Comparison of Linear Growth Patterns in the First Three Years of Life Across Two Generations in Guatemala

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ABSTRACT. ***Objective.*** **The secular increase in height is assumed to result from long-term improvements in nutritional intakes and reductions in infectious disease burdens. Nutritional supplementation in early life reduces stunting in chronically undernourished populations. It is not known whether these improvements have an impact on the growth of subsequent generations. Our objective was to estimate the intergenerational effect on offspring length of improved nutrition in the mother's early childhood.**

Methods. **We studied 283 mother–child pairs (mothers born 1969–1977; children born 1996–1999). The mothers had received nutritional supplementation—either atole (enhanced protein-energy) or fresco (moderate energy, no protein), with both containing vitamins and minerals—prenatally and up to age 7 y as part of a community trial conducted in 4 villages in Guatemala. Length was measured on repeated occasions to 36 months of age in both mothers and children. Growth was modeled as a fractional polynomial.**

Results. **Children grew faster than their mothers. Children of mothers who received atole grew faster than children of women who received fresco. In both groups, lengths of individual children were positively correlated with lengths of their own mothers at the same ages. Correlations were generally stronger when the mothers had received atole in early life.**

Conclusion. **We have confirmed a secular trend in growth of children in a developing country setting. The rate of child growth reflects, in part, the growth pattern of the mother, including improvements to that pattern resulting from nutritional supplementation.** ***Pediatrics*** **2004;113:e270–e275. URL: http://www.pediatrics.org/cgi/content/full/113/3/e270;** ***children, energy, Guatemala, growth, intergenerational effects, nutrition, protein, supplementation.***

ABBREVIATION. SD, standard deviation.

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In many countries, there has been a secular trend of increased attained height.[1] It has been recognized for many years that inadequate early nutrition and high burdens of infectious disease contribute to growth deficiency in children.[2] Stunting, which has its origins in prenatal and early postnatal growth failure,[3] increases the risk, later in life, for adverse pregnancy outcomes, including low birth weight,[4] thus perpetuating the cycle of undernutrition.

Growth deficits attributable to undernutrition can sometimes be ameliorated with improved nutrition in the first few years of life.[5] Increasing the growth rates of girls, if it translates to improved growth rates in their children, represents a powerful long-term strategy for improving public health in developing countries. We have previously shown that provision of enhanced nutrition supplementation early in postnatal life results in improved growth,[5] whereas exposure to nutritional supplementation, especially after age 3, results in improved growth in the subsequent generation.[6] However, that analysis did not compare the growth patterns of the 2 generations, and we are aware of no other research that has specifically compared growth patterns across generations. We therefore evaluated the associations between the growth patterns of mothers and their children. Specifically, we tested the hypothesis that improved growth as a result of improved nutrition in the first 2 years of life among girls would result in better growth in their offspring. The study, originally a community-randomized controlled trial of nutritional supplementation, was conducted in Guatemala.

METHODS

The data for the present analysis derive from research conducted between 1969 and 1999 among 3 generations of residents of 4 villages in eastern Guatemala. From 1969 to 1977, the Institute of Nutrition of Central America and Panama conducted a controlled intervention trial in 4 rural communities to study the effects of nutrition supplementation on child growth and development. The 4 villages were paired by size and allocated randomly within pairs to 1 of 2 supplements. One pair received atole, a nutritious drink with a high-protein (6.4 g/100 mL) and moderate-energy (91 kcal/100 mL) content. The other pair received Fresco, a nonprotein, fruit-flavored sweetened drink that provided 33 kcal/100 mL. Both supplements were fortified with selected vitamins and minerals. Supplements were freely available to all village residents twice each day (mid-morning and mid-afternoon) in a central location in the village, although only intakes of supplement by pregnant and lactating women and children younger than 7 years were recorded. Child length was measured using a portable length board at 15 days and then at 3-month intervals through age 2 y, after which height was measured every 6 months using a portable stadiometer. Compared with the fresco group, the cohort of children who were provided with atole supplement experienced reduced infant mortality rates and improved growth rates through 3 years of age, and birth weight was associated with maternal energy intake in both the atole and fresco groups.[7]

