

Breast-Feeding and Risk for Childhood Obesity

Does maternal diabetes or obesity status matter?

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OBJECTIVE — We sought to evaluate whether maternal diabetes or weight status attenuates a previously reported beneficial effect of breast-feeding on childhood obesity.

RESEARCH DESIGN AND METHODS — Growing Up Today Study (GUTS) participants were offspring of women who participated in the Nurses' Health Study II. In the present study, 15,253 girls and boys (aged 9–14 years in 1996) were included. Maternal diabetes and weight status and infant feeding were obtained by maternal self-report. We defined maternal overweight as BMI ≥ 25 kg/m². Childhood obesity, from self-reported height and weight, was based on the Centers for Disease Control and Prevention definitions as normal, at risk for overweight, or overweight. Maternal status categories were nondiabetes/normal weight, nondiabetes/overweight, or diabetes. Logistic regression models used generalized estimating equations to account for nonindependence between siblings.

RESULTS — For all subjects combined, breast-feeding was associated with reduced overweight (compared with normal weight) in childhood. Compared with exclusive use of formula, the odds ratio (OR) for exclusive breast-feeding was 0.66 (95% CI 0.53–0.82), adjusted for age, sex, and Tanner stage. Results did not differ according to maternal status (nondiabetes/normal weight OR 0.73 [95% CI 0.49–1.09]; nondiabetes/overweight 0.75 [0.57–0.99]; and diabetes 0.62 [0.24–1.60]). Further adjustment for potential confounders attenuated results, but results remained consistent across strata of maternal status (*P* value for interaction was 0.50).

CONCLUSIONS — Breast-feeding was inversely associated with childhood obesity regardless of maternal diabetes status or weight status. These data provide support for all mothers to breast-feed their infants to reduce the risk for childhood overweight.

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Recent meta-analyses concluded that having been breast-fed is associated with a 13–22% reduced odds for overweight or obesity in childhood and later in life (1,2), and the meta-analysis by Harder et al. (3) confirmed a dose-response effect according to duration of breast-feeding. The basis for such an effect

may be behavioral (4), related to maternal feeding styles that are less controlling and more responsive to infant cues of hunger and satiety (5). Alternatively, or additionally, the infant's physiologic response to the nutritional or hormonal content of breast milk may explain effects of breast-feeding on growth (6–9). How-

ever, several issues are unresolved, including the potential for residual confounding to explain the effect (10,11). Moreover, it is possible that the impact of breast-feeding on childhood obesity may be attenuated or reversed among children whose mothers have diabetes (12–15) or may be enhanced if mothers are overweight or obese (16,17).

Increased glucose and insulin content of breast milk of diabetic mothers (18) may contribute to effects of breast-feeding on infant growth, although some investigators have found no difference in macronutrient content of breast milk of well-controlled diabetic mothers (19). Alternatively, genetic susceptibility, birth weight, insulinemia, or other characteristics of infants born of a diabetic intrauterine environment may alter their response to breast- or formula feeding. Of particular concern is the report by Plagemann et al. (12), which found that offspring of mothers with type 1 or gestational diabetes who consumed diabetic breast milk during the 1st week of life were more likely to be overweight and to have worse glucose tolerance at 2 years of age than offspring of mothers who consumed banked nondiabetic breast milk, analyzed as a function of volume of milk ingested. Effects of milk consumed in this 1st week were confirmed in the same cohort, after accounting for intake in the 2nd to 4th week of life (13). However, among offspring of mothers with type 1 diabetes, Kerssen et al. (15) found no association of infant feeding modality in the first 6 weeks of life with weight or BMI at 1 year of age. Pettitt et al. (14) found that among Pima Indians, a protective effect of breast-feeding on subsequent development of type 2 diabetes in offspring appeared to be present in mothers with or without diabetes during pregnancy, although the sample size was small.

Previously, a protective, dose-dependent effect of breast-feeding to reduce the risk of overweight in adolescents was reported by Gillman et al. (20) from a study of the offspring of participants in the Nurses' Health Study II (Growing Up Today Study [GUTS]), which included over

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Abbreviations: GUTS, Growing Up Today Study.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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15,000 subjects. The large size of this cohort, unselected for maternal diabetes or obesity status, allows direct comparison of the association of breast-feeding on childhood obesity across maternal status, which previous studies have not done.

