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Original Article

Effect of complementary feeding with lipid-based nutrient supplements and corn–soy blend on the incidence of stunting and linear growth among 6- to 18-month-old infants and children in rural Malawi

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Abstract

Low nutritional value of complementary foods is associated with high incidence of childhood growth stunting in low-income countries. This study was done to test a hypothesis that dietary complementation with lipid-based nutrient supplements (LNS) promotes linear growth and reduces the incidence of severe stunting among at-risk infants. A total of 840 6-month-old healthy infants in rural Malawi were enrolled to a randomised assessor-blinded trial. The participants received 12-month supplementation with nothing, milk–LNS, soy–LNS, or corn–soy blend (CSB). Supplements provided micronutrients and approximately 280 kcal energy per day. Outcomes were incidence of severe and very severe stunting [length-for-age *z*-score, (LAZ) < –3.00 and <–3.50, respectively], and change in LAZ. The incidence of severe stunting was 11.8%, 8.2%, 9.1% and 15.5% ($P = 0.098$) and that of very severe stunting 7.4%, 2.9%, 8.0% and 6.4% ($P = 0.138$) in control, milk–LNS, soy–LNS and CSB groups, respectively. Between 9 and 12 months of age, the mean change in LAZ was –0.15, –0.02, –0.12 and –0.18 ($P = 0.045$) for control, milk–LNS, soy–LNS and CSB groups, respectively. There was no significant between-group difference in linear growth during other age-intervals. Although participants who received milk–LNS had the lowest incidence of severe and very severe stunting, the differences between the groups were smaller than expected. Thus, the results do not provide conclusive evidence on a causal association between the LNS supplementation and the lower incidence of stunting. Exploratory analyses suggest that provision of milk–LNS, but not soy–LNS promotes linear growth among at-risk infants mainly between 9 and 12 months of age.

Keywords: complementary feeding, lipid-based nutrient supplements, infants, children, linear growth, stunting.

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Introduction

Almost one-third of all under 5-year-old children in low- or middle-income countries and over 40% of those living in Africa are estimated to be stunted, i.e. they have suffered from linear growth failure that has made them shorter than expected for their age (Black *et al*. 2008). Stunting is not only associated with reduced final height, but also with increased morbidity, mortality, developmental delay or deficits, poor school performance and lower cognitive function in childhood, and less income as an adult (Pelletier *et al*. 1995; Grantham-McGregor *et al*. 2007; Victora *et al*. 2008). Given these adverse outcomes and the frequency of the condition, it is not surprising that prevention of childhood stunting has been identified as a major global health priority (UNICEF 2009).

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On a population level, stunting is associated with a number of harmful exposures, including inadequate diet and frequent infections (Martorell *et al*. 1994). However, most interventions addressing these risk factors have so far failed to markedly improve linear growth or prevent stunting among infants and young children (Dewey & Adu-Afarwuah 2008). Recently results from studies in Ghana and Malawi suggested that consumption of lipid-based nutrient supplements (LNS), a novel class of micronutrient–fortified, ready-to-use products, might boost length gain and reduce growth failure and the incidence of severe stunting among 6–18-month-old infants (Adu-Afarwuah *et al*. 2007; Phuka *et al*. 2008; Phuka *et al*. 2009). While these findings were encouraging, they are also limited; the Malawi study did not include a parallel no-intervention control group and the non-intervention group in Ghana study had no weekly follow-up visits compared with the intervention groups.

The main aim of the present study was to test a hypothesis that provision of LNS would reduce the incidence of severe stunting or other forms of linear growth faltering among 6–18-month-old infants in Malawi, southern Africa. Two separate LNS products were tested, one that contained dried skim milk and thus resembled products used in earlier prevention trials with LNS (Adu-Afarwuah *et al*. 2007; Phuka *et al*. 2008), and another one in which the milk powder was substituted with soy flour. The latter choice was motivated by the use of soy in nationally recommended complementary foods (Malawi MoHP 2010), its cheaper price and also its acceptability to vegetarians. To improve on the earlier trials, we also designed the study with two control groups: one of these included children who received no intervention during the period of interest while participants in the other control group were given rations of micronutrient-fortified corn–soy blend (CSB), a nationally recommended complementary food for infants and young children (Malawi MoHP 2010). Because of our earlier finding that LNS provision might have the strongest impact on the most disadvantaged infants (Phuka *et al*. 2009), we selected the incidence of severe stunting as the primary outcome measure.

