

# Infant growth and health outcomes associated with 3 compared with 6 mo of exclusive breastfeeding<sup>1-3</sup>

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## ABSTRACT

**Background:** Opinions and recommendations about the optimal duration of exclusive breastfeeding have been strongly divided, but few published studies have provided direct evidence on the relative risks and benefits of different breastfeeding durations in recipient infants.

**Objective:** We examined the effects on infant growth and health of 3 compared with 6 mo of exclusive breastfeeding.

**Design:** We conducted an observational cohort study nested within a large randomized trial in Belarus by comparing 2862 infants exclusively breastfed for 3 mo (with continued mixed breastfeeding through  $\geq 6$  mo) with 621 infants who were exclusively breastfed for  $\geq 6$  mo. Regression to the mean, within-cluster correlation, and cluster- and individual-level confounding variables were accounted for by using multilevel regression analyses.

**Results:** From 3 to 6 mo, weight gain was slightly greater in the 3-mo group [difference: 29 g/mo (95% CI: 13, 45 g/mo)], as was length gain [difference: 1.1 mm (0.5, 1.6 mm)], but the 6-mo group had a faster length gain from 9 to 12 mo [difference: 0.9 mm/mo (0.3, 1.5 mm/mo)] and a larger head circumference at 12 mo [difference: 0.19 cm (0.07, 0.31 cm)]. A significant reduction in the incidence density of gastrointestinal infection was observed during the period from 3 to 6 mo in the 6-mo group [adjusted incidence density ratio: 0.35 (0.13, 0.96)], but no significant differences in risk of respiratory infectious outcomes or atopic eczema were apparent.

**Conclusions:** Exclusive breastfeeding for 6 mo is associated with a lower risk of gastrointestinal infection and no demonstrable adverse health effects in the first year of life. *Am J Clin Nutr* 2003;78:291-5.

**KEY WORDS** Breastfeeding, gastrointestinal infection, respiratory infection, growth, atopic eczema

## INTRODUCTION

The debate over the optimal duration of exclusive breastfeeding has been long and heated. The belief that breast milk alone is nutritionally insufficient after 3 or 4 mo, combined with the fact that weaning foods given in many developing countries are both nutritionally inadequate and contaminated, has given rise to the so-called “weanling’s dilemma” (1, 2). Breastfeeding is a life-and-death issue in developing countries; a recent meta-analysis reported markedly reduced mortality (especially mortality due to infectious disease) with breastfeeding, even into the second year of life (3).

In most developed countries, however, uncontaminated, nutritionally adequate complementary foods are readily available, and growth faltering is relatively uncommon. With the resurgence of breastfeeding initiation in developed countries, recent attention has turned to the importance of promoting its duration and exclusivity. The epidemiologic evidence is now overwhelming that, even in developed countries, breastfeeding protects against gastrointestinal and (to a lesser degree) respiratory infection and that the protective effect is enhanced with greater duration and exclusivity of breastfeeding (4-8).

Although growth faltering is uncommon in developed countries, available data indicate that infants following recent World Health Organization (WHO) feeding recommendations (ie, to exclusively breastfeed until 4-6 mo of age and to continue breastfeeding with added complementary foods up to 2 y of age) show a deceleration in both weight and length gains relative to the international WHO/Centers for Disease Control and Prevention (CDC) growth reference from 3 to 12 mo, with partial catch-up thereafter (9-13).

In the past few years, a split has developed concerning the recommended optimal duration of exclusive breastfeeding. Until May 2001, the WHO recommended exclusive breastfeeding for 4-6 mo (14), while the United Nations Children’s Fund (UNICEF) recommended exclusive breastfeeding for  $\approx 6$  mo (15). This difference led to vigorous and often acrimonious debate, not only between the 2 United Nations agencies but also in the larger infant nutrition and public health communities (16). The American Academy of Pediatrics has been ambivalent about this issue; in 2 different sections of their 1998 Pediatric Nutrition Handbook (17), they alternatively recommend human milk as the “exclusive nutrient source... during the first 6 mo” (page 18) and “to delay introduction of solid

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foods until 4 to 6 mo" (page 38). Because of the ongoing controversy and polarization with respect to this issue, we carried out an observational cohort study nested within a large randomized trial in the Republic of Belarus in an attempt to identify the health effects of these alternative approaches to infant feeding.

