

## Supplementary Online Content

Wang G, Hu FB, Mistry KB, et al. Association between maternal prepregnancy body mass index and plasma folate concentrations with child metabolic health. *JAMA Pediatr*. Published online June 13, 2016. doi:10.1001/jamapediatrics.2016.0845.

**eFigure 1.** Flowchart of the Sample Included in the Analysis.

**eFigure 2.** Association Between Maternal Folate and Offspring Metabolic Biomarkers in the Boston Birth Cohort.

**eTable 1.** Comparison of Prenatal and Early Childhood Characteristics Between Included and Excluded Samples.

**eTable 2.** Individual and Combined Effect of Maternal Folate Concentration And Pre-Pregnancy BMI Categories on Child Insulin Concentration With Additional Adjustment for Child Adiposity in the Boston Birth Cohort (BBC).

**eTable 3.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Leptin Concentration With Additional Adjustment for Child Adiposity in the Boston Birth Cohort (BBC).

**eTable 4.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Adiponectin/Leptin Ratio With Additional Adjustment for Child Adiposity in the Boston Birth Cohort (BBC).

**eTable 5.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score and Overweight Or Obesity at Age 2-5 Years in the Boston Birth Cohort (BBC).

**eTable 6.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score and Overweight or Obesity at Age 6-9 Years in the Boston Birth Cohort (BBC).

**eTable 7.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score and Overweight Or Obesity at Age 2-9 Years (Black Only) in the Boston Birth Cohort (BBC).

**eTable 8.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score at Age 2-9 Years Stratified by Preterm Birth in the Boston Birth Cohort (BBC).

**eTable 9.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score and Overweight or Obesity at Age 2-9 Years With Additional Adjustment for C-Section and Planned Pregnancy in the Boston Birth Cohort (BBC).

**eTable 10.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Metabolic Biomarkers With Additional Adjustment for C-Section and Planned Pregnancy in the Boston Birth Cohort (BBC).

**eTable 11.** Propensity Score-Based Matched Analysis for Comparison of Low Folate to Adequate Folate Concentration in the Boston Birth Cohort (BBC).

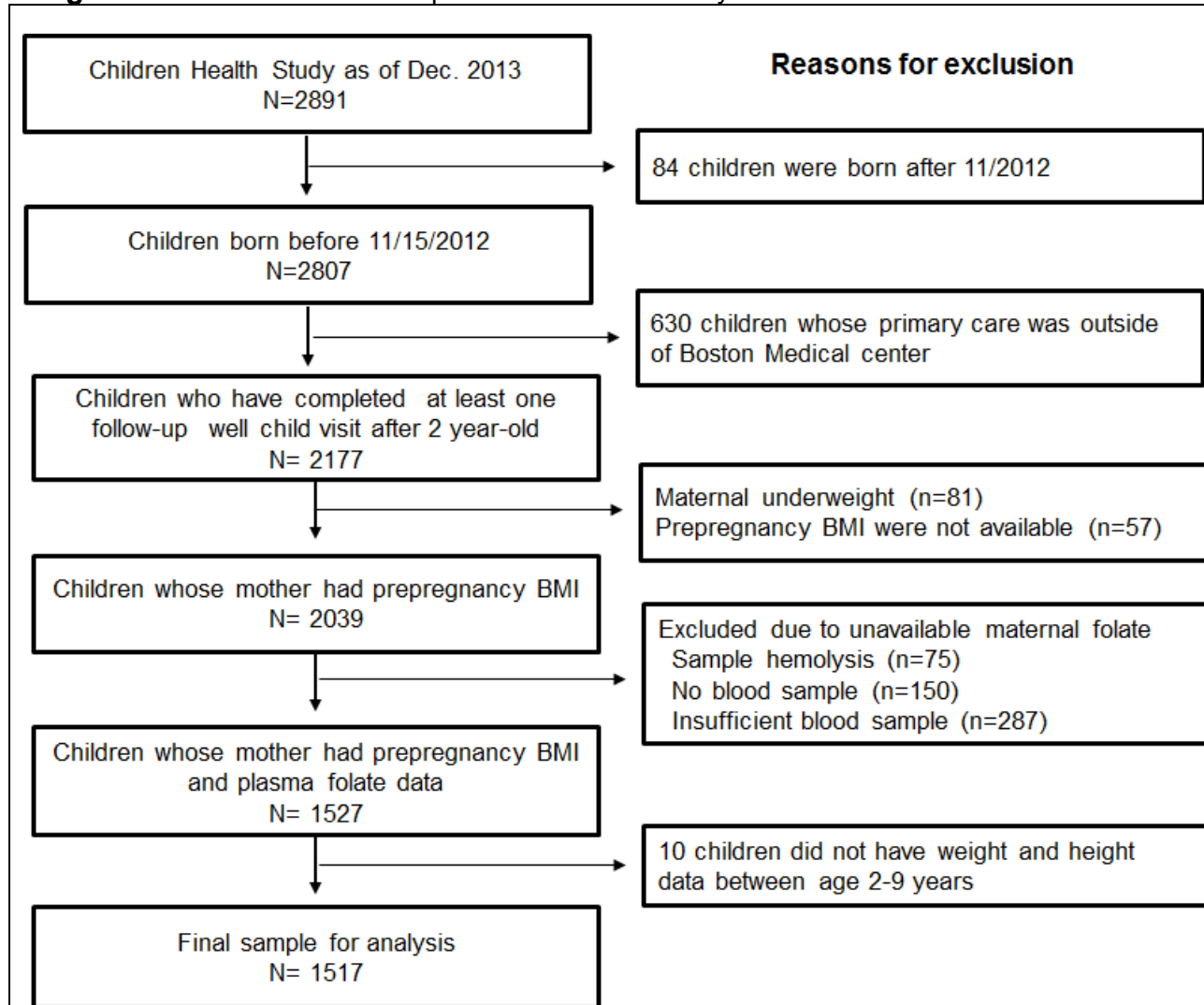
**eTable 12.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Metabolic Biomarkers in the First 2 Years of Life in the Boston Birth Cohort (BBC).

**eTable 13.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score at Age 2-9 Years With and Without Adjustment for Child Plasma Folate Concentration in the Boston Birth Cohort (BBC).

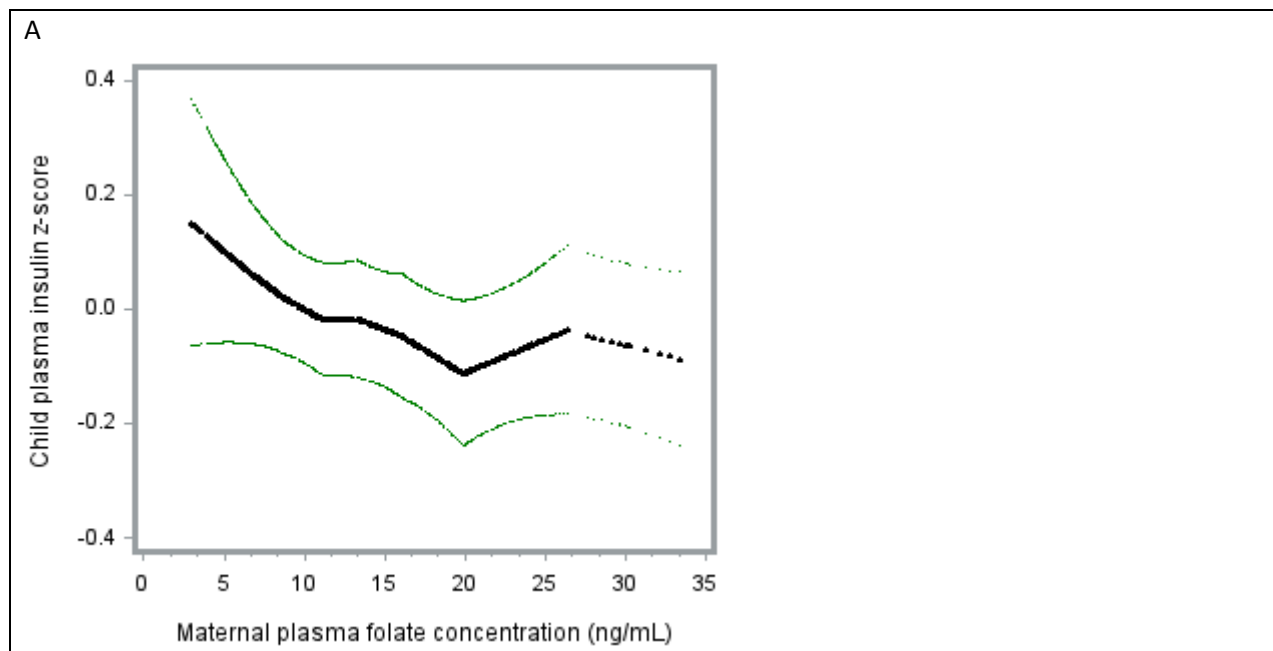
**eTable 14.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Overweight or Obesity at Age 2-9 Years With And Without Adjustment for Child Plasma Folate Concentration in the Boston Birth Cohort (BBC).

