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Continuation of oral nutritional supplementation supports continued growth in nutritionally at-risk children with picky eating behaviour: A post-intervention, observational follow-up study

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Abstract

Objectives: To evaluate the 120-day post-intervention growth trajectory of picky-eating children aged 2 to 6 years who previously completed a 90-day, randomized, controlled trial of oral nutritional supplementation (ONS) plus dietary counselling (DC) (SDC, n = 98) compared with DC alone (n = 105).

Methods: A total of 203 children were included. Children were free to consume ONS during follow-up. Information on ONS consumption was collected. Weight-for-age percentile (WAP) and height-for-age percentile (HAP) were measured at Day 90 (beginning) and Day 210 (end point).

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Results: Despite continued weight gain, there was a significant decline in WAP in both groups during the post-intervention period. However, children who took ONS voluntarily had a smaller loss in WAP compared with those who did not. Children in the SDC group showed no difference in a decline in HAP between those who took ONS during follow-up and those who did not. However, children in the DC group showed a marginally larger decline in HAP in those who did not take ONS during the follow-up compared with those who did.
Conclusions: Continued parental self-administration of ONS to their children slows down the loss of growth percentiles, supporting continued weight gain in picky-eating children at nutritional risk.

Keywords
Oral nutritional supplement, at-risk children, growth, picky eating, dietary counselling, energy intake

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Introduction

Picky eating behaviour is a relatively common problem during childhood with a prevalence of 8% to 50% in different published studies.[1,2] There is inconsistent evidence on the association between picky eating and weight status due to variations in the definition of picky eating. However, a systematic review showed that severe or persistent picky eating in children is associated with increased odds of underweight.[3] Additionally, a recent longitudinal study showed that picky eaters were more likely to be underweight and less likely to be overweight.[4] Picky eaters may also become locked in a cycle of recurring illness and faltering growth, with a negative effect on their long-term growth and cognitive abilities.[5,6] Therefore, the long-term aim of interventions for children with picky eating behaviour who are at nutritional risk is to improve eating patterns and support appropriate growth, especially in children with slow and poor growth.[7,8]

Evidence suggests that even mild undernutrition defined as a z-score ≥ -2 and < -1 also increases the risk of child mortality from respiratory tract infections.[9] Additionally, there is a linear association between growth and cognitive performance, even in the mild form of growth faltering.[10] Therefore, a preventive approach with early intervention in children with mild growth deficits may help children achieve their growth potential. We recently conducted a 90-day, prospective, randomized, controlled trial to investigate a preventive approach of intervention in children aged 24 to 72 months who were mildly underweight, defined as a weight-for-age percentile (WAP) between the 3rd and 15th percentiles (World Health Organization [WHO] Child Growth Standards) at enrolment. These children had picky eating behaviour with acute upper respiratory tract infections. We found that children who received oral nutritional supplementation (ONS) along with dietary counselling had a significantly higher weight gain and

lower incidence of upper respiratory tract infections compared with children who received dietary counselling alone.[11]

Although provision of ONS is effective in promoting catch-up growth in children at nutritional risk, limited research has monitored the sustainability of growth and energy intake on nutritionally at-risk children with picky eating behaviour and post-nutrition intervention. Therefore, we conducted this observational, follow-up study for 120 days post-completion of a 90-day, prospective, randomized, controlled trial. This study aimed to evaluate the growth trajectory (WAP, height-for-age percentile [HAP], and body mass index [BMI]-for-age) and energy intake of children with picky eating behaviour after nutritional intervention using ONS and dietary counselling were discontinued. We hypothesize that there are sustainable effects of ONS supplementation on growth in children at nutritional risk after nutritional intervention. Additionally, we also hypothesize that children who continue or start to consume ONS during this follow-up period will have better growth maintenance.

Methods

Study design and participants

This study was a prospective, observational follow-up study with no treatments provided to the subjects. Subjects who had successfully completed the ONS study without significant adverse safety events and without major deviation to the protocol were asked to participate in this follow-up study to assess the growth parameters for an additional 4 months. The primary objective was to assess the growth of these preschool children for an additional 4 months (from Day 90 to day 210) after completion of the ONS study. The secondary objectives were to assess energy consumption and appetite in these preschool children.

Briefly, the original ONS study was a prospective, multicentre, open-label study, which was conducted in Indian children who were defined as picky eaters. These children were aged between 2 and 6 years old, they presented with acute upper respiratory tract infection, and had WAP between the 3rd and 15th percentiles as per WHO growth charts. Picky eating was defined as having at least two of the following: 1) eating only a limited number of foods; 2) being unwilling to try new foods; 3) refusing to eat vegetables and/or foods from other food groups; 4) showing strong food likes and dislikes; and 5) displaying behaviour that disrupted mealtime.[1,12] The intervention and post-intervention studies were conducted at the Paediatric Outpatient Department from six clinics and hospitals across India. The original study design is shown in Figure 1. Eligible children were randomized to receive either ONS (Pediasure, Abbott Healthcare Private Limited, Mumbai, India) and dietary counselling (SDC group) or dietary counselling alone (DC group). The dose of ONS for children aged between 24 and 48 months was a minimum of one serving (224 mL per serving) of ONS per day, and that for children aged between 49 and 72 months of age, a minimum of two servings (224 mL per serving) per day for 90 days. One serving (224 mL) of study product provided 224 kcal of energy, 6.42 g of protein, 22.9 g of carbohydrates, and 10.7 g of fat. Dietary counselling provided to both groups was conducted by six dietitians who were trained in the standardized protocol for conducting dietary counselling. Parents were advised on the selection of appropriate food groups in food preparation and the importance of meal frequency, including three main meals and two to four snacks, to meet the child's nutritional requirements. Parents of children in the intervention group were instructed to provide the ONS during snack time between main meals.

