Breast-feeding and Mental and Motor Development at 5½ Years

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Objective.—Breast-feeding is associated with better child development outcomes, but uncertainty remains primarily due to the close relationship between breast-feeding and socioeconomic status. This study assesses the issue in a low socioeconomic status sample where breast-feeding was close to universal.

Methods.—Seven hundred eighty-four Chilean children were followed longitudinally from infancy. All but four were initially breastfed, 40% nursed beyond 12 months, and infant growth was normal. Child development was assessed at 5½ years by a cognitive, language, and motor test battery. The duration of breast-feeding as the sole milk source was analyzed as a continuous variable, adjusting for a comprehensive set of background factors.

Results.—The relationship between breast-feeding and most 5½-year developmental outcomes was nonlinear, with poorer outcome for periods of breast-feeding as the sole milk source for <2 months or >8 months—statistically significant for language, motor, and one comprehensive cognitive test, with a suggestive trend for IQ.

Conclusions.—The observed nonlinear relationships showed that breast-feeding as the sole milk source for <2 months or >8 months, compared with 2–8 months, was associated with poorer development in this sample. The latter finding requires replication in other samples where long breast-feeding is common and socioeconomic status is relatively homogeneous.

KEY WORDS: breast-feeding; mental development; motor development

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Whether or not breast-feeding is advantageous to mental and motor development has generated much interest, with over 50 relevant studies[1–11] (see Jain et al[12] for a review of 40 earlier studies). Many studies report a positive association between breast-feeding and better developmental outcomes as assessed in infancy, childhood, or adulthood. A recent meta-analysis concluded that a 3-point increment in cognitive function was associated with breast-feeding over formula feeding.[13] However, a number of other studies found no significant association between breast-feeding and development after adjustment for confounders.[14–23] Furthermore, many studies reporting a positive association did not control for the most influential factors—maternal intelligence and stimulation in the home.[24]

Two recent critical reviews[12,25] used methodological standards proposed by Bauchner et al[26] to evaluate the available studies. Standards included adequate sample size, identification of target population, high-quality feeding data, control of susceptibility bias, blinding, outcome based on standardized individual measures obtained when the child was ≥2 years old, and format of results indicating clinical significance. Of the 40 studies in the latest review,[12] only two met all the criteria. One of them reported a positive association between breast-feeding and cognitive development,[27] whereas the other did not.[23] The critical reviews concluded that pervasive methodological weaknesses warrant caution in interpreting the results of available studies.

Other limitations of the literature deserve mention. Research on this issue has been conducted almost exclusively in Europe, the United States, Australia, and New Zealand, where breast-feeding is highly confounded with socioeconomic status. Also, most studies have compared infants who were breastfed to infants fully formula-fed. Since the decision to breastfeed can be closely related to socioeconomic status, the results of such comparisons may be inherently biased. As well, there is a need for more attention to motor development, which has been assessed in less than half of the previous studies.

Given the ubiquitous connection between breast-feeding and family factors, plus the mixed results of previous studies, our prediction was that there would be no relationship in a socioeconomically homogeneous population, where breast-feeding was universal, between breast-feeding and developmental outcomes at 5½ years.

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METHODS

Sample

Data for this analysis were collected in the course of a study of the behavioral and developmental effects of preventing iron deficiency anemia in healthy full-term infants.[28] The infancy phase of the study was conducted between 1991 and 1996 in urban communities near Santiago, Chile. Infants were identified as potential study participants at the 4-month health maintenance visit. The entrance criteria were gestational age ≥37 weeks, birth weight ≥3.0 kg, singleton birth, and absence of major congenital anomalies, major birth or neonatal complications, cesarean section, jaundice requiring phototherapy, hospitalization for other than an uncomplicated problem, chronic illness, or iron therapy. The 3.0 kg birth weight cutoff was used because some clinics had a pre-existing program to provide iron to infants weighing <3.0 kg.

