Postintervention growth of Malawian children who received 12-mo dietary complementation with a lipid-based nutrient supplement or maize-soy flour

John C Phuka, Kenneth Maleta, Chrissie Thakwalakwa, Yin Bun Cheung, Andre’ Briand, Mark J Manary, and Per Ashorn

ABSTRACT

Background: Therapeutic feeding with micronutrient-fortified lipid-based nutrient supplements (LNSs) has proven useful in the rehabilitation of severely malnourished children. We recently reported that complementary feeding of 6–18-mo-old infants with an LNS known as FS50 was associated with improved linear growth and a reduction in the incidence of severe stunting during the supplementation period.

Objective: Our objective was to assess whether a reduction in stunting seen with 12-mo LNS supplementation was sustained over a subsequent 2-y nonintervention period.

Design: One hundred eighty-two 6-mo-old healthy rural Malawian infants were randomly assigned to receive daily supplementation for 12 mo with 71 g of maize-soy flour [likunt phala (LP); control group, 282 kcal] or either 50 g of FS50 (264 kcal; main intervention group), or 25 g of FS25 (130 kcal). Main outcome measures were incidence of severe stunting and mean z score changes in weight-for-age, length-for-age, and weight-for-length during a 36-mo follow-up period.

Results: The cumulative 36-mo incidence of severe stunting was 19.6% in LP, 3.6% in FS50, and 10.3% in FS25 groups (P = 0.03). Mean weight-for-age changes were −1.09, −0.76, and −1.22 (P = 0.04); mean length-for-age changes were −0.47, −0.37, and −0.71 (P = 0.10); and mean weight-for-length changes were −1.52, −1.18, and −1.48 (P = 0.27). All differences were more marked among individuals with baseline length-for-age below the median. Differences in length developed during the intervention at age 10–18 mo, whereas weight differences continued to increase after the intervention.

Conclusions: Twelve-month-long complementary feeding with 50 g/d FS50 is likely to have a positive and sustained impact on the incidence of severe stunting in rural Malawi. Half-dose intervention may not have the same effect. This trial was registered at clinicaltrials.gov as NCT00131209.


INTRODUCTION

Stunting, or statural growth failure, affects ≈170 million children <5 y of age, with a prevalence of 40% in southern Asia and 50% in sub-Saharan Africa (1–5). The condition is associated with many long-term consequences, such as poor cognitive or school performance, delayed motor development, impaired physical performance, reduced income in adulthood, obstetric emergencies, and lower birth weight in offspring (4, 6–15).

Because of these adverse sequelae and the persistence of stunting after the age of 2 y (16, 17), prevention strategies are a global health priority. To date, however, few interventions have proven successful in markedly promoting sustainable linear growth of children <2 y old in low-resource settings (18).

In recent years, the treatment of children with severe acute malnutrition has drastically changed through the use of lipid-based nutrient supplements (LNSs) (19–25). These products typically contain milk protein, sugar, and a mixture of micronutrients, embedded in a lipid base (26). Because of their positive impact on severely malnourished individuals, ease of production and use, excellent storage properties, and flexibility of the fortified micronutrient composition, modified LNSs have also been considered a potential means for the prevention of stunting. Actual research data on this possibility are still scarce, but 3 recent clinical trials from sub-Saharan Africa suggest that provision of small daily doses of complementary LNS to 6–18-mo-old infants can promote their linear growth and yield other health benefits (27–29). To date, however, no longer term results have been published from trials using LNSs to prevent stunting.

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2 AB is a staff member of the World Health Organization. The author alone is responsible for the views expressed in this publication, which do not necessarily represent the decisions or the stated policy of the World Health Organization. The funders of this trial had no role in its implementation, analysis, or reporting.

3 Supported by the Academy of Finland (grants 200720 and 109796), the Foundation for Paediatric Research in Finland, and the Medical Research Fund of Tampere University Hospital. The micronutrient mixture used in the production of fortified spread was provided free of charge by Nutriset Inc (Malaunay, France). JCP and CT received personal stipends from the Nestle Foundation.

