Adult consequences of growth failure in early childhood1–3

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ABSTRACT

Background: Growth failure is associated with adverse consequences, but studies need to control adequately for confounding.

Objective: We related height-for-age $z$ scores (HAZs) and stunting at age 24 mo to adult human capital, marriage, fertility, health, and economic outcomes.

Design: In 2002–2004, we collected data from 1338 Guatemalan adults (aged 25–42 y) who were studied as children in 1969–1977. We used instrumental variable regression to correct for estimation bias and adjusted for potentially confounding factors.

Results: A 1-SD increase in HAZ was associated with more schooling (0.78 grades) and higher test scores for reading and nonverbal cognitive skills (0.28 and 0.25 SDs, respectively), characteristics of marriage partners (1.39 y older, 1.02 grade more schooling, and 1.01 cm taller) and, for women, a higher age at first birth (0.77 y) and fewer number of pregnancies and children (0.63 and 0.43, respectively). A 1-SD increase in HAZ was associated with increased household per capita expenditure (21%) and a lower probability of living in poverty (10 percentage points). Conversely, being stunted at 2 y was associated with less schooling, a lower test performance, a lower household per capita expenditure, and an increased probability of living in poverty. For women, stunting was associated with a lower age at first birth and higher number of pregnancies and children. There was little relation between either HAZ or stunting and adult health.

Conclusion: Growth failure in early life has profound adverse consequences over the life course on human, social, and economic capital. Am J Clin Nutr 2013;98:1170–8.

INTRODUCTION

Globally, ~165 million preschool children are stunted, which is defined as a height-for-age $z$ score (HAZ)$^4$ less than $-2$ by using the WHO Child Growth Standards (1). Stunting usually develops <2 y of age (2) and, despite improvement in $z$ scores subsequently (3, 4), growth failure before age 2 y is an important cause of short adult stature (5). Causes of stunting are well known and range from poverty at the societal and household levels to the interaction between diets deficient in quantity or quality and infection at the individual level (1). Stunting is a marker of systemic dysfunction during a sensitive phase of child development. At the same time that growth failure is occurring, growth and development of other organ systems, including the brain and neurologic development, are affected. Therefore, stunting is a summary indicator of all influences that have an effect on growth and development during the first 1000 d of life from conception to 2 y. Consequently, stunting has been linked to many adverse outcomes related to later physical and cognitive development (6).

We investigated relations between height-for-age and stunting at age 24 mo and human, social, and economic capital of Guatemalan adults aged $\geq 25$ y. To our knowledge, our study is unique for 2 reasons. First, we included a more-comprehensive set of outcomes than in any other previous prospective study, including human capital (schooling, intelligence, and reading), marriage, fertility, health (cardiovascular disease risk factors and physical performance), the labor market, and household poverty. Second, because growth failure occurs in contexts of poverty and low education and where caregivers make decisions under severe constraints, we controlled for confounding and measurement error through the use of instrumental variables (IVs), which is an approach that allows for the possibility of making causal inferences.

SUBJECTS AND METHODS

Study setting

We linked data on growth in early life collected as part of a community-randomized food-supplementation trial conducted in rural Guatemala in 1969–1977 to follow-up data collected in 2002–2004.

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2 Supported by the NIH (grants TW-05598 and HD-046125), the National Science Foundation/Economics (grants SES 0136616 and SES 0211404), and Grand Challenges Canada (grant 0072-03). This is a free access article, distributed under terms (http://www.nutrition.org/publications/guidelines-and-policies/license/) that permit unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

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4 Abbreviations used: HAZ, height-for-age $z$ score; INCAP, The Institute of Nutrition of Central America and Panama; IV, instrumental variable; OLS, ordinary least squares; pp, percentage points; SIA, Serie Interamericana.
The Institute of Nutrition of Central America and Panama Longitudinal Study (1969–1977)

The Institute of Nutrition of Central America and Panama (INCAP) conducted a food-supplementation trial between 1969 and 1977 to test the effect of improved protein intakes on physical and mental development in children in 4 villages near Guatemala City (7, 8). One village from each of 2 pairs matched for population size was randomly assigned to receive atole, which is a nutritious supplement that provided 6.4 g protein/100 mL and 91 kcal energy/100 mL. In 2 other villages, residents received fresco, which is a drink that contained no protein and had 33 kcal/100 mL. Both supplements were fortified with micronutrients in equal concentrations by volume. Supplements were available to all village residents 2 times/d at a central location in each village. INCAP provided identical medical services to all 4 villages. Lengths at 3 y of age were similar in atole and fresco villages in 1968 before the supplementation program began. The nutritional intervention only improved child growth rates when consumed during the first 3 y of life and did so equally for boys and girls; most of the effect was before age 2 y (9). For children exposed to supplementation to 3 y of age, lengths were greater by 2.9 cm in atole and by 0.5 cm in fresco villages compared with baseline values, with a net difference of 2.4 cm in favor of children in atole villages ($P < 0.005$) (10).

