

Are Adolescents Who Were Breast-fed Less Likely to Be Overweight?

Analyses of Sibling Pairs to Reduce Confounding

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Background: Cohort analyses suggesting that breast-feeding protects against being overweight have been criticized for inadequately controlling for confounding associated with the self-selection of feeding practices.

Methods: Using nationally representative U.S. data from the National Longitudinal Study of Adolescent Health (1994–1996), we performed traditional cohort analyses ($n = 11,998$) using logistic regression to estimate the relation between breast-feeding and adolescent overweight (body mass index ≥ 85 percentile, based on year 2000 CDC growth charts), controlling for known potential confounders. Breast-feeding also was assessed in a subsample of 850 sibling pairs to account for unmeasured genetic and environmental factors.

Results: Among girls in the full cohort, the odds of being overweight declined among those who had been breast-fed at least 9 months; odds ratios ranged from 0.90 (95% confidence interval = 0.74–1.09) for <3 months of breast-feeding to 0.78 (0.64–0.96) for ≥ 9 months. A similar effect was seen in boys, although these trends were less consistent. In contrast, an analysis of sibling pairs provided no evidence of breast-feeding effects on weight within discordant trends.

Conclusion: Cohort data indicate that odds of being overweight decrease as breast-feeding duration increases, at least among girls. However, sibling analyses suggest that this relationship may not be causal but rather attributable to unmeasured confounding related to mothers' choice to breast-feed, or to other childhood risk factors for overweight. Our results illustrate the utility of sibling analyses in understanding the true effect of early life exposures (such as breast-feeding) on health outcomes over time, independent of confounding

factors that may not be satisfactorily controlled using traditional prospective cohort methods.

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Causes of the obesity epidemic in the United States^{1,2} are not fully understood. Cohort analyses suggest that breast-feeding may reduce the risk of obesity in childhood and adolescence,^{3–9} with evidence of a dose-dependent relationship.^{9,10} Several biologic mechanisms support this observation, including metabolic responses to bioactive substances unique to breast milk, the effect of nutrient composition on insulin responses, and alterations in regulation of feeding.^{8,11–13}

Inconsistencies and null findings,^{8,9,14–18} however, have fueled controversy in this area. Cohort studies have been criticized for inadequate control of confounding factors associated with the decision to initiate and/or continue breast-feeding,⁸ such as maternal care-giving, mother-child interactions or other health-related behaviors. These factors are difficult to measure in large cohorts, and they also affect obesity risk, leading to possible erroneous attribution of risk reduction to breast-feeding rather than other protective behaviors.

Other factors commonly measured in cohort studies (eg, parental education) may be only theoretically important confounders of the breast-feeding-overweight relationship. In numerous studies reporting both crude and adjusted models, inclusion of these potential confounders produced little change in effect estimates^{4,5,7,10,15,17,18} and yielded no increase in precision.^{5,7,10,15,17} Although the underlying factors that these variables are intended to approximate may be important confounders, typically only crude proxies have been measured in large cohort studies. Previous analyses have devoted scant attention to understanding the actual confounding effects of these covariates once included in adjusted etiologic models.

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We used matched full-sibling adolescent pairs to reduce the influence of poorly measured or unmeasured confounding. This analytic strategy helps to address early-life effects on health^{19–23} by providing additional household- and maternal-level controls. Using one sibling as a control for another accounts for multiple shared environmental and genetic sources of variation that are not assessed in traditional cohort designs, and allows a more accurate description of the causal breast-feeding–weight relationship.

Our objectives were to determine whether breast-feeding exposure and duration are protective against adolescent overweight using traditional cohort analyses in a large, nationally representative sample with measured weight and height, and then to explore how this effect varies within matched full-sibling pairs that have been fed differently (compared with those fed similarly). We hypothesized that if breast-feeding protects against being overweight, a breast-fed child is less likely to become overweight compared with a sibling who was not breast-fed. However, sibling pairs fed similarly should have similar risks of being overweight. Therefore, the between-sibling difference in obesity risk should be greater among sibling pairs fed differently compared with those fed similarly.

