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Early Life

Effect of fortified complementary food supplementation on child growth in rural Bangladesh: a cluster-randomized trial

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Abstract

Background: Growth faltering in the first 2 years of life is high in South Asia where prevalence of stunting is estimated at 40–50%. Although nutrition counselling has shown modest benefits, few intervention trials of food supplementation exist showing improvements in growth and prevention of stunting.

Methods: A cluster-randomized controlled trial was conducted in rural Bangladesh to test the effect of two local, ready-to-use foods (chickpea and rice-lentil based) and a fortified blended food (wheat-soy-blend++, WSB++) compared with Plumpy'doz, all with nutrition counselling vs nutrition counselling alone (control) on outcomes of linear growth (length and length-for-age z-score, LAZ), stunting (LAZ < -2), weight-for-length z-score (WLZ) and wasting (WLZ < -2) in children 6–18 months of age. Children ($n = 5536$) were enrolled at 6 months of age and, in the food groups, provided with one of the allocated supplements daily for a year.

Results: Growth deceleration occurred from 6 to 18 months of age but deceleration in LAZ was lower (by 0.02–0.04/month) in the Plumpy'doz ($P = 0.02$), rice-lentil (< 0.01), and chickpea (< 0.01) groups relative to control, whereas WLZ decline was lower only in Plumpy'doz and chickpea groups. WSB++ did not impact on these outcomes. The prevalence of stunting was 44% at 18 months in the control group, but lower by 5–6% ($P \leq 0.01$) in those receiving Plumpy'doz and chickpea. Mean length and LAZ at 18 months

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were higher by 0.27–0.30 cm and 0.07–0.10 (all $P < 0.05$), respectively, in all four food groups relative to the control.

Conclusions: In rural Bangladesh, small amounts of daily fortified complementary foods, provided for a year in addition to nutrition counselling, modestly increased linear growth and reduced stunting at 18 months of age.

Key words: Complementary food, stunting, growth, micronutrients, supplementation, Bangladesh

Key Messages

- Few systematic reviews of supplementation effects on child growth exist, given the heterogeneity of formulations and study designs and the prevention vs treatment approaches used in trials.
- Our randomized, controlled trial in rural Bangladesh found two local and two international complementary foods which, when provided daily to children from 6 until 18 months of age, significantly reduced linear growth deceleration and the prevalence of stunting at 18 months of age by 4–6% over and above nutrition counselling alone.
- Use and promotion of such products may be important in food-insecure settings in addition to other strategies and approaches for alleviating the large burden of childhood stunting in South Asia.

Introduction

Childhood stunting (length-for-age z-score, LAZ < -2) is well recognised as a public health problem of global proportions that requires urgent attention. Recent estimates show that globally 162 million children under 5 years of age, 160 million of whom reside in low- and middle-income countries (LMIC), may experience stunting.[1] Wasting (weight-for-length z-score, WLZ < -2) also affects around 52 million children at any given time. A critical period of child growth is in the first 2–3 years of life when growth faltering is common and exclusive breastfeeding in the first 6 months, and appropriate complementary feeding after 6 months, are essential to meet the nutritional needs of the growing child. In addition to a lack of access due to limited availability and affordability of a diverse diet, traditional home-prepared complementary foods used in many contexts are either too viscous or watered down, monotonous, and have low energy and micronutrient density and poor protein quality.[2–4] Childhood stunting and undernutrition may also have prenatal origins, for which interventions in pregnancy are needed.[5] However, behaviour change and nutritional interventions in the postnatal period show some promise for improving linear growth among children, despite the tenuous evidence for their benefit from rigorous randomized trials.[6] Education on appropriate complementary feeding alone in four studies in food-secure populations and one in a food-insecure setting (with total number of children 991 in the intervention and 949 in the control groups) showed a reduction in the odds of stunting by 29%.[7] In seven studies that provided complementary foods with or without education in food-insecure populations, height-for-age z-score was higher among those in the intervention group, but height and weight gain and stunting prevalence were not different.[7] Closer examination of the individual study effects and sample size reveals the sum total of evidence for a benefit related to food supplementation to be weak.[6]

Even as fortified blended foods such as corn-soy or wheat-soy continue to be commonly used in feeding programmes and in emergencies, increasingly, high-energy and micronutrient dense lipid-based formulations are of interest, having been demonstrated to be successful in community-based treatment of severe and moderate acute malnutrition[8] and in prevention of acute malnutrition.[9] Several studies have compared lipid-based products and fortified blended foods for impact on growth among moderately malnourished children 6–60 months of age, but have found unconvincing differences in childhood linear and ponderal growth,[10,11] although the lipid-based supplements did somewhat better in showing improved weight gain and in reducing stunting.[12–14] More importantly, however, the type of commercial lipid-based formulations used may be difficult to procure and not widely available in low-resource settings, creating an urgent need for testing of local complementary food supplements using a variety of culturally preferred ingredients procured and manufactured in the region, that can be used in local programmes. We designed a study to fill this gap by simultaneously testing in an cluster-randomized, controlled trial the effect of two innovative and well-designed, locally developed and produced products, and an enhanced fortified blended food, in promoting linear growth and reducing stunting and wasting in a typical poor rural area of northern Bangladesh.

Methods

Study area and population

The study was conducted in the rural north-western study site that our research group established in 1999, located in 18 Unions of the Gaibandha and one Union of the Rangpur district, under the 'JiVitA Project' of the Johns Hopkins University in Bangladesh non-governmental organization. The 435 km^2 study area has been divided into 596 clusters of communities (sectors) and is home to about 650 000 people. The population is majority Muslim with a poor, agrarian semi-subsistence economy; rice, pulses, vegetables, fisheries and homestead food production are the main sources of income generation.

Study design, hypothesis and sample size

The field study was designed as an unblinded, randomized, controlled, community-based trial in which infants were enrolled at 6 months of age into five different study groups from September 2012 until May 2014. The trial evaluated three specially formulated complementary food supplements (CFSs) and an international product (Plumpy'doz) compared with a control (no food supplement), in addition to nutrition counselling provided to all. The main outcomes were LAZ change between 6 and 18 months and LAZ, length and stunting ($LAZ < -2$) at 18 months as well as WLZ and wasting ($WLZ < -2$) at 18 months. We hypothesized that compared with nutrition counselling alone (as control), each of the four CFS products given daily for 12 months in addition to nutrition counselling would increase LAZ and WLZ by > 0.2 z-scores, improve linear growth and reduce the prevalence rates of stunting (by $\geq 10\%$ in absolute terms) and wasting at 18 months. We further hypothesized that each of the three CFS products would perform as well as an international 'standard' lipid-based Plumpy'doz in impacting on growth, defining an inferiority margin for an end-of-trial status at 18 months of age of 0.2 z-scores.