Infants were screened at 5–6 months to prevent any with iron deficiency anemia from entering the study. At 6 months, infants consuming ≥250 mL/day cow's milk or formula were randomly assigned to high- or low-iron–fortified formula or unmodified cow's milk plus multivitamins without iron. Infants taking <250 mL/day, including those infants who received breast milk as the sole milk source, were randomly assigned to a liquid multivitamin with or without iron. After randomization, the infancy study entailed collection of information on feeding during weekly home visits, measurement of maternal and family factors, and developmental assessment of the infant at 12 months. Refusal/dropout before random assignment totaled 6.0%. Attrition after group assignment was 7.8%. There were no differences between those who did or did not complete the study in infant characteristics, family characteristics, or iron supplementation. A total of 1657 infants completed the infancy phase of the study. Full details have been previously published.[28]

The follow-up at 5½ years did not include the entire sample due to funding constraints. It focused on the high-iron and no-added iron conditions (n = 1252 in infancy). Developmental assessment and measurement of maternal and family factors were collected for 784 subjects (37% attrition). The sample population was highly mobile and approximately half of those not tested moved out of the area or were unable to be located. The other half declined to participate or repeatedly missed testing appointments. There were no differences between those who were or were not tested at 5½ years in gestational age, birth weight/length, number of children in household, single parent status, parental education, maternal IQ, depression, and age. Children not in the 5½ year follow-up had somewhat lower socioeconomic status ($P < .01$) and less supportive home environments ($P < .05$), but differences were small (1 point or less).

The research protocols for both the infancy and 5½-year phases were approved by the institutional review boards of the University of Michigan Medical Center, Ann Arbor, and of Institute of Nutrition and Food Technology, University of Chile, Santiago.

Developmental Assessment at 5½ Years

Developmental outcomes at 5½ years included the Wechsler Preschool and Primary Scale of Intelligence–Revised (WPPSI-R),[29] the Beery-Buktenica Developmental Test of Visual-Motor Integration,[30] the Preschool Language Scale, 3rd Edition (PLS-3),[31] the Broad Cognitive Abilities – Standard Scale (BCA) of *The Batería Woodcock-Muñoz-Revisada*[32] (the parallel Spanish version of the Woodcock-Johnson-Revised), and the short form of the Bruininks-Oseretsky Test of Motor Proficiency.[33] All evaluations were conducted by psychologists specially trained and standardized for each measurement (≥80% intertester reliability). Psychologists were unaware of the child's feeding status in infancy.

Measurement of Breast-Feeding in Infancy

Breast-feeding data were based on maternal recall for the period before study enrollment at 4-6 months. Prior to enrollment, infants were fed according to Chilean custom at the time, which often entailed mixed breast- and bottle-feeding. All but 8 infants completing the infancy phase of the study were initially breast-fed, 4 of whom were reassessed at 5½ years. Formula use was uncommon, and clinics distributed unmodified cow's milk as part of a legally required and effective program for preventing generalized undernutrition in infancy. Fieldworkers obtained subsequent information on milk feeding concurrently at subject enrollment and weekly home visits thereafter until the infant's first birthday. Mothers were almost always the informant. The following information was obtained: method of milk feeding, date of first bottle (cow's milk or formula), the average daily amount of milk or formula during the preceding week, and, if weaned by 12 months, the date of complete weaning from the breast.

Our analysis considered the period of nursing as the sole milk source (up to 12 months). We did not analyze the age of weaning from the breast, because 40% of the sample was still nursing at 12 months when the infancy phase ended, and breast-feeding data were not revisited during the 5½-year phase. It was also not possible to consider the length of exclusive breast-feeding per WHO definitions, since systematic data on the introduction of solid foods and juice were not collected. However, previous studies in the same communities showed that families generally followed Chilean pediatric recommendations of introducing fruits and cereals at 4 months of age, meat and vegetables at 6 months, and legumes and eggs at 9 months.[34]

Background Factors

Project psychologists obtained detailed family information at the 5½-year evaluation. Socioeconomic status was measured by the Graffar scale, which differentiates families at the lower end of the socioeconomic status spectrum.[35] It includes questions about household composition, parental education, work, housing ownership, and major household possessions. Maternal depressive symptomatology was measured by the Spanish-language version of the Center for Epidemiologic Studies Depression Scale.[36] Family support for child development was as-

sessed by the questionnaire version of the Home Observation for Measurement of the Environment-Revised (HOME).[37]

Maternal IQ was measured in infancy with a short form of the Wechsler Adult Intelligence Scale-Revised.[38,39] Data were available for 452 subjects. Only a random 10% of subjects enrolled in the last 2 years of the infancy study could be assessed due to lack of funds. Because data were not missing completely at random, we used multiple imputations to impute missing IQ for the remaining 332 subjects.[40]

