Efficacy trials of a micronutrient dietary supplement in schoolchildren and pregnant women in Tanzania

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Abstract

Traditionally, the main strategies used to control micronutrient deficiencies have been food diversification, consumption of medicinal supplements, and food fortification. In Tanzania, we conducted efficacy trials using a dietary supplement as a fourth approach. These were randomized, double-blind, placebo-controlled efficacy trials conducted separately first in children and later in pregnant women. The dietary supplement was a powder used to prepare an orange-flavored beverage. In the school trial, children consumed 25 g per school day attended. In the pregnancy trial, women consumed the contents of two 25-g sachets per day with meals. This dietary supplement, unlike most medicinal supplements, provided 11 micronutrients, including iron and vitamin A, in physiologic amounts. In both trials we compared changes in subjects consuming either the fortified or the nonfortified supplement. Measures of iron and vitamin A status were similar in the groups at the baseline examination, but significantly different at follow-up, always in favor of the fortified groups. Children receiving the fortified supplement had significantly improved anthropometric measures when compared with controls. At four weeks postpartum, the breast milk of a supplemented group of women had significantly higher mean retinol content than did the milk of mothers consuming the nonfortified supplement. The advantages of using a fortified dietary supplement, compared with other approaches, include its ability to control several micronutrient deficiencies simultaneously; the use of physiologic amounts of nutrients, rather than megadoses that require medical supervision; and the likelihood of better compliance than with the use of pills because subjects liked the beverage used in these trials.

Key words: Iron, micronutrients, powder beverage, pregnancy, supplement, Tanzania, vitamin A

Introduction

Micronutrient deficiencies, particularly of iron, iodine, and vitamin A, have been recognized for many years as serious health problems in developing countries [1], including in Tanzania [2]. Well over two billion people worldwide are believed to suffer from these deficiencies, with women of reproductive age and young children at greatest risk. It is also known that in many developing countries, zinc deficiencies are also prevalent; inadequate intakes of vitamin C may adversely influence iron absorption; vitamin E is an important antioxidant; and the following vitamin B-complex deficiencies also have adverse results: riboflavin (widespread ariboflavinosis), vitamin B_{12} (anemia), vitamin B_6 (neuropathies), folate (anemia and spina bifida), and niacin (pellagra). Very few developing countries have in place strategies to control these micronutrient deficiencies.

Standard strategies to overcome micronutrient deficiencies

Despite the wide prevalence and devastating consequences [3] of micronutrient deficiencies worldwide, the established approaches to control them have remained much the same for more than three decades and consist mainly of the following three strategies:

» *Dietary diversification.* Clearly the aim of nutritionists is to ensure that people consume a variety of foods that together provide adequate quantities of all the essential micronutrients necessary for health. Actions

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taken may include nutrition-education programs to achieve behavioral change, as well as increasing and diversifying regional and/or household production and consumption of micronutrient-rich foods.

» *Food fortification.* The addition of a micronutrient to a food item that is widely consumed by a population at risk of a deficiency has been a widely used strategy for many years in industrialized countries. The classic example is the iodization of salt now practiced in many countries. Other examples are vitamin A added to dairy products and iron to baby cereals.
» *Medicinal supplementation.* This includes the provision of a micronutrient often through the healthcare system usually in the form of a pill, liquid, or injection. It may include (a) periodic administration of megadoses of a specific micronutrient, such as vitamin A or iodine, or (b) regular provision of medicinal amounts of a micronutrient in amounts much higher than the recommended daily intakes (RDI), for example, iron supplements during pregnancy.

Disadvantages and limitations of standard strategies

These three strategies have had both successes and failures, and each has disadvantages and limitations. Many agree that food diversification offers the best long-term approach that is likely to be sustainable [4]. But often it requires either major change in agricultural production, including home gardens, or in higher incomes for the poor, allied with nutrition education. Therefore, progress is slow in many non-industrialized countries, and in some African countries with a deteriorating economic situation, food diversification is unlikely to reduce substantially micronutrient deficiencies in the near future. The conditions needed for successful fortification vary depending on the foods widely eaten in a country and the nutrients being considered for fortification. In some countries several commonly eaten foods do pass through commercial processing where fortification is feasible. Salt iodization has greatly reduced iodine deficiency disorders in many countries, including Tanzania. But in many non-industrialized countries it is difficult to find a suitable food vehicle to fortify with iron or vitamin A. To be suitable for fortification, a food must be consumed regularly by those at risk of the deficiency—often children and women in poor families. Especially in rural areas, those suffering from micronutrient deficiencies may purchase few manufactured or processed foods.

There are two kinds of medicinal supplements. First there are those taken in pharmacologic doses daily or at frequent intervals, and second are those prescribed to be consumed in megadoses at intervals of 4 to 24 months. Ferrous sulfate and folate are examples of the former, and vitamin A and Lipiodol® (iodinated poppy seed oil) and oral iodine are examples of the latter. Medicinal supplementation is dependent on a delivery system, which is often relatively costly if the supplement is to reach those at risk. Other problems include poor compliance, which is common with iron prescribed during pregnancy, and low participation rates, such as when massive dose vitamin A supplements are offered over time.

Common problems in implementing the standard strategies

A World Bank review of micronutrient programs [5] found three common problems arising from the implementation of any or all of these strategies: (1) lack of appropriate consumer demand; (2) lack of appropriate delivery infrastructure with adequate access for poor women and isolated populations; and (3) lack of honest, efficient, and technically competent enforcement systems for food fortification.

Appeal of micronutrient dietary supplements as a fourth approach

Micronutrient dietary supplements offer a fourth approach and one that can control several micronutrient deficiencies simultaneously. This approach differs from medicinal supplementation in that several micronutrients are provided at the same time; the micronutrients are provided in physiologic amounts, rather than in megadoses; the supplements can be self "prescribed" or purchased in the marketplace, rather than through the healthcare system; and they are usually pleasant to take, and therefore avoid problems of compliance often associated with medicinal supplements. However, micronutrient dietary supplements have not been very widely used to control common deficiencies in developing countries. The dietary supplement we used has some features of fortification and others related to more common forms of supplementation.

Trials of a micronutrient dietary supplement in Tanzania

In the Dodoma Region of Tanzania, two separate double-blind, placebo-controlled field efficacy trials have been completed using a multiple-micronutrient-fortified dietary supplement. The first trial [6, 7] was conducted with young primary schoolchildren and the second with pregnant women, some of whom were followed postpartum during 4 weeks of lactation [8].

Micronutrient deficiencies including iron deficiency, vitamin A deficiency, and iodine deficiency disorders are recognized as important public health problems in Tanzania [2]. The trials were collaborative involving the Tanzania Food and Nutrition Centre (TFNC), Cornell University (Ithaca, NY, USA), United Nations Children's Fund (UNICEF), the Micronutrient Initiative (MI) (Canada), and The Procter & Gamble Co. (P&G) (Cincinnati, Ohio, USA).

The dietary supplement used was a fortified powdered fruit drink. It was developed and produced by scientists at P&G in Ohio, especially for these trials in Tanzania. However nutritionists at TFNC and Cornell University, in consultation with P&G and others, made the decision about which micronutrients to include and in what quantities.

The dietary supplement was supplied to the research team in individual-serving paper sachets each containing 25 g of a fine white powder. The contents of a sachet, when added to 250 ml of water, turned orange and produced a pleasant tasting orange-flavored beverage. The micronutrient content of each fortified sachet is shown in table 1. As indicated in the table, niacin was not included in the supplement for the school study, but was included for the pregnancy trial.

For each trial, P&G provided an equal quantity of nonfortified supplement (placebo) identical in appearance and taste to the fortified supplement. The sachets containing the fortified and nonfortified beverage supplements differed only in the color of the package. The study participants as well as the research team did not know which sachets were fortified and which were not until the results had been analyzed, when the code was broken. Different-colored sachets were used for each of the trials.

Table 1. Nutrient levels in each micronutrient fortified sachet[a]

Nutrient	Amount of nutrient in 25 g sachet	% RDI[b] Value per sachet
Iron (Ferrochel®)	5.4 mg	30
Vitamin A (retinyl palmitate)	1,750 IU	35
Iodine	45 μg	30
Zinc	5.25 mg	35
Ascorbic acid	72 mg	120
Riboflavin	0.6 mg	35
Folic acid	0.14 mg	35
Vitamin B_{12}	3 μg	50
Vitamin B_6	0.7 mg	35
Vitamin E	10.5 mg	35
Niacin[c]	5.0 mg	30

a. In the school trial, children consumed one sachet per school day attended. Women in the pregnancy trial were instructed to consume two sachets per day, one with the morning and a second with the evening meal.

b. RDI = recommended daily intake

c. Niacin was not included in the school trial.

Efficacy trial in schoolchildren

This was a randomized, double-blind, placebo-controlled efficacy trial. The children who participated were recruited from six rural primary schools in Mpwapwa District in the Dodoma Region of Tanzania. The main objective of the trial was to determine whether a dietary supplement providing 10 micronutrients in physiologic amounts resulted 6 months later in differences in measures of iron status, serum retinol, and child growth when compared with children receiving a nonfortified supplement identical in appearance and taste. Children were randomly assigned to be in either the fortified or nonfortified group. The children, teachers, and researchers did not know which sachets—the blue ones labeled "J" or the green ones labeled "K"—were fortified. The content of each sachet was added to 250 ml of previously boiled water to form a pleasant tasting orange-flavored beverage. During the morning break children lined up according to the two groups and were served their beverage. Teachers recorded attendance in the compliance notebooks.

The results presented here relate mainly to the 774 young primary schoolchildren examined at baseline and 6 months later at the follow-up examinations. All had participated and consumed on each school day attended one sachet of either the fortified or nonfortified beverage. Details relating to subject selection, methodology used, and detailed results in relation to iron nutrition status, serum retinol levels, and anthropometry have been reported elsewhere [6]. Baseline characteristics of children in the fortified and nonfortified groups were similar in terms of mean age, gender distribution, anthropometric measures (weight, height, and body mass index [BMI]), hemoglobin and serum retinol levels, and presence of helminthic infections in their stool samples.

Baseline measurements of both groups

The beverage was very well liked and consumption rates were very high. The percentage of days of possible consumption during the trial did not differ between the two groups (79.9% in the fortified and 81.1% in the nonfortified group). At baseline, 18.5% of the fortified group and 19.1% of the nonfortified group had hemoglobin levels below 110g/L. Findings show that 21.4% of the fortified group and 20.6% of the nonfortified group had serum retinol levels below 200 μg/L. Anthropometry showed that 50.5% of children in the fortified group and 49.5% of children in the unfortified group had height-for-age Z-scores below –2. In none of these measurements are the differences significant between the two groups at baseline.