Sample size calculations for a cluster-randomized trial of non-inferiority were performed as per Blackwelder *et al.*[15] Based on available published data from similar non-intervened populations,[16,17] we estimated an endpoint LAZ in the control group of −1.70, with a standard deviation of 1.0. Existing data on intracluster correlation of 0.08 for LAZ at 6 months of age in our study population ($n = 2286$) was used to estimate a maximum design effect of 1.5, which was applied to adjust the final calculated sample sizes. Other assumptions included power ($1 - \beta$) of 90%, type 2 error (α) of 0.05 and an expected 5% loss to follow-up. Our sample size estimate was predicated on a mean difference in endpoint z-score (for LAZ or WLZ) of up to 0.20 between CFS groups and the standard, which also allowed us to test whether the difference between the negative control (counselling) and the intervention arms differed beyond 0.20 z-scores. As we intended to compare three intervention arms with each of the control and standard groups, the size of the comparison groups was inflated by a correction factor of 1.7 (the square root of the number of intervention groups, $n = 3$). This led to a final sample size of 831 children per intervention group and 1413 children in the control and standard groups, for a total of 5319 (rounded to 5320) children to be enrolled into the trial.

Interventions

The nutrition counselling provided to all study participants consisted of home-based, age-specific messages on infant and young child feeding, health and hygiene provided by extensively trained counsellors using the Alive and Thrive (www.aliveandthrive.org) modules.

Two lipid-based ready-to-use foods (RUFS, rice-lentil and chickpea-based) were locally developed at the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b, Dhaka, Bangladesh), and tested for acceptability[18] before their use in the trial. Based on the recipe that was developed and tested, a local company (Olympic Industries Ltd, Dhaka, Bangladesh) was contracted to manufacture the supplements for the study. The raw ingredients were procured from the local market and quality of grains checked. Sorting and processing was done as required. Once manufactured, Olympic packaged the products into laminated, labelled sachets. Products were made in bulk in lots, and samples from each lot were sent to SGS [www.sgsgroup.fr/] for microbiological, chemical and nutrient testing. Food technologists at the World Food Programme (WFP) discussed each report, and a lot was deemed acceptable or rejected based on not exceeding the microbiological and contaminant limits set for this type of product consumed by the specific target group. Plumpy'doz (medium quantity lipid-based nutritional supplement, LNS), an international, commercially produced product, was provided by Nutriset, Mulaunay, France. The WFP provided a fortified blended food called wheat-soy-blend plus plus (WSB++, also known as Super Cereal Plus or SC+), a product used by WFP worldwide for targeted supplementary feeding for the management of acute malnutrition and for prevention of wasting and stunting. This requires cooking, which was also tested in the study. All food procurement and transportation to the field site was facilitated and managed by WFP. Dosage and nutritive value of the four food products that were used are provided in Supplementary Table 1 (available as Supplementary data at *IJE* online). The CFSs were isocaloric, with the caloric level chosen guided by the energy intake recommended for preventing undernutrition when feeding children Plumpy'doz (46 g or 250 kcal/day). We decided to use half the dose (125 kcal) when feeding children who were 6 to 12 months of age and the full dose (250 kcal) for between 12 and 18 months of age. Plumpy'doz was provided in light-protected, lidded plastic pots of 325 g, with one pot intended to be consumed every 2 weeks at the younger age [~23 g or 1.5 tablespoons (tbs)/day] and one pot to be consumed per week from 12 until 18 months of age (~46 g or 3 tbs/day or 250 kcal). The rice-lentil RUFS, locally developed to be similar in macro- and micronutrient composition to a LNS and as an alternative to the local 'khichuri' (mixture of rice-lentil and other ingredients) recipe, and the chickpea-based RUFS, designed from recipes being considered in the region (India, Pakistan), were provided in serving sachets of 28 g of rice-lentil and 23 g of chickpea product.[18] In addition to rice-lentil and chickpea, both RUFS contained sugar, soybean oil and whole-milk powder. WSB++ was procured in 1.5-kg packs and repackaged into daily portions of 32 g flour, under controlled hygienic conditions, and delivered at home to be cooked into a water-based porridge. Caregivers were given a weekly supply of the two RUFSs and WSB++ sachets, to feed children one sachet per day during the younger, and two sachets per day during the older age period. Single portions provided approximately 125 kcal per sachet. Older children were given two sachets providing 250 kcal/day.

Randomization

Cluster-randomization of the 596 predefined communities in JiVitA, called 'sectors', was done by blocks of 19 (total 32 blocks, last block had 7 sectors). A random-number seed was selected by a statistician not involved in the study, using a random number generator, and a random number between 0 and 1 drawn from a uniform distribution was assigned to each sector. Additionally, a block number was assigned to each sector in groups of 19. For blocks 1–31, the first five sectors by sort order were assigned to treatment group 1, the next five to treatment group 2, and so on. For block 32, the two larger controls were assigned two sectors and the intervention groups 1 sector each. This resulted in 157 assigned to each of the control groups and 94 sectors assigned to each of the intervention groups, yielding a ratio of 5:3 (or 1.7) required for the multiple comparison correction factor.

Data collection and procedures

Enumeration and enrolment procedures

Before study start-up, the JiVitA study area maintained a pregnancy surveillance in a cohort of women of reproductive age enumerated throughout the study area to identify new pregnancies, using urine-based testing as part of a previous trial which ended in May 2011. The identified pregnancies were tracked and live births recorded until April 2012. In February and March of 2012, we also conducted a vital status and household and address update of all previous JiVitA study participants (women and children), at which time we identified women who became pregnant after our pregnancy surveillance was completed and tracked live births in this group. Finally, we also conducted an area-wide enumeration of all 0–3 month old children about 3 months before starting the enrolment, to identify surviving children eligible to be enrolled in the study when they completed 6 months of age. From these three sources, a list of eligible children was generated. These were visited when they were 5 months of age to obtain informed consent from the parents before enrolment in the study at 6 months of age.

Enrolment interview and follow-up visits

Families who had consented to be enrolled were visited at home for a baseline enrolment interview in the week the child turned 6 months of age, across all five groups. To ensure full exposure to a year of supplementation, per protocol, consented children who were not met despite repeated visits were excluded from the study once they had reached their 7-month birthday. Trained female interviewers ($n = 45$) conducted interviews to assess household socioeconomic status including parental education and occupation, household asset ownership and perceptions of household food security in the previous 6 months, using a nine-question Food Access Survey Tool (FAST) method.[23] Infant breastfeeding and complementary feeding history (including intakes of animal milk, powdered milk or infant formulas, common complementary foods, oil- and sugar-rich products like biscuits, etc), a previous 3-month morbidity history of symptoms of acute lower respiratory infection, diarrhoea and fever as well as a vaccination history and practices related to sanitation and hygiene, were also assessed. Anthropometry was done at this time using standard methods. Weight to the nearest 10 g was measured on digital scales designed for infant weighing (model BD585, Tanita Corporation of America, Arlington Heights, IL, USA), and checked daily for accuracy using a defined set of standard weights. Supine length was measured using a locally developed length board standardized against the infant/child Shorrboard (Weight and Measure, LLC, Olney, MD, USA). Mid upper arm circumference (MUAC) was measured at the midpoint of the left arm, using a non-stretch insertion tape. Head and chest circumferences were also recorded. Length and circumferential measures were obtained and recorded in triplicate and the median reading was used in the analysis. The inter- and intra-worker technical errors of measurement (TEM) were set at 1.0% and 1.5%, respectively, and each anthropometrist was trained and standardized to meet these cut-offs at the outset and at the midpoint of the study. Repeat infant anthropometry assessments were conducted during home visits every 3 months after the baseline at 9, 12, 15 and 18 months of age. At each 3-monthly visit, diet and breastfeeding history were assessed.

