

Eggs in Early Complementary Feeding and Child Growth: A Randomized Controlled Trial

Lora L. Iannotti, PhD,^a Chessa K. Lutter, PhD,^b Christine P. Stewart, PhD,^c Carlos Andres Gallegos Riofrío, MA,^d Carla Malo, BS,^d Gregory Reinhart, PhD,^e Ana Palacios, MD, MA,^e Celia Karp, BS,^d Melissa Chapnick, RD, MS, MPH,^a Katherine Cox, BA,^a William F. Waters, PhD^d

abstract

BACKGROUND: Eggs are a good source of nutrients for growth and development. We hypothesized that introducing eggs early during complementary feeding would improve child nutrition.

METHODS: A randomized controlled trial was conducted in Cotopaxi Province, Ecuador, from March to December 2015. Children ages 6 to 9 months were randomly assigned to treatment (1 egg per day for 6 months [$n = 83$]) and control (no intervention [$n = 80$]) groups. Both arms received social marketing messages to encourage participation in the Lulun Project (*lulun* meaning “egg” in Kichwa). All households were visited once per week to monitor morbidity symptoms, distribute eggs, and monitor egg intakes (for egg group only). Baseline and end point outcome measures included anthropometry, dietary intake frequencies, and morbidity symptoms.

RESULTS: Mothers or other caregivers reported no allergic reactions to the eggs. Generalized linear regression modeling showed the egg intervention increased length-for-age z score by 0.63 (95% confidence interval [CI], 0.38–0.88) and weight-for-age z score by 0.61 (95% CI, 0.45–0.77). Log-binomial models with robust Poisson indicated a reduced prevalence of stunting by 47% (prevalence ratio [PR], 0.53; 95% CI, 0.37–0.77) and underweight by 74% (PR, 0.26; 95% CI, 0.10–0.70). Children in the treatment group had higher dietary intakes of eggs (PR, 1.57; 95% CI, 1.28–1.92) and reduced intake of sugar-sweetened foods (PR, 0.71; 95% CI, 0.51–0.97) compared with control.

CONCLUSIONS: The findings supported our hypothesis that early introduction of eggs significantly improved growth in young children. Generally accessible to vulnerable groups, eggs have the potential to contribute to global targets to reduce stunting.



^aBrown School, Institute for Public Health, Washington University in St Louis, St Louis, Missouri; ^bSchool of Public Health, University of Maryland, College Park, Maryland; ^cDepartment of Nutrition, University of California Davis, Davis, California; ^dInstitute for Research in Health and Nutrition, Universidad San Francisco de Quito, Quito, Pichincha, Ecuador; and ^eThe Mathile Institute for the Advancement of Human Nutrition, Dayton, Ohio

Dr Iannotti conceptualized and designed the study design, managed the study, analyzed and interpreted the data, drafted the initial manuscript, and reviewed and revised the manuscript; Drs Lutter and Stewart conceptualized and designed the study design, interpreted the data, and reviewed and revised the manuscript; Mr Gallegos Riofrío and Dr Waters conceptualized and designed the study design, managed the study, interpreted the data, and reviewed and revised the manuscript; Drs Reinhart and Palacios conceptualized and designed the study design, and reviewed and revised the manuscript; Ms Malo, Karp, and Chapnick collected the data and reviewed and revised the manuscript; Ms Cox provided support in managing the study, analyzed the data, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

WHAT'S KNOWN ON THIS SUBJECT: To our knowledge, no intervention trials have examined eggs during the complementary feeding period for growth outcomes. One review of other complementary foods in food-insecure populations showed an average effect of 0.39 height-for-age z score.

WHAT THIS STUDY ADDS: This randomized controlled trial showed that eggs introduced during infancy increased length-for-age z score by 0.63 and reduced stunting by 47%. There was no evidence of egg allergies. Eggs, generally affordable and accessible, have the potential to contribute to global stunting targets.

To cite: Iannotti LL, Lutter CK, Stewart CP, et al. Eggs in Early Complementary Feeding and Child Growth: A Randomized Controlled Trial. *Pediatrics*. 2017; 140(1):e20163459

The World Health Assembly set a global target to reduce childhood stunting by 40% by 2025. If trends continue, we will fail to meet the target by an estimated 27 million children.¹ Stunting is a complex public health problem arising from poverty and other environmental and biological factors. As such, its reduction has been a programmatic and policy enigma with relatively slow progress thus far. The consequences of stunting are well established to be increased mortality and lost developmental potential.² Certain populations are disproportionately affected. Our study focused on rural, indigenous populations of the Ecuadorian highlands where intragenerational stunting is evident and the prevalence among children <5 years (42.3%) exceeds the national average (25.2%).^{3,4}

Interventions to address stunting have largely employed fortified foods or supplements, but limited evidence exists for locally available nutritious foods. Eggs provide >50% of adequate intakes for critical nutrients in breastfeeding infants and may also offer immune protection.⁵ They are more affordable than other animal-source foods and are relatively simple to store and prepare. Evidence, primarily from upper-income countries, suggests that eggs introduced during infancy neither increases allergy risk nor reduces egg sensitization.^{6,7} Infants living in a middle-to-upper income setting with a preexisting egg allergy may be more likely to experience a reaction, but the minimal evidence from resource-poor settings suggests little to no risk for allergic reaction.^{8,9} Our study aimed to test the nutritional efficacy of giving 1 egg per day for 6 months to children beginning at ages 6 to 9 months. We hypothesized that increased consumption of eggs would improve biomarkers (specifically choline, betaine, and vitamin B₁₂) as well child growth. We report herein

our findings on child growth and stunting; biomarker outcomes are reported in a separate publication.

