

Growth and Micronutrient Status in Children Receiving a Fortified Complementary Food^{1,2}

Chessa K. Lutter,^{3*} Alicia Rodríguez,⁴ Guillermo Fuenmayor,⁴ Luz Avila,⁴ Fernando Sempertegui,⁵ and Jessica Escobar⁶

³Pan American Health Organization, Washington, DC 20037; ⁴Institute of Science and Technology, Ministry of Public Health of Ecuador, Quito, Ecuador; ⁵Faculty of Medicine, Central University of Ecuador, Quito, Ecuador; and ⁶Ministry of Health, El Salvador, San Salvador, El Salvador

Abstract

Linear growth retardation and anemia are the most prevalent nutritional problems in the world; effective interventions are urgently needed. We evaluated Ecuador's National Food Nutrition Program (PANN 2000) that included a micronutrient-fortified complementary food (FCF), *Mi Papilla*, in poor periurban and rural communities of Ecuador. The program is preventive and targeted to all infants and young children living in poor communities and receiving government health services. We compared dietary intake, micronutrient status, and growth over 11 mo in a cohort of children from the catchment areas of the PANN 2000 with same-age control children in nearby communities eligible to enter the program 1 y later. PANN 2000 children enrolled in the program when they were age 9–14 mo and were age 20–25 mo at the final survey. They consumed significantly more energy, protein, fat, iron, zinc, vitamin A, and calcium than control children because of their FCF consumption. Anemia, 76% in both groups at baseline, fell to 27% in PANN 2000 children but only to 44% in control children ($P < 0.001$). The odds of being anemic were 58% lower for PANN 2000 children ($P = 0.003$). The effects on linear growth and weight were limited to children who were older when the program began (12–14 mo) and were significant for weight (interaction with age, 0.38 kg; $P = 0.029$) and positive but not significant for length (0.66 cm; $P = 0.08$). An FCF, including ferrous sulfate, delivered through public health services, is highly effective in improving weight and hemoglobin and reducing anemia. *J. Nutr.* 138: 379–388, 2008.

Introduction

Growth faltering and anemia are widespread among children in the developing world who are <24 mo old (1,2). Poor nutrition during these critical formative years has both short- and long-term consequences (3,4). Short-term consequences include significant morbidity and mortality and delayed physical and mental development (5,6). Long-term consequences include impaired intellectual performance, work capacity, and reproductive capacity and increased risk of chronic diseases (7,8).

The relative effectiveness of interventions to change behaviors vs. provision of foods to improve young child nutrition is not known. Several studies show the efficacy of providing complementary foods to young children living in poverty on anemia and growth under research conditions (9,10). Others have shown an effect on linear growth of improved feeding behaviors (11,12). Less information is available on the effectiveness of such interventions when administered as individual interventions or together through public health services where delivery is embedded in routine care and compliance is not controlled (13).

The nutritional situation of infants and young children in Ecuador is characterized by linear growth retardation and a high prevalence of anemia consistent with global findings (2). The prevalence of anemia (hemoglobin < 110 g/L) of 72% in children <1 y of age (14) is higher than found in the only nationally representative nutrition survey 11 y earlier (15). A study in the 5 poorest provinces in Ecuador in children aged 12–59 mo showed serum retinol < 0.70 $\mu\text{mol/L}$ (20 $\mu\text{g/dL}$) in 18% of rural children and 13% of urban children (16).

Ecuador launched its National Food Nutrition Program (PANN 2000)⁷ in 2000 during an acute economic crisis to prevent malnutrition in young children by improving feeding behaviors and dietary quality. It represents a substantial departure from the previous nutrition program. To reach the poorest children during their most vulnerable period of development, it targeted all children between birth and 24 mo living in conditions of extreme poverty rather than children < 5 y of age with low weight-for-age, many of whom were already likely to be permanently stunted, but with adequate weight-for-height. Rather than providing staple foods to the malnourished child's family, the program sought to improve the quality of the young child's diet by providing a specifically designed fortified complementary food (FCF) beginning at 6 mo. PANN 2000 is a national publicly financed program present throughout the country. Administered by the Ministry of Public Health (MSP),

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⁷ Abbreviations used: FCF, fortified complementary food; MSP, Ministry of Public Health; PANN 2000, National Food Nutrition Program of Ecuador.

* To whom correspondence should be addressed. E-mail: lutterch@paho.org.

PANN 2000 reached ~125,000 infants and young children at the time of the evaluation in 1607 health centers in the poorest parishes.

The evaluation reported here was conducted in poor periurban and rural communities in Ecuador. The impact of 11 mo of participation in PANN 2000 was evaluated in the catchment populations of 10 participating government health clinics and 6 nearby control clinics. We evaluated both the process of the implementation of PANN 2000 and the impact with respect to maternal knowledge about child nutrition, maternal behavior and feeding practices, dietary intakes, micronutrient status, morbidity, and growth.

Methods

Study site and population. The evaluation was undertaken in the Canton of Santo Domingo de Los Colorados in the Province of Pinchincha, located ~3 h by car from the capital of Ecuador in a low-lying malaria-endemic coastal area. Santo Domingo is a rapidly growing area because of its favorable location between the coast and the highlands. It comprises poor urban, periurban, and rural communities known to have a high level of both in- and out-migration and is characterized by low and insecure income, poor housing, and a general lack of 1 or more essential services (piped water, reliable electricity supply, sewage disposal). It has a prevalence of stunting (length-for-age Z-score < -2 SD) of 24.6, similar to the national median (17). The evaluation design took advantage of the planned rolling implementation of PANN 2000. Health centers in communities where the program began served as the program group and health centers in neighboring, apparently similar communities, where the program was to be implemented 1 y later, served as the control group.

Design. This evaluation was quasi-experimental with nonrandomly chosen control subjects. Initially, the communities in the lowest (5th) poverty quintile were targeted for PANN 2000 with the incorporation of the 4th quintile at a later date. Thus, a priori the program group was expected to be poorer than the control group. Randomization was not possible as the government was committed to intervene in the poorest communities. No effort was made to affect program implementation so that its effectiveness would be evaluated under actual conditions.