From 1996 to 1999, we conducted a prospective study of pregnancy and child growth in the same 4 villages. All women of childbearing age, regardless of participation in the original supplementation study, were regularly screened for pregnancy, and identified pregnancies were followed through delivery. Mothers and children were then studied intensively until the child reached 36 months of age. Child length was measured at birth, monthly through age 6 months, every 3 months through age 24 months, and then at 30 and 36 months using a portable length board. All phases of the study were approved by the Institutional Review Boards at Emory and Institute of Nutrition of Central America and Panama, and informed consent was obtained for all measurements.

Statistical Methods

Data are available for 3 generations, which we denote as grandmothers (G1; participated as adults in the 1969–1977 study), mothers (G2; children during the 1969–1977 study), and children (G3; born during the 1996–1999 study). Data from individuals from the G2 and G3 generations are included in this analysis. G3 births to in-migrant women, which were followed and studied during 1996–1999 but for whom maternal early growth patterns are unknown, and to out-migrants, who were not studied in the follow-up, were excluded from this analysis.

Variable Definitions

Length is the primary variable. Because of study closeout in 1999, few G3 children reached 36 months of age during the data collection period, and the G3 length data are right censored. To be eligible for the present analysis, at least 3 measures of length before age 24 months had to be available for both the mother and the child. Child age at the time of each body length measurement was rounded to the nearest month. Treatment group is a dichotomous variable indicating the type of nutrition intervention (atole or fresco). Gestational age was categorized as term (37 or more completed weeks), preterm (36 or fewer completed weeks), or unknown. Child birth order was categorized as 1 when born as the first or second child of the family and 0 when otherwise. Twin status is a dichotomous variable. Socioeconomic status was derived from a scale that was based on household assets in 1996, scaled to result in a mean of 0 and a standard deviation (SD) of 1 in the total population.

Model Development

We modeled growth as a fractional polynomial function of age,[8] using all available data through age 36 months for G2 mothers and for G3 boys and girls separately. As there is a wide range of possible models available, we restricted our analysis to 6 models of fractional polynomials of degree = 2 involving terms of ln(x), sqrt(x), x, x^2, and x^3.[9,10] From among these models, we chose the final model for analysis on the basis of considerations of model fit and coherence of the model with known growth trajectories of preadolescent children. The final model selected was length = $\beta_0+\beta_1$[ln(age + 9)] + β_2[sqrt(age + 9)], where age is expressed in months. A shift in scale for age is necessary as ln(age) is undefined at age = 0 (birth). This model resulted in the smallest Akaike information criterion value in modeling the growth of the G2 mothers and the G3 children, whether considered as a single pooled sample or stratified by gender (data not shown).

We compared the growth pattern of the G2 and G3 generations by comparing the resulting coefficients. Specifically, we tested the significance of the partial-F statistic for a full model of the form

length = β_0 + β_1[ln(age + 9)] + β_2[sqrt(age + 9)] + β_3(group) + β_4[ln(age + 9)*group] + β_5[sqrt(age + 9)] (1)

against a reduced model of the form

β_0 + β_1[ln(age + 9)] + β_2[sqrt(age + 9)] (2)

where group is an indicator variable that takes the value 1 or 0 for specific contrasts and the models are fitted for the subset of the study population of interest for the specified contrast. A 3 degree of freedom test of H_0:β_3 = β_4 = β_5 = 0 was used to assess the overall coincidence of the fitted lines. Thus, for example, by setting the group variable to 1 if the G2 mother was born in an atole village and 0 if not and by restricting the analysis to the G2 data, we can test whether the growth pattern of the G2 mothers was affected by the type of supplement received. We compared growth patterns of boys versus girls and mothers versus children within treatment groups, as well as patterns of growth of boys and girls within the G3 generation across treatment groups. These analyses were performed with adjustment for birth order (first vs other), twin status (yes/no), and gestational age (term, preterm, missing) by adding terms for these covariate in models 1 and 2