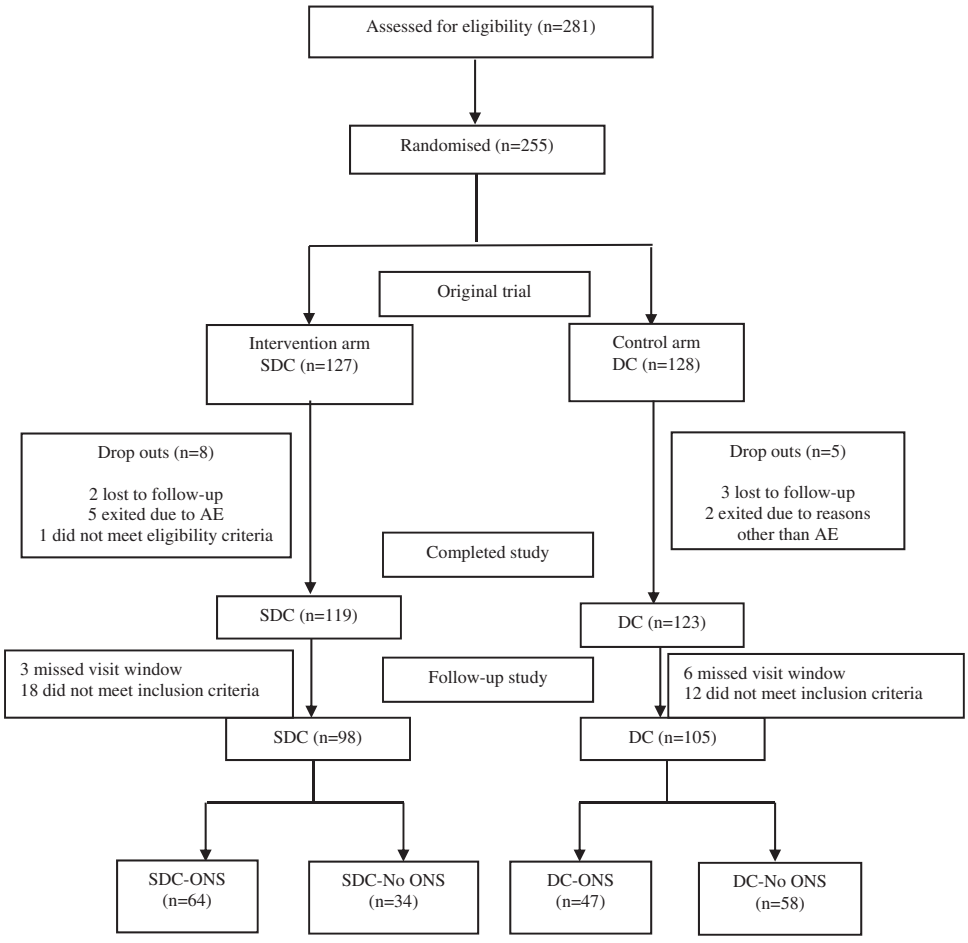

Figure 1. Flow of participants from the original trial to the current follow-up
Abbreviations: SDC, oral nutritional supplementation and dietary counselling; DC, dietary counselling alone; ONS, oral nutritional supplementation, AE, adverse event.

Study groups

In this follow-up observational study (Day 90 to Day 210), all of the subjects who were previously assigned to either the SDC or DC group did not receive any type of intervention. They were followed-up in a real-life scenario (no dietary counselling or nutritional supplementation was provided) for an additional 4 months. However, subjects were free to consume ONS or health drinks at their own preference during the follow-up period. In a follow-up visit at Day 210, parents or caregivers were asked to report the consumption patterns of any ONS and health drinks over the 120-day post-intervention period, including the brand name, the frequency, and the average amount consumed each time. Subjects were considered to have consumed ONS if they were reported to consume any ONS or other health drinks with micronutrient fortification. Regular milk, such as cow's milk, is low in a number of essential nutrients for growth and development, including B vitamins,

vitamin C, and choline.[13] Cow's milk is also associated with iron deficiency anaemia. Therefore, cow's milk was excluded from ONS classification. On the basis of whether subjects consumed ONS (any form of fortified milk supplement of any dose) during the 4 months, they were divided into four subgroups as follows: subjects in the previous SDC group who took any form of ONS voluntarily (SDC-ONS); subjects in the previous SDC group who did not take any ONS during the next 4 months (SDC No-ONS); subjects in the previous DC group who took any form of ONS voluntarily (DC-ONS); and subjects in the previous DC group who did not take any ONS during the next 4 months (DC No-ONS). Growth measurements and energy consumption were collected at the beginning and end point of this follow-up study at Day 90 and Day 210. The SDC-ONS and DC-ONS subgroups were further divided into four sub-subgroups to evaluate the association between different compliance levels, such as full compliance versus partial compliance, and growth. These four sub-subgroups included the following: SDC-ONS-Full compliance subjects in the previous SDC group who took any form of ONS voluntarily at a similar amount as in the intervention period (SDC-ONS-Full compliance); subjects in the previous SDC group who took any form of ONS voluntarily at a lower dose compared with that consumed in the intervention period (SDC-ONS-Partial compliance); subjects in the previous DC group who took any form of ONS voluntarily at the recommended dose on the product label for each brand (DC-ONS-Full compliance); and subjects in the previous DC group who took any form of ONS voluntarily below the recommended dose on the product label for each brand (DC-ONS-Partial compliance). Subdivision of subgroups leads to a smaller number of subjects in each sub-subgroup, which may result in a decrease in statistical power in data analysis. Therefore, the four subgroups, including SDC-ONS, SDC No-ONS, DC-ONS, and DC No-ONS, were used in most of the analyses to reduce complexity. The sub-subgroups are presented using figures.

Ethics

The study was performed in accordance with the ethical principles that had their origin in the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000). The study was approved by the Institutional Review Board or Independent Ethics Committee, depending on study site requirements. Written informed consent was obtained from each child's parent or legal guardian. This study was registered with Clinical Trial Registry India (ctri.nic.in) and clinicaltrials.gov with the registration numbers CTRI/2014/07/004717 and NCT02056275, respectively.

Anthropometric assessment

Anthropometric measurements were performed by trained research staff using standardized methods. Body weight was measured with light clothes and shoes and jackets removed using an electronic weighing scale after calibrating the scale to zero (Wensar Aliston; Sanjay Scientific Company, Ghatkopar West, Mumbai, India) and recording the weight to the nearest 0.1 kg. Height was measured without shoes or hat using a stadiometer (Prestige Stadiometer; Sanjay Scientific Company) and it was recorded to the nearest 0.1 cm. Weight and height measurements were performed twice. A third measurement was required if the difference between the first two measurements exceeded the defined limits (>100 g for weight and 0.4 cm for length). BMI (kg/m^2) was calculated using measured weight and height. The anthropometric measurements were used to calculate weight-for-age, height-for-age,

and BMI-for-age based on WHO Child Growth Standards.

Dietary assessment

Dietary intake was collected using a single 24-hour food recall conducted by trained dieticians at each study site at baseline, Day 90, and the end of the study (Day 210). A list of the most commonly consumed foods and drinks for this child population of the three main meals (breakfast, lunch and dinner) and snacks had been compiled taking into account the energy and macronutrient values of different serving sizes based on the Indian food composition tables published by the National Institute of Nutrition.[14] Energy and macronutrient consumption was then calculated for each child at each study visit.

Appetite assessment

Parents were asked to score the child's appetite over the last 24 hours using the Visual Analogue Scale of 0 to 10. In this scale, 0 is the lowest score indicating a very poor appetite and 10 is considered a very good appetite.