Supplementation and nutrition counseling

One field distributor (FD) was assigned to each of the study areas' 596 sectors and was responsible for visiting the homes of enrolled children to provide the foods and to assess daily morbidity. Based on the findings of formative research,[24] in the first week of enrolment in the WSB++ arm, FDs visited the mothers daily for the first 2–3 days to teach them the standard recipe (amount of water and cooking time) for cooking this fortified blended food. Mothers were informed that the food being provided was a snack and breastfeeding and other foods should be given as usual. The snack was instructed to be given at any time between meals, and the child did not need to eat it all at once. For the cooked food, specific instructions were given regarding pre-heating left-over cooked food. For all supplement groups, each week the FDs visited the homes of enrolled children twice to count sachets and ask about daily consumption of the CFS. Using maternal recall at each visit, FDs obtained daily histories of amount of CFS offered to and consumed by the child, and amount left over or shared. The amount consumed was assessed using seven categories of none, a fourth, a third, half, two-thirds, three-fourths and the entire daily portion. A weekly supply of seven (or 14 for older children) sachets was provided once every week on Sunday. Across all sectors, during the twice-weekly home visits, FDs obtained a daily history of fever, cough, difficulty/rapid breathing, diarrhoea (four or more watery stools per day) and diarrhoeal dysentery (blood or mucus in stool) and recorded information about health check-ups related to reported morbidity. In addition, FDs provided advice to mothers to take a sick child to a local health facility for treatment. The protocol for required number of visits to be made by FDs to each household was identical across all five groups.

Nutrition counselling was provided to mothers of all children (including controls) enrolled in the trial by 40 well-trained female 'counsellors' over a total of nine home-based counselling visits conducted monthly from 6 to 10 months of age, bi-monthly at 12, 14 and 16 months of age and a final visit at 17 months of age. A total of 11 age-specific infant and young child feeding messages (ranging from adding animal-source foods to an infant's diet and hand-washing, to feeding a sick child) were reinforced through interactive sessions lasting ∼30–45 min during which the counsellor assessed mothers on current feeding behaviours, reinforced good practices, introduced new behaviours and encouraged mothers to try the new behaviours. Locally developed, nationally approved, coloured pamphlets with pictures and messages were used during the counselling and given to mothers. All child feeding counselling visits were scheduled just after the child completed his/her monthly 'birthday', and messages specific for the child's age were provided until the next scheduled counselling visit. If mothers missed a previous month's counselling session, counsellors provided them with the missed messages during the next scheduled session.

Management of severe acute malnutrition (SAM)

At each assessment, children with weight-for-length z-score (WLZ) of < -3 underwent a community management of SAM protocol as per the national guidelines. The special nutritious foods they received were one of the two local RUFS used in the trial, in amounts determined based on the weight of the SAM child as per the guideline. Children undergoing the SAM protocol continued to remain in the trial protocol, and continued to receive the intervention as per their allocation group. The proportion of children treated for SAM was $< 1\%$ at below 12 months of age and up to 2% thereafter, and did not differ by treatment group (data not shown).

Statistical analysis

All analyses were done on an intention-to-treat basis. Baseline household, maternal, and child characteristics were compared by treatment group using generalized estimating equations (GEE), linear, logistic and multinomial regression for continuous outcomes, and dichotomous and categorical variables with more than two levels, respectively, to account for the cluster-randomization. Adherence to supplementation was estimated using data collected twice weekly on the amount of the daily portion of food consumed by the child. Percent adherence to supplementation was estimated as the total amount of food consumed summed up across the entire duration of supplementation, with the denominator as intended daily portions over 365 days. This was based on self-reported daily consumption and sachet counts done semi-weekly by the FDs.

Anthropometric data on weight and length were used to construct indices of LAZ, WLZ and WAZ using the WHO child growth standards.[25] To examine treatment effects on growth rate (change in anthropometric measure per month) from 6 to 18 months of age, mixed-effects models were used with age included as a quadratic term, which improved the fit of the models as shown recently.[26] Fixed

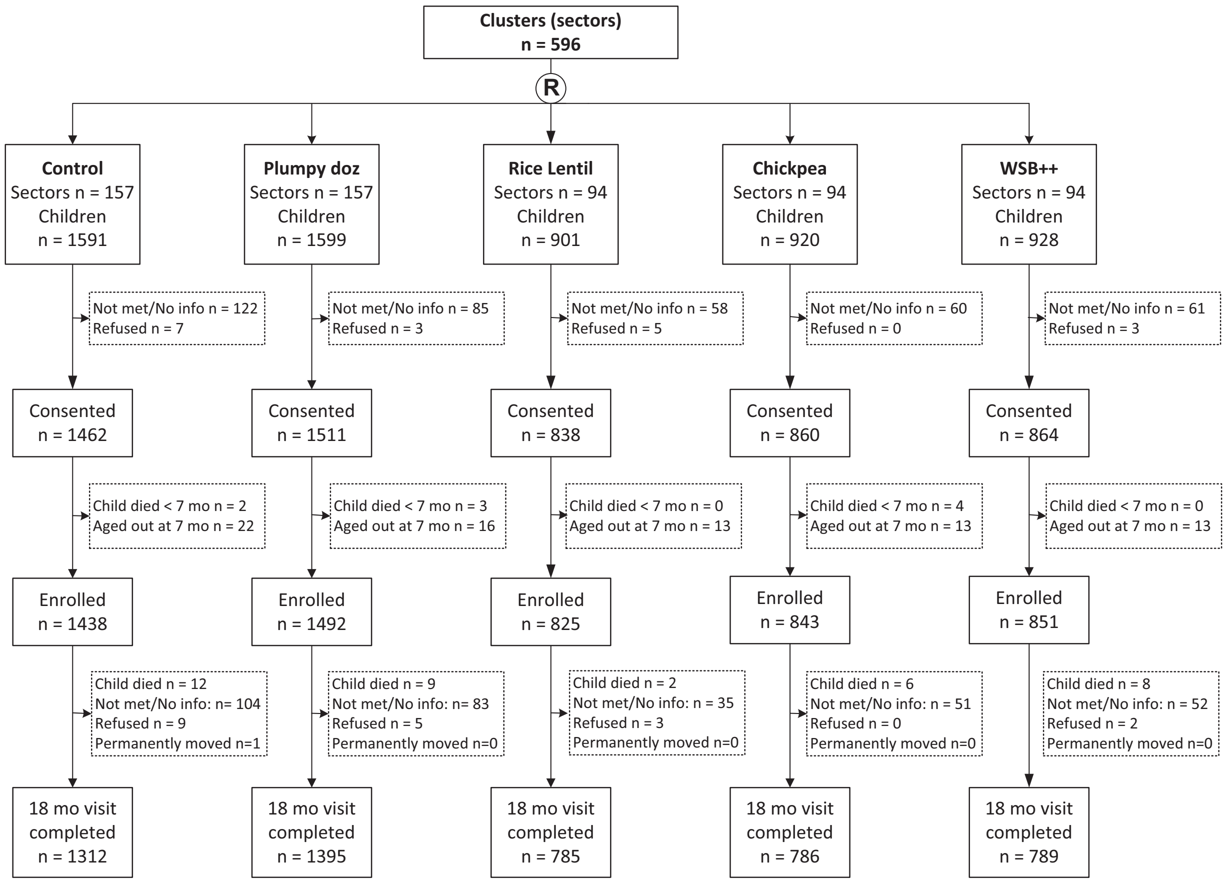

Figure 1. Study participants and follow-up by complementary food supplement group.

