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Predictors of infant body composition at 5 months of age: The Healthy Start Study

Katherine A Sauder, PhD¹, Jill L Kaar, PhD¹, Anne P Starling, PhD², Brandy M Ringham, PhD³, Deborah H Glueck, PhD³, and Dana Dabelea, MD, PHD^{1,2}

¹Department of Pediatrics, University of Colorado School of Medicine, Aurora CO, USA

²Department of Epidemiology, Colorado School of Public Health, Aurora CO, USA

³Department of Biostatistics and Informatics, Colorado School of Public Health, Aurora CO, USA

Abstract

Objective—To examine associations of demographic, perinatal, and infant feeding characteristics with offspring body composition at ~5 months.

Study design—We collected data on 640 mother/offspring pairs from early pregnancy through ~5 months of age. We assessed offspring body composition with air displacement plethysmography at birth and ~5 months. Linear regression analyses examined associations between predictors and fat-free mass (FFM), fat mass (FM), and percent fat mass (adiposity) at ~5 months. Secondary models further adjusted for body composition at birth and rapid infant growth.

Results—Greater pre-pregnant BMI and gestational weight gain were associated with greater FFM at ~5 months, but not after adjustment for FFM at birth. Greater gestational weight gain was also associated with greater FM at ~5 months, independent of FM at birth and rapid infant growth, although this did not translate into increased adiposity. Greater percent time of exclusive breastfeeding was associated with lower FFM (–311g, $p<0.001$), greater FM (+224g, $p<0.001$), and greater adiposity (+3.51%, $p<0.001$). Compared with offspring of non-Hispanic white mothers, offspring of Hispanic mothers had greater adiposity (+2.72%, $p<0.001$) and offspring of non-Hispanic black mothers had lower adiposity (–1.93%, $p<0.001$). Greater adiposity at birth predicted greater adiposity at ~5 months, independent of infant feeding and rapid infant growth.

Conclusions—There are clear differences in infant body composition by demographic, perinatal, and infant feeding characteristics, although our data also show that increased adiposity at birth persists through ~5 months of life. Our findings warrant further research into implications of differences in infant body composition.

Corresponding Author: Katherine Sauder, 12474 E 19th Ave – F426, Aurora, CO 80045, USA; katherine.sauder@ucdenver.edu; (p) 303-724-8715; (f) 303-724-7724.

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Keywords

Breastfeeding; maternal obesity; race; ethnicity; body composition

The developmental origins of obesity theory posits that early life exposures, including intrauterine exposures, influence obesity risk across the lifespan.¹ There is compelling evidence that intrauterine exposure to maternal obesity is associated with increased obesity in offspring across the lifespan.² We and others have previously reported that greater maternal pre-pregnant body mass index (BMI) and gestational weight gain are each associated with greater offspring body size and adiposity at birth^{3, 4, 5}. However, the degree to which these associations persist into the postnatal period is not well understood.

There is evidence that intrauterine exposure to maternal obesity is associated with greater offspring fat mass and/or adiposity in the first few months of life.^{6, 7} Other studies report no associations,^{8–10} or evidence of slowed “catch-down” growth, in fat mass and/or adiposity during infancy among offspring exposed to maternal obesity.^{11, 12} Some of the discrepancy between studies may be explained by differences in methodology, including the age at which infant body composition is measured. Other important considerations that vary across studies include adjustment for size at birth or speed of growth, as well as evaluation of the effect of infant feeding (breastmilk, formula, complementary foods). Infant feeding is particularly important to examine, as it has been shown to modify the effect of adverse intrauterine exposures on offspring obesity risk.¹³

The main purpose of this analysis was to evaluate whether maternal pre-pregnant BMI, gestational weight gain and breastfeeding exclusivity are independently associated with offspring body size and composition at 5 months. In addition, we sought to determine whether these effects are independent of body composition at birth and early infant growth status. We also explored interactions between pre-pregnant BMI, gestational weight gain, and breastfeeding to understand whether infant feeding modified the effect of intrauterine exposure to maternal obesity on offspring body composition.

