What are the new guidelines and position papers in pediatric nutrition: a 2015-2020 overview

Iva Hojsak[a, b], Michael Chourdakis[c], Konstantinos Gerasimidis[d], Jessie Hulst[e, f], Koen Huysentruyt[g], Jose M. Moreno-Villares[h], Koen Joosten[i]

[a]Children's Hospital Zagreb, University of Zagreb Medical School, Zagreb, Croatia

[b]University J.J. Strossmayer Medical School, Osijek, Croatia, ivahojsak@gmail.com

[c]School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Greece

[d]Human Nutrition, School of Medicine, College of Medicine, Veterinary and Life Sciences, Royal Hospital for Sick Children, University of Glasgow, Glasgow, United Kingdom, Konstantinos.Gerasimidis@glasgow.ac.uk

[e]Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, The Hospital for Sick Children, Toronto, Ontario, Canada

[f]Department of Pediatrics and Nutritional Sciences, Faculty of Medicine, University of Toronto, Toronto, ON, Canada, jessie.hulst@sickkids.ca

[g]Department of Pediatric Gastroenterology, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium, koen.huysentruyt@uzbrussel.be

[h]Department Pediatrics Clinica Universidad de Navarra, Madrid, Spain, josemanuel.moreno@salud.madrid.org

[i]Department of Pediatric Intensive Care, Sophia Children's Hospital – Erasmus Medical Center, Rotterdam, The Netherlands, k.joosten@erasmusmc.nl

Corresponding author:

Assist. Professor Iva Hojsak, MD, PhD

Children's Hospital Zagreb

Klaićeva 16, HR-10000 Zagreb

Phone: +38514600130

E mail: ivahojsak@gmail.com

Abbreviations

AA: Amino Acid**, ASPEN:** American Society for Parenteral and Enteral Nutrition**, CSPEN:** Chinese Society for Clinical Nutrition and Metabolism**, ESPEN:** European Society for Clinical Nutrition and Metabolism, **CRBSI**: catheter related bloodstream infections, **CVC:** Central venous catheter, **EPA:** European Paediatric Association, **ESPGHAN:** European Society of Gastroenterology, Hepatology and Nutrition, **ESPNIC:** The European Society of Paeditric and Neonatal Intensive Care, **ESPID:** the European Society of Pediatric Infectious Diseases, **ESPR:** European Society Pediatric Research**, FAO:** Food and Agriculture Organization, **FUF-YC:** Follow-up formula for young children (FUF-YC), **GFHGNP:** French-speaking Pediatric Hepatology, Gastroenterology and Nutrition, **FAO:** Food and Agriculture Organization**, LEAP:** Learning Early about Peanut Allergy, **LGG:** *L. rhamnosus* GG, **n-3 fatty acids:** Omega−3 fatty acids, **NICE;** National Institute for Health and Care Excellence**, NASPGHAN:** North American Society For Pediatric Gastroenterology, Hepatology & Nutrition, **SAM**: severe acute malnutrition, **PICU:** pediatric intensive care unit, **PN**: Parenteral Nutrition, **PUFA:** Polyunsaturated fatty acids, **REE:** resting energy expenditure, **SAM:** severe acute malnutrition, **SFA:** Saturated fatty acids, **SIG:** Special Interest Group, **RCT:** randomized controlled trials, **RR:** risk ratio, **RUTFs:** Ready-to-Use-Therapeutic Foods, **TFA:** Trans-fatty acids, **WHO:** World Health Organization

Abstract

Background: Nutrition related publications in pediatric population cover wide range of topics and therefore it is usually difficult for clinicians to get an overview of recent nutrition related guidelines or recommendations.

Methods: The Special Interest Group (SIG) of Pediatrics of European Society for Clinical Nutrition and Metabolism (ESPEN) performed a literature search to capture publications in the last five years aiming to provide the latest information concerning nutritional issues in children in general and in specific diseases and to discuss progression in the field of pediatric nutrition evidence-based practice.

Results: Eight major topics were identified as the most frequently reported including allergy, critical illness, neonatal nutrition, parenteral and enteral nutrition, micronutrients, probiotics and malnutrition. Furthermore, it was noted that many reports were disease focused or included micronutrients and were, therefore, represented as tables.

