

General and abdominal fat outcomes in school-age children associated with infant breastfeeding patterns^{1–3}

Büşra Durmuş, Denise HM Heppe, Olta Gishti, Rashindra Manniesing, Marieke Abrahamse-Berkeveld, Eline M van der Beek, Albert Hofman, Liesbeth Duijts, Romy Gaillard, and Vincent WV Jaddoe

ABSTRACT

Background: Breastfeeding may have a protective effect on the development of obesity in later life. Not much is known about the effects of infant feeding on more-specific fat measures.

Objective: We examined associations of breastfeeding duration and exclusiveness and age at the introduction of solid foods with general and abdominal fat outcomes in children.

Design: We performed a population-based, prospective cohort study in 5063 children. Information about infant feeding was obtained by using questionnaires. At the median age of 6.0 y (95% range: 5.7 y, 6.8 y), we measured childhood anthropometric measures, total fat mass and the android:gynoid fat ratio by using dual-energy X-ray absorptiometry, and preperitoneal abdominal fat by using ultrasound.

Results: We observed that, in the models adjusted for child age, sex, and height only, a shorter breastfeeding duration, nonexclusive breastfeeding, and younger age at the introduction of solid foods were associated with higher childhood general and abdominal fat measures (P -trend < 0.05) but not with higher childhood body mass index. The introduction of solid foods at a younger age but not breastfeeding duration or exclusivity was associated with higher risk of overweight or obesity (OR: 2.05; 95% CI: 1.41, 2.90). After adjustment for family-based sociodemographic, maternal lifestyle, and childhood factors, the introduction of solid food between 4 and 4.9 mo of age was associated with higher risks of overweight or obesity, but the overall trend was not significant.

Conclusions: Associations of infant breastfeeding and age at the introduction of solid foods with general and abdominal fat outcomes are explained by sociodemographic and lifestyle-related factors. Whether infant dietary composition affects specific fat outcomes at older ages should be further studied. *Am J Clin Nutr* 2014;99:1351–8.

INTRODUCTION

A shorter breastfeeding duration is associated with higher risks of obesity, cardiovascular disease, and type 2 diabetes in adulthood (1–3). Studies in children have also suggested that a shorter duration of breastfeeding is related to higher BMI and fat mass, but results have not been consistent (3–5). Previously, we observed that shorter breastfeeding was associated with increased infant length and weight growth but not with risks of overweight and obesity at the age of 3 y (6). Results from studies that focused on associations of the early introduction of solid foods with increased risk of overweight and obesity in

children have also been inconsistent (5, 7–10). BMI does not distinguish lean mass from fat mass. In adults, specific body fat measures and waist circumference were independent of BMI related with adverse health outcomes and risk of mortality (11–13). Studies in children and adolescents on specific fat measurements have been scarce, and reported associations with cardiometabolic outcomes have not been consistent (11, 14–17). However, few studies have examined the effects of infant feeding on specific measures of general and abdominal body fat distributions. Mechanisms that underlie a potential beneficial effect of breastfeeding on obesity in later life may include infant growth patterns, behavioral factors such as self-regulatory feeding capabilities of the infant, and nutritional factors in human breast milk (4, 18–23). However, the observed association of breastfeeding duration with later overweight may also be confounded. Mothers who breastfed their infants have, in general, healthier family-related lifestyle habits and are less likely to overfeed their infants independent of the choice of feeding model (18, 24).

Therefore, in 5063 children participating in a population-based prospective cohort study, we examine associations of breastfeeding duration and exclusiveness and the age at introduction of solid foods with BMI and general and abdominal body fat outcomes in children at the age of 6 y. We specifically explored whether any association was explained by family-based sociodemographic, maternal lifestyle, and childhood factors.

¹ From the Generation R Study Group (BD, DHMH, OG, RG, and VVWJ) and the Departments of Pediatrics (DHMH, OG, LD, RG, and VVWJ) and Epidemiology (BD, DHMH, OG, AH, LD, RG, and VVWJ), Erasmus University Medical Center, Rotterdam, Netherlands; the Department of Radiology, Radboud University, Nijmegen, Netherlands (RM); and Nutricia Research, Utrecht, Netherlands (MA-B and EMvdB).

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³ Address reprint requests and correspondence to VVW Jaddoe, Generation R Study Group, Room (Na29-15), Erasmus Medical Center, PO Box 2040, 3000 CA, Rotterdam, Netherlands. E-mail: v.jaddoe@erasmusmc.nl.

