BMJ Open Associations of maternal diet with infant adiposity at birth, 6 months and 12 months

Sarah Gonzalez-Nahm,¹ Cathrine Hoyo,² Truls Østbye,³ Brian Neelon,⁴ Carter Allen,⁴ Sara E Benjamin-Neelon⁹

ABSTRACT

To cite: Gonzalez-Nahm S, Hoyo C, Østbye T, *et al.* Associations of maternal diet with infant adiposity at birth, 6 months and 12 months. *BMJ Open* 2019;**9**:e030186. doi:10.1136/ bmjopen-2019-030186

Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2019-030186).

Received 03 March 2019 Revised 13 August 2019 Accepted 16 August 2019

Check for updates

© Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

 ¹Health, Behavior and Society, Johns Hopkins Bloomberg
 School of Public Health, Baltimore, Maryland, USA
 ²Biological Sciences, North Carolina State University, Raleigh, North Carolina, USA
 ³Community and Family
 Medicale, Duke University
 Medical Center, Durham, North Carolina, USA
 ⁴Public Health Sciences, Division of Biostatistics, The Medical University of South Carolina, USA

Correspondence to

Dr Sarah Gonzalez-Nahm; sarah.nahm@jhu.edu **Objectives** To assess associations between maternal prenatal diet quality and infant adiposity.

Design The design was a prospective birth cohort. **Setting** We used data from the Nurture study, a cohort of women and their infants residing in the southeastern USA. **Participants and exposure assessment** Between 2013 and 2015, we enrolled 860 women between 20 and 36 weeks' gestation. After reconsenting at delivery and excluding women with implausible calorie intakes, we measured dietary intake using the Block food frequency questionnaire, and assessed diet quality using a modified Alternate Healthy Eating Index 2010 (AHEI-2010), which assessed intake of 10 food categories, including fruits, vegetables, whole grains, nuts/legumes, fats, meats, beverages and sodium (excluding alcohol).

Outcomes We assessed birth weight for gestational age z-score, small and large for gestational age, low birth weight and macrosomia. Outcomes at 6 and 12 months were weight-for-length z-score, sum of subscapular and triceps skinfold thickness (SS+TR) and subscapular-to-triceps skinfold ratio (SS:TR).

Results Among mothers, 70.2% were black and 20.9% were white; less than half (45.2%) reported having a high school diploma or less. Among infants, 8.7% were low birth weight and 8.6% were small for gestational age. Unadjusted estimates showed that a higher AHEI-2010 score, was associated with a higher birth weight for gestational z-score (β =0.01; 95% Cl 0.002 to 0.02; p=0.02) and a greater likelihood of macrosomia (OR=1.04; 95% Cl 1.004 to 1.09; p=0.03). After adjustment, maternal diet quality was not associated with infant adiposity at birth, 6 or 12 months.

Conclusions Although poor maternal diet quality during pregnancy was not associated with infant adiposity in our study, maternal diet during pregnancy may still be an important and modifiable factor of public health importance.

BACKGROUND

Early childhood obesity is a risk factor for obesity later in life.¹⁻⁴ In the USA, ~13.9% of children ages 2–5 years are considered obese.⁵ A number of risk factors for the early onset of obesity have been identified.^{6–8} Birth weight may predict later obesity risk; with those at the extremes of the birth weight

Strengths and limitations of this study

- This study used prospective data from a racially diverse sample of mother–infant dyads to study associations between maternal diet during pregnancy and infant adiposity.
- This study provides data on infant weight throughout multiple time points during infancy.
- We did not adjust for multiple testing and results should be interpreted with caution.

distribution having the greatest risk of obesity later in life.^{9 10} Infant birth weight relative to gestational age is a widely used indicator of fetal growth. Infants born small for gestational age (SGA) tend to experience excessive catch-up growth, which has also been linked to a higher risk of obesity and chronic disease in childhood and adulthood.¹¹ Overweight and excessive adiposity during infancy have also been associated with a greater risk of becoming obese later in life.¹²

The fetal origins hypothesis posits that the in utero period is a critical window, during which health trajectories are established.^{13–15} Maternal diet during this developmental window has been shown to be an important exposure.^{16–18} The study of specific nutrients in relation to birth outcomes has shed light on associations between a greater maternal carbohydrate intake during pregnancy and a greater infant birth weight, and between a greater fat intake and lower infant birth weight.¹⁹ In addition, lower levels of specific nutrients, such as B vitamins, have been associated with poor offspring outcomes.^{20 21} Although the association between intake of specific nutrients and health outcomes provides useful information, the study of dietary patterns provides information on disease risk that enables the design of public health interventions that are more easily understood and implemented, as people consume foods rather than nutrients in isolation. Severe caloric restriction during times of famine has been associated with dyslipidemia, obesity and type 2 diabetes.^{22 23} In addition, poor maternal adherence to a Mediterranean diet pattern during pregnancy has been associated with a greater odds of infant DNA methylation at *MEG3-IG*,²⁴ a greater waist circumference in young children²⁵ and lower infant birth weight.²⁶

