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Differential Response to Early Nutrition Supplementation: Long-Term Effects on Height at Adolescence

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Background. The classical risk approach to predicting who benefits from an intervention is unsound because it relies on the theoretical assumption that those at risk will necessarily benefit. A better approach to systematically test who benefits from nutrition supplementation is proposed using interactive models.

Methods. Differential effects of nutrition supplementation during early childhood on stature at adolescence were studied in 245 males and 215 females to identify determinants of long-term benefit from food supplementation. Factors studied included family socioeconomic status (SES) and children's home diet and diarrhoea during the first 3 years of life. To determine whether a factor conferred benefit, the statistical significance of the interaction between this factor and the intervention was tested. Data from the INCAP supplementation trial in Guatemala and from the follow-up of the same subjects at adolescence were used.

Results. Ordinary least squares (OLS) showed that high rates of diarrhoea in males and poor SES in females were significant determinants of benefit from supplementation at adolescence, and that the effects were mediated by length at 3 years old. Results of two-stage least squares (2SLS) analysis showed that length at 36 months, maturation and maternal height were significant determinants of height at adolescence but SES was not.

Conclusions. Nutrition supplementation in early childhood has long-lasting effects on body size and the larger benefits acquired by some groups of children remain throughout early adulthood. The relevance of these findings for screening and targeting of nutritional interventions is discussed.

The World Health Organization (WHO) recommends the use of the 'risk-approach' for the selection of beneficiaries for nutrition interventions.[1] This approach consists of the identification of risk factors that are associated with outcomes such as malnutrition, morbidity and mortality. These are used as screening tools to target interventions to the most needy. The ultimate goal of this approach is to improve the effectiveness of health services in reaching the most vulnerable and at-risk individuals.

The main limitation of the risk factor approach, however, is that it relies on the assumption that predictors of risk also predict benefit. This assumption may not always hold. A more appropriate approach to predicting benefit is proposed here. It involves testing directly the interaction between a characteristic hypothesized to determine benefit and the intervention.

Overall benefits from nutritional supplementation during infancy on early growth and on stature at adolescence have been demonstrated.[2–5] Studies carried out by the Institute of Nutrition of Central America and Panama (INCAP) showed that daily supplementation of children from birth to 3 years with an average of 10% of their recommended dietary allowances (RDA) for energy,[6] improved growth during the pre-school period.[2] Differences in length observed at 3 years of age

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remained at adolescence, although slightly attenuated, and were mainly due to differences already established by 3 years of age.[5]

While the previous INCAP research focused on the overall effects of supplementation (main effects), the issue addressed in the present paper is the differential response to the intervention (interactive effect). Data from the INCAP supplementation[7] and follow-up studies[8] were used to explore the following questions: 1) whether children with certain characteristics benefited more from the supplementation than others during the pre-school period; 2) whether these benefits remained at adolescence; and 3) whether the benefits seen at adolescence were due to differences already established during the pre-school period. Characteristics studied as potential determinants of benefit were diarrhoea and home diet during the first 3 years of life and family socioeconomic status at the time of the supplementation trial.

The practical relevance of identifying determinants of benefit is that these characteristics may be considered in future studies as potential screening tools to maximize the impact and cost-effectiveness of nutrition interventions.

METHODS

Data and Sample

The data were collected by INCAP during a longitudinal supplementation trial conducted in rural Guatemala between 1969 and 1977, and a follow-up study in 1988–1989. Detailed descriptions of these two studies are presented elsewhere.[7,8] Brief summaries follow.

The supplementation trial consisted of the random allocation of two villages to receive a high-calorie, high-protein drink (Atole, which contained 91 kcal and 6.1 g of protein per 100 ml), while two other villages were assigned to a low-calorie, non-protein drink (Fresco, which contains 33 kcal per 100 ml and no protein). The supplements were made available at a central location to all pregnant and lactating women and to all children ≤7 years. Individual supplement intake was carefully measured to the nearest millilitre.

