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Elevated Body Mass Index and Decreased Diet Quality among Women and Risk of Birth Defects in Their Offspring

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Abstract

Background—We examined whether risks of 32 birth defects were higher than expected in the presence of overweight or obese body mass index (BMI) and low diet quality, based on estimating individual and joint effects of these factors and calculating relative excess risk due to interaction.

Methods—Analyses included mothers of 20,250 cases with birth defects and 8617 population-based controls without birth defects born from 1997 to 2009 and interviewed for the National Birth Defects Prevention Study. We used logistic regression to generate adjusted odds ratios (AORs) reflecting the combined effects of BMI and diet quality. We focused analyses on 16 birth defects (n = 11,868 cases, 8617 controls) for which initial results suggested an association with BMI or diet quality.

Results—Relative to the reference group (normal weight women with not low diet quality, i.e., >lowest quartile), AORs for low diet quality among normal weight women tended to be >1, and AORs for overweight and obese women tended to be stronger among women who had low diet quality than not low diet quality. For 9/16 birth defects, AORs for obese women who had low diet quality—the group we hypothesized to have highest risk—were higher than other stratum-specific AORs. Most relative excess risk due to interactions were positive but small (<0.5), with confidence intervals that included zero.

Conclusion—These findings provide evidence for the hypothesis of highest birth defect risks among offspring to women who are obese and have low diet quality but insufficient evidence for an interaction of these factors in their contribution to risk.

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Additional Supporting information may be found in the online version of this article.

Keywords

nutrition; obesity; congenital anomalies; diet; neural tube defects

Introduction

Elevated prepregnancy body mass index (BMI) has been associated with increased risks of many birth defects (Waller et al., 2007; Gilboa et al., 2010). Intakes of folate and other micronutrients from vitamin/mineral supplements as well as from foods have been associated with reduced risks of birth defects (Botto et al., 2004). Diet quality represents a more holistic approach to characterizing dietary intake than examining single micronutrients or food groups. Recent studies indicate that overall better maternal diet quality is also associated with reduced risks of birth defects, independent of intake of supplements or specific dietary nutrients (Carmichael et al., 2012; Feldkamp et al., 2014). Many biologic pathways could contribute to associations of birth defects with elevated BMI or with lower diet quality, including for example glycemic control and oxidative stress (Carmichael et al., 2010). No particular etiologic explanation has been established for either elevated BMI or lower diet quality.

Studying the combined influence of elevated BMI and lower maternal diet quality could further our understanding of the underlying etiologies associated with either factor alone. Understanding risks associated with joint exposures is also important from a prevention standpoint; i.e., it is important to know whether women with multiple risk factors are at particularly high risk of certain outcomes. In the current study, we used data from the National Birth Defects Prevention Study (NBDPS) to examine the independent as well as combined effects of maternal diet quality and BMI on risks of birth defects.

Materials and Methods

STUDY DESIGN

The NBDPS is a multi-state, population-based case–control study of clinically well-defined birth defects. This analysis included deliveries that had estimated due dates from 1997 to 2009. The study is an approved activity of the Institutional Review Boards of the participating study centers and the Centers for Disease Control and Prevention. Detailed study methods and descriptions of surveillance systems in the 10 states that contributed data to this analysis (AR, CA, GA, IA, MA, NC, NJ, NY, TX, UT) have been published (Yoon et al., 2001; Reefhuis et al., 2015). Case information was obtained from hospital reports and medical records and entered into a standardized database for clinician review and classification. Detailed case classification criteria have been published previously (Rasmussen et al., 2003). Cases resulting from known single gene or chromosomal abnormalities (syndromic cases) were ineligible, given their presumed genetic determinants. Infants whose birth defects were believed to be secondary to another defect (e.g., median cleft lip in the presence of holoprosencephaly) were ineligible. As controls, each participating center randomly selected at least 100 liveborn infants without major birth defects per study year from birth certificates or birth hospitals to represent the population from which the cases were derived. Maternal interviews were conducted using a standardized, computer-based questionnaire, primarily by telephone, in English or Spanish, between 6 weeks and 24 months after the infant's estimated date of delivery. Exposures to many factors were assessed, relative to the woman's estimated date of conception, which was derived by subtracting 266 days from the estimated date of delivery. Interviews were conducted with mothers of 68% of cases and 65% of controls. Median time from actual date of delivery to interview was 10.4 months for cases (interquartile range, 8.0 months) and 7.6 months for controls (interquartile range, 6.5 months).

