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Malnutrition and Catch-Up Growth during Childhood and Puberty

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Introduction

Children in resource-poor settings are prone to malnutrition resulting from a suboptimal nutrition and various environmental hindrances. According to the 2019 joint report of UNICEF, WHO, and the World Bank on levels and trends in child malnutrition, we are far from a world free of malnutrition. Indeed, global rates remain alarmingly high. In 2018, an estimated 14 million children younger than 5 years (21.9%) were affected by stunting, and wasting continued to threaten the lives of an estimated 49 million (7.3%). The report revealed that insufficient progress has been made to reach the World Health Assembly targets set for 2025 and the Sustainable Development Goals set for 2030 [1].

It is becoming evident that in order to effectively prevent and treat childhood malnutrition in low- and middle-income countries, a combination of interventions in several disciplines is needed: nutritional, for both mother and child; environmental, including access to basic health, water, hygiene, and sanitation services; and indirectly, agricultural and financial [2]. The nutritional interventions must be multisectoral and sustainable over the long term, and many countries appear to be moving in the right direction [1].

The prevention and treatment of stunting and wasting also require an in-depth understanding of the mechanisms underlying their development. Extensive research has

been directed specifically at deciphering the intricate relationship between the gut microbiome and the occurrence of enteric dysfunction. Recent findings suggest that interventions directed at the gut microbiota may help in the treatment of malnourished children [3].

This chapter reviews the most recent data on childhood malnutrition and catch-up growth, published between July 1, 2018, and June 30, 2019, and addresses several topics:

1 Evaluation and assessment of malnutrition in childhood and adolescence.

An interesting review of the genetic contribution to the evolvement of malnutrition [4] and 2 reviews on adolescent malnutrition [5, 6]

2 Nutritional interventions to prevent and treat malnutrition in children.

Several Cochrane database systemic reviews of RCTs and quasi-RCTs [7–10] and several summaries of clinical trials [11–13], assessing the effectiveness of different nutritional intervention approaches in the prevention and treatment of malnutrition in young children.

3 The microbiome and childhood malnutrition.

Several reviews summarizing the interplay between the microbiome and malnutrition and potential strategies for modulating the gut microbiota during childhood as prevention and treatment strategies against undernutrition [14–16].

Key articles reviewed for this chapter

Evaluation and Assessment of Malnutrition in Childhood and Adolescence

Does malnutrition have a genetic component?

Duggal P, Petri WA Jr.

Annu Rev Genomics Hum Genet 2018;19:247–262

Perspective: challenges in use of adolescent anthropometry for understanding the burden of malnutrition

Tumilowicz A, Beal T, Neufeld LM, Frongillo EA

Adv Nutr 2019;10:563–575

Addressing knowledge gaps in adolescent nutrition: toward advancing public health and sustainable development

Canavan CR, Fawzi WW

Curr Dev Nutr 2019;3:nzz062

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Nutritional Interventions to Prevent and Treat Malnutrition in Children

Preventive lipid-based nutrient supplements given with complementary foods to infants and young children 6–23 months of age for health, nutrition, and developmental outcomes

Das JK, Salam RA, Hadi YB, Sadiq Sheikh S, Bhutta AZ, Weise Prinzo Z, Bhutta ZA

Cochrane Database Syst Rev 2019;5:CD012611

Ready-to-Use Therapeutic Food (RUTF) for home-based nutritional rehabilitation of severe acute malnutrition in children from six months to five years of age

Schoonees A, Lombard MJ, Musekiwa A, Nel E, Volmink J

Cochrane Database Syst Rev 2019;5:CD009000

Community-based supplementary feeding for food insecure, vulnerable and malnourished populations: An overview of systematic reviews

Visser J, McLachlan MH, Maayan N, Garner P

Cochrane Database Syst Rev 2018;11:CD010578

Effectiveness of provision of animal-source foods for supporting optimal growth and development in children 6–59 months of age

Eaton JC, Rothpletz-Puglia P, Dreker MR, Iannotti L, Lutter C, Kaganda J, Rayco-Solon P

Cochrane Database Syst Rev 2019;2:CD012818

Consumption of animal-source protein is associated with improved height-for-age z scores in rural Malawian children aged 12–36 months

Kaimila Y, Divala O, Agapova SE, Stephenson KB, Thakwalakwa C, Trehan I, Manary MJ, Maleta KM

Nutrients 2019;11:480

Maximizing recovery and growth when treating moderate acute malnutrition with whey-containing supplements

Stobaugh H

Food Nutr Bull 2018;39(suppl 2):S30–S34

Higher levels of dairy result in improved physical outcomes: a synthesis of 3 randomized controlled trials in Guinea-Bissau comparing supplements with different levels of dairy ingredients among children 6–59 months, 5–19 year olds, and mothers in preschools, primary schools, and villages, and the implications for programs

Schlossman N

Food Nutr Bull 2018;39(suppl 2):S35–S44

The Microbiome and Childhood Malnutrition

Gut microbiota alterations and dietary modulation in childhood malnutrition: The role of short chain fatty acids

Pekmez CT, Dragsted LO, Brahe LK

Clin Nutr 2019;38:615–630

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World Rev Nutr Diet. Basel, Karger, 2020, vol 120, pp 158–180 (DOI: 10.1159/000503646)

A sparse covarying unit that describes healthy and impaired human gut microbiota development

Raman AS, Gehrig JL, Venkatesh S, Chang HW, Hibberd MC, Subramanian S, Kang G, Bessong PO, Lima AAM, Kosek MN, Petri WA Jr., Rodionov DA, Arzamasov AA, Leyn SA, Osterman AL, Huq S, Mostafa I, Islam M, Mahfuz M, Haque R, Ahmed T, Barratt MJ, Gordon JI

Science 2019;365:140

Effects of microbiota-directed foods in gnotobiotic animals and undernourished children

Gehrig JL, Venkatesh S, Chang HW, Hibberd MC, Kung VL, Cheng J, Chen RY, Subramanian S, Cowardin CA, Meier MF, O'Donnell D, Talcott M, Spears LD, Semenkovich CF, Henrissat B, Giannone RJ, Hettich RL, Ilkayeva O, Muehlbauer M, Newgard CB, Sawyer C, Head RD, Rodionov DA, Arzamasov AA, Leyn SA, Osterman AL, Hossain MI, Islam M, Choudhury N, Sarker SA, Huq S, Mahmud I, Mostafa I, Mahfuz M, Barratt MJ, Ahmed T, Gordon JI

Science 2019;365:139

Evaluation and Assessment of Malnutrition in Childhood and Adolescence

Does malnutrition have a genetic component?