Statistical analyses

Categorical variables were analysed using the chi-square or Fisher's exact test. All continuous variables were checked for normality using the Shapiro–Wilk test, histograms, and normal probability plots, and were determined as non-normal if found significant ($P < 0.001$). For comparison between groups, the changes from baseline during the intervention and post-intervention periods were analysed using analysis of variance or the two-sample, two-sided Wilcoxon rank-sum test (if the data were non-normal). For testing changes within the SDC and DC groups, the one-sample paired t-test (or signed-rank test if data were not normal) was used. All hypothesis testing, except for the tests for interaction and normality, was performed using two-sided, 0.05 level tests. Tests for interactions and normality were performed using two-sided 0.10, and 0.001 level tests, respectively. All statistical analyses were performed using SAS release 9.3 (SAS Institute Inc., Cary, NC).

Results

Subjects

Of 255 screened subjects, 242 completed the original ONS study and 203 participated in this follow-up study (response rate of 79.6%) (Figure 1). The baseline characteristics of the subjects at Day 90 are shown in Table 1. The mean ages of the SDC and DC groups at follow-up were 3.9 and 4.0 years, respectively. In each group, approximately two-thirds of the subjects were boys. The two groups did not differ in age, sex distribution, and weight. However, children in the DC group were significantly taller ($P = 0.014$) with a higher HAP ($P = 0.003$), and they had a lower WAP ($P < 0.001$), lower BMI ($P < 0.001$), and lower BMI-for-age percentile ($P < 0.001$) than did the SDC group. Comparison of baseline characteristics between the subjects who participated in this follow-up study and those who were not enrolled (Figure 1) showed no significant differences (data not shown). There were no differences in various growth parameters between the two subgroups in each study group (SDC-ONS vs. SDC No-ONS, and DC-ONS vs. DC No-ONS) (Table 1).

ONS

During the 120-day follow-up period, 65.3% of children in the SDC group and 44.8% of children in the DC group were reported to consume ONS. Approximately 50.0% of children in the SDC group and 14.3% of children in the DC group self-

Table 1. Baseline characteristics of subjects at Day 90.

Characteristics	Intervention (SDC) n = 98	SDC-ONS n = 64	SDC No-ONS n = 34	P value (SDC-ONS vs. SDC No-ONS)	Control (DC) n = 105	DC-ONS n = 47	DC No-ONS n = 58	P value (DC-ONS vs. DC No-ONS)	P value (SDC vs. DC)
Age (years)	3.9 (1.2)	3.8 (1.2)	4.0 (1.2)	0.367[a]	4.0 (1.2)	4.2 (1.3)	3.9 (1.1)	0.234[a]	0.229[a]
Sex									
Male, n (%)	64 (65.3)	43 (67.2)	21 (61.8)	0.591[b]	65 (61.9)	29 (61.7)	36 (62.1)[b]	0.969[b]	0.615[b]
Female, n (%)	34 (34.7)	21 (32.8)	13 (38.2)		40 (38.1)	18 (38.3)	22 (37.9)		
Weight (kg)	13.6 (2.0)	13.5 (2.0)	13.6 (2.0)	1.00[a]	13.5 (2.0)	13.7 (2.2)	13.4 (1.7)	1.00[a]	0.946[a]
Height (cm)	94.0 (10.4)	93.4 (9.7)	95.1 (11.7)	1.00[d]	97.4 (9.6)	98.2 (10.3)	96.8 (8.9)	1.00[d]	0.014[a]
BMI (kg/m^2)	15.5 (1.8)	15.6 (1.7)	15.2 (1.9)	0.611[d]	14.3 (1.4)	14.2 (1.3)	14.3 (1.4)	0.829[d]	<0.001[c]
Weight-for-age percentile	12.1 (8.3)	13.0 (8.5)	10.4 (7.6)	0.155[a]	8.0 (4.3)	7.2 (3.9)	8.7 (4.5)	0.155[a]	<0.001[a]
Height-for-age percentile	12.4 (17.8)	12.1 (17.5)	12.9 (18.5)	0.837[a]	18.7 (22.3)	17.0 (22.7)	20.1 (22.0)	0.837[a]	0.003[a]
BMI-for-age percentile	46.5 (32.1)	48.8 (13.7)	42.0 (32.6)	0.486[d]	25.9 (25.3)	25.2 (23.4)	26.5 (26.9)	0.782[d]	<0.001[a]

Data are presented as mean (SD).

[a]Two-sample, two-sided Wilcoxon rank-sum test.

[b]Chi-square test.

[c]Analysis of variance model adjusted for study site, treatment group, and sex.

[d]Analysis of variance adjusted for multiple comparisons of new subgroups using stepdown Bonferroni adjustment.

Abbreviations: BMI, body mass index; ONS: oral nutritional supplementation; DC: dietary counselling alone; SDC: subjects received ONS and DC during the 90-day intervention period; SDC-ONS: subjects were previously supplemented and took ONS voluntarily during the next 4 months; SDC No-ONS: subjects were previously supplemented and did not take any ONS during the next 4 months; DC-ONS: subjects previously received DC and took any form of ONS voluntarily during the next 4 months; DC No-ONS: subjects previously received DC, but did not take any ONS during the next 4 months.

supplemented with the same ONS that was given to the SDC group in the intervention period. A total of 15.3% of children in the SDC group and 30.5% of children in the DC group self-supplemented with other health drinks. The remainder of the children (34.7% in the SDC group and 55.2% in the DC group) did not consume any ONS or other health drinks. The mean $\pm$ SD intake of ONS was 152.7 ± 39.7 mL and 128.3 ± 38.5 mL in the SDC-ONS and DC-ONS groups, respectively.

Energy intake

The SDC group had significantly higher energy intake at baseline and Day 90 compared with the DC group ($P < 0.05$) (Figure 2). However, this difference was no longer significant at Day 210.

At Day 90, there was no significant difference in energy intake between the SDC-ONS and SDC No-ONS subgroups (Figure 3). At Day 210, the SDC-ONS subgroup showed a significantly higher energy intake ($P < 0.001$) compared with the SDC No-ONS subgroup. We observed no difference in energy intake from Day 90 to Day 210 within the SDC-ONS subgroup, while the SDC No-ONS subgroup showed a significant decrease in energy intake over this time ($P < 0.001$) (Table 2). These findings indicated that the SDC-ONS subgroup was able to maintain energy intake during the post-intervention period compared with the SDC No-ONS subgroup.