METHODS

Study Design and Participants

We conducted a randomized controlled trial (RCT) with parallel design in 5 rural parishes of the Cotopaxi Province in Ecuador: Pastocalle, Toacaso, Guaytacama, Tanicuchi, and Mulalo. Cotopaxi, located to the south of Quito, has a population of ~457 000 persons and is composed of the *mestizo* ethnic majority, of which ~22% self-identified as indigenous in the last census.¹⁰ The Universidad San Francisco de Quito (USFQ), responsible for field activities, canvassed the catchment parishes to identify and recruit mother (caregiver)-infant pairs. Inclusion criteria were as follows: infant aged 6 to 9 months, singleton birth, and infant in good health. Infants were not included if they had a congenital heart condition, severe acute malnutrition, or egg allergy. If mothers were not available, other caregivers were enrolled. A rolling recruitment process was used over a 5-month period to ensure that the sample size was reached in the relatively low-population density rural region.

The study was reviewed and approved by ethics committees of USFQ, Washington University in St Louis, and the Pan American Health Organization. Written informed consent was obtained from mothers or other caregivers before baseline data collection was initiated.

Randomization and Masking

A block randomization procedure was conducted at the data collection sites. Potentially eligible mother (caregiver)-infant pairs were transported to data collection sites on the basis of geographic location. These groups of generally 8 to 10

pairs were assigned randomly equally in a 1:1 ratio through an allocation concealment mechanism. Mothers or other caregivers were shown the forms labeled “alpha” and “beta,” which were then hidden, sealed, and placed in a container. Each participant then drew a form for group assignment. Field study team investigators were masked to group assignments with the exception of 1 individual responsible for enrolling and monitoring participants throughout the study. Because of the nature of the intervention, it was impossible to blind participants to study group assignment after enrollment. During the data analysis phase, investigators involved in sensitivity analyses were also masked to group assignment.

Procedures

The intervention consisted of 1 medium-sized egg (~50 g) per day, and the egg supply was provided on a weekly basis to children in the treatment group over a 6-month period. Eggs were procured from small-to-medium-sized poultry farms in the surrounding areas.

During weekly visits, mothers or other caregivers in the treatment group were reminded to give 1 egg per day to the index child. Members of the study team maintained a log report from their weekly visits with information about egg delivery, egg consumption by the child in the previous week, and any morbidities experienced (for example, skin rash, diarrhea, fever, or cough). Families in the control group were also visited every week and monitored for morbidities. Referrals to health care facilities were made when children were seriously ill.

USFQ, in collaboration with a local communication firm, developed and implemented a social marketing strategy to support the recruitment, reduce attrition, and promote full participation. A key outcome of the social marketing was the creation

of the project's brand, including its name, the Lulun Project (*lulun* meaning "egg" in Kichwa). Other components included social media, entertainment for children at data collection sites, demand-driven workshops, and flyers and posters to reinforce the role of the project in communities. The project brand and activities were designed to invoke indigenous traditions and symbols while remaining meaningful for an international audience. The field team built rapport with caregivers by combining the abovementioned strategy with standardized techniques to explain the study rationale, procedures, risks, and benefits.

Outcomes

The primary outcomes for this longitudinal study were improved anthropometric measures of child growth. Mixed methods were employed, including the collection of quantitative and qualitative data. At baseline and at end point (6 months after the intervention), caregiver-child pairs were transported to centrally located research sites or were visited at the child's household. Information was collected on socioeconomic and demographic variables, including water, hygiene, and sanitation practices and conditions; child morbidities; child diet; and child anthropometry. Child dietary intake was measured by using 24-hour recall frequency of dietary intake of foods commonly consumed in the area. This method, used globally in Demographic and Health Surveys, has been previously validated and was based on extensive formative research for foods commonly consumed in this context.^{11,12} Morbidities were assessed through 2-week recalls, with particular focus on diarrheal and respiratory conditions that are highly prevalent in this region and symptoms that might be associated with an egg allergy. Other morbidities

included fever; skin rash; persistent cough; congestion or runny nose; panting, wheezing, or difficulty breathing; and toothache or teething.

Anthropometric measures were collected at baseline and follow-up time points according to international protocols.¹³ Before the start of the study, enumerators participated in training and validation exercises over a 3-day period. Pairs of enumerators took 2 measures of child length by using a seca 417 portable infantometer (seca GmbH & Co KG, Hamburg, Germany) to the nearest 1 mm. When measures differed by 5 mm or more, a third measure was taken and averaged with the closest measure. Weight was measured by using the seca Model 874 Electronic Digital Scale (seca GmbH & Co KG) with the mother-child tare feature to the nearest 0.01 kg. Again, 2 measures were taken and when they differed by 0.05 kg or more, a third measurement was taken and averaged with the other 2 for analysis. Anthropometric measures were converted to z scores for length-for-age (LAZ), weight-for-age (WAZ), weight-for-length (WLZ), and BMI (BMIZ).¹³ Stunting was defined as LAZ < -2, underweight WAZ < -2, wasting WLZ < -2, and thin BMIZ < -2.

