Impact of Early and Concurrent Stunting on Cognition

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Abstract

Undernutrition is associated with poor cognitive development, late entry into school, decreased years of schooling, reduced productivity, and smaller adult stature. We use longitudinal data from 1674 Peruvian children participating in the Young Lives study to assess the relative impact of early stunting (stunted at 6-18 months of age) and concurrent stunting (stunted at 4.5-6 years of age) on cognitive ability. Anthropometric data were longitudinally collected for children at 6-18 months of age and 4.5-6 years of age at which time verbal and quantitative ability were also assessed. We estimate that an increase in concurrent height-for-age z-scores (HAZ) by one standard deviation was associated with an increase in a child's score on the Peabody Picture Vocabulary Test (PPVT) by 2.35 points (CI: 1.55-3.15) and a 0.16 point increase on the Cognitive Development Assessment (CDA) (CI: 0.05-0.27). Further, we report that the estimate for concurrent HAZ and PPVT is significantly higher than the estimate for early stunting and PPVT. We found no significant difference between early and concurrent estimates for HAZ and CDA. Children from older mothers, children whose mothers had higher education levels, children living in urban areas, children who attended preschool, children with fewer siblings, and children from wealthier backgrounds scored higher on both assessments. Cognitive skills of children entering school were associated with early stunting but the strongest association was found with concurrent stunting suggesting that interventions preventing linear growth faltering should not only focus on the under twos but include children up to five years of age.

Key words: stunting, chronic undernutrition, cognitive development, preschool children, Peru

<center>Introduction</center>

Approximately 150 million children, or roughly one quarter of children worldwide, experience stunting (low height-for-age), while 20% are underweight (de Onis 2008). Children who are moderately to severely underweight have a 5-8 times greater risk of dying than well nourished children. Even children who are mildly underweight have a risk of death that is twice as high as well nourished children (Black et al. 2003). Undernutrition is responsible for 2.2 million deaths and 21% of Disability-Adjusted Life-Years (DALYs) among children less than five years of age. Maternal and child undernutrition is estimated to account for 3.5 million deaths and 11% of all global DALYs (Black et al. 2008). Micronutrient deficiencies account for 10% of deaths and DALYs in children less than five years of age (Bhutta et al. 2008).

Undernutrition is also associated with poor developmental outcomes (Adair 1999, Berkman et al. 2002, Daniels & Adair 2004, Li et al. 2003, Alderman et al. 2006, Victora et al. 2008). Children who experience stunting in early childhood are more likely to have vocabulary deficits (Sigman et al. 1991, Walker et al. 2000, Grantham-McGregor 2002) and other deficiencies in school performance and intelligence (Grantham-McGregor 1995). As Grantham-McGregor and colleagues have noted (2007), with respect to poor outcomes associated with undernutrition, death is the tip of the iceberg.

While much is known about the association between undernutrition and cognitive development, gaps in knowledge persist. National level statistics on cognitive development in children are lacking. While there are numerous cross-sectional studies indicating an association between concurrent undernutrition and cognitive ability, there are few longitudinal studies that do so (Grantham-McGregor et al. 2007). The major longitudinal studies linking undernutrition to poor cognitive development evaluate the relationship between undernutrition and early development (e.g. motor development) as well as cognitive development in adolescence or later. Some longitudinal studies examine the association between early nutritional insult and cognitive abilities of children entering school (Martorell et al. 2002, Cheung et al. 2001, Berkman et al. 2002, Kuklina et al. 2004, Cheung 2006) but additional longitudinal studies are needed.

In this paper we describe the prevalence of undernutrition among Peruvian children in early infancy (6–18 months of age) and childhood (4.5–6 years of age). We test the hypothesis that early stunting (at 6-18 months of age) has a greater impact on cognitive abilities of children entering school than concurrent stunting (4.5–6 years of age).

Materials and Methods

Study Design and Background

The Young Lives study, which uses a prospective cohort design, is a multi-country research study investigating the consequences of childhood poverty, how poverty is passed from one generation to the next, and the effectiveness of poverty-reduction policies (www.younglives.org.uk). The study has followed 12,000 children since 2002 and plans are to follow these children over a total period of 15 years. The study includes four countries: Ethiopia, India, Peru and Vietnam. These countries were selected to represent a broad range of political, social, geographical, and cultural contexts and circumstances. Each country follows two groups of children, one group beginning at approximately one year of age and the other enrolled at about eight years of age. To meet our study objectives, we describe methods related to the sampling of children from the younger Peruvian cohort.

The study covers urban, peri-urban, and rural areas including respondents from all three main geographic regions in Peru—coastal, highland, and jungle. Impoverished populations were oversampled. The study is managed in Lima, Peru by researchers from the Instituto de Investigación Nutricional (IIN) and Grupo de Análisis para el Desarrollo (GRADE).

Study Participants

In the first round in 2002, 2052 children aged 6–17.9 months from 74 communities were recruited. A multi-stage sampling strategy was used. Districts were chosen by employing a list ranking of all the districts in Peru according to poverty level. The poverty rank was based on measures of infant mortality, schooling, housing and access to services. The highest ranking five percent of the districts were excluded to ensure that the study oversampled impoverished districts. Researchers then systematically selected 20 districts using a randomly selected individual starting point and fixed population interval. This randomization process

was repeated 10 times until researchers arrived at a sampling framework that included the geographical areas of Amazon jungle, mountains and coast with a spread across the whole country. Using maps of each district a house was then randomly chosen as the starting point and subsequent houses were visited in systematic fashion until 100 children were enrolled. (Wilson et al. 2006). Because some districts were too small to yield 100 households with eligible children contiguous districts were added until 100 children were enrolled.