Duggal P[1], Petri WA Jr[2]

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Annu Rev Genomics Hum Genet 2018;19:247–262

Abstract: Malnutrition is a complex disorder, defined by an imbalance, excess, or deficiency of nutrient intake. The visible signs of malnutrition are stunted growth and wasting, but malnourished children are also more likely to have delays in neurocognitive development, vaccine failure, and susceptibility to infection. Despite malnutrition being a major global health problem, we do not yet understand the pathogenesis of this complex disorder. Although lack of food is a major contributor to childhood malnutrition, it is not the sole cause. The mother's prenatal nutritional status, enteric infections, and intestinal inflammation also contribute to the risk of childhood malnutrition and recovery. Here, we discuss another potential risk factor, host and maternal genetics that may play a role in the risk of malnutrition via several biological pathways. Understanding the genetic risks of malnutrition may help to identify ideal targets for intervention and treatment of malnutrition.

Comments Challenging the common assumption that malnutrition is an acquired condition, with a small, if any, contribution of the host, this review summarizes current data on genes that may be involved in the pathways leading to malnutrition. The genes mentioned have been shown to predispose or protect an individual from acquiring a specific micro- or macronutrient deficiency; to confer susceptibility to developing diarrhea by specific enteric infections; or may take part in the pathways leading to chronic en-

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teric inflammation. If so, this could explain why some children are more prone to malnutrition and stunting and suggest new directions for the development of targeted nutritional interventions.

Perspective: challenges in use of adolescent anthropometry for understanding the burden of malnutrition

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Adv Nutr 2019;10:563–575

Abstract: Improving nutritional status during adolescence is an opportunity to improve the lives of this generation and the next. Estimating the burden of malnutrition at a population level is fundamental to targeting interventions and measuring progress over time, and for adolescents, we usually depend on survey data and the 2007 WHO Growth Reference to do so. There is substantial risk of misguided conclusions regarding adolescent prevalence estimates, however, when underlying methodological limitations of the indicators and reference are not adequately considered. We use national prevalence estimates among girls and young women 10–22 years of age from the 2014 State of Food Security and Nutrition in Bangladesh report as an example to demonstrate that determining the true prevalence of undernutrition, overweight, and obesity is complicated by racial/ethnic variation across populations in timing of the adolescent growth spurt, growth potential, and body build. Further challenging the task are inherent limitations of the body mass index as an indicator of thinness and adiposity, and cutoffs that poorly distinguish a well-nourished population from a malnourished one. We provide recommendations for adolescent nutrition policy and program decision-making, emphasizing the importance of (1) critically interpreting indicators and distributions by age when using the 2007 WHO Growth Reference; (2) examining what is happening before and after adolescence, when interpretation of anthropometry is more straightforward, as well as trends over time; and (3) complementing anthropometry with other information, particularly dietary intake. Finally, we advocate that nutrition researchers prioritize exploration of better methods to predict peak height velocity, for development of standardized indicators to measure dietary quality among adolescents, and for studies that will illuminate causal paths so that we can effectively improve adolescent dietary intake and nutritional status.

Addressing knowledge gaps in adolescent nutrition: toward advancing public health and sustainable development

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Curr Dev Nutr 2019;3:nzz062

Abstract: Adolescence marks a critical period of growth in the life course. Malnutrition among adolescents includes suboptimal dietary intake of macronutrients and micronutrients as well as overweight and obesity linked to poor dietary quality. We discuss adolescent nutrition and outline 3 knowledge gaps toward advancing adolescent health. First, micronutrient and macronutrient

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supplements have significant potential to improve nutritional status, but information on the most effective implementation strategies is lacking. Second, food system interventions offer a promising avenue to improve access to healthy foods, and school settings may be an important entry point for improving diets. Third, nutrition programs should be combined with delayed pregnancy interventions for greatest impact given the adverse effects of early pregnancy on maternal and infant health and nutrition outcomes. Evidence-based solutions for adolescent nutritional supplementation, food system and dietary intake interventions, and integration with sexual and reproductive health strategies present crucial opportunities for improving adolescent health and well-being.

Comments Improving the nutritional status of adolescents and young adults may better their present life, their future life, and that of their offspring. However, we still need to overcome some major methodological issues when evaluating this age group. These perspectives outline the knowledge gaps and challenges in diagnosing malnutrition and stunting in adolescents and in designing future studies on and effective interventions for these diagnoses. First of all, data required for developing adolescent growth standards are missing, yet these do not seem feasible to conduct a prospective, multicenter observational reference study similar to the WHO MRGS in adolescents. Additionally, significant differences in timing of puberty and peak height velocity interfere with the interpretation of existing data. Late outcomes of adolescent undernutrition cannot be properly assessed through cross-sectional studies as some undernourished adolescents experience very late catch-up growth. And finally, the BMIZ and HAZ cutoffs for the definition of wasting and stunting are not aligned with adult cutoffs for these same conditions, making it impossible to compare data on prevalence from different age groups. The authors highlight the need to find better methods to predict peak height velocity for the sake of cross-sectional surveys and the need for studies that will clarify causal paths and true outcomes so that we can effectively assess the barriers and develop solutions.

Nutritional Interventions to Prevent and Treat Malnutrition in Children

Preventive lipid-based nutrient supplements given with complementary foods to infants and young children 6–23 months of age for health, nutrition, and developmental outcomes

Das JK[1], Salam RA[1], Hadi YB[2], Sadiq Sheikh S[1], Bhutta AZ[3], Weise Prinzo Z[4], Bhutta ZA[5,6]

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Cochrane Database Syst Rev 2019;5:CD012611

Background: One nutritional intervention advocated to prevent malnutrition among children is lipid-based nutrient supplements (LNS). LNS provide a range of vitamins and minerals, but unlike

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most other micronutrient supplements, LNS also provide energy, protein and essential fatty acids. Alternative recipes and formulations to LNS include fortified blended foods (FBF), which are foods fortified with vitamins and minerals, and micronutrient powders (MNP), which are a combination of vitamins and minerals.

Objectives: To assess the effects and safety of preventive LNS given with complementary foods on health, nutrition and developmental outcomes of non-hospitalised infants and children 6–23 months of age, and whether or not they are more effective than other foods (including FBF or MNP).

This review did not assess the effects of LNS as supplementary foods or therapeutic foods in the management of moderate and severe acute malnutrition.

Search Methods: In October 2018, we searched CENTRAL, MEDLINE, Embase, 21 other databases and 2 trials registers for relevant studies. We also checked the reference lists of included studies and relevant reviews and contacted the authors of studies and other experts in the area for any ongoing and unpublished studies.

Selection Criteria: Randomised controlled trials (RCTs) and quasi-RCTs that evaluated the impact of LNS plus complementary foods given at point-of-use (for any dose, frequency, duration) to non-hospitalised infants and young children aged 6–23 months in stable or emergency settings and compared to no intervention, other supplementary foods (i.e. FBF), nutrition counselling or multiple micronutrient supplements or powders for point-of-use fortification of complementary foods.