Statistical Analysis

Our original sample size calculations were based on the hypothesized effect size (difference-in-difference with control) of 0.35 over the 6-month period ($\alpha = .05$ and $1 - \beta = .90$), a magnitude that we considered reasonable for micronutrient biomarkers on the basis of existing literature.^{14,15} We estimated that we would require 90 children per group, assuming a 20% attrition rate. This effect size for LAZ is comparable to that reported in other trials of complementary feeding practices.¹⁶

Intention-to-treat analyses were applied for all inference analyses. Stunting prevalence in this

population exceeded the acceptable threshold for use of odds ratios (0.2105). Thus, prevalence ratios (PRs) were used to examine the egg effect and were considered analogous to relative risk in this longitudinal study.¹⁷ For the binomial outcomes of stunting and underweight, we estimated prevalence ratios by using generalized linear regression (GLM) modeling with robust Poisson. The GLM, also applied for the continuous outcomes, allowed for nonnormal distribution of parameters. Log-binomial models using the maximum likelihood estimate and the logarithm of the probability as the link function were also performed, but failed to converge. The robust Poisson, with a classic sandwich estimator to correct the inflated variance of standard Poisson, is less affected by outliers.¹⁷ Adjusted regression models included age and sex of the child and corresponding baseline measures.¹⁸ For the morbidity symptom and dietary intake models, baseline anthropometry was tested but not found to be significant. Data analyses were performed with Stata software (version 13.1; StataCorp, College Station, TX). The trial is registered at clinicaltrials.gov, identifier NCT02446873.

RESULTS

Through a rolling recruitment process from February to June 2015, 175 mother (caregiver)-infant pairs were assessed for eligibility. Four mother-infant pairs did not meet all the inclusion criteria, and another 8 mothers declined to participate because of logistics or moving from the area, blood draw concerns, or unknown reasons (Fig 1). One hundred thirty eight (85%) of the 163 enrolled and randomly assigned dyads were mother-infant pairs, whereas 25 (15%) of the enrolled were other caregivers, including grandmothers ($n = 12$), aunts ($n = 7$), fathers ($n = 4$), and sisters aged

15 and 19 years ($n = 2$), with no difference by treatment group. One hundred sixty-three children were assigned randomly to either a control group ($n = 83$) or an intervention group ($n = 80$). Losses to follow-up were less than originally anticipated ($n = 11$, 7% attrition). Reasons for losses to follow-up included refusal for final blood draw, temporary relocation, permanent relocation, and 2 pairs with unknown reasons.

Baseline characteristics presented in Table 1 were comparable. Infants were on average 7.6 months of age (SD 1.1), and 66 (41%) of 160 infants were firstborn. The mean age of mothers was 25.4 (SD 6.7) years, although 36 (23%) of 160 mothers were <19 years of age. Out of the 133 reporting, 24 mothers (18%) indicated they were single (unmarried and without a partner). Mothers completed an average of 9.0 (SD 3.1) years of education, and 73 (46%) of 160 mothers were employed outside the home. A large proportion of households were reported to be engaged in some form of food production (134 [84%] of 160 households), with tubers being the predominant crop (121 [76%] of the households). Similarly, 135 (84%) of 160 households reported owning and raising animals for food and income, with small animals, including guinea pigs and rabbits, being the most common (100 households, 63%). In addition, 93 (58%) households raised poultry.

We examined the effect of the egg intervention on child dietary intake by using a 24-hour frequency of intake of commonly consumed foods as one of the secondary outcomes (Supplemental Table 4). At end point, there was a significant, positive difference in the prevalence of children from the intervention group consuming any eggs compared with the control group. Both study arms, however, were observed to have increased the frequency of egg consumption within the previous

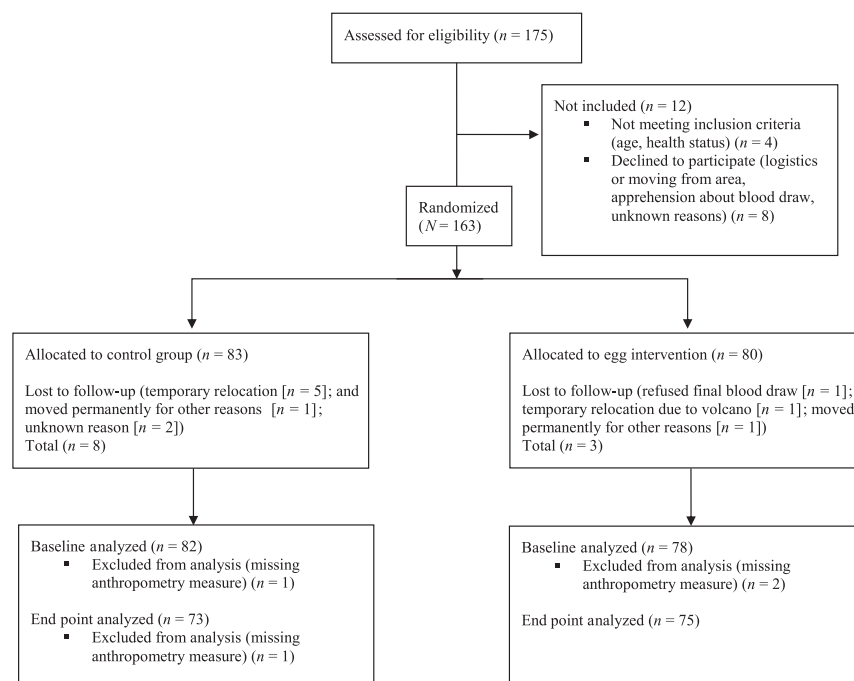


FIGURE 1
Flow diagram.

24 hours (Supplemental Table 4). Over time, both groups reported an increase in consumption of sugary foods, drinks, and sodas. In the intervention group, the prevalence of reported consumption of sugary foods, such as chocolate, sweets, candies, pastries, cakes, or cookies, was 29% lower at end point when compared with the control group ($P = .032$). The prevalence of consumption of soda was also slightly (but not statistically significantly) lower (10% vs 14%, $P = .137$). No significant differences were observed for other food items between the intervention and control groups.