This process resulted in a sample that approximates to 95 percent of the children in Peru excluding the wealthiest 5 percent of households. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the London South Bank University, London School of Hygiene and Tropical Medicine, University of Reading and the Ethics Committee of the Instituto de Investigación Nutritional in Lima, Peru. Written informed consent was obtained from the parent or legal guardian of the children enrolled in the study. For illiterate respondents, verbal consent was obtained by interviewers prior to the interviews and was witnessed and formally recorded. Study approval was also obtained from Peru's Ministry of Health and from local authorities and community leaders.

Data Collection

Interview questionnaires were developed by international experts from several fields. The questionnaires consisted of a core survey used in all four countries participating in the Young Lives study. A community questionnaire was also used to assess population size (e.g. urban vs. rural) and geographic location (e.g. jungle, highland, coast). Investigators from each country added country-specific questions. The questionnaire used in Peru included information on the following: household composition, child health (including acute and chronic illness), caregiver characteristics, livelihoods, socio-economic status (assets), social capital, anthropometry of the child, childcare, and cognitive development.

Anthropometric data were obtained through the use of standardized digital platform scales (Soehnle) accurate to 100g and locally made rigid measures accurate to 2mm, with fixed head and moveable foot piece. The core questionnaire was translated into Spanish and then revised and modified through field testing and a pilot study before being used to collect data from the full cohort. Fieldworkers were trained extensively before interviewing began with special

emphasis on economic sections of the questionnaire and how to properly use the questionnaire in rural areas. Members from each team were trained and standardized in anthropometric measurement according to WHO protocols. The training of fieldworkers culminated in a large pilot study where the data collection instrument, fieldworkers, and entire data collection system were tested in a mixed rural-urban district. The process of training, testing and revision took approximately three months.

First round data were collected in 2002 when children were 6–18 months of age. Second round data collection took place in 2006 and 2007 when the same children were 4.5–6 years old. Data collection was conducted by three teams consisting of six interviewers each. Field managers and study investigators oversaw all three teams. Each of the three teams worked in 6–7 districts. Interviews lasted 2–4 hours and each district took 2–3 weeks to complete 100 interviews. In total, more than 40,000 households were contacted in order to find and enroll both the younger and older cohort of children.

Investigators used several methods to minimize the loss of participants at follow-up. First, after the initial enrollment and baseline interview, participants received information about the study and at each subsequent visit they were given a present of a certificate with a photo of the child at each round, families were asked to give names and addresses or telephone numbers for family or friends with whom they were likely to maintain contact. The field staff visited the household once between the data gathering rounds in order to maintain contact and deliver the photos. Families were also asked to let the project team know if they moved and were given telephone numbers and a stamped addressed envelope to facilitate this. Finally, during round 2, interviewers returned to the home as many times as needed until they were able to conduct the interview, were turned away, or were able to confirm the person no longer lived at the residence. Households with participating children were contacted almost annually to ensure continued involvement in the study. Additionally, children who did move were still contacted. If children moved within Peru, every effort was made to interview them. If children moved outside the country, they were contacted, but no effort was made to interview them. Only 3.5 percent of children were lost to follow-up during the four years between round 1 and round 2.

Data from round 1 was entered using Delphi (Austin, TX, USA), a data entry software program, and then transferred into Microsoft Access (version 2000, Seattle, WA, USA). Data

from round 2 was entered directly into Microsoft Access (round 2). Both data entry systems used pre-programmed skip patterns and data and acceptable range controls. Additional information on the Young Lives Peruvian cohorts can be found at: http://www.ninosdelmilenio.org/.

Cognitive Outcomes

Several cognitive development assessments were pilot tested in the field. Based on these results, Young Lives researchers selected the Peabody Picture Vocabulary Test (PPVT) to assess listening comprehension and vocabulary skills and the Cognitive Development Assessment (CDA) to assess quantitative reasoning of children 4.5-6 years of age. The PPVT has been in use since 1959 and has several variations (PPVT-I, PPVT-II, PPVT-III, and PPVT-R). The PPVT has shown a strong correlation with other intelligence measures such as the Wechsler and McCarthy Scales (Campbell 1998, Gray et al. 1999, Campbell et al. 2001). The PPVT-R (Spanish version) consists of 125 items and was used for the Young Lives cohort (Dunn et al. 1986, Dunn & Dunn 1997). The PPVT has been used extensively as a measure of cognitive ability in many studies (Desai et al. 1989, Baydar & Brooks-Bunn 1991, Blau & Grossberg 1992, Parcel & Menaghan 1994, Rosenzweig & Wolpin 1994, Grantham-McGregor et al. 1997, Blau 1999, Walker et al. 2000, McCulloch & Joshi 2002, Kordas et al. 2004, Walker et al. 2005, Paxson & Norbert 2007). The Spanish version was reviewed by local language experts and then pilot tested to ensure that respondents were able to understand the questions.

The PPVT is orally administered, not timed, and is given individually. During the PPVT test, the child is presented with a stimulus word and a set of pictures and is asked to select the picture that best represents the word's meaning. Test items are ordered from easiest to hardest. Each child is only given items within his or her critical range and is not given the entire set of questions. The critical range is established by the child's chronological age, which corresponds with a specific start point on the test. The test administrator begins at the starting point and proceeds until a ceiling (the point at which the respondent has 6 errors in a stretch of 8 responses) is reached. The PPVT yields raw scores that can then be standardized using a sample of PPVT test scores for other Latin American countries (Dunn et al. 1986).

