Introduction

Globally, 149 million children are stunted (i.e., length-for-age Z score less than –2) and the rate of decline has been unacceptably slow. The burden of this problem is in southern Asia and sub-Saharan Africa, where many communities remain impoverished. Childhood stunting is an indicator of poor linear growth and chronic undernutrition and is associated with adverse health, developmental, and eventual socioeconomic consequences for the affected children. The international community has agreed that stunting is a global child health and nutrition priority. As a result, there has been a global impetus to design, evaluate, and implement interventions to address this problem and inform policy changes. The hope is that these strategies will accelerate progress towards the global nutrition target of a 40% reduction in under-5 stunting by 2025.

In this chapter, we have put together an interesting selection of recently published papers on stunting and growth covering diverse areas of research and the evolving perspectives. The mechanisms of stunting have remained elusive and this has slowed down the development of interventions. We therefore include recent data on studies that have evaluated pathways to or factors associated with stunting in greater detail. Evidence of the association of stunting with maternal mental health, wasting in children, and the role of enteropathogens are outlined. We also include the most recent data on the efficacy of interventions that have been tested to address stunting in early childhood in low- and middle-income countries. These interventions are primarily nutrition (maternal and child) interventions alone or combined with water, sanitation, and hygiene (WASH) strategies. The findings from these studies and the accompanying perspectives provide key research questions that need to be explored in future
research in this field. Finally, we have included some thought-provoking perspectives on whether the investments being made for the development of interventions to address stunting are somewhat misplaced, as stunting may not after all be the best marker of childhood undernutrition? These papers remind us the importance of continuing to refine our research agendas and questions with the emerging evidence, as we seek to address childhood undernutrition.

### Key articles reviewed for this chapter

#### Pathways

**Maternal common mental disorder as predictors of stunting among children aged 6–59 months in Western Ethiopia: a case-control study**
Girma S, Fikadu T, Abdisa E
*Int J Pediatr* 2019;2019:4716482

**The relationship between wasting and stunting: a retrospective cohort analysis of longitudinal data in Gambian children from 1976 to 2016**

**Use of quantitative molecular diagnostic methods to investigate the effect of enteropathogen infections on linear growth in children in low-resource settings: longitudinal analysis of results from the MAL-ED cohort study**
*Lancet Glob Health* 2018;6:e1319–e1328

**Biomarkers of environmental enteric dysfunction and associations with child linear growth in rural Odisha, India (OR10-06-19)**
Sinharyo S, Reese H, Clasen A T
*Curr Dev Nutr* 2019;3(suppl 1); nzz034.OR10-06-19, https://doi.org/10.1093/cdn/nzz034.OR10-06–19

#### Consequences

**The aggregate income losses from childhood stunting and the returns to a nutrition intervention aimed at reducing stunting**
Galasso E, Wagstaff A
*Econ Hum Biol* 2019;34:225–238
Lifetime economic impact of the burden of childhood stunting attributable to maternal psychosocial risk factors in 137 low/middle-income countries


BMJ Glob Health 2019;4:e001144

Water, Sanitation, and Hygiene

Independent and combined effects of improved water, sanitation, and hygiene, and improved complementary feeding, on child stunting and anaemia in rural Zimbabwe: a cluster-randomised trial


Lancet Glob Health 2019;7:e132–e147

The WASH benefits and SHINE trials. interpretation of findings on linear growth and diarrhoea and Implications for policy: perspective of the investigative teams (P10-136-19)


Thresholds of socio-economic and environmental conditions necessary to escape from childhood malnutrition: a natural experiment in rural Gambia

Husseini M, Darboe MK, Moore SE, Nabwera HM, Prentice AM

BMC Med 2018;16:199

Environmental enteric dysfunction and child stunting

Budge S, Parker AH, Hutchings PT, Garbutt C

Nutr Rev 2019;77:240–253

Intervention

A multicountry randomized controlled trial of comprehensive maternal nutrition supplementation initiated before conception: the women first trial


PROCOMIDA, a food-assisted maternal and child health and nutrition program, reduces child stunting in Guatemala: a cluster-randomized controlled intervention trial

Olney DK, Leroy J, Bliznashka L, Ruel MT

J Nutr 2018;148:1493–1505
Pathways

Maternal Common Mental Disorder as Predictors of Stunting among Children Aged 6–59 Months in Western Ethiopia: A Case-Control Study

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Background: Child malnutrition in low- and middle-income countries still continues to be an alarming. Africa and Asia bear the greatest share of all forms of malnutrition. The association between maternal common mental disorder and stunting has not been studied well even in developed countries; much less in developing countries and even the findings are conflicting. Thus, the purpose of the present research was to investigate the relationship of maternal common mental disorder and child stunting.

Methods: Institution based unmatched case-control study design was employed from March to April 2017. Two hundred thirty-four sampled children (78 cases and 156 controls) were randomly selected. Anthropometric measurements (height/length and weight) were taken by calibrated instruments. Maternal common mental disorder (CMD) was measured by using the locally validated Self-Reporting Questionnaire (SRQ-20). Data entry was done by Epi data version 3.1 and analysis was done by SPSS 21.0 statistical software.