Follow-up study (2002–2004)

We resurveyed the individuals in 2002–2004 (11, 12). Of the 2392 individuals enrolled in the original study, 1855 (78%) subjects were alive and living in Guatemala; 272 (11%) subjects had died; 162 (7%) subjects had migrated internationally; and 101 (4%) subjects were not traceable. A total of 1571 subjects completed at least one interview (11). For 1338 subjects, enough information was collected for inclusion in the study. With the use of a conservative definition whereby deaths were regarded as cases lost to follow-up (denominator: 2392), attrition was 44.1%. If, instead, deaths were classified as having been traced (denominator: 2120) (13), attrition was 36.9%. These rates were similar to those reported in other cohort studies in low- and middle-income countries, most of which had shorter durations of follow-up (6). All participants provided informed consent; the study was approved by Emory University’s Institutional Review Board.

Variable characterization

Characterization of linear growth and stunting

Length was measured at age 15 d and at or near 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48, 54, 60, 72, and 84 mo of age. We calculated a continuous measure of attained linear growth (ie, HAZ), by using WHO growth standards (14, 15). Stunting was defined as an HAZ less than –2.0. The average HAZ fell over infancy, reaching –3.2 at 24 mo. After this age, the average HAZ increased and approached –2.3 at age 72 mo. We chose 24 mo for the age at which the consequences of growth were assessed. We had direct observations on HAZ at age 24 mo for 696 individuals; we imputed values for subjects without a measure at 24 mo of age but with measures at other ages (n = 642). We assessed the robustness of our results to the use of imputed values and alternative choices of ages for the assessment of relations with HAZ [see section A (Supplemental Figure 1 and Supplemental Tables 1 and 2) under “Supplemental data” in the online issue].

Characterization of outcomes collected in 2002–2004

Outcome variables are defined in Table 1. We determined the ages at which individuals started and left school and the highest grade attained by interview. Subjects who passed a literacy screen test or who had completed $>$6 grades of schooling were administered the Inter-American Reading Series [Serie Inter-americana (SIA)] vocabulary (Level 3) and reading comprehension (Level 2) test modules, with a maximum combined score of 85 points (22). Subjects who did not pass the literacy screen (18% of the sample) were assigned a score of zero. All participants took the Raven’s Standard Progressive Matrices test, which is an assessment of nonverbal cognitive ability (23). We administered the first 3 scales for a maximum possible score of 36. SIA and Raven test scores are internally standardized to a mean ± SD of 0 ± 1 within the sample.

A marital history was administered to each individual in the sample. Marriage referred to any union, whether by common law or officially sanctioned. The module included questions on marital history and partner characteristics and provided the following outcomes: age at first marriage, age, grade attainment, and height of partner.

Women were asked in detail about their fertility history. From this questioning, we derived the age at first birth, total number of pregnancies, and number of surviving children (16). Fertility variables were cumulative to the date of interview; all analyses were adjusted for age.

We collected measurements of body size and composition, blood pressure, tests of physical fitness, and a finger-stick whole-blood sample from which plasma glucose and a lipid profile were measured (17). We considered the following measures: overweight or obese; isometric hand strength and predicted maximal oxygen uptake, hypertensive or prehypertensive state, and diabetic or prediabetic state. We also included the metabolic syndrome (17).

Individuals were interviewed about all of their income-generating activities, including wage labor, agricultural activities, and nonagricultural own-business activities (18). We included the following outcomes: wage rates; hours worked in the previous 12 mo; total net annual income from wage work, own-account agricultural, and own-business activities; whether an individual currently worked in clerical, administrative, technical, or professional positions; and whether an individual operated his or her own nonagricultural business for <9 mo/y.

Respondents provided information on household food and nonfood expenditures. With the use of these data and household compositions, we calculated the per capita household expenditure. We defined a household as poor if its per capita expenditure was below the Guatemalan poverty line (19).