Methods

Study area

The study was conducted in Lungwena and Malindi, two rural Malawian communities with a total population of approximately 60 000 people. Infant undernutrition in the area is common with a high prevalence of early childhood stunting and underweight. Almost all children are breastfed until two years, but exclusive breastfeeding period is normally very short and almost all children are introduced to complementary foods by 4 months of age. The principal complementary food is maize, usually first served as a thin porridge and later in infancy substituted by a thicker porridge and complemented with soups from vegetables and fish (Vaahtera *et al*. 2001). The main staple, maize, is normally grown and harvested between December and March and dietary inadequacies in food consumption and nutrient intakes are common especially in the months preceding the only annual harvest (Hotz & Gibson 2001).

Key messages

- Dietary complementation with lipid-based nutrient supplements (LNS) has been suggested to improve linear growth and reduce the incidence of stunting.
- In the current sample, statistically significant between-group differences were observed in the mean length-for-age change between 9 and 12 months of age. There were parallel differences in the mean length gain, incidence of severe or very severe stunting or several other growth outcomes over the entire 12-month supplementation period, but none of these results reached statistical significance.
- The study findings suggest that provision of milk-containing LNS may slow down the process of infant growth faltering around the time of the transition into the childhood phase of growth.

Eligibility criteria, enrolment, and randomisation

The study was designed as a community-based randomised trial comparing the efficacy of four intervention schemes involving three intervention groups and one delayed-intervention group. Trial participants were recruited from 28 January 2008 to 25 May 2009. The inclusion criteria included age 5.50–6.50 months, residence in the study area, and informed consent from at least 1 authorised guardian. The exclusion criteria were weight for length (WFL) < 80% of the World Health Organization (WHO) reference median or presence of oedema, severe illness warranting hospitalisation on the enrolment day, history of peanut allergy, concurrent participation in another clinical trial, and any symptoms of food intolerance within 30 min after ingesting a 5-*g* test dose of LNS (either milk- or soy-based) used in the trial.

Initially the exclusion criteria also included severe stunting (length-for-age *z*-score; LAZ < –3.00), but this criterion was dropped at 6 weeks into the trial (17 March 2008, when 97 of the 840 participants had been enrolled). This change in eligibility criteria was prompted by our observation that approximately 23% of the infants who underwent the eligibility assessment met this criterion. The proportion was much higher than we had anticipated, mostly due to the fact that in this study we were using the 2006 WHO Child Growth Standards (World Health Organisation (WHO) Multicentre Growth Reference Study Group 2006), whereas our earlier studies and estimates had used the Centers for Disease Control and Prevention (CDC) 2000 references (Kuczmarski *et al*. 2002). Our earlier study (Phuka *et al*. 2009) suggested that the more severely stunted infants grew more when receiving the LNS intervention and, hence we wanted to include such infants who might benefit most from it.

Potentially eligible participants were identified through community census in the study area with a preliminary screening done to assess for eligibility. During recruitment, trained data collectors contacted all the families of children of eligible age whose parents showed a preliminary interest in the trial. Infants were invited to an enrollment session, where they were screened for eligibility, and guardians were given detailed information on the trial contents. Before enrollment, a guardian signed a written consent form for trial participation.

Blocked randomisation, with each block containing 16 allocations evenly distributed for the four groups, was used to assign participants to intervention groups. A set of identical-appearing opaque envelopes from one randomisation block was shuffled and a guardian was requested to choose one envelope. The envelope contained an identification number and the allocation to one of the four interventions. The randomisation list and envelopes were made by an individual not involved in trial implementation, and the code was not disclosed to the researchers or to those assessing the outcomes until all data had been entered and verified in a database.

Interventions and follow-up

Eligible infants were randomly assigned to 1 of 4 intervention schemes for a 12-month period. Infants in the control group were not provided with any supplemental complementary food during the primary follow-up, but received a delayed supplementation with 71 g per day-fortified corn–soy flour between 18 and 30 months of age. Participants in the other three groups received either 71 g day^{-1} of micronutrient-fortified CSB, 54 g day^{-1} of micronutrient- fortified LNS with milk protein base (milk–LNS) or 54 g day^{-1} of micronutrient- fortified LNS with soy protein base (soy–LNS) between 6 and 18 months of age.

The supplements were home delivered at 2-week intervals (at each supplement delivery, either two 500-g bags of CSB, or five 150-g jars LNS were given). The corn–soy flour was purchased from a local producer (Rab Processors, Blantyre, Malawi). The investigational LNS were produced at a Malawian non-governmental organisation, Project Peanut Butter (Blantyre, Malawi), from peanut paste, milk powder (which made up 25% of the milk–LNS product weight), or soy flour (which made up 20% of the soy–LNS product weight), vegetable oil, sugar and multiple micronutrient mixture (Nutriset Inc, Malaunay, France). The products were made mostly from the same ingredients as commercially available

