

Nutritional Supplementation in Early Childhood, Schooling, and Intellectual Functioning in Adulthood

A Prospective Study in Guatemala

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Objective: To estimate the association of improved nutrition in early life with adult intellectual functioning, controlling for years of schooling.

Design: Prospective cohort study.

Setting: Four villages in Guatemala, as well as locations within Guatemala to which cohort members migrated.

Participants: Individuals who had participated as children in a nutrition supplementation intervention trial from March 1, 1969, through February 28, 1977 (N=2392). From May 1, 2002, through April 30, 2004, adequate information for analysis was obtained from 1448 of 2118 individuals (68.4%) not known to have died.

Interventions: Individuals exposed to atole (a protein-rich enhanced nutrition supplement) at birth through age 24 months were compared with those exposed to the supplement at other ages or to fresco, a sugar-sweetened beverage. We measured years of schooling by interview.

Main Outcome Measures: Scores on the *Serie Interamericana* (InterAmerican Series) tests of reading comprehension and the Raven Progressive Matrices, obtained from May 1, 2002, through April 30, 2004.

Results: In models controlling for years of schooling and other predictors of intellectual functioning, exposure to atole at birth to age 24 months was associated with an increase of 3.46 points (95% confidence interval, -1.26 to 8.18) and 1.74 points (95% confidence interval, 0.53-2.95) on the InterAmerican Series and Raven Progressive Matrices tests, respectively. There was no statistical interaction between exposure to atole at birth to age 24 months and years of schooling on either outcome ($P=.24$ and $P=.60$, respectively).

Conclusion: Improved early-life nutrition is associated with increased intellectual functioning in adulthood after taking into account the effect of schooling.

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SCHOOLING IS A KEY COMPONENT of the development of literacy, reading comprehension, and cognitive functioning, and thus of human capital.^{1,2} The educational returns of investments in schooling should have their greatest effect among well-prepared children.³ Early-life preparation for schooling through direct investments in intellectual development is effective.^{4,5} However, the literature suggests that in resource-poor environments, poor nutritional status in early childhood—usually measured by growth retardation in height or stunting—is associated with poor performance on cognitive tests in later childhood or in adulthood.⁶⁻⁸ Therefore, both nutrition and early-childhood intellectual enrichment are likely to be important determinants of intellectual functioning in adulthood.

We have been observing prospectively a cohort of Guatemalan men and women who participated as children in a nutritional supplementation intervention trial.⁹ In the present study, we assess the joint contributions of enhanced early-life nutrition and schooling to intellectual functioning in adult men and women.

METHODS

SUBJECTS AND SETTING

Longitudinal Study

The Institute of Nutrition of Central America and Panama (INCAP) conducted a study of child growth and development between March 1, 1969, and February 28, 1977, in 4 villages whose residents were of mixed Spanish and American Indian descent, located 40 to 110 km east of Guatemala City, Guatemala.¹⁰ The 4 vil-

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lages were divided into 2 pairs based on size, then randomly assigned to 1 of 2 treatments. In 1 village in each pair, residents were offered atole, a dietary supplement made from the vegetable protein mixture Incaparina (EDT USA Corp, Miami, Florida), dry skim milk, and sugar that provided protein (6.4 g/100 mL) and 900 kcal/L. In the other village, residents were offered fresco, which contained no protein or fat and 330 kcal/L, all from sugar. Beginning in October 1971, both supplements were fortified with micronutrients in equal concentrations by volume. The supplements were available twice daily at a central location in each village. Between the ages of 15 and 36 months, children who were exposed to atole had a net increase of 8.7 g protein and 94 kcal/d (29.0% and 10.4% of total intake, respectively) compared with children exposed to fresco.¹⁰ Exposure to atole improved growth rates and reduced the prevalence of stunting at age 3 years.¹⁰⁻¹²

The 2002-2004 Follow-up

Between 2002 and 2004, the cohort was resurveyed.^{13,14} Data collection occurred at INCAP facilities in the study villages, at INCAP headquarters in Guatemala City, or at respondents' homes. All data collection followed protocols that were approved by the institutional review boards of INCAP and Emory University, and all study participants gave written informed consent.