Methods

The Healthy Start study is an ongoing pre-birth cohort in Denver, Colorado. From 2009–2014, we recruited women in early pregnancy from obstetric clinics at the University of Colorado Anschutz Medical Campus. Women were eligible if they were ≥16 years of age, <24 weeks pregnant with a single fetus, had no chronic medical conditions (Type 2 diabetes, cancer, etc), and no history of obstetric complications (prior stillbirth or birth <25 weeks). Participants completed research visits in early pregnancy (median 17 weeks), mid-pregnancy (median 27 weeks) and at delivery (median 1 day post-birth). The original protocol included a postnatal phone interview (median 5.2 months), which was converted to an in-person visit in January 2011. The study was approved by the Colorado Multiple Institutional Review Board and all women provided written informed consent.

We enrolled 1410 women in Healthy Start, of which 1102 were eligible for the in-person infant visit when it was added to the protocol (Figure; available at www.jpeds.com).

Participants were eligible for the current analysis if infants were full-term (gestational age ≥ 37 weeks), had body composition measurements at birth and ~ 5 months, and complete data on all covariates.

Exposure assessments

Women self-reported demographic information at enrollment including date of birth, race/ethnicity, education, annual household income, and gravidity. At the pregnancy and delivery visits, women self-reported smoking, alcohol consumption, and vitamin use. Following delivery, we obtained data on pre-pregnancy body mass index (BMI), gestational weight gain, diagnosis of gestational diabetes, date of delivery, mode of delivery, offspring sex, birth weight, birth length, and gestational age at birth from clinical records. At the ~ 5 month visit, women reported breastfeeding status, use of formula (including infant age at introduction and relative proportion of formula to breastmilk), and introduction of solid foods (i.e., age at which the infant began consuming foods other than breastmilk, formula, or water on a daily basis). We quantified breastfeeding with breastmilk-months, a metric which reflects both duration and exclusivity of breastfeeding. For example, 6 months of exclusive breastfeeding equates to 6 breastmilk-months while 4 months of exclusive breastfeeding followed by 2 months of 50% breastmilk and 50% formula equates to 5 breastmilk-months. To account for differences in age at the infant visit, we divided breastmilk-months by offspring age to obtain the percent time each infant was exclusively breastfed. This data can be interpreted on a continuous scale, such that 0% indicates exclusively formula-fed, 50% indicates half breastfed, half formula-fed, and 100% indicates exclusively breastfed from birth to the ~ 5 month visit.

Outcome assessments

Offspring body composition was measured at the in-person delivery and infant visits via air displacement plethysmography (PEA POD, COSMED, Rome, Italy), which has excellent validity and reliability in infants.^{14, 15} The PEA POD device measures total body volume by detecting differences in air pressure between a test chamber in which the infant is placed and a control chamber with known air pressure.¹⁶ Body mass and volume measurements are used to calculate body density, and fat and fat-free mass density coefficients¹⁷ are used to obtain estimates of fat-free mass (g), fat mass (g), and adiposity (percent fat mass). Trained research personnel measured each offspring outcome twice, with a third measurement obtained when percent fat mass differed by $>2.0\%$. The average of the two closest readings was used for analysis. We quantified early infant growth by calculating birth and ~ 5 month sex-specific weight-for age z-scores (WAZ) using the 2006 World Health Organization growth charts. Rapid growth was defined as a change >0.67 in WAZ from birth to the ~ 5 month visit, which corresponds to upward crossing of a percentile band on standardized growth charts and indicates a clinically significant increase in weight.¹⁸