METHODS

National Longitudinal Study of Adolescent Health

The National Longitudinal Study of Adolescent Health cohort is a nationally representative school-based study of youths (grades 7–12), augmented with selected subsamples (eg, sibling pairs). Survey procedures have been described elsewhere²⁴ and were approved by the Institutional Review Board of the University of North Carolina at Chapel Hill. Wave I of the in-home survey (1994–1995) included 20,745 adolescents and their parents. Wave II (1996) included 14,738 wave I adolescents. Only school-aged adolescents (including dropouts) were followed in wave II; adolescents who had graduated were not followed.

This analysis excluded participants who were severely disabled ($n = 84$), pregnant ($n = 214$; because of the likelihood of weight misclassification), Native Americans ($n = 125$; because of small sample size), or missing data on breast-feeding ($n = 2259$) or weight or height ($n = 220$) data. The sample for the cohort analyses totaled 11,998. Comparing the participants included in our analysis with those who were not, there were differences by ethnicity (57% vs. 37% white; 21% vs. 26% black; 17% vs. 19% Hispanic; 5% vs. 13% Asian) and parental education (15% vs. 18% parents with less than a high school education; 26% vs. 30% parents with a college degree or higher), but not by maternal obesity (18% vs. 20% obese mothers).

The outcome measure of being overweight was based on measured height and weight from wave II and defined according to recommendations by expert panels.^{25,26} “At risk for overweight” is defined as a body mass index (BMI) ≥ 85 th and < 95 th percentile of age- and sex-specific National Center for Health Statistics/Centers for Disease Control and Prevention 2000 reference curves,²⁷ and “overweight” as BMI ≥ 95 th percentile. These 2 outcomes have been combined according to convention (and hereafter referred to as “overweight” for simplicity) as a BMI ≥ 85 th percentile. Individuals who were older than 20 years of age ($n = 11$) were considered 20 years of age for the purposes of overweight status assessment. Information on whether the adolescent had been breast-fed was obtained from in-home wave I parental interviews. Breast-feeding refers to any breast-feeding, with or without complementary feeding; this exposure variable was categorized as never breast-fed, or breast-fed: < 3 , 3–5.99, 6–8.99, 9–11.99, 12–23.99, or ≥ 24 months. Covariates were measured by traditional survey methods and included parental self-reported maternal obesity status (yes/no); parental education, household income and ethnicity (by parental and adolescent report); and current smoking habits (smoker vs. nonsmoker); and pubertal status (early, average, or late maturer)²⁸ by adolescent self-report. Low birthweight (LBW) status was defined as less than 2500 g; information was derived from parental report of adolescents’ birthweight.

Full Cohort Analyses

Statistical analyses were conducted using STATA (Release 7.0, Stata Corp, College Station, TX). Poststratification sample weights used in descriptive analyses allow these results to be nationally representative. Survey design effects of multiple stages of cluster sampling were controlled using SVY commands.

Logistic regression was used to estimate the effect of breast-feeding on adolescent overweight. We collapsed categories of breast-feeding duration because of small sample sizes at the longest durations. We conducted crude stratified analyses to examine potential effect measure modification, and we identified confounding using causal diagrams.²⁹ We fit a parsimonious logistic regression by specifying a model with potential effect measure modification and confounding variables.^{30,31} First, we removed potential effect measure modifiers from the model if there was apparent homogeneity across strata. Remaining effect measure modification terms were then reduced using likelihood ratio tests, with $\alpha = 0.10$ to limit the likelihood of erroneously eliminating important variables. Lastly, potential confounders were removed from the model if their inclusion did not satisfy an a priori change-in-estimate criterion (a change in the odds ratio [OR] of $\geq 10\%$). Of all covariates evaluated, only the ethnicity and income variables resulted in changes in the OR that met our a priori criteria for inclusion in the final model. Gender was

identified as an important effect measure modifier, and therefore all models were stratified by gender. Logistic regressions predicting likelihood of overweight were repeated in the sibling sample to test whether a protective effect of breast-feeding was present, without accounting for sibship.

