Journal of Developmental Origins of Health and Disease

www.cambridge.org/doh

Original Article

Cite this article: Horta BL, Coca KP, Desai M, Dias MS, B. Jaccottet M, and Ross MG. (2024) Breastfeeding moderates the association of maternal pre-pregnancy nutritional status with offspring body composition at 30 years. *Journal of Developmental Origins of Health and Disease* **15**: e3, 1–7. doi: 10.1017/S2040174424000047

Received: 15 March 2023 Revised: 31 January 2024 Accepted: 8 February 2024

Keywords:

Maternal pre-pregnancy body mass index; breastfeeding; offspring body composition; cohort

Corresponding author: Bernardo L. Horta; Email: blhorta@gmail.com

© The Author(s), 2024. Published by Cambridge University Press in association with The International Society for Developmental Origins of Health and Disease (DOHaD).



Breastfeeding moderates the association of maternal pre-pregnancy nutritional status with offspring body composition at 30 years

Bernardo L. Horta¹, Kelly P. Coca², Mina Desai³, Mariane S. Dias¹, Manoella B. Jaccottet¹ and Michael G. Ross³

¹Postgraduate Program in Epidemiology, Federal University of Pelotas, Pelotas, Brazil; ²Escola Paulista de Enfermagem, Universidade Federal de São Paulo, São Paulo, Brazil and ³Perinatal Research Laboratory, The Lundquist Institute at Harbor-UCLA Medical Center, Department of Obstetrics and Gynecology, Torrance, CA, USA Department of Obstetrics and Gynecology, David Geffen School of Medicine, University of California, Los Angeles, CA, USA

Abstract

Maternal pre-pregnancy body mass index is positively associated with offspring obesity, even at adulthood, whereas breastfeeding decreases the risk of obesity. The present study was aimed at assessing whether breastfeeding moderates the association of maternal pre-pregnancy body mass index with offspring body composition at adulthood, using data from 3439 subjects enrolled in a southern Brazilian birth cohort. At 30 years of age, maternal pre-pregnancy body mass index was positively associated with offspring prevalence of obesity, abdominal obesity, as well as body mass index and fat and lean mass index. Breastfeeding moderated the association of maternal pre-pregnancy obesity with offspring adiposity at 30 years of age. For those breastfed<6 months, body mass index was 4.13 kg/m² (95% confidence interval: 2.98; 5.28) higher among offspring of obese mothers, in relation to offspring of normal weight mothers, whereas among those breastfed >6 months the magnitude of the difference was small [2.95 kg/m² (95% confidence interval: 1.17; 4.73)], *p*-value for interaction = 0.03. Concerning obesity, among those who had been breastfed < 6 months, the prevalence of obesity was 2.56 (95% confidence interval: 1.98; 3.31) times higher among offspring of obese mothers. On the other hand, among those who were breastfed ≥ 6 months, the prevalence of obesity was 1.82 (95% confidence interval: 1.09; 3.04) times higher among offspring of obese mothers. Therefore, among overweight mothers breastfeeding for more than 6 months should be supported, as it may mitigate the consequences of maternal overweight on offspring body composition.

Introduction

Evidence suggests that maternal overweight during pregnancy has long-term consequences on offspring body composition, increasing the risk of obesity.¹⁻⁶ Although most of the studies evaluated children,^{1,2,5,6} it has also been^{3,4} reported that offspring of overweight mothers have higher body mass index, fat mass index and waist circumference, even at adulthood. As childhood obesity is a strong predictor of adolescent and adult obesity⁷ the lifelong impact is not unexpected.

The mechanisms associated with the developmental programing of offspring obesity by maternal overweight during pregnancy are multifactorial.¹ It has been suggested that this association could be due do shared family characteristics, environmental characteristics, or genetic factors because it has been observed that the magnitude of the association of maternal and paternal pre-pregnancy body mass index with offspring body mass index is similar.^{1,8-10} Indeed, Bond et al¹¹ observed that genotype explained 43% of the association of maternal pre-pregnancy body mass index with offspring body mass index and environmental characteristics, it has been suggested that factors such as diet and physical activity could explain this association between maternal and offspring body composition. Indeed, Burgess et al¹² reported that overweight or obese mothers were more likely to offer foods or beverages with added sugar to their infants, and that the intake of added sugar was a mediator of the association of maternal pre-pregnancy body mass index with rapid weight gain in infancy. In contrast, studies have failed to observe an association between maternal pre-pregnancy body mass index with rapid weight gain in infancy.

Furthermore, animal studies have reported that intrauterine exposure to maternal overweight may be associated with changes in the hypothalamic axis, impaired appetite control and altered adipogenic regulation that would also be associated with the programing of overweight/obesity.^{15,16}

Factors which may mitigate the impact of maternal overweight on offspring include responsive parenting,¹⁷ improved sleep,¹⁸ and breastfeeding.¹⁹ Specifically, evidence suggests that breastfeeding protects against overweight,¹⁹ and the better appetite control among breastfed subjects is a possible mechanism that would explain the association between breastfeeding and overweight.²⁰ Indeed, it has been reported that breastfeeding moderates the effect of variants in the fat mass and obesity-associated gene (FTO),²¹⁻²³ which is related to the development of overweight via a compromised appetite control.²⁴ Assuming that breastfeeding is associated with improved satiety control, we hypothesized that it could also moderate the association of maternal pre-pregnancy body mass index with offspring body composition.

