Promotion of breastfeeding intervention trial (PROBIT)

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Promotion of Breastfeeding Intervention Trial (PROBIT)
A Randomized Trial in the Republic of Belarus

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B REASTFEEDING HAS BEEN WIDELY reported to reduce the risk of infection[1-11] and atopic disease[1,12-15] in the recipient infant and child. The effect of breastfeeding in protecting against infection is more striking, and thus easier to demonstrate, in settings where poverty, malnutrition, and poor hygiene are preva-

Context Current evidence that breastfeeding is beneficial for infant and child health is based exclusively on observational studies. Potential sources of bias in such studies have led to doubts about the magnitude of these health benefits in industrialized countries.

Objective To assess the effects of breastfeeding promotion on breastfeeding duration and exclusivity and gastrointestinal and respiratory infection and atopic eczema among infants.

Design The Promotion of Breastfeeding Intervention Trial (PROBIT), a cluster-randomized trial conducted June 1996–December 1997 with a 1-year follow-up.

Setting Thirty-one maternity hospitals and polyclinics in the Republic of Belarus.

Participants A total of 17 046 mother-infant pairs consisting of full-term singleton infants weighing at least 2500 g and their healthy mothers who intended to breastfeed, 16 491 (96.7%) of which completed the entire 12 months of follow-up.

Interventions Sites were randomly assigned to receive an experimental intervention (n = 16) modeled on the Baby-Friendly Hospital Initiative of the World Health Organization and United Nations Children's Fund, which emphasizes health care worker assistance with initiating and maintaining breastfeeding and lactation and postnatal breastfeeding support, or a control intervention (n = 15) of continuing usual infant feeding practices and policies.

Main Outcome Measures Duration of any breastfeeding, prevalence of predominant and exclusive breastfeeding at 3 and 6 months of life and occurrence of 1 or more episodes of gastrointestinal tract infection, 2 or more episodes of respiratory tract infection, and atopic eczema during the first 12 months of life, compared between the intervention and control groups.

Results Infants from the intervention sites were significantly more likely than control infants to be breastfed to any degree at 12 months (19.7% vs 11.4%; adjusted odds ratio [OR], 0.47; 95% confidence interval [CI], 0.32-0.69), were more likely to be exclusively breastfed at 3 months (43.3% vs 6.4%; $P<.001$) and at 6 months (7.9% vs 0.6%; $P = .01$), and had a significant reduction in the risk of 1 or more gastrointestinal tract infections (9.1% vs 13.2%; adjusted OR, 0.60; 95% CI, 0.40-0.91) and of atopic eczema (3.3% vs 6.3%; adjusted OR, 0.54; 95% CI, 0.31-0.95), but no significant reduction in respiratory tract infection (intervention group, 39.2%; control group, 39.4%; adjusted OR, 0.87; 95% CI, 0.59-1.28).

Conclusions Our experimental intervention increased the duration and degree (exclusivity) of breastfeeding and decreased the risk of gastrointestinal tract infection and atopic eczema in the first year of life. These results provide a solid scientific underpinning for future interventions to promote breastfeeding.
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lent.[2-5] All of the scientific evidence regarding breastfeeding and morbidity in healthy, full-term infants is based on observational studies, because it is neither feasible nor ethical to randomly assign such infants to be breastfed vs formula-fed. Such studies are plagued by numerous sources of bias related to measurement, selection, confounding, and reverse causality.[16-18] These potential biases have created doubt about the magnitude, and even the existence, of a protective effect of breastfeeding against infection in developed country settings.[18]

A rigorous and feasible research strategy to overcome these biases would be to assess whether infants who are randomly allocated to a breastfeeding promotion intervention experience a reduced risk of infection. The mother's decision to initiate breastfeeding is usually made prenatally or even before becoming pregnant and prenatal interventions are often logistically difficult and expensive.[19] Therefore, it may be preferable to focus on improving duration and exclusivity among women who have decided to initiate breastfeeding. The World Health Organization (WHO) and United Nations Children's Fund (UNICEF) have combined 10 such interventions ("steps") in developing the Baby-Friendly Hospital Initiative (BFHI, available at http://www.unicef.org/programme/nutrition/infantfe/tensteps.htm).[20] Based on systematic reviews of controlled clinical trials available in the Cochrane Database of Systematic Reviews,[21-24] evidence suggests that duration and exclusivity of breastfeeding are increased by help with positioning and other aspects of breastfeeding technique (step 5), demand feeding (step 8), and postnatal support (step 10).

