Linear Growth and Child Development in Low- and Middle-Income Countries: A Meta-Analysis

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abstract

BACKGROUND AND OBJECTIVE: The initial years of life are critical for physical growth and broader cognitive, motor, and socioemotional development, but the magnitude of the link between these processes remains unclear. Our objective was to produce quantitative estimates of the cross-sectional and prospective association of height-for-age *z* score (HAZ) with child development.

METHODS: Observational studies conducted in low- and middle-income countries (LMICs) presenting data on the relationship of linear growth with any measure of child development among children $<$12 years of age were identified from a systematic search of PubMed, Embase, and PsycINFO. Two reviewers then extracted these data by using a standardized form.

RESULTS: A total of 68 published studies conducted in 29 LMICs were included in the final database. The pooled adjusted standardized mean difference in cross-sectional cognitive ability per unit increase in HAZ for children $\leq$2 years old was +0.24 (95% confidence interval [CI], 0.14–0.33; I^2 = 53%) and +0.09 for children $>$2 years old (95% CI, 0.05–0.12; I^2 = 78%). Prospectively, each unit increase in HAZ for children $\leq$2 years old was associated with a +0.22-SD increase in cognition at 5 to 11 years after multivariate adjustment (95% CI, 0.17–0.27; I^2 = 0%). HAZ was also significantly associated with earlier walking age and better motor scores ($P < .05$).

CONCLUSIONS: Observational evidence suggests a robust positive association between linear growth during the first 2 years of life with cognitive and motor development. Effective interventions that reduce linear growth restriction may improve developmental outcomes; however, integration with environmental, educational, and stimulation interventions may produce larger positive effects.

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In 2011 an estimated 314 million children <5 years of age in low- and middle-income countries (LMICs) experienced mild to severe stunting.[1] Restricted linear growth is primarily a result of inadequate nutrition and infectious disease and has long been recognized as a principal cause of morbidity and mortality throughout childhood.[2,3] It is also well established that the initial years of life are critical for cognitive, motor, and socioemotional development, but the degree to which physical growth, child development, and their determinants are directly linked remains difficult to untangle.[4,5]

Studies investigating the relationship between physical growth and child development date back more than a century.[6,7] Reviews of this literature to date have presented only qualitative findings that focus primarily on cognitive outcomes and have generally found that restricted linear growth is associated with reduced cognitive capacity.[5,8–11] Given that growth restriction is used as a proxy for children's broader developmental status in LMICs, quantitative summary estimates are needed to determine the magnitude of the direct links between physical growth and broader child development.[5] These estimates are also needed to design intervention studies with optimal statistical power to determine the effect of risk factors and interventions classically associated with restricted linear growth on child development outcomes.

In this systematic review and meta-analysis we present all published studies to date conducted in LMICs including data on the relationship of linear growth with child cognitive, motor, and socioemotional development domains. We produce crude and multivariate adjusted pooled estimates for cross-sectional and prospective studies to inform the ability to use linear growth as an indicator of children not reaching their developmental potential and to estimate the possible direct link of exposures leading to restricted linear growth and child development.

METHODS

We conducted a systematic literature review of observational studies conducted in LMICs presenting data on the relationship of child linear growth (crude height or height-for-age *z* score [HAZ]) with any measurement of cognitive, motor, or socioemotional functioning. We include any measure of children's intelligence (IQ), executive function, reasoning, language, or academic (eg, early math or reading skills) as representations of cognition. Motor development was represented by measure of both fine and gross motor capacities, including age of attainment of particular skills (eg, walking). Socioemotional development included measures of behavior problems, attachment, emotionality, social competence, and temperament. Studies were excluded from the review if they were conducted among nongeneralizable populations (eg, children with conditions such as HIV, hypopituitarism, Turner syndrome, or neurologic problems; studies restricted to low birth weight or preterm infants; or children living in extreme social situations such as institutions or areas of armed conflict), they were conducted in a high-income country, they were based on nonhuman study populations, they included samples <50 subjects, the mean age of the study population was >12 years, or the study outcome was designed to represent nonnormative development, including significant mental or physical disability. We included only studies of children <12 years of age to examine the relationship of HAZ with child development during the early to middle childhood (ie, preadolescent and prepubertal) period.