Results: Finding of this study found out about three-fourths of cases (71.8%) and three-fourths of controls (69.9%) were residing in rural and urban areas, respectively. Regarding maternal common mental disorder, more than half of cases mother (53.8%) and more than one-tenth of controls mother (13.5%) were found to have common mental disorder. The study showed that children of mothers who had common mental disorder were found to be 3 times more likelihood of developing stunting than children whose mothers had not common mental disorder.

Conclusion and Recommendation: The study indicated that maternal common mental disorder was significantly associated with stunting. Therefore, emphasis should be given in preventing, managing, and maintaining maternal mental health in order to prevent stunting.
Maternal CMD which is composed of depressive, anxiety and somatic symptoms is highly prevalent, and it is one of the major contributors to the global burden of disease in low- and middle-income countries (LMICs). Using a case-control design, the study aims to unravel the specific association between maternal CMD and stunting. This study found that children whose mothers had CMD were 3 times more likely to be stunted than children whose mothers had no CMD. These data further support the known link between maternal mental health and childhood undernutrition. A major challenge in this field is finding interventions that work and are scalable in LMICs.


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Background: The etiologic relationship between wasting and stunting is poorly understood, largely because of a lack of high-quality longitudinal data from children at risk of undernutrition.

Objectives: The aim of this study was to describe the interrelationships between wasting and stunting in children aged <2 years.

Methods: This study involved a retrospective cohort analysis, based on growth-monitoring records spanning 4 decades from clinics in rural Gambia. Anthropometric data collected at scheduled infant welfare clinics were converted to z scores, comprising 64,342 observations on 5,160 subjects (median: 12 observations per individual). Children were defined as “wasted” if they had a weight-for-length z score less than –2 against the WHO reference and “stunted” if they had a length-for-age z score less than –2.

Results: Levels of wasting and stunting were high in this population, peaking at approximately (girls-boys) 12–18% at 10–12 months (wasted) and 37–39% at 24 months of age (stunted). Infants born at the start of the annual wet season (July-October) showed early growth faltering in weight-for-length z score, putting them at increased risk of subsequent stunting. Using time-lagged observations, being wasted was predictive of stunting (OR 3.2; 95% CI 2.7–3.9), even after accounting for current stunting. Boys were more likely to be wasted, stunted, and concurrently wasted and stunted than girls, as well as being more susceptible to seasonally driven growth deficits.

Conclusions: We provide evidence that stunting is in part a biological response to previous episodes of being wasted. This finding suggests that stunting may represent a deleterious form of adaptation to more overt undernutrition (wasting). This is important from a policy perspective as it suggests we are failing to recognize the importance of wasting simply because it tends to be more acute and treatable. These data suggest that stunted children are not just short children but are children who earlier were more seriously malnourished and who are survivors of a composite process.

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The relationship between wasting and stunting is poorly understood. In recent decades, the nutrition community has separated child wasting and stunting along the humanitarian/development divide resulting in different policies, programs, research, and funding for these 2 manifestations of child undernutrition. The rationale behind the conceptual separation of stunting and wasting in terms of etiology and programs has been questioned in a number of recent reviews and publications [1, 2]. Using longitudinal cohort data from Gambia, the study sought to describe the interrelationships between wasting and stunting in children. The data showed that being wasted was predictive of stunting (OR 3.2; 95% CI 2.7–3.9), even after accounting for current stunting, meaning that the effects of wasting may be longer term manifesting as slow linear growth. There are compelling reasons for both treatment and prevention interventions to consider them jointly and with awareness of the relation between them.

Use of quantitative molecular diagnostic methods to investigate the effect of enteropathogen infections on linear growth in children in low-resource settings: longitudinal analysis of results from the MAL-ED cohort study


Background: Optimum management of childhood diarrhoea in low-resource settings has been hampered by insufficient data on aetiology, burden, and associated clinical characteristics. We used quantitative diagnostic methods to reassess and refine estimates of diarrhoea aetiology from the Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED) cohort study.

Methods: We re-analysed stool specimens from the multisite MAL-ED cohort study of children aged 0–2 years done at eight locations (Dhaka, Bangladesh; Vellore, India; Bhaktapur, Nepal; Naushero Feroze, Pakistan; Venda, South Africa; Haydom, Tanzania; Fortaleza, Brazil; Lo reto, Peru), which included active surveillance for diarrhoea and routine non-diarrhoeal stool
collection. We used quantitative PCR to test for 29 enteropathogens, calculated population-level pathogen-specific attributable burdens, derived stringent quantitative cutoffs to identify aetiology for individual episodes, and created aetiology prediction scores using clinical characteristics.