We also computed person-specific growth curves, by fitting the mixed effect models for the *i*th mother and her *j*th child pairs

Length_{mi} = β_{m0} + β_{m1}[ln(age + 9)] + β_{m2}[sqrt(age + 9)] + β_{mi0} + β_{mi1}[ln(age + 9)] (3)

Length_{cij} = β_{c0} + β_{c1}[ln(age + 9)] + β_{c2}[sqrt(age + 9)] + β_{ci0} + β_{ci1}[ln(age + 9)] (4)

where {β_{m0} + β_{m1}[ln(age + 9)] + β_{m2}[sqrt(age + 9)]} represents the G2 (mother's) population growth curve and {β_{c0} + β_{c1}[ln(age + 9)] + β_{c2}[sqrt(age + 9)]} represents the G3 (children's) population growth curve; β_{mi0} and β_{mi1} are random intercept and slope deviations (with respect to logarithm of age) of the *i*th mother from the population growth curve; and β_{ci0} and β_{ci1} are random intercept and slope deviations (with respect to logarithm of age) of the *j*th child's length from the population growth. These models provide individual growth curves, for example, (β_{m0} + β_{mi0}) + (β_{m1} + β_{mi1})[ln(age + 9)] + β_{m2}[sqrt(age + 9)] and (β_{c0} + β_{ci0}) + (β_{c1} + β_{ci1}) [ln(age + 9)] + β_{c2}[sqrt(age + 9)] for the *i*th mother and her child's growth curves, respectively. We did not include a random square root term in our models because we found that there was very little individual deviation from the population square root term. To determine whether the G3 child's growth curve is similar to his or her mother's growth curve, we computed the correlation of the child's growth slope with respect to logarithm of age with the mother's growth slope, ie, corr(β_{c1} + β_{ci1}, β_{m1} + β_{mi1}) = corr(β_{ci1}, β_{mi1}). This is the correlation between the linear deviation from the group mean and can be estimated by using the pair estimates for (β_{ci1}, β_{mi1}) predicted from models 3 and 4. Because the (β_{ci1}, β_{mi1}) are predicted values, the usual standard error formula for the sample correlation coefficient cannot be used for statistical inference. We used a bootstrap approach to obtain valid standard error for the estimated correlation. Specifically, we took 200 bootstrap samples, in which each bootstrap sample is a random sample with replacement from all G2 mothers. Then we fitted the above mixed-effect models for the selected mothers and all her children, respectively, for each bootstrap sample and computed correlation estimates for corr(β_{ci1}, β_{mi1}) based on the 200 bootstrap samples. The standard deviation of these 200 correlation estimates is the bootstrap standard error for the estimated correlation from the original sample. For comparison purpose, we also computed the correlation between mother and offspring using available observed lengths at 3-month intervals through age 24 months and at 30 months. We compared the observed correlations across treatment groups using a *t* test after transforming the correlation coefficients to ensure normality. The above analyses were conducted for atole and fresco villages separately, and we have adjusted for G2 and G3 twin status, birth order, and gestational age, and G3 gender by including the covariates terms in the models.

All analyses were conducted using SAS software version 8.2 (SAS Institute, Cary, NC). SAS procedure MIXED was used to fit models 1 through 4. We adjusted for repeated measurements of length variable taken for the same individual by specifying a spatial correlation structure with age as distance.

RESULTS

Our data set included 283 mother–child pairs born to 197 women. The mothers provided a mean of 8.6 measures of length (range: 3–12), whereas the children provided a mean of 9.7 measures of length (range: 3–19). Selected characteristics of the 2 generations, by treatment allocation in 1969–1977, are presented in Table 1.