Tracing, Contact, and Sample Size

Of the 2392 persons in the 1969-1977 sample, 1855 (77.6%) were determined to be alive and living in Guatemala, 274 (11.5%) had died—most from infectious diseases in early childhood, 162 (6.8%) had migrated abroad, and nothing could be learned about the remaining 101 (4.2%). During 2002-2004 data collection, 1571 individuals (65.7%) completed at least 1 survey instrument, and 1448 individuals (60.5% of the original cohort and 68.4% of those not known to have died) provided adequate data to be included in the present analysis.

VARIABLES

Schooling

We ascertained years of schooling by interview (n=1471). Schooling was considered a continuous variable (range, 0-18 years). At the time this cohort was recruited, there was no systematic kindergarten program in Guatemala. In addition, we categorized schooling as the completion of primary school (sixth grade) compared with those who did not complete primary school. We focus on the completion of primary school because this is a Millennium Development Goal³; furthermore, primary schooling is compulsory in Guatemala.

Reading Comprehension

Respondents who reported the completion of less than 3 years of schooling, or those who reported completing 3 to 5 years of schooling but could not read the headline of a local newspaper article fluently (n=452), received a literacy test consisting of a series of letters, words, and phrases of increasing complexity. The test was scored. All other respondents were presumed to be literate and were assigned the maximum score of 35 points.

We administered the *Serie Interamericana* (InterAmerican Reading Series) (SIA)¹⁵ to 1197 individuals who completed the literacy test with fewer than 5 errors or were presumed to be literate, as previously described. The SIA originally was developed to assess reading abilities of Spanish-speaking children

in Texas. The SIA has demonstrated adequate test-retest reliability (intraclass correlation coefficients 0.85 and 0.87 for reading and vocabulary, respectively) and internal consistency (Cronbach α =0.79-0.98) in previous studies in this population.¹⁶ We used reading comprehension level 2 and vocabulary level 3. The SIA was self-administered in a quiet environment. We summed the scores on the literacy test with those on the SIA.

Cognitive Functioning

We administered the Raven Progressive Matrices, a nonverbal assessment of cognitive ability, to 1452 individuals.^{17,18} The test consists of a series of pattern-matching exercises, with the patterns getting progressively more complex and hence harder to match correctly. The Raven Progressive Matrices have shown adequate test-retest reliability (intraclass correlation coefficient, 0.87) and internal consistency, as well as construct validity in earlier studies in this population.¹⁶ We administered scales A to C, 12 items each. Results are presented as the number of correct answers.

Characterizing Exposure to Supplement

The original intervention study included all children in the villages younger than 7 years at study launch, pregnant women, and newborns. Supplementation was provided from March 1, 1969, through February 28, 1977. Children were followed up through age 7 years or the end of the study. Thus, all children were exposed to 1 of 2 supplements at some point, and children could have been exposed to the intervention at a range of ages: prenatally through supplement intake by the mother and postnatally through maternal supplement intake transmitted as breast milk as well as through the child's own consumption.

For each child, we created a variable that takes a value of 1 when the respondent was exposed to any form of supplementation for the entire window at birth to age 24 months (hereinafter "0 to 24 months") and 0 otherwise (denoted as "exposure to supplementation at ages 0 to 24 months"). We also created a variable ("supplement type") that takes the value 1 if the child lived in one of the atole villages, and 0 otherwise. The interaction term between the 2 variables (denoted as "exposure to atole at ages 0 to 24 months") represents the differential effect of exposure to atole compared with fresco at ages 0 to 24 months, after subtracting the difference between individuals exposed to atole compared with fresco at other ages (ie, those coded 0 for "exposure to supplementation from ages 0 to 24 months"). The interaction term, therefore, provides an estimate of the double-difference effect of atole relative to fresco for a given window of exposure. Because this formulation is not dependent on actual intake of the supplement, our approach represents the intent-to-treat effect of exposure to atole at ages 0 to 24 months.

Other Variables

We developed dummy variables for the study villages, capturing fixed characteristics of these localities that might affect education-related outcomes. We also derived indicators of household proximity to the feeding center in each village to account for differences in accessibility that have been shown to be associated with intake,¹⁹ as well as indicators for parental characteristics related to schooling or to intellectual potential, namely, household socioeconomic status in 1967 (for participants born before 1971) or in 1975 (for participants born after 1970),²⁰ maternal and paternal schooling attainment, and maternal and paternal age when the participant was born.^{14,21} We used archival and updated village histories²²⁻²⁴ to derive measures for the avail-

Table 1. Characteristics of 1448 Respondents by Exposure to a Nutrition Supplement^a and Schooling^b

