ACTA PÆDIATRICA
NURTURING THE CHILD

Acta Pædiatrica ISSN 0803-5253

REGULAR ARTICLE

Intervention study shows suboptimal growth among children receiving a food supplement for five months in a slum in Bangladesh

Nuzhat Choudhury[1], Sabri Bromage[2], Md. Ashraful Alam[1], A.M. Shamsir Ahmed[3], M. Munirul Islam[1], M. Iqbal Hossain[1], Mustafa Mahfuz[1], Dinesh Mondal[1], Rashidul Haque[1], Tahmeed Ahmed (tahmeed@icddrb.org)[1]

1.Nutrition and Clinical Services Division, ICDDR,B, Dhaka, Bangladesh
2.Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA
3.Disease Prevention and Control Division, University of Queensland School of Public Health, Herston, QLD, Australia

Keywords
Bangladesh, children, growth, malnutrition, ready-to-use supplementary food

Correspondence
Tahmeed Ahmed, Nutrition and Clinical Services Division, 68 Shaheed Tajuddin Ahmed Sarani, Mohakhali, Dhaka 1212, Bangladesh.
Tel: +880 2 982 7001-10; Ext. 2300 |
Fax: +880 2 982 7101 |
Email: tahmeed@icddrb.org

Received
22 February 2016; revised 24 May 2016; accepted 12 July 2016.

DOI:10.1111/apa.13528

ABSTRACT

Aim: This study assessed weight and height changes among underweight children who received a locally produced, cereal-based, ready-to-use supplementary food.

Methods: We recruited 500 underweight Bangladeshi children aged 6–23 months from a Dhaka slum and individually matched them by sex and neighbourhood with 480 well-nourished controls. The intervention group received the daily food supplement for five months, and both groups received daily micronutrient supplements. Their weight, height, mid-upper-arm circumference and head circumference were measured monthly.

Results: The children's mean daily weight gain decreased from 1.27 to 0.66 grams per kilogram per day (g/kg/day) in the intervention group and 0.77 to 0.49 g/kg/day in the controls after adjusting for age differences between the two groups from baseline to five months of follow-up. The mean monthly height gain decreased from 1.13 to 1.03 millimetres per metre per month in the intervention children and 1.26 to 1.01 in the controls. The weight gain was highest in the intervention children who were most wasted at baseline and the controls who were least stunted.

Conclusion: The children showed suboptimal growth despite food supplements, highlighting the need for ongoing research to develop inexpensive, locally sourced food supplements to improve the nutrition of underweight children in Bangladesh.

INTRODUCTION

Childhood under-nutrition remains a serious global health problem, particularly in South Asia and sub-Saharan Africa and is recognised as the leading underlying cause of mortality among children in low- and middle-income countries (1). Moderate childhood underweight, one manifestation of childhood under-nutrition, is defined by weight-for-age Z-scores (WAZ) of ≥ -3 and < -2. Globally, more than 100 million children under five years of age are underweight, and these children account for 14% of total mortality among under fives (2). In Bangladesh, 33% of children under five are underweight (3), as a result of poverty and food insecurity, a lack of variety in their diet, inadequate child feeding practices, poor access to and use of health services and poor sanitation (4). The caregivers of these children in Bangladesh are typically given just health and nutrition education, but this type of intervention has shown limited effectiveness (5).

The former National Nutrition Program of Bangladesh provided a cereal-based, ready-to-use supplementary food called the Pushti packet, which was prepared by local community health workers, in addition to dietary counselling, for the management of underweight children. The Pushti packet was an unfortified mixture of toasted rice powder (26.3 g), roasted lentil powder (13.2 g), molasses (6.6 g) and vegetable oil (3.9 g) (6). The total energy obtained from one 50 g Pushti packet was 188 kilocalories. Moderately underweight children were prescribed two packets per day and severely underweight children were prescribed three packets. However, there is limited

Key notes

- This study assessed weight and height changes among 500 underweight children from a Bangladesh slum who received a locally produced, cereal-based, ready-to-use supplementary food and 480 well-nourished controls.
- After five months, suboptimal weight and height gain were observed among both the underweight, food-supplemented slum children and well-nourished, unsupplemented controls.
- Research should continue to develop effective, fortified, locally produced ready-to-use supplementary foods to improve the nutrition of underweight children in Bangladesh.

evidence to suggest that the Pushti packet was an effective choice for increasing body weight among underweight children. Severely malnourished children are capable of supporting a weight gain of 8 g/kg/day (7), and it has been recommended that the diets of moderately malnourished children support a weight gain of at least 5 g/kg/day (8). However, there are few details in the literature on the desired, practicably attainable or actual rates of growth among moderately underweight children in a country such as Bangladesh, particularly in the context of a community intervention programme. The lack of evidence regarding an optimal intervention, and its expected impact, has been a major deterrent to effective programming for the huge population of rural and slum children living in Bangladesh and other low- and middle-income countries.

This study was conducted to measure the weight and height gain among underweight slum children supplemented with daily Pushti packets for five months and among unsupplemented well-nourished controls. We compared each groups' rates of absolute and relative weight and height gain at baseline, five months and 12 months after enrolment. The study also sought to identify the independent contributions of different baseline characteristics on predicted gains in both weight and height within each study group from baseline to five months of follow-up.