TABLE 1. Selected Characteristics of 2 Generations of Participants in the Oriente Longitudinal Study, Guatemala, 1969–1999, by Type of Supplementation Received

	Atole (Mean ± SD [N]* or % [N])	Fresco (Mean ± SD [N]* or % [N])	P†
G3 (child) characteristics			
Gestational age, week	39.4 ± 2.2 (120)	38.6 ± 4.9 (101)	.1
Birth weight, kg	3.04 ± 0.47 (132)	2.95 ± 0.47 (123)	.2
Birth length, cm	48.6 ± 2.2 (130)	48.2 ± 2.3 (117)	.13
Male	52.9% (140)	55.2% (143)	.7
First or second born	43.6% (140)	61.5% (143)	<.01
Twin	2.2% (139)	1.4% (139)	.3
G2 (maternal) characteristics			
Gestational age, week	39.9 ± 2.27 (63)	39.2 ± 4.01 (63)	.2
Birth weight, kg	3.09 ± 0.40 (69)	3.0 ± 0.42 (73)	.2
Birth length, cm	49.3 ± 2.2 (69)	49.5 ± 2.1 (61)	.59
First or second born	22.5% (89)	30.3 (89)	.2
Twin	4.5% (89)	2.3% (89)	.2
SES in 1996	−0.2 ± 0.9 (93)	−0.3 ± 1.0 (96)	.7
Completed primary school (≥6th grade)	20.6% (97)	40.8% (98)	<.01

SES indicates socioeconomic status.
* N = number of nonmissing values for that variable.
† t test for continuous variables, χ^2 test or Fisher exact test for discrete variables.

The G1 generation was stunted as adults, and their height did not differ by treatment allocation.[11] Both G2 and G3 generations experienced marked growth failure. Birth lengths were 0.61 SD below the World Health Organization reference population median, and by 12 months of age the G2 generation mean length was 2.35 SD below the median, whereas the G3 generation was less stunted at 12 months, at 1.45 SD below the median, after experiencing a period of rapid growth in the first 3 months of life (Fig 1). In the G3 generation, there was some improvement in the mean z score after 18 months of age. The polynomial functions resulting from models fit on selected subsets of the study population are provided in Table 2. Both terms were statistically significant ($P < .01$) in all G3 models, whereas the square root term was not significant ($P > .10$) for both atole and fresco G2 women. Table 2 also provides specific tests of overall coincidence. All but 1 of the pairs of fitted growth lines were noncoincident; the exception was for G3 girls, for whom the hypothesis of coincidence between those born into atole villages and those born into fresco villages could not be rejected ($P = .17$). On the basis of the fitted growth curves, the G3 children were longer than their mothers in both atole and fresco groups at all ages, with boys being taller than girls (Fig 2). All of these lines fit the data well, with r^2 values in the range .88 to .92.

The correlation between the linear deviation from the group mean was 0.45 (95% confidence interval: 0.31–0.59 based on the bootstrap standard error) for the atole group and 0.24 (95% confidence interval: 0.07–0.41 based on the bootstrap standard error) for the fresco group. Mother–child correlations in ob-