Data Analysis

To allow for nonlinear relationships between days of breast-feeding as the sole milk source and developmental outcome, we used a generalized additive model.[41] A generalized additive model makes no assumption about the form of the relationship between independent and outcome variables, in contrast to general linear models that assume a linear association and fit a straight line to the data to describe the relationship. We used multiple generalized cross-validations for automatic selection of the smoothing parameters. The error term was assumed to be normally distributed with constant variance. The partial residuals of the generalized additive model were plotted for the duration of breast-feeding as the sole milk source and each developmental outcome, together with their 95% confidence intervals. Partial residuals indicate the relative influence of a given explanatory variable on the prediction. Thus, the plots indicate the nature of the relationship between breast-feeding and 5½-year outcomes.

The models included the following covariates identified a priori as important in the breast-feeding and child development literature[7,12,13,24,25,42]: gender, birth weight, child's age at testing, maternal education, IQ, depression, age, number of children, father absence, paternal education, HOME score, and socioeconomic status. Since maternal age and number of children (average 2.4) were substantially correlated ($r = 0.51$, $P < .0001$), we excluded number of children. We also controlled for three other important factors: overall nutritional status (weight-for-height z scores at 12 months), iron deficiency anemia at 12 months, and iron supplementation group in the infancy study.[28]

We also wanted to facilitate comparisons with previous studies. Therefore, we conducted additional analyses of breast-feeding as a categorical variable to allow calculation of effect sizes. We converted breast-feeding data (in days) to months by using 30.4 days per month (365 days per year/12 months). We categorized the duration of breast-feeding as the sole milk source into 3 groups: 0–61 days as "<2 months" (n = 275; 35%); 62–243 days as "2–8 months" (n = 421; 54%); and >243 days as ">8 months" (n = 88; 11%). Groups were based on the inflection points from the results of the continuous analyses for the BCA, PLS-3, and IQ (WPPSI-R). Effect sizes for each 5½-year outcome were calculated by determining the difference in means between groups, divided by the sample standard deviation. Assessing the magnitude of effects also offset the risk that our relatively large sample size might result in statistically significant differences that would not be clinically meaningful. To identify background differences related to early or late introduction of cow's milk/formula we examined the variables listed in Table 1 by breast-feeding groups using ANOVA.

Table 1. Sample Characteristics ($n = 784$)

	Values*
Child	
Child's age at testing, months	66.1 ± 0.0
Gender, % male	53 (415/784)
Birth weight, grams	3555 ± 13.2
12-month weight-for-height (z score)	0.5 ± 0.0
Family	
Maternal age, years	26.7 ± 0.2
Father absent, %	19 (151/783)
Paternal education, years	9.7 ± 0.1
Maternal education, years	9.8 ± 0.1
Maternal IQ	84.3 ± 0.4
Maternal depressive symptoms†	19.8 ± 0.5
Home environment‡	34.8 ± 0.2
Socioeconomic index§	36.3 ± 0.3

*Values are means ± SE for continuous variables and percentages and *n*/total*n* for the categorical variables.

†Measured by Center for Epidemiologic Studies Depression Scale.

‡Assessed by Home Observation for Measurement of the Environment-Revised.