Sibling Pair Subsample and Analyses

To expand the findings of traditional cohort analyses, we selected a subsample of subjects matched with a full-sibling adolescent to control for shared genetic and environmental characteristics.³² Our analyses consisted of all full-sibling, nontwin pairs ($n = 850$) identified in the full cohort, with complete height, weight, and breast-feeding data for both siblings. SVY commands were used to control for household clustering. Statistical power for the multinomial logistic regression was assessed using nQuery Advisor (Release 5.0, Statistical Solutions; Saugus, MA). Our analytic design accounts for sibling pairs and tests whether differences in feeding practices influence weight outcomes of 2 siblings with shared environmental exposures and genetic background. If breast-feeding protects against overweight, we would expect differences in feeding practices to yield differences in weight status. This hypothesis was tested using continuous and categorical outcomes representing weight.

Sibling pairs were ordered by BMI-for-age Z-score, with the heavier sibling identified as sibling 1. Linear regression first was used to predict within-pair Z-score differences from indicator variables of breast-feeding status (ever versus never breast-fed) for concordant and discordant breast-feeding pairs (Eq 1).

$$E(Z \text{ score difference}) = \beta_0 + \beta_1 (\text{Lighter sib BF}) \\ + \beta_2 (\text{Heavier sibling BF}) + \beta_3 (\text{Both sibs BF}) \\ + \beta_4 (\text{covariate}_1) + \dots + \beta_k (\text{covariate}_k) \quad (1)$$

We hypothesized that among pairs that were discordantly fed, the breast-fed sibling would be lighter (ie, have a lower BMI-for-age Z-score) than the nonbreast-fed sibling. Using linear regression to predict BMI-for-age Z-score differences, we expected large, positive differences in Z-scores if the lighter sibling was breast-fed and the heavier sibling was not breast-fed; therefore, if breast-feeding is protective against overweight, we expect the regression coefficient β_1 to be greater than 0. Potential confounders were again identified by causal diagrams, and were evaluated by the a priori change-in-estimate criterion.

Second, a separate analysis used multinomial (polytomous) logistic regression addressing the hypothesis that among discordantly fed sibling pairs, the breast-fed sibling is less likely to become overweight (compared with the nonbreast-fed sibling) and that these differences in risk are greater than those among pairs who have been fed similarly.

These analyses result in ORs comparing several predicted outcomes (ie, the odds of both siblings becoming overweight versus that of only one sibling becoming overweight, and the odds of neither sibling becoming overweight versus that of only one sibling becoming overweight).³³ Dichotomous exposure variables were defined as: the heavier sibling not breast-fed, the lighter sibling breast-fed; the heavier sibling breast-fed, the lighter sibling not breast-fed; both siblings breast-fed; and neither sibling breast-fed (referent).

These modeling strategies included assessment of potential confounders (age, sex, birth order, and LBW status) that differed between siblings. Family characteristics (such as parental education or household income) were not included in the models since these are shared between siblings (which is a strength of this analytic approach). As in previous analyses, sibling pairs are ordered by BMI-for-age Z-score. Thus in the discordant overweight group, sibling 1 is overweight, and sibling 2 is normal weight.

RESULTS

Full Sample Analyses

Characteristics of the nationally representative adolescent cohort are given by breast-feeding duration in Table 1. Half (52%) were never breast-fed, whereas 15% were breast-fed for less than 3 months, and 33% were breast-fed for 3 months or greater, with few differences by sex or maternal obesity. Breast-feeding initiation was lowest in non-Hispanic black children, and highest among children of Asian parents, as well as more highly educated parents. Approximately 25% of girls ($n = 1179$) and 27% of boys ($n = 1172$) had a BMI ≥ 85 th percentile and thus were considered to be overweight. Age of participants ranged from 12 to 21 years. The final cohort analysis sample was 72% non-Hispanic white, 13% non-Hispanic black, 11% Hispanic, and 3% Asian, and evenly distributed by sex.

