Selling Sprinkles micronutrient powder reduces anemia, iron deficiency, and vitamin A deficiency in young children in Western Kenya: a cluster-randomized controlled trial

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ABSTRACT

Background: Although the efficacy of micronutrient powders [MNPs; eg, Sprinkles MNP (Sprinkles Global Health Initiative)] in the reduction of anemia has been established, the effectiveness of these powders in real-world programs has seldom been assessed.

Objective: In this study, we evaluated the effect of community-based marketing and distribution of Sprinkles MNP on childhood rates of anemia and iron and vitamin A deficiency.

Design: In a cluster-randomized trial in children aged 6–35 mo in Western Kenya, 60 villages were randomly assigned to either intervention or control groups. Community vendors marketed and sold sachets of Sprinkles MNP in intervention villages. Biweekly household visits monitored the use of Sprinkles MNP. Hemoglobin, ferritin, retinol binding protein, malaria, and anthropometric measures were assessed at baseline (n = 1063) and 12 mo of follow-up (n = 862). Data were analyzed by using an intention-to-treat analysis and generalized linear mixed models.

Results: On average, 33% of households in intervention villages purchased Sprinkles MNP; the average weekly intake per child was 0.9 sachets (~11.3 mg Fe and ~328 μg vitamin A). Compared with control subjects, intervention children had greater improvements in hemoglobin concentrations (increase of 0.9 compared with 0.6 g/dL, respectively; P = 0.02), iron deficiency (decrease of 19.3% compared with 5.3%, respectively; P = 0.001), and vitamin A deficiency (decrease of 7.5% compared with an increase of 2.5%, respectively; P = 0.01). Results adjusted for age, sex, socioeconomic status, and maternal education showed a significant association between the hemoglobin, iron, and vitamin A concentrations of children and the number of Sprinkles MNP sachets the children consumed. The prevalence of malaria, wasting, and stunting did not change significantly in either group.

Conclusion: Even with relatively low and infrequent use, Sprinkles MNP sales through community vendors were associated with decreased rates of anemia and iron and vitamin A deficiency in children in a resource-poor setting. This trial was registered at clinicaltrials.gov as NCT01088958.

Topic:

- anemia
- iron
- hemoglobin
- iron deficiency anemia
- child
- follow-up
- kenya

- malaria
- micronutrients
- mothers
- powder dose form
- vitamin a deficiency
- world health
- ferritin
- vitamin a
- iron deficiency
- community

Issue Section:
International nutrition

INTRODUCTION

Micronutrient interventions, particularly vitamin A and zinc supplementation of children and fortification of foods with iron and iodine, have been shown to be among the most cost-effective global development efforts (1). Despite the well-recognized benefits of supplement interventions, their implementation has been hindered by the poor adherence of recipients to dosing regimens, inadequate supplement supplies, low coverage rates, and concerns about dose-related side effects and safety (2).

In response to these operational constraints, micronutrient powders (MNPs)[5], such as Sprinkles MNP (Sprinkles Global Health Initiative), were developed as a novel approach for delivering iron and other micronutrients. MNPs are single-serving packets of vitamins and minerals in powdered form that are mixed into any semisolid food before consumption (3). MNPs were designed to improve adherence by reducing the side effects of iron through the use of microencapsulated ferrous fumarate as the iron source as well as the buffering effect of the food to which MNPs are added (4).

Numerous efficacy trials, including a recent Cochrane review, have demonstrated that MNP use is associated with a significant reduction in the incidence of anemia, and MNPs have higher acceptability and produce fewer side effects than do iron drops in infants and children (5, 6). In addition, MNPs are lightweight and simple to store and

transport, easy to use, relatively inexpensive, and unlikely to result in overdose (7). Because of these advantages, the distribution of MNPs is becoming the preferred iron-deficiency prevention strategy in several countries (8). Bangladesh, Mongolia, and Bolivia all have national MNP programs, and several other countries are planning large-scale MNP distribution (9–12). However, the effectiveness of MNP programs in real-world settings has rarely been assessed. Because the government of Kenya plans to scale up the distribution of MNPs, evidence on the effectiveness of market-based distribution is needed to inform stakeholders. In this study, we sought to determine whether sales of MNPs through a community-based program helped to reduce rates of anemia and iron and vitamin A deficiency in children in a rural population with high rates of malnutrition and poor access to health care.