STUDY VARIABLES

Mother's prepregnancy BMI was based on her self-reported prepregnancy weight divided by height-squared (kg/m^2). Obesity was defined as BMI ≥ 30.0, overweight as 25.0 to 29.9, and normal weight as 18.5 to 24.9 kg/m^2 (National Institutes of Health, 1998). Underweight (<18.5 kg/m^2) women were excluded. Mothers reported their average intake of foods during the year before they became pregnant using a 58-item food frequency questionnaire (FFQ) developed by Willett and colleagues for The Nurse's Health Study (Willett et al., 1985). Intake of breakfast cereals, sodas, and food supplements were assessed by separate, more detailed questions, which covered intake during the 3 months before pregnancy. Because few women (mothers of 10% of cases and 10% of controls) consumed food supplements (e.g., powdered drink supplements) and nutrient data were not available for many of these products, food supplements were not included in nutrient calculations. The USDA nutrient database (version 25) was the source of nutrient values (USDA-Agricultural-Research-Service, 2012). Beginning with deliveries in 2006, several new food items were added to the FFQ; to ensure comparability of data across the duration of the study, we did not consider these additional food items in nutrient calculations.

We created a diet quality index (DQI) based on a previously validated index that reflects pregnancy-specific nutritional recommendations (Haines et al., 1999; Bodnar and Siega-Riz, 2002) but adapted to the NBDPS FFQ (Carmichael et al., 2012). The DQI is the summary score of six positively scored components (grains, vegetables, fruits, folate, iron, and calcium) and two negatively scored components (percent of calories from fat, and sweets); for each subject, each component was scored from zero to three based on quartiles of the distribution among controls, and then the components were summed to obtain the final value for the DQI. A higher value indicates better diet quality. The DQI used in these analyses differs from the original in that it excludes the meal pattern component but includes a sweets component and scores each component based on quartiles rather than absolute values. A detailed description of the food items included in each component, how the indices differ from the originals, and how they were calculated is available elsewhere (Carmichael et al., 2012).

Additional variables of interest included several potential confounders, which were selected a priori: maternal age (continuous, years); race-ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other); education (<, =, or > high school); parity (0, one or more); alcohol consumption, smoking, and intake of folic acid-containing vitamin/mineral supplements during the month before pregnancy or the first 2 months of pregnancy; and energy intake.

EXCLUSIONS

We considered for analysis 27,808 unique cases and 10,200 controls. We then made the following exclusions: 1151 cases and 407 controls with maternal energy intake less than 500 kcal or greater than 5000 kcal and mothers with more than one food item missing (i.e., not queried) from the food frequency questionnaire; 2535 cases and 910 controls with underweight (<18.5 kg/m^2) or missing BMI; 665 cases and 68 controls whose mothers had type I/II diabetes diagnosed before or during the index pregnancy, given that diet–birth defect associations could differ for women with diabetes; and subjects with incomplete covariate data (544 cases and 198 controls). Remaining were 22,913 cases and 8617 controls. We analyzed 20,250 cases from 18 noncardiac and 14 cardiac-related categories of birth defects for which there were at least 250 cases (see Supplementary Table 1, which is available online).

ANALYSES

We examined the combined effects of BMI and diet quality by creating a six-level variable: (1) not low diet quality (i.e., in the highest three quartiles, based on the distribution among the controls) and normal weight (reference), (2) low diet quality (i.e., in the lowest quartile) and normal weight, (3) not low diet quality and overweight, (4) low diet quality and overweight, (5) not low diet quality and obese, and (6) low diet quality and obese (the group we hypothesize to have highest risk). We used logistic regression to calculate adjusted odds ratios (AORs) and 95 percent confidence intervals (CIs) associated with each level of this variable, adjusted for the potential confounders listed above. For birth defect categories for which at least one of the stratum-specific AORs suggested an association with risk (i.e., at least one 95% CI excluded 1.0), we estimated the relative excess risk due to interaction (RERI) and its 95% CI to reflect departure from additivity of effects, following the approach described previously by others (Andersson et al., 2005) and used by Correa et al. in their NBDPS analysis of the joint effects of diabetes and multivitamin intake (Correa et al., 2012). RERI provides an assessment of additive interaction in the framework of an exponential (logistic regression) model, which is typically used to assess multiplicative rather than interaction. RERI was estimated separately for overweight and obese BMI.