Data Collection and Analysis: Two review authors independently screened studies for relevance and, for those studies included in the review, extracted data, assessed risk of bias and rated the quality of the evidence using the GRADE approach. We carried out statistical analysis using Review Manager software. We used a random-effects meta-analysis for combining data as the interventions differed significantly. We set out the main findings of the review in "Summary of findings" tables.

Main Results: Our search identified a total of 8,124 records, from which we included 17 studies (54 papers) with 23,200 children in the review. The included studies reported on one or more of the pre-specified primary outcomes, and 5 studies included multiple comparison groups.

Overall, the majority of trials were at low risk of bias for random sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias, but at high risk of bias for blinding of participants and personnel due to the nature of the intervention. Using the GRADE approach, we judged the quality of the evidence for most outcomes as low or moderate.

LNS+Complementary Feeding Compared with no Intervention: Thirteen studies compared LNS plus complementary feeding with no intervention. LNS plus complementary feeding reduced the prevalence of moderate stunting by 7% (risk ratio [RR] 0.93, 95% CI 0.880.98; nine studies, 13,372 participants; moderate-quality evidence), severe stunting by 15% (RR 0.85, 95% CI 0.74–0.98; 5 studies, 6151 participants; moderate-quality evidence), moderate wasting by 18% (RR 0.82, 95% CI 0.74–0.91; 8 studies; 13,172 participants; moderate-quality evidence), moderate underweight by 15% (RR 0.85, 95% CI 0.80–0.91; 8 studies, 13,073 participants; moderate-quality evidence), and anaemia by 21% (RR 0.79, 95% CI 0.69–0.90; 5 studies, 2,332 participants; low-quality evidence). There was no impact of LNS plus complementary feeding on severe wasting (RR 1.27, 95% CI 0.66–2.46; 3 studies, 2,329 participants) and severe underweight (RR 0.78, 95% CI 0.54–1.13; 2 studies, 1,729 participants).

Adverse effects did not differ between the groups (RR 0.86, 95% CI 0.74–1.01; 3 studies, 3,382 participants).

LNS+Complementary Feeding Compared with FBF: Five studies compared LNS plus complementary feeding with other FBF, including corn soy blend and UNIMIX. We pooled 4 of the 5 studies in meta-analyses and found that, when compared to other FBF, LNS plus complementary feeding significantly reduced the prevalence of moderate stunting (RR 0.89, 95% CI 0.82–0.97; 3 studies, 2,828 participants; moderate-quality evidence), moderate wasting (RR 0.79, 95% CI 0.65–0.97; 2

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studies, 2,290 participants; moderate-quality evidence), and moderate underweight (RR 0.81, 95% CI 0.73–0.91; 2 studies, 2,280 participants; moderate quality evidence). We found no difference between LNS plus complementary feeding and FBF for severe stunting (RR 0.41, 95% CI 0.12–1.42; 2 studies, 729 participants; low-quality evidence), severe wasting (RR 0.64, 95% CI 0.19–2.81; 2 studies, 735 participants; moderate-quality evidence), and severe underweight (RR 1.23, 95% CI 0.67–2.25; 1 study, 173 participants; low quality evidence).

LNS+Complementary Feeding Compared with MNP: Four studies compared LNS plus complementary feeding with MNP. We pooled data from 3 of the 4 studies in meta-analyses and found that compared to MNP, LNS plus complementary feeding significantly reduced the prevalence of moderate underweight (RR 0.88, 95% CI 0.78–0.99; 2 studies, 2,004 participants; moderate-quality evidence) and anaemia (RR 0.38, 95% CI 0.21–0.68; 2 studies, 557 participants; low-quality evidence). There was no difference between LNS plus complementary feeding and MNP for moderate stunting (RR 0.92, 95% CI 0.82–1.02; 3 studies, 2,365 participants) and moderate wasting (RR 0.97, 95% CI 0.77–1.23; 2 studies, 2,004 participants).

Authors' Conclusions: The findings of this review suggest that LNS plus complementary feeding compared to no intervention is effective at improving growth outcomes and anaemia without adverse effects among children aged 6–23 months in low- and middle-income countries (LMIC) in Asia and Africa, and more effective if provided over a longer duration of time (over 12 months). Limited evidence also suggests that LNS plus complementary feeding is more effective than FBF and MNP at improving growth outcomes.

Comments

Supplementary feeding is a strategy for providing extra food to children beyond their regular home diets. There are several common types of supplementary feeding designed to manage and improve malnutrition. One type is lipid-based nutrient supplements (LNS), a family of products that supply energy derived mainly from lipids in addition to a range of micronutrients, proteins, and essential fatty acids. LNS are nutrient-dense, require no cooking before use, and can be stored for months even in warm conditions. Other types of supplements include fortified blended foods (FBF) that are composed of cereals mixed with other ingredients, such as whey, soy protein isolate, dried skimmed milk, sesame, cashews, and chickpea paste, fortified with vitamins and minerals, and multiple micronutrient powders (MNP), supplied as single-dose packets of vitamins and minerals in powder form that can be spread on any ready-to-eat semi-solid food.

In 2019, a Cochrane systematic review by Das et al. [7] suggested that LNS plus complementary feeding is a safe and effective intervention for improving growth outcomes and anemia in healthy, nonhospitalized children aged 6–23 months. The intervention seemed to be more effective if provided for longer than 1 year. Although the data comparing LNS plus complementary feeding with other nutritional interventions were sparse, the authors found limited evidence that intervention with LNS plus complementary feeding probably reduces moderate stunting, moderate wasting, and moderate underweight compared to FBF and is probably more effective than MNP at reducing moderate underweight and improving height and weight. They also provided several directions for future studies to fill research gaps in the field. These include analyses of the impact of LNS and other nutritional interventions on psychomotor and neurodevelopmental outcomes, comparison of different nutritional interventions (different products as well as nutrition education alone), and further investigations of the long-term impact of different nutritional interventions on growth and development.

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Ready-to-Use Therapeutic Food (RUTF) for home-based nutritional rehabilitation of severe acute malnutrition in children from six months to five years of age

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Cochrane Database Syst Rev 2019;5:CD009000

Background: Management of severe acute malnutrition (SAM) in children comprises 2 potential phases: stabilisation and rehabilitation. During the initial stabilisation phase, children receive treatment for dehydration, electrolyte imbalances, intercurrent infections and other complications. In the rehabilitation phase (applicable to children presenting with uncomplicated SAM or those with complicated SAM after complications have been resolved), catch-up growth is the main focus and the recommended energy and protein requirements are much higher. In-hospital rehabilitation of children with SAM is not always desirable or practical – especially in rural settings – and home-based care can offer a better solution. Ready-to-use therapeutic food (RUTF) is a widely used option for home-based rehabilitation, but the findings of our previous review were inconclusive.