Table 1. Nutrient composition of the 3 supplements used in the study

Nutrient	Milk–LNS	Soy–LNS	CSB
Amount of food supplement (g)	54	54	71
Energy (kcal)	285	276	284
Protein (g)	8.2	7.5	10.4
Fat (g)	17.9	18.5	3.1
Retinol (μg RE)	400	400	139
Folate (μg)	160	160	43
Niacin (mg)	6	6	3.5
Panthothenic acid (mg)	2	2	–
Riboflavin (mg)	0.5	0.5	0.3
Thiamin (mg)	0.5	0.5	0.13
Vitamin B6 (mg)	0.5	0.5	0.34
Vitamin B12 (μg)	0.9	0.9	0.9
Vitamin C (mg)	30	30	48
Vitamin D (μg)	5	5	–
Calcium (mg)	366	366	72
Copper (mg)	0.4	0.4	–
Iodine (μg)	90	90	–
Iron (mg)	6	6	5.5
Magnesium (mg)	78.5	78.5	–
Selenium (μg)	20	20	–
Zinc (mg)	6.0	6.0	3.6
Phosphorus (mg)	186	186	–
Potassium (mg)	319	307	–
Manganese (mg)	0.6	0.6	–

CSB, corn–soy blend; milk–LNS, milk powder-containing lipid-based nutrient supplement; soy–LNS, soy–flour-containing lipid-based nutrient supplement.

Plumpy Nut™ or PumpyDoz™, but their nutrient composition was closer to the 'preventive' supplement named Nutributter™.

Table 1 shows the micronutrients and their quantities in the three supplements. The daily CSB and LNS ration provided approximately 280 kcal of energy and a sufficient dose of selected micronutrients to meet their recommended daily allowances when added to intakes from breast milk and complementary foods. Milk–LNS and soy–LNS contained an identical range and quantities of micronutrients. CSB contained fewer micronutrients and for most nutrients, the daily supplement ration contained a lower dose than that for LNS. Phytate content of the supplements was not assessed.

Guardians for infants in the intervention groups were provided with spoons and advised to feed their babies with normal healthy diets and additionally offer them daily either 10 spoonfuls of CSB, cooked into a complementary porridge, or eight spoonfuls of milk–LNS or soy–LNS, divided into two to four daily servings. All mothers were encouraged to continue breastfeeding on demand and to feed their infants only as much of the food supplement as the infants wanted to consume at a time.

Participants were visited every 2 weeks at their homes to collect information on supplement use and possible adverse events. Empty food containers were collected at these visits. At 12-week intervals after enrolment up to week 52, participants had a visit at the trial office where they underwent an anthropometric assessment. Unclothed infants were weighed using an electronic infant weighing scale (SECA 735; Chasmors Ltd, London, England), and weights were recorded to the nearest 10 g. Length was measured to the nearest 1 mm using a high-quality length board (Kiddimetre; Raven Equipment Ltd, Essex, England). All anthropometric measurements were done by three trained research assistants. The technical error of each research assistant's measurements and the coefficient of reliability were assessed during weekly standardisation measurements from at least three participants. Anthropometric indexes LAZ, weight-for-age (WAZ) and weight-for-length (WLZ) were calculated using WHO Child Growth Standards (2010 STATA igrowup package) (WHO 2010).

At enrolment, the participants' blood haemoglobin concentration was measured from a venous sample using cuvettes and a reader (HemoCue AB, Angelholm, Sweden). Malaria was diagnosed microscopically from Giemsa stained thick and thin blood films. Malaria treatment was provided according to the national guidelines to all participants with clinical malaria. All participants found to have a blood haemoglobin concentration below 80 g l^{-1} were treated with iron supplementation in accordance with the national treatment guidelines (1–6 mg per kilogram body weight per day for one month). Participants developing moderate or severe wasting (WFL < 80% of the WHO reference median) during the intervention were temporarily suspended from the study and referred for appropriate management but continued follow-up and resumed trial supplementation after nutrition treatment.

Outcome measures

The primary outcome was the incidence of severe stunting (LAZ < –3.00) during the 12-month follow-up. To allow direct comparison with the results from our earlier trials in which severe stunting was defined using an older CDC growth reference (13), we used the incidence of very severe stunting (LAZ < –3.5) as our first secondary outcome. In the studied age group, a length that gives a *z*-score of –3.0 when using the older reference corresponds to a *z*-score of –3.5 if calculated with the WHO growth reference (12). Other secondary outcomes included the incidence of moderate-to-severe stunting (LAZ < –2), mean change in LAZ, and the prevalence of various forms of stunting at the end of the intervention. Hence, the focus of the study was on stunting and linear growth, but for completeness, we also described changes in weight and the incidence of underweight and wasting.

