Risk of Overweight Among Adolescents Who Were Breastfed as Infants

Matthew W. Gillman, MD, SM
Sheryl L. Rifas-Shiman, MPH
Carlos A. Camargo, Jr, MD, DrPH
Catherine S. Berkey, ScD
A. Lindsay Frazier, MD, MPH
Helaine R. H. Rockett, MS, RD
Alison E. Field, ScD
Graham A. Colditz, MD, DrPH

ATES OF OVERWEIGHT AMONG children, adolescents, and adults in the United States and other developed countries have been rising markedly over the past 4 decades.1,2 While obesity at any age during childhood predicts obesity in adult life, the predictive value of obesity in adolescence is higher than in earlier childhood.3 Adolescent obesity is associated with cardiovascular risk factors,4 orthopedic conditions,5 lower self-esteem,6 and adverse social and economic outcomes in young adulthood.7 Childhood and adolescent obesity also predicts morbidity and mortality decades later.8,9 Once present, overweight is hard to treat. For these reasons, prevention is paramount.

Both physiological and behavioral mechanisms raise the possibility that breastfeeding during infancy could reduce the risk of overweight in later childhood and adolescence.10-13 Some epidemiologic studies suggest a protective effect in the first 6 years of life, but few reliable data exist for older ages. During the second year of life, for example, children who had been breastfed for at least 12 months have lower weight-for-height values than those breastfed for shorter durations.14 In a recent study among German school children at age 5 to 6 years, duration of breastfeeding was inversely associated with obesity and overweight.15 In 2 linked case-control investigations of Canadian 12- to 18-year-olds, Kramer16 reported inverse relationships between obesity and having been breastfed and, to a lesser extent, breast-

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feeding duration. However, that study was published 2 decades ago, when breastfeeding rates were lower and diet and physical activity patterns were different. Although data on several confounding factors existed, Kramer did not use multivariate techniques to control for them simultaneously. Results of other more recent studies have been variable, perhaps owing to substantial limitations, including lack of data on length of breastfeeding or on important confounders, inadequate sample sizes, and end points measured at relatively young ages.16-21

The purpose of this study was to investigate relationships of type and duration of infant feeding with the prevalence of overweight in older children and adolescents.

METHODS

Subjects

The subjects in the Growing Up Today Study are sons and daughters of subjects in the ongoing Nurses' Health Study II, a cohort study of over 116000 female registered nurses.22 From Nurses' Health Study II study records, we identified 40968 subjects who had at least 1 child aged 9 to 14 years in 1996. We contacted the 34 174 of those who promptly responded to the most recent Nurses' Health Study II questionnaire, 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. Approximately 68% of the girls (n=9039) and 58% of the boys (n=7843) 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 16 448 (97%) of the mothers completed this questionnaire. Human subjects committees at

the Harvard School of Public Health and Brigham and Women's Hospital, Boston, Mass, approved the study.

For this analysis, we excluded 343 participants outside the age range 9 to 14 years on the baseline questionnaire in 1996, 417 whose mothers did not respond to the supplemental 1997 questionnaire, 476 who had missing or outlying values for height or weight on the baseline questionnaire, 146 whose mothers reported a gestation of less than 34 completed weeks, and 159 with childhood medical conditions that might have interfered with growth. These conditions were diabetes mellitus (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 48 other selected infectious, endocrine, metabolic, neurologic, renal, respiratory (not asthma), and orthopedic conditions, and congenital anomalies (n=48). Thus we based the analyses on 15341 participants: 8186 girls and 7155 boys.

Measurements

We ascertained all information except household income from mailed self-report questionnaires. Among other variables, each Growing Up Today Study participant reported age, sex, race/ethnicity, height, weight, pubic hair sexual maturity (Tanner stage) rating using validated pictograms, 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 estimates of the 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 infant 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, formula only; and (2) duration of breastfeeding in the categories 0, less than 1 month, 1 to 3 months, 4 to 6 months, 7 to 9 months, and greater than 9 months. We also asked about the timing (in months) of introduction of solid foods, cow's milk, and infant formula, including type of formula.