Potentially confounding variables

We controlled for individual, family, and village characteristics. Individual characteristics included sex and year of birth. Family characteristics included the completed grades of schooling of the mother and father, whether a parent had died by the time the individual reached 15 y of age, an index of household wealth before the intervention (19) and the distance to the village center. Village fixed effects were represented by village dummy
### TABLE 1
Early-life growth failure and subsequent outcome variables: definitions and descriptive statistics

| Variable                        | Definition                                                                 | Sample size (all) | All            | F          | M          |
|---------------------------------|---------------------------------------------------------------------------|-------------------|----------------|------------|------------|
| HAZ at 24 mo                    | Height-for-age z score at 24 mo                                           | 1338              | -3.18 ± 1.09²  | -3.12 ± 1.06 | -3.24 ± 1.12 |
| Stunted at 24 mo                | =1 if height-for-age z score at 24 mo was less than -2                   | 1338              | 0.86 ± 0.34    | 0.86 ± 0.35 | 0.87 ± 0.33 |
| F (%)                           |                                                                           | 1338              | 49.8           | —          | —          |
| Schooling-related outcomes      |                                                                           |                   |                |            |            |
| Age started school              | Age (in y) when individual began attending primary school                | 1201              | 6.80 ± 1.09    | 6.78 ± 1.00 | 6.82 ± 1.19 |
| Age left school                 | Age (in y) when individual stopped attending school                      | 1201              | 12.51 ± 2.95   | 12.06 ± 2.86 | 13.02 ± 2.97 |
| Highest grade attained          | Highest grade of schooling completed                                     | 1238              | 4.70 ± 3.45    | 4.30 ± 3.31 | 5.15 ± 3.56 |
| SIA z score                     | Inter-American Series test score of reading and vocabulary, standardized with mean 0 and SD 1 within the sample | 1271              | 0 ± 1          | -0.072 ± 0.98 | 0.082 ± 1.02 |
| Raven z score                   | Raven’s Standard Progressive Matrices test score, standardized with a mean ± SD of 0 ± 1 in the sample | 1267              | 0 ± 1          | -0.23 ± 0.88 | 0.27 ± 1.06 |
| Marital market outcomes         |                                                                           |                   |                |            |            |
| Age at first marriage           | Age (in y) at time of first union formation                               | 1056              | 20.80 ± 4.10   | 19.76 ± 3.98 | 22.16 ± 3.79 |
| Partner’s age                   | Age (in y) of partner at time of current union formation                  | 1254              | 33.30 ± 7.16   | 36.24 ± 7.31 | 30.41 ± 5.68 |
| Partner’s highest grade attained| Partner’s highest grade of schooling completed                            | 1052              | 4.65 ± 3.37    | 4.94 ± 3.57  | 4.45 ± 3.20 |
| Partner’s height                | Partner’s height (in cm)                                                  | 935               | 155.7 ± 8.03   | 162.5 ± 5.72 | 150.5 ± 5.19 |
| Fertility-related outcomes (F only) (16) |                                                                           |                   |                |            |            |
| Age at first birth              | Age (in y) at time of first birth                                         | 592               | 20.84 ± 3.81   | —           | —          |
| Number of pregnancies           | Number of reported pregnancies including miscarriages and stillbirths     | 671               | 3.23 ± 2.16    | —           | —          |
| Number of children              | Number of surviving children                                              | 671               | 2.71 ± 1.86    | —           | —          |
| Health-related outcomes (17)    |                                                                           |                   |                |            |            |
| Overweight or obese             | = 1 if BMI (in kg/m$^2$) > 25.0                                          | 1160              | 0.17 ± 0.37    | 0.25 ± 0.43 | 0.09 ± 0.29 |
| Hand strength                   | Isometric strength of dominant hand measured in newtons                   | 1161              | 31.69 ± 9.13   | 25.57 ± 4.95 | 39.40 ± 7.15 |
| $\dot{V}$O$_2$max               | Maximal oxygen uptake (mL · kg$^{-1}$ · min$^{-1}$) predicted from recovery rates after administration of step-test | 1141              | 18.75 ± 8.50   | 22.38 ± 8.11 | 14.76 ± 7.01 |
| Hypertensive or prehypertensive | = 1 if systolic or diastolic blood pressure was >120 or 80 mm Hg, respectively | 1422              | 0.31 ± 0.46    | 0.20 ± 0.40 | 0.43 ± 0.49 |
| Diabetic or prediabetic         | = 1 if plasma glucose concentrations were between 100 and 125 mg/dL (prediabetic) or >126 mg/dL (diabetic) | 1186              | 0.21 ± 0.41    | 0.21 ± 0.41 | 0.20 ± 0.40 |