The Promotion of Breastfeeding Intervention Trial (PROBIT) builds on the scientific evidence concerning components of the BFHI. Not only is PROBIT the first randomized trial of the BFHI as a whole, but the large number of infants and mothers studied provides an opportunity to assess the direct relationship between a breastfeeding promotion intervention and infant health and the experimental link between infant feeding and infant morbidity in healthy mothers and their infants.

METHODS
Research Design

This study was a multicenter randomized controlled trial using cluster randomization. Maternal hospitals and their corresponding polyclinics, the "clusters" randomized in our study, were originally paired according to geographic region within Belarus (Minsk city, Minsk region, Brest, Mogilev, Gomel, Vitebsk, and Grodno), urban vs rural status, number of deliveries per year (±500 if <2500, or ≥2500), and breastfeeding initiation rates at hospital discharge (±5%). Most of the maternity hospitals located in large cities (Minsk, Vitebsk, Brest, and Mogilev) are affiliated with several polyclinics.

To maximize efficiency, enrollment of mothers was limited to those whose infants were to be followed up at a single selected polyclinic affiliated with each of these large maternity hospitals. Intervention allocation was based on a double-randomization procedure. First, a random number table was used to assign a 2-digit random number to each of the study sites. Within each pair, the hospital and polyclinic sites corresponding to the higher and lower numbers were assigned to interventions A and B, respectively. Later, at a public gathering of the Canadian and Belarussian investigators, a coin flip determined that B sites would receive the experimental intervention, and A sites would receive the control intervention.

We chose to carry out this trial in Belarus rather than North America or Western Europe because maternity hospital practices in Belarus and other former Soviet republics are similar to those in North America and Western Europe 20 to 30 years ago and thus provide a greater potential contrast between intervention and control study sites. However, Belarus resembles Western developed countries in 1 very important respect: basic health services and sanitary conditions are very similar. An uncontaminated water supply is ensured and monitored throughout the republic by public health authorities, and hospital clinics are abundant and readily accessible, even in rural areas.

Mothers were considered eligible for participation if they expressed an intention to breastfeed on admission to the postpartum ward, had no illnesses that would contraindicate breastfeeding or severely compromise its success, and had given birth to a healthy singleton infant of 37 weeks' or more gestation, 2500 g or more birth weight, and Apgar score 5 or higher at 5 minutes. The study received approval from the institutional review board of the Montreal Children's Hospital, and signed consent in Russian was obtained from all participating mothers.

Intervention

The experimental intervention was modeled on the BFHI. Because no breastfeeding support groups existed in Belarus at the time PROBIT was designed, step 10 (postnatal support) of the BFHI was expanded to include the intervention polyclinics. Participants, usually the chief obstetrician and chief pediatrician, from each of the intervention maternity hospitals and polyclinics, respectively, received the 18-hour BFHI lactation management training course, which was organized by the European Regional Office of the WHO. The course emphasized methods to maintain lactation, promote exclusive and prolonged breastfeeding, and resolve common problems.

Full implementation of the experimental intervention required 12 to 16 months to train all midwives, nurses, and physicians providing care to study mothers and infants during labor, delivery, and the postpartum hospital stay, and all pediatricians and nurses working at the polyclinics. Monitoring visits by members of the Canadian and Belarussian Steering prior to and during recruitment and follow-up at each site ensured that the hospital and polyclinic procedures and policies were consistent with the BFHI at the intervention sites, and that the control sites did not institute any changes that would ren-

der their maternity hospitals or polyclinics more baby friendly.

Data Collection

Sociodemographic and clinical information was recorded on an enrollment form completed during the postpartum stay. In Belarus, infants are seen monthly for routine well-child visits and whenever they are ill. At 1, 2, 3, 6, 9, and 12 months, polyclinic pediatricians completed a data form containing detailed information about infant feeding; measurement of infant weight, length, and head circumference; the occurrence of symptoms of gastrointestinal or respiratory tract infection, rash, other illnesses; and hospitalizations since birth or the most recent clinic visit. In the case of 1 or more missed clinic visits, data were updated at the next study visit to include all illness occurring since the previous study visit and the date of weaning, if applicable.