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 questionnaire about the mother's smoking habits during the early life of the child. From the 1995 Nurses' Health Study II questionnaire, we ascertained mothers' other lifestyle habits that may relate to children's growth, including dietary restraint, history of weight cycling, diet, and physical activity.22

To obtain estimates of household income, we mapped each subject's address to a census tract. We used US Census data from 1990 to assign the median household income for that census tract to the individual subject.

Validity of Exposure and Outcome Assessments

Maternal recall of breastfeeding provided the main exposure variables for this study. Several articles have addressed the validity of maternal recall of their children's infant feeding habits. Vobecky et al23 compared maternal recall 8 to 9 years after birth with prospectively collected information from a longitudinal study in infancy. The correlation coefficient for duration of breastfeeding was 0.95. In a study of maternal recall 20 years after birth, Kark et al24 estimated a correlation coefficient of 0.86 between recalled duration of breastfeeding and infant clinical records. With regard to reproducibility, correlation coefficients for breastfeeding duration were 0.91 for maternal report 4 months apart among Malaysian women 15 to 50 years after birth25 and 0.86 for maternal report 2 years apart among participants.
in the Nurses’ Health Study a mean of 53 years after birth.20 These and other studies indicate that maternal recall of breastfeeding duration has sufficient reliability and validity to be used in epidemiologic studies. In our study, the mothers are all registered nurses, thus providing confidence in the accuracy of their reports.

We used the adolescents’ self-report of height and weight to determine our study outcomes. While self-reports of these measures are known to be valid in adults, recent data also suggest high validity among children and adolescents. In samples ranging in age from 11 to 16 years, Shannon et al27 and Strauss28 report correlation coefficients in the range 0.84 to 0.94 for self-reported vs actual weight and 0.62 to 0.91 for height. In a more recent study, Goodman et al29 estimated a correlation of 0.92 between body mass index (BMI: weight in kilograms divided by the square of height in meters [kg/m2]) calculated from self-report vs measured height and weight among participants in the National Longitudinal Study of Adolescent Health. Despite the tendency for heavier children to underreport their weight, only 3.8% of youth in Goodman et al’s study were misclassified as obese.

### Data Analysis

Our 2 exposures of interest were predominance of breastfeeding in the first 6 months of life and duration of breastfeeding. For predominance of breastfeeding, our primary analysis compared subjects who were mostly or only fed breast milk vs those fed mostly or only infant formula. For the duration of breastfeeding, our primary analysis examined subjects who were breastfed at least 7 months compared with those who were breastfed for 3 months or less. In additional analyses, we compared subjects in each duration category with those in a referent group, comprising the categories never breastfed and breastfed less than 1 month. We also examined duration as a continuous variable, using the values 0, 0.5, 2, 5, 8, and 11 months for the 6 duration categories. For the continuous variable, we report outcomes by a 3-month increment in breastfeeding duration.

Although controversy exists regarding terminology, we chose to use overweight, defined as BMI exceeding the age- and sex-specific 95th percentile in a national sample of US children, as our main outcome.50 We also examined “at risk for overweight,” defined as BMI between the 85th and 95th percentile, as a secondary outcome.