In 1988–1989, a cross-sectional study was carried out in the same villages to evaluate the effect of improved nutrition during early childhood on physical and psychosocial status at adolescence. A series of anthropometric measurements were taken on the subjects who had been supplemented in early childhood and were then adolescents or young adults.

The sample includes 245 males and 215 females aged 14–20 years who had been exposed to the supplement from birth to 3 years of age and who had anthropometric measurements (length/height) at 36 months and at adolescence.

Variables

The variables used in the present analysis were: length at 36 months, height at adolescence and maternal height (all measured to the nearest millimetre, using standard measurement and standardization techniques;[9] supplement group (Fresco = 0 and Atole = 1); home diet: mean daily energy intake from home diet (kcal/day), estimated by multiple 24-hour recalls conducted with mothers every 3 months between 15 and 36 months of age;[7] diarrhoea: per cent days ill with diarrhoea (as defined by the mother) between birth and 36 months of age collected by recall every 2 weeks during home visits;[7] socioeconomic status: information about housing quality and family possessions measured in 1975 and 1988, and analysed with principal components analysis to derive one factor (standardized variable, mean = 0, sd = 1);[5] maturation: skeletal age derived from left hand wrist x-rays using the TW-2 (RUS) method.[10]

The variables home diet, diarrhoea and socioeconomic status were dichotomized for the multiple regression analyses using the median as cutoff point (sex-specific median was used for home diet and diarrhoea), because the association between these variables and the outcomes (length at 36 months and height at adolescence) was not linear. A square term for skeletal age was included in the male models because the relationship with height was not linear.[5]

Analytical Methodology

The analysis was based on the conceptual model presented in Figure 1. It was hypothesized that length at 3 years of age is determined by a combination of biological (left side) and socioeconomic (right side) factors, which may interact with supplementation and modify its effect on growth. The influence of these factors on height at adolescence is thought to be mostly mediated by length at 3 years of age. Thus, no residual effect of these variables on height at adolescence is expected when length at 36 months is included in the models. The main determinants of height at adolescence are thought to be length at 3 years, maturation (skeletal age) and maternal height. The latter is thought to reflect both genetic factors and past socioeconomic characteristics of the mother's family. We also hypothesized that recent socioeconomic factors (SES in 1988) may influence attained height at adolescence and that this effect may be modified by length at 36 months old.

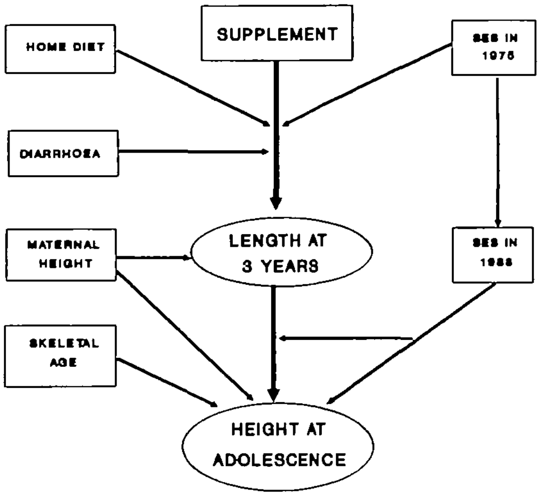

FIGURE 1 *Conceptual model of the determinants of length at 3 years and of height at adolescence*

The analysis had three objectives:

1) to test whether family SES, and children's diarrhoea and home diet during the first 3 years of life were modifiers of the effect of supplementation on length at 3 years of age;
2) to test whether these same factors were effect modifiers of height at adolescence;
3) to test whether the effect of these factors disappeared when length at 3 years was included in the adolescent model, which would suggest that the effects were mediated by length at 36 months of age.