**Findings:** We analysed 6,625 diarrhoeal and 30,968 non-diarrhoeal surveillance stools from 1,715 children. Overall, 64.9% of diarrhoea episodes (95% CI 62.6–71.2) could be attributed to an aetiology by quantitative PCR compared with 32.8% (30.8–38.7) using the original study microbiology. Viral diarrhoea (36.4% of overall incidence, 95% CI 33.6–39.5) was more common than bacterial (25.0%, 23.4–28.4) and parasitic diarrhoea (3.5%, 3.0–5.2). Ten pathogens accounted for 95.7% of attributable diarrhoea: Shigella (26.1 attributable episodes per 100 child-years, 95% CI 23.8–29.9), sapovirus (22.8, 18.9–27.5), rotavirus (20.7, 18.8–23.0), adenovirus 40/41 (19.0, 16.8–23.0), enterotoxigenic Escherichia coli (18.8, 16.5–23.8), norovirus (15.4, 13.5–20.1), astrovirus (15.0, 12.0–19.5), Campylobacter jejuni or C. coli (12.1, 8.5–17.2), Cryptosporidium (5.8, 4.3–8.3), and typical enteropathogenic *E. coli* (5.4, 2.8–9.3). 86.2% of the attributable incidence for Shigella was non-dysenteric. A prediction score for shigellosis was more accurate (sensitivity 50.4% [95% CI 46.7–54.1], specificity 84.0% [83.0–84.9]) than current guidelines, which recommend treatment only of bloody diarrhoea to cover Shigella (sensitivity 14.5% [95% CI 12.1–17.3], specificity 96.5% [96.0–97.0]).

**Interpretation:** Quantitative molecular diagnostics improved estimates of pathogen-specific burdens of childhood diarrhoea in the community setting. Viral causes predominated, including a substantial burden of sapovirus; however, Shigella had the highest overall burden with a high incidence in the second year of life. These data could improve the management of diarrhoea in these low-resource settings.

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**Comments**

Diarrhea due to pathogens, such as Shigella and enterotoxigenic *Escherichia coli*, has been associated with poor height attainment and poor weight gain, respectively, whereas rotavirus has been shown to have little effect on ponderal or linear growth. The study analyzed stool samples from the Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development (MAL-ED). This was a multisite longitudinal birth cohort that assessed the effect of enteric infections and other risk factors on linear growth [3]. In their analysis, they used PCR technique that has high sensitivity compared to culture and immunoassays methods previously used. Data showed that subclinical infections with bacteria had larger and more consistent associations with larger decrements in LAZ than those of viruses or protozoa. Shigella infection resulted in the largest population-level difference in LAZ. This suggests that focused strategies to reduce subclinical infection may contribute to reducing prevalence of stunting.

**Biomarkers of environmental enteric dysfunction and associations with child linear growth in rural Odisha, India (OR10-06-19)**

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*Curr Dev Nutr* 2019;3(suppl 1); nzz034. OR10-06-19, https://doi.org/10.1093/cdn/nzz034. OR10-06-19

**Objectives:** Intestinal dysfunction due to mucosal inflammation, known as environmental enteric dysfunction (EED), has been hypothesized to contribute to stunting in low- and middle-income countries (LMICs). Given that consensus is lacking on gold standard biomarkers for EED and on
relationships with child linear growth, we examined 3 biomarkers of EED and height-for-age z-score (HAZ) among children under age 5 years in rural Odisha, India.

**Methods:** We conducted a sub-study within Gram Vikas MANTRA, a matched cohort study of a household-level water and sanitation intervention in Odisha, India. We collected stool samples and anthropometry data for children under age 5 \((n = 209)\) in 2 rounds (October 2016 – January 2017 and July – October 2017). We analyzed stool samples for 3 biomarkers of EED: myeloperoxidase (MPO), neopterin (NEO), and α1-anti-trypsin (AAT). We assessed correlations between values and used linear regression to analyze associations between each biomarker and HAZ. All analyses were adjusted for relevant covariates and village-level clustering.

**Results:** Mean HAZ for children under 5 in our sample population was –1.52 (SD 1.34). Median biomarker values (25th, 75th percentiles) were 1,052.71 ng/mL (682.76, 3,208.22) for MPO, 2,104.21 nmol/L (1,193.64, 3,490.10) for NEO, and 0.406 mg/g (229.44, 743.78) for AAT. Correlations between the biomarkers were relatively low, with the highest correlation \((\rho = 0.45)\) between MPO and AAT. We observed an inverse association between MPO and HAZ \((\beta = -0.000027, p < 0.001)\) but no association between NEO and HAZ \((\beta = 0.000031, p = 0.46)\) or AAT and HAZ \((\beta = -0.000072, p = 0.52)\).

**Conclusions:** In our sample population, median values for NEO and AAT were similar to those from other studies of children in LMICs. MPO had substantially lower values than in other reports but was still strongly associated with HAZ. Previous studies have produced conflicting evidence on relationships between each biomarker of EED and HAZ. Our results contribute evidence that intestinal inflammation may play an important role in growth faltering in young children, possibly through mucosal dysfunction. MPO is a major component of the primary granules in neutrophils and hence reflects luminal neutrophilic infiltration. Priorities for a future research agenda on EED and growth will be discussed.