Conclusion: Overall, it has been shown that most reports on nutrition topics in pediatrics were systematic reviews or guidelines/position papers of relevant societies, but many of them basing the conclusion on a limited number of high-quality randomized controlled trials or large observational cohort studies.

Key words: guidelines, feeding, allergy, parenteral, enteral, micronutrients, malnutrition

Introduction

In 2015 the Special Interest Group (SIG) of Pediatrics was founded following a survey among members of The European Society for Clinical Nutrition and Metabolism (ESPEN), which showed that there was an unmet need for more pediatric related topics and representation within the activities of the society and its annual congress (1). In line with this need, the SIG of Pediatrics reported a search on existing clinical trials at the 38th annual ESPEN congress in 2018. It was found that 430 clinical nutrition trials in pediatrics were registered and that research focused primarily on a variety of specific diseases and obesity (2). Here, the SIG group has conducted a literature search to give an overview of guidelines, position papers from scientific societies, systematic reviews and meta-analysis published over the last 5 years. Eight major topics were identified, and other topics were categorized under a miscellaneous category. The aim of this overview is to provide the latest information concerning major nutritional recommendations and systematic reviews in children in general and in specific diseases and to discuss progression in the field of pediatric evidence-based nutrition practice.

Methods

Review of the literature in the PubMed database was performed using the following terms: (child or children or pediatric) AND (nutrition or feeding or feed or eating or diet)). For every specific disease or condition more detailed literature search was performed. Only articles published in English and in a pediatric population (up to 18 years of age) from January 1st, 2015 to October 1st, 2020 were included. The search was limited to guidelines, position papers, recommendations of pediatric societies and systematic reviews covering a wide range of clinical nutrition literature. The eight major general topics including allergy, critical illness, neonatal intensive care, enteral and parenteral nutrition (PN), vitamins, minerals and trace elements, malnutrition, probiotics are presented in more detail while nutritional topics in specific diseases and micronutrients are presented in Table 1 and Table 2.

Results

Allergy and eosinophilic disorders

Major randomized controlled trials (RCT) that evaluated early vs late introduction of allergens were published in 2015 and 2016 and were subsequently analyzed in a meta-analysis (3). The LEAP Trial (Learning Early about Peanut Allergy) demonstrated an 11-25% absolute reduction in the risk of developing peanut allergy in high-risk infants when peanuts were introduced early in the complementary feeding, between 4 and 11 months of age (4). A meta-analysis that included 5 trials (1915 participants in total) showed that early egg introduction between 4 to 6 months was associated with a reduced egg allergy risk (risk ratio [RR] 0.56 [95% CI 0.36–0.87], p<0.009), with similar findings in studies including populations at normal-risk, high risk, and very high-risk of allergy (3).

The first interim guidelines were published early after the LEAP trial because new Level 1 of evidence was available prompting a need to assist the clinical decision making regarding the peanut introduction (5). In later years the National Institute of Allergy and Infectious Diseases (NIAID) published addendum guideline (6-11). These guidelines categorize infants into 3 categories. In infants with severe eczema, egg allergy or both evaluation by sIgE and/or skin-prick test and, if necessary, an oral food challenge is strongly recommended. This test should guide introduction of peanut-containing foods (earlier age for peanut introduction being 4-6 months). In children with mild-to-moderate eczema, peanut containing foods should be introduced at about 6 months and in children with no eczema or food allergies, age-appropriate peanut containing foods introduction in accordance with family preferences and cultural practices is recommended (7).

A position paper by the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) on complementary feeding stated that allergenic foods may be introduced when complementary feeding is commenced any time after 4 months (17 weeks) but infants at high risk of peanut allergy (those with severe eczema, egg allergy, or both as defined in the LEAP study) should

have peanut introduced (e.g., as smooth peanut butter) between 4-11 months, following evaluation by an appropriately trained professional (12).

In 2017 the Asia Pacific Association of Pediatric Allergy, Respirology and Immunology (APAPARI) published a consensus statement in regard to the allergenic foods for the prevention of food allergy (13). This statement also recognized 3 groups of infants based on allergy risk, but provides guidelines depending on the availability of allergy expertise in specific area.