Objectives: To assess the effects of home-based RUTF used during the rehabilitation phase of SAM in children aged between 6 months and 5 years on recovery, relapse, mortality and rate of weight gain.

Search Methods: We searched the following databases in October 2018: CENTRAL, MEDLINE, Embase, 6 other databases and 3 trials registers. We ran separate searches for cost-effectiveness studies, contacted researchers and healthcare professionals in the field, and checked bibliographies of included studies and relevant reviews.

Selection Criteria: Randomised controlled trials (RCTs) and quasi-RCTs, where children aged between 6 months and 5 years with SAM were, during the rehabilitation phase, treated at home with RUTF compared to an alternative dietary approach, or with different regimens and formulations of RUTF compared to each other. We assessed recovery, deterioration or relapse and mortality as primary outcomes; and rate of weight gain, time to recovery, anthropometrical changes, cognitive development and function, adverse outcomes and acceptability as secondary outcomes.

Data Collection and Analysis: We screened for eligible studies, extracted data and assessed risk of bias of those included, independently and in duplicate. Where data allowed, we performed a random-effects meta-analysis using Review Manager 5, and investigated substantial heterogeneity through subgroup and sensitivity analyses. For the main outcomes, we evaluated the quality of the evidence using GRADE, and presented results in a 'Summary of findings' table per comparison.

Main Results: We included 15 eligible studies (n = 7,976; effective sample size = 6,630), four of which were cluster trials. Eight studies were conducted in Malawi, 4 in India, and 1 apiece in Kenya, Zambia, and Cambodia. Six studies received funding or donations from industry whereas 8 did not, and one study did not report the funding source. The overall risk of bias was high for 6 studies, unclear for 3 studies, and low for 6 studies. Among the 14 studies that contributed to meta-analyses, none (n = 5), some (n = 5) or all (n = 4) children were stabilised in hospital prior to commencement of the study. One small study included only children known to be HIV-infected, another study stratified the analysis for "recovery" according to HIV status, while the remaining studies included HIV-uninfected or untested children. Across all studies, the intervention lasted between 8 and 16 weeks. Only 5 studies followed up children postintervention (maximum of 6 months), and generally reported on a limited number of outcomes. We found 7 studies with 2,261 children comparing

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home-based RUTF meeting the World Health Organization (WHO) recommendations for nutritional composition (referred to in this review as standard RUTF) with an alternative dietary approach (effective sample size = 1,964). RUTF probably improves recovery (risk ratio [RR] 1.33; 95% CI 1.16 to 1.54; 6 studies, 1,852 children; moderate-quality evidence), and may increase the rate of weight gain slightly (mean difference [MD] 1.12 g/kg/day, 95% CI 0.27 to 1.96; 4 studies, 1,450 children; low-quality evidence), but we do not know the effects on relapse (RR 0.55, 95% CI 0.30 to 1.01; 4 studies, 1,505 children; very low-quality evidence) and mortality (RR 1.05, 95% CI 0.51 to 2.16; 4 studies, 1,505 children; very low-quality evidence). Two quasi-randomised cluster trials compared standard, home-based RUTF meeting total daily nutritional requirements with a similar RUTF but given as a supplement to the usual diet (213 children; effective sample size = 210). Meta-analysis showed that standard.

RUTF meeting total daily nutritional requirements may improve recovery (RR 1.41, 95% CI 1.19 to 1.68; low quality evidence) and reduce relapse (RR 0.11, 95% CI 0.01 to 0.85; low-quality evidence), but the effects are unknown for mortality (RR 1.36, 95% CI 0.46 to 4.04; very low-quality evidence) and rate of weight gain (MD 1.21 g/kg/day, 95%CI – 0.74 to 3.16; very low-quality evidence).

Eight studies randomised 5,502 children (effective sample size = 4456) and compared standard home-based RUTF with RUTFs of alternative formulations (e.g., using locally available ingredients, containing less or no milk powder, containing specific fatty acids, or with added pre- and probiotics). For recovery, it made little or no difference whether standard or alternative formulation RUTF was used (RR 1.03, 95% CI 0.99 to 1.08; 6 studies, 4,188 children; high-quality evidence). Standard RUTF decreases relapse (RR 0.84, 95% CI 0.72 to 0.98; 6 studies, 4,188 children; high-quality evidence). However, it probably makes little or no difference to mortality (RR 1.00, 95% CI 0.80 to 1.24; 7 studies, 4,309 children; moderate-quality evidence) and may make little or no difference to the rate of weight gain (MD 0.11 g/kg/day, 95% CI −0.32 to 0.54; 6 studies, 3,807 children; low-quality evidence) whether standard or alternative formulation RUTF is used.

Authors' Conclusions: Compared to alternative dietary approaches, standard RUTF probably improves recovery and may increase rate of weight gain slightly, but the effects on relapse and mortality are unknown. Standard RUTF meeting total daily nutritional requirements may improve recovery and relapse compared to a similar RUTF given as a supplement to the usual diet, but the effects on mortality and rate of weight gain are not clear. When comparing RUTFs with different formulations, the current evidence does not favour a particular formulation, except for relapse, which is reduced with standard RUTF. Well-designed, adequately powered, pragmatic RCTs with standardized outcome measures, stratified by HIV status, and that include diarrhoea as an outcome, are needed.

Comments

Ready-to-use therapeutic food (RUTF) is a widely used strategy for home-based rehabilitation of children with severe acute malnutrition (SAM). The products are energy-dense and typically include milk powder, sugar, peanut butter, vegetable oil, vitamins, and minerals. They are usually made according to a standard composition defined by the WHO. RUTF may serve as complete nutrition that meets all the nutritional requirements of a child recovering from SAM or as a supplement to the usual family diet. It requires no preparation and has long shelf-life without refrigeration. RUTF is available as a homogenous paste for consumption by children as young as 6 months or as a solid product that can be soaked in clean, boiling water to form porridge for young infants or consumed as a biscuit by older children.

A Cochrane systematic review by Schoonees et al. [8] suggested that RUTF probably improves recovery from malnutrition and may increase the rate of weight gain compared to alternative dietary approaches. However, its effects on relapse and mortality are unknown. The authors emphasize several limitations of existing studies, namely,

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absence of a clear definition of SAM, use of different outcome measures (such as recovery and anthropometric outcomes), and lack of data on adverse effects (such as diarrhea and allergic reactions), compliance, and cost-effectiveness.

Community-based supplementary feeding for food insecure, vulnerable and malnourished populations: An overview of systematic reviews

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Cochrane Database Syst Rev 2018;11:CD010578

Background: Supplementary feeding may help food insecure and vulnerable people by optimising the nutritional value and adequacy of the diet, improving quality of life and improving various health parameters of disadvantaged families. In low- and middle-income countries (LMIC), the problems supplementary feeding aims to address are entangled with poverty and deprivation, the programmes are expensive and delivery is complicated.