Data analyses

Analyses were conducted in SAS 9.4 (SAS Institute, Cary, NC, USA). We fit separate multivariable linear regression models for the outcomes of fat-free mass, fat mass, and adiposity. The primary predictors of interest were maternal pre-pregnant BMI, gestational weight gain, and percent time of exclusive breastfeeding. We used a backwards stepwise

model-fitting approach, wherein non-significant covariates were removed, starting with the highest p-value. As covariates, we considered the continuous variables of maternal age, gravidity, weeks of daily prenatal vitamin use, gestational age at birth, and offspring age at the postnatal visit; categorical variables of race/ethnicity, education, and household income; and binary variables for introduction of solids by the ~5 month visit, diagnosis of gestational diabetes, any maternal smoking during pregnancy, any maternal alcohol consumption during pregnancy, mode of delivery, and offspring sex. We also considered second- and third-order interactions, hypothesized *a priori*, between maternal pre-pregnant BMI, gestational weight gain, and percent time of exclusive breastfeeding. Examination of jackknifed studentized residuals confirmed the assumptions of normality and homoscedasticity. Variance inflation factors were inspected to confirm that multicollinearity between predictors was not prohibitive (all <2.0). We removed covariates which were statistically non-significant ($p>0.05$) for all body composition measures, including the interaction terms, and present three models for interpretation. Model 1 includes the primary predictors (pre-pregnant BMI, gestational weight gain, breastfeeding exclusivity) and significant covariates (race/ethnicity and sex). Model 2 includes Model 1 predictors plus the respective body composition measure at birth (e.g. fat-free mass at birth for the model predicting fat-free mass at ~5 months). Model 3 includes Model 2 predictors and additionally adjusts for the binary status of rapid growth in WAZ from birth to ~5 months.

Results

Of the 1102 participants eligible for the postnatal exam, complete data were available for 640 participants (Figure). As shown in Table I, these 640 participant-dyads were similar to the larger eligible cohort with respect to maternal-offspring characteristics, including race/ethnicity, education, pre-pregnancy BMI, gestational weight gain, infant feeding, and infant size and body composition at birth and ~5 months.

The associations of maternal, perinatal, and infant feeding characteristics with offspring body composition at ~5 months is reported in Table II in sequentially adjusted models. The interactions between pre-pregnant BMI, gestational weight gain, and breastfeeding were all statistically non-significant; thus we present and interpret only the main effects.

Pre-pregnant BMI and gestational weight gain—Increasing pre-pregnant BMI and gestational weight gain were each associated with increasing offspring fat-free mass at ~5 months (Model 1, +6g, $p<0.05$ for both), but these associations were attenuated to non-significance after adjustment for fat-free mass at birth (Model 2) and remained non-significant with additional adjustment for rapid infant growth (Model 3). In contrast, increasing gestational weight gain was associated with increasing absolute fat mass at ~5 months (Model 1, +5g, $p=0.08$), and this association was independent of both fat mass at birth (Model 2, +4g, $p=0.26$) and rapid infant growth (Model 3, +6g, $p<0.05$). However, neither pre-pregnant BMI nor gestational weight gain were associated with fat mass percent (adiposity) at 5 months.

Exclusive breastfeeding—A greater percent time of exclusive breastfeeding was associated with reduced fat-free mass (−311g, $p<0.001$) and increased fat mass (244g,

$p < 0.001$), resulting in significantly greater adiposity (3.51%, $p < 0.001$). These associations were consistent across all three models, thus independent of race/ethnicity, sex, maternal factors, body composition at birth and rapid infant growth status.

Demographic characteristics

Race/ethnicity—In Model 1, compared with offspring of non-Hispanic white mothers, offspring of Hispanic mothers had significantly greater fat mass (+267g, $p < 0.001$) and adiposity (2.72%, $p < 0.001$), while offspring of non-Hispanic black mothers had significantly lower fat mass (+141g, $p = 0.02$) and adiposity (−1.93%, $p < 0.001$), independent of maternal pre-pregnant BMI, gestational weight gain, and breastfeeding exclusivity. These effects persisted after adjustment for body composition at birth (Model 2) and rapid infant growth (Model 3); however, with these additional adjustments, offspring of non-Hispanic black mothers also displayed significantly higher fat-free mass (+165g, $p < 0.001$) compared with offspring of non-Hispanic white women.