PATIENTS AND METHODS

Participants

This intervention study was conducted in the Bauniabadh section of Mirpur, a subdistrict of the Bangladeshi capital, Dhaka. Bauniabadh, a typical urban slum, is one of eight field sites covered by the Malnutrition and Enteric Infections: Consequences for Child Health and Development Network study (MAL-ED) (9). In 2009, a child feeding centre was established in Bauniabadh to provide supplementary feeding for moderately and severely underweight children. The feeding centre is staffed by trained and experienced field workers and supervised by a physician. In this study, local children aged 6–23 months presenting with moderate or severe underweight at the centre between February 2009 and April 2011 were eligible for inclusion in the study's intervention group. If a child was severely underweight with a WAZ of <-3, he or she was referred to the site clinic for nutrition counselling and treatment. Children who were identified as severely malnourished, with a weight-for-height Z-score (WHZ) of <-3 and/or bilateral pedal oedema, were referred to icddr,b, formerly known as the International Centre for Diarrhoeal Disease Research, Bangladesh at Dhaka hospital, for treatment. Each intervention child was matched with a well-nourished control, with a WAZ of >-1, of the same sex and from the same neighbourhood in the Bauniabadh area. We excluded children with evidence of severe diarrhoea or pneumonia, persistent diarrhoea, a cleft lip or palate, blindness, tuberculosis, jaundice, neurologic handicap, renal or cardiac failure at enrolment.

Description of study groups

The intervention children began receiving the Pushti packet supplements when they enrolled in the study. Moderately underweight children were provided with two Pushti packets, containing 376 kilocalories, every day for a maximum of five months. At least one daily sachet was administered under direct observation at the feeding centre, and the other was to the child to eat at home. Severely underweight children received a third Pushti packet per day, giving them an additional 188 kilocalories. Both the intervention and control groups initially received one sachet of *Monimix* micronutrient powder (Renata Limited, Dhaka, Bangladesh), containing 12.5 mg of iron, 5 mg of zinc, 300 μg of vitamin A, 150 μg of folic acid and 50 mg of vitamin C, every day for two months. Participants who enrolled after August 2010 received daily packets for four months. The intervention and control children who were at least one year of age received 200 mg of the antihelminthic drug albendazole upon enrolment. In both groups, diarrhoeal episodes were treated with oral rehydration solution and oral zinc treatment in line with the World Health Organization and UNICEF recommendations, which are 20 mg of zinc sulphate daily for 10 days, with a half the dose for infants. All the children received typhoid, hepatitis B and *Hemophilus influenzae* vaccines. In addition, the caregivers of the intervention and control group children were encouraged to have their children vaccinated against poliomyelitis, tuberculosis, diphtheria, pertussis, tetanus and measles at the nearest vaccination centre.

Health and nutrition education was at the core of the behavioural change communication for both the intervention and control groups. Caregivers of all children were strongly encouraged to attend health and nutrition sessions that took place at the feeding centre every week. Each session focused on selected health and nutrition issues, preferably one issue at each session. Issues included preparation of nutritious food using ingredients available to the family, the importance of hand washing, sanitation and immunisation, home management of diarrhoea and how to recognise the warning signs of common childhood illnesses. Pretested information, education and communication materials were used during the sessions, which were conducted by trained field research supervisors.

Data collection

Each child had his or her weight, height, mid-upper-arm circumference (MUAC) and head circumference measured at baseline and every following month for 12 months. Seca 727 digital scales were used to measure weight to the nearest 100 grams (Seca, Hamburg, Germany). Trained field staff measured standing height or length to the nearest 0.1 cm using a locally manufactured stadiometer (icddr,b, Dhaka, Bangladesh). MUAC and head circumference were measured using specialised tape measures. Data on household food insecurity, the child's early feeding practices, household assets, income and size and the mother's age, body mass index (BMI) and education were obtained at enrolment using questionnaires from the MAL-ED study.

Of these variables, only infant and young child feeding practices were assessed after baseline at months one, two, three, four, five, nine and 12 using a monthly recall instrument administered to the caregiver, which included 24-hour recall of food groups and indicators of appropriate breastfeeding and complementary feeding practices.

Statistical analysis

The mother's BMI was calculated using her height and weight. For each month, each child's Z-scores of weight-for-height (WHZ) and height-for-age (HAZ) was calculated based on World Health Organization child growth standards (10). Baseline household food security data were used to calculate a household food insecurity access index scaled from zero to 27 (11), and principal component regression was applied to household assets data to derive an assets scale (12) from zero to 100. A monthly average dietary diversity score was calculated for each child by averaging the number of food groups recalled across all available monthly recalls for the infant and young child feeding practices.

Baseline characteristics were tabulated as means and standard deviations for continuous measures and numbers and percentages for categorical measures. For each monthly interval, we estimated the mean daily absolute change in weight in grams per day, and the monthly absolute change in height in millimetres per month (mm/mo) were estimated by subtracting the previous month's measure from that of the current month and dividing the result by 30 days in the case of weight (7). Mean relative weight and height change were expressed as grams per kilogram per day (g/kg/day) and millimetres per metre per month (mm/m/mo), respectively, by dividing daily absolute weight changes and monthly absolute height changes by the previous month's recorded mass and height measurement in terms of kilograms and metre, respectively. To control for differences in the baseline age distribution between the intervention and control groups, the mean rates of growth were adjusted for a third-order polynomial of baseline age, calculated as age plus age squared plus age cubed. For selected monthly intervals – zero to one, five to six and 11 to 12, two-tailed independent-samples t-tests were conducted to determine whether differences in absolute and relative changes in weight and height between the intervention and control children were statistically significant at α=0.05. With 95% confidence and 20% attrition, a minimum sample size of 500 for each study group was identified as necessary to detect a difference in mean relative weight gain of at least 0.2 g/kg/day between the groups (13).