For the calculation of incidence, participants with the particular form of malnutrition (e.g. very severe stunting, severe wasting) at enrolment were excluded from the specific analysis. Incidence was calculated as the first time a participant developed a given form of malnutrition (e.g. very severe stunting). Relapses after recovery from the malnutrition were not counted as 'new' cases of malnutrition.

Data management and statistical methods

The sample size of 210 participants per group gave 85% power (5% two-sided type I error) to detect a difference in the incidence of severe stunting between 15% in the control group and 5% in the intervention groups. This allowed for an attrition of 10% during the follow-up and exclusion of 5% who were severely stunted at baseline, based on the initial enrollment criterion.

The collected data were recorded on paper forms, transcribed to paper case report forms, and double entered into a tailor made Microsoft Access 2003 database (Microsoft Corp., Redmond, WA, USA). The two entries were electronically compared, and extreme or otherwise suspicious values were confirmed or corrected.

Statistical analyses were performed using Stata 11.0 (Stata Corp, College Station, TX, USA) on an intention-to-treat basis. Analysis of variance and Student's *t*-test was used to compare continuous outcomes between the four intervention groups, and the multi-group extension of Fisher's exact test for categorical outcomes. To take into account multiple comparisons between the different groups, we used a gatekeeping procedure of first testing the global null hypothesis of all four groups being equal. Pairwise comparisons were considered confirmatory only if the global null hypothesis was rejected.

Participant's compliance to the trial was assessed in terms of compliance to scheduled health facility visits, food sharing and food leftover at each 2-week visit. Compliance in terms of observed leftovers and mothers' report of usage was analysed using the generalised estimating equation approach with Huber–White robust standard error to allow for correlated data (multiple visits per child).

Ethics, study registration, and participant safety

The trial was performed according to International Conference on Harmonisation/Good Clinical Practice guidelines, and regulatory guidelines in Malawi. The trial protocol was reviewed and approved by the University of Malawi College of Medicine research and ethics committee 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.

A data safety and monitoring board continuously monitored the incidence of suspected serious adverse events (SAEs), defined as any untoward medical occurrence that either resulted in death or was life threatening or required inpatient hospitalisation or prolongation of existing hospitalisation or resulted in persistent or significant disability or incapacity or other serious medical conditions.

Results

Of the 1385 infants who were identified through community census, 490 were either ineligible or not brought to an enrolment session. A further 55 were found ineligible in a more detailed assessment. The remaining 840 infants were randomised into four