Characteristic	Nutrition Supplementation				Completed Primary School	
	Atole		Fresco		No (n=782)	Yes (n=666)
	Exposed at Ages 0-24 mo (n=386)	Exposed at Ages Other Than 0-24 mo (n=384)	Exposed at Ages 0-24 mo (n=336)	Exposed at Ages Other Than 0-24 mo (n=342)		
Male sex, No. (%)	178 (46.1)	178 (46.4)	167 (49.7)	150 (43.9)	305 (39.0)	368 (55.2)
Age in 2002, y	30.43 (1.84)	33.42 (5.14)	30.28 (1.90)	33.60 (5.26)	32.47 (4.24)	31.31 (4.09)
Socioeconomic status in 1967 or 1975 ^c	0.01 (0.91)	0.03 (0.77)	-0.02 (0.88)	-0.02 (0.91)	-0.10 (0.76)	0.12 (0.97)
Maternal schooling, y	1.18 (1.49)	1.13 (1.53)	1.54 (1.80)	1.61 (1.84)	1.02 (1.48)	1.74 (1.80)
Paternal schooling, y	1.35 (1.93)	1.16 (1.76)	2.13 (2.15)	2.11 (2.24)	1.18 (1.64)	2.23 (2.35)
Maternal age at respondent's birth, y	27.63 (7.11)	27.41 (7.13)	26.96 (7.25)	28.00 (6.77)	27.73 (6.95)	27.24 (7.22)
Paternal age at respondent's birth, y	33.22 (8.45)	32.92 (8.26)	32.76 (8.49)	32.56 (7.85)	32.99 (8.33)	32.74 (8.19)
Student to teacher ratio at age 7 y	41.00 (6.24)	43.47 (7.54)	34.18 (5.38)	40.40 (12.61)	40.94 (9.11)	38.75 (8.72)
Student to teacher ratio at age 12 y	37.76 (3.72)	39.41 (7.23)	34.74 (4.18)	33.89 (4.28)	37.09 (5.93)	35.99 (5.01)
Permanent structure of primary school at age 7 y, No. (%)	64 (16.58)	100 (26.04)	312 (92.86)	210 (61.40)	299 (38.24)	387 (58.11)
Permanent structure of primary school at age 12 y, No. (%)	334 (86.53)	142 (36.98)	336 (100.00)	328 (95.91)	569 (72.76)	571 (85.74)
Highest grade completed, y	4.28 (3.57)	3.77 (3.20)	5.63 (3.25)	5.26 (3.43)	2.19 (1.69)	7.63 (2.54)
Reading comprehension score ^d	67.86 (30.45)	61.34 (32.40)	71.42 (24.86)	67.76 (29.07)	50.48 (29.21)	86.25 (14.88)
Raven Progressive Matrices score ^e	18.85 (6.22)	17.42 (6.00)	17.44 (6.19)	16.99 (5.99)	15.51 (4.80)	20.28 (6.53)

^aVillages were randomized to receive atole (a protein-rich food supplement) or fresco (a carbohydrate beverage). Age at exposure to the supplement was derived from the birth date of the child and the period of intervention.

^bData are given as mean (SD) unless otherwise indicated.

^cFirst component of a principal components analysis using household assets and home construction materials in 1967 for individuals born before 1971 or in 1975 for those born after 1970.

^dSum of scores on the literacy prescreen (range, 0-35 points) and the *Serie Interamericana* (InterAmerican Series) tests of reading comprehension (level 2: range, 0-40 points) and vocabulary (level 3: range, 0-45 points). Individuals presumed literate were assigned 35 points on the literacy pretest.

^eNumber of correct answers (range, 0-36).