RESEARCH DESIGN AND METHODS

The subjects are participants in the GUTS, who are offspring of subjects in the Nurses' Health Study II, a cohort study of over 116,000 female registered nurses (21). From the Nurses' Health Study II study records, we identified 40,968 subjects who had at least one child aged 9–14 years in 1996. We contacted 34,174 of those who promptly responded to the most recent Nurses' Health Study II questionnaires, requesting permission to contact their children. A total of 18,526 women provided information for 26,765 children: 13,261 girls and 13,504 boys. In the fall of 1996, we sent each of these children a letter inviting them to participate in the study along with a sex-specific questionnaire, assuring them that we would not convey their individual responses to anyone, including their mothers. Of the children, ~68% of the girls ($n = 9,039$) and 58% of the boys ($n = 7,843$) returned completed questionnaires, thereby assenting to participate in the cohort study. In the spring of 1997, we sent a supplemental questionnaire to the participants' mothers to obtain information on early life factors. A total of 16,550 (98%) of the mothers completed this questionnaire. In 1999, 13,640 (81% of 16,882) mothers responded to a second supplemental questionnaire, which concentrated on the child's medical history and mother's prenatal diabetes and weight history. Human subject committees at the Harvard School of Public Health and Brigham and Women's Hospital, Boston, Massachusetts, approved the study.

For this analysis, of the 16,882 initially enrolled subjects, we excluded 343 participants outside the age range 9–14 years on the baseline questionnaire in 1996, 426 whose mothers did not respond to the supplemental 1997 questionnaire, 31 who had impossible combinations of infant feeding type and duration of breast-feeding, 470 who had missing or outlying values for height or weight on the baseline questionnaire, 56 missing maternal overweight/diabetes status, 145 whose mothers reported a gestation of <34 completed weeks, and 158 with childhood medical conditions that might have interfered

with growth. These conditions were diabetes ($n = 41$), juvenile rheumatoid arthritis ($n = 24$), inflammatory bowel disease ($n = 18$), cerebral palsy ($n = 17$), Down syndrome ($n = 6$), acute lymphocytic leukemia ($n = 5$), and other selected infectious, endocrine, metabolic, neurologic, renal, respiratory (not asthma), and orthopedic conditions and congenital anomalies ($n = 47$). Thus, we based the analyses on 15,253 participants.

We ascertained all information except household income from mailed self-report questionnaires. Among other variables, each GUTS participant reported age, sex, race/ethnicity, height, weight, pubic hair sexual maturity (Tanner stage) rating using validated pictograms (22), age at menarche for menarcheal girls, diet and physical activity in the previous 12 months using validated frequency questionnaires, and average time spent watching television on weekdays and on weekends.

From the 1997 supplemental questionnaire to mothers, we obtained child's birth weight, birth length, category of gestational age (<34, 34–37, and >37 weeks), medical conditions during childhood, and infant feeding practices. The infant feeding questions included 1) the predominant liquid-feeding method in the first 6 months of life (on a 5-point scale: breast milk only, more breast milk than infant formula, both equally, more formula than breast milk, or formula only) and 2) the duration of breast-feeding in the following categories: 0, <1, 1–3, 4–6, 7–9, and >9 months.

From the 1999 supplemental questionnaire to mothers, we ascertained diagnosis with gestational diabetes during the index pregnancy. For maternal BMI, we used mother's weight in 1997 and, if missing, used weight closest to 1997 to estimate mother's BMI (1995, 1993, or 1991). From the Nurses' Health Study II questionnaires, we obtained information on the mother's weight at age 18 years and in 1989, 1991, 1993, and 1995; height; and birth order of the child. We obtained information from the 1989 Nurses' Health Study II original baseline questionnaire about mother's diabetes status and smoking habits during the early life of the child. From the 1995 Nurses' Health Study II questionnaire, we ascertained mothers' other lifestyle habits, which may relate to children's growth, including diet and physical activity (21).

To obtain estimates of household income, we mapped each subject's address

to a census tract. We used U.S. census data from 1990 to assign the median household income for that census tract to the individual subject.

Validity of exposure and outcome assessments

Issues related to the validity of the main exposure variable (maternal report of infant feeding) and outcome (self-reported height and weight) used in this study have been previously discussed in detail (20). Mother's weight and diabetes status were also self-reported in the study. Troy et al. (23) reported a high correlation between self-reported weight ($r = 0.87$) and height ($r = 0.94$) at age 18 years and those documented on entry to nursing school among a subset of Nurses' Health Study II participants. The validity of self-reported diabetes has been verified in the Nurses' Health Study cohort. Among a subsample of 62 women who were regarded as diabetic cases based on self-reported information, 61 (98%) of the diagnoses were further confirmed by medical record review (24). With regard to self-reported gestational diabetes, among a sample of 114 women in the Nurses' Health Study II cohort who had reported on a supplementary questionnaire that they had a first diagnosis of gestational diabetes in a singleton pregnancy between 1989 and 1991, 94% of the women were confirmed by medical records to have a physician diagnosis of gestational diabetes, and all women had evidence of impairment of glucose tolerance (25).

