HHS Public Access

Author manuscript

Pediatr Obes. Author manuscript; available in PMC 2017 October 01.

Published in final edited form as:

Pediatr Obes. 2016 October ; 11(5): 434–441. doi:10.1111/ijpo.12084.

Exploring the association between maternal prenatal multivitamin use and early infant growth: The Healthy Start Study

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Abstract

Background—Prenatal multivitamin supplementation is recommended to improve offspring outcomes, but effects on early infant growth are unknown.

Objectives—We examined whether multivitamin supplementation in the year before delivery predicts offspring mass, body composition, and early infant growth.

Methods—Multivitamin use was assessedlongitudinally in 626 women from the Healthy Start Study. Offspring body size and composition was measured with air displacement plethysmography at birth (<3 days) and postnatally (median 5.2 months). Separate multiple linear regressions assessed the relationship of weeks of daily multivitamin use with offspring mass, body composition, and postnatal growth, after adjustment for potential confounders (maternal age, race, pre-pregnant BMI; offspring gestational age at birth, sex; breastfeeding exclusivity).

Results—Maternal multivitamin use was not related to offspring mass or body composition at birth, or rate of change in total or fat-free mass in the first 5 months. Multivitamin use was inversely associated with average monthly growth in offspring percent fat mass ($\beta = -0.009$, $p=0.049$) between birth and the postnatal exam. Offspring of non-users had a monthly increase in percent fat mass of 3.45%, while offspring at the top quartile of multivitamin users had a monthly increase in percent fat mass of 3.06%. This association was not modified by exclusive breastfeeding.

Conclusions—Increased multivitamin use in the preconception and prenatal periods was associated with a slower rate of growth in offspring percent fat mass in the first 5 months of life.

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Conflict of Interest

The authors declare no conflict of interest.

This study provides further evidence that in utero nutrient exposures may affect offspring adiposity beyond birth.

Keywords

Prenatal vitamins; body composition; adiposity; pregnancy; fetal programming

Introduction

Research on developmental origins of health and disease indicates that the intrauterine environment can have immediate and long-lasting effects on offspring health (1, 2). Maternal malnutrition during pregnancy is associated with both low birthweight and macrosomia, as well as future offspring risk of diabetes, obesity, and cardiovascular disease (3). Universal recommendations exist only for iron and folic acid supplementation in pregnancy (4), but clinicians in developed countries commonly recommend multiple vitamin and mineral supplementation to prevent prenatal micronutrient deficiencies (5). However, in the presence of food fortification and access to nutrient-adequate diets, such supplementation may result in women exceeding the upper limits for dietary reference intakes in pregnancy (6). In a study of 222 pregnant Caucasian American women, average dietary and supplemental intake of 20 micronutrients was 2-3 times higher than prenatal recommendations (7). Animal studies report that intrauterine exposure to high levels of micronutrients increases susceptibility to obesity and metabolic abnormalities in offspring, possibly through altering DNA methylation (8, 9).

Evidence for postnatal effects of intrauterine micronutrient exposure in humans is limited. Most studies have focused on undernourished populations, and used low birthweight as an outcome (10). A recent publication from the Nurses' Health Study reported no association between prenatal multivitamin use and offspring obesity in childhood and early adulthood. However, this analysis was limited by retrospective data collection and self-reported measures of adult weight and childhood body size (11). Additionally, it did not consider body composition (fat mass, fat-free mass) or the role of rapid early growth, a potential mediator between intrauterine exposures and subsequent health and disease in offspring (12). Other authors have suggested that infant feeding (breastmilk, formula, or mixed) should also be considered since the choice of infant feeding method is associated with offspring growth trajectories (13).

The present study prospectively examined the association between maternal multivitamin supplementation in the preconception and prenatal period with offspring mass and body composition at birth and rate of growth in the first 5 months postnatally. We hypothesized greater exposure to prenatal multivitamin supplementation would be associated with greater mass at birth and increased rate of growth in the first 5 months for total mass and adiposity (percent fat mass). We further hypothesized that the association between maternal multivitamin use and early infant growth would be modified by exclusive breastfeeding.