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SUBJECTS AND METHODS

Study design

This study was embedded in the Generation R Study, which is a population-based prospective cohort study from fetal life onwards in Rotterdam, Netherlands (25). Enrollment in the study was aimed in the first trimester but was allowed until the birth of the child. All children were born between April 2002 and January 2006. Of all eligible children in the study area, 61% of children were participating in the study at birth (25). The study protocol was approved by the Medical Ethical Committee of the Erasmus Medical Center, Rotterdam (MEC 198.782/2001/31). Written informed consent was obtained from all parents. Information on breastfeeding was available in 6616 singleton, live-born children. A total of 6054 of these children participated in follow-up measurements until the age of 6 y; of these, 5063 children participated in detailed measurements for the current study at the median age of 6.0 y (90% range: 5.7, 6.8) (see Supplemental Figure S1 under "Supplemental data" in the online issue).

Infant feeding assessments

Information on the breastfeeding initiation and continuation was obtained from delivery reports and postal questionnaires at the ages of 2, 6, and 12 mo after birth as previously described (6, 25). Briefly, mothers were asked whether they ever breastfed their child (yes or no) and at what age they stopped breastfeeding. The duration of exclusive breastfeeding was defined by using information about at what age other types of milk or solids were introduced in the first 6 mo of life according to a short food-frequency questionnaire. In breastfed children, the breastfeeding duration was categorized into 4 groups as follows: 1) >0 to 1.9 mo, 2) 2–3.9 mo; 3) 4–5.9 mo, and 4) ≥ 6 mo. The information on the exclusiveness of breastfeeding was categorized into the following 2 categories: 1) nonexclusive until 4 mo of age and 2) exclusive until 4 mo of age. Nonexclusive until 4 mo of age indicates infants who received both breastfeeding and formula feeding or solids during the first 4 mo of life. Exclusive until 4 mo of age indicated infants who had been breastfed without any other milk, solids, or fluids during the first 4 mo of life. Analyses that focused on the breastfeeding duration and exclusivity were performed after the exclusion of never-breastfed children. Information on the introduction of solid foods included fruit and vegetable snacks and was obtained from the same food-frequency questionnaire. The age at the introduction of solid foods was categorized as 1) <4 mo, 2) 4–4.9 mo, and 3) ≥ 5 mo.

General and abdominal fat outcomes

At age 6 y, follow-up measurements were performed in a dedicated research center by a well-trained staff. We measured height in a standing position to the nearest millimeter without shoes by using a Harpenden stadiometer (Holtain Ltd) and weight by using a mechanical personal scale (SECA), and we calculated BMI (in kg/m^2). Age- and sex-adjusted SD scores (SDSs) for all growth characteristics were obtained with Dutch reference growth charts (Growth Analyzer 3.5, Dutch Growth Research Foundation.) (26). Childhood overweight was defined by International Obesity Task Force cutoffs (27).

Total body and regional fat masses was measured by using a dual-energy X-ray absorptiometry (DXA) scanner (iDXA, 2008; GE-Lunar) and analyzed with enCORE software (v.12.6; GE-Lunar) (30, 31). Previous studies have validated adiposity assessment by using a DXA scanner compared with computed tomography (28–30). Quality-assurance tests were run every day by using a standard calibration block of tissue-equivalent material supplied by the manufacturer. Children were placed without shoes, heavy clothing, and metal objects in a supine position on the DXA table with their hands lying flat and pronated and were asked to remain motionless (30). Total fat mass (kg) was presented as the percentage of total body weight (kg) measured by using DXA, and the android:gynoid fat ratio was calculated. The android:gynoid fat ratio reflects the central body fat distribution in the abdomen (android) and hip (gynoid) regions (30).

Abdominal ultrasound examinations were performed by using ultrasound. This method has been described in detail and has been validated previously (31, 32). Briefly, preperitoneal fat thicknesses were measured with a linear (L12-5 MHz) transducer (23), which was placed perpendicular to the skin surface on the median upper abdomen. We scanned longitudinally just below the xiphoid process to the navel along the midline (linea alba). All measurements were performed offline. The preperitoneal fat mass distance (preperitoneal distance) was measured as the distance of the linea alba to the peritoneum on top of the liver. The preperitoneal fat mass area was measured as areas of 2-cm length along the midline starting from the maximum preperitoneal distance in the direction of the navel (preperitoneal area) (24).

Covariates

Information on maternal age, prepregnancy BMI, educational level, ethnicity, and parity was obtained from the first questionnaire at enrollment in the study. Ethnicity and educational level were defined according to the classification of Statistics Netherlands (33, 34). Information on maternal smoking during pregnancy (yes or no) was retrieved from questionnaires during pregnancy. Gestational age at birth, birth weight, and sex were obtained from midwife and hospital registries at birth. The average television-watching time at the age of 6 y was assessed by using questionnaires (35).