SUBJECTS AND METHODS

Participants

Between March 2007 and March 2009, we conducted a community-based, cluster-randomized trial to evaluate the effectiveness of the Nyando Integrated Child Health and Education Project (13), which involved the promotion and sale of evidence-based health products, including Sprinkles MNP, in Western Kenya. Details of the study have been described elsewhere (13–15).

The 2 primary objectives of the study were to measure *1*) the effectiveness of the distribution of Sprinkles MNP through an integrated health promotion and income-generating program and *2*) the impact of the sales of Sprinkles MNP on anemia, iron deficiency, and vitamin A deficiency. Three months after a baseline survey in March 2007, Sprinkles MNP was marketed and distributed in the intervention villages; vendors, however, were not prevented from selling Sprinkles MNP in control villages. The monitoring of sales and use took place in both arms of the study via biweekly household monitoring visits. A follow-up survey was conducted in March 2008 to measure the biological impact. After the conclusion of the follow-up survey, we expanded project interventions in control villages.

The study population consisted of children aged 6–35 mo who lived in Nyando Division, which is a largely rural region within the Nyanza Province in Western Kenya that has ~80,000 people and 15,000 households. Most residents are of Luo origin, practice polygamy, and engage in subsistence farming. Malaria transmission in the region is intense and occurs throughout the year, with peaks in the rainy seasons (June to August and November to December). According to the 1999 Kenya National Anemia Survey, 77% of children <30 mo of age were anemic (16). In Western Kenya, more than one-half of pediatric hospital deaths were attributable to anemia (17).

We obtained informed consent (signature or thumbprint) from an adult in the households of all study participants. Children who were severely anemic (hemoglobin concentrations <7.0 g/dL) or with clinical malaria (fever with a positive malaria smear) during baseline and follow-up visits were referred for treatment to the nearest hospital or clinic and included in the analysis. Any participant shown to be ill during biweekly visits was referred for medical care. Institutional review boards of the Kenya Medical Research Institute and the US CDC approved the study.

Procedures

Sample-size estimates were based on the predicted change of hemoglobin in children who consumed Sprinkles MNP by accounting for cluster design. To detect a 10-percentage-point difference of anemia between the intervention and comparison group after 12 mo of intervention with 80% power, a confidence level of 95%, design effect of 1.5, and with allowance for a loss of 20% of subjects, we needed to include 580 children in each arm (with expectation of a decrease in anemia from 60% to 50% in the intervention group).

We used a 2-stage cluster-sampling strategy to select potential study participants. During the first stage, we randomly selected 30 intervention and 30 control villages from a total of 144 villages in Nyando Division (14). The randomization sequence was generated offsite by using a computerized random-number generator. Survey and laboratory field staffs were blinded to treatment groups. Villages were sampled with the probability proportion to size according to the 1999 Kenya Housing and

Population Census. Villages in and near the urban centers of Ahero and Awasi (n = 38) and villages in which Safe Water and AIDS Project (SWAP) groups were already active (n = 4) were excluded from selection (13). During the second stage, we randomly selected 25 children aged 6–35 mo from participating villages; in villages with fewer than 25 children, all such children were recruited.

In intervention villages, sachets of Sprinkles MNP that containing a standard formulation of 12.5 mg Fe as microencapsulated ferrous fumarate, 375 μg vitamin A, 5 mg Zn, 150 μg folic acid; 35 mg vitamin C, 5 μg vitamin D_3, 6 mg vitamin E, 6 mg niacin; 0.6 mg Cu, 50 μg iodine, 0.5 mg thiamine, riboflavin, and vitamin B-6, and 0.9 mg vitamin B-12 were marketed and sold to households with preschool children aged 6–59 mo. Sprinkles MNP was manufactured by Sprinkles Global Health Initiative, shipped by air to Kenya, and distributed by groups of women trained by SWAP (14). Sprinkles MNP was sold alone or with other SWAP health products, which included water disinfectant, soap, insecticide-treated bed nets, and condoms. Although these other health products were generally available and socially marketed in both intervention and control villages, SWAP vendors only promoted and sold them in intervention villages. Sachets of Sprinkles MNP were purchased wholesale by SWAP vendors for one Kenya shilling (~1.3 US cents). Vendors were instructed to resell them at retail in their village and surrounding areas for 2 Kenya shillings (~2.7 US cents) per sachet.