The Alternate Healthy Eating Index 2010 (AHEI-2010) allows scoring of an individual's diet quality based on the dietary guidelines, but also on foods and nutrients that have been found to be predictive of chronic disease risk.²⁷ Evidence suggests an association between a high AHEI-2010 score and lower risk of chronic diseases, such as cancer,^{28 29} and a lower risk of gestational diabetes.³⁰ Prenatally, a higher maternal prenatal AHEI-2010 is associated with a lower odds of SGA.³¹

Emond and colleagues recently assessed the association between maternal AHEI-2010 score and various infant weight and size outcomes at birth in the New Hampshire birth cohort,³¹ a predominantly White cohort of women and infants in the northern USA. We build on this prior work and assess the association between maternal AHEI-2010 score and several infant outcomes associated with obesity in a cohort of predominantly Black women from the southern USA, as Black women have higher likelihood of delivering a SGA infants.³² We examined the following five primary outcomes: birth weight for gestational age z-scores, SGA, large for gestational age (LGA), low birth weight and macrosomia. In addition, we examined infant weight-for-length (WFL) z-score and sum of subscapular and triceps skinfold thickness (SS+TR) for overall adiposity, and their ratio (SS:TR) for central adiposity,³³ when infants were 6 and 12 months of age.

METHODS

Study design and population

For this secondary data analysis, we included women and their infants who participated in the Nurture study, an observational birth cohort from the Southeastern USA intended to study the associations between multiple caregivers and infant adiposity. Recruitment has been described in detail elsewhere.³⁴ Briefly, we recruited and enrolled women between 20 and 36 weeks' gestation (second and third trimesters) from a private prenatal clinic and the local health department. At delivery, women were required to reconfirm their interest in the study and reconsent to participate in the study for themselves and their infants. Women were included if they had a singleton pregnancy with no known congenital anomalies, were at least 18 years of age, spoke English, intended to keep the baby, and had plans to stay in the area until at least 12 months' postpartum. At delivery, we excluded women who had infants born prior to 28 weeks' gestation, had congenital anomalies that could affect growth or development, were not able to take food by mouth at time of discharge, or who had been in the hospital for three or more weeks prior to discharge.

We enrolled 860 women during pregnancy, and of those, 799 (92.9%) delivered a single live infant who met our inclusion criteria and 747 completed a food frequency questionnaire (FFQ). Of those, 666 mothers (77.4%) agreed to participate in the study for themselves and their infants after birth, and 652 had completed an FFQ during pregnancy (online supplementary figure 1). We present results on a sample size of 817 imputed mother–infant pairs at birth, and 623 imputed mother–infant pairs at 6 and 12 months (after exclusions for implausible caloric intakes).

Exposure: maternal diet

We collected data on maternal diet during pregnancy at enrollment via the Block FFQ,³⁵ for which women were asked to think about their diet over the last 30 days. We scored responses using the AHEI-2010,²⁷ excluding the alcohol category, as alcohol intake in our sample was very low (median=0.07 grams), and even moderate alcohol consumption during pregnancy is not recommended. This approach is consistent with previous studies of maternal diet in pregnancy.^{36 37} Women's diets were scored based on their frequency and quantity of intake of the following 10 diet components: (1) vegetables, (2) fruit, (3) whole grains, (4) sugar-sweetened beverages, (5) nuts and legumes, (6) red/processed meat, (7) trans fat, (8) long-chain omega-3 fatty acids (docosahexaenoic acid and eicosapentaenoic acid), (9) polyunsaturated fatty acids and (10) sodium. We assigned a score of 0-10 points for each category based on recommended intake,²⁷ allowing for a final score of 0-100.

