Impact of peanut consumption in the LEAP Study: Feasibility, growth, and nutrition

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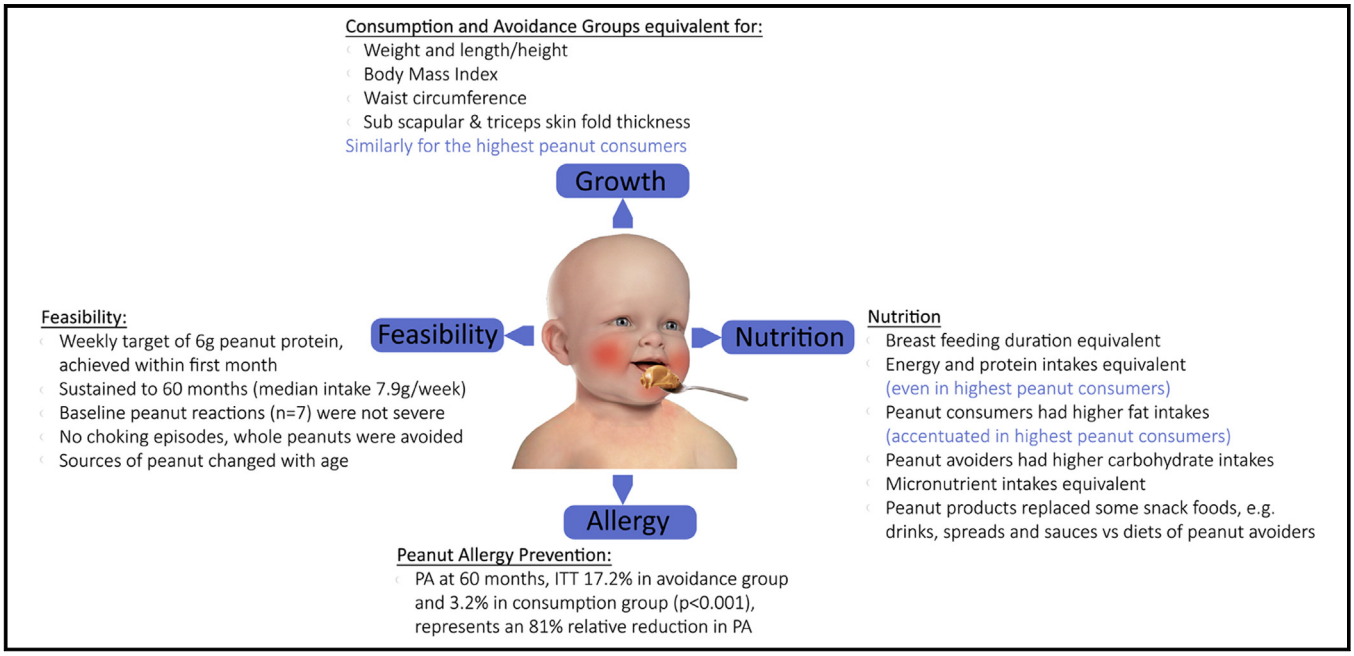
GRAPHICAL ABSTRACT



Background: Early introduction of peanut is an effective strategy to prevent peanut allergy in high-risk infants; however, feasibility and effects on growth and nutritional intake are unknown.

Objective: We sought to evaluate the feasibility of introducing peanut in infancy and explore effects on growth and nutritional intake up to age 60 months.

Methods: In the Learning Early About Peanut Allergy trial, 640 atopic infants aged 4 to 11 months were randomly assigned to consume (6 g peanut protein per week) or avoid peanut until age 60 months. Peanut consumption and early feeding practices were assessed by questionnaire. Dietary intake was evaluated with prospective food diaries. Anthropometric measurements were taken at all study visits.

Results: Peanut was successfully introduced and consumed until 60 months, with median peanut protein intake of 7.5 g/wk (interquartile range, 6.0-9.0 g/wk) in the consumption group compared with 0 g in the avoidance group. Introduction of peanut in breast-feeding infants did not affect the duration of breast-feeding. There were no differences in anthropometric measurements or energy intakes between groups at any visits. Regular peanut consumption led to differences in dietary intakes. Consumers had higher intakes of fat and avoiders had higher carbohydrate intakes; differences were greatest at the upper quartiles of peanut consumption. Protein intakes remained consistent between groups.

Conclusions: Introduction of peanut proved feasible in infants at high risk of peanut allergy and did not affect the duration of breast-feeding nor impact negatively on growth or nutrition. Energy balance was achieved in both groups through variations in intakes from fat and carbohydrate while protein homeostasis was maintained. (J Allergy Clin Immunol 2016;138:1108-18.)

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Key words: *Food allergy, allergy prevention, peanut, infant feeding, breast-feeding, nutrition, growth, prospective food diary, protein homeostasis*

Abbreviations used
BMI: Body mass index
DRV: Dietary reference value
FFQ: Food frequency questionnaire
LEAP: Learning Early About Peanut Allergy
LRNI: Lower reference nutrient intake
%TE: Percentage of total energy
RNI: Reference nutrient intake
UK: United Kingdom
WHO: World Health Organization

We recently reported that early introduction of dietary peanut results in a marked reduction in the development of peanut allergy in high-risk infants.[1] The Learning Early About Peanut Allergy (LEAP) study intervention disagrees with current World Health Organization (WHO) advice, which recommends that infants should be exclusively breast-fed for the first 6 months of life (no other food or water).[2] Similar to the dietary practices in the United States and Australia, the mean age of introduction of peanut-containing foods in the United Kingdom (UK) is 36 months and only around 8% to 10% of infants eat peanut before age 1 year.[3-5]

Many professional allergy societies now recommend the LEAP study intervention of early peanut introduction in infancy followed by ongoing regular consumption until age 60 months for the prevention of peanut allergy in high-risk infants.[6,7] This advice may in time be extended to encompass all children regardless of their risk of peanut allergy. Although regular consumption of peanut from an early age appears to be an effective strategy for the prevention of peanut allergy in high-risk infants as well as in infants recruited from a general population, there could be unexpected consequences for growth and nutrition.[1,8] Anecdotally, no adverse health consequences have been associated with this practice in countries such as Israel, where peanut is regularly consumed by infants and young children. Epidemiological studies describe beneficial health effects of regular nut consumption in children and adolescents including a lower body mass index (BMI), a higher healthy eating index, and higher intakes of micronutrients.[9,10] Furthermore, there is a long tradition of using peanut as the mainstay of nutritional fortification programs in developing countries and even in the United States as part of the supplemental nutrition program for Women, Infants and Children.[11] Despite these dietary practices, intervention studies involving regular consumption of peanut or similar energy-dense foods in early childhood are lacking in the literature.