effects were specified as CFS allocation (vs control) and random effects comprised the individual subject and randomization cluster with interaction between child age and CFS variables included in the models. The following generic models were run:

$$Y = \beta_{0(\text{random intercept})} + \beta_{1(\text{intervention})} + \beta_{2(\text{age})} + \beta_{3(\text{age}^2)} + \beta_{4(\text{age x intervention } \beta 1 \text{ x } \beta 2)} + \beta_{5(\text{age x intervention } \beta 1 \text{ x } \beta 3)}$$

For dichotomous outcomes of stunting, wasting and underweight at 18 months of age, we used GEE logistic regression analysis with an identity link and an exchangeable correlation to account for the cluster randomization and to derive absolute risk differences and 95% confidence intervals (CI). Predicted monthly rate [standard error (SE)] of change in growth outcomes using average marginal effects, and difference (95% CI) using contrasts of average marginal effects, were estimated from the mixed-effects models.

For continuous outcomes of LAZ, WLZ, WAZ, length, head circumference and MUAC at 18 months, GEE linear regression analysis was employed to examine food supplementation effects. Episodes of pneumonia, diarrhoea and dysentery, defined using the day of onset to the last day with reported symptoms followed by two consecutive symptom-free days, and person-year of follow-up, were used to estimate incidence density. GEE logistic regression analysis with a log link was used to calculate relative risks (RR) and 95% CI for these morbidity outcomes. Non-inferiority was examined comparing the three CFSs to Plumpy'doz with LAZ as the outcome, using a GEE linear regression analysis and plotting the treatment effect and 95% CI alongside the $\pm$ 0.2 LAZ margin. Data analysis was done using SAS version 9.3 (Cary, NC) and Stata 12.0 (College Station, TX).

Ethical approval and data safety and monitoring process

The study received ethical approval from the Ethical Review Committee (ERC) at icddr,b, Bangladesh and the Institutional Review Board (IRB) of the Johns Hopkins Bloomberg School of Public Health, MD, USA. Written parental consent was obtained at the time of enrolment. A data safety and monitoring board (DSMB) was formed comprising an epidemiologist (chair), biostatistician, nutritionist, paediatrician and public health expert. The DSMB met three times: once before the start of the study to review the study protocol and processes, midway through the

Table 1. Baseline parental and household characteristics of enrolled children by CFS group ($n = 5421$)

Characteristics	Control		Plumpy'doz		Rice-lentil		Chickpea		WSB++	
Maximum *n*	1428		1484		817		837		839	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Household size	5.0	1.7	5.0	1.8	5.0	1.8	5.1	1.9	5.0	1.8
Paternal age	30.9	7.1	31.2	7.5	30.8	7.1	31.2	7.1	30.9	7.1
Maternal age	24.3	5.6	24.1	5.4	24.2	5.4	24.1	5.3	24.1	5.4
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Maternal education										
No schooling	357	25.1	361	24.3	190	23.3	193	23.1	197	23.6
Class 1 to 9	916	64.3	950	64.0	546	66.9	543	64.9	533	63.8
SSC passed	77	5.4	74	5.0	31	3.8	47	5.6	41	4.9
11 years and above	75	5.3	99	6.7	49	6.0	54	6.4	65	7.8
Religion										
Muslim	1319	92.4	1374	92.6	762	93.3	754	90.1	778	92.7
Hindu	107	7.5	108	7.3	51	6.2	83	9.9	60	7.2
Other	2	0.1	2	0.1	4	0.5	0	0	1	0.1
Household food insecurity[a]										
HFI 9	712	49.9	760	51.2	429	52.5	432	51.6	418	49.8
HFI 10–15	520	36.4	537	36.2	291	35.6	294	35.1	309	36.8
HFI >= 16	196	13.7	187	12.6	97	11.9	111	13.3	112	13.4
Assets										
Cattle[b]	701	49.1	774	52.2	408	49.9	418	49.9	452	53.9
Any land	996	69.8	1046	70.6	563	69.0	608	72.7	566	67.5
Electricity	450	31.5	480	32.4	252	30.9	272	32.5	233	27.8
Latrine										
None/field/bush	273	19.1	264	17.8	141	17.3	137	16.4	138	16.4
Open	14	1.0	18	1.2	6	0.7	6	0.7	12	1.4
Pit	52	3.6	70	4.7	43	5.3	27	3.2	35	4.2
Water Sealed/slab	1088	76.2	1131	76.2	627	76.7	666	79.6	654	78.0
Flush	1	0.1	1	0.1	0	0	1	0.1	0	0

SSC, Secondary School Certificate.

[a]HFI, Household Food Insecurity assessed using a modified questionnaire with nine questions by summing five ordered responses (1 = never, 2 = rarely, 3 = sometimes, 4 = often and 5 = mostly); HFI score ranged from 9 to its possible maximum of 45.[23]

[b]Using GEE linear or multinomial logistic regression analysis, goat/sheep ownership *P*-value: 0.009.

study and at the end. The DSMB reviewed and approved the study for its randomization, accrual of planned sample size, comparability by group, protection of human subjects in accordance with international research and ethical guidelines and monitoring of adherence to supplementation. The DSMB also monitored the study for any evidence of harm and found none. Given the shortness of the intervention period, no interim analysis of intervention differences of study outcomes was undertaken.

Results

Enrolment in the study was done from 2 September 2012 until 15 May 2013. Based on enumerated births and infants < 6 months of age in the study area, a total of 5941 children were eligible for enrolment in the study (Figure 1). Parental consent was obtained for 5536 (93.2%) of these when they reached 5 months of age, whereas 387 (6.5%) were not met with despite repeated visits because of travel outside the study area, and 18 (0.3%) refused participation. Following consent, losses were due to child deaths or not being met with until 7 months of age, when they were no longer eligible for enrolment in the study. Thus we enrolled a total of 5449 children, over 1400 in the two control groups and over 800 each in the other three food supplement groups. Loss to follow-up at 18 months was 7% and did not differ by supplement group.

Baseline comparison was done across a range of household, parental and child factors (Tables 1–2). The groups were balanced on a large number of variables, with small

Table 2. Child anthropometry, breastfeeding, diet and morbidity history at the enrolment interview by CFS group