The primary study outcome was the risk of 1 or more episodes of gastrointestinal tract infection. Secondary outcomes included the risk of 2 or more episodes of any respiratory tract infection (including upper respiratory tract infection, otitis media, croup, wheezing, or pneumonia), 2 or more upper respiratory tract infections; atopic eczema; recurrent (≥2 episodes) wheezing; the prevalence of any breastfeeding at 3, 6, 9, and 12 months of age; and the prevalence of exclusive and predominant breastfeeding at 3 and 6 months. Consistent with WHO definitions,[25] infants were considered as exclusively breastfed for 3 or 6 months if they received no solids, nonbreast milk, or water or other liquids (other than vitamins or medications) at all visits up to and including the 3- and 6-month visits, respectively. They were considered predominantly breastfed at these ages if they received no solids or nonbreast milk; juices, water, teas, and other liquids were permitted in this category. The criteria for gastrointestinal and upper respiratory tract infection were based on the algorithms of Rubin et al,[6] modified to ensure a minimum duration of 2 days: at least 2 symptoms among increased stool frequency, loose stools, vomiting, and temperature greater than 38.5°C for gastrointestinal tract infection and at least 2 symptoms among runny nose, cough, fast breathing, and temperature greater than 38.5°C for upper respiratory tract infection. Rashes were classified as atopic eczema if they lasted at least 2 weeks or recurred after clearing for at least 1 week, were itchy, and occurred on the face and/or the extensor surfaces of the arms and/or the extensor surfaces of the legs.

Sample Size

Based on the available evidence concerning the effectiveness of the individual components of the BFHI, we estimated that the intervention would reduce breastfeeding discontinuation by 3 months from 50% (reported in a prior Belarussian Ministry of Health survey) to 35%. Three months of any breastfeeding was chosen as the primary basis for calculating breastfeeding prevalence based on the data of Howie et al[7]; in initially breastfed infants who were weaned at 13 weeks vs those breastfed to any degree and for at least 13 weeks, the relative risk of gastrointestinal tract infection (the primary outcome) associated with early weaning was approximately 2. From our previous surveillance studies in French day care centers using similar surveillance techniques and definitions,[26] we estimated that the expected delay in weaning would reduce the risk of 1 or more episodes of gastrointestinal tract infection from 60% to 54%.

Assuming 500 mothers and infants enrolled at each maternity hospital, a design using 15 pairs of study sites would provide a power of greater than 80% to detect such a difference at a 2-sided α level of .05, even assuming a worst-case scenario of high variability between sites and totally ineffective pairing.[27,28] To ensure that 15 hospital pairs would be included in the final study sample, we randomized 17 pairs to provide a margin of security against withdrawals or unforeseen logistical problems at a few sites. As it turned out, 2 of the maternity hospitals refused to carry out their allocated intervention following randomization, and 1 of the

Figure 1. Flowchart of Study Sites and Participants
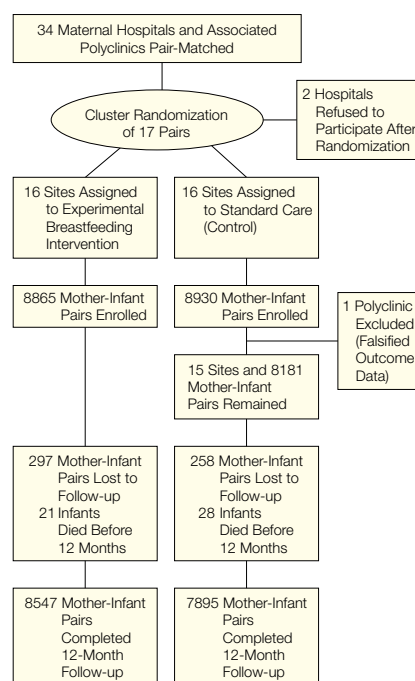
polyclinics was discovered to have falsified their outcome data, leaving 31 sites (16 intervention and 15 control) and 15 intact original pairs (**FIGURE 1**).

Cohort Recruitment, Data Validation, and Follow-Up

Recruitment began in June 1996 and by October 1996 all randomized sites were recruiting mothers and infants. To ensure an adequate sample size at each of the study sites, recruitment continued until the end of December 1997. After eliminating the 749 mother-infant pairs enrolled at the site excluded because of falsified outcome data, a total of 17 046 mother-infant pairs were enrolled at the 31 remaining sites, making this, to our knowledge, the largest randomized trial ever undertaken in the area of human lactation.