Baseline prevalence of stunting was 38%, and mean LAZ was -1.90 (SD 1.01). Children in the egg group showed a higher prevalence of stunting and underweight than the control group at baseline. Child growth outcomes were improved in the egg group compared with control group across all anthropometric measures (Table 2). LAZ was significantly increased by 0.63 (95% confidence interval [CI], 0.38–0.88) at end point in the egg

group, and prevalence of stunting was reduced by 47% (PR, 0.53; 95% CI, 0.37–0.77) after adjusting for child age, sex, and the corresponding baseline anthropometry measure. Other covariates, including diarrhea morbidities, were not found to be significant predictors or mediators of anthropometric outcomes. There was a shift in the distribution of LAZ from baseline to end point for the egg group only, with statistically significant difference-in-difference between groups (Fig 2). Similarly, WAZ was increased in the treatment group compared with the control group by 0.61 (95% CI, 0.45–0.77), and the prevalence of underweight was reduced by 74%, again adjusting for child age, sex of the child, and baseline anthropometry. Weight-for-length and BMIz also increased significantly in the treatment group compared with the control group. No children developed immediate allergic reactions after consuming the eggs, as observed or reported at baseline, end point, or in the weekly monitoring visits made to households throughout the study period.

Respiratory symptoms of cough and congestion were the most commonly reported morbidities at both baseline and end point. Fever was also highly prevalent and not significantly

different by group at both time points. The prevalence of reported acute diarrhea in the previous 7 days was higher in the egg group (20 [26%] of 78 children) compared with

the control group (12 [15%] of 82 children) at baseline and increased by 5.5% points in the egg group only, resulting in a significant increase in the PR (Table 3).

TABLE 1 Baseline Characteristics, by Trial Arm

	Control (n = 82)	Eggs (n = 78)
Child		
Age, mo	7.7 (1.2)	7.4 (1.1)
Female, %	43 (52)	30 (39)
First born, %	34 (42)	32 (41)
Maternal		
Maternal age, y	25.6 (7.0)	25.2 (6.4)
Teenage mother (19 y or less), %	19 (23)	17 (22)
Education completed, y	9.2 (3.3)	8.8 (2.8)
Mother employed outside home, %	34 (41)	39 (50)
Caregiver reporting, %		
Mothers	69 (84)	66 (85)
Grandmothers	7 (2)	5 (3)
Aunts	3 (4)	4 (5)
Fathers	2 (2)	2 (3)
Sisters	1 (1)	1 (1)
Household		
No. of household members	6.2 (2.4)	6.1 (2.0)
Food production, %		
Any crops	70 (85)	64 (82)
Tubers	64 (78)	57 (73)
Legumes	41 (50)	31 (40)
Fruit or vegetables	44 (54)	38 (49)
Livestock ownership, %		
Any livestock	68 (83)	67 (86)
Poultry	48 (59)	45 (58)
Cows	32 (39)	30 (39)
Sheep, goats	15 (18)	18 (23)
Guinea pigs, rabbits	50 (61)	50 (64)
Conditional cash transfer program (Bono de Desarrollo Humano), %	21 (26)	19 (24)
Improved water source, %	81 (99)	77 (99)
Treat water, %	61 (74)	55 (71)
Flush toilet, %	76 (93)	67 (86)
Gas or electricity cooking fuel, %	70 (85)	65 (83)

Data are mean (SD) or no. (%).

DISCUSSION

This RCT tested the simple food-based intervention of providing 1 egg per day for 6 months, beginning early in the complementary feeding period, compared with control or usual infant feeding practices. We found that this produced a significant and biologically meaningful effect on child growth, notably LAZ and reduced stunting. Effect sizes for the anthropometric outcomes were substantially greater than what has been previously found in other complementary feeding trials. Adjusted longitudinal analyses of egg compared with control groups showed LAZ increased by 0.63 (95% CI, 0.38–0.88) and stunting was reduced by 47% (PR, 0.53; 95% CI, 0.37–0.77). The LAZ effect was a one-third or more increase in the global average effect size from other experimental trials of complementary foods in food-insecure populations: 0.39 (standardized mean difference; 95% CI, 0.05–0.73).¹⁹ Although the intake frequency of sugar-sweetened foods increased from baseline in both groups, there was a reduced intake frequency in the intervention group

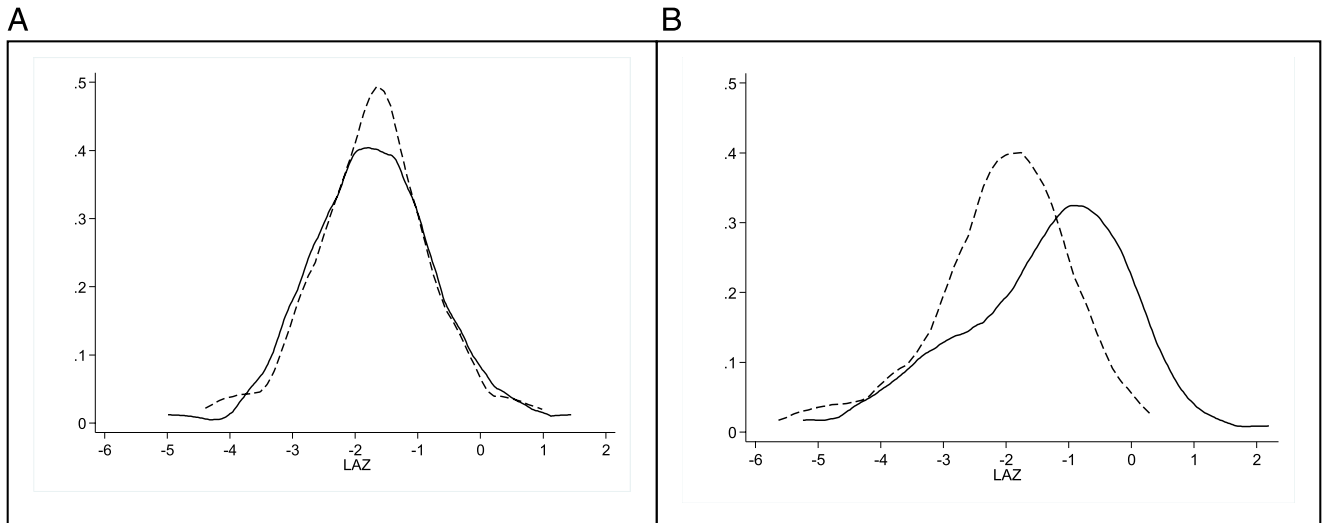
TABLE 2 Effect of the Intervention on Child Growth in a Randomized Controlled Trial of Eggs in Ecuador