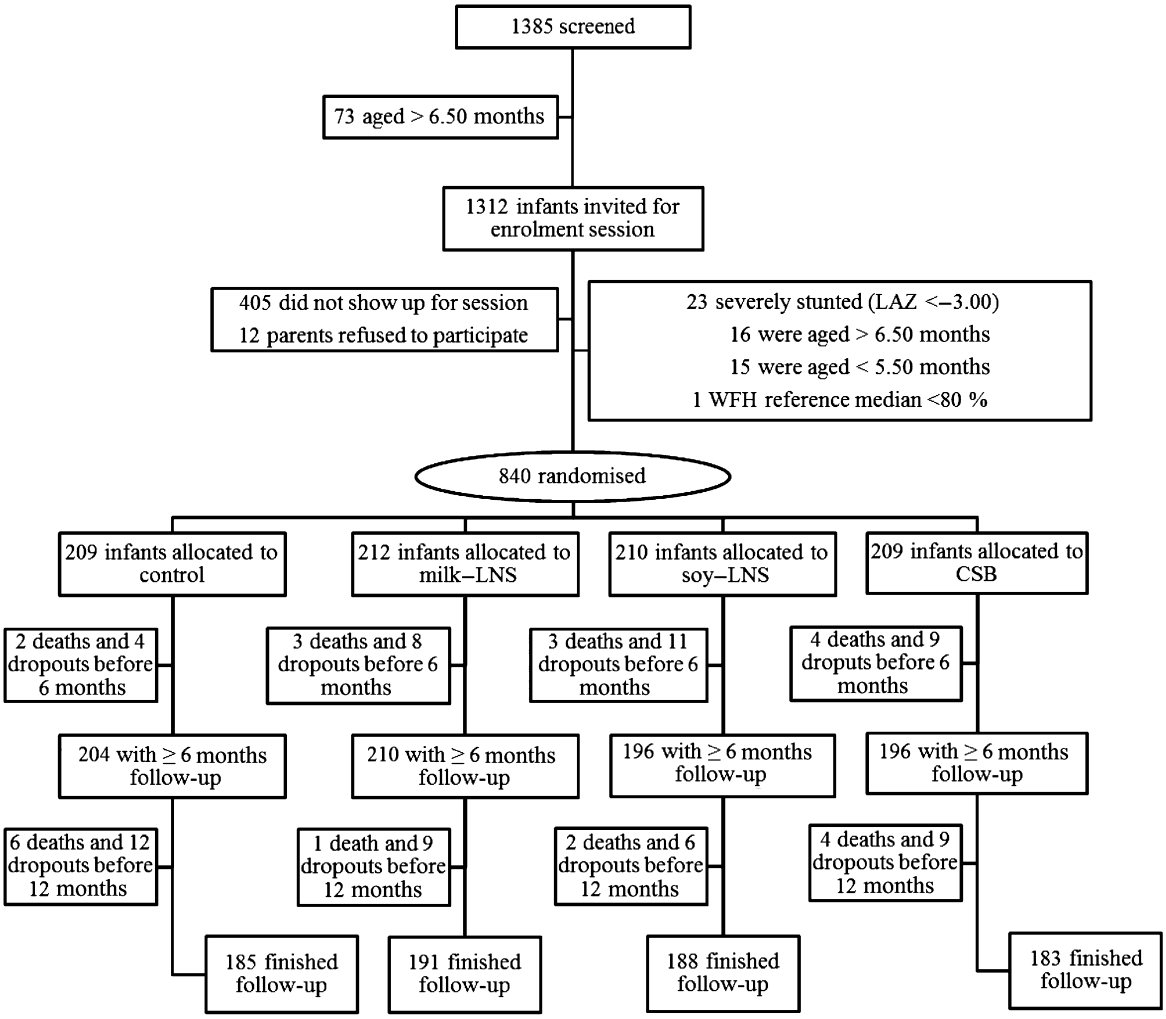

Fig. 1. Flow diagram of participant progress throughout the study. CSB, corn–soy blend; LAZ, length-for-age *z*-scores; milk–LNS, milk-containing lipid-based nutrient supplements; soy–LNS, soy-containing lipid-based nutrient supplements; WFH, weight-for-height.

intervention groups as shown in Fig. 1. None of the infants was allergic to a 5-g test dose of milk–LNS.

Table 2 shows the baseline demographics, anthropometrics and parental characteristics of the participants by intervention group. The summary statistics were largely comparable in the four groups although the CSB group had slightly fewer boys and lower mean initial weight and LAZ. At enrolment, the prevalence of severe and very severe stunting in the combined sample was approximately 8.5% and 3.5%, respectively. All except one child were breastfeeding at enrolment, but none of them exclusively. The proportion of children receiving breast milk remained very high throughout the study (99.7% at 12 months and 96.8% at 18 months of age).

During the 12 month follow up, 25 children (3.0%) died and 68 (8.1%) dropped out (Fig. 1). Hence, final measurements were obtained from 747/840 (88.9%) participants. The success of follow-up was not significantly different between intervention groups ($P = 0.852$). A total of 45 participants had no anthropometric data at all after enrolment (13 deaths, 32 drop-outs) and there was no difference in this proportion between the intervention groups ($P = 0.847$).

Table 2. Baseline characteristics of participants at enrolment

Variable	Control ($n = 209$)	Milk–LNS ($n = 212$)	Soy–LNS ($n = 210$)	CSB ($n = 209$)
Infant sex, male [n (%)]	111 (53.1)	107 (50.5)	103 (49.1)	98 (46.9)
Age, months (mean ± SD)	6.02 ± 0.23	6.02 ± 0.25	6.04 ± 0.25	6.03 ± 0.24
Weight, kg(mean ± SD)	7.02 ± 0.89	7.09 ± 0.97	7.00 ± 0.88	6.95 ± 1.01
Length, cm (mean ± SD)	63.2 ± 2.2	63.2 ± 2.4	63.0 ± 2.4	62.9 ± 2.3
Weight-for –age z score (mean ± SD)	–0.80 ± 1.06	–0.70 ± 1.10	–0.80 ± 1.12	–0.85 ± 1.21
Length-for-age z score (mean ± SD)	–1.64 ± 0.97	–1.59 ± 1.05	–1.68 ± 1.11	–1.72 ± 0.97
Weight-for-length z score (mean ± SD)	0.41 ± 1.05	0.50 ± 1.05	0.46 ± 1.00	0.42 ± 1.11
Very severely stunted [n (%)]	7/209 (3.4)	6/212 (2.8)	10/210 (4.8)	6/209 (2.9)
Severely stunted [n (%)]	14 (6.7)	17 (8.0)	24 (11.4)	16 (7.7)
Blood hemoglobin concentration, g/dl (mean ± SD)	9.4 ± 1.7	9.6 ± 1.7	9.3 ± 1.7	9.5 ± 1.6
Maternal BMI, kg m^{-2} (mean ± SD)	20.6 ± 2.4	20.7 ± 2.2	21.0 ± 2.4	20.7 ± 2.4
Maternal education, years (mean ± SD)	3.6 ± 3.4	4.0 ± 3.7	3.0 ± 3.1	3.7 ± 3.1

CSB, corn–soy blend; milk–LNS, milk powder containing lipid-based nutrient supplement; soy–LNS, soy-flour containing lipid-based nutrient supplement; SD, standard deviation.