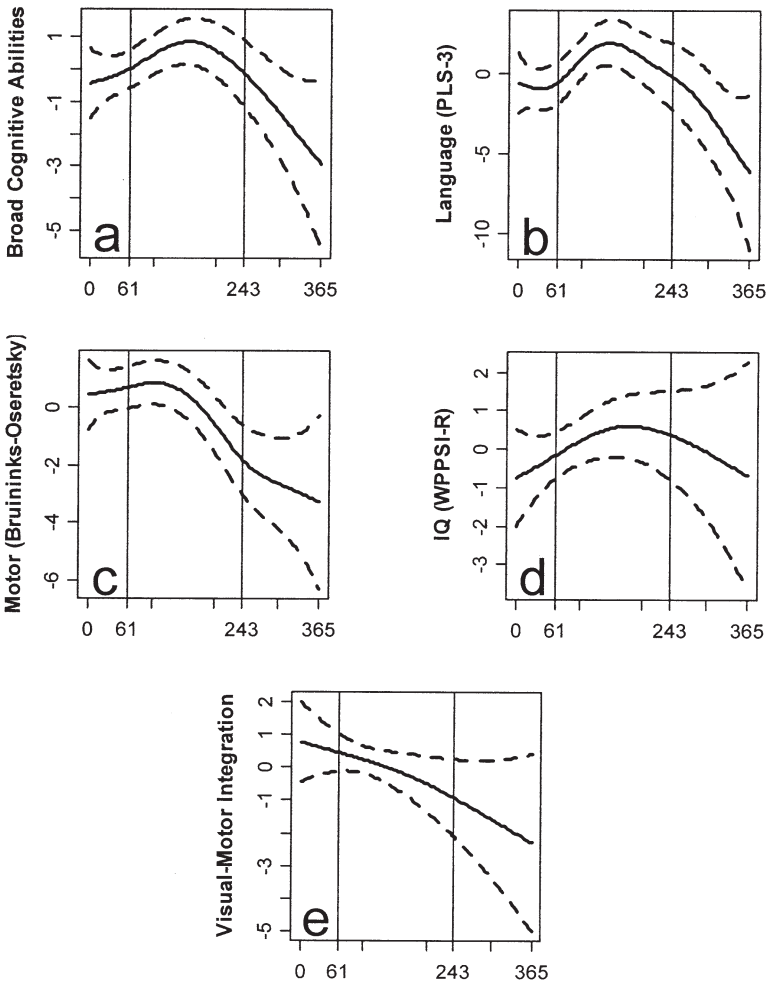
§Measured by the Graffar scale, designed specifically to differentiate families at the lower end of the socioeconomic spectrum. A score of 36 falls in the medium range of the lower class spectrum.

All analyses were carried out with SAS version 9.1 (SAS Institute Inc, Cary, NC), R version 2.1.1,[43] and the mgcv package version 1.3-7.[44] An alpha level of 0.05 was defined for tests of statistical significance.

RESULTS

Characteristics of the 5½-year sample are shown in Table 1. Fathers were absent from 19% of the households. Both parents averaged slightly more than 9 years of schooling. Maternal depressive symptoms were common, as is often the case in mothers of young children in economically stressed environments.[45] The average maternal IQ in the mid 80s was similar to that of US women of lower socioeconomic groups with less than a high school education.[46,47]

The Figure shows the relationship between breast-feeding as the sole milk source as a continuous variable (in days) and developmental outcomes at 5½ years. The relationship is shown after adjusting for the comprehensive set of covariates specified above. A significant nonlinear effect was found for 3 of 5 outcomes: Broad Cognitive Abilities – Standard Scale of *The Batería Woodcock-Muñoz-Revisada* ($\chi^2 = 8.20$; $P < .01$), Preschool Language Scale-3rd Edition ($\chi^2 = 10.53$; $P < .01$), and the Bruininks-Oseretsky Test of Motor Proficiency ($\chi^2 = 4.29$; $P < .05$). For the Wechsler Preschool and Primary Scales of Intelligence-Revised, the nonlinear effect showed a suggestive trend ($\chi^2 = 3.17$; $P = .07$). Neither the linear nor nonlinear effect was statistically significant



(a–e) Relationship between duration of breast-feeding and developmental outcomes at 5½ years. The partial residuals (solid line) of the generalized additive model are plotted for each developmental outcome, together with their 95% confidence intervals (broken line). Confidence intervals are wider at the beginning and end (0 and 365 days) due to lower numbers of subjects. Results are shown after adjustment for all background factors listed in Table 1.

for the Visual-Motor Integration Test. Poorer outcomes on the cognitive and language assessments (Figure a, b, and d) were found for both the short and long extremes of breast-feeding as the sole milk source. Poorer outcome on the motor test was found for the long extreme only (Figure c).

Among the covariates in the models, HOME score was the strongest predictor for the cognitive and language outcomes, followed by maternal IQ for the cognitive outcomes and paternal education for the language outcome. For the motor outcome, gender was the strongest predictor, followed by HOME score.