Statistical analysis

First, we assessed differences in subject characteristics between the different breastfeeding categories by using 1-factor ANOVA tests for continued variables and chi-square tests for categorical variables. Second, we explored associations of breastfeeding and age at the introduction of solid foods with childhood outcomes at the age of 6 y by using multiple linear regression models. These models were first adjusted for child age at visit, sex, and height only (crude models) and subsequently in addition for potential confounders. We tested the role of 1) family-based sociodemographic factors (maternal age, ethnicity, and education), 2) maternal lifestyle-related factors (pregnancy BMI, parity, and smoking during pregnancy), and 3) childhood factors (gestational age at birth, birth weight, and television watching). These covariates were included in the regression models on the basis of their associations with fat outcomes in previous studies, a significant association with outcomes, or a change in effect estimates



>10%. Because the preperitoneal abdominal fat had a skewed distribution, we applied a ln transformation. To enable the comparison of effect estimates, results are presented in outcome SDSs, which were calculated as follows:

$$(\text{Observed value} - \text{mean}) \div \text{SD} \quad (1)$$

We used age-adjusted SDSs for BMI on the basis of Dutch reference growth charts (26). We did not create age-adjusted SDSs for total body and abdominal fat measurements because these were performed in a small age range. We also examined associations of breastfeeding with childhood outcomes in absolute values. Tests for trends were performed by treating the categorized variable as a continuous term. Finally, we used logistic regression models to examine associations of breastfeeding and age at the introduction of solid foods with risks of childhood overweight or obesity. A sensitivity analysis performed in European mothers only showed similar results as for the total group (data not shown). We did not observe a significant interaction term between breastfeeding and solid-food categories and child sex (P -interaction > 0.05) in relation to fat outcomes. To reduce the potential bias associated with missing data, we performed multiple imputations of missing covariates by generating 5 independent datasets by using the Markov chain Monte Carlo method, after which pooled effect estimates were calculated (36). Imputations were based on relations between covariates, determinants, and outcomes. We did not impute missing determinants or outcomes. Statistical analyses were performed with Statistical Package of Social Sciences software (version 20.0 for Windows; SPSS Inc).

RESULTS

Subject characteristics

Of all children, 92.4% ($n = 4678$) had ever been breastfed of whom 20.4% had been exclusively breastfed until 4 mo. Compared with mothers who never breastfed their children, mothers who ever breastfed their children had a lower weight and BMI, were higher educated, and were less likely to smoke ($P < 0.01$) (Table 1). Children who were never breastfed had a lower birth weight and gestational age at birth. See Supplemental Tables S1–S3 under “Supplemental data” in the online issue for distributions of maternal and childhood characteristics according to breastfeeding duration and exclusiveness and age at introduction of first solid-food categories.

Infant feeding and childhood general and abdominal fat outcomes

Associations of ever breastfeeding and breastfeeding duration and exclusivity and the timing of the introduction of solid foods with general and abdominal body fat–distribution outcomes at the age of 6 y were analyzed in different linear regression models. Models adjusted for child age at visit, sex, and height only are shown in Table 2. Breastfeeding duration and exclusivity were not associated with childhood BMI, whereas a shorter breastfeeding duration and nonexclusive breastfeeding were associated with higher total fat mass, android:gynoid fat ratio, and preperitoneal abdominal fat (P -trend < 0.05). An earlier introduction of solid foods was associated with higher

childhood BMI, total fat mass, and android:gynoid fat ratio but not with higher preperitoneal abdominal fat (P -trend < 0.05).

Fully adjusted effect estimates with adjustments for both maternal and infant covariates are given in Table 3 and show that, except for the association of a shorter breastfeeding duration with BMI, all associations attenuated into nonsignificance. The maternal educational level was the strongest confounder in these associations. See Supplemental Tables S4–S6 under “Supplemental data” in the online issue for models adjusted for family-based sociodemographic, maternal lifestyle, and childhood factors separately. See Supplemental Table S7 under “Supplemental data” in the online issue for associations of breastfeeding with BMI, in different adjusted models, which showed that adjustment for maternal age, ethnicity, and educational level attenuated all significant associations. See Supplemental Tables S8 and S9 under “Supplemental data” in the online issue for associations of infant feeding with childhood adiposity outcomes in absolute values. The duration of breastfeeding >12 mo was also not associated with lower amounts of fat mass in childhood (see Supplemental Table S10 under “Supplemental data” in the online issue).