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**Comments**

There is growing interest in understanding the role environmental enteric dysfunction (EED) plays in childhood malnutrition in order to inform interventions. However, as there is still no gold standard biomarker to support the diagnosis of EED, this study in India takes an interesting approach and examines the relationship of 3 different biomarkers of EED with stunting.

**Consequences**

**The aggregate income losses from childhood stunting and the returns to a nutrition intervention aimed at reducing stunting**

Galasso E, Wagstaff A

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*Econ Hum Biol* 2019;34:225–238

We undertake 2 calculations, one for all developing countries, the other for 34 developing countries that together account for 90% of the world’s stunted children. The first asks how much lower a country’s per capita income is today as a result of having a fraction of its workforce been stunted in childhood. We use a development accounting framework, relying on micro-econometric estimates...
of the effects of childhood stunting on adult wages through their effects on years of schooling, cognitive skills, and height, parsing out the relative contribution of each set of returns to avoid double counting. We estimate that, on average, the per capita income penalty from stunting is between 5–7%, depending on the assumption. In our second calculation we estimate the economic value and the costs associates with scaling up a package of nutrition interventions using the same methodology and set of assumptions used in the first calculation. We take a package of 10 nutrition interventions that has data on both effects and costs, and we estimate the rate-of-return to gradually introducing this program over a period of 10 years in 34 countries that together account for 90% of the world’s stunted children. We estimate a rate-of-return of 12%, and a benefit-cost ratio of 5:1–6:1.

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Comments

The economic cost associated with childhood stunting has previously been estimated; however, the rate of return expected by the application of various nutrition interventions is less well understood and hardly estimated. The study applies a unique approach to estimate the rate of return that would be expected if interventions were to be applied. In one study, the rate of returns from a package of 10 nutrition interventions over a period of 10 years in 34 countries was estimated at 12%.

Lifetime economic impact of the burden of childhood stunting attributable to maternal psychosocial risk factors in 137 low/middle-income countries

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Introduction: The first 1,000 days of life is a period of great potential and vulnerability. In particular, physical growth of children can be affected by the lack of access to basic needs as well as psychosocial factors, such as maternal depression. The objectives of the present study are to: (1) quantify the burden of childhood stunting in low/middle-income countries attributable to psychosocial risk factors; and (2) estimate the related lifetime economic costs.

Methods: A comparative risk assessment analysis was performed with data from 137 low/middle-income countries throughout Asia, Latin America and the Caribbean, North Africa and the Middle East, and sub-Saharan Africa. The proportion of stunting prevalence, defined as less than –2 SDs from the median height for age according to the WHO Child Growth Standards, and the number of cases attributable to low maternal education, intimate partner violence (IPV), maternal depression and orphanhood were calculated. The joint effect of psychosocial risk factors on stunting was estimated. The economic impact, as reflected in the total future income losses per birth cohort, was examined.
**Results:** Approximately 7.2 million cases of stunting in low/middle-income countries were attributable to psychosocial factors. The leading risk factor was maternal depression with 3.2 million cases attributable. Maternal depression also demonstrated the greatest economic cost at USD 14.5 billion, followed by low maternal education (USD 10.0 billion) and IPV (USD 8.5 billion). The joint cost of these risk factors was USD 29.3 billion per birth cohort.

**Conclusion:** The cost of neglecting these psychosocial risk factors is significant. Improving access to formal secondary school education for girls may offset the risk of maternal depression, IPV and orphanhood. Focusing on maternal depression may play a key role in reducing the burden of stunting. Overall, addressing psychosocial factors among perinatal women can have a significant impact on child growth and well-being in the developing world.

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**Comments**

The burden of childhood stunting in low- and middle-income countries has previously been quantified. The contribution of food and water, sanitation, and hygiene (WASH) interventions to the prevention and treatment of childhood stunting has also been well documented. In this study, using a large dataset from 137 countries, maternal-related risk factors are highlighted and the cases attributed to these factors estimated. Specifically, maternal depression and low levels of education are strong predictors of stunting and demonstrated the greatest impact cost at USD 14.5 billion and USD 10.0 billion, respectively. These new data call for a shift in focus and expand intervention packages targeting stunting across the globe.

**Water, Sanitation, and Hygiene**

**Independent and combined effects of improved water, sanitation, and hygiene, and improved complementary feeding, on child stunting and anaemia in rural Zimbabwe: a cluster-randomised trial**

Humphrey JH1,2, Mbuya MNN1–5, Ntozini R2, Moulton LH1, Stoltzfus RJ3, Mampingwa NV2, Mutasa K2, Majo F2, Mutasa B2, Mangwadu G2, Chasokela CM3, Chigumira A5, Chasekwa B2, Smith LE2,6, Tielsch JM7, Jones AD9, Manges AR9, Maluccio JA10, Prendergast AJ1,2,11 for the Sanitation Hygiene Infant Nutrition Efficacy (SHINE) Trial Team

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*Lancet Glob Health* 2019;7:e132–e147