Changes in hemoglobin, serum ferritin, and serum retinol levels

After 6 months, hemoglobin levels had declined significantly in both the fortified and nonfortified groups, although the decline of 6.7 g/L in the nonfortified group was significantly larger than the decline of 3.2 g/L in the fortified group (table 2). We have discussed elsewhere [6] our belief concerning the reasons why hemoglobin levels declined in both groups between baseline and follow-up. We believe this was mainly a seasonal effect because the follow-up exams were performed at a time of year when food is often in short supply prior to the next harvest and a period when malaria transmission is very high. As shown, serum ferritin levels increased significantly in the fortified group, but there was no significant change in the nonfortified group. In those children with anemia at the baseline (Hb < 110 g/L [9]) there was a significantly higher rise in hemoglobin concentration (9.2 g/L) in the fortified group compared with a nonsignificant rise in the nonfortified group (0.3 g/L). At baseline, there was no significant difference in the percentage of children with anemia (18.5% versus 19.1%). At follow-up, there was a significant difference (chi-square = 0.005) in the percentage of children in the two groups who were still anemic (26.3% versus 35.6%). In terms of serum retinol determinations, the percentage of children in the fortified group whose serum retinol was below 200 µg/L declined from 21.4% to 11.3% between baseline and follow-up (table 3). This was a very significant improvement. In contrast, the percentage decline in those with deficient serum retinol levels was not significant in the nonfortified group.

Anthropometric-measurement changes

In terms of anthropometry, there were no significant differences in mean weight, height, and BMI between groups at the baseline examination [7]. However, at follow-up, incremental changes in weight (1.79 versus 1.24 kg, a difference of 0.55 kg); in height (3.2 cm versus 2.6 cm, a difference of 0.6 cm); and in BMI units (0.88 versus 0.53, a difference of 0.35) were significantly higher in the fortified compared with the nonfortified group (results not shown).

Efficacy trial in pregnant women

The pregnancy trial in the Dodoma Region in Tanzania in 1999 enrolled pregnant women attending six different clinics, five in Mpwapwa and one in Kongwa Districts [8]. At baseline, 579 women were screened; 140 were excluded mainly because their pregnancies were too advanced (50%) or because their hemoglobin levels were below 80 g/L (26%). Of the 439 women who enrolled in the study, the main results presented here relate to 259 women who both participated in the supplementation trial and who had not delivered 8 weeks after their initial examination. (Fifty-nine supplemented mothers delivered their infants before 8 weeks of follow-up had elapsed and another 121 women were lost to follow-up.)

The objective of the trial was to evaluate the effect of the micronutrient supplement on iron status, hemoglobin, and serum retinol levels. In a subgroup of women, breast milk was obtained 4 weeks postpartum to determine retinol levels.

At each clinic site, after the baseline examination, pregnant women were randomly assigned to receive either the micronutrient-fortified or the nonfortified dietary supplement. Each woman was carefully instructed on how to mix the contents of one sachet with about 250 ml of clean boiled water to produce a single serving of the orange-flavored beverage. They

TABLE 2. Concentrations of hemoglobin and serum ferritin in children at baseline and after 6 months of supplementation, and the respective changes compared with baseline

	Nonfortified			Fortified			
Endpoint	*n*	Mean (SD)	Paired *t* test *p* value	*n*	Mean (SD)	Paired *t* test *p* value	Between group *p* value
Hemoglobin (g/L)							
Baseline	376	119.7 (13)		373	119.2 (14)		.639
Follow-up	376	112.9 (15)		373	116.0 (13)		.001
Difference[a]		–6.7 (13)	.001		–3.2 (13)	.001	.001
Serum ferritin[b] (µg/L)							
Baseline	148	33.88 (30.97–37.83)		149	29.51 (29.97–33.02)		.054
Follow-up	148	36.31 (33.43–40.13)		149	45.71 (42.20–50.15)		.001
Difference		2.05 (28)	.180		15.90 (33)	.001	.001

a. Difference is mean within-individual incremental change between baseline measurements and measurements after 6-month intervention.
b. Geometric mean ± 95% confidence interval (CI).

TABLE 3. Percentage of children with serum retinol concentration below 200 μg/L in the fortified and nonfortified group at baseline and follow-up examinations

Serum Retinol % below 200 μg/L	*n*	Fortified %	*n*	Nonfortified %	Between group significance
Baseline	364	21.4	370	20.6	NS
Follow-up	364	11.3	370	19.7	.001
Difference		10.4		0.9	.001
Significance of difference		.001		NS	

NS = Not significant

were requested to consume two sachets daily, one with the morning and the second with the evening meal. Each woman was provided with a plastic mug and a 2-week supply of supplement and was requested to collect new supplies every 2 weeks at the clinic for the duration of the 8-week intervention period. During each follow-up visit they brought back the empty sachets that were counted, thus serving as one method of measuring compliance [10].

Baseline measurements of both groups

Data collected at baseline included assessment of gestational age; information on parity and gravidity of the current pregnancy; history of medical problems and health status; phlebotomy to collect 5 ml of blood (2 ml of serum) for immediate determination of hemoglobin and later analyses of serum ferritin and C-reactive protein (CRP) levels; finger-prick capillary blood to prepare dried spots on filter paper for subsequent determination of retinol and thyroid stimulating hormone levels; and anthropometric data, including height, weight, mid-upper arm circumference, and triceps skinfold thickness. Most of the appropriate measurements were repeated at the 8-week follow-up examination.

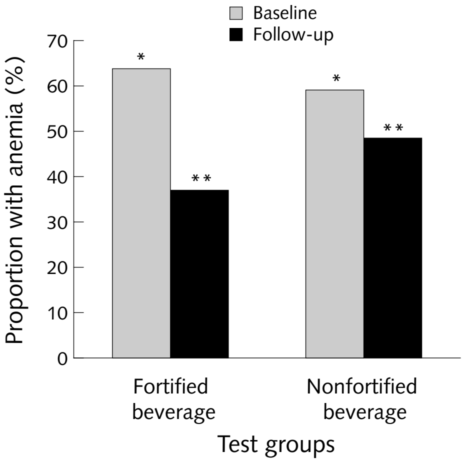
Similarities between groups

There was no significant difference at the baseline in terms of hemoglobin and serum ferritin levels of those women who completed the study when compared with those who did not. An equal number of subjects were lost from each treatment group. There were also no significant differences in the age, educational level, parity, gravidity, or anthropometric measurements in women in the two groups. Women in the group receiving the fortified supplement had a marginally higher gestational age when compared with those receiving the nonfortified supplement. The prevalence of parasitic infestation was low and did not differ between treatment groups, nor did history of malarial infection or additional iron supplementation. No significant differences were found in levels of thyroid stimulating hormone (TSH) between groups, or between baseline and follow-up examinations. Most subjects were using iodized salt.

Hemoglobin-level changes

At baseline, 61.4% of the study participants were anemic (hemoglobin level below 110 g/L [9]) with no significant difference between the experimental and the control groups. At the end of 8 weeks of supplementation, both groups experienced a decrease in the incidence of anemia. The proportion of anemic women in the control group declined from 59.1% to 48.5%. In contrast, women in the fortified beverage group experienced an almost 27% decline from 63.8% to 37%, producing a highly significant difference (P = .019) in the proportion of anemic women between the nonfortified and fortified groups at the end of the treatment period (48.5% versus 37%, respectively) (fig. 1).

Table 4 shows that both groups experienced a significant increase in hemoglobin concentration. However, mothers in the fortified-beverage group had a mean increase of 9 g/L while mothers in the nonfortified group had mean increase of only 4 g/L. Therefore, fortified group women experienced a 5 g/L significantly higher increase in hemoglobin concentration when compared with nonfortified group women (P = .015).



* p = .438 ** p = .019

FIG. 1. Comparison of proportion of women with anemia (hemoglobin < 110 g/L [9]) at baseline and at follow-up in the fortified and nonfortified beverage groups

TABLE 4. Hemoglobin, ferritin, and serum retinol concentrations in women before and after supplementation

Indicator	Fortified beverage				Nonfortified beverage (placebo)			
	n	Mean	(SD)	Sig.	n	Mean	(SD)	Sig.
Hemoglobin (g/L)								
Baseline	127	105	(14.2)		132	105	(14.9)	
Follow-up	127	114	(14.0)		132	109	(15.1)	
Difference	127	9		.000	132	4		.000
Ferritin (µg/L)								
Baseline	118	184.7	(2.31)		116	189.1	(2.4)	
Follow-up	118	215.1	(2.1)		116	169.2	(1.97)	
Difference	118	30.4		.012	116	–19.9		.166
Serum Retinol (µmol/L) (not delivered)[a]								
Baseline	116	1.04	(0.36)		126	1.00	(0.33)	
Follow-up	116	0.78	(0.27)		126	0.78	(0.29)	
Difference	116	–0.26		.000	126	–0.22		.000
Serum Retinol (µmol/L) (delivered)[b]								
Baseline	28	0.93	(0.29)		18	1.02	(0.34)	
Follow-up	28	1.08	(0.32)		18	0.96	(0.25)	
Difference	28	0.15		.078	18	–0.06		.509

a. Mother has not yet delivered at 8-week follow-up
b. Mother had delivered before 8-week follow-up

Changes in serum ferritin levels

As shown in table 4, there was no significant difference at the baseline in the mean ferritin concentration of the two groups (184.7 versus 189.1 µg/L). At the 8-week follow-up, however, the mean serum ferritin level was significantly higher (45.9 µg/L) in the fortified-beverage group than in the nonfortified group (P = .009). Mothers in the fortified-beverage group had a significant mean increase of 30.4 µg/L, while mothers consuming the nonfortified beverage experienced a nonsignificant mean drop of 19.9 µg/L. Therefore, the fortified beverage appeared to result in a net improvement in ferritin concentration.

Changes in serum retinol levels

The results of the serum retinol determinations, including the changes between baseline and follow-up examinations in both groups of subjects are also shown in table 4. Data are included for any woman in either group who had not delivered her infant, and also for the smaller number of women who had delivered prior to the completion of 8 weeks of supplementation. As shown in table 4 there was a decline in serum retinol levels between the baseline and follow-up examination prior to delivery in both groups. It is known that serum retinol levels decline during the last weeks of pregnancy and that it takes rather large doses of medicinal vitamin A to reverse this decline [11]. However, in those mothers who had delivered their infants, the mothers consuming the fortified supplement had a significant improvement in serum retinol levels (fig. 2), whereas there was a marginally significant decline in mean serum retinol levels in mothers receiving the nonfortified supplement. At follow-up, mothers who had delivered and were in the fortified group had mean serum retinol levels 0.12 µmol/L higher than similar mothers consuming the nonfortified supplement. In a separate analysis, we found that serum retinol levels were positively correlated with increases in hemoglobin [8], illustrating the importance of an adequate vitamin A status in the control of anemia.