Methods

Participants were from The Healthy Start Study, a pre-birth cohort of mother-offspring dyads. Women were recruited from the obstetric clinic at the University of Colorado from 2009-2014. This study was approved by the Colorado Multiple Institutional Review Board and all participants provided written informed consent. Women were eligible for Healthy Start if they were ≥16 years of age, were <24 weeks gestation at enrollment, were expecting a singleton birth, and had no history of serious chronic disease, prior stillbirth, or very preterm birth (<25 weeks gestation). A total of 1410 women were enrolled and completed research visits in early pregnancy (median 17 weeks gestation), mid-pregnancy (median 27 weeks gestation), and delivery (median 1 day after birth). The postnatal research visit (median 5.2 months) was added later to the protocol. Of the 1159 women who completed the postnatal visit, 424 were missing data on offspring body composition at birth (n=137) or at the postnatal visit (n=287; of these, 99 were missing postnatal body composition because they exceeded the 10kg weight limit of the device). Of the 735 with complete body composition data, 24 were excluded due to preterm births (<37 weeks gestation), 6 had incomplete multivitamin data, 62 had body composition assessed >3 days after birth, 12 had missing maternal diet data, and 5 were missing breastfeeding data (total of 533 missing). Complete data were available for 626 mother-offspring pairs (54% of the eligible cohort, 85% of those with complete body composition data).

Data Collection

Maternal prenatal multivitamin use was assessed via self-report. At each research visit, women described multivitamin use in the 12 weeks prior to conception (for the early pregnancy visit), since the prior visit (for the mid-pregnancy and delivery visits), or since delivery (for the postnatal visit). When applicable, women were asked about starting and stopping date, dosage, and brand/type. Multivitamin use was quantified as weeks of daily use. For example, a woman who reported taking multivitamins daily from 12 weeks prior to conception through delivery at 40 weeks gestation had 52 weeks of daily use, whereas a woman who reported taking multivitamins every other day for the same period had 26 weeks of daily use. Due to missing data on the brand/type of multivitamin used, we considered all prenatal multivitamins equivalent and did not investigate associations with specific brands/types.

Offspring body composition was assessed at the delivery and postnatal visits without clothing via air displacement plethysmography (PEAPOD, COSMED, Rome, Italy), which uses a 2-compartment model to estimate fat mass (adipose tissue; g and % of total mass) and fat-free mass (water, bone; g and % of total mass). Plethysmography has excellent validity and reliability in infants (14, 15). Trained personnel conducted 2 measurements on each infant, with a third measurement taken if the percent fat mass differed by >2%. The average of the 2 closest readings was used for analysis, and total mass (g) was calculated by summing fat mass (g) and fat-free mass (g).

Data on relevant covariates were collected at the research visits and through medical record review. Maternal race/ethnicity, highest level of education completed, annual household income, and gravidity (number of previous pregnancies) were assessed via self-report at the

early pregnancy visit. Maternal age at delivery (years) was calculated from self-reported date of birth and date of delivery. Maternal pre-pregnancy BMI was calculated from self-report or medical record pre-pregnancy weight and height measured at the early pregnancy visit. Gestational weight gain was calculated from pre-pregnancy weight and the last weight recorded in the medical record prior to delivery, and classified according to the 2009 Institute of Medicine recommendations (16). Physical activity in pregnancy was assessed at each research visit with the Pregnancy Physical Activity Questionnaire (17) and quantified as average total energy expenditure in MET-hours/week. Diet in pregnancy was assessed 2-8 times with Automated Self-Administered 24-hour dietary recalls (18) and average daily energy intake (kilocalories) was calculated. Smoking in pregnancy (yes/no) was assessed via self-report at each research visit. Offspring gestational age at birth (weeks) was estimated via prenatal ultrasound measurements and/or self-reported first day of last menstrual period. Date of conception was estimated from gestational age at birth and date of delivery. Data on breastfeeding and introduction of solid foods were obtained by maternal report at the postnatal visit.