## SUBJECTS AND METHODS

The methods undertaken in the Promotion of Breastfeeding Intervention Trial (PROBIT) are described in detail in previous publications (18, 19). Briefly, 31 maternity hospitals and 1 each of their affiliated polyclinics (ie, the clinics where children are followed for routine health care) were randomly assigned to receive a breastfeeding promotion intervention modeled on the WHO/UNICEF Baby-Friendly Hospital Initiative (experimental group) or to continue the maternity hospital and polyclinic practices in effect at the time of randomization (control group). Healthy, breastfed, term newborns weighing  $\geq 2500$  g at birth were enrolled during their postpartum hospital stay. Follow-up data were collected at polyclinic visits at 1, 2, 3, 6, 9, and 12 mo; home visits were made when a polyclinic visit was missed. At each of these visits, we obtained data on infant feeding, illness, and growth. Because differences in growth were not major hypotheses of PROBIT, which focused on reductions in infection and atopic eczema (18, 19), no attempts were made to standardize measurements of weight, length, and head circumference.

Classification of the degree of breastfeeding was based on WHO definitions. We classified infants as exclusively breastfed at 3 mo if the cross-sectional feeding information obtained at 1, 2, and 3 mo indicated that no liquid or solid foods other than breast milk were being administered to the infant. An infant was considered to be exclusively breastfed at 6 mo if, in addition to the above criteria, he or she was not receiving any other liquid or solid foods at the 6-mo visit. (Although the controversy about the optimal duration of exclusive breastfeeding concerns whether to breastfeed for 4 or 6 mo, we did not collect infant feeding information at 4 mo; therefore, our comparison was between breastfeeding durations of 3 and 6 mo.)

A total of 17 046 subjects were recruited from the 31 randomized sites; 555 (3.3%) subjects were lost to follow-up before 12 mo. A 32nd site was also originally to be included as part of the study, but it was excluded because of documented falsification of outcome data (18, 19). Of the entire randomly assigned cohort, 2862 infants were exclusively breastfed for 3 mo and were introduced nonbreast milk liquids, solids, or both by 6 mo of age but continued to partially breastfeed through 6 mo; 621 infants were exclusively breastfed for  $\geq 6$  mo. These 2 subcohorts made up the subjects studied in this observational analysis and are referred to as the 3-mo and 6-mo groups, respectively.

We used the algorithms of Rubin et al (20) to classify gastrointestinal and upper respiratory infection, which were modified to ensure a minimum duration of infection of 2 d. Other types of respiratory infections under study included croup, otitis media, wheezing, and pneumonia; subjects were classified as having one of these infections if the infection had been diagnosed by the chief polyclinic pediatrician and if the duration of infection was  $\geq 2$  d. Rashes were considered to represent atopic eczema if they lasted  $\geq 2$  wk or recurred after clearing for  $\geq 1$  wk, were itchy, and occurred on the face or extensor surfaces of the arms or the extensor surfaces of the legs. Audits for the recorded data on any breastfeeding duration  $\geq 3$  mo,  $\geq 1$  episode of gastrointestinal infection, and  $\geq 2$  episodes of respiratory infection were conducted on 20 polyclinic charts and 10 maternal

interviews that were randomly selected by the investigators from each study site. The results of these audits showed high concordance between the data from the PROBIT forms and both the polyclinic chart and maternal interview data; no differences in under- or overreporting were observed between the experimental and control sites (18, 19).