Because the observers of the clinical outcomes were the same pediatricians involved in implementing the experimental or control interventions, they could not be blinded to the intervention vs control status of the study infants. One routine audit of data valid-

ity was therefore carried out at each study site. Twenty polyclinic charts were selected at random and the data contained therein bearing on gastrointestinal tract infections, respiratory tract infections, and any breastfeeding at 3 months were compared with the data on these outcomes recorded on the PROBIT polyclinic visit forms. Of the 20 audited polyclinic charts, maternal interviews were also carried out for 10. The audit compared the occurrence of 1 or more gastrointestinal tract infections and 2 or more respiratory tract infections. For breastfeeding at 3 months, agreement was considered present if the date of weaning in the polyclinic chart or by maternal interview was within 15 days of the date recorded on the PROBIT polyclinic visit forms.

Of the 17 046 mother-infant pairs enrolled, only 555 (3.3%) were lost at some time during their first year, including 297 (3.4%) in the intervention group and 258 (3.2%) in the control group (Figure 1). However, because information on breastfeeding duration and illness episodes was updated at each clinic visit, analysis of each outcome is based on all infants remaining in the study at the time that outcome was measured, even if they were lost to follow-up before 12 months.

Data Analysis

All outcomes were analyzed based on the intention-to-treat principle, ie, according to randomized allocation to the experimental vs control intervention. But removal of 2 study sites from 2 different original pairs and data falsification at a third site undermined our original plan to analyze the trial data using paired *t* tests. As recommended by an external monitoring committee, we based our primary analytic strategy on stratification rather than pairing, with multivariate modeling of group- and individual-level covariates to allow statistical inference at the level of individual women and infants. We used a dichotomous stratification for region, west (Brest and Grodno) vs east (all others), and urban vs rural location. We compared the intervention and control groups at baseline using the PROC MIXED procedure in SAS for continuous variables and PROC FREQ for categorical variables (version 6.12; SAS Institute, Cary, NC). The primary analysis of study outcomes was implemented using the GLIMMIX procedure in the same version of SAS, with the cluster as the unit of analysis and cluster-based indicators for region and urban vs rural status. To control for individual-level covariates, multivariate models (using GLIMMIX in SAS) for breastfeeding outcomes contained individual-level terms for birth weight (2500-2999, 3000-3499, ≥3500 g), maternal age (<20, 20-34, ≥35 years), and history of having breastfed a previous infant for 3 months for longer (yes vs no). For gastrointestinal and respiratory tract infection, the individual-level covariates included birth weight and number of other children living in the household (0, 1, ≥2); maternal smoking during pregnancy (yes vs no) was also included for respiratory tract infection. Finally, for analysis of atopic eczema and other rashes, only family atopic history (positive history of asthma, allergic rhinitis, or atopic eczema in the mother, the father, or a sibling) was included as an individual-level covariate. Results of all GLIMMIX models are reported as adjusted odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS

As shown in TABLE 1, the randomization produced intervention and control sites with similar distributions of maternal age, maternal education, atopic family history, previous breastfeeding experience, other children living in the household, smoking during pregnancy, cesarean delivery, and infant sex distribution. Small differences in several of these categorical variables are attributable to the cluster-based randomization. The mean birth weight, gestational age, and 5-minute Apgar scores were virtually identical in the 2 groups.

TABLE 2 summarizes the audit results for any breastfeeding, 1 or more episodes of gastrointestinal tract infection, and 2 or more episodes of respira-

Table 1. Baseline Comparison of Intervention and Control Groups*

Variable	Intervention Group (n = 16 Sites, 8865 Mother-Infant Pairs)	Control Group (n = 15 Sites, 8181 Mother-Infant Pairs)
Mothers		
Maternal age, y		
<20	14.4	13.5
20-34	81.4	82.3
≥35	4.2	4.2
Maternal education		
Incomplete secondary	4.6	3.2
Complete secondary	33.9	30.4
Advanced secondary or partial university	53.4	47.1
Complete university	14.1	13.0
Positive atopic family history	5.2	3.5
Breastfed previous child ≥3 mo	24.4	24.7
Other children living in household		
0	59.8	56.1
1	32.3	34.9
≥2	7.9	9.1
Smoking during pregnancy	2.8	1.8
Cesarean delivery	12.6	10.5
Infants		
Male	51.7	51.9
Mean birth weight, g	3448	3446
Mean gestational age, wk	39.4	39.3
Mean 5-min Apgar score	8.5	8.6

*Data are presented as percentages unless otherwise indicated.

tory tract infection. Chance-corrected agreement was high for all 3 outcomes, as shown by the high levels of κ, and there was no difference in degree of overreporting or underreporting according to intervention vs control status.