Search Strategy

We conducted a comprehensive systematic literature search of PubMed (from 1966 to December 20, 2014), Embase (from 1974 to December 20, 2014), and PsycINFO (from 1872 to December 20, 2014). The PubMed search consisted of ("child" or "infant") AND ("cognitive" or "cognition" or "psychomotor" or "sensorimotor" or "motor" or "intelligence" or "IQ" or "language" or "executive function" or "attention" or "memory" or "learning" or "information processing" or "literacy" or "reading" or "math" or "school readiness" or "pre-academic" or "academic" or "mental health" or "behavior problem" or "emotional" or "emotion" or "socioemotional" or "temperament" or "self-regulation" or "attachment" or "self-esteem" or "self-esteem" or "self-efficacy" or "social competence" or "peer relationship" or "prosocial behavior" or "internalizing" or "externalizing" or "hyperactivity" or "impulsivity" or "aggression") AND ("height" or "stunt*" or "height-for-age" or "HAZ"), and these search terms were customized for Embase and PsycINFO databases. There were no language or publication restrictions.

Study Selection

Two reviewers (C.R.S. and D.C.M.) independently screened titles and abstracts and then reviewed full texts of selected studies to assess eligibility. Reference lists of included studies and previous reviews were scanned to identify any potentially relevant publications not found through the electronic search. Any discrepancy between the reviewers was resolved through discussion.

Data Abstraction

Two reviewers (C.R.S. and D.C.M.) independently extracted data by using a standardized data extraction form. The data collected from each study included information on study design, location, number of participants, height or HAZ distribution, time of height assessment, child development measurement tool, time of child development assessment, confounders, and measures of association. We also collected SD of the child development outcome if standardized mean differences (SMDs) or standardized mean scores were not presented. Discrepancies between the reviewers were resolved through discussion, by contacting the authors, or by consultation with a third reviewer (W.W.F. or G.D.).

Statistical Analysis

The objective of the meta-analysis was to produce a series of quantitative estimates of the relationship between linear growth and development separately for the cognitive, motor, and socioemotional domains stratified by study design and statistical adjustment. For each child development domain we sought to produce a pooled summary of the crude cross-sectional correlation of HAZ with the domain score, crude SMD in domain score for each unit increase in HAZ in cross-sectional studies, multivariate adjusted SMD in domain score for each unit increase in HAZ in cross-sectional studies, crude SMD in domain score for each unit increase in HAZ and in prospective cohort studies, and multivariate adjusted SMD in domain score for each unit increase in HAZ in prospective cohort studies. As a secondary meta-analysis we also present SMDs for each of these summary estimates by design and statistical adjustment for stunted versus nonstunted children; however, these estimates may underestimate the relationship if the nonstunted control group has suboptimal growth or a mean HAZ <0. We produced pooled estimates using SMDs because of substantial differences in the scoring systems used in the many child development tools included in the review. If an SMD was not presented, standardized mean *z* scores by group or within sample and the SD of the child development score was used to calculate an SMD estimate. For the socioemotional domain, we present only a qualitative overview because we were unable to present summary estimates in this domain because of the small number of studies and differences in the aspects of socioemotional development that each tool measured. Similarly, we were also unable to produce summary estimates for studies examining the relationship between change in HAZ or height over time and child development because of the small number of studies and significant differences in timing of height measurements and the type of statistical analysis used.