Within each study group, two multivariable linear regression models were run to estimate the independent effects of baseline child, maternal and household characteristics on absolute changes in weight-adjusted-for-height in grams and height in millimetres between zero and five months. Weight-adjusted-for-height is a residual-adjusted measure that is assumed to be independent of height, calculated by regressing weight onto height and extracting the resulting residuals (14). Given the degree of heterogeneity with respect to the baseline characteristics between groups, stratified models were run by study groups rather than a pooled model in which a group term was included as a covariate. Comparisons of stratified models were strengthened by including the same covariates in both the intervention and control models. In both the intervention and control models, we included the child's baseline WHZ, HAZ, age, sex, length of exclusive breastfeeding and dietary diversity score, household food security score, mother's baseline age, education and BMI and household income and size. The child's baseline age was modelled using both a linear and a quadratic term to account for nonlinear associations. For each model, all pairwise interactions were tested between the variables sex, baseline age, WHZ and HAZ. Linear models were fit using the GENMOD procedure in SAS version 9.13 (SAS Institute, Cary, North Carolina, USA).

A separate set of multivariable regression models were run for each study group using the same outcome and explanatory variables as in the linear models, in which child's baseline WHZ, HAZ and age were modelled as generalised additive functions (15) using penalised splines (16) to assess potential nonlinearity in these variables' associations with change in weight-adjusted-for-height and height across the range of the observed distributions of the explanatory variables. The statistical significance of each predictor was calculated using a Wald test comparing the estimated effect of each predictor to the null hypothesis of no effect (17). Nonlinear models were fitted using the GAM package in R version 3.11 (R Foundation for Statistical Computing, Vienna, Austria).

Ethical approval

Ethical approval was obtained from the icddr,b Institutional Review Board. Informed and signed consent was obtained individually from the caregivers of the participants, and all data were coded to remove identifying information and to ensure confidentiality.

RESULTS

Of 1,156 children we screened, 980 (87%) were enrolled in the study, with 500 assigned to the intervention group and 480 to the control group. The numbers of intervention and control children who were followed up for at least five months were 391 (78.2%) and 371 (77.2%), respectively. Figure 1 describes the study profile. No two children came from the same household. No adverse reactions to the Pushti packet were observed or reported. Baseline characteristics of the intervention and control children are provided in Table 1.

Figure 2 provides plots of the age-adjusted mean rates of absolute and relative weight and height gain for each study group for each monthly interval, as well as each group's mean monthly WAZ and HAZ. The corresponding numerical estimates for rates of weight and height growth are provided in Table 2 for selected intervals. Between months zero and one, the mean daily absolute weight gain among

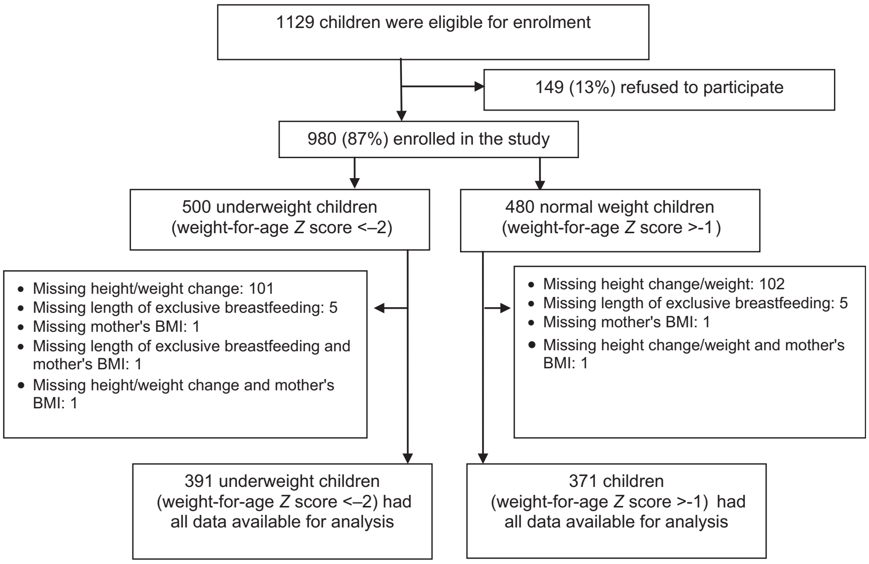

Figure 1 Study profile.

the intervention children significantly exceeded that of the control group (8.70 versus 6.57 g/day, $p < 0.001$), as did the mean daily relative weight gain (1.27 versus 0.77 g/kg/day, $p < 0.001$). Differences in the mean daily absolute weight gain between the study groups were not significant at months five to six or 11 to 12, but the mean relative weight gain was significantly greater in the intervention than the control group at months five to six (0.66 versus 0.49 g/kg/day, $p = 0.036$) and months 11 to 12 (0.69 versus 0.52 g/kg/day, $p = 0.045$). The difference in the mean absolute change in height was only significant at months zero to one, at 7.70 mm/mo in the intervention versus 8.97 in the controls ($p = 0.011$).

In both study groups, a precipitous and lasting decline in the mean rate of absolute and relative weight gain was observed after the first month of enrolment, while mean absolute and relative height gain peaked during the third month and steadily declined over the course of the study (Figure 2). Mean WHZ remained close to zero among control children throughout the study period, while WHZ increased steadily among the intervention children, who were significantly more wasted at baseline. Mean HAZ decreased at approximately the same rate in both groups, and the intervention children were significantly more stunted at baseline than the control group.

The results of the linear regression models for change in weight-adjusted-for-height are displayed in Table 3. Intervention children who were more wasted at baseline gained significantly more weight-adjusted-for-height after five months of follow-up, with 17.6 g gained for each 0.1 unit decrement in baseline WHZ ($p < 0.001$). Baseline WHZ was not significantly associated with the change in weight-adjusted-for-height among controls. Conversely, baseline HAZ was not associated with the change in weight-adjusted-for-height among intervention children, but was positively associated with gains among the controls (10.1 g per 0.1 increase in HAZ, $p = 0.004$). In both study groups, the baseline age in months exhibited a U-shaped association with the changes in weight-adjusted-for-height, particularly among the controls. The estimated contributions of baseline WHZ, HAZ and age on changes in weight-adjusted-for-height in each study group are plotted in Figure S1 as predictions from the nonlinear model.