To maximize the potential to measure program impacts, the age criterion for selection was 6–11 mo at baseline. A census was undertaken to identify households with eligible infants in the catchments of all 10 health clinics serving the health district of Los Rosales where PANN 2000 was to be implemented first and in the 6 health clinics in the neighboring health district of La Concordia where PANN 2000 was to be implemented 1 y later. Parents were informed of the evaluation protocol and asked to sign a consent form; there were few refusals. The evaluation was conducted by the research arm of MSP, which functioned autonomously from the PANN 2000 implementing team and was approved by the ethics committee of both MSP and the Pan American Health Organization. All control children were entered into PANN 2000 within 1 mo of the final survey.

The PANN 2000 program. PANN 2000 has 5 major components: 1) information, education, and communication; 2) training of health workers in infant and young child nutrition and counseling skills; 3) community participation; 4) provision of a FCF (*Mi Papilla*); and 5) monitoring and evaluation. The first component aimed to raise awareness of the importance of good nutrition during early childhood, inform families and communities about PANN 2000, and encourage families with young children to enroll. The training component aimed to provide health workers with information and skills needed to implement the program and to improve their knowledge and communication skills so that mothers were given appropriate age-specific child-feeding messages, including the use of *Mi Papilla*. The community participation component consisted of forming parent committees to select a distribution point for *Mi Papilla* and identify children in the targeted age range.

Mi Papilla consists of a daily ration of 65 g dry product that provides 275 kcal/d (1150.6 kJ/d) and has an energy density of 1.2 kcal/g (5.0 kJ/g) when mixed with the appropriate amount of water. It is designed to provide 10 g protein; 6 g lipid; 100% of the daily requirement of iron (as ferrous sulfate), folic acid, and zinc (as zinc sulfate); 60% of the daily requirement of vitamin C, the B vitamins, and magnesium; and 30% of the daily requirement of vitamin A, calcium, and phosphorus (Table 1). Macronutrients are provided by dry skim milk (minimum 15% of energy), sugar (maximum 10% of energy), cereal and legume flours (rice, corn, rye, soy), and vegetable oil (3% of total energy provided by the essential fatty acids linoleic and linolenic acid). The manufacturer can decide the exact proportions of cereal and legume flours, but they must provide the required nutrient profile. *Mi Papilla* is precooked and requires only a clean source of water for preparation and feeding. It complies with the Codex Alimentarius Standard for Processed Cereal-Based Foods for Infants and Children (Standard 74–1981) (20). Its quality is ensured through microbiological, bromatological, and micronutrient analyses.

Evaluation. We hypothesized that 3 program components (training of health workers in infant and young child feeding and counseling skills, delivery of information, education, and communication, and providing a FCF) would lead to a series of changes in feeding practices and dietary quality that would ultimately improve the growth and micronutrient status of children. The baseline survey was conducted just before the projected implementation of PANN 2000 in March 2002 in infants aged 6–11 mo. However, program implementation was delayed for 3 mo and the final survey was rescheduled to occur 3 mo after originally planned. Children were aged 9–14 mo when enrolled and 20–25 mo at the final

TABLE 1 Summary of nutritional requirements and nutritional characteristics of *Mi Papilla* per daily ration of 65 g and per 100 g

Energy and nutrients	Dietary reference values (18) ¹			<i>Mi Papilla</i>	
	6–8 mo	9–11 mo	12–24 mo	65 g	100 g
Energy, ² kcal	615 (202)	686 (307)	894 (548)	275	423
Protein, g	9.1 (2.0)	9.6 (3.1)	10.9 (5.0)	10	16
Fat, g				6	10
Vitamins					
Vitamin A, ³ µg RE	350 (13)	350 (42)	400 (126)	83	127
Folic acid, µg	32 (0)	32 (0)	50 (3)	32.5	50
Niacin, mg	5 (3)	5 (4)	8 (7)	3.5	5.4
Riboflavin, mg	0.4 (0.2)	0.4 (0.2)	0.6 (0.4)	0.31	0.48
Thiamin, mg	0.3 (0.1)	0.3 (0.2)	0.5 (0.4)	0.3	0.42
Vitamin B-6, mg	0.4 (0)	0.4 (0)	0.7 (0)	0.4	0.6
Vitamin B-12, µg	0.4 (0)	0.4 (0)	0.5 (0)	0.46	0.7
Vitamin C, mg	25 (0)	25 (0)	30 (8)	16	24
Vitamin D, µg	7 (6.6)	7 (6.7)	7 (6.7)		
Vitamin E, mg				2.3	3.6
Minerals					
Calcium, mg	525 (336)	525 (353)	350 (196)	156	240
Chloride, mg	500 (217)	500 (241)	800 (569)		
Copper, mg	0.3 (0.1)	0.3 (0.1)	0.4 (0.3)		
Iodine, µg	60 (0)	60 (0)	70 (10)		
Iron, ⁴ mg	11 (10.8)	11 (10.8)	6 (5.8)	6.5	10
Magnesium, mg	80 (51)	80 (58)	85 (66)	31	48
Phosphorus, mg	400 (306)	400 (314)	270 (193)	156	240
Zinc, mg	5.0 (2.2)	5.0 (2.3)	6.5 (2.4)	6.5	10

¹ A blank space indicates that *Mi Papilla* was not fortified with the nutrient; however, the nutrient may be present if it occurs naturally in the product.

² Institute of Medicine (19). The first figure is the total daily energy requirement. The figure in parentheses is the estimated amount of energy required from complementary foods, assuming average breast milk intake. 1 kcal = 4.184 kJ.

³ RE, Retinol equivalents.

⁴ Medium bioavailability as defined in (19).

survey. Therefore, although the final survey took place 14 mo after the baseline, the PANN 2000 group received the program for only 11 mo.