(Continued)
| Variable                                      | Definition                                                                 | Sample size (all) | Values                      |
|----------------------------------------------|---------------------------------------------------------------------------|-------------------|-----------------------------|
| Metabolic syndrome                          | = 1 if yes to ≥3 of the following variables: waist circumference > 102 cm for M and > 88 cm for F, triglyceride concentration ≥ 150 mg/dL, HDL cholesterol concentration < 40 mg/dL for M and < 50 mg/dL for F, blood pressure ≥ 130/85 mm Hg, and fasting glucose concentration ≥ 110 mg/dL. Drug therapy was extremely rare. | 1186              | All: 0.31 ± 0.46  F: 0.40 ± 0.49  M: 0.18 ± 0.39 |
| Labor market outcomes (18)                   |                                                                           |                   |                             |
| Wage rates                                   | Net income (Quetzales) from wage work, own-account agriculture, and own-business activities divided by hours worked conditional on earning any income in previous 12 mo. Exchange rate was 7.9 Quetzales per US$1 in 2004. | 1037              | 10.13 ± 12.12  8.55 ± 12.26  11.41 ± 11.87 |
| Hours worked                                 | Hours worked in the previous 12 mo                                         | 1041              | 2095 ± 1260  1613 ± 1382  2489 ± 990 |
| Total earned income                          | Net income (Quetzales) from wage work, own-account agriculture and own-business activities conditional on earning any income in previous 12 mo | 1037              | 20682 ± 25590  12562 ± 24905  27284 ± 24222 |
| Skilled labor or white collar worker         | = 1 if individuals currently work in clerical, administrative, technical, or professional positions, conditional on working | 1132              | 0.25 ± 0.43  0.11 ± 0.32  0.37 ± 0.48 |
| Operates own business                        | = 1 if individual operates own nonagricultural business for more than 9 mo | 1239              | 0.23 ± 0.42  0.37 ± 0.48  0.20 ± 0.40 |
| Expenditure and poverty (19)                 |                                                                           |                   |                             |
| Per capita household expenditure             | Per capita household expenditure (Quetzales)                              | 1335              | 7431 ± 6024  7877 ± 6764  6988 ± 5154 |
| Household is poor                            | = 1 if per capita household expenditure was below the poverty line (4319 Quetzales per capita) | 1335              | 0.29 ± 0.45  0.28 ± 0.45  0.30 ± 0.46 |
| Social confounders (20, 21)                  |                                                                           |                   |                             |
| Maternal schooling                           | Highest grade of schooling completed of mothers; maximum value is 12     | 1338              | 1.30 ± 1.62  1.22 ± 1.59  1.37 ± 1.65 |
| Paternal schooling                           | Highest grade of schooling completed of fathers; maximum value is 12    | 1338              | 1.68 ± 2.06  1.70 ± 2.01  1.67 ± 2.10 |
| Household wealth index score                 | Linear index encapsulating an array of household consumer durable goods and housing characteristics, measured at the nuclear family level in 1967 and calculated by using principal components analysis | 1338              | −3.08 ± 0.90  −3.08 ± 0.90  −3.09 ± 0.89 |
| Village school permanent structure when child was 7 y old | = 1 if primary school building was made of concrete when individual was 7 y old | 1338              | 0.51 ± 0.50  0.51 ± 0.50  0.51 ± 0.50 |
| Village student:teacher ratio when child was 7 y old | Number of students divided by the number of teachers in village school when individual was 7 y old | 1338              | 39.65 ± 8.61  40.01 ± 8.95  39.22 ± 8.22 |

1 HAZ, height-for-age z score; SIA, Serie Interamericana; V\textsubscript{O}\text{max}, maximal oxygen uptake.
2 Mean ± SD (all such values).
variables, which captured all time-invariant characteristics of these localities. From community developmental histories, we constructed proxy measures for schooling availability and quality, namely whether the primary school was a permanent, cement-block structure and the primary school student:teacher ratio, in both cases when each individual was 7 y old (21).