	Baseline		End Point		Effect Size or PR		Effect Size or PR	
	Control (n = 82)	Egg (n = 78)	Control (n = 73)	Egg (n = 75)	Unadjusted		Adjusted ^a	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	β (95% CI)	P	β (95% CI)	P
LAZ (SD)	-1.71 (0.92)	-2.09 (1.08)	-1.71 (1.00)	-1.39 (1.35)	.64 (0.40–0.89)	<.001	.63 (0.38–0.88)	<.001
WAZ (SD)	-0.40 (0.92)	-0.91 (1.24)	-0.55 (0.85)	-0.34 (1.06)	.71 (0.53–0.90)	<.001	.61 (0.45–0.77)	<.001
WLZ (SD)	0.86 (0.99)	0.55 (0.99)	0.36 (0.81)	0.45 (0.84)	.42 (0.20–0.65)	<.001	.33 (0.14–0.51)	<.001
BMIz (SD)	0.80 (1.00)	0.42 (1.10)	0.64 (0.82)	0.68 (0.86)	.45 (0.20–0.70)	<.001	.29 (0.08–0.49)	.006
	%	%	%	%	PR (95% CI) ^b	P	PR (95% CI) ^b	P
Stunted	26 (32)	37 (47)	29 (40)	21 (28)	0.70 (0.44–1.12)	.14	0.53 (0.37–0.77)	.001
Underweight	4 (5)	10 (13)	5 (7)	4 (5)	0.78 (0.22–2.80)	.70	0.26 (0.10–0.70)	.008

Table shows results for end-point mean (SD) anthropometric measures and prevalence (no. [%], of undernutrition), as well as GLM modeling for unadjusted and adjusted effect size and PR for anthropometric outcomes, by group.

^a Adjusted for child age, sex of the child, and baseline anthropometry for the same dependent variable.

^b PR was estimated using GLM with robust Poisson.



	<i>n</i>	Mean change (SD)	95% CI
A. Control group	73	0.04 (0.08)	-0.11 to 0.19
B. Egg group	75	0.68 (0.10)	0.49 to 0.88

*t*test *P* < .001

FIGURE 2

Change in LAZ distribution at baseline (dashed) and at end point (solid). A, Control group. B, Egg group.

TABLE 3 Effect of the Intervention on Child 7-d Morbidity Symptoms in a Randomized Controlled Trial of Eggs in Ecuador

	Baseline		End Point		PR		PR	
	Control (<i>n</i> = 82)	Egg (<i>n</i> = 78)	Control (<i>n</i> = 73)	Egg (<i>n</i> = 75)	Unadjusted		Adjusted ^a	
					β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>
Fever	29 (35%)	27 (35%)	18 (24%)	24 (32%)	1.33 (0.79–2.25)	.28	1.44 (0.86–2.42)	.17
Respiratory conditions								
Difficulty breathing	21 (26%)	25 (32%)	7 (10%)	6 (8%)	.86 (0.30–2.44)	.77	1.05 (0.32–3.39)	.94
Cough	34 (42%)	40 (51%)	24 (32%)	29 (39%)	1.21 (0.78–1.87)	.40	1.25 (0.94–1.39)	.33
Congestion	35 (43%)	37 (47%)	18 (24%)	31 (42%)	1.72 (1.06–2.80)	.40	1.61 (0.98–2.62)	.06
Acute diarrhea	12 (15%)	20 (26%)	11 (15%)	23 (31%)	2.09 (1.10–3.98)	.03	1.97 (0.99–3.89)	.05
Skin conditions								
Rash	31 (38%)	21 (27%)	17 (23%)	10 (14%)	.59 (0.29–1.20)	.15	.61 (0.29–1.26)	.18
Bruises, scrapes, cuts	14 (17%)	13 (17%)	11 (15%)	6 (8%)	.55 (0.21–1.40)	.21	.47 (0.19–1.16)	.10
Toothache and/or teething	9 (11%)	9 (12%)	8 (11%)	5 (7%)	.63 (0.21–1.83)	.39	.64 (0.22–1.84)	.41

Table shows results for baseline and end-point prevalence (no. [%] of morbidity) symptoms by weekly recall and GLM modeling with robust Poisson.

^a Adjusted for child age, sex of the child, and baseline morbidity symptoms for the same dependent variable.

compared with the control group. No immediate allergic reactions to egg consumption were observed in the young children from this resource-poor setting, where the prevalence of food allergy is low.

