

# Preventing Iron Deficiency in Infants and Preschool Children in Argentina

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*This paper summarizes the results of most major studies of iron deficiency and anemia in infants and children in Argentina. Possible reasons for high prevalences of iron deficiency and anemia in certain population groups are given, and plans for future interventions, based on these data, are discussed.*

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## Introduction

Argentina is home to many different climates, ecologies, natural resources, lifestyles, and dietary patterns. Like other countries in the region, it is a transitional society. As such, large population segments currently have no major health and nutrition problems, whereas others suffer such problems as overnutrition, high morbidity and mortality rates, shorter life expectancy, and nutritional deficiencies, including obvious protein-energy malnutrition.

Argentina used to have the highest per capita meat consumption in the world as well as one of the highest per capita energy availabilities. Bovine meat has been for decades one of the least expensive protein sources, available to most families. Based on this dietary pattern, iron deficiency was not assumed to be a health problem by physicians and health authorities. However, the supplementation of medicinal iron to infants and pregnant women has been officially recommended for many years.<sup>1</sup> This recommendation was fully endorsed by the Argentine Pediatric Society in 1983.<sup>2</sup>

In the late 1970s, a Pan American Health Organization (PAHO)-sponsored nutrition survey was conducted in the northwest provinces of Argentina, which are the least developed and have the lowest per capita income. Unfortunately much of the information obtained in the survey was not published, but it did show a high prevalence of anemia and low iron intakes in all ages and biologic groups.<sup>3</sup>

For this paper we collected all available information on the prevalence of iron deficiency and anemia in Argen-

tina. Only population studies that are sufficiently representative are mentioned. A more thorough analysis of the findings of surveys of small children is discussed, as are plans for future interventions. These studies have been performed by CESNI over a 10-year period in three different locations of Argentina.

The first study was conducted in 1986 in the Greater Buenos Aires area.<sup>4</sup> One-third of the nation's population live in this region. Their eating patterns, living patterns, and health standards are similar to those of all other major cities in the country, whose total populations constitute 70% of the Argentine population. In the Greater Buenos Aires area, all socioeconomic and educational levels are represented. The Federal District of Buenos Aires City is not included in this survey because its population is very homogeneous.

The second survey was conducted a year later in the province of Misiones, with a large rural population and a subtropical climate and where uncinariasis is prevalent. At the time of the study, the economic, sanitary, and educational indicators of Misiones were in the lowest segment of those found in the nation's provinces.<sup>5</sup>

The most recent study was undertaken within the activities of the Tierra del Fuego project.<sup>6</sup> Tierra del Fuego is the nation's southernmost province and has enjoyed an economic and population boom owing to the growth of electronic industries, oil exploitation (inland and off shore), tourism, fisheries, and sheep raising. Tierra del Fuego is an island shared with Chile separated from the mainland by the Magellan Strait. The climate is cold, windy, and rather humid and rainy.

Ninety-six percent of Tierra del Fuego's population reside in two cities of similar size: Ushuaia and Río Grande. The province has the highest percentage of children relative to its total population. Health indicators are the best in the country, even better than those of the Federal District. Illiteracy is rare and per capita expenditures on social and welfare issues are the highest in the country. There is no extreme poverty. Tierra del Fuego's population does not have a local cultural feeding pattern. Food is purchased in the same supermarket chains that exist in Buenos Aires and other large cities. Analysis of the diets of Fuegian children shows no differences from the diets of children in Buenos Aires.<sup>7</sup>

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**Table 1.** Population Studies of Iron Deficiency in Argentina Among Infants 9–24 Months Old