At baseline, information was collected on family composition, socioeconomic conditions, maternal knowledge of and practices for breast-feeding and complementary feeding, and dietary intake. To assess micronutrient status, 5 mL venous blood was collected using sterile equipment and zinc-free tubes and immediately covered with aluminum foil to avoid contact with air and light. The serum was separated by centrifugation and placed in amber-colored vials. Samples were placed in dry ice, transported to the central laboratory, and stored at -80°C until analyzed. Collection and processing of blood samples were conducted according to the MSP procedures (21). Hemoglobin was measured in situ using 10 μL capillary blood and processed with a hemoglobinometer HemoCue B (HemoCue AN). The accepted variation coefficient was 1.5%. Serum retinol was determined using HPLC (21) and serum zinc was determined by flame atomic absorption spectrometry (22).

Community health workers associated with each health center conducted weekly in-home morbidity surveillance and were trained to recognize cases of diarrhea, cough, and difficulty breathing using standard protocols and to document intake of *Mi Papilla* the day before the visit (yes or no). Reported illness symptoms during the previous 24 h were used as an estimate of overall population morbidity incidence. At baseline and 13 mo later, children were weighed on a clock balance accurate to 100 g (ITAC) and calibrated weekly and recumbent length was measured using locally made, rigid stadiometers accurate to 0.1 cm. Field workers were trained and standardized using WHO guidelines (23). To estimate dietary intake, a 24-h recall at baseline and at the final survey were administered to the child's mother by trained nutritionists. Household utensils and locally made food models were used to estimate portion sizes and standard tables were used to calculate the weight of the food consumed using *ProPAN* (Process for the Promotion of Child Feeding) software (24). When a food consumed was not found in the standard tables, it was weighed using a digital balance (Soehnle DC 8115, maximum weight 2 kg, precision 1 g). Z scores were calculated using the new WHO Child Growth Standard (25).

Sample size. Sample size calculations were based on the hypothesized differences PANN 2000 would make in growth, daily energy intake, serum retinol, and hemoglobin and based on a 2-tailed test, a significance level of 0.05%, and a statistical power of 0.8. The effects of the clusters (the unit of sampling was the health center) and different sizes of the clusters were presumed to be modest and not adjusted for in sample size calculations. Based on published studies, we expected a positive effect on linear growth of 0.65 ± 4.0 cm, energy intake of 195 ± 225 kcal/d (815.9 ± 941.1 kJ/d), hemoglobin of 20 ± 1.4 g/L, and serum retinol of 0.25 ± 0.24 $\mu\text{mol/L}$ (7.3 ± 7.0 $\mu\text{g/dL}$). Because the necessary sample size depended on the outcome in question, we used a hierarchical nested design. The overall sample was selected to assess effect on growth (calculated at 250 per group), a subsample was selected to assess micronutrient status (calculated at 75 per group), and a subsample of the micronutrient sample was used to assess diet (calculated at 60 per group). To allow for attrition, these samples were increased by $\sim 25\%$ and varied by group and subsample as all eligible children in the catchment area were invited to participate. Hemoglobin was assessed in most children in the overall sample as was morbidity.

Data analysis. Data were collected on forms that were previously pilot tested, checked by field supervisors, entered into EPI-Info 6.04, and

converted to SPSS 12.0 for analysis. Distributions of all variables were checked for normality and transformed where necessary to achieve a normal distribution; when a normal distribution was not possible, non-parametric statistical tests were applied. Socioeconomic information was analyzed using principal component analysis and 3 clusters of associated variables were identified: housing, possessions, and parental education. Food intake was converted to nutrients using *ProPAN*, which includes food composition data from Latin American and United States food composition tables (24). We compared outcomes using Student's *t* test, chi-square, McNemar's test, ANOVA, multiple regression, and logistic regression. Variables controlled in the regression models were selected because of their relationship to child growth and included child age, child age squared, initial value (e.g. baseline weight-for-age Z score or hemoglobin), maternal education, maternal age, housing index, socioeconomic index, morbidity index, employment of household head, child sex, program, and the interaction of program with all other covariates. In the final model, only covariates that were significant at the 0.1 level (0.15 for interactions) were kept. To assess bias that may have resulted from loss to follow-up or loss to measurement, a dummy variable indicating loss-to-follow-up status was regressed on the same covariates in the final models (26). The Generalized least means procedure (SAS 8.02) was used to examine the models for the clustering effect of the health center (the unit of sampling) and adjust them, if necessary.

All analyses were conducted using an intention-to-treat analysis method in which all children in the program group, irrespective of intervention exposure and intake of *Mi Papilla*, were included in the analysis as the program group. Outcomes reported all pertain to the individual level. Definitions of outcomes were decided a priori: maternal knowledge about child nutrition and feeding, caregiver behavior and feeding practices, dietary intakes of energy, macro-, and micronutrients, and *Mi Papilla*; hemoglobin, transferrin saturation, serum zinc, and serum retinol; final attained length, weight, and associated Z scores; and prevalence of underweight and stunting (< -2 SD) and overweight (> 2 SD). For morbidity outcomes, diarrhea was defined as 3 or more liquid or semiliquid stools in 24 h and cough with difficulty breathing was defined as increased respiratory frequency ($> 40/\text{min}$ in children < 1 y of age and $> 50/\text{min}$ in older children) and thorax retraction (deepening of the abdomen toward the ribs during inhalation) according to parental reporting.