Table 3. Change in weight and length among participants during the 12-month intervention, by study group

Outcome	Study group				P-value
	Control	Milk–LNS	Soy–LNS	CSB	
Change in length, cm (mean ± SD)	13.0 ± 2.0	13.2 ± 1.7	13.0 ± 2.0	12.9 ± 2.6	0.427
Change in length-for-age z-score (mean ± SD)	–0.31 ± 0.72	–0.23 ± 0.68	–0.28 ± 0.76	–0.38 ± 0.68	0.325
Change in weight, kg (mean ± SD)	2.42 ± 0.77	2.53 ± 0.78	2.46 ± 0.88	2.32 ± 0.88	0.119
Change in weight-for-age z-score (mean ± SD)	–0.30 ± 0.72	–0.21 ± 0.77	–0.25 ± 0.92	–0.37 ± 0.87	0.280
Change in weight-for-length z-score (mean ± SD)	–0.66 ± 0.93	–0.57 ± 1.02	–0.62 ± 1.05	–0.69 ± 1.03	0.585

CSB, corn–soy blend; milk–LNS, milk powder containing lipid-based nutrient supplement; soy–LNS, soy-flour containing lipid-based nutrient supplement; SD, standard deviation. P-value obtained by analysis of variance.

All mothers reported that their infants readily ate the provided supplement and diversion of any portion to someone other than the intended beneficiary was reported at only 69 of 18 906 (0.36%) supplement delivery interviews: 29 in milk–LNS, 19 in soy–LNS, and 21 in CSB groups ($P = 0.383$). From the 2-weekly home visits during which leftover trial products were checked, the percentage of visits with leftovers found were 1.3%, 1.3%, and 0.6% in the milk–LNS, soy–LNS, and CSB groups respectively ($P < 0.001$).

During the one year intervention period, children who received milk–LNS had the most length gain both in terms of cm and z-scores whereas children who received CSB had the least. None of the differences between the intervention groups and the control children was, however, statistically significant (Table 3). Looking into the consecutive measurements within the one year period, the biggest difference was seen in the age period between 9 to 12 months (Fig. 2). During this time children who received milk–LNS had a negligible change in their mean LAZ (–0.02 z-score units) whereas children in the Control, soy–LNS and CSB group dropped their mean LAZ by –0.15, –0.12 and –0.18 z-score units, respectively ($P = 0.045$). (Sample size varied from 520 to 747 across age intervals of measurements.) Pairwise comparisons showed statistically significant differences in change in LAZ between milk–LNS and control groups ($P = 0.029$) and CSB group ($P = 0.014$), but not soy–LNS group ($P = 0.079$) in this age interval.

A total of 86 infants developed severe stunting during the intervention. The number of those who developed very severe stunting, moderate-to-severe

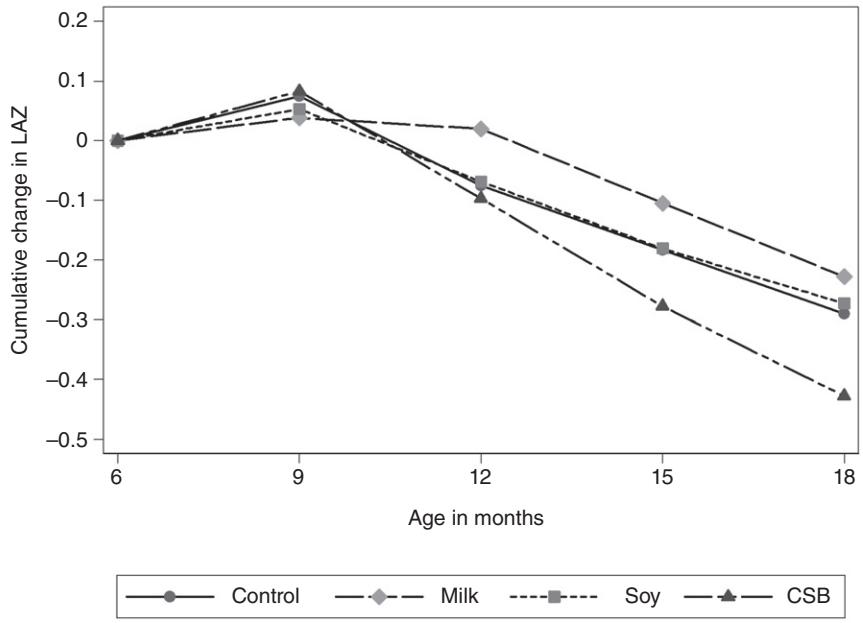

Fig. 2. Cumulative change in mean length-for-age *z*-scores by age and study group. CSB, corn–soy blend; milk–LNS; milk-containing lipid-based nutrient supplements; soy–LNS, soy-containing lipid-based nutrient supplements.