Objectives: (1) To summarize the evidence from systematic reviews of supplementary feeding for food insecure, vulnerable and malnourished populations, including children under 5 years of age, school-aged children, pregnant and lactating women, people with HIV or tuberculosis (or both), and older populations. (2) To describe and explore the effects of supplementary feeding given to people in these groups, and to describe the range of outcomes between reviews and range of effects in the different groups.

Methods: In January 2017, we searched the Cochrane Database of Systematic Reviews, MEDLINE, Embase and nine other databases. We included systematic reviews evaluating community-based supplementary feeding, and concerning food insecure, vulnerable and malnourished populations. Two review authors independently undertook selection of systematic reviews, data extraction and "Risk of bias" assessment. We assessed review quality using the AMSTAR tool, and used GRADEpro "Summary of findings" tables from each review to indicate the certainty of the evidence for the main comparisons. We summarised review findings in the text and reported the data for each outcome in additional tables. We also used forest plots to display results graphically.

Main Results: This overview included eight systematic reviews (with last search dates between May 2006 and February 2016). Seven were Cochrane Reviews evaluating interventions in pregnant women; children (aged from birth to 5 years) from LMIC; disadvantaged infants and young children (aged 3 months to 5 years); children with moderate acute malnutrition (MAM); disadvantaged school children; adults and children who were HIV positive or with active tuberculosis (with or without HIV). One was a non-Cochrane systematic review in older people with Alzheimer's disease. These reviews included 95 trials relevant to this overview, with the majority (74%) of participants from LMIC. The number of included participants varied between 91 and 7,940 adults, and 271 and more than 12,595 children. Trials included a wide array of nutritional interventions that varied in duration, frequency and format, with micronutrients often reported as cointerventions. Follow-up ranged from 6 weeks to 2 years; 3 trials investigated outcomes at 4–17 years of age. All reviews were rated as high quality (AMSTAR score between 8 and 11). The GRADE certainty ratings ranged from very low to moderate for individual comparisons, with the evidence often comprising only 1 or 2 small trials, thereby resulting in many underpowered analyses (too small to detect small but important differences). The main outcome categories reported across reviews were death, anthropometry (adults and children) and other markers of nutritional status, disease-related outcomes, neurocogni-

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tive development and psychosocial outcomes, and adverse events. Mortality data were limited and underpowered in meta-analysis in all populations (children with MAM, in children with HIV, and in adults with tuberculosis) with the exception of balanced energy and protein supplementation in pregnancy, which may have reduced the risk of stillbirth (risk ratio [RR] 0.60, 95% CI 0.39–0.94; 5 trials, 3,408 women). Supplementation in pregnancy also improved infant birth weight (mean difference [MD] 40.96 g, 95% CI 4.66–77.26; 11 trials, 5,385 participants) and reduced risk of infants born small-for-gestational age (RR 0.79, 95% CI 0.69–0.90; 7 trials, 4,408 participants). These effects did not translate into demonstrable long-term benefits for children in terms of growth and neurocognitive development in the 1–2 trials reporting on longer-term outcomes. In one study (505 participants), high-protein supplementation was associated with increased risk of small-for-gestational age babies. Effects on growth in children were mixed. In children under 5 years of age from LMIC, one review found that supplementary feeding had a little or no effect on child growth; however, a more recent review in a similar population found that those who received food supplementation gained an average of 0.12 kg more in weight (MD 0.12 kg, 95% CI 0.05–0.18; 9 trials, 1,057 participants) and 0.27 cm more in height (MD 0.27 cm, 95% CI 0.07–0.48; 9 trials, 1,463 participants) than those who were not supplemented. Supplementary food was generally more effective for younger children (younger than 2 years of age) and for those who were poorer or less well-nourished. In children with MAM, the provision of specially formulated food improved their weight, weight-for-height z scores and other key outcomes such as recovery rate (by 29%), as well as reducing the number of participants dropping out (by 70%). In LMIC, school meals seemed to lead to small benefits for children, including improvements in weight z scores, especially in children from lower-income countries, height z scores, cognition or intelligence quotient tests, and maths and spelling performance. Supplementary feeding in adults who were HIV positive increased the daily energy and protein intake compared to nutritional counselling alone. Supplementation led to an initial improvement in weight gain or body mass index but did not seem to confer long-term benefit. In adults with tuberculosis, one small trial found a significant benefit on treatment completion and sputum conversion rate. There were also significant but modest benefits in terms of weight gain (up to 2.60 kg) during active tuberculosis. The one study included in the Alzheimer's disease review found that 3 months of daily oral nutritional supplements improved nutritional outcomes in the intervention group. There was little or no evidence regarding people's quality of life, adherence to treatment, attendance at clinic or the costs of supplementary feeding programmes.

Authors' Conclusions: Considering the current evidence base included, supplementary food effects are modest at best, with inconsistent and limited mortality evidence. The trials reflected in the reviews mostly reported on short-term outcomes and across the whole of the supplementation trial literature it appears important outcomes, such as quality of life and cost of programmes, are not systematically reported or summarized.

Comments Visser et al. [9] conducted a Cochrane database review of published systematic reviews to summarize the current evidence on the effectiveness of supplementary feeding for food-insecure, vulnerable, and malnourished populations, including children, pregnant and lactating women, people with HIV or tuberculosis, and the elderly. The main results relevant to the present chapter were mixed. In children under 5 years of age from low- and middle-income countries, supplementary feeding seems to have a small impact on growth. The benefits observed include weight and height gains, especially in younger children (<2 years old) and poorer or more undernourished children. Some benefit could also be seen in children with moderate acute malnutrition (MAM) in terms of weight gain, improvement of other growth outcomes, and recovery rate. In schoolchildren, school meals seemed to promote small improvements in weight, height, intelligence test scores, and school performance. The authors con-

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clude that the current evidence-based data on the effectiveness of supplementary food are modest at best, and findings on mortality are inconsistent and limited. Most of the studies were short term and did not investigate adherence to treatment, quality of life, or costs. The authors emphasize that to address the complex and multidimensional nature of food insecurity and malnutrition, an integrated approach is needed, combining supplementary feeding with other interventions. They list several important aspects to be considered in the development of a nutrition-based program for the prevention and treatment of malnutrition. These include targeting participants who are undernourished and vulnerable; selecting the place of administration (on-site versus home) that will minimize leakage, promote adherence, and allow for proper supervision; providing sufficient energy and nutrients (at least 30% of the dietary reference intakes); and starting early (in infants and children) to optimize benefit.