Results

Sample size and loss to follow-up. Sample sizes for the program and control groups at baseline and the follow-up show differential loss to measurement depending on the specific subsample (Table 2). Few losses occurred in the sample followed weekly for morbidity surveillance over the 11-mo observation. The rate of weekly follow-up for these children was slightly $> 80\%$ for both groups. In contrast, the loss to measurement of children who were followed for the other study components varied between 16 and 50% depending on the evaluation component. There is no indication that loss to measurement differed by group. The 80% follow-up by the team responsible for weekly morbidity surveillance was due to the fact that it was done by community health workers who could easily revisit the home to collect complete data. In contrast, the other teams

TABLE 2 Sample size at baseline and final surveys and proportion not measured for anthropometry, micronutrient status, and diet and weekly morbidity surveillance

	Program			Control		
	Baseline <i>n</i>	Final <i>n</i>	Percent not measured	Baseline <i>n</i>	Final <i>n</i>	Percent not measured
Anthropometry	338	170	50	296	149	50
Morbidity (weekly)	324	324	0	262	262	0
Micronutrient status	102	74	27	101	80	21
Diet	83	49	41	61	51	16

traveled from the capital to the evaluation area for baseline and final measurements in the health clinics and had less flexibility to follow up with children who did not come to the clinic.

Sample description at baseline. At baseline, program and control groups were similar with respect to many but not all variables (Table 3). Contrary to expectations, a significantly greater proportion of program families had electricity and cement houses and mothers also had significantly more years of

completed schooling. Nonetheless, groups did not differ in breast-feeding status, bottle use, or any anthropometric indicators. There were also no differences in intake of energy and most micronutrients except protein and calcium intakes were significantly higher in the program group. All serum micronutrient concentrations were similar except for retinol, which was significantly higher in the program group (Table 3). The prevalence of subclinical vitamin A deficiency [serum retinol < 0.70 $\mu\text{mol/L}$ (20 $\mu\text{g/dL}$)] was also significantly lower in the

TABLE 3 Child and family characteristics at baseline¹

	Program	Control	P-value
Family and child characteristics, <i>n</i>	338	296	
Child age, <i>mo</i>	9.2 \pm 1.9	9.1 \pm 1.8	0.583
Child currently breast-feeding, %	80.4	80.5	0.967
Child currently using bottle, %	50.4	49.8	0.877
Mother's age, <i>y</i>	26.1 \pm 7.1	26.3 \pm 7.3	0.838
Mother's completed schooling, <i>y</i>	7.4 \pm 3.3	6.8 \pm 3.8	0.023
Both parents live with child, %	81.6	80.5	0.477
Family size, <i>n</i>	6.03 \pm 2.79	5.49 \pm 2.22	0.008
Cement house, %	75.7	65.9	0.006
Electricity, %	93.5	87.8	0.018
Telephone, %	13.0	9.8	0.215
Television, %	73.9	70.9	0.423
Refrigerator, %	42.3	39.2	0.466
Energy and nutrient intake, <i>n</i>	83	51	
Energy, ⁴ <i>kcal</i>	554.1 \pm 445.2	437.1 \pm 391.6	0.100
Energy per kg, <i>kcal/kg</i>	64.1 \pm 48.3	55.8 \pm 51.3	0.320
Protein, <i>g</i>	16.6 \pm 14.6	11.4 \pm 9.5	0.017
Fat, <i>g</i>	14.7 \pm 16.3	13.5 \pm 22.7	0.705
Energy as fat, %	23.0%	22.7%	0.883
Iron, <i>mg</i>	3.2 \pm 3.2	2.6 \pm 3.1	0.251
Zinc, <i>mg</i>	2.04 \pm 2.1	1.49 \pm 1.7	0.088
Vitamin A, $\mu\text{g RE}$	249.5 \pm 352.8	256.9 \pm 470.9	0.913
Vitamin C, <i>mg</i>	21.9 \pm 24.2	23.6 \pm 31.7	0.723
Calcium, <i>mg</i>	287.4 \pm 419.1	172.0 \pm 256.1	0.057
Anthropometric indicators, <i>n</i>	338	296	
Weight, <i>kg</i>	8.10 \pm 1.1	8.02 \pm 1.1	0.406
Length, <i>cm</i>	68.5 \pm 3.5	68.1 \pm 3.5	0.141
Weight-for-age Z score	-0.58 \pm 1.1	-0.65 \pm 1.0	0.439
Length-for-age Z score	-1.20 \pm 1.2	-1.35 \pm 1.1	0.114
Weight-for-length Z score	0.17 \pm 1.0	0.19 \pm 1.0	0.713
Underweight (weight-for-age < -2 SD), %	10.4	6.8	0.109
Stunted (length-for-age < -2 SD), %	24.3	26.1	0.609
Wasted (weight-for-length < -2 SD), %	2.4	2.7	0.787
Overweight (weight-for-length > 2 SD), %	3.0	2.4	0.645
Micronutrient status, <i>n</i>	102	101	
Anemia (Hb < 110 g/L), %	76.1	76.4	1.000
Hemoglobin, ² <i>g/L</i>	101.6 \pm 11.2	102.4 \pm 10.2	0.410
Transferrin, <i>g/L</i>	2.92	2.97	0.350
Serum ferritin, ³ $\mu\text{g/L}$	19.5 (12.1, 91.2)	23.5 (12.3, 42.7)	0.320
Deficient iron stores (serum ferritin < 12.0 $\mu\text{g/L}$), %	24.5	24.8	1.000
Serum Zn, $\mu\text{mol/L}$ ($\mu\text{g/dL}$)	11.1 \pm 4.3 (72.3 \pm 27.94)	10.4 \pm 4.0 (68.0 \pm 26.02)	0.260
Zn deficiency (serum Zn < 9.9 $\mu\text{mol/L}$ [65 $\mu\text{g/dL}$]), %	41.0	42.0	1.0
Serum retinol, $\mu\text{mol/L}$ ($\mu\text{g/dL}$)	0.95 \pm 0.25 (27.34 \pm 7.11)	0.87 \pm 0.23 (24.89 \pm 6.54)	0.010
Vitamin A deficiency (serum retinol < 0.70 $\mu\text{mol/L}$ [20 $\mu\text{g/dL}$]), %	13.1	24.3	0.050

¹ Values are means \pm SD, medians (ranges), or %.

² Hemoglobin was assessed using the Hemocue method and data are available on 226 and 208 infants in the program and control groups, respectively.