Statistical analyses

We estimated the relations of the set of outcomes with HAZ (continuous) and stunting (dichotomous), both at 24 mo. We used ordinary least squares (OLS) regression with the confounders previously described controlled for, but because OLS estimates may be subject to residual confounding by other, unobserved factors that are correlated with both growth and the outcomes (24–26), we also used an IV approach, whereby we treated HAZ (or stunting) as endogenous (Figure 1). In the first stage, we generated the predicted HAZ (or stunting) from IVs that we assumed were unrelated to the unmeasured confounders and were related to outcomes only through HAZ (or stunting). If these assumptions held, the estimated effect of the predicted HAZ (or stunting) was not biased by unmeasured confounders. IVs included 2 variables that represented the following effects of the nutritional intervention: 1) exposure to the randomized intervention from ages 0–24 mo and 2) exposure to the intervention from ages 0–24 mo and residing in an atole village (8). An individual participant was considered to be exposed 1) to either atole or fresco, which depended only on their village of birth; and 2) to the study intervention, either for the whole of a specified age range, or not, which depended only on their date of birth. Individuals with no or partial exposure in that age range were considered unexposed. Other IVs were maternal height and whether the individual was a twin. We estimated IV models by using a 2-step generalized method of moments (26).

Some variables were log transformed to normalize their distributions (Table 2). Because there were siblings in the sample, heteroscedasticity-robust SEs were calculated by allowing for clustering within mothers as well as correction for the 2-step estimation procedure (27). We report marginal effects, \( P \) values, and 95% CIs. When the outcome variable was in logarithms, we calculate the marginal effects of a 1-SD change in HAZ or the change from stunted to not stunted by using the following formula (28):

\[
100 \times (e^{\text{estimated coefficient}} - 1)
\]  

(1)

When the outcome was dichotomous, the coefficient \( \times 100 \) was the marginal effect in percentage points (pp).

For all outcomes except those relating to the labor market or fertility, models were estimated by pooling men and women because the coefficients did not differ significantly by sex (online supplemental material, section B, Supplemental Tables 3 and 4). For dichotomous outcomes, in addition to linear regressions we estimated probit regressions (see section C, Supplemental Table 5, under “Supplemental data” in the online issue). We tested the validity of IV estimates (see section D, Supplemental Tables 6–9, under “Supplemental data” in the online issue). Last, because the analyses were based on only a portion of the original sample, we implemented a correction procedure for attrition (see section E, Supplemental Table 10, under “Supplemental data” in the online issue) (29). Data were analyzed with Stata version 12 software (27).

RESULTS

Descriptive statistics are shown in Table 1, and OLS and IV results are shown in Table 2. In Table 2, estimated marginal effects in 1 (OLS) and 3 (IV) show changes in outcomes associated with a 1-SD improvement in HAZ. Estimates in 5 (OLS) and 7 (IV) show changes in outcomes associated with being stunted relative to not being stunted.

Both HAZ and stunting had many significant associations with schooling, marriage, female fertility, the labor market, and poverty outcomes in OLS analyses (Table 2, 1 and 5). When we used IV analyses (Table 2, 3 and 7), in general, the magnitudes of relations were magnified and remained significant for all but health and labor market outcomes. For these outcomes, some relations became nonsignificant with IV analyses, and the change in magnitude varied across coefficients.