	Study (Year Performed)		
	Greater Buenos Aires (1985) <sup>a</sup>	Misiones (1986) <sup>b</sup>	Tierra del Fuego (1994) <sup>c</sup>
Prevalence of anemia (%) <sup>d</sup>			
< 11 g Hb/dL	49 (55–34) <sup>e</sup>	55 (62–39)	24 (13–44)
< 10 g Hb/dL	26	24	8.6
< 9 g Hb/dL	13	23	0.9
Iron nutrition indicators (%)			
MCV > 80 $\mu^3$	38	NA	NA
ZPP > 100 $\mu\text{mol/mol}$ heme	57	NA	42
SF < 12 $\mu\text{g/L}$	60	55	52
Response to Fe treatment of anemic infants (%)	78	NA	NA
% iron sufficient (Hb > 11, SF > 12, ZPP < 100)	15	NA	38
% iron deficient, nonanemic (Hb > 11, SF < 12, ZPP < 100)	12	NA	25
% iron deficient, $\downarrow$ erythropoiesis (Hb > 11, SF < 12, ZPP > 100)	12	NA	11
% iron deficient, anemia (Hb < 11, SF < 12, ZPP > 100)	30	NA	14
<b>Dietary Information</b>			
<b>Iron</b>			
Iron intake (mg/day)	5.6 $\pm$ 3.5	4.0 $\pm$ 2.6	5.9 $\pm$ 4.5
Heme iron intake (mg/day)	0.9	0.4	0.8
% daily intake	18	10	14
Nonheme iron intake (mg/day)	4.5 $\pm$ 0.8	4.0 $\pm$ 0.8	5.1 $\pm$ 4.5
Absorbable nonheme iron intake (mg/day) <sup>f</sup>	0.5 $\pm$ 0.4	0.3 $\pm$ 0.3	0.3 $\pm$ 0.2
Dietary iron density (mg/1000 kcal)	4.55	NA	4.7
Bioavailable iron intake < 1 mg/day (%)	90	96	95
Iron intake < 15 mg/day (%)	98	100	96
Iron intake < 10 mg/day (%)	92	90	88
<b>Iron supplementation at:</b>			
< 3 months (%)	78	88	9
< 6 months (%)	92	98	12
% below RDA for ascorbic acid	61	80	40
<b>Birth weight (g)</b>			
< 2500	7.5	6.8	7.2
2500–3000	8.4	9.2	9.8
> 3000	84.5	83.7	84.8
<b>% of children weaned from breast-feeding at:</b>			
< 3 months	40	26	18
< 6 months	57	36	40
< 9 months	66	49	56
<b>% of children introduced to cow's milk at:</b>			
< 3 months	52	41	21
< 6 months	78	—	55
< 9 months	89	—	75

Note: NA = not available, SEL = socioeconomic level, MCV = mean corpuscular volume, ZPP = zinc protoporphyrin, SF = serum ferritin.

<sup>a</sup>Sample randomized by conglomerates, stratified by educational level of the head of the family. Sampling fraction, 1:300 households. SEL: low to high, ages 9–24 months ( $n = 593$ ).

<sup>b</sup>Probabilistic design, stratified by geographic criteria in two stages and self-weighted. Sampling fraction, 1:67 households. SEL: high to low, ages 9–24 months ( $n = 464$ ).

<sup>c</sup>Simple random sample. Sampling fraction, 1:4 households in the city of Ushuaia. SEL: low to high ( $n = 231$ ).

<sup>d</sup>Reference 22.

<sup>e</sup>Low SEL–high SEL.

<sup>f</sup>Reference 9.

### Anemia in Children 8 to 24 Months Old

Table 1 summarizes the main findings of iron nutrition status in the three CESNI (Center for Studies on Infant Nutrition) infant population studies mentioned above. All so-

cioeconomic levels were represented in the three surveys. Anemia was present in all levels but with lower prevalences among those of higher socioeconomic status. Anemia was not severe; most infants had hemoglobin values between 10 and 11 g/dL. The high prevalence of high zinc protopor-

**Table 2.** Odds Ratio (Confidence Interval) for Risk of Hemoglobin Below 11 g/dL

Factor	Greater Buenos Aires	Tierra del Fuego
Birth weight < 3000 g	3.05 (1.74–5.36)	1.31 (0.95–1.79)
Height <i>z</i> score < -1 SD	2.09 (1.24–3.51)	0.96 (0.8–1.16)
Introduction of cow's milk before 3 months	1.90 (1.15–3.12)	1 (0.78–1.28)
Age less than 18 months	1.72 (1.32–2.83)	2.03 (1.02–4.02)
Breast-feeding less than 3 months	1.36 (0.79–2.32)	1.02 (0.83–1.25)
Iron supplementation	1.60 (0.96–2.67)	1.94 (0.46–8.16)
Low socioeconomic level	1.84 (1.12–3.02)	1.11 (0.99–1.24)
Maternal practical illiteracy	1.32 (0.71–2.46)	1.05 (0.92–1.19)
Poor pediatric care	2.34 (1.37–3.99)	0.99 (0.9–1.07)

phyrin (ZPP) and low serum ferritin confirm the sideropenic etiology of anemia.