To adjust for covariates and to account for correlated values among siblings (n=4479, 29.2% of the cohort), we used logistic regression models with estimation by generalized estimating equations.31 For the outcome of overweight, we compared odds of exceeding the 95th percentile of BMI with odds of being less than the 95th percentile. For “at risk for overweight,” we compared odds of being between the 85th and 95th percentile with being less than the 85th percentile. In our base model, we included age and Tanner stage, since BMI varies with these 2 variables in adolescence.32,33 We also combined boys and girls and adjusted for sex, since results of sex-specific analyses were similar. In our next model, we added child’s energy intake, total physical activity, and hours of television watched, since these variables represent proxies for energy balance.31 In the third model, we added mother’s BMI, which represents a number of interrelated variables. Finally, we added several variables that were potential confounders because they represent social or economic factors or reflect maternal habits that could affect the child’s growth. We also included birth weight, since in this cohort it is directly related to adolescents’ BMI (unpublished data). Since menarcheal status did not confound the associations among girls, to simplify the sex-adjusted models we did not include it as a covariate. We explored the use of many different terms for mother’s body size, including BMI at age 18 years, in 1989, or in 1995; her BMI at age 18 years along with weight gain from age 18 until 1995; and a parity-adjusted least-squares regression model to interpolate her BMI at the time of the child’s conception. Since each approach gave similar estimates, we used mother’s BMI in 1995 in all models. If the 1995 weight was missing, we used the weight at the cycle closest to 1995 to estimate BMI. We report odds ratios (ORs) and 95% confidence intervals (CIs).

### RESULTS

The mean (SD) age of participants in 1996 was 11.9 (1.6) years; 93.6% were white. A total of 5.0% of the girls and 8.9% of the boys were overweight. TABLE 1 shows age-adjusted mean adolescent BMI and proportions of subjects who were overweight, by type of infant feeding in the first 6 months of life. In both boys and girls, mean BMI and risks of being overweight generally rose across categories, with the lowest values in the category breast milk only. Adolescents who were breastfed longer had lower age-adjusted mean BMI and lower risks of being overweight (TABLE 2).

Using multivariate models, we found that adolescents who were mostly or only fed breast milk vs mostly or only fed infant formula in the first 6 months of life were at an approximately 22% lower risk of being overweight (OR in fully adjusted model, 0.78; 95% CI, 0.66-0.91) (TABLE 3). We observed moderate confounding effects of maternal BMI and slight attenuation of estimates by adjusting for children’s energy balance, as represented by energy intake, physical activity, and inactivity.

Inverse associations were also present between duration of breastfeeding and risk of overweight (TABLE 4). Adolescents who were breastfed for at least 7 months were approximately 20% less likely to be overweight than those breastfed for no more than 3 months (fully adjusted OR, 0.80; 95% CI, 0.67-0.96). Compared with the referent group comprising subjects who had never been breastfed or breastfed less than 1 month, categories of longer duration were associated with lower risks of overweight (FIGURE). A model using duration of breastfeeding as a con-
We also assessed the associations of breastfeeding with "at risk for overweight," which was present in 12.5% of girls and 14.5% of boys. The age-, sex-, and Tanner stage–adjusted OR for adolescents who were fed mostly or only breast milk in the first 6 months of life was 0.84 (95% CI, 0.76-0.93), compared with those who were fed mostly or only formula. The fully adjusted OR estimate was 0.95 (95% CI, 0.84-1.07). Regarding duration, the ORs for having been breastfed at least 7 months vs 3 months or less were 0.82 (95% CI, 0.73-0.91) adjusted for age, sex, and Tanner stage, and 0.93 (95% CI, 0.81-1.05) with full adjustment for covariates.

Mothers who fed their infants only breast milk in the first 6 months of life had the lowest mean BMI (24.5 kg/m²) whereas those who fed their infants only formula had the highest mean value (25.7 kg/m²). Similarly, mothers who breastfed their infants for a longer period had lower mean BMI than mothers who did so for a shorter time. For example, mothers who breastfed their infants for at least 7 months had a mean BMI of 24.6 kg/m², compared with 25.7 kg/m² for mothers who did so for 3 months or less. Mothers’ BMI was also a strong predictor of offspring overweight. Comparing moth-

### Table 1. Mean Age-Adjusted Body Mass Index (BMI) and Proportions of Subjects Classified as Overweight at Age 9 to 14 Years, by Category of Infant Feeding in the First 6 Months of Life*