In this study, we evaluated the hypothesis that breastfeeding moderates the association of maternal pre-pregnancy body mass index with offspring body composition at adulthood.

Methods

In 1982, the maternity hospitals located in Pelotas, a southern Brazilian city, were daily visited and the births were identified from labor ward records. Those livebirths (n = 5914) whose family lived in the urban area of the city were examined and their mothers interviewed soon after delivery. These subjects have been prospectively followed at different ages. In 1984 and 1986, a census was carried in the urban area of the city and those children enrolled in the cohort were identified, examined, and their mothers interviewed. From June 2012 to February 2013 (mean age of 30.4 years), study participants were invited to visit the research clinic to be interviewed and examined. The study methodology has been described in detail elsewhere.^{25,26} The Ethical Review Board of the Faculty of Medicine of the Federal University of Pelotas approved the study protocol (Of. 16/12), and written informed consent was obtained from all subjects.

For the assessment of maternal pre-pregnancy body mass index in kg/m², information on maternal weight at the beginning of the pregnancy was extracted from antenatal card or, when absent, by self-report. For maternal height, mothers were measured by hospital staff, using locally made portable stadiometers, and this information was retrieved from the hospital records. Overweight was defined by a body mass index at the beginning of the pregnancy \geq 25 and < 30 kg/m², and obesity by a body mass index \geq 30 kg/m².²⁷

Information on duration of breastfeeding and age at introduction of complementary foods was collected in the 1984 and 1986 visits and the information collected closest to the age of weaning was used to minimize recall bias. Standard World Health Organization definitions were used to assess duration of predominant and total breastfeeding.²⁸ Predominant breastfeeding was defined as the age at which foods other than breastmilk, teas, or water were introduced, and total breastfeeding as birth to the age at which breastfeeding completely stopped.

With respect to body composition assessment at 30 years of age, body mass index was estimated dividing the weight (in kg) by the squared height in meters. Weight was measured once to the nearest 0.1 kg using a scale coupled to the BodPod (COSMED, Rome, Italy) and height was also measured once with a portable stadiometer -SECA 240 (SECA Instruments, Hamburg, Germany). Waist circumference was measured twice, after a gentle expiration, using an inextensible tape with an accuracy of 0.1 cm (CESCORF, Brazil) at the narrowest part of the trunk, identified as the midpoint between the lowest rib margin and the iliac crest. We used the average of two waist circumference measurements. Fat and lean mass were estimated using dual X-ray absorptiometry (Lunar Prodigy; GE Healthcare[®], Madison, Wisconsin, USA), and fat and lean mass index were calculated by dividing these measurements by squared height in meters. Overweight and obesity were defined by a body mass index \geq 25 to < 30 and \geq 30 kg/m²,²⁷ respectively, and abdominal obesity by a waist circumference \geq 102 cm in men and \geq 88 cm in women.²⁹

The following variables that had been assessed in the perinatal study were considered as possible confounders:

- Family income, the mothers were asked about the total income, in five categories of minimum wages (≤ 1, 1.1–3, 3.1–6; 6.1–10, > 10), earned by the family members;
- Parental schooling, years of schooling successfully completed;
- Household asset index was based on the ownership of household goods and estimated using factor analysis;
- Maternal skin color was rated by the interviewer;
- Maternal smoking during the pregnancy, those mothers who reported smoking cigarettes at any time during pregnancy were considered as smokers;
- Parity, the number of time that the mother had given birth to a live neonate;
- Birthweight, hospital staff weighed the newborns, using pediatric scales (Filizola, Sao Paulo, Brazil) that were weekly calibrated by the research team.

Analyses were carried out using Stata version 15.0. ANOVA was used to compare means and chi-square test for proportions, according to categories of maternal pre-pregnancy body mass index and breastfeeding duration. In the multivariate analyses, confounding variables were selected based on known characteristics that were associated with maternal pre-pregnancy body mass index and offspring body composition. For continuous outcomes (body mass index, fat mass index, and waist circumference) multiple linear regression was used to adjust the estimate for possible confounding variables. The adjusted prevalence ratio of obesity was estimated using Poisson regression with robust adjustment of the variance.³⁰ In order to evaluate whether duration of breastfeeding modified the association of maternal prepregnancy body mass index with offspring body composition at 30 years of age, we stratified the analysis according to categories of breastfeeding duration and tested for interaction between maternal pre-pregnancy body mass index and duration of breastfeeding. With respect to the interaction between maternal pre-pregnancy body mass index and breastfeeding duration, the statistical evidence was clear when breastfeeding was categorized as < 6 vs. ≥ 6 months, and a more detailed categorization of breastfeeding did not result in a stronger association, whereas the precision of the estimates decreased.