Statistical Analyses

Analyses were conducted in SAS 9.4 (SAS Institute, Cary, NC, USA). Separate univariate multiple linear regression models were fit for each of the outcomes at birth (total mass, fat-free mass, fat mass, and percent fat mass) and postnatally (rate of change in total mass, fat-free mass, fat mass, percent fat mass). The models controlled for potential confounders as described below. In each model, the strength of the association between weeks of daily multivitamin use and the outcomes was assessed. Postnatal rate of change was calculated by subtracting body composition measures at birth from body composition measures at the postnatal visit and dividing by offspring age in months at the postnatal visit (e.g. [total mass at postnatal visit – total mass at birth] / age at postnatal visit = average growth per month). We also tested an *a priori* hypothesized interaction between weeks of multivitamin use and exclusive breastfeeding. We conducted exploratory analyses to determine whether early (12 weeks pre-conception through the first trimester) or late (second and third trimesters) multivitamin use was more strongly related to offspring outcomes.

For descriptive purposes, we classified the women as non-users of multivitamins or into quartiles of multivitamin use. For continuous variables, we estimated means and standard deviations for participant characteristics and outcome measures with general linear models and defined category of multivitamin use as a class variable. To obtain p for trend, we entered multivitamin use as a continuous variable (weeks of daily use). For categorical variables, we calculated group frequencies and estimated the p value for the overall variable from the Cochran-Mantel-Haenszel test.

For the main analysis, we considered weeks of daily multivitamin use as a continuous variable in 2 different adjusted models. Model 1 included maternal age at delivery (continuous), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, other), education (less than 12^{th} grade, high school degree, some college or associate's degree, 4 years of college, graduate degree), offspring sex (male, female), gestational age at birth (continuous), and, for postnatal analyses only, exclusive breastfeeding (<0.5 months

[predominately formula], 0.5-3 months [early mixed feeding], 3-5 months [late mixed feeding], ≥5 months [exclusive breastfeeding]). Model 2 included the covariates in Model 1 plus annual household income (<$40,000, $40,000-$70,000, ≥$70,000, missing/don't know), gravidity (continuous), maternal pre-pregnant BMI (continuous), prenatal average daily energy (continuous), prenatal energy expenditure (continuous), prenatal smoking (yes, no), gestational weight gain (inadequate, adequate, excessive), and, for postnatal analyses only, started solids (yes/no), and maternal use of multivitamins in the postnatal period (yes/no). Residuals were inspected for normality. Two-sided alpha for statistical significance was set at $p<0.05$. Tables depict mean and SD unless otherwise noted.

Results

Of the 1159 eligible mother-offspring pairs in Healthy Start, complete data were available for 626 pairs. There were no notable differences between excluded and included participants (data not shown). Characteristics of the final sample by prenatal multivitamin use (non-users and quartile of multivitamin users) are presented in Tables 1 and 2.

In univariate analyses we observed a significant increase in offspring total mass and fat-free mass at birth across increasing categories of prenatal multivitamin use ($p=0.0004$ and $p=0.0003$, respectively), but no difference in fat mass or percent fat mass (Table 2). However, after adjustment in multivariable models (Table 3), we found no significant association between weeks of daily prenatal multivitamin use and offspring measures of body size and composition at birth.

In univariate analyses we observed no significant associations between weeks of daily prenatal multivitamin use and offspring body size or body composition at 5 months postnatally (Table 2). In multivariable analyses predicting growth rate, we observed a significant inverse association between multivitamin use and growth rate of adiposity (percent fat mass) in the fully-adjusted Model 2 ($\beta= -0.009$, $p=0.049$) (Table 3). In contrast, multivitamin use was not associated with offspring growth rate for total mass or fat-free mass (g). Offspring of mothers who did not use prenatal multivitamins had an adjusted monthly rate of growth in percent fat mass of 3.45%. In comparison, offspring of mothers in the top quartile of weeks of daily multivitamin use had an adjusted monthly rate of growth in percent fat mass of 3.06%. These rate differences translate to an extra 2.00% adiposity (percent fat mass) at 5 months for offspring of non-multivitamin users compared to the top quartile of daily multivitamin users. These associations were not modified by exclusive breastfeeding. Exploratory analyses that included separate predictors for early pregnancy use (12 weeks pre-conception through the first trimester) and late pregnancy use (second and third trimesters) showed that neither early nor late use predicted outcomes, suggesting that timing of prenatal multivitamin use is not as important as overall dose.

Discussion

We found that increased maternal multivitamin use in the preconception and prenatal period did not influence body composition at birth or growth in total or fat-free mass in the first 5 months of life, but was associated with a slower relative growth in percent fat mass. Percent

fat-free mass increases as fat-free mass decreases; thus, our results also indicate that offspring of mothers with increasing multivitamin use had a greater rate of growth in percent fat-free mass in the first 5 months. This effect was not modified by exclusive breastfeeding status postnatally, and was also independent of breastfeeding exclusivity.