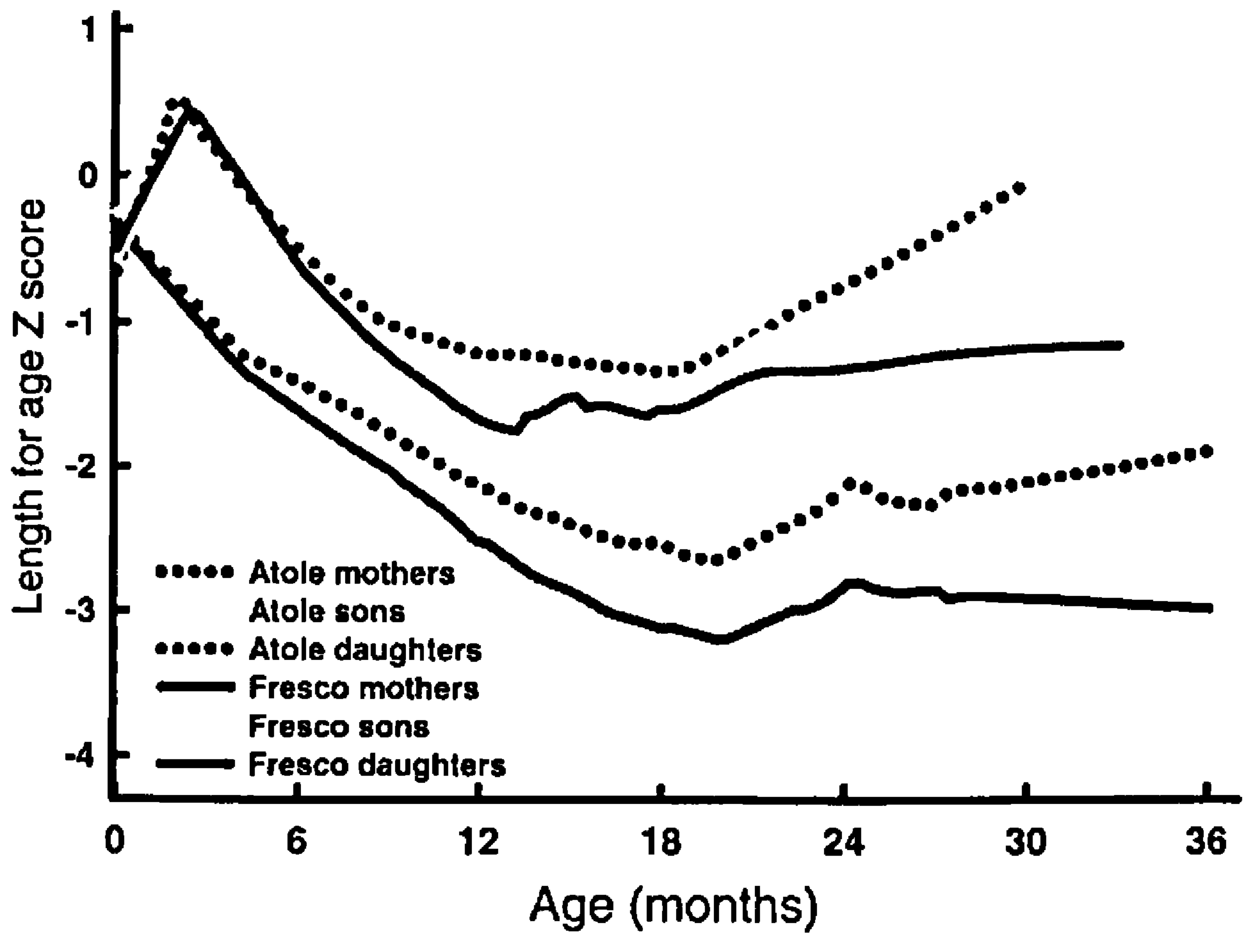

Fig 1. Growth of women and their children in the first 3 years of life, expressed as deviations from the World Health Organization reference population, Guatemala 1969–1977 and 1996–1999.

TABLE 2. Coefficients for a Polynomial Model* of Linear Growth From Birth to 36 Months, Among Selected Subsets of Women Exposed Early in Life to Nutrition Supplementation and Their Own Children, Guatemala, and Tests of Homogeneity of Coefficients Across Generations, Genders, and Treatment Groups