Effectiveness of provision of animal-source foods for supporting optimal growth and development in children 6–59 months of age

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Cochrane Database Syst Rev 2019;2:CD012818

Background: Adequate nutrients early in life promote cognitive development and are critical for proper growth and functioning. The effect of individual nutrients consumed through food is often not the same as consuming the same nutrients in supplementary form due to "food synergy," the biological and chemical interrelations that occur between nutrients. Animal-source foods, such as eggs, meat, fish, and dairy, are energy dense and contain multiple micronutrients and essential fatty acids with high bioavailability. The benefits of animal-source foods may include higher food synergy relative to fortified foods as well as decreasing dependence on external suppliers of fortified foods.

Objectives: To assess the effectiveness of animal-source foods compared to any other feeding interventions or no intervention in improving growth and developmental outcomes in children aged 6–59 months.

Search Methods: We searched CENTRAL, MEDLINE, Embase, CINAHL, 18 other databases, and 3 trials registers up to August 2018. We also contacted authors and known experts in the field for assistance in identifying ongoing or unpublished data, and searched the reference lists of included studies and reviews, and websites of relevant organizations, for other studies that may not have been captured by our electronic searches.

Selection Criteria: We included randomized controlled trials and quasi-randomized controlled trials of any duration, where children between 5 and 59 months (6 years) of age were provided with an animal-source food (e.g., consumption of milk, meat, or eggs), prepared with any cooking method, compared with any intervention or no intervention.

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Data Collection and Analysis: Two review authors independently assessed trial eligibility using prespecified criteria, extracted data, assessed risk of bias, and graded the quality of the evidence using the GRADE approach.

Main Results: Study characteristics – We included 6 studies that analyzed data from 3,036 children aged 5–50 months. The studies were conducted in China, the Democratic Republic of Congo, Ecuador, Guatemala, Pakistan, the USA, and Zambia, and lasted between 5 and 12 months. Three studies were funded, in part, by government entities; one study was supported by a nonprofit organization. Two studies did not report a funding source. Three studies compared the effects of feeding an animal-source food with a fortified (iron or iron and zinc), or unfortified cereal; two used a control group with no intervention; one compared a meat-based diet to a dairy-based diet. The types of animal-source foods tested included yogurt, eggs, cheese, lyophilized (freeze-dried) beef product, ground and frozen pork, puréed and jarred beef with gravy or pork, and powdered whey protein. We judged 4 studies to be at unclear risk of bias overall; 3 studies because they were funded by an industry with a plausible interest in the outcome of the intervention; and one study because there was insufficient information to assess 5 of the 7 bias "Risk of bias" domains. We judged 2 of the 6 studies to be at high risk of bias overall; one study because there was significant baseline imbalance in length-for-age z scores (LAZ) between groups and evidence of selective reporting; the other study because there was both a significant baseline imbalance in LAZ and weight-for-age z scores (WAZ) between groups, and a large-scale social media campaign that may have influenced care received at home in the control group.

Key Results: *– Animal-source foods versus cereal-based foods or no intervention*

Five studies (2,972 children) measured change in linear growth with either height-for-age z scores (HAZ) or LAZ. Three studies (592 children) reported a significant increase in HAZ and LAZ in the intervention group compared to the control group. Two studies (2,380 children) reported a decline in LAZ in both groups. In one study (1,062 children) there was no difference between the groups in the rate of decline; in the other (1,318 children) the decrease in LAZ was significantly smaller in the intervention group. Five studies (2,972 children) measured weight gain using WAZ. Three studies (592 children) reported a significant increase in WAZ in the intervention group compared to the control group. In 2 studies (2380 children), WAZ decreased in both groups. In one of these studies (1,318 children), the decrease in the intervention group was significantly smaller than in the control group. In the other study (1,062 children), there was no difference between the groups. Three studies (1,612 children) reported impacts on all-cause morbidity, but metrics were inconsistent between studies. One study with yogurt (402 children) reported a significant reduction in duration and incidence of diarrhea and upper respiratory infections in the intervention group. One study with eggs (148 children) reported a significant increase in the incidence of diarrhea in the intervention group, but this may have been due to cultural associations with eggs and gastrointestional problems. There were no other significant differences in fever, respiratory infections, or skin conditions between groups. The third study (1,062 children) found no differences between intervention and control groups across morbidity measures. No studies reported data on anemia.

Meat-based diet versus dairy-based diet. One study (64 children) measured change in LAZ and WAZ in infants fed either a meat-based diet or dairy-based diet. There was a significant increase in LAZ among infants consuming the meat-based diet and a significant decrease in LAZ among infants consuming a dairy-based diet. WAZ increased in both groups, with no significant difference between groups. The study did not assess all-cause morbidity or anemia.

Quality of the evidence. We rated the quality of the evidence as very low overall due to baseline imbalances between intervention and control groups, high heterogeneity in meta-analysis, and imprecision due to wide confidence intervals and inconsistent direction of effects. We have little confidence in the results; further research is likely to change the estimate of magnitude and direction of treatment effect.

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Authors' Conclusion: Given the limited quality of the evidence, we are uncertain of the effects of the provision of animal-source food versus cereal products or no intervention on the growth or development of children. More adequately powered trials with deliberately selected animal-source foods are needed.

Consumption of animal-source protein is associated with improved height-for-age z scores in rural Malawian children aged 12–36 months

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Abstract: Linear growth faltering, caused by insufficient diet, recurrent infections and environmental enteric dysfunction (EED), continues to plague young children in low- and middle-income countries (LMICs). Diets in LMICs are primarily plant based, and thus have poor-quality protein and low levels of essential micronutrients. The aim of this study was to assess the association of the type and protein quality of food consumed with stunting, EED and acute malnutrition in children aged 6–36 months in Limera and Masenjere, 2 rural Southern Malawian communities. This is a secondary analysis of 2 randomized controlled trials that tested the effects of common bean and cowpea flour on stunting in children aged 6–36 months. We used data from 2 interactive 24-h dietary recalls conducted 12 weeks after enrolment into each trial. Food intakes were compared between the regions using chi-square and Student *t* test. There were 355 children that participated in the dietary recalls. The diets of children were of poor quality, but the children from Limera consumed more fish (54 vs. 35%, $p = 0.009$) and more bioavailable protein (26.0 ± 10.3 vs. 23.1 ± 8.1 g/day, $p = 0.018$, respectively) than children in Masenjere. Food type and protein quality were not associated with any of the outcomes except an association between animal protein consumption and improvement in height-for-age z scores in children aged 12–36 months ($p = 0.047$). These findings support the notion that animal-source food (ASF) consumption in this vulnerable population promotes linear growth.