Infant sex—In Model 1, compared with male offspring, female offspring had lower fat-free mass (−482g, $p < 0.001$), with no significant differences in absolute fat mass levels, thus resulting in increased adiposity at ~5 months (+2.30%, $p < 0.001$), independent of race/ethnicity, maternal BMI and gestational weight gain. Further adjustment for body composition at birth (Model 2) and rapid growth status (Model 3) did not influence these results.

Body composition measures at birth were significant predictors of the respective body composition measures at ~5 months, independent of prenatal and postnatal factors. For example, a 1% increase in adiposity at birth was associated with a 0.3% increase in adiposity at ~5 months, independent of demographic maternal, infant feeding characteristics and rapid growth.

Rapid infant growth—Finally, offspring who exhibited rapid growth in WAZ had significantly greater fat-free mass, fat mass, and adiposity at ~5 months. Of note, these effects were independent of body composition measures at birth.

Other predictors that were considered and removed due to statistical non-significance include: maternal age, education, household income, gravidity, gestational diabetes, prenatal smoking, prenatal alcohol consumption, weeks of daily prenatal vitamin use, mode of delivery, introduction to solids, and second- and third-order interactions between pre-pregnant BMI, gestational weight gain, and breastfeeding.

Discussion

We found that increasing maternal gestational weight gain was significantly associated with an increase in offspring fat mass at ~5 months, independent of race/ethnicity, pre-pregnant BMI, fat mass at birth, breastfeeding exclusivity and rapid infant growth. However, due to similar effects on fat free mass, these did not translate in a significant increase in relative fat mass (adiposity). Increased breastfeeding was associated with reduced fat-free mass, but increased fat mass, and increased relative fat mass (adiposity). Offspring who grew rapidly

from birth to ~5 months gained substantially more fat mass than fat-free mass, resulting in 5% more adiposity at ~5 months, independent of all other pre and postnatal factors considered. Importantly, our data provided evidence that increased infant adiposity at birth persists through 5 months of age, independent of demographic, maternal, and early infant feeding and growth characteristics.

We previously reported that maternal pre-pregnant BMI and gestational weight gain were each independent predictors of offspring fat mass, fat-free mass, and adiposity at birth.³ Here we show that maternal pre-pregnant BMI is no longer significantly associated with fat mass and adiposity ~5 months, and the association with fat free mass is attenuated to non-significance by adjustment for fat-free mass at birth. Furthermore, although gestational weight gain was a significant predictor of fat mass at ~5 months, independent of both fat mass at birth, breastfeeding, and early infant growth, the increase in fat mass did not translate into a corresponding increase in adiposity (fat mass percent). Thus, pre-pregnant BMI and gestational weight gain were no longer significantly associated with adiposity at ~5 months. However, they did predict greater adiposity at birth,³ which in turn, as we show here, is a significant predictor of adiposity at ~5 months, regardless of early growth patterns. As offspring continue to grow, adopt more postnatal behaviors modeled by mothers/families, and transition through other critical developmental periods such as puberty, it is possible that associations between maternal and offspring obesity will again become apparent. Given the complexity of early life influences on infant body composition, further work is needed to understand how infant body composition is related to future health and disease risk.

Infants with a greater percent time of exclusive breastfeeding were smaller overall at ~5 months: fat-free mass was lower by 311g and fat mass was higher by 224g resulting in a net body size decrease of 98g among infants exclusively breastfed for 100% of the time versus 0% during the first ~5 months. Although these exclusively breastfed babies are smaller overall, they have an increased relative fat mass (adiposity). These findings are seemingly in contrast to the collective body of evidence suggesting a small but consistent protective effect of breastfeeding against obesity¹⁹ and adiposity²⁰ across the life course. However, our findings are consistent with a 2012 meta-analysis of 15 smaller studies that reported reduced fat-free mass, greater fat mass, and greater adiposity among breastfed offspring at 3–6 months compared with formula-fed offspring.²¹ Further, by 12 months of age, formula-fed infants have significantly more fat-free mass and a tendency towards increased fat mass ($p=0.16$) and adiposity ($p=0.07$).²¹ Differences in size and adiposity between feeding groups could be explained by the higher protein content of formula compared with breastmilk, or by differences in appetite control and satiety that become more pronounced as in later infancy as offspring are weaned onto solid foods. We have shown here that breastfeeding has complex and diverging effects on infant size and composition at ~5 months, and further studies are needed to determine whether differences in body composition early in life associated with breastfeeding exclusivity influence future obesity and chronic disease risk.