Outcomes: infant adiposity at birth, 6 and 12 months

We obtained birth weight, birth length and gestational age from the medical record. We calculated birth weight for gestational age using the intergrowth 21st reference population.³⁸ We classified infants as SGA if they had a birth weight for gestational age z-score <10th percentile for the study sample, and LGA as >90th percentile for the study sample. We also classified infants as low birth weight if they weighed <2500 g at birth, and we categorised those with birth weights >4000 g as macrosomia. In addition, we assessed infant adiposity at 6 and 12 months. Trained study staff measured infant length, weight and skinfold thicknesses in triplicate and we used the average of the three measures. We measured recumbent length to the nearest one-eighth inch using a ShorrBoard Portable Length Board and we assessed weight to the nearest 0.1 pound with a Seca Infant Scale. Data collectors also obtained skinfold measurements using Holtain skin callipers using standard techniques.³⁹ We calculated WFL z-scores at 6 and 12 months using WHO standards.⁴⁰ We calculated the ratio of subscapular skinfolds to tricep skinfolds (SS:TR) and the sum of subscapular and tricep skinfolds (SS+TR) at 6 and 12 months, which provide estimates of central and total adiposity, respectively.

Statistical analysis

We performed multiple linear regression to estimate the association between maternal AHEI-2010 score and the following outcomes: (1) birth weight for gestational age z-score, (2) WFL z-score at 6 and 12 months, (3) SS:TR skinfolds at 6 and 12 months and (4) SS+TR skinfolds at 6 and 12 months. We also performed multiple logistic regression to estimate the association between maternal AHEI-2010 score and (1) SGA, (2) LGA, (3) low birth weight and (4) macrosomia. We excluded participants with implausible calorie intakes from our analysis (<500 or >5000 kcal; n=43). We adjusted for race (Black/White/ other), parity, maternal prepregnancy body mass index (BMI), maternal education (high school graduate or less/greater than high school), maternal age, maternal smoking during pregnancy, age at infant measurement and maternal dietary kcal intake for outcomes at birth. For adiposity and growth outcomes at 6 and 12 months, we also included birth weight and breastfeeding as covariates. We included calorie intake in our models to account for the potential that women with greater AHEI-2010 scores may have overall greater caloric intake, reflecting a greater variety of food consumption. We assessed AHEI-2010 scores continuously. To address the issue of missing data, we performed multiple imputation by generating 1000 imputed datasets and fitting models to each imputed dataset. We then aggregated model parameter estimates across imputations using standard approaches that account for the variability within and across imputed datasets.⁴¹ We conducted all analyses using SAS V.9.4 with a significance level of α =0.05.

Patient and public involvement

Human subjects were not involved in the development or conduct of this analysis. We will disseminate the results of this study through scientific publications.

RESULTS

The study unimputed subjects' sociodemographic characteristics are displayed in table 1. Women were predominantly Black (70.2%), with White women making up 20.9% and women of other/multiple races 8.9%. Less than half reported having a high school diploma or less (45.2%), and 14.8% reported smoking during pregnancy. Among infants, 8.7% were low birth weight, 8.6% were considered SGA, 13.1% were considered LGA and 7.7% had macrosomia. The average woman in our sample was overweight with a mean (SD; SD) prepregnancy BMI of $30.1 (9.3) \text{ kg/m}^2$. Mean birth weight for gestational age z-score was 0.08 (1.0), and mean WFL z-scores were 0.40 (1.0) at 6 months and 0.66 (1.0) at 12 months. The mean (SD) gestational age at FFQ completion was 29.0 (4.8). Mean maternal AHEI-2010 score was 50.8 (8.8) with a range of 16.9-76.3, and mean caloric intake was 2073.8 (931.1) (table 2). Women with lower quality diets were more likely to be Black, have lower income and education and were more likely to be smokers, and were on average

 Table 1
 Maternal and infant characteristics of the Nurture study sample by quartile of AHEI-2010 score (unimputed data)

data)		
	AHEI-2010	
	Maternal characteristics	
	N (%)	
Race		
Black	426 (70.2)	
White	127 (20.9)	
Other	54 (8.9)	
Education		
≤High School graduate	275 (45.2)	
Some college/college or higher degree	334 (54.8)	
Annual household income		
<us\$20000< td=""><td colspan="2">331 (58.9)</td></us\$20000<>	331 (58.9)	
US\$20000-40000	126 (22.4)	
US\$20001-70000	60 (10.7)	
>US\$70000	45 (8.0)	
Smoking		
Yes	81 (14.8)	
No	466 (85.2)	
	Mean (SD)	
Maternal age (years)	27.4 (5.8)	
Prepregnancy BMI (kg/m ²)	30.1 (9.3)	
Parity	1.2 (1.5)	
	Infant characteristics	
	N (%)	
Low birth weight		
Yes	52 (8.7)	
No	544 (91.3)	
Macrosomia		
Yes	46 (7.7)	
No	550 (92.3)	
SGA		
Yes	51 (8.6)	
No	545 (91.4)	
LGA		
Yes	78 (13.1)	
No	518 (86.9)	
	Mean (SD)	
Gestational age (weeks)	38.5 (2.0)	
Birth weight (g)	3193.06 (581.8)	
BW/GA z-score	0.08 (1.0)	
WFL z-score 6 months	0.40 (1.1)	
WFL z-score 12 months	0.66 (1.0)	
	Continued	