Infant feeding and risks of overweight or obesity

As shown in Figure 1, in models adjusted for child age and sex only, a younger age at the introduction of solid food was associated with increased risks of childhood overweight or obesity (OR: 2.05; 95% CI: 1.41, 2.90). After adjustment for family-based sociodemographic, maternal lifestyle, and childhood factors, a shorter duration of breastfeeding was associated with lower risk of childhood overweight or obesity. Also, the introduction of solid food between 4 and 4.9 mo of age was associated with increased risk of childhood overweight or obesity, but the overall trend was not significant. See Supplemental Figures S2–S4 under “Supplemental data” in the online issue for models adjusted for family-based sociodemographic, maternal lifestyle, and childhood factors separately.

DISCUSSION

Results from this population-based, prospective study suggested that the observed associations of breastfeeding duration and exclusivity or the timing of the introduction of solid foods with body fat outcomes in childhood were explained by family-based sociodemographic, maternal lifestyle, and childhood factors.

Methodologic considerations

We used a population-based, prospective cohort design that included a large number of subjects who we studied from early fetal life onwards. Of the total group of singleton, live-born children, information on breastfeeding was available for 70% of them. We did not expect that this nonresponse at baseline led to biased effect estimates because biased estimates in large cohort studies mainly arise from the loss to follow-up rather than from nonresponse at baseline (37). Of all children with information on breastfeeding, <24% of them did not participate in the follow-up measurements at the age of 6 y. This loss to follow-up would have led to a selection bias if the associations of infant feeding with body fat distribution outcomes would have differed between those included and not included in the final analyses. We



TABLE 1
Subject characteristics according to the category of breastfeeding ($n = 5063$)¹

	Total group ($n = 5063$)	Never breastfed ($n = 385$)	Ever breastfed ($n = 4678$)	<i>P</i>
Maternal characteristics				
Age (y)	31.5 (22.3, 39.9) ²	31.4 (20.8, 40.0)	31.5 (20.2, 39.9)	0.72
Height (cm)	168.1 ± 7.4 ³	168.0 ± 7.0	168 ± 7.4	0.95
Weight (kg)	65.0 (49.0, 98.0)	64.5 (50.0, 112.0)	65.0 (49.0, 97.0)	<0.01
Prepregnancy BMI (kg/m ²)	22.6 (18.2, 34.3)	23.1 (18.2, 38.6)	22.5 (18.2, 34.0)	<0.01
Education (%)				
Lower	7.3	6.8	7.3	<0.01
Middle	40.2	62.0	38.4	
Higher	52.6	31.2	54.3	
Ethnicity (%)				
Dutch or European	66.5	78.2	65.5	<0.01
Non-European	33.5	21.8	34.4	
Smoking during pregnancy (%)				
Ever	24.3	38.8	23.1	<0.01
Never	75.7	61.2	76.9	
Parity (%)				
0	57.4	49.6	58.0	<0.01
≥1	42.6	50.4	42.0	
Birth characteristics				
Boys (%)	49.8	49.9	49.7	0.96
Gestational age (wk)	40.1 (36.0, 42.3)	39.9 (35.6, 42.4)	40.1 (36.1, 42.3)	<0.01
Preterm birth (%)	4.3	4.9	4.2	0.52
Weight (g)	3452 ± 540	3398 ± 565	3456 ± 538	0.04
Low birth weight (%)	3.7	5.2	3.5	0.09
Small for gestational age (%)	10.0	12.0	9.8	0.18
Introduction of solid foods (%)				
<4 mo of age	8.3	16.8	7.6	<0.01
4–4.9 mo of age	60.9	68.4	60.3	
≥5 mo of age	30.8	14.8	32.1	
Childhood characteristics				
Age at visit (y)	6.0 (5.7, 6.8)	6.0 (5.6, 7.2)	6.0 (5.6, 7.4)	0.81
Height (cm)	118.9 ± 5.7	118.5 ± 5.8	118.9 ± 5.7	0.13
Weight (kg)	22.9 ± 3.9	22.9 ± 4.3	22.9 ± 3.8	0.83
BMI (kg/m ²)	15.8 (13.6, 20.6)	15.8 (13.6, 22.2)	15.8 (13.6, 20.5)	0.51
Total fat mass (%)	23.8 (16.2, 37.8)	24.4 (16.1, 37.5)	23.8 (16.2, 37.8)	0.26
Android:gynoid fat ratio	0.24 (0.16, 0.41)	0.24 (0.15, 0.41)	0.24 (0.16, 0.40)	0.88
Preperitoneal abdominal fat area (cm ²)	0.38 (0.16, 1.08)	0.37 (0.16, 1.10)	0.38 (0.16, 1.09)	0.28
Overweight or obesity (%)	15.8	15.6	15.8	0.92

¹ Differences in maternal, infant, and childhood characteristics (compared within the never-breastfed group) were evaluated by using ANOVA for continuous variables and chi-square tests for categorical variables. Preterm birth was defined as gestational age <37 wk. Low birth weight was defined as birth weight <2500 g. Small for gestational age was defined as gestational age- and sex-adjusted birth weight <10%. Subject characteristics according to breastfeeding duration and exclusivity and age at the introduction of solid groups are given in supplementary materials (see Tables S1–S3 under “Supplemental data” in the online issue).