³ Excluded are 11 children (10.8%) in the program group and 8 children (7.9%) in the control group who had C-reactive protein > 100 mg/L, indicating current infection. Median (first quartile, third quartile).

⁴ 1 kcal = 4.184 kJ.

program group (Table 3). No child had a serum retinol level < 0.35 $\mu\text{mol/L}$ (10 $\mu\text{g/dL}$), which indicates severe deficiency. The prevalence of anemia was extremely high and ~10% of children in both groups had C-reactive protein levels > 952 nmol/L (10 mg/dL), indicating current infection. One-quarter of children had serum ferritin values below 12.0 $\mu\text{g/L}$, indicating deficient iron stores. Slightly >40% of the children had serum zinc < 10.7 $\mu\text{mol/L}$ (65 $\mu\text{g/dL}$), indicating zinc deficiency.

Description of the sample at final survey. Intake of *Mi Papilla* significantly improved dietary quantity and quality and did not interfere with breast-feeding patterns. At the final survey, most children, 85.8% in the program group and 91.6% in the control group, were no longer breast-fed ($P = 0.100$). *Mi Papilla* was consumed 72.9% of the time, with 4 children never consuming it and 42 children consuming it every day before the weekly morbidity surveillance visit. *Mi Papilla* contributed significantly to intake, providing nearly one-quarter of all energy, carbohydrates, protein, and fat, 40–45% of calcium, vitamin A, and vitamin C, and ~70% of iron and zinc intake (Table 4; Fig. 1). On the day of the 24-h recall, *Mi Papilla* was consumed by 57.4% of the program children, who consumed a

total of 56.6 ± 24.0 g. When all children with dietary recalls were included in the denominator (both those that consumed *Mi Papilla* and those that did not), consumption was 32.5 ± 33.5 g, or one-half the daily ration. Both total energy intake and energy intake per kilogram body weight were significantly higher in the program group as was the intake of fat. Intakes of iron, zinc, and calcium were also higher in program children. Consumption of *Mi Papilla* did not replace usual intake but increased net intake of energy and other nutrients; daily energy increased by 240 kcal and iron increased by nearly 9 mg.

The incidence of diarrhea, cough, and difficulty breathing (with or without cough) as reported by the mother during 42 weekly home visits declined over the period of follow-up and for diarrhea and cough did not differ between groups (data not shown).

Mothers in the program group were not more likely to report hearing messages or receiving counseling about breast-feeding and/or complementary feeding in health services compared with mothers in the control group (data not shown). In both groups, very few reported hearing messages on the radio or in health services. Breast-feeding and complementary feeding practices, apart from feeding *Mi Papilla*, did not improve in children in the

TABLE 4 Child characteristics at final survey¹

Characteristic	Program	Control	P-value
Energy and nutrient intake, <i>n</i>	49	61	
Energy, ² <i>kcal</i>	969.7 \pm 458.2	790.7 \pm 404.1	0.024
Energy per kg, <i>kcal/kg</i>	91.4 \pm 45.5	73.3 \pm 40.6	0.038
Protein, <i>g</i>	32.8 \pm 18.9	23.1 \pm 13.9	0.001
Fat, <i>g</i>	29.3 \pm 35.8	16.9 \pm 13.6	0.009
Energy as fat, %	24.5%	19.3%	0.007
Iron, <i>mg</i>	8.8 \pm 5.8	3.5 \pm 2.0	<0.0001
Zinc, <i>mg</i>	7.83 \pm 5.6	2.6 \pm 1.8	<0.0001
Vitamin A, $\mu\text{g RE}$	367.0 \pm 446.6	177.6 \pm 218.7	0.003
Vitamin C, <i>mg</i>	54.7 \pm 32.3	41.8 \pm 39.9	0.057
Calcium, <i>mg</i>	447.7 \pm 340.5	223.9 \pm 270.4	<0.0001
Anthropometric indicators, <i>n</i>	170	149	
Weight, <i>kg</i>	10.72 \pm 1.30	10.5 \pm 1.18	0.099
Length, <i>cm</i>	81.0 \pm 3.8	80.7 \pm 3.5	0.407
Weight-for-age Z score	-0.62 \pm 0.91	-0.88 \pm 1.03	0.021
Length-for-age Z score	-1.50 \pm 0.99	-1.77 \pm 1.15	0.027
Weight-for-length Z score	0.19 \pm 0.87	0.04 \pm 0.97	0.159
Underweight (weight-for-age < -2 SD), %	4.7	13.4	0.006
Stunted (length-for-age < -2 SD), %	31.8	41.9	0.061
Wasted (weight-for-length < -2 SD), %	0.6	0.0	0.350
Overweight (weight-for-length > 2 SD), %	2.4	2.7	0.843
Micronutrient status, <i>n</i>	74	80	
Anemia (Hb < 110 g/L), %	27.6	44.2	0.005
Hemoglobin, ³ <i>g/L</i>	114.6 \pm 8.8	109.7 \pm 10.3	<0.0001
Transferrin, <i>g/L</i>	3.01	2.93	0.560
Serum ferritin, ⁴ $\mu\text{g/L}$	17.4 (10.4, 27.6)	19.3 (10.4, 27.4)	0.390
Deficient iron stores (serum ferritin < 12.0 $\mu\text{g/L}$), %	29.7	26.6	0.721
Serum Zn, $\mu\text{mol/L}$ ($\mu\text{g/dL}$)	13.6 \pm 4.1 (89.0 \pm 26.7)	13.2 \pm 3.4 (86.3 \pm 22.5)	0.463
Zn deficiency (serum Zn < 9.9 $\mu\text{mol/L}$ [65 $\mu\text{g/dL}$]), %	11.4	14.9	0.633
Serum retinol, $\mu\text{mol/L}$ ($\mu\text{g/dL}$)	1.08 \pm 0.23 (31.0 \pm 6.7)	0.99 \pm 0.27 (28.4 \pm 7.8)	0.035
Vitamin A deficiency [serum retinol < 0.70 $\mu\text{mol/L}$ (20 $\mu\text{g/dL}$)], %	6.7	15.4	0.122