Results

Most mothers were non-Hispanic white, had greater than high school education, and took vitamin/mineral supplements during pregnancy. The distribution of these covariates was similar among all cases combined and controls, including BMI and the diet quality index (Table 1).

We identified nine noncardiac and seven cardiac-related birth defect categories for which stratum-specific AORs suggested they were associated with diet quality, overweight or obesity, that is, the 95% CI excluded 1.0 for at least one stratum-specific AOR (n = 11,868 unique cases). Results for these birth defects are presented in Table 2. AORs comparing low versus not low diet quality among normal weight women tended to be >1, but 95% CIs excluded 1.0 only for anencephaly, cleft lip with cleft palate, congenital diaphragmatic hernia, and tetralogy of Fallot. AORs for overweight and obese women tended to be stronger among women who had low diet quality than not low diet quality; for the few exceptions (omphalocele and obese BMI, gastroschisis and overweight BMI, tetralogy of Fallot and obese BMI, and hypoplastic left heart syndrome and overweight BMI), the pair of AORs were very similar to each other.

For 9 of the 16 birth defects in Table 2, the AORs for women who were obese and had low diet quality—that is, the group we hypothesized to have highest risk—were higher than the other stratum-specific AORs. AORs for gastroschisis among overweight and obese women were <1, driven by the known inverse association of BMI with risk.

Most RERIs were positive but small (<0.5), with CIs that included zero; thus, statistical evidence was not provided to show that the effect of elevated BMI and lower diet quality in combination was greater than expected (based on an additive model). However, among overweight women, the RERIs were positive for 12 of the 16 birth defects shown in Table 2; and among obese women, the RERIs were positive for 11. The largest RERIs were for anencephaly and overweight BMI (0.58), spina bifida and obese BMI (0.55), and anomalous pulmonary venous return and obese BMI (0.75). Only the RERI for anorectal atresia/stenosis and overweight women had a 95% CI that excluded zero (RERI 0.47; 95% CI, 0.03–0.92).

Discussion

This study examined the independent and combined effects of overweight or obese maternal BMI and low diet quality on risks of 32 types of structural birth defects. Our hypothesis was that risks would be highest among women who were obese *and* had low diet quality. Results indicated an association of elevated (overweight or obese) BMI alone, or lower diet quality alone, with 16 of the studied birth defects. Although for nine of these birth defects, risks were highest in magnitude among women who were obese *and* had low diet quality (as hypothesized), statistical evidence that these risks were significantly higher was lacking.

Previous analyses of data from NBDPS suggest increased risk of birth defects among women who are overweight or obese BMI (Waller et al., 2007; Gilboa et al., 2010) or who have low diet quality (Carmichael et al., 2012; Feldkamp et al., 2014). We are unaware of studies that have examined the effects of these two factors in combination. Studies have examined other aspects of nutrition in combination. For example, an analysis of NBDPS data reported that risks of birth defects among offspring born to women with pregestational diabetes were markedly less elevated among women who took vitamin/mineral supplements periconceptionally (Correa et al., 2012). This finding is in concordance with experimental studies suggesting a protective effect of anti-oxidant nutrients against the development of neural tube defects among offspring born to diabetic dams (Loeken, 2005). Another multi-site birth defects study reported that the association of obesity with risk of spina bifida was similar regardless of mother's periconceptional folic acid intake (Parker et al., 2013). We chose to focus on diet quality because higher maternal diet quality scores have been associated with reduced risks of several birth defects in the NBDPS, including neural tube defects, orofacial clefts and gastroschisis (Carmichael et al., 2012; Feldkamp et al., 2014).

The NBDPS is one of the largest population-based case–control studies of structural birth defects to date and is also unique in its inclusion of a wide variety of types of birth defects, all rigorously ascertained (Reefhuis et al., 2015). Potential limitations include recall bias, selection bias and residual confounding. The retrospective design is subject to recall bias. We believe it is unlikely that recall bias would occur for a complex exposure like diet quality or for maternal prepregnancy weight or height (which are not a well-known risk factor for birth defects in the lay community); that is, it is unlikely that mothers of cases would be more likely to misreport their dietary intake or weight or height than mothers of controls. However, we acknowledge that data are not available to explicitly assess the presence of recall bias in this study. A previous analysis indicated that NBDPS controls were similar to the base population with respect to a variety of characteristics, which reduces our concerns about selection bias (Cogswell et al., 2009). This finding, along with the study's multisite, population-based design, enhance its potential generalizability. The NBDPS interview enabled adjustment for a variety of potential confounders, but we acknowledge that residual confounding by unmeasured factors remains possible. We also note that there is substantial variability in BMI among obese women; ideally, it would be interesting to examine the study question among women with varying levels of obesity, but sample sizes seemed too limited to support such analyses.