² Median; 95% range in parentheses (all such values for variables with skewed distribution).

³ Mean ± SD (all such values).

observed that children who did not participate in follow-up measurements at the age of 6 y were less frequently breastfed and breastfed for a shorter period. This effect might have led to an underestimation of the possible adverse effects of no breastfeeding. The assessment of breastfeeding initiation and duration by using questionnaires seems to be a valid method, especially when recall spans after a short period (<3 y), which was the case in our study. In our study, we used 3 questionnaires to assess infant feeding during the first 12 mo of life. We performed detailed measurements of childhood body fat distribution outcomes. DXA quantifies the fat content with a high precision and has the capacity for a regional analysis but cannot differentiate the amount of the 2 abdominal fat compartments (24, 26). Ultrasound is a reliable method to differentiate between abdominal visceral and subcutaneous fat compartments by using

an area measurement as a proxy for these fat compartments (38, 39). Both DXA and abdominal ultrasound have been validated against computed tomography (39). We did not correct for multiple testing because all outcomes were strongly correlated. However, because of the higher number of tests performed, false-positive associations might have occurred. Finally, although we performed adjustments for a large number of potential maternal and childhood confounders, residual confounding might still have occurred, as in any observational study.

Interpretation of main findings

A recent systematic review suggested that, compared with breastfed infants, formula-fed infants had higher fat-free mass in the first year of life, after which associations reversed with higher

TABLE 2

Associations of infant feeding with general and abdominal fat distribution outcomes at the age of 6 y adjusted for child age, sex, and height (*n* = 5063)¹

	Difference in outcome-measure SDSs			
	BMI (SDS) (<i>n</i> = 5063)	Total fat mass (SDS) (<i>n</i> = 4925)	Android:gynoid fat ratio (SDS) (<i>n</i> = 4925)	Preperitoneal abdominal fat area (SDS) (<i>n</i> = 4075)
Breastfeeding				
Never (<i>n</i> = 385)	0.03 (−0.06, 0.13)	0.07 (−0.02, 0.16)	0.02 (−0.03, 0.07)	−0.04 (−0.10, 0.01)
Ever (<i>n</i> = 4678)	Reference	Reference	Reference	Reference
Duration				
>0–1.9 mo of age (<i>n</i> = 1000)	0.04 (−0.03, 0.12)	0.20 (0.16, 0.23)*	0.11 (0.06, 0.15)*	0.15 (0.14, 0.16)*
2–3.9 mo of age (<i>n</i> = 836)	−0.00 (−0.08, 0.07)	0.06 (−0.01, 0.14)	0.05 (0.01, 0.09)*	0.04 (−0.05, 0.12)
4–5.9 mo of age (<i>n</i> = 479)	0.02 (−0.08, 0.11)	0.02 (−0.03, 0.06)	0.06 (0.01, 0.12)*	0.05 (−0.00, 0.11)
≥6 mo of age (<i>n</i> = 1258)	Reference	Reference	Reference	Reference
<i>P</i> -trend	0.36	0.01	0.01	0.01
Exclusive for 4 mo				
No (<i>n</i> = 2661)	0.02 (−0.05, 0.08)	0.12 (0.09, 0.15)*	0.04 (0.00, 0.07)*	0.05 (0.02, 0.09)*
Yes (<i>n</i> = 1041)	Reference	Reference	Reference	Reference
First solid foods				
<4 mo of age (<i>n</i> = 277)	0.17 (0.05, 0.28)*	0.23 (0.12, 0.34)*	0.15 (0.03, 0.28)*	0.08 (−0.04, 0.21)
4–4.9 mo of age (<i>n</i> = 2036)	0.10 (0.03, 0.16)*	0.16 (0.09, 0.22)*	0.13 (0.05, 0.20)*	0.03 (−0.05, 0.10)
≥5 mo of age (<i>n</i> = 1030)	Reference	Reference	Reference	Reference
<i>P</i> -trend	<0.01	<0.01	<0.01	0.21

¹ All values are linear regression coefficients; 95% CIs in parentheses. Models were adjusted for child age at visit, sex, and height. Nonexclusive breastfeeding until 4 mo of age included partial breastfeeding until 4 mo of age and partial breastfeeding thereafter as well as partial breastfeeding until 4 mo of age and not thereafter. Exclusive breastfeeding until 4 mo of age included exclusive breastfeeding until 6 mo of age, exclusive breastfeeding until 4 mo of age and partial breastfeeding thereafter, and exclusive breastfeeding until 4 mo of age and not thereafter. **P* < 0.05. SDS, SD score.

fat mass in formula-fed infants (40). A study in 216 children observed an inverse association of the breastfeeding duration with DXA-derived total body fat in girls at the age of 9 y (7, 41).