The CDA was developed by the International Evaluation Association for the purpose of studying the impact of attending pre-school on cognitive development in four-year old children. The CDA has three main components or subtests: quantity, time, and spatial relations. The Young Lives study used only the quantity subtest, which measures a child's notion of amount. Young Lives researchers pilot tested both the spatial relations and time subtests. The spatial relations subtest was not used in the Young Lives study due to the large amount of time it took to administer. The time subtest was not used because of low reliability among the Young Lives sample in Peru. The CDA was translated into Spanish for use in the Young Lives cohort. The translation was verified by a local Spanish language expert and then pilot tested.

The CDA quantity subtest consists of 15 items. Each item includes three or four images that the child is asked to consider in response to a question posed by the interviewer. For example, the interviewer shows the child a picture with several smaller images of cats and dogs and says, "Look at the cats and dogs and point to the picture where the dog has less food than the cat." The child must then consider the different amounts of food and quantify them in order to determine the correct picture. Correct responses receive a score of 1 point while incorrect responses are given a score of 0.

Validity and reliability were established during pilot testing to ensure the appropriateness of using the PPVT and the CDA for the Young Lives sample. Young Lives researchers measured validity by assessing the degree to which evidence and theory supported the interpretations of test scores. Researchers estimated the correlation between each test score and variables such as age and educational level to determine whether these measures were supported by previous empirical evidence from the literature. For example, on average, children in higher grades of school should get better results than children in lower grades or children who no longer attend school. Furthermore, parental education should be positively correlated with scores on tests). Reliability was established according to Classical Test theory (CTT) and Item Response theory (IRT) (Baker & Kim 2004, Crocker & Algina 1986). The CTT was applied by using split-half reliability coefficients to assess internal consistency. This was followed by the estimation of reliability coefficients using the Spearman-Brown prophecy formula. The IRT was applied by using the Person reliability index. Both assessments were found to have acceptable psychometric properties based on both Classical Test Theory and Item Response Theory for children who spoke Spanish as their native

language. Native Quechua speakers scored below the acceptable thresholds for both measures. For example, for Quechua speakers, Cronbach's Alpha for the reliability coefficients of the CDA were below acceptable standards for the CTT (the acceptable level was 0.6 but the level for Quechua speakers was 0.4). The person reliability index among Quechua speakers (0.4) was also below the standard (0.5). The relatively poor performance of the tests in Quechua speakers was thought to be due to difficulties with the translation particularly due to the variation in the vocabulary of Quechua spoken in different parts of the country. As a result, only Spanish speakers (n=1706) were included in our analyses.

Covariates

Height-for-age z-scores from both rounds of data were used. Z-scores are based on the international reference standard from the World Health Organization (available at: http://www.who.int/childgrowth/en/). The z-score is calculated through an interpolation function that accounts for sex, age, and height. We defined moderate stunting as a height-for-age z-score between -2.0 and -2.99 standard deviations below the mean on the international reference standard. We defined severe stunting as a height-for-age z-score less than -3.0 standard deviations below the mean on the international reference standard. A height-for-age z-score less than -2.0 from round one was categorized as early stunting, while a height-for-age z-score less than -2.0 from round two was referred to as concurrent stunting, because it was concurrent with our cognitive assessments. Additionally, we calculated weight-for-age and weight-for-height z-scores based on the same cut-offs used for stunting. Because there were few children with low weight-for-height, we did not include this variable as a predictor of cognitive ability.

Using the conceptual framework outlined by Black and colleagues for the determinants and consequences of undernutrition, we controlled for potential confounding variables available in the Young Lives study (Black et al. 2008). These variables included: age, sex, site (urban/rural), region (coast/highland/jungle), maternal education, maternal age, religion, preschool attendance, primary school attendance, and a wealth index. The wealth index is based on work from the World Bank and is used in UNICEF's Multiple Indicator Cluster Surveys. The index is a continuous score from 0–1 that is a composite of housing quality, consumer durables, and services (e.g. drinking water, toilet, electricity, etc.) (Filmer &

Pritchett 2001).

Data Analysis

Z-scores were calculated with the EpiNut module of EpiInfo (version 2000, Centers for Disease Control and Prevention, Atlanta, GA, USA). All statistical analyses were conducted using Statistical Analysis Systems statistical software version 9.1 (SAS Institute, Cary, NC, USA). Study participants and prevalence of stunting, wasting, and underweight were described. More than 2000 children were enrolled at baseline, however, we only analyzed data for children who had anthropometric information at baseline and follow-up and who spoke Spanish (n=1674).

In order to test our hypothesis that early stunting (6-18 months of age) has a greater impact on the cognition of children entering school than concurrent stunting (4.5-6 years of age), we went through three processes. First, we reviewed the literature and conducted univariate analyses to identify variables that should be included in multivariate models. We then used mixed effects regression to determine the relative impact of early versus concurrent stunting (when children were 6-18 months of age and 4.5-6 years of age, respectively) on each cognitive outcome. Finally, we compared the coefficients for early and concurrent stunting for each cognitive model using a Wald test. This test determined whether or not the coefficients for each model were significantly different. Mixed effects regression models are considered appropriate when sampling is based on clusters. We present unadjusted models as well as models that account for known confounders. With the MIXED procedure from SAS we produced models with an unrestricted covariance structure for random effects, a random intercept for variation between clusters, and fixed effects for all other variables in the model (e.g. early stunting, concurrent stunting, maternal age, maternal education, area population, preschool attendance, child age, wealth index, and number of siblings). We retained or dropped variables from the models based on p values (<0.1) and conceptual considerations and reported regression coefficients and 95% confidence intervals for all retained variables. We checked all models for interaction and for compliance with model assumptions. Interaction terms were checked for all retained variables for each model. None were retained based on p values (<0.1).