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We recently reported findings from a randomized trial in Malawi, which showed a 0% incidence of severe stunting [length-for-age z score (LAZ) ≤ −3] between 6 and 18 mo of age among infants receiving daily dietary supplementation with 50 g LNS for 1 y, compared with 13% among those receiving an iso-energetic dose of maize-soy flour and 4% among those receiving 25 g/d LNS (29). In the current article, we extend the follow-up of the same children to the subsequent 2-y period with no further dietary intervention. The new analysis focused on the incidence of stunting as well as mean length and weight gain between 6 and 42 mo of age.

SUBJECTS AND METHODS

Study area and timing

The study was conducted between 11 October 2004 and 8 January 2008 in Lungwena, a rural Malawian community with a high prevalence of early childhood stunting and underweight children (1, 30). The staple food, maize, was grown during a single rainy season between December and March. Exclusive breastfeeding for babies was almost nonexistent and infant diet was typically complemented with thin maize porridge from 2 to 6 mo of age.

Eligibility criteria, enrollment, and randomization of the trial participants

Inclusion criteria included age of 5.50–6.99 mo, residence in the study area, and an informed consent from at least one authorized guardian. Exclusion criteria were low weight-for-length z score (WLZ; < −2.0), presence of edema, history of peanut allergy, severe illness warranting hospitalization on the enrollment day, concurrent participation in another clinical trial, or any symptoms of food intolerance ≤ 30 min after the ingestion of a 6-g test dose of the peanut-based LNS used as a trial intervention.

For enrollment, trained health surveillance assistants contacted all families who were known to live in the area with a child between 5 and 7 mo of age. Infants were invited to an enrollment session where they were screened for eligibility, and guardians were given detailed information on the trial contents.

For group allocation, guardians picked one from a set of identically appearing opaque envelopes, each containing a paper indicating an identification number and a randomly assigned allocation to 1 of the 3 interventions. The randomization list and envelopes were made by persons not involved in trial implementation, and those assessing the outcomes were blinded throughout the study.

Interventions and follow-up

There were 3 intervention schemes given for 12 mo from the age of 6 mo, after which the participants were monitored for another 24 mo without additional intervention. Infants in the control group were provided with an average of 71 g/d of micronutrient-fortified maize and soy flour, locally called likuni phala (LP). Participants in the other 2 groups received, on average, either 50 or 25 g/d of an LNS known as fortified spread (FS; FS50 or FS25). The supplements were home delivered at 3 weekly intervals (at each food delivery, three 500-g bags of LP, four 262-g jars of FS50, or two 262-g jars of FS25 were provided).

LP was purchased from a local producer (Rab Processors, Limbe, Malawi). LNS was produced at a Malawian nongovernmental organization (Project Peanut Butter, Blantyre, Malawi) from peanut paste, milk powder, vegetable oil, sugar, and pre-made micronutrient mixture (Nutriset, Malaunay, France). All supplements were fortified with micronutrients, but the level of fortification varied between the products. The difference between the FS50 and FS25 supplementation was the amount of food base given (50 compared with 25 g/d). The micronutrient content, however, was adjusted so that children in both FS50 and FS25 groups received similar daily micronutrient doses. The energy and nutrient contents of a daily ration of each supplementation scheme are shown in Table 1.

FS50 and FS25 could be eaten raw, whereas the maize-soy flour (LP) required cooking into porridge before consumption. The guardians were provided with spoons and advised to daily offer their infants porridge containing 12 spoonfuls of LP, 8 spoonfuls of FS50, or 4 spoonfuls of FS25, which were divided into 2–3 daily doses. All mothers were encouraged to continue breastfeeding on demand and to feed their infants only as much of the food supplement as the infant wanted to consume at a feeding.

During the intervention, the participants were visited weekly at their homes to collect information on supplement use and possible adverse events during the intervention period. Empty food containers were collected every 3 wk. At 4, 8, 12, 18, and 36 mo after enrollment, the participants visited the research office at a nearby health center and underwent a physical examination and anthropometric assessment.

