a live infant, we excluded 45 infants born < 34 weeks gestation (Table I). Of the 2083 remaining women, 1653 (79%) had at least one fetal ultrasound at 16 to 20 weeks gestation. To avoid using the ultrasound data for dating as well as growth, we excluded 203 women whose ultrasound indicated a gestational age that was 10 days of the predicted due date based on last menstrual period (LMP). Of those, we further excluded 678 whose ultrasound was missing one or more measures of fetal abdominal diameter, biparietal diameter, or femur length, which are measures needed to calculate estimated fetal weight (EFW). Because these ultrasounds were clinical studies intended for a fetal survey to detect structural anomalies, most of the missing biometric data was due to missing abdominal diameter (673 of 678). The biparietal diameter and femur length for the 772 participants with all three measures were similar to those among the 678 participants we excluded (41.0 v. 39.9 mm and 26.8 v. 26.9 mm, respectively), suggesting no systematic bias by availability of biometric measures. Finally, 334 participants were missing measurements of BMI (kg/m²) or BP (mmHg) at age 3, yielding a final cohort of

438 mother-fetus-child subjects for analysis. Compared with the participants missing age 3 outcome measures, the mothers in the final cohort were older (mean age 31.1 v. 30.1 years), more likely to be married (92% v. 86%), be college graduates (67% v. 51%), and have household incomes > \$70,000 (66% v. 53%). Children were more likely to be of white race (61% v. 51%). Other maternal and child characteristics, including maternal BMI, did not differ among included and excluded groups.

We abstracted measurements of abdominal diameter (AD), biparietal diameter (BPD) and femur length (FL) from fetal ultrasounds obtained at 16 to 20 weeks gestation, and birth weight from the hospital medical record. We converted abdominal diameter to abdominal circumference (AC) using the geometric formula: $Circumference = \pi r^2$. We calculated EFW using the formula by Hadlock et al: $\text{Log}_{10} \text{ EFW} = 1.335 - 0.0034(\text{AC})(\text{FL}) + 0.0316 (\text{BPD}) + 0.0457 (\text{AC}) + 0.1623 (\text{FL})$. [16] We used this formula because it has previously been found to have the least bias and best precision in predicting measured weight at birth compared with 13 other formulas. [17].

During an in-person visit at age 3 years, trained research assistants weighed children with a digital scale (model 881; Seca, Hamburg, Germany) and obtained height and subscapular and triceps skinfold measurements using standardized techniques. [18] They used a standardized protocol to measure child BP with a Dinamap Pro100 (Critikon, Inc, Tampa, FL) automated oscillometric recorder, taking up to 5 measurements 1 minute apart in each child. The child's position, activity level, the extremity used, cuff size, and measurement sequence number at the time of BP measurement were recorded. Research staff participated in biannual in-service training to ensure measurement validity (I.J. Shorr, MPS personal oral communication, 2004–2007). Inter- and intra-rater measurement error were within published reference ranges. [19]

Our main outcomes were adiposity and BP at age 3 years. We calculated age- and sex-specific BMI z-score using U.S. national reference data [20] and used this measure as a continuous variable as well as examined obesity (age- and sex-specific BMI 95th percentile). We used the sum and ratio of subscapular (SS) and triceps (TR) skinfold thicknesses to represent adiposity and central adiposity, respectively. [21] We used systolic BP at age 3 years as our main BP outcome because it predicts later BP better than diastolic BP, and is measured with more validity in children. [22]

Mothers reported information about their age, education, household income, marital status, parity, duration of breastfeeding at one year, smoking status and child sex and race/ethnicity in structured interviews and questionnaires. We calculated prepregnancy BMI (kg/m^2) from maternal self-report of height and prepregnancy weight. We calculated total gestational weight gain as the difference between the last recorded clinical weight before delivery and the self-reported prepregnancy weight. We previously reported the validity of self-reported prepregnancy weight in our cohort. [23] We categorized women as having gained inadequate, adequate, or excessive weight according to 2009 Institute of Medicine guidelines for weight gain during pregnancy. [24] We obtained glucose tolerance status based on glycemic screening from the medical record. Definitions of glucose tolerance status are described elsewhere. [25] We abstracted the first three maternal systolic BP levels after 28 weeks gestation from the medical record and calculated the mean.