Results

Of all survey respondents, nearly three-quarters lived in urban areas, most lived in coastal (40.2%) or highland (43.0%) regions compared to the jungle region (16.8%), and nearly half of all children were female 'Table 1'. Catholicism was the predominant maternal religion and nearly all mothers described themselves as *mestizo*. The mean age of children during the first round was 12 months, 86.1% of children attended preschool, and the mean score for wealth index was 0.42.

Prevalence of stunting, wasting and underweight in round 1 are described in Table 2. The percentage of children who were stunted in round 2 rose approximately 5 percentage points while prevalence of underweight children in round 2 decreased slightly.

Figure 1 illustrates the distribution of height-for-age z-scores (HAZ) for children from each round of data collection. The figure does not depict changes across time for individual children, but does display general trends in the population by age. During the first round of data collection, there is a general decline in HAZ from 6–18 months of age. Children from urban and rural areas appear to decline at a similar rate. Additional decline takes place between 18 and 56 months of age.

Unadjusted regression estimates between covariates and verbal score are presented in table 3. Children from urban areas performed better on verbal cognitive tests than those from rural areas. Higher early and concurrent HAZ scores were also associated with better verbal scores. Those who attended preschool fared better than those who did not. Additional variables significantly associated with verbal score were wealth index, maternal age, and number of siblings. A higher level of completed maternal education was also associated with a higher verbal score.

Adjusted results demonstrate that children with higher concurrent z-scores, children with older mothers, children with mothers who had increased education, children living in urban areas, children who attended preschool, children with fewer siblings, and children from wealthier circumstances were more likely to score higher on the PPVT verbal assessment than their counterparts 'Table 3'.

What is most notable about findings presented in table 3 is the large difference between

adjusted estimates for early and concurrent stunting: improving height-for-age z-scores of *infants* by one standard deviation increased their score on the Peabody Picture Vocabulary Test (PPVT) by only 0.20 points (95% CI: -0.59, 0.99) but improving their *concurrent* height-for-age z-scores (i.e., when they were 4.5-6 years of age) contributed to a 2.23 point increase (95% CI: 1.29, 3.17). Further, we found that the differences in estimates were statistically significant (p-value=0.0083). Thus, concurrent stunting had a greater impact on vocabulary test scores than early stunting.

Table 4 displays unadjusted regression estimates between covariates (including HAZ) and quantitative scores. The child's age at round 1, maternal education, wealth index, and number of siblings were all significantly associated with quantitative scores. In addition, higher early and concurrent HAZ scores were associated with higher quantitative scores. The adjusted model was similar except early stunting was no longer associated with quantitative score. As with verbal scores, the impact of concurrent stunting on CDA scores appeared greater than the impact of early stunting. However, the difference between coefficients was not significant. Thus, we cannot conclude that concurrent stunting had a significantly greater impact on CDA scores than early stunting despite the notable difference in magnitude.

Coefficients for models where the CDA test score is the dependent variable are small in comparison to coefficients for PPVT test scores. However, it must be remembered that there were approximately 10 times as many items on the PPVT test. Thus, multiplying coefficients in models predicting CDA test scores by 10 helps when comparing coefficients from both models.

Because of the very low prevalence of wasting at the early assessment, we did not model the relationship between wasting and the cognitive measures.

Discussion

We show that there are a variety of factors that predict verbal and quantitative test scores among young Peruvian children. These include wealth, living in an urban setting, increased maternal education and age, preschool attendance and fewer siblings. Our findings also indicate that children who demonstrate linear growth restriction concurrent with cognitive measurements when they enter school (4.5–6 years of age) are more likely to score poorly on

cognitive tests than their better-nourished peers. While our findings do not demonstrate an association between children who experience linear growth restriction at an early age (6–18 months) poor performance on cognitive tests when controlling for concurrent growth restriction, models with only early stunting (i.e., no concurrent stunting indicator in the model) do show a strong association between early height-for-age z-scores and both cognitive outcomes (data not shown). What is more notable about our results is the greater impact of concurrent stunting than early stunting, both for verbal and for quantitative measures of cognition. These findings do not support our hypothesis that early stunting is more important in predicting cognition than concurrent stunting. Our results, though, are consistent with cross-sectional studies that demonstrate associations between early nutritional insult and intelligence scores during the early school years (Agarwal et al. 1989, Beasley et al. 2000, Cheung 2006, Paxson & Norbert 2007) as well as longitudinal studies that report an association between early nutrition and later adolescent cognitive ability and academic achievement (Martorell et al. 1992, Grantham-McGregor 1995, Grantham-McGregor et al. 1997, Martorell 1997, Hack 1998, Mendez & Adair 1999, Beasley et al. 2000, Cheung et al. 2001, Glewwe et al. 2001, Berkman 2002, Kuklina et al. 2004, Ivanovic et al. 2004). However, the results reported here examine intelligence at the time that students enter school which has not been well studied using longitudinal data.

Our results illustrate the importance of assessing HAZ beyond 18 months of age. Specifically, in this sample children continued to experience stunting past 18 months, sometimes falling an additional standard deviation between 18 and 56 months of age. This is consistent with findings that show that height-for-age scores begin faltering immediately after birth and continue into the third year of life (Martorell 1999, Shrimpton et al. 2001).