The prevalence of anemia in the earlier studies (in Misiones and Greater Buenos Aires) was almost twice that found in Tierra del Fuego. Total iron intake and dietary iron density (mg iron/1000 kcal) were similar in the Greater Buenos Aires and Tierra del Fuego studies. Iron intake of 90% of infants was below 11 mg/day (basal requirement considering a global iron bioavailability of 10%), and 70% were below the requirement to prevent anemia.<sup>8,9</sup>

Heme iron intake, as a percentage of daily iron intake, was also similar in Greater Buenos Aires and Tierra del Fuego but was significantly lower in Misiones, amounting to 18%, 14%, and 10%, respectively. Ninety percent of infants in Tierra del Fuego had an intake of bioavailable iron<sup>9</sup> below the 95th percentile of the requirement for absorbed iron.<sup>8</sup> Supplementary iron was given for a longer time in Tierra del Fuego than in the other locations. Birth weights were similar in the three populations. Duration of breast-feeding was longer in Misiones, which is mainly rural, than in the other studies.

The odds ratio of several risk factors related to anemia were different in Greater Buenos Aires and Tierra del Fuego. In Greater Buenos Aires, birth weight, *z* score for height, early introduction of cow's milk (before the third month), age below 18 months, low socioeconomic level, and inadequate pediatric care have odds ratios with confidence intervals greater than 1. In Tierra del Fuego the only condition significantly associated with the risk of anemia was age less than 18 months (Table 2).

These findings are consistent with the analysis of the same factors in a multivariate model using hemoglobin as the dependent variable. Age, birth weight, *z* score for height, mother's educational level (as a dummy variable), quality of pediatric care (another dummy variable), cesarean delivery, length of breast-feeding (in months), total daily cow's milk intake, heme iron intake, and duration of iron supplementation explain more than 24% of the variation of the hemoglobin level in Greater Buenos Aires (adjusted  $r^2 = 0.243$ ,  $p < 0.000$ ) but less than 6% in Tierra del Fuego (adjusted  $r^2 = 0.069$ ,  $p = 0.16$ ), where the only two variables statistically associated with hemoglobin levels

were age below 18 months and heme iron intake. Logistic regression (performed only in Tierra del Fuego) using risk of anemia as the dependent variable and the different conditions potentially related to iron deficiency as the independent variables was not able to demonstrate a significant association between them and the occurrence of anemia in infants.

Infections as a cause of low hemoglobin values can be ruled out in the three surveys because a history of upper respiratory infection, diarrhea, or fever of any origin during the previous three weeks was a criterion for rejecting infants for the hematologic studies.

As noted above, in Tierra del Fuego, not a single risk factor, or group of factors, could be statistically associated with iron deficiency. Conversely, in the Greater Buenos Aires and Misiones studies, the early introduction and amount of cow's milk consumed by infants emerged as an important risk factor (Table 3). In Greater Buenos Aires and Misiones the cow's milk universally consumed was fluid and pasteurized, whereas in Tierra del Fuego the milk consumed was dry or sterilized. Although it is well known that there is induction of microscopic blood fecal losses in small infants fed pasteurized milk,<sup>10,11</sup> we are not aware of studies investigating this immunologic response with dry or sterilized milk, which might denature cow's milk protein, rendering it less immunogenic.

Another difference in the studies related to compliance with the recommendation to give supplemental iron to infants fed cow's milk during the first 2 years of life.

**Table 3.** Iron Status and Early Introduction of Cow's Milk

Introduction of cow's milk	Age (months)			
	0	1–3	4–6	7
Greater Buenos Aires <sup>a</sup>				
Hb < 10.5	18	63	28	31
Hb > 11.5	10	47	34	46
Tierra del Fuego <sup>b</sup>				
Hb < 10.5	2	5	8	4
Hb > 11.5	9	9	24	23

<sup>a</sup> $\chi^2 = 7.97$ ,  $p < 0.05$ .

<sup>b</sup> $\chi^2 = 2.54$ , NS.