**Background:** Child stunting reduces survival and impairs neurodevelopment. We tested the independent and combined effects of improved water, sanitation, and hygiene (WASH), and improved infant and young child feeding (IYCF) on stunting and anaemia in Zimbabwe.
Methods: We did a cluster-randomised, community-based, 2 × 2 factorial trial in 2 rural districts in Zimbabwe. Clusters were defined as the catchment area of between 1 and 4 village health workers employed by the Zimbabwe Ministry of Health and Child Care. Women were eligible for inclusion if they permanently lived in clusters and were confirmed pregnant. Clusters were randomly assigned (1:1:1:1) to standard of care (52 clusters), IYCF (20 g of a small-quantity lipid-based nutrient supplement per day from age 6 to 18 months plus complementary feeding counselling; 53 clusters), WASH (construction of a ventilated improved pit latrine, provision of 2 handwashing stations, liquid soap, chlorine, and play space plus hygiene counselling; 53 clusters), or IYCF plus WASH (53 clusters). A constrained randomisation technique was used to achieve balance across the groups for 14 variables related to geography, demography, water access, and community-level sanitation coverage. Masking of participants and fieldworkers was not possible. The primary outcomes were infant length-for-age Z score and haemoglobin concentrations at 18 months of age among children born to mothers who were HIV negative during pregnancy. These outcomes were analysed in the intention-to-treat population. We estimated the effects of the interventions by comparing the 2 IYCF groups with the 2 non-IYCF groups and the 2 WASH groups with the 2 non-WASH groups, except for outcomes that had an important statistical interaction between the interventions.

Findings: Between Nov 22, 2012, and March 27, 2015, 5,280 pregnant women were enrolled from 211 clusters. 3,686 children born to HIV-negative mothers were assessed at age 18 months (884 in the standard of care group from 52 clusters, 893 in the IYCF group from 53 clusters, 918 in the WASH group from 53 clusters, and 991 in the IYCF plus WASH group from 51 clusters). In the IYCF intervention groups, the mean length-for-age Z score was 0.16 (95% CI 0.08–0.23) higher and the mean haemoglobin concentration was 2.03 g/L (1.28–2.79) higher than those in the non-IYCF intervention groups. The IYCF intervention reduced the number of stunted children from 620 (35%) of 1,792 to 514 (27%) of 1,879, and the number of children with anaemia from 245 (13.9%) of 1,759 to 193 (10.5%) of 1,845. The WASH intervention had no effect on either primary outcome. Neither intervention reduced the prevalence of diarrhoea at 12 or 18 months. No trial-related serious adverse events, and only 3 trial-related adverse events, were reported.

Interpretation: Household-level elementary WASH interventions implemented in rural areas in low-income countries are unlikely to reduce stunting or anaemia and might not reduce diarrhoea. Implementation of these WASH interventions in combination with IYCF interventions is unlikely to reduce stunting or anaemia more than implementation of IYCF alone.

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Comments

This was a rigorously designed and implemented trial using improved water, sanitation, and hygiene (WASH) interventions, optimizing breastfeeding and complementary feeding strategies and play spaces for infants and toddlers in rural Zimbabwe. The WASH interventions had no effect on the length-for-age Z scores (LAZ) or anaemia in children at 18 months of age. The feeding strategies resulted in a modest increase in LAZ of 0.16 and a 2 g/L increase in hemoglobin levels. The WASH strategies that they used in this trial did not appear to achieve the levels of environmental hygiene that are required to prevent infant and young child morbidities such as environmental enteric dysfunction that are involved in the causal pathways of childhood stunting and anaemia.
The WASH benefits and SHINE trials. Interpretation of findings on linear growth and diarrhoea and implications for policy: perspective of the investigative teams (P10-136-19)

Humphrey J1, Pickering A2, Null C3, Winch P4, Mangwedu G5, Arnold B6, Prendergast A7, Njenga S8, Rahman M8, Ntozini R9, Benjamin-Chung J10, Stewart C4, Huda T8, Moulton L12, Colford J10, Luby S12

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Objectives: We recently completed 3 efficacy trials (Bangladesh, Kenya, Zimbabwe) testing the independent and combined effects of improved complementary feeding (CF) and intensive household water quality, sanitation, and hygiene (WASH) on child diarrhea and length-for-age-Z-score (LAZ) at 18–24 months. Intervention uptake was high. In all 3 trials: CF increased LAZ but WASH had no effect on LAZ. WASH reduced diarrhea in Bangladesh but not in Kenya or Zimbabwe. We present a synthesis of trial findings and their implications.

Methods: Reviews of the literature and reanalysis of trial data were conducted.