TABLE 3 and **FIGURE 2** summarize the results for any breastfeeding. In the control group, 60% of mothers (range among sites, 46%-78%) were still breastfeeding to some degree at 3 months, considerably higher than the 50% we had estimated based on data prior to initiating our trial. Nonetheless, the intervention group had significantly higher rates of continued breastfeeding at 3 months (73%; range, 64%-87%) and throughout the first year. Even larger differences were observed for degree of breastfeeding, although extremely low rates of exclusive and, at 6 months, predominant breastfeeding in the control group led to GLIMMIX models that did not adequately converge and hence to unreliable estimates of the adjusted ORs. Statistical significance for these comparisons was assessed using unpaired t tests. The proportion of women exclusively breastfeeding at 3 months was 7-fold higher in the experimental group (43.3% vs 6.4%; $P < .001$ by unpaired t test) and more than 12-fold higher at 6 months (7.9% vs 0.6%; $P = .01$). Nearly twice as many women in the intervention group were predominantly breastfeeding at 3 months (51.9 vs 28.3%; adjusted OR, 0.28; 95% CI, 0.16-0.49) and nearly 7 times as many at 6 months (10.6% vs 1.6%; $P = .003$).

As shown in **TABLE 4**, the proportion of infants in the control group who experienced 1 or more episodes of gastrointestinal tract infection in the first year was only 13.2%, far lower than the 60% we had estimated. Nonetheless, the intervention significantly reduced this risk by 40%. For the various respiratory tract infection as outcomes under study, reductions in risk in the intervention group were small and statistically nonsignificant.

TABLE 5 summarizes the results for atopic eczema and other rashes. The occurrence of atopic eczema was reduced by 46% in the intervention group, with a similar reduction in the risk for nonec-

zematous rashes. To verify that the reduction in risk of noneczematous rashes was not merely due to protection against viral exanthems and other infection-related rashes, we also examined the risk for occurrence of noneczematous, noninfectious rashes; the risk reduction was of comparable magnitude. Multivariate models showed a significant asso-

ciation between positive family atopic history and both noneczematous rash (adjusted OR, 1.50; 95% CI, 1.22-1.85) and noneczematous, noninfectious rash (adjusted OR, 1.49; 95% CI, 1.20-1.85), suggesting that some of these rashes may have been atopic despite not meeting our clinical criteria for atopic eczema.

Table 2. Audit Results for Main Outcome Measures*

| Outcome	Polyclinic Chart		Maternal Interview	
	Intervention Group	Control Group	Intervention Group	Control Group
≥1 Gastrointestinal tract infection				
κ (95% CI)	0.91 (0.83-0.99)	0.85 (0.76-0.94)	0.76 (0.61-0.92)	0.74 (0.57-0.90)
Underreporting, %	1	2	3	2
Overreporting, %	1	1	1	4
≥2 Respiratory tract infections				
κ (95% CI)	0.77 (0.70-0.85)	0.86 (0.80-0.92)	0.65 (0.54-0.77)	0.63 (0.51-0.75)
Underreporting, %	8	5	6	4
Overreporting, %	3	2	11	15
Breastfeeding at 3 months				
κ (95% CI)	0.93 (0.88-0.98)	0.91 (0.87-0.96)	0.89 (0.81-0.97)	0.94 (0.89-0.99)
Underreporting, %	2	2	3	1
Overreporting, %	1	2	1	2

*CI indicates confidence interval.

Table 3. Frequencies for Any Breastfeeding and Odds Ratios for Having Been Weaned at 3, 6, 9, and 12 Months*

Infant Age, mo	Intervention Group, %	Control Group, %	Adjusted Odds Ratio (95% CI)†
3	72.7	60.0	0.52 (0.40-0.69)
6	49.8	36.1	0.52 (0.39-0.71)
9	36.1	24.4	0.51 (0.36-0.73)
12	19.7	11.4	0.47 (0.32-0.69)

*CI indicates confidence interval. Tabulated percentages are mean percentages for 16 intervention and 15 control sites.
†Adjusted for birth weight, maternal age, and previous breastfeeding history.