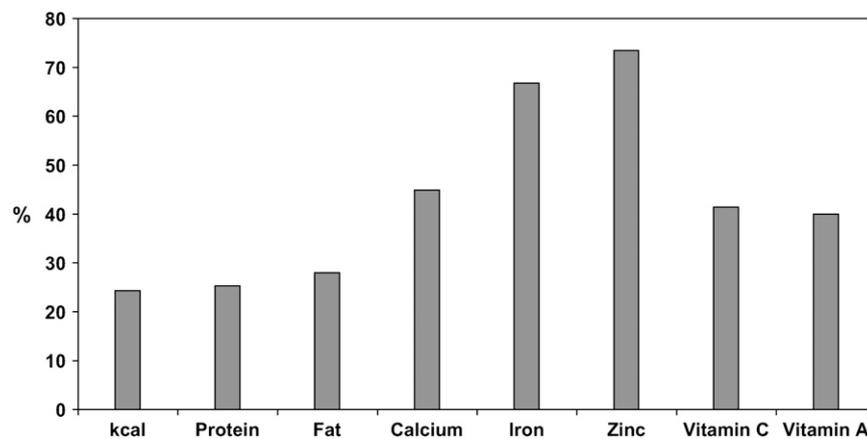
¹ Values are means \pm SD, medians (ranges), or %.

² 1 kcal = 4.184 kJ.

³ Hemoglobin was assessed using Hemocue method and data are available on 116 and 155 children in the program and control groups, respectively.

⁴ Excluded are 7 children (9.5%) in the program group and 9 children (11.3%) in the control group who had C-reactive protein > 100 mg/L, indicating current infection. Median (first quartile, third quartile).

FIGURE 1 Percentages of energy and nutrient intakes provided by *Mi Papilla* in program children ($n = 35$) on the day of the 24-h recall. 1 kcal = 4.184 kJ.



program group. There were no differences in the proportion of mothers in either group that reported that “breastmilk is the best food for infants < 6 mo,” “the ideal consistency of porridge for infants is thick,” “the consistency of the main meal given to the infant yesterday was thick,” or “breastmilk is the best food for infants < 6 mo” at the final compared with the baseline survey.

Nonadjusted program effects using the intention to treat method were positive and significant for length-for-age ($P = 0.027$) and weight-for-age ($P = 0.021$) Z scores and the prevalence of underweight ($P = 0.006$) (Table 4). The level of significance for the difference in stunting was 0.061, favoring the program group. There were no differences in the likelihood to be wasted or overweight.

Children in the program group had significantly higher hemoglobin values and were significantly less likely to be anemic than were children in the control group (Table 4). There were no between-group differences in levels of transferrin saturation or ferritin. Mean levels of serum zinc and the proportion of children considered zinc deficient did not differ between groups. The prevalence of vitamin A deficiency declined in both groups and no significant differences were found ($P = 0.12$). As in the baseline survey, no children had serum retinol values < 0.35 $\mu\text{mol/L}$ (10 $\mu\text{g/dL}$). Mean hemoglobin in program children increased by 13.7 g/L, whereas in control children it only increased by 5.6 g/L ($P < 0.0001$) (data not shown).

Multiple regression and logistics regression analysis. The effect of PANN 2000 on linear growth was a function of child age when entered into the program. The overall effect was positive (0.37 cm) but not significant ($P = 0.137$) when we controlled for the covariates child age; child age squared; baseline length; the indices for socioeconomic level, housing, education, and employment of household head; and the interaction term for child age at baseline and program. When stratified by the age groups of 9–11 mo vs. 12–14 mo, a program effect of 0.66 cm was observed ($P = 0.08$) in the older children (Table 5). The coefficient for younger children was small and positive but not significant. A similar response for weight, significantly favoring only the children who were older at baseline, was also observed (Table 5). However, the interaction term of child age at baseline and program was significant ($P = 0.029$), indicating that the effect of the program on weight depended on the age of the child when the program began. At the final survey, an 8-kg child who was 12 mo old when the program began was 0.241 kg heavier than a control child of a similar initial weight and age, whereas an 8-kg child who was 13 mo old

when the program began was 0.617 kg heavier than a control child of a similar initial weight and age.

Loss to measurement did not appear to bias these results; this was determined using the method described in “Methods” in which a dummy variable indicating loss to follow-up status was regressed on the variables in the regression models. These variables included child age at baseline, child age at baseline squared, child sex, baseline length (or weight), maternal education, maternal age, housing index, socioeconomic index, employment of the household head, program, and the interaction of the program with each independent variable. None of the main effects or interactions yielded P -values < 0.13. For final weight, no variable was significantly associated with loss to follow-up (data not shown). Intuitively, the results made sense as neither program nor control children for whom final anthropometry was measured had initial weight-for-age Z scores different from those of children who were not measured. The effect of sampling at the unit of the health center was also not significant ($P = 0.87$) and therefore the results were also not adjusted for health center. For final length, baseline length ($P = 0.04$) and baseline age ($P = 0.008$) were significant, indicating that children who were shorter and younger at baseline were more likely to be lost to measurement. However, program status was not significant, indicating that being in the program vs. the control group was not related to being lost to measurement and therefore unlikely to bias the final result.

The odds of being underweight were 75% lower for children in the program when we controlled for the covariates mentioned above ($P = 0.007$). The odds of being underweight were 7% lower for every year of maternal age and 81% lower for every 1 SD increase in weight-for-age at baseline with other variables being controlled for. The odds of being stunted were not significantly different.