Critical illness and pediatric intensive care

In 2016 an updated Cochrane systematic review was published concerning nutritional support in critically ill children (14). Only one trial was found as relevant and involved seventy-seven children with burns. A systematic review concerning the use of PN identified only 6 small RCTs that investigated the impact of a different dose or composition of PN in critically ill infants or children treated in the pediatric intensive care unit (PICU) (15). The few RCTs suggested that surrogate endpoints (e.g. laboratory parameters) can be affected by providing parenteral nutrition to critically ill children, but the studies were not statistically powered to draw robust clinical conclusions. From 2016 onwards the Chinese group of experts from the Emergency Group of Chinese Pediatrics Society, Pediatrics group of Chinese Emergency Society, American Society for Parenteral and Enteral Nutrition (ASPEN) and European Society of Paeditric and Neonatal Intensive Care (ESPNIC) guidelines for nutritional support in critically ill children were published, as well as a consensus statement for the Asia-Pacific and Middle East region (16-19). Furthermore, both the combined ESGPHAN/ESPEN/European Society Pediatric Research (ESPR)/ Chinese Society for Clinical Nutrition and Metabolism (CSPEN) guidelines on pediatric parenteral nutrition (2018) and the Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children (2019) contain information concerning nutritional support of the critically ill child (20-27). These recommendations were mainly influenced by the results of the PEPaNIC trial, an RCT which included 1440 patients and showed that withholding PN for one week (Late-PN) while

giving micronutrients resulted in fewer new infections and reduced the duration of PICU stay as compared to initiating PN at day 1 (Early-PN) (28).

Finally, two manuscripts were published with specific topics. One about the current evidence and guidelines for the optimal prescription and delivery of nutrition for pediatric patients receiving extracorporeal membrane oxygenation (ECMO) (29) and one systematic review about estimation of resting energy expenditure (REE) using predictive equations in critically ill children (30). It was concluded that no equation could successfully predict REE within ±10% of measured energy expenditure in >50% of observations. Furthermore, it was stated that indirect calorimetry is urgently needed for the critically ill pediatric population. This statement is debatable because it hasn't been proven yet that use of indirect calorimetry may have impact on the outcome and also because there is lack of appropriate equipment at this moment.

Neonatal intensive care

Most manuscripts concerned nutrition in preterm infants but no large RCT trials were found. Two manuscripts described the current evidence on optimal protein intake and the relationship between arginine intake in PN and plasma arginine concentrations (31, 32). A topic of interest is feeding the late and moderately preterm infants, discharge criteria for the late preterm infant, transitioning breastfeeding after discharge from the neonatal intensive care unit and weaning and complementary feeding (33-36). In a systematic review which was published in 2016 (before new ESPGHAN guidelines on PN were published, see below in the topic PN) the effect of early initiation of PN with high protein and relatively high caloric intake on homeostasis in very preterm infants during the first few postnatal weeks was considered. It was concluded that optimal PN following new guidelines in very preterm infants, despite their demonstrated benefits on growth, may induce adverse effects on ionic homeostasis (37). In two reviews, feeding practices in infants born at term were described and related to supplementation of long chain polyunsaturated fatty acids and the use of glucose gel as treatment strategy for transient neonatal hypoglycemia (38, 39). Additionally, the management and

nutrition of neonates during the COVID-19 pandemic was presented in a review of the existing guidelines and recommendations (40) finding that all guidelines recommended to continue breastfeeding or feeding with expressed maternal milk with except for Chinese recommendations that suggested avoiding breastfeeding.

To address the current state of knowledge and to support systematic reviews that will be used to develop evidence-based guidance for the nutritional care of preterm and high-risk newborn infants, a consortium in the US initiated the Pre-B Project. This consortium will address specific themes concerning the nutritional care of preterm infants (41, 42).

Oral and enteral nutrition

Information related to human milk/breast feeding was addressed in two studies. The society of Pediatric nurses (SPN) developed clinical practice guidelines for the use of human milk and breastfeeding for the hospitalized infant/child beyond immediate neonatal care in order to promote prolonged exclusive breastfeeding (43). It consists of best evidence for lactation support and care, operational definitions and 10 recommended steps for the protection and promotion of human milk and breastfeeding in vulnerable infants. The other study related to breast milk is a systematic review including 36 studies with quantitative information on the direct relation between maternal nutrition and breast-milk composition (44). Overall, available information was found to be scarce and diverse with most evidence for the link between fish consumption and high docosahexaenoic acid in breast milk and dietary vitamin C and its concentration in breast milk.