We found a strong association between wealth index and cognitive scores. This is similar to findings from a recent study in Ecuador that demonstrated an association between socioeconomic status and verbal scores among preschool children (Paxson & Norbert 2007). Additionally, our findings are similar to those of Daniels using data from the Philippines. She found associations between cognitive scores and birth order, maternal and paternal education, maternal height, household assets, number of siblings, household income, place of residence, presence of electricity and environmental cleanliness (Daniels & Adair 2004).

Stunting was common in this sample: more than one in five children were stunted when 6-18 months and 4.5-6 years old (22.9% and 27.8%, respectively). The level of stunting at 6-18 months of age (22.9%) was the same as that reported by a national survey (Demographic and Health Surveys 2000) for Peruvian children 6-23 months of age. In 2007, the percent of children in the Young Lives cohort who were stunted at 4.5-6 years of age was slightly higher than for children 48-59 months of age in the DHS (27.8% and 24.9%, respectively) (Demographic and Health Surveys 2008). WHZ scores were similar for YL children 6-18 months old and DHS children 6-23 months of age (1.6% and 1.5%, respectively). For children at about 5 years of age, 0.8% were low weight-for-height among the DHS sample and 0% among YL children. While underweight was more common among DHS one-year olds than the YL cohort (8.7% versus 4.8%), there were similar levels of underweight among 5 year olds (4.8% DHS and 4.3% YL).

Our study suffers from several limitations. While this study benefits from a longitudinal design, the timing of assessment during the first round is problematic. Children received one anthropometric assessment sometime between 6 and 18 months of age. As a result, children who were assessed early were likely to experience more post-assessment growth restriction than children who were assessed later in the 6–18 month period, thus limiting the comparability of the HAZ between children at round 1. Previous research suggests that height-for-age at 2 years is the best predictor of human capital (Victora et al. 2008). Because we lacked anthropometric measures at 2 years of age, we evaluated early and concurrent HAZ separately to determine how these time points might differ in predicting cognition. When comparing findings from HAZ measures at both time points, concurrent stunting had a noticeably greater impact on verbal and quantitative test scores than early stunting. It may be that concurrent stunting is a better predictor of cognition than early nutritional insult but additional research is needed to confirm or refute this conclusion.

An additional limitation of this research is the degree to which this sample represents Peru as a whole. Young Lives researchers deliberately oversampled from poorer communities. Also, because the reliability and validity of the cognitive assessments was not adequate for Quechua speaking children, nearly 300 indigenous children were excluded from the study. Based on Young Lives data, it can be noted that Quechua children were less likely than Spanish speaking children to attend pre-school (73.6% versus 85.5%, respectively). In addition, their mothers were more likely to have no education whatsoever (40.3% versus

4.6%, respectively). However, while the nature of the sampling design and the exclusion of Quechua speaking children limit the generalizability of these findings to all Peruvian children, HAZ measures from our data are quite similar to nationally representative data collected by two demographic surveys conducted in the past decade.

It should also be noted that the quantitative assessment of cognition in Peru excluded the spatial relations and time subtests; consequently, the CDA reflected children's notions of quantity only. Lastly, despite the longitudinal design of this study, it is constrained by the observational nature of data collection. Thus, we are unable to fully control for unfavorable environmental factors such as care-giving behaviors that restrict both growth and delay or disrupt cognitive development (Grantham-McGregor 2002).

For the past several decades, academicians, policy makers, donors and program planners and implementers have rightfully advocated for the prevention of undernutrition during infancy. However, our findings suggest that when cognition is the outcome of interest, it is equally important to ensure that older children are well-nourished. These findings argue for a more comprehensive life course approach to addressing stunting and its negative sequela. In particular, if our findings are substantiated by others, raising awareness about the importance of concurrent stunting seems warranted. Efforts to address stunting could take a variety of forms but should involve multiple audiences, including parents, clinicians, educators, program planners and implementers and policymakers. Program activities aimed at older children might include extra nutritional snacks at home or at school, pre-school lunch programs and regular growth monitoring—even as children enter pre-school and begin their primary education. Growth monitoring should be accompanied by appropriate counseling for parents and teachers. As Glewwe has demonstrated, investments in children's nutrition can yield a threefold financial return in academic achievement (Glewwe et al. 2001).

Poor nutritional status alone does not account for children's cognitive deficits (Grantham-McGregor 2002). Our study confirms that other factors such as wealth, maternal education, area of residence and number of siblings are also important determinants of verbal and quantitative ability. Consequently, program and policies that reduce poverty, increase educational opportunities for adolescent girls and women and promote birth spacing are also of importance. Additional efforts to improve children's cognition include psychosocial stimulation at a variety of levels including the home, neighborhood and institutions such as

day care, pre-school and school; school readiness initiatives; and mental health support, among others (Committee on Integrating the Science of Child Development 2000).

Our findings suggest that broad-based efforts to promote adequate nutrition need to aim to prevent stunting during infancy but should continue at least to when children enter school.

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Conflict of Interest

The authors declare they have no competing interests.