Statistical Analysis

Because weight is highly correlated with gestational age, we first adjusted EFW and birth weight for gestational age at each measurement time point. We then ranked EFW and birth weight into sex-specific quartiles, coded 1 to 4. To represent fetal weight gain, we created a

16 category variable according to quartile of second trimester EFW and birth weight, with participants in the lowest quartile of both EFW and birth weight as the reference group.

We examined bivariate relationships among our main exposures, other covariates, and our outcomes. For trend p-values, we used Mantel-Haenszel Chi-Square for categorical characteristics and linear regression for continuous outcomes. After testing model assumptions, we used multivariable linear and logistic regression models to examine independent associations of second trimester EFW, birth weight and, separately, the change in fetal weight quartile from the second trimester until birth with our main outcomes. To estimate the associations with systolic BP at age 3 years, we used mixed effects regression models incorporating all available BP measurements from each child as repeated outcome measurements. Model 1 included the main exposure and child's sex and age at the 3-year visit. Model 2 also included maternal age, marital status, education, household income and child race/ethnicity. Model 3 included factors known to affect fetal growth which may mediate the relationship between fetal weight gain and childhood BMI and BP including maternal prepregnancy BMI, gestational glucose tolerance and weight gain, maternal blood pressure in the third trimester, and smoking status. We also included breastfeeding duration as a potential confounder (as a proxy for maternal behaviors) on the associations between fetal growth and child obesity and BP outcomes. All models estimating BP were adjusted for BP measurement conditions including cuff size, extremity used, child state and position, and measurement sequence number as well as child height.

Next we used parameter estimates from our multivariate model to estimate the predicted probability of obesity at age 3 years in 9 categories of fetal weight gain based on tertiles of second trimester EFW and birth weight. We used tertiles instead of quartiles for this analysis of the dichotomous outcomes because some cells contained small numbers. We used typical characteristics from our cohort as values of covariates. We used mean values for continuous variables and mode values for categorical variables.

Finally, we performed a sensitivity analysis with further restriction of our cohort to mothers who reported that they were "certain" of their last "normal" menstrual period during interviewing in the first trimester (N = 347). Calculations of EFW during the second trimester depend on accurate gestational age. We felt that maternal report of certainty of normalcy of their last menstrual period may be more accurate to predict gestational age than concordance with second trimester ultrasound prediction of due date. We found no differences in our effect estimates and show findings from our original cohort of 438 mother-infant pairs. We performed data analysis with SAS 9.3 (SAS Institute, Cary NC).

Results

The mean (SD) gestational age at the second trimester 16–20 week ultrasound was 18.2 (0.7) weeks (Table I). Fetal biometry measures were 124.9 (11.4) mm for abdominal circumference, 41.4 (2.3) mm for biparietal diameter, and 26.9 (2.0) mm for femur length. EFW at 16–20 weeks adjusted for gestational age was 234 (30) grams and birth weight adjusted for gestational age was 3518 (420) grams. At age 3 years, mean (SD) BMI was 16.5 (1.4) kg/m² and BMI z-score was 0.43 (0.99) units. Nine percent of the children had BMI 95th percentile for age and sex. The mean (SD) sum and ratio of subscapular and triceps skinfold thicknesses was 16.4 (4.0) mm and 0.64 (0.15), respectively and systolic BP at was 92.3 (10.7) mmHg.

On bivariate analysis, infants in the highest EFW quartile had the highest mean birth weight and shortest mean gestational length (Table I). Mothers of children in the highest quartile of EFW during the second trimester were older, breastfed longer, and more were married or

cohabitating compared with mothers of children in the lowest quartile of EFW (Table I). More infants in the highest quartile of EFW were white and fewer were black than children in the first quartile of EFW. We did not observe differences in prepregnancy BMI, gestational glucose tolerance, third trimester systolic BP, smoking status, parity, household income, education, child sex or height according to quartile of EFW (Table I).