Table 2 details the results of the logistic regression. In general, ORs declined with increasing duration of breast-feeding. We also assessed breast-feeding as a dichotomous variable. Adjusting for ethnicity, parental education, LBW, maternal obesity, household income, age, puberty and smoking status of adolescent, the odds of being overweight given that the adolescent had ever been breast-fed were 0.83 (95% confidence interval [CI] = 0.72–0.95) among girls and 0.90 (95% CI = 0.76–1.05) among boys. Income was the only potential confounder that produced $\geq 10\%$ change in the OR.

When the sibling subsample was analyzed without accounting for sibship and shared environments, the odds of being overweight among adolescents who were breast-fed was 0.78 (95% CI = 0.63–0.97). The odds of being overweight among those breastfed at least 3 months was 0.69 (95% CI = 0.54–0.87).

TABLE 1. Breast-feeding Duration by Adolescent Weight Status and Background Characteristics, National Longitudinal Study of Adolescent Health, 1994–1996

	No.	Breast-feeding Status; Proportion (Standard Error)*						
		Never	<3 Months	3 to <6 Months	6 to <9 Months	9 to <12 Months	12 to <24 Months	≥24 Months
Total	11,998	0.52 (0.01)	0.15 (0.01)	0.11 (0.01)	0.08 (0.005)	0.07 (0.005)	0.06 (0.01)	0.02 (0.002)
Weight status								
At risk for overweight	3,055	0.56 (0.02)	0.15 (0.01)	0.10 (0.01)	0.07 (0.01)	0.06 (0.01)	0.05 (0.01)	0.02 (0.004)
Normal weight	8,943	0.51 (0.02)	0.15 (0.01)	0.11 (0.01)	0.08 (0.01)	0.07 (0.01)	0.07 (0.01)	0.02 (0.002)
Sex								
Male	5,929	0.53 (0.02)	0.15 (0.01)	0.10 (0.01)	0.08 (0.01)	0.07 (0.01)	0.06 (0.01)	0.01 (0.002)
Female	6,069	0.51 (0.02)	0.15 (0.01)	0.12 (0.01)	0.07 (0.01)	0.06 (0.01)	0.02 (0.01)	0.02 (0.003)
Ethnicity								
White	6,858	0.49 (0.02)	0.16 (0.01)	0.11 (0.01)	0.08 (0.01)	0.07 (0.01)	0.06 (0.01)	0.02 (0.002)
Black	2,491	0.78 (0.02)	0.08 (0.01)	0.06 (0.01)	0.02 (0.004)	0.02 (0.005)	0.03 (0.01)	0.00 (0.002)
Hispanic	1,979	0.46 (0.02)	0.19 (0.01)	0.12 (0.02)	0.08 (0.01)	0.06 (0.01)	0.07 (0.01)	0.02 (0.01)
Asian	624	0.29 (0.03)	0.16 (0.03)	0.16 (0.02)	0.14 (0.03)	0.10 (0.02)	0.14 (0.03)	0.02 (0.01)
Parental education [†]								
Not high school graduate	1,846	0.67 (0.03)	0.11 (0.01)	0.07 (0.01)	0.04 (0.01)	0.03 (0.01)	0.05 (0.01)	0.02 (0.01)
High school graduate	3,551	0.64 (0.02)	0.14 (0.01)	0.08 (0.01)	0.05 (0.01)	0.05 (0.01)	0.04 (0.01)	0.01 (0.002)
Some college	3,439	0.48 (0.02)	0.17 (0.01)	0.13 (0.01)	0.08 (0.01)	0.07 (0.01)	0.06 (0.01)	0.01 (0.003)
College graduate	3,118	0.34 (0.02)	0.15 (0.01)	0.14 (0.01)	0.12 (0.01)	0.10 (0.01)	0.11 (0.01)	0.03 (0.01)
Maternal obesity								
Not obese	9,665	0.52 (0.02)	0.15 (0.01)	0.11 (0.01)	0.08 (0.01)	0.07 (0.01)	0.07 (0.01)	0.02 (0.002)
Obese	2,116	0.52 (0.02)	0.17 (0.01)	0.11 (0.01)	0.07 (0.01)	0.06 (0.01)	0.05 (0.01)	0.01 (0.004)

*Percentages are weighted to be nationally representative.