To calculate a summary correlation coefficient, we used the DerSimonian and Laird method with random effects models.[12] Studies that presented correlations by subgroups of age or gender are included in the summary measure separately, and because of the lack of study independence they will lead to an underestimation of the pooled SE and confidence intervals (CIs). For pooled summary SMD estimates we used generic inverse variance weighting.[13] We used the Q-statistic and its P value and I^2 statistics to examine between-study heterogeneity.[14,15] If the Q-statistic P value was <0.10 and I^2 was $>50\%$, heterogeneity was considered to be substantial, and random effects models were used. A priori we also decided to explore heterogeneity in estimates by age at HAZ measurement. We examined subgroup estimates stratified for the ≤2 years and >2 years age groups (≥50% of the sample) for all analyses, and the χ^2 test was used to assess statistical significance of difference in pooled estimates between groups for SMDs. If significant differences by age subgroup were determined, stratified results are presented. We used funnel plots to assess publication bias, and statistical significance was defined as $P < .05$. We used SAS (version 9.2; SAS Institute, Inc, Cary, NC), RevMan (version 5.1; The Cochrane Collaboration, Copenhagen, Denmark), and MedCalc (version 12.5; MedCalc Software bvba, Ostend, Belgium) for the analyses.

RESULTS

Literature Search

A summary of the literature search and final database study selection process is presented in Fig 1. Briefly, we identified a total of 9044 records from Embase, PubMed, and PsycINFO, of which 7578 were unique citations after we removed duplicates. We screened these record titles and abstracts and identified 444 citations for full-text review. We also identified 14 additional studies from reference lists to be included in the full-text review. We were unable to obtain full text for 4 articles, and abstracts only were available for 17 citations (see Supplemental Information for a list of these references). After a detailed review of available full-text articles, we included 68 reports in the final database.

Study Characteristics

The 68 reports included in the final database consisted of 56 distinct study populations in 29 different LMICs and represented a range of study designs from small cohorts to large cross-sectional multicountry demographic surveys.[16–83] We present study characteristics and results in Supplemental Tables 2–7 for cognitive, motor, and socioemotional domains, respectively. Some studies presented data on multiple developmental domains, resulting in 52 studies reporting cognitive domain associations,* 22 with motor associations,† and 13 with socioemotional associations.‡

*Refs 22–26, 28–30, 32, 34–40, 42–53, 55, 56, 58, 60–62, 64–66, 68, 69, 71, 73–79, 82, and 83.

†Refs 17, 21, 25, 27, 29, 31, 33, 46, 48, 50, 54, 57–61, 66, 67, 72, 73, 77, and 81.

‡Refs 19, 20, 25, 26, 29, 50, 51, 63, 67, 70, 73, 80, and 82.

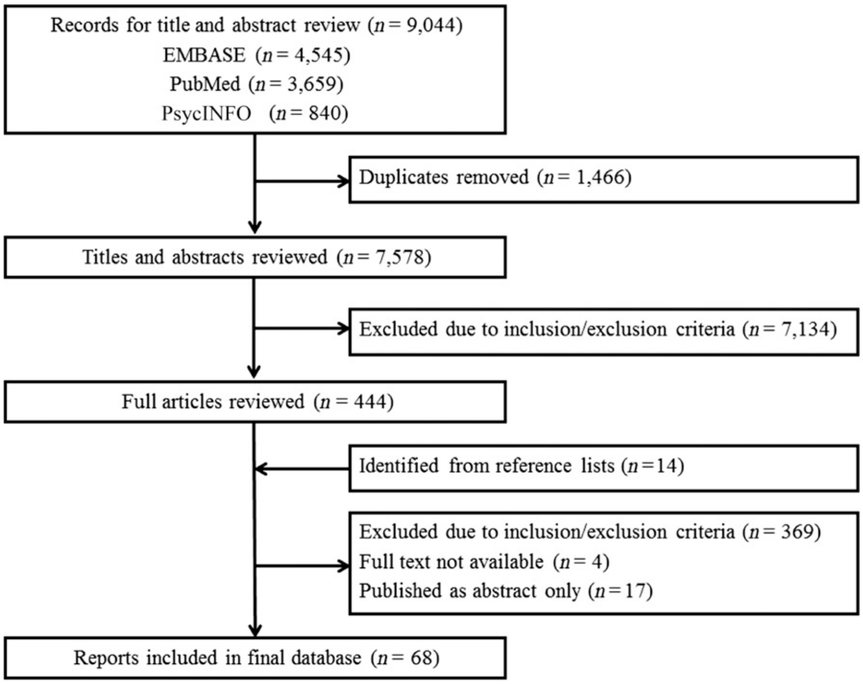

FIGURE 1
Flow diagram of literature search and study identification process.