Ordinary least squares (OLS) regression analysis was used and the statistical significance of the effect modifiers was tested by including in the models a two-way interaction term between each of the characteristics studied and the variable supplementation (0 = Fresco; 1 = Atole). The equations corresponding to each of the three objectives were as follows:

$$\text{LENGTH AT 36 MONTHS} = a_0 + a_1\text{SUP} + a_2\text{MH} + a_3\text{SES (1975)} + a_4\text{DIET} + a_5\text{DIARRHOEA} + a_6\text{SUP*SES (1975)} + a_7\text{SUP*DIET} + a_8\text{SUP*DIARRHOEA} + e_1 \quad (1)$$

$$\text{HEIGHT AT ADOLESCENCE} = b_0 + b_1\text{SUP} + b_2\text{MH} + b_3\text{SES (1975)} + b_4\text{DIET} + b_5\text{DIARRHOEA} + b_6\text{SUP*SES (1975)} + b_7\text{SUP*DIET} + b_8\text{SUP*DIARRHOEA} + b_9\text{SKA} + b_{10}\text{SKA}^2 + e_2 \quad (2)$$

*An endogenous (also called 'jointly independent' or 'jointly determined') variable is defined as a variable whose values are determined within the model, as opposed to an 'exogenous' (or 'predetermined') variable, whose values are determined outside the model.[11]

$$\text{HEIGHT AT ADOLESCENCE} = c_0 + c_1\text{SUP} + c_2\text{MH} + c_3\text{SES (1975)} + c_4\text{DIET} + c_5\text{DIARRHOEA} + c_6\text{SUP*SES (1975)} + c_7\text{SUP*DIET} + c_8\text{SUP*DIARRHOEA} + c_9\text{SKA} + c_{10}\text{SKA}^2 + c_{11}\text{LENGTH AT 36 MONTHS} + e_3 \quad (3)$$

where,

SUP	=	supplement (Fresco = 0; Atole = 1)
MH	=	maternal height (cm)
SES (1975)	=	socioeconomic status in 1975 (low = 0; high = 1)
DIET	=	home diet: mean kcal/day (low = 0; high = 1)
DIARRHOEA	=	% days with diarrhoea (low = 0; high = 1)
SUP*SES	=	2-way interaction between supplement and socioeconomic status
SUP*DIET	=	2-way interaction between supplement and home diet
SUP*DIARRHOEA	=	2-way interaction between supplement and diarrhoea
SKA	=	skeletal age
SKA^2	=	skeletal age square (for males only)
e	=	error term

Note that equation 3 is statistically and conceptually incorrect because it contains an endogenous* variable (length at 36 months), which is determined by some of the exogenous variables (e.g. maternal height) that are hypothesized to be determinants of the dependent variable of the equation (height at adolescence). This equation is used only for comparison purposes, to demonstrate whether the interactions seen at adolescence (equation 2) disappear once length at 36 months of age is controlled for. However, because length at 36 months of age is endogenous, the errors of this variable in equation 3 may be correlated with the error term of the equation (e_3). The use of OLS in this situation is not appropriate because it may provide biased and inconsistent estimates of the regression coefficients.[11] Two-stage least squares (2SLS) is widely used for the estimation of models where one or more variables are endogenous and thus correlated with the error term.[12] A description of the method and examples of its uses in epidemiological research are provided elsewhere.[13,14] Briefly, 2SLS consists of:

1) regressing the endogenous variable on its predictors and
2) using the predicted values to replace the observed values in the overall equation.

In the present study, 2SLS was used to estimate height at adolescence (equation 4), using the predicted values (as opposed to the observed values) for length at 36 months to avoid problems of endogeneity in the overall equation. The model also included the variable socioeconomic status measured in 1988, and the hypothesized interaction between SES in 1988 and length at

TABLE 1 *Descriptive results by sex and supplementation group*[a]

