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Pre- and post-natal maternal anxiety and early childhood weight gain

Nobutoshi Nawa Maureen M.Black, Ricardo Araya, Lorenzo Richiardi, Pamela J.Surkan

Abstract

Background

While maternal depression has been linked to impaired child growth, the relationship between anxiety and child weight gain is unknown. The study objective was to investigate maternal pre- and post-natal anxiety in relation to child weight gain.

Methods

Data included 1168 children in the Avon Longitudinal Study of Parents and Children. Child height and weight were measured at the median ages of 25 and 31 months postnatally and used to calculate body mass index (BMI). Maternal anxiety was measured with the Crown-Crisp Experiential Index at 18 and 32 gestational weeks, and two and 21 months postpartum. Mothers scoring in the top 15% at one or more of the four time points were considered to have anxiety. Maternal depressive symptoms were measured using the Edinburgh Postnatal Depression Scale-7 (EPDS-7) at these same time points. Maternal depression was defined as EPDS-7 scores of >10. We used Generalized Estimating Equations to assess whether child BMI trajectories varied by the presence of maternal anxiety. Parallel analyses were conducted for maternal depression.

Results

Among children of mothers who had anxiety at least at one timepoint, the BMI changes associated with a three-month increase in child age increased by 0.06 (95% CI:0.004-0.12) compared to BMI changes in children of mothers without anxiety. Maternal depressive symptoms were not associated with child BMI trajectories.

Limitations

Maternal anxiety and depressive symptoms were based on maternal self-report.

Conclusion

Maternal anxiety around childbirth was associated with modest increases in child BMI gain during the child's second year of life

Abbreviations: ALSPAC, avon longitudinal study of parents and children
BMI, body mass index
EPDS, edinburgh postnatal depression scale
CiF, children in focus
GEE, generalized estimating equations

1. Introduction

While there has been much interest in maternal depression and impaired child growth (e.g. including undernutrition and overweight) (Lampard et al., 2014, Patel et al., 2004, Surkan et al., 2008a, Surkan et al., 2008b, Surkan et al., 2011), research on the association between maternal anxiety and child weight gain has been limited (Ding et al., 2014). Anxiety is common in the perinatal period (Ford et al., 2017, National Institute for Health and Care Excellence (NICE) 2014, O'Hara and Wisner, 2014) and is associated with several adverse maternal caregiving and child health outcomes (Fallon et al., 2016, Hurley et al., 2015, Hurley et al., 2008, Paul et al., 2013).

Regarding possible mechanisms that could link perinatal anxiety to child growth, maternal anxiety during pregnancy increases maternal and fetal glucocorticoid levels (Gitau et al., 1998, Van den Bergh et al., 2005) which could affect child weight gain or increases in BMI after birth (Stout et al., 2015, Street et al., 2012). Moreover, in utero exposure to maternal psychosocial stress has been associated with changes in metabolic function, reflected in increases in BMI as well as in changes in lipid profile and glucose-insulin metabolism among young adults (Entringer et al., 2012, Entringer et al., 2008). A study of infant feeding found that postpartum anxiety was associated with shorter duration of breastfeeding, with lower rates of exclusive breastfeeding, and with formula supplementation in the hospital (Fallon et al., 2016). Breastfeeding difficulties and non-exclusive or early cessation of breastfeeding may also mediate the association between maternal postpartum depression and poor infant growth (Madeghe et al., 2016, Stewart, 2007, Surkan et al., 2011).

Maternal symptoms of depression, anxiety, and stress have been associated with nonresponsive feeding styles (Hurley et al., 2008), higher energy consumption by infants in the first six months of life (Hurley et al., 2015), and earlier than recommended introduction of solid foods (Eidelman et al., 2012, Hurley et al., 2015). However, in spite of the connection to fetal glucocorticoid levels, infant feeding and dietary patterns, the relationship between maternal anxiety and early childhood growth has scarcely been investigated.

Weight gain from two to three years of age has been identified as a potential risk factor for hypertension and obesity later in life, suggesting the potential importance of obesity prevention in this developmental period (Munthali et al., 2017, Perng et al., 2016). The primary aim of this study was to investigate the relationship between maternal pre- or post-natal anxiety and changes in child Body Mass Index (BMI) using longitudinal data extending into the second year of childhood. A secondary aim was to study the association between pre- or post-natal depression and child BMI, and to investigate if the associations between symptoms of anxiety and depression in relation to child growth are independent.