Data collection and processing

Baseline and follow-up data were collected in March 2007 and March 2008, respectively, by using surveys that included interviews of mothers of study participants and measurements of heights, weights, and selected biomarkers of children. Estimates of the use of Sprinkles MNP by children and the health status of children were based on biweekly interviews of the mothers of study participants.

Baseline and follow-up surveys were conducted by trained fieldworkers who administered questionnaires to the mothers of study participants to collect demographic and socioeconomic data (baseline survey only) and information

concerning hygiene, sanitation, and child-feeding practices and the morbidity status of their children (ie, diarrhea, fever, and cough) during the previous 24 h. Fieldworkers also measured heights or lengths of children by using a wooden measuring board that was accurate to 0.1 cm (Irwin Shorr Productions) and weights of children by using a digital scale that was accurate to 0.1 kg (Seca Corp).

Trained laboratory technicians collected capillary blood samples from a finger stick for use in hemoglobin measurements, malaria smear preparations, and purple top Microtainer collection (Becton Dickinson) to assess iron status, vitamin A status, and the presence of inflammation. Hemoglobin concentrations were measured in the field with HemoCue B-Hemoglobin photometers, which were calibrated daily; children with hemoglobin concentrations <11.0 g/dL were classified as anemic (18). Thick blood smears were prepared, stained with Giemsa, and observed under a light microscope at the Kenyan Medical Research Institute/CDC malaria laboratory in Kisian, Kenya. In addition, ~400–500 μL capillary blood was collected into heparinized microcontainers and transported on ice to the project laboratory within 6 h of collection where zinc protoporphyrin (ZP) concentrations were measured in duplicate with a hematofluorometer (Aviv Biomedical) that was standardized daily. ZP concentrations >90 μmol/mol heme (after the application of a correction factor recommended by Aviv and the CDC quality-assurance laboratory) were considered elevated and indicative of iron deficiency (19).

Remaining blood from samples were centrifuged, and the plasma was separated, collected, and stored at −40°C before being transported to a German laboratory that measured concentrations of ferritin, soluble transferrin receptor (TfR), retinol binding protein (RBP), and C-reactive protein (CRP) by using a sandwich enzyme-linked immunosorbent assay technique (20). The following thresholds were used to define abnormal concentrations of these biochemical indicators: <12 μg ferritin/L, >8.3 mg TfR/L, <0.7 μmol RBP/L, and >10 mg CRP/L (20). Approaches to account for the effect of infection or inflammation on ferritin and RBP concentrations included the exclusion of individuals with inflammation based on elevated values of one or more acute-phase proteins (eg, CRP) (21) or the use of correction factors to adjust for

effects of inflammation (22, 23). In line with current WHO and CDC recommendations, we excluded subjects with elevated CRP concentrations from analyses of the relation between the intake of Sprinkles MNP and concentrations of ferritin and RBP (21). We calculated the TfR and ferritin index of children and considered index values >500 to be elevated (24); we calculated total-body iron stores of children and considered values <0 mg Fe/kg body weight to be low (25). The CDC laboratory oversaw the quality control and quality assurance of specimen analyses. All indicators were measured twice, and the average of the duplicate measures was used; the intraassay and interassay CVs were <10%.

We estimated the intake of Sprinkles MNP of children by dividing the number of sachets of Sprinkles MNP reported as purchases or gifts during biweekly household visits by the number of children aged 6–59 mo (ie, the population to whom Sprinkles MNP were promoted) who lived in that household.

Statistical analysis

We used an intention-to-treat analysis to compare key outcomes in the intervention group with key outcomes in the control group. To determine whether our results were biased by children lost to follow-up, we compared baseline characteristics of children who completed the study with baseline characteristics of children lost to follow-up by using Student's *t* test for continuous variables and the chi-square test of proportion for categorical variables. In addition, we compared the consumption of Sprinkles MNP and loss to follow-up by treatment group. We divided participants into socioeconomic quintiles on the basis of household-asset scores that were calculated by assigning values to housing materials and household possessions (26).

After the intention-to-treat analysis, we compared main outcomes by treatment group and adjusted results for any baseline characteristics that may have differed by treatment group by using general linear models that accounted for covariates and clustering (PROC GLIMMIX, SAS version 9.2; SAS Institute Inc); we considered $P < 0.05$ to be indicative of significant differences between groups. Data cleaning and analyses were performed with SAS software (version 9.2; SAS Institute Inc) and Epi

Info (version 3.3.2; CDC). We used the WHO Child Growth Standards (WHO Anthro) to calculate *z* scores for underweight (weight-for-age *z* score less than −2), stunting (length-for-age or height-for-age *z* score less than −2), and wasting (weight-for-length or weight-for-height *z* score less than −2).