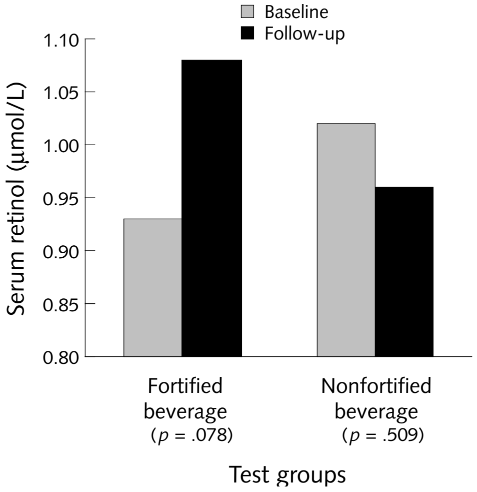


FIG. 2. Changes in serum retinol in women who had already delivered at the time of follow-up (N = 46)

Breast milk retinol levels

Samples of breast milk were obtained approximately 4 weeks postpartum in 50 mothers in the fortified group and 34 in the nonfortified group. The results are provided in table 5, which shows that mothers in the fortified group had mean breast milk retinol levels of 1.24 μmol/L compared with 1.06 μmol/L in mothers consuming the nonfortified beverage. The difference is highly significant. In a separate analysis, we found that serum and breast milk retinol levels were significantly positively correlated. Breast milk retinol levels were not significantly associated with other measures of nutrition status, such as hemoglobin or serum ferritin levels. Therefore, the results show that the fortified supplement was significantly associated with higher breast milk retinol levels.

TABLE 5. Comparison of breast milk retinol (μmol/L) in mothers belonging to the two treatment groups

	Fortified		Nonfortified	
	N	Mean (SD)	N	Mean (SD)
Breast milk retinol[a]	50	1.24 (.34)	34	1.06 (.30)

a. $t = 2.574$, df 82, $p = .012$

Benefits of the micronutrient dietary supplement

These trials were initially designed to test the efficacy of a newly developed multiple-micronutrient supplement both in schoolchildren and in pregnant women. The results summarized above illustrate that the fortified supplement when compared with the nonfortified supplement had a positive impact on measures of iron (in terms of hemoglobin and serum ferritin levels) and vitamin A status (in serum retinol levels) in both children and women; it appeared to improve the growth of children; and it also seemed to increase levels of retinol in breast milk from mothers consuming the fortified beverage.

As previously mentioned, the major micronutrient deficiencies identified in Tanzania are iron, iodine, and vitamin A deficiency [2]. The ultimate objective of the trial was not only to deliver adequate levels of bioavailable iron, stable vitamin A, and iodine via the beverage that schoolchildren and pregnant women found to be highly palatable and pleasant to take, but also to provide in physiologic amounts many other essential minerals and vitamins, including zinc, vitamin C, and folate (table 1). From unpublished dietary evidence, daily consumption of the beverage raised the intakes of the 10 micronutrients (11 in the pregnancy trial) to levels above accepted recommended dietary intakes. Therefore, the multiple-micronutrient-fortified powdered fruit drink delivers nutrients in a tasty beverage that is convenient and affordable.

Product acceptance

During the pregnancy trial, we employed, with UNICEF support, a social anthropologist with extensive Tanzanian experience to examine social attitudes toward the use of this beverage supplement. We recognized that frequently a new health or nutrition intervention, even if scientifically demonstrated to be efficacious, does not assure that people are likely to accept or adopt the product tested. The anthropologist concluded [10], without qualification, that women (1) like the beverage as a delivery vehicle; (2) prefer this dietary supplement to pills such as ferrous sulphate, (3) consider it beneficial to health, and (4) are willing, and able, to utilize the supplement properly and follow instructions concerning its use.

We found that the Ministry of Health very frequently fails to make available iron and folate tablets to pregnant women, and in Tanzania (as is the case in many countries), it has been shown that compliance in taking these tablets is low. So our trial leads us to believe that a dietary supplement such as this would be popular, be widely consumed, and could have major benefits. In the case of Tanzania we are exploring ways to have it locally manufactured.

Micronutrient dietary supplements offer a viable fourth approach, one that can control several deficiencies using a single intervention. This approach is different from the three standard approaches mentioned earlier, because it delivers micronutrients that fill the nutrition gap via a vehicle that is, or becomes, well accepted by the target group.

Early successes in dietary supplementation

The supplementation of diets with a specific food substance high in one or more micronutrients recognized as potentially deficient in the regular diet is not a new concept. Up to about 60 years ago, children in industrialized or industrializing countries received a regular dose of cod liver oil to stave off the effects of vitamin A and D deficiencies. In the early 1900s, rickets (the consequence of prolonged deficient vitamin D intake or lack of sunshine) was very common among children in the poor communities of industrialized cities where the diets were comprised of a small range of foods and there was limited access to outdoor areas and thus direct sunlight. In some countries, on the shelves of remote, small rural and urban shops, one can still find bottles of a concoction of halibut oil high in vitamins A and D or of Ribena® (GlaxoSmithKline Group), to provide vitamin C. Glucosade, a supplement claiming to provide instant energy, is widely sold; its main nutrient is glucose. Other products, some labeled as "tonics," are widely available in many countries worldwide. However these supplements and tonics often do not include those minerals and vitamins most lacking in local diets. Often, these products are a very costly way of providing micronutrients to target groups that have limited income.

In Europe and North America, the promotion of cod liver oil and other healthful dietary supplements empowered mothers with affordable options to prevent rickets in their children, and where such solutions were not affordable, those dietary supplements were available free of charge through public health clinics. The development of better health care systems, affordable and diversified food supplies, and a growing appreciation of the health benefits of outdoor play presumably also underlie the decline of rickets in industrialized countries [12]. Unfortunately, the concept of regular dietary-supplement consumption has not been translated from industrialized countries to the populations of nonindustrialized countries that continue to be at risk of, or suffer from, micronutrient deficiencies.

Recently in South Africa, a trial of a micronutrient-fortified biscuit was successfully tested and yielded positive results [13]. There is also extensive literature on the successful use of dietary or food supplements such as Incaparina in Guatemala to provide additional energy, protein, and other nutrients to children [14].

Implementing a new dietary supplement

In conclusion, the dietary-supplement strategy recognizes the key principles incorporated in one or all of the other three commonly used intervention methods as follows: behavioral change via social marketing, diversification of food intake, supply of specific vitamins in specific foods, and regular doses of vitamins and minerals specific to regionally or locally recognized deficiencies. These are the underlying mechanisms by which micronutrient deficiencies are addressed. Just as food diversification seeks to create a supply, demand, and taste for a new food item, so should the promotion of a dietary supplement; and, just as medicinal supplements aim to provide a significant (albeit pharmacologic) dose of specific nutrients, a well-developed supplement could do the same using physiologic amounts.

Dietary supplements may potentially overcome some of the problems identified with other approaches to micronutrient deficiencies. Where sufficient appreciation and desire for the food item is generated—developed through commercial marketing strategies—supply should be ensured through market demand. Political will and external, public resources are not necessary inputs, although they could be of benefit in generating a rapid development of demand and supply or for ensuring access through subsidies and/or free supply where income is not sufficient. The argument for a contribution from commercial manufacturers to the cost of subsidies and for social-marketing promotions should not be overlooked given the potential for longer-term sales development.

As with the dietary supplement practices of old, this approach can empower mothers and families with a healthful, care-giving practice that they control and can ideally access with security at reasonable cost. Importantly, it is technically possible to include several micronutrients within a single food item, thus the process of addressing a situation where there are several deficiencies is simplified—a clear advantage over current fortification and medicinal-supplementation strategies.

Other versions of the test product

The dietary supplement described here was produced by food scientists at The Procter & Gamble Co. in Cincinnati and was especially manufactured to contain the range and amount of micronutrients we requested for the trials in Tanzania. The same dietary supplement, also in the form of a powder to make a fruit-flavored beverage, has more recently been tested elsewhere, sometimes with alternative packaging and different flavoring other than orange. It has been extensively tested in the Philippines [15], is being manufactured and commercially marketed under the brand name NutriStar® in Venezuela (P&G), and is being tested in an efficacy trial in adolescent girls in Bangladesh.

Public-private partnerships

The Tanzanian trials described here provide an excellent example of public-private partnerships and true collaborative efforts. In the work in Tanzania, collaboration involved the TFNC; UNICEF staff based in New York, Nairobi, and Dar es Salaam; the Micronutrient Initiative in Canada; The Procter & Gamble Co.; Cornell University's Division of Nutritional Sciences; and importantly also local institutions and civil society in the Dodoma Region of Tanzania. This collaboration and long-term partnerships have been rewarding to all and have been maintained over many years.

Plan for overcoming micronutrient deficiencies in Tanzania

Tanzania is currently taking steps to address the serious problems of iron, vitamin A, and iodine deficiencies. Wisely, a variety of strategies are being used. Among the interventions being tried are iron and folate supplements administered to pregnant women; programs to deworm children in part to reduce anemia; fermentation and germination of grains to improve iron utilization and to reduce the action of phytates;

vitamin A supplementation in high-risk children in many health units; efforts to increase the production and consumption of carotene-rich foods; legislation to ensure iodization of salt from the major manufacturers; and other actions to address diseases, such as malaria, that influence nutrition status [16].

These two studies in Tanzania are considered an important first step in testing and further developing the mechanism of dietary supplementation for addressing micronutrient deficiencies. A distinction is being made here between medicinal supplements such as ferrous sulphate tablets and dietary supplements. Differences include the fact that medicinal supplements are taken under medical supervision and control, whereas dietary supplements for children are controlled by the mother or family, and for the pregnant woman by the mother herself. Another important difference is that this dietary supplement provided physiologic “doses” of 11 micronutrients, where medicinal supplements provide doses of micronutrients much above the RDI and often only one or two micronutrients per dose.

It is not expected or intended that this approach will replace current programs and strategies, but instead that it will provide policy makers, health planners, and, more importantly, mothers and families, with an additional option. The decision on which strategy to pursue or promote and how public dollars will be directed must be assessed on a case-by-case basis. Moreover, consistent with current understandings and experiences, which show that no single approach will be effective in all settings and at all times, the further development of this fourth option can provide an effective means to fill the gaps left by the other three approaches.

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Effect of a multiple-micronutrient-fortified fruit powder beverage on the nutrition status, physical fitness, and cognitive performance of schoolchildren in the Philippines

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Abstract

This study aimed to determine the effect of a multiple-micronutrient-fortified beverage on the micronutrient status, physical fitness, and cognitive performance of schoolchildren. The study was a randomized, double-blind, placebo-controlled trial of schoolchildren assigned to receive either the fortified or nonfortified beverage with or without anthelmintic therapy. Data on hemoglobin level, urinary iodine excretion (UIE) level, physical fitness, and cognitive performance were collected at baseline and at 16 weeks post-intervention. The fortified beverage significantly improved iron status among the subjects that had hemoglobin levels < 11 g/dl at baseline. The proportion of children who remained moderately to severely anemic was significantly lower among those given the fortified beverage. In the groups that received the fortified product, the median UIE level increased, whereas among those who received the placebo beverage, the median UIE level was reduced significantly. Iron- and/or iodine-deficient subjects who received the fortified beverage showed significant improvements in fitness (post-exercise reduction of heart rate) and cognitive performance (nonverbal mental ability score). The study showed that consumption of a multiple-micronutrient-fortified beverage for 16 weeks had significant effects on iron status, iodine status, physical fitness, and cognitive performance among iron- and/or iodine-deficient Filipino schoolchildren. Anthelmintic therapy improved iron status of anemic children and iodine status of the iron-adequate children at baseline but it had no effect on physical fitness and cognitive performance. The results from the clinical study showed that a multiple-micronutrient-fortified beverage could play an important role in preventing and controlling micronutrient deficiencies.