Cognitive Domain

A summary of the cognitive domain findings is presented in Table 1, and individual study descriptors and results are found in Supplemental Tables 2 and 3. A total of 11 studies presented cross-sectional unadjusted correlations of HAZ with cognitive domain score, which produced a pooled correlation of 0.28 (95% CI, 0.19–0.36; I^2 = 92%)[§] (Supplemental Fig 5). When data were stratified by age, there was no difference in correlations for studies assessing cognitive correlations between children ≤2 years of age (pooled correlation 0.22; 95% CI, 0.12–0.32)[42,66,73] and children >2 years of age (pooled correlation 0.31; 95% CI, 0.19–0.41).[23,25,32,44,49,60,65,74] A total of 10 cross-sectional studies presented multivariate adjusted SMDs for the relationship between HAZ and cognition.[‖] The SMD in cognitive score for each unit increase in HAZ was significantly greater for studies conducted among children ≤2 years old as compared with study populations >2 years old (test for subgroup differences $P < .01$). For children ≤2 years old, each unit increase in HAZ was associated with a +0.24-SD increase in cross-sectional cognitive ability (95% CI, 0.14–0.33; I^2 = 53%), whereas for children >2 years old each unit increase in HAZ was associated with only a +0.09 SMD in the cognitive score (95% CI, 0.05–0.13; I^2 = 74%) (Fig 2). A total of 5 prospective cohort studies presented a multivariate adjusted SMD for each unit increase in HAZ, and a pooled analysis determined that each unit increase in HAZ ≤2 years was associated with a +0.22 SD increase in cognition at 5 to 11 years of age with no significant heterogeneity (95% CI, 0.17–0.27; I^2 = 0%) (Fig 3).[22,28,43,48,83,84] Summary estimates for stunted versus nonstunted participants are presented in the Supplemental Information by study design and use of statistical adjustment (Supplemental Figs 6–9). Seven studies presented multivariate adjusted associations examining change in length/height or HAZ over time with cognitive scores.[22,28,35,37,58,69,82] Because of differences in timing of height assessment and statistical analyses we were not able to pool these estimates; however, most studies suggest that improvements in HAZ over time or recovery from a stunted to a nonstunted HAZ is associated with improved cognition.

§Refs 23, 25, 32, 42, 44, 49, 60, 65, 66, 73, and 74.

‖Refs 23, 28, 36, 39, 51, 55, 56, 58, 65, and 77.

Motor Domain

A summary of the motor domain meta-analyses is presented in Table 1, and study descriptors and results are found in Supplemental Tables 4 and 5. Four cross-sectional studies presented the correlation of HAZ with motor score, and the summary pooled correlation was 0.24 (95% CI, 0.11–0.36; I^2 = 84%)[17,25,67,73] (Supplemental Fig 9). The pooled SMD for the 2 studies that presented multivariate adjusted cross-sectional motor scores was +0.39 for each 1-unit increase in HAZ (95% CI, 0.30–0.47; I^2 = 31%)[58,77] (Supplemental Fig 11). In addition, 3 studies among children ≤2 years old presented the multivariate cross-sectional association of HAZ with odds of walking; when these studies were pooled, each 1-unit increase in HAZ was associated with 2.03 (95% CI, 1.57–2.64; I^2 = 46%) times the odds of walking[54,57,72] (Supplemental Fig 12). Two prospective cohort studies determined that each unit increase in HAZ among children ≤3 years old was associated with a 0.29-SD increase (95% CI, 0.15–0.42; I^2 = 0%) in motor score at 5 to 8 years of age after multivariate adjustment[29,48] (Fig 4). The unadjusted cross-sectional SMD for stunted versus nonstunted children is presented in Supplemental Fig 10. One study presented data on change in HAZ over time and motor development and determined that increases in HAZ from birth to 1 year were significantly