<table>
<thead>
<tr>
<th>Category</th>
<th>Boys (n = 7155)†</th>
<th>Girls (n = 8186)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Mean BMI, kg/m²</td>
</tr>
<tr>
<td>Breast milk only</td>
<td>2199</td>
<td>18.9</td>
</tr>
<tr>
<td>More breast milk than infant formula</td>
<td>2311</td>
<td>19.1</td>
</tr>
<tr>
<td>Both equally</td>
<td>472</td>
<td>19.3</td>
</tr>
<tr>
<td>More infant formula than breast milk</td>
<td>1370</td>
<td>19.5</td>
</tr>
<tr>
<td>Infant formula only</td>
<td>878</td>
<td>19.3</td>
</tr>
</tbody>
</table>

*Definition of overweight was BMI >95th percentile for age and sex from US data.30
†There were 5 missing values for boys and 8 for girls.

### Table 2. Mean Age-Adjusted Body Mass Index (BMI) and Proportions of Subjects Classified as Overweight at Age 9 to 14 Years, by Duration of Breastfeeding in Infancy*

<table>
<thead>
<tr>
<th>Duration, mo</th>
<th>Boys (n = 7155)†</th>
<th>Girls (n = 8186)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Mean BMI, kg/m²</td>
</tr>
<tr>
<td>0</td>
<td>698</td>
<td>19.4</td>
</tr>
<tr>
<td>&lt;1</td>
<td>393</td>
<td>19.4</td>
</tr>
<tr>
<td>1-3</td>
<td>1079</td>
<td>19.4</td>
</tr>
<tr>
<td>4-6</td>
<td>1513</td>
<td>19.1</td>
</tr>
<tr>
<td>7-9</td>
<td>1109</td>
<td>19.1</td>
</tr>
<tr>
<td>&gt;9</td>
<td>2191</td>
<td>18.9</td>
</tr>
</tbody>
</table>

*Definition of overweight was BMI >95th percentile for age and sex from US data.30
†There were 172 missing values for boys and 199 for girls.

### Table 3. Odds Ratio of Overweight Among Adolescents Who Were Mostly or Only Fed Breast Milk, Compared With Mostly or Only Fed Formula, in the First 6 Months of Life*

<table>
<thead>
<tr>
<th>Model Covariates</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age, sex, and Tanner stage</td>
<td>0.66 (0.58-0.76)</td>
</tr>
<tr>
<td>2. Model 1 + weekly hours of television and physical activity, and daily energy intake</td>
<td>0.72 (0.62-0.83)</td>
</tr>
<tr>
<td>3. Model 2 + mother’s body mass index</td>
<td>0.81 (0.70-0.94)</td>
</tr>
<tr>
<td>4. Model 3 + birth weight, birth order, household income, and mother’s smoking, dietary restraint, weight cycling, and weight concerns</td>
<td>0.78 (0.66-0.91)</td>
</tr>
</tbody>
</table>

*OR indicates odds ratio; CI, confidence interval. Definition of overweight was body mass index >95th percentile for age and sex from US data.30

### Table 4. Odds Ratio of Overweight Among Adolescents by Duration of Breastfeeding in Infancy, Comparing Subjects Who Were Breastfed for at Least 7 Months With Subjects Who Were Breastfed 3 Months or Less*

<table>
<thead>
<tr>
<th>Model Covariates</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age, sex, and Tanner stage</td>
<td>0.65 (0.56-0.75)</td>
</tr>
<tr>
<td>2. Model 1 + weekly hours of television and physical activity, and daily energy intake</td>
<td>0.71 (0.61-0.83)</td>
</tr>
<tr>
<td>3. Model 2 + mother’s body mass index</td>
<td>0.81 (0.69-0.96)</td>
</tr>
<tr>
<td>4. Model 3 + birth weight, birth order, household income, and mother’s smoking, dietary restraint, weight cycling, and weight concerns</td>
<td>0.80 (0.67-0.96)</td>
</tr>
</tbody>
</table>

*OR indicates odds ratio; CI, confidence interval. Definition of overweight was body mass index >95th percentile for age and sex from US data.30
ers with BMI less than 25 kg/m² vs greater than 30 kg/m², the adjusted OR was 0.27 (95% CI, 0.21-0.33).