RESULTS

Baseline survey

Of 1420 children selected as potential study participants, 1063 children (74.9%) were enrolled in the study, 561 children lived in intervention villages, and 502 children lived in control villages (Figure 1). Of the 357 children who were not enrolled in the study, 61.6% of children were not encountered on 3 attempted household visits, 35.3% of children were outside of the required age range, and 3.1% of children did not receive parental consent. The mean age of enrolled children was 19.9 mo, 51.7% of enrolled children were boys, and ∼2 of 3 of enrolled children were anemic. Baseline characteristics of children in intervention and control groups were similar (Table 1).

TABLE 1

Demographic characteristics and nutritional status of study participants at baseline[1]

	Intervention (*n* = 561)	**Control (*n* = 502)**
Household		
Size	5.5 ± 4.1[2]	5.1 ± 3.6
No electricity (%)	99.4	99.2
Dung or mud walls (%)	96.9	96.1
SES quintile (%)[3]		
1 (lowest)	17.1	24.1
2	19.5	22.7
3	23.3	19.4
4	18.2	15.2
5 (highest)	22.0	18.6
Mothers		
Age (y)	26.7 ± 7.2	26.2 ± 7.1
Less than complete primary school education (%)	54.3	53.5
Children		
Boys (%)	50.3	53.4
Age (mo)	20.4 ± 8.5	19.3 ± 8.4
Ever breastfed (%)	94.2	91.4

	Intervention (*n* = 561)	Control (*n* = 502)
Currently breastfeeding (%)	55.7	59.3
ITN use (%)	83.6	83.3
Hemoglobin (g/dL)	10.3 ± 1.5	10.2 ± 1.5
Anemic (hemoglobin concentration <11.0 g/dL) (%)	64.7	66.6
Malaria positive (%)	20.2	17.3
Elevated CRP (>10 mg/mL) (%)	17.3	15.0
Underweight (WAZ <−2) (%)	12.3	14.0
Stunted (HAZ <−2) (%)	30.2	25.9
Wasted (WHZ <−2) (%)	5.0	5.5

1
CRP, C-reactive protein; HAZ, height-for-age *z* score; ITN, insecticide-treated net; SES, socioeconomic status; WAZ, weight-for-age *z* score; WHZ, weight-for-height *z* score.

2
Mean ± SD [all such values (continuous variables)].

3
P = 0.02 (chi-square test).

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FIGURE 1.

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Trial profile.

Biweekly home visits

Of 6880 biweekly visits to households in intervention villages, 33% of visits were to households that had purchased Sprinkles MNP in the previous 2 wk. Although nearly 93% of children used Sprinkles MNP, most children consumed fewer than 2 sachets/wk (Figure 2). The average estimated intake per child was 0.9 sachets (~11.3 mg Fe and 338 μg vitamin A)/wk. One-fourth of children were classified as consistent users of Sprinkles MNP (ie, reported having purchased Sprinkles MNP at >50% of biweekly household visits). Nearly 40% of children in control villages also had used Sprinkles MNP because of vendors who sold Sprinkles MNP outside their own villages.

FIGURE 2.

Average weekly use of Sprinkles micronutrient powder (Sprinkles Global Health Initiative) in enrolled children in intervention and control villages, June 2007 to May 2008. *Five children whose mothers were vendors were excluded.

Follow-up survey

Approximately 19% of children were lost to follow-up, mostly because their parents moved outside the study area to escape political violence after Kenyan elections in December 2007. In addition, 5 children in the intervention group and 7 children in the control group died during the follow-up period. The percentage of children lost to follow-up did not differ significantly between treatment groups. The final sample of 862 children, aged 18–47 mo, who had data collected in the follow-up survey was similar to children lost to follow-up.

The mean hemoglobin concentration increased by 0.9 g/dL in the intervention group and by 0.6 g/dL in the control group; the increase in the intervention group was significantly greater than in the control group ($P = 0.02$) (Table 2). There was a 27.2% absolute reduction and 40.9% relative reduction in the prevalence of anemia in the

intervention group compared with a 20.1% absolute and a 29.9% relative reduction in the control group; the difference in anemia reduction between the 2 groups was not significant ($P = 0.10$). More than one-half of children in the intervention group who were anemic at baseline were not anemic at follow-up, which was a significantly higher proportion than that in the comparison group ($P = 0.006$).