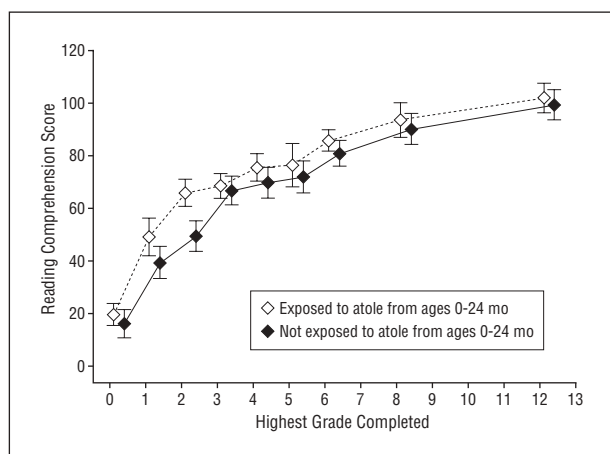


Figure 1. Performance on the *Serie Interamericana* (InterAmerican Reading Series) reading comprehension tests among participants in the 2002-2004 follow-up survey to a longitudinal study in Guatemala conducted from 1969-1977, by exposure to atole at birth to age 24 months and schooling (ie, highest grade attained). Data are least-squares means and 95% confidence intervals and are adjusted for sex; year of birth; socioeconomic status in 1967 or 1975; maternal and paternal years of schooling, maternal and paternal age at respondent's birth (years, log transformed); distance from house to feeding center (2 dummies); student to teacher ratio when the respondent was aged 7 and 12 years; school construction materials when the respondent was aged 7 and 12 years (permanent materials vs other); and clustering of subjects within family and families within village. Data for grades 7 through 9 and for grades 10 and higher are pooled because of small sample sizes and are presented at the group median (grades 8 and 12, respectively).

ability of a permanent structure for the primary school and primary school student-teacher ratios when the respondent was aged 7 and 12 years. Although these schooling variables re-

flect community characteristics, they vary by single-year age cohorts within each village and relate school availability to the period in a child's life when critical decisions about schooling are made.

STATISTICAL ANALYSIS

In the analysis, we retained 1448 individuals for whom data on schooling, reading comprehension, and the Raven Progressive Matrices were available. Missing values for specific covariates (eg, maternal and paternal schooling; 23.8% of individuals had missing values for 1 or more covariates) were handled using multiple imputation procedures.²⁵ Five replicate data sets were created using PROC MI in SAS statistical software, version 9.1 (SAS Institute, Cary, North Carolina). Each data set was then analyzed using standard procedures for complete data, and the results from these analyses were combined using PROC MIANALYZE in SAS.

Associations of exposure to the intervention and schooling, considered in separate models as a continuous measure and as a binary variable, with the reading comprehension scores and with the Raven scores were modeled using linear regression. We present estimates and 95% confidence intervals (CIs).

Our base model included terms for exposure to supplementation at ages 0 to 24 months, supplement type, and the interaction term exposure to atole at ages 0 to 24 months. We then added schooling to the model. Using interaction terms, we tested whether the estimated association of exposure to atole at ages 0 to 24 months with the outcomes varied by schooling attainment. We controlled for sex, village, year of birth (continuous), and the community and household covariates described in the "Other Variables" subsection.

In our population, individuals reside within 4 villages, and 84.7% of participants have 1 or more siblings in the study. There-

Table 2. General Linear Mixed Model^a Estimates of Mean Differences in Schooling Attainment and Reading Comprehension and Raven Progressive Matrices Scores

Characteristic	Estimate (95% Confidence Interval)			
	Reading Comprehension Score		Raven Progressive Matrices Score	
	Main Effects	Main Effects and Interaction	Main Effects	Main Effects and Interaction
Schooling attainment, y	6.54 (6.21 to 6.88)	6.46 (5.84 to 7.07)	0.90 (0.82 to 0.99)	0.85 (0.69 to 1.01)
Supplement exposure at ages 0-24 mo	0.79 (-2.40 to 3.97)	5.16 (-0.71 to 11.04)	-0.39 (-1.22 to 0.43)	-0.71 (-2.24 to 0.82)
Supplement type, atole vs fresco	4.97 (-3.58 to 13.52)	-0.31 (-9.34 to 8.71)	2.69 (1.66 to 3.73)	2.23 (0.73 to 3.72)
Exposure to atole at ages 0-24 mo	3.46 (-1.26 to 8.18)	5.07 (-2.50 to 12.64)	1.74 (0.53 to 2.95)	2.16 (0.19 to 4.13)
Supplement exposure at ages 0-24 mo × schooling attainment	NA	-0.75 (-1.63 to 0.13)	NA	0.06 (-0.17 to 0.29)
Supplement type × schooling attainment	NA	1.26 (0.41 to 2.12)	NA	0.09 (-0.13 to 0.32)
Exposure to atole at ages 0-24 mo × schooling attainment	NA	-0.72 ^b (-1.92 to 0.48)	NA	-0.08 ^c (-0.39 to 0.23)

Abbreviation: NA, not applicable.