Table 4. Incidence of severe undernutrition during the 12-month intervention, by study group

Outcome	Number of participants with the indicated outcome / total number of participants (%)				
	Control	Milk–LNS	Soy–LNS	CSB	*P*-value
Ever developed severe stunting (LAZ < –3.00)	23/195 (11.8%)	16/195 (8.2%)	17/186 (9.1%)	30/193 (15.5%)	0.098
Ever developed very severe stunting (LAZ < –3.50)	15/202 (7.4%)	6/206 (2.9%)	16/200 (8.0%)	13/203 (6.4%)	0.138
Ever developed moderate-to-severe stunting (LAZ < –2.0)	41/138 (29.7%)	40/140 (28.6%)	46/128 (35.9%)	50/126 (39.7%)	0.177
Ever developed severe underweight (WAZ < –3.00)	11/205 (5.4%)	3/208 (1.4%)	10/206 (4.9%)	12/200 (6.0%)	0.107
Ever developed severe wasting (WLZ < –3.00)	2/209 (1.0%)	2/212 (0.9%)	4/210 (1.9%)	3/209 (1.4%)	0.797

CSB, corn–soy blend; LAZ, length-for-age *z*-score; milk–LNS, milk-containing lipid-based nutrient supplements; soy–LNS, soy-containing lipid-based nutrient supplements; WAZ, weight-for-age *z*-score; WLZ, weight-for- length *z*-score. *P*-value obtained by Fisher's exact test.

stunting, severe underweight, and severe wasting were 50, 177, 36, and 11, respectively. Children in the milk–LNS group had less of these events whereas those in the CSB group had more (except very severe stunting), but none of the differences between the groups was statistically significant (Table 4). At the end of the 12-month intervention, the prevalence of severe stunting and other forms of undernutrition was slightly lower in the milk–LNS group than the other groups but again the differences were not statistically significant (Table 5).

All interventions were well tolerated by the participants. Besides the 25 deaths (8 in control, 4 in milk–LNS, 5 in soy–LNS, 8 in CSB; Fig. 1), 34 other participants were hospitalised (12 in control, 7 in milk–LNS, 6 in soy–LNS, 9 in CSB) and 3 were recorded as having experienced another SAE during the follow-up. Fifty-nine (95.2%) of the SAEs were

Table 5. Prevalence of severe undernutrition at the end of 12-month intervention, by study group

Outcome	Number of participants with the indicated outcome / total number of participants (%)				
	Control	Milk–LNS	Soy–LNS	CSB	*P*-value
Severely stunted (LAZ < –3.00)	26/185 (14.1%)	21/191 (11.0%)	30/188 (16.0%)	29/180 (16.1%)	0.454
Very severely stunted (LAZ < –3.50)	12/185 (6.5%)	8/191 (4.2%)	17/188 (9.0%)	11/180 (6.1%)	0.290
Moderately-to-severely stunted (LAZ < –2.00)	81/185 (43.8%)	79/191 (41.4%)	89/188 (47.3%)	98/180 (54.4%)	0.066
Severely wasted (WLZ < –3.00)	2/184 (1.1%)	0/191 (0%)	3/188 (1.6%)	3/180 (1.7%)	0.370

CSB, corn–soy blend; milk–LNS, milk-containing lipid-based nutrient supplements; LAZ, length-for-age *z*-score; soy–LNS, soy-containing lipid-based nutrient supplements; WLZ, weight-for- length *z*-score. *P*-value obtained by Fisher exact test.

considered unrelated and the rest probably unrelated to the trial interventions.

Discussion

This trial was carried out to test a hypothesis that 12-month-long dietary supplementation with LNS would promote linear growth and reduce the incidence of severe growth faltering among rural Malawian infants and young children. Although statistically not significant, the sample findings were consistent with the hypothesis, as participants receiving dietary complementation with milk-containing LNS gained on average approximately 0.2 cm more in length and 110 g more in weight and had a lower incidence of severe stunting during the follow-up than control children. The internal validity of the trial was high because of broad inclusion criteria, random group allocation, similarity of the intervention groups at enrolment, comprehensive follow-up, and blinding of the outcome assessors. The between-group differences were, however, smaller than anticipated and in many analyses the probability of the observed differences being due to random variation was above the traditionally accepted 5% threshold. Because of this, the primary null-hypothesis of no difference between the groups could not be conclusively rejected. Nevertheless, the inherent consistency of the findings on various aspects of growth, as well as their biological plausibility and coherence with earlier studies (Adu-Afarwuah *et al*. 2007; Phuka *et al*. 2008; Phuka *et al*. 2009) suggest a causal relationship between the milk–LNS intervention and moderately improved growth outcomes.