In a multivariable linear regression model adjusted for sex and exact age at the 3-year visit, we found a 0.32 (95% C.I., 0.06, 0.59) unit higher BMI z-score among infants with EFW in the highest versus lowest quartile (Table II, Model 1). Estimates were similar with additional adjustment for demographic variables (0.34 [95% C.I. 0.07, 0.61]) (Table II, Model 2), as well as for maternal factors which affect fetal growth including maternal prepregnancy BMI and glucose tolerance, gestational weight gain, smoking status and third trimester BP and breastfeeding duration (0.32 [95% CI 0.04, 0.60]) (Table II, Model 3). In a logistic model adjusted for sex and age, the odds ratio for obesity (BMI 95th percentile v. < 85th percentile) was 4.77 (95% C.I. 1.68, 13.51) among children with EFW in the highest versus lowest quartile. Estimates were similar with additional adjustment for demographic variables (OR 5.16 [95% C.I. 1.72, 15.46]) (Table II, Model 2) and slightly attenuated with additional adjustment for maternal factors which affect fetal growth and breastfeeding duration (OR 4.50 [95% C.I. 1.38, 14.68]) (Table II, Model 3). We did not find associations of EFW quartile with the sum and ratio of subscapular and triceps skinfold thicknesses or systolic BP at age 3 (Table II).

Adjusting for sex, age and gestational age at birth, children in the highest versus lowest quartile of birth weight had higher BMI z-scores (0.44 [95% C.I. 0.18, 0.71]) and higher odds of obesity (OR 4.61 [95% C.I. 1.62, 13.18]) (Table II, Model 1). The associations did not change with adjustment for demographics, maternal factors which affect fetal growth, or breastfeeding duration (Table II, Model 3). We did not find associations between birth weight and sum and ratio of subscapular and triceps skinfold thicknesses or systolic BP (Table II, Model 3).

In models that examined both EFW and birth weight, we found that changing from the 1st quartile in the second trimester to the 4th quartile at birth, which represents more rapid fetal weight gain, was associated with a 0.85 unit (95% C.I. 0.30, 1.39) higher increase in BMI z-score, than remaining in the 1st quartile at both time points (Table III). We also found that infants who remained relatively large, i.e. those with weights in the 4th quartile at both time points, had higher BMI z-scores compared with those who were in the lowest quartile at both time points (0.63 [95% C.I. 0.17, 1.09]). Infants who remained in the 2nd quartile at both time points (0.86 [95% C.I. 0.34, 1.37]) and similarly had higher BMI z-scores. We found a more modest association between fetal weight gain and BMI z-score among infants who dropped from the 4th quartile in mid-pregnancy to the 3rd quartile at birth (0.59 [95% C.I. 0.13, 1.06]) and those who dropped from the 4th quartile to the 2nd quartile (0.54 [95% C.I. 0.02, 1.06]) (Table III). We did not find associations between more rapid fetal weight gain and systolic BP at age 3 years, but we found that children who started in the 4th quartile of EFW in the second trimester and dropped to the 2nd quartile at birth had systolic BP 5.53 mmHg (95% C.I. 1.08, 9.98) higher than the reference group (Table III).

In Figure 2, we show that the covariate-adjusted predicted probability of obesity (< 95th percentile v. < 85th percentile at age 3 years) was highest for infants who remained relatively large in the highest weight tertile at the second trimester and at birth (15.0%) and also high for infants with more rapid fetal weight gain who changed from the first to the third tertile in the second half of pregnancy (13.9 %). The predicted probability of obesity was lowest among infants who remained in the lowest tertile in the second trimester and second tertile at

birth (0%) and also low among infants who remained in the lowest tertile at both time points (0.8%).