Prepregnancy obesity and low diet quality are both important but complex factors that are associated with risks of several birth defects. Inquiries examining combined contributions of known or suspected risk factors are important for furthering etiologic understandings. These studies are rare, likely owing to the large sample sizes often required to investigate combinatorial factors. Based on an additive model of interaction, results of this study did not show statistical evidence that co-occurrence of elevated BMI and low diet quality increases women's risk more than having only one of these risk factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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TABLE 1

Descriptive Characteristics of Mothers of Case and Control Infants, National Birth Defects Prevention Study, 1997 to 2009

	Percent[a]	
	Cases (*n* = 20,250)	**Controls (*n* = 8,617)**
Race-ethnicity		
Non-Hispanic white	63	62
Black	9	11
Hispanic	21	20
Other	7	7
Education		
Less than high school	14	14
Equal to high school	25	24
Greater than high school	60	62
Parity		
0	43	40
≥ 1	57	60
Smoking[b]		
None	80	82
Any	20	18
Alcohol consumption[b]		
None	62	62
Any	38	38
Folic acid-containing vitamin/mineral supplement use[b]		
None	21	21
Any	79	79
Pre-pregnancy body mass index (kg/m^2)		
Normal weight (18.5–24.9)	55	57
Overweight (25.0–29.9)	25	24
Obesity (≥30.0)	20	19
Diet quality index[c]		
Low (score 0–8)	33	29
Not low (score 9–24)	67	71
Body mass index and diet quality index combined[c]		
Normal weight, not low diet quality	38	41
Normal weight, low diet quality	17	17
Overweight, not low diet quality	16	17
Overweight, low diet quality	8	7
Obese, not low diet quality	13	13

	Percent[a]	
	Cases (*n* = 20,250)	**Controls (*n* = 8,617)**
Obese, low diet quality	7	6
	Mean (SD)	
Maternal age at delivery (years)	27.92 (6.18)	27.88 (6.02)
Energy intake (kcals)	1565.4 (682.41)	1595.59 (673.83)

[a]Numbers may not add to 100% due to rounding.

[b]From 1 month before through 2 months after conception.

[c]Diet quality defined as "low" if the score was in the lowest quartile, based on the distribution among the controls, and as "not low" otherwise.

SD, standard deviation.

TABLE 2

Independent and Joint Effect Estimates for Maternal BMI and Diet Quality with Risk of Birth Defects, National Birth Defects Prevention Study, 1997 to 2009

Non-cardiac birth defect category	Maternal BMI	Diet quality index[a]	No. cases[b]	No. controls[b]	AOR (95% CI)[c]	RERI for overweight or obese BMI[d]	95% CI lower limit	95% CI upper limit
Anencephaly	Normal	Not low	154	3504	Reference			
	Normal	Low	84	1423	**1.60 (1.19,2.16)**			
	Overweight	Not low	66	1489	0.94 (0.70,1.27)			
	Overweight	Low	49	600	**2.16 (1.51,3.08)**	0.58	−0.16	1.31
	Obese	Not low	59	1111	1.14 (0.84,1.56)			
	Obese	Low	32	490	**1.67 (1.11,2.52)**	−0.08	−0.88	0.72
Spina bifida	Normal	Not low	310	3504	Reference			
	Normal	Low	134	1423	1.04 (0.83,1.31)			
	Overweight	Not low	170	1489	**1.25 (1.03,1.53)**			
	Overweight	Low	79	600	**1.45 (1.10,1.90)**	0.15	−0.29	0.60
	Obese	Not low	153	1111	**1.53 (1.24,1.88)**			
	Obese	Low	96	490	**2.15 (1.66,2.79)**	0.55	−0.02	1.12
Cleft lip with cleft palate	Normal	Not low	534	3440	Reference			
	Normal	Low	252	1410	**1.21 (1.02,1.44)**			
	Overweight	Not low	231	1469	1.00 (0.84,1.18)			
	Overweight	Low	106	592	1.24 (0.98,1.57)	0.03	−0.31	0.38
	Obese	Not low	202	1095	1.15 (0.96,1.37)			
	Obese	Low	113	483	**1.63 (1.29,2.06)**	0.27	−0.16	0.69
Anorectal atresia/ stenosis	Normal	Not low	278	3504	Reference			
	Normal	Low	108	1423	0.93 (0.73,1.19)			
	Overweight	Not low	125	1489	1.03 (0.83,1.29)			
	Overweight	Low	70	600	**1.45 (1.09,1.94)**	**0.47**	**0.03**	**0.92**
	Obese	Not low	111	1111	1.24 (0.98,1.56)			