Results

In the 2012–13 follow-up visit, we were able to evaluate 3701 participants of the cohort, which corresponded to a follow-up rate of 68.1%, after adding the 325 deaths identified among the cohort members. Information on duration of breastfeeding and body composition outcomes was available for 3439 subjects. Table 1 shows that about one of every three mothers had four or less years of schooling, the prevalence of maternal pre-pregnancy overweight and obesity was 18.5 and 4.7%, respectively, and the prevalence of

Table 1. Characteristics of the participants included in the analysis

	N (%)
Gender	
Male	1694 (49.3)
Female	1745 (50.7)
Family income at birth(minimum wage) <1	676 (19.7)
≤ 1 1.1 -3	1700 (49.6)
3.1 - 6	670 (19.6)
6.1 - 10 > 10	198 (5.8) 180 (5.3)
	160 (5.5)
Maternal schooling (in years) ≤4	1097 (31.9)
5-8	1488 (43.3)
9-11	376 (11.0)
≥ 12	474 (13.8)
Maternal pre-pregnancy body mass index Normal weight	2266 (76.8)
Overweight	546 (18.5)
Obese	138 (4.7)
Birthweight (in grams)	
< 2500	245 (7.1)
2500–2999 3000–3499	812 (23.6) 1298 (37.8)
3500–3999	874 (25.4)
≥ 4000	209 (6.1)
Duration of breastfeeding (in months)	720 (21.2)
<1 1–2.9	729 (21.2) 884 (25.7)
3–5.9	794 (23.1)
≥6	1032 (30.0)
Duration of predominant breastfeeding (in months)	
<1 1–1.9	882 (26.5) 454 (13.6)
2-2.9	676 (20.3)
≥3	1319 (39.6)
Variables measured at 30 years	
Body mass index in kg/m ² , mean (SD)	26.8 (5.5)
Fat mass index in kg/m ² , mean (SD)	8.73 (4.55)
Lean mass index in kg/m ² , mean (SD)	18.12 (2.69)
Prevalence of abdominal obesity (%)	657 (19.0)
Body mass index in categories	
Normal	1460 (42.5)
Overweight Obese	1191 (34.6) 788 (22.9)
Total	3439 #

#The total of some variables does not sum to 3439 because of missing data.

low birthweight was 7.1%. With respect to duration of breastfeeding, 30.0% of offspring were breastfed for at least 6 months, whereas duration of predominant breastfeeding was short, with about six of every ten subjects predominantly breastfed for less than three months. At 30 years of age, mean body mass index was 26.8 kg/m^2 , and the prevalence of obesity and abdominal obesity was 22.9% and 19.0%, respectively.

Table 2 shows that in the unadjusted analyses, maternal prepregnancy body mass index was positively associated with offspring body mass index, fat mass index, lean mass index, and the prevalence of obesity and abdominal obesity at 30 years of age. On the other hand, breastfeeding duration was not associated with body composition at 30 years of age. When controlled for possible confounding variables, maternal pre-pregnancy body mass index was positively associated with offspring body mass index, fat mass index, lean mass index, and prevalence of obesity and abdominal obesity. The prevalence of obesity was 2.31 (95% confidence interval: 1.84; 2.92) times higher among offspring of obese mothers in relation to those of normal weight mothers, whereas body mass index was 3.75 kg/m² (95% confidence interval: 2.79; 4.72) higher among offspring of obese mothers in comparison with those of normal weight mothers. Maternal pre-pregnancy body mass index was also associated with offspring overweight (Data not shown) (Table 3).

Despite the lack of impact of breastfeeding on body composition at 30 years of age, breastfeeding significantly moderated the association of maternal pre-pregnancy body mass index with offspring adiposity at 30 years of age. Fig 1 shows that the association of maternal pre-pregnancy body mass index with offspring outcomes (prevalence of obesity and abdominal obesity, body mass index, and fat mass index) was stronger among those breastfed for less than 6 months, with p-values for interaction ranging from 0.03 to 0.13. For those breastfed for less than 6 months, body mass index was 4.13 kg/m² (95% confidence interval: 2.98; 5.28) higher among those subjects whose mother was obese before the pregnancy, in relation to offspring of normal weight mothers, whereas among those breastfed for 6 or more months the magnitude of the difference was small [2.95 kg/m² (95% confidence interval: 1.17; 4.73)], p-value for interaction = 0.03. With relation to obesity, among those who had been breastfed for less than 6 months, the prevalence of obesity was 2.56 (95% confidence interval: 1.98; 3.31) times higher among offspring of obese mothers. On the other hand, among those who were breastfed for 6 months or more, the prevalence of obesity was 1.82 (95% confidence interval: 1.09; 3.04) times higher among offspring of obese mothers. The formal test for interaction was statistically significant (p-value = 0.04). For predominant breastfeeding, we did not observe any clear pattern of effect modification (Fig 2).

Discussion

In our study, based on a cohort that has been prospectively followed since birth in a southern Brazilian city, we observed that maternal pre-pregnancy overweight and obesity is strongly associated with offspring obesity, BMI, fat mass index, lean mass index and abdominal obesity at 30 years of age. We further observed that breastfeeding moderates the impact of maternal prepregnancy body mass index on offspring body composition at 30 years of age. Among those subjects who had been breastfeed for 6 months or more, the association of maternal pre-pregnancy overweight and obesity with offspring body mass index and obesity was weaker than among those who had been breastfed for less than 6 months. For abdominal obesity and fat mass index the magnitude of the associations was also smaller among those breastfed for more than 6 months, but we could not rule out that these differences were due to the chance. Our findings suggests that breastfeeding may help to reduce the long-term consequences of maternal prepregnancy overweight on offspring body composition, decreasing the "transmission" of obesity across generations.