Discussion

Our findings differ from those of Durmus et al of the Generation R cohort in the Netherlands who found an inverse relationship between second trimester fetal weight and ultrasound measured abdominal fat mass in the preperitoneal area, representing visceral abdominal fat at age 2, but did not find associations between fetal weight, fetal weight gain and other ultrasound measures of central adiposity which are related to adverse metabolic outcomes. [13] We found positive associations between second trimester weight, more rapid fetal weight gain and childhood BMI, but no association between the ratio of subscapular to triceps skinfold thicknesses, another measure of central adiposity. The participant characteristics including maternal age, BMI, maternal smoking status, gestational age, birth weight and childhood BMI were similar in both our own and the Generation R cohort.[13] Thus, the varied findings between fetal weight and childhood obesity could be attributed to the different outcome measures used in each cohort. Additional studies among populations at higher risk of childhood obesity are needed to further understand the relationship between fetal weight, fetal weight gain and childhood obesity.

In our 16-category analysis of fetal weight gain, we found the strongest associations with childhood obesity among infants who moved from the 1st to the 4th quartile during the second half of gestation. This may suggest that the smallest fetuses with rapid weight gain have the greatest risk of long-term obesity outcomes. Alternatives to this interpretation are that we had relatively few subjects in each of the 16 categories, resulting in somewhat unstable estimates, or that we inadequately modeled fetal weight gain, as we had only 2 measurement time points and clinical fetal biometry measurements. Studies with multiple fetal biometry measurements and long term childhood follow-up may better characterize patterns of fetal growth in relation to childhood outcomes.

In addition to infants with more rapid fetal weight gain, persistently large fetuses also had higher BMI z-scores in childhood. This suggests that fetal weight gain from conception to mid-pregnancy may also be an important predictor of childhood obesity. Currently, studies show that higher maternal BMI is associated with higher EFW in mid-pregnancy [26] and older maternal age and higher parity are associated with longer crown-rump lengths, representing larger fetuses, in early pregnancy.[27] Further recognition of modifiable predictors of fetal weight gain in early pregnancy may provide new clues for childhood obesity prevention.

Contrary to our hypothesis, we did not find associations of EFW, birth weight, or fetal weight gain with childhood BP. van Houten et al of the Generation R cohort similarly reported no association between BP at age 2 with fetal weight gain from the second or third trimester until birth.[14] Others have described an inverse association with birth weight and blood pressure in later childhood and adulthood. [9, 28–30] Authors propose that low birth weight may represent fetal under-nutrition or relative fetal growth restriction and that this stressful intrauterine environment leads to higher blood pressure later in life.[9] These studies used birth weight as a proxy for fetal growth. We did note that dropping from the 4th to the 2nd quartile was associated with increased systolic BP, but this result was not consistent across other quartiles, and may be a chance finding. We did not evaluate BP among children older than age 3 and it is possible that fetal growth may be related to BP in later childhood. However, we found previously in our cohort that more rapid infant weight gain in the first six months of life was associated with higher childhood blood pressure at

age 3.[5] Alternatively, postnatal rather than prenatal growth may be more important for childhood BP.

Strengths of this study include its prospective study design and evaluation of multiple prenatal factors that can alter fetal growth as well as many potential confounders. We carefully measured BP and anthropometry measures in childhood. Limitations of the study include the use of clinical ultrasound measures that were intended to detect structural anomalies, which substantially reduced the number of participants available for analysis. Although we did not find differences in the fetal biometry measurements of the remaining participants, we cannot exclude the possibility of selection bias. Error in fetal biometry measurement was likely non-differential, a conservative bias. Because we used clinical ultrasound data, we evaluated EFW only at one time point in the second trimester. EFW during other times of gestation would allow for more complex modeling of fetal weight gain and may elucidate whether different periods of growth during gestation are more or less important for later outcomes. We did not evaluate additional measures of body composition other than BMI-z score and sum and ratio of SS and TR skinfold thicknesses. Finally, the relatively high socioeconomic status and few minorities in our cohort may reduce generalizability.