### TABLE 1
Energy and nutrient content of a daily ration of each food supplement used in this trial

<table>
<thead>
<tr>
<th>Variable</th>
<th>LP</th>
<th>FS50</th>
<th>FS25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (g)</td>
<td>71</td>
<td>50</td>
<td>25</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>282</td>
<td>256</td>
<td>127</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>10.3</td>
<td>7.0</td>
<td>3.6</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>NA</td>
<td>13.8</td>
<td>6.6</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>3.1</td>
<td>16.9</td>
<td>8.5</td>
</tr>
<tr>
<td>Retinol (µg RE)</td>
<td>138</td>
<td>400</td>
<td>400</td>
</tr>
<tr>
<td>Folate (µg)</td>
<td>43</td>
<td>160</td>
<td>160</td>
</tr>
<tr>
<td>Niacin (mg)</td>
<td>3</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Pantothenic acid (mg)</td>
<td>NA</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Riboflavin (mg)</td>
<td>0.3</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Thiamine (mg)</td>
<td>0.1</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Vitamin B-6 (mg)</td>
<td>0.3</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Vitamin B-12 (µg)</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Vitamin C (mg)</td>
<td>48</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Vitamin D (µg)</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>71</td>
<td>366</td>
<td>283</td>
</tr>
<tr>
<td>Copper (mg)</td>
<td>NA</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Iodine (µg)</td>
<td>NA</td>
<td>135</td>
<td>135</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>5</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>NA</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Selenium (µg)</td>
<td>NA</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>3.6</td>
<td>8.4</td>
<td>8.4</td>
</tr>
</tbody>
</table>

1 FS25, fortified spread 25 g/d; FS50, fortified spread 50 g/d; LP, likuni phala; NA, not available; RE, retinol equivalents.
Measurement of outcome variables

The primary outcome for the initial trial was weight gain. Secondary outcomes included the following: mean changes in length, head circumference, and mid-upper-arm circumference; the anthropometric indexes weight-for-age z score (WAZ), length-for-age z score (LAZ/HAZ), and WHZ; and the incidence of underweight children, wasting, and stunting. In this secondary phase, we focused the analyses on the incidence of severe stunting (LAZ/HAZ < -3 z score units) or moderate-to-severe stunting (LAZ/HAZ < -2 z score units) and changes in the mean anthropometric indexes.

Weight was measured with naked infants by using an electronic infant weighing scale (SECA 834; Chasmos Ltd, London, United Kingdom) and recorded to the nearest 10 g. Length (at ≤24 mo of age) and height (at >24 mo) were measured to the nearest 1 mm with a high-quality length board (Kiddimetre; Raven Equipment Ltd, Essex, United Kingdom) and a high-quality stadiometer (Harpenden stadiometer; Child Growth Foundation, London, United Kingdom). Mid-upper-arm and head circumferences were measured with nonstretchable plastic tapes (Lasso-o tape; Harlow Printing Ltd, South Shields, United Kingdom). Anthropometric indexes (WAZ, LAZ, and WHZ) were calculated with Epi-Info 3.3.2 software (Centers for Disease Control and Prevention, Atlanta, GA) with the use of the the CDC 2000 growth reference charts (31).

Sample size calculation

Sample size was calculated from expected weight gain at the end of the initial 12-mo intervention period. Assuming a SD of 1.40 kg in all intervention groups and a difference of 0.75 kg between the means in the main intervention group (FS50) and the control group (LP), a sample size of 55 infants/group was calculated to provide the trial with 80% power and 95% confidence. To allow for ≈10% attrition, the target enrollment was 60 infants/group.

Data management and analysis

Data were recorded on paper forms, transcribed to paper case report forms, and entered twice into a custom Microsoft Access 2003 database program (Microsoft Corp, Redmond, WA). The double entries were electronically compared, and extreme values were confirmed or corrected.