	Control		Plumpy'doz		Rice-lentil		Chickpea		WSB++	
Maximum *n*	1438		1492		825		843		851	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age at enrolment, months	6.13	0.0	6.26	0.26	6.25	0.25	6.24	0.25	6.26	0.27
Weight, kg	6.80	0.91	6.83	0.93	6.76	0.83	6.79	0.92	6.73	0.88
Length, cm	64.32	2.55	64.32	2.50	64.11	2.63	64.33	2.55	64.11	2.68
LAZ	−1.33	1.04	−1.34	1.05	−1.40	1.09	−1.33	1.08	−1.43	1.10
WLZ	−0.40	1.03	−0.36	1.08	−0.38	1.00	−0.42	1.08	−0.44	1.00
WAZ	−1.19	1.08	−1.17	1.09	−1.22	0.97	−1.21	1.10	−1.28	1.07
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Sex, male	686	48.6	767	51.8	400	49.0	419	50.5	419	49.5
Stunting, LAZ < -2	323	23.1	369	25.1	215	26.5	206	25.0	249	29.5
Wasting, WLZ < -2	82	5.9	91	6.2	41	5.1	49	5.9	45	5.3
Underweight, WAZ < -2	283	20.2	288	19.5	155	19.0	173	20.9	196	23.2
Exclusive BF in the first 3 mo[a]	794	63.6	853	64.0	478	64.2	463	60.1	500	65.6
Exclusive BF in the first 6 mo[b]	277	19.6	426	28.8	240	29.4	207	25.0	233	27.5
24-h dietary intake (any)										
Other animal milk	139	9.8	134	9.1	59	7.2	74	8.9	64	7.6
Rice	666	47.2	598	40.4	321	39.3	356	42.9	359	42.4
Suji	285	20.2	228	15.4	136	16.7	169	20.4	122	14.4
Khichuri	42	3.0	29	2.0	17	2.1	16	1.9	16	1.9
Egg	104	7.4	122	8.2	59	7.2	68	8.2	51	6.0
Green leafy vegetables	80	5.7	77	5.2	42	5.1	31	3.7	37	4.4
Fish	116	8.2	100	6.8	59	7.2	64	7.7	57	6.7
Meat/chicken	17	1.2	7	0.5	2	0.2	11	1.3	11	1.3
Biscuit	477	33.8	382	25.8	208	25.5	201	24.2	224	26.4
Morbidity in the past 3 months										
Difficulty breathing	608	43.1	616	41.6	348	42.6	332	40.0	356	42.0
Diarrhoea	149	10.6	154	10.4	83	10.2	71	8.6	77	9.1
Dysentery	111	7.9	121	8.2	53	6.5	54	6.5	67	7.9
High fever	711	50.4	759	51.3	398	48.8	411	49.6	466	55.0

BF, breastsfeeding; Suji, wheat semolina porridge.

[a]Breastfeeding and no other liquids (including water or semi-solids) introduced in the child's diet.

[b]Breastfeeding and no other liquids or semi-solids given in the past 24 h, 6 months after birth. Using GEE logistic regression analysis; *P*-value for exclusive breastfeeding in 1st 6 mo, any consumption of powdered milk, rice, suji (with/without milk), meat and biscuits 0.05. Using GEE linear regression analysis, stunting *P*-value: 0.03, age enrolment: $P < 0.0001$.

differences seen in goat/sheep ownership, exclusive breastfeeding for the first 6 months, previous 24-h intake of some foods and age at enrolment. Household food insecurity was moderate and experienced among 50% of households in the study area. Mean weight at 6 months was around 6.8 kg and mean length 64 cm across groups (Table 2). The prevalence of stunting at enrolment ranged between 23% and 29% in the five groups and differed between groups, whereas wasting prevalence was 5–6% and did not differ.

Adherence to supplementation was high in the four groups and did not differ between groups ($P > 0.05$) (Figure 2). Median percent (intraquartile range) adherence was 93 (81–98), 92 (81–98), 91 (79–97) and 90 (76–96) in the Plumpy'doz, rice-lentil, chickpea and WSB++ groups, respectively (data not shown). Adherence was slightly higher, with median ranging 94-95 in all four groups, among children 12–18 months old compared with 6–12 month olds.

LAZ declined with age in all five groups (Figure 3, Table 3) and, when adjusting for baseline, was lower in all food groups compared with the control (Supplementary Figure 2, available as Supplementary data at *IJE* online). The rate of decline over the intervention period was lower in LAZ (0.02–0.04/month) in the Plumpy'doz, chickpea and rice-lentil groups compared with the control (Table 3). Increases in length of 0.06 cm/month (mo) to 0.09 cm/mo and in weight of 0.02 kg/mo to 0.04 kg/mo were also observed in these three groups relative to the control (all $P < 0.05$). WLZ rate of change was higher in the

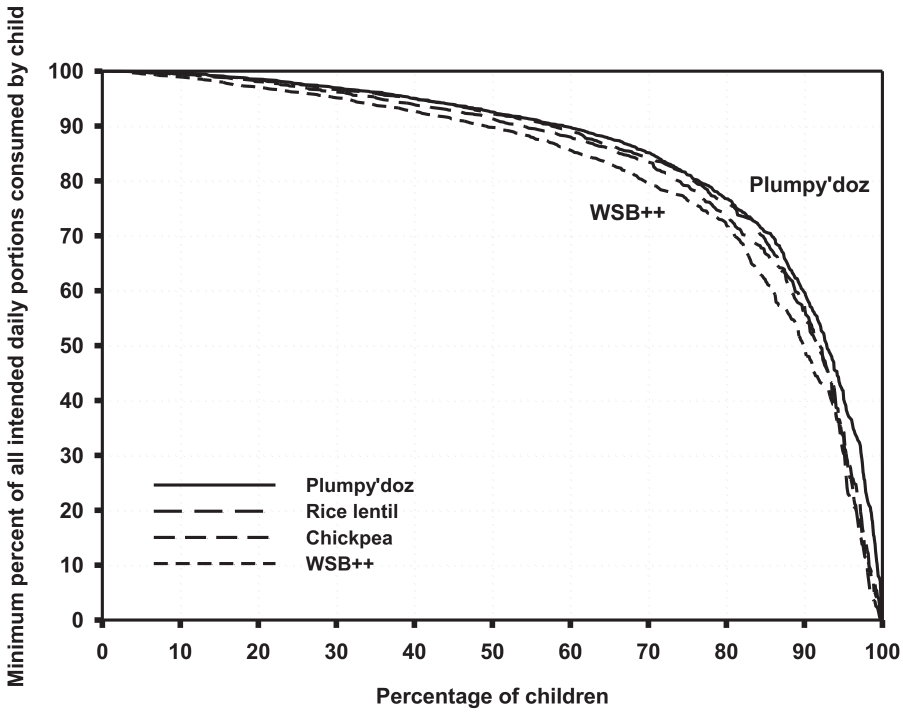

Figure 2. Adherence to supplementation by complementary food supplement group. Example of WSB++: 50% of children had compliance rates of 89.8% and above; 20% of children had compliance rates of 97.1% and above.