TABLE 1 Summary of Pooled Meta-Analysis Results by Developmental Domain

	No. of Studies	Pooled Estimate (95% CI)	I^2, %	Figure
Cognitive domain				
Unadjusted cross-sectional correlation	11	0.28 (0.19–0.36)	92	Supplemental Fig 5
Adjusted cross-sectional SMD per unit increase in HAZ*				
≤2 y of age	3	0.24 (0.14–0.33)	53	Fig 2
>2 y of age	7	0.09 (0.05–0.13)	74	Fig 2
Adjusted prospective SMD per unit increase in HAZ	5	0.22 (0.17–0.27)	0	Fig 3
Motor domain				
Unadjusted cross-sectional correlation	4	0.24 (0.11–0.36)	84	Supplemental Fig 9
Adjusted cross-sectional SMD per unit increase in HAZ	2	0.38 (0.31–0.46)	31	Supplemental Fig 11
Adjusted cross-sectional odds ratio for walking per unit increase in HAZ	3	2.00 (1.68–2.37)	46	Supplemental Fig 12
Adjusted prospective SMD per unit increase in HAZ	2	0.29 (0.15–0.42)	0	Fig 4

*$P < .01$ for significant difference between age subgroups.

associated with reduced time to walking.[57]

Socioemotional Domain

Study descriptors and results for the included 13 studies are found in Supplemental Tables 6 and 7. It was difficult to synthesize results for the socioemotional domain because of the small number of studies and poor comparability of socioemotional development outcomes assessed at different ages (eg, fussing, socialization, exploration, aggression). In multivariate analyses, 3 studies found no significant relationship of HAZ or stunting with different aspects of socioemotional development,[19,51,82] 1 study found significantly improved social scores with increased HAZ,[29] and another study found that increased height was associated with increased aggression.[70]

DISCUSSION

The results of this study suggest that linear growth is positively associated with cognitive and motor development among children living in LMICs. We found that each unit increase in HAZ during the first 2 years of life was independently associated with a +0.24-SD shift in concurrent cognitive ability and a +0.22-SD shift in cognition at 5 to 11 years of age. This suggests that, without intervention, early cognitive deficits may persist throughout childhood for children experiencing restricted linear growth during the first 2 years of life. Nevertheless, this study suggests there is substantial variation in child development that is not linked to linear growth. The associations of HAZ with current and future motor development skills were of similar magnitude to those seen in the cognitive domain. We were unable to produce results for socioemotional development because of the small number of studies and differences in the constructs each study attempted to measure.

The independent association of HAZ with cognitive and motor

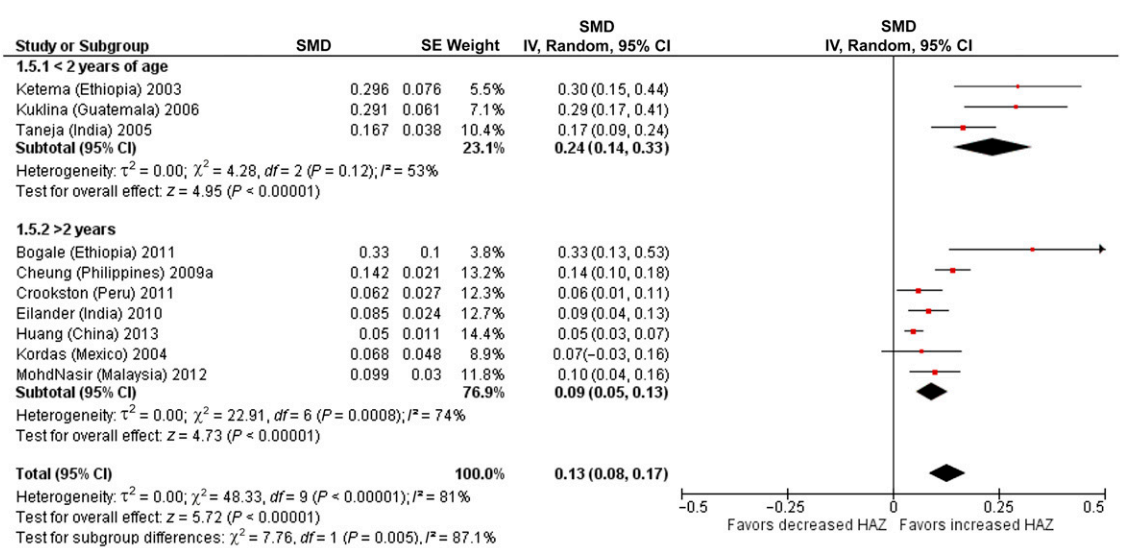

FIGURE 2
Multivariate adjusted cross-sectional SMD in cognition per unit increase in HAZ stratified by age at measurement. IV, inverse variance.