The LEAP intervention recommended an intake of 6 g peanut protein per week, equivalent to 3 teaspoons of peanut butter, on the basis of the upper quartile of intake observed in infants in Israel (7.1 g peanut protein per month).[3] It is unknown whether this dietary recommendation is challenging to incorporate into the diet of the infant, or will lead to an imbalanced diet if eaten throughout childhood.

The objectives of this study were to evaluate the feasibility of introduction of peanut in infancy and the effects of regular ongoing consumption on growth, nutrition, and diet of infants with atopy enrolled onto a randomized controlled trial. Using data from the LEAP study, we compared infants randomized to consumption or avoidance of peanut during the first 5 years of life.

Graphical abstract image illustration: Jarrod Nielsen, Medical Media Kits.

This study was funded by the National Institute of Allergy and Infectious Diseases (award nos. UM1AI109565, NO1-AI-15416, and HHSN272200800029C) and others. This research was performed as a project of the Immune Tolerance Network, an international clinical research consortium headquartered at the Benaroya Research Institute and supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Additional support came from Food Allergy Research & Education (FARE), McLean, Virginia; the Medical Research Council & Asthma UK Centre; the UK Department of Health through the National Institute for Health Research comprehensive Biomedical Research Centre award to Guy's & St Thomas' National Health Service (NHS) Foundation Trust, in partnership with King's College London and King's College Hospital NHS Foundation Trust. The clinical trials unit is supported by the National Peanut Board, Atlanta, Georgia. The UK Food Standards Agency provided additional support for the costs of phlebotomy.

Disclosure of potential conflict of interest: M. Feeney has received research support from the National Institute of Allergy and Infectious Diseases (NIAID, National Institutes of Health [NIH]; grant nos. NO1-AI-15416 [contract] and UM1AI109565), UK Food Standards Agency (FSA), Food Allergy & Research Education (FARE), and Medical Research Council (MRC) and Asthma UK Centre; has received the BRC award to Guy's and St Thomas' National Health Service (NHS) Foundation from the UK Department of Health through the National Institute for Health Research (NIHR); and has received support for the Paediatric Allergy Clinical Trial's Unit from the National Peanut Board. G. Du Toit has received research support from the NIAID, NIH (grant nos. NO1-AI-15416 [contract] and UM1AI109565) and UK's FSA, FARE, and MRC and Asthma UK Centre; has received the BRC award to Guy's and St Thomas' NHS Foundation from the UK Department of Health through NIHR; has received support for the Paediatric Allergy Clinical Trial's Unit from the National Peanut Board; and has an equity holding in FoodMaestro. G. Roberts has received research support from the NIAID, NIH (grant nos. NO1-AI-15416 [contract] and UM1AI109565) and has received research support from FARE. P. H. Sayre has received research support from the NIH. K. Lawson has received research and travel support, fees for participation in review activities, payment for writing/reviewing the manuscript, and provision of writing assistance, medicines, equipment, or administrative support from the NIAID/NIH (grant no. UM2AI117870). H. T. Bahnson has received research support from the NIAID/NIH (grant no. UM2AI117870 and contract no. HHSN272200800029C). M. L. Sever has received research and travel support, fees for participation in review activities, payment for writing/reviewing the manuscript, and provision of writing assistance, medicines, equipment, or administrative support from the NIAID/NIH (grant no. UM2AI117870). S. Radulovic has received research support from the NIAID, NIH (grant nos. NO1-AI-15416 [contract] and UM1AI109565) and UK's FSA, FARE, and MRC and Asthma UK Centre; has received the BRC award to Guy's and St Thomas' NHS Foundation from the UK Department of Health through NIHR; and has received support for the Paediatric Allergy Clinical Trial's Unit from the National Peanut Board. G. Lack has received research support from the NIAID, NIH (grant nos. NO1-AI-15416 [contract] and UM1AI109565) and UK's FSA, FARE, and MRC and Asthma UK Centre; has received the BRC award to Guy's and St Thomas' NHS Foundation from the UK Department of Health through NIHR; has received support for the Paediatric Allergy Clinical Trial's Unit from the National Peanut Board; is on the DBV Technologies Scientific Advisory Board; has stock/stock options in DBV Technologies; and has received travel support from the National Mexican Congress of Allergy, the EAACI, the ASCIA, PAAM, the WAC, the WAO, the Institute of Medicine Committee Meeting, and the American Academy of Allergy, Asthma & Immunology. M. Plaut declares no relevant conflicts of interest. The peanut snack used in the study, called Bamba, was purchased from Osem at a discounted rate.

Received for publication February 3, 2016; revised March 30, 2016; accepted for publication April 13, 2016.

Available online June 10, 2016.

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0091-6749/$36.00

http://dx.doi.org/10.1016/j.jaci.2016.04.016

TABLE I. Infant feeding characteristics

Feeding characteristics	Avoiders (N = 321)	Consumers (N = 319)	Total (N = 640)	*P* value
Breast and formula feeding				
Participant breast-fed?				.25*
Yes, n (%)	292 (91.0)	298 (93.4)	590 (92.2)	
Age at cessation of breast-feeding (mo)				.15†
n (%)	289 (90)	290 (90.9)	579 (90.5)	
Mean ± SD	7.5 ± 5.8	8.1 ± 5.8	7.8 ± 5.8	
Breast-feeding at randomization?				.23*
Yes, n (%)	127 (39.6)	141 (44.2)	268 (41.9)	
Number of months breast-fed postrandomization				.56†
n (%)	127 (39.6)	141 (44.2)	268 (41.9)	
Mean ± SD	4.9 ± 4.8	4.7 ± 4.9	4.8 ± 4.9	
Given formula before randomization?				.52*
Yes, n (%)	287 (89.4)	290 (90.9)	577 (90.2)	
Age solid food introduced at baseline (mo)				
Earliest age any solid introduced				.93†
n (%)	321 (100)	319 (100)	640 (100)	
Mean ± SD	5.0 ± 0.9	5.0 ± 0.8	5.0 ± 0.9	
Dairy‡				.85†
n (%)	214 (66.7)	212 (66.5)	426 (66.6)	
Mean ± SD	6.2 ± 1.1	6.2 ± 1.1	6.2 ± 1.1	
Hen's egg				.28†
n (%)	99 (30.8)	100 (31.3)	199 (31.1)	
Mean ± SD	7.2 ± 1.3	7.3 ± 1.4	7.2 ± 1.4	
Wheat				.99†
n (%)	246 (76.6)	238 (74.6)	484 (75.6)	
Mean ± SD	6.4 ± 1.0	6.4 ± 1.0	6.4 ± 1.0	
Finfish				.73†
n (%)	188 (58.6)	195 (61.1)	383 (59.9)	
Mean ± SD	6.8 ± 1.1	6.8 ± 1.1	6.8 ± 1.1	
Soya				.38†
n (%)	85 (26.5)	75 (23.5)	160 (25.0)	
Mean ± SD	6.8 ± 1.7	6.6 ± 1.6	6.7 ± 1.7	
Tree nuts				.12†
n (%)	5 (1.6)	9 (2.8)	14 (2.2)	
Mean ± SD	7.4 ± 0.8	8.1 ± 1.0	7.9 ± 1.0	
Average peanut consumption (g/wk) (Source: FFQ§)				
First month of intervention				<.01†
n (%)	313 (97.5)	298 (93.4)	611 (95.5)	
Median	0.0	7.5	0.0	
First 6 mo of intervention				<.01†
n (%)	321 (100)	319 (100)	640 (100)	
Median	0.0	7.9	0.0	