Table 4 shows the results of the linear regression models for change in height. Among the intervention children, baseline WHZ was positively associated with change in height (0.4 mm per 0.1 increment in WHZ, $p < 0.001$). The association between baseline WHZ and height gain in controls was also positive but marginally significant ($\beta = 0.2$, $p = 0.069$). In both study groups, baseline HAZ was negatively associated with height gain (–0.4 mm in intervention and –0.2 mm in controls, $p < 0.001$ and $p = 0.006$, respectively). Figure S2 provides predictions for the effects of baseline WHZ, HAZ and age on height gain from the nonlinear model.

Average monthly reported dietary diversity was associated with increased height gains in both the intervention and controls of 2.4 mm and 1.6 mm, respectively ($p = 0.001$ and $p = 0.013$) (Table 4). Other variables positively associated with height gain among the intervention children were length of exclusive breastfeeding (0.8 mm per month, $p = 0.024$), mother's baseline age (0.3 mm per year, $p = 0.027$) and mother's education (0.6 mm per year, $p = 0.009$). Although sex was not significantly associated with height gain in the intervention or control groups, a significant interaction was observed between sex and baseline HAZ in the intervention group ($p = 0.007$), with each 0.1 decrement in baseline HAZ being associated with a 0.4 mm greater change in height among the girls than in boys (data not shown).

Table 1 Enrolment characteristics of study population

Characteristic	Intervention: No of obs	Intervention: Mean/median or proportion	Control: No of obs.	Control: Mean/median or proportion	p
Subject characteristics at enrolment					
Sex (% female)	500	48.4	480	48.33	ns
Birthweight (kg), mean±SD	47	2.66 ± 0.54	83	2.99 ± 0.48	<0.001
First born (%)	499	46.89	479	45.09	ns
Age at enrolment (mo), mean±SD	500	14.23 ± 5.32	480	12 ± 4.91	<0.001
Age distribution at enrolment (%)					
6–8 months	115	23.0	182	37.92	<0.001
9–11 months	81	16.2	88	18.33	
12–23 months	304	60.8	210	43.75	
Weight at enrolment (kg), mean±SD	500	7.14 ± 1.07	480	8.82 ± 1.2	<0.001
Height at enrolment (cm), mean±SD	500	70.35 ± 5.47	480	72.53 ± 5.75	<0.001
MUAC at enrolment (cm), mean±SD	499	13 ± 0.83	479	14.69 ± 1.5	<0.001
Head circumference at enrolment (cm), mean±SD	499	43.19 ± 2.01	480	43.97 ± 1.96	<0.001
Practices optimum IYCF (consuming milk, 4 + food groups, age-specific minimum time frequency), %	500	42.0	479	39.04	ns
Length of exclusive breastfeeding (mo), mean±SD	494	6.38 ± 1.79	474	6.28 ± 1.58	<0.001
Maternal characteristics					
Age (y), mean±SD	500	24.78 ± 5.37	480	25.05 ± 4.9	ns
Weight (kg), mean±SD	498	43.97 ± 7.72	478	50.11 ± 9.08	<0.001
Height (cm), mean±SD	498	148.24 ± 6.19	478	150.46 ± 5.36	<0.001
BMI, mean±SD	498	20.01 ± 3.25	478	22.12 ± 3.79	<0.001
Education (%, minimum primary)	500	43.4	480	58.54	<0.001
Marital status (%, currently married)	500	98.8	480	99.79	ns
Household characteristics					
Using pipe water for drinking (%)	500	98.8	480	99.38	ns
Using sanitary latrine (%)	500	65.6	480	63.54	ns
Median monthly income, BDT (range)	500	7000 (5000–9000)	480	8000 (6000–12000)	<0.001
Family size, mean±SD	500	4.66 ± 2.0	480	4.69 ± 1.92	ns
Living in the same household (<1 year), %	500	42.6	480	36.04	0.036
Wealth index, %					
Poorest	145	29.0	52	10.83	<0.001
Poor	114	22.8	82	17.08	
Middle	96	19.2	99	20.63	
Rich	84	16.8	112	23.33	
Richest	61	12.2	135	28.13	
Household food insecurity access (%)					
Food secure	252	50.4	302	62.92	<0.001
Mildly food insecure	58	11.6	51	10.63	
Moderately food insecure	114	22.8	83	17.29	
Severely food insecure	76	15.2	44	9.17	

ns: not significant at α = 0.05 level.

DISCUSSION

Ready-to-use supplementary foods made from local ingredients are an appealing choice for improving complementary feeding, in that they are relatively cheap to manufacture, are usually accepted by children and have been shown to be effective in preventing or ameliorating child malnutrition in diverse populations (18). In this intervention study, malnourished Dhaka slum children with a WAZ of less than −2 were provided a locally prepared, rice and lentil-based food supplement daily for five months and their growth was compared to that of well-nourished unsupplemented controls individually matched by sex and neighbourhood and with a WAZ of more than −1. Exceedingly suboptimal growth was observed in both groups during the study, and this indicates that the Pushti packet was an ineffective measure for improving public nutrition and further highlights the severity of malnutrition among slum children. These results provide support for the development of more nutritious food supplements in Bangladesh and evidence about how such supplements might be strategically administered and what kind of gains might be elicited.