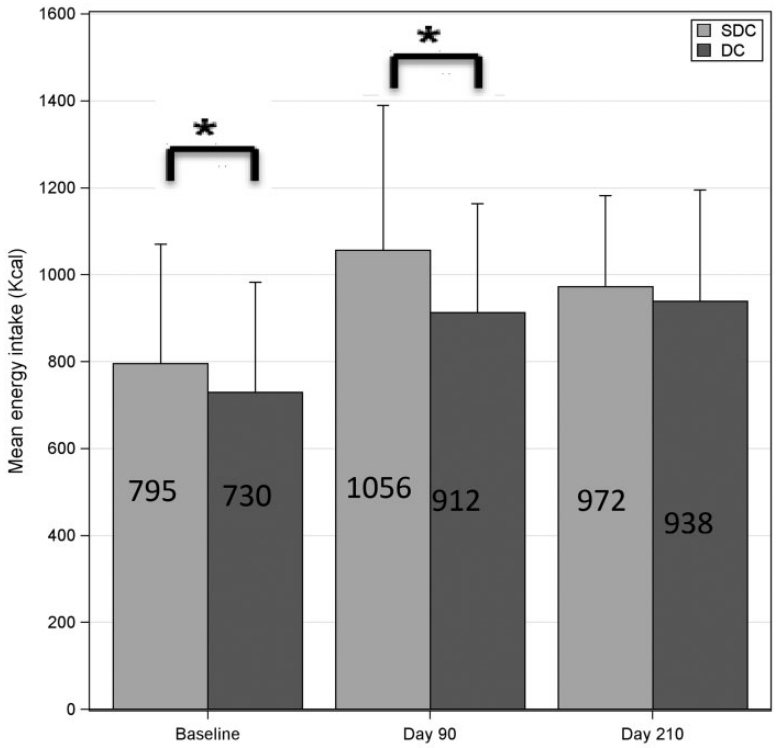

Figure 2. Mean energy intake between the SDC and DC groups
Error bars refer to SD. P values were obtained from the two-sample, two-sided Wilcoxon rank-sum test. *$P < 0.05$.
Abbreviations: SDC, oral nutritional supplementation and dietary counselling; DC, dietary counselling alone.

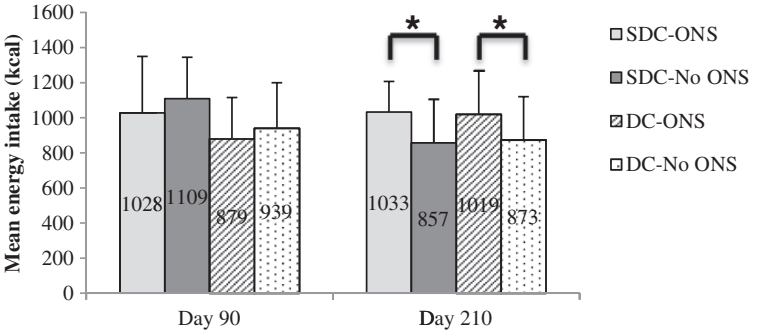

Figure 3. Mean energy intake between the SDC and DC subgroups
Error bars refer to SD. P values were obtained from the two-sample, two-sided Wilcoxon rank-sum test. *$P < 0.05$.
Abbreviations: SDC, oral nutritional supplementation and dietary counselling; DC, dietary counselling alone; ONS, oral nutritional supplementation.

Table 2. Change in energy intake from Day 90 to Day 210.

Study group	Change in energy intake (kcal)	P value
SDC	−84 (293)	0.006
SDC-ONS	5 (257)	0.406[a]
SDC No-ONS	−252 (285)	<0.001
DC	26 (260)	0.305
DC-ONS	140 (264)	<0.001
DC No-ONS	−66 (218)	0.025

Data are presented as mean (SD).
[a]The P value was obtained from the Wilcoxon rank-sum test. All other P values were obtained using the paired t-test.
Abbreviations: DC: dietary counselling alone; SDC: subjects received ONS and DC during the 90-day intervention period; SDC-ONS: subjects were previously supplemented and took ONS voluntarily during the next 4 months; SDC No-ONS: subjects were previously supplemented and did not take any ONS during the next 4 months; DC-ONS: subjects previously received DC and took any form of ONS voluntarily during the next 4 months; DC No-ONS: subjects previously received DC, but did not take any ONS during the next 4 months.

The DC-ONS and DC No-ONS subgroups had similar energy intakes at Day 90 (Figure 3). At Day 210, we observed a significantly higher energy intake in the DC-ONS subgroup compared with the DC No-ONS subgroup ($P = 0.005$). This finding resulted in a significant increase in energy intake in the DC-ONS subgroup from Day 90 to Day 210 ($P < 0.001$), while the DC No-ONS subgroup showed a significant decrease in energy intake during the same period ($P = 0.025$) (Table 2).

Appetite scores

The SDC group had a significantly higher mean appetite score than did the DC group at Day 90 ($P = 0.024$) (Table 3). This score remained significantly higher in the SDC group compared with the DC group at Day 210 ($p=0.013$). Subgroup analyses showed that there were no significant differences in appetite scores between the SDC-ONS and SDC No-ONS subgroups, as well as between the DC-ONS and DC No-ONS subgroups, at Day 90. However, the SDC-ONS ($P = 0.0006$) and DC-ONS ($P < 0.0001$) subgroups had significantly higher appetite scores than did the SDC No-ONS and DC No-ONS subgroups, respectively, at Day 210 (Table 3).

Table 3. Mean appetite score by study groups.

	Day 1	Day 90	Day 210
SDC	3.2 (1.2)	5.7 (1.2)	5.7 (1.3)
SDC-ONS	3.2 (1.2)	5.8 (1.25)	5.9 (0.2)
SDC No-ONS	3.1 (1.1)	5.6 (1.27)	5.0 (0.2)
P value (SDC-ONS vs. SDC No-ONS)	1.00[a]	0.412[a]	0.0006[b]
DC	3.1 (1.2)	5.5 (1.4)	5.4 (1.4)
DC-ONS	3.2 (1.1)	5.0 (1.48)	5.7 (0.2)
DC No-ONS	3.0 (1.3)	5.5 (1.50)	4.7 (0.2)
P value (DC-ONS vs. DC No-ONS)	1.00[a]	0.238[a]	<0.0001[b]
P value (SDC vs. DC)	0.790[a]	0.024[a]	0.013[b]

Data are presented as mean (SD).
[a]P values were obtained from from two-sample, two-sided Wilcoxon rank-sum test.
[b]P values were obtained from analysis of variance adjusting for centre and subgroup.
Abbreviations: DC: dietary counselling alone; SDC: subjects received ONS and DC during the 90-day intervention period; SDC-ONS: subjects were previously supplemented and took ONS voluntarily during the next 4 months; SDC No-ONS: subjects were previously supplemented and did not take any ONS during the next 4 months; DC-ONS: subjects previously received DC and took any form of ONS voluntarily during the next 4 months; DC No-ONS: subjects previously received DC, but did not take any ONS during the next 4 months.