Non-cardiac birth defect category	Maternal BMI	Diet quality index[a]	No. cases[b]	No. controls[b]	AOR (95% CI)[c]	RERI for overweight or obese BMI[d]	95% CI lower limit	95% CI upper limit
	Obese	Low	66	490	**1.67 (1.24,2.25)**	0.49	−0.04	1.02
Transverse limb deficiency	Normal	Not low	201	3504	Reference			
	Normal	Low	93	1423	1.22 (0.93,1.60)			
	Overweight	Not low	92	1489	1.05 (0.82,1.36)			
	Overweight	Low	51	600	**1.59 (1.14,2.22)**	0.32	−0.27	0.91
	Obese	Not low	69	1111	1.08 (0.81,1.43)			
	Obese	Low	36	490	1.37 (0.94,2.01)	0.08	−0.52	0.67
Craniosynostosis	Normal	Not low	419	3504	Reference			
	Normal	Low	196	1423	1.09 (0.90,1.33)			
	Overweight	Not low	189	1489	1.11 (0.92,1.33)			
	Overweight	Low	104	600	**1.39 (1.09,1.77)**	0.17	−0.21	0.55
	Obese	Not low	148	1111	1.18 (0.96,1.44)			
	Obese	Low	86	490	**1.46 (1.13,1.90)**	0.21	−0.24	0.65
Diaphragmatic hernia	Normal	Not low	211	3504	Reference			
	Normal	Low	142	1423	**1.63 (1.28,2.08)**			
	Overweight	Not low	77	1489	0.87 (0.66,1.13)			
	Overweight	Low	59	600	**1.63 (1.19,2.24)**	0.12	−0.42	0.67
	Obese	Not low	78	1111	1.19 (0.91,1.56)			
	Obese	Low	41	490	1.40 (0.98,2.01)	−0.42	−1.05	0.21
Omphalocele	Normal	Not low	114	3504	Reference			
	Normal	Low	50	1423	1.05 (0.73,1.51)			
	Overweight	Not low	58	1489	1.20 (0.86,1.65)			
	Overweight	Low	25	600	1.23 (0.77,1.95)	−0.02	−0.7	0.67
	Obese	Not low	56	1111	**1.57 (1.13,2.19)**			
	Obese	Low	25	490	1.51 (0.95,2.39)	−0.1	−0.96	0.74
Gastroschisis	Normal	Not low	488	3504	Reference			
	Normal	Low	260	1423	1.18 (0.97,1.43)			

Non-cardiac birth defect category	Maternal BMI	Diet quality index[a]	No. cases[b]	No. controls[b]	AOR (95% CI)[c]	RERI for overweight or obese BMI[d]	95% CI lower limit	95% CI upper limit
	Overweight	Not low	122	1489	**0.63 (0.50,0.78)**			
	Overweight	Low	62	600	0.78 (0.57,1.07)	−0.01	−0.32	0.31
	Obese	Not low	40	1111	**0.27 (0.19,0.38)**			
	Obese	Low	15	490	**0.24 (0.14,0.42)**	−0.20	−0.42	0.08