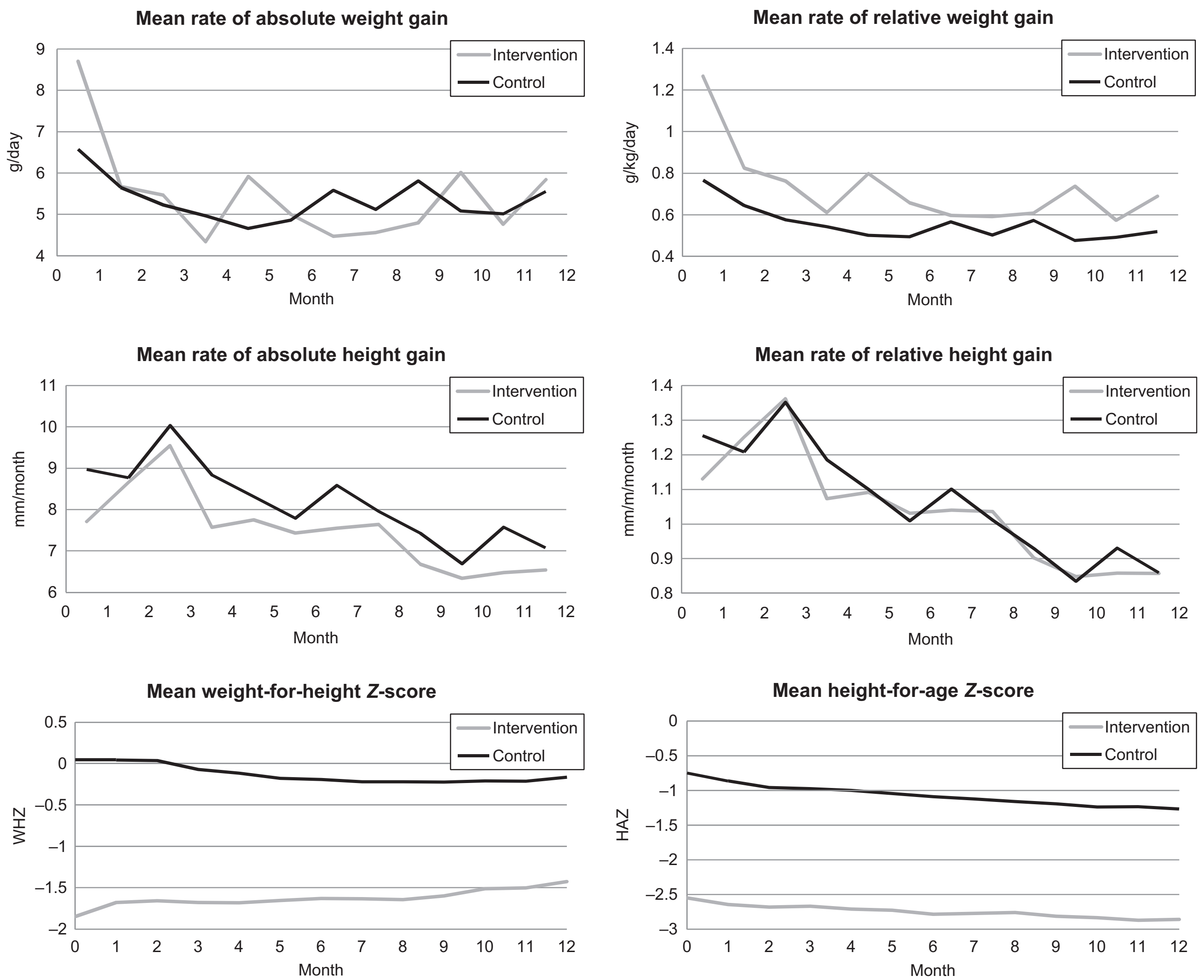

Figure 2 Mean monthly growth rates and anthropometric Z-scores in intervention and control groups. Means are linear least-square means adjusted for a third-order polynomial of baseline age (age + age^2 + age^3). Intervention (zero-five months): n = 397, control (5-12 months): n = 326, intervention (zero-five months): n = 377 and control (5-12 months): n = 286.

Ethical considerations precluded the use of a malnourished control group in this study. The study was therefore unable to isolate the effect of the food supplement per se, as there were important biological and socio-economic differences between the intervention and control children, aside from the provision of the food supplement, which might have been responsible for the observed differences in growth between the two groups. Instead, this study was designed to describe the pattern and determinants of growth within a group of malnourished food-supplemented and well-nourished unsupplemented controls and, while the food supplement may have improved growth in the intervention group, this effect could not be quantified. Furthermore, lack of a malnourished control group warranted analyses stratified by study group, which reduced our statistical power to identify the factors associated with growth. On the other hand, as the growth of malnourished controls was expected to be slower than that observed in the intervention group, the well-nourished controls provided a useful alternative contrast as they gave an idea about whether the food supplementation would allow their malnourished counterparts to attain similar growth rates and anthropometry. A similar experimental design was employed effectively in a study of multiple micronutrient supplementations among premenarchal girls in India (19). A second important limitation of our study was that children in the intervention and control groups were not matched by baseline age, and this meant that the age distributions of the children in each group were significantly different from one another. To address this, we have presented baseline age-adjusted measures of growth in each study group, in order to validly compare the monthly growth of children aged 6–23 months at baseline.