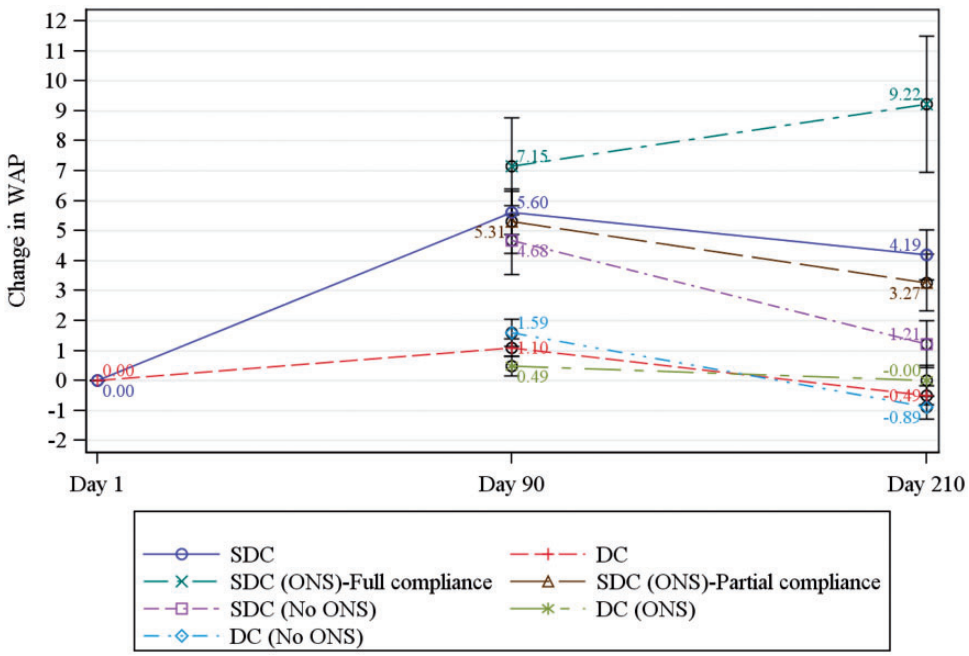

Figure 4. Mean change in weight-for-age percentile from baseline
P values were obtained from the two-sample, two-sided Wilcoxon rank-sum test.
Abbreviations: SDC, oral nutritional supplementation and dietary counselling; DC, dietary counselling alone; ONS, oral nutritional supplementation.

Table 4. Rate of weight and height gain between groups and subgroups.

	Weight (kg)		Height (cm)	
Period	Days 1–90	Days 90–210	Days 1–90	Days 90–210
SDC	0.90 (0.51)	0.40 (0.35)	1.29 (1.43)	0.69 (0.84)
SDC-ONS (n = 64)	0.92 (0.53)	0.52 (0.37)	1.52 (1.59)	0.57 (0.55)
SDC No-ONS (n = 34)	0.87 (0.46)	0.17 (0.11)	0.86 (0.94)	0.57 (0.55)
P value (SDC-ONS vs. SDC No-ONS)	0.681	<0.001	0.08	0.3
DC	0.51 (0.28)	0.34 (0.29)	0.96 (1.17)	0.58 (0.69)
DC-ONS (n = 47)	0.46 (0.23)	0.49 (0.31)	0.82 (0.96)	0.81 (0.80)
DC No-ONS (n = 58)	0.56 (0.31)	0.22 (0.21)	1.27 (1.56)	0.39 (0.51)
P value (DC-ONS vs. DC No-ONS)	0.347	<0.001	0.461	<0.001
P value (SDC vs. DC)	<0.001	0.269	0.076	0.065

Data are presented as mean (SD).

P values were obtained from the two-sample, two-sided Wilcoxon rank-sum test.

Abbreviations: DC: dietary counselling alone; SDC: subjects received ONS and DC during the 90-day intervention period; SDC-ONS: subjects were previously supplemented and took ONS voluntarily during the next 4 months; SDC No-ONS: subjects were previously supplemented and did not take any ONS during the next 4 months; DC-ONS: subjects previously received DC and took any form of ONS voluntarily during the next 4 months; DC No-ONS: subjects previously received DC, but did not take any ONS during the next 4 months.

WAP and rate of weight change

The SDC group gained significantly more WAP (5.60 ± 7.15 percentile) than did the DC group (1.10 ± 2.99 percentile) from Day 1 to Day 90 ($P < 0.001$) (Figure 4). When interventions were ceased, both groups showed losses in WAP from Day 90 to Day 210, but this difference was not significant between the groups. During the entire 210-day study period, the SDC group showed a mean increase of 4.19 ± 8.21 percentiles in WAP compared with the DC group, which showed a decrease of 0.49 ± 3.27 percentiles ($P < 0.001$). Despite the loss of WAP from Day 90 to Day 210, both groups continued to gain weight, although there was no significant difference in the change in weight between the groups (Table 4).

The SDC-ONS and SDC No-ONS subgroup together with the DC-ONS and DC No-ONS subgroups showed a decline in the mean change in WAP from Day 90 to Day 210 (Figure 4). However, the supplemented subgroups (SDC-ONS and DC-ONS) showed a significantly slower decline than did the non-supplemented subgroups (SDC No-ONS and DC No-ONS) ($P < 0.001$). When we divided the subgroups by compliance level, the SDC-ONS-Full compliance sub-subgroup showed a significantly greater increase in the mean change in WAP from Day 90 to day 210 than did the SDC-ONS-Partial compliance sub-subgroup ($P = 0.002$) (Figure 4). Within-group comparison showed that WAP was not significantly increased from Day 90 to Day 210 in the SDC-ONS-Full compliance sub-subgroup. However, the SDC-ONS-Partial compliance sub-subgroup showed a significant loss in the mean change in WAP from Day 90 to Day 210 ($P < 0.0001$). This finding suggests that the SDC-ONS-Full compliance sub-subgroup maintained the growth gained in the 90-day intervention period. There was no significant difference in growth between the two DC-ONS sub-subgroups (data not shown). From Day 0 to Day 210, the SDC No-ONS subgroup had a significantly greater net increase in the mean change in WAP than did the DC No-ONS ($P = 0.001$). This finding suggested that provision of ONS and dietary counselling

helped sustain growth better than did only dietary counselling.

From Day 90 to Day 210, we observed significant increases in weight for all groups and subgroups, despite a decline in WAP, as mentioned above (Table 4). The post-intervention supplemented subgroups (SDC-ONS and DC-ONS) showed marked weight gain compared with the non-supplemented subgroups (SDC No-ONS and DC No-ONS) ($P < 0.001$). Despite the observed weight gain among the groups and subgroups, except for the sub-subgroup SDC-ON-Full compliance in which weight gain resulted in an increase in the mean change in WAP (data not shown), weight gain was likely to have been slower than that of the standard growth trajectory of the reference population. This could have led to the overall decline in WAP.