Cardiac birth defect category	Maternal BMI	Diet quality index	No. cases	No. controls	AOR (95% CI)	RERI for overweight or obese (95% CI)	95% CI lower limit	95% CI upper limit
Tetralogy of Fallot	Normal	Not low	309	3504	Reference			
	Normal	Low	154	1423	**1.26 (1.01,1.56)**			
	Overweight	Not low	142	1489	1.06 (0.86,1.31)			
	Overweight	Low	87	600	**1.65 (1.26,2.15)**	0.33	−0.14	0.80
	Obese	Not low	134	1111	**1.38 (1.11,1.72)**			
	Obese	Low	57	490	1.32 (0.97,1.80)	−0.32	−0.82	0.19
Anomalous pulmo- nary venous return	Normal	Not low	98	3504	Reference			
	Normal	Low	49	1423	1.12 (0.77,1.63)			
	Overweight	Not low	40	1489	0.92 (0.63,1.34)			
	Overweight	Low	16	600	0.86 (0.49,1.50)	−0.20	−0.87	0.47
	Obese	Not low	30	1111	0.91 (0.60,1.38)			
	Obese	Low	27	490	**1.75 (1.11,2.77)**	0.75	−0.11	1.6
Hypoplastic left heart syndrome	Normal	Not low	170	3504	Reference			
	Normal	Low	82	1423	1.15 (0.86,1.53)			
	Overweight	Not low	90	1489	1.26 (0.96,1.64)			
	Overweight	Low	37	600	1.20 (0.82,1.76)	−0.20	−0.77	0.37
	Obese	Not low	67	1111	1.24 (0.92,1.66)			
	Obese	Low	38	490	**1.50 (1.03,2.20)**	0.12	−0.53	0.78
Right ventricular outflow tract defects – excluding Ebstein cases	Normal	Not low	448	3504	Reference			

Cardiac birth defect category	Maternal BMI	Diet quality index	No. cases	No. controls	AOR (95% CI)	RERI for overweight or obese (95% CI)	95% CI lower limit	95% CI upper limit
	Normal	Low	219	1423	1.20 (1.00,1.44)			
	Overweight	Not low	254	1489	**1.33 (1.12,1.57)**			
	Overweight	Low	137	600	**1.74 (1.39,2.17)**	0.22	−0.19	0.64
	Obese	Not low	201	1111	**1.37 (1.14,1.64)**			
	Obese	Low	132	490	**2.00 (1.60,2.51)**	0.43	−0.05	0.90
Pulmonary valve stenosis	Normal	Not low	355	3345	Reference			
	Normal	Low	177	1376	1.20 (0.98,1.46)			
	Overweight	Not low	209	1406	**1.39 (1.16,1.67)**			
	Overweight	Low	111	580	**1.75 (1.37,2.22)**	0.17	−0.30	0.63
	Obese	Not low	161	1065	**1.38 (1.13,1.68)**			
	Obese	Low	104	468	**1.97 (1.54,2.53)**	0.41	−0.12	0.94
Atrial septal defect (secundum)	Normal	Not low	601	3504	Reference			
	Normal	Low	273	1423	1.17 (0.99,1.39)			
	Overweight	Not low	281	1489	1.07 (0.92,1.25)			
	Overweight	Low	149	600	**1.51 (1.23,1.86)**	0.27	−0.08	0.62
	Obese	Not low	266	1111	**1.33 (1.13,1.56)**			
	Obese	Low	137	490	**1.66 (1.33,2.06)**	0.15	−0.25	0.56
Atrial septal defect (not otherwise specified)	Normal	Not low	177	3504	Reference			
	Normal	Low	83	1423	1.20 (0.90,1.61)			
	Overweight	Not low	81	1489	0.99 (0.75,1.30)			
	Overweight	Low	50	600	**1.64 (1.16,2.31)**	0.44	−0.15	1.03
	Obese	Not low	67	1111	1.10 (0.82,1.47)			
	Obese	Low	34	490	1.35 (0.91,2.00)	0.04	−0.59	0.66

[a] Diet quality defined as “low” if the score was in the lowest quartile, based on the distribution among the controls, and as “not low” otherwise.

[b] Results are for 11,868 unique cases and a maximum of 8,617 controls; the total number of controls was lower for cleft lip with or without cleft palate and pulmonary valve stenosis due to variability in the time period of collection of these case groups for some centers.

[c] Adjusted for maternal age, race-ethnicity, education, parity, any periconceptional alcohol consumption, smoking, intake of folic acid-containing vitamin/mineral supplements during the month before pregnancy or the first 2 months of pregnancy, and energy intake.

[d]RERI = Relative excess risk due to interaction, which reflects departure from additivity of effects of overweight BMI and low diet quality or obese BMI and low diet quality in combination.

Boldface type indicates AORs with 95% CIs that exclude 1.0. AOR, adjusted odds ratio; BMI, body mass index; 95% CI = 95% confidence interval.