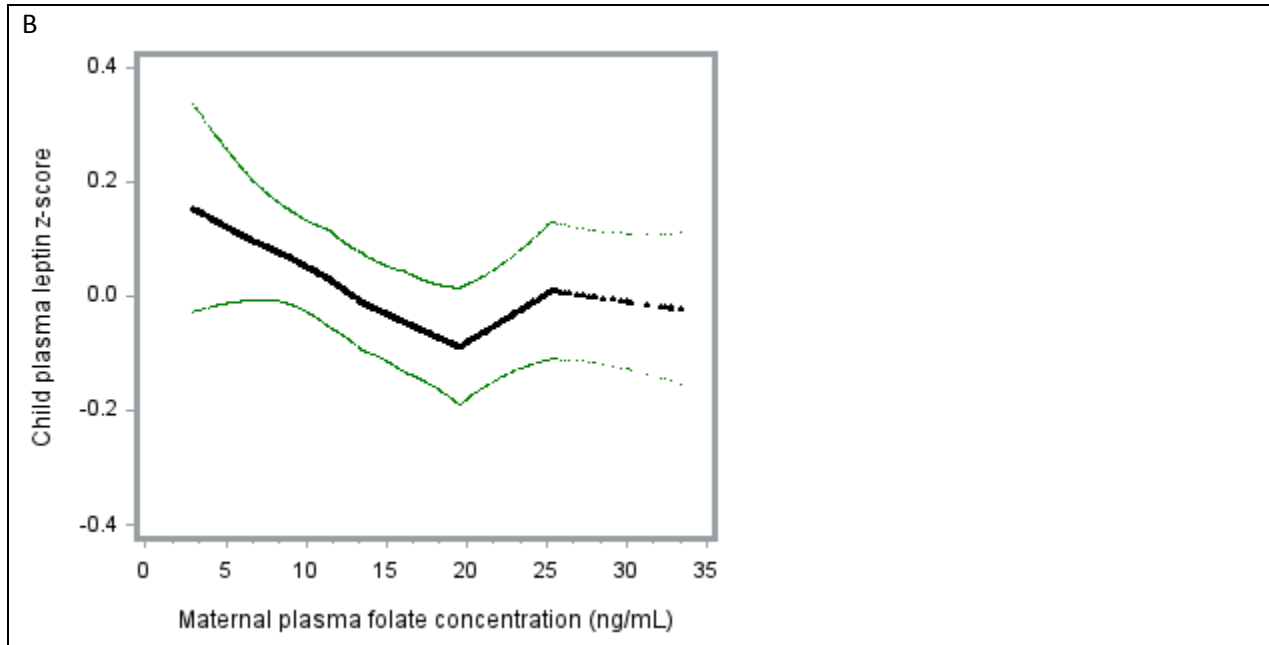
This supplementary material has been provided by the authors to give readers additional information about their work.

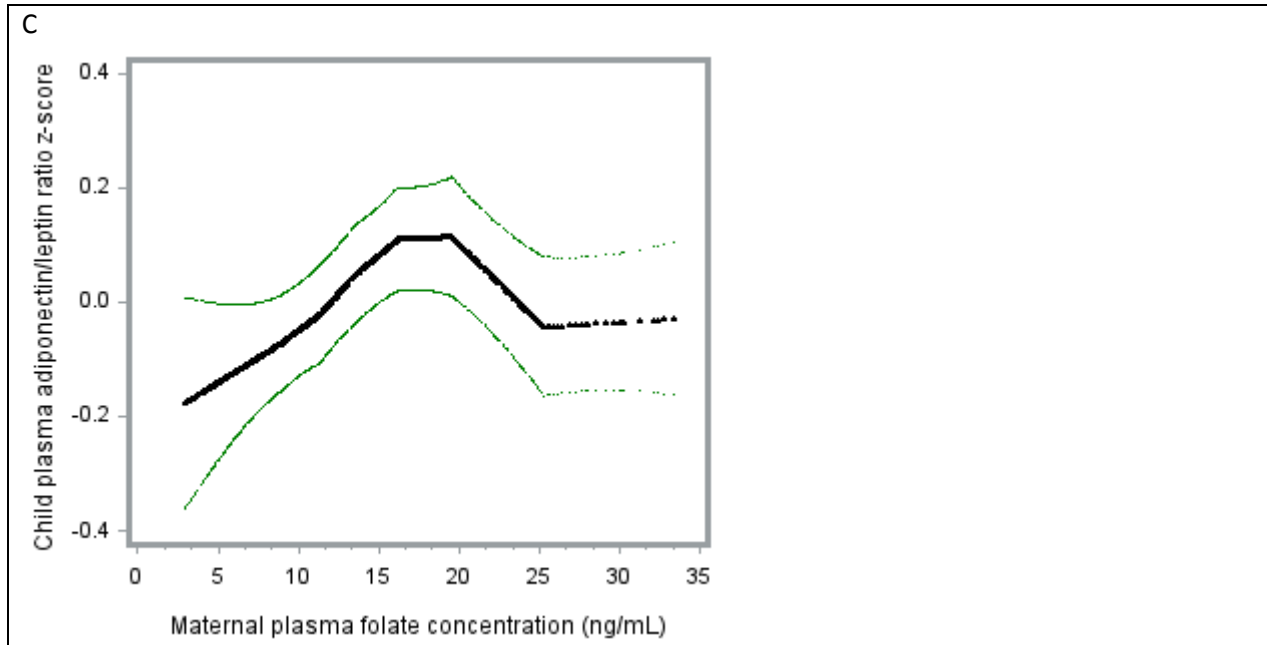
**eFigure 1.** Flowchart of the Sample Included in the Analysis



**eFigure 2.** Association Between Maternal Folate and Offspring Metabolic Biomarkers in the Boston Birth Cohort







SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

Panel A displays the association between maternal plasma folate concentration and offspring plasma insulin z-score. Due to a small sample size (n=34), the curve is truncated at 35 ng/mL.

Panel B displays the association between maternal plasma folate and offspring plasma leptin z-score. Due to a small sample size (n=39), the curve is truncated at 35 ng/mL.

Panel C displays the association between maternal plasma folate concentration and offspring plasma adiponectin/leptin ratio z-score. Due to a small sample size (n=37), the curve is truncated at 35 ng/mL.