<u>Key Messages</u>

1. A variety of factors put children at risk of poor cognitive development including poverty, living in a rural environment, low maternal education and age, more siblings and failure to attend preschool
2. In some settings, concurrent nutritional status may be at least as important as early nutritional status in predicting cognitive performance
3. Stunting should be assessed beyond 18 months of age
4. Broad-based efforts to promote adequate nutrition should aim to reduce stunting during infancy and should continue at least to when children enter school. Children older than two years of age should not be neglected
5. Efforts to address stunting and poor cognitive performance must involve parents, clinicians, educators, program planners and implementers and policymakers. Activities aimed at older children might include extra snacks at home and school, pre-school lunch programs and regular growth monitoring—even as children enter pre-school and begin their primary education

457   <u>References</u>

459   Adair L.S. (1999) Filipino children exhibit catch-up growth from age 2 to 12 years. *J Nutr*
460   **129**, 1140-1148.

462   Agarwal D.K., Upadhyay S.K. & Agarwal K.N. (1989) Influence of malnutrition on
463   cognitive development assessed by Piagetian tasks. *Acta Paediatr Scand* **78**, 115-122.

465   Alderman H., Hoddinott J. & Kinsey W. (2006) Long-term consequences of early
466   childhood malnutrition. *Oxford Economic Papers* **58**, 450-474.

468   Baker F. & Kim S. (2004) *Item Response Theory: Parameter Estimation Techniques.*
469   Dekker, New York, 2nd edition.

471   Baydar N. & Brooks-Gunn J. (1991) Effects of maternal employment and child-care
472   arrangements on pre-schoolers' cognitive and behavioral outcomes: evidence from the
473   children of the National Longitudinal Survey. *Dev Psychol* **27**, 932-945.

475   Beasley N.M.R., Hall A., Tomkins A.M., Donnelly C., Ntimbwa P., Kivuga J. *et al*.
476   (2000) The health of enrolled and non-enrolled children of school age in Tanga,
477   Tanzania. *Acta Trop* **76**, 223-229.

479   Berkman D.S., Lescano A.G., Gilman R.H., Lopez S.L., Black M.M. (2002) Effects of
480   stunting, diarrhoeal disease, and parasitic infection during infancy on cognition in late
481   childhood: a follow-up study. *Lancet* **359**, 564-571.

483   Bhutta Z.A., Ahmed T., Black R.E., Cousens S., Dewey K., Giugliani E. et al. (2008)
484   What works? interventions for maternal and child undernutrition and survival. *Lancet*
485   **371**, 417-440.

487   Black R.E., Morris S.S. & Bryce J. (2003) Where and why are 10 million children dying
488   every year? *Lancet* **361**, 2226–2234.

490   Black R.E., Allen L.H., Bhutta Z.A., Caulfield L.E., de Onis M., Ezzati M., *et al*. (2008)

491   Maternal and child undernutrition: global and regional exposures and health

492   consequences. *Lancet* **371**, 243-260.

493

494   Blau F.D. & Grossberg A.J. (1992) Maternal labor supply and children's cognitive

495   development. *Rev Econ Stat* **743**, 474-481.

496

497   Blau D.M. (1999) The effect of income on child development. *Rev Econ Stat* **81**, 261-

498   276.

499

500   Campbell J.M. (1998) Review of the Peabody Picture Vocabulary Test, third edition.

501   *Journal of Psychoeducational Assessment* **16**, 334-338.

502

503   Campbell J.M., Bell S.K. & Keith L.K. (2001) Concurrent validity of the Peabody Picture

504   Vocabulary Test third edition as an intelligence and achievement screener for low SES

505   African American children. *Assessment* **8**, 85–94.

506

507   Cheung Y.B., Yip P.S.F. & Karlberg J.P.E. (2001) Fetal growth, early postnatal growth

508   and motor development in Pakistani infants. *Int J Epidemiol* **30**, 66-72.

509

510   Cheung Y.B. (2006) Growth and cognitive function of Indonesian children: zero-inflated

511   proportion models. *Stat Med* **25**, 3011-3022.

512

513   Committee on Integrating the Science of Child Development (2000) From neurons to

514   neighborhoods: the science of child development. Washington DC: National Academy

515   Press.

516

517   Crocker L. & Algina J. (1986) *Introduction to Classical and Modern Test Theory*. New

518   York: Holt, Rinehart and Winston.

519

520   Daniels M.C. & Adair L.S. (2004) Growth in young Filipino children predicts schooling

521   trajectories through high school. *J Nutr* **134**, 1439-1446.

522

523 de Onis M. (2008) Child growth and development. In *Nutrition and Health in Developing*

524 *Countries*, *2nd edition* (eds R.D. Semba & M.W. Bloem), pp. 113-137. Totowa, NJ:

525 Humana Press.

526

527 Demographic and Health Surveys. (2000) Peru 2000 Standard DHS. Calverton (MD):

528 MEASURE DHS, Macro International.

529 Available: www.measuredhs.com/countries/country_main.cfm?ctry_id=33 (accessed

530 March 9, 2010).

531

532 Demographic and Health Surveys. (2008) Peru 2004-2008 Continuous DHS. Calverton

533 (MD): MEASURE DHS, Macro International.

534 Available: www.measuredhs.com/countries/country_main.cfm?ctry_id=33 (accessed

535 March 9, 2010).

536

537 Desai S.P., Chase-Lansdale L. & Michael R.T. (1989) Mother or market? effects of

538 maternal employment on the intellectual ability of 4-year-old children. *Demography* **26**,

539 545-561.

540

541 Dunn L., Padilla E., Lugo D., & Dunn, L. (1986) *Manual del examinador para el test de*

542 *vocabulario en imágenes Peabody (Peabody Picture Vocabulary Test). Adaptación*

543 *Hispanoamericana*. Minnesota: AGS.