*P value is from a χ^2 test comparing the percentage of subjects in the avoidance group to the consumption group.
†P value is from a Wilcoxon rank sum test comparing the distributions in the avoidance group to the distributions in the consumption group.
‡Dairy refers to solid foods (eg, yogurt or cheese).
§Source of peanut consumption comes from the FFQ.

METHODS

Study design

This study represents a planned secondary analysis from the LEAP trial, a randomized, open-label, controlled trial comparing 2 strategies to prevent peanut allergy: consumption or avoidance of peanut in high-risk infants. The primary outcomes and adverse event profile of this trial have been previously published.[1]

Dietary intervention

Infants aged 4 months to less than 11 months with severe eczema and/or egg allergy were randomly assigned to consume or avoid peanut until age 60 months. Participants randomized to peanut consumption (except those who were diagnosed with peanut allergy) were advised to eat at least 6 g peanut protein per week distributed over 3 or more meals per week until age 60 months. The preferred peanut source was Bamba, a snack food manufactured from peanut butter and puffed maize; this snack was suitable for infants and could also be easily softened to a smooth texture (with warm milk or water) and added to other infant foods, such as oatmeal. Smooth peanut butter (Sunpat and Duerr's brands) was also provided by the study center; for safety, it was advised that this be loosened using warm (cooled, boiled) water before feeding infants.[12] Because of choking risk, it was also recommended that whole peanuts be avoided during early childhood.[12] Participants randomized to avoidance (and participants who were diagnosed with peanut allergy) were given detailed dietary advice on how to avoid exposure to peanut during study participation. They were advised that avoidance of products with peanut precautionary allergen labeling (where peanut was not a listed ingredient) was unnecessary unless diagnosed peanut allergic. Further details of the dietary advice provided are available in this article's Online Repository (see Figs E1 and E2 at www.jacionline.org).

Peanut consumption monitoring

Peanut consumption was monitored using a validated food frequency questionnaire (FFQ) at intervals as detailed in the schedule of events; adherence criteria are detailed elsewhere.[1,13] For subgroup analyses, peanut

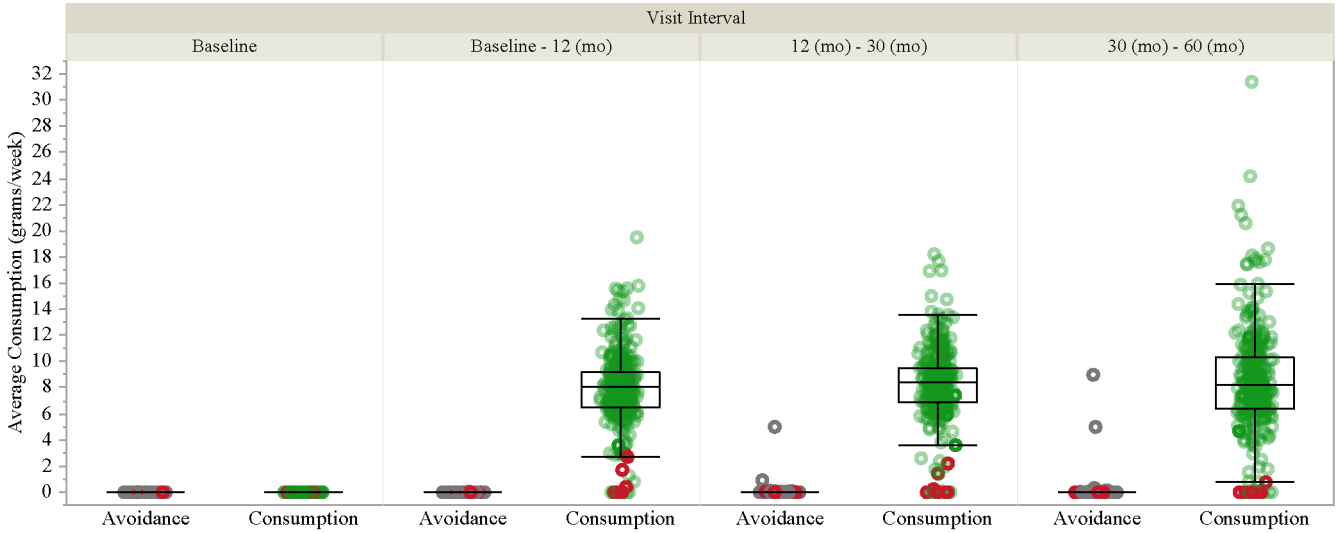

FIG 1. Average peanut consumption over time (grams peanut protein per week). Peanut consumption summarized throughout the study from FFQs completed at baseline and between study visits. Median weekly consumption during the first 2 years of life (per-protocol adherence) has been previously published.[1] *Gray dots* denote subjects randomized to the avoidance group. *Green dots* denote subjects randomized to the consumption group. *Red circles* denote participants who were peanut allergic at 60 months.

consumers were divided into quartiles on the basis of average peanut consumption throughout the study as measured by the FFQ.

Growth and anthropometric measurements

Anthropometric measurements were taken in duplicate and the mean value recorded by trained staff at each study visit. Length and height were measured to the nearest 0.1 cm, using an infant measuring table (<2 years) or wall-mounted stadiometer (Harpenden, Crymych, UK) and weight to the nearest 0.1 kg using an electronic scale (Marsden M700, Rotherham, UK). Waist circumference was measured to the nearest 0.1 cm using an anthropometric measuring tape, and triceps and subscapular skinfold thickness was measured to the nearest 0.1 mm using skinfold calipers (Holtain, Crymych, UK). BMI was calculated as weight/(height × height). Measurements were transformed into z scores using the WHO Child Growth Standards.[14]

Nutritional intake monitoring

A 3-day food diary was completed before (or shortly after) each study visit. Detailed instructions were provided by study dietitians on how to complete the diary accurately. Food diaries were checked for completeness by a dietitian/dietetic assistant at the study visit and additional information or clarification sought where required including cooking methods and portion sizes. Those who had not completed some or all of the food diary were asked to return the diary by mail after the clinic visit.