Although this information was obtained retrospectively by questioning the mothers, differences between the older studies and Tierra del Fuego are obvious. Perhaps the issue of supplementary iron prescription and compliance is related to the time elapsed between the earlier studies and the most recent in Tierra del Fuego. The publication of the Misiones and Greater Buenos Aires studies produced concern in the pediatric community and health authorities. During this decade, studies about developmental delays occurring in iron-deficient infants have generated great public concern. This possibly increased the prescription of and compliance with supplemental iron regimes, and perhaps induced improvements in the quality of infant diets, increasing intakes of absorption enhancers such as ascorbic acid and decreasing intakes of maté and tea in bottles and during meals. These two popular beverages have known negative effects on iron bioavailability.

We can speculate from the findings of the Tierra del Fuego study, given the good health standards of the population and its compliance with recommendations for infant care and prevention of iron deficiency, that the prevalence of anemia found in infants represents the lowest figure possible without food fortification programs in our country.

#### Anemia in Preschool Children

The only population study available on preschool children is in Tierra del Fuego. The results indicate that the prevalence of anemia in preschool children (11%) is about half that in infants. In all cases anemia was mild: 19% had serum ferritin below 12 µg/dL and 14% had ZPP values > 100 µmol/mol Hb. Another study, from Armelini,<sup>12</sup> showed similar figures, although it was not a true population study.

#### Anemia in Nonpregnant Women of Fertile Age

Data from five studies are available (Table 4<sup>3,6,14-16</sup>). The earliest one was conducted in the province of Salta in 1979.<sup>3</sup> The study in the province of Corrientes (northeast Argentina) was conducted in low-income suburbs of Corrientes City, with a high prevalence of parasitic infestation (22% of surveyed women had uncinaria). Only hemoglobin values were obtained.<sup>14</sup> The study of adolescents in Buenos Aires City (mid and mid-low socioeconomic levels) by Carmuega et al.<sup>15</sup> showed a steady increase in anemia in girls with the progression of the pubertal spurt. The prevalence of anemia at the end of adolescence in females was 18%; in males it was very low.

Women studied in CESNI's Greater Buenos Aires<sup>16</sup> survey were relatives living in the same households of participating infants. Mothers were subjects if their babies were older than 18 months and if they had not breast-fed them for at least the previous 12 months.<sup>16</sup> Iron stores were calculated according to Cook and Finch<sup>17</sup> and were < 150

**Table 4.** Prevalence of Anemia in Women of Child-bearing Age<sup>a</sup>

Population Study	Prevalence (%)	
Salta (1976) ( <i>n</i> = 136) <sup>b</sup>	40.7	
Corrientes Province (1978) ( <i>n</i> = 96) <sup>c</sup>	34.3	
Adolescents in Buenos Aires City (1993) ( <i>n</i> = 386) <sup>d</sup>	12.1	
Tanner scale	Females	Males
I and II	4	20
III	14	4
IV	15	7
V	18	0
Greater Buenos Aires (1986) ( <i>n</i> = 184) <sup>e</sup>	27.7	
MCV > 80 fL	12.3	
ZPP > 80 µmol/mol Hb	42.3	
SF < 12 µg/L	35.5	
Two indicators	21.6	
Tierra del Fuego (1994) ( <i>n</i> = 143) <sup>f</sup>	11	
SF < 12 µg/L	18	
ZPP > 80 µmol/mol Hb	21	
Below iron RDA	87	
Below vitamin C RDA	63	

<sup>a</sup>Definition of anemia according to reference 13.

<sup>b</sup>Reference 3.

<sup>c</sup>Reference 14.

<sup>d</sup>Reference 15.

<sup>e</sup>Reference 16.

<sup>f</sup>Reference 6.