Key words: Children, fortified powder beverage, iodine, iron, multiple micronutrient

Introduction

Micronutrient malnutrition has been recognized not only to be widespread but also, if uncorrected, to cause serious health, developmental, and economic problems [1–4]. More than 2 billion people worldwide are affected by micronutrient malnutrition [1–4]. In addition, children in developing countries are prone to infection, including chronic infection with a variety of parasites [5–7]. The combined effects of undernourishment and chronic helminth infections can be serious. In areas where both are common, much of the student population may carry a significant health burden [2, 5–7], with resulting delays in physical, emotional, and intellectual growth that have the potential to prevent the children from reaching their full potential in both physical and mental development.

The nutrition status of children in developing countries reflects the fact that, for much of the world's population, adequate nutrition is hindered by a plethora of geopolitical, cultural, and economic issues [8, 9]. In fact, one of five people in developing countries does not regularly consume enough food to meet minimum nutrition requirements [9]. Deficiencies of iron, iodine, and vitamin A are considered important global health problems [1–4], due to both widespread prevalence and the potential for such nutritional deficits to create serious health problems [10]. Deficiencies of zinc [11] and folate [12] are also common. Vitamin

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C can be seasonally difficult to obtain in some regions [10], and in some groups, cultural practices restricting exposure to sunlight for female children create deficits of vitamin D [13].

Iron deficiency and anemia

The most widespread nutrition problem in the world is anemia [2–4, 14], affecting an estimated 2.15 billion people globally, with women and children affected the most. As much as 90% of anemia cases result directly from a deficiency of iron [14].

In children, anemia has been shown to affect both physical and cognitive development. Anemia produces pronounced lethargy with a decreased physical capacity for activity, which in children results in less time spent playing or exploring [1–4, 15–18]. Cognitive function is impaired in anemic schoolchildren, as evidenced by poorer school performance and lower scores on tests of concentration and cognitive development [16–20]. "Subclinical" iron deficiency is also recognized as a public health issue in schoolchildren. Non-anemic iron deficiency has been demonstrated to have subtle but demonstrably adverse health consequences, including lethargy, decreased physical capacity, decreased immune function, increased infection, and increased morbidity from infection [21, 22].

Iodine deficiency

Iodine deficiency, the single most preventable cause of mental retardation in the world, is another critical public health issue; approximately 40% of the world's population lives in areas where the risk of iodine deficiency disorder (IDD) is significant [23–25]. The prevalence of iodine deficiency is estimated to be approximately 250 million cases worldwide, with 50 million people suffering from goiter [26] and another 3.5 million affected by congenital IDD-associated cretinism [26, 27]. IDD causes neurologic abnormalities and impairment, with cognitive effects that range from mild motor or cognitive deficits to severe congenital or developmental retardation [25]. The impact of IDD on intelligence quotient (IQ) scores has been estimated at a decrease of 10–15% [24], or about 10 points [28].

Multiple micronutrient deficiencies

In developing countries, where people may be deficient in several micronutrients at one time, multiple-micronutrient supplementation may be necessary for optimal effect. In addition, many critical vitamins are interdependent with regard to efficacy and optimal absorption. Vitamin A is critical for iron metabolism and utilization; response to iron supplementation is measurably diminished if vitamin A deficiency is also present and is not simultaneously treated [29, 30]. Vitamin C is also necessary for optimal iron absorption [31, 32]. Deficiencies of vitamin A and iron, in turn, decrease thyroid metabolism, which subsequently decreases the response to supplemental iodine [27].

Intervention methods

Although long-term resolution of micronutrient deficiencies in the developing world will probably include educational programs and nutrition diversification [6], short-term urgency and practical considerations have favored two approaches to intervention. These include fortification of commonly consumed foods and supplementation [33].

Micronutrient supplementation has largely produced positive results with respect to growth and nutrition status [34–37]. A positive effect of iron supplementation on cognitive functions has been observed in schoolchildren, as well [16–18, 38–40]. Iron supplementation has been demonstrated to improve development and cognitive function in both anemic [41] and nonanemic iron-deficient schoolchildren [21]. Iodine supplementation has been shown to reverse the effects of IDD, with the exception of congenital retardation or severe early iodine deficiency [25, 42]. Zinc supplementation, as well, has been shown to improve growth and cognitive performance [34].

Although supplementation has been proven effective in resolving micronutrient deficiencies, logistical, cultural, and economic issues in field supplementation have hindered major progress in alleviating the public health problem that multiple micronutrient deficiencies represent in the developing world [43]. Recent efforts have focused on the fortification of common foods, an approach considered to be effective as well as very inexpensive [44–46].

Field efficacy trial in the Philippines

This study evaluated the effect of a multiple-micronutrient-fortified beverage on iron and iodine status and functional endpoints (fitness and mental abilities). Compliance (or acceptability of beverage) of subjects was assessed. The fruit-flavored beverage contained physiologic levels of 11 micronutrients, including iron, vitamin A, and iodine [46]. In addition, the fortified beverage utilized a fortification approach that delivers highly bioavailable micronutrients without changing the taste or appearance of the consumed final product [46].

Subjects

This study was a randomized, double-blind, placebo-controlled field efficacy trial that evaluated a micronutrient-fortified dietary supplement in the presence or absence of anthelmintic therapy in schoolchildren in the Philippines. The proposal was given human subjects approval by the NCP ethical review committee, whose members include representatives from Helen Keller International (Philippines) and United Nations Children's Fund (UNICEF). A total of 851 children in grades 1–6 were enrolled and 808 were subsequently evaluated. Children were recruited from four elementary schools in the municipality of Balete, located in the province of Batangas in the Philippines. Selection of participating schools considered the prevalence of both macronutrient and micronutrient deficiencies. Overall prevalence of moderate-to-severe malnutrition in this district's schools is 25%. Written consent from the parent or guardian was obtained for all students enrolled. The actual intervention and assessment of nutrition status were conducted from October 1998 to March 1999.

Research design

Study participants were assigned, through randomization at the individual level, to one of four different treatment groups. This provided at least 200 subjects per treatment group, yielding at least 80% power in detecting small effects for fortified beverage and/or albendazole at $\alpha = 0.05$. The sample size computation was generated using the Power Analysis and Sample Size version 1.0 program developed by Hintze [47]. Subsamples of the total groups were selected for urinary iodine excretion (UIE) level determination, dietary assessment, and a socioeconomic survey. For UIE determination, 320 subjects/group were required for 80% power to detect a difference of 10 at $\alpha = 0.05$. For the socioeconomic and dietary assessments, a subsample of 200 children was selected. Both the researchers and the study participants were blinded to the treatment assignment of each child. The delivery of the intervention was strictly supervised and observed by field assistants to prevent contamination or sharing of the beverage.

The study design is shown in figure 1. Group 1 received fortified beverage with anthelmintic therapy; group 2 received fortified beverage with placebo anthelmintic therapy; group 3 received nonfortified beverage with anthelmintic therapy; and group 4 received nonfortified beverage with placebo anthelmintic therapy. Each study subject received a 200-ml serving of either fortified or nonfortified beverage twice each school day for a total of 16 weeks. A single serving (25 g sachets) contained iron (4.8 mg), vitamin A (700 IU), iodine (48 µg), zinc (3.75 mg), vitamin C (75 mg), riboflavin (0.46 mg), folic acid (0.06 mg), vitamin B_{12} (0.5 µg), vitamin B_6 (0.5 mg), vitamin E (2.5 mg), and niacin (2.5 mg) (see box 1). Anthelmintic treatment consisted of one 400-mg albendazole tablet given at the start and end of the intervention. Placebo beverage and placebo anthelmintic pills were indistinguishable from their counterparts in appearance, smell, and taste.

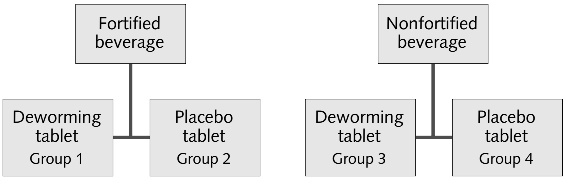

FIG. 1. Clinical study design

Methods

Assessments of overall health and nutrition status as well as a 3-day recall of dietary intake were obtained both at baseline and immediately post-intervention. The general health of study subjects was evaluated through a physical exam and a medical history. Children with a hemoglobin level ≤ 8 g/dl were treated and excluded from the study.

Anthropometric assessments included weight, height, and analysis of nutrition status using the Epi Info version 6 software (Epidemiology Program Office, Center for Disease Control and Prevention, US Department of Health and Human Services). Hemoglobin was instantly measured using the HemoCue® kit (Hemocue AB, Angelholm, Sweden). UIE was determined from urine samples, immediately transferred to cryovials that were sealed, stored at –20° C, and submitted to the Philippine Food and Nutrition Research Institute for iodine content analysis using the perchloric method.

Stool specimens were collected at baseline, 3 weeks after the deworming was given, and again at the end of intervention. Quantitative stool examination was done using the Kato-Katz technique [48]. Slides were prepared and counted for hookworm eggs in the field laboratory; egg counts for *Ascaris lumbricoides* and *Trichuris trichiura* eggs were performed at both the field and the central laboratory.

BOX 1. Contents of single serving (25 g)

Iron	4.8 mg
Vitamin A	700 IU
Iodine	48 µg
Zinc	3.75 mg
Vitamin C	75 mg
Riboflavin	0.46 mg
Folic acid	0.06 mg
Vitamin B_{12}	0.5 µg
Vitamin B_6	0.5 mg
Vitamin E	2.5 mg
Niacin	2.5 mg

Physical fitness was assessed using a modification of the Harvard step test by Montoye for cardiovascular endurance of different age groups [49] and pushups for muscular endurance [50]. This modification of the Harvard step test did not require additional weight load (per kg of body weight) but it varied step height per age. Auscultation of the chest for heart rate measurement was done by trained research staff. Heart rate was taken at rest, immediately after exercise, and at four 1-minute intervals post-exercise. Resting heart rate was taken only after the subject had remained seated for 5 minutes. Each subject was assigned a research staff member who took both baseline and endline measurements. The duration of the step test was maintained at 3 minutes (180 seconds). The frequency of the steps was set at 24 cycles/minute and the cadence maintained by a metronome amplified through an audio system. The height of the step was adjusted according to the height of the child. Children were given detailed instructions and were allowed to practice before the actual test was performed. Heart rates recorded during recovery were analyzed at each time point as well as through a fitness index score, which was equal to the duration of the test (180 seconds) divided by the sum of heart rates for the 5-minute recovery period. A random sub-sample of boys aged 8–12 years also performed standard pushups and the number of properly performed pushups were observed and recorded by trained research staff.

Cognitive ability was measured using a standardized written mental-abilities test called the Primary Mental Abilities Test for Filipino Children (PMAT-FC), developed by Dr. Nelia T. Vargas-Benito in 1993. The test measures the following three basic mental abilities: verbal, nonverbal, and quantitative. Specifically, the test covers general knowledge and comprehension, verbal relationships, fundamental mathematical comprehension and skills, numerical sequencing, and ability to perceive and apply relationships based on meaningless stimuli. First-grade students were tested individually by an interview with a test administrator. Grade 2 students were tested as a group but a test administrator read aloud the test questions to assist students without true reading proficiency. Children in grades 3 through 6 were tested as a group and students read and answered questions on their own.