Table 2 Mean absolute and relative change in weight and height between zero and one, five and six, and 11 and 12 months

	Mean absolute change,g/day or mm/mo (SD)			Mean relative change, g/kg/day or mm/m/mo (SD)		
Interval	Intervention	Controls	p	Intervention	Controls	p
0 to 1 months						
Change in weight	8.70 (8.72)	6.57 (8.96)	<.001	1.27 (1.32)	0.77 (1.05)	<.001
Change in height	7.70 (8.08)	8.97 (8.63)	0.011	1.13 (1.18)	1.26 (1.22)	0.061
5 to 6 months						
Change in weight	5.00 (7.31)	4.86 (8.82)	0.831	0.66 (0.95)	0.49 (0.92)	0.036
Change in height	7.43 (8.64)	7.79 (7.37)	0.529	1.03 (1.16)	1.01 (0.95)	0.776
11 to 12 months						
Change in weight	5.84 (7.60)	5.55 (9.41)	0.689	0.69 (0.88)	0.52 (0.86)	0.045
Change in height	6.54 (5.04)	7.08 (5.28)	0.368	0.86 (0.66)	0.86 (0.66)	0.981

Means are linear least-square means adjusted for a third-order polynomial of baseline age (age + age^2 + age^3). Standard deviations were estimated prior to adjustment. Intervention: n(zero–one month) = 347, n(five–six month) = 359, n(11–12 month) = 304. Controls: n(zero–one month) = 446, n(five–six month) = 343, n(11–12 month) = 286.

Table 3 Multiple linear regressions to identify factors associated with absolute change in weight-adjusted-for-height (g) between zero and five months

	Intervention		Controls	
Parameter	β	p	β	p
Baseline WHZ (0.1 unit)	−17.6	<.001	−1.1	0.798
Baseline HAZ (0.1 unit)	−1.3	0.583	10.1	0.004
Baseline age (mo.)	−66.6	0.006	−128.8	<.001
Baseline age^2 (mo.^{2})	2.2	0.006	4.3	<0.001
Female sex	−22.9	0.561	−16.0	0.749
Length of exclusive breastfeeding (mo)	13.3	0.258	1.2	0.945
Dietary diversity (avg # food grps/mo)	16.1	0.493	21.1	0.410
HFIA score (0–27)	−2.9	0.493	−5.9	0.377
Mother's baseline age (years)	−1.0	0.810	2.9	0.606
Mother's education (years)	−6.5	0.371	5.1	0.555
Mother's baseline BMI (kg/m^3)	−0.0	0.997	1.6	0.822
Household income (per 1000 BDT)	0.5	0.925	0.6	0.856
Asset index (0–100)	1.6	0.447	−1.2	0.583
Household size (persons)	−9.3	0.437	11.8	0.444

Intervention: n = 391, Controls: n = 371.

Table 4 Multiple linear regressions to identify factors associated with absolute change in height (mm) between zero to five months

	Intervention		Controls	
Parameter	β	p	β	p
Baseline WHZ (0.1 units)	0 .4	<.001	0.2	0.069
Baseline HAZ (0.1 units)	−0.4	<.001	−0.2	0.006
Baseline age (mo)	−1.4	0.072	−1.3	0.085
Baseline age^2 (mo^2)	0.0	0.815	−0.0	0.699
Female sex	2.1	0.099	−0.1	0.932
Length of exclusive breastfeeding (mo)	0.8	0.024	0.4	0.319
Dietary diversity (avg # food grps/mo)	2.4	0.001	1.6	0.013
HFIA score (0–27)	0.1	0.635	−0.1	0.441
Mother's baseline age (years)	0.3	0.027	0.0	0.895
Mother's education (years)	0.6	0.009	0.1	0.807
Mother's baseline BMI (kg/m^3)	−0.3	0.158	−0.1	0.438
Household income (per 1,000 BDT)	0.3	0.112	−0.1	0.159
Asset index (0–100)	−0.1	0.155	0.1	0.207
Household size (persons)	−0.0	0.985	0.2	0.679

Interaction observed between female sex and baseline HAZ (0.1 units) in intervention group: β = −0.4 (p = 0.007) (model including interaction term not shown). Intervention: n = 391, Controls: n = 371.

Despite variations attributable to baseline age and anthropometry, and the positive effects of other selected predictors such as dietary diversity of complementary foods, length of breastfeeding and the mother's age and education, the overall pattern of growth was extremely suboptimal in both study groups. Among the malnourished intervention children, the maximum observed relative weight gain did not exceed 1.27 g/kg/day. Despite some improvement in WHZ among the intervention children over the full 12 months of observation, a significant secular decline in mean HAZ was observed in both study groups. There are several possible reasons for these findings. Our results show that 43% of the study households were food insecure, which was 8% above the national average (3), and food insecurity has been associated with insufficient or inconsistent provision of calories, nutrients, and inadequate feeding practices (4). Secondly, the Pushti packet was only moderately dense in carbohydrates and energy and a poor source of oils, protein or micronutrients. Based on its composition, supplementation would not necessarily have been expected to dramatically improve the quality of complementary feeding, which is generally poor in Bangladesh (20,21). To attain the desired weight gain, a severely malnourished child weighing 7.0–8.4 kg would need three 92 g food supplement packets per day, containing 1,500 kilocalories in total, which is 266% of the calorific content of three Pushti packets (22). Severely malnourished children in this study would have therefore had to consume 936 kilocalories per day through complementary foods, which may have been difficult to achieve. Thirdly, environmental enteropathy, which has been implicated in poor growth among children in rural Bangladesh (23), may also be an important factor with respect to this study population, in which over a third of households lacked access to a sanitary latrine, despite almost universal (98%) access to piped water, and in which incidence of diarrhoeal disease was high at 4.69 episodes per child per year (24). The environmental and economic deprivation observed in this slum population may have significantly blunted the response to food supplementation in both study groups. Such effects were difficult to characterise given our stratified analysis and the fact that all of the children lived in the same slum, but were probably at least as important as the apparent contributions of baseline age and anthropometry. It is likely that improving sanitation, food security and poverty would have augmented the effectiveness of food supplementation in this setting (25).