[†]Parental education was defined as the highest level of education achieved for either parent.**TABLE 2.** Results of Logistic Regression Analysis Predicting Adolescent Overweight (≥85th Percentile BMI-For-Age) By Breast-feeding Exposure, Stratified by Sex

Breast-feeding Duration	Boys		Girls	
	Unadjusted Model Odds Ratio (95% CI)	Reduced* Model Odds Ratio (95% CI)	Unadjusted Model Odds Ratio (95% CI)	Reduced* Model Odds Ratio (95% CI)
None [†]	1.00	1.00	1.00	1.00
<3 months	1.03 (0.86–1.22)	1.03 (0.85–1.24)	0.79 (0.66–0.95)	0.90 (0.74–1.09)
≥3 to <6 months	0.80 (0.63–1.03)	0.81 (0.63–1.04)	0.70 (0.55–0.89)	0.82 (0.64–1.05)
≥6 to <9 months	0.83 (0.61–1.11)	0.86 (0.63–1.17)	0.61 (0.45–0.82)	0.73 (0.54–1.00)
≥9 months	0.81 (0.65–1.00)	0.83 (0.67–1.04)	0.63 (0.51–0.78)	0.78 (0.64–0.96)

*Adjusted for ethnicity and income.

[†]Reference group.

Sibling Pair Analyses

In the sibling subsample, both siblings were breast-fed in 46% of pairs (n = 374 pairs), and neither sibling was breast-fed in 41% of pairs (n = 364). Discordant breast-feeding (only one sibling breast-fed) occurred in 13% of

pairs (n = 112). Among the 374 pairs in which both siblings were breast-fed, breast-feeding duration differed in 267 sibling pairs (71%). Sixty-two percent (n = 531) of the sibling subsample were pairs in which neither sibling was overweight, 26% (n = 217) included 1 overweight

sibling, and 12% ($n = 102$) were pairs in which both were overweight.

In the linear regression model predicting BMI-for-age Z-score differences, β_1 was not greater than zero [regression coefficient (standard error): $\beta_1 = -0.004$ (0.11); $\beta_2 = -0.09$ (0.11); $\beta_3 = -0.06$ (0.06)]. Birth order, sibling LBW status, sex and sibling age difference did little to change the regression coefficients.

In a separate model of all sibling pairs, difference in breast-feeding duration between siblings (duration in sibling 1 minus duration in sibling 2) was not a good predictor of the Z-score difference ($\beta_{\text{duration difference}} = 0.01$ (0.01)), with the regression coefficient not in the expected direction. These results were similar among: only those in which both were breast-fed, only those that were discordantly fed (ie, pairs in which both were breast-fed but for different lengths of time, as well as those in which only one sibling was breast-fed), and only those in which both were breast-fed but for different lengths of time.

The results of the multinomial logistic regression model are presented in Table 3. We expect the odds of discordance in overweight to be high among pairs in which only the lighter sibling was breast-fed, indicating that the nonbreast-fed sibling is overweight and the breast-fed sibling is normal weight. ORs among pairs where only the lighter sibling was breast-fed are expected to be >1.0 , whereas ORs among pairs where only the heavier sibling was breast-fed are expected to be <1.0 .

Compared with pairs in which neither sibling was breast-fed and neither was overweight, the odds that the lighter sibling of a discordant pair was breast-fed were 1.22 (95% CI = 0.64–2.32) times higher and the odds that the heavier sibling was breast-fed were 1.27 (95% CI = 0.65–1.25) times higher, suggesting little effect of breast-feeding on weight status. In contrast, when compared with pairs in which both siblings were not breast-fed and both were overweight, the odds that the lighter sibling of a discordant pair

was breast-fed were 0.52 and the odds that the heavier sibling was breast-fed were 2.03, a result opposite to our original hypothesis.