Eggs are a complete food, safely packaged and arguably more accessible in

resource-poor populations than other complementary foods, specifically fortified foods. Despite these features, few trials in young children have examined the impacts of eggs on child growth and development. In a review of the evidence, our group found no comparable intervention study in young children from resource-poor populations in which

growth was a measured outcome.⁵ One Australian study examined the effects of n-3 fatty acid–enriched egg yolks during the complementary feeding period, compared with regular eggs and a control group, on biomarker outcomes.²⁰ Investigators showed an increase in erythrocyte docosahexaenoic acid concentrations in the n-3–enriched egg intervention

compared with the other groups and an increase in plasma iron and transferrin saturation in both egg groups when compared with the control group.²⁰ Other studies have indirectly tested the nutritional effects of eggs that are promoted through education and social marketing programs and small livestock production.^{21–24} Observational studies have linked eggs to child growth, including a recent large-scale study in India, which showed that lower egg consumption among children 0 to 23 months doubled the odds of stunting.²⁵

We hypothesized that eggs, as a high-quality food introduced early during the complementary feeding period, would have positive impacts on child growth in this population with marginal diets. Both egg yolk and egg whites contain constituents that might separately be linked to growth, although it was likely it was the combination of egg yolk and egg whites that produced the effect observed. Compared with other foods, eggs contain high concentrations of choline, a nutrient previously found to promote growth in animal models primarily.²⁶ The assemblage of amino acids in eggs has long been recognized for its quality and even applied to evaluate protein content in other foods.²⁷ Proteins are necessary for muscle tissue accretion, but may also improve absorption kinetics for minerals and other essential nutrients.²⁸ Finally, other bioactive compounds may have contributed to the large effect size, such as insulin-like growth factor 1.²⁹ The preparation methods may have also influenced the availability of energy and nutrients. In our qualitative research (W.F.W., C.A.G.R., C.K., C.K.L., C.P.S., L.L.I., unpublished observations) we showed that mothers and other caregivers primarily offered the children soft- or hard-boiled eggs, though other

cooking methods were also used, including frying the eggs with oil, preparing them as an omelet (with beets, broccoli, carrots, chard, or turnips), or adding raw eggs to soup or drinks. The limited variability in preparation, also demonstrated in the quantitative frequency of egg intake by preparation method, may explain why this variable was not found to mediate growth outcomes.

Our study carefully monitored allergic reactions to eggs, yet no incidents were observed or reported by caregivers during the weekly home visits. Egg allergies are among the most common immunoglobulin E-mediated food allergies in infants and young children, although relatively few studies have been conducted in resource-poor populations.⁹ Hence, despite mixed evidence, there is consensus that eggs may be introduced earlier in the complementary feeding period without risk of increased allergy incidence, as reflected in the revised guidelines of the American Academy of Pediatrics in 2008, among others globally.^{6,30} Concerns remain in Ecuador, although as a result of this study, the country's Ministry of Health is updating its complementary feeding guidelines to recommend the introduction of eggs at 7 months. Our study showed no effect for the egg intervention on reducing morbidity symptoms, but there was an increased prevalence of reported acute diarrhea by the caregivers in the egg group. This may have been caused by the egg intervention, potentially a non-immunoglobulin E-mediated allergy or foodborne illness because of improper preparation or handling of the eggs. However, there is also the possibility for some bias in the reporting of diarrhea, arising from attitudes and concerns about gastrointestinal problems associated with eggs in the diets of young children, as we observed in our qualitative research (W.F.W., C.A.G.R., C.K., C.K.L., C.P.S., L.L.I., unpublished

observations). Previous studies have also shown inaccurate reporting of acute diarrhea, especially in breastfed children.³¹

Similar to many low- and middle-income countries globally, Ecuador is in the throes of a nutrition and epidemiologic transition. The recent 2012 Ecuadorian National Health and Nutrition Survey showed 8.6% of children to be overweight or obese, and 13.1% of households to be experiencing double the burden with overweight or obese mothers and stunted children <5 years old.^{3,4} We observed an increase in consumption frequency of sugary foods, drinks, and soda for both groups by end point. The egg group, however, showed a lower prevalence of consumption of sugary foods such as chocolates, sweets, candies, pastries, cakes and cookies compared with the control group. We did not provide nutrition education in this study beyond the social marketing for participation in the Lulun Project and compliance for egg consumption. High-quality foods like eggs can serve a vital replacement role, whether through calorie replacement or other appetite mechanisms to address problems of the nutrition transition in other parts of the world.

Some limitations in this study should be recognized. First, although the randomization process generated comparable groups on all other observed characteristics, there were baseline differences in anthropometric and reported diarrheal symptom measures between the 2 groups. There may have been differences in growth trajectories or catch-up growth with this variation in background stunting prevalence. We accounted for these differences by adjusting for baseline anthropometric measure in all analyses and found only minor reductions in the intervention effect size. Similarly, baseline morbidity symptoms were included in regression modeling

with little or no effects. Birth weight and gestational age at birth are 2 factors that may have also influenced growth trajectories that were not tested in our study, largely because the information is often not known or recalled with accuracy. Another limitation may have been that the study was originally designed and powered to test the effect of an egg intervention on micronutrient biomarkers. Although the social marketing campaign included messages that encouraged mothers or other caregivers to give the egg to the index child only, we are aware that sharing with siblings may have occurred. However, if this occurred, it would only serve to have attenuated the effect size. Finally, although eggs are a widely available and accessible food source in most parts of the world, findings may not be generalizable to other contexts because of background stunting

prevalence or cultural acceptability, although well-designed social marketing campaigns may overcome problems of acceptability.