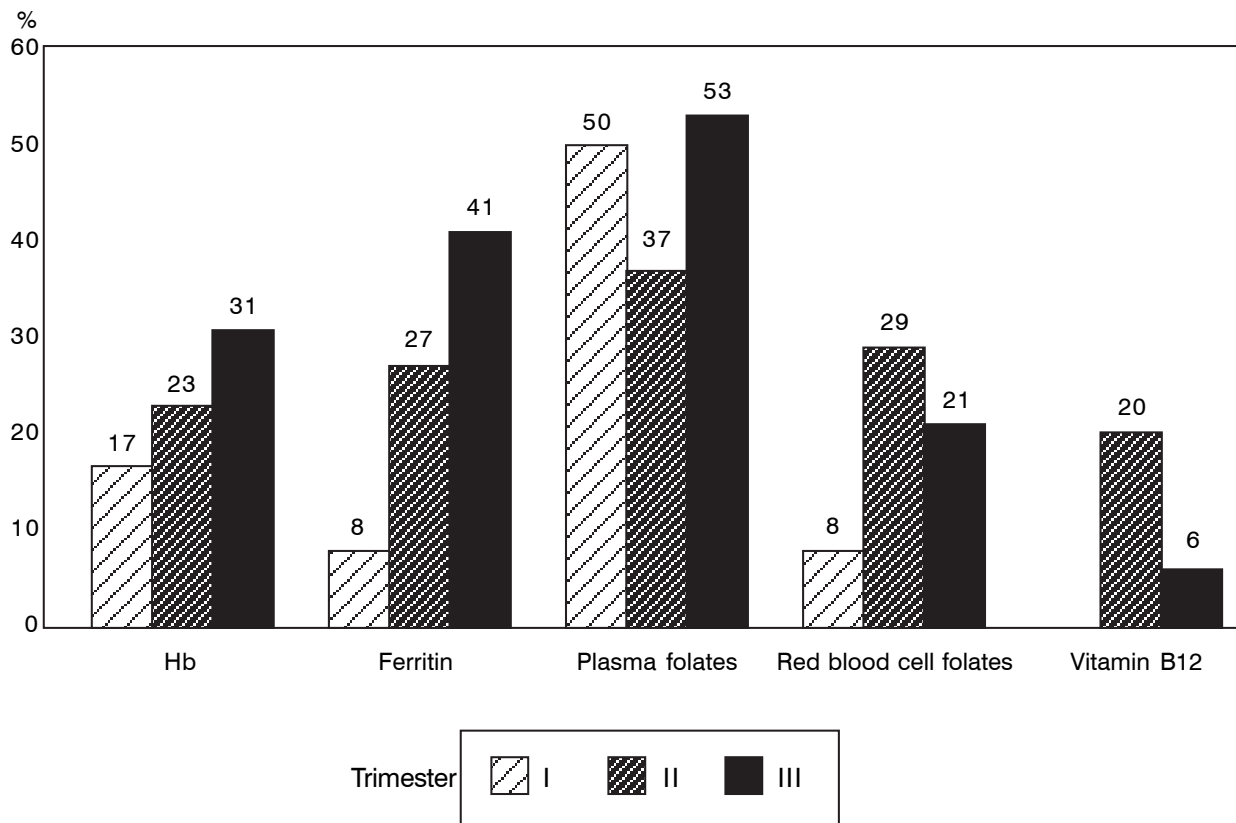
MCV = mean corpuscular volume, ZPP = zinc protoporphyrin, SF = serum ferritin, fL = femtoliter.

mg in 49%, < 300 mg in 64%, and < 600 mg in 81% of women. The median of iron stores was estimated to be 180 mg; in the 10th percentile it was < 390 mg and in the 90th percentile it was < 750 mg. In Tierra del Fuego, as was the case with infants, the prevalence of anemia was lower than in the previous studies.

#### Anemia in Pregnant Women

The only population study on anemia in pregnant women available is the Tierra del Fuego study. Prevalence of anemia and indicators of iron nutritional status by trimester of pregnancy are shown in Figure 1. The prevalence of hemoglobin values below 11 g/dL was 17%, 23%, and 31% in trimesters 1, 2, and 3, respectively. The prevalence of serum ferritin values below 12 µg/L was 8%, 27%, and 41%, respectively. Median iron intake was 8.3 mg/day (range 5.5–10.8); heme iron intake was 0.9 mg/day (0.44–1.7) and bioavailable nonheme iron intake was 0.49 mg/day (0.3–0.8). Eighty-eight percent of women had intakes below 1 mg bioavailable iron.

Vitamin A nutriture was investigated, given its association with anemia. Of pregnant women, 8.7% had serum retinol levels below 20 µg/dL. This rather high prevalence was unexpected because the deficiency of this vitamin had never been studied before in Argentina.