For quantitative variables, means and standard deviations were calculated for each treatment group and by combining groups 1 and 2 for the fortified group and groups 3 and 4 as the nonfortified group (fig. 1). Analysis of variance (ANOVA) was performed to test for differences of the means among the treatment groups. If the F-test from the ANOVA was significant, a multiple range test was done to identify which pairwise comparison of means was significant. Further analyses were conducted on different subsets of subjects who were grouped based on hemoglobin and/or UIE levels at baseline. The subset analyses were carried out because treatment effects of supplementation have been demonstrated to be more visible among subjects who are micronutrient deficient at baseline [17, 35, 46, 51, 52]. Subset analyses, therefore, identified groups of individuals more likely to benefit from the intervention.

Results

The nutrition profile at baseline of the subjects enrolled in this study largely mirrored the findings of the national survey conducted in 1998. Of the 808 elementary students evaluated, 52% (419 subjects) were anemic (hemoglobin < 12 g/dl). Five percent of all students were severely anemic (hemoglobin levels > 8 to < 10 g/dl) and about 21% were moderately to severely anemic (hemoglobin < 11 g/dl). The children from whom endline hemoglobin data were unavailable are evenly distributed across the four treatment groups. There was no significant difference in the hemoglobin level of the children across treatment groups at baseline. Approximately 90% of all the students evaluated were iodine deficient (UIE ≤ 100 μg/L), with 35% measured as severely deficient (UIE < 20 μg/L).

There were no significant differences between treatment groups with regard to age, socioeconomic demographic characteristics, 24-hr typical dietary intake, or any anthropometric measurement (table 1). Overall, 54% (369/677) of all subjects had at least one type of helminth infection and most of the infections were calculated to be of light intensity. A total of 290 (43%), 150 (22%), and 74 (11%) were positive for *Ascaris, Trichuris*, and hookworm respectively. There was no significant difference in the cumulative prevalence, prevalence of mixed infections, and the prevalence of *Ascaris, Trichuris,* and hookworm infection among the four treatment groups. There were no significant differences between treatment groups with regard to compliance or acceptance of the beverage; 95.9% of children who received fortified beverage liked the beverage as much or more than the juice they typically drank at home (versus 96.3% of children who drank placebo beverage). Among non-anemic subjects, the group receiving fortified beverage had a slightly lower baseline UIE level than those in the placebo group (37.00 versus 47.89 μg/L, respectively, $p = .035$). No other significant differences between treatment groups in any baseline biochemical analysis were observed. There were also no differences observed between groups with regard to baseline cognitive function, physical fitness, or general medical history.

Anthropometric status

Analysis of the children's anthropometric status at post-intervention revealed that there was a slight increase in weight and height for all four treatment groups (table 2). When the children were grouped

TABLE 1. Characteristics of study participants at baseline by treatment group

	Treatment group				
Variable	Fortified, dewormed	Fortified, not dewormed	Nonfortified, dewormed	Nonfortified, not dewormed	*P*-value
n	203	209	213	206	
Age [a]	10.1 ± 2.1	9.8 ± 2.1	9.9 ± 2.2	9.9 ± 2.3	.37
% Male	53.7	49.8	53.5	51.9	.84
Anthropometric status					
n	203	209	213	206	
Weight (kg) [b]	24.59 ± 6.07	24.27 ± 6.60	24.52 ± 6.75	24.23 ± 6.69	.93
Height (cm) [b]	127.19 ± 11.65	126.04 ± 12.08	126.71 ± 11.95	125.99 ± 12.18	.70
Weight-for-age z-score [b, c]	–1.70 ± 0.78	–1.60 ± 0.71	–1.65 ± 0.70	–1.70 ± 0.71	.46
Height-for-age z-score [b, c]	–1.85 ± 0.93	–1.72 ± 0.97	–1.76 ± 0.89	–1.83 ± 0.88	.40
Weight-for-height z-score [b, c, d]	3.75 ± 5.29	3.23 ± 5.26	3.47 ± 5.31	3.41 ± 5.29	.97
Iron status					
n	196	200	207	205	
Hemoglobin level (g/dl) [b]	11.91 ± 1.33	11.86 ± 1.25	11.93 ± 1.23	11.92 ± 1.23	.95
% Non-anemic (Hb ≥ 12 g/dl)	44.9	48.5	50.7	48.3	.71
% Iron-deficient					
Hb ≥11 to <12 g/dl	33.7	29.0	29.0	33.2	.60
Hb <11 g/dl	21.4	22.5	20.3	18.5	.79
Iodine status					
n	136	156	156	163	
Urinary iodine level (μg/L) [b]	40.82 ± 42.19	41.08 ± 40.07	46.14 ± 46.47	48.33 ± 48.38	.36
% Non-iodine deficient (UIE ≥ 100 μg/L)	8.8	9.6	12.8	11.0	.69
% Iodine-deficient					
UIE ≥ 50 μg/L to < 100 μg/L	17.6	19.2	19.9	23.9	.56
UIE ≥ 20 μg/L to < 50 μg/L	40.4	34.0	28.8	34.4	.23
UIE < 20 μg/L	33.1	37.2	38.5	30.7	.44
Physical fitness					
n	181	186	186	194	
Fitness index score [b]	62.13 ± 9.93	61.32 ± 9.87	63.56 ± 10.04	62.98 ± 9.35	.13
Push-up capacity [b, e]	6.38 ± 4.10	5.44 ± 2.20	6.44 ± 3.77	6.25 ± 3.56	.71
Cognitive performance					
n	186	185	188	183	
Verbal ability score [b]	7.56 ± 4.28	7.33 ± 4.20	8.10 ± 3.96	7.45 ± 4.35	.30
Non-verbal ability score [b]	2.65 ± 1.54	2.55 ± 1.58	2.63 ± 1.50	2.73 ± 1.50	.73
Quantitative ability score [b]	7.67 ± 2.84	7.36 ± 3.31	7.68 ± 3.24	7.22 ± 3.05	.40
Total score [b]	17.88 ± 6.83	17.24 ± 7.37	18.41 ± 7.13	17.37 ± 7.18	.37
Parasitic infection prevalence (%)					
n	159	172	175	171	
Ascaris	40	46	43	42	.70
Trichuris	24	25	17	23	.30
Hookworm	13	15	7	9	.10
Cumulative	55	58	53	53	.70
Mixed	21	23	14	19	.14

a. Values are means ± SD.
b. Values are means ± SE.
c. Z-scores were computed based on the NCHS standards.
d. Sample size for the groups was 119, 131, 129, and 126, respectively.
e. Sample size for the groups was 29, 25, 32, and 28, respectively.

by type of beverage received, regardless of deworming treatment, those given the fortified beverage had slightly higher increases in weight and height than did the children given the nonfortified beverage. When analyzed according to deworming group, those who received the deworming tablet were found to have a slightly higher increase in weight. However, the differences observed in all these instances were not statistically significant.

Anemia and iodine deficiency

At baseline, most subjects (52%) were anemic. The consumption of the fortified beverage had no significant effect on iron status when hemoglobin levels of < 12 g/dl was used as a cutoff. However, a significant improvement in iron status was demonstrated among the subjects who had hemoglobin levels < 11 g/dl at baseline. An analysis of the changes in iron status relative to the severity of anemia at baseline revealed a strong association between the efficacy of the fortified beverage and the severity of anemia at baseline (table 3). The highest increase in hemoglobin level was obtained in the subgroup that had < 10 g/dl hemoglobin level at baseline, even though the difference was not significant ($p < .10$). By contrast, the subjects who had adequate iron status (≥ 12 g/dl hemoglobin) at baseline showed a slight reduction in hemoglobin level. The correlation between baseline hemoglobin level and the effect of the fortified beverage on iron status was highly significant ($p < .0001$). The number of children who remained moderately or severely anemic at the end of the 16-week intervention period was also significantly lower among children who received the fortified beverage (14.9% versus 28.75%, respectively, $p = .03$) (results not shown). The benefit of the fortified product on iron status is similar to that of deworming. Deworming significantly improved the iron status of moderately to severely anemic subjects at baseline, (12.04 g/dl in dewormed children versus 11.6 g/dl in children not dewormed, $p = .02$) (results not shown).

Children who consumed the fortified beverage showed dramatic improvement in iodine status (table 4). In children who received the fortified product, the median UIE level increased from 41.31 µg/L at baseline to 67.98 µg/L after the 16-week intervention. Among those who received the placebo beverage, the median UIE level reduced significantly from 46.99 µg/L at baseline to 39.74 µg/L after intervention. The increase in UIE level after supplementation is strongly associated with iodine status at baseline. Subjects who were iodine replete at baseline (≥ 100 µg/L) experienced a significant drop in UIE level at

TABLE 2. Effect of the fortified beverage on anthropometric status

Variable	Treatment Group		*P*-value
	Fortified	Nonfortified	
n	412	419	
Weight (kg)[a]			
Baseline	24.66 ± 0.20	24.68 ± 0.20	.95
Post-intervention	26.16 ± 0.22	26.15 ± 0.22	.97
Change	1.50 ± 0.05	1.47 ± 0.05	.69
Height (cm)[a]			
Baseline	126.89 ± 0.33	126.99 ± 0.33	.83
Post-intervention	129.22 ± 0.34	129.29 ± 0.34	.88
Change	2.33 ± 0.04	2.30 ± 0.04	.64
Weight-for-age z-score[a]			
Baseline	−1.63 ± 0.04	−1.66 ± 0.04	.62
Post-intervention	−1.52 ± 0.04	−1.54 ± 0.04	.66
Change	0.12 ± 0.01	0.12 ± 0.01	.91
Height-for-age z-score[a]			
Baseline	−1.77 ± 0.05	−1.78 ± 0.05	.84
Post-intervention	−1.69 ± 0.05	−1.71 ± 0.05	.81
Change	0.08 ± 0.01	0.08 ± 0.01	.73
Weight-for-height z-score[a, b]			
Baseline	−0.75 ± 0.13	−0.82 ± 0.14	.31
Post-intervention	−0.69 ± 0.14	−0.74 ± 0.14	.57
Change	0.05 ± 0.05	0.07 ± 0.05	.52

a. Values are adjusted means ± SE.
b. Sample size for the groups was 231 and 236, respectively.