Data analysis

Our two exposures of interest were breast-feeding exclusivity in the first 6 months of life and duration of breast-feeding. For breast-feeding exclusivity, our analysis compared subjects in each breast-feeding type category, with those only formula fed as the referent group. For the duration of breast-feeding, our analysis examined subjects in each duration category compared with those never breast-fed as the referent group.

The outcome, childhood obesity, was defined based on the Centers for Disease Control and Prevention definitions according to age- and sex-specific BMI as normal (up to the 85th percentile), at risk for overweight (85th to 95th percentile), or overweight (>95th percentile) (<http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm>). Maternal overweight was defined as BMI ≥ 25 kg/

m². Mothers were classified as having diabetes if they reported having diabetes on the 1989 Nurses' Health Study II baseline questionnaire, for which the diagnoses occurred before the birth of the index child, or reported having gestational diabetes, for which the diagnosis occurred during the pregnancy of the index child or on the 1999 supplemental questionnaire. Maternal diabetes and weight status were defined categorically as nondiabetes/normal weight, nondiabetes/overweight, or diabetes. The diabetes category included women who had preexisting diabetes ($n = 56$) and those with gestational diabetes ($n = 417$).

To adjust for covariates and to account for correlated values among siblings ($n = 11,810$ families, 77% of the cohort), we used logistic regression models with estimation by generalized estimating equations (26). We compared odds of exceeding the 95th percentile of BMI with the odds of being less than the 85th percentile for all subjects combined and for subjects in each level of maternal diabetes and weight status. We focused on the contrast between youth exceeding the 95th percentile and those less than the 85th percentile because misclassification of youth with excess adipose tissue was less likely in the group exceeding the 95th percentile than in the intermediate group. Furthermore, our previous work established a protective effect for both exclusivity and duration of breast-feeding that was intermediate for the "at risk for overweight group," as would be expected under a dose-response effect for breast-feeding in relation to weight status in childhood. In our base model, we included sex, age, and Tanner stage since BMI varies with age and Tanner stage in adolescence (27,28). We further adjusted for mother's BMI and prepregnancy smoking behavior, child's race, birth weight, gestational age, birth order, weekly hours of television and physical activity, and daily energy intake and household income. We report odds ratios (ORs) and 95% CIs as the measures of association.

We evaluated the association of breast-feeding with childhood obesity in the full cohort, then in stratified analyses according to maternal obesity and diabetes status. Effect modification was tested formally (maternal status \times breast-feeding exclusivity and maternal status \times breast-feeding duration) in the fully adjusted models.

RESULTS— Of 15,253 study participants, 13.4% were at risk for overweight and another 6.7% were overweight. The mean (\pm SD) age of study participants was 11.9 ± 1.6 , and 53.2% were girls. Mothers of these subjects included 56.4% who were nondiabetic subjects and of normal weight, 40.5% who were nondiabetic subjects and overweight, and 3.1% who had diabetes, including 56 with preexisting diabetes and 417 with gestational diabetes.

Table 1 shows unadjusted characteristics of subjects according to the subjects' weight status and their mothers' weight and diabetes status. Compared with lower weight status youth, overweight youth were more likely to have mothers who were overweight or who had diabetes. Overweight youth were also more likely to have been predominantly or exclusively formula fed and to have been breast-fed for shorter periods of time. Similarly, mothers who were either overweight themselves or who had diabetes appeared more likely to predominantly or exclusively formula feed their sons or daughters and to breast-feed for shorter periods of time.

Infant feeding practices were further compared between youth who were of normal weight ($n = 12,182$) and those who were overweight ($n = 1,026$). Shown in Table 2, for all subjects combined, feeding with breast milk only compared with feeding with formula only was associated with reduced likelihood of being overweight in childhood (OR 0.66 [95% CI 0.53–0.82], adjusted for age, sex, and Tanner stage). This analysis was repeated after stratification by maternal diabetes and weight status, also shown in Table 2. ORs and 95% CIs were very similar, except for a wider CI in the subgroup of mothers with diabetes, likely due simply to the smaller sample size in this subgroup compared with the other two subgroups. Further details of the analysis are given in Table 2, wherein each category of breast-feeding exclusivity was compared with feeding with formula only. After adjustment for potentially confounding variables related to youth and maternal lifestyle and BMI, the association was attenuated somewhat (Table 2). Results were not different across strata of maternal obesity and diabetes status ($P = 0.50$ for interaction in the fully adjusted model).