**eTable 1.** Comparison of Prenatal and Early Childhood Characteristics Between Included and Excluded Samples<sup>a</sup>

Variables	Participants older than 2 years	Participants included in the study	Participants excluded in the study	Participants primary care outside BMC
No.	2807 <sup>b</sup>	1517	1290 <sup>b</sup>	630
<b>Maternal characteristics</b>				
Maternal age, mean(SD), year	28.2(6.5)	28.6(6.5)	28.4(6.6)	28.6(6.5)
Race/ethnicity, No.(%)				
Black	1662(59.2)	1019(67.2)	643(49.8)	259(41.1)
Hispanic	598(21.3)	290 (19.1)	308(23.9)	228(36.2)
Other	530(18.9)	208(13.7)	322(25.0)	138(21.9)
Missing	17(0.6)	0(0.0)	17(1.3)	5(0.8)
Education, No.(%)				
High school and lower	1788(63.7)	988(65.1)	800(62.0)	402(63.8)
College and higher	969(34.5)	529(34.9)	440(34.1)	210(33.3)
Missing	50(1.8)	0(0.0)	50(3.9)	18(2.9)
Parity, No.(%)				
Nulliparous	1189(42.4)	618(40.7)	571(44.3)	270(42.9)
Multiparous	1617 (57.6)	899(59.3)	718(55.7)	360(57.1)
Missing	1(0.0)	0(0.0)	1(0.02)	0(0.0)
Smoking, No.(%)				
Never	2243(79.9)	1264(83.3)	979(75.9)	479(76.0)
Quitter	207(7.4)	111(7.3)	96(7.4)	41(6.5)
Continuous	312(11.1)	142(9.4)	170(13.2)	94(14.9)
Missing	45(1.6)	0(0.0)	45(3.5)	16(2.6)
<b>Child characteristics</b>				
Gender, No.(%)				
Boy	1421(50.6)	765(50.4)	656(50.8)	333(52.9)
Girl	1386(49.4)	752(49.6)	634(49.2)	297(47.1)
Preterm birth, No.(%)				
No	2012(71.7)	1162(76.6)	850(65.9)	401(63.7)
Yes	795(28.3)	355(23.4)	440(34.1)	229(36.3)
Low Birthweight, No.(%)				
No	2056(73.3)	1174(77.4)	882(68.4)	432(68.6)

Yes	751(26.7)	343(22.6)	408(31.6)	198(31.4)
Abbreviation: BMC, Boston Medical Center.				
<p><sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Of 2891 participants in Children Health study as of Dec. 2013, 84 participants were new enrolled and their information hasn't been entered into database.</p>				
<p><sup>b</sup>84 participants whose information hasn't been entered into database were excluded in the analysis.</p>				



**eTable 2.** Individual and Combined Effect of Maternal Folate Concentration And Pre-Pregnancy BMI Categories on Child Insulin Concentration With Additional Adjustment for Child Adiposity in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal			Crude		Model 1		Model 2
OWO	Folate	n	$\beta$ (95%CI)		$\beta$ (95%CI)		$\beta$ (95%CI)
	<b>Quartile<sup>b</sup></b>						
	Q4	194	ref		ref		ref
	Q3	158	0.07(-0.14 to 0.29)		0.09(-0.13 to 0.30)		0.06(-0.15 to 0.27)
	Q2	196	0.11(-0.10 to 0.31)		0.11(-0.09 to 0.31)		0.09(-0.10 to 0.29)
	Q1	197	0.21(0.01 to 0.42)		0.19(-0.02 to 0.39)		0.15(-0.06 to 0.35)
			0.07(0.00 to 0.13)		0.06(-0.01 to 0.12)		0.05(-0.02 to 0.11)
	<b>Binary<sup>b</sup></b>						
	Q2-Q4	548	ref		ref		ref
	Q1	197	0.15(-0.01 to 0.32)		0.12(-0.04 to 0.29)		0.09(-0.07 to 0.26)
NL		341	ref		ref		ref
OW <sup>c</sup>		218	0.11(-0.06 to 0.29)		0.15(-0.02 to 0.33)		0.14(-0.03 to 0.31)
OB <sup>c</sup>		186	0.18(-0.01 to 0.36)		0.20(0.01 to 0.39)		0.14(-0.05 to 0.33)
P for trend			0.047		0.024		0.086
<b>Combined effect</b>							
NL	Q2-Q4	250	ref		ref		ref
	Q1	91	0.11(-0.13 to 0.36)		0.04(-0.21 to 0.29)		0.03(-0.22 to 0.27)
OW	Q2-Q4	167	0.11(-0.09 to 0.31)		0.13(-0.07 to 0.32)		0.12(-0.08 to 0.32)
	Q1	51	0.25(-0.06 to 0.55)		0.27(-0.04 to 0.57)		0.23(-0.08 to 0.53)
OB	Q2-Q4	131	0.14(-0.08 to 0.35)		0.14(-0.08 to 0.37)		0.10(-0.13 to 0.32)
	Q1	55	0.38(0.08 to 0.68)		0.39(0.09 to 0.69)		0.28(-0.02 to 0.59)
<b>Stratified by BMI categories</b>							
NL	Q1	91	ref		ref		ref
	Q2-Q4	250	-0.11(-0.35 to 0.12)		-0.04(-0.28 to 0.20)		-0.03(-0.27 to 0.21)
OW	Q1	51	ref		ref		ref
	Q2-Q4	167	-0.13(-0.45 to 0.18)		-0.16(-0.48 to 0.15)		-0.10(-0.41 to 0.21)
OB	Q1	55	ref		ref		ref
	Q2-Q4	131	-0.24(-0.59 to 0.10)		-0.28(-0.63 to 0.06)		-0.23(-0.58 to 0.12)

Abbreviation: BMI, body mass index (calculated as weight in kilograms multiply by height in meters squared); NL, normal weight; OW, overweight; OB, obesity. SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>; n=745.

Model1: adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity (p>0.05).

Model 2: Model 1+child weight for height z- score

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>Additional adjustment for plasma folate concentration.

**eTable 3.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Leptin Concentration With Additional Adjustment for Child Adiposity in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal			Crude		Model 1		Model 2
OWO	Folate	n	$\beta$ (95%CI)		$\beta$ (95%CI)		$\beta$ (95%CI)
	<b>Quartile<sup>b</sup></b>						
	Q4	246	ref		ref		ref
	Q3	239	-0.08(-0.25 to 0.09)		-0.10(-0.27 to 0.08)		-0.15(-0.30 to 0.00)
	Q2	248	0.02(-0.15 to 0.20)		0.03(-0.14 to 0.20)		-0.05(-0.20 to 0.10)
	Q1	252	0.16(-0.01 to 0.33)		0.15(-0.02 to 0.32)		0.01(-0.14 to 0.16)
			0.06(0.00 to 0.11)		0.06(0.00 to 0.11)		0.01(-0.04 to 0.06)
	<b>Binary<sup>b</sup></b>						
	Q2-Q4	733	ref		ref		ref
	Q1	252	0.18(0.04 to 0.32)		0.17(0.03 to 0.31)		0.08(-0.05 to 0.20)
NL		452	ref		ref		ref
OW <sup>c</sup>		283	0.03(-0.12 to 0.17)		0.00(-0.15 to 0.15)		-0.05(-0.18 to 0.08)
OB <sup>c</sup>		250	0.25(0.10 to 0.40)		0.24(0.08 to 0.40)		0.08(-0.06 to 0.22)
			0.005		0.018		0.570
<b>Combined effect</b>							
NL	Q2-Q4	336	ref		ref		ref
	Q1	116	0.15(-0.05 to 0.36)		0.13(-0.08 to 0.33)		0.08(-0.11 to 0.26)
OW	Q2-Q4	214	0.03(-0.13 to 0.20)		-0.01(-0.18 to 0.16)		-0.04(-0.18 to 0.11)
	Q1	69	0.17(-0.08 to 0.42)		0.14(-0.12 to 0.39)		-0.01(-0.23 to 0.21)
OB	Q2-Q4	183	0.23(0.05 to 0.40)		0.20(0.02 to 0.38)		0.06(-0.10 to 0.22)
	Q1	67	0.47(0.22 to 0.73)		0.47(0.20 to 0.73)		0.19(-0.05 to 0.42)
<b>Stratified by BMI categories</b>							
NL	Q1	116	ref		ref		ref
	Q2-Q4	336	-0.15(-0.36 to 0.05)		-0.14(-0.35 to 0.06)		-0.09(-0.27 to 0.10)
OW	Q1	69	ref		ref		ref
	Q2-Q4	214	-0.14(-0.39 to 0.11)		-0.18(-0.42 to 0.06)		-0.06(-0.29 to 0.16)
OB	Q1	67	ref		ref		ref
	Q2-Q4	183	-0.25(-0.55 to 0.05)		-0.31(-0.61 to -0.01)		-0.12(-0.37 to 0.12)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity. SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>; n=985.