Continued

Table 1 Continued	
	Mean (SD)
SS+TR 6 months	17.29 (3.4)
SS+TR 12 months	16.14 (3.1)
SS:TR 6 months	0.83 (0.2)
SS:TR 12 months	0.83 (0.2)
Any breastfeeding (weeks)	16.0 (18.8)

AHEI, Alternate Healthy Eating Index;BMI, body mass index; BW/GA, birth weight for gestational age; LBW, SGA, small for gestational age; LGA, large for gestational age; SS, subscapular skinfolds; TR, triceps skinfolds; WFL, weight for length.

younger (p<0.01). Lower AHEI-2010 scores were associated with a lower consumption of all food and nutrient categories with the exception of trans fats and sweetened beverages. Women excluded from this analysis on the basis of implausible calorie reporting were, on average younger, had higher BMI, had a lower level of income and education, and were more likely to be Black (p<0.001).

In the unadjusted linear regression models (online supplementary table 1), we observed that a 1-unit increase in maternal AHEI-2010 score was associated with a 0.01 increase in infant BW/GA z-scores (β =0.01; 95% CI 0.002 to 0.02; p=0.02). Results from our unadjusted logistic regression models (online supplementary table 2) also suggested that an increase in maternal diet score was associated with an increased likelihood of macrosomia (OR=1.04; 95% CI 1.004 to 1.09; p=0.03). After adjusting for covariates, linear and logistic regression models (tables 3 and 4) showed no statistically significant associations between maternal AHEI-2010 scores during pregnancy and infant adiposity at birth, 6 or 12 months.

Table 2 Mean (SD) of maternal diet variables		
	Mean (SD)	
AHEI-2010 score	50.8 (8.8)	
Vegetables (sv/day)	4.9 (2.9)	
Fruit (sv/day)	7.8 (5.3)	
Whole grains (g/day)	30.7 (22.7)	
Nuts/legumes (sv/day)	5.6 (5.6)	
EPA and DHA (mg/day)	71.9 (77.4)	
PUFA (% energy)	7.5 (1.8)	
Trans fats (% energy)	1.3 (0.4)	
Red and processed meats (sv/day)	9.4 (5.5)	
Sodium (mg/day)	3284.0 (1581.8)	
Sweet beverages (sv/day)	6.1 (5.2)	
Total daily kcal intake (kcal/day)	2073.81 (931.1)	

AHEI, Alternate Healthy Eating Index;DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PUFA, polyunsaturated fatty acids; sv, servings.

Table 3Linear regression*† of the association betweenmaternal diet score and (1) BW/GA z-score, (2) WFLz-score at 6 months, (3) WFL z-score at 12 months, (4)SS+TR skinfolds at 6 months, (5) SS+TR skinfolds at 12months, (6) SS:TR skinfolds at 6 and (7) SS:TR at 12 months(unstandardised beta estimates and 95% CI)

β (95% CI)		P value
BW/GA z-score	0.01 (-0.002 to 0.02)	0.10
WFL z-score 6 months	0.002 (-0.009 to 0.01)	0.74
WFL z-score 12 months	0.01 (-0.01 to 0.02)	0.34
SS+TR 6 months	0.002 (-0.01 to 0.01)	0.74
SS+TR 12 months	0.01 (-0.01 to 0.02)	0.56
SS:TR 6 months	–0.001 (–0.003 to 0.001)	0.46
SS:TR 12 months	-0.002 (-0.004 to 0.001)	0.14

*Estimates at birth adjusted for maternal race, parity, maternal education, maternal prepregnancy BMI, maternal age, maternal smoking during pregnancy, maternal daily kcal intake. †Six-month and 12-month estimates adjusted for maternal race, parity, maternal education, maternal prepregnancy BMI, maternal age, maternal smoking during pregnancy, maternal daily kcal intake, birth weight, weeks of breastfeeding and infant age at measurement.

AHEI-2010, Alternate Healthy Eating Index-2010; BMI, body mass index; BW/GA, birth weight for gestational age; SS, subscapular skinfolds; TR, triceps skinfolds; WFL, weight for length.