Duration of breast-feeding was considered using the category "never breast-fed" as the reference group, and among all

subjects, a protective effect was observed with increasing duration of breast-feeding (OR for breast-feeding duration >9 months was 0.63 [95% CI 0.50–0.78], adjusted for age, sex, and Tanner stage) (Table 3). An unexpected finding emerged in this analysis; the OR for breast-feeding duration <1 month was 1.36 (95% CI 1.02–1.82). Results for the fully adjusted model were attenuated somewhat. Results did not differ across strata of maternal diabetes or obesity status (P for interaction was 0.66 in the fully adjusted model).

Of the 6,174 nondiabetic mothers who had BMI ≥ 25 kg/m², 62% had BMI 25–29.0 and 48% had BMI ≥ 30 . There were no differences in the association of breast-feeding exclusivity or breast-feeding duration with childhood overweight between nondiabetic mothers who were normal weight, overweight, or obese ($P > 0.5$ for interaction terms). Finally, we evaluated potential effect modification within the group of mothers with diabetes, according to weight status (normal weight, 51%; overweight, 49%), and tests for interaction were nonsignificant ($P > 0.5$).

CONCLUSIONS— In the present study, the prevalence of overweight in youth decreased as exclusivity and duration of breast-feeding increased. These findings held true for youth whose mothers had diabetes or who were overweight, as well as for youth whose mothers were of normal glucose tolerance and normal weight. The importance of this result lies in the potential for breast-feeding to reduce excess risk of obesity and diabetes, which may occur among offspring of diabetic or overweight mothers (14,29–31).

Our findings are in contrast to those reported by Plageman et al. (12), which suggested a potential adverse effect of diabetic breast milk on glucose tolerance and relative weight at age 2 years. The study by Plageman et al. included only offspring of women with diabetes (type 1 diabetes, $n = 83$; gestational diabetes, $n = 29$; total $n = 112$ of 368 originally eligible), and comparisons were made based on infant feeding during the 1st week of life, when all mothers and infants remained at the hospital maternity ward and all were encouraged to breast-feed. Supplemental feeding with banked breast milk of unrelated, nondiabetic women was offered to infants based on the clinical judgment of the ward pediatrician. Comparisons of exposure to volume of dia-

Table 1—Subject characteristics according to offspring weight status and maternal diabetes/weight status (n = 15,253)

	Offspring weight status				Maternal diabetes/weight status			
	Normal	At risk for overweight	Overweight	P value	Nondiabetes/normal weight	Nondiabetes/overweight	Diabetes	P value
n	12,182	2,045	1,026		8,606	6,174	473	
Maternal status								
Nondiabetes, BMI <25 kg/m ²	7,458 (61)	848 (41)	300 (29)	<0.0001				
Nondiabetes, BMI ≥25 kg/m ²	4,355 (36)	1,135 (56)	684 (67)					
Diabetes	369 (3)	62 (3)	42 (4)					
Infant feeding				<0.0001				<0.0001
Breast milk only	3,872 (32)	570 (28)	253 (25)		2,830 (33)	1,715 (28)	150 (32)	
Predominantly breast	3,879 (32)	644 (32)	293 (29)		2,770 (32)	1,922 (31)	124 (26)	
Breast and formula equally	816 (7)	136 (7)	72 (7)		579 (7)	413 (7)	32 (7)	
Predominantly formula	2,174 (18)	407 (20)	257 (25)		1,499 (17)	1,241 (20)	98 (21)	
Formula only	1,438 (12)	287 (14)	150 (15)		926 (11)	880 (14)	69 (15)	
Duration of breast-feeding				<0.0001				<0.0001
Never breast-fed (months)	1,438 (12)	287 (14)	150 (15)		926 (11)	880 (14)	69 (15)	
<1	562 (5)	112 (6)	82 (8)		368 (4)	357 (6)	31 (7)	
1–3	1,738 (14)	323 (16)	182 (18)		1,202 (14)	965 (16)	76 (16)	
4–6	2,525 (21)	424 (21)	208 (20)		1,787 (21)	1,286 (21)	84 (18)	
7–9	1,872 (15)	309 (15)	150 (15)		1,367 (16)	894 (15)	70 (15)	
>9	4,005 (33)	581 (29)	251 (25)		2,924 (34)	1,770 (29)	143 (30)	
Mean age (years)	12.0 ± 1.6	11.8 ± 1.5	11.7 ± 1.5	<0.0001	11.9 ± 1.6	12.0 ± 1.6	11.7 ± 1.5	<0.0001
Sex				<0.0001				0.66
Girls	6,718 (55)	1,011 (49)	389 (38)		4,608 (54)	3,261 (53)	249 (53)	
Boys	5,464 (45)	1,034 (51)	637 (62)		3,998 (46)	2,913 (47)	224 (47)	
Tanner stage				<0.0001				<0.0001
0 (missing value)	344 (3)	67 (3)	32 (3)		239 (3)	185 (3)	19 (4)	
1	2,738 (22)	426 (21)	220 (21)		2,053 (24)	1,205 (20)	126 (27)	
2	2,910 (24)	471 (23)	279 (27)		2,121 (25)	1,426 (23)	113 (24)	
3	2,209 (18)	371 (18)	184 (18)		1,539 (18)	1,137 (18)	88 (19)	
4	2,641 (22)	408 (20)	188 (18)		1,786 (21)	1,370 (22)	81 (17)	
5	1,340 (11)	302 (15)	123 (12)		868 (10)	851 (14)	46 (10)	