The studied population is experiencing a rapid nutrition transition; the prevalence of obesity among the daughters at 30 years of age (23.4%) was about 5 times higher than that observed in the mothers at the beginning of the pregnancy (4.7%). In Pelotas, the prevalence of maternal obesity at the beginning of the pregnancy, increased from 4.4% in 1982 Pelotas Birth Cohort to

Table 2. Prevalence of obesity, and mean body mass index, fat mass index and abdominal obesity at 30 years according to maternal pre-pregnancy body mass index and duration of breastfeeding

	Prevalence ratio of obesity at 30 years (%)	Body mass index (kg/m²) at 30 years – Mean (95% CI)	Fat mass index (kg/m ²) at 30 years – Mean (95% Cl)	Lean mass index (kg/m²) at 30 years – Mean (95% Cl)	Prevalence of abdominal obesity (%)
Maternal pre-pregnancy body	P < 0.001 #	P < 0.001 #	P < 0.001 #	P < 0.001 #	P < 0.001 #
mass index					
Normal	19.0	26.2 (26.0; 26.4)	8.28 (8.11; 8.46)	17.95 (17.85; 18.06)	15.6
Overweight	31.8	28.2 (27.7; 28.7)	9.70 (9.31; 10.08)	18.50 (18.27; 18.73)	26.2
Obese	41.3	29.7 (28.5; 30.8)	11.02 (10.07; 11.97)	18.82 (18.38; 19.27)	34.7
Duration of total	P = 0.62 ##	P = 0.88 ##	P = 0.54 ##	P = 0.21 #	P = 0.99 #
breastfeeding (months)					
<1	23.9	26.9 (26.5; 27.3)	8.84 (8.51; 9.17)	18.07 (17.88; 18.27)	19.1
1- 2.9	23.5	26.8 (26.4; 27.1)	8.68 (8.40; 8.96)	18.05 (17.87; 18.22)	18.9
3–5.9	23.3	27.0 (26.6; 27.3)	8.86 (8.54; 9.19)	18.11 (17.93; 18.29)	19.2
≥6	21.5	26.8 (26.4; 27.2)	8.59 (8.30; 8.88)	18.21 (18.04; 18.38)	19.0
Duration of predominant	P = 0.79 ##	P = 0.94 ##	P = 0.99 ##	P = 0.71 ##	P = 0.37 ##
breastfeeding (months)					
<1	23.8	26.9 (26.5; 27.3)	8.76 (8.46; 9.06)	18.16 (17.98; 18.34)	19.8
1-1.9	24.0	26.9 (26.4; 27.4)	8.81 (8.40; 9.21)	18.14 (17.90; 18.39)	20.2
2-2.9	23.7	26.8 (26.4; 27.2)	8.71 (8.38; 9.04)	18.01 (17.81; 18.21)	19.3
>=3	22.3	26.9 (26.6; 27.2)	8.78 (8.52; 9.03)	18.14 (18.00; 18.29)	18.5

#test of linear trend.

##test of heterogeneity.

Table 3. Association of body composition at 30 years (Obesity, Body mass index, fat mass index and abdominal obesity) according to maternal pre-pregnancy body mass index and infant feeding. Estimates were adjusted for confounding variables

	Adjusted regression coefficient					
	Prevalence ratio of obesity at 30 years	Body mass index (kg/ m²) at 30 years	Fat mass index (kg/m²) at 30 years	Lean mass index (kg/m²) at 30 years	Prevalence ratio of abdominal obesity at 30 years	
Maternal pre-pregnancy body mass index ¹	P < 0.001 #	P < 0.001 #	P < 0.001 #	<i>P</i> < 0.001 #	P < 0.001 #	
Normal	Reference (1)	Reference (0)	Reference (0)	Reference (0)	Reference (1)	
Overweight	1.79 (1.53; 2.10)	2.24 (1.71; 2.78)	1.56 (1.11; 2.00)	0.67 (0.41; 0.94)	1.79 (1.50; 2.14)	
Obese	2.31 (1.84; 2.92)	3.75 (2.79; 4.72)	3.04 (2.23; 3.84)	0.89 (0.41; 1.37)	2.39 (1.83; 3.11)	
Duration of total breastfeeding (months) ²	P = 0.66 ##	<i>P</i> = 0.68 ##	<i>P</i> = 0.50 ##	<i>P</i> = 0.95 ##	P = 0.98 ##	
<1	Reference (1)	Reference (0)	Reference (0)	Reference (0)	Reference (1)	
1-2.9	0.96 (0.79; 1.17)	-0.07 (-0.66; 0.52)	-0.04 (-0.53; 0.45)	-0.06 (-0.35; 0.23)	0.97 (0.78; 1.22)	
3–5.9	0.99 (0.81; 1.21)	0.17 (-0.42; 0.77)	0.16 (-0.34; 0.66)	0.00 (-0.30; 0.29)	1.01 (0.80; 1.27)	
≥ 6	0.89 (0.74; 1.09)	-0.16 (-0.73; 0.41)	-0.19 (-0.67; 0.28)	0.02 (-0.26; 0.30)	1.01 (0.81; 1.26)	
Duration of predominant breastfeeding (months) ²	<i>P</i> = 0.96 ##	<i>P</i> = 0.99 ##	P = 0.93 ##	P = 0.84 ##	P = 0.90 ##	
<1	Reference (1)	Reference (0)	Reference (0)	Reference (0)	Reference (1)	
1-1.9	1.02 (0.81; 1.28)	0.09 (-0.57; 0.76)	0.17 (-0.38; 0.73)	-0.05 (-0.37; 0.28)	1.07 (0.84; 1.38)	
2-2.9	1.01 (0.82; 1.23)	-0.02 (-0.61; 0.58)	0.08 (-0.41; 0.57)	-0.13 (-0.42; 0.16)	1.01 (0.80; 1.27)	
≥3	0.97 (0.82; 1.15)	0.06 (-0.45; 0.56)	0.12 (-0.30; 0.53)	-0.08 (-0.33; 0.17)	0.98 (0.81; 1.19)	