Our supplemental analysis restricted to Black women and their infants showed similar results to the overall analysis (online supplementary tables 3 and 4), with no changes in statistical significance. Similarly, supplemental analysis excluding preterm infants resulted in no significant changes to our findings (online supplementary tables 5 and 6).

Additionally, we present results of a supplemental analysis (online supplementary table 7 and online supplementary table 8) using a stricter upper limit (>3500 kcal) for implausible reporting of caloric intake. Our supplemental unadjusted analyses using a stricter calorie limit resulted

Table 4Logistic regression* of the association of maternaldiet score with (1) SGA, (2) LGA, (3) low birth weight and (4)macrosomia (adjusted ORs and 95% CI)				
	OR (95% CI)	P value		
SGA	0.98 (0.94 to 1.01)	0.16		
LGA	1.02 (0.98 to 1.05)	0.33		

0.99 (0.95 to 1.03)

1.04 (0.98 to 1.9)

0.60

0.07

Low birth weight

Macrosomia

*Adjusted for maternal race, parity, maternal education, maternal prepregnancy BMI, maternal age, maternal smoking during pregnancy, maternal daily kcal intake, infant gender. .AHEI, Alternate Healthy Eating Index;BMI, body mass index; LGA, large for gestational age; SGA, small for gestational age. in a similar association between maternal diet score and an increase in BW/GA z score (β =0.1; 95% CI 0.003 to 0.2; p=0.01). We also observed an association between an increase in maternal diet score and a slightly lower odds of SGA (OR=0.97; 95% CI 0.93 to 0.99; p=0.04). However, consistent with our main findings, these associations did not remain statistically significant after adjustment for covariates.

DISCUSSION

Our study suggests that maternal diet quality during pregnancy, measured by the AHEI-2010, was not associated with infant weight or adiposity at birth, 6 or 12 months after adjustment for maternal race, maternal education, maternal age, maternal smoking, prepregnancy BMI, parity, maternal calorie intake, weeks of breastfeeding and infant age at measurement.

Our findings should be interpreted with caution, as our sample size and potential for measurement error in both the exposure and outcomes may have hindered our ability to see an association between maternal AHEI-2010 score and infant adiposity. We presented the results of imputed data to improve our statistical power; however, the prevalence of SGA, low birth weight and macrosomia were still fairly low in our study sample (<10%). Also, although we had trained data collectors measure infant weight, length and skinfold thicknesses directly, obtaining accurate measurements in infants can be challenging, especially in infants with smaller skinfolds. If data collectors systematically overestimated infants' skinfold thicknesses and mothers with lower diet quality are more likely to have an infant with low skinfold thickness, then these results may be biassed toward the null. Additionally, although the use of the Block FFQ has been validated in multiple populations, measuring diet through questionnaires still presents a challenge. Participants may have had trouble accurately recalling their diets, or they may have been subject to social desirability bias. If women who consumed a low quality diet generally mis-reported a higher quality diet, then this may have also biassed our results towards the null.

Although our study showed no statistically significant findings after adjustment, several previous studies have shown a link between maternal diet during pregnancy and infant anthropometric outcomes at birth, including SGA and birth weight.^{19 42 43} In a recent publication, Emond and colleagues reported an association between a lower maternal AHEI-2010 score during pregnancy and an increased likelihood of having an SGA infant in a predominantly White, non-Hispanic population.³¹ The results of our analysis did not show such an association in a sample of predominantly Black women and infants. However, our ability to observe a statistically significant association after adjustment was likely hindered, in part, by our sample size and the small number of infants considered SGA. Given the previously established association between Black race and size at birth,⁴⁴ we conducted

a supplemental analysis, in which we restricted to Black women and their infants. We also found no statistically significant associations between maternal diet and infant weight and adiposity at birth, 6 and 12 months among Black women and their infants. This contradicted our hypothesis that the association between maternal diet and SGA would have become stronger when assessing only Black women and their infants.