This study raises the possibility that greater fetal weight in mid-pregnancy and fetal weight gain either before or after this time point may be important risk factors for childhood obesity and its consequences. The need exists to understand more about the modifiable predictors of intrauterine weight gain and the timing of such weight gain in relation to long-term child outcomes, and refine better methods to measure fetal body composition throughout gestation.

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Abbreviations

BMI	Body mass index
BP	Blood pressure
EFW	Estimated fetal weight
LMP	Last menstrual period
AD	Abdominal diameter
AC	Abdominal circumference
BPD	Biparietal diameter
FL	Femur length
SS + TR	Sum of subscapular and triceps skinfold thicknesses
SS/TR	Ratio of subscapular and triceps skinfold thicknesses

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Figure 1.

US= ultrasound; LMP= last menstrual period; AD = abdominal diameter; BPD= biparietal diameter; FL= femur length; EFW= estimated fetal weight; BMI= body mass index; BP= blood pressure

Figure 2.

Predicted probability of obesity (BMI $\geq 95^{\text{th}}$ v. $< 85^{\text{th}}$ percentile) at age 3 years according to sex-specific tertile of second trimester estimated fetal weight (EFW) and birth weight, with adjustment for gestational age at both time points, maternal age, education, marital status, prepregnancy body mass index, glucose tolerance, gestational weight gain, third trimester systolic BP, and smoking during pregnancy, household income, breastfeeding duration, and child sex, race/ethnicity and exact age at the 3 year visit. We used typical participant characteristics for covariates, including mean values for continuous variables and mode values for categorical variables.

Table 1
 Characteristics of 438 Mother-Child Pairs According to Sex-Specific Quartile of Second Trimester Estimated Fetal Weight

	Overall	Sex-Specific Quartile of Second Trimester EFW				P for trend
		1	2	3	4	
N	438	108	110	110	110	
Maternal Characteristics						
		Mean ± SD				
Maternal age, years	31.0 ± 4.8	29.9 ± 5.4	31.0 ± 4.3	31.4 ± 4.8	31.7 ± 4.4	<0.001
Prepregnancy BMI, kg/m²	24.7 ± 5.1	24.4 ± 5.3	25.3 ± 5.8	24.6 ± 4.5	24.5 ± 4.5	0.91
Third Trimester Systolic BP, mmHg	110.6 ± 8.4	109.7 ± 8.1	111.3 ± 8.7	110.5 ± 8.4	110.9 ± 8.5	0.43
		N (%)				
Gestational weight gain, Institute of Medicine category						
Excessive	249 (57)	55 (51)	63 (58)	68 (62)	63 (58)	0.35
Adequate	142 (33)	40 (37)	35 (32)	35 (32)	32 (29)	
Inadequate	44 (10)	13 (12)	11 (11)	6 (6)	14 (13)	
Gestational glucose tolerance						
Gestational Diabetes	20 (5)	4 (4)	7 (6)	5 (5)	4 (4)	0.30
Impaired Glucose Tolerance	14 (3)	4 (4)	4 (4)	5 (5)	1 (1)	
Transient Hyperglycemia	34 (8)	7 (7)	6 (5)	11 (11)	10 (9)	
Normal Glucose Tolerance	368 (84)	92 (65)	93 (85)	88 (81)	95 (77)	
Smoked during pregnancy	49 (11)	13 (12)	13 (12)	11 (10)	12 (11)	0.54
Nulliparous	232 (53)	63 (58)	54 (49)	63 (57)	52 (47)	0.24
College graduate	293 (67)	68 (63)	74 (67)	79 (72)	72 (66)	0.55
Household income >\$70,000	262 (66)	57 (59)	67 (60)	76 (75)	62 (62)	0.44
Married or cohabitating	401 (92)	92 (86)	102 (93)	104 (95)	103 (95)	0.02