The effect of the program on the risk of being anemic was significant (OR = 0.58; CI = 0.24, 0.75; $P = 0.003$). Baseline hemoglobin was negatively related to final hemoglobin and also significant ($P < 0.002$); children with higher baseline hemoglobin experienced less change in hemoglobin than those with lower hemoglobin. There was no interaction between baseline hemoglobin and program. Loss to follow-up does not appear to bias the results (data not shown). Neither program nor control children who were followed had baseline hemoglobin levels or maternal education different from those of children not followed. The effect of sampling at the unit of the health center was marginally significant ($P = 0.06$); however, the effects on the unstandardized coefficients was small and the final model was

TABLE 5 Multiple regressions for predicted effects on length and weight in older children at baseline (12–14 mo)¹

	Unstandardized coefficients		P-value	95% CI
Length, cm (n = 130)				
	β	SE		
Constant	73.86	38.57		
Child age at baseline, mo	-10.05	6.71	0.137	-23.33, 3.23
Length at baseline, cm	0.91	0.07	<0.001	0.77, 1.06
Program	0.66	0.37	0.080	-0.80, 1.41
Child age at baseline squared	0.45	0.30	0.133	-0.14, 1.03
Weight, kg (n = 130)				
Constant	5.13	1.48		
Weight at baseline, kg	0.83	0.63	<0.001	0.70, 0.95
Child age at baseline, mo	-0.12	0.12	0.318	-0.36, 0.12
Program	-3.90	1.91	0.043	-7.67, -0.12
Child age at baseline \times program	0.38	0.17	0.029	0.04, 0.71

¹ The full model included the covariates child age; child age squared; baseline length or weight; the indices for socioeconomic level, housing, education, and employment of household head; and the interaction term child age at baseline \times program. None of the indices was significant and the interaction term was significant only for weight. The reduced models are presented here.

not adjusted for health center. When covariates were controlled for, the odds of being anemic were 58% lower for children in the program. Children of mothers with higher education and children with higher baseline hemoglobin scores were less likely to be anemic; the odds of being anemic were 8% lower for every year of maternal education and 34% lower for every 10 g/L additional hemoglobin at baseline when other covariates were controlled for. The results do not appear to be influenced by loss to measurement. There was no effect of health center clustering ($P = 0.64$).

Discussion

Our evaluation showed that a FCF delivered through the health system during a critical period of growth and development was

highly effective in reducing the prevalence of underweight and anemia, with the results for linear growth (0.66 cm) being biologically important but not significant ($P = 0.08$). The results of the dietary analysis support this conclusion: program children consumed significantly more energy and iron than control children and overall dietary quality substantially improved. At the same time, we show that the other program components, training of health workers and delivery of information, education, and communication, did not have the anticipated effects in improving breast-feeding and complementary feeding practices, apart from the feeding of *Mi Papilla* (Fig. 2). Counseling has been shown to be effective in improving feeding behaviors and growth, when few consistent messages are given and implementation is well supervised (11,12). The challenge in a large public health program is to achieve high-quality, consistent

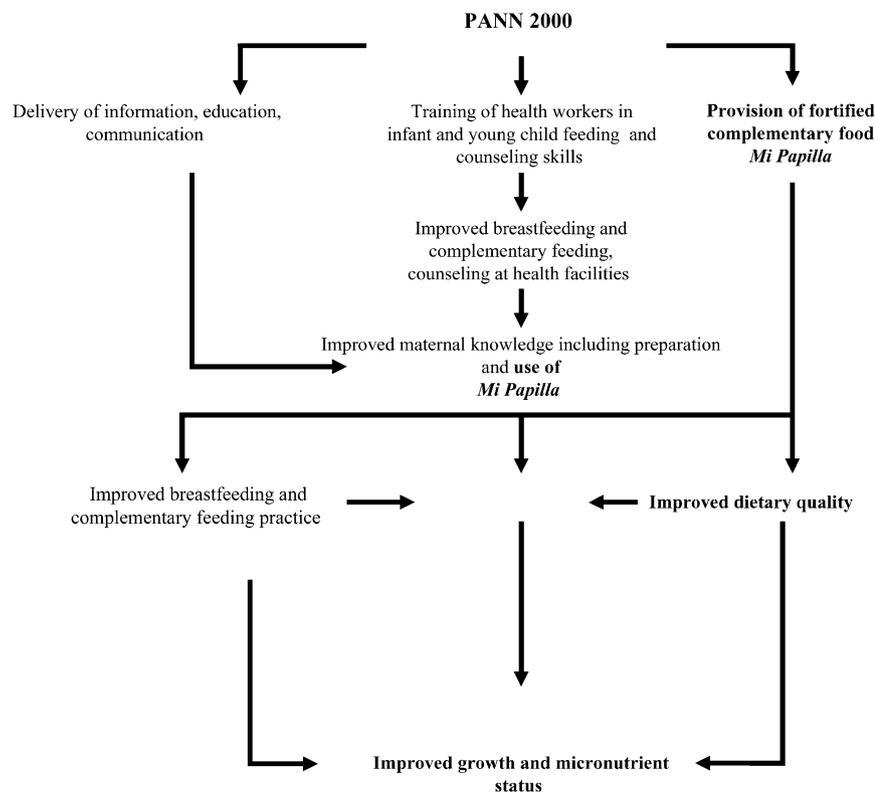


FIGURE 2 Conceptual model of Ecuador's PANN 2000 and potential pathways for achieving the desired outcome. Pathways that were shown to be successful are in bold.

counseling with good coverage. It is a challenge that merits attention as it is likely that the effects of improved dietary quality on growth could have been enhanced if behaviors had also improved.

The effect on anemia was particularly dramatic. In Chile, infants who did not receive iron between ages 6 and 12 mo (either through infant formula or supplement drops) processed information slower than infants who did receive iron (27). Studies of long-term effects of iron deficiency anemia in Costa Rica and Chile show that children who were anemic as infants had lower test scores at age 5 y than children who had not been anemic (28,29). In Costa Rica where participants have been followed into adulthood, these differences not only persist but increase, with particularly negative effects for participants of low socioeconomic status (28). These results are consistent with neuromaturation studies showing that anemic infants have slower auditory brainstem response times than nonanemic infants and that these differences persist long after anemia has been corrected.