Foods and drinks were entered into Dietplan 6 (Forestfield Software Limited, Horsham, UK) and analyzed to produce average daily energy, macronutrient, and micronutrient intakes. Portion weights were assigned on the basis of information from manufacturers or food packaging and/or estimated from standard food portion sizes all scaled down for age on the basis of details recorded in the food diary and portion size resources.[15-20]

Nutrient intakes were compared with UK dietary reference values (DRVs) by age and sex.[21-23] Further details on nutritional intake monitoring are available in this article's Online Repository at www.jacionline.org.

Types of foods consumed (average daily consumption in grams) over the duration of the study were compared between avoidance and consumption groups. All food codes entered into Dietplan were mapped to 61 food groups on the basis of those reported elsewhere.[24] In addition, we separated out peanut-containing foods and specialist allergen-free products (eg, wheat/gluten-free cereals) that are more frequently eaten in this population than in the general population.

Statistical analysis

All analyses were carried out in the intention-to-treat population comparing the 2 randomized treatment groups cross-sectionally. Anthropometry and skin fold measurements were compared using general linear models adjusted for treatment assignment and sex. Percentage of total energy (%TE) intake was compared using equivariance t tests. The proportion of participants with micronutrient intakes below lower reference nutrient intake (LRNI) levels were compared with Fisher exact tests. Micronutrient intakes, total protein intake, percent of total protein intake, and average daily consumption of different types of foods were compared using Wilcoxon tests.

RESULTS

Study participants

The median age of participants at screening was 7.8 months (interquartile range, 6.3-9.1 months). The median duration of study participation was 4.4 years. Additional baseline characteristics have been previously published.[1]

Peanut consumption

In the consumption group, average peanut intake exceeded the recommended study intake within the first month (median, 7.5 g/wk; interquartile range, 6.0-9.0 g/wk) postrandomization, was sustained during the first 6 months of the intervention (median, 7.9 g/wk; interquartile range, 6.6-9.2 g/wk), and on average increased throughout the study (Table I and Fig 1). Median peanut intake in the avoidance group remained at 0 g throughout the study.

The main sources of peanut changed over time (see Fig E3 in this article's Online Repository at www.jacionline.org): up until age 21 months, participants consumed Bamba as their predominant source of peanut protein, with peanut butter becoming the

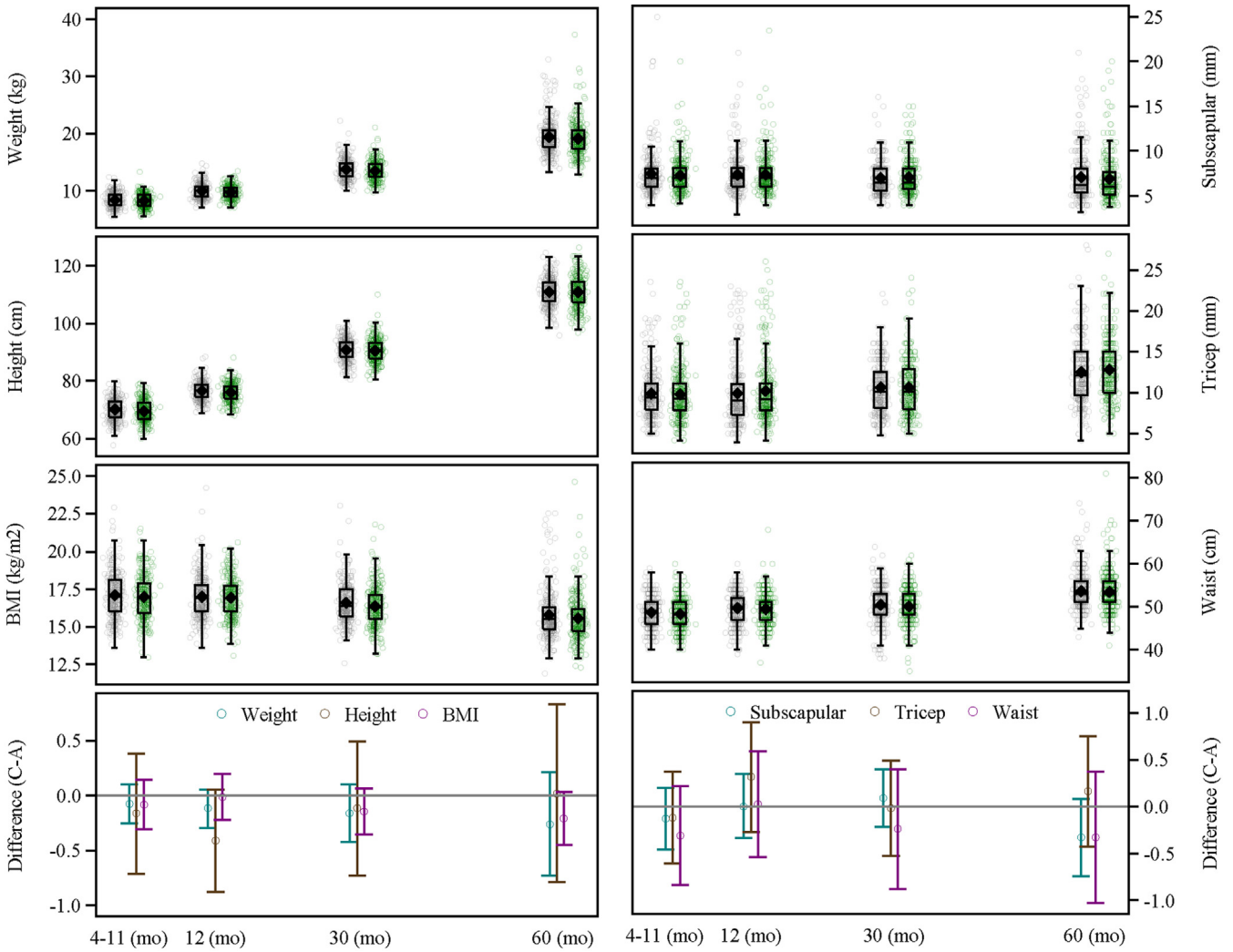

FIG 2. Growth and anthropometry in avoidance and consumption groups (ITT sample). Measures are weight, height, BMI, subscapular skinfold thickness, triceps skinfold thickness, and waist circumference. The *bottom panel* displays the difference in means (consumption – avoidance) and 95% CIs between the 2 randomized groups resulting from a model adjusted for randomization assignment and sex. *ITT,* Intent to treat.

main source as participants got older. Other sources, including peanut-containing breakfast cereals and confectionary (eg, cookies, chocolate, or snack bars containing peanut) were minor sources of peanut protein. Crushed or ground whole peanuts were eaten by some participants from age 12 months.