We compared the 2 study groups at baseline and at 3 mo with the use of *t* tests for continuous variables and chi-square tests for categorical variables. The primary analysis of study outcomes was based on linear mixed models (PROC MIXED) for continuous (growth) outcomes and generalized linear mixed models (PROC GLIMMIX) for dichotomous outcomes, accounting for both cluster-level (geographic region, urban compared with rural location, and hospital) and individual-level (birth weight, maternal education, and number of siblings in the household) covariates. Weight-for-age, length-for-age, and weight-for-length *z* scores were calculated by using EPIINFO 2000 (CDC, Atlanta) based on the sex- and age-specific WHO/CDC reference (21). The mixed models for growth outcomes controlled for anthropometric measures from birth to 3 mo (to control for regression to the mean) and accounted for within-cluster (within-hospital) correlation and for the repeated-measures nature of these outcomes. Maternal smoking (any smoking during pregnancy) was also included as an individual-level covariate for analysis of respiratory tract infection. Finally, for analysis of atopic eczema, family atopic history (a positive history of asthma, allergic rhinitis, or atopic eczema in the mother, the father, or a sibling) was also included as an individual-level covariate. The results of the PROC MIXED models are reported as adjusted differences (and the 95% CIs), whereas those for GLIMMIX models are reported as adjusted odds ratios (and the 95% CIs). Incidence density ratios (IDRs) and their 95% CIs were estimated according to Poisson modeling within GLIMMIX by using the same cluster- and individual-level covariates listed above. All statistical analyses were carried out with the use of SAS software (version 8.2; SAS Institute, Inc, Cary, NC).

## RESULTS

At baseline, infants who were exclusively breastfed for  $\geq 3$  mo were not significantly different from the other PROBIT infants who were not exclusively breastfed for  $\geq 3$  mo with respect to mean birth weight (3442 compared with 3437 g, respectively), birth length (51.9 cm for both), and head circumference (35.1 compared with 34.9 cm, respectively). Maternal age, family atopic history, and number of other children at home were also not significantly different between the 2 groups (data not shown). Not surprisingly, however, mothers who did not exclusively breastfeed their infants for  $\geq 3$  mo were less well-educated (12.8 compared with 16.6% completed university;  $P < 0.0001$ ) and were more likely to smoke cigarettes during pregnancy (2.5% compared with 1.5%;  $P < 0.001$ ).

Baseline data for the 3-mo and 6-mo study groups are compared in **Table 1**. No significant differences between the 2 groups were observed, except for a significantly higher prevalence of family atopic history and lower mean birth length and head circumference in the 6-mo group. Differences in intakes of formula, juices, cereals, and other solid foods at 6 mo were observed between the 2 groups. In the 3-mo group, 14.5% were receiving infant formula (most, 1–4 times/d), 83.6% were receiving juices (usually once or twice per

TABLE 1

Baseline comparison of mothers and their infants exclusively breastfed for 3 or  $\geq 6$  mo

Variable	3-mo Group (n = 2862)	6-mo Group (n = 621)
Mothers [n (%)]		
Maternal age		
<20 y	374 (13.1)	81 (13.0)
20–34 y	2374 (82.9)	511 (82.3)
$\geq 35$ y	114 (4.0)	29 (4.7)
Maternal education [n (%)]		
Incomplete secondary	115 (4.0)	28 (4.5)
Complete secondary	871 (30.4)	198 (31.9)
Advanced secondary or partial university	1397 (48.8)	297 (47.8)
Complete university	479 (16.7)	98 (15.8)
Positive atopic family history [n (%)]	111 (3.9)	46 (7.4) <sup>1</sup>
Other children living in household [n (%)]		
0	1658 (57.9)	331 (53.3)
1	969 (33.9)	235 (37.8)
$\geq 2$	235 (8.2)	55 (8.9)
Smoking during pregnancy [n (%)]	46 (1.6)	5 (0.8)
Cesarean delivery [n (%)]	333 (11.6)	66 (10.6)
Infants		
Male [n (%)]	1458 (50.9)	301 (48.5)
Gestational age (wk)	39.4 $\pm$ 1.0 <sup>2</sup>	39.5 $\pm$ 0.9
Birth weight (g)	3441 $\pm$ 415	3445 $\pm$ 408
Birth length (cm)	52.0 $\pm$ 2.1	51.6 $\pm$ 2.2 <sup>3</sup>
Head circumference at birth (cm)	35.2 $\pm$ 1.4	34.8 $\pm$ 1.7 <sup>3</sup>
5-min Apgar score	8.6 $\pm$ 0.7	8.5 $\pm$ 0.6 <sup>3</sup>
Weight at 3 mo (g)	6189 $\pm$ 650	6222 $\pm$ 674
Length at 3 mo (cm)	61.0 $\pm$ 2.4	60.9 $\pm$ 2.5
Head circumference at 3 mo (cm)	40.5 $\pm$ 1.4	40.5 $\pm$ 1.6