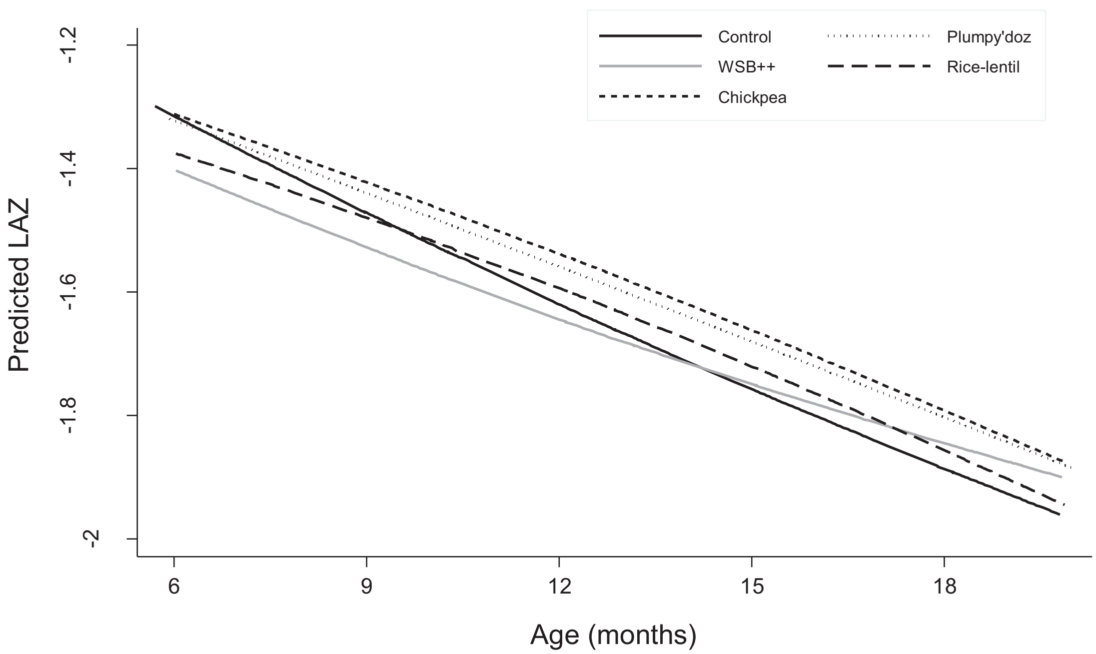

Figure 3. Predicted length for age z-score from 6 until 18 months of age by complementary food supplement group, using a mixed-effects linear regression model with age included as a quadratic term.

Plumpy'doz and chickpea (by 0.04/mo) compared with the control but not in the rice-lentil or WSB++ groups. Although WSB++ did not demonstrate gains in LAZ or WLZ, its use was associated with a higher rate of change in WAZ relative to the control group (0.02/mo). Weight and circumferential measurements in the Plumpy'doz group, and weight alone in the chickpea group, were higher at 18 mo relative to control (Supplementary Table 2, available as Supplementary data at *IJE* online).

Table 3. Effect of CFS on rate of change in linear and ponderal growth among children followed from 6 to 18 months of age

	Control	Plumpy'doz	Rice-lentil	Chickpea	WSB++
LAZ/mo, mean[a] (SE)	−0.06 (.01)	−0.04 (.01)	−0.02 (.01)	−0.03 (.01)	−0.05 (.01)
Treatment effect[b] β (95% CI)	–	.02 (.004, .04)	.04 (.02, .06)	.03 (.01, .06)	.01 (−.02, .03)
P-value		0.02	< 0.01	< 0.01	0.49
WLZ/mo, mean[a] (SE)	−0.22 (.01)	−0.18 (.01)	−0.22 (.01)	−0.18 (.01)	−0.20 (.01)
Treatment effect[b] β (95% CI)		.04 (.01, .06)	−.00 (−.03, .03)	.04 (.01, .07)	.021 (−.01, .05)
P-value		< 0.01	0.86	< 0.01	0.16
WAZ/mo mean[a] (SE)	−0.10 (.01)	−0.07 (.01)	−0.08 (.01)	−0.06 (.01)	−0.08 (.01)
Treatment effect[b] β (95% CI)		.04 (.02, .05)	.02 (.005, .04)	.04 (.03, .06)	.02 (.003, .04)
P-value		< 0.001	0.01	< 0.001	0.02
Length cm/mo, mean[a] (SE)	1.57 (.02)	1.63 (.02)	1.66 (.02)	1.65 (.02)	1.58 (.02)
Treatment effect[b] β (95% CI)		.06 (.02, .11)	.09 (.03, .15)	.08 (.02, .14)	.01 (−.05, .07)
P-value		0.02	< 0.01	0.01	0.76
Weight kg/mo, mean[a] (SE)	0.24 (.01)	0.28 (.01)	0.26 (.01)	0.28 (.01)	0.26 (.01)
Treatment effect[b] β (95% CI)		.03 (.02, .05)	.02 (.003, .04)	.04 (.02, .05)	.01 (−.002, .03)
P-value		< 0.001	0.02	< 0.001	0.09

[a]Mixed-effects model derived monthly growth rates (SE) estimated using average marginal effects.
[b]Treatment effect β (95% CI) and *P*-value of treatment effect derived using contrasts of average marginal effects.

Table 4. Effect of CFS on the prevalence of stunting, wasting, underweight and attained length and LAZ in children at 18 months of age after a year of supplementation

	Control N = 1265	Plumpy'doz N = 1344	Rice-lentil N = 755	Chickpea N = 769	WSB++ N = 770
Stunting (LAZ < -2), %	44.2	40.3	43.7	39.1	44.3
Difference (95% CI),[a] %	–	−5.0, (−8.8, −1.2)	−2.2 (−6.5, 2.0)	−6.2 (−10.6, −1.8)	−3.9 (−8.1, 0.4)
P-value		0.01	0.30	0.006	0.07
Wasting (WLZ < -2), %	16.4	13.8	15.6	16.1	17.6
Difference (95% CI)[1], %	–	−2.5 (−5.2, 0.0)	−0.5 (−3.6, 2.6)	0.0 (−3.5, 3.4)	1.5 (−2.0, 4.9)
P-value		0.06	0.74	0.97	0.40
Underweight (WAZ < -2), %	39.1	32.6	38.6	34.6	40.1
Difference (95% CI)[a]	–	−6.2 (−9.4, 3.0)	0.0 (−3.8, 3.8)	−5.1 (−8.7, -1.6)	−1.2 (−5.0, 2.5)
P-value		< 0.001	0.99	0.005	0.52
Length, mean (SD) cm	76.3 (3.0)	76.6 (2.9)	76.4 (3.0)	76.6 (3.0)	76.39 (3.0)
Difference[a] (95% CI)		0.30 (0.14, 0.47)	0.27 (0.07, 0.47)	0.27 (0.05, 0.48)	0.27 (0.08, 0.46)
P-value		< 0.001	< 0.01	0.01	< 0.01
LAZ, mean (SD)	−1.91 (1.02)	−1.80 (0.99)	−1.86 (1.01)	−1.80 (1.05)	−1.87 (1.00)
Difference[a] (95% CI)		0.10 (0.04, 0.16)	0.07 (0.00, 0.14)	0.08 (0.01, 0.16)	0.10 (0.03, 0.17)
P-value		< 0.001	0.04	0.03	< 0.01

[a]Using GEE linear regression analysis adjusting for baseline status

Rates of stunting and wasting increased with age (Supplementary Figure 1). The prevalence of stunting at 18 months of age was lower and the absolute risk reduction was −5.0% (95% CI: −8.8%, −1.2%) in the Plumpy'doz, −6.2% (95% CI: −10.6%, −1.8%) in the chickpea (−6.2%) and −3.9% (95% CI: −8.1%, 1.04%) in the WSB++ groups (Table 4). The prevalence of underweight at 18 months of age was lower only in the Plumpy'doz and chickpea groups ($p < 0.05$) whereas none of the food supplements reduced wasting compared with controls. Cumulative incidence of wasting from 6 until 18 months was 20.7% in the control group, which was lower than in the Plumpy'doz by 17% (RR = 0.83, 95% CI: 0.72, 0.97) but not other food groups (data not shown). By 18 months of age, intakes of all four foods led to an increase in length (0.27–0.30 cm) and LAZ (by 0.07–0.10) adjusted for baseline anthropometric measures (all $P \leq 0.01$, Table 4).