When we controlled for baseline WHZ, HAZ and age, gains in weight-adjusted-for-height were observed to be greatest among the most wasted and least stunted children, whereas gains in height were greatest among the least wasted and most stunted. These findings imply that the wasted children, independent of baseline HAZ and age, were metabolically optimised for weight gain, while the stunted children, independent of baseline WHZ and age, were optimised for catch-up linear growth. Conversely, these findings implicate adequate HAZ as a prerequisite for healthy weight gain and adequate WHZ as a prerequisite for healthy linear growth. Without such prerequisites, metabolic resources may not be optimally allocated for growth. Older children, independent of baseline WHZ and HAZ, exhibited smaller gains in height, presumably because of a more advanced chronological phase that was less conducive to linear growth. The observation that intermediate age children in both study groups, of 12–15 months at baseline, gained the least weight-adjusted-for-height may reflect a chronobiological effect combined with age-related differences in the intrahousehold distribution of complementary feeding and childcare.

Taken together, the results of this study suggest that new food supplements the aim to elicit maximum weight gain should be targeted at the most wasted, least stunted children, whereas programmes that aimed to elicit maximal gains in height should target the most stunted, least wasted and youngest children. Such recommendations rely on the assumption that the associations estimated between the baseline characteristics and Pushti packet consumption would be reasonably comparable to those that would be found in another study of a food supplement in Bangladesh. As such, multiple products may warrant formulation to elicit improvements in wasting and stunting most efficiently. In practice, such recommendations should also be aware of not only the maximal attainable growth, but of the appropriate rate at which malnourished children could and should gain weight-for-height relative to gains in height-for-age, in order to prevent wasting as a result of rapid catch-up growth. This important possibility was studied by the pioneering Kingston Project, which provided food supplementation to malnourished Jamaican children (26).

In a preliminary analysis of an earlier study comparing the effectiveness of the Pushti packet and a ready-to-use therapeutic food called Plumpy'Nut (Nutriset, Normandy, France) in underweight Dhaka children, with a WAZ of less than −2 from the same slum of Bauniabadh, Plumpy'Nut was found to be significantly more effective in increasing weight at every month for five months of follow-up (Mustafa Mahfuz, personal communication, November 2015). Nonetheless, the potential cost savings of using a locally produced food supplement has spurred research into more effective alternatives to the Pushti packet. A much larger study of rural Bangladeshi children compared locally developed fortified rice and lentil and chickpea-based food supplements, a fortified-blended supplement called WSB++ (World Food Programme, Rome, Italy), and the Plumpy'-Doz (Nutriset, Normandy, France) supplement. This showed that declines in WHZ were smaller in the chickpea-based and Plumpy'Doz groups, but not in the rice and lentil or WSB++ group (27). Although length-for-age (LAZ) declined with age in all study groups, as observed among both groups in this study, the predicted LAZ at 18 months was slightly lower in the rice and lentil group than among the other intervention groups. However, it is likely that both locally produced food supplements would elicit significant improvements over the Pushti packet, which is nutritionally inferior and not as well accepted by children (6). The Bangladeshi National Nutrition programme was phased out in 2011, citing the Pushti packet as an inadequate source of calories and micronutrients (28). This study provides experimental evidence that this was a good decision.

CONCLUSION

Our findings agree retrospectively with the decision to discontinue the Pushti packet. While this experiment was not designed to isolate the effect of this food supplement, the exceedingly poor growth observed among supplemented children strongly suggests that it could not have been highly effective as administered in this setting. These data support on-going research to develop inexpensive, locally sourced, ready-to-use supplementary foods to improve the nutrition of underweight children in Bangladesh, as well as recommendations on how such supplements could be most effectively administered to improve growth in weight and height in a population of slum children. This study also suggests that the environmental and economic conditions in slums need to be improved before such food supplements can be effective.

ACKNOWLEDGEMENT

The authors thank William A Petri Jr and Richard L Guerrant for their technical support.

FINANCE STATEMENT

This research was funded by University of Virginia, with support from Malnutrition and Enteric Infections: Consequences for Child Health and Development Network Investigators in the Foundation for the National Institutes of Health, the Fogarty International Center and with overall support from the Bill & Melinda Gates Foundation. icddr,b also receives core/unrestricted support from the governments of Bangladesh, Canada, Sweden and the United Kingdom. Sabri Bromage was supported in part by National Institutes of Health grant 5T32ES007069.

CONFLICT OF INTEREST

The authors have no conflict of interests to disclose.