Infant feeding prerandomization and postrandomization

There were no differences in breast-feeding characteristics between treatment groups before or after randomization (Table I). The introduction of peanut did not result in a significantly shorter duration of breast-feeding in the peanut consumption group, even when adjusted for maternal highest level of education, gestational age at birth, and ethnicity. The mean duration of breast-feeding postrandomization was 4.7 months in the consumption group and 4.9 months in the avoidance group ($P = .56$). At the time of randomization, 290 participants had introduced infant formula in the consumption group and 287 in the avoidance group. Solid foods were introduced at a mean age of 5 months (range, 2.0-7.0 months) in both groups. There were no differences in the age at which the following food allergens were introduced prerandomization: dairy foods (excludes infant formula), egg, wheat, fish, soya, and tree nuts.

Growth, anthropometry, and nutritional intakes

Anthropometric measures and nutrient intakes were compared between randomized groups and in subgroup analyses that compared the highest quartile of peanut consumers with the peanut avoidance group.

There were no differences in weight, height, BMI, or other anthropometric measurements (waist circumference, subscapular and triceps skin fold thickness) between the consumption and avoidance groups at any time during the study (Fig 2). Even when comparing the highest quartile of peanut consumers to peanut avoiders, there were no differences in anthropometric measures (see Fig E4 in this article's Online Repository at

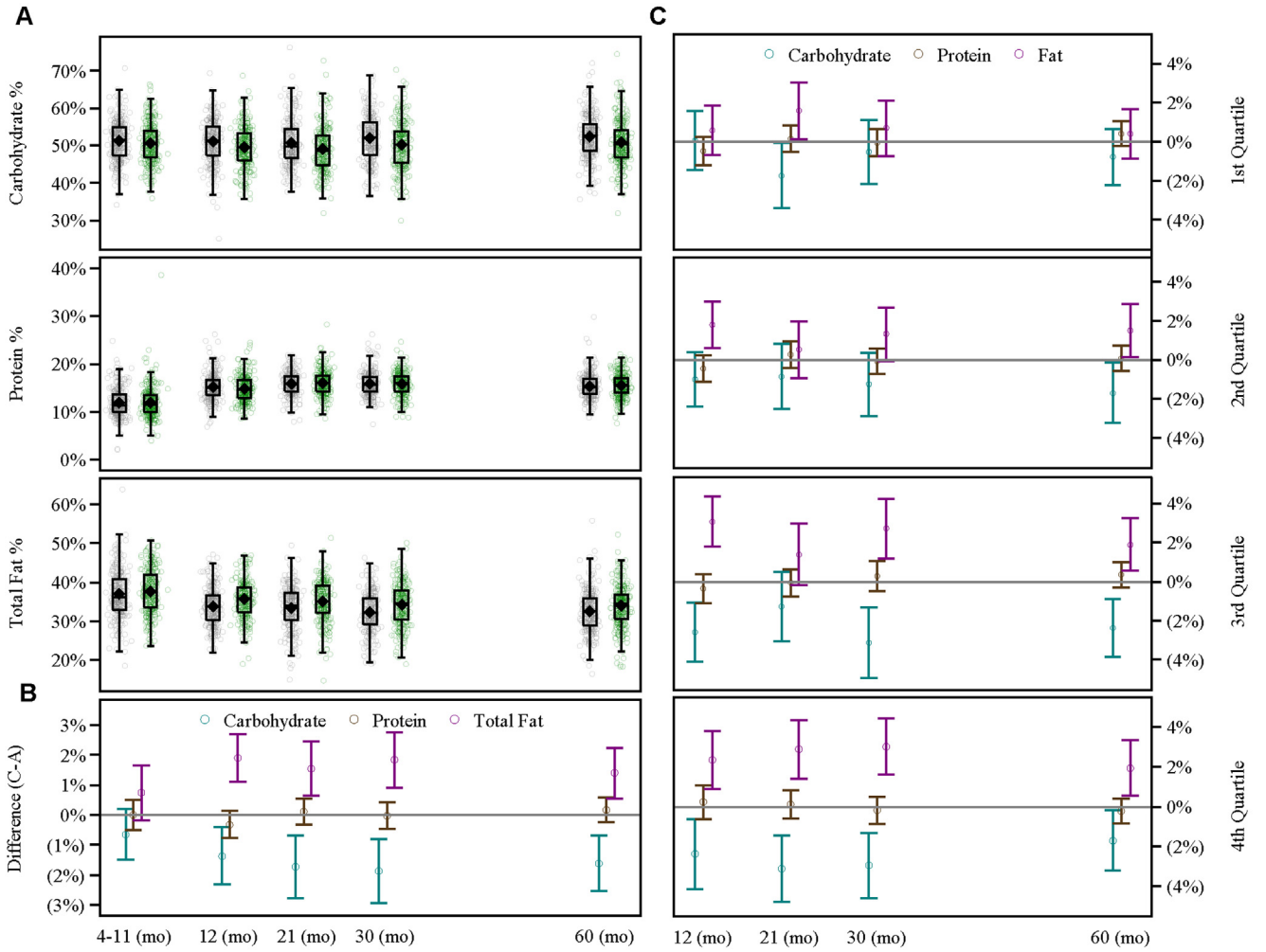

FIG 3. Macronutrient intakes in avoidance and consumption groups as %TE (ITT sample) and differences in mean macronutrient intakes by quartile of peanut consumption. **A,** All data for both randomized groups. **B,** Difference in means (consumption – avoidance) and 95% CIs between the 2 randomized groups resulting from equivariance *T* tests. **C,** Difference in means (consumption – avoidance) and 95% CIs between the avoidance group and each quartile of peanut consumption resulting from equivariance *T* tests. *ITT,* Intent to treat.

www.jacionline.org). There were also no differences in anthropometric measurements when compared with WHO Child Growth Standards (see Table E1 in this article's Online Repository at www.jacionline.org).

Food diary return rates

There were no differences between randomized groups in the numbers of food diaries returned (see Table E2 in this article's Online Repository at www.jacionline.org).

Energy and macronutrient intakes

There were no differences in total energy intakes between randomized groups at any study time point and for the highest quartile of peanut consumers compared with peanut avoiders (see Fig E5 in this article's Online Repository at www.jacionline.org).