2. Methods

2.1. Sample

Data originated from a substudy of pregnant women enrolled in the Avon Longitudinal Study of Parents and Children (ALSPAC), which recruited 14,541 pregnant women in Avon, UK expecting to deliver between April 1, 1991 and December 31, 1992. 14,541 was the initial number of pregnancies for which the mother enrolled in the ALSPAC study and had either returned at least one questionnaire or attended a "Children in Focus" clinic by July 19, 1999. Of these initial pregnancies, there were 14,676 fetuses, resulting in 14,062 livebirths and 13,988 children who were alive at one year of age (Boyd et al., 2013, Fraser et al., 2013). (See the study website for details on available data, (University of Bristol, 2018a, University of Bristol, 2018b)). Infants with major

congenital abnormalities, cerebral palsy, and non-singleton births were excluded (ud Din et al., 2013). We used data from the Children in Focus (CiF) group, corresponding to 10% of the ALSPAC cohort, who attended clinics at the University of Bristol. The CiF group was chosen at random from the last 6 months of ALSPAC births (1432 families who attended at least one clinic visit). Mothers who had moved out of the area, were lost to follow-up, or were enrolled in another study of infant development in Avon were excluded (Clegg et al., 2015, Taylor et al., 2017, University of Bristol, 2018a, University of Bristol, 2018b). Thus, while CiF data were collected at various time intervals between 4 and 61 months of age, we included children who had weight and height measurements at the median ages of 25 and 31 months. This study was approved by the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Secondary data analysis was deemed exempt by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board.

3. Measures

3.1. Dependent variables

3.1.1. Child body mass index (BMI)

Child height was measured using a Leicester Height Measure and weight was measured using a Seca 835 Scale (Seca, Hamburg, Germany) in clinics at the University of Bristol when children were at the median ages of 25 (IQR: 0.2) and 31 (IQR: 0.2) months, respectively. The mean age for the first measurement was 25 months (SD: 0.2, min: 24.5, max: 26.5); the mean age for the second measurement was 31 months (SD: 0.2, min: 30.5, max: 31.8). Child BMI was calculated by dividing weight (in kilograms) by height (in meters) squared.

3.2. Independent variables

3.2.1. Maternal anxiety

In our analysis, maternal anxiety was based on the eight-item anxiety sub-scale of the Crown-Crisp Experiential Index (Birtchnell et al., 1988, Blackmore et al., 2011, Capron et al., 2015, Collin et al., 2015, Cookson et al., 2009, Crown and Crisp, 1966, Glover et al., 2004, Heron et al., 2004, O'Connor et al., 2002, Sutherland and Cooper, 1992, Vaz Jdos et al., 2013, Wiles et al., 2006). We aimed to compare the growth of children of mothers with and without anxiety, rather than studying child growth in relation to an incremental one-unit change in maternal anxiety level. Mothers with a score in the top 15% of the Crown-Crisp Experimental Index (a score \geq 85th percentile) were regarded as anxious (henceforth referred to as having 'anxiety'). This cutoff was based on the prevalence of antenatal and postnatal anxiety in the UK (National Institute for Health and Care Excellence (NICE), 2014), and it has been previously used in studies with the ALSPAC dataset (Blackmore et al., 2011, Collin et al., 2015, Glover et al., 2004, Heron et al., 2004, O'Connor et al., 2002, Vaz Jdos et al., 2013). We used data from 18 and 32 gestational weeks to indicate maternal prenatal anxiety and at eight weeks and 21 months postpartum to indicate maternal postpartum anxiety. The 85th percentile value of the Crown-Crisp Experimental Index at 18 gestational weeks was 8, the value at 32 gestational weeks was 9, the value at 8 weeks postpartum was 6 and the value at 21 months postpartum was 6. We used a fixed cutoff for the two prenatal time points (cutoff: 8) and another fixed cutoff for the two postnatal time points (cutoff: 6). Mothers were considered to have anxiety if their anxiety scores were in the top 15% at one or more of the four time points (two prenatal and two postnatal time points). We also analyzed the timing and chronicity of anxiety. Timing was assessed by examining anxiety at each of the four time points separately in relation to

child weight gain using continuous scores from the Crown-Crisp Experiential Index. Chronicity was assessed by examining women who had anxiety at 1) only one time point; and 2) at least two time points.