¹Adjusted for: family income at birth, parental schooling, household asset index, maternal skin color, maternal smoking during pregnancy, and parity.

²Adjusted for 1 and birthweight. #test of linear trend.

#test of linear trend.

##test of heterogeneity.

18.7% in 2015 Birth Cohort.³¹ In spite of such rapid increase in the prevalence of obesity, we observed that breastfeeding decreased the magnitude of the association of maternal pre-pregnancy overweight/obesity with offspring body mass index and obesity.

Overweight is positively associated with the development of metabolic disorders,³² and it has been reported that maternal prepregnancy body mass index is also associated with offspring metabolic cardiovascular risk factors.³³⁻³⁵ Furthermore, Dias et al³³ observed that offspring body mass index at adulthood captured all the association of maternal pre-pregnancy body mass index with offspring systolic blood pressure and non-high-density lipoprotein (non-HDL) cholesterol. Suggesting, therefore, that by moderating the association between maternal pre-pregnancy body mass index and offspring adiposity, breastfeeding may also have a long-term

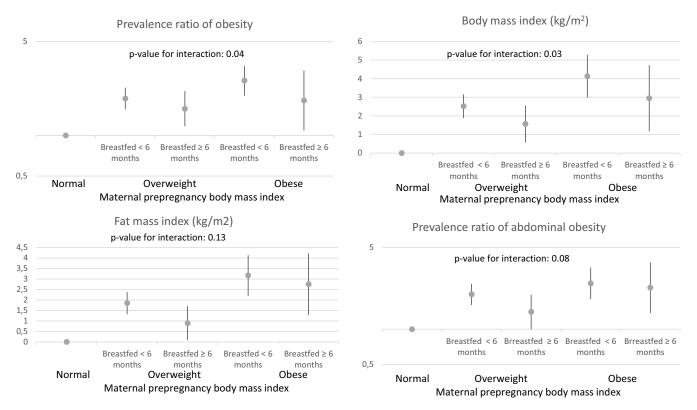


Figure 1. Association of body composition at 30 years with maternal pre-pregnancy body mass index, according to breastfeeding duration. Estimates were adjusted for confounding by: family income at birth, parental schooling, household asset index, maternal skin color, maternal smoking during pregnancy, and parity.

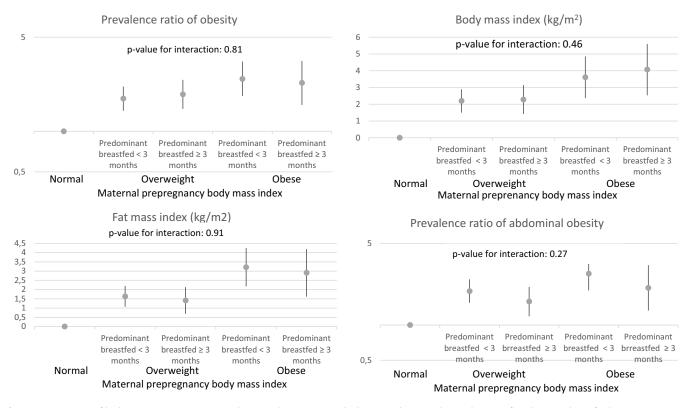


Figure 2. Association of body composition at 30 years with maternal pre-pregnancy body mass index, according to duration of predominant breastfeeding. Estimates were adjusted for confounding by: family income at birth, parental schooling, household asset index, maternal skin color, maternal smoking during pregnancy, and parity.

impact on the development of metabolic cardiovascular disorders among offspring of obese mothers. Furthermore, the rapid increase in the prevalence of maternal pre-pregnancy overweight/obesity reinforces the relevance of identifying factors that mitigate its longterm consequences on the offspring.