Statistical analysis was performed by using Stata 9.0 (StataCorp, College Station, TX) on an intention-to-treat basis. Infants with no anthropometric data after enrollment were included only in the comparison of baseline characteristics. The analyses of anthropometric measures used data from young children who were available at 42 mo of age; data from infants and young children with at least one measurement after enrollment were analyzed for incidence of stunting with the use of the survival analysis method to control for censoring.

For continuous and categorical outcomes, the 3 intervention groups were compared by using analysis of variance (ANOVA) and Fisher’s exact test, respectively. Post hoc pairwise comparisons for statistically significant intergroup differences were analyzed using the Tukey wholly significant difference test. Survival analysis was used to determine the cumulative probability of severe or moderate stunting among different groups, and the differences were tested by the log-rank test. An event was considered to have occurred at midpoint when it occurred between the time the event was detected and the previous measurement. Individuals with severe or moderate-to-severe stunting at enrollment were excluded from survival analyses on the incidence of that outcome. Effect sizes were calculated by dividing the difference in mean z scores between FS50 and either FS25 or LP groups by the pooled SDs of the 2 means.

Ethics, study registration, and participant safety

The trial was performed according to International Conference of Harmonisation—Good Clinical Practice guidelines (ICH-GCP), and it adhered to the principles of the Declaration of Helsinki and the regulatory guidelines in Malawi. Before the onset of enrollment, the trial protocol was reviewed and approved by the College of Medicine Research and Ethics Committee (University of Malawi) and the Ethical Committee of Pirkanmaa Hospital District (Finland). Key details of the protocol were published at the clinical trial registry of the National Library of Medicine, Bethesda, MD. Before enrollment and again between the initial 12-mo intervention and the subsequent 24-mo follow-up, participant guardians were briefed about the study, and they signed a written consent form for trial participation.

A data safety and monitoring board continuously monitored the incidence of suspected serious adverse events during the intervention period, defined as any untoward medical occurrence that resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, or resulted in a persistent or significant disability or incapacity or other serious medical condition.

RESULTS

Of the 303 initially screened infants, 182 were enrolled in the complementary feeding trial. Of these, 10 died and 4 were lost to follow-up during the 12-mo food-supplementation period; thus, 168 participated in the postintervention follow-up. During the 24-mo postintervention follow-up, there were 6 deaths and 13 further losses to follow-up, which left 149 participants who completed the 36-mo assessment (Figure 1). There was no statistically significant difference in the proportion of deaths and number of dropouts between the food intervention groups (P = 0.72 and 0.26, respectively).

Selected baseline characteristics of the participants by intervention group are shown in Table 2. At enrollment, mean anthropometric measurements were comparable in the LP and FS50 groups, whereas infants in the FS25 group were, on average, slightly heavier and taller (Table 2). The prevalences (number of infants) of severe stunting and severe underweight at enrollment in the LP, FS50, and FS25, groups, respectively, were as follows: severe stunting: 3.3% (n = 2), 6.6% (n = 4), and 1.7% (n = 1); severe underweight: 1.6% (n = 1), 3.3% (n = 2), and 0.0% (n = 0).

Figure 2 describes a time-to-event analysis of stunting in different intervention groups. By the end of the 12-mo intervention period, 13.3% (n = 7), 0.0% (n = 0), and 3.5% (n = 2) of the participants in the LP, FS50, and FS25 groups, respectively, had developed severe stunting (29). In the postintervention follow-up, 4–7% of the participants in each group...
developed the condition, which increased the cumulative 3-y incidence (number of cases) of severe stunting to 19.6% (n = 11) in LP, 3.6% (n = 2) in FS50, and 10.3% (n = 6) in FS25 groups (P = 0.03, log-rank test; Figure 2A). The point estimate (95% CI) for the difference between the LP and FS50 groups was 16% (5–26%), and the number needed to treat or prevent one case of severe stunting was 6 (4–20). The cumulative incidence of moderate-to-severe stunting was more similar in the 3 groups, although infants in the FS50 group tended to develop the condition on average somewhat later (P = 0.50, log-rank test; Figure 2B).