	Overall	Sex-Specific Quartile of Second Trimester EFW				P for trend
		1	2	3	4	
<i>Second Trimester Fetal Characteristics, adjusted for gestational age, 16–20 wks</i>						
		<i>Mean ± SD</i>				
Gestational age at ultrasound, weeks	18.2 ± 0.7	18.2 ± 0.7	18.1 ± 0.7	18.2 ± 0.7	18.3 ± 0.7	0.09
Estimated fetal weight, grams	233.8 ± 30.0	198.9 ± 17.0	225.3 ± 5.2	241.4 ± 4.7	269.0 ± 26.4	<0.0001
Abdominal circumference, mm	124.9 ± 11.4	112.6 ± 10.8	122.5 ± 3.9	128.2 ± 3.8	135.9 ± 9.2	<0.0001
Biparietal diameter, mm	41.1 ± 2.3	39.2 ± 1.6	40.8 ± 1.7	41.8 ± 1.8	42.8 ± 2.3	<0.0001
Femur length, mm	26.9 ± 2.0	24.9 ± 1.6	26.5 ± 1.1	27.3 ± 1.3	28.8 ± 1.8	<0.0001
<i>Infant/Child Characteristics</i>						
Gestational age at birth, weeks	39.7 ± 1.4	40.1 ± 1.3	39.7 ± 1.5	39.6 ± 1.5	39.4 ± 1.4	<0.0001
Birth weight adjusted for gestational age, grams	3518 ± 420	3329 ± 434	3500 ± 373	3540 ± 377	3699 ± 415	<0.0001
BMI age 3 years, kg/m ²	16.5 ± 1.4	16.3 ± 1.2	16.5 ± 1.7	16.4 ± 1.3	16.7 ± 1.4	0.08
BMI z-score age 3 years	0.43 ± 0.99	0.32 ± 0.91	0.44 ± 1.12	0.36 ± 0.95	0.62 ± 0.97	0.06
SS + TR, mm	16.4 ± 4.0	16.3 ± 3.7	16.7 ± 4.4	16.2 ± 3.3	16.3 ± 4.5	0.81
SS/TR	0.64 ± 0.15	0.66 ± 0.15	0.62 ± 0.17	0.65 ± 0.14	0.64 ± 0.14	0.58
Height, cm	97.6 ± 4.6	97.1 ± 4.4	97.6 ± 4.9	97.1 ± 4.1	98.5 ± 4.9	0.05
Systolic BP, mmHg	92.3 ± 10.7	92.4 ± 11.8	92.8 ± 10.9	91.5 ± 10.2	92.4 ± 9.7	0.78
		<i>N (%)</i>				
Obesity (BMI 95 th percentile for age and sex)	40 (9)	5 (5)	10 (9)	6 (6)	19 (18)	0.01
Female sex	223 (51)	55 (51)	56 (51)	56 (51)	56 (51)	1.00
Race/ethnicity						
White	265 (61)	56 (52)	68 (62)	72 (65)	69 (63)	0.04

	Overall	Sex-Specific Quartile of Second Trimester EFW				P for trend
		1	2	3	4	
Black	68 (16)	23 (21)	21 (19)	8 (7)	16 (15)	
Hispanic	29 (7)	5 (5)	10 (9)	6 (5)	8 (7)	
Other	76 (17)	24 (22)	11 (10)	24 (22)	17 (15)	
Duration of breastfeeding, months	6.7 (4.4)	5.8 (4.4)	6.6 (4.3)	7.1 (4.5)	7.4 (4.3)	0.01

EFW= estimated fetal weight; BMI= body mass index; BP = blood pressure; SS + TR= sum of subscapular and triceps skinfold thicknesses; SS/TR= ratio of subscapular and triceps skinfold thickness

Table 2
Associations of Second Trimester Estimated Fetal Weight and Birth Weight with Adiposity and Blood Pressure at Age 3 Years