Our findings contribute to the growing body of literature on maternal diet during pregnancy and infant weight and adiposity. Previous studies have found an association between increased intake of sodium during the first trimester of pregnancy and a greater WFL z-score and adiposity measures at 6 months,⁴⁵ and another reported an association between maternal consumption of a Mediterranean diet pattern and body composition at age 4 years.²⁵ However, this is not the first study to report null findings on the association between maternal nutrition and infant size or adiposity. A previous study found no association between maternal vitamin D intake during pregnancy and infant size or body composition at 5 months.⁴⁶ Another study found no association between a low glycemic index diet and infant adiposity throughout the first year of life.⁴⁷ The lack of a statistically significant association between maternal diet quality and infant weight and adiposity in our study may be related to the timing of exposure assessment. We did not have dietary data reflecting intake during the first trimester, which the literature suggests is an important period for in utero programming. Previous literature has also shown that different timing of exposure assessment during the in utero period can result in different outcomes in offspring throughout the life course.^{48 49}

Our study had several strengths. We used a diet measure that has been shown to be associated with chronic disease risk, and is easily translatable to public health recommendations. In addition, we used a racially diverse study population that had data prospectively collected by trained study staff, therefore recall bias in outcome measures is less of an issue. However, our study also had limitations. First, the study was limited by the use of self-reported maternal diet data. While the Block FFQ has been shown to be a valid dietary assessment tool, there is always the potential for social desirability bias. Second, we investigated weight and adiposity status at different time points rather than growth or weight gain over time. Although there is literature showing a link between weight status and obesity risk, there is a greater body of literature showing an association between weight gain over the first year of life and obesity risk. $^{4.50-52}$ Third, it is possible our study was limited by multiple testing, and that we observed our results by chance. Fourth, although previous studies have used 5000 kcal as the upper limit for implausible calorie reporting during pregnancy,^{53 54} there is literature supporting the use of a stricter (3500 kcal) limit.^{55 56} We conducted supplemental analysis with the stricter cut point and found no change in statistical significance or direction of our findings. Finally, our sample was limited

geographically to women recruited from two prenatal clinics in the southeastern USA, and results may not be generalisable to other populations of women. We were also unable to include potentially important covariates, such as maternal physical activity and gestational weight gain due to a lack of available data on these factors.

CONCLUSIONS

Assessing child outcomes beyond the first year of life will provide additional insights into whether the association between maternal diet during pregnancy and infant weight persists through childhood. Future studies should use larger, diverse cohorts, with longer follow-up periods to assess differences in maternal diet by important covariates, such as race and maternal BMI, and associations with adiposity later in childhood. The results of this study add to the growing literature on associations of maternal diet during pregnancy on offspring weight and adiposity outcomes, and reinforces the importance of maternal diet during pregnancy. Despite a lack of statistically significant results in this study, it is still worth investigating the role of maternal diet during pregnancy on infant and child adiposity outcomes, as in utero programming may dictate offspring obesity risk. Maternal diet during pregnancy is a modifiable factor that can potentially be used to help prevent future obesity, and may even mitigate an elevated obesity risk in children. These results can inform clinical practice by providing diet recommendations that are easy to convey and understand.

Contributors SG-N and CA conducted the analysis. SG-N drafted the manuscript. SEB-N and BN oversaw the analysis. SEB-N, BN, CA, TO and CH reviewed and edited the manuscript. SG-N, SEB-N, CH, TO, BN and CA approved the final manuscript.

Funding This study was supported by a grant from the National Institutes of Health (R01DK094841).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Women provided written, informed consent for themselves and their infants to participate in the study. The Institutional Review Board of Duke University Medical Centre approved this study and its protocol (reference number: Pro00036242).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

REFERENCES

- Evensen E, Emaus N, Kokkvoll A, *et al.* The relation between birthweight, childhood body mass index, and overweight and obesity in late adolescence: a longitudinal cohort study from Norway, the Tromsø study, fit futures. *BMJ Open* 2017;7:e015576.
- Baird J, Fisher D, Lucas P, et al. Being big or growing fast: systematic review of size and growth in infancy and later obesity. BMJ 2005;331.
- Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics* 1998;101:518–25.