HAP and rate of height change

During the intervention phase, both groups showed a loss in HAP. The DC group showed a significantly larger loss in HAP than did the SDC group from Day 1 to Day 90 ($P < 0.001$) (Figure 5). Despite the loss in HAP, there tended to be a gain in height in the SDC and DC groups, but there was no significant difference between the groups ($P = 0.076$) (Table 4). This finding suggested that, similar to WAP described above, the increase in height was insufficient to meet the growth trajectory of the reference population, which resulted in a decline in HAP.

From Day 90 to Day 210 of the post-intervention phase, there was no significant difference in the mean change in HAP between the SDC-ONS and SDC No-ONS subgroups (Figure 5). There was also no

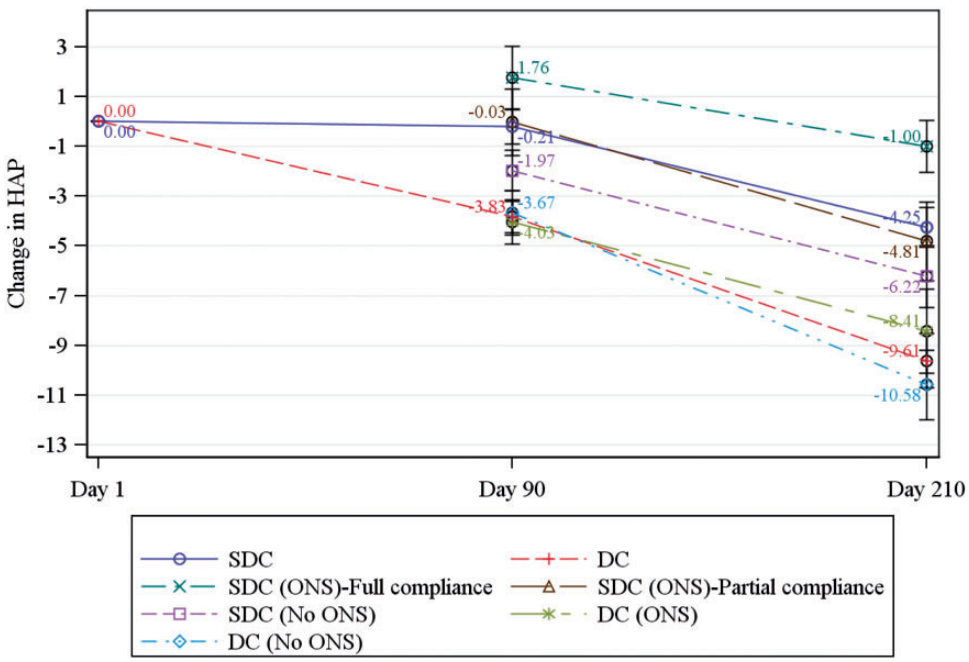

Figure 5. Mean change in height-for-age percentile from baseline
P values were obtained from the two-sample, two-sided Wilcoxon rank-sum test.
Abbreviations: SDC, oral nutrition supplementation and dietary counselling; DC, dietary counselling alone; ONS, oral nutritional supplementation.

significant difference in the mean change in HAP between the SDC-ONS-Partial compliance and SDC-ONS-Full compliance sub-subgroups. Despite gaining height (Table 4), there was no significant difference in height gain from Day 90 to Day 210 between the SDC-ONS and SDC No-ONS subgroups. The DC-ONS subgroup had a marginally smaller decline in HAP compared with the DC No-ONS subgroup from Day 90 to Day 210 (Figure 5) ($P = 0.052$). This finding could have been due to the observation that the DC-ONS subgroup showed a greater height gain compared with the DC No-ONS subgroup ($P < 0.001$) (Table 4).

BMI-for-age percentile

During the intervention phase, the SDC group had a significantly larger increase in the BMI-for-age percentile than did the DC group from Day 1 to Day 90 ($P < 0.001$). During the post-intervention phase, the SDC and DC groups showed a significant increase in the BMI-for-age percentile ($P < 0.0001$), with a similar rate of change in each group (data not shown). However, subgroup analysis showed that the SDC-ONS subgroup had a significantly larger improvement in the BMI-for-age percentile compared with the SDC No-ONS subgroup from Day 90 to Day 210 ($P < 0.001$). Similarly, the DC-ONS subgroup had a significantly larger improvement in the BMI-for-age percentile compared with the DC No-ONS subgroup from Day 90 to Day 210 ($P < 0.01$).

Discussion

This was a prospective, observational follow-up study that assessed the growth trajectory of preschool children with picky eating behaviour for an additional 4 months after discontinuation of nutritional intervention using dietary counselling with or without ONS. We found that the SDC and DC groups had a significant decline in the growth percentile. However, children who consumed ONS in accordance with their parents' practice during the post-intervention period had less loss of the growth percentile compared with children who did not. This finding suggested that continuation of ONS helped maintain improved growth achieved from the intervention period.

Malnutrition of children aged under 5 years is a major public health problem in India.[19,20] Malnutrition affects children at the most crucial time of growth and development, which can lead to impairment ranging from physical to cognitive growth and susceptibility to infection.[19] In nutritionally at-risk children with picky eating behaviour, meeting daily nutrient intake recommendations may be challenging.[21] Some studies have examined the possible effect of picky eating on growth. These studies reported that preschoolers with picky eating behaviour were more likely to be underweight.[22–25] Underweight is an important risk factor for poor cognitive development, learning disabilities, long-term behavioural problems, increased prevalence and severity of infection, and high mortality rates.[26,27] However, some studies have also showed no significant association between picky eating behaviour and the child's growth.[1,12] Some factors that can explain this inconsistency among studies include different methods of calculating underweight status, such as using different growth references and cutoffs for defining underweight, a lack of homogeneity in age in the study populations, and using different criteria for classifying picky eating behaviour.

Several studies have evaluated the beneficial effect of ONS on catch-up growth in children at nutritional risk.[6,15–17] One randomized, controlled intervention trial was conducted in preschool aged children with

evidence of suboptimal growth (weight-for-height below the 25th percentile) and picky eating behaviour. This trial showed greater increases in growth parameters in children who received ONS plus dietary counselling compared with those who received only dietary counselling.[6] Another recent study demonstrated that ONS with dietary counselling improved nutrient adequacy in young Chinese children with picky eating behaviour and with weight-for-height below the 25th percentile.[16] In a 48-week nutritional intervention study, provision of ONS combined with dietary counselling promoted catch-up growth in weight and improved linear growth during the growth maintenance phase.[18] This helped to sustain proportional growth in children at nutritional risk.