TABLE 2

Changes in mean hemoglobin concentration, anemia prevalence, and anemia recovery rate in study participants after distribution of Sprinkles MNP by study group[1]

	Intervention (*n* = 427)	**Control (*n* = 407)**	***P* across groups**
Hemoglobin (g/dL)			
Baseline	10.3 (10.1, 10.5)[2]	10.2 (10.0, 10.4)	0.32
12-mo follow-up	11.2 (11.0, 11.4)	10.8 (10.6, 11.0)	0.001
Difference (g/dL)[3]	+0.9	+0.6	0.02
Anemia (hemoglobin concentration <11.0 g/dL)			
Baseline (%)	66.5	67.3	0.80

	Intervention (*n* = 427)	Control (*n* = 407)	*P* across groups
12-mo follow-up (%)	39.3	47.2	0.02
Absolute difference (%)[3]	−27.2	−20.1	0.10
Anemia recovery rate (%)[4]	53.2	42.0	0.006

1
Means across groups tested by using ANOVA with clustering accounted for; the percentage across and within groups was compared by using the chi-square test with clustering accounted for (reflects *n* = 18 and *n* = 10 missing hemoglobin values in intervention and control groups, respectively). Sprinkles MNP was manufactured by Sprinkles Global Health Initiative. MNP, micronutrient powder.

2
Mean; 95% CI in parentheses (all such values).

3
P for effect of heterogeneity from mixed model (double difference between groups across time) with cluster accounted for.

4
n = 558 anemic at baseline.

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The prevalence of iron deficiency as measured by ferritin concentrations <12.0 ng/mL decreased by 19.3% in the intervention group compared with 5.3% in the control group (*P* = 0.001), and the prevalence of vitamin A deficiency decreased by 7.5% in the intervention group compared with a 2.5% increase in the control group (*P* = 0.01) (Table 3). These differences remained significant even after children with elevated CRP values were included in the analyses, and analyses were adjusted for any baseline differences that differed by treatment group (data not shown). Compared with control subjects, intervention children did not have significant improvements in TfR, the TfR and ferritin index, total-body iron stores, or ZP (Table 4). Changes in the

prevalence of malaria parasitemia, stunting, wasting, and underweight did not differ significantly by study group (data not shown).

TABLE 3

Changes in prevalence of iron deficiency and vitamin A deficiency in study participants after distribution of Sprinkles MNP by study group[1]

Deficiency	Intervention	Control	*P* across groups
Iron (ferritin concentration <12.0 ng/mL)[2]			
n	254	246	—
Baseline (%)	41.7	43.9	0.62
12-mo follow-up (%)	22.4	38.6	<0.001
Absolute difference (%)[3]	−19.3	−5.3	0.001
Vitamin A (RBP concentration <0.7 μg/L)[2]			
n	254	246	—
Baseline (%)	17.7	13.0	0.15

Deficiency	Intervention	Control	*P* across groups
12-mo follow-up (%)	10.2	15.5	0.08
Absolute difference (%)[3]	−7.5	+2.5	0.01

1
Means across groups were tested using ANOVA with clustering accounted for; the percentage across and within groups was compared by using the chi-square test with clustering accounted for. Sprinkles MNP was manufactured by Sprinkles Global Health Initiative. CRP, C-reactive protein; MNP, micronutrient powder; RBP, retinol binding protein.

2
Excluded samples with elevated CRP concentrations >10 mg/dL (*n* for the intervention group reflects missing blood data in 76 subjects and exclusion of 97 subjects with elevated CRP; *n* for the control group reflects missing blood data in 82 subjects and exclusion of 79 subjects with elevated CRP).

3
P for effect of heterogeneity from mixed model (double difference between groups across time) with cluster accounted for.