DISCUSSION

These analyses illustrate the difficulties of assessing the influence of breast-feeding on later weight, as well as the potential impact of unmeasured (or poorly measured) confounding in cohort analyses. The use of an alternative study design (ie, matched sibling analyses) helped to address these shortcomings. The findings from our traditional cohort analyses are similar to those previously cited in the literature, suggesting a potentially protective effect of having been breast-fed on overweight status.^{3–8} These results also support findings of a strong effect with increasing duration of breast-feeding,^{9,10} although previous research in this area is not consistent.^{8,13–18} However, in the sibling subsample, discordant breast-feeding of sibling pairs did not predict BMI Z-score differences or discordant overweight status. These alternative results suggest that the effect of breast-feeding on overweight may be weak or absent. This relationship may be induced by confounding because of environmental and genetic factors, reflecting characteristics of mothers or families that choose to breast-feed.

Though the best method to establish a causal effect of breast-feeding on overweight (independent of other factors) is a randomized controlled trial, such trials randomizing breast-feeding are unethical. Alternative data collection and analysis strategies must be explored, such as the present analysis of sibling pairs exposed to differing feeding practices but sharing physical and familial environments. By using matched pairs and thereby controlling for a variety of unmeasured (or poorly measured) confounders, our results indicate the lack of a positive effect of breast-feeding on overweight in this sample. Although the sibling sample size is smaller than traditional epidemiologic cohorts, it is larger than other sibling samples^{19–22} and allowed sufficient power to detect an

TABLE 3. Relative Odds of Discordant Overweight Pairs (in Which One Sibling Is Overweight and One Sibling Is Normal Weight), Compared With the 2 Concordant Outcomes

Breast-feeding Status	Adjusted OR* (95% CI) of Discordant Overweight Pairs	
	Compared With Neither Sibling Overweight [†]	Compared With Both Siblings Overweight [†]
Neither sibling breast-fed [‡]	1.0	1.0
Lighter sibling breast-fed	1.22 (0.64–2.32)	0.52 (0.22–1.24)
Heavier sibling breast-fed	1.27 (0.65–2.50)	2.03 (0.64–6.43)

*Adjusted for age difference between siblings, sex pairs (male/male, male/female, female/male, or female/female), birth order, and birthweight status of the sibling pair (both LBW, neither LBW, only lighter adolescent sibling LBW, only heavier adolescent sibling LBW).

[†]Outcome reference group.

[‡]Exposure reference group.

effect. Similar sibling study designs have been used to evaluate relationships between intrauterine exposure to type II diabetes and risk of adolescent/early adult overweight and diabetes^{19,20}; maternal feeding practices and preadolescent overweight²¹; extreme low birthweight and subsequent cognitive development²²; and infant weight gain and childhood obesity.²² These results provide a unique perspective that adds to the current literature and allows for further hypothesis generation, and to our knowledge, this sibling analysis is the first study of its kind to assess this relationship.

Breast-feeding could be linked to later becoming overweight through numerous underlying processes, many of which are difficult to measure. Although much discussion has focused on possible biologic mechanisms, there has been little research on other influential environmental and behavioral factors that may confound this relationship. A mother's decision to initiate and continue breast-feeding is highly self-selective and nonrandom in nature. Traditionally unmeasured characteristics that may be associated with breast-feeding, such as maternal care-giving, health behavior or physical environment, likely also affect later risk of overweight.

Covariates measured in large cohort studies may not adequately capture the underlying factors that affect the breast-feeding–overweight relationship, thereby limiting the ability to statistically control for confounding. The analyses presented here, as well as previous analyses,^{4,5,7,10,15,17,18} demonstrate that many of these potential confounders result in minimal changes in the point estimate, indicating little or no actual confounding. Such comparisons highlight the shortcomings of traditional efforts to control for confounding, even with use of models adjusted for numerous survey-derived variables.

The sibling-pair study design can reduce important unmeasured confounding by maternal and household influences. Despite the strengths of this approach, however, these results may be limited in generalizability, as sibling pairs who are discordantly breast-fed or discordantly overweight may not be representative of all U.S. adolescents. Simply having another adolescent sibling may be a factor that limits generalizability.

In addition, this study may also be limited by the potential residual confounding related to why a mother chooses to breast-feed one sibling and not another. We attempted to address this possible source of confounding by controlling for sibling LBW status in the models. Other specific factors may confound our results if they influenced a mother to breast-feed one child and not another, and differentially affected risk of overweight later in life. For example, these models may be confounded by neonatal complications in the birth of one of the siblings if the effect of these complications had a reduction in later odds of adolescent overweight (and was not reflected in birthweight status).