IV results for HAZ (Table 2, 3) indicate that a 1-SD increase in HAZ at 24 mo was associated with a higher grade attainment (0.78 grades) and a delay in the age of leaving school (0.54 y). A 1-SD increase in HAZ was associated with increased test scores for reading and vocabulary (0.28 SIA \( z \) scores) and nonverbal cognitive skills (0.25 Raven \( z \) scores). With respect to spousal characteristics, a 1-SD increase in HAZ was associated with older age (1.39 y), more schooling (1.02 grade), and being taller.
| TABLE 2 | Early-life growth failure and outcomes across the life course 1 |
|---------|---------------------------------------------------------------|
|         | HAZ at 24 mo                                                  | Stunted (HAZ less than –2.0) at 24 mo |
|         | 1 OLS  2 P  3 IV  4  P                                      | 5 OLS  6 P  7 IV  8 P               |
| Schooling-related outcomes |                                                |
| Age started school (y)    | −0.09 (−0.15, −0.02) 0.018 −0.21 (−0.43, 0.02) 0.068 | 0.13 (−0.03, 0.28) 0.103 0.86 (−0.21, 1.93) 0.114 |
| Age left school (y)       | 0.38 (0.22, 0.54) 0.001 0.54 (0.07, 1.01) 0.025    | −0.76 (−1.29, −0.22) 0.006 −3.14 (−5.90, −0.38) 0.026 |
| Highest grade attained    | 0.51 (0.35, 0.67) 0.001 0.78 (0.25, 1.30) 0.003    | −0.93 (−1.48, −0.39) 0.001 −4.64 (−7.82, −1.47) 0.004 |
| SIA z score               | 0.17 (0.12, 0.23) 0.001 0.28 (0.10, 0.47) 0.003    | −0.26 (−0.43, −0.10) 0.002 −1.26 (−2.26, −0.27) 0.013 |
| Raven z score             | 0.15 (0.10, 0.21) 0.001 0.25 (0.09, 0.41) 0.002    | −0.27 (−0.44, −0.09) 0.004 −1.12 (−2.02, −0.33) 0.006 |
| Marriage market outcomes  |                                                |
| Age at first marriage (y) | 0.18 (−0.07, 0.43) 0.165 0.40 (−0.19, 0.98) 0.185 | −0.89 (−1.59, −0.19) 0.103 −2.58 (−5.37, 0.20) 0.069 |
| Partner’s age (y)         | 0.50 (0.18, 0.82) 0.002 1.39 (0.41, 2.37) 0.006    | −0.44 (−1.29, 0.42) 0.316 −6.78 (−11.71, −1.86) 0.007 |
| Partner’s highest grade attained | 0.32 (0.11, 0.54) 0.003 1.02 (0.42, 1.62) 0.001 | −0.68 (−1.38, 0.02) 0.056 −4.40 (−7.70, −1.11) 0.009 |
| Partner’s height (cm)     | 0.58 (0.20, 0.96) 0.003 1.01 (0.02, 2.00) 0.046    | −1.03 (−2.19, 0.12) 0.079 −3.28 (−7.46, 0.90) 0.124 |
| Fertility-related outcomes (F) |                                            |
| Age at first birth (y)    | 0.07 (−0.26, 0.40) 0.669 0.77 (0.03, 1.51) 0.043    | −0.91 (−1.87, 0.58) 0.063 −4.26 (−7.44, −0.89) 0.008 |
| Number of pregnancies     | −0.05 (−0.17, 0.07) 0.403 −0.63 (−1.05, −0.21) 0.003 | 0.27 (−0.04, 0.58) 0.085 2.39 (0.67, 4.11) 0.006 |
| Number of children        | −0.03 (−0.13, 0.06) 0.442 −0.43 (−0.82, −0.04) 0.032 | 0.22 (−0.04, 0.47) 0.095 1.74 (0.25, 3.24) 0.022 |
| Health outcomes           |                                                |
| Overweight or obese (pp)  | 6 (3, 8) 0.001 5 (3, 13) 0.209                          | −8 (−17, 1) 0.066 −22 (−64, 15) 0.226 |
| Log hand strength (%)     | 4 (3, 5) 0.001 5 (2, 8) 0.003                           | −6 (−9, −3) 0.001 −22 (−35, −7) 0.008 |
| Log VO2max (%)            | 3 (0, 6) 0.023 4 (3, 12) 0.255                          | −5 (−12, 2) 0.159 −21 (−46, 11) 0.183 |
| Hypertensive or prehypertensive (pp) | 4 (2, 7) 0.002 6 (1, 13) 0.067 | −6 (−14, 3) 0.178 −27 (−59, 6) 0.107 |
| Diabetic or prediabetic (pp) | 3 (2, 3) 0.846 3 (4, 9) 0.472                          | −8 (−15, 0) 0.046 −19 (−50, 12) 0.237 |
| Metabolic syndrome (pp)   | 3 (0, 5) 0.068 4 (3, 11) 0.237                          | −5 (−13, 4) 0.267 −21 (−54, 13) 0.221 |
| Labor market outcomes     |                                                |
| M Log wage rates (%)      | 13 (6, 20) 0.001 14 (2, 32) 0.080                      | −16 (−33, 4) 0.115 −52 (−82, −21) 0.136 |
| Log hours worked (%)      | −3 (−7, 1) 0.189 −11 (−20, 0) 0.044                   | 19 (1, 39) 0.038 77 (−12, 458) 0.111 |
| Log total earned income (%) | 10 (2, 19) 0.014 4 (12, 22) 0.691                      | −3 (−25, 26) 0.816 −23 (−75, 256) 0.643 |
| Skilled laborer or white collar worker (pp) | 6 (2, 9) 0.002 8 (3, 18) 0.173 | −1 (−14, 12) 0.861 −31 (−97, 36) 0.360 |
| Operates own business (pp) | 1 (2, 4) 0.372 4 (3, 11) 0.279                        | −2 (−12, 8) 0.702 −27 (−76, 22) 0.276 |
| F Log wage rates (%)      | 12 (2, 23) 0.019 5 (20, 36) 0.745                      | −14 (−36, 15) 0.302 −18 (−74, 166) 0.748 |
| Log hours worked (%)      | 17 (2, 34) 0.030 20 (12, 63) 0.252                     | −17 (−43, 21) 0.336 −48 (−86, 92) 0.327 |
| Log total earned income (%) | 30 (9, 55) 0.003 9 (27, 51) 0.641                      | −27 (−55, 17) 0.196 −30 (−87, 274) 0.681 |
| Skilled laborer or white collar worker (pp) | 9 (3, 16) 0.003 2 (1, 6) 0.147 | −12 (−23, −1) 0.039 −41 (−75, −7) 0.017 |
| Operates own business (pp) | 2 (1, 5) 0.227 11 (3, 19) 0.010                       | 1 (−9, 11) 0.081 −35 (−74, 4) 0.075 |