%TE from carbohydrate was higher in the avoidance group compared with the consumption group at all postrandomization time points. Conversely, the %TE from fat was higher in the consumption group compared with the avoidance group at all postrandomization time points (Fig 3, *B*). A cross-sectional comparison of macronutrient intakes across quartiles of peanut consumption found that small differences in contributions of carbohydrate and fat to %TE were accentuated in the upper quartiles of peanut consumption whereas %TE from protein remained consistent at all postrandomization time points for all quartiles of peanut consumption (Fig 3, *C*) and in the avoidance group. When macronutrient subgroups were compared, %TE from starch was significantly higher at 21 and 30 months and %TE from sugars was significantly higher at 30 and 60 months in the avoidance group (see Fig E6, *A*, in this article's Online Repository at www.jacionline.org). There were no differences between randomized groups in % TE from saturated or polyunsaturated fatty acids at any time point. Intakes of monounsaturated fatty acids were significantly higher in the consumption group at 60 months (see Fig E6, *B*).

TABLE II. Average daily intake of select micronutrients as percentage of the reference nutrient intake (RNI*)

	4-11 (mo)			12 (mo)		
Micronutrient	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value
Iron			.50			.64
Mean ± SD	156.6 ± 82.8	151.3 ± 77.6		136.8 ± 51.3	142.4 ± 64.8	
Median	141.4	140.5		134.3	135.1	
Q1-Q3	103.2-196.6	94.9-191.1		98.1-173.1	103.7-172.1	
Calcium			.35			.02
Mean ± SD	118.7 ± 47.6	113.9 ± 43.7		213.1 ± 82.4	197.7 ± 82.5	
Median	112.9	109.9		205.1	191.5	
Q1-Q3	85.0-145.2	81.9-143.2		160.1-263.7	140.2-243.1	
Zinc			.85			.23
Mean ± SD	105.6 ± 38.0	104.9 ± 38.5		120.0 ± 35.6	115.7 ± 36.5	
Median	98.9	101.4		116.7	111.3	
Q1-Q3	78.3-123.9	72.4-128.8		93.7-141.9	90.8-139.7	
Vitamin D			.45			.58
Mean ± SD	77.0 ± 55.1	72.2 ± 54.5		69.9 ± 51.5	73.5 ± 62.3	
Median	83.3	79.8		70.8	76.6	
Q1-Q3	28.4-115.3	15.0-114.1		18.0-105.9	22.2-104.7	

P values are based on Wilcoxon tests comparing all avoiders to all consumers within each visit. Summary statistics are displayed as mean ± SD, median, and interquartile range.
*The RNI is the amount of a nutrient sufficient for 97% of the population.

TABLE III. Proportion of participants with average daily intakes of select micronutrients below the lower reference nutrient intake (LRNI*)

	4-11 (mo)			12 (mo)			21 (mo)			30 (mo)			60 (mo)		
Micronutrient	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value
Iron	21 (6.9%)	24 (8.0%)	.64	10 (3.5%)	9 (3.3%)	1.00	11 (4.1%)	9 (3.5%)	.82	15 (5.8%)	7 (2.7%)	.13	5 (1.7%)	0 (0.0%)	.06
Calcium	2 (0.7%)	5 (1.7%)	.28	0 (0.0%)	1 (0.4%)	.49	2 (0.7%)	0 (0.0%)	.50	2 (0.8%)	1 (0.4%)	1.00	4 (1.3%)	1 (0.3%)	.37
Zinc	33 (10.8%)	34 (11.4%)	.90	8 (2.8%)	10 (3.6%)	.64	6 (2.2%)	10 (3.9%)	.32	14 (5.4%)	14 (5.5%)	1.00	41 (13.8%)	39 (13.4%)	.90

Percentages are calculated from the total number of participants in each treatment group with available data within each visit. *P* values are based on Fisher exact tests.
*The LRNI is the amount that is adequate for only around 2.5% of the population.

When compared with UK DRVs, mean protein intakes in both groups were well above the reference nutrient intake (RNI) while fat intakes met DRVs at all study visits.[21] Mean carbohydrate intakes fall just above the recommended 50%TE for children aged 2 years and older in the avoidance group at all postrandomization time points. In the consumption group, carbohydrate intakes fall just below the DRV at 12 and 21 months, are at the DRV at 30 months, and just above at 60 months.[22]

Sodium, calcium, iron, zinc, vitamin D

As peanut-containing foods often have added sodium, we assessed this intake between peanut avoiders and consumers. Sodium intake was elevated for all participants (144%-244% above UK recommendations); this intake was not significantly different between randomized groups or in the highest peanut consumers compared with peanut avoiders (see Table E3, *A-C*, in this article's Online Repository at www.jacionline.org).[23,25]

Calcium, iron, zinc, and vitamin D intakes (expressed as a percentage of the RNI) were compared because intakes of these micronutrients are often compromised in children with food allergies.[26-28] There were no differences in intakes for calcium (except at 12 months), iron, or zinc. There were no differences between groups in intakes of vitamin D; however, intake decreased over time. There is no RNI for vitamin D above age 3 years so intake as a percentage of RNI at 60 months could not be calculated (Table II).

There were no differences in the proportion of participants with intakes of iron, calcium, or zinc below the LRNI (Table III). A higher than expected proportion of participants in both randomized groups had intakes of iron and zinc below the LRNI: at baseline and at age 12, 21, and 30 months for iron and at all time points for zinc (apart from the peanut avoidance group at 21 months).

Foods consumed

Participants randomized to consumption ate significantly less of the following food groups: "crisps/chips and savory snacks," "high fiber bread," "fruit juices and smoothies," "spreads" (eg, jam and yeast extract), "low-energy-dense sauces" (includes gravy, ketchup, mustard, tomato-based pasta sauce), "sunflower/other oils and fat spreads," and "dairy-free spreads" (see Tables E4 and E5 in this article's Online Repository at www.jacionline.org).

To see whether the consumption of peanut, a source of vegetable protein, led to a reduced intake of protein from other sources in order to maintain overall protein homeostasis, we

TABLE II. *(Continued)*

21 (mo)			30 (mo)			60 (mo)		
Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value
		.87			.49			.86
113.3 ± 50.4	109.6 ± 34.7		100.9 ± 32.0	102.2 ± 30.3		129.0 ± 35.3	128.5 ± 34.1	
106.4	106.1		97.2	99.7		124.7	122.4	
84.5-133.2	85.6-129.4		79.6-119.5	81.3-120.0		105.5-146.6	104.3-149.8	
		.33			.09			.25
224.4 ± 76.1	218.2 ± 72.2		212.9 ± 69.0	205.2 ± 71.0		177.1 ± 62.9	170.7 ± 55.9	
226.3	211.9		211.8	196.7		171.9	165.6	
171.9-268.5	154.9-276.5		159.8-258.5	154.9-243.7		133.5-209.6	129.3-198.5	
		.12			.35			.96
116.4 ± 35.4	110.7 ± 29.9		104.0 ± 27.7	102.9 ± 28.8		88.4 ± 25.0	88.5 ± 24.3	
110.8	109.3		103.4	100.6		86.6	86.3	
93.6-133.3	92.2-127.0		86.6-119.6	82.9-120.4		70.1-105.7	71.6-103.2	
		.11			.06			
41.5 ± 41.3	36.2 ± 38.3		34.1 ± 36.5	30.0 ± 35.5				
24.5	19.5		20.0	16.7				
9.8-64.3	8.3-50.6		9.9-43.4	8.2-40.2		Not	applicable	