Results: WASH and stunting: Copious observational studies have demonstrated a strong association between household-level WASH and child LAZ. We conducted an observational analysis (nested birth cohort) from our control arms. In adjusted analyses of all 3 trials, having an improved latrine when the pregnant woman was enrolled was associated with ∼0.2LAZ increase in her child at 18–24 months. The frequently reported association between household WASH indicators and child growth may be confounded and drawing causal inference misguided. WASH and diarrhea: Promoters visited intervention households 6 times per month in Bangladesh and monthly in Kenya and Zimbabwe. We conducted a systematic literature review: virtually all evidence that household water chlorination and handwashing reduce diarrhea comes from studies with daily to fortnightly intervention contact. In studies with follow-up after the trial ending, behaviors steeply declined and the effect on child diarrhea disappeared. Household water chlorination and handwashing promotion implemented through sporadic message delivery may not reduce child diarrhea. Enteropathogen transmission: Despite achieving substantial contrast between WASH and non-WASH households, children in the WASH arms still experienced high enteropathogen transmission, illustrating the recalcitrance of pervasive fecal contamination in rural low-income communities to even intense intervention.

Conclusions: Household WASH interventions are unlikely to reduce child stunting and may not reduce child diarrhea. We call for substantial investment in research to identify and in programming to deliver much more efficacious interventions.

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Comments: This was a useful perspective from the study team who conducted 3 cluster randomized trials to evaluate the efficacy of optimizing infant-feeding strategies and enhancing environmental hygiene (chlorinated water, improved sanitation and hygiene interventions, i.e., handwashing with soap, WASH) on linear growth and diarrhea in the infants, in 3 low- and middle-income countries (Bangladesh, Kenya, and Zimbabwe). The findings showed that WASH interventions alone had no effect on linear growth and only had an effect on diarrhea in Bangladesh where there was more intensive household follow-up. Combined breastfeeding and complementary feeding strategies had a small but significant increase on the mean length-for-age Z score by 0.13–0.25 in the initial analysis. Interestingly, a subanalysis showed a small but significant
effect on infant linear growth of about 0.2 LAZ scores when pregnant women had access to improved latrines. Their insights into the limitations of their interventions and study design provides a platform for future research on early childhood exposures to enteropathogens whose pathways were not sufficiently interrupted by the interventions in these trials. Evaluation of interventions that focus on the appropriate strategies for disposal of infant and domestic animal feces to ensure that infants and older children are not exposed to these environmental contaminants is warranted.

### Thresholds of socio-economic and environmental conditions necessary to escape from childhood malnutrition: a natural experiment in rural Gambia

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**Background:** Childhood malnutrition remains highly prevalent in low-income countries, and a 40% reduction in under-5 year stunting is WHO’s top Global Target 2025. Disappointingly, meta-analyses of intensive nutrition interventions reveal that they generally have low efficacy at improving growth. Unhygienic environments also contribute to growth failure, but large WASH Benefits and SHINE trials of improved water, sanitation and hygiene (WASH) recently reported no benefits to child growth.

**Methods:** To explore the thresholds of socio-economic status (SES) and living standards associated with malnutrition, we exploited a natural experiment in which the location of our research centre within a remote rural village created a wide diversity of wealth, education and housing conditions within the same ecological setting and with free health services to all. A composite SES score was generated by grading occupation, education, income, water and sanitation, and housing and families were allocated to 5 groups (SES1 = highest). SES ranged from very poor subsistence-farming villagers to post graduate staff with overseas training. Nutritional status at 24 m was obtained from clinic records for 230 children and expressed relative to WHO Growth Standards.

**Results:** Height-for-age (HAZ) and weight-for-age (WAZ) Z-scores were strongly predicted by SES group. HAZ varied from –0.67 to –2.23 (p < 0.001) and WAZ varied from –0.90 to –1.64 (p < 0.001), from SES1 to SES5, respectively. Weight-for-height (WHZ) showed no gradient. Children in SES1 showed greater dispersion so were further divided in a post hoc analysis. Children resident in Western housing on the research compound (SES1A) had HAZ = +0.68 and WAZ = +0.36. The residual gradient between those in SES1B and SES5 spanned only 0.65 Z-score for HAZ (–1.58 to –2.23) and was not significant for WAZ or WHZ.

**Conclusions:** The large difference in growth between children in SES1A living in Western-type housing and SES1B children living in the village, and the very shallow gradient between SES1B and SES5, implies a very high SES threshold before stunting and underweight will be eliminated. This may help to explain the lack of efficacy of the recent WASH interventions and points to the need for what is termed ‘Transformative WASH’. Good quality housing, with piped water into the home, may be key to eliminating malnutrition.
This observational study was conducted in a rural Gambian community that for nearly 4 decades has had free access to primary health care services and a nutrition supplementation/rehabilitation center. In addition, breastfeeding in the first 18–24 months is the norm. It was a small study of 230 children with detailed information on parental socioeconomic status. At 2 years, the height-for-age Z score (HAZ) was strongly associated with socioeconomic status. In addition, children who resided in Western-style housing where there was limited contact with domestic animals, in-door running water, and flushing toilets had significantly better HAZ. The authors emphasized the fact that addressing stunting will require high thresholds of socioeconomic development in poor communities in low resource settings for this to be achieved.