	BMI	95 th percentile ^a	BMI z-score	SS + TR (mm)	SS/TR ^b	Systolic BP ^c (mmHg)
Quantile of Second Trimester EFW ^d						
	Odds Ratio (95% C.I.)			Effect Estimate (95% C.I.)		
Model 1: Age- and sex- adjusted						
1	1.0 (ref)		0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
2	1.95 (0.64, 5.98)		0.15 (−0.12, 0.41)	0.43 (−0.66, 1.51)	−4.33 (−8.48, −0.18)*	1.20 (−1.19, 3.59)
3	1.18 (0.35, 4.02)		0.04 (−0.22, 0.31)	−0.04 (−1.12, 1.04)	−1.76 (−5.91, 2.38)	−1.01 (−3.33, 1.31)
4	4.77 (1.68, 13.51)*		0.32 (0.06, 0.59)*	0.03 (−1.05, 1.12)	−2.44 (−6.63, 1.76)	0.13 (−2.20, 2.46)
Model 2: M1 + demographics ^e						
1	1.0 (ref)		0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
2	1.82 (0.57, 5.81)		0.14 (−0.13, 0.41)	0.14 (−0.96, 1.24)	−3.09 (−7.26, 1.09)	1.18 (−1.27, 3.62)
3	1.18 (0.33, 4.16)		0.08 (−0.19, 0.34)	−0.14 (−1.24, 0.96)	−0.21 (−4.38, 3.96)	−0.95 (−3.35, 1.45)
4	5.16 (1.72, 15.46)*		0.34 (0.07, 0.61)*	−0.09 (−1.21, 1.02)	−1.59 (−5.84, 2.65)	0.24 (−2.24, 2.72)
Model 3: M2 + factors that affect fetal growth ^f + breastfeeding duration						
1	1.0 (ref)		0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
2	1.62 (0.46, 5.64)		0.17 (−0.11, 0.45)	0.15 (−1.04, 1.34)	−3.63 (−8.10, 0.84)	1.02 (−1.54, 3.58)
3	0.58 (0.13, 2.56)		0.04 (−0.24, 0.32)	−0.28 (−1.47, 0.91)	0.40 (−4.07, 4.90)	−0.66 (−3.10, 1.78)
4	4.50 (1.38, 14.68)*		0.32 (0.04, 0.60)*	−0.07 (−1.28, 1.14)	−1.01 (−5.59, 3.57)	0.80 (−1.77, 3.37)
Quantile of Birth Weight ^d						
Model 1: Age- and sex- adjusted						
1	1.0 (ref)		0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
2	1.77 (0.56, 5.63)		0.11 (−0.15, 0.37)	0.29 (−0.80, 1.37)	0.00 (−4.14, 4.14)	1.57 (−0.79, 3.94)
3	2.25 (0.74, 6.89)		0.22 (−0.04, 0.48)	0.50 (−0.58, 1.59)	−2.82 (−7.00, 1.37)	1.14 (−1.21, 3.50)
4	4.61 (1.62, 13.18)*		0.44 (0.18, 0.71)*	0.47 (−0.63, 1.57)	−1.95 (−6.19, 2.29)	0.27 (−2.09, 2.63)
Model 2: M1 + demographics ^e						

	BMI	95 th percentile ^a	BMI z-score	SS + TR (mm)	SS/TR ^b	Systolic BP ^c (mmHg)
<i>Quartile of Second Trimester EFW^d</i>		<i>Effect Estimate (95% C.I.)</i>				
		<i>Odds Ratio (95% C.I.)</i>				
1		1.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
2		2.26 (0.67, 7.60)	0.15 (-0.11, 0.42)	0.31 (-0.79, 1.40)	0.75 (-3.41, 4.91)	1.69 (-0.75, 4.14)
3		2.91 (0.91, 9.32)	0.27 (0.01, 0.54)	0.45 (-0.65, 1.55)	-1.64 (-5.85, 2.57)	1.37 (-1.13, 3.87)
4		6.90 (2.24, 21.28)*	0.54 (0.27, 0.81)*	0.39 (-0.74, 1.53)	-0.39 (-4.76, 3.99)	0.69 (-1.79, 3.18)
Model 3: M2 + factors that affect fetal growth ^f + breastfeeding duration						
1		1.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)	0.0 (ref)
2		3.07 (0.79, 11.93)	0.15 (-0.12, 0.43)	0.46 (-0.73, 1.65)	1.24 (-3.23, 5.72)	1.73 (-0.88, 4.34)
3		2.76 (0.73, 10.39)	0.22 (-0.06, 0.50)	0.48 (-0.72, 1.68)	-1.19 (-5.73, 3.35)	1.81 (-0.81, 4.43)
4		10.50 (2.79, 39.54)*	0.53 (0.24, 0.81)*	0.45 (-0.80, 1.70)	-0.10 (-4.89, 4.69)	0.91 (-1.78, 3.59)