The significant difference in anemia occurred despite attempts to treat anemic children identified at baseline in both groups with ferrous sulfate. Data were not collected on the compliance; however, at baseline, only ~11% of mothers in both groups reported giving an iron supplement in the 2 wk before the interview and we are not aware of any peer-reviewed studies showing that iron supplementation programs for infants and young children, although highly efficacious in clinical trials (30), are effective in a public health setting. The prevalence of anemia at baseline (76%) is higher than that reported in the only nationally representative nutrition survey (15) 11 y earlier, despite programs to improve micronutrient status, and illustrates the challenge of reducing iron deficiency anemia in infants and young children.

Iron status during the first 2 y of life is highly dynamic, which may explain why *Mi Papilla* did not affect serum ferritin despite having a significant positive effect on hemoglobin and anemia prevalence. In a study of well-nourished infants with a low prevalence of iron deficiency anemia, dietary iron predicted hemoglobin but not serum ferritin values during infancy (31). In this study, there was no correlation between dietary iron and serum ferritin before age 18 mo, a finding consistent with some (32,33) but not all studies (34) of iron metabolism during early childhood.

The fact that increased dietary zinc in program children did not lead to improved zinc status compared with control children suggests that the compound in *Mi Papilla*, zinc sulfate, was not effective. There are several possible reasons for this finding: it may not be bioavailable in a food matrix, zinc intake from traditional complementary foods provided the physiologic requirement, and/or plasma zinc may be an insensitive biomarker of zinc status. Previous studies showed zinc sulfate to be bioavailable in adults, although absorption was less from porridge than from bread, presumably because of the greater phytate content in porridge (35). Zinc sulfate provided as a supplement to young children is bioavailable and improves serum zinc status and linear growth (36). However, a recent study in Peru shows that zinc sulfate when given with food did not affect zinc plasma concentration in young children (37) and it is possible that high-phytate meals depress zinc absorption in zinc-FCF (38). The physiologic zinc requirement for children ages 1–3 y is 0.74 mg/d and the estimated average requirement is 2.5 mg/d (39). At the final survey, the daily zinc intake from traditional complementary foods, excluding that from *Mi Papilla*, was 2.9 for program children and 2.6 mg for control children. These intakes exceed the estimated average require-

ment; therefore, it is possible that physiologic requirements were met and the saturation point for absorption was approached (40).

Serum retinol concentration increased and the prevalence of subclinical vitamin A deficiency decreased in both groups and the program had no apparent effect on vitamin A status. The level of vitamin A is relatively low in *Mi Papilla* and provides only about one-third of the recommended daily intake. This amount of vitamin may have been dwarfed by high-dose supplements received by about one-half of the children in both groups in the 6 mo before the final survey.

The program had a far greater effect on the weight gain than on linear growth and only in children aged 12–14 mo when they began consuming *Mi Papilla*. This finding is counterintuitive to the perception that younger children in the most rapid phase of growth are more likely to respond to improved food intake. However, indicators of risk do not necessarily correspond to indicators of benefit (41). The gastric capacity of older children is greater, allowing them to eat more of the FCF with less displacement of usual intake. Also, older children are more likely to be weaned, which increases the proportion of total nutritional requirements provided by food intake. Greater improvements in linear growth may not have been observed because most of the stunting detected at the final survey had already occurred when baseline measures were taken. During the course of the evaluation, the relative increase in stunting in program and control children was only 24 and 38%, respectively. To ensure maximum impact of public health interventions that provide a FCF, greater efforts need to be made to extend the duration of exclusive breast-feeding to prevent growth faltering that occurs during the first 6 mo of life.

There have been few evaluations of the effect on growth of public health programs to improve diet and results are mixed (42). A recent evaluation in Mexico showed that the only subgroup to benefit from a FCF started supplementation before age 6 mo and was in the poorer half of the socioeconomic strata (43). After 2 y of follow-up, these children grew 1.1 cm more than children of the same age and socioeconomic strata who received the FCF for only 1 y. In India, children aged 4–12 mo who were randomly assigned to receive a milk-based cereal and nutrition counseling consumed more energy and gained 250 g more than children who only received counseling (44). Linear growth was not affected. In Peru, children who received a FCF did not improve in linear growth more than a similarly aged control group over 11 mo even in those who were youngest (aged 6–11 mo) at baseline (45).

The strength of our results is that they are from a public health program delivered through routine health services. The data showing improved dietary intake in the program group is congruent with the effects in this group on growth and micronutrient status. However, there were also some weaknesses in the design and implementation. The evaluation was not randomized nor could it be blinded except for the analysis of the blood samples, and the loss to final measurement was large for some evaluation components. Seemingly similar program and control communities were selected, and although the differences found between them were adjusted for in the analysis, this adjustment may have been incomplete. The lack of blinding could have led to bias; however, data collection was standardized, all interviews were structured, and different sets of interviewers collected data on diet and anthropometry. Although it is possible that knowledge of the group influenced data collectors' interpretation of responses or the recording of the dietary recall data, it is difficult to see how anthropometric measures could have been affected. Also, the determinations of serum retinol,

iron indicators, and serum zinc were blinded and consistent with the dietary data.

We examined possible bias that may have been introduced by loss to final measurement by asking 2 questions: was the loss to measurement different for program vs. control children, and was the loss to measurement related to any of the variables in the regression model showing a positive effect of the program on weight or length? With respect to weight, both answers were negative. With respect to length, the probability of loss to measurement was associated with age and length at baseline but not program, showing that such loss is unlikely to have biased the results.

Linear growth retardation and anemia are the 2 most prevalent forms of malnutrition in Latin America and other regions of the world, affecting the health and development of millions of children. The FCF of the program described here was highly effective in reducing anemia; the effects on linear growth, while positive, failed to reach significance. Several countries in Latin America have implemented programs that include a FCF and others are contemplating such programs. Our evaluation provides further evidence they can be effective. However, it also points to the challenges and importance of simultaneously improving exclusive breast-feeding and complementary feeding behaviors so that the effect of improved dietary quality on growth can be maximized.

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