TABLE 3. Effect of fortified beverage on iron status (hemoglobin g/dl ± SE)

Evaluation	Treatment Group		*P*-value
	Fortified	Nonfortified	
All subjects (*n* = 809)			
Baseline	11.90 ± 0.06	11.95 ± 0.06	.58
Post-intervention	12.19 ± 0.06	12.16 ± 0.06	.72
Change	0.29 ± 0.08	0.21 ± 0.08	.47
Hb < 10g/dl at baseline (*n* = 44)			
Baseline	9.33 ± 0.12	9.42 ± 0.13	.55
Post-intervention	11.91 ± 0.33	11.14 ± 0.38	.10
Change	2.58 ± 0.35	1.72 ± 0.40	.08
Hb < 11g/dl at baseline (*n* = 167)			
Baseline	10.24 ± 0.07	10.25 ± 0.08	.93
Post-intervention	12.01 ± 0.14	11.63 ± 0.15	.05
Change	1.72 ± 0.15	1.35 ± 0.16	.09
Hb < 12 g/dl at baseline (*n* = 419)			
Baseline	11.00 ± 0.05	11.01 ± 0.05	.89
Post-intervention	12.02 ± 0.08	11.85 ± 0.08	.15
Change	1.02 ± 0.09	0.85 ± 0.09	.18
Hb ≥ 12 g/dl at baseline (*n* = 390)			
Baseline	12.89 ± 0.06	12.86 ± 0.06	.69
Post-intervention	12.35 ± 0.09	12.46 ± 0.09	.40
Change	−0.54 ± 0.11	−0.40 ± 0.10	.35

post-intervention, whereas the highest improvement in iodine status was observed in subjects who had UIE levels below 20 μg/L. The data suggest that the bioavailability of iodine is tightly regulated by the iodine status of the subjects at baseline. Regression analysis showed there is a significant ($p < .0001$) correlation between improvement in iodine status and baseline iodine status. Although it is not as dramatic as that of the fortified beverage, it is interesting to note that anthelmintic treatment had some effect on iodine status at post-intervention ($p < .07$) In fact, among subjects with baseline hemoglobin levels ≥ 12 g/dl, the increase in UIE level among the dewormed (21.7 μg/L) was significantly higher than that of the placebo group (5.98 μg/L) (results not shown). Although preliminary, the data suggest that there is a positive interaction of baseline iron status and anthelmintic treatment on iodine status.

The interaction between iron and iodine status on both iron and iodine status at the end of the intervention was also evaluated by using a regression analysis (not shown). There was no correlation between iodine status at baseline and iron status at post-intervention ($p = .92$). The effect of baseline hemoglobin level on change in iodine status seems to show some correlation ($p = .18$). The subjects with hemoglobin levels ≥ 11 to < 12 g/dl at baseline had significantly ($p < .01$) less post-intervention increase in UIE levels than did those with hemoglobin levels > 12 g/dl at baseline (results not shown).

Physical fitness

The effect of the fortified beverage on changes in heart rate was dramatic and consistent. The fortified beverage consistently showed beneficial effect in reducing post-exercise heart rates (table 5). Significant difference in changes in heart rate was consistently observed among the subjects with hemoglobin levels < 12 g/dl and hemoglobin levels < 12 g/dl and UIE levels < 50 μg/L at the baseline. Interestingly, the fortified beverage also showed significant and more dramatic effect in reducing heart rate among the children with hemoglobin levels > 12 g/dl and UIE levels > 20 to < 50 μg/L, hemoglobin levels > 12 g/dl and UIE levels > 50 to < 100 μg/L, and UIE levels > 20 to < 50 μg/L at baseline (table 5).

The increases in fitness index scores in the subjects who received the fortified and nonfortified beverage were 1.25 and 0.29, respectively. Although the score is higher in the treated subjects than in the placebo group, it was not significant ($p = .11$). It is likely that the difference observed is due to the fortified beverage, because the anthelmintic-treated subjects had lower increases in fitness index scores compared with the untreated group (dewormed = 0.53, placebo = 0.10; $p =$

TABLE 4. Effect of fortified beverage on iodine status (UIE level μg/L ± SE)

Evaluation	Treatment Group		*P*-value
	Fortified	Nonfortified	
All subjects ($n = 611$)			
Baseline	41.31 ± 2.56	46.99 ± 2.45	.11
Post-intervention	67.98 ± 2.70	39.74 ± 2.58	< .0001
Change	26.68 ± 3.44	–7.25 ± 3.29	< .0001
UIE < 20 μg/L at baseline ($n = 226$)			
Baseline	11.12 ± 0.55	11.71 ± 0.55	.43
Post-intervention	60.69 ± 3.77	27.77 ± 3.73	< .0001
Change	49.57 ± 3.76	16.06 ± 3.72	< .0001
UIE ≥ 20 to < 50 μg/l at baseline ($n = 199$)			
Baseline	31.78 ± 0.86	33.55 ± 0.91	.15
Post-intervention	70.23 ± 4.86	45.05 ± 5.16	< .0001
Change	38.44 ± 4.85	11.49 ± 5.14	< .0001
UIE ≥ 50 to < 100μg/l at baseline ($n = 122$)			
Baseline	70.14 ± 2.04	67.96 ± 1.77	.42
Post-intervention	82.86 ± 6.58	55.9 ± 5.7	.002
Change	12.72 ± 6.78	–12.06 ± 5.88	.006
UIE ≥ 100 μg/l at baseline ($n = 64$)			
Baseline	148.53 ± 9.77	153.90 ± 8.64	.64
Post-intervention	83.88 ± 9.56	56.4 ± 8.45	.02
Change	–64.65 ± 13.95	–97.50 ± 12.33	.05

TABLE 5. Effect of fortified beverage on changes in heart rates (bpm ± SE)

Time after exercise	Treatment Group		*P*-value
	Fortified	Nonfortified	
All subjects ($n = 742$)			
1 minute	–2.91 ± 0.76	–1.19 ± 0.75	.11
2 minutes	–2.29 ± 0.71	–0.41 ± 0.70	.06
3 minutes	–2.19 ± 0.67	–0.65 ± 0.67	.10
4 minutes	–1.98 ± 0.64	–0.53 ± 0.63	.11
Hb < 12 g/dl ($n = 390$)			
1 minute	–1.65 ± 0.53	–0.24 ± 0.53	.06
2 minutes	–1.30 ± 0.51	0.17 ± 0.51	.04
3 minutes	–0.95 ± 0.48	0.24 ± 0.48	.07
4 minutes	–0.83 ± 0.44	0.10 ± 0.44	.13
Hb < 12 g/dl and UIE ≤ 50 μg/L ($n = 191$)			
1 minute	–2.08 ± 0.70	–0.25 ± 0.73	.06
2 minutes	–1.87 ± 0.71	–0.45 ± 0.74	.02
3 minutes	–1.47 ± 0.69	0.63 ± 0.72	.03
4 minutes	–0.88 ± 0.63	0.40 ± 0.65	.15
UIE ≥ 20 to < 50 μg/L ($n = 175$)			
1 minute	–3.64 ± 1.54	0.65 ± 1.60	.05
2 minutes	–2.78 ± 1.47	1.87 ± 1.54	.03
3 minutes	–3.63 ± 1.39	1.57 ± 1.46	.01
4 minutes	–3.05 ± 1.37	2.19 ± 1.43	.01

.44). It is important to note that deworming had either no effect or a negative effect on fitness index scores (data not shown). On the other hand, the effect of deworming on change in heart rate was inconclusive.

Cognitive performance

The effects of the fortified beverage on mental ability scores are presented in table 6. Consumption of fortified beverage showed no significant effect on changes in total cognitive score of all subjects. By contrast, the subjects who were both iron deficient (hemoglobin < 11 g/dl) and mildly iodine deficient (UIE > 50 to < 100 µg/L) at baseline showed significant increases in changes of total cognitive ($p < .02$), nonverbal ability ($p < .03$), and verbal ability ($p < .02$) scores.

Among subjects who were moderately to severely anemic (hemoglobin < 11 g/dl) at baseline, children receiving the fortified beverage showed significant improvement in changes in nonverbal ability score ($p < .05$). The iron-deficiency-anemia-mediated impact of the fortified beverage on verbal ability scores was enhanced to some extent by iodine deficiency (table 6). Changes in quantitative scores were inconsistent; the effect of fortified beverage on quantitative scores is inconclusive (data not shown). Improvement in mental ability scores is specific to the fortified beverage, because anthelmintic treatment showed either no effect or had a negative effect (data not shown).

Discussion

Baseline data demonstrate that both iron and iodine deficiencies are prevalent among Filipino schoolchildren. At baseline, 52% and 21% were anemic, using Hb levels of < 12 g/dl and < 11 g/dl as cutoff points, respectively. Likewise, about 90% and 37% were iodine deficient at baseline, using UIE levels of < 100 µg/L and <20 µg/L as cutoff points, respectively. The prevalence of micronutrient deficiencies observed at baseline is higher than that observed in the 1998 Philippine national survey [48]. According to this relatively recent survey, anemia and iodine deficiency among schoolchildren are about 37% and 36%, respectively. A little over half of all children examined had at least one type of helminth infection, but most of those infected had light infections. This should be taken into account when interpreting the benefit of concomitant deworming and fortification.

Although it is well recognized that food fortification is among the preferred and cost-effective approaches in combating micronutrient malnutrition, its effectiveness in developing countries is yet to be demonstrated. One of the limiting factors is the lack of simple and affordable technology to fortify foods with stable and bioavailable nutrients without compromising commonly accepted taste and appearance [46, 53, 54]. In fact, compliance has been identified as one of the key limiting factors in combating micronutrient malnutrition through supplementation [55]. The results showed that the fortification of the powder fruit drink with multiple micronutrients (three minerals and eight vitamins) had no significant impact on the amount of beverage consumed and overall compliance. When asked to compare the fortified beverage with the juice they usually drink at home, 20% of the children liked the beverage better and 76% showed no preference, with only 4% preferring juice.

This randomized, double-blind, placebo-controlled study showed that repeated consumption of the fortified beverage has a significant impact on improving the iron status of the subjects with hemoglobin levels < 11 g/dl at baseline. The data suggest that utilization of iron from the fortified beverage is highly regulated by the iron status of the subjects. The highest increase

TABLE 6. Effect of fortified beverage on changes in mental ability scores

Nutrition status at baseline	*n*	Treatment Group Fortified	 Nonfortified	*P*-value
Change in cognitive score				
All	742	1.82 ± 0.22	1.66 ± 0.22	.62
Hb < 11 g/dl and UIE > 50 to < 100µg/L	24	5.29 ± 1.74	0.42 ± 1.31	.02
Change in nonverbal-ability score				
All	742	0.21 ± 0.10	0.18 ± 0.10	.84
Hb < 11 g/dl	144	0.50 ± 0.23	–0.07 ± 0.25	.08
Hb < 11 g/dl and UIE ≤ 20 µg/L	44	1.37 ± 0.50	0.09 ± 0.50	.06
Hb < 11 g/dl and UIE ≤100 µg/L	101	0.82 ± 0.27	–0.04 ± 0.30	.03
Hb < 11 g/dl and UIE > 50 to ≤ 100 µg/L	24	2.08 ± 0.81	–0.18 ± 0.61	.03
Change in verbal-ability score				
All	742	0.76 ± 0.14	0.60 ± 0.14	.42
Hb < 11 g/dl and UIE > 50 to < 100 µg/L	24	1.05 ± 0.83	–1.3 ± 0.62	.02

was obtained in the subjects with hemoglobin levels < 10 g/dl at baseline (table 3). Regression analysis also showed that the increases in hemoglobin levels at post-intervention were significantly correlated with baseline iron status. This corroborates data obtained by others among Tanzanian schoolchildren with the same delivery system [33]. Note that the iron consumed daily in the study was not only at physiologic levels but also consumed only during the school days for 16 weeks.