Effect sizes in the three CFSs were similar to that for Plumpy'doz based on the pre-specified margin of non-inferiority of ± 0.2 LAZ (Figure 4).

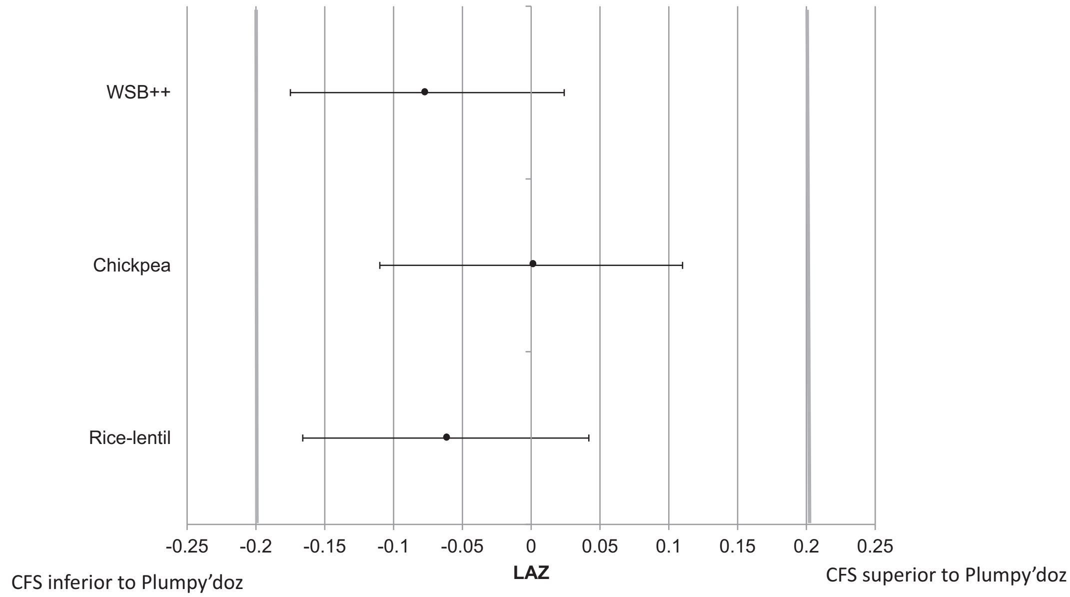

Figure 4. Relative risk and 95% CI of treatment effects on length for age z-score by complementary food supplement group relative to Plumpy'doz. Grey vertical lines indicate margin of non-inferiority of ± 0.2.

There were no differences in the incidence of pneumonia, diarrhoea or diarrhoeal dysentery across the intervention groups. Mean duration of each episode was lower in the WSB++ group for all three morbidities by about 0.25–1 day, lower in the rice-lentil group for diarrhoea and dysentery and lower in the Plumpy'doz group for pneumonia and diarrhoea (all $p < 0.05$, Table 5).

In total, 39 children died after enrolment in the study (data not shown). Mortality rates were ≤ 1% and did not differ between the intervention arms. Rates of hospitalizations in the past 6 months assessed at baseline, 12 and 18 months, ranged between 0.8% and 2.2% and did not differ by intervention group. We examined the frequency of breastfeeding and diet provided at home at each of the follow-up visits, which did not differ between the five groups (data not shown).

Discussion

In a rural area in Bangladesh where growth faltering and stunting are common, complementary foods bridging an energy and macro- and micronutrient intake gap, when provided daily for a year, reduced linear growth deceleration between 6 and 18 months of age and stunting at 18 months of age. We saw an absolute difference of 4–6% in the prevalence of stunting in three of the four supplemented groups, a difference that was significant in two and almost significant in the third group. This reduction has public health importance given that our intervention was only a year long and covered only 365 of the critically important first 1000 days from conception to 2 years of age. Annual goals in reductions in stunting prevalence set for 2025 by the World Health Assembly would be of similar magnitude. Three of the four foods provided appeared to have a comparable effect, albeit modest, on reducing linear growth deceleration. Although prevalence of wasting at 18 months was not different by group, Plumpy'doz reduced cumulative incidence of wasting by 17% compared with the control.

Our trial was unblinded, and that may result in potential bias in assessments of outcomes, although the large study area (reducing likelihood of contamination), cluster-randomization with clearly demarcated sector lines, objectivity of anthropometric measurements and sector-specific workers may have reduced bias. Another limitation was that we did not continue supplementation until 24 months of age, to examine the effect of continued supplementation, although a full year of feeding, especially during the critical period when growth faltering has been shown to be the most pronounced,[27] increased our ability to show an impact.

There are several explanations for finding modest benefits on linear growth outcomes in our study. Of note, low birthweight affected approximately half of newborns in this rural population in Bangladesh.[28,29] Low birthweight and small size for gestational age are associated with an increased risk of stunting during childhood,[5] suggesting that additional feeding of nutritious foods between 6 and 18 months of age may have a limited effect. Also, exclusive breastfeeding up to 6 months of age was only 20–30% and stunting rates were already high, ranging from 23% to 29%, suggesting that interventions with nutritionally adequate complementary foods, consumed between 6 and 18 months of age, would not only have to prevent but also reverse accrued growth deficits. Furthermore, the formulation of supplements to stimulate 'catch-up' growth while

Table 5. Effect of CFS on annual episodes and duration of pneumonia, diarrhoea and dysentery in children followed from 6 to 18 months of age

	Control	Plumpy'doz	Rice-lentil	Chickpea	WSB++
Pneumonia (cough with difficulty/rapid breathing with fever)					
Episodes, *n*	1808	1886	875	912	930
PY	1335	1403	786	792	800
Incidence density	1.35	1.34	1.11	1.15	1.16
RR (95% CI)[a]	1	0.98 (0.80, 1.20)	0.87(0.68, 1.12)	0.82 (0.65, 1.04)	0.89 (0.69, 1.14)
P-value		0.82	0.28	0.10	0.36
Duration, days mean (SD)	3.65 (2.74)	3.40 (1.76)	3.40 (1.89)	3.54 (1.92)	3.29 (1.77)
Diff, days mean (95% CI)[b]		−0.25 (−0.50, 0)	−0.25 (−0.57, 0.07)	−0.11 (−0.42, 0.20)	−0.35 (−0.66, −0.04)
P-value		0.047	0.13	0.49	0.02
Diarrhoea (≥ 4 watery stools/day)					
Episodes, *n*	2973	3014	1772	1579	1667
PY	1334	1402	785	791	800
Incidence density	2.23	2.15	2.26	2.00	2.08
RR (95% CI)	1	0.97 (0.85, 1.10)	1.04 (0.90, 1.20)	0.91 (0.79, 1.05)	0.97 (0.83, 1.13)
P-value		0.61	0.58	0.19	0.66
Duration, days mean (SD)	3.44 (1.89)	3.22 (1.70)	3.21 (1.63)	3.34 (1.76)	3.20 (1.63)
Diff, days mean (95% CI)[b]		−0.22 (−0.37, −0.07)	−0.23 (−0.41,−0.06)	−0.11 (−0.29, 0.08)	−0.25 (−0.42,−0.07)
P-value		0.004	0.01	0.26	0.01
Diarrhoeal dysentery (blood/mucus in stool)					
Episodes	5314	5569	3294	2870	2994
PY	1334	1402	785	792	800
Incidence density:	3.98	3.97	4.19	3.63	3.74
RR (95% CI)	1	1.03 (0.90, 1.19)	1.12 (0.95, 1.33)	0.94 (0.80, 1.11)	0.99 (0.84, 1.16)
P-value		0.64	0.18	0.47	0.92
Duration, days mean (SD)	5.52(7.39)	4.98 (8.67)	4.77(3.80)	5.16(8.64)	4.51(3.66)
Diff, days mean (95% CI)2		−0.54 (−1.18, 0.11)	−0.75 (−1.35,−0.15)	−0.36 (−1.11, 0.38)	−1.01(−1.60,−0.42)
P-value		0.10	0.01	0.34	0.001