Table 2 shows the results of categorical analyses comparing developmental outcomes in groups based on the duration of breast-feeding as the sole milk source (0–61 days are categorized as "<2 months," 62–243 days are categorized as "2–8 months," and >243 days are categorized as ">8 months"). There was a significant nonlinear effect for the same 3 outcomes in the continuous variable analysis: BCA, PLS-3, and the Bruininks-Oseretsky Test of Motor Proficiency. Children in the middle group (2–8 months) averaged 0.14 and 0.17 SD units higher on the BCA and PLS-3, respectively, than the <2 months group and 0.22 SD units higher than the >8 months group. On the motor test, there was no difference in scores between the <2 months and 2–8 months groups; the >8 months group scored 0.39 SD units lower than the rest of the sample. Although the nonlinear relationship for the Visual-Motor Integration was not statistically significant, the magnitude of effects comparing the 2–8 months group and >8 months group was 0.20 SD units, which falls within the range found for statistically significant outcomes.

Regarding background differences that related to breast-feeding groups, early introduction of milk/formula was associated with more father absence ($P < .01$) and higher maternal depressive symptoms ($P < .01$). Children with later introduction had greater weight-for-height z scores at 12 months ($P < .01$) and were 1 week younger for the 5½-year follow-up ($P < .05$).

Table 2. Categorical Analyses Results Showing Developmental Outcomes and Effect Sizes by Breast-feeding Group*

	Breastfeeding group						
	< 2 months $n = 275$	2–8 months $n = 421$	> 8 months $n = 88$	*t*-statistic	Nonlinear *P*†	Effect size < 2 vs 2–8	Effect size 2–8 vs >8
Broad Cognitive Abilities (Woodcock-Muñog)	461.7 ± 0.5	462.8 ± 0.4	461.1 ± 0.8	−2.27	.02	.14	.22
Preschool Language Scale-3rd Edition	89.8 ± 0.7	91.8 ± 0.6	89.2 ± 1.3	−2.46	.01	.17	.22
Bruininks-Oseretsky Test of Motor Proficiency	52.7 ± 0.5	52.7 ± 0.4	49.6 ± 0.9	−2.42	.02	0	.39
Wechsler Preschool and Primary Scales of Intelligence–Revised (IQ)	87.1 ± 0.6	88.4 ± .05	88.1 ± 1.2	−.97	.33	.12	.03
Visual-Motor Integration Test	97.8 ± 0.7	97.3 ± 0.6	95.0 ± 1.3	−.92	.36	.05	.20

*718 children had breast-feeding data, developmental outcomes, and covariates.

†Significance levels are shown for adjusted means and refer to tests of nonlinear effects between breast-feeding groups and developmental outcomes. Values are means ± SE and are adjusted for gender, birth weight, age of child at testing, father absence, paternal education, maternal education, IQ, depression and age, HOME score, socioeconomic status, weight-for-height z score at 12 months, iron deficiency anemia, and iron supplementation group.

DISCUSSION

We found a nonlinear relationship between the duration of breast-feeding as the sole milk source and most developmental outcomes at 5½ years. The highest scores were observed among the children who received breast milk as the sole milk source for 2–8 months. Our finding that breast-feeding as the sole milk source past 2 months resulted in better cognitive and language outcomes than those breastfed <2 months resembles numerous studies that report a positive association between breast-feeding and developmental outcome. The effect sizes we observed, though small, are similar to effect sizes reported in the literature (see Jain et al[12] for a review of reported effect sizes). In our sample, although the association between a short duration of breast-feeding as the sole milk source and higher maternal depression and more father absence points to background factors that may adversely affect breast-feeding early on, poorer 5½ year outcomes remained statistically significant controlling for these and other background factors.

Our findings regarding the short duration of breast-feeding as the sole milk source seem to support the biologic and interactional effects of breast-feeding considered in most previous studies. Breast milk components not previously found in formulas, such as long-chain polyunsaturated fatty acids, are thought to promote development. Another reason is interactional, that is, nursing itself may foster the mother-child relationship, stimulating the breast-fed infant and enhancing development. Our <2 months group had the shortest window to receive these biologic and interactional benefits. In addition, the use of unmodified powdered cow's milk may have been detrimental to development.

In contrast to the short duration findings, our observation of poorer outcome at the longest duration of breast-feeding as the sole milk source (>8 months) is distinct from most previous studies. It is also puzzling, given the many known benefits of breast-feeding. Compared with children receiving breast milk as the sole milk source for 2–8 months, children who received no other milk for >8 months had lower cognitive and language test scores, like the short-duration breast-feeding group. They also had the lowest motor scores of all groups, scoring 0.39 SD units in mean test performance below those who received some milk or formula before 8 months.