544

545 Dunn L. & Dunn L. (1997) *Examiner's manual for the PPVT-III.* Form IIIA and IIIB.

546 Minnesota: AGS.

547

548 Filmer D. & Pritchett L. (2001) Estimating wealth effects without expenditure data or

549 tears: an application to educational enrolments in states of India. *Demography* **38**, 115-

550 132.

551

552 Glewwe P., Jacoby H.G. & King E.M. (2001) Early childhood nutrition and academic

553 achievement: a longitudinal analysis. *J Public Econ* **81**, 345-368.

554

555   Grantham-McGregor S. (1995) A review of studies of the effect of severe malnutrition on
556   mental development. *J Nutr* **125**, 2233S–2238S.

557

558   Grantham-McGregor S.M., Walker S.P., Chang S.M., Powell C.A. (1997) Effects of early
559   childhood supplementation with and without stimulation on later development in stunted
560   Jamaican children. *Am J Clin Nutr* **66**, 247–253.

561

562   Grantham-McGregor S. (2002) Linear growth retardation and cognition. *Lancet* **359**, 542.

563

564   Grantham-McGregor S., Cheung Y.B., Cueto S., Glewwe P., Richter L., Strupp B. (2007)
565   Developmental potential in the first 5 years for children in developing countries. *Lancet*
566   **369**, 60-70.

567

568   Gray S., Plante E., Vance R., & Henrichsen, M. (1999) The diagnostic accuracy of four
569   vocabulary tests administered to preschool-age children. *Language, Speech, and Hearing*
570   *Services in Schools* **30**, 196–206.

571

572   Hack M. (1998) Effects of intrauterine growth retardation on mental performance and
573   behavior, outcomes during adolescence and adulthood. *Eur J Clin Nutr* **52,** Suppl. l, S65–
574   S70.

575

576   Ivanovic D.M., Perez H.T., Olivares M.D., Diaz N.S., Leyton B.D., Ivanovic R.M. (2004)
577   Scholastic achievement: a multivariate analysis of nutritional, intellectual,
578   socioeconomic, sociocultural, familial, and demographic variables in Chilean school-aged
579   children. *Nutrition* **20**, 878-889.

580

581   Kordas K., Lopez P., Rosado J.L. Vargas, G.G., Rico, J.A., Cebrián, M.E., *et al.* (2004)
582   Blood lead, anemia, and short stature are independently associated with cognitive
583   performance in Mexican school children. *J Nutr* **134**, 363–371.

584

585   Kuklina E.V., Ramakrishnan U., Stein A.D., Barnhart H.H., Martorell R. (2004) Growth
586   and diet quality are associated with the attainment of walking in rural Guatemalan infants.
587   *J Nutr* **134**, 3296-3300.

588

589   Li H., Barnhart H.X., Stein A.D. *et al*. (2003) Effects of early childhood supplementation
590   on the educational achievement of women. *Pediatrics* **112**, 1156–1162.

591

592   Martorell R., Rivera J., Kaplowitz J., Pollitt E. (1992) Long term consequences of growth
593   retardation during early childhood. In *Human growth: basic and clinical aspects* (eds M.
594   Hernandez & J. Argenta), pp. 143-149. Amsterdam: Elsevier.

595

596   Martorell R. (1997) Undernutrition during pregnancy and early childhood: consequences
597   for cognitive and behavioral development. In *Early child development: investing in our*
598   *children's future* (eds M.E. Young), pp. 39-83. Amsterdam: Elsevier Science BV.

599

600   Martorell R. (1999) The nature of child malnutrition and its long-term implications. *Food*
601   *Nutr Bull* **19**, 288–292.

602

603   McCulloch A. & Joshi H.E. (2002) Child development and family resources: evidence
604   from the second generation of the 1958 British Birth Cohort. *J Popul Econ* **15**, 283–304.

605

606   Mendez M.A. & Adair L.S. (1999) Severity and timing of stunting in the first two years
607   of life affect performance on cognitive tests in late childhood. *J Nutr* **129**, 1555–1562.

608

609   Parcel T.L. & Menaghan E.G. (1994) Early parental work, family social capital and early
610   childhood outcomes. *AJS* **99**, 972-1009.

611

612   Paxson C. & Norbert S. (2007) Cognitive development among young children in
613   Ecuador: the roles of wealth, health and parenting. *J Hum Resour* **42**, 49–84.

614

615   Pollitt E., Watkins W.E. & Husaini M.A. (1997) Three-month nutritional supplementation
616   in Indonesian infants and toddlers benefits memory function 8 years later. *Am J Clin Nutr*
617   **66**, 1357–1363.

618

619   Pollitt E. (2000) Developmental sequel from early nutritional deficiencies: conclusive and
620   probability judgments. *J Nutr* **130** Suppl. 1, S350–S353.

621

622   Rosenzweig M.R. & Wolpin K.I. (1994) Are there increasing returns to the
623   intergenerational production of human capital? maternal schooling and child intellectual
624   achievement. *J Hum Resour* **29**, 670-693.

625
626   Shrimpton R., Victora C., de Onis M., Costa Lima R., Blössner M., Clugston G. (2001)
627   Worldwide timing of growth faltering: implications for nutritional interventions.
628   *Pediatrics* **107**, 75–81.

629
630
631   Sigman M., McDonald M.A., Neumann C., Bwibo N. (1991) Prediction of cognitive
632   competence in Kenyan children from toddler nutrition, family characteristics and abilities.
633   *J Child Psychol Psychiatry* **32**, 307–320.