Data are n (%) or means ± SD.

betic breast milk versus volume of nondiabetic banked breast milk were made based on the weight of the infant before and after each feeding. Thus, the finding of increased relative weight at age 2 years in association with increased volume of diabetic breast milk could simply reflect appropriate growth in a successfully breast-fed baby for whom the ward pediatrician did not recommend frequent supplemental feedings, rather than an indication of a deleterious effect of breast milk of diabetic mothers. The study of Kerssen et al. (15) showed no effect of infant feeding on weight or BMI at age 1 year for infants of 229 mothers with type 1 diabetes, although the sample size within each infant feeding group was small ($n = 39$, $n = 43$, and $n = 50$ for breast milk, formula, and mixed feeding, respectively). In contrast, our study included a larger sample size of women with

diabetes ($n = 473$) and a large sample of women without diabetes, enabling direct comparison of the estimated association of infant feeding with childhood overweight according to maternal diabetes and weight status.

Studies of the health effects of breast-feeding raise many methodological issues because decisions made regarding infant feeding may be strongly related to rate of growth, hunger or perceived hunger, and maternal dietary beliefs and health habits. One issue is reverse causality; i.e., deciding to supplement due to perceptions by the mother of infant hunger or need to enhance growth (32). The reverse causality scenario may, in fact, not be a bias but a real explanation of beneficial effects of prolonged breast-feeding in that mothers who choose to supplement may overfeed their infants and contribute to excess weight gain later in childhood. This phe-

nomenon may explain the unexpected finding in the present study of an OR greater than the null value for the category of breast-feeding (>0 but <1 month) (Table 3). If such an apparent deleterious association was real for infants who are breast-fed <1 month, it could reflect decisions to supplement infants who are hungry and growing rapidly. Infants who experience rapid growth in early weeks of life are at increased risk for overweight later in life (33,34).

Another issue commonly cited as problematic in studies of infant feeding and long-term health outcomes is residual confounding, in which analyses do not adequately account for factors associated with maternal and child health habits that may explain observed health effects of infant feeding (10). Residual confounding, in the present study, seems unlikely because stratification by maternal obesity

Table 2—Association of infant feeding type in the first 6 months of life with subject overweight status according to maternal diabetes and weight status*

Infant feeding type	Maternal diabetes/weight status			
	Nondiabetes, BMI <25 kg/m ²	Nondiabetes, BMI ≥25 kg/m ²	Diabetes	All
Overweight vs. normal weight, adjusted for age, sex, and Tanner stage (n = 13,204)†				
Breast milk only	0.73 (0.49–1.09)	0.75 (0.57–0.99)	0.62 (0.24–1.60)	0.66 (0.53–0.82)
Predominantly breast	0.79 (0.53–1.17)	0.84 (0.65–1.10)	0.28 (0.08–0.92)	0.73 (0.59–0.90)
Breast and formula equally	0.73 (0.41–1.29)	1.07 (0.74–1.56)	0.22 (0.03–1.46)	0.84 (0.62–1.13)
Predominantly formula	0.96 (0.63–1.46)	1.25 (0.96–1.64)	0.91 (0.33–2.50)	1.09 (0.88–1.35)
Formula only	1.00	1.00	1.00	1.00
Overweight vs. normal weight, adjusted for age, sex, Tanner stage, and maternal and child characteristics (n = 12,321)‡				
Breast milk only	0.89 (0.57–1.38)	0.85 (0.64–1.14)	0.79 (0.29–2.16)	0.84 (0.66–1.07)
Predominantly breast	0.91 (0.59–1.40)	0.89 (0.67–1.17)	0.27 (0.07–0.97)	0.84 (0.67–1.07)
Breast and formula equally	0.81 (0.44–1.50)	1.02 (0.68–1.53)	0.34 (0.05–2.39)	0.90 (0.65–1.26)
Predominantly formula	1.03 (0.65–1.62)	1.17 (0.87–1.56)	0.77 (0.23–2.54)	1.08 (0.85–1.37)
Formula only	1.00	1.00	1.00	1.00