^a Controlled for sex; year of birth; socioeconomic status in 1967 or 1975; maternal and paternal years of schooling; maternal and paternal age at respondent's birth (years, log transformed); distance from house to feeding center (2 dummies); student to teacher ratio when the respondent was aged 7 and 12 years; school construction materials when the respondent was aged 7 and 12 years (permanent materials vs other); also accounting for clustering of subjects within family and families within village.

^b $P = .60$ for the interaction term.

^c $P = .24$ for the interaction term.

fore, we used the SAS procedure MIXED to fit linear-mixed models, which account for the clustering of subjects within family and families within village.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

Almost 50% of the study sample was male, and male respondents were more likely to have completed primary school than were female respondents (**Table 1**). The mean age was 32 years. Parental years of schooling was higher among individuals not exposed to atole at ages 0 to 24 months. This difference is attributable to longstanding differences in schooling observed in 1 village that was randomized to fresco. Fewer individuals exposed to atole at ages 0 to 24 months attended a school that was a permanent structure at age 7 years, but that difference was no longer apparent by age 12 years. Socioeconomic status in childhood, parental years of schooling, and the probability that the school was a permanent structure were all higher among individuals who completed primary school.

READING COMPREHENSION

The mean reading comprehension score was 66.9 (range, 0-118) (Table 1). Reading comprehension scores had a curved relationship with schooling, with the slope steepest at low levels of schooling (**Figure 1**). In a linear model, each year of schooling was associated with a 6.54-point increment in the score (95% CI, 6.21-6.88). In adjusted models that did not include schooling, exposure to atole at ages 0 to 24 months was associated with a 6.72-point increment in the reading comprehension score (95% CI, -0.02 to 13.46). With additional adjustment for

schooling as a continuous variable, exposure to atole at ages 0 to 24 months was associated with a 3.46-point increment in the reading comprehension score (95% CI, -1.26 to 8.18) (**Table 2**), whereas adjustment for completion of primary school resulted in an estimate of 6.39 points (95% CI, 0.79-11.99) (**Table 3**). No interaction between exposure to atole at ages 0 to 24 months and schooling was observed on the reading comprehension score when schooling was considered a continuous variable ($P = .24$ for the interaction term) (Table 2) or a binary variable ($P = .26$) (Table 3).

We repeated the analysis with the addition of a quadratic term for schooling attainment and using spline regression with 1 node to capture the nonlinear relationship between schooling and the reading comprehension score. The results were consistent with those from the linear model (data not shown).

RAVEN PROGRESSIVE MATRICES

The mean Raven score was 17.7 (range, 0-36). The Raven score was approximately linearly related to schooling attainment (**Figure 2**). Each year of schooling was associated with a 0.90-point increment in the Raven score (95% CI, 0.82-0.99). In adjusted models that did not include schooling, exposure to atole at ages 0 to 24 months was associated with a 2.19-point increment in the Raven score (95% CI, 0.80-3.57). With additional adjustment for schooling, exposure to atole at ages 0 to 24 months was associated with a 1.74-point increment in the Raven score (95% CI, 0.53-2.95). Adjustment for completion of primary school resulted in an estimate of 2.09 points (95% CI, 0.79-3.39). No interaction between exposure to atole at ages 0 to 24 months and schooling was observed for the Raven score when schooling was included as a continuous variable ($P = .60$) (Table 2) or as a binary variable ($P = .15$) (Table 3).

Table 3. Completion of Primary School and General Linear Mixed Model^a Estimates of Mean Differences in Reading Comprehension and Raven Progressive Matrices Scores

Characteristic	Estimate (95% Confidence Interval)			
	Reading Comprehension Score		Raven Progressive Matrices Score	
	Main Effects	Main Effects and Interaction	Main Effects	Main Effects and Interaction
Completion of primary school ^b	34.06 (31.41 to 36.71)	37.04 (31.98 to 42.09)	4.34 (3.74 to 4.95)	4.16 (2.99 to 5.33)
Exposure at ages 0-24 mo	0.35 (-3.44 to 4.13)	5.93 (0.15 to 11.71)	-0.44 (-1.33 to 0.44)	-0.16 (-1.50 to 1.19)
Supplement type, atole vs fresco	3.39 (-3.59 to 10.36)	4.15 (-3.56 to 11.87)	2.25 (1.14 to 3.36)	2.22 (0.83 to 3.60)
Exposure to atole at ages 0-24 mo	6.39 (0.79 to 11.99)	2.03 (-5.46 to 9.51)	2.09 (0.79 to 3.39)	1.39 (-0.36 to 3.13)
Exposure at ages 0-24 mo × completion of primary school	NA	-9.05 (-16.18 to -1.93)	NA	-0.49 (-2.15 to 1.17)
Supplement type × completion of primary school	NA	-0.00 (-6.99 to 6.98)	NA	-0.04 (-1.66 to 1.58)
Exposure to atole at ages 0-24 mo × completion of primary school	NA	5.65 ^c (-4.22 to 15.52)	NA	1.70 ^d (-0.60 to 4.00)