Among the 149 participants who completed the follow-up, mean 3-y gains in weight, height, and mid-upper-arm and head circumferences were highest in the FS50 group and lowest in the FS25 group. Average values for the anthropometric indexes WAZ, HAZ, and weight-for-height z score (WHZ) decreased in all groups, but the reductions were smallest among the FS50 group and largest in the FS25 group. However, intergroup differences reached statistical significance among unselected children only for WAZ change (Table 3). During the follow-up period, those who received LP or FS25, on average, had larger reductions in their WAZ compared with FS50 children: 0.33 (95% CI: −0.39, 0.69) vs. 0.46 (95% CI: 0.10, 0.82) z score units for LP and FS25 groups, respectively. Similarly, those who received LP or FS25 had larger reductions in their HAZ during the follow-up: 0.10 (95% CI: −0.23, 0.43) and 0.34 (95% CI: 0.02, 0.67) z score units for LP and FS25 groups.

TABLE 2
Baseline characteristics of the 182 participants at enrollment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LP (n = 61)</td>
</tr>
<tr>
<td>Male sex</td>
<td>24/61 (39.3)²</td>
</tr>
<tr>
<td>PCR-confirmed HIV infection</td>
<td>0/55 (0.0)</td>
</tr>
<tr>
<td>Age (mo)</td>
<td>5.91 ± 0.41³</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>6.92 ± 0.93</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>62.8 ± 2.1</td>
</tr>
<tr>
<td>Mid-upper-arm circumference (cm)</td>
<td>13.4 ± 0.9</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>43.0 ± 1.5</td>
</tr>
<tr>
<td>Weight-for-age z score</td>
<td>−0.65 ± 1.07</td>
</tr>
<tr>
<td>Length-for-age z score</td>
<td>−1.20 ± 0.82</td>
</tr>
<tr>
<td>Weight-for-length z score</td>
<td>0.48 ± 1.08</td>
</tr>
</tbody>
</table>

¹FS25, fortified spread 25 g/d; FS50, fortified spread 50 g/d; LP, likuni phala; PCR, polymerase chain reaction.
²n/total n; percentage in parentheses (all such values).
³Mean ± SD (all such values).
respectively. Adjusting the analyses for baseline weight resulted in findings similar to the unadjusted analyses (data not shown).

Because of our earlier observation that there was a strong interaction between a child’s length at 6 mo of age and his or her weight and length gains during the intervention ($P = 0.002$ and $P = 0.04$, respectively) (29), we also conducted stratified analyses on these outcomes during the postintervention follow-up. As shown in Table 3, the largest and smallest anthropometric gains were seen in the FS50 and FS25 groups, respectively, both among children with baseline height below the population median and those above it. However, the absolute differences in weight and length were bigger, and they more often reached statistical significance in the initially shorter participants (Table 3). Among these infants, those who received FS50 had, on average, a $0.61$ kg (95% CI: $-0.15, 1.37$ kg) higher weight gain or a $0.53$ (95% CI: $0.07, 0.99$) $z$ score unit smaller reduction in WAZ than did LP children and a $0.91$ kg (95% CI: $0.19, 1.24$) higher weight gain or a $0.53$ (95% CI: $0.07, 0.99$) $z$ score unit smaller reduction in WAZ than did FS25 children. Differences in height gains showed a similar pattern but did not reach statistical significance (Table 3).

### Table 3: Outcome changes during 36 mo of follow-up in young children who received different doses of fortified spread (FS) and likuni phala (LP)$^1$