<sup>1,3</sup>Significantly different from 3-mo group: <sup>1</sup> $P < 0.001$  (chi-square test), <sup>3</sup> $P < 0.001$  ( $t$  test).

<sup>2</sup> $\bar{x} \pm$  SD.

day), 54.8% were receiving cereals (most, 1 time/d), and 78.2% were receiving other solid foods (most, 1 time/d) at 6 mo; only 5.2% were receiving water, 5.1% cow milk, and 0.2% other milks.

Weight and length gains in the 3-mo and 6-mo groups are compared in **Table 2**. For the period from 3 to 6 mo, both measures were higher in the 3-mo group, ie, those infants who received complementary foods in addition to continued breastfeeding between 3 and 6 mo. Some catch-up in length gain occurred in the 6-mo group between 9 and 12 mo. As shown in **Table 3**, the differences in weight gain were reflected in slightly (0.08–0.09) but significantly higher weight-for-age  $z$  scores in the 3-mo group at 6, 9, and 12 mo, although the means remained at  $\approx 0.5$ – $0.6$  in both groups. For length-for-age, the mean  $z$  scores were near 0 (the WHO/CDC reference mean) at 6 and 9 mo, although they were significantly higher in the 3-mo group. By 12 mo, however, the difference in length-for-age had disappeared, and both groups exceeded the reference mean. Differences in weight-for-length  $z$  scores were not statistically significant at any age.

Weight-for-age  $z$  scores  $< -2$  were rare at all 3 ages in both groups: 0 of 620 compared with 2 of 2841 at 6 mo, 1 of 612 compared with 3 of 2796 at 9 mo, and 1 of 617 compared with 4 of 2849 at 12 mo in the 6-mo compared with the 3-mo groups, respectively. Low ( $< -2$ ) length-for-age  $z$  scores were more common,

TABLE 2

Comparison of weight and length gains in infants exclusively breastfed for 3 or  $\geq 6$  mo<sup>1</sup>

	3-mo Group	6-mo Group	Difference (95% CI) <sup>2</sup>
Weight gain (g/mo)			
3–6 mo	640 $\pm$ 186 <sup>3</sup>	612 $\pm$ 180	28 (12, 44)
6–9 mo	454 $\pm$ 177	449 $\pm$ 171	5 (–11, 21)
9–12 mo	355 $\pm$ 172	354 $\pm$ 176	1 (–15, 17)
Length gain (mm/mo)			
3–6 mo	20.3 $\pm$ 7.0	19.2 $\pm$ 6.4	1.1 (0.5, 1.6)
6–9 mo	15.3 $\pm$ 6.5	14.8 $\pm$ 6.5	0.5 (–0.1, 1.1)
9–12 mo	13.3 $\pm$ 6.3	14.2 $\pm$ 6.8	–0.9 (–1.5, –0.3)

<sup>1</sup>Adjusted with the use of the MIXED procedure (SAS Institute Inc, Cary, NC) for geographic region, urban or rural location, hospital of birth, maternal education, number of siblings in household, birth weight or length, and weight or length gain from birth to 3 mo.

<sup>2</sup>The tabulated difference is statistically significant at  $P < 0.05$  if the 95% CI excludes the null value of 0.