3.2.2. Maternal depression

Symptoms of maternal depression were measured using the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987). Because the EPDS contains three items that correspond to anxiety (and we were interested in differentiating the effects of anxiety and depression), a subscale of EPDS that includes only items related to depressive symptoms (EPDS-7) was used in the analysis. In our dataset, using linear regression we confirmed that the total scores for these three items were highly correlated with the Crown-Crisp Experiential Index score ($P < 0.01$; beta coefficients ranged from 0.98 to 1.12, which were all significantly different from zero). The total EPDS-7 subscale score was divided by the total number of items (seven) and was multiplied by ten to create a total score equivalent to the original ten-item EPDS (Kabir et al., 2008, Venkatesh et al., 2014). A score of >10 on the EPDS-7 was used to identify mothers with depressive symptoms (Kabir et al., 2008, Venkatesh et al., 2014). Data from 18 and 32 gestational weeks were used for maternal prenatal depressive symptoms. Data collected at eight weeks and 21 months postpartum were used to assess maternal postpartum depressive symptoms. For our overall assessment, mothers were classified as having depression if the EPDS-7 score was >10 at least at one of the four time points.

3.3. Covariates

Covariates included maternal age, pre-pregnancy weight, height, parity, education, and race/ethnicity, as well as paternal education, marital status, and child gender (Table 1). Covariates were chosen based on prior studies assessing associations between maternal mental status such as depression and early child growth (Ertel et al., 2010, Surkan et al., 2012, Surkan et al., 2014, Surkan et al., 2008a). Maternal age, pre-pregnancy weight, and height were used as continuous variables, while parity, education, race/ethnicity, paternal education, marital status, and child gender were categorical variables (Table 1).

Table 1. Characteristics of study participants from the ALSPAC Children in Focus sample .

Variable		Total ($n = 1168$)	
		N or Mean	% or SD
Parental characteristics			
Maternal age (years)	Mean	28.7	4.5
Maternal pre-pregnancy weight (kg)	Mean	62.8	11.2
Maternal height (cm)	Mean	164.4	6.4
Parity	Mean	0.8	1
Maternal education	Lower than O-level	221	18.9
	O-level	402	34.4
	A-level	302	25.9
	Degree	163	14
	Missing	80	6.8

Variable	Total (<i>n</i> = 1168)	
	<i>N</i> or Mean	% or SD
Paternal education	Lower than O-level	183 15.7
	O-level	233 19.9
	A-level	297 25.4
	Degree	210 18
	Missing	245 21
Marital status	Single	224 19.2
	Married	915 78.3
	Missing	29 2.5
Maternal race/ethnicity	Other than White	23 2
	White	1109 94.9
	Missing	36 3.1
Breastfeeding duration (months)	Never breastfed	221 18.9
	≤5	462 39.6
	6–11	253 21.7
	≥12	125 10.7
	Missing	107 9.2
Maternal anxiety at 18 gestational weeks	Yes	178 15.2
	No	873 74.7
	Missing	117 10
Maternal anxiety at 32 gestational weeks	Yes	218 18.7
	No	841 72.0
	Missing	109 9.3
Maternal anxiety at 8 weeks postpartum	Yes	220 18.8
	No	893 76.5
	Missing	55 4.7
Maternal anxiety at 21 months postpartum	Yes	225 19.3
	No	816 69.9
	Missing	127 10.9
Maternal anxiety at one or more of the four time points	Yes	354 30.3
	No	541 46.3
	Missing	273 23.4
Maternal EPDS-7 score at 18 gestational weeks	≤10	944 80.8
	>10	108 9.2
	Missing	116 9.9
Maternal EPDS-7 score at 32 gestational weeks	≤10	932 79.8
	>10	152 13
	Missing	84 7.2
Maternal EPDS-7 score at 8 weeks postpartum	≤10	1043 89.3