In the original intervention study, we found that nutritional intervention combining ONS and dietary counselling for 90 days was effective in improving energy intake and weight in picky-eating children who were at nutritional risk and presented with acute upper respiratory tract infection. During the follow-up period (Day 90 to Day 210) where all interventions were discontinued, self-provision of ONS increased total energy intake, whereas discontinued use of ONS decreased energy intake. The parents of the subjects reported better appetite following self-consumption of ONS, as reflected by higher appetite scores at Day 210 compared with Day 90. This finding is similar to a recent study that reported increased appetite scores following long-term supplementation in children at nutritional risk.[18] Adequate intake of certain micronutrients, such as zinc and iron as a result of supplementation, may positively influence the child's appetite. These micronutrients have been shown to be involved in appetite regulation[28,29] and improvement in appetite in young children who have evidence of growth faltering.[30,31]

With regard to growth parameters, in the original study, the SDC treatment group had significantly greater weight gain over the study period (Day 1 to Day 90) compared with the DC control group. However, during the follow-up phase from Day 90 to Day 210, we observed a significant decline in WAP, despite continued weight gain. Subgroup analyses showed that continued provision of ONS at similar doses as in the intervention period helped maintain the improved growth achieved during the intervention period. Additionally, continuation of smaller volumes of ONS after cessation of treatment slowed down the loss in WAP in the self-supplemented subgroups (SDC-ONS and DC-ONS) compared with the non-supplemented subgroups (SDC No-ONS and DC No-ONS). This finding is consistent with previous studies, which showed that continuous use of ONS after the catch-up growth phase helps maintain growth.[18,32] Additionally, these studies also demonstrated that long-term use of ONS was not associated with an increased risk of overweight and obesity in children at nutritional risk.[18,32] These results suggest that for growth maintenance in picky-eating children at nutritional risk, supplementation with ONS is effective in maintaining or slowing down the trend for loss of growth and helps support continued weight gain.

The SDC and DC groups showed a decline in HAP from the onset of the study, but this decline was significantly slower in the SDC group compared with the DC group during the intervention phase from Day 1 to Day 90. Despite self-supplementation from Day 90 to Day 210, there was no significant difference in the rate of HAP decline between the SDC-ONS and SDC No-ONS subgroups, although there was a marginally larger decline in the DC No-ONS subgroup compared with the DC-ONS subgroup. The decline in HAP observed throughout the study groups and subgroups occurred despite an increase in height from Day 1 to Day 210. This lack of improvement in

HAP may be attributed to the relatively short study duration of supplementation (Day 1 to Day 90), inconsistent self-provision of ONS during the follow-up phase (Day 90 to Day 210), and lower volumes of ONS consumed. These factors could be reasons why we did not observe an improvement in HAP, especially among the supplemented group.

Collectively, the growth parameters showed that subjects in the SDC and DC groups showed loss in WAP and HAP during the extension phase from Day 90 to Day 210. However, subjects who consumed ONS of any form during the extension phase had significantly smaller WAP losses than did those who did not consume ONS, regardless of their previously assigned treatment groups. Furthermore, those who self-supplemented from Day 90 to Day 210 had a greater increase in weight change, and, to a lesser extent, height gain. These findings suggest that continuation of ONS may be needed for continued growth maintenance for children at nutritional risk.

Interestingly, subjects in the SDC and DC groups had an increase in the BMI-for-age percentile during the extension phase, with a similar rate of change within the groups. However, this increase may have been due to disproportional loss of WAP and HAP, or the children gained weight faster than their change in height.

In this study, approximately 50% of children in the SDC group and 14% of those in the DC group consumed the same ONS, which was provided in the intervention period. This finding indicated that the majority of children self-supplemented with the same ONS, at least in the SDC group, after the initial intervention phase. Nonetheless, the mean volume of approximately 130 mL (other health drinks) to 150 mL (the same ONS) was less than the dose that children received during the intervention phase (224–448 mL). Therefore, the nutrient content of self-supplemented ONS (the same ONS or other health drinks) may have been lower than that administered in the intervention phase.

The strengths of this study include its prospective design in which children who had undergone different treatments were monitored for an additional 4 months under free-living conditions. This reflects the real-life situation of whether provision of ONS can be sustained. Children with picky eating behaviour are also rarely studied in Asian countries. Our study provided important data on continued growth and energy intake of nutritionally at-risk children after cessation of treatment. Children's height and weight were objectively measured and WHO percentiles were used for comparison between treatment groups.

The present study has some limitations. Although 24-hour dietary recalls are recognized as one of the most appropriate methods to estimate dietary intake, including macronutrients, there might be recall bias and under-reporting of food intakes.[33] Additionally, the use of a single 24-hour recall imparts limitations on sufficient characterization of a patient's usual intake as a result of day-to-day variation. Nonetheless, the 24-hour recall procedure is appropriate for studying energy and nutrient intake in children in large samples and is used in nutrition surveys in several countries.[22,34] This recall procedure is also considered reasonably accurate for providing group mean estimates of children intakes. Similarly, the information on ONS consumption patterns over the post-intervention period was collected using parental reporting, which was subject to possible recall bias. However, we observed an increase in energy intake in accordance with an increase in body weight in the two subgroups who consumed ONS. Therefore, the 24-hour recall method appears to have provided a reasonable measure of energy intake in this study. Another limitation is the subjective parental assessment of the child's appetite level, which may be

prone to bias, especially in children who received ONS. Furthermore, there was a lack of controlling of potential confounding factors, which are known to be associated with a child's health, such as socioeconomic status and parental education. Nearly two-thirds of the child population in this study were boys. Picky eating appears to affect girls and boys equally, as shown in a cross-sectional study of 200 Indian children younger than 5 years old,[35] as well as in other child populations.[1] Therefore, the generalizability of the findings in this study may be limited to settings with a similar sex distribution.

Conclusions

In conclusion, self-supplementation with ONS after cessation of treatment increases energy and macronutrient intake and slows down the loss of the growth percentile during the post-intervention period in nutritionally at-risk children with picky eating behaviour. Additionally, continuation of ONS at a similar dose as that in the intervention period helps maintain growth in the post-intervention period. Therefore, continuation of ONS may be needed for growth maintenance in children at nutritional risk with picky eating behaviour.

Author contributions

AG, BK, IS, and VS conceived and designed the study. AG, BK, AK, DC, PP, and SS were responsible for recruitment of subjects and data collection. MP was responsible for overall supervision of the study. AG, BK, IS, VS, AK, DC, PP, SS, MP, YB, YLL, VMHT, and DH participated in data analysis and interpretation. VMHT and DH drafted the manuscript. All authors read and approved the final manuscript.

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Declaration of conflicting interest

IS, VS, YLL, VT, and DH, are employees of Abbott Nutrition. YB is an employee of Cognizant Technologies Solution Pvt. Ltd, which is a Contract Research Organization providing statistical services to Abbott Nutrition.