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TABLE 4

Changes in prevalence of secondary measures of iron deficiency in study participants after distribution of Sprinkles MNP in intervention villages by study group[1]

Secondary measure	Intervention	Control	*P* across groups
TfR (>8.3 mg/L)			
n	351	325	—
Baseline (%)	33.3	36.0	0.47
12-mo follow-up (%)	21.9	25.5	0.27
Absolute difference (%)[2]	−11.4	−10.5	0.71
TfR and ferritin index (>500)			
n	351	325	—
Baseline (%)	45.0	47.4	0.54
12-mo follow-up (%)	24.5	31.1	0.06
Absolute difference (%)[2]	−20.5	−16.3	0.22
Total-body iron stores (<0 mg Fe/kg body weight)			
n	351	325	—
Baseline (%)	36.8	40.9	0.27
12-mo follow-up (%)	17.4	25.0	0.02
Absolute difference (%)[2]	−19.4	−15.9	0.19
ZP (>90 μmol/mol)			

Secondary measure	Intervention	Control	*P* across groups
n	344	315	—
Baseline (%)	81.7	84.1	0.41
12-mo follow-up (%)	53.8	62.1	0.03
Absolute difference (%)[2]	−27.9	−22.0	0.43

1
Means across groups were tested by using ANOVA with clustering accounted for (reflects $n = 76$ and $n = 82$ missing TfR in intervention and control groups, respectively, and $n = 83$ and $n = 92$ missing ZP values in intervention and control groups, respectively). Sprinkles MNP was manufactured by Sprinkles Global Health Initiative. MNP, micronutrient powder; TfR, soluble transferrin receptor; ZP, zinc protoporphyrin.

2
P for effect of heterogeneity from mixed model (double difference between groups across time) with cluster accounted for.

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Because some children in control villages used Sprinkles MNP during the study period, we conducted an as-treated analysis to assess the impact of the use of Sprinkles MNP on biomarkers of children in both groups combined (Figure 3). For this analysis, we divided children into the following 3 groups: nonusers, infrequent users (>0–2 sachets/wk), and frequent users (>2 sachets/wk) and observed a significant trend of Sprinkles MNP use with measures of ferritin and RBP at follow-up ($P = 0.04$ and $P = 0.01$, respectively) (Figure 3). There were no significant baseline differences in demographic characteristics, socioeconomic status, or nutritional status between users and nonusers of Sprinkles MNP (data not shown). Results adjusted for age, sex, socioeconomic status, and maternal education showed the frequency of use of Sprinkles MNP to be positively associated with mean ferritin, RBP, and hemoglobin values [adjusted OR: 1.4 ($P = 0.05$), adjusted OR: 3.3 ($P = 0.006$), and

adjusted OR: 1.4 (P = 0.08), respectively). In the adjusted analysis, children who used >2 sachets/wk had a 0.54 g/dL greater increase in hemoglobin concentration compared with that of nonusers (P = 0.027).

FIGURE 3.

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Percentage of children with anemia, iron deficiency, and vitamin A deficiency at follow-up by category of use of Sprinkles micronutrient powder (Sprinkles Global Health Initiative). *Mixed model $P < 0.05$ adjusted for age, sex, socioeconomic status, and maternal education.

DISCUSSION

We showed that the distribution of MNPs through a potentially self-sustaining community-based marketing approach was effective in reducing rates of iron and vitamin A deficiency and increasing the rate of recovery from anemia in young children. Even though children in the intervention group consumed an average of only 0.9 sachets/wk, we showed significant improvement in their hemoglobin and vitamin A status and in some measures of their iron status. The vitamin A findings suggested that MNP distribution might be an effective adjunct intervention to biannual high-dose vitamin A supplementation or fortification of staple foods with vitamin A.

Results of previous clinical trials of Sprinkles MNP distributed at no cost to recipients have shown anemia recovery rates to be similar to the 53% that we showed (Table 2). For example, the recovery rate was 54% in 6-mo-old Cambodian infants given Sprinkles MNP with 12.5mg Fe daily for 12 mo (27). Similarly, the flexible administration of 60 sachets of Sprinkles MNP to anemic Bangladesh children aged 6–24 mo was shown to result in a 54% anemia cure rate over 3 mo and a 65% cure rate over 4 mo (28).