These findings clearly need to be replicated in other samples where many infants are breast-fed into the second half of the first year of life and socioeconomic status is relatively homogeneous. Indeed, there is little basis for direct comparisons with previous studies, and caution is warranted in terms of generalizing these results. We found only 2 studies analyzing the duration of breast-feeding that reported a proportion of infants with long breast-feeding (>8 months) similar to our sample.[4,48] The majority of other studies either contrasted children who received at least some breast-feeding with those who never breast-fed, unlike our study where breast-feeding was virtually universal and extensive, or did not look at breast-feeding into later infancy.

That said, a very early study[49] reported that infants breast-fed ≥10 months scored lower on cognitive measures than those breast-fed shorter durations or not at all. However, important background differences were also observed. A recent study on breast-feeding duration[4] reported a positive dose-response relationship for Verbal, Performance, and Full Scale IQ scores (Wechsler Adult Intelligence Scale) among adult males who were breast-fed as infants up to 9 months but lower mean scores for those breast-fed >9 months. Lower scores in the long extreme were not discussed, perhaps because the differences in adjusted means between groups breast-fed 7–9 months and >9 months were not statistically significant nor were tests for a nonlinear relationship. Using published data for that study, we calculated the magnitude of effects between the 7–9 months and >9 months groups. The effect size was 0.13 SD units—similar to differences interpreted as meaningful in the breast-feeding and development literature. While small, it is important to note, as did Rogan and Gladen,[42] that even a small change in mean IQ can affect both the number of children falling below any given cutoff of concern and the number considered high-functioning. Despite differences in definitions of breast-feeding and statistical analysis, these two studies

and ours highlight the need for a closer look at breast-feeding in later infancy.

Possible explanations for the poorer outcomes we found with longer breast-feeding as the sole milk source include nutritional limitations, behavioral factors, harmful exposures, and unmeasured background factors. Perhaps breast-feeding no longer fully met the infants' nutritional needs in the second half of the first year of life. Although iron deficiency anemia did not differ between groups and was covaried in our analyses, there could have been other micronutrient deficiencies such as zinc. The children in the >8 months group had the highest weight-for-height *z* scores at 12 months, which argues against zinc deficiency, but some other unidentified nutrient might have been inadequate given the rapid growth. The sample's rapid growth could also suggest that, from an evolutionary standpoint, breast milk may have been able to fully meet the needs of infants in the past who were not growing so quickly, but could not do so in our heavy population of infants.

Behavioral factors are another possibility. Infants who receive breast milk as the sole milk source into the second 6 months of life might miss the developmental window for easily accepting other foods, and thus, develop nutrient deficiencies. Alternatively, long-duration breast-feeding could reflect a limited repertoire of maternal response to infant distress. Harmful substances might be another factor. If environmental contaminants are found in breast milk, children with long breast-feeding as the sole milk source might have higher levels of toxic substances and be at greater risk for associated developmental ill effects.

There were no statistically significant differences in the study's comprehensive set of maternal or familial characteristics that might explain the lower test scores in the >8 months group. However, mothers providing breast milk as the sole milk source for a long time might have differed in unmeasured ways. Maternal characteristics such as dominance, insecurity, and self-esteem were not assessed. These and other unmeasured background factors might explain the findings. It should also be noted that our sample was of quite low socioeconomic status, and the results may not apply to populations with higher socioeconomic status.

In sum, this study found a nonlinear relationship between the duration of breast-feeding as the sole milk source and 3 of 5 developmental outcomes at 5½ years, before and after adjustment for important confounders, with a suggestive trend for a 4th outcome. The observed nonlinear relationships showed that breast-feeding as the sole milk source for <2 months or >8 months in this sample was associated with poorer development than breast-feeding as the sole milk source for 2–8 months. Our results regarding the short duration of breast-feeding agree with numerous prior studies. Our findings regarding the long duration of breast-feeding as the sole milk source are uncommon in the breast-feeding and child development literature, but there are few comparable studies. The latter findings should not detract from the well-known benefits of breast-feeding. Rather, they should invite replication in other samples where breast-feeding is extensive and socioeconomic status is relatively homogeneous.

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