We also noted significant differences in infant body composition according to race/ethnicity and sex. As compared with non-Hispanic whites, offspring of Hispanic mothers had increased fat mass and adiposity, while offspring of non-Hispanic black mothers had lower fat mass and adiposity, independent of all other pre-and postnatal factors considered. The

racial/ethnic differences we observed could reflect genetics or other unmeasured cultural differences,²² including beliefs surrounding ideal body size for children or nuances in early infant feeding that were not assessed in the present study. The sex differences we observed are consistent with prior studies.²³ Further research is needed to understand both the causes and long-term significance of racial/ethnic and sex differences in early infant body composition.

Our study has limitations and strengths. Our analysis included only 58% of the eligible cohort, mostly due to pre-term birth exclusions, missing data on covariates, or missed postnatal visit. The lower sample size may have reduced power to detect significant effects. However, the analytic sample was similar to the eligible cohort in terms of maternal characteristics, perinatal predictors, and body composition at birth, mitigating potential concerns regarding loss to follow-up bias. A strength of the study is the prospective pre-birth cohort design, which enabled us to collect detailed data on exposures throughout pregnancy and early infancy. Measuring infant body composition by air displacement plethysmography is also a strength, as this method provides better estimates of overall adiposity than skinfold thicknesses, BMI, or abdominal ultrasound.

In summary, we report differences in infant body composition at ~5 months by demographic, prenatal and early postnatal characteristics. We show that infant body composition, particularly increased adiposity, persists from birth to ~5 months, independent of other early life factors, and that offspring who grow rapidly accumulate more fat mass than fat-free mass, resulting in substantially greater adiposity. These findings warrant further research into the long-term implications of differences in infant body composition at a very early age.

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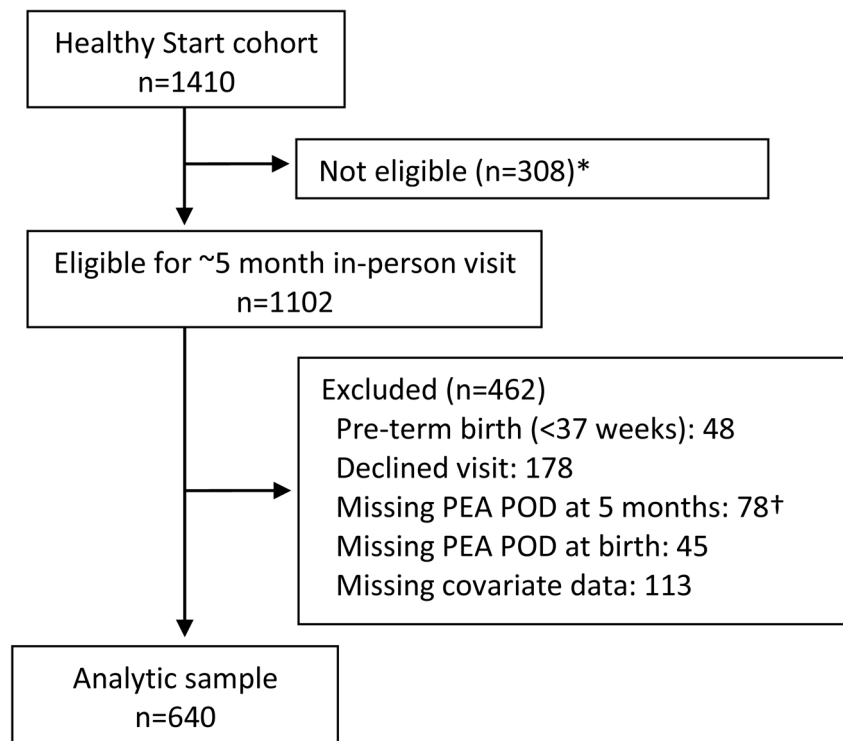
Abbreviations

WAZ weight-for-age z-score

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**Figure.**

Study flow diagram.