- Ekelund U, Ong K, Linné Y, *et al.* Upward weight percentile crossing in infancy and early childhood independently predicts fat mass in young adults: the Stockholm weight development study (SWEDES). *Am J Clin Nutr* 2006;83:324–30.
- Hales CM, Carroll MD, Fryar CD, et al. Prevalence of obesity among adults and youth: United States 2015-2016. NCHS data brief, no 288. Hyattsville, MD: National Center for Health Statistics, 2017.
- Monasta L, Batty GD, Cattaneo A, et al. Early-Life determinants of overweight and obesity: a review of systematic reviews. Obesity Reviews 2010;11:695–708.
- Thompson AL, Bentley ME. The critical period of infant feeding for the development of early disparities in obesity. Soc Sci Med 2013;97:288–96.
- Emmett PM, Jones LR. Diet, growth, and obesity development throughout childhood in the Avon longitudinal study of parents and children. *Nutr Rev* 2015;73(suppl 3):175–206.
- 9. Ong KK. Size at birth, postnatal growth and risk of obesity. *Horm Res Paediatr* 2006;65(Suppl 3):65–9.
- Schellong K, Schulz S, Harder T, et al. Birth weight and long-term overweight risk: systematic review and a meta-analysis including 643,902 persons from 66 studies and 26 countries globally. PLoS One 2012;7:e47776.
- Wills AK, Strand BH, Glavin K, et al. Regression models for linking patterns of growth to a later outcome: infant growth and childhood overweight. BMC Med Res Methodol 2016;16:41.
- Smego A, Woo JG, Klein J, *et al.* High body mass index in infancy may predict severe obesity in early childhood. *J Pediatr* 2017;183:87–93.
- Barker DJP. The fetal and infant origins of adult disease the womb may be more important than the home. *BMJ* 1990;301.
- Gluckman PD, Hanson MA, Cooper C, *et al.* Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med* 2008;359:61–73.
- Godfrey KM, Gluckman PD, Hanson MA. Developmental origins of metabolic disease: life course and intergenerational perspectives. *Trends Endocrinol Metab* 2010;21:199–205.
- Symonds ME, Mendez MA, Meltzer HM, et al. Early life nutritional programming of obesity: mother-child cohort studies. Ann Nutr Metab 2013;62:137–45.
- Lillycrop KA, Burdge GC. Maternal diet as a modifier of offspring epigenetics, 2015: 88–95.
- Murrin C, Shrivastava A, Kelleher CC. Maternal macronutrient intake during pregnancy and 5 years postpartum and associations with child weight status aged five. *Eur J Clin Nutr* 2013;67:670–9.
- Sharma SS, Greenwood DC, Simpson NAB, et al. Is dietary macronutrient composition during pregnancy associated with offspring birth weight? an observational study. Br J Nutr 2018;119:330–9.
- Dominguez-Salas P, Moore SE, Cole D, et al. Dna methylation potential: dietary intake and blood concentrations of one-carbon metabolites and cofactors in rural African women. Am J Clin Nutr 2013;97:1217–27.
- Hoyo C, Daltveit AK, Iversen E, et al. Erythrocyte folate concentrations, CpG methylation at genomically imprinted domains, and birth weight in a multiethnic newborn cohort. *Epigenetics* 2014;9:1120–30.
- Li C, Lumey LH. Exposure to the Chinese famine of 1959–61 in early life and long-term health conditions: a systematic review and metaanalysis. *Int J Epidemiol* 2017;46:1157–70.
- Lumey LH, Khalangot MD, Vaiserman AM. Association between type 2 diabetes and prenatal exposure to the Ukraine famine of 1932-33: a retrospective cohort study. *Lancet Diabetes Endocrinol* 2015;3:787–94.
- Gonzalez-Nahm S, Mendez M, Robinson W, et al. Low maternal adherence to a Mediterranean diet is associated with increase in methylation at the MEG3-IG differentially methylated region in female infants. *Environ Epigenet* 2017;3:1–10.
- Fernández-Barrés S, Romaguera D, Valvi D, *et al.* Mediterranean dietary pattern in pregnant women and offspring risk of overweight and abdominal obesity in early childhood: the INMA birth cohort study. *Pediatr Obes* 2016;11:491–9.
- Parlapani E, Agakidis C, Karagiozoglou-Lampoudi T, et al. The Mediterranean diet adherence by pregnant women delivering prematurely: association with size at birth and complications of prematurity. J Matern Fetal Neonatal Med 2017:1–8.
- Chiuve SE, Fung TT, Rimm EB, *et al.* Alternative dietary indices both strongly predict risk of chronic disease. *J Nutr* 2012;142:1009–18.
- Qin B, Moorman PG, Kelemen LE, et al. Dietary quality and ovarian cancer risk in African-American women. Am J Epidemiol 2017;185:1281–9.