These types of confounders are not specific to sibling analyses but rather are problematic in all observational epidemiologic methods, including traditional cohort analyses. Some previous studies have controlled for preterm birth^{3,10} or gestational age,¹⁸ or have excluded for abnormalities during birth,^{4,6} but much of the existing literature has not taken these issues into account.^{5,7,14,15,17} Our data may also be limited by parent-recalled breast-feeding status. Although these types of recalled measures are reasonable reproducible^{3,34} and valid,³⁵ they may be less accurate than data collected prospectively.

The protective effect of breast-feeding on later overweight status has been accepted in various clinical settings, as evidenced by its inclusion in a recent policy statement by the American Academy of Pediatrics on the prevention of pediatric overweight and obesity.³⁶ Given the numerous benefits of breast-feeding,³⁷ nearly all mothers should be advised to breast-feed, and initiatives to increase breast-feeding should be actively pursued. However, the etiology of obesity is multidimensional, and our findings suggest that any potential effect of breast-feeding may be outweighed by the influences of other household characteristics.

In a broader context, our findings suggest the need to find alternative means of testing exposures that cannot be manipulated (eg, breast-feeding), and to explore other methods of observational study design to lend strength to observed associations and enhance evidenced-based health beliefs, practices and recommendations. In addition to traditional cohort analyses, other approaches such as the sibling analyses presented here should continue to be vigorously explored to tease apart the underlying determinants of health and disease across the life-course and address the issue of unmeasured confounding related to a variety of influences related to the biologic, social, cultural and/or physical environment.

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REFERENCES

1. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. *JAMA*. 2002;288:1723–1727.
2. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999–2000. *JAMA*. 2002;288:1728–1732.
3. Leise AD, Hirsch T, von Mutius E, Keil U, Leupold W, Weiland SK. Inverse association of overweight and breast feeding in 9 to 10-y-old children in Germany. *Int J Obes*. 2001;25:1644–1650.
4. Gillman MW, Rifas-Shiman SL, Camargo CA, et al. Risk of overweight among adolescents who were breastfed as infants. *JAMA*. 2001;285:2461–1467.
5. Armstrong J, Reilly JJ, Child Health Information Team. Breastfeeding and lowering the risk of childhood obesity. *Lancet*. 2002;359:2003–2004.
6. Bergmann KE, Bergmann RL, von Kries R, et al. Early determinants of childhood overweight and adiposity in a birth cohort study: role of breast-feeding. *Int J Obes*. 2003;27:162–172.
7. Toschke AM, Vignerova J, Lhotska L, Osancova K, Koletzko B,