*5 month postnatal visit introduced later in study protocol.

†76 declined measure, 2 exceeded PEA POD weight limit of 10 kg.

Table 1

Characteristics of mothers and offspring participating in the Healthy Start study.

	Postnatal cohort n=1102	Analytic cohort n=640
Maternal characteristics		
Age at delivery (years)	28.8 (6.1)	29.1 (6.0)
Race		
Hispanic	261 (24%)	155 (24%)
Non-Hispanic white	613 (56%)	364 (57%)
Non-Hispanic black	153 (14%)	85 (13%)
Other	75 (7%)	36 (6%)
Education		
<12 years	130 (12%)	77 (12%)
High school degree	191 (17%)	94 (15%)
College classes or college degree	781 (71%)	469 (73%)
Household income		
<\$40,000	304 (28%)	179 (28%)
\$40,000–\$70,000	219 (20%)	127 (20%)
>\$70,000	387 (35%)	226 (35%)
Missing/don't know	192 (17%)	108 (17%)
Gravidity (n)	1.4 (1.5)	1.4 (1.6)
Smoking during pregnancy (n)	81 (7%)	41 (6%)
Alcohol during pregnancy (n)	220 (20%)	130 (20%)
Gestational diabetes (n)	44 (4%)	24 (4%)
Pre-pregnant BMI (kg/m ²)	25.7 (6.1)	25.7 (6.3)
Underweight	35 (3%)	20 (3%)
Lean	564 (51%)	324 (51%)
Overweight	288 (26%)	174 (27%)
Obese	215 (20%)	122 (19%)
Gestational weight gain (kg)	13.6 (6.5)	13.9 (6.2)
Inadequate (n)	270 (25%)	138 (22%)
Adequate (n)	319 (29%)	196 (31%)
Excessive (n)	513 (47%)	306 (48%)
Prenatal multivitamins (weeks of daily use)	35.0 (13.4)	35.6 (13.5)
Offspring characteristics		
Female (n)	536 (49%)	324 (51%)
Gestational age at birth (weeks)	39.4 (1.6)	39.6 (1.1)
Cesarean delivery (n)	226 (21%)	129 (20%)
Body size, composition at birth		
Weight (g)	3237 (498)	3281 (422)
Weight-for-age z-score	−0.17 (0.92)	−0.05 (0.89)
Fat-free mass (g)	2841 (346)	2846 (325)
Fat mass (g)	297 (152)	296 (147)

	Postnatal cohort n=1102	Analytic cohort n=640
Adiposity (%)	9.2 (3.9)	9.1 (3.9)
Age at postnatal visit (months)	5.5 (1.5)	5.1 (1.2)
Breastfeeding category (n)		
Exclusive breastfeeding	393 (42%)	287 (45%)
Formula only	60 (6%)	39 (6%)
Mixed feeding	492 (52%)	312 (49%)
Percent time exclusively breastfed	0.73 (0.37)	0.72 (0.36)
Started solids (n)	387 (43%)	296 (46%)
Body size, composition at ~5 months		
Weight (g)	6929 (980)	6818 (864)
Weight-for-age z-score	-0.46 (0.94)	-0.49 (0.91)
Fat-free mass (g)	5147 (650)	5149 (618)
Fat mass (g)	1649 (493)	1669 (491)
Adiposity (%)	24.0 (5.4)	24.2 (5.3)
Early infant growth		
Change in weight-for-age z-score 0.67 (n)	153 (17%)	74 (12%)

Data are mean (SD) or n (%).

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Table 2

Predictors of infant body composition at ~5 months of age.