Variables	Males				Females			
	Fresco	(n = 127)	Atole	(n = 118)	Fresco	(n = 99)	Atole	(n = 116)
	X[b]	(SD)[b]	X	(SD)	X	(SD)	X	(SD)
Length at 36 months (cm)	85.32	(4.05)	86.93	(3.81)*	83.61	(3.57)	86.33	(3.50)*
Height at adolescence (cm)	158.33	(7.60)	157.76	(9.18)	148.78	(4.74)	150.52	(5.33)*
Maternal height (cm)	148.81	(5.12)	148.81	(5.07)	149.32	(5.64)	149.04	(5.19)
Home diet[c] (kcal/day)	767.40	(231.85)	716.34	(218 29)	695.32	(242 24)	668.39	(188.51)
Supplement[d] (kcal/day)	20.87	(18.28)	127.52	(90.44)*	16.84	(13.05)	114.84	(77.45)*
Diarrhoea[e] (% days)	7 69	(6.65)	8.82	(8.19)	7.88	(7.85)	6.46	(6.24)
SES[f] in 1975	–0.12	(0.78)	–0.10	(0.96)	0.00	(1.02)	–0.07	(0.90)
SES[f] in 1988	0.19	(0.95)	–0.07	(0.92)*	0.10	(0.99)	0.05	(0.87)
Skeletal age (years)	16.61	(1.62)	16.05	(1.82)*	16.09	(1.54)	16 14	(1.45)

[a] Supplementation groups: 0 = Fresco = Low-calorie, non-protein drink; 1 = Atole = High-calorie, high-protein drink.
[b] X = Mean; SD = Standard deviation.
[c] Home diet: Mean kilocalories/day from home diet between 15 and 36 months of age.
[d] Supplement: Mean kilocalories/day from supplement intake between 0–36 months of age.
[e] Diarrhoea: Per cent days with diarrhoea between 0–36 months of age.
[f] SES = Socioeconomic status; SES (1975) = Socioeconomic status measured in 1975; SES (1988) = Socioeconomic status measured in 1988.
Standardized factor scores from principal components analysis are presented with mean = 0 and standard deviation (SD) = 1.
* T-test of the difference between Atole and Fresco statistically significant ($P < 0.05$).

36 months of age. The model for equation 4 is as follows:

$$\text{LENGTH AT ADOLESCENCE} = d_0 + d_1\text{LENGTH AT 36 MONTHS} + d_2\text{SES (1988)} + d_3\text{MH} + d_4\text{SKA} + d_5\text{LENGTH (36)*SES (1988)} + e_4 \quad (4)$$

where,

LENGTH AT 36 MONTHS = the predicted values for length at 36 months, derived from equation 1
SES (1988) = socioeconomic status in 1988
LENGTH (36)*SES (1988) = 2-way interaction between length at 36 months and socioeconomic status in 1988.

The 2SLS analysis was performed using the PROC SYSLIN procedure of the PC-SAS statistical program, version 6.04.

RESULTS

Descriptive data for all variables are provided in Table 1, by sex and supplementation group. In females, differences between supplementation groups were statistically significant only for the two outcomes studied (length at 36 months and height at adolescence). Except for the obvious difference in supplement intake, there were no other differences between the Atole and Fresco groups in any of the independent variables. In males, length at 36 months was statistically greater among the Atole group, but height at adolescence was not. A previous analysis showed that when differences in maturation were controlled for, male adolescents from the Atole group were taller than the Fresco group.[5] Adolescents from the Atole group had lower SES in 1988, statistically significant in males but not significant in females.

Tables 2 and 3 present the results of the OLS regression analyses for males and females, respectively. Diarrhoea was a statistically significant effect modifier in males (interaction: supplement * diarrhoea), for both length at 36 months and height at adolescence. As expected, the interactive effect of diarrhoea and supplement was no longer statistically significant when length at 3 years of age was included in the adolescent model (model 3). These results show that diarrhoea was an important modifier of the effect of supplementation at 3 years of age in males, and that this effect remained throughout adolescence. The effect was mediated by length at 3 years, and thus, disappeared when this latter variable was controlled for in the adolescent model. Figure 2 illustrates the interaction between supplement and diarrhoea in males. Differences in adjusted mean

TABLE 2 *Determinants of length at 3 years, height at adolescence and height at adolescence controlling for length at 3 years of age in males (OLS[a] models)*