Model1: adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity (p>0.05).

Model 2: Model 1+child weight for height z-score

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>Additional adjustment for plasma folate concentration.

**eTable 4.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Adiponectin/Leptin Ratio With Additional Adjustment for Child Adiposity in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal			Crude	Model 1	Model 2
OWO	Folate	n	$\beta$ (95%CI)	$\beta$ (95%CI)	$\beta$ (95%CI)
	<b>Quartile<sup>b</sup></b>				
	Q4	240	ref	ref	ref
	Q3	231	0.23(0.05 to 0.40)	0.23(0.05 to 0.40)	0.27(0.11 to 0.44)
	Q2	243	0.02(-0.16 to 0.19)	0.00(-0.17 to 0.18)	0.07(-0.10 to 0.23)
	Q1	247	-0.10(-0.28 to 0.07)	-0.09(-0.27 to 0.09)	0.02(-0.15 to 0.18)
			-0.05(-0.11 to 0.00)	-0.05(-0.10 to 0.01)	-0.02(-0.07 to 0.04)
	<b>Binary<sup>b</sup></b>				
	Q2-Q4	714	ref	ref	ref
	Q1	247	-0.18(-0.32 to -0.04)	-0.16(-0.31 to -0.02)	-0.10(-0.23 to 0.04)
NL		444	ref	ref	ref
OW <sup>c</sup>		274	-0.02(-0.17 to 0.13)	-0.00(-0.15 to 0.15)	0.03(-0.11 to 0.17)
OB <sup>c</sup>		243	-0.14(-0.29 to 0.02)	-0.13(-0.30 to 0.03)	0.00(-0.15 to 0.15)
P for trend			0.125	0.195	0.886
<b>Combined effect</b>					
NL	Q2-Q4	330	ref	ref	ref
	Q1	114	-0.10(-0.31 to 0.11)	-0.05(-0.26 to 0.17)	0.00(-0.20 to 0.19)
OW	Q2-Q4	206	-0.01(-0.18 to 0.16)	0.03(-0.14 to 0.20)	0.05(-0.11 to 0.21)
	Q1	68	-0.15(-0.41 to 0.10)	-0.13(-0.39 to 0.13)	-0.02(-0.27 to 0.22)
OB	Q2-Q4	178	-0.07(-0.25 to 0.11)	-0.04(-0.22 to 0.15)	0.08(-0.10 to 0.25)
	Q1	65	-0.43(-0.69 to -0.17)	-0.41(-0.68 to -0.14)	-0.20(-0.45 to 0.05)
<b>Stratified by BMI categories</b>					
NL	Q1	114	ref	ref	ref
	Q2-Q4	330	0.10(-0.11 to 0.31)	0.06(-0.15 to 0.28)	0.01(-0.19 to 0.22)
OW	Q1	68	ref	ref	ref
	Q2-Q4	206	0.14(-0.12 to 0.40)	0.17(-0.08 to 0.42)	0.11(-0.14 to 0.35)
OB	Q1	65	ref	ref	ref
	Q2-Q4	178	0.37(0.08 to 0.66)	0.42(0.12 to 0.71)	0.28(0.02 to 0.54)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity. SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>; n=961.

Model1: adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity ( $p>0.05$ ).

Model 2: Model 1+child weight for height z-score

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>Additional adjustment for plasma folate concentration.

**eTable 5.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score and Overweight Or Obesity at Age 2-5 Years in the Boston Birth Cohort (BBC).<sup>a</sup>

Maternal		Child BMI z-score			Child overweight or obesity	
BMI	Folate	N	Mean (SD)	$\beta$ (95%CI)	Case n(%)	OR (95%CI)
	<b>Quartile<sup>b</sup></b>					
	Q4	373	0.58(1.13)	ref	131(35.1)	1.00
	Q3	368	0.54(1.37)	-0.10(-0.27 to 0.08)	139(37.8)	1.06(0.77 to 1.46)
	Q2	367	0.47(1.33)	-0.13(-0.30 to 0.05)	117(31.9)	0.83(0.60 to 1.14)
	Q1	371	0.84(1.35)	0.22(0.04 to 0.40)	165(44.5)	1.38(1.01 to 1.89)
	Folate per quartile decrease			0.06(0.00 to 0.12)		1.08(0.97 to 1.19)
	<b>Binary<sup>b</sup></b>					
	Q2-Q4	1108	0.53(1.28)	ref	387(34.9)	1.00
	Q1	371	0.84(1.35)	0.29(0.15 to 0.44)	165(44.5)	1.44(1.12 to 1.86)
NL		678	0.38(1.25)	ref	202(29.8)	1.00
OW <sup>c</sup>		431	0.65(1.26)	0.20(0.05 to 0.35)	168(39.0)	1.41(1.08 to 1.84)
OB <sup>c</sup>		370	0.98(1.37)	0.49(0.33 to 0.65)	182(49.2)	2.04(1.53 to 2.72)
P for trend				<0.001		<0.001
<b>Combined effect</b>						
NL	Q2-Q4	514	0.32(1.22)	ref	146(28.4)	1.00
	Q1	164	0.56(1.30)	0.22(0.00 to 0.44)	56(34.1)	1.22(0.82 to 1.81)
OW	Q2-Q4	323	0.57(1.23)	0.18(0.01 to 0.35)	121(37.5)	1.38(1.01 to 1.88)
	Q1	108	0.89(1.33)	0.48(0.23 to 0.74)	47(43.5)	1.76(1.13 to 2.76)
OB	Q2-Q4	271	0.87(1.37)	0.43(0.25 to 0.62)	120(44.3)	1.72(1.24 to 2.39)
	Q1	99	1.28(1.33)	0.84(0.57 to 1.10)	62(62.6)	3.70(2.29 to 5.99)
<b>Stratified by BMI categories</b>						
NL	Q1	164	0.56(1.30)	ref	56(34.2)	1.00
	Q2-Q4	514	0.32(1.22)	-0.20(-0.42 to 0.02)	146(28.4)	0.88(0.58 to 1.33)
OW	Q1	108	0.89(1.33)	ref	47(43.5)	1.00
	Q2-Q4	323	0.57(1.23)	-0.29(-0.55 to -0.03)	121(37.5)	0.77(0.48 to 1.24)
OB	Q1	99	1.28(1.33)	ref	62(62.6)	1.00
	Q2-Q4	271	0.87(1.37)	-0.47(-0.77 to -0.17)	120(44.3)	0.43(0.26 to 0.73)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity. SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>; n=1479.

Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity (p>0.05).

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>Additional adjustment for plasma folate concentration.