- Von Kries R. Overweight and obesity in 6- to 14- year-old Czech children in 1991: Protective effect of breast-feeding. *J Pediatr*. 2002; 141:764–769.
8. Dewey KG. Is breastfeeding protective against child obesity? *J Hum Lact*. 2003;19:9–18.
 9. Grummer-Strawn LM, Mei Z. Does breastfeeding protect against pediatric overweight? Analysis of longitudinal data from the Centers for Disease Control and Prevention Pediatric Nutrition Surveillance System. *Pediatrics*. 2004;113:81–86.
 10. von Kries R, Koletzko B, Sauerwald T, et al. Breast feeding and obesity: cross sectional study. *BMJ*. 1999;319:147–150.
 11. Hamosh M. Does infant nutrition affect adiposity and cholesterol levels in the adult. *J Pediatr Gastroenterol Nutr*. 1988;7:10.
 12. Locke R. Preventing obesity: the breast milk-leptin connection. *Acta Paediatr*. 2002;91:891–896.
 13. Savino F, Costamagna M, Prino A, Oggero R, Silvestro L. Leptin levels in breast-fed and formula-fed infants. *Acta Paediatr*. 2002;91:897–902.
 14. Hediger ML, Overpeck MD, Ruan WJ, Troendle JF. Early infant feeding and growth status of US-born infants and children, ages 4–71 mo. *Am J Clin Nutr*. 2000;72:159–167.
 15. Hediger ML, Overpeck MD, Kuczmariski RJ, Ruan WJ. Association between infant breastfeeding and overweight in young children. *JAMA*. 2001;285:2453–2460.
 16. Butte NF, Wong WW, Hopkinson JM, Smith EO, Ellis KJ. Infant feeding mode affects early growth and body composition. *Pediatrics*. 2000;106:1355–1366.
 17. Li L, Parsons TJ, Power C. Breast feeding and obesity in childhood. *BMJ*. 2003;327:904–905.
 18. Victora CG, Barros FC, Lima RC, et al. Anthropometry and body composition of 18 year old men according to duration of breast feeding. *BMJ*. 2003;327.
 19. Dabelea D, Hanson RL, Lindsay RS, et al. Intrauterine exposure to diabetes conveys risk for type 2 diabetes and obesity: a study of discordant sibships. *Diabetes*. 2000;49:2208–2211.
 20. Dabelea D, Pettitt DJ. Intrauterine diabetic environment confers risks for type 2 diabetes mellitus and obesity in the offspring, in addition to genetic susceptibility. *J Pediatr Endocrinol Metab*. 2001;14:1085–1091.
 21. Saelens BE, Ernst MM, Epstein LH. Maternal child feeding practices and obesity: a discordant sibling analysis. *Int J Eat Disord*. 2000;27: 459–463.
 22. Kilbride HW, Thorstad K, Daily DK. Preschool outcome of less than 801-gram preterm infants compared with full-term siblings. *Pediatrics*. 2004;113:742–47.
 23. Stettler N, Faith MS. A sibling analysis of the association between early infancy weight gain and childhood obesity [abstract]. *Circulation*. 2004; 109:291.
 24. Popkin BM, Udry JR. Adolescent obesity increases significantly in second and third generation US immigrants. *J Nutr*. 1998;128:701–706.
 25. Himes JH, Dietz WH. Guidelines for overweight in adolescent preventive services: Recommendations from an expert committee. The Expert Committee on Clinical Guidelines for Overweight in Adolescent Preventive Services. *Am J Clin Nutr*. 1994;59:307–316.
 26. WHO Expert Committee. Physical Status: The Use and Interpretation of Anthropometry. WHO Technical Report Series 854. Geneva, Switzerland: World Health Organization; 1995.
 27. Kuczmariski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC Growth Charts: United States. Advance Data From Vital and Health Statistics; no 314. Hyattsville, MD: National Center for Health Statistics; 2000.
 28. Adair LS, Gordon-Larsen P. Maturational timing and overweight prevalence in US adolescent girls. *Am J Public Health*. 2001;91:642–4.
 29. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology*. 1999;10:37–48.
 30. Kleinbaum DG, Klein M. *Logistic Regression*. 2nd ed. New York: Springer; 2002.
 31. Greenland S. Modeling and variable selection in epidemiologic analysis. *Am J Public Health*. 1989;79:340–9.
 32. Nelson MC, Gordon-Larsen P, Adair LS. The protective effect of breast-feeding on adolescent overweight disappears with use of sibling controls (abstract). *FASEB J*. 2003;17(5 Part 2 Suppl):A1089.
 33. Rothman KJ, Greenland S. *Modern Epidemiology*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1998.
 34. Tomeo CA, Rich-Edwards JW, Michels KB, et al. Reproducibility and validity of maternal recall of pregnancy-related events. *Epidemiology*. 1999;10:774–777.
 35. Troy LM, Michels KB, Hunter DJ, et al. Self-reported birthweight and history of having been breastfed among young women: an assessment of validity. *Int J Epidemiol*. 1996;25:122–127.
 36. American Academy of Pediatrics, Committee on Nutrition. Prevention of pediatric overweight and obesity. *Pediatrics*. 2003;112:424–430.
 37. American Academy of Pediatrics, Work Group on Breastfeeding. Breastfeeding and the Use of Human Milk. *Pediatrics*. 1997;100:1035–1039.