Variable	Total (<i>n</i> = 1168)	
	<i>N</i> or Mean	% or SD
	>10	93 8
	Missing	32 2.7
Maternal EPDS-7 score at 21 months postpartum	≤10	963 82.4
	>10	90 7.7
	Missing	115 9.8
Maternal EPDS-7 score >10 at one or more of the four time points	Yes	228 19.5
	No	709 60.7
	Missing	231 19.8
Child characteristics		
Birthweight (g)	Mean	3460 507
Low birthweight	Yes	37 3.2
	No	1122 96.1
	Missing	9 0.8
Birth length (cm)	Mean	50.7 2.1
Gestational age (weeks)	Mean	39.5 1.6
Preterm birth	Yes	49 4.2
	No	1119 95.8
	Missing	0 0
Gender	Male	638 54.6
	Female	530 45.4
	Missing	0 0
Child BMI at 25 months*	Mean	16.5 1.2
Child BMI at 31 months*	Mean	16.7 1.3

*

Because there was variation in when children attended study visits, these dates refer to the median number of months when height and weight measurements were taken for children in our sample.

Information on maternal age and marital status was obtained from mothers at eight gestational weeks of pregnancy. Self-reported maternal pre-pregnancy weight and maternal height were collected from mothers at 12 gestational weeks. Information on parity was obtained from mothers at 18 gestational weeks, while information on maternal education and maternal race/ethnicity were obtained from mothers at 32 gestational weeks.

Self-reported maternal race/ethnicity was dichotomized into “White”, versus “other than White”. Original categories included “White,” “Black/Caribbean,” “Black/African,” “Black/other,” “Indian,” “Pakistani,” “Bangladeshi,” “Chinese,” and “any other ethnic group”. Child sex was noted at the time of delivery. Information about paternal education was obtained from fathers at 18 gestational weeks.

Other information on birth conditions and breastfeeding listed in Table 1 were derived as described below. Birthweight was collected from obstetric medical records, direct measurement by ALSPAC study staff after delivery, and from birthweight from the birth notification that was submitted to the health authority by the medical attendant at the time of birth (Anand and Pharoah, 2000). If all birthweights from each data source were the same, that value was used. If there was an inconsistency between data sources and the difference was ≥ 100 g, the birthweight was considered missing. If the difference was < 100 g, the lower value was used. Low birthweight was defined as birthweight < 2500 g. For birth length, we used crown-heel length measured after delivery by ALSPAC study personnel. Gestational age was calculated based on the date of the mother's last menstrual period (LMP). When there was an inconsistency between the LMP and ultrasound assessment, ultrasound was used. Preterm birth was defined as gestational age < 37 weeks. Mothers were asked questions regarding breastfeeding at 6 and 15 months postpartum. Breastfeeding duration was categorized as never breastfed, ≤ 5 , 6–11, and ≥ 12 months. Because it is possible that birthweight, gestational age at birth, and breastfeeding duration are on the causal pathway between maternal anxiety and early childhood growth, and there were no statistically significant associations between postnatal maternal anxiety and childbirth conditions such as gestational age (or preterm birth) and birthweight (or low birthweight), we did not adjust for them.

3.4. Statistical analyses

All statistical analyses were conducted using R, version 3.4.3 (R Core Team, 2017). Since child BMI was measured repeatedly at two time points, Generalized Estimating Equations (GEE) (Liang and Zeger, 1986) using the “gee” package, version 4.13–19 were applied to account for the underlying correlation between repeated observations from the same child (Carey et al., 2015). To assess whether child BMI trajectories varied by the presence of maternal anxiety, the model included an interaction term for maternal anxiety and child age. Child age was centered at the median age of the child's first measurement (of the two), which was 25 months of age. Also, child age was scaled so that the effect of a one-unit change in age could be interpreted as the effect of change over 3 months.

To handle missing values on covariates (missing values ranged from 2.5% for marital status to 21% for paternal education), multiple imputation was used to estimate missing covariate values. Variables included in the imputation included gestational age, birthweight, breastfeeding duration, maternal smoking during pregnancy, paternal age, paternal anxiety, paternal depression, paternal history of depression, paternal race/ethnicity, child weight and height. Fifty imputed datasets were created using the “mice” package, version 2.46.0 (van Buuren and Groothuis-Oudshoorn, 2011). The results of analyses using all the imputed datasets were combined using Rubin's rules for multiple imputation (Rubin, 1987, Sterne et al., 2009) using the norm package, version 1.0–9.5 (Novo and Schafer, 2013).