TABLE IV. Comparison of sources of protein (animal or vegetable) in avoidance and consumption groups (total grams consumed and percent of total protein intake)

	12 (mo)			21 (mo)			30 (mo)			60 (mo)		
Intake	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value
Total intake (g)												
Animal			.08			.73			.20			.88
Mean ± SD	24.7 ± 9.7	23.2 ± 9.3		27.8 ± 10.5	27.6 ± 10.6		26.8 ± 9.7	25.7 ± 9.7		30.5 ± 12.3	29.6 ± 11.1	
Median	24.0	22.3		28.0	27.6		26.7	25.6		29.1	29.9	
Vegetable			.48			.16			.30			.56
Mean ± SD	13.1 ± 5.4	12.9 ± 5.2		16.2 ± 6.4	16.7 ± 5.7		17.2 ± 6.5	17.7 ± 5.9		22.1 ± 6.6	22.5 ± 6.8	
Median	12.5	11.8		14.9	16.1		16.3	16.8		21.4	21.7	
Other			.02			.52			.19			.41
Mean ± SD	0.7 ± 1.1	0.5 ± 1.0		0.9 ± 1.1	1.0 ± 2.0		1.4 ± 1.7	1.3 ± 1.7		2.2 ± 2.2	2.2 ± 2.7	
Median	0.2	0.1		0.5	0.5		0.9	0.8		1.5	1.5	
Percent of total intake												
Animal			.23			.14			.16			.79
Mean ± SD	63.9 ± 14.2	63.0 ± 20.1		60.9 ± 15.2	59.6 ± 13.9		58.2 ± 14.1	56.4 ± 14.0		54.3 ± 13.2	53.4 ± 13.9	
Median	65.3	63.9		63.7	62.6		60.1	58.1		55.3	55.9	
Vegetable			.36			.15			.08			.63
Mean ± SD	35.0 ± 12.4	36.0 ± 12.0		37.1 ± 14.5	38.1 ± 13.1		38.7 ± 13.6	40.8 ± 13.7		41.5 ± 12.8	42.5 ± 13.7	
Median	33.3	34.2		34.2	36.2		36.8	39.4		40.0	40.1	
Other			.06			.44			.21			.48
Mean ± SD	1.7 ± 2.8	1.5 ± 2.6		2.1 ± 2.5	2.2 ± 4.2		3.1 ± 3.7	2.8 ± 3.6		4.1 ± 4.0	4.2 ± 4.9	
Median	0.6	0.2		1.2	1.2		2.1	1.8		2.8	2.7	

Animal sources included the following food groups: milk/milk products, infant formula, eggs/egg dishes, meat/meat products, and fish/fish products.
Vegetable sources included cereal/cereal products, milk substitutes, meat alternatives, vegetables/potatoes, nuts/seeds, savory snacks, and fruit.
Other sources included fat spreads/oils, sugar and confectionery, nonalcoholic beverages, and miscellaneous.
P values are based on Wilcoxon tests comparing all avoiders to all consumers within each visit.

compared the sources of protein (expressed as total intake in grams and percent of total protein intake) in the avoidance and consumption groups. There were no differences between randomized groups in protein intake from different sources at any postrandomization time point (except for "other" sources at 12 months) (Table IV). However, when we compared the highest quartile of peanut consumers to the avoiders, we found significantly higher intakes of vegetable protein and lower intakes of animal protein expressed as a percent of total grams at 21, 30, and 60 months (Table V).

DISCUSSION

The LEAP study successfully introduced peanut to the diet of infants randomized to peanut consumption. The recommended intake was achieved in the first month of the study and maintained

TABLE V. Comparison of sources of protein (animal or vegetable) for all avoiders compared to the highest quartile of peanut consumption (total grams consumed and percent of total protein intake)

	12 (mo)			21 (mo)			30 (mo)			60 (mo)		
Intake	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value	Avoiders	Consumers	*P* value
Total intake (g)												
Animal			.73			.79			.25			.33
Mean ± SD	24.7 ± 9.7	23.7 ± 8.9		27.8 ± 10.5	28.0 ± 10.5		26.8 ± 9.7	25.3 ± 8.6		30.5 ± 12.3	28.5 ± 11.7	
Median	24.0	23.6		28.0	27.0		26.7	24.8		29.1	29.6	
Vegetable			.22			<.01			.01			<.01
Mean ± SD	13.1 ± 5.4	14.6 ± 6.0		16.2 ± 6.4	18.2 ± 5.0		17.2 ± 6.5	19.2 ± 5.9		22.1 ± 6.6	24.7 ± 7.1	
Median	12.5	12.6		14.9	17.9		16.3	18.3		21.4	23.8	
Other			.10			.31			.81			.18
Mean ± SD	0.7 ± 1.1	0.5 ± 0.9		0.9 ± 1.1	1.1 ± 1.3		1.4 ± 1.7	1.3 ± 1.3		2.2 ± 2.2	2.3 ± 3.5	
Median	0.2	0.0		0.5	0.8		0.9	0.9		1.5	1.2	
Percent of total intake												
Animal			.19			.02			.02			.03
Mean ± SD	63.9 ± 14.2	59.7 ± 15.1		60.9 ± 15.2	58.3 ± 11.6		58.2 ± 14.1	54.5 ± 11.6		54.3 ± 13.2	49.9 ± 13.9	
Median	65.3	65.8		63.7	60.6		60.1	55.6		55.3	52.8	
Vegetable			.21			.03			.01			.03
Mean ± SD	35.0 ± 12.4	38.0 ± 14.3		37.1 ± 14.5	39.5 ± 10.6		38.7 ± 13.6	42.4 ± 10.9		41.5 ± 12.8	45.8 ± 13.6	
Median	33.3	34.0		34.2	38.2		36.8	40.4		40.0	42.3	
Other			.11			.39			.79			.17
Mean ± SD	1.7 ± 2.8	1.5 ± 2.4		2.1 ± 2.5	2.4 ± 3.2		3.1 ± 3.7	3.1 ± 3.2		4.1 ± 4.0	4.2 ± 6.1	
Median	0.6	0.2		1.2	1.6		2.1	2.0		2.8	2.2	

P values are based on Wilcoxon tests comparing all avoiders to the highest quartile of peanut consumers within each visit.