Environmental enteric dysfunction and child stunting
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In 2017, an estimated 1 in every 4 (23%) children aged <5 years were stunted worldwide. With slow progress in stunting reduction in many regions and the realization that a large proportion of stunting is not due to insufficient diet or diarrhea alone, it remains that other factors must explain continued growth faltering. Environmental enteric dysfunction (EED), a subclinical state of intestinal inflammation, can occur in infants across the developing world and is proposed as an immediate causal factor connecting poor sanitation and stunting. A result of chronic pathogen exposure, EED presents multiple causal pathways, and as such the scope and sensitivity of traditional water, sanitation, and hygiene (WASH) interventions have possibly been unsubstantial. Although the definite pathogenesis of EED and the mechanism by which stunting occurs are yet to be defined, this paper reviews the existing literature surrounding the proposed pathology and transmission of EED in infants and considerations for nutrition and WASH interventions to improve linear growth worldwide.

This review provides current insights into environmental enteric dysfunction (EED), a pervasive, subclinical condition that is a key factor in the causal pathway of stunting and poor neurodevelopmental outcomes among children in poor communities in low- and middle-income countries. Also, that EED is not amenable to the current water, sanitation, and hygiene (WASH) interventions which focus on reducing episodes of diarrhea, whereas stunting is only weakly associated with diarrhea. The review suggests that more holistic approaches that also address environmental contamination by domestic animals would be more successful at limiting pathogen exposure in children in these environments. In addition, it emphasizes that future research should test integrated WASH, nutrition, caregiver practices, and early child development interventions.
A multicountry randomized controlled trial of comprehensive maternal nutrition supplementation initiated before conception: the women first trial

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This manuscript is also discussed in Chapter 9 by Yogev and Hiersch, page 185.

Background: Reported benefits of maternal nutrition supplements commenced during pregnancy in low-resource populations have typically been quite limited.

Objectives: This study tested the effects on newborn size, especially length, of commencing nutrition supplements for women in low-resource populations ≥3 months before conception (Arm 1), compared with the same supplement commenced late in the first trimester of pregnancy (Arm 2) or not at all (control Arm 3).

Methods: Women First was a 3-arm individualized randomized controlled trial (RCT). The intervention was a lipid-based micronutrient supplement; a protein-energy supplement was also provided if maternal body mass index (kg/m²) was <20 or gestational weight gain was less than recommendations. Study sites were in rural locations of the Democratic Republic of the Congo (DRC), Guatemala, India, and Pakistan. The primary outcome was length-for-age z score (LAZ), with all anthropometry obtained <48 h post-delivery. Because gestational ages were unavailable in DRC, outcomes were determined for all 4 sites from WHO newborn standards (non-gestational-age-adjusted, NGAA) as well as INTERGROWTH-21st fetal standards (GAA).

Results: A total of 7,387 non pregnant women were randomly assigned, yielding 2,451 births with NGAA primary outcomes and 1465 with GAA outcomes. Mean LAZ and other outcomes did not differ between Arm 1 and 2 using either NGAA or GAA. Mean LAZ (NGAA) for Arm 1 was greater than for Arm 3 (effect size: +0.19; 95% CI 0.08, 0.30, p = 0.0008). For GAA outcomes, rates of stunting and small-for-gestational-age were lower in Arm 1 than in Arm 3 (RR 0.69; 95% CI 0.49–0.98, p = 0.0361 and RR 0.78; 95% CI 0.70–0.88, p < 0.001, respectively). Rates of preterm birth did not differ among arms.

Conclusions: In low-resource populations, benefits on fetal growth-related birth outcomes were derived from nutrition supplements commenced before conception or late in the first trimester.

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Comments

Initiating nutrition supplements in the preconceptual period is a suggested strategy to correct maternal underweight and micronutrient deficiencies. In the women first...
trail, nutritional supplements were given before conception and during pregnancy (second and third trimester) with the aim of reducing the prevalence of stunting at birth. From these data, supplementing women before conception or in the first trimester may be more beneficial than not supplementing women at all. These data call for strategies to improve women nutrition before conception that may coincide with a focus on adolescent nutrition.

PROCOMIDA, a food-assisted maternal and child health and nutrition program, reduces child stunting in Guatemala: a cluster-randomized controlled intervention trial
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J Nutr 2018;148:1493–1505

Background: Food-assisted maternal and child health and nutrition (FA-MCHN) programs may foster child growth during the first 1,000 days (pregnancy and the first 2 years of a child’s life), but evidence is scant.

Objective: We evaluated the impact of an FA-MCHN program, PROCOMIDA, on linear growth (stunting [length-for-age z score (LAZ) less than –2] and length-for-age difference [LAD]) among children aged 1–24 months. PROCOMIDA was implemented in Guatemala by Mercy Corps and was available to beneficiaries throughout the first 1,000 days.