The relationship between milk or milk products and growth, body composition and/or bone health in healthy children was assessed in two studies. A meta-analysis including 17 trials found that children aged 6-18 years consuming milk and milk products were more likely to achieve a lean body phenotype (45) compared to control groups, whereas no significant differences in terms of height were found. The systematic review of 13 controlled trials by de Lamas et al (46) about the effect of dairy product consumption on height and bone mineral content in children <18 years showed a

similar inconclusive relationship with linear growth but a positive association with increase in bone mineral content.

The Committee on Nutrition of the ESPGHAN published two position papers based on extensive literature search and expert opinion; the first one about complementary feeding (12) is an update of the 2008 position paper with a focus on healthy term infants in Europe and includes new evidence from RCTs on introduction of gluten and allergenic foods. The second paper covers the topic of Young Infant Formula (47) and states that it's routine use is not recommended in children from 1-3 years of life, but that can be useful as part of a strategy to increase the intake of vitamin D, iron, and polyunsaturated fatty acid and decrease the intake of protein compared with unfortified cow's milk.

Protein Quality of Follow-up formula for young children (FUF-YC) and Ready-to-Use-Therapeutic Foods (RUTFs) was the topic of an FAO Expert Working group paper (48). Specific recommendations on protein requirements and corresponding amino acid (AA) requirements were made based on currently available protein and indispensable amino acid digestibility data. Furthermore, it provides practical guidelines and assistance to countries and the industry on how protein quality should be assessed.

Two systematic reviews and one position paper were published regarding enteral nutrition and post-pyloric feeds. The ESPGHAN position paper (49) based on systematic literature search 1982-2018, states that jejunal feeding is a safe and effective means of enteral feeding when gastric feeding is insufficient to meet nutritional needs. It also advises to involve a multidisciplinary team in the decision making and follow-up of patients with a jejunal tube. A systematic review (50) about gastrojejunostomy tube complications published before this position paper, assessed 48 studies (1996-2016) representing >2700 procedures. It showed a significant overall complication risk, especially in children <10 kg (perforation rate 3.1% vs 0.1%; relative risk 9.4 compared to children >10 kg), and a need for frequent replacement/revision. A systematic review about the safety of early enteral nutrition after gastrointestinal anastomosis surgery was recently published by Braungart et al (51). The conclusion, based on limited studies (n=10) and patients (n=451), was that there is no clear

disadvantage of providing early (<24 hours, range 2-72 hours) enteral feeding versus a prolonged nil by mouth approach.

Parenteral nutrition

Most papers came from the 2018 ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric PN, a revision of the previous document prepared by the same organizations in 2005 (22-27, 52-60). The recommendations were developed as a combination of available literature between 2004 and 2017 and the opinions of experts. GRADE approach was used to assess the quality of evidence. Recommendations were assigned according to the level of evidence (58).

The most relevant consideration in these guidelines include the use of Schofield's equation for calculation of resting energy expenditure, although the use of indirect calorimetry is desirable in a subgroup of patients with suspected metabolic alterations or malnutrition (22). The guidelines, following the results of PEPaNIC study suggest withholding PN for one week in critically ill children while giving micronutrients (28). Regarding amino acids supply the most relevant recommendation was not to go above 3.5 g/kg in preterm infants (postnatal day 2 onwards should be between 2.5 g/kg/day and 3.5 g/kg/day and should be accompanied by non-protein intakes of more than 65 kcal/kg/day and adequate micronutrient intakes) (26). Intravenous lipid emulsions (ILE) should be an integral part of parenteral nutrition either exclusive or complementary to enteral feeding (27). In preterm infants, lipid emulsions can be started immediately after birth and no later than on day two of life and for those in whom enteral feeding has been withdrawn, they can be started at time of PN initiation. Lipid intake should not exceed 3 g/kg/day in term infants and 4 g/kg/day in preterm infants (27).