To further validate the biological impact on hemoglobin that was observed in this study, we calculated the predicted change in the mean hemoglobin concentration in

the intervention group (on the basis of the amount of iron in Sprinkles MNP that group members were estimated to have consumed) (29), which was only slightly higher than the 0.9-g/dL increase that we observed. In addition, the absolute increase in hemoglobin concentration in the intervention group and the 0.3-g/dL increase overall were similar to the effects of treatment reported in recent Cochrane reviews of iron supplementation and MNP trials (6, 30). The increases in hemoglobin concentrations that we showed may not have been due to iron alone because other micronutrients in Sprinkles MNP can enhance hematopoeisis by increasing iron absorption (vitamin C and riboflavin) or metabolism (copper, vitamin A, vitamin B-12, riboflavin, and vitamin C) (31). Furthermore, some of the increase in hemoglobin that we observed may have been attributable to the effects of other interventions associated with anemia reduction (eg, the distribution of insecticide-treated bed nets) (32). However, the observed use of bed nets was not different between treatment groups (data not shown).

The anemia recovery rates in our intervention group likely would have been even higher had the iron content of Sprinkles MNP been greater or the Sprinkles MNP been used more frequently. In a similar setting in Western Kenya, the anemia recovery rate was 75% in children who received daily supplements of 3–6 mg Fe/kg with malaria treatment of 12 wk (33). However, because of recent concerns about the safety of daily iron supplementation in malarial areas (2), the optimal dose and method of iron delivery is uncertain. It is possible that in highly iron-deficient populations, less frequent iron intake over time may be a safe but still effective distribution approach. More research on the safety and effectiveness of iron intake in malarial areas is needed, particularly in regard to iron-dosing regimens as well as different iron preparations including MNPs (34).

After the 2007 change of the Kenya Ministry of Health in the method of distributing vitamin A supplements from mass distribution campaigns to routine distribution in health facilities, coverage fell from ~80% in 2006 to 22% in 2008 in the Nyanza Province (35). Our finding of a 42% relative reduction in the prevalence of vitamin A deficiency in children in the intervention group suggested that MNPs could be

considered as a possible adjunct to vitamin A supplementation in young children in areas with a low coverage of biannual supplementation.

Although not a primary outcome of our study, we showed no significant association between the use of Sprinkles MNP and 4 secondary indicators of iron status (Table 4). All iron biomarkers were affected by factors other than iron status, which may explain why ferritin, when effect of inflammation was accounted for, was the most sensitive indictor in this setting. Although there are no global recommendations on the use of these indicators for the evaluation of the impact of iron interventions, the US NIH recently established the Biomarkers of Nutrition and Development to explore such issues (36).

This study had several limitations. First, because it was limited to one division in the Nyanza Province, the results of the study were not representative of the province or Kenya as a whole. Second, the biweekly home visits may have motivated mothers of children in the intervention group to purchase Sprinkles MNP. To address this potential bias from the Hawthorne effect, follow-up data were collected from a subsample of children from households that did not participate in biweekly monitoring. Although these children had significant reductions in anemia and iron and vitamin A deficiency, these reductions were smaller than those in actual study households, which suggested that home visits may have biased our results toward an overestimate of the effectiveness of the intervention (data not shown). Third, the distribution of Sprinkles MNP in control villages may have biased our results in the other direction (ie, toward an underestimate of the effectiveness of the intervention). Fourth, ~19% of children were lost to follow-up, and an additional 20% of children had incomplete laboratory values (although this limitation probably had little effect on study results because demographic characteristics and use of Sprinkles MNP in these children were not different from those in other study participants). Finally, our analyses did not account for the effect of Sprinkles MNP alone because Sprinkles MNP was sometimes sold with other health products. Indications of a trend effect of the use of Sprinkles MNP on anemia and iron and vitamin A deficiency (Figure 3)

provided support that the use of Sprinkles MNP was largely responsible for the observed effect.

In conclusion, we have shown that market-based community distribution of Sprinkles MNP in a resource-poor, malaria-endemic area can be effective in the improvement of anemia recovery rates and some measures of iron deficiency and vitamin A deficiency in children aged 6–35 mo even though most children received less than recommended doses of iron. These findings suggest a need for additional investigation into the minimum amounts of micronutrients necessary to prevent anemia and iron and vitamin A deficiency and for additional evaluation of models of distribution of Sprinkles MNP as part of potentially sustainable programs for the prevention of these conditions.

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The authors' responsibilities were as follows—PSS, LJR, BAW, CM, MEDJ, and RQ: designed the research; PSS, LJR, UM, MEDJ, and RQ: conducted the research; PSS and RF-A: analyzed data; PSS: wrote the manuscript and had primary responsibility for the final content of the manuscript; and all authors: read and approved the final manuscript. None of the authors had a personal or financial conflict of interest.

FOOTNOTES

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