It is well-established that nutrient deprivation during pregnancy is associated with adverse health outcomes for offspring (19). More recently, associations of fetal over-nutrition with subsequent obesity and metabolic diseases have been reported (20, 21), and rapid early growth has been implicated in the development of later obesity (22). In the present cohort, we previously reported that increased maternal glucose levels during pregnancy, even within the normal range, independently predicted offspring adiposity at birth (23, 24). However, the effect of high micronutrient exposure in utero and early life growth in adiposity is unclear. Evidence in humans is lacking, while studies in Wistar rats report that intrauterine exposure to high (10-fold increase) multivitamin diets increases food intake, body weight, and symptoms of the metabolic syndrome in offspring (9). These effects have been amplified by post-weaning consumption of obesogenic diets (8) and attenuated by post-weaning consumption of diets rich in multivitamins or folate (25). It has been hypothesized that increased availability of methyl donors or metabolic co-factors (such as choline, methionine, or folate) increase obesity or metabolic dysfunction by altering DNA methylation and gene expression (26).

This complex interplay between fetal nutrition and postnatal growth reported in animal models is difficult to translate to human research. In the present study, we found that increased multivitamin use during pregnancy was not associated with overall or fat-free mass (g) rates of growth in the first 5 months of life, but a relatively slower rate of growth in adiposity in offspring, an effect that was not modified by breastfeeding exclusivity. There are several possible explanations for why these results are different from the animal studies. First, the high-multivitamin diet used in the animal studies contained a 10-fold increase in multivitamins compared to the standard diet. In the present study, we were unable to estimate micronutrient intake in absolute terms due to incomplete data on specific brands and types of multivitamins. However, there is evidence that women may be consuming 2-3 times the recommended daily amounts of micronutrients in pregnancy from combined dietary and supplemental sources (7). Therefore, while micronutrient intake in pregnancy may be elevated, it is unlikely that the intrauterine exposure to micronutrients in humans is comparable to the dose tested in the animal studies. Second, the animal studies reported a significant adverse effect of prenatal multivitamin supplementation on offspring at 12-48 weeks post-weaning, periods that correspond to adolescence and young adulthood in humans (8, 9, 25). In contrast, the majority of offspring in Healthy Start were not yet weaned at the time of the postnatal body composition measurements. It is possible that the hypothesized detrimental effects of high multivitamin supplementation do not manifest until later in life, and then only in conjunction with an obesogenic diet. This possibility is supported by the observation of lower body weight at the time of weaning in offspring of rats who consumed high multivitamin diets in pregnancy (9), but needs to be tested in longitudinal human cohorts.

In contrast to the animal literature that suggests an adverse effect of high prenatal multivitamin supplementation on offspring obesity and cardiometabolic health, our results indicate that daily multivitamin use throughout the preconception and prenatal period have no deleterious effects on body size at birth and overall rate of growth in early life, and may in fact be somewhat protective, at least with regard to relative growth in adiposity. We acknowledge that the effect we observed was small and the clinical or biological relevance is unclear. Normative data on infant body composition and growth is still emerging. Fields and colleagues (27) published longitudinal body composition data measured with air displacement plethysmography in 160 exclusively breastfed infants. From birth to 5 months of age, the infants gained an average of 3.0% fat mass each month (females: 2.91%/month, males: 3.10%/month) (27). Assuming an increase of 3.0%/month in fat mass (adiposity) represents normal growth in the first 5 months, our study indicates that offspring of mothers who did not use prenatal multivitamins gained fat mass (%) at a greater rate (3.45%/month), while offspring of mothers who used multivitamins throughout the preconception and prenatal periods gained fat mass (%) at a normal rate (3.06%). Additional longitudinal assessment of offspring body composition and growth in pre-birth cohorts such as Healthy Start is needed to further examine whether in utero exposure to multivitamin supplementation is associated with obesity and cardiometabolic risks, or protection from such risks, later during childhood or adolescence.