The timing of introduction of solid foods, cow’s milk, or infant formula neither predicted the outcomes nor confirmed the observed associations (data not shown).

COMMENT

Our findings indicate that infants who were predominantly fed breast milk in the first 6 months of life had a lower prevalence of overweight 9 to 14 years later. Compared with infants predominantly fed infant formula, the estimated relative reduction in risk was approximately 22%. In addition, the apparent protective effects were larger with increasing duration of breastfeeding.

At least 2 mechanisms could explain how breastfeeding protects against later overweight. The first is behavioral. Children naturally regulate their energy intake, but parents’ behavior can override the appetite signals. In cross-sectional studies, Birch and colleagues found that preschool children of parents who used a high degree of control over how much the children ate had lower self-regulation of energy intake, and in girls, higher adiposity. During infancy, it is possible that bottle feeding promotes more parental control, and thus less self-regulation, than breastfeeding. Parents who bottle feed their infants often do so on a regular schedule, and since the remaining volume of formula is visible, they may have the infant finish the bottle even when satiated. By contrast, mothers who breastfeed may be more responsive to the infant’s signals for frequency and volume of feedings. In 1 study, at 6 to 9 months of age, breastfed infants consumed less nonmilk food offered to them than formula-fed infants. Recent qualitative research supports the notion that parents who do not accurately perceive their infants’ hunger cues may be increasing their risk of later obesity. In focus groups of mothers participating in a nutrition program for low-income families, most thought a heavy infant was healthy, supplemented the diets of their infants to assuage fears that they were not getting enough to eat, and used food to shape their children’s noneating behaviors.

A second mechanism could involve the metabolic consequences of ingesting breast milk. Lucas and colleagues found lower serum concentrations of insulin, a hormone that promotes fat storage, in breastfed infants than in infants fed cow’s milk-based formula. Also, in contrast to the linear intake of milk in 10 minutes of formula feeding, 80% to 90% of breast milk is consumed in the first 4 minutes. Since the hind milk is both consumed in small amounts and more energy dense, infants may absorb less energy per volume of breast milk than infant formula. In addition, breast milk may modify growth factors that inhibit adipocyte differentiation in vitro. Overfeeding itself during infancy may also have long-term harmful effects. Animal and some human studies indicate that overfed infants have increased adipocyte number and fat content. Female baboons overfed during infancy, but not thereafter, have much greater adiposity at age 5 years than those normally fed or underfed. These studies suggest that infancy may be a critical period for long-term effects of feeding and that breastfeeding may program the infant to defend against later energy imbalance. Early life metabolic programming is a well-known phenomenon in animals and is receiving increasing attention among humans.

In our analyses, adjustment for maternal BMI attenuated the inverse associations between breastfeeding and later overweight. A mother’s adiposity is directly related to adiposity in her child, for both genetic and environmental reasons. In addition, maternal body mass tends to be higher, and breastfeeding rates lower, in lower socioeconomic strata. Although confounding by socioeconomic status could thus explain the effect of adjusting for maternal BMI, adjustment for other related variables, such as maternal smoking, household income, and birth weight, did not alter the effect estimates. Furthermore, all of the mothers are registered nurses, minimizing variability by education and occupation. Since lactation places demand for energy on the mother, another possibility is that mothers who breastfeed lose more weight during the postpartum period, leading to lower mean BMI 9 to 14 years later. However, empirical evidence shows that postpartum weight loss among lactating mothers is highly variable. A further alternative is that maternal adiposity prevents successful initiation or maintenance of breastfeeding. Hilson et al found that after adjusting for socioeconomic variables, rates of delivery room breastfeeding did not differ by maternal BMI. The women with higher BMI, however, had lower breastfeeding rates at hospital discharge and afterward. Possible explanations include mechanical difficulties in initiating breastfeeding as well as metabolic derangements. Obese rats initiate lactation less successfully than slim rats, perhaps because they produce less breast milk than controls and/or the milk contains altered quantities of nutrients. In addition, Rutishauser and Carlin have reported that women with a BMI exceeding 26 kg/m² at 1 month postpartum were 50% more likely than thinner women to cease breastfeeding in the ensuing 5 months, after adjustment for confounding variables.