Figure 2. Comparison of Proportion of Infants Still Breastfeeding (to Any Degree) During Year of Follow-up
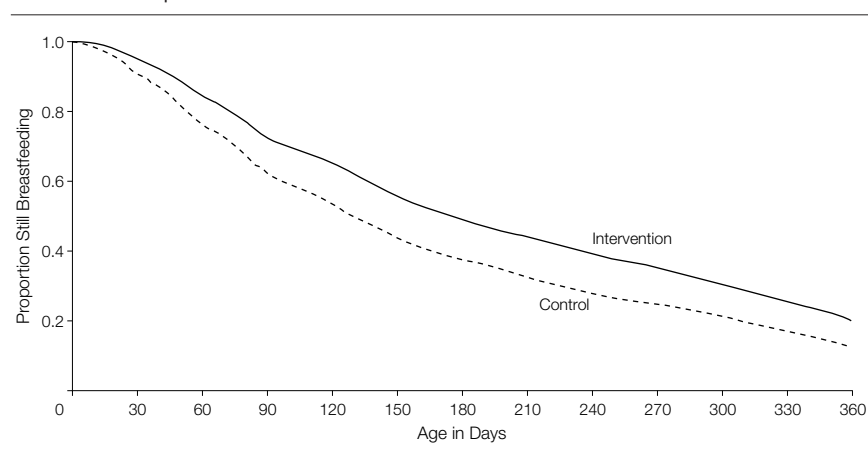
Table 4. Frequencies and Odds Ratios for Infectious Diseases*

Outcome	Intervention Group, %	Control Group, %	Adjusted Odds Ratio (95% CI)†
≥1 Gastrointestinal tract infection	9.1	13.2	0.60 (0.40-0.91)
≥1 Hospitalization for gastrointestinal tract infection	3.2	3.6	0.92 (0.62-1.37)
≥2 Respiratory tract infections‡	39.2	39.4	0.87 (0.59-1.28)
≥2 Upper respiratory tract infections	36.1	36.2	0.87 (0.58-1.30)
≥1 Episode of otitis media	6.2	6.0	1.01 (0.54-1.88)
≥1 Episode of croup	0.5	0.4	0.86 (0.38-1.94)
≥2 Episodes of wheezing	0.6	0.7	0.70 (0.29-1.70)
≥1 Hospitalization for respiratory tract infection	17.9	20.5	0.85 (0.57-1.27)

*CI indicates confidence interval. Tabulated percentages are mean percentages for 16 intervention and 15 control sites.
†Adjusted for birth weight and number of other children in household; respiratory tract infection outcomes also adjusted for maternal smoking during pregnancy.
‡Includes upper respiratory tract infection, otitis media, croup, wheezing, and pneumonia.

Table 5. Frequencies and Odds Ratios for Atopic Eczema and Other Rashes*

Outcome	Intervention Group, %	Control Group, %	Adjusted Odds Ratio (95% CI)†
Any rash	12.3	18.3	0.56 (0.38-0.81)
Atopic eczema	3.3	6.3	0.54 (0.31-0.95)
Noneczematous rash	9.9	13.5	0.59 (0.38-0.92)
Noneczematous, noninfectious rash‡	8.8	11.9	0.61 (0.40-0.93)

*CI indicates confidence interval. Tabulated percentages are mean percentages for 16 intervention and 15 control sites.
†Adjusted for family atopic history.
‡A noninfectious rash denotes a rash that did not occur within 2 days of a gastrointestinal or respiratory tract infection.

A total of 49 deaths occurred among study infants during the 12 months of follow-up, 21 in the intervention group and 28 in the control group, for a total infant mortality rate of 2.3 vs 3.7 per 1000 live births, and an adjusted OR of 0.78 (95% CI, 0.52-1.42). Of note was the occurrence of only 1 death attributed to the sudden infant death syndrome (SIDS) among infants in the intervention group vs 5 SIDS deaths among infants in the control group (*P*=.12 by unpaired *t* test; multivariate model did not converge).