To our knowledge this is the first study to report that breastfeeding moderates the association of maternal pre-pregnancy body mass index with offspring body composition. Concerning the validity of our findings, as previously reported, attrition rate was low and independent of breastfeeding duration and socioeconomic status,³⁶ among those subjects who had been breastfed for 6 or more months, 71.7% were followed up at years of age, whereas among those breastfed for<1 month this proportion was 69.4% Therefore, it is unlikely that the observed associations were due to selection bias. Residual confounding is also unlikely because estimates were adjusted for several variables that were measured in early childhood, decreasing the likelihood of measurement error due to recall bias. Moreover, in the studied population breastfeeding duration was independent of socioeconomic status.³⁶ Because low birthweight is positively associated with obesity³⁷ and negatively with breastfeeding duration,³⁶ it could be argued that the observed association could be due to confounding by birthweight. On the other hand, birthweight is impacted by maternal body mass index, and therefore a basic requisite for confounding is not fulfilled. In spite of that, breastfeeding significantly moderated the association of maternal pre-pregnancy body mass index with offspring body composition, even after controlling for birthweight. Interviewer bias is unlikely because anthropometrical assessment at 30 years of age was carried out by trained assessors that were unaware of the subject exposure to maternal overweight during pregnancy, as well as infant feeding. On the other hand, for some mothers, data on maternal prepregnancy weight was not available at the antenatal card and it was self-reported by the mothers. Therefore, a measurement error is likely, and duration of breastfeeding may have been misclassified. A study that validated the maternal recall of breastfeeding duration observed that about 25% of the mothers tended to misclassify the duration of breastfeeding, but usually to the nearest category.³⁸ Because these measurement errors are unrelated to offspring body composition, the misclassification was non-differential, which tends to underestimate the magnitude of the association. Consequently, it is unlikely that the observed associations were caused by classification errors.

Type-1 error inflation could be considered as another explanation for the observed associations because we carried out several tests to assess the effect modification by infant feeding.³⁹ On the other hand, the inflation is smaller than the expected because the body composition outcomes are correlated.⁴⁰ Furthermore, breastfeeding duration decreased the magnitude of the association of maternal pre-pregnancy overweight with the four outcomes evaluated, and the number of tests of interaction that reached the level of statistical significance was higher than that would be expected by chance.

With respect to the biological mechanisms that would explain the observed associations, as previously mentioned, intrauterine exposure to maternal overweight is associated with changes in the hypothalamic axis that would contribute to hyperphagia and impaired appetite control.^{15,16} On the other hand, it has been reported that breastfeeding is associated with an improved appetite control,²⁰ and breastfeeding moderates the effect of a gene that is associated with an impaired appetite control.²¹⁻²³ By increasing satiety control, breastfeeding would moderate the association of intrauterine exposure to maternal overweight with offspring adiposity. Additionally, breast milk oligosaccharides and satiety-inducing short chain fatty acids may have contributory impact.⁴¹

Because the duration of breastfeeding in the studied population was short, we were unable to assess the impact of being breastfed as recommended by international agencies.⁴² Our findings reinforce the relevance of promoting and specifically supporting breastfeeding among overweight mothers, since breastfeeding may mitigate the consequences of intrauterine exposure to maternal overweight on offspring body composition.

Funding statement. This project was supported in part by National Institutes of Health, Eunice Kennedy Shriver National Institute of Child (Grant # R01HD099813).

This article is based on data from the 1982 Pelotas Birth Cohort study conducted by Postgraduate Program in Epidemiology at Federal University of Pelotas with the collaboration of the Brazilian Public Health Association. The project is supported by the Department of Science and Technology of the Ministry of Health (Department of Science and Technology (DECIT/Brazilian Ministry of Health). From 2004 to 2013, the Wellcome Trust supported the 1982 Pelotas Birth Cohort. The International Development Research Center, World Health Organization, Overseas Development Administration, European Union, National Support Program for Centers of Excellence (PRONEX), the Brazilian National Research Council (CNPq), and the Brazilian Ministry of Health supported previous phases of these studies. The European Union, National Support Program for Centers of Excellence (PRONEX), the Brazilian National Research Council (CNPq), and the Brazilian Ministry of Health and Children's Pastorate supported previous phases of the study. BLH is supported by the CNPq, and has has a visiting researcher fellow - Amazonas State Research Support Foundation - FAPEAM.

Competing interests. The authors declare that they have no conflict of interest.

Ethical standard. This study was carried out according to guidelines established in the Declaration of Helsinki and all procedures involving human subjects were approved by Research Ethics Committee of the College of Medicine, Federal University of Pelotas.