<table>
<thead>
<tr>
<th>Variable</th>
<th>All participants</th>
<th>Baseline LAZ &lt; median</th>
<th>Baseline LAZ ≥ median</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LP group (n = 50)</td>
<td>FS50 group (n = 46)</td>
<td>FS25 group (n = 53)</td>
</tr>
<tr>
<td>Change in weight (kg)</td>
<td>$5.61 \pm 1.12^2$</td>
<td>$6.00 \pm 1.31$</td>
<td>$5.58 \pm 1.08$</td>
</tr>
<tr>
<td>Change in height (cm)</td>
<td>$28.4 \pm 2.7$</td>
<td>$28.6 \pm 2.8$</td>
<td>$27.9 \pm 3.1$</td>
</tr>
<tr>
<td>Change in mid-upper-arm circumference (cm)</td>
<td>$1.3 \pm 1.1$</td>
<td>$1.4 \pm 1.3$</td>
<td>$1.0 \pm 1.1$</td>
</tr>
<tr>
<td>Change in head circumference (cm)</td>
<td>$5.6 \pm 0.7$</td>
<td>$5.8 \pm 0.9$</td>
<td>$5.6 \pm 0.8$</td>
</tr>
<tr>
<td>Change in weight-for-age $z$ score</td>
<td>$-1.99 \pm 0.90$</td>
<td>$-0.76 \pm 0.99$</td>
<td>$-1.22 \pm 0.84$</td>
</tr>
<tr>
<td>Change in height-for-age $z$ score</td>
<td>$-0.47 \pm 0.76$</td>
<td>$-0.37 \pm 0.83$</td>
<td>$-0.71 \pm 0.87$</td>
</tr>
<tr>
<td>Change in weight-for-length $z$ score</td>
<td>$-1.52 \pm 1.20$</td>
<td>$-1.18 \pm 1.28$</td>
<td>$-1.48 \pm 0.92$</td>
</tr>
</tbody>
</table>

$^1$ FS25, 25 g/d; FS50, 50 g/d; LAZ, length-for-age $z$ score.

$^2$ Obtained by ANOVA.
To demonstrate the timing of growth failure in the 3 intervention groups, we plotted the changes of children’s mean anthropometric indexes as a function of the trial duration (Figure 3). As shown, the difference in HAZ between LP and FS groups started to develop after 4 mo (when children were 10 mo old) and reached a peak 4–8 mo later (at 14–18 mo of age). In contrast, differences in WAZ or WHZ increased gradually during the 12-mo intervention and continued to grow wider during the 2-y postintervention follow-up (Figure 3). The patterns were similar among participants with baseline height above or below the median, but absolute values were more pronounced among those who were shorter at the beginning (data for individuals with higher baseline HAZ not shown). The corresponding attained weight or height by age and intervention group, both among all children and only those with baseline LAZ below the median, is shown in Figure 4.

DISCUSSION

We previously reported findings from a randomized controlled trial that reported a lower incidence of severe linear growth failure (stunting) among infants whose diet was supplemented for 1 y with a specific formula (FS50) of micronutrient-fortified LNS rather than an iso-energetic ration of maize and soy flour (LP) (29). In the present study, we analyzed the duration of the effect by extending the growth follow-up for an additional 2 y without providing further food supplements. After the intervention, severe stunting continued to occur slightly more often in the control group, so that over the entire 3-y follow-up, its incidence was almost 20% in the LP group but only 4% in the FS50 group. Hypothesis testing suggested that the observed difference was unlikely to be caused by chance alone. Selection and implementation bias was avoided by procedures such as population-based enrollment, use of a control group, randomized group allocation and blinding of outcome assessors, strict control of dropouts, and the use of standardized outcome variables. The observed results are thus consistent with the idea that 1-y supplementation of infant diet with 50 g/d FS50 is associated in rural Malawi with a reduced incidence of severe stunting during a period that covers the intervention and subsequent 2 y.

Similar to our earlier results (29), the growth difference between the intervention and the control group was largest when measured with dichotomous and more severe outcomes or among those individuals who were somehow already disadvantaged (mildly stunted) at enrollment. Differences in mean length or height developed mostly during the intervention (at 10–18 mo of age), whereas weight differences became more pronounced later,
in the second and third year of life. Although no conclusive ex-
planation can be given to this phenomenon, the results are con-
sistent with the idea that FS50 supplementation somehow affected
the timing of acceleration in the infants’ linear growth velocity
(32). Such acceleration, known as the infancy-to-childhood
growth spurt (IC spurt), occurs at an average age of 9 mo in in-
dustrialized countries but often much later in low-income settings
(17, 33). Each month of delay in IC spurt is associated, on average,
with \( \approx 0.5 \text{-cm deficit in length gain by } 5 \text{ y} \) (17, 33).