	N	Intercept	β_1 (Log Term)	β_2 (Square Root Term)	Coincidence†	
					Partial *F*	*P* Value
Mothers vs daughters						
Mothers	106	−1.5	23.58	−0.92	76.2	<.001
Daughters	130	−30.4	49.43	−10.75		
Mothers vs sons						
Mothers	127	0.2	22.03	−0.33	161.0	<.001
Sons	153	−34.2	53.41	−12.16		
Mothers: atole vs fresco						
Atole	97	−3.6	24.41	−0.79	13.1	<.001
Fresco	100	0.3	23.27	−1.13		
Daughters: atole vs fresco						
Atole	66	−29.8	49.02	10.38	1.7	.17
Fresco	64	−24.7	44.32	−8.61		
Sons: atole vs fresco						
Atole	74	−32.4	54.99	−12.84	4.2	.007
Fresco	79	−26.6	48.03	−9.89		
Atole: mothers vs daughters						
Mothers	55	−0.5	24.69	−1.08	37.2	<.001
Daughters	66	−29.6	51.76	−11.67		
Atole: sons vs daughters						
Sons	74	35.2	54.75	12.74	6.8	<.001
Daughters	66	−30.0	48.11	−9.96		
Fresco: mothers vs daughters						
Mothers	51	1.6	21.62	−0.49	42.9	<.001
Daughters	64	−27.9	46.52	−9.60		
Fresco: sons vs daughters						
Sons	79	−26.9	48.02	−9.87	4.1	.008
Daughters	64	−23.1	44.45	−8.67		

* Length = $\beta_0 + \beta_1 * \log(\text{Age} + 9) + \beta_2 * \text{sqrt}(\text{Age} + 9)$ estimated by repeated measures regression to account for multiple siblings within families and adjusted for birth order (first vs other), twin status (yes/no), and gestational age (term, preterm, missing).
† Tests of coincidence used a 3 degree of freedom partial F-test.