CONCLUSIONS

This RCT demonstrated that 1 egg per day, starting early in complementary feeding from 6 to 9 months and continuing for 6 months, significantly improved linear growth and reduced stunting in this Andean population. Moving forward, there is a need for effectiveness studies to identify scalable strategies to increase egg availability and access to vulnerable households and promote eggs early in the complementary feeding period in different cultural contexts. The efficacy of eggs might also be examined during pregnancy for impacts on fetal growth and maternal nutrition. In our view, eggs have the potential to be an affordable and

environmentally sustainable high-quality food source in populations at risk for both undernutrition and overweight and obesity.

ACKNOWLEDGMENTS

This study was funded by the Mathile Institute for the Advancement of Human Nutrition.

ABBREVIATIONS

BMIz: body mass index z score
CI: confidence interval
GLM: generalized linear regression
LAZ: length-for-age z score
PR: prevalence ratio
RCT: randomized controlled trial
USFQ: The Universidad San Francisco de Quito
WAZ: weight-for-age z score
WLZ: weight-for-length z score

The trial is registered with clinicaltrials.gov (identifier NCT02446873).

DOI: <https://doi.org/10.1542/peds.2016-3459>

Accepted for publication Mar 30, 2017

Address correspondence to Lora L. Iannotti, PhD, Washington University in St Louis, Campus Box 1196, One Brookings Drive, St Louis, MO 63130. E-mail: liannotti@wustl.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2017 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: At the time of the study, Drs Reinhart and Palacios worked for The Mathile Institute, which funded the study. The Mathile Institute has no vested interest in the outcome(s) of the study. The Mathile Institute is a not-for-profit organization that financially supports basic research in the global nutrition sector pertaining to infant and young children nutrition; the other authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: All phases of this trial were supported by The Mathile Institute for the Advancement of Human Nutrition.

POTENTIAL CONFLICT OF INTEREST: At the time of the study, Drs Reinhart and Palacios worked for The Mathile Institute, which funded the study. The Mathile Institute has no vested interest in the outcome(s) of the study. The Mathile Institute is a not-for-profit organization that financially supports basic research in the global nutrition sector pertaining to infant and young children nutrition; the other authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. International Food Policy Research Institute (IFPRI). *Global Nutrition Report 2016: From Promise to Impact: Ending Malnutrition by 2030*. Washington, DC: International Food Policy Research Institute (IFPRI); 2016
2. Black RE, Victora CG, Walker SP, et al; Maternal and Child Nutrition Study Group. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet*. 2013;382(9890):427–451
3. Freire WB, Ramirez-Luzuriaga MJ, Belmont P, et al. *Tomo I: Encuesta Nacional de Salud y Nutrición de la población ecuatoriana de cero a 59 años. ENSANUT-ECU 2012*. Quito, Ecuador: Ministerio de Salud Pública/ Instituto Nacional de Estadísticas y Censos; 2014
4. Freire WB, Silva-Jaramillo KM, Ramírez-Luzuriaga MJ, Belmont P, Waters WF. The double burden of undernutrition and excess body weight in Ecuador. *Am J Clin Nutr*. 2014;100(6):1636S–1643S
5. Iannotti LL, Lutter CK, Bunn DA, Stewart CP. Eggs: the uncracked potential for improving maternal and young child