For sensitivity analyses, we used polynomial regression to analyze associations between maternal anxiety and child continuous BMI measured at 25 months of age. For maternal anxiety, we first used a combined continuous anxiety variable, which was defined as the mean of the anxiety scores from each of the four time points. We also used a combined continuous prenatal anxiety variable and a combined continuous postnatal anxiety variable, which were defined as the mean of the two prenatal anxiety scores and as the mean of the two postnatal anxiety scores, respectively. Finally, we examined the association between these maternal anxiety variables and child continuous BMI measured at 31 months of age. To reduce multicollinearity, we centered the mean for linear and higher-order polynomial terms of the anxiety variables. When fitting a polynomial model, we first tested whether the coefficient of the highest-order polynomial term was significantly different from zero. If the p-value of the coefficient was ≥ 0.05 , the highest-order polynomial term was removed

from the model (Fitzmaurice et al., 2012). The model was adjusted for maternal age, pre-pregnancy weight, height, parity, education, race/ethnicity as well as paternal education, marital status, child gender, and child age at the time of BMI assessment.

To illustrate the change in child BMI from 25 months to 31 months postpartum among children of mothers with and without anxiety, the standard error for the adjusted mean of child BMI in both groups at 25 months and 31 months postpartum was calculated using the “emmeans” package, version 1.3.4 (Lenth et al., 2019).

4. Results

As displayed in Table 1, among the 1168 mothers included in the study, mean maternal age was 28.7 years (SD: 4.5), 19.2% of mothers were single, and 94.9% of mothers were white. 30.3% (354) of mothers reported anxiety at one or more of the four time points, while 19.5% (228) of mothers reported depression at one or more of the four time points. About 14.8% of mothers reported both anxiety and depression and 14.4% of mothers reported anxiety at one or more time points without reporting depression at any time point. In contrast, only 3.2% of mothers reported depression at one or more of the time points without reporting anxiety at any time point. The percentage of mothers who reported anxiety at two, three, and all four time points were 7.2%, 5.4%, and 3.6%, respectively. The prevalence of mothers having anxiety and depression at each prenatal and postpartum period is shown in Table 1.

Table 2 shows the results for associations between maternal anxiety symptoms as well as maternal depression at one or more time points and child BMI after multiple imputation. For children of mothers having maternal anxiety at one or more time points, the change in BMI with a three-month increase in child age was 0.06 BMI units greater (95% CI: 0.004–0.12) than the change for children of mothers without anxiety after covariate adjustments. There was no evidence of an association between the presence of maternal depressive symptoms at one or more time points and the change in BMI with child age, after adjusting for covariates. In addition, there was no evidence of an interaction between depression and anxiety.

Table 2. Associations between maternal symptoms of anxiety and of depression reported at one time point or more and child BMI after multiple imputation.^a

	Crude		Model1 ^b	
	β	95%CI	β	95%CI
Child age	0.07	(0.03, 0.11)	0.07	(0.03, 0.11)
Maternal anxiety (ref: no)	-0.16	(-0.34, 0.01)	-0.16	(-0.33, 0.02)
Maternal anxiety (ref: no) × child age	0.06	(0.003, 0.11)	0.06	(0.004, 0.12)
Child age	0.09	(0.05, 0.12)	0.09	(0.05, 0.12)
Maternal EPDS-7 (ref: ≤10)	-0.19	(-0.39, -0.001)	-0.18	(-0.38, 0.02)
Maternal EPDS-7 (ref: ≤10) × child age	0.02	(-0.03, 0.08)	0.03	(-0.03, 0.08)

Bold values indicate statistical significance at $p < 0.05$.

a

Age was centered at 25 months and was scaled so that the effect of a one-unit change in age can be interpreted as the effect corresponding to a 3 month change.

b

Adjusted for maternal age, pre-pregnancy weight, height, parity, education, race/ethnicity as well as paternal education, marital status, and child gender.