Factors that induce the IC spurt in infants are unknown at
present, but dietary intake of cow milk may play a role in the
process (34). Theoretically, it is thus possible that the observed
linear growth differences in our trial were due to the cow milk
protein fraction in FS50 (10 g in the 50-g/d dose), an increased
intake of which might have led, on average, to a 4 mo earlier
induction of IC spurt in the intervention compared with the
control group. This suggestion, while still hypothetical, receives
some support from the fact that children grew less in the group
that received a lower dose of FS (FS25), which had the same
micronutrient content but only half the amount of milk.

Contrary to the findings on linear growth, weight differences
between the groups grew larger, especially after the intervention.
Whereas part of this finding may be attributed to the timing of
the IC spurt, other variables are likely to play a role as well.
Possible explanations include the impact of FS50 supplemen-
tation on the children’s general health and susceptibility to in-
fec tions or on appetite. Alternatively, the guardians may have
continued to provide nutritious snacks to children who had
earlier received FS50 but not to those who had received LP.
Although these are biologically plausible explanations, we have
no data to support any of these possibilities.

A third important point from our results is the comparison of
outcomes among children who received the higher (50 g/d) and the
lower (25 g/d) doses of FS. The higher dose was designed to provide
approximately the recommended amount of energy from sup-
plement foods for 6-mo-old infants without affecting the breast

FIGURE 4. Attained weight and length in all participants and those with baseline length-for-age z score (LAZ) below median during the follow-up. LP, likuni phala; FS50, fortified spread 50 g/d; FS25, fortified spread 25 g/d.
milk intake of the recipients (37, 38). Because the price for such a dose (≈$0.20/d) would be relatively high for the rural families in Malawi, we wanted to see if half of the dose would produce the same growth outcomes but more inexpensively. Unfortunately, this was not the case; children in the lower-dose group had both a higher incidence of severe stunting and lower mean weight and height gains during the intervention and especially thereafter. A comparable phenomenon was earlier observed in a Malawan dose-finding trial, in which underweight infants were given different doses of LNS for 12 wk (39). Although a smaller (20 g/d) dose of a similar supplement (Nutributter; Nutriset, Malauany, France) yielded positive results on linear growth and motor development among 6–12-mo-old infants in Ghana (27), the larger dose may thus be more appropriate in the Malawan setting. The apparent discrepancy may be explained by the much higher degree of stunting in the Malawan setting or the fact that the higher dose was not tested in the Ghanaian setting (27, 29).

The 2 main limitations of our trial were the lack of comprehensive data on the participants’ dietary intakes during or after the intervention and the lack of a nonsupplemented control group. Breast milk intakes were comparable in all trial groups before the intervention and 4 wk after its onset, but subsequent dietary intakes are unknown (40). Furthermore, because of the lack of an unsupplemented control group, we can make solid conclusions only on the relative value of the FS50 and maize-soy flour (LP) supplementations but not on their independent effect. In this comparison, the effect size on linear growth was comparable with other complementary-feeding trials that made comparisons with unsupplemented control children (18). However, in our setting, even the control intervention (LP supplementation) may have had some impact on the growth outcomes, as suggested by better outcomes in the control group than in the half-dose LNS group. If compared with no-food control children, the growth-promoting effect of LNS might thus prove even more favorable than what was observed in this sample. Further trials should investigate this possibility.

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The authors’ responsibilities were as follows—JCP, KM, CT, AB, MJM, and PA: designed the trial; JCP and CT: responsible for data collection; YBC: responsible for analytical strategy; and YBC, KM, and PA: supervised the analysis. All authors commented on the analysis and participated in writing of the manuscript. JCP had full access to all the data in the study and is responsible for its integrity and the accuracy of the data analysis. AB was a consultant to Nutriset until December 2003, and the company also supported the planning of another research project by the same study team.

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