References

- Godfrey KM, Reynolds RM, Prescott SL, *et al.* Influence of maternal obesity on the long-term health of offspring. *Lancet Diabetes Endocrinol.* 2017; 5(1), 53–64. DOI: 10.1016/S2213-8587(16)30107-3.
- Reilly JJ, Armstrong J, Dorosty AR, *et al.* Early life risk factors for obesity in childhood: cohort study. *BMJ*. 2005; 330(7504), 1357. DOI: 10.1136/bmj. 38470.670903.E0.
- Eriksson JG, Sandboge S, Salonen M, Kajantie E, Osmond C. Maternal weight in pregnancy and offspring body composition in late adulthood: findings from the Helsinki birth cohort study (HBCS). *Ann Med.* 2015; 47(2), 94–99. DOI: 10.3109/07853890.2015.1004360.
- da Dias MS, Matijasevich A, Barros AJ, et al. Influence of maternal prepregnancy nutritional status on offspring anthropometric measurements and body composition in three Brazilian birth cohorts. *Public Health Nutr.* 2021; 24(5), 882–894. DOI: 10.1017/S1368980020004887.
- Gaillard R, Steegers EAP, Duijts L, et al. Childhood cardiometabolic outcomes of maternal obesity during pregnancy. *Hypertension*. 2014; 63(4), 683–691. DOI: 10.1161/HYPERTENSIONAHA.113.02671.
- Pinot de Moira A, Power C, Li L. Changing influences on childhood obesity: a study of 2 Generations of the 1958 British birth cohort. *Am J Epidemiol.* 2010; 171(12), 1289–1298. DOI: 10.1093/aje/kwq083.
- Simmonds M, Llewellyn A, Owen CG, Woolacott N. Predicting adult obesity from childhood obesity: a systematic review and meta-analysis. *Obesi Revi.* 2016; 17(2), 95–107. DOI: 10.1111/obr.12334.
- Paliy O, Piyathilake CJ, Kozyrskyj A, Celep G, Marotta F, Rastmanesh R. Excess body weight during pregnancy and offspring obesity:

potential mechanisms. *Nutrition*. 2014; 30(3), 245–251. DOI: 10.1016/j.nut. 2013.05.011.

- Santos Ferreira DL, Williams DM, Kangas AJ, et al. Association of prepregnancy body mass index with offspring metabolic profile: analyses of 3 European prospective birth cohorts. *PLoS Med.* 2017; 14(8), e1002376. DOI: 10.1371/journal.pmed.1002376.
- Sharp GC, Lawlor DA, Richmond RC, *et al.* Maternal pre-pregnancy BMI and gestational weight gain, offspring DNA methylation and later offspring adiposity: findings from the avon longitudinal study of parents and children. *Int J Epidemiol.* 2015; 44(4), 1288–1304. DOI: 10.1093/ije/ dyv042.
- Bond TA, Karhunen V, Wielscher M, *et al.* Exploring the role of genetic confounding in the association between maternal and offspring body mass index: evidence from three birth cohorts. *Int J Epidemiol.* 2020; 49(1), 233–243. DOI: 10.1093/ije/dyz095.
- Burgess B, Morris KS, Faith MS, Paluch RA, Kong KL. Added sugars mediate the relation between pre-pregnancy BMI and infant rapid weight gain: a preliminary study. *Int J Obes.* 2021; 45(12), 2570–2576. DOI: 10.1038/s41366-021-00936-w.
- Mintjens S, Gemke RJBJ, van Poppel MNM, Vrijkotte TGM, Roseboom TJ, van Deutekom AW. Maternal prepregnancy overweight and obesity are associated with reduced physical fitness but do not affect physical activity in childhood: the Amsterdam born children and their development study. *Childhood Obesity*. 2019; 15(1), 31–39. DOI: 10.1089/chi. 2018.0171.
- Alves JM, Angelo BC, Zink J, *et al.* Child physical activity as a modifier of the relationship between prenatal exposure to maternal overweight/obesity and neurocognitive outcomes in offspring. *Int J Obes.* 2021; 45(6), 1310–1320. DOI: 10.1038/s41366-021-00794-6.
- Zambrano E, Nathanielsz PW. Mechanisms by which maternal obesity programs offspring for obesity: evidence from animal studies. *Nutr Rev.* 2013; 71, S42–S54. DOI: 10.1111/nure.12068.
- Desai M, Ross MG. Maternal-infant nutrition and development programming of offspring appetite and obesity. *Nutr Rev.* 2020; 78(Supplement_2), 25–31. DOI: 10.1093/nutrit/nuaa121.
- Katzow MW, Messito MJ, Mendelsohn AL, Scott MA, Gross RS. Protective effect of prenatal social support on the intergenerational transmission of obesity in low-income hispanic families. *Child Obes*. 2023; 19(6), 382–390. DOI: 10.1089/chi.2021.0306.
- Kennelly MA, Ainscough K, Lindsay KL, Cronin M, McAuliffe FM. 336: an antenatal lifestyle intervention in overweight and obese pregnancy improves sleep behaviour and maternal wellbeing. *Am J Obstet Gynecol.* 2019; 220(1), S234–S235. DOI: 10.1016/j.ajog.2018.11.357.
- Horta BL, Rollins N, Dias MS, Garcez V, Pérez-Escamilla R. Systematic review and meta-analysis of breastfeeding and later overweight or obesity expands on previous study for World Health Organization. *Acta Paediatr.* 2023; 112(1), 34–41. DOI: 10.1111/apa.16460.
- Brown A, Lee M. Breastfeeding during the first year promotes satiety responsiveness in children aged 18-24 months. *Pediatr Obes.* 2012; 7(5), 382–390. DOI: 10.1111/j.2047-6310.2012.00071.x.
- Dedoussis GVZ, Yannakoulia M, Timpson NJ, et al. Does a short breastfeeding period protect from FTO -induced adiposity in children? *Int J Pediatr Obes.* 2011; 6(2-2), e326–e335. DOI: 10.3109/17477166.2010. 490269.
- 22. Abarin T, Yan Wu Y, Warrington N, Lye S, Pennell C, Briollais L. The impact of breastfeeding on FTO-related BMI growth trajectories: an application to the Raine pregnancy cohort study. *Int J Epidemiol.* 2012; 41(6), 1650–1660. DOI: 10.1093/ije/dys171.
- Horta BL, Victora CG, França GVA, et al. Breastfeeding moderates FTO related adiposity: a birth cohort study with 30 years of follow-up. Sci Rep. 2018; 8(1), 2530. DOI: 10.1038/s41598-018-20939-4.