Variable	Length at 3 years Model 1		Height at adolescence Model 2		Height at adolescence controlling for length at 3 years Model 3	
	B	(*P*-value)	B	(*P*-value)	B	(*P*-value)
Intercept	50.57	(0.00)	-72.93	(0.00)	-108.07	(0.00)
Supplement (SUP)[b]	0 50	(0.58)	-1.43	(0.32)	-2.38	(0.04)
Maternal height (cm)	0.23	(0.00)	0.53	(0.00)	0.31	(0.00)
Diarrhoea[c] (% days)	-1.75	(0.01)	-1.70	(0.09)	-0.08	(0.92)
Diet[d] (kcal/day)	1 24	(0.05)	1.48	(0.14)	0.15	(0.84)
SES (1975)[e]	1.05	(0.11)	-0.05	(0.96)	-1.08	(0.19)
Skeletal age (years)			16.23	(0.00)	14.89	(0.00)
Skeletal age square			-0.42	(0.00)	-0.39	(0.00)
Length at 36 months (cm)					0.97	(0.00)
2-WAY INTERACTIONS:						
SUP * Diarrhoea[c]	2 04	(0.02)	3.01	(0.03)	1.15	(0.31)
SUP * Diet[d]	0.85	(0.35)	0.27	(0 85)	-0.17	(0 88)
SUP * SES (1975)[e]	0.14	(0.88)	2.15	(0.14)	2.12	(0.06)

[a] OLS = Ordinary least squares regression analysis.
[b] Supplement type: Fresco (0), Atole (1).
[c] Diarrhoea: Per cent days with diarrhoea between birth and 36 months:
Low (0) <6.51% (median for males)
Higher (1) ≥6.51%.
[d] Diet: Mean kilocalories/day from home diet between 15 and 36 months:
Low (0) < 728.17 kcal/day (median for males)
Higher (1) ≥728.17 kcal/day.
[e] SES = Socioeconomic status; SES (1975) = SES measured in 1975.
Standardized factor scores from principal components analysis were used in the analysis: Low SES (0) = Factor score <0; High SES (1) = Factor score ≥0.

length/height between Atole and Fresco are presented for all three outcomes (a taller bar indicates larger benefit from supplementation, i.e. a larger difference between Atole and Fresco). This Figure shows that the male children who benefited more from the supplementation were those with greater rates of diarrhoea in early infancy. Among this group, the difference in length at 36 months in favour of the Atole group was 3.03 cm, compared to 0.98 cm for the group with less diarrhoea. Among the high diarrhoea group, the difference remained statistically significant at adolescence and was only slightly reduced in size (difference of 2.63 cm in favour of the Atole group at adolescence). Among male adolescents who had lower rates of diarrhoea in childhood, the difference between the Atole and Fresco group was small (–0.38 cm) and not statistically significant. Thus, benefits from supplementation in males were restricted to children with high rates of diarrhoea during infancy. In this sample, males with high diarrhoea rates were those who spent on average more than 6.5% of the time with diarrhoea in their first 3 years of life.

In females, SES was an effect modifier at 36 months of age and at adolescence, and the effect at adolescence disappeared when length at 36 months was controlled for (Table 2). Figure 3 illustrates the interaction between supplement type and SES and shows that girls from poorer families benefited more than girls from wealthier families, both at 3 years old and at adolescence. When length at 36 months was controlled for, SES was no longer a significant effect modifier of supplementation on height at adolescence. Thus, in females, SES was a determinant of benefit from the supplementation at 3 years of age and at adolescence, and differences seen at adolescence were already established by 3 years of age.