Results are from multivariate analysis of data for 438 mother-child pairs participating in Project Viva.

EFW= estimated fetal weight; BMI= body mass index; SS + TR= sum of subscapular and triceps skinfold thicknesses; SS/TR= ratio of subscapular to triceps skinfold thicknesses; BP= blood pressure

^aThe comparison group was children with BMI values in the 5th to <85th percentile

^bSubscapular to triceps skinfold thickness ratio multiplied $\times$ 100 and additionally adjusted for BMI-z score at age 3 years

^cAll models for BP adjusted for BP measurement conditions (child's state and position, extremity used, cuff size, and measurement sequence number) and height at the 3 year visit

^dSecond trimester EFW and birth weight are adjusted for gestational age at each time point

^eDemographic covariates include maternal age, education, marital status, household income, and child race/ethnicity

^fFactors that affect fetal growth include maternal prepregnancy BMI, gestational glucose tolerance, gestational weight gain, third trimester systolic BP and smoking status during pregnancy

* Denotes p -value <0.05

Table 3
Associations of Weight Gain from Second Trimester to Birth with BMI-z score and Systolic BP at Age 3 Years^a

Quartile of Second Trimester EFW	Quartile of Birth Weight							
	1		2		3		4	
	BMI-z score	Systolic BP ^b	BMI-z score	Systolic BP ^b	BMI-z score	Systolic BP ^b	BMI-z score	Systolic BP ^b
1	0.0 (ref)	0.0 (ref)	-0.03 (-0.52, 0.45)	3.73 (-0.55, 8.02)	0.23 (-0.35, 0.81)	4.21 (-0.97, 9.38)	0.85 (0.30, 1.39)*	4.20 (-0.08, 8.47)
2	0.14 (-0.34, 0.62)	2.55 (-1.76, 6.86)	0.86 (0.34, 1.37)*	4.98 (0.25, 9.71)	-0.01 (-0.49, 0.46)	4.55 (0.08, 9.01)	0.60 (0.10, 1.11)*	2.10 (-3.22, 7.42)
3	0.22 (-0.32, 0.76)	4.72(-0.68, 10.13)	-0.11 (-0.58, 0.35)	0.57 (-3.32, 4.47)	0.43 (-0.07, 0.93)	2.27 (-2.24, 6.78)	0.56 (0.04, 1.07)*	1.64 (-2.73, 6.02)
4	0.04 (-0.63, 0.71)	0.86 (-5.03, 6.74)	0.54 (0.02, 1.06)*	5.53 (1.08, 9.98)*	0.59 (0.13, 1.06)*	3.35 (-0.97, 7.66)	0.63 (0.17, 1.09)*	3.08 (-1.07, 7.23)

Results are from multivariate analysis of data for 438 mother-child pairs participating in Project Viva.

BMI= body mass index; EFW= estimated fetal weight; BP = blood pressure

^aThe multivariate model adjusted for gestational age at second trimester US and birth, maternal age, education, marital status, prepregnancy BMI, gestational glucose tolerance, gestational weight gain, third trimester systolic BP and smoking during pregnancy, household income and child sex, race/ethnicity, breastfeeding duration and exact age at the 3-year visit.

^b All models for BP adjusted for BP measurement conditions (child's state and position, extremity used, cuff size, and measurement sequence number) and height at the 3 year visit

* Denotes *p*-value <0.05