We observed a significant increase in offspring birthweight across categories of multivitamin use in univariate models that was attenuated and no longer significant in adjusted models. Multiple micronutrient supplementation during pregnancy is recommended to prevent low birthweight, particularly in developing countries (28). Our results indicate that prenatal multivitamin use is not strongly associated with birthweight in this sample of ethnically-diverse urban women in Colorado.

The present study has some limitations and several strengths. As noted previously, we were unable to estimate absolute intake of supplemental micronutrients, which prevents us from drawing conclusions about deficiency/over-sufficiency status or optimal maternal intake of specific micronutrients with regard to offspring adiposity. Similarly, we did not evaluate individual micronutrient intake or assess circulating levels of specific micronutrients, and therefore can only comment on multiple micronutrient supplementation. Multivitamin data were collected via self-report which is subject to reporting errors; however, every effort to minimize reporting errors and recall bias was made by assessing multivitamin use multiple times throughout pregnancy. Strengths include the prospective cohort design, a large ethnically diverse sample, and measures of offspring body composition in addition to birthweight.

In conclusion, prenatal multivitamin supplementation was not associated with overall or fat-free mass rates of growth in early life, but was associated with a relatively slower rate of growth in adiposity from birth to 5 months. Our study suggests that, in an urban population from Western United States, prenatal multivitamin supplementation during pregnancy has no deleterious effects on infant body size and composition, and may in fact be protective against early life adiposity. Future follow-up is needed to test whether any differences in

early life growth are associated with clinically meaningful differences in adiposity or chronic disease risk in childhood and beyond.

Acknowledgements

The authors thank the Healthy Start Study Project Coordinator, Mrs. Mercedes Martinez, and the study investigators, participants, and personnel. This work was supported by the NIH (R01DK076648 – DD; UL1TR001082 - NIH/NCATS Colorado CTSA; P30DK56350 – UNC Nutrition Obesity Research Center). KAS is supported by an NIH post-doctoral institutional training grant to the University of Colorado (T32DK07658). Contents are the authors' sole responsibility and do not necessarily represent official NIH views. KAS and DD designed the study; KAS, BMR, and DHG performed the statistical analysis; and KAS drafted the first version of the manuscript. All authors interpreted the results, critically revised the manuscript, and approved the final version.

This work was supported by The National Institutes of Health.

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What is already known about this subject

- Prenatal multivitamin supplementation is recommended to improve offspring outcomes
- In animal models, exposure to high levels of multivitamins is associated with increased obesity and metabolic dysfunction in offspring
- In humans, effects of high multivitamin supplementation on offspring adiposity are unknown

What this study adds

- Prenatal multivitamin supplementation was not associated with mass or body composition at birth
- Increased multivitamin use in the preconception and prenatal periods was associated with a slower rate of growth in offspring percent fat mass in the first 5 months of life
- This study provides further evidence that in utero nutrient exposures may affect offspring adiposity beyond birth