**eTable 6.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score and Overweight or Obesity at Age 6-9 Years in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal		Child BMI z-score			Child overweight or obesity	
BMI	Folate	N	Mean(SD)	$\beta$ (95%CI)	Case, n(%)	OR (95%CI)
	<b>Quartile<sup>b</sup></b>					
	Q4	206	0.74(1.09)	ref	83(40.3)	1.00
	Q3	155	0.84(1.22)	0.02(-0.21 to 0.25)	72(46.5)	1.21(0.77 to 1.90)
	Q2	183	0.86(1.11)	0.09(-0.13 to 0.31)	84(45.9)	1.24(0.81 to 1.89)
	Q1	240	0.98(1.21)	0.17(-0.04 to 0.37)	123(51.3)	1.45(0.97 to 2.17)
	Folate per quartile decrease			0.06(-0.01 to 0.12)		1.12(0.99 to 1.28)
	<b>Binary<sup>b</sup></b>					
	Q2-Q4	544	0.81(1.13)	ref	239(43.9)	1.0
	Q1	240	0.98(1.21)	0.13(-0.04 to 0.30)	123(51.3)	1.27(0.92 to 1.77)
NL		339	0.59(1.14)	ref	122(36.0)	1.0
OW <sup>c</sup>		249	0.88(1.10)	0.23(0.05 to 0.41)	119(47.8)	1.48(1.04 to 2.11)
OB <sup>c</sup>		196	1.31(1.13)	0.63(0.43 to 0.84)	121(61.7)	2.58(1.73 to 3.84)
P for trend				<0.001		<0.001
<b>Combined effect</b>						
NL	Q2-Q4	241	0.58(1.09)	ref	85(35.3)	1.00
	Q1	98	0.59(1.25)	-0.02(-0.28 to 0.24)	37(37.8)	1.05(0.63 to 1.75)
OW	Q2-Q4	180	0.85(1.07)	0.18(-0.04 to 0.39)	82(45.6)	1.35(0.89 to 2.05)
	Q1	69	0.96(1.18)	0.32(0.03 to 0.62)	37(53.6)	1.91(1.09 to 3.37)
OB	Q2-Q4	123	1.18(1.22)	0.52(0.27 to 0.76)	72(58.5)	2.31(1.43 to 3.73)
	Q1	73	1.53(0.94)	0.85(0.55 to 1.15)	49(67.1)	3.46(1.91 to 6.27)
<b>Stratified by BMI categories</b>						
NL	Q1	98	0.59(1.25)	ref	37(37.8)	1.00
	Q2-Q4	241	0.58(1.09)	0.06(-0.22 to 0.33)	85(35.3)	1.00 (0.59 to 1.71)
OW	Q1	69	0.96(1.18)	ref	37(53.6)	1.00
	Q2-Q4	180	0.85(1.07)	-0.17(-0.46 to 0.13)	82(45.6)	0.64 (0.34 to 1.18)
OB	Q1	73	1.53(0.94)	ref	49(67.1)	1.00
	Q2-Q4	123	1.18(1.22)	-0.41(-0.72 to -0.10)	72(58.5)	0.56 (0.27 to 1.14)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity. SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>; n=784.

Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity (p>0.05).

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>Additional adjustment for plasma folate concentration.

**eTable 7.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score and Overweight Or Obesity at Age 2-9 Years (Black Only) in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal		N	Child BMI z-score		Child overweight or obesity	
BMI	Folate		Mean (SD)	$\beta$ (95%CI)	Case, n(%)	OR (95%CI)
	<b>Quartile<sup>b</sup></b>					
	Q4	251	0.63(1.14)	ref	92(36.7)	1.00
	Q3	238	0.51(1.33)	-0.15(-0.36 to 0.06)	89(37.4)	0.98(0.66 to 1.44)
	Q2	245	0.62(1.25)	-0.04(-0.25 to 0.17)	94(38.4)	1.02(0.69 to 1.49)
	Q1	285	0.97(1.26)	0.33(0.13 to 0.54)	137(48.1)	1.58(1.09 to 2.30)
	Folate per quartile decrease			0.11(0.05 to 0.18)		1.16(1.03 to 1.30)
	<b>Binary<sup>b</sup></b>					
	Q2-Q4	734	0.59(1.24)	ref	275(37.5)	1.00
	Q1	285	0.97(1.26)	0.40(0.23 to 0.56)	137(48.1)	1.59(1.18 to 2.14)
NL		431	0.43(1.24)	ref	135(31.3)	1.00
OW <sup>c</sup>		307	0.76(1.17)	0.30(0.13 to 0.48)	133(43.3)	1.63(1.18 to 2.26)
OB <sup>c</sup>		281	1.04(1.29)	0.54(0.36 to 0.73)	144(51.2)	2.09(1.49 to 2.93)
P for trend				<0.001		<0.001
<b>Combined effect</b>						
NL	Q2-Q4	308	0.32(1.23)	ref	87(28.2)	1.00
	Q1	123	0.70(1.23)	0.40(0.15 to 0.65)	48(39.0)	1.58(0.99 to 2.52)
OW	Q2-Q4	226	0.70(1.12)	0.34(0.14 to 0.54)	93(41.2)	1.66(1.14 to 2.43)
	Q1	81	0.92(1.27)	0.61(0.32 to 0.89)	40(49.4)	2.46(1.45 to 4.16)
OB	Q2-Q4	200	0.89(1.30)	0.49(0.28 to 0.71)	95(47.5)	1.96(1.32 to 2.91)
	Q1	81	1.41(1.20)	1.02(0.73 to 1.32)	49(60.5)	3.40(1.95 to 5.92)
<b>Stratified by BMI categories</b>						
NL	Q1	123	0.70(1.23)	ref	48(39.0)	1.00
	Q2-Q4	308	0.32(1.23)	-0.34(-0.60 to -0.08)	87(28.2)	0.70 (0.43 to 1.14)
OW	Q1	81	0.92(1.27)	ref	40(49.4)	1.00
	Q2-Q4	226	0.70(1.12)	-0.26(-0.54 to 0.01)	93(41.2)	0.68(0.39 to 1.19)
OB	Q1	81	1.41(1.20)	ref	49(60.5)	1.00
	Q2-Q4	200	0.89(1.30)	-0.60(-0.92 to -0.29)	95(47.5)	0.53(0.30 to 0.96)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity. SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>; n=1019.

Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity (p>0.05).

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>Additional adjustment for plasma folate concentration

**eTable 8.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score at Age 2-9 Years Stratified by Preterm Birth in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal		Term (n=1162)			Preterm (n=335)		
BMI	Folate	N	Mean(SD)	$\beta$ (95%CI)	N	Mean(SD)	$\beta$ (95%CI)
	<b>Quartile<sup>b</sup></b>						
	Q4	315	0.60(1.08)	ref	64	0.64(1.35)	ref
	Q3	280	0.63(1.31)	-0.04(-0.23 to 0.14)	100	0.41(1.37)	-0.37(-0.77 to 0.03)
	Q2	290	0.63(1.18)	-0.01(-0.19 to 0.17)	89	0.37(1.52)	-0.39(-0.80 to 0.02)
	Q1	277	0.91(1.29)	0.20(0.01 to 0.39)	102	0.84(1.34)	0.20(-0.21 to 0.61)
	Folate per quartile decrease			0.06(0.00 to 0.12)			0.09(-0.04 to 0.22)
	<b>Binary<sup>b</sup></b>						
	Q2-Q4	885	0.62(1.19)	ref	253	0.45(1.42)	ref
	Q1	277	0.91(1.29)	0.21(0.06 to 0.37)	102	0.84(1.34)	0.48(0.17 to 0.79)
NL		552	0.43(1.21)	ref	141	0.34(1.39)	ref
OW <sup>c</sup>		328	0.81(1.15)	0.27(0.11 to 0.43)	115	0.41(1.30)	0.09(-0.23 to 0.42)
OB <sup>c</sup>		282	1.06(1.20)	0.47(0.29 to 0.64)	99	1.06(1.44)	0.72(0.37 to 1.06)
P for trend				<0.001			0.001
<b>Combined effect</b>							
NL	Q2-Q4	433	0.38(1.18)	ref	94	0.22(1.38)	ref
	Q1	119	0.59(1.28)	0.15(-0.08 to 0.39)	47	0.58(1.38)	0.40(-0.06 to 0.87)
OW	Q2-Q4	245	0.76(1.11)	0.26(0.08 to 0.45)	88	0.34(1.29)	0.08(-0.29 to 0.46)
	Q1	83	0.98(1.26)	0.43(0.16 to 0.70)	27	0.64(1.30)	0.58(0.03 to 1.14)
OB	Q2-Q4	207	0.96(1.18)	0.40(0.20 to 0.60)	71	0.90(1.53)	0.65(0.25 to 1.05)
	Q1	75	1.34(1.22)	0.77(0.48 to 1.06)	28	1.46(1.12)	1.23(0.68 to 1.78)
<b>Stratified by BMI categories</b>							
NL	Q1	119	0.59(1.28)	ref	47	0.58(1.38)	ref
	Q2-Q4	433	0.38(1.18)	-0.13(-0.38 to 0.11)	94	0.22(1.38)	-0.31(-0.78 to 0.15)
OW	Q1	83	0.98(1.26)	ref	27	0.64(1.30)	ref
	Q2-Q4	245	0.76(1.11)	-0.19(-0.46 to 0.08)	88	0.34(1.29)	-0.44(-0.99 to 0.10)
OB	Q1	75	1.34(1.22)	ref	28	1.46(1.12)	ref
	Q2-Q4	207	0.96(1.18)	-0.41(-0.72 to -0.11)	71	0.90(1.53)	-0.67(-1.24 to -0.10)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity. SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>.

Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity (p>0.05).

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>Additional adjustment for plasma folate concentration.

**eTable 9.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score and Overweight or Obesity at Age 2-9 Years With Additional Adjustment for C-Section and Planned Pregnancy in the Boston Birth Cohort (BBC).<sup>a</sup>

Maternal		N	Child BMI z-score		Child overweight or obesity	
BMI	Folate Quartile <sup>b</sup>		Mean (SD)	$\beta$ (95%CI)	Case, n(%)	OR (95%CI)
	Q4	379	0.61(1.13)	ref	132(34.8)	1.00
	Q3	380	0.57(1.33)	-0.11(-0.28 to 0.06)	147(38.7)	1.10 (0.80 to 1.50)
	Q2	379	0.57(1.27)	-0.08(-0.25 to 0.09)	135(35.6)	0.97 (0.71 to 1.33)
	Q1	379	0.89(1.30)	0.19(0.02 to 0.36)	176(46.4)	1.44 (1.05 to 1.96)
	Folate per quartile decrease			0.06(0.00 to 0.11)		1.10 (1.00 to 1.22)
	<b>Binary<sup>b</sup></b>					
	Q2-Q4	1138	0.58(1.24)	ref	414(36.4)	1.0
	Q1	379	0.89(1.30)	0.25(0.11 to 0.39)	176(46.4)	1.41 (1.09 to 1.81)
NL		693	0.41(1.25)	ref	212(30.6)	1.0
OW <sup>c</sup>		443	0.71(1.20)	0.22(0.07 to 0.36)	185(41.8)	1.45(1.12 to 1.89)
OB <sup>c</sup>		381	1.06(1.26)	0.53(0.37 to 0.68)	193(50.7)	1.95(1.47 to 2.59)
P for trend				<0.001		<0.001
<b>Combined effect</b>						
NL	Q2-Q4	527	0.35(1.22)	ref	151(28.7)	1.00
	Q1	166	0.59(1.31)	0.19(-0.02 to 0.40)	61(36.7)	1.32 (0.89 to 1.95)
OW	Q2-Q4	333	0.65(1.17)	0.21(0.05 to 0.38)	131(39.3)	1.42 (1.05 to 1.93)
	Q1	110	0.90(1.27)	0.43(0.19 to 0.68)	54(49.1)	2.02 (1.30 to 3.14)
OB	Q2-Q4	278	0.95(1.27)	0.46(0.28 to 0.64)	132(47.5)	1.84 (1.33 to 2.54)
	Q1	103	1.37(1.19)	0.85(0.59 to 1.11)	61(59.2)	2.82 (1.77 to 4.52)
<b>Stratified by BMI categories</b>						
NL	Q1	166	0.59(1.31)	ref	61(36.8)	1.00
	Q2-Q4	527	0.35(1.22)	-0.16(-0.38 to 0.06)	151(28.7)	0.79(0.53-1.19)
OW	Q1	110	0.90(1.27)	ref	54(49.1)	1.00
	Q2-Q4	333	0.65(1.17)	-0.22(-0.46 to 0.03)	131(39.3)	0.70(0.44-1.12)
OB	Q1	103	1.37(1.19)	ref	61(59.2)	1.00
	Q2-Q4	278	0.95(1.27)	-0.45(-0.73 to -0.18)	132(47.5)	0.60(0.36-1.01)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity. SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>; n=1517.

Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, C-section, planned pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity (p>0.05).

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>Additional adjustment for plasma folate concentration.



1 **eTable 10.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child  
 2 Metabolic Biomarkers With Additional Adjustment for C-Section and Planned Pregnancy in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal		Insulin z-score (n=757)		Leptin z-score (n=1009)		Adiponectin/leptin ratio z-score (n=985)	
BMI	Folate Quartile <sup>b</sup>	Mean(SD)	β (95%CI)	Mean(SD)	β (95%CI)	Mean(SD)	β (95%CI)
	Q4	-0.13(0.97)	ref	-0.02(0.95)	ref	-0.03(0.97)	ref
	Q3	-0.05(1.10)	0.21(-0.05 to 0.47)	-0.08(0.95)	-0.10(-0.33 to 0.12)	0.17(0.95)	0.20(-0.03 to 0.43)
	Q2	-0.01(1.04)	0.18(-0.08 to 0.43)	0.01(0.96)	-0.01(-0.23 to 0.21)	-0.02(0.93)	-0.02(-0.24 to 0.21)
	Q1	0.09(0.99)	0.28(0.01 to 0.56)	0.14(1.06)	0.15(-0.10 to 0.39)	-0.14(1.10)	-0.18(-0.43 to 0.07)
	Folate per quartile decrease		0.08(0.00 to 0.17)		0.05(-0.03 to 0.12)		-0.07(-0.14 to 0.01)
	<b>Binary<sup>b</sup></b>						
	Q2-Q4	-0.06(1.03)	ref	-0.03(0.95)	ref	0.04(0.95)	ref
	Q1	0.09(0.99)	0.16(-0.08 to 0.40)	0.14(1.06)	0.18(-0.02 to 0.39)	-0.14(1.10)	-0.24(-0.45 to -0.03)
NL		-0.10(0.99)	ref	-0.06(0.96)	ref	0.03(0.99)	ref
OW <sup>c</sup>		0.01(1.01)	0.06(-0.14 to 0.26)	-0.04(0.92)	0.06(-0.14 to 0.26)	0.01(0.95)	-0.03(-0.24 to 0.17)
OB <sup>c</sup>		0.08(1.09)	0.18(-0.04 to 0.39)	0.20(1.08)	0.18(-0.04 to 0.39)	-0.12(1.03)	-0.07(-0.29 to 0.15)
P for trend			0.007		0.128		0.520
<b>Combined effect</b>							
NL	Q2-Q4	-0.13(0.98)	ref	-0.10(0.92)	ref	0.06(0.95)	ref
	Q1	-0.02(1.02)	0.03(-0.32 to 0.38)	0.05(1.05)	0.14(-0.16 to 0.44)	-0.04(1.11)	-0.07(-0.38 to 0.24)
OW	Q2-Q4	-0.02(1.03)	0.26(0.01 to 0.51)	-0.06(0.93)	0.07(-0.15 to 0.29)	0.04(0.92)	0.02(-0.21 to 0.24)
	Q1	0.12(0.91)	0.36(-0.07 to 0.79)	0.05(0.92)	0.13(-0.24 to 0.51)	-0.08(1.01)	-0.25(-0.64 to 0.13)
OB	Q2-Q4	0.01(1.13)	0.21(-0.07 to 0.49)	0.12(1.02)	0.13(-0.11 to 0.36)	-0.01(0.98)	0.02(-0.22 to 0.26)
	Q1	0.24(1.00)	0.62(0.20 to 1.03)	0.39(1.20)	0.50(0.12 to 0.87)	-0.39(1.13)	-0.48(-0.87 to -0.08)
<b>Stratified by BMI categories</b>							
NL	Q1	-0.02(1.02)	ref	0.05(1.05)	ref	-0.04(1.11)	ref
	Q2-Q4	-0.13(0.98)	-0.04(-0.39 to 0.31)	-0.10(0.92)	-0.18(-0.48 to 0.11)	0.06(0.95)	0.13(-0.18 to 0.44)
OW	Q1	0.12(0.91)	ref	0.05(0.92)	ref	-0.08(1.01)	ref
	Q2-Q4	-0.02(1.03)	-0.14(-0.55 to 0.26)	-0.06(0.93)	-0.23(-0.58 to 0.13)	0.04(0.92)	0.35(-0.02 to 0.71)
OB	Q1	0.24(1.00)	ref	0.39(1.20)	ref	-0.39(1.13)	ref
	Q2-Q4	0.01(1.13)	-0.58(-1.09 to -0.07)	0.12(1.02)	-0.32(-0.75 to 0.11)	-0.01(0.98)	0.51(0.06 to 0.95)

3 Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity.  
 4 SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

5  
 6 <sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by  
 7 electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized  
 8 into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>.