There are few intervention studies with iron-fortified foods in schoolchildren [3, 33]. The effect of fortified biscuits on micronutrient status in schoolchildren in South Africa showed a decrease in hemoglobin levels after 6 months and a significant increase in hemoglobin levels after 12 months of intervention [3]. Many of the other iron intervention studies in schoolchildren use supplementation at pharmaceutical doses [17, 35, 37]. In these studies, significant changes in iron status were observed only among the anemic subjects [17, 35].

Repeated consumption of the multiple-micronutrient-fortified beverage by Filipino schoolchildren resulted in significant improvement in iodine status (table 4). The highest increase in UIE level was obtained among the subjects who were severely iodine deficient (UIE < 20 μg/L) at baseline. By contrast, a decrease in UIE levels was observed among those who were iodine adequate (UIE > 100 μg/L) at baseline. Furthermore, the results demonstrate that the utilization of iodine from the fortified product is tightly regulated. Regression analysis showed that baseline iodine status is negatively correlated with change in UIE levels at the end of the study. No interaction was observed between iodine status at baseline and increases in hemoglobin levels at post-intervention. However, although the association between iron status at baseline and post-intervention change in UIE level was nonsignificant, the subjects who were iron adequate at baseline had a significantly higher increase in UIE levels than those who had baseline hemoglobin levels between 11 and 12 g/dl. Note, however, that the increase in UIE levels observed among the subjects who were iron deficient (hemoglobin < 11 g/dl) at baseline was not significantly different from that in subjects who were iron adequate (hemoglobin > 12 g/dl) and mildly anemic (hemoglobin ≥11 g/dl to < 12 g/dl) at baseline.

Very few studies on the interaction between iron and iodine status have been reported in the literature. According to Zimmermann, et al. [27] the effect of iodine supplementation is impaired in goitrous children with iron-deficiency anemia. Furthermore, results from an iron supplementation study showed efficacy of iodized salt in goitrous children to be significantly improved by iron treatment [56]. It is possible that the marked improvement in iodine status observed in children consuming the fortified beverage could be due to the delivery of both iron and iodine through a single product.

Multiple studies have shown that micronutrient malnutrition, particularly of iron and iodine, has negative effects on growth, strength, mental development, and learning [15–20, 32–42]. Our results showed that the fortified beverage had no effect on growth of the schoolchildren. Limited studies have shown significant effect of iron supplementation on growth in schoolchildren [35, 37, 57]. However, these studies used pharmaceutical doses of iron in anemic subjects. A recent study by Latham et al. [33], however, did find a significant effect on growth (height and weight gain) and body mass index after repeated consumption of a fortified beverage after 6 months. It is likely that the lack of positive response observed in the Filipino study could be due to the short duration of the intervention phase (4 months).

Several clinical studies of iron supplementation in Guatemala [12, 58], Sri Lanka [14, 16, 17, 59], Indonesia [60], and Africa [63] have demonstrated a strong relationship between increased hemoglobin levels and common work performance capacity indicators, such as work productivity, heart rate, blood lactate, and oxygen intake. All of these studies used iron supplements instead of fortified foods, and none studied schoolchildren. The effect of the fortified beverage, even though the nutrients are consumed daily at physiologic levels, is interesting. The increase in the fitness index score of the subjects who received the fortified beverage was higher, even though it was not significant ($p < .11$), than in those who received the nonfortified beverage. The average change in heart rate as a function of time after exercise was consistently lower among those in the fortified group than in the nonfortified group (table 5). However, it reached significance only at 2 minutes after exercise ($p < .06$). Among subjects with hemoglobin levels < 12 g/dl at baseline, reduction in heart rate of those in the fortified group was significantly higher than in the nonfortified group at 1 and 2 minutes. There is an indication that iodine status may have an adverse effect on fitness in schoolchildren. Among the subjects who were moderately iodine deficient (UIE > 20 to < 50 μg/L) at baseline, those who received fortified beverage had significantly higher reduction in heart rate at 1, 2, 3, and 4 minutes after exercise. It is unclear why this particular group consistently responded positively to the fortified beverage by showing significantly increasing fitness as indicated by reduction of heart rate. It is likely that the level of iodine (96 μg) consumed per day and the duration of the study (4 months) were not adequate to provide benefits to those with UIE levels < 20 μg/L at baseline. By contrast, the group with baseline UIE levels > 50 μg/L probably already had adequate amounts of iodine, which were not affected by the fortified beverage.

Several studies of infants, preschool children, and schoolchildren have shown that iron-deficient subjects had lower cognitive development and school performance [5, 16–32, 38–41]. In infants, iron supplementation was effective in improving iron status but not in correcting mental development deficit [19, 20]. Significant improvement in cognitive performance by iron supplementation in preschool and schoolchildren has been observed in Indonesia [17, 38, 61], India [39], and the United States [21, 22]. Unlike the study reported here, these studies used pharmaceutical doses of iron. Also, positive cognitive benefits were observed only in the subjects who were iron deficient at baseline.

Very limited studies have assessed the impact of iodine supplementation on cognitive performance in preschool and schoolchildren. In a controlled study done in Bolivia, improvement in IQ was demonstrated in all those schoolchildren who showed significant reduction in goiter [62]. Recently, results from a 1-year intervention study among iodine-deficient schoolchildren showed a significant improvement in mental performance among those children with increased UIE levels [42]. Our data demonstrate that consumption of a fortified beverage had a significant effect on nonverbal ability scores among subjects who were moderately to severely anemic (hemoglobin < 11 g/dl). Interestingly, the subjects who were both iron deficient (hemoglobin < 11 g/dl) and mildly iodine deficient (UIE > 50 to < 100 µg/L) at baseline had significantly increased total cognitive, nonverbal ability, and verbal ability scores.

Overall our results are consistent with results reported by others [17, 22, 38, 39, 61]. The significant cognitive benefits of the fortified beverage occurred only among subjects who were either anemic or both anemic and iodine deficient at baseline. Also, our results support the recently published data by Stoltzfus et al. [5], in which a physiologic level of iron supplementation for 1 year had a significant benefit on language and motor development among anemic preschool children. The effect of iron supplementation was limited to children with more severe anemia (hemoglobin < 8 g/dl) at baseline. Data published thus far, including ours, are consistent with the conclusion made by Sternberg et al. [26] that inadequate levels of vitamins and minerals in the blood reduces intellectual performance below a child's optimal level. Vitamins and minerals, in addition to a child's standard diet, seem to be particularly associated with a rise in nonverbal cognitive performance.

Conclusion

Our results show that daily delivery of multiple micronutrients including iron and iodine (at physiologic levels) via a commonly accepted powder fruit drink showed a significant effect on iron and iodine status. The utilization of both iron and iodine is highly regulated. Only the subjects who were deficient at baseline showed an increase in either hemoglobin or UIE levels. In addition, the repeated consumption of the fortified powder drink had a significant benefit in improving physical fitness (indicated by reduction in heart rate) and mental ability (indicated by nonverbal and verbal ability scores). Again, these functional benefits were obtained among subjects who were either iron and/or iodine deficient.

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Drinking to their health: Social analysis of a micronutrient-fortified beverage field trial

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Abstract

Anthropologic research was conducted among pregnant and lactating women in rural Tanzania in conjunction with clinical trials of a micronutrient-fortified beverage. Use of the beverage was examined through interviews and ethnographic observation in clinics and at home. Women liked the taste of the beverage, considered it beneficial to their health, preferred it to pills or injections, and most were willing and able to use it according to instructions. Most consumed the beverage according to schedule in the hope of improving pregnancy outcomes. However, public health facilities in Tanzania are not currently equipped to ensure regular delivery of micronutrient supplements, and many of the women with the worst nutrition profiles are also those who would be least able to purchase supplements on the open market. Successful distribution of micronutrient supplements in forms that appeal to consumers, such as a fortified beverage, will require programmatic attention to locally appropriate social marketing and to the challenges of reaching those with extremely low incomes.

Key words: Compliance, fortified beverage, medical anthropology, micronutrient malnutrition, product acceptance, social analysis

Research objectives

This paper discusses the anthropologic component of a micronutrient-fortified beverage field trial in Mpwapwa, Tanzania [1], which was conducted in association with clinical trials detailed elsewhere in this supplement [2] (see Box 1). The United Nations Children's Fund (UNICEF) funded research conducted in 1999 and 2000, in close cooperation with nutritionists and technicians from Cornell University (Ithaca, New York) and the Tanzania Food and Nutrition Centre (TFNC), during the clinical-trial period with expectant and nursing mothers. The anthropologic component was initiated to determine how such a beverage or similar micronutrient package would be accepted and consumed if clinical data indicated the program should go to scale. Among the study objectives, we sought to learn from and avoid common development pitfalls, investigate social reaction to the micronutrient beverage, and investigate potential obstacles to widespread distribution of such a product in East Africa.

In designing the study we sought to make recommendations that would be both practical and pos-

BOX 1. Efficacy trial of a micronutrient dietary supplement in pregnant women in Tanzania

Food technologists at The Procter & Gamble Co. (P&G) produced both the micronutrient-fortified beverage mix and an identical tasting and looking nonfortified beverage mix, which served as the experimental and placebo treatments respectively. For the pregnancy study, two types of sachets were used with one colored green and labeled "G" and the other colored blue and labeled "H." Neither the researchers nor the study participants were aware of the identity of the package contents. The composition of the supplement in each sachet had been agreed to after extensive consultation by nutritionists at Cornell University, Tanzania Food and Nutrition Centre (TFNC), Micronutrient Initiative (MI), United Nations Children's Fund (UNICEF), and P&G and is further detailed by Latham and others elsewhere in this volume.

Sources: Ash et al. [1], Makola et al. [2].

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sible for the intended beneficiaries. Examples of well-intentioned projects gone awry abound in international health and development activities. However, when projects incorporate social scientific analysis into their structure, efforts to introduce and encourage beneficial but unfamiliar activities have an increased likelihood of being effective.

The social science component of the current research was intended to raise questions about the viability of introducing a multiple-micronutrient–fortified beverage into poor areas in ways that might reach the mothers and children with the worst nutritional profiles. Research questions included the following: Did women find compelling reasons to use the beverage? Did they find ways to work it into their daily routines? Did they seek to share its potential benefits with their children? Did some sell the powder to raise cash? Did they have problems keeping the powder safe from pilfering? Did other household members help or hinder women's use of the beverage? Also, given all the other competing demands on impoverished consumers' time and resources, how might a market for such a product be encouraged? And, finally, what additional structural obstacles would need to be overcome in the health sector in order for widespread distribution to be a success?

Study design: applying anthropology to micronutrient research

With these questions in mind, an anthropologic research project was launched that looked very different from the clinical trials to which it was attached. The variables in subjects' lives that epidemiologic research seeks to control for are the very ones that anthropology seeks to highlight. Whereas clinical research relies on the collection of measurable physiologic data, anthropology investigates unquantifiable factors through discussion and observation. While epidemiologic research requires appropriate, often large, sample sizes to have the statistical power to make valid conclusions, anthropology in complex societies is at its best when it delves deeply into the lives of a relatively small sample of a larger population. When clinical studies prick and poke subjects for blood samples and parasite counts, anthropologic research tries to set subjects at ease so they will express thoughts that they would otherwise keep hidden from outsiders and authority figures. When conducted in tandem, we found these two very different types of research to be quite complementary.