Maximizing recovery and growth when treating moderate acute malnutrition with whey-containing supplements

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Food Nutr Bull 2018;39(suppl 2):S30–S34

Background: Much debate exists about the utility of dairy ingredients in the supplementary foods used to treat childhood moderate acute malnutrition (MAM).
Objective: To review the evidence regarding the effectiveness of dairy-containing supplements, particularly specially formulated foods containing whey permeate and whey protein concentrate, in treating children with MAM.

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Methods: A summary of a conference presentation regarding an overview of current evidence behind the use of whey in supplementary foods, including results of a randomized double-blinded clinical effectiveness trial involving 2,259 Malawian children treated for MAM using either a soy ready-to-use supplementary food (RUSF) or a novel whey RUSF treatment.
Results: While the majority of the evidence base only suggests potential benefits of including whey in supplementary foods to treat MAM, a recent study specifically demonstrates that a whey RUSF produced superior recovery and growth outcomes in treating children with MAM when compared with a soy RUSF.
Conclusions: The use of whey ingredients has been shown to improve outcomes in the treatment of MAM; however, further research is needed to identify the ideal amount and type of dairy protein required to produce the best outcomes for the lowest cost.

Higher levels of dairy result in improved physical outcomes: a synthesis of 3 randomized controlled trials in Guinea-Bissau comparing supplements with different levels of dairy ingredients among children 6–59 months, 5–19 year olds, and mothers in preschools, primary schools, and villages, and the implications for programs

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Background: This article synthesizes the results of 3 cluster randomized controlled trials of dairy-containing ready-to-use supplementary foods (RUSFs) to treat malnutrition in primary schools, preschools and villages in Guinea-Bissau, one of the world's poorest countries. Together, these studies document widespread malnutrition across infants, young children, adolescents, and pregnant and lactating women and point to intervention options that were not previously presented.
Objective: To combine the evidence from the United States Department of Agriculture-funded pilot studies in Guinea-Bissau on the effects of dairy protein supplementation to gain a broader perspective on the role of dairy containing RUSFs in various age-groups, the importance of the mother-child dyad and family food dynamics for infant and child growth. Translate the results into action and the next generation of effective products.
Methods: A comparative analysis of data and synthesis of evidence from 3 published studies and ongoing research conducted by our team in Guinea-Bissau.
Results and Conclusions: Higher dairy supplements have the potential to achieve broad benefits for malnutrition, especially in mothers and early childhood (first 1,000 days and 36–59 months).

Higher levels of dairy protein also can prevent moderate acute malnutrition in children younger than 2 years, independent of the family food dynamic. Community-level nutrition behavior change education should target older children and adolescents at the community level and through the preschool/school platform.

Comments Both the quality and quantity of protein are known to be important for growth in children. Eggs, meat, fish, and dairy are good sources of high-quality proteins and contain multiple micronutrients and essential fatty acids with high bioavailability. Numerous studies have suggested that animal-source protein improves nutritional outcomes in

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undernourished populations [17]. Several papers [10–13], including one Cochrane systematic review [10], published in the last year focused on the role of animal-source protein in the prevention and treatment of malnutrition in high-risk pediatric populations from low-income regions.

A Cochrane systematic review by Eaton et al. [10] compared the effectiveness of animal-source foods with any other feeding interventions or no intervention in improving growth and developmental outcomes in children aged 6–59 months. Of the 6 studies included, 5 (total 2,972 children) measured changes in linear growth and weight. Four studies reported a significant superiority for the animal-based intervention group compared to the control group in the changes of linear growth and weight, and one found no between-group differences. However, the authors rated the quality of the evidence as very low owing to baseline imbalances between the intervention and control groups and the high heterogeneity in the meta-analysis. As a result, they report little confidence in the results and highlight the need for more high-quality randomized control trials with deliberately selected animal-source foods.

A study by Kaimila et al. [11] assessed the association of the source and quality of nutritional protein with stunting, environmental enteric dysfunction (EED), and acute malnutrition in children aged 6–36 months residing in 2 rural Southern Malawian communities, Limera and Masenjere. The children from Limera consumed a higher amount of protein from animal sources (mainly fish), and this was found to be associated with better linear growth at ages 12–36 months. Overall, these results suggest that populations in regions characterized by higher consumption of animal-source proteins have lower rates of stunting, acute malnutrition, and EED than populations from areas with lower consumption of these foods, regardless of the level of nutrient intake and the quality of sanitation practices. Furthermore, although the children from Masenjere had a higher dietary diversity score and more of them met the minimum required dietary diversity compared to the children from Limera, their rate of stunting was higher. This observation suggests that the source of the protein may be more important than the diversity of the diet for improving anthropometric status. However, it contrasts with other studies reporting a positive association between higher dietary diversity and improved anthropometric outcomes [18–20]. Additional studies of this issue are warranted.

Milk and dairy products are known to be important for growth in children [21]. Both interventional and observational studies [21–24] have provided evidence that milk products positively affect linear growth. However, the exact mechanisms by which they do so remain unclear. Potential contributory factors are bioactive peptides found in milk proteins, insulin-like growth factor, and various minerals, including calcium and zinc [25]. The milk proteins whey and casein are very high-quality proteins and are rich in branched-chain amino acids (BCAA) [26]. BCAA are metabolized by muscle, promoting protein synthesis and reducing the need to break down lean tissue for energy. This is important in the recovery from acute malnutrition, in which one of the goals is to build lean tissue mass [26]. Milk proteins, especially whey, also exert several general health benefits via their enhancement of immune system responses [26]. Whey protein is particularly advantageous because it is water soluble, mixes easily, and is rapidly digested [27].

A recent randomized, double-blind controlled clinical trial by Stobaugh et al. [12, 28] studied the effectiveness of whey-based compared to soy-based ready-to-use supplementary food (RUSF) on recovery from MAM in 2,259 Malawian children. The total amount of protein provided by the soy-based RUSF was approximately 50% higher than that of the whey-based RUSF for each dose received. Nevertheless, compared to

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the patients fed the soy-based RUSF, the whey-based RUSF group had a higher rate of recovery in addition to better secondary growth outcomes. Thus, although the whey-based RUSF contained less protein and energy than the soy-based RUSF, it was more effective in children with MAM.

These findings were supported in a recent paper by Schlossman [13] summarizing the results of 3 cluster randomized controlled studies of the effectiveness of dairy-based RUSF in preventing malnutrition in infants, young children, adolescents, and pregnant and lactating women. The studies were conducted in Guinea-Bissau, one of the world's poorest countries. Participants were recruited from preschools, schools, and village health centers and assigned to 2 intervention groups and a control group. The first intervention group received RUSF in which 15% of the protein was derived from dairy (whey), and the second group received RUSF in which 33% of the protein was derived from dairy (50% whey and 50% nonfat dry milk), with the balance of the protein from soy isolate. The nutritional profile of the RUSFs was otherwise identical. The control group did not receive RUSF. The authors found that the supplements higher in dairy protein had a potential to achieve broad benefits in the treatment and prevention of MAM in all the age groups studied, and especially in mothers and young children. Furthermore, intake of the higher dairy protein supplements was associated with fewer reported illnesses in children. According to these results, 15% protein from dairy is probably not enough. More research is needed to determine the optimal protein content for optimal physical as well as for cognitive development.