Abbreviation: NA, not applicable.

^aControlled for sex; year of birth; socioeconomic status in 1967 or 1975; maternal and paternal years of schooling; maternal and paternal age at respondent's birth (years, log transformed); distance from house to feeding center (2 dummies); student to teacher ratio when the respondent was aged 7 and 12 years; school construction materials when the respondent was aged 7 and 12 years (permanent materials vs other); also accounting for clustering of subjects within family and families within village.

^bReference group is individuals who did not complete primary school.

^c*P* = .26 for the interaction term.

^d*P* = .15 for the interaction term.

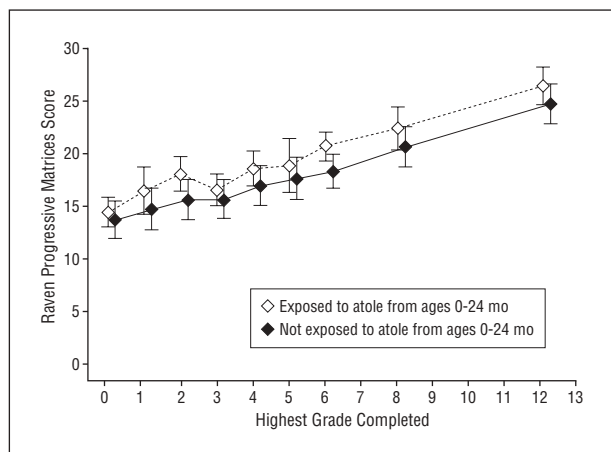


Figure 2. Performance on the Raven Progressive Matrices among participants in the 2002-2004 follow-up survey to a longitudinal study in Guatemala conducted from 1969 through 1977, by exposure to atole at birth to age 24 months and schooling. Data are least-squares means and 95% confidence intervals, and are adjusted for sex; year of birth; socioeconomic status in 1967 or 1975; maternal and paternal years of schooling; maternal and paternal age at respondent's birth (years, log transformed); distance from house to feeding center (2 dummies); student to teacher ratio when the respondent was aged 7 and 12 years; school construction materials when the respondent was aged 7 and 12 years (permanent materials vs other); and clustering of subjects within family and families within village. Data for grades 7 through 9 and for grades 10 and higher are pooled because of small sample sizes and are presented at the group median (grades 8 and 12, respectively).

COMMENT

It is presumed that investments in schooling will have greater returns if the children arrive at school well prepared.²⁶ Decisions about schooling are made by parents in accordance with their perceptions of the child's potential, the costs and expected returns of schooling, and societal values about investments in schooling. The child's

potential, as perceived early in life by the parents, thus may influence the quantity of schooling that might be obtained and the resulting cognitive attainments. Nutrition in early life is associated with markers of child development in this population,^{27,28} and exposure to atole for most of the first 3 years of life was associated with an increase of 0.4 years in attained schooling, with the association being stronger for females (1.2 years of schooling).²¹ Thus, schooling might be in the causal pathway between early childhood nutrition and adult intellectual functioning. Our estimates for the effect of exposure to atole at ages 0 to 24 months on reading comprehension scores were attenuated from 6.39 to 3.46 points with adjustment for schooling (notably, adjustment for the completion of primary schooling did not attenuate this estimated association; this may represent inadequate control for schooling). No such attenuation was observed for the Raven scores, regardless of the measure used to represent schooling. Our data are consistent with the model that early-life nutritional intervention results in improvements in growth and development, which in turn induce further parental investments, including schooling; both the improved nutrition and the higher levels of schooling are associated with improvements in adult cognitive functioning. Our data specifically suggest that early-life nutrition is independently associated with the Raven score, but that the association with reading comprehension is at least partially mediated through its association with increasing schooling. Early-life psychosocial interventions have strong associations with cognitive development⁴; these were not evaluated systematically in our study. Elsewhere, we suggest that the association between schooling and intellectual functioning in adulthood is substantially attenuated with adjustment for factors that predict height at age

7 years²⁹; those results further reinforce the importance of early life circumstances in the development of cognitive functioning over the life course.