Similarly, Robinson et al (5) observed an inverse association of the breastfeeding duration with body fat in 536 children at the age of 4 y. These findings are in line with the results of a large

TABLE 3

Associations of infant feeding with general and abdominal fat distribution outcomes at the age of 6 y adjusted for child age, sex, height, family-based sociodemographic, maternal lifestyle, and childhood factors (*n* = 5063)¹

	Difference in outcome-measure SDSs			
	BMI (SDS) (<i>n</i> = 5063)	Total fat mass (SDS) (<i>n</i> = 4925)	Android:gynoid fat ratio (SDS) (<i>n</i> = 4925)	Preperitoneal abdominal fat area (SDS) (<i>n</i> = 4075)
Breastfeeding				
Never (<i>n</i> = 385)	−0.01 (−0.10, 0.08)	0.01 (−0.08, 0.09)	−0.04 (−0.14, 0.06)	−0.08 (−0.19, 0.02)
Ever (<i>n</i> = 4678)	Reference	Reference	Reference	Reference
Duration				
>0–1.9 mo of age (<i>n</i> = 1000)	−0.08 (−0.15, −0.01)*	0.03 (−0.04, 0.10)	−0.03 (−0.11, 0.05)	0.02 (−0.07, 0.10)
2–3.9 mo of age (<i>n</i> = 836)	−0.03 (−0.10, 0.05)	0.00 (−0.07, 0.07)	−0.00 (−0.09, 0.08)	−0.02 (−0.10, 0.07)
4–5.9 mo of age (<i>n</i> = 479)	0.03 (−0.06, 0.12)	0.03 (−0.06, 0.11)	−0.06 (−0.16, 0.00)	0.06 (−0.04, 0.16)
≥6 mo of age (<i>n</i> = 1258)	Reference	Reference	Reference	Reference
>0–1.9 mo of age (<i>n</i> = 1000)	0.03	0.47	0.43	0.90
Exclusive for 4 mo				
No (<i>n</i> = 2661)	−0.05 (−0.12, 0.01)	−0.01 (−0.07, 0.05)	−0.06 (−0.13, 0.01)	−0.05 (−0.13, 0.02)
Yes (<i>n</i> = 1041)	Reference	Reference	Reference	Reference
First solid foods				
<4 mo of age (<i>n</i> = 277)	0.01 (−0.11, 0.12)	−0.02 (−0.12, 0.09)	−0.03 (−0.16, 0.10)	−0.09 (−0.21, 0.05)
4–4.9 mo of age (<i>n</i> = 2036)	0.04 (−0.03, 0.10)	0.06 (−0.01, 0.12)	0.06 (−0.01, 0.13)	−0.04 (−0.12, 0.03)
≥5 mo of age (<i>n</i> = 1030)	Reference	Reference	Reference	Reference
<i>P</i> -trend	0.51	0.38	0.63	0.13

¹ All values are linear regression coefficients; 95% CIs in parentheses. Models are adjusted for child age at visit, sex, and height plus family-based sociodemographic confounders (maternal age, ethnicity, and education), maternal lifestyle-related factors (prepregnancy BMI, parity, and smoking during pregnancy), and childhood factors (gestational age at birth, birth weight, and television watching). Results from models adjusted for family-based sociodemographic confounders, maternal lifestyle-related factors, and childhood factors separately are given in the supplementary materials (see Tables S4 and S5 under “Supplemental data” in the online issue). Nonexclusive breastfeeding until 4 mo of age included partial breastfeeding until 4 mo of age and partial breastfeeding thereafter as well as partial breastfeeding until 4 mo of age and not thereafter. Exclusive breastfeeding until 4 mo of age included exclusive breastfeeding until 6 mo of age, exclusive breastfeeding until 4 mo of age and partial breastfeeding thereafter, and exclusive breastfeeding until 4 mo of age and not thereafter. **P* < 0.05. SDS, SD score.