	Model 1		Model 2		Model 3	
	β (SE)	P	β (SE)	P	β (SE)	P
Fat-free mass (g)						
Race (reference = NHW)						
Hispanic	79 (45)	0.08	53 (38)	0.16	18 (36)	0.62
Black	93 (56)	0.10	201 (49)	<0.001	165 (46)	<0.001
Other	19 (77)	0.80	44 (66)	0.51	2 (63)	0.97
Pre-pregnant BMI (kg/m ²)	6 (3)	0.05	-1 (3)	0.72	0 (2)	0.99
Gestational weight gain (kg)	6 (3)	0.03	0 (3)	0.94	1 (2)	0.56
Sex (ref = male)	-482 (35)	<0.001	-345 (31)	<0.001	-355 (30)	<0.001
GA at birth (ref = 37 weeks)	112 (16)	<0.001	8 (16)	0.61	16 (15)	0.29
Percent time exclusively breastfed (%)	-311 (53)	<0.001	-417 (46)	<0.001	-375 (44)	<0.001
Fat-free mass at birth (%)			1 (0)	<0.001	1 (0)	<0.001
Rapid growth in WAZ (ref = no)					411 (47)	<0.001
R ²		0.50		0.64		0.68
Fat mass (g)						
Race (reference = NHW)						
Hispanic	267 (47)	<0.001	272 (46)	<0.001	221 (42)	<0.001
Black	-141 (59)	0.02	-110 (59)	0.06	-169 (53)	0.002
Other	88 (81)	0.28	101 (80)	0.21	36 (72)	0.62
Pre-pregnant BMI (kg/m ²)	3 (3)	0.30	0 (3)	0.98	1 (3)	0.67
Gestational weight gain (kg)	5 (3)	0.08	4 (3)	0.26	6 (3)	0.03
Sex (ref = male)	50 (37)	0.18	25 (37)	0.50	-15 (33)	0.65
GA at birth (ref = 37 weeks)	34 (17)	0.05	21 (17)	0.23	40 (16)	0.01
Percent time exclusively breastfed (%)	224 (56)	<0.001	204 (55)	0.0003	276 (50)	<0.001
Fat mass at birth (%)			1 (0)	<0.001	1 (0)	<0.001
Rapid growth in WAZ (ref = no)					651 (54)	<0.001
R ²		0.13		0.16		0.31
Adiposity (%)						

	Model 1		Model 2		Model 3	
	β	p	β	p	β	p
Race (reference = NHW)						
Hispanic	2.72 (0.50)	<0.001	2.80 (0.49)	<0.001	2.36 (0.46)	<0.001
Black	-1.93 (0.63)	0.002	-1.70 (0.62)	0.01	-2.23 (0.59)	0.0002
Other	1.08 (0.86)	0.21	1.22 (0.85)	0.15	0.67 (0.80)	0.40
Pre-pregnant BMI (kg/m ²)	0.00 (0.03)	0.94	-0.03 (0.03)	0.43	-0.01 (0.03)	0.63
Gestational weight gain (kg)	0.04 (0.03)	0.25	0.02 (0.03)	0.49	0.05 (0.03)	0.13
Sex (ref = male)	2.30 (0.39)	<0.001	1.92 (0.39)	<0.001	1.56 (0.37)	<0.001
GA at birth (ref = 37 weeks)	-0.01 (0.18)	0.93	-0.08 (0.18)	0.64	0.10 (0.17)	0.55
Percent time exclusively breastfed (%)	3.51 (0.59)	<0.001	3.36 (0.59)	<0.001	4.00 (0.55)	<0.001
Adiposity at birth (%)			0.22 (0.05)	<0.001	0.29 (0.05)	<0.001
Rapid growth in WAZ (ref = no)					5.57 (0.59)	<0.001
R ²		0.17		0.19		0.28

NHW, non-Hispanic White; BMI, body mass index; GA, gestational age; WAZ, weight-for-age z-score

* Estimates obtained from multivariable linear regression models conducted separately for each outcome. Other predictors considered and removed due to statistical non-significance include: maternal age, education, household income, gravidity, gestational diabetes, prenatal smoking, prenatal alcohol consumption, weeks of daily prenatal vitamin use, mode of delivery, introduction to solids, and second- and third-order interactions between pre-pregnant BMI, gestational weight gain, and breastfeeding.