Table 1

Characteristics of mothers according to prenatal multivitamin use category*

			Quartile of Prenatal Vitamin Users								
	Non-users		**1**		**2**		**3**		**4**		**p for trend**
Sample size	30		149		156		142		149		
Age at delivery (years)	26.9	(5.2)	25.6	(6.5)	26.7	(6.2)	29.4	(5.4)	31.8	(4.1)	0.0001
Race/ethnicity (n)											
Hispanic	7	(23%)	45	(30%)	60	(38%)	25	(18%)	18	(12%)	0.0001
Non-Hispanic White	16	(53%)	60	(40%)	56	(36%)	100	(70%)	116	(78%)	
Non-Hispanic Black	4	(13%)	36	(24%)	29	(19%)	12	(8%)	7	(5%)	
Other	3	(10%)	8	(5%)	11	(7%)	5	(4%)	8	(5%)	
Education (n)											
Less than 12th grade	7	(23%)	39	(26%)	27	(17%)	10	(7%)	2	(1%)	0.0001
High school degree or GED	4	(13%)	34	(23%)	40	(26%)	14	(10%)	2	(1%)	
Some college or associate's degree	6	(20%)	38	(26%)	48	(31%)	36	(25%)	31	(21%)	
Four years of college (BA, BS)	5	(17%)	19	(13%)	22	(14%)	43	(30%)	52	(35%)	
Graduate degree (Master's, PhD)	8	(27%)	19	(13%)	19	(12%)	39	(27%)	62	(42%)	
Household income (n)											
< $40,000	6	(20%)	54	(36%)	56	(36%)	31	(22%)	30	(20%)	0.0001
$40,000 - $70,000	9	(30%)	22	(15%)	30	(19%)	32	(23%)	28	(19%)	
> $70,000	9	(30%)	46	(31%)	43	(28%)	14	(10%)	6	(4%)	
Missing or don't know	6	(20%)	27	(18%)	27	(17%)	65	(46%)	85	(57%)	
Pre-pregnancy BMI (kg/m^2)	26.2	(7.4)	25.3	(5.8)	26.7	(7.4)	25.4	(5.4)	24.9	(6.1)	0.14
Gravidity	1.5	(1.5)	1.6	(1.6)	1.4	(1.7)	1.3	(1.6)	1.2	(1.3)	0.30
Smoking in pregnancy (n)	3	(10%)	6	(4%)	10	(6%)	6	(4%)	5	(3%)	0.28
Physical activity (MET-h/week)	181.6	(149.6)	159.6	(87.1)	154.3	(85.0)	164.7	(82.8)	164.7	(81.5)	0.55
Average daily calories	2044	(290)	2042	(394)	2017	(384)	2012	(366)	2032	(323)	0.95
Gestational diabetes (n)	0	(0%)	6	(4%)	8	(5%)	2	(1%)	6	(4%)	0.62
Gestational weight gain											
Inadequate	5	(17%)	38	(26%)	47	(30%)	24	(17%)	30	(20%)	0.04
Adequate	9	(30%)	37	(25%)	39	(25%)	38	(27%)	59	(40%)	

	Non-users		Quartile of Prenatal Vitamin Users 1		2		3		4		p for trend
Excessive	16	(53%)	74	(50%)	70	(45%)	80	(56%)	60	(40%)	
Prenatal multivitamins (weeks of daily use)											
Pre-conception (12w prior)	0.0	(0.0)	0.5	(2.0)	0.2	(1.3)	4.3	(4.6)	11.8	(0.8)	0.0001
1st trimester	0.0	(0.0)	3.7	(3.5)	7.4	(1.8)	11.3	(1.8)	13.0	(0.0)	0.0001
2nd trimester	0.0	(0.0)	9.9	(4.3)	13.4	(1.5)	13.1	(1.9)	14.0	(0.2)	0.0001
3rd trimester	0.0	(0.0)	8.3	(4.8)	12.0	(1.5)	12.0	(2.6)	12.6	(1.2)	0.0001
Total	0.0	(0.0)	22.5	(7.0)	33.0	(1.5)	40.7	(3.8)	51.4	(1.4)	0.0001
Range of total use	0.0		1.2 - 30.2		30.3 - 35.4		35.5 - 47.9		48.0 - 54.1		
Postnatal vitamin use (n)	20	(67%)	86	(58%)	114	(73%)	122	(86%)	137	(92%)	0.0001

*For continuous variables, group means (SD) were estimated from general linear models with category of multivitamin use/non-use entered as a class variable, and p for trend was obtained by specifying multivitamin category as a continuous variable. For categorical variables, group frequencies were calculated for each category of multivitamin use/non-use, and the p value for the overall variable was estimated from the Cochran–Mantel–Haenszel test.

Pediatr Obes. Author manuscript; available in PMC 2017 October 01.