634
635   Victora C.G., Adair L., Fall C., Hallal PC, Martorell R, Ritcher L. *et al*. (2008) Maternal
636   and child undernutrition: consequences for adult health and human capital. *Lancet* **371**,
637   340-357.

638
639   Walker S.P., Grantham-McGregor S.M., Powell C.A., Chang S.M. (2000) Effects of
640   growth restriction in early childhood on growth, IQ and cognition at age 11-12 years and
641   the benefits of nutritional supplementation and psychosocial stimulation. *J Pediat* **137**,
642   36-41.

643
644   Walker S.P., Chang S.M., Powell C.A., Grantham-McGregor S.M. (2005) Effects of early
645   childhood psychosocial stimulation and nutritional supplementation on cognition and
646   education in growth-stunted Jamaican children: prospective cohort study. *Lancet* **366**,
647   1804–1807.

648
649   Wilson I., Huttly S.R.A. & Fenn B. (2006) A case study of sample design for longitudinal
650   research: Young Lives. *Int. J. Social Research Methodology* **9**, 351-356.

651
652
653

Table 1. Characteristics of study participants

Characteristics[a]	N=1675[b]
Child Characteristics	
Child age (months)	12.04 (3.55)[c]
Sex, female (%)	49.46
Attended preschool, yes (%)	86.14
Mother Characteristics	
Maternal age (years)	26.69 (6.62)
Maternal education in years	8.74 (3.98)
Maternal ethnicity (%)	
Caucasian	4.96
Mestizo	91.88
Indigenous[d]	2.57
Other	0.60
Household Characteristics	
Region (%)	
Coast	40.20
Highland	43.01
Jungle	16.79
Area (%)	
Urban	74.07
Rural	25.93
Wealth index (score 0-1)	0.42 (0.21)

[a] Data reported in table come from round 1 (when child was 6–18 months of age) except preschool attendance
[b] Maximum missing value for any category was 11 (or 0.7%)
[c] Mean (SD)
[d] Indigenous could mean any of a variety of different ethnic groups living in the highlands, coastal areas or jungle.

Table 2. Prevalence of stunting, wasting and underweight by round

Characteristics	Round 1 N=1675[1]	Round 2 N=1675[a]
Stunted (%)	22.94	27.80
Wasted (%)	1.63	--
Underweight (%)	4.82	4.31

[a] Maximum missing value for any measure was 16 or (1.0%)

Table 3. Linear regression results for predictors of verbal score

Independent Variable[a]	N	Unadjusted Model[b]		Adjusted Model[c]	
		Estimate	95% CI	Estimate	95% CI
Intercept		--	--	62.90	57.27, 68.53
Round 1 HAZ	1649	2.63	1.90, 3.37	0.20	-0.59, 0.99
Round 2 HAZ	1649	4.70	3.87, 5.53	2.23	1.29, 3.17
Maternal Age in Years	1649	0.06	-0.06, 0.19	0.24	0.11, 0.38
Maternal Education in Years	1649	1.99	1.77, 2.20	1.39	1.15, 1.62
Area Population					
Rural	421	--	--	--	--
Urban	1228	11.35	8.34, 14.35	4.58	1.81, 7.35
Preschool Attendance					
No	226	--	--	--	--
Yes	1423	9.86	7.30, 12.43	3.69	1.29, 6.08
Wealth Index	1649	44.26	37.32, 51.21	20.23	13.14, 27.31
Number of siblings	1649	-2.11	-2.68, -1.54	-1.14	-1.78, -0.50

[a] Data reported in table come from round 1 (when child was 6-18 months of age) except preschool attendance, wealth index, and number of siblings.
[b] Unadjusted models include an individual model for each independent variable.
[c] Post regression Wald test comparing HAZ coefficients from both rounds = 6.97, p-value= 0.0083

Table 4. Linear regression results for predictors of quantitative score

Independent Variable[a]	N	Unadjusted Model[b]		Adjusted Model[c]	
		Estimate	95% CI	Estimate	95% CI
Intercept		--	--	6.68	5.89, 7.47
Round 1 Height-for-age Z Score	1649	0.10	0.01, 0.20	0.03	-0.09, 0.14
Round 2 Height-for-age Z Score	1649	0.36	0.25, 0.47	0.15	0.02, 0.28
Child Age	1649	0.12	0.09, 0.15	0.11	0.08, 0.14
Maternal Age in Years	1649	0.01	-0.01, 0.03	0.02	0.00, 0.04
Maternal Education in Years	1649	0.14	0.11, 0.17	0.09	0.05, 0.12
Area Population					
Rural	421	--	--	--	--
Urban	1228	1.14	0.77, 1.51	0.56	0.20, 0.93
Preschool Attendance					
No	226	--	--	--	--
Yes	1423	1.22	0.89, 1.55	0.54	0.21, 0.88
Wealth Index	1649	3.67	2.77, 4.58	1.60	0.63, 2.57
Number of siblings	1649	-0.15	-0.23, -0.08	-0.10	-0.19, -0.02

[a] Data reported in table come from round 1 (when child was 6-18 months of age) except preschool attendance, wealth index, and number of siblings.
[b] Unadjusted models include an individual model for each independent variable.
[c] Post regression Wald test comparing HAZ coefficients from both rounds = 1.26, p-value= 0.2622

Figure 1. Cross-sectional* data for median height-for-age z-score (HAZ) by age at assessment and area for round 1 and round 2. *Child was measured once during round 1 and once during round 2; () = sample size for age group.