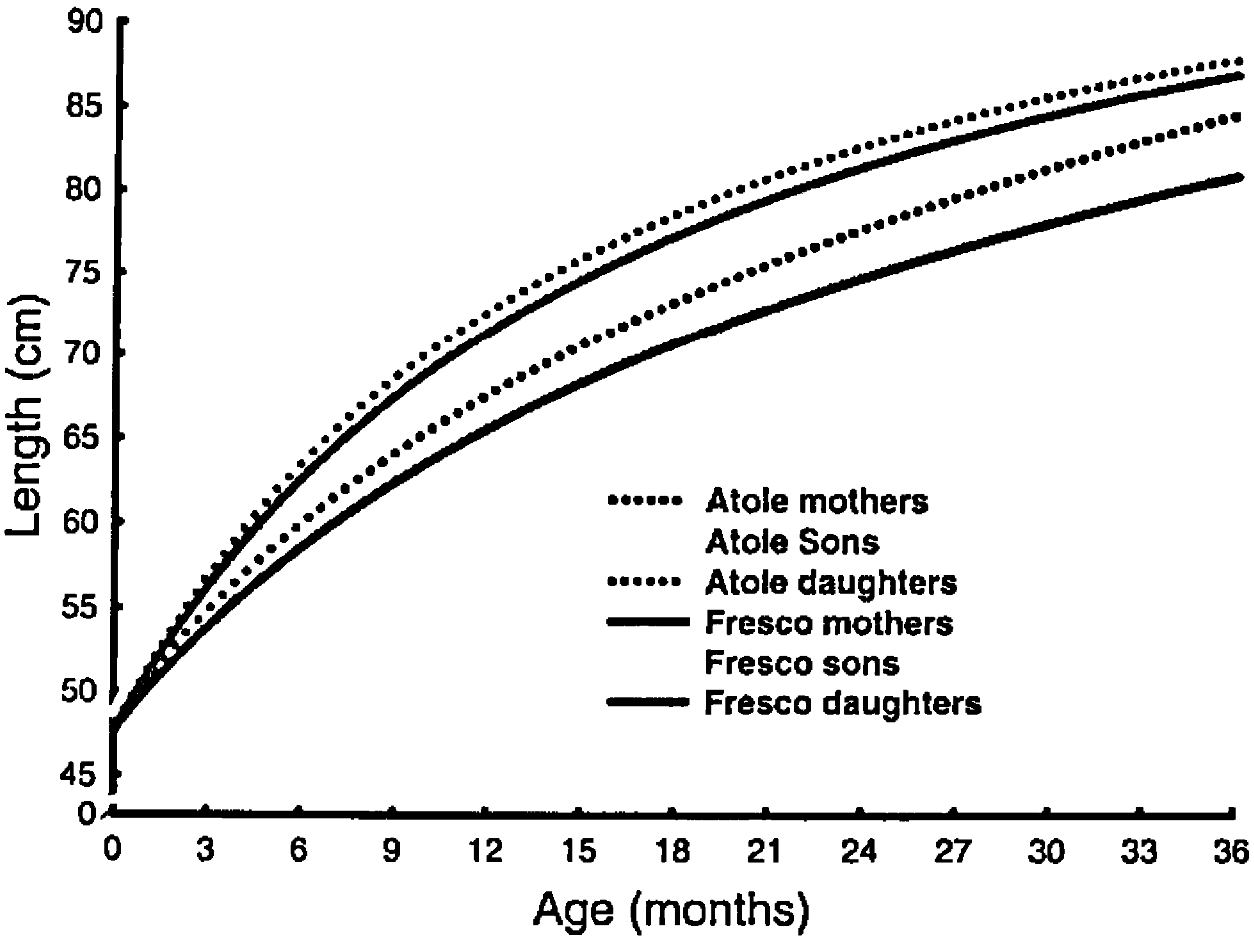

Fig 2. Fitted length between birth and 36 months for women who participated in the Oriente Longitudinal Study, 1969–1977, and their children studied between 1996 and 1999, by type of supplementation received, Guatemala.

served length at several ages are presented in Table 3. The correlations all were positive, ranging from 0.21 to 0.53 in the atole group (with 7 of 10 being significant at $P < .05$) and 0.14 to 0.37 in the fresco group (with 4 of 10 being significant at $P < .05$). Although the correlations of the atole group were generally higher (8 of 10 comparisons), pairwise comparisons of correlations at each age were not heterogeneous ($P > .05$) at every age.

DISCUSSION

Our data are the first that we are aware of that test the impact of a specific intervention, nutritional intervention in childhood, on both the intervened population and the subsequent generation. Children in these 4 villages in Guatemala are growing faster than their mothers' generation. These data thus confirm the overall, global secular trends in linear growth

TABLE 3. Pairwise Correlation* in Length at 3-Month Age Intervals From Birth to 30 Months Between Women Who Received Nutritional Supplementation Early in Life and Their Own Children, Guatemala

	Birth	3 Months	6 Months	9 Months	12 Months	15 Months	18 Months	21 Months	24 Months	30 Months
Atole villages										
No. of pairs	94	64	64	68	49	42	43	53	49	43
r	.26	.53	.51	.27	.29	.21	.33	.42	.46	.51
P	.02	<.001	.001	.04	.06	.2	.06	.004	.003	.001
Fresco villages										
No. of pairs	70	56	43	47	52	37	45	48	42	45
r	.14	.33	.22	.18	.32	.19	.34	.37	.31	.23
P	.3	.02	.2	.3	.03	.3	.04	.02	.08	.2

* Adjusted for maternal and offspring birth order, twin status and gestational age, child gender, and intrafamilial clustering.

and are encouraging. Furthermore, we observed a positive, generally significant association between G2 and G3 length at several ages among those pairs in which the mother received atole and a weaker association among pairs in which the mother received fresco.

Transgenerational effects on health have been documented since 1934, when Kermack et al[12] showed that improvements in infant mortality followed improvements in the mortality experience of women of reproductive age. Since then, a rich literature has documented that improving maternal health and education is important for child health.