Methods: We used a longitudinal, cluster-randomized controlled trial with groups varying in family ration sizes (full [FFR], reduced [RFR], and none [NFR]) and individual ration types provided to mothers (pregnancy to 6 mo postpartum) and children (6–24 months of age) [corn-soy blend (CSB), lipid-based nutrient supplement (LNS), micronutrient powder (MNP)]: (1) FFR + CSB (n = 576); (2) RFR + CSB (n = 575); (3) NFR + CSB (n = 542); (4) FFR + LNS (n = 550); (5) FFR + MNP (n = 587); (6) control (n = 574). Program impacts compared with control, and differential impacts between groups varying family ration size or individual ration type, were assessed through the use of linear mixed-effects models and post hoc simple effect tests (significant if p < 0.05).

Results: PROCOMIDA significantly reduced stunting at age 1 month in FFR + CSB, RFR + CSB, and FFR + MNP groups compared with control (5.05, 4.06, and 3.82 percentage points [pp], respectively). Stunting impact increased by age 24 months in FFR + CSB and FFR + MNP relative to control (impact = 11.1 and 6.5 pp at age 24 months, respectively). For CSB recipients, the FFR compared with RFR or NFR significantly reduced stunting (6.47–9.68 pp). CSB reduced stunting significantly more than LNS at age 24 months (8.12 pp).

Conclusions: FA-MCHN programs can reduce stunting during the first 1,000 days, even in relatively energy/food-secure populations. Large family rations with individual rations of CSB or MNP were most effective. The widening of impact as children age highlights the importance of intervening throughout the full first 1,000 days.

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Comments There is a window of opportunity to correct stunting in the first 24 months of life. High-energy/protein food supplements given earlier in life may increase growth of stunted children. PROCOMIDA was a cluster randomized trial that aimed to prevent
childhood stunting by delivering sufficient food, promoting the adoption of optimal health, nutrition, hygiene practices, and improving the provision and utilization of preventive health services. The program managed to reduce prevalence of stunting at 24 months by 11.1% point in the intervention group receiving full family ration (FFR) + corn-soy blend (CSB) package. The findings add to existing knowledge that combining nutrition supplementation, hygiene, and access to health services with family food rations may have even better impact.

**Perspective**

**Perspective: What Does stunting really mean? A critical review of the evidence**

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The past decade has seen an unprecedented increase in attention to undernutrition, and drastically reducing child stunting has become a global development objective. The strong focus on linear growth retardation and stunting has enabled successful advocacy for nutrition, but with this focus has come some confusion and misunderstanding about the meaning of linear growth retardation and stunting among researchers, donors, and agencies active in nutrition. Motivated by the belief that a sharp focus will further accelerate progress in reducing undernutrition, we critically reviewed the evidence. The global attention to stunting is based on the premise that any intervention aimed at improving linear growth will subsequently lead to improvements in the correlates of linear growth retardation and stunting. Current evidence and understanding of mechanisms do not support this causal thinking, with 2 exceptions: linear growth retardation is a cause of difficult births and poor birth outcomes. Linear growth retardation is associated with (but does not cause) delayed child development, reduced earnings in adulthood, and chronic diseases. We thus propose distinguishing 2 distinctly different meanings of linear growth retardation and stunting. First, the association between linear growth retardation (or stunting) and other outcomes makes it a useful marker. Second, the causal links with difficult births and poor birth outcomes make linear growth retardation and stunting outcomes of intrinsic value. In many cases a focus on linear growth retardation and stunting is not necessary to improve the well-being of children; in many other cases, it is not sufficient to reach that goal; and for some outcomes, promoting linear growth is not the most cost-efficient strategy. We appeal to donors, program planners, and researchers to be specific in selecting nutrition outcomes and to target those outcomes directly.

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**Comments**

This interesting and thought-provoking write-up seeks to clear up the confusion and misunderstanding about what stunting really means among researchers, donors, and agencies active in nutrition.
Stunting, starvation and refeeding: a review of forgotten 19th and early 20th century literature

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Aim: To scrutinize to what extent modern ideas about nutrition effects on growth are supported by historic observations in European populations.

Method: We reviewed 19th and early 20th century paediatric journals in the Staatsbibliothek zu Berlin, the third largest European library with an almost complete collection of the German medical literature. During a 3-day visit, we inspected 15 bookshelf meters of literature not available in electronic format.

Results: Late 19th and early 20th century breastfed European infants and children, independent of social strata, grew far below World Health Organisation (WHO) standards and 15–30% of adequately-fed children would be classified as stunted by the WHO standards. Historic sources indicate that growth in height is largely independent of the extent and nature of the diet. Height catch-up after starvation was greater than catch-up reported in modern nutrition intervention studies and allowed for unimpaired adult height.

Conclusion: Historical studies are indispensable to understand why stunting does not equate with undernutrition and why modern diet interventions frequently fail to prevent stunting. Appropriateness and effect size of modern nutrition interventions on growth need revision.

Comments

Using data from historical studies in Europe, this interesting review argues that stunting does not equate to undernutrition. They concluded that “the historic literature lacks evidence of a strong association between food, child growth and adult height.” Therefore, focusing on modern diet interventions to address stunting diverts attention away from focusing on interventions that can truly address childhood undernutrition. They argue that the “upstream” factors including improvements in living conditions, food quality, and socioeconomic empowerment of communities are required for stunting to be addressed.

References