Organizational aspects of PN as well as a chapter on home parenteral nutrition was also included in these guidelines, but most of the recommendations were based on expert opinions (56). Individually tailored PN solutions should generally be used when the nutritional requirements cannot be met by

the available range of commercially available PN formulations (59). Lastly, a chapter is included emphasizing possible PN complications and how to avoid them (60).

NICE guidelines 2020 on neonatal PN advise to start PN in preterm neonates as soon as possible, within 8 hours after birth at the latest, and favor the use of standardized neonatal parenteral nutrition ("standardized bags"). In contrasts to the ESPGHAN guidelines, it recommends amino acid amount to go up to 4 g/kg/day (61). The guidelines include a section on information and support for parents and caregivers. Irish guidelines, published in 2020 (62), are mainly based on ESPGHAN guidelines.

A literature review (non-systematic) was published regarding trace elements provision and dosing in pediatric PN (63). Based on current evidence, the authors conclude that there is a need to review the formulation of commercial solutions that contain multiple-trace elements and to enable individual trace elements additives to be available for specific indications. Literature supports the removal of chromium provision, whereas the use of manganese and molybdenum supplementation is debated (63). Preterm neonates may have higher parenteral requirements in iodine, selenium and copper than previously recommended (63).

Ultrasound guidance may be used in order to reduce complications during venous catheterization (57). The use of heparin flushes for maintaining patency was not recommended, and the use of locks for preventing or treating catheter related bloodstream infections (CRBSI) was discussed and taurolidine line lock had the most evidence for the use in preventing CRBSI (57). Adherence to CVC care protocols is essential in reducing infectious complications (64).

An additional three papers referred to strategies and recommendations for preservation of CVCs in children (65-67). In particular, the VANGUARD Task Force, not specifically for PN use, had details on the elements of an individualized plan of care and emphasizes a patient-centered, multidisciplinary approach (65). Phua et al (66) reviewed all studies gathering information on Candida catheter blood related infection in Home PN patients. Major guidelines advocate catheter removal prior to systemic antifungal treatment, although some studies suggest more conservative treatment with the use of

catheter lock solutions, but evidence is not yet firmly established (66). In the third, which is a systematic review on the use of anticoagulants for the prevention and treatment of catheter-related thrombosis in adults and children on PN (67), the authors conclude there is insufficient evidence to allow consensus to be reached on the topic, mainly because of the low quality of most papers included.

Micronutrients

There have been several Cochrane systematic reviews, guidelines, meta-analyses and position papers on a) assessment of micronutrient status and b) micronutrient supplementation in healthy and sick children (Table 2). Recommendations are also made for clinical practice but also for public health in low-medium-income countries. Majority of the available guidelines/recommendations focused on recommendations for vitamin D intake (68-71). In a societal position paper endorsed by ESPGHAN, there is debate on the various approaches available to assess micronutrient status in sick children and discuss their advantages and disadvantages (72). The authors conclude that a multimodal approach, including clinical examination, dietary assessment, and laboratory biomarkers is the optimal way to ascertain the micronutrient status of individual patients. They also highlight that in the presence of acute inflammatory conditions, micronutrient measurements in plasma are unlikely to reflect true body status and recommend their replacement by other biomarkers and assessments such as dietary assessment and functional assays. One opinion paper from the European Academy in Paediatrics, one metanalysis and regional practice guidelines focused on the optimal recommendations for vitamin D intake (69). The European Academy in Paediatrics does not justify the routine screening for vitamin D deficiency in healthy children. They propose evaluation of vitamin D status in children belonging to high-risk groups. They also recommend that all infants up to 1 year of age should receive an oral supplementation of 400 IU/day of vitamin D. In the systematic review by Brett et al serum responses to vitamin D intake differ according to the baseline vitamin D status, dietary intakes, and delivery mode, but not age, sex, or latitude (68). In a regional guideline for the

Gulf countries, the recommendations for vitamin D intake vary according to age, pregnancy, prematurity, obesity and skin color (70).

Over the past two years two Cochrane systematic reviews and metanalyses explored the effect of vitamin K and vitamin D in improving the outcomes of people with cystic fibrosis (73) and sickle cell