Data are OR (95% CI). *Estimates are from logistic regression models with general estimating equation estimation adjusting for clustered, nonindependent observations among siblings. †P value for interaction between infant feeding type and maternal diabetes/weight status was 0.20. ‡Adjusted for mother's BMI and prepregnancy smoking behavior, child's race, birth weight, gestational age, birth order, weekly hours of television and physical activity, and daily energy intake and household income. P value for interaction between infant feeding type and maternal diabetes/weight status was 0.50.

and diabetes status would result in subgroups of mothers, within which health habits may be more similar. Furthermore, a dose-dependent association of breastfeeding duration has been confirmed by meta-analysis, and it seems unlikely that

dose-dependent residual confounding would occur across multiple studies. A recent analysis of GUTS data (11) showed that the estimated impact of breastfeeding duration on childhood overweight was nearly identical within

sibships compared with the estimated association overall (not within families), thus indicating that residual confounding related to family health habits was an unlikely explanation for beneficial association of breast-feeding on childhood

Table 3—Association of breast-feeding duration with subject overweight status according to maternal diabetes and weight status*

Breast-feeding duration	Maternal diabetes/weight status			
	Nondiabetes, BMI <25 kg/m ²	Nondiabetes, BMI ≥25 kg/m ²	Diabetes	All
Overweight vs. normal weight, adjusted for age, sex, and Tanner stage (n = 13,163)†				
>9 months	0.70 (0.47–1.04)	0.76 (0.58–1.00)	0.30 (0.10–0.89)	0.63 (0.50–0.78)
7–9 months	0.84 (0.54–1.31)	0.88 (0.65–1.19)	0.69 (0.22–2.14)	0.78 (0.61–0.99)
4–6 months	0.84 (0.55–1.28)	0.88 (0.66–1.16)	0.39 (0.12–1.31)	0.78 (0.62–0.97)
1–3 months	0.86 (0.55–1.35)	1.12 (0.83–1.50)	0.85 (0.28–2.54)	0.97 (0.77–1.22)
<1 month	0.96 (0.53–1.76)	1.59 (1.11–2.26)	1.65 (0.48–5.71)	1.36 (1.02–1.82)
Never breast-fed	1.00	1.00	1.00	1.00
Overweight vs. normal weight, adjusted for age, sex, Tanner stage, and maternal and child characteristics (n = 12,281)‡				
>9 months	0.84 (0.54–1.31)	0.84 (0.63–1.13)	0.37 (0.13–1.04)	0.79 (0.62–1.00)
7–9 months	0.99 (0.62–1.58)	0.96 (0.69–1.33)	1.01 (0.28–3.66)	0.95 (0.73–1.24)
4–6 months	0.96 (0.61–1.51)	0.91 (0.67–1.22)	0.29 (0.07–1.14)	0.88 (0.68–1.12)
1–3 months	0.96 (0.59–1.55)	1.04 (0.76–1.42)	0.98 (0.30–3.20)	0.99 (0.77–1.28)
<1 month	0.92 (0.48–1.77)	1.46 (1.01–2.13)	1.11 (0.22–5.60)	1.22 (0.89–1.68)
Never breast-fed	1.00	1.00	1.00	1.00

Data are OR (95% CI). *Estimates are from logistic regression models with general estimating equation estimation adjusting for clustered, nonindependent observations among siblings. †P value for interaction between breast-feeding duration and maternal diabetes/weight status was 0.63. ‡Adjusted for mother's BMI and prepregnancy smoking behavior, child's race, birth weight, gestational age, birth order, weekly hours of television and physical activity, and daily energy intake and household income. P value for interaction between breast-feeding duration and maternal diabetes/weight status was 0.66.