<sup>3</sup> $\bar{x} \pm$  SD.

but they did not differ significantly between the 6-mo and 3-mo groups at 6, 9, and 12 mo, respectively: 14 of 619 compared with 42 of 2841 [RR: 1.53 (95% CI: 0.84, 2.78)], 14 of 611 compared with 44 of 2795 [RR: 1.46 (95% CI: 0.80, 2.64)], and 4 of 617 compared with 28 of 2849 [RR: 0.66 (95% CI: 0.23, 1.87)], respectively. As with weight-for-age, weight-for-length  $z$  scores  $< -2$  were also rare at all 3 ages: 0 of 619 compared with 7 of 2841 at 6 mo, 2 of 611 compared with 8 of 2795 at 9 mo, and 1 of 617 compared with 4 of 2849 at 12 mo, respectively, in the 6-mo and 3-mo groups, respectively. High ( $> 2$ )  $z$  scores were far more common than were low  $z$  scores at all 3 ages, especially for weight-for-age and weight-for-length, but the scores did not differ significantly between the 2 feeding groups.

Despite the slightly higher head circumference at birth in the 3-mo group (**Table 1**), mean ( $\pm$ SD) head circumference was similar in the 3-mo and 6-mo groups at 6 mo [43.44  $\pm$  1.46 compared with 43.34  $\pm$  1.53 cm; difference: 0.10 (95% CI: –0.02, 0.22) cm] and 9 mo [45.45  $\pm$  1.43 compared with 45.52  $\pm$  1.46 cm; difference: –0.06 (95% CI: –0.18, 0.06) cm]; it was significantly higher in the 6-mo group, however, at 12 mo [47.06  $\pm$  1.49 compared with 47.25  $\pm$  1.50 cm; difference: –0.19 (95% CI: –0.31, –0.07) cm].

The incidence of atopic and infectious outcomes during the first 12 mo of life is shown in **Table 4**. No significant difference was observed in the risk of atopic eczema,  $\geq 2$  episodes of wheezing,  $\geq 2$  episodes of any respiratory or upper respiratory infection,  $\geq 1$  episode of otitis media, or hospitalization for respiratory infection.

The risk of one or more episodes of gastrointestinal infection was significantly lower in the 6-mo group [adjusted OR: 0.61 (95% CI: 0.41, 0.93)], even after control for geographic origin, urban compared with rural location, maternal education, birth weight, and number of siblings in the household. The reduction in the risk of hospitalization for gastrointestinal infection was not statistically significant however. To further explore the timing of the protective effect against gastrointestinal infection, we used a Poisson model (within GLIMMIX) to estimate the adjusted IDR during the periods 0–3, 3–6, and 6–12 mo; the analysis for 6–12 mo was restricted to those infants who continued breastfeeding (ie, were not weaned) throughout the period. As expected, no

**TABLE 3**  
Comparison of anthropometric z scores in infants exclusively breastfed for 3 or ≥6 mo<sup>1</sup>

	3-mo Group	6-mo Group	Difference (95% CI) <sup>2</sup>
Weight-for-age z score			
6 mo	0.61 ± 0.83 <sup>3</sup>	0.53 ± 0.84	0.08 (0.02, 0.15)
9 mo	0.57 ± 0.86	0.48 ± 0.88	0.09 (0.02, 0.15)
12 mo	0.61 ± 0.86	0.53 ± 0.94	0.08 (0.02, 0.15)
Length-for-age z score			
6 mo	0.05 ± 0.94	-0.06 ± 0.95	0.11 (0.03, 0.18)
9 mo	0.08 ± 0.96	-0.06 ± 0.97	0.14 (0.06, 0.21)
12 mo	0.13 ± 0.91	0.12 ± 0.90	0.01 (-0.07, 0.09)
Weight-for-length z score			
6 mo	0.64 ± 1.00	0.64 ± 0.96	-0.01 (-0.09, 0.08)
9 mo	0.73 ± 0.99	0.75 ± 0.98	-0.02 (-0.10, 0.07)
12 mo	0.80 ± 0.95	0.71 ± 0.98	0.09 (-0.01, 0.17)

<sup>1</sup>Adjusted with the use of the MIXED procedure (SAS Institute Inc, Cary, NC) for geographic region, urban or rural location, hospital of birth, maternal education, number of siblings in household, and weight-for-age, length-for-age, or weight-for-length at birth and at 3 mo.