The anthropologic study was designed to get people talking. We first met with most of the women immediately after their initial clinical screening, introducing them to the beverage while engaging them in friendly banter. In this way a relationship was established that was followed with home visits in many cases. The home visits generally lasted 30–90 minutes. We conducted semi-structured interviews, meaning we made sure to discuss certain crucial topics centering around individual impressions of the beverage and circumstances of its use, while also allowing conversation to include topics ranging from life histories to breastfeeding and birth planning to household economics. We could not, given the time available, collect quantitative data that would enable us to say that, for example, "X" percent of women would purchase a micronutrient product at price point "Y." With these parameters in mind and by following accepted anthropologic methods of participant observation, we can say, however, that the information we gathered is broadly representative of families in Tanzania and, by extension, is relevant to much of eastern, central, and southern Africa.

At the same time that we were talking with women and their families about where the micronutrient beverage fit in their lives, we were also talking with health personnel and observing health service facilities. We did this because many health programs are based on the assumption that health services will be delivered in remote areas in ways that correspond closely with planners' intentions. By observing health services as they are actually available to a not atypical set of Tanzanians, we were able to identify some of the issues that will affect the logistics and supply side of micronutrient-supplement distribution in this part of the world, beyond the immediate questions of consumer acceptability uncovered by the work with study participants.

Key findings: favorable and cautionary

The key findings that most gratify the team that formulated the micronutrient beverage are that most women liked it, preferred it as a delivery vehicle over pills or injections, considered it beneficial to their health, and were willing and able to use it according to instructions. When viewed in conjunction with the physiologic data presented by Latham [3] and others [2], the findings present a strong argument for going forward with a micronutrient beverage in East Africa. There is a second set of findings that is equally important, though, and is somewhat cautionary. These findings center around the fact that the women and children with the worst nutrition profiles, who would therefore benefit most from a supplement like a micronutrient beverage, are also by and large the poorest, most politically marginal members of society who would be least able to afford any daily cost of purchasing such a product.

Though the specific social relations of poverty we found in this research are unique to East Africa, these findings will hold for much of the rest of the world and should therefore be a topic of serious consideration for any public or private organization pursuing the distribution of such a product to poor consumers who are at risk of micronutrient deficiency.

Favorable findings

The first set of findings is clear. Women liked the beverage, and they and their families did all they could to ensure that they consumed it on a regular basis. While many studies of "compliance" find low adherence to tablet regimens [4], we found that 74% consumed between 75% and 100% of their beverage sachets (with a mean consumption in these top three quartiles of 110 out of 112 possible sachets) and 92% consumed at least one-half of their sachets (with a mean consumption in the top two-thirds of the bottom quartile of 83 out of 112 sachets, or 74%) (table 1).

Most women found the taste pleasant, mentioning that it is similar to a popular flavor of soda. Their reasons for drinking the beverage had little to do with a craving for orange-flavored drink mix, though. Rather, most responded to the suggestion by medical experts that the product could have health benefits for themselves and their babies.

Most of the women in the study were from households that relied on farm products, petty trade, and casual labor to bring in about $10 (US dollars) per month per person, to meet all household needs for food, medicine, education, clothing, and shelter. Within their families, most women had little power to direct household resources toward their health. Unmarried pregnant women, who were perceived to be "soiling" the household, had even less claim than most for family support. Many of the women, therefore, willingly accepted the beverage as something they could use to improve their health that did not require approval from family members with greater authority over resources.

Equally significant is that other family members also were eager for the pregnant women among them to use the product. Husbands, sisters, and mothers-in-law all helped protect the product for the pregnant women and made sure they drank the beverage according to the daily schedule and got their refills every 2 weeks.

TABLE 1. Compliance of supplementation of two servings per day during the first 8 weeks of the study

Number of Packets[a]		Consumption[b] *n*/*N* (%)
Mean	Range	
0	0	2/318 (0.6%)
28	25–28	7/318 (2.2%)
55	44–56	15/318 (4.7%)
83	64–84	58/318 (18.2%)
110	86–114	236/318 (74.2%)

a. Number of sachets consumed during first 8 weeks of study is based on the number of empty packages returned during follow-up.

b. Proportion of mothers who consumed stated amount.

Children are central to Tanzanian social life, and most adults were enthusiastic about having a product available that might help offspring survive pregnancy and infancy. In a country with an estimated infant mortality rate (IMR) of 99/1,000 live births [5], in which it is not uncommon for a woman to have only a few children reach adulthood from as many as a dozen pregnancies, both pregnant women and their families were eager to do what they could to shift the odds in their favor.

In local parlance, the beverage was discussed as something that could "increase blood." People agreed that certain foods could increase blood, including scarce foods like meat and sporadically available foods like dark leafy vegetables. (Parenthetically, we therefore recommend that any micronutrient supplement manufactured for the East African market be available in a dark purple formula.) Few families, though, normally made special efforts to use diet to increase the blood of pregnant women until very late in the pregnancy, just before the anticipated blood loss during delivery. The information we gave—that increasing blood early in pregnancy could help mother and baby and that increasing the blood of nursing women might improve the quality of the milk for the infant—was not part of local ethnomedical understandings prior to the study. However, when given this information, most people evaluated it and incorporated it into their models of physiologic processes.

Families were then eager to adopt the beverage for pregnant women, because it was a non-cumbersome way to achieve the revised goal of increasing the mother's blood during and after pregnancy. Similar information regarding health benefits for children would stimulate demand for feeding micronutrient supplements to children. Though understanding of diet and bodily processes will vary from place to place, thus making research about local health conceptions important before implementing micronutrient-supplement programs elsewhere, the central objectives of improving maternal and child health will be shared by many poor families worldwide.

Cautionary findings

The second, cautionary set of findings presents much more of a challenge to those who wish to promote micronutrient supplements. These findings will also vary in their particularities from place to place, but will present similar obstacles overall throughout the non-wealthy world. Chiefly, the public supply stream is often broken, and the main consumer base consists of those people least able to allocate the cash needed to support a private micronutrient-supplement industry. Health services and supplies are largely inadequate in Tanzania, as they are in impoverished areas from Peru to Haiti to

Indonesia—preventive health care is minimal where doctors are few, facilities are Spartan, and supplies are scarce even for emergency medicine. In a country like Tanzania where even free medical supplies—such as the iron-folate tablets that are supposed to be available for pregnant women—often do not reach their intended recipients, any model of public distribution of micronutrient supplements will need to confront aggressively the serious institutional and supply stream weaknesses that currently prevent women and children from accessing many of those public health services that are nominally available to them.

Additionally, when considering a private model of selling micronutrient supplements directly to consumers, we found that the best of intentions to purchase such a product will often crash against the realities of household economics in impoverished areas. A basic graph of supply and demand, drafted with rough figures, indicates a fundamental fact of economics—in a totally free market, some consumers will always be left out. In the case of micronutrient supplements, the people who can least afford the cost of the product are exactly the "target demographic" with whom we ought to be most concerned (figures 1 and 2).

When food is a daily struggle, as it is especially in female-headed households, supplements will necessarily be a lower priority than food or medicine. When women have restricted access to household income, as in many households with a strong patriarchal organization, it is difficult for them to make the independent decision to purchase supplements for themselves or their children. Among the 64% of women we tested with hemoglobin concentrations indicating moderate-to-severe anemia, many reported having resources available, either through their own small income or family decisions about household expenditures, to only eat nutrient-rich foods such as meat, eggs, or milk as seldom as once or twice a month. Even the staple diet, maize meal and beans, can be difficult to afford during the leanest months. As much as mothers and children may like a fortified beverage or other micronutrient product, whether for flavor or for anticipated health benefits, a private company would face considerable obstacles in creating a viable business model selling to the poorest groups with the least nutritious diets.

Applying the lessons: research into action

What we found through anthropologic research with the women in the study and through evaluating their health-services environment is a substantial challenge. Women and children enjoy drinking a micronutrient-fortified beverage. Families with good information appreciate the importance of improving the health profiles of mothers and children through the regular use of micronutrient supplements, and appropriate social marketing can inspire them to go to great lengths to acquire them. However, public distribution of such supplements can become mired in existing inefficiencies, and private sales will often miss the most important markets—in effect, micronutrient supplementation programs risk resembling other well-intentioned programs that assume rather than analyze and address the situational realities of consumer demand.

Overcoming these challenges should be of central concern in discussing the future of public-private partnerships in micronutrient supplementation. By working together on the beverage, for example, The Procter & Gamble Co. (P&G), Micronutrient Initiative (MI), UNICEF, TFNC, and the Cornell team developed a product that appeals to consumers and is relatively inexpensive to produce. Other products might be even less expensive to produce, such as fortified mixes for the family cooking pot or nutrient pre-mixes that can be ground into staple foods at the community grain mill. Careful social science research can establish whether

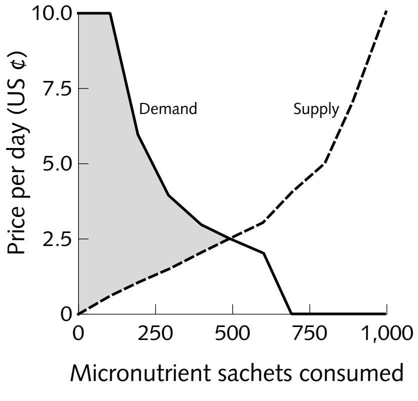

FIG. 1. Model supply and demand curves showing met demand

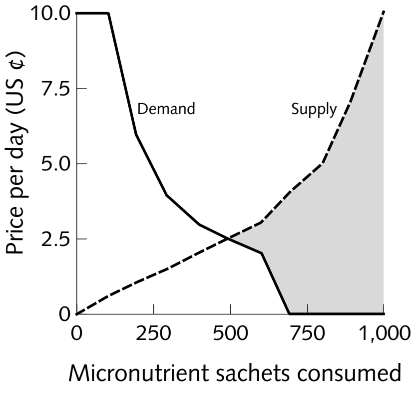

FIG. 2. Model supply and demand curves showing unmet demand

such products are attractive to consumers in various international markets.

Where public and private organizations can then proceed to collaborate to good effect is in the transition beyond the general notion that such a product is tasty and beneficial, toward stimulating consumer demand for micronutrient products and establishing effective distribution models. Marketing activities should not simply aim to motivate consumers to want the product, but must also address ways in which it is practical for the neediest consumers to obtain it, especially the many rural poor who are so often missed by campaigns designed in urban centers. For example, partners can undertake innovative social marketing campaigns with NGOs to expound on the benefits of micronutrient supplements for mothers and children, not only through media campaigns for urban consumers but also through rolling, face-to-face rural outreach programs featuring community theater, music, and nondidactic adult education. At the same time, it is vital at the outset to consider subsidizing the availability of micronutrient products at crucial contact points such as maternal and child health clinics, schools, kindergartens, refugee camps, or hospitals. Such educational and distributional efforts would raise awareness of micronutrient health and supplementation, stimulate a demand for such products on the open market, and also reach those consumers who can most benefit from and least afford to purchase micronutrient products.

Acknowledgment

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