(Continued)
TABLE 2  (Continued)

| Expenditure and poverty outcomes | Stunted (HAZ less than $-2.0$) at 24 mo | $p$ | OLS | $p$ | IV | $p$ |
|----------------------------------|----------------------------------------|-----|-----|-----|-----|-----|
| Log per capita household expenditure (%) | $-3 (9.13)$ | 0.011 | $-3 (9.13)$ | 0.012 | $-3 (9.13)$ | 0.012 |

All values are marginal effects (95% CIs) unless otherwise indicated. For each outcome, we estimated a separate regression model using OLS, IV, and IV analyses. We also estimated a separate regression model for each outcome, using OLS and IV analyses. We carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also estimated a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses. We also carried out the following analyses: (a) OLS; (b) IV; (c) a separate regression model for each outcome, using OLS and IV analyses.

DISCUSSION

To our knowledge, this study provided new evidence on the relation between growth failure at 24 mo and adult outcomes. Previous studies have included a limited set of adult outcomes, particularly in regards to marriage, fertility, and economic outcomes (6). With the use of data from the 1988–1989 follow-up study of this study cohort and OLS regressions, we linked stunting at 3 y with anthropometric characteristics, schooling, and test performance in the subsample of 18–25-y-olds (30). In the current study, we used data collected 15 y later, when most participants had finished schooling, were married, and had
chosen an occupation. This method allowed for the inclusion of a wider array of adult outcomes including the marriage market, fertility, health, labor market, and expenditure and poverty.

The current study also used IV methods, which have the potential to adjust for both observed and unobserved confounders in observational studies, and, therefore, to support attribution of causality (24–26). Common in econometric research, IV methods have been used increasingly in epidemiologic and biomedical research (25). In one instance, C-reactive protein haplotypes associated with plasma C-reactive protein were used as instruments in studies of the metabolic syndrome (31). Other applications of IV methods have included the use of a calendar period as an instrument in AIDS research (32), geographic location as an instrument in cardiovascular research (33), and the maximum potential cumulative cash transfers that a family could receive from Mexico’s Oportunidades program to study the impact of cash transfers on height-for-age, verbal and cognitive performance, and behavior (34).

Our use of IVs was motivated primarily by the concern that HAZ at 24 mo was the outcome of parental and family choices made under various constraints, and reasons for such choices may have influenced adult outcomes in ways that did not operate directly through what HAZ represents. A second but equally important concern was with random error in the measurement of HAZ. Although the direction of bias in OLS results from the first source of correlation is ambiguous, depending on the specific sources and their correlation with the error term, the sign of bias from random measurement error is attenuation toward zero. Although HAZ was measured by using standardized techniques with minimal error (35), we used the predicted HAZ in part of the sample and this likely introduced some random error. Finally, we interpreted HAZ to be a proxy of factors that influenced growth and development in early life; it is likely that there was random error in how well HAZ represented these causes. Because of this, OLS estimates may have understated the magnitude of the relation between HAZ (or stunting) and adult outcomes of interest as we showed.

We showed that our IV variable analyses met tests of validity (see “Supplemental data” in the online issue), which provided support to the claim that the relation between growth failure and adult outcomes we estimated was causal. We did not consider HAZ or stunting at 2 y to be the causal factor per se. Rather the cause was the cascade of factors at societal, household, and individual levels, such as those depicted in the UNICEF conceptual framework (36), which ultimately determines nutrient availability at the cellular level and directly has an effect on growth and development in the first 1000 d of life.