<sup>2</sup>The tabulated difference is statistically significant at  $P < 0.05$  if the 95% CI excludes the null value of 0.

<sup>3</sup> $\bar{x} \pm SD$ .

significant difference was observed from 0 to 3 mo (when both groups were exclusively breastfed); the adjusted IDR in the 6-mo group was 0.97 (95% CI: 0.46, 2.04). The protective effect was very strong during the 3–6-mo period [adjusted IDR: 0.35 (95% CI: 0.13, 0.96)] but did not persist at 6–12 mo [adjusted IDR: 0.90 (95% CI: 0.46, 1.78)].

## DISCUSSION

The main benefit associated with exclusive breastfeeding for 6 mo compared with that associated with exclusive breastfeeding at 3 mo was a significant reduction in the risk of gastrointestinal infection. This benefit was limited to the actual period (from 3 to 6 mo) during which feeding differed in the 2 study groups, ie, the protective effect did not persist beyond 6 mo but was of substantial magnitude despite the extremely low incidence of gastrointestinal infection in both study groups (Table 4). Continued exclusive breastfeeding for 6 mo reduced the incidence density by nearly two-thirds from 3 to 6 mo.

Complementary feeding between 3 and 6 mo was associated with increases in both weight gain and length gain during that period, although by 12 mo the difference in weight-for-age z score was only 0.08, and no significant difference was observed in either length-for-age or weight-for-length. Weight-for-age and

weight-for-length z scores remained well above the reference mean of 0 through 12 mo, which reflects both the selection criteria (inclusion of healthy newborns with a birth weight ≥ 2500 g and a gestational age ≥ 37 wk) for participation in PROBIT (18, 19) and the rapid average weight gain of PROBIT infants (22). The latter may reflect culturally determined infant feeding practices in Belarus.

An intriguing finding was a significantly larger head circumference at 12 mo in the 6-mo group. This difference was small (0.19 cm), however, and may have occurred by chance. Whether the difference will persist over time and whether it is associated with the previously reported benefits in neurocognitive function associated with prolonged breastfeeding (23–29) is uncertain but will be an important focus of the future follow-up of PROBIT infants.

Despite the substantially and significantly lower risk of atopic eczema associated with random assignment to the experimental intervention in our initial trial (19), no significant difference was observed for this outcome (or for recurrent wheezing) in the observational comparison of infants in the 3-mo and 6-mo groups. When combined with the results of our trial, these observational findings suggest that exclusive breastfeeding for 3 mo with continued breastfeeding through ≥ 6 mo provides equivalent protection against atopic eczema to exclusive breastfeeding for 6 mo. These data are consistent with those from other studies included

**TABLE 4**  
Comparison of first-year incidence of atopic and infectious outcomes in infants exclusively breastfed for 3 or ≥6 mo<sup>1</sup>

Outcome	3-mo Group (n = 2862)	6-mo Group (n = 621)	Adjusted OR (95% CI) <sup>2</sup>
	n (%)	n (%)	
Atopic eczema	78 (2.7)	17 (2.7)	1.14 (0.65, 2.02)
≥ 2 Episodes of wheezing	6 (0.2)	2 (0.3)	1.49 (0.66, 3.36)
≥ 1 Episode of gastrointestinal infection	213 (7.4)	31 (5.0)	0.61 (0.41, 0.93)
Hospitalization for gastrointestinal infection	64 (2.2)	11 (1.8)	0.75 (0.38, 1.04)
≥ 2 Episodes of any respiratory infection	969 (33.9)	190 (30.6)	0.86 (0.69, 1.07)
≥ 2 Episodes of upper respiratory infection	887 (31.0)	175 (28.2)	0.85 (0.68, 1.06)
≥ 1 Episode of otitis media	147 (5.1)	41 (6.6)	1.14 (0.76, 1.64)
Hospitalization for respiratory infection	411 (14.4)	69 (11.1)	0.96 (0.71, 1.30)


<sup>1</sup>Adjusted with the use of the GLIMMIX procedure (SAS Institute Inc, Cary, NC) for geographic region, urban or rural location, hospital of birth, birth weight, maternal education, number of siblings in household, and (for wheezing and respiratory infectious outcomes) maternal smoking.