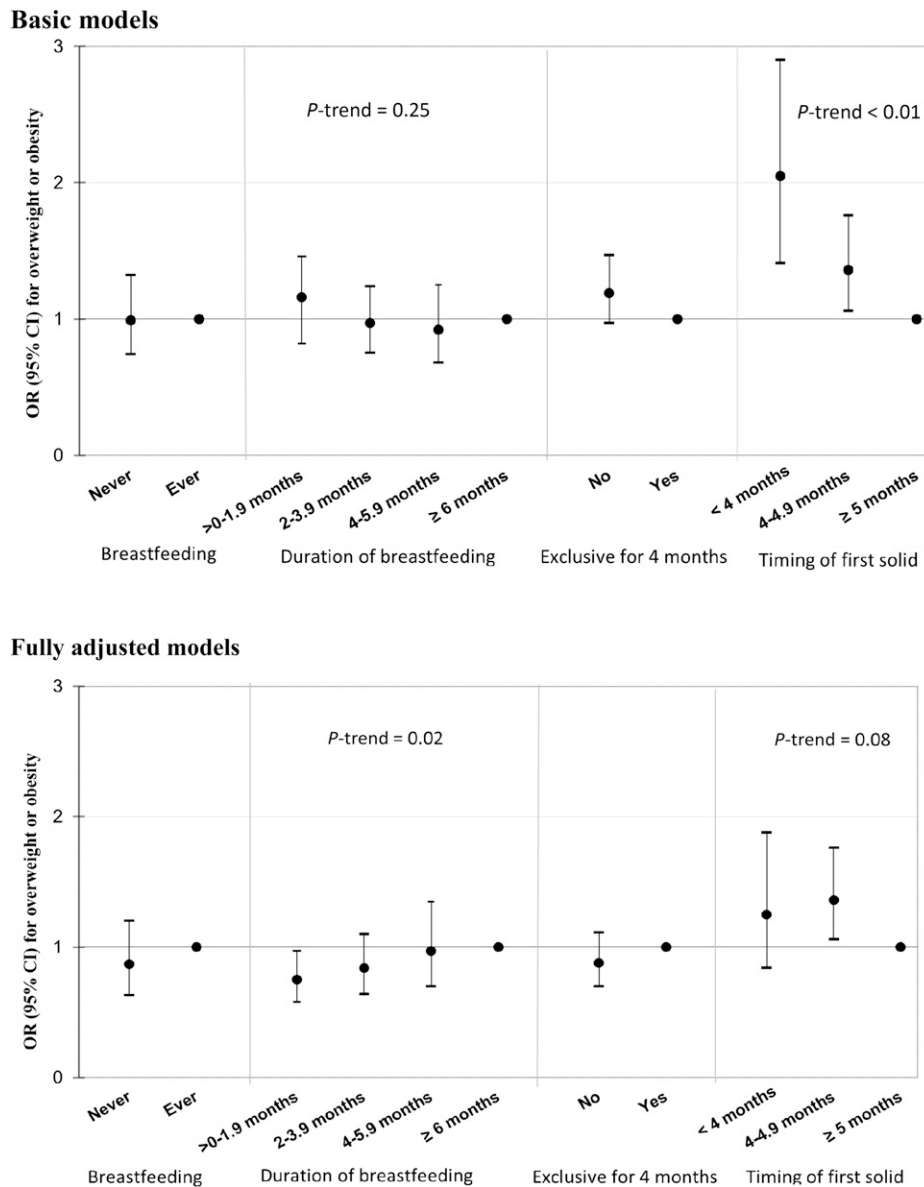


FIGURE 1. Associations [ORs (95% CIs)] of infant feeding with risk of childhood overweight or obesity ($n = 5063$). Basic models and fully adjusted models are shown. Values were determined by using multiple logistic regression models. Basic models were adjusted for child age at visit and sex. Fully adjusted models were additionally adjusted for family-based sociodemographic factors (maternal age, ethnicity, and education), maternal lifestyle-related factors (prepregnancy BMI parity and smoking during pregnancy), and childhood factors (gestational age at birth, birth weight, and television watching). Results from the models adjusted for family-based sociodemographic confounders, maternal lifestyle-related factors, and childhood factors separately are given in the supplementary materials (see Figures S2–S4 under “Supplemental data” in the online issue). Nonexclusive breastfeeding until 4 mo of age included partial breastfeeding until 4 mo of age and partial breastfeeding thereafter as well as partial breastfeeding until 4 mo of age and not thereafter. Exclusive breastfeeding until 4 mo of age included exclusive breastfeeding until 6 mo of age, exclusive breastfeeding until 4 mo of age and partial breastfeeding thereafter, and exclusive breastfeeding until 4 mo of age and not thereafter.