We also analyzed the association between the presence of maternal depression, measured by original EPDS instead of the EPDS-7, at one or more time points and BMI trajectories using the dataset generated with multiple imputation. Adjusted results suggested no association between the presence of maternal depressive symptoms at one or more time points and BMI trajectories.

In a sensitivity analysis, we analyzed the associations between maternal anxiety or maternal depression at one or more time points and child BMI in the original (unimputed) dataset and obtained similar results (Supplementary Table 1 and Supplementary Fig. 1). In our analysis of the timing of anxiety (examining anxiety at each of the four time points separately in relation to child weight gain using the continuous Crown-Crisp Experimental Index scores), we found that the interaction term for age and the continuous anxiety variable that was assessed at 32 gestational weeks was positive ($P = 0.03$), suggesting that maternal anxiety at 32 gestational weeks was associated with a very small increased change in BMI. The p -values for the interaction term for age and the continuous anxiety measure assessed at the other time points were all ≥ 0.05 . We also created a combined continuous anxiety variable, which was defined as the mean of the anxiety scores from all four time points (Cronbach's alpha = 0.83). There was a positive interaction for the combined continuous anxiety measure with child age, but the associated p -value was 0.18. For chronicity, among children of mothers who had anxiety at only one point, the change in BMI associated with a three-month increase in child age increased by 0.04 (95% CI: -0.03, 0.11) compared to BMI changes in children of mothers without anxiety. Among children of mothers who had anxiety during at least two time points, the change in BMI associated with a three-month increase in child age was greater and increased by 0.08 (95% CI: 0.01, 0.15) compared to BMI changes in children of mothers without anxiety, suggesting a dose response relationship. Finally, we used polynomial regression to analyze associations between maternal anxiety and child continuous BMI measured at 25 or 31 months of age. The results suggest that the associations with BMI at these time points were not curvilinear (i.e., the quadratic term was not significant when the second-order polynomial model was fit). However, a linear association was observed between the continuous prenatal anxiety variable (the mean of the two prenatal anxiety scores) and BMI measured at 25 months of age. A one-unit increase in the continuous prenatal anxiety variable was associated with 0.03 decrease in child BMI measured at 25 months of age (95% CI: -0.06, -0.0006). When we examined each prenatal time point separately, we found modest decreases in child BMI measured at 25 months of age in relation to a one-unit increase in anxiety at 18 and 32 gestational weeks ($\beta = -0.02$, 95% CI: -0.05, 0.006; $\beta = -0.03$, 95% CI: -0.05, -0.002), respectively. This association was virtually the same when we also adjusted for birthweight and gestational age at birth in addition to other covariates. The p -value for the association between the continuous postnatal anxiety variable and child BMI measured at 25 months of age was 0.18.

5. Discussion

In this study, we found that while child BMI increased from 25 to 31 months of age in the whole sample, children of mothers experiencing any pre- or post-natal anxiety had a modestly larger increase in BMI with age than the children of mothers without anxiety. In contrast, there was no evidence of an association between maternal depression and early child BMI or weight gain. Anxiety and depression are two of the most common prenatal mental problems (National Institute for Health and Care Excellence (NICE), 2014) and also affect 15–20% of mothers during the first year postpartum (Ford et al., 2017, National Institute for Health and Care Excellence (NICE) 2014,

O'Hara and Wisner, 2014). Although comorbidity between anxiety and depression is common (Eysenck et al., 2006), different events can trigger, and are associated with, anxiety compared to depression (Eysenck et al., 2006). In our sample, there was also some overlap between anxiety and depression (14.1%), however a similar proportion of mothers reported anxiety without reporting depression (11.1%). In spite of the high burden of pre- or post-natal anxiety, most research has focused on the effects of pre- or post-natal depression and child growth (Lampard et al., 2014, Surkan et al., 2011). To our knowledge, this is the first study to investigate the relation between maternal anxiety and child growth, using change in BMI as an indicator. Rapid early childhood growth has been identified as a risk factor for later obesity (Baird et al., 2005, Monteiro and Victora, 2005). We found that among children of mothers with anxiety the change in BMI associated with a three-month increase in child age increased modestly (by 0.06) compared to the change in BMI among children of mothers without anxiety. Of note, the equivalent change in BMI associated with change in child age over the whole study period (six months: from 25 to 31 months of age) among children of mothers with anxiety corresponds to a 0.12 increase. Relative to the finding that among all children the increase in BMI from 25 to 31 months of age was only 0.2 (from 16.5 to 16.7), the magnitude of the association between anxiety and child weight gain was notable (60% of total weight gain), suggesting that this finding is important and that the associations should be replicated and examined in other ages early in childhood.