<sup>2</sup>The tabulated odds ratio (OR) is statistically significant at  $P < 0.05$  if the 95% CI excludes the null value of 1.



in a recent systematic review including longer-term atopic outcomes (especially asthma) as well (30).

Two important limitations of our study should be mentioned. First, although PROBIT was designed as a randomized trial, the study groups reported herein are based on an observational design. In other words, randomized allocation has been ignored in these analyses and, thus, residual confounding might theoretically have biased our results. Second, anthropometric measurements were not standardized among study sites (*see* Subjects and Methods); the increased (random) error in measuring weight, length, and head circumference should have been nondifferential and therefore might have reduced the observed differences in growth outcomes between the 2 study groups.

In summary, Belarussian infants breastfed exclusively for  $\geq 6$  mo had a significantly lower incidence and incidence density of gastrointestinal infection between 3 and 6 mo of age than did infants exclusively breastfed for 3 mo (with continued mixed breastfeeding through 6 mo); morbidity due to respiratory infection and atopic eczema in the first year of life was not significantly different between the 2 groups. No persistent benefits of introducing complementary foods between 3 and 6 mo were shown. We observed more rapid weight and length gains between 3 and 6 mo in infants who were introduced to complementary foods between 3 and 6 mo, but little difference remained by 12 mo. Combined with other evidence that was recently systematically reviewed (30), there are no apparent risks in recommending, as a general policy, exclusive breastfeeding for the first 6 mo of life. Thus, our findings support the World Health Assembly's recently revised infant feeding recommendation that mothers exclusively breastfeed their infants for 6 mo (31). Future follow-up of the PROBIT cohort should provide information about possible long-term consequences of these differences in duration of exclusive breastfeeding. 

MSK, ZS, ID, J-PC, SS, BC, EH, GS, and IM participated in the study design. ID, IV, GS, NB, and TD collected the data. TG, TD, MSK, RWP, J-PC, and SS analyzed the data. MSK, RWP, J-PC, SS, BC, and EH wrote the manuscript. None of the authors had any financial or personal interest in any company or organization sponsoring the research.

## REFERENCES

- Rowland M, Barrell R, Whitehead R. Bacterial contamination in traditional Gambian weaning foods. *Lancet* 1978;1:136–8.
- Rowland M. The weanling's dilemma: are we making progress? *Acta Paediatr Scand* 1986;323(suppl):33–42.
- WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet* 2001;355:451–5.
- Howie PW, Forsyth JS, Ogston SA, Clark A, du V Florey C. Protective effect of breast feeding against infection. *BMJ* 1990;300:11–6.
- Cunningham AS, Jelliffe DB, Jelliffe EFP. Breast-feeding and health in the 1980's: a global epidemiologic review. *J Pediatr* 1991;118:659–66.
- Beaudry M, Dufour R, Marcoux S. Relation between infant feeding and infections during the first six months of life. *J Pediatr* 1995;126:191–7.
- Dewey K, Heinig M, Nommsen-Rivers L. Differences in morbidity between breast-fed and formula fed infants. *J Pediatr* 1995;126:696–702.
- Raisler J, Alexander C, O'Campo P. Breast-feeding and infant illness: a dose-response relationship? *Am J Public Health* 1999;89:25–30.
- WHO Working Group on Infant Growth. An evaluation of infant growth. Geneva: World Health Organization, 1994.
- Dewey K, Peerson J, Brown K, et al. Growth of breast-fed infants

deviates from current reference data: a pooled analysis of US, Canadian, and European data sets. *Pediatrics* 1995;96:495–503.