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References

1. Mascola AJ, Bryson SW and Agras WS. Picky eating during childhood: a longitudinal study to age 11 years. *Eat Behav* 2010; 11: 253–257.
2. Cochrane SH, Leslie J and O'Hara DJ. Parental education and child health: intracountry evidence. *Health Policy Educ* 1982; 2: 213–250.
3. Brown CL, Vander Schaaf EB, Cohen GM, et al. Association of Picky Eating and Food Neophobia with Weight: A Systematic Review. *Child Obes* 2016; 12: 247–262.
4. Antoniou EE, Roefs A, Kremers SP, et al. Picky eating and child weight status development: a longitudinal study. *J Hum Nutr Diet* 2016; 29: 298–307.
5. Black RE, Allen LH, Bhutta ZA, et al. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet* 2008; 371: 243–260.
6. Alarcon PA, Lin LH, Noche M, Jr., et al. Effect of oral supplementation on catch-up growth in picky eaters. *Clin Pediatr (Phila)* 2003; 42: 209–217.
7. Ong C, Phuah KY, Salazar E, et al. Managing the 'picky eater' dilemma. *Singapore Med J* 2014; 55: 184–189; quiz 190.
8. Mc Cormick C. Monitoring, reporting and addressing child rights and protection violations in 'non-listed' countries. *Disasters* 2013; 37(Suppl 1): S121–S138.

9. Olofin I, McDonald CM, Ezzati M, et al. Associations of suboptimal growth with all-cause and cause-specific mortality in children under five years: a pooled analysis of ten prospective studies. *PLoS One* 2013; 8: e64636.
10. Sudfeld CR, McCoy DC, Fink G, et al. Malnutrition and its determinants are associated with suboptimal cognitive, communication, and motor development in Tanzanian Children. *J Nutr* 2015; 145: 2705–2714.
11. Ghosh A, Kishore B, Shaikh I, et al. Effect of oral nutritional supplementation on growth and recurrent upper respiratory tract infections. *J Int Med Res* 2018
12. Wright CM, Parkinson KN, Shipton D, et al. How do toddler eating problems relate to their eating behavior, food preferences, and growth? *Pediatrics* 2007; 120: e1069–e1075.
13. Griebler U, Bruckmuller MU, Kien C, et al. Health effects of cow's milk consumption in infants up to 3 years of age: a systematic review and meta-analysis. *Public Health Nutr* 2016; 19: 293–307.
14. NIN, *Nutrition Value of Indian Foods*, 2011, National Institute of Nutrition. Indian Council of Medical Research.
15. Fiore P, Castagnola E, and Merolla R. Effect of nutritional intervention on physical growth in children at risk of malnutrition. *Int Pediatr* 2002; 17: 179–183.
16. Sheng X, Tong M, Zhao D, et al. Randomized controlled trial to compare growth parameters and nutrient adequacy in children with picky eating behaviors who received nutritional counseling with or without an oral nutritional supplement. *Nutr Metab Insights* 2014; 7: 85–94.
17. Fisberg M, Maulen-Radovan IE, Tormo R, et al. Effect of oral nutritional supplementation with or without synbiotics on sickness and catch-up growth in preschool children. *Int Pediatr* 2002; 17: 216–222.
18. Huynh DTT, Estorninos E, Capeding RZ, et al. Longitudinal growth and health outcomes in nutritionally at-risk children who received long-term nutritional intervention. *J Hum Nutr Diet* 2015; 28: 623–635.
19. Bhutia DT. Protein energy malnutrition in India: the plight of our under five children. *J Family Med Prim Care* 2014; 3: 63–67.
20. Sahu SK, Kumar SG, Bhat BV, et al. Malnutrition among under-five children in India and strategies for control. *J Nat Sci Biol Med* 2015; 6: 18–23.
21. Meshram, II, Arlappa N, Balakrishna N, et al. Trends in the prevalence of undernutrition, nutrient and food intake and predictors of undernutrition among under five year tribal children in India. *Asia Pac J Clin Nutr* 2012; 21: 568–576.
22. Dubois L, Farmer AP, Girard M, et al. Preschool children's eating behaviours are related to dietary adequacy and body weight. *Eur J Clin Nutr* 2007; 61: 846–855.
23. Galloway AT, Fiorito L, Lee Y, et al. Parental pressure, dietary patterns, and weight status among girls who are "picky eaters". *J Am Diet Assoc* 2005; 105: 541–548.
24. Ekstein S, Laniado D, and Glick B. Does picky eating affect weight-for-length measurements in young children? *Clin Pediatr (Phila)* 2010; 49: 217–220.
25. Xue Y, Lee E, Ning K, et al. Prevalence of picky eating behaviour in Chinese school-age children and associations with anthropometric parameters and intelligence quotient. A cross-sectional study. *Appetite* 2015; 91: 248–255.
26. Chatoor I, Surles J, Ganiban J, et al. Failure to thrive and cognitive development in toddlers with infantile anorexia. *Pediatrics* 2004; 113: e440–e447.
27. Tomkins A. Malnutrition, morbidity and mortality in children and their mothers. *Proc Nutr Soc* 2000; 59: 135–146.
28. Shay NF and Mangian HF. Neurobiology of zinc-influenced eating behavior. *J Nutr* 2000; 130(Suppl 5S): 1493S–1499S.
29. Topaloglu AK, Hallioglu O, Canim A, et al. Lack of association between plasma leptin levels and appetite in children with iron deficiency. *Nutrition* 2001; 17: 657–659.
30. Stoltzfus RJ, Chway HM, Montresor A, et al. Low dose daily iron supplementation improves iron status and appetite but not anemia, whereas quarterly anthelminthic treatment improves growth, appetite and anemia in Zanzibari preschool children. *J Nutr* 2004; 134: 348–356.

31. Umeta M, West CE, Haidar J, et al. Zinc supplementation and stunted infants in Ethiopia: a randomised controlled trial. *Lancet* 2000; 355: 2021–2026.
32. Lebenthal Y, Yackobovitch-Gavan M, Lazar L, et al. Effect of a nutritional supplement on growth in short and lean prepubertal children: a prospective, randomized, double-blind, placebo-controlled study. *J Pediatr* 2014; 165: 1190–1193 e1.
33. Willett WC. *Nutritional epidemiology*. 2nd ed. New York Oxford: University Press, 1998.
34. Johnson RK, Driscoll P, and Goran MI. Comparison of multiple-pass 24-hour recall estimates of energy intake with total energy expenditure determined by the doubly labeled water method in young children. *J Am Diet Assoc* 1996; 96: 1140–1144.
35. Sukumaran A and Elizabeth FJ. Prevalence of Food Neophobia and Picky Eating: A Descriptive study among mothers of under-five children attending selected paediatric units of AIMS, Kochi, Ernakulam, Kerala State, India. *JETIR* 2015; 2.