- Church C, Moir L, McMurray F, et al. Overexpression of Fto leads to increased food intake and results in obesity. Nat Genet. 2010; 42(12), 1086–1092. DOI: 10.1038/ng.713.
- Victora CG, Barros FC. Cohort profile: the 1982 Pelotas (Brazil) birth cohort study. *Int J Epidemiol.* 2006; 35(2), 237–242. DOI: 10.1093/ije/dyi 290.
- Horta BL, Gigante DP, Goncalves H, et al. Cohort profile update: the 1982 Pelotas (Brazil) birth cohort study. Int J Epidemiol. 2015; 44(2), 441–441e. DOI: 10.1093/ije/dyv017.
- 27. World Health Organization. Obesity : preventing and managing the global epidemic : report of a WHO Consultation. (2000).
- WHO & UNICEF. Indicators for assessing infant and young child feeding practices definitions and measurement methods. (2021).
- Lean MEJ, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. *BMJ*. 1995; 311(6998), 158–161. DOI: 10.1136/bmj.311.6998.158.
- Barros AJ, Hirakata VN. Alternatives for logistic regression in crosssectional studies: an empirical comparison of models that directly estimate the prevalence ratio. *BMC Med Res Methodol*. 2003; 3(1), 21. DOI: 10.1186/ 1471-2288-3-21.
- Horta BL, Barros FC, Lima NP, et al. Maternal anthropometry: trends and inequalities in four population-based birth cohorts in Pelotas, Brazil, 1982– 2015. Int J Epidemiol. 2019; 48(Supplement_1), i26–i36. DOI: 10.1093/ije/ dyy278.
- Khan SS, Ning H, Wilkins JT, et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. JAMA Cardiol. 2018; 3(4), 280. DOI: 10.1001/jamacardio.2018.0022.
- 33. da Dias MS, Matijasevich A, Menezes AMB, et al. Association between maternal prepregnancy body mass index with offspring cardiometabolic risk factors: analysis of three Brazilian birth cohorts. J Dev Orig Health Dis. 2022; 13(2), 161–167. DOI: 10.1017/S2040174421000179.
- Brandt S, Moß A, Lennerz B, et al. Plasma insulin levels in childhood are related to maternal factors - results of the ulm birth cohort study. Pediatr Diabetes. 2014; 15(6), 453–463. DOI: 10.1111/pedi.12109.
- Hochner H, Friedlander Y, Calderon-Margalit R, et al. Associations of maternal prepregnancy body mass index and gestational weight gain with adult offspring cardiometabolic risk factors. *Circulation*. 2012; 125(11), 1381–1389. DOI: 10.1161/CIRCULATIONAHA.111.070060.
- 36. Victora CG, Horta BL, de Mola CL, et al. Association between breastfeeding and intelligence, educational attainment, and income at 30 years of age: a prospective birth cohort study from Brazil. *Lancet Glob Health*. 2015; 3(4), e199–e205. DOI: 10.1016/S2214-109X(15)70002-1.
- Zhao Y, Wang SF, Mu M, Sheng J. Birth weight and overweight/obesity in adults: a meta-analysis. *Eur J Pediatr.* 2012; 171(12), 1737–1746. DOI: 10.1007/s00431-012-1701-0.
- Huttly SRA, Barros FC, Victora CG, Beria JU, Vaughan JP. Do mothers overestimate breast feeeding duration? An example of recall bias from a study in southern Brazil. *Am J Epidemiol.* 1990; 132(3), 572–575. DOI: 10.1093/oxfordjournals.aje.a115693.
- Brunner J, Austin PC. Inflation of Type I error rate in multiple regression when independent variables are measured with error. *Canad J. Stat.* 2009; 37(1), 33–46. DOI: 10.1002/cjs.10004.
- Gao X, Becker LC, Becker DM, Starmer JD, Province MA. Avoiding the high Bonferroni penalty in genome-wide association studies. *Genet Epidemiol.* 2010; 34(1), 100–105. DOI: 10.1002/gepi.20430.
- Maessen SE, Derraik JGB, Binia A, Cutfield WS. Perspective: human milk oligosaccharides: fuel for childhood obesity prevention? *Adv Nutr.* 2020; 11(1), 35–40. DOI: 10.1093/advances/nmz093.
- Achike M, Akpinar-Elci M. The role of maternal prepregnancy body mass index in breastfeeding outcomes: a systematic review. *Breastfeedi Med.* 2021; 16(9), 678–686. DOI: 10.1089/bfm.2020.0376.