- Nielsen G, Thomsen B, Michaelsen K. Influence of breastfeeding and complementary food on growth between 5 and 10 months. *Acta Paediatr* 1998;87:911–7.
- Hediger M, Overpeck M, Ruan W, Troendle J. Early infant feeding and growth status of US-born infants and children aged 4–71 mo: analyses from the third National Health and Nutrition Examination Survey, 1988–1994. *Am J Clin Nutr* 2000;72:159–67.
- Haschke F, van't Hof M, Euro-Growth Study Group. Euro-Growth references for breast-fed boys and girls: influence of breast-feeding and solids on growth until 36 months of age. *J Pediatr Gastroenterol Nutr* 2000;31:S60–71.
- World Health Organization. Nutrition. Information and attitudes among health personnel about early feeding practices. *Wkly Epidemiol Rec* 1995;28:117–20.
- United Nations Children's Fund. Facts for life. Wallingford, United Kingdom: P&LA, 1993.
- Lutter C. Length of exclusive breastfeeding: linking biology and scientific evidence to a public health recommendation. *J Nutr* 2000;130:1335–8.
- Committee on Nutrition, American Academy of Pediatrics. Pediatric nutrition handbook. 4th ed. Elk Grove Village, IL: American Academy of Pediatrics, 1998.
- Kramer MS, Chalmers B, Hodnett ED, et al. Promotion of breastfeeding intervention trial (PROBIT): a cluster-randomized trial in the Republic of Belarus. In: Koletzko B, Michaelsen KF, Hernell O, eds. Short and long term effects of breast feeding on child health. New York: Kluwer Academic/Plenum Publishers, 2000:327–45.
- Kramer MS, Chalmers B, Hodnett ED, et al. Promotion of breastfeeding intervention trial (PROBIT): a randomized trial in the Republic of Belarus. *JAMA* 2001;285:413–20.
- Rubin D, Leventhal J, Krasilnikoff P, et al. Relationship between infant feeding and infectious illness: a prospective study of infants during the first year of life. *Pediatrics* 1990;85:464–71.
- US Department of Health, Education and Welfare. NCHS growth curves for children, birth-18 years. Washington, DC:US DHEW, 1977. [DHEW Publication (PHS) 78-1650.]
- Kramer MS, Guo T, Platt RW, et al. Breastfeeding and infant growth: biology or bias? *Pediatrics* 2002;110:343–7.
- Lucas A, Morley R, Cole T, et al. Breast milk and subsequent intelligence quotient in children born preterm. *Lancet* 1992;339:261–4.
- Lanting C, Fidler V, Huisman M, et al. Neurological differences between 9-year old children fed breast-milk or formula-milk as babies. *Lancet* 1994;344:1319–22.
- Horwood L, Fergusson D. Breastfeeding and later cognitive and academic outcomes. *Pediatrics* [serial online] 1998;101:e9. Internet: <http://www.pediatrics.org/cgi/content/full/101/1/e9> (accessed 30 April 2003).
- Anderson J, Johnstone B, Remley D. Breast-feeding and cognitive development: a meta-analysis. *Am J Clin Nutr* 1999;70:525–35.
- Vestergaard M, Obel C, Henriksen T, Sørensen H, Skajaa E, Østergaard J. Duration of breastfeeding and developmental milestones during the latter half of infancy. *Acta Paediatr* 1999;88:1327–32.
- San Giovanni J, Berkey C, Dwyer J, Colditz G. Dietary essential fatty acids, long chain polyunsaturated fatty acids, and visual resolution acuity in healthy fullterm infants: a systematic review. *Early Hum Dev* 2000;57:165–88.
- San Giovanni J, Parra-Cabrera S, Colditz G, Berkey C, Dwyer J. Meta-analysis of dietary essential fatty acids and long chain polyunsaturated fatty acids as they relate to visual resolution acuity in healthy preterm infants. *Pediatrics* 2000;105:1292–8.
- Kramer MS, Kakuma R. The optimal duration of exclusive breastfeeding. A systematic review (Cochrane Review). In: The Cochrane Library. Oxford, United Kingdom: Update Software, 2002. (Issue 3.)
- World Health Organization. Infant and young child nutrition. Geneva: World Health Organization, 2001. (no. 54.2.)