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Several factors strengthen confidence in the validity of our findings. Stronger associations were evident for overweight, defined as BMI exceeding the 95th percentile for age and sex, than for “at risk for overweight,” that is, between the 85th and 95th percentiles. The overweight category is more likely to comprise subjects with true adiposity as opposed to large body build that comprises more nonfat tissue.7,40 In addition, substantial associations remained after adjustment for relevant confounding variables. Further support derives from the dose-response relationship reflected by reduced rates with longer duration of breastfeeding. Compared with earlier studies of infant feeding and later obesity, we had a larger sample, leading to more precise effect estimates, and we examined the overweight outcomes at older, more clinically relevant, ages than almost all other studies.

For the variable measuring predominance of breast milk in the first 6 months, we could not ascertain what proportion of the breast milk was administered by pumped breast milk in a bottle rather than by nursing. However, we also found robust associations for duration of breastfeeding, which is less subject to this potential limitation. Also, this limitation would not apply to the etiologic hypothesis that the contents of breast milk itself are protective. The highest category for length of breastfeeding on our questionnaire was 9 months or more. Nonetheless, the finding of less overweight with longer duration of breastfeeding is consistent with the recommendation of the American Academy of Pediatrics to maintain breastfeeding for the first 12 months of life.3

Since we did not obtain data during the preschool and school-age period for each child, we were unable to examine growth trajectories over time, including the point of adiposity rebound.40 Residual and unmeasured confounding are always of concern in an observational study where the subjects choose the level of exposure and not all covariates are measured with optimal precision. Although our subjects hail from all 50 states and several US territories, they comprise a largely racially homogeneous population. More of the participants were breastfed than among the contemporaneous general US population,40 and, especially among the girls, overweight rates were lower.2 Our results, however, are compatible with those from a population with lower prevalence and duration of breastfeeding,15 and we found similar ORs for boys and girls.

In conclusion, we found that infants who were breastfed were less likely than infants who were formula fed to manifest overweight as adolescents. Although complete control for cultural determinants of both overweight and duration of breastfeeding is not achievable in an observational study, we observed substantial effect sizes after adjustment for numerous confounding variables, minimal concern with other forms of bias, a dose-response relationship, consistency with previous literature, and biological plausibility. The benefits of breastfeeding likely include prevention of childhood atopic, infectious, and neurologic conditions, lowering mother’s risk of breast cancer, and reduction of undue family expenditures.30-32 Our study suggests that breastfeeding may also prevent later overweight, raising the possibility that continued promotion of breastfeeding could attenuate the dramatically rising prevalence of obesity in the United States and elsewhere.

Author Contributions: Study concept and design: Gillman, Camargo, Field, Colditz.
Acquisition of data: Gillman, Berkey, Frazier, Rockett, Camargo, Field, Colditz.
Analysis and interpretation of data: Gillman, Rifas-Shiman, Camargo, Berkey, Frazier, Rockett, Field, Colditz.
Drafting of the manuscript: Gillman.
Critical revision of the manuscript for important intellectual content: Gillman, Rifas-Shiman, Camargo, Berkey, Frazier, Rockett, Field, Colditz.
Statistical expertise: Berkey, Field.
Obtained funding: Gillman, Colditz.
Administrative, technical, or material support: Rifas-Shiman, Rockett, Colditz.
Study supervision: Gillman.
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