COMMENT

Our breastfeeding promotion intervention, modeled on the BFHI, succeeded in increasing the duration and exclusivity of breastfeeding in the first year of life. These effects occurred against a background of a higher-than-expected breastfeeding duration in the control group. The latter may well be attributable to deteriorating economic conditions in the country during the trial and the higher costs of formula feeding. Even though locally made formula was readily

available, it cost nearly 20% of an average monthly salary by the end of the study. The higher-than-expected breastfeeding duration in the control group might also be due to the receding memory and reduced fear of breastfeeding related to the Chernobyl incident in 1986.

Despite our initial overestimate of the incidence of gastrointestinal tract infection, the risk of such infection was reduced by 40% in the intervention group. This represents a clinically substantial reduction in risk of this important cause of infant morbidity and confirms recent results of a small randomized trial in Mexico.[29] The lower-than-expected incidence of gastrointestinal tract infection is probably related to the fact that all of the study infants were breastfed initially and that most, even in the control group, were breastfed for more than 3 months. The prolonged (approximately 3 years in most cases) obligatory maternity leave and absence of day care centers for infants in Belarus probably also played a role. The low inci-

dence of otitis media and wheezing may have a similar explanation. We do not believe the low incidence of gastrointestinal tract infection reflects underreporting because the definition and surveillance methods used were similar to those we used previously in France,[28] where the incidence was far higher, and because our routine audits confirmed the figures reported on our data forms.

We observed no significant reduction in risk for the respiratory tract infectious outcomes under study. This may also be due to the universal breastfeeding initiation in our study cohort, as well as the high rates of breastfeeding for 3 months or longer, even in the control group. It also reflects the reduced protective effect of breastfeeding against respiratory tract infection that has been noted consistently in previous epidemiologic studies.[1,2,7,8] We do not believe that the absence of a protective effect reflects nondifferential error in measurement of respiratory tract infections because these infections were significantly associated with maternal cigarette smoking (OR, 1.45; CI, 1.17-1.79) for the risk of 2 or more respiratory tract infections.

The experimental intervention also appears to have been successful in reducing the risk of atopic eczema in the first year of life. Although we were surprised that the risk of noneczematous, noninfectious rashes was also reduced in the intervention group, our results suggest that some of these rashes may have been true atopic eruptions that were misclassified by our clinical criteria.

Several limitations of our study should be acknowledged. All of the infectious outcomes were based on clinical criteria; no culture or serologic data were collected. Such data would have added substantial costs and logistical problems to an already large and complex study. Nonetheless, our data audits indicate extremely close agreement between the data recorded on our study data forms and those recorded in the polyclinic charts, as well as high concordance with information obtained from direct maternal interviews. More importantly, we saw no evidence from these audits that

infectious outcomes were underreported in the experimental group or overreported in the control group. Because we were unable to audit the data for atopic eczema and other rashes, the apparent protective effect of the intervention on these outcomes should be interpreted with caution. Our experimental intervention may have been insufficient to effect a reduction in respiratory tract infectious outcomes; more prolonged and exclusive breastfeeding than we were able to achieve might have succeeded in reducing respiratory tract infection. Our study did not have sufficient statistical power to detect an effect of the intervention on mortality. Nonetheless, the observed trend toward a reduced risk of SIDS in the intervention group, although not statistically significant, is consistent with several previous epidemiologic studies reporting a protective effect associated with breastfeeding.[30]

Finally, although basic health services and sanitary conditions are quite similar to those in North America and Western Europe, 2 aspects of the Belarussian health care system may limit the generalizability of our findings. First, the highly centralized Belarussian system undoubtedly helped in implementing the experimental intervention; the intervention maternity hospitals and polyclinics made remarkable changes, documented during our monitoring visits, in their approach to breastfeeding within a very brief prerecruitment period (12-16 months). Second, the prolonged (6-7 days) postpartum stay for routine vaginal deliveries far exceeds those currently found in the West and may help establish good breastfeeding practices and instill maternal confidence.

Despite these limitations, we believe that PROBIT provides an essential scientific underpinning, not only for the BFHI, but for future breastfeeding promotion interventions in both developed and developing country settings. Moreover, the creation of 2 large randomized cohorts with substantial differences in the degree and duration of breastfeeding creates a unique opportunity for future study of longer-term health outcomes, including growth, asthma and other atopic diseases, neurocognitive development, and common adult chronic diseases.

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Dr Helsing participated in the design of the intervention.

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Death must be distinguished from dying, with which it is often confounded.
—Sydney Smith (1771-1845)