Our study population showed marked linear growth failure at 24 mo of age with a mean HAZ less than −3 and a prevalence of stunting of 86%. We showed that individuals who were stunted suffered profound adverse consequences in adulthood. These individuals scored worse on tests of reading and intelligence. As measured by grade attainment and height, individuals who were stunted matched with poorer-quality partners. Women had their first child at younger ages and had more pregnancies and more children. Growth failure in early life resulted in individuals being more likely to live in poor households as adults. Conversely, better growth, as indicated by HAZ, led to better adult outcomes.

We did not find significant associations of growth failure with most measures of health or with women’s wage rates. For many health measures, such as the metabolic syndrome, this sample may have been too young to have been able to observe an effect. Also, linear growth in early childhood has weak, if any, relations, with cardiovascular disease risk factors. Instead, weight-for-length, particularly after 4 y of age, is more consistently and strongly related to these outcomes (5). Our IV findings strongly suggested an impact on men’s but not women’s wage rates. The majority of women who were working in the sample engaged in low-productivity activities such as agricultural processing (8, 18), which may explain the absence of effects of HAZ on women’s wage rates, despite the positive effects on the sector of occupation.

Our results may be extrapolated to settings with significant levels of stunting that also are undergoing the nutrition transition. The results were consistent with the large literature from other observational studies across diverse populations (6). However, our IV estimates appeared greater in magnitude than in many previous studies. For example, a 1-SD increase in HAZ at 24 mo was associated with 0.5 additional grades of schooling in a study of 5 cohorts from low- and middle-income countries, including in our cohort (6). Our OLS estimate was identical but our IV estimate was larger (0.8 grades). This comparison suggests that the impact of stunting may have been underestimated in the literature because of unmeasured confounders and measurement errors.

Our findings may have been limited, first, by the substantial level of attrition. However, the regression models we used controlled for a large number of covariates, many of which also were associated with attrition (11). Therefore, these results controlled in part for possible selectivity effects of attrition in the sample. Moreover, procedures to address a possible attrition bias did not change our results appreciably. We interpreted these findings to mean that our results were unlikely to be biased by attrition.

A second possible limitation was that growth failure in early life may have been correlated with other factors that affected outcomes over the life course. Our estimates, however, included 1) covariates for age to control for cohort effects, which captured unmeasured events common to all individuals of a given age; 2) controls for parental and household characteristics; 3) village fixed effects, which controlled for all unmeasured time-invariant events that were common to residents of the same village; and 4) time-varying village characteristics measured at the age of school entry. In addition, the IV estimation explicitly accounted for correlations between growth failure and other unmeasured factors that may have affected these outcomes.

Despite these potential limitations, our study has multiple strengths. The original study included measurements of growth in early life. The period of follow-up was >25 y and included high-quality data across a wide range of life course outcomes. Appropriate and robust statistical methods were used.

We did not elucidate explicitly the pathways through which growth failure operates. The results, however, suggested the following sequence. Early life growth failure is a marker of dysfunction and malnutrition that also affects neurological development, which has long-term consequences for schooling. Lowered grade attainment results in poorer matches in the marriage market, and in women, it leads to higher fertility. Fewer grades of schooling reduce the likelihood of entry into higher return labor market activities; and lower cognitive skills reduce earnings for men. Lower earnings, together with poorer matches in the marriage market, result in lower levels of household expenditure and greater risk of being poor.
In conclusion, this study fills important gaps by examining a range of consequences in adulthood of growth failure in early life with the use of appropriate statistical methods to account for potential confounding and to compare directly the relative strengths of associations across a wide range of outcomes. We showed that growth failure has substantial effects on important outcomes, especially family formation, reproduction, men’s wage rates, and the prevention of poverty, which are likely mediated through schooling and cognitive achievement. Our analyses provide a powerful rationale for the current focus on improving childhood nutrition and promoting linear growth from conception to age 2 y because it confers lifelong benefits to individuals as well as their families.

We thank other members of the Human Capital Study team (Ann DiGirolamo, Ruben Grajeda, Humberto Méndez, Usha Ramakrishnan, and Luis Fernando Ramírez) and Alexis Murphy, Scott McNiven, and Meng Wang for their excellent research assistance in the preparation of data for this article.

The authors’ responsibilities were as follows—JH, JRB, JAM, MR-Z, ADS, and RM: designed the research; PM: was field director; JAM and MR-Z: trained field workers and supervised data collection in economics and health, respectively; JH, JRB, and JAM: performed statistical analyses; JH, JRB, JAM, ADS, and RM: wrote the first drafts of the manuscript; ARQ, MR-Z, and KMY: provided comments; RM: had primary responsibility for the final content of the manuscript; and all authors: read and approved the final manuscript. None of the authors had a conflict of interest.

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