overweight. We note that the final models show that adjustment for multiple potential confounders did attenuate findings. However, one could argue that adjustment for current diet- and physical activity-related variables is an overadjustment because energy balance is ultimately determined by calorie balance, regardless of other important characteristics. Establishing healthful habits early in life may be a valid explanation for at least part of the beneficial impact of breast-feeding on later health outcomes. Prospectively collected data suggest that familial health habits may explain beneficial effects of breast-feeding beyond infancy reported by studies that relied on retrospectively collected data (35). Finally, the prevalence of being “at risk for overweight” in the present cohort of offspring of participants in the Nurses’ Health Study II (13.4%) was similar to that of U.S. youth from a similar time (14%) (27), although the prevalence of “overweight” was somewhat lower (6.7 vs. 11% for the present cohort vs. the national sample, respectively). This difference in prevalence of overweight might be due to study respondents being more likely to engage in healthful behaviors compared with non-responders. Such differences would not be expected to compromise the internal validity of analyses conducted and presented herein.

In conclusion, our findings provide reasonable assurance that for offspring of diabetic mothers, adverse effects on weight status by adolescence are unlikely and further support the recommendation by the American Academy of Pediatrics to encourage breast-feeding through the 1st year of life (36). It is possible that the beneficial effects of breast-feeding may contribute to breaking the cycle of overweight and diabetes, which may occur among offspring of diabetic mothers.

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References

- Owen CG, Martin RM, Whincup PH, Smith GD, Cook DG: Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. *Pediatrics* 115:1367–1377, 2005
- Arenz S, Ruckerl R, Koletzko B, von KR: Breast-feeding and childhood obesity: a systematic review. *Int J Obes Relat Metab Disord* 28:1247–1256, 2004
- Harder T, Bergmann R, Kallischnigg G, Plagemann A: Duration of breastfeeding and risk of overweight: a meta-analysis. *Am J Epidemiol* 162:397–403, 2005
- Birch LL, Fisher JO: Development of eating behaviors among children and adolescents. *Pediatrics* 101:539–549, 1998
- Tavera EM, Scanlon KS, Birch L, Rifas-Shiman SL, Rich-Edwards JW, Gillman MW: Association of breastfeeding with maternal control of infant feeding at age 1 year. *Pediatrics* 114:e577–e583, 2004
- Picciano MF: Nutrient composition of human milk. *Pediatr Clin North Am* 48:53–67, 2001
- Lucas A, Boyes S, Bloom SR, Aynsley-Green A: Metabolic and endocrine responses to a milk feed in six-day-old term infants: differences between breast and cow’s milk formula feeding. *Acta Paediatr Scand* 70:195–200, 1981
- Heine WE: The significance of tryptophan in infant nutrition. *Adv Exp Med Biol* 467:705–710, 1999
- Savino F, Nanni GE, Maccario S, Costamagna M, Oggero R, Silvestro L: Breast-fed infants have higher leptin values than formula-fed infants in the first four months of life. *J Pediatr Endocrinol Metab* 17:1527–1532, 2004
- Nelson MC, Gordon-Larsen P, Adair LS: Are adolescents who were breast-fed less likely to be overweight? Analyses of sibling pairs to reduce confounding. *Epidemiology* 16:247–253, 2005
- Gillman MW, Rifas-Shiman SL, Berkey CS, Frazier AL, Rockett HR, Camargo CA Jr, Field AE, Colditz GA: Breast-feeding and overweight in adolescence. *Epidemiology* 17:112–114, 2006
- Plagemann A, Harder T, Franke K, Kohlhoff R: Long-term impact of neonatal breast-feeding on body weight and glucose tolerance in children of diabetic mothers. *Diabetes Care* 25:16–22, 2002
- Rodekamp E, Harder T, Kohlhoff R, Franke K, Dudenhausen JW, Plagemann A: Long-term impact of breast-feeding on body weight and glucose tolerance in children of diabetic mothers: role of the late neonatal period and early infancy. *Diabetes Care* 28:1457–1462, 2005
- Pettitt DJ, Knowler WC: Long-term effects of the intrauterine environment, birth weight, and breast-feeding in Pima Indians. *Diabetes Care* 21 (Suppl. 2):B138–B141, 1998
- Kerssen A, Evers IM, de Valk HW, Visser GH: Effect of breast milk of diabetic mothers on bodyweight of the offspring in the first year of life. *Eur J Clin Nutr* 58:1429–1431, 2004
- Li C, Kaur H, Choi WS, Huang TT, Lee RE, Ahluwalia JS: Additive interactions of maternal prepregnancy BMI and breast-feeding on childhood overweight. *Obes Res* 13:362–371, 2005
- Baker JL, Michaelsen KF, Rasmussen KM, Sorensen TI: Maternal prepregnant body mass index, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain. *Am J Clin Nutr* 80:1579–1588, 2004
- Jovanovic-Peterson L, Fuhrmann K, Hedden K, Walker L, Peterson CM: Maternal milk and plasma glucose and insulin levels: studies in normal and diabetic subjects. *J Am Coll Nutr* 8:125–131, 1989
- van Beusekom CM, Zeegers TA, Martini IA, Velvis HJ, Visser GH, van Doormaal JJ, Muskiet FA: Milk of patients with tightly controlled insulin-dependent diabetes mellitus has normal macronutrient and fatty acid composition. *Am J Clin Nutr* 57:938–943, 1993
- Gillman MW, Rifas-Shiman SL, Camargo CA Jr, Berkey CS, Frazier AL, Rockett HR, Field AE, Colditz GA: Risk of overweight among adolescents who were breastfed as infants. *JAMA* 285:2461–2467, 2001
- Rich-Edwards JW, Goldman MB, Willett WC, Hunter DJ, Stampfer MJ, Colditz GA, Manson JE: Adolescent body mass index and infertility caused by ovulatory disorder. *Am J Obstet Gynecol* 171:171–177, 1994
- Morris N, Udry J: Validation of a self-administered instrument to assess stage of adolescent development. *J Youth and Adol* 9:271–280, 1980
- Troy LM, Hunter DJ, Manson JE, Colditz GA, Stampfer MJ, Willett WC: The validity of recalled weight among younger women. *Int J Obes Relat Metab Disord* 19:570–572, 1995
- Manson JE, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Krolewski AS, Rosner B, Hennekens CH, Speizer FE: Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 338:774–778, 1991
- Solomon CG, Willett WC, Rich-Edwards J, Hunter DJ, Stampfer MJ, Colditz GA, Manson JE: Variability in diagnostic evaluation and criteria for gestational diabetes. *Diabetes Care* 19:12–16, 1996
- Liang KY, Zeger SL: Longitudinal data analysis using generalized linear models. *Biometrika* 73:13–22, 1986
- Troiano RP, Flegal KM: Overweight children and adolescents: description, epidemiology, and demographics. *Pediatrics* 101:497–504, 1998
- Berkey CS, Rockett HR, Field AE, Gillman MW, Frazier AL, Camargo CA Jr, Colditz GA: Activity, dietary intake, and weight changes in a longitudinal study of preadolescent and adolescent boys and girls. *Pediatrics* 105:1–9, 2000
- Pettitt DJ, Baird HR, Aleck KA, Bennett PH, Knowler WC: Excessive obesity in offspring of Pima Indian women with diabetes during pregnancy. *N Engl J Med* 308:242–245, 1983