**Figure 1.** Nutritional anemia according to trimester of pregnancy, % of women with abnormal values in Tierra del Fuego survey.

### Interventions to Improve the Iron Status of At-Risk Groups in Tierra Del Fuego

Interventions to improve the iron nutriture of the population vary according to the risk groups targeted.

#### Infants

Food fortification programs do not generally exist in Argentina, except for salt iodization. The most suitable vehicle for iron fortification in infants was selected from the dietary patterns observed in the Greater Buenos Aires and Tierra del Fuego surveys. The contribution of different foodstuffs to daily energy intake was similar in both locations. Cow's milk was introduced in the diets of 30% of infants 4 to 12 months of age. Ninety-five percent of infants regularly received milk in their feedings. During the second half of the first year of life and the entire second year, milk provides at least 30% of the total daily energy intake in those infants receiving cow's milk. Consumption of cow's milk and volumes of intake are independent of socioeconomic level or level of parental education. Milk is largely consumed as fluid UHT by infants in the upper socioeconomic level and as reconstituted full-fat dry milk by infants of lower socioeconomic status. Consumption of infant formulas is negligible.

The high consumption of fluid milk by infants in Tierra del Fuego and in all of Argentina is an established habit.

Therefore, the fortification iron compound to be used must be technologically feasible and bioavailable in dry as well as in fluid milk. Therefore, both forms of milk, fluid and dry, will soon be fortified with ferrous sulfate encapsulated with phospholipids (15 mg/L, as recommended by the Argentine Codex Alimentarius). This compound does not affect the organoleptic properties of milk and can be used in all usual culinary preparations.<sup>18</sup> The bioavailability, shelf life, and pharmacology of this compound were tested in animals and healthy male adults.<sup>18</sup>

Before recommending it as a fortification compound to be used in the Tierra del Fuego project, we conducted a bioavailability study with adult male volunteers, utilizing the method of incorporating absorbed labeled iron into the hemoglobin. The study showed that the absorption of this fortification iron compound was 10% in infants with marginal iron nutrition, which is the case of children in Tierra del Fuego and in other regions of the country.<sup>19</sup>

If nonfortified milk is replaced with milk fortified with 15 mg encapsulated ferrous sulfate per liter, the percentage of infants not meeting the requirement of absorbed iron would likely drop from 90% to 30%.<sup>8</sup> If the 5th percentile of this requirement is considered, only 10% of infants would not reach such intake.

Fortified milk will be complemented with an ad hoc-designed low-cost, precooked, gluten-free infant cereal composed of corn and rice, to be prepared with milk and

fortified with the same ferrous sulfate compound plus vitamins, calcium, and zinc. One serving a day of this cereal provides the following percentage RDAs: 48% iron, 67% ascorbic acid, 67% zinc, 36% copper, 29% vitamin D, and 40% vitamin A, and would allow 95% of the infant population to meet their iron needs and their vitamin C and vitamin A requirements in combination with present food sources. This cereal will be sold at stores and distributed to beneficiaries of mother-child food assistance programs.

### Schoolchildren

School milk programs are a tradition in Argentina and in Tierra del Fuego, where they currently include reconstituted nonfortified, full-fat dry milk. The project distributes 200 mL fortified milk per day to children in all schools in the province, providing 3 mg iron/day. If absorption is estimated at 10% of intake, 0.3 mg/day will be added to their total available iron intake. This means a drop from 90% to 50% in the proportion of children with iron intakes below the 95th percentile of the FAO/WHO 1988 guidelines and from 60% to 5% of children below the 5th percentile.

The school milk program will be complemented with a package containing three cookies (37 g) enriched with bovine hemoglobin (6.27 mg iron/100 g cookies).<sup>20,21</sup> Assuming that the average absorption of hemoglobin iron is 23%, with three cookies containing 2.3 mg iron, the iron needs of all of the schoolchildren in Tierra del Fuego will be met.

### Breast-fed Infants

For infants exclusively breast-fed, medicinal iron as ferrous sulfate or another iron salt of equivalent absorption will be prescribed at 4 months of age and older, according to recommendations of the Ministry of Health and the Argentine Pediatric Society<sup>1</sup> (15 mg ferrous sulfate/day). Compliance will be evaluated by primary health care providers during their scheduled monthly visits to the homes of all infants in the province.

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