population-based study in the United Kingdom in 4325 children aged 9 y that showed a protective effect of a longer breastfeeding duration on total body fat at the age of 9 y (42). However, in the latter study, associations of breastfeeding duration with body fat outcomes attenuated after adjustment for confounders. Results from the Promotion of Breastfeeding Intervention Trial also did not show beneficial effects of the breastfeeding duration and exclusivity on fat distribution measured by waist circumference, waist-to-hip ratio, and subscapular skinfold thickness at the age of 6.5 y (43). In a study among 14,726 children from 8 European countries, exclusive breastfeeding for specifically 4–6 mo was

related with lower risks of overweight and waist-to-hip ratio and lower body fat at the age of 9 y (44). The authors only took a limited number of potential confounders into account. We had more detailed measures of general and abdominal fat available than only BMI. Previous studies in adults suggested that specific body fat measures are independent of BMI related cardiovascular and metabolic disease (12, 13). Studies in children and adolescents have been scarce and reported inconsistent results (11, 14–16). In models adjusted for child age, sex, and height, we observed associations of a shorter breastfeeding duration and nonexclusivity with higher general and abdominal fat but not



with higher BMI. These differences in results might have been attributable to the fact that BMI is an imprecise measure of adiposity in children because it also includes lean and bone masses. However, associations attenuated after adjustment for maternal and infant confounders. In contrast with previous studies (4, 22), in the fully adjusted models, a shorter breastfeeding duration was associated with lower BMI. We could not explain this finding.

Studies that focused on associations of breastfeeding and age at the introduction of solid food with risk of childhood overweight and obesity also showed inconsistent results (7, 8, 10, 45). Previous studies reported that the introduction of solid foods at a younger age than 4 mo was associated with increased body fat or weight in childhood (8, 46) or a greater weight gain during infancy (47, 48), which predicted later adiposity (49). Other studies did not observe these associations (7, 9). We showed a significant association of the introduction of solid food before 4.9 mo of age with risk of overweight or obesity at the age of 6 y, but these associations attenuated into nonsignificant after adjustment for confounders. Similarly, a systematic review in 24 studies from developed countries showed no consistent association between the early introduction of solid food and risk of overweight and obesity in infancy and childhood (9).

Results from our study suggested that associations of infant feeding with body fat distribution in childhood were explained by family-based sociodemographic, maternal lifestyle, and childhood factors. We observed that the maternal educational level was the strongest confounder in these associations. A lower parental socioeconomic status is unlikely to be the causal factor per se that leads to adiposity in offspring. A lower socioeconomic status might reflect various unhealthy lifestyle habits such as the use of high-caloric food in the diet, overnutrition of children, lower levels of physical activity, or psychological factors as emotional deprivation in childhood. Additional studies are needed to explore which specific factors explain the associations of lower socioeconomic status with adiposity in offspring. The lack of support for a causal association of breastfeeding with childhood fat outcomes is in line with findings from the Promotion of Breastfeeding Intervention Trial. Kramer et al (18) suggested that the observed, potential causal association of breastfeeding with childhood fat mass outcomes might be confounded by differences in the socioeconomic status of breastfeeding and formula-feeding mothers. Reversed causation may also partly explain the observed associations because thinner infants may prefer to be breastfed or prolonged breastfed.

However, other explanations are possible for the lack of associations in the final models. We only used breastfeeding or the timing of solid foods as exposure and did not have information about breast-milk composition. Differences in breast milk composition, such as the long-chain PUFA content across populations and over time, might complicate direct comparisons between studies (50). DHA is thought to delay the timing of adiposity rebound by downregulating adipose tissue hyperplasia (50). Also, associations of shorter breastfeeding with overweight might appear at older ages or be confined to specific populations such as preterm infants. Additional studies are needed to explore these specific hypotheses.

In conclusion, in this population-based, prospective cohort study, we observed that associations of breastfeeding and timing of the introduction of solid foods with general and abdominal

body fat outcomes in children are explained mainly by family-based sociodemographic, maternal lifestyle, and childhood factors. Additional studies are needed to evaluate whether breast-milk composition or infant feeding habits affect fat mass at older ages.

The Generation R Study is conducted by the Erasmus Medical Center in close collaboration with the School of Law and Faculty of Social Sciences of the Erasmus University Rotterdam; the Municipal Health Service Rotterdam area, Rotterdam; the Rotterdam Homecare Foundation, Rotterdam; and the Stichting Trombosedienst and Artsenlaboratorium Rijnmond, Rotterdam. We gratefully acknowledge the contribution of participating mothers, general practitioners, hospitals, midwives, and pharmacies in Rotterdam.

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