30. Gillman MW, Rifas-Shiman S, Berkey CS, Field AE, Colditz GA: Maternal gestational diabetes, birth weight, and adolescent obesity. *Pediatrics* 111:e221–e226, 2003
31. Stettler N, Bovet P, Shamlaye H, Zemel BS, Stallings VA, Paccaud F: Prevalence and risk factors for overweight and obesity in children from Seychelles, a country in rapid transition: the importance of early growth. *Int J Obes Relat Metab Disord* 26:214–219, 2002
32. Kramer MS, Guo T, Platt RW, Shapiro S, Collet JP, Chalmers B, Hodnett E, Sevkovskaya Z, Dzikovich I, Vanilovich I: Breastfeeding and infant growth: biology or bias? *Pediatrics* 110:343–347, 2002
33. Stettler N, Kumanyika SK, Katz SH, Zemel BS, Stallings VA: Rapid weight gain during infancy and obesity in young adulthood in a cohort of African Americans. *Am J Clin Nutr* 77:1374–1378, 2003
34. Stettler N, Stallings VA, Troxel AB, Zhao J, Schinnar R, Nelson SE, Ziegler EE, Strom BL: Weight gain in the first week of life and overweight in adulthood: a cohort study of European American subjects fed infant formula. *Circulation* 111:1897–1903, 2005
35. Burke V, Beilin LJ, Simmer K, Oddy WH, Blake KV, Doherty D, Kendall GE, Newnham JP, Landau LI, Stanley FJ: Breastfeeding and overweight: longitudinal analysis in an Australian birth cohort. *J Pediatr* 147:56–61, 2005
36. Gartner LM, Morton J, Lawrence RA, Naylor AJ, O'Hare D, Schanler RJ, Eidelman AI: Breastfeeding and the use of human milk. *Pediatrics* 115:496–506, 2005