<u>6</u>

- Park S-Y, Boushey CJ, Wilkens LR, et al. High-Quality Diets Associate With Reduced Risk of Colorectal Cancer: Analyses of Diet Quality Indexes in the Multiethnic Cohort. *Gastroenterology* 2017;153:386–94.
- Tobias DK, Zhang C, Chavarro J, et al. Prepregnancy adherence to dietary patterns and lower risk of gestational diabetes mellitus. Am J Clin Nutr 2012;96:289–95.
- Emond JA, Karagas MR, Baker ER, et al. Better diet quality during pregnancy is associated with a reduced likelihood of an infant born small for gestational age: an analysis of the prospective new Hampshire birth cohort study. J Nutr 2018;148:22–30.
- 32. Bediako PT, BeLue R, Hillemeier MM. A comparison of birth outcomes among black, Hispanic, and black Hispanic women. *J. Racial and Ethnic Health Disparities* 2015;2:573–82.
- Boeke CE, Oken E, Kleinman KP, et al. Correlations among adiposity measures in school-aged children. BMC Pediatr 2013;13.
- Benjamin Neelon SE, Østbye T, Bennett GG, et al. Cohort profile for the nurture observational study examining associations of multiple caregivers on infant growth in the southeastern USA. *BMJ Open* 2017;7:e013939.
- Block G, Hartman AM, Dresser CM, *et al.* A data-based approach to diet questionnaire design and testing. *Am J Epidemiol* 1986;124:453–69.
- Mantzoros CS, Sweeney L, Williams CJ, et al. Maternal diet and cord blood leptin and adiponectin concentrations at birth 2010;29:622–6.
- Shapiro ALB, Kaar JL, Crume TL, et al. Maternal diet quality in pregnancy and neonatal adiposity: the healthy start study. Int J Obes 2016;40:1056–62.
- Villar J, Ismail LC, Victora CG, *et al*. International standards for newborn weight, length, and head circumference by gestational age and sex: the newborn cross-sectional study of the INTERGROWTH-21st project. *Lancet* 2014;384:857–68.
- Shorr I. How to weigh and measure children. New York: United Nations, 1986.
- 40. World Health Organization. The who growth standards. Available: http://www.who.int/childgrowth/standards/en/
- Rubin DB. Multiple imputation for nonresponse in surveys. John Wiley & Sons, 2004.
- 42. Gómez Roig MD, Mazarico E, Ferrero S, *et al.* Differences in dietary and lifestyle habits between pregnant women with small fetuses and appropriate-for-gestational-age fetuses. *J Obstet Gynaecol Res* 2017;43:1145–51.

- MS L, Chen QZ, JR H, et al. Maternal dietary patterns and fetal growth: a large prospective cohort study in China. Nutrients 2016;8.
- Grobman WA, Parker CB, Willinger M, et al. Racial disparities in adverse pregnancy outcomes and psychosocial stress. Obstet Gynecol 2018;131:328–35.
- 45. Horan M, McGowan C, Gibney E, *et al*. Maternal nutrition and glycaemic index during pregnancy impacts on offspring adiposity at 6 months of Age—Analysis from the ROLO randomised controlled trial. *Nutrients* 2016;8:7.
- Sauder K, Koeppen H, Shapiro A, et al. Prenatal vitamin D intake, cord blood 25-hydroxyvitamin D, and offspring body composition: the healthy start study. *Nutrients* 2017;9:790.
- Kizirian NV, Kong Y, Muirhead R, et al. Effects of a low–glycemic index diet during pregnancy on offspring growth, body composition, and vascular health: a pilot randomized controlled trial. Am J Clin Nutr 2016;103:1073–82.
- Tobi EW, Lumey LH, Talens RP, et al. Dna methylation differences after exposure to prenatal famine are common and timing- and sexspecific. Hum Mol Genet 2009;18:4046–53.
- Heijmans BT, Tobi EW, Stein AD, et al. Persistent epigenetic differences associated with prenatal exposure to famine in humans. Proc Natl Acad Sci U S A 2008;105:17046–9.
- Cl D, Stettler N, Sharp S, et al. Prediction of childhood obesity by infancy weight gain: an individual-level meta-analysis. *Paediatric and Perinatal Epidemiology* 2012;26:19–26.
- Ong K, Loos R. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. *Acta Paediatr* 2006;95:904–8.
- Monteiro POA, Victora CG. Rapid growth in infancy and childhood and obesity in later life - a systematic review. *Obesity Reviews* 2005;6:143–54.
- Starling AP, Sauder KA, Kaar JL, *et al.* Maternal dietary patterns during pregnancy are associated with newborn body composition. J *Nutr* 2017;147:1334–9.
- Meltzer HM, Brantsaeter AL, Ydersbond TA, et al. Methodological challenges when monitoring the diet of pregnant women in a large study: experiences from the Norwegian mother and child cohort study (MobA). Matern Child Nutr 2008;4:14–27.
- Rhee JJ, Sampson L, Cho E, *et al.* Comparison of methods to account for Implausible reporting of energy intake in epidemiologic studies. *Am J Epidemiol* 2015;181:225–33.
- Willett WC. Nutritional epidemiology. New York, NY: Oxford University Press, 1998.