Age–interval-specific analyses from our sample indicated that the mean length-for-age remained constant from 6 to 12 months among participants who received milk–LNS (i.e. no growth faltering occurred), whereas it decreased by 0.1–0.2 *z*-score units between 9 and 12 months of age among other infants. From the age of 12–18 months, the mean length-for-age fell at approximately equal rate in all groups. One possible explanation for these findings is a specific effect of milk powder on linear growth in early childhood. According to the Infancy–Childhood–Puberty model of growth, the interval from 6 to 12 months of age is the period when an infant changes from the infancy phase of growth to the childhood phase (Karlberg 1989; Liu *et al*. 1998a, 2000). A delay in this shift [called the infancy-childhood (IC) spurt] has been associated with the high incidence of growth retardation in some low-income settings (Liu *et al*. 1998a,b). Factors leading to the IC spurt remain unclear, but insulin-like growth factor and numerous other biologically active substances that are present in cow's milk – and hence also in milk–LNS – have been suggested to play a role (Low *et al*. 2001; Wiley 2005; Wiley 2012). This hypothesis is supported by several studies suggesting that animal source foods, especially bovine milk promote length or height gain in human children (Hoppe *et al*. 2006; de Beer 2012).

The apparent difference in linear growth and the incidence of severe stunting between participants who received milk-containing as opposed to soy-containing LNS could be a spurious finding or related to the lack of milk or other differences in the composition of the soy–LNS. Depending on the type

and extent of processing, soy products contain antinutrients that might negatively affect linear growth, such as enzyme inhibitors, phytate and lectins (Sarwar 1997; Hoppe *et al*. 2008). Although soy is cheaper than milk, has a favorable protein profile, and is increasingly used in therapeutic LNS preparations (de Pee & Bloem 2009), our results do not support its use in the formulation for preventive LNS. Similarly, the observation that the growth outcomes were worse among participants who received fortified CSB than among non-supplemented controls (e.g. incidence of moderate-to-severe stunting was 39.7% vs. 29.7%, respectively) does not lend support to the Malawian national recommendation of using CSB as a complementary food (Malawi MoHP 2010). Unlike the energy- and nutrient-dense LNS, the intake of which does not appear to alter breast milk intakes (Galpin *et al*. 2007), CSB is typically fed as a high-volume dilute porridge, which may more easily result in displacement of breast milk or other nutritious foods in the child's diet. The relatively poor growth outcomes in the CSB group could also explain why the effects observed in the current trial (in which the LNS groups were compared with a no-supplement control group) were smaller than those observed in a previous trial conducted in the same area in which the LNS groups were compared with a group given CSB (Phuka *et al*. 2009). However, these potential explanations are speculative and require confirmation. The current study was designed to compare each intervention group to the control group, but not to make direct comparisons between the intervention groups.

As a whole, the results from the current trial and those of the two earlier ones (Adu-Afarwuah *et al*. 2007; Phuka *et al*. 2008; Phuka *et al*. 2009) are consistent with a hypothesis that provision of milk-containing LNS may slows down the process of infant growth faltering around the time of the transition into the childhood phase of growth in environmental conditions similar to those in rural Malawi. Unfortunately the intervention appears insufficient to promote catch-up growth or even to maintain normal growth after the first year of life in this population, possibly because of increasing nutrient needs, high incidence and prevalence of morbidity and environmental enteropathy (Prentice & Paul 2000; Goto *et al*. 2009; Humphrey 2009), or programming of postnatal growth rate due to malnutrition *in utero*. The failure to reverse linear growth faltering is not surprising, because stunting typically involves multiple aetiologies (Waterlow 1994) and very few single-pronged interventions have ever achieved catch-up growth in length, either in a trial or programmatic setting (Dewey & Adu-Afarwuah 2008). Long-term reduction in stunting most likely requires a health and nutrition package that comprehensively covers the critical '1000 days', i.e. the period from conception to approximately the point when the child turns 2 years old (Piwoz *et al*. 2012).

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Contributions

All authors participated in the design of the trial. PA, KM coordinated and supervised the research team. CM, CT coordinated the research team at local centres and were responsible for data collection. YBC, CM designed the details of statistical analysis and analysed the data. CM, KM, PA wrote the first draft of the manuscript. All authors commented on the analysis, reviewed and approved the final manuscript.

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