Our study was conducted in a resource-poor setting where stunting has been widespread among children and opportunities for schooling have been limited. In the early 1960s, schools consisted of single rooms with multiple ages and grades being taught simultaneously by a single teacher. We lack detailed measures for the quality of schooling but were able to control for 2 community-level characteristics that varied across villages and over time, namely, the student-teacher ratio and the materials used to construct the schools. We also controlled for year of birth, which captures any similar secular trends in schooling quality across all villages.

There have been 2 prior investigations of the relationship between nutrition in early life and later intellectual functioning in this cohort. Pollitt et al¹⁶ examined the cohort in 1988, when cohort members were aged 11 to 25 years and some, especially the younger members, were still in school. Li et al³⁰ studied a sample of women who were living in the study villages and delivered an infant between 1991 and 1996. Both studies reported that exposure to atole in early childhood was associated with a larger estimate of the effect of schooling on reading comprehension. We did not observe this interaction in our study, which included a larger proportion of the cohort at ages when all had completed their schooling. Pollitt et al did not observe any association between exposure to atole and the Raven score, and Li et al did not examine this association.

The study population was not individually randomized to receive atole or fresco. With only 2 pairs of villages randomized, baseline differences among the villages are not fully addressed by randomization. These differences include patterns of schooling; rates of schooling were, and continue to be, higher in the fresco villages. We controlled for village and several individual and community factors potentially related to both decisions about school enrollment and later cognitive functioning. We were concerned that adult literacy programs, targeted at those with little formal schooling, might have biased our results. In practice, few respondents reported attending adult literacy programs.

Our analysis does not consider the dosage of nutrition supplement received, which previously has been shown to be related to factors such as the distance from the home to the feeding center.¹⁹ In addition, the potential for attrition bias must be considered. The major cause of attrition was mortality (274 deaths, representing 29.0% of all nonstudied individuals). We were able to obtain data on outcome measures for 60.5% of the cohort (68.4% of those not known to have died). For attrition to bias our results, those who were not studied would need to differ selectively with respect to their exposure to the intervention, with their schooling attainment, and with their current cognitive functioning. The first has been shown to have occurred,¹³ but we lack information on the latter two. To preserve the sample size while preventing introduction of further bias, we used multiple imputation to address covariate nonresponse; we did not impute values for the key outcome variables.

Our intervention was food-based and resulted in increased intakes of protein, fat, carbohydrates, and a range of micronutrients in those exposed to atole. Hence, we interpret our findings as suggestive of a role for high-quality food and not for specific nutrients.

Major efforts are under way to improve the nutrition of disadvantaged young children,³¹ and the second Millennium Development Goal is to achieve universal primary schooling everywhere by 2015.³² Even if the only effect of improved early-life interventions, whether nutritional or behavioral, is to induce parents to provide more schooling for their children, such interventions have a potential for high returns.³³ The increment in the Raven Progressive Matrices scores associated with exposure to atole at ages 0 to 24 months represents the equivalent of 1.6 additional years of schooling. Our data, which suggest an effect of exposure to an enhanced nutritional intervention in early life that is independent of any effect of schooling, provide additional evidence in support of intervention strategies that link early investments in children³⁴ to continued investments in early-life nutrition and in schooling.¹

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Author Contributions: Dr Stein had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Stein, Martorell, and Ramakrishnan. *Acquisition of data:* Stein, Grajeda, Martorell, and Ramirez-Zea. *Analysis and interpretation of data:* Stein, Wang, DiGirolamo, Martorell, Ramakrishnan, and Yount. *Drafting of the manuscript:* Stein and Martorell. *Critical revision of the manuscript for important intellectual content:* Wang, DiGirolamo, Grajeda, Martorell, Ramakrishnan, Ramirez-Zea, and Yount. *Statistical analysis:* Wang. *Obtained funding:* Stein and Martorell. *Administrative, technical, or material support:* Grajeda and Martorell. *Study supervision:* Stein and Ramirez-Zea.

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We have seen that, although American communities are already aiding youth, all can do even better.

—From *The Adolescent Years* by William W. Wattenberg, 1955.