- nutrition among the world's poor. *Nutr Rev*. 2014;72(6):355–368
6. Greer FR, Sicherer SH, Burks AW; American Academy of Pediatrics Committee on Nutrition; American Academy of Pediatrics Section on Allergy and Immunology. Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics*. 2008;121(1):183–191
 7. Bellach J, Schwarz V, Ahrens B, et al. Randomized placebo-controlled trial of hen's egg consumption for primary prevention in infants [published online ahead of print August 12, 2016]. *J Allergy Clin Immunol*. doi:10.1016/j.jaci.2016.06.045
 8. Palmer DJ, Metcalfe J, Makrides M, et al. Early regular egg exposure in infants with eczema: a randomized controlled trial. *J Allergy Clin Immunol*. 2013;132(2):387–392.e1
 9. Boye JL. Food allergies in developing and emerging economies: need for comprehensive data on prevalence rates. *Clin Transl Allergy*. 2012;2(1):25
 10. INEC (Instituto Ecuatoriano de Encuestas y Censo). *Resultados del censo 2010 de población y vivienda en el Ecuador: Fascículo Provincial Cotopaxi*. Quito, Ecuador: INEC (Instituto Ecuatoriano de Encuestas y Censo). Available at: www.ecuadorencifras.gob.ec/wp-content/descargas/Manualateral/Resultados-provinciales/cotopaxi.pdf. Accessed December 8, 2015
 11. Arimond M, Wiesmann D, Becquey E, et al. Simple food group diversity indicators predict micronutrient adequacy of women's diets in 5 diverse, resource-poor settings. *J Nutr*. 2010;140(11):2059S–2069S
 12. Gallegos CA, Freire W, Waters W. *Assessment of the food situation of the population of Ecuador* [In Spanish]. Quito, Ecuador: Secretaría Nacional de Planificación y Desarrollo (SENPLADES); 2010
 13. World Health Organization (WHO). *The WHO Child Growth Standards*. Geneva, Switzerland: World Health Organization; 2006. Available at: www.who.int/childgrowth/en/. Accessed May 25, 2016
 14. Taneja S, Strand TA, Kumar T, et al. Folic acid and vitamin B-12 supplementation and common infections in 6–30-month-old children in India: a randomized placebo-controlled trial. *Am J Clin Nutr*. 2013;98(3):731–737
 15. Jones KM, Ramirez-Zea M, Zuleta C, Allen LH. Prevalent vitamin B-12 deficiency in twelve-month-old guatemalan infants is predicted by maternal B-12 deficiency and infant diet. *J Nutr*. 2007;137(5):1307–1313
 16. Dewey KG, Adu-Afaruwah S. Systematic review of the efficacy and effectiveness of complementary feeding interventions in developing countries. *Matern Child Nutr*. 2008;4(suppl 1):24–85
 17. Petersen MR, Deddens JA. A comparison of two methods for estimating prevalence ratios. *BMC Med Res Methodol*. 2008;8:9
 18. Victora CG, de Onis M, Hallal PC, Blössner M, Shrimpton R. Worldwide timing of growth faltering: revisiting implications for interventions. *Pediatrics*. 2010;125(3). Available at: www.pediatrics.org/cgi/content/full/125/3/e473
 19. Bhutta ZA, Das JK, Rizvi A, et al; Lancet Nutrition Interventions Review Group; Maternal and Child Nutrition Study Group. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet*. 2013;382(9890):452–477
 20. Makrides M, Hawkes JS, Neumann MA, Gibson RA. Nutritional effect of including egg yolk in the weaning diet of breast-fed and formula-fed infants: a randomized controlled trial. *Am J Clin Nutr*. 2002;75(6):1084–1092
 21. Guldán GS, Fan HC, Ma X, Ni ZZ, Xiang X, Tang MZ. Culturally appropriate nutrition education improves infant feeding and growth in rural Sichuan, China. *J Nutr*. 2000;130(5):1204–1211
 22. de Pee S, Bloem MW, Satoto, et al. Impact of a social marketing campaign promoting dark-green leafy vegetables and eggs in central Java, Indonesia. *Int J Vitam Nutr Res*. 1998;68(6):389–398
 23. Nielsen H, Roos N, Thilsted SH. The impact of semi-scavenging poultry production on the consumption of animal source foods by women and girls in Bangladesh. *J Nutr*. 2003;133(11 suppl 2):4027S–4030S
 24. Galal OM, Harrison GG, Abdou AI, Zein el Abedin A. The impact of a small-scale agricultural intervention on socio-economic and health status. *Food Nutr (Roma)*. 1987;13(1):35–43
 25. Aguayo VM, Nair R, Badgaiyan N, Krishna V. Determinants of stunting and poor linear growth in children under 2 years of age in India: an in-depth analysis of Maharashtra's comprehensive nutrition survey. *Matern Child Nutr*. 2016;12(suppl 1):121–140
 26. Zeisel SH, da Costa KA. Choline: an essential nutrient for public health. *Nutr Rev*. 2009;67(11):615–623
 27. Dubin S, McKee K, Battish S. Essential amino acid reference profile affects the evaluation of enteral feeding products. *J Am Diet Assoc*. 1994;94(8):884–887
 28. Lönnerdal B, Lien EL. Nutritional and physiologic significance of alpha-lactalbumin in infants. *Nutr Rev*. 2003;61(9):295–305
 29. Scavo L, Alemany J, Roth J, de Pablo F. Insulin-like growth factor I activity is stored in the yolk of the avian egg. *Biochem Biophys Res Commun*. 1989;162(3):1167–1173
 30. Fleischer DM, Spergel JM, Assa'ad AH, Pongracic JA. Primary prevention of allergic disease through nutritional interventions. *J Allergy Clin Immunol Pract*. 2013;1(1):29–36
 31. Schmidt WP, Cairncross S. Household water treatment in poor populations: is there enough evidence for scaling up now? *Environ Sci Technol*. 2009;43(4):986–992

Eggs in Early Complementary Feeding and Child Growth: A Randomized Controlled Trial

Lora L. Iannotti, Chessa K. Lutter, Christine P. Stewart, Carlos Andres Gallegos Riofrío, Carla Malo, Gregory Reinhart, Ana Palacios, Celia Karp, Melissa Chapnick, Katherine Cox and William F. Waters

Pediatrics 2017;140;

DOI: 10.1542/peds.2016-3459 originally published online June 7, 2017;

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/140/1/e20163459
Supplementary Material	Supplementary material can be found at: http://pediatrics.aappublications.org/content/suppl/2017/06/05/peds.2016-3459.DCSupplemental
References	This article cites 26 articles, 8 of which you can access for free at: http://pediatrics.aappublications.org/content/140/1/e20163459.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Current Policy http://classic.pediatrics.aappublications.org/cgi/collection/current_policy Developmental/Behavioral Pediatrics http://classic.pediatrics.aappublications.org/cgi/collection/development:behavioral_issues_sub Growth/Development Milestones http://classic.pediatrics.aappublications.org/cgi/collection/growth:development_milestones_sub Nutrition http://classic.pediatrics.aappublications.org/cgi/collection/nutrition_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: https://shop.aap.org/licensing-permissions/
Reprints	Information about ordering reprints can be found online: http://classic.pediatrics.aappublications.org/content/reprints

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since . Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2017 by the American Academy of Pediatrics. All rights reserved. Print ISSN:

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Eggs in Early Complementary Feeding and Child Growth: A Randomized Controlled Trial

Lora L. Iannotti, Chessa K. Lutter, Christine P. Stewart, Carlos Andres Gallegos Riofrío, Carla Malo, Gregory Reinhart, Ana Palacios, Celia Karp, Melissa Chapnick, Katherine Cox and William F. Waters

Pediatrics 2017;140;

DOI: 10.1542/peds.2016-3459 originally published online June 7, 2017;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/140/1/e20163459>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since . Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2017 by the American Academy of Pediatrics. All rights reserved. Print ISSN:

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