References

1. GBD Compare [Internet]. Seattle: Institute for Health Metrics and Evaluation, 2016. Available at: http://vizhub.healthdata.org/gbd-compare/ (accessed on February 19, 2016).
2. Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, De Onis M, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* 2013; 382: 427–51.
3. National Institute of Population Research and Training, Mitra and Associates. Bangladesh demographic and Health Survey 2011. Dhaka, Bangladesh, and Calverton MD: NIPORT, Mitra and Associates, Macro International; 2013.
4. Ahmed N, Barnett I, Longhurst R. *MQSUN determinants of child undernutrition in bangladesh literature review*. Washington, DC: PATH, 2015.
5. Begum HA, Mascie-Taylor C, Nahar S. The impact of food supplementation on infant weight gain in rural Bangladesh; an assessment of the Bangladesh Integrated Nutritional Program (BINP). *Public Health Nutr* 2007; 10: 49–54.
6. Ahmed T, Choudhury N, Hossain MI, Tangsuphoom N, Islam MM, de Pee S, et al. Development and acceptability testing of ready-to-use supplementary food made from locally available food ingredients in Bangladesh. *BMC Pediatr* 2014 Jun; 14: 164.
7. Sphere Project. Sphere Handbook: Humanitarian Charter and Minimum Standards in Disaster Response [Internet]. Geneva: The Sphere Project, 2011. Available at: http://www.sphereproject.org/handbook/ (accessed on February 19, 2016).
8. Golden MH. Proposed recommended nutrient densities for moderately malnourished children. *Food Nutr Bull* 2009 Sep; 30(3 Suppl): S267–342.
9. Ahmed T, Mahfuz M, Islam MM, Mondal D, Hossain MI, Ahmed AS, et al. The MAL-ED cohort study in Mirpur, Bangladesh. *Clin Infect Dis* 2014; 59(Suppl 4): S280–6.
10. WHO Multicentre Growth Reference Study Group. *WHO child growth standards: growth velocity based on weight, length and head circumference: methods and development*. Geneva: World Health Organization, 2009.
11. Coates J, Swindale A, Bilinsky P. *Household Food Insecurity Access Scale (HFIAS) for measurement of food access: indicator guide*. Washington, DC: Food and Nutrition Technical Assistance Project, Academy for Educational Development, 2007.
12. Rutstein SO, Johnson K.The DHS wealth index. DHS comparative reports no. 6. Calverton, MD: ORC Macro; 2004.
13. Dupont WD, Plummer WD. Power and sample size calculations for studies involving linear regression. *Control Clin Trials* 1998; 19: 589–601.
14. Hu F. Measurements of Adiposity and Body Composition. In: F Hu, editor. *Obesity epidemiology*. New York: Oxford University Press, 2008: 74.
15. Wood SN. Stable and efficient multiple smoothing parameter estimation for generalized additive models. *JASA* 2012; 99: 673–86.
16. Eilers PH, Marx BD. Flexible smoothing with B-splines and penalties. *Stat Sci* 1996; 11: 89–102.
17. Wood SN. On p-values for smooth components of an extended generalized additive model. *Biometrika* 2012; 100: 221–28.
18. Lenters LM, Wazny K, Webb P, Ahmed T, Bhutta ZA. Treatment of severe and moderate acute malnutrition in low- and middle-income settings: a systematic review, meta-analysis and Delphi process. *BMC Public Health* 2013; 13(Suppl 3): S23.
19. Khadilkar AV, Kadam NS, Chiplonkar SA, Khadilkar VV. Effect of micronutrient supplementation on height velocity of underprivileged girls in comparison with un-supplemented healthy controls. *J Pediatr Endocrinol Metab* 2014; 27: 245–52.
20. Kimmons JE, Dewey KG, Haque E, Chakraborty J, Osendarp SJ, Brown KH. Low nutrient intakes among infants in rural Bangladesh are attributable to low intake and micronutrient density of complementary foods. *J Nutr* 2005; 135: 444–51.
21. Rasheed S, Haider R, Hassan N, Pachon H, Islam S, Jalal CS, et al. Why does nutrition deteriorate rapidly among children under 2 years of age? Using qualitative methods to understand community perspectives on complementary feeding practices in Bangladesh. *Food Nutr Bull* 2011; 32: 192–200.
22. Bahwere P, Binns P, Collins S, Dent N, Guerrero S, Hallam A, et al. *Community-Based Therapeutic Care (CTC): a field manual*, 1st ed. Oxford, UK: Valid International, 2006.
23. Lin A, Arnold BF, Afreen S, Goto R, Huda TM, Haque R, et al. Household environmental conditions are associated with enteropathy and impaired growth in rural Bangladesh. *Am J Trop Med Hyg* 2013; 89: 130–7.
24. Mondal D, Minak J, Alam M, Liu Y, Dai J, Korpe P, et al. Contribution of enteric infection, altered intestinal barrier function, and maternal malnutrition to infant malnutrition in Bangladesh. *Clin Infect Dis* 2012; 54: 185–92.
25. Mahmud I, Mbuya N. *Water, sanitation, hygiene, and nutrition in Bangladesh: can building toilets affect children's growth? world bank studies*. Washington, DC: World Bank, 2016.
26. Heikens GT, Schofield WN, Dawson S, Grantham-McGregor S. The Kingston project. I. Growth of malnourished children during rehabilitation in the community, given a high energy supplement. *Eur J Clin Nutr* 1989; 43: 145–60.
27. Christian P, Shaikh S, Shamim AA, Mehra S, Wu L, Mitra M, et al. Effect of fortified complementary food supplementation on child growth in rural Bangladesh: a cluster-randomized trial. *Int J Epidemiol* 2015; 44: 1862–76.
28. World Food Program. Bangladesh Nutrition Strategy 2012–2016 [Internet]. Rome: World Food Program, 2012 Available at: http://www.wfp.org/sites/default/files/ (accessed on February 19, 2016).

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1 Contribution of baseline WHZ, HAZ and age on absolute change in weight-adjusted-for-height (g) between zero to five months. Left column: intervention group (p, baseline WHZ<0.001; p, baseline HAZ=0.890; p, baseline Age=0.128). Right column: control group (p, baseline WHZ=0.791; p, baseline HAZ=0.010; p, baseline age=0.002). Estimates are adjusted for all variables included in Tables 2 and 3. Dotted lines indicate 95% confidence intervals.

Figure S2 Contribution of baseline WHZ, HAZ and age on absolute change in height (mm) between zero-five months. Left column: intervention group (p, baseline WHZ<0.001; p, baseline HAZ<0.001; p, baseline Age<0.001). Right column: control group (p, baseline WHZ<0.244; p, baseline HAZ=0.019; p, baseline age<0.001). Estimates are adjusted for all variables included in Tables 2 and 3. Dotted lines indicate 95% confidence intervals.