In both generations, the majority of children were stunted, with few exceeding the 50th percentile of the World Health Organization reference curves. The G3 generation was shorter at birth than their mothers. This probably reflects regression to the mean. The mothers are the survivors among their generation, in which infant mortality was still elevated, and hence are selected for increased birth weight and length relative to their birth cohort. The G3 generation in this study is experiencing lower rates of morbidity and mortality, and hence the survival selection by birth size is reduced, increasing the prevalence of individuals with lower weight and length at birth in the sample. Nevertheless, the prevalence of stunting has decreased markedly over time. The pattern of growth in the first 2 to 3 months of life also differed, with the G3 generation expressing an increase in length for age z score to month 3 followed by a falling off, whereas the G2 generation seemed to lose percentile ranking consistently from birth. We lack an immediate explanation for this observation, which may relate to minor differences in the method of ascertaining length at birth.

The burden of infection on growth failure has been well documented,[13] and we have observed in our data a reduction of >60% in the proportion of days that children spend ill with gastrointestinal or respiratory disease (unpublished data). Thus, in addition to the effects of nutritional supplementation on the growth of the mothers, improvements in sanitation, immunization, and food availability all probably contribute to the improved growth patterns of the G3 generation.

Earlier studies in this population documented the similarity of the populations at baseline with respect to G1 height and growth of children.[14] Furthermore, our earlier studies documented no secular trend in height of adults who were born between 1905 and 1959 but an increase of 2.5 to 3.3 cm in height between 3-year-olds who were born in 1965 and in 1985.[15] That study did not link adult and child height across generations and did not assess growth longitudinally. To the extent that differences in adult height are established by age 24 months,[1,5] Figure 2 suggests that girls in the G3 generation might achieve adult heights 7 to 8 cm greater than those of their mothers, with the boys another 3 to 4 cm taller yet.

We had expected to see some regression to the mean among the offspring of those women who benefited most from supplementation in the previous generation. The trend toward stronger associations in the atole group therefore is counter to our initial hypothesis. The correlation of growth through age 3 across generations probably reflects underlying genetic potential,[16] as well as persistent differences across families in access to economic resources and household characteristics such as availability of clean water. The observed results strongly suggest that the benefits of supplementation, which resulted in improved growth in the G2 generation when provided in the first 3 years of life, persist to some degree in the next generation. These results thus reinforce a previous result[6] that supplementation per se had an impact on the growth of the next generation, especially when provided after age 3 years. That analysis did not include data on maternal growth and did not consider the individual growth patterns of the study children but merely considered exposure to supplementation as a single exposure.

Limitations of our data need to be considered. We were unable to study the G3 offspring of out-migrants, who differ from the women who remained in the village in several aspects[17] that might have affected G3 growth patterns. Our sample size is relatively small, and thus all of our estimates are somewhat imprecise. This is particularly true for the observed correlations at specific ages, and those analyses lacked power to examine modest differences in strength of association across treatment groups. Nevertheless, we were able to document differences in growth patterns between mothers and children and between boys and girls within treatment types. Finally, we used a fractional polynomial of rank m = 2 to model growth. Although the model explained >85% of variance in length-by-age across the generations, genders, and treatment groups, growth is clearly a complex process, and this model may be insensitive to small between-group differences, and like any regression approach, the potential for misclassification exists. Interpretation of the fit of any model is especially problematic at the upper age range studied, and for growth in particular, more complex models are required to capture the changing patterns of growth velocity over the life span. Nevertheless, over the limited age range studied, the model has utility and seems to fit the data well, and use of the same model across populations confers the ability to conduct comparisons subject to the same set of limitations. Fitting of a more complex model would have required even more data points per individual, resulting in larger numbers of exclusions from our already limited sample size.

We conclude that there has been a secular trend in early childhood growth across generations in Guatemala, which was further enhanced by provision of improved nutrition to the mothers. The better growth of the younger generation should result in greater attained heights and fat-free mass in adulthood,[5,18] potentially resulting in improved educational attainment[19] and hence adult productivity in both genders and improved prospects for safe delivery as the girls enter their own reproductive life.

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