Although the aim of this study was not to test potential mechanisms that might explain the association between maternal anxiety and BMI changes, one plausible mechanism is through the increase of maternal glucocorticoid or corticotropin-releasing hormone levels during pregnancy, which may result in elevated levels of fetal glucocorticoid that might eventually affect child weight gain or increases in BMI after birth (Gitau et al., 1998, Stout et al., 2015, Street et al., 2012, Van den Bergh et al., 2005). Prior studies have also reported associations between maternal anxiety and infant feeding and dietary patterns (Fallon et al., 2016, Hurley et al., 2015, Hurley et al., 2008, Paul et al., 2013). Maternal anxiety has been linked to controlling feeding practices (e.g., forcing a child to eat) (Farrow and Blissett, 2005) and to earlier introduction of solid foods (Hurley et al., 2008), which may affect child weight gain and growth. Thus, it is plausible that maternal anxiety may contribute to changes in child biological processes and/or maternal parenting styles, potentially resulting in increased risk of overweight.

In our analyses of the timing of anxiety (examining anxiety at each of the four time points separately in relation to child weight gain), we found that maternal anxiety at 32 gestational weeks was associated with an increased change in BMI. We also found a negative association between prenatal anxiety modeled as a continuous variable (especially with anxiety at 32 gestational weeks) and continuous BMI measured at 25 months of age. In contrast, no association was observed between the continuous prenatal anxiety variable (i.e. the mean of the two continuous prenatal anxiety scores) and continuous BMI measured at 31 months of age. These results are consistent with previous studies investigating the effects of fetal exposure to corticotropin-releasing hormone, which suggested that elevated placental CRH level was associated with rapid postnatal increases in BMI and that the sensitive period for the effect of placental CRH was during the early third trimester (around 30 gestational weeks) (Ellman et al., 2008, Stout et al., 2015). These results, in combination with the association we observed between maternal pre- or post-natal anxiety and changes in child BMI trajectories, should increase interest in future studies on potential pre- and/or postnatal mediators of the association between maternal anxiety and child BMI.

When we analyzed the association between maternal pre- or post-natal anxiety and changes in child BMI trajectories using a dichotomous anxiety variable (having anxiety at least at one of the four time points versus not), the association was significant, whereas, when we used the combined continuous anxiety variable, which was defined as the mean of the four anxiety scores, the

association was still positive but not significant. Given that the association between child BMI trajectories and maternal anxiety was more evident for maternal anxiety at 32 gestational weeks, this finding may suggest that the association between anxiety and child BMI trajectories may not be linear or not equal across the four time points. However, we should emphasize that we did find an association between maternal pre- or post-natal anxiety and changes in child BMI trajectories when using a dichotomous variable and we observed a possible dose-response relationship in our analysis of chronicity, once again highlighting the importance of exploring the effects of anxiety at time points other than 32 gestational weeks in future studies.