Table 2

Characteristics of offspring according to prenatal multivitamin use category*

			Quartile of Prenatal Vitamin Users								
	Non-users		1		2		3		4		p for trend
Sample size	30		149		156		142		149		
Female gender (n)	18	(60%)	81	(54%)	87	(56%)	75	(53%)	65	(44%)	0.03
At birth											
Gestational age (weeks)	39.3	(1.1)	39.5	(1.1)	39.4	(1.1)	39.9	(1.1)	39.8	(1.1)	0.0001
Total mass (g)	2943.2	(431.6)	3085.7	(384.9)	3051.1	(370.1)	3181.6	(443.2)	3201.7	(408.2)	0.0004
Fat-free mass (g)	2691.9	(317.7)	2799.4	(305.9)	2775.2	(305.2)	2882.6	(349.8)	2896.4	(323.5)	0.0003
Fat mass (g)	251.3	(163.2)	286.4	(136.4)	276.0	(137.4)	299.0	(152.3)	305.2	(141.8)	0.20
Fat mass (%)	8.1	(4.5)	9.0	(3.7)	8.9	(3.7)	9.1	(3.9)	9.3	(3.7)	0.60
At postnatal visit											
Age (months)	5.0	(1.5)	5.2	(1.2)	5.2	(1.3)	5.2	(1.3)	5.0	(1.2)	0.89
Breastfeeding											
Exclusive <0.5 months	10	(33%)	39	(26%)	35	(22%)	26	(18%)	21	(14%)	0.0001
Exclusive 0.5 to <3 months	6	(20%)	39	(26%)	43	(28%)	21	(15%)	19	(13%)	
Exclusive 3 to <5 months	2	(7%)	24	(16%)	26	(17%)	20	(14%)	14	(9%)	
Exclusive ≥5 months	12	(40%)	47	(32%)	52	(33%)	75	(53%)	95	(64%)	
Started solids (n)	15	(50%)	80	(54%)	75	(48%)	59	(42%)	52	(35%)	0.001
Total mass (g)	6589.2	(892.4)	6874.9	(877.5)	6855.7	(929.5)	6768.7	(910.4)	6863.8	(761.0)	0.44
Fat-free mass (g)	4985.6	(605.1)	5213.5	(649.6)	5155.8	(663.7)	5147.6	(638.3)	5171.1	(561.5)	0.48
Fat mass (g)	1603.7	(574.6)	1661.4	(516.8)	1699.9	(523.3)	1621.1	(498.2)	1692.7	(423.4)	0.59
Fat mass (%)	23.9	(6.4)	23.9	(5.7)	24.5	(5.5)	23.7	(5.3)	24.5	(4.7)	0.59
Total mass growth rate (g/mo)	749.2	(157.5)	747.1	(158.6)	757.8	(162.9)	710.3	(146.9)	747.0	(160.1)	0.11
Fat-free mass growth rate (g/mo)	468.5	(88.5)	471.7	(87.3)	470.1	(99.7)	445.7	(94.9)	460.4	(91.8)	0.12
Fat mass growth rate (g/mo)	280.7	(122.6)	275.3	(118.5)	287.7	(106.9)	264.6	(101.8)	286.6	(103.8)	0.36
Fat mass growth rate (%/mo)	3.4	(1.8)	3.0	(1.5)	3.2	(1.4)	3.0	(1.4)	3.2	(1.4)	0.29

*For continuous variables, group means (SD) were estimated from general linear models with category of multivitamin use/non-use entered as a class variable, and p for trend was obtained by specifying multivitamin category as a continuous variable. For categorical variables, group frequencies were calculated for each category of multivitamin use/non-use, and the p value for the overall variable was estimated from the Cochran–Mantel–Haenszel test.

Table 3

Association between weeks of daily prenatal multivitamin use and rate of change in offspring size and body composition in the first 5 months of life

	Model 1*			Model 2†		
	β	SE	P value	β	SE	P value
Birth (median 1 day)						
Total mass (g)	1.14	1.14	0.32	1.56	1.11	0.16
Fat-free mass (g)	0.82	0.88	0.35	1.09	0.87	0.21
Fat mass (g)	0.32	0.44	0.48	0.48	0.43	0.27
Adiposity (%)	0.008	0.012	0.49	0.012	0.012	0.30
Postnatal (median 5.2 months)						
Total mass growth rate (g/mo)	−0.17	0.49	0.73	−0.41	0.48	0.40
Fat-free mass growth rate (g/mo)	0.11	0.27	0.67	0.04	0.27	0.89
Fat mass growth rate (g/mo)	−0.29	0.34	0.40	−0.44	0.34	0.19
Adiposity growth rate (%/mo)	−0.006	0.005	0.182	−0.009	0.004	0.049

*Adjusted for maternal factors (age at delivery, race/ethnicity, education) and offspring factors (sex, gestational age at birth). Postnatal analyses additionally adjusted for exclusive breastfeeding.

†Adjusted for factors in model 1 plus additional maternal factors (household income, gravidity, pre-pregnancy BMI, average daily calories, physical activity, smoking, gestational weight gain). Postnatal analyses additionally adjusted for solids and maternal postnatal vitamin use.