throughout, confirming the ease with which peanut can be introduced to the infant diet. Although Bamba and peanut butter accounted for the majority of peanut intake during the early years of the trial, peanut butter consumption increased after 21 months, showing that the intervention can be undertaken using various peanut products. Despite eating different peanut-containing foods, even whole peanuts from the age of 12 months, no episodes of participant choking or aspiration were reported. However, clinicians should still emphasize that whole peanuts and chunks of peanut butter are a choking hazard in young children and should not be consumed before age 5 years.[6,7,12]

The timing of introduction of other allergenic foods was equivalent between groups before randomization. A high proportion of LEAP infants were breast-feeding at the time of introducing peanut and, reassuringly, peanut consumption did not affect the duration of breast-feeding. Although the study intervention does not comply with WHO guidelines on exclusive breast-feeding, it did not negatively impact breast-feeding itself. This is important due to concerns that introduction of solid foods before age 6 months will reduce breast-feeding duration.[29] Our finding is supported by other studies.[30,31] We know that in the United Kingdom, 30% of infants have already been introduced to solid foods by age 4 months and 75% by age 5 months, that is, do not comply with the WHO guidelines on exclusive breast-feeding.[5] In addition, for some infants, the introduction of allergenic foods between age 4 and 6 months may be important for allergy prevention.[32-34] Our results show that in high-risk infants, early consumption of peanut from age 4 months is safe and effective for allergy prevention.

Peanut consumption did not lead to differences in weight, height, BMI, or other anthropometric measurements even among the highest quartile of peanut consumers.

Macronutrient intakes in both groups were in line with UK recommendations apart from carbohydrate, which fell close to the recommended intake (DRV for 2- to 5-year-olds defined in 2015). When compared with US dietary reference intakes, which have wider ranges than the UK dietary reference intakes, both groups meet acceptable macronutrient distribution ranges for protein, fat, and carbohydrate at all study visits.[35] Sodium intakes were above UK-recommended maximum intakes in both groups but below US-recommended maximum intakes.[25] Although iron and zinc intakes were low for some participants, similar proportions of young children with intakes below the LRNI have been reported by the recent UK national dietary survey.[36]

Nutritional priorities of maintenance of energy and protein homeostasis are achieved in different ways in peanut consumers compared with avoiders. Peanut consumption led to a higher fat intake and a lower carbohydrate intake compared with avoidance while energy balance was maintained in both groups. These differences in fat and carbohydrate intakes were accentuated in the highest quartile of peanut consumers while protein intake stayed constant across quartiles of peanut consumption and in the avoidance group. We believe this shows evidence of protein regulation occurring in children from an early age. The addition of peanut-containing foods did not affect %TE intake from protein because intake from other sources (animal protein sources) was decreased to maintain protein homeostasis; energy balance was maintained by adjusting nonprotein energy intakes (ie, fat and carbohydrate). Similarly, an experimental study found that adult participants restored protein homeostasis through increased selection of high-protein foods such that they had a 13% higher protein intake after a 14-day low-protein diet compared with after a high-protein diet.[37]

Peanut consumers made different food choices to peanut avoiders. They had a lower intake of fat spreads and oils compared with the avoidance group; however, their overall intake of fat as % TE was higher. This likely reflects their using peanut butter in place of fat spreads. Peanut butter tends to be spread more generously and also parents/caregivers may have given larger portions to ensure the participants achieved their target peanut protein intake (a generous teaspoon or 8 g of smooth peanut butter contains approximately 2 g of peanut protein).

Peanut consumers also ate significantly less crisps/chips and savory snacks, high-fiber bread, fruit juices and smoothies, spreads (eg, jam and yeast extract), low-energy-dense sauces (includes gravy, ketchup, mustard, tomato-based pasta sauce), compared with peanut avoiders. Many of these foods have a high carbohydrate content supporting the lower carbohydrate intakes found in the consumption group. We are unable to say whether reduced consumption of these foods is due to the development of different taste preferences through repeat peanut exposure from infancy (increased liking for fruit and vegetables has been observed in children with repeat exposure from infancy), or whether having a predetermined snack means that other popular snack choices are not selected. Alternatively, regulatory processes may influence self-selection of specific foods to avoid imbalances in protein and total energy intake, which we observe occurs with intakes of different protein sources in the highest peanut consumers.[38-40]

The nutritional intake data are subject to the limitations of estimated food diaries, which are well described including the challenges of accurately quantifying portion sizes, overreporting, underreporting, and misreporting of dietary intakes by participants and missing nutritional data in UK food tables.[41] Nonetheless, this method provides a level of detail about dietary intake that cannot be obtained by other methods such as FFQs.[42] We have also previously described the limitations associated with the use of FFQs for the accurate determination of peanut intake.[13] The favorable LEAP nutritional results may not be generalizable to children in the general population who have less dietetic support with peanut consumption, less frequent monitoring of peanut intakes, and of growth and nutritional intakes during treatment.

Our study has several strengths. The high study retention over 5 years (98%), high adherence to the randomized intervention (92%), regular collection of peanut consumption and avoidance information by the FFQ (median number of 80 phone contacts per participant) ensure robust data were gathered. This is enhanced by the high return rate of food diaries (83% returned ≥4 food diaries) with collection on 5 occasions from infancy to 60 months alongside detailed growth data. In addition, we show that infants and young children not only maintain energy balance in response to dietary manipulation but also regulate their protein intakes.

In conclusion, this is the first randomized trial to introduce peanut in infancy and demonstrates that the intervention is easily achieved and has no adverse dietary sequelae. In addition to a reduction in peanut allergy at age 60 months, peanut consumption did not negatively impact growth in childhood even at the highest quartile of consumption. These findings are reassuring in the context of new consensus communications to feed peanut early to high-risk, atopic infants.[6,7] Interestingly, we found that despite peanut consumers making different food choices to peanut avoiders, both achieved nutritional priorities of energy and protein homeostasis. This occurs through a trade-off between carbohydrate and fat contributions to energy intake.

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We thank Daniel Rotrosen and David Raubenheimer for their critical insights and helpful comments; the many nurses, dietitians, doctors, and administrative staff of the Guy's and St Thomas' NHS Foundation Trust Children's Allergy Service for clinical and logistical assistance over the period of the study; Poling Lau for administrative support in the preparation of this manuscript; and Anna Tseng and Bunmi Raji for dietetic cover. We acknowledge Lia Weiner and Maya Barton for statistical and programming support. Above all, we are indebted to all the children and their families who generously took part in this study.

Clinical implications: Peanut consumption as a strategy to prevent peanut allergy, introduced in infancy and maintained to age 5 years, is nutritionally safe even when consumption occurs at high levels. Caregivers should be advised regarding feeding of suitable peanut products to ensure uptake and avoid choking risks in young children.

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