To conclude, this review of the 2018 published data on nutritional interventions for the prevention and treatment of malnutrition in children provides a comprehensive survey of the existing literature in the field. The Cochrane database studies (3 systematic reviews and 1 overview) [7–10] show that supplementary feeding is an effective strategy to prevent and treat malnutrition in young children from vulnerable populations. Specifically, the data suggest that effective and safe interventions for improving growth outcomes in malnourished young children should include LNS plus complementary feeding. Furthermore, RUTF improves recovery from malnutrition. The standard RUTF that meets the total daily nutritional requirements may be more effective for recovery than RUTF given as a supplement to the usual diet. Animal-source proteins and milk proteins improve nutritional outcomes in undernourished populations and are probably superior to other protein sources.

However, all the Cochrane systematic reviews listed several major limitations to the included studies and assigned most of them a low or moderate quality-of-evidence rating. The main limitations were a high risk of bias for blinding of participants and personnel owing to the nature of the intervention, report of only short-term outcomes, and failure to address some important outcome factors, such as compliance, adverse events, mortality, psychomotor and neurological development, quality of life, and cost. Furthermore, there was a large heterogeneity among the nutritional intervention protocols in terms of duration, format, and nutrient composition, precluding conclusions regarding specific supplementary foods or practices. Visser et al. [9], in their summary of Cochrane systematic reviews, called for new studies focusing on relevant and understudied outcomes, with follow-up over longer periods of time (>2 years). They emphasized the need for investigations of approaches that integrate supplementary feeding programs with other interventions to address the complex issues of malnutrition and food insecurity.

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Gut microbiota alterations and dietary modulation in childhood malnutrition: The role of short chain fatty acids

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Abstract: The gut microbiome affects the health status of the host through different mechanisms and is associated with a wide variety of diseases. Both childhood undernutrition and obesity are linked to alterations in composition and functionality of the gut microbiome. One of the possible mechanisms underlying the interplay between microbiota and host metabolism is through appetite-regulating hormones (including leptin, ghrelin, glucagon-like peptide-1). Short-chain fatty acids, the end product of bacterial fermentation of non-digestible carbohydrates, might be able to alter energy harvest and metabolism through enteroendocrine cell signaling, adipogenesis and insulin-like growth factor-1 production. Elucidating these mechanisms may lead to development of new modulation practices of the gut microbiota as a potential prevention and treatment strategy for childhood malnutrition. The present overview will briefly outline the gut microbiota development in the early life, gut microbiota alterations in childhood undernutrition and obesity, and whether this relationship is causal. Further we will discuss possible underlying mechanisms in relation to the gut-brain axis and short chain fatty acids, and the potential of probiotics, prebiotics and synbiotics for modulating the gut microbiota during childhood as a prevention and treatment strategy against undernutrition and obesity.

Comments There is a bidirectional relationship between the microbiome and childhood malnutrition: undernutrition interferes with the maturation and diversity of the microbiome, while microbial dysbiosis adversely affects the host's susceptibility to enteric infection, chronic inflammation, and other important mechanisms related to weight gain and growth. One of the ways in which the gut microbiota may exert its effect on the host's nutritional status is by the production and utilization of short-chain fatty acids (SCFAs). This review focuses on the different pathways in which SCFAs could be involved: enteroendocrine signaling and appetite control; the IGF-1 axis; providing a source of energy for colonic cells; and helping to maintain the epithelial gut barrier. This review provides an interesting perspective on the interplay between the microbiome and malnutrition.

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A sparse covarying unit that describes healthy and impaired human gut microbiota development

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Abstract: Characterizing the organization of the human gut microbiota is a formidable challenge given the number of possible interactions between its components. Using a statistical approach initially applied to financial markets, we measured temporally conserved covariance among bacterial taxa in the microbiota of healthy members of a Bangladeshi birth cohort sampled from 1 to 60 months of age. The results revealed an "ecogroup" of 15 covarying bacterial taxa that provide a concise description of microbiota development in healthy children from this and other low-income countries, and a means for monitoring community repair in undernourished children treated with therapeutic foods. Features of ecogroup population dynamics were recapitulated in gnotobiotic piglets as they transitioned from exclusive milk feeding to a fully weaned state consuming a representative Bangladeshi diet.

Comments Important cohort study from a low- and middle-income country defining the taxonomy of healthy microbiota in a cohort of healthy children (under 5 years of age) with no growth failure. The findings are comparable to those observed from microbiota maturation among healthy children in Peru. Given the importance of microbiome in health and growth and potential interventions, these findings help develop standards and criteria for monitoring and evaluation and potential benchmarks for defining uptake and change. The findings of the 15 co-varying bacterial taxa need to be validated through additional studies in Asia (such as the MalED cohort) and also compared with findings from Africa in cohorts with healthy children without growth failure.

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Effects of microbiota-directed foods in gnotobiotic animals and undernourished children

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Abstract: To examine the contributions of impaired gut microbial community development to childhood undernutrition, we combined metabolomic and proteomic analyses of plasma samples with metagenomic analyses of fecal samples to characterize the biological state of Bangladeshi children with severe acute malnutrition (SAM) as they transitioned, after standard treatment, to moderate acute malnutrition (MAM) with persistent microbiota immaturity. Host and microbial effects of microbiota-directed complementary food (MDCF) prototypes targeting weaning-phase bacterial taxa underrepresented in SAM and MAM microbiota were characterized in gnotobiotic mice and gnotobiotic piglets colonized with age- and growth-discriminatory bacteria. A randomized, double-blind controlled feeding study identified a lead MDCF that changes the abundances of targeted bacteria and increases plasma biomarkers and mediators of growth, bone formation, neurodevelopment, and immune function in children with MAM.

Comments Landmark study from a cohort of Bangladeshi children with moderate acute malnutrition identifying and validating the benefit of diets that improved the microbiome (based on preidentified bacterial taxa in the same population and also among healthy children in Peru) and biomarkers of growth and immune function. The work was systematic in identifying types of diets that led to improvement and normalization of microbiota in gnotobiotic animals (mice and piglets) as well as molecular signals of improved

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growth and immune function. When tested among a small cohort of 60 malnourished children in Bangladesh over a 1-month period, the diet (based on chickpea, banana, and soy and peanut flours) helped the microbiomes mature and improve the molecular signals for healthy growth. These important findings point the way for longer-term studies of dietary (and other) approaches to prevent growth failure and reduce enteropathy of malnutrition among young children in low- and middle-income countries.

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