An episode was defined using the day of onset with reported symptoms to the last day with symptoms followed by two consecutive symptom-free days.
PY, person-year; diff, difference.
[a]Using GEE logistic regression analysis with a log-link to estimate RR.
[b]Using GEE linear regression analysis.

also minimizing the substitution and potential suboptimal nutritional effects of traditional home foods is a difficult challenge. Additionally, gaps of macro- and micronutrients are not well characterized and vary widely, and the requirements to successfully achieve catch-up growth are not established.[30,31] The energy content of the foods provided in our study met about 20–30% of children's requirement from food, with requirements for most micronutrients being met, especially in the older children (12 until 18 months) when the ration was doubled. Breastfeeding and dietary data collected throughout the study indicated that there was no reduction in the frequency of intake and types of foods in the groups that received the food supplement, suggestive of limited substitution perhaps related to the small quantity of the supplement provided. However, it is possible that our daily rations did not adequately bridge the nutrient gap in this highly undernourished population.

Our unsupplemented control group received nutrition counselling based on previous evidence that education about child feeding alone can increase weight gain (mean effect size = 0.28, range -0.06, 0.96) and linear growth (mean effect size 0.20, range 0.04, 0.64).[32] Our complementary food formulations showed evidence of promoting linear growth beyond any effect achieved by dietary counselling alone, as provided to all participants.

Studies similar to ours, supplementing children from 6 months of age, have been varied and could be categorized into feeding durations of 3–4months,[14,33,34] 6 months[8,35,36] and 12 months.[12,37,38] One trial of Plumpy'doz supplementation (at 46 g/d) for 4 months in Chad[33] increased growth velocity by +0.03 LAZ and 0.09 cm in length per month, similar to our study, although it did not record a reduction in stunting or wasting as observed in our trial. One study in Haiti showed age-adjusted increase of 0.13 LAZ after 6 months of LNS supplementation.[36] None of the other studies showed statistically significant differences in height gain over their duration, although provision of a fortified spread relative to a maize-soy flour product for 12 months reduced severe stunting in Malawi, an impact which persisted for 2 years after the end of the study.[12,39] One trial that provided different doses of supplements for children between 6 and11 months and 12 and 18 months in Malawi did not find differences in height gain or the prevalence of stunting,[37] whereas another trial providing 280 kcal per day, with milk-LNS, soy-LNS and corn-soy-blend, showed the lowest incidence of severe stunting in the milk-LNS group. No difference in linear growth was observed with supplementation relative to the control.[39]

The growth deficits observed in our study are comparable to those seen with other non-nutritional health interventions or associated with risk factors. For example, using seven longitudinal studies, cumulative diarrhoeal burden equivalent to 23 days per year has been associated with a lower length of 0.38 cm by 2 years of age compared with being diarrhoea free.[40] Our CFSs after 1 year improved length by 0.30 cm at 18 months. Similarly, a recent meta-analysis of 10 trials of antibiotics showed an increase in linear growth of 0.04 cm/mo,[41] similar to our study, albeit these data may not be directly applicable to children under 2 years of age. Finally, a recent meta-analysis of five Water, Sanitation and Hygiene (WASH) interventions showed an impact on HAZ of 0.08;[42] our effect sizes across the four food groups for LAZ ranged from 0.07 to 0.1.

We showed that the locally produced ready-to-use foods were likely to be non-inferior to the positive control at a margin of 0.2 LAZ. Given the significant effect sizes of 0.1 LAZ seen with CFSs vs nutrition counselling alone, we cannot rule out that these foods may have been inferior to Plumpy'doz; however, our study did not have the power to show this. Although one may raise the question that 0.1 LAZ or 0.30 cm of length difference is not a meaningful improvement in linear growth, that it was accompanied by 4–6% reduction in stunting is suggestive of a public health impact, larger than that set as an annual nutrition target for 2025 at 3% by the World Health Assembly and the reduction in stunting recorded recently in the state of Maharashtra, India.[43]

Moreover, our data may be generalizable to the rural northern subcontinent where high prevalence of stunting and similar cultural and environmental conditions prevail.

Conclusions and programmatic implications

Among populations living with food insecurity, nutrition counselling alone may not be able to reduce the pervasive levels of stunting. Locally developed and produced ready-to-use complementary food supplements that were previously shown to be acceptable were tested in our trial, and may fill an important gap. These foods were culturally appropriate and acceptable and provide essential nutrients in a concentrated form. Fortified blended food, such as WSB++, on the other hand are commonly used in national programmes, unlike the lipid-based products that are generally provided in small quantities to complement the daily diet. As yet there is no one fix or magic bullet to reducing stunting, and other causes including environmental enteropathy among others may be important. Other considerations are the affordability of these foods not addressed in our study, especially for the most marginalized populations, and ensuring daily intakes, which would need to be replicated under programmatic and less controlled situations. Use and promotion of these foods may be important in concert with nutrition counselling and other strategies, including improving adolescent and maternal nutrition to address the huge burden of stunting in South Asia.

Supplementary Data

Supplementary data are available at *IJE* online.

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Commentary: Please sir, I want some more (and something else)

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Stunting has gained unprecedented attention, largely because of the importance of the first 1000 days to lifelong well-being.[1] We know that healthy physical growth is an essential component of normal development and that it does not simply happen. It is the result of awareness, adequate resources and (not or) clean environments, each sustained from conception onwards. Some argue that these conditions are also essential during the development of the progeny's parents, and possibly even grandparents. Yet it is unlikely that either a lack of knowledge or growth constraints experienced by today's parents during their own development account substantially for the ongoing persistence of stunting.[2] Rather, it is the enduring discrepancies between what is known about human growth, societies' aspirations for their children's well-being and the resources dedicated to child health, that require attention and give heightened significance to the Bangladeshi study by Prof. Christian *et al*. reported in this issue.[3]

The investigators set out to assess the effects on linear growth of fortified complementary food supplementation in children 6 to 18 months of age, living in rural Bangladesh and at high risk of food insecurity and undernutrition. They assessed the effectiveness of two 'innovative and well-designed, locally developed and produced products and also an enhanced fortified blended food, in promoting linear growth and reducing stunting and wasting'. They also included a fourth group supplemented with a lipid-based product, Plumpy-doz. Food supplements provided 20–30% of estimated energy needs and met requirements for 'most' micronutrients, 'especially in older children' who received larger rations. Child feeding, health and hygiene advice was also provided to all caregivers in experimental and control

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