© 2016 American Medical Association. All rights reserved.

9 Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, C-section,  
10 planned pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy  
11 obesity ( $p>0.05$ ).  
12

13 <sup>b</sup>Additional adjustment for maternal pre-pregnancy BMI category; <sup>c</sup>Additional adjustment for plasma folate concentration.

**eTable 11.** Propensity Score-Based Matched Analysis for Comparison of Low Folate to Adequate Folate Concentration in the Boston Birth Cohort (BBC)<sup>a</sup>

Variable	Maternal low folate (<9 ng/mL)	Maternal adequate folate (≥9 ng/mL)	P value
n	375	375	
Maternal folate concentration, median(IQR), ng/mL	14.53(10.93-17.40)	37.19(28.63-52.22)	0.000
Odds ratio	1.39 (1.04-1.86)		0.03
OWO rate (%)	143(38.1)	173(46.1)	0.03
Race (%)			0.86
Black	282(75.2)	281(74.9)	
Hispanic	61(16.3)	58(15.5)	
Other	32(8.5)	36(9.6)	
Education (%)			0.87
High school and below	257(68.5)	259(69.1)	
College and above	118(31.5)	116(30.9)	
Maternal smoking			0.99
Never	295(78.6)	294(78.4)	
Quitter	34(9.1)	35(9.3)	
Continuous	46(12.3)	46(12.3)	
Parity			0.65
0	135(36.0)	141(37.6)	
≥1	240(64.0)	234(62.4)	
Gender (%)			0.71
Boy	196(52.3)	201(53.60)	
Girl	179(47.7)	174(46.40)	
Maternal diabetes (%)			0.82
No	333(88.8)	335(89.3)	
Yes	42(11.2)	40(10.7)	
Maternal BMI category, n (%)			1.00
18.5-24.9 kg/m <sup>2</sup>	163(43.5)	163(43.5)	
25.0-29.9 kg/m <sup>2</sup>	111(29.6)	110(29.3)	
≥30 kg/m <sup>2</sup>	101(26.9)	102(27.2)	
Maternal age, mean±SD, year	28.4(6.4)	28.4(6.4)	0.96
Maternal BMI, mean±SD, kg/m <sup>2</sup>	27.4(6.6)	27.6(7.1)	0.72
Maternal vitamin B12, mean±SD, pmol/L	254.5(81.4)	29.3(89.0)	0.44
Perceived stress during pregnancy, n(%)			0.93
Low	302(80.5)	301(80.3)	
High	73(19.5)	74(19.7)	
Child's birthweight, mean±SD, g	2995(733)	2961(845)	0.55
Gestational age, mean±SD, week	38.0(2.9)	37.8(3.4)	0.39
Child's age, mean±SD, year	6.8(2.4)	6.9(2.4)	0.53
Breastfeeding, n(%)			0.81
Formula	102(27.2)	110(29.3)	
Breastfeeding	11(2.9)	11(2.9)	
Both	262(69.9)	254(67.8)	

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); OWO, overweight or obesity.

SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record.

**Analysis:** We applied a non-parametric multivariable logistic regression model to calculate propensity scores for low (<9.0 ng/mL) and adequate folate ( $\geq 9$  ng/mL) concentration, using the following covariates: maternal age, education, race, smoking status, parity, vitamin B12 concentration, BMI, diabetes status, perceived stress during pregnancy, child's age, gender, birthweight, gestational age at birth, and breastfeeding.

**eTable 12.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Metabolic Biomarkers in the First 2 Years of Life in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal		Insulin z-score (n=441)		Leptin z-score (n=559)		Adiponectin/leptin ratio z-score(n=543)	
BMI	Folate	Mean(SD)	β (95%CI)	Mean(SD)	β (95%CI)	Mean(SD)	β (95%CI)
	<b>Quartile<sup>b</sup></b>						
	Q4	-0.15(0.96)	ref	0.03(0.95)	ref	-0.05(0.95)	ref
	Q3	0.02(1.10)	0.17(-0.09 to 0.44)	-0.04(0.96)	-0.10(-0.32 to 0.13)	0.14(0.95)	0.20(-0.02 to 0.43)
	Q2	0.00(1.04)	0.17(-0.09 to 0.42)	0.02(0.98)	0.00(-0.22 to 0.22)	-0.06(0.96)	-0.03(-0.26 to 0.19)
	Q1	0.14(1.08)	0.26(-0.02 to 0.53)	0.21(1.09)	0.14(-0.10 to 0.38)	-0.26(1.16)	-0.18(-0.43 to 0.06)
	Folate per quartile decrease		0.08(-0.01 to 0.16)		0.05(-0.03 to 0.12)		-0.07(-0.15 to 0.01)
	<b>Binary<sup>b</sup></b>						
	Q2-Q4	-0.05(1.03)	ref	0.00(0.96)	ref	0.01(0.95)	ref
	Q1	0.14(1.08)	0.15(-0.09 to 0.38)	0.21(1.09)	0.17(-0.03 to 0.38)	-0.26(1.16)	-0.24(-0.45 to -0.03)
NL		-0.12(0.98)	ref	-0.02(0.97)	ref	-0.02(1.00)	ref
OW <sup>c</sup>		0.08(1.00)	0.27(0.05 to 0.50)	0.05(0.92)	0.06(-0.14 to 0.26)	-0.05(0.97)	-0.03(-0.24 to 0.17)
OB <sup>c</sup>		0.10(1.18)	0.29(0.04 to 0.53)	0.16(1.09)	0.17(-0.04 to 0.38)	-0.09(1.05)	-0.08(-0.30 to 0.13)
P for trend			0.007		0.146		0.472
<b>Combined effect</b>							
NL	Q2-Q4	-0.13(0.96)	ref	-0.06(0.96)	ref	0.01(0.96)	ref
	Q1	-0.05(1.05)	0.02(-0.33 to 0.37)	0.13(1.01)	0.13(-0.17 to 0.43)	-0.13(1.15)	-0.07(-0.38 to 0.24)
OW	Q2-Q4	0.06(1.02)	0.25(0.00 to 0.51)	0.04(0.94)	0.07(-0.15 to 0.29)	0.00(0.94)	0.02(-0.21 to 0.24)
	Q1	0.17(0.96)	0.36(-0.07 to 0.79)	0.09(0.88)	0.12(-0.26 to 0.50)	-0.27(1.09)	-0.26(-0.64 to 0.13)
OB	Q2-Q4	-0.01(1.17)	0.21(-0.07 to 0.49)	0.08(1.00)	0.12(-0.12 to 0.35)	0.02(0.97)	0.01(-0.23 to 0.25)
	Q1	0.41(1.18)	0.58(0.17 to 1.00)	0.46(1.36)	0.48(0.11 to 0.86)	-0.50(1.25)	-0.48(-0.88 to -0.09)
<b>Stratified by BMI categories</b>							
NL	Q1	-0.05(1.05)	ref	0.13(1.01)	ref	-0.13(1.15)	ref
	Q2-Q4	-0.13(0.96)	-0.01(-0.35 to 0.34)	-0.06(0.96)	-0.16(-0.46 to 0.13)	0.01(0.96)	0.12(-0.19 to 0.45)
OW	Q1	0.17(0.96)	ref	0.09(0.88)	ref	-0.27(1.09)	ref
	Q2-Q4	0.06(1.02)	-0.17(-0.57 to 0.24)	0.04(0.94)	-0.22(-0.56 to 0.13)	0.00(0.94)	0.35(-0.02 to 0.71)
OB	Q1	0.41(1.18)	ref	0.46(1.36)	ref	-0.50(1.25)	ref
	Q2-Q4	-0.01(1.17)	-0.47(-0.97 to 0.03)	0.08(1.00)	-0.36(-0.79 to 0.06)	0.02(0.97)	0.52(0.08 to 0.96)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity.  
SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>.

Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity ( $p>0.05$ ).

<sup>b</sup>Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup>additional adjustment for plasma folate concentration.

**eTable 13.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child BMI Z-Score at Age 2-9 Years With and Without Adjustment for Child Plasma Folate Concentration in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal				Model 1	Model 2
BMI	Folate	N	Mean (SD)	$\beta$ (95%CI)	$\beta$ (95%CI)
	<b>Quartile<sup>b</sup></b>				
	Q4	210	0.59(1.10)	ref	ref
	Q3	207	0.74(1.34)	0.05(-0.17 to 0.27)	0.06(-0.16 to 0.28)
	Q2	197	0.68(1.20)	0.05(-0.17 to 0.28)	0.06(-0.16 to 0.28)
	Q1	189	0.95(1.29)	0.28(0.05 to 0.51)	0.29(0.06 to 0.52)
	Folate per quartile decrease			0.08(0.01 to 0.16)	0.08(0.01 to 0.16)
	<b>Binary<sup>b</sup></b>				
	Q2-Q4	614	0.67(1.21)	ref	
	Q1	189	0.95(1.29)	0.25(0.06 to 0.44)	0.25(0.06 to 0.44)
NL		359	0.45(1.23)	ref	ref
OW <sup>c</sup>		239	0.81(1.11)	0.27(0.07 to 0.46)	0.26(0.07 to 0.46)
OB <sup>c</sup>		205	1.14(1.27)	0.54(0.34 to 0.75)	0.54(0.33 to 0.75)
P for trend				<0.001	<0.001
<b>Combined effect</b>					
NL	Q2-Q4	270	0.41(1.21)	ref	ref
	Q1	89	0.60(1.29)	0.10(-0.18 to 0.38)	0.09(-0.19 to 0.38)
OW	Q2-Q4	185	0.74(1.01)	0.21(-0.01 to 0.43)	0.21(-0.01 to 0.43)
	Q1	54	1.05(1.37)	0.53(0.19 to 0.86)	0.52(0.18 to 0.86)
OB	Q2-Q4	159	1.04(1.32)	0.46(0.23 to 0.70)	0.46(0.23 to 0.70)
	Q1	46	1.50(0.96)	0.91(0.54 to 1.28)	0.90(0.54 to 1.27)
<b>Stratified by BMI categories</b>					
NL	Q1	89	0.60(1.29)	ref	ref
	Q2-Q4	270	0.41(1.21)	-0.03(-0.32 to 0.26)	-0.03(-0.31 to 0.26)
OW	Q1	54	1.05(1.37)	ref	ref
	Q2-Q4	185	0.74(1.01)	-0.32(-0.66 to 0.01)	-0.32(-0.66 to 0.01)
OB	Q1	46	1.50(0.96)	ref	ref
	Q2-Q4	159	1.04(1.32)	-0.51(-0.90 to -0.12)	-0.50(-0.90 to -0.11)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity.

SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB:  $\geq$ 30kg/m<sup>2</sup>; n=803.

Model 1: Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentration during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity ( $p>0.05$ ).

Model 2: Model 1+child folate concentration;

<sup>b</sup> Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup> Additional adjustment for plasma folate concentration.

**eTable 14.** Individual and Combined Effect of Maternal Folate Concentration and Prepregnancy BMI Categories on Child Overweight or Obesity at Age 2-9 Years With And Without Adjustment for Child Plasma Folate Concentration in the Boston Birth Cohort (BBC)<sup>a</sup>

Maternal				Model 1		Model 2
BMI	Folate	N	Case, n(%)	OR (95%CI)		OR (95%CI)
	<b>Quartile<sup>b</sup></b>					
	Q4	210	72(34.3)	1.00		1.00
	Q3	207	92(44.4)	1.43(0.93 to 2.18)		1.46(0.96 to 2.25)
	Q2	197	75(38.1)	1.15(0.74 to 1.76)		1.17(0.76 to 1.80)
	Q1	189	93(49.2)	1.77(1.14 to 2.74)		1.79(1.15 to 2.77)
	Folate per quartile decrease			1.16(1.01 to 1.33)		1.16(1.01 to 1.33)
	<b>Binary<sup>b</sup></b>					
	Q2-Q4	614	239(38.9)	1.00		1.00
	Q1	189	93(49.2)	1.50(1.05 to 2.14)		1.49(1.04 to 2.14)
NL		359	112(31.2)	1.00		1.00
OW <sup>c</sup>		239	106(44.4)	1.57(1.09 to 2.25)		1.56(1.09 to 2.24)
OB <sup>c</sup>		205	114(55.6)	2.38(1.61 to 3.53)		2.38(1.61 to 3.53)
P for trend				<0.001		<0.001
<b>Combined effect</b>						
NL	Q2-Q4	270	80(29.6)	1.00		1.00
	Q1	89	32(36.0)	1.11 (0.65 to 1.91)		1.10 (0.64 to 1.89)
OW	Q2-Q4	185	75(40.5)	1.34 (0.88 to 2.03)		1.33 (0.88 to 2.03)
	Q1	54	31(57.4)	2.72 (1.44 to 5.14)		2.71 (1.43 to 5.11)
OB	Q2-Q4	159	84(52.8)	2.11 (1.36 to 3.28)		2.11 (1.36 to 3.28)
	Q1	46	30(65.2)	3.71 (1.83 to 7.54)		3.71 (1.82 to 7.54)
<b>Stratified by BMI categories</b>						
NL	Q1	89	32(36.0)	1.00		1.00
	Q2-Q4	270	80(29.6)	1.04 (0.58 to 1.85)		1.04 (0.58 to 1.86)
OW	Q1	54	31(57.4)	1.00		1.00
	Q2-Q4	185	75(40.5)	0.47(0.23 to 0.94)		0.47(0.23 to 0.94)
OB	Q1	46	30(65.2)	1.00		1.00
	Q2-Q4	159	84(52.8)	0.46(0.21 to 1.00)		0.47(0.21 to 1.01)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NL, normal weight; OW, overweight; OB, obesity.

SI conversion factor: To convert folate to nmol/L, multiply by 2.266.

<sup>a</sup>The BBC uses a rolling enrollment; the study sample consists of children enrolled from 1998-2012 who have been followed from birth up to the last visit recorded by electronic medical record. Q2-Q4 folate concentration range: 2.9-<9.0 ng/mL, Q1 folate concentration range: 9.0-81.9 ng/mL. Maternal prepregnancy BMI was categorized into three groups: NL: BMI 18.5-24.9 kg/m<sup>2</sup>, OW: 25-29.9kg/m<sup>2</sup>, and OB: ≥30kg/m<sup>2</sup>; n=803.

Model 1: Adjusted for maternal age, race, education, smoking, parity, perceived stress during pregnancy, diabetes, plasma vitamin B12 concentrations during pregnancy, infant's gestational age category, birthweight, and breastfeeding. There was no significant interaction between maternal folate status and prepregnancy obesity (p>0.05).

Model 2: Model 1+child folate concentration

<sup>b</sup> Additional adjustment for maternal prepregnancy BMI category;

<sup>c</sup> Additional adjustment for plasma folate concentration.