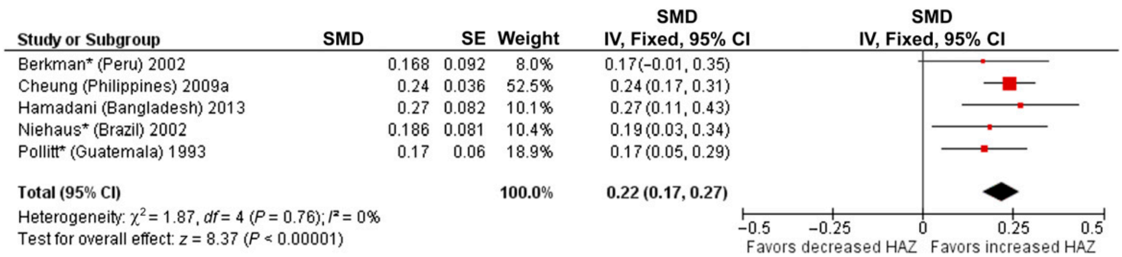

FIGURE 3

Multivariate adjusted prospective SMD in cognition per unit increase in HAZ. * Estimate obtained from Fischer Walker et al.[43] IV, inverse variance.

development after multivariate adjustment in both cross-sectional and prospective studies supports the possibility of a biological mechanism whereby early exposure to malnutrition and infection leads simultaneously to restricted linear growth and deficits in brain development that may persist throughout childhood.[85] Decades of animal and human research have shown that prenatal and early life malnutrition negatively affect neuronal growth, pruning, and connectivity within regions of the brain associated with both motor and attentional functioning.[85,86] A few trials of energy supplementation have also indicated improved cognitive development for undernourished children or those at high risk of malnutrition.[87–89]

Our finding that linear growth in the first 2 years of life appears to be a stronger independent predictor of both early and later childhood cognition as compared with growth after 2 years of age also corroborates a growing body of neuroscientific research showing that exposure to environmental and biological adversity during early sensitive periods of brain development can be particularly detrimental to cognitive development.[90] We found a significantly muted cross-sectional association of HAZ with cognition for children >2 years old. A partial explanation may be that the biologically relevant time period during which malnutrition acts on child development is during infancy or early toddlerhood, and because of growth catch-up the association is diluted at older ages.[91] Studies examining changes in HAZ over time also suggest that early growth catch-up or reversal of stunting status is associated with improved cognition.[22,35,58,69,82]

Another possible mechanism is that chronic infection or protein energy malnutrition may delay or prohibit advancement of early motor skills, which then leads to cognitive delays by way of reduced ability of the child to explore and extract learning opportunities from the physical and social environment.[54,67] This mechanism is a component of the functional isolation hypothesis, in which infants or children with significant growth restriction may experience reduced ability to engage in their environments and a lack of responsiveness by caregivers.[92,93] In addition, mothers of children with growth restriction may have low expectations about developmental milestones as a result of their short stature. In our pooled analysis, each unit increase of HAZ was independently associated with approximately twice the odds of being able to walk and a +0.29-SD shift in overall motor score. In support, animal models have also suggested that loss of muscle and decreased muscle fiber size caused by malnutrition may directly lead to motor delay, and studies have also found that children who are less active and lethargic are given fewer opportunities to advance motor skills.[54,94] This mechanism illustrates the significant interconnection of child development domains, particularly during infancy, and future studies should attempt to measure noncognitive domains to assess potential causal cognitive pathways.