Our analysis showed no clear association between maternal depressive symptoms and child BMI trajectory. Prior research investigating associations between maternal depression and child growth in high-income countries have reported mixed results (Drewett et al., 2004, Ertel et al., 2010, Grote et al., 2010, Lampard et al., 2014, Surkan et al., 2012, Surkan et al., 2014, Wright et al., 2006). Some of these studies reported no association (Drewett et al., 2004, Grote et al., 2010), whereas others have observed associations between maternal depression and impaired child growth (Ertel et al., 2010, Surkan et al., 2012, Surkan et al., 2014, Wright et al., 2006), or obesity (Ertel et al., 2010, Lampard et al., 2014). Of note, using the ALSPAC data, Drewett et al. (2004) found no association between postnatal maternal depression as assessed by the EPDS (score >12) and failure-to-thrive over the first nine months (Drewett et al., 2004). Although we assessed associations between maternal depression and child BMI at different time points than in that study, the results of Drewett et al. (2004) are consistent with ours. In contrast, other studies using the EPDS as a measure of maternal depressive symptoms have found associations between these symptoms and child weight gain (Ertel et al., 2010, Wright et al., 2006). However, it can be argued that their measures reflected both depression and anxiety symptoms, as they used all ten EPDS items. The EPDS consists of depression (seven items) and anxiety sub-scales (three items) (Matthey et al., 2003, Venkatesh et al., 2014). Given the high degree of comorbidity between anxiety and depression (Eysenck et al., 2006) and the possible effects of maternal anxiety on child growth, future research on the relation between maternal depression and child BMI should consider separating the symptoms of depression and anxiety. Typically, studies have used the whole EPDS (or all items on other depressive symptom scales), without excluding the anxiety components (Drewett et al., 2004, Ertel et al., 2010, Grote et al., 2010, Wright et al., 2006).

Our study has several limitations. First, maternal anxiety and depressive symptoms were based on maternal self-report and these scales are not diagnostic tools. Second, maternal pre-pregnancy weight and height were self-reported. Third, the source of anxiety was unknown. Some maternal anxiety could have been triggered by concern about the child's poor growth, leading to efforts to stimulate child growth. Fourth, although we used a fixed cutoff for the two prenatal time points (cutoff: 8), the level of distress may differ across these two time points. This is also the case for postnatal anxiety. Fifth, the change in child BMI trajectory was assessed only in one childhood age range (from 25 to 31 months of age), and the BMI of children born to a mother with anxiety was lower at 25 months than the BMI of children of mothers without anxiety. Further studies investigating the effects of anxiety on child BMI and child BMI trajectories in different age groups are needed. Sixth, this weight gain may just represent a catch-up to average weight from lower infant weight in early infancy. Further research on how maternal anxiety affects weight at birth and in early infancy is required. Seventh, we were not able to adjust for poverty level or food insecurity as potential sources of anxiety, which should be considered in future research. Eighth, in our dataset we did not have biomarkers for anxiety (e.g., blood levels of stress hormones such as cortisol). In addition, data on mothers' medications and treatment for anxiety were not available. Our results should be confirmed with larger studies using different indicators for maternal anxiety. Future studies may also investigate whether the relation between maternal anxiety and child growth is mediated by maternal parenting styles and/or maternal hormonal levels.

Regarding the clinical implications of these findings, the American Academy of Pediatrics states that pediatricians can play an important role in screening and identifying mothers with postnatal depression and in providing comprehensive support to their families, which is critical given the adverse effects of depression on the health of mothers and their children (Earls, 2010, Paul et al., 2013). Also, the UK National Institute for Health and Care Excellence guidelines recommended that primary care providers consider screening women for depression and anxiety during pregnancy and in the postnatal period to identify, monitor, and possibly intervene (National Institute for Health and Care Excellence (NICE), 2014). However, these recommendations do not address the relationship between maternal anxiety and children's physical development. Based on our results, healthcare providers may need to pay attention to the weight gain of children of mothers with anxiety (especially in the early third trimester), and introduction of screening for history of anxiety during pregnancy might be useful. Furthermore, healthcare providers may also need to be attentive to maternal anxiety among mothers of children with excess growth.

Our study showed that the presence of maternal pre- or post-natal anxiety was associated with modest changes in child BMI trajectories, which has important implications given the rising trends in obesity levels in early childhood (de Onis et al., 2010). Contrary to some literature from high-income settings, we did not find a link between maternal pre- or post-natal depression and child BMI. Given the high prevalence of perinatal anxiety and depression, our findings suggest the need for further research in this area and the importance of providing comprehensive support to mothers with symptoms of anxiety during the prenatal and postnatal period.

CRedit authorship contribution statement

Nobutoshi Nawa: Writing - original draft, Formal analysis, Writing - review & editing. **Maureen M. Black:** Conceptualization, Writing - review & editing. **Ricardo Araya:** Conceptualization, Writing - review & editing. **Lorenzo Richiardi:** Conceptualization, Writing - review & editing. **Pamela J. Surkan:** Conceptualization, Writing - review & editing.

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