Maternal height showed no interactive effect with supplementation but it was an important positive determinant of all outcomes studied in both males and

TABLE 3 *Determinants of length at 3 years, height at adolescence and height at adolescence controlling for length at 3 years of age in females (OLS[a] models)*

Variable	Length at 3 years Model 1		Height at adolescence Model 2		Height at adolescence controlling for length at 3 years Model 3	
	B	(*P*-value)	B	(*P*-value)	B	(*P*-value)
Intercept	53.19	(0 00)	72.36	(0.00)	31.20	(0.00)
Supplement (SUP)[b]	3.72	(0.00)	4.12	(0.00)	1.11	(0.35)
Maternal height (cm)	0.20	(0.00)	0 46	(0.00)	0.31	(0.00)
Diarrhoea[c] (% days)	-0.23	(0.75)	0.30	(0.75)	0.46	(0.56)
Diet[d] (kcal/day)	0.99	(0.17)	1.18	(0.22)	0.39	(0.63)
SES (1975)[e]	0.91	(0.21)	2.55	(0.01)	1.85	(0.02)
Skeletal age (years)			0.36	(0.04)	0.38	(0.01)
Length at 36 months (cm)					0.77	(0.00)
2-WAY INTERACTIONS:						
SUP * Diarrhoea[c]	-0.96	(0.31)	-1.37	(0.29)	-0.54	(0.62)
SUP * Diet[d]	0.81	(0.40)	-0.30	(0.82)	-0.88	(0.42)
SUP * SES (1975)[e]	-1.62	(0.10)	-2.51	(0.06)	-1.32	(0.24)

[a] OLS = Ordinary least squares regression analysis.
[b] Supplement type: Fresco (0), Atole (1).
[c] Diarrhoea: Per cent days with diarrhoea between birth and 36 months:
Low (0) <5.14% (median for females)
Higher (1) ≥5.14%.
[d] Diet: Mean kilocalories/day from home diet between 15 and 36 months:
Low (0) < 656.33 kcal/day (median for females)
Higher (1) ≥656.33 kcal/day.
[e] SES = Socioeconomic status; SES (1975) = SES measured in 1975.
Standardized factor scores from principal components analysis were used in the analysis: Low SES (0) = Factor score <0; High SES (1) = Factor score ≥0.

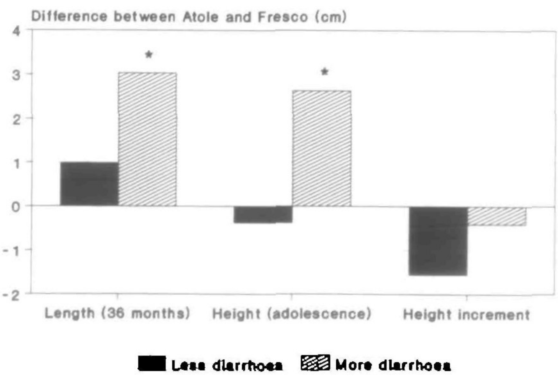

FIGURE 2 *Interaction between type of supplement (Atole/Fresco) and per cent days ill with diarrhoea, in males*

Height increment = Height at adolescence controlling for length at 3 years of age.
Less diarrhoea = <6.51% of days spent with diarrhoea during the first 3 years of life.
More diarrhoea = ≥6.51% of days spent with diarrhoea during the first 3 years of life.
*The 2-way interaction between supplementation and diarrhoea is statistically significant ($P < 0.05$).

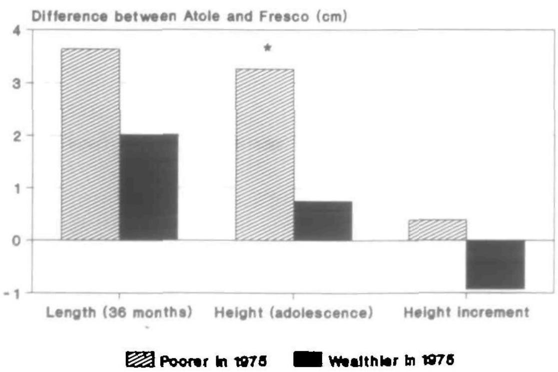

FIGURE 3 *Interaction between type of supplement (Atole/Fresco) and socioeconomic status in 1975, in females*

Height increment = height at adolescence controlling for length at 3 years.
Poorer in 1975 = Factor scores from principal components analysis <0 (see Methods).
Wealthier in 1975 = Factor scores ≥0.
*The 2-way interaction between supplementation and socioeconomic status in 1975 is statistically significant ($P < 0.05$).

TABLE 4 *Determinants of height at adolescence, controlling for length at 3 years and its determinants, in males and females (2SLS[a] models)*

Variable	Height at adolescence (Males) Model 4		Height at adolescence (Females) Model 4	
	B	(*P*-value)	B	(*P*-value)
Intercept	101.20	(0.00)	36.22	(0.01)
Maternal height (cm)	0.33	(0.00)	0.37	(0.00)
SES (1988)[b]	–0.70	(0.46)	–1.30	(0.19)
Skeletal age (years)	15.76	(0.00)	0.35	(0.01)
Skeletal age square	–0.42	(0.00)		
Length at 3 years (cm)	0.75	(0.00)	0.61	(0.00)
2-WAY INTERACTION:				
Length at 36 months				
* SES (1988)[b]	2.23	(0.15)	2 14	(0.11)

[a] 2SLS = Two-stage least squares analysis.
[b] SES = Socioeconomic status; SES (1988) = SES measured in 1988.
Standardized factor scores from principal components analysis were used in the analysis: Low SES (0) = Factor score <0; High SES (1) = Factor score ≥0.

females. Home diet during the first 3 years of life was not an effect modifier but was positively associated with growth, particularly in males. Children who consumed more calories from home diet during the first 3 years of life were taller at adolescence, and this effect was due to the positive effect of home diet on length at 3 years of age.

Table 4 presents the results of the 2SLS analysis of the determinants of growth between 3 years and adolescence. Skeletal age, maternal height and length at 36 months were statistically significant determinants of adolescents' height. The hypothesized interaction between SES in 1988 and length at 36 months on adolescents' height was not statistically significant for either gender. The model which included SES as a main effect only, also indicated a lack of association between SES in 1988 and height at adolescence (model not shown).

DISCUSSION

Differential Response to Supplementation

Our results support the hypothesis that some groups of children benefit more than others from food supplementation during early infancy, and that these benefits continue throughout adolescence and young adulthood. Diarrhoea and SES were the main determinants of benefit in our sample from rural Guatemala. Male children who spent on average more than 6.5% of their first 3 years of life with diarrhoea benefited more from the supplementation than children from the same villages who had less diarrhoea. In females, greater benefits from the supplementation were obtained among those who lived in poorer households. These benefits were seen both at 3 years of age and at adolescence, and the effects seen at adolescence were explained by differences already observed at 3 years of age. Home diet had a positive effect on growth throughout adolescence but was not a determinant of benefit, which suggests an additive effect with supplementation. In sum, our results show that nutrition interventions in early childhood have long lasting effects on body size and that the benefits acquired early in life remain throughout young adulthood.

Gender differences in response to supplementation have been documented in previous analyses of these data[5] and were attributed mainly to differences in maturity. In the present study, sex differences in the determinants of benefit were found, i.e. diarrhoea was significant in males and SES in females. One possible explanation for the absence of interaction between supplement and diarrhoea in girls could be their lower diarrhoeal morbidity compared to males. The median percentage of days sick with diarrhoea in the first 3 years of life was 6.51% and 5.14% for males and females, respectively. In absolute terms, this corresponds to a difference of 15 days for the period between zero and 3 years of age. This hypothesis was tested by using the male cutoff point (6.51%) to stratify low and high diarrhoea in females. The results did not confirm this hypothesis, and still showed a non-statistically significant interaction between supplement and diarrhoea when the cutoff for males was used. An alternative hypothesis, which cannot be tested with existing data, is that diarrhoeal illnesses may have been less severe in girls, and thus less detrimental to their growth. Previous studies that documented the interaction between diarrhoea and supplementation in early childhood did not stratify by sex, nor test the three-way interaction between supplementation, sex and diarrhoea.[15,16]

Socioeconomic status was a significant determinant of benefit in females but not in males. This may occur because diarrhoea, a more proximal determinant of nutritional status, was significant in the male model. This hypothesis was tested by excluding diarrhoea from the male model and testing the interaction between supplement and socioeconomic status. The interaction remained non-significant. Regardless of the fact that our hypothesis was not verified statistically, it is well known that diarrhoea is one of the main mechanisms by which socioeconomic status negatively affects children's growth.

Determinants of Adolescent Height

The 2SLS model showed that length at 3 years of age, maternal height and maturation were important determinants of height at adolescence. Maternal height was strongly associated with growth at all ages, even after controlling for current SES. Coefficients for maternal height were larger in the adolescents compared to the children models, suggesting that multigenerational factors, probably genetic, play a more important role at adolescence than at 3 years of age.

Current SES was not associated with height at adolescence, neither as main effect nor in interaction with length at 36 months of age. We had hypothesized that small 3 year olds might experience some catch-up growth between 3 years and adolescence, and that this catch-up may have been influenced by socioeconomic factors, thus hypothesizing a two-way interaction between length at 36 months and socioeconomic factors. Such an interaction was not confirmed by our analyses. Thus, our results provide additional evidence to previous findings in this population, that catch-up growth is not observed in later childhood and adolescence, and that growth during this period is probably less sensitive to socioeconomic influences than in the pre-school period.[17]

Practical Relevance of the Study

To our knowledge, this is the first analysis of the long-term differential response to early nutrition supplementation on later attained body size. The practical relevance of this area of research, which aims at identifying determinants of benefit, relates to the importance of the selection of beneficiaries for appropriate targeting of nutrition interventions. Screening with well-defined selection criteria improves targeting, which in turn, maximizes impact and cost-effectiveness. Studies to identify the characteristics of children who benefit from nutrition interventions are thus essential to assist programmes in the choice of screening and targeting mechanisms. The present study is unique in that 1) it used a methodology to predict benefit directly through response, rather than presuming that risk will predict benefit and 2) it goes beyond the identification of children who benefit in the short-term to test whether these same individuals benefit in the long-term when they reach adolescence and young adulthood.

Based on our findings, the logical recommendations for nutrition interventions would be to screen poor families and children with high rates of diarrhoea. Screening on diarrhoea rates, however, would imply screening after the damage is already done. Diarrhoea may be a good indicator of risk and of response to nutrition supplementation, but it would not be an efficient 'predictive' indicator.[18] Socioeconomic status, on the other hand, could be an effective screening tool, and special efforts should be made to develop simple, locally relevant indicators of family SES. In rural populations in the developing world, which rely largely on subsistence agriculture, accurate information on income is tremendously difficult to obtain. The common use of land ownership as a proxy for income has also been shown to be flawed because of differential endowments between regions.[19] In the present study, a socioeconomic indicator based on housing quality and family possessions was developed after careful assessment of local conditions. The indicator was found useful for research purposes and was simple enough to be included in the collection of census data. For use as a screening tool in large-scale primary health care programmes, however, the indicator would need to be simplified further, and validated against a more detailed survey of family SES.

Another important consideration is whether screening should be done at the individual or at the community level. Although this question was not addressed directly in the present analysis, it is generally recognized that individual screening is costly and time-consuming,[20,21] and may result in rivalries and sensitivities within communities when some children and their families are excluded from the interventions. Thus, the additional effort of individually screening children based on socioeconomic differences, as opposed to screening and targeting entire communities, must be weighed against potential benefits. In some cases, it may be more practical and efficient to screen poor communities, and to target all children below a certain age. Using the same data set, Schroeder *et al.*[22] showed that supplementation had the greatest impact on growth in children <3 years old, with the largest benefits in the first year. Thus, in poor communities where little variation in SES is found between families, it may be simpler and more efficient to target all children below a certain age and to start interventions as early as possible in the first year of life. The age cutoff point should be selected according to available resources.

The effectiveness and feasibility of applying these recommendations for individual versus community screening and targeting of food distribution programmes are currently being tested in Guatemala.

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