It is also important to note the significant attenuation of the association of HAZ with cognitive development in multivariate adjusted versus unadjusted analyses in both cross-sectional and prospective studies. For example, a prospective

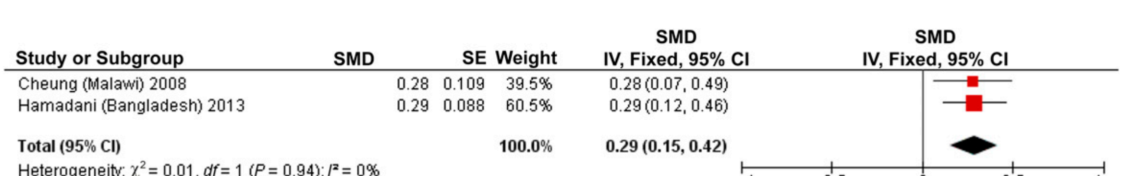

FIGURE 4

Multivariate adjusted prospective SMD in motor domain per unit increase in HAZ.

cohort study of Filipino infants found stunting at 2 years of age was associated with a −0.40-SD deficit in cognition at 8 years in crude analysis, but after adjustment for socioeconomic, caregiver, and demographic factors the *z* score deficit for stunted infants was significantly reduced to −0.14.[64] This large change indicates the strong potential for residual and unmeasured confounding to lead to overestimation of the direct effect of linear growth on cognitive and motor abilities in adjusted estimates because of unmeasured and residual confounding; however, multivariate adjusted estimates of the association of HAZ with cognition and motor development are homogeneous despite these analytical differences. This suggests that the contribution of unmeasured confounding above and beyond measures of socioeconomic status and age, which are included in most adjusted analyses, may be small. Nevertheless, this large attenuation also suggests that integrating nutritional, environmental, educational, and stimulation interventions may produce large positive effects on child development. Although limited in number and sample size, interventions that integrate both nutrition and stimulation interventions appear to be particularly promising for promoting multiple domains of child functioning.[87] In addition, these experimental studies offer the opportunity to begin to untangle the many pathways that potentially link children's physical growth and broader cognitive, motor, and socioemotional development.

Although this systematic review and quantitative meta-analysis provides several important advantages over past qualitative work, we were limited by several factors that should be addressed in future studies. Foremost, because of the observational nature of the included studies we are unable to determine a causal link between underlying factors that lead to restricted linear growth and child cognitive and motor development. Second, the lack of comparable evidence in the socioemotional domain prevents us from drawing conclusions about the nature of relationships between growth and social and emotional development at different ages during childhood. The significantly smaller number of studies examining socioemotional development as compared with cognitive and motor domains illustrates the need to better understand and measure the diversity and complexity of social and emotional skills acquired by children over time and globally across cultures. In addition, there was significant heterogeneity in most pooled analyses presented in this study, which may be attributed in large part to the diversity of measurement tools and related constructs included in the analyses. For example, the inclusion of measures of IQ, attention, reasoning, language, and preacademic skills as representations of cognition probably generated some degree of imprecision in estimates. In the future, more unified measurement tools are needed that take advantage of both broad and construct-specific measurement strategies to allow more analogous comparisons. In addition, we were unable to examine the complete shape or dose response of the relationship of HAZ with child development because of the lack of analyses presenting estimates for HAZ ≥ -1 in LMICs. Many studies presented adjusted estimates for stunting (HAZ < -2), and a few presented data for mild growth restriction (HAZ ≥ -2 and < -1), but the magnitude and shape of the relationship remain unclear for HAZ ≥ -1, specifically if there are any additional benefits to obtaining HAZs > 0.

Our findings suggest that restricted growth and stunting can be used as an incomplete proxy for delayed child development broadly and that the underlying causes of growth restriction may also have direct effects on cognitive and motor development. These findings can also be viewed as a possible mechanism to the more distal relationship of increased height with schooling attainment determined in a recent pooled analysis of long-term follow-up studies.[95] A multitude of risk factors and effective interventions for restricted linear growth that span prepregnancy through early and middle childhood have been identified, but for the majority of these risk factors and interventions the impact on child development remains understudied or unclear.[4] Future research is needed to determine the effectiveness of interventions used to prevent and treat linear growth restriction on child development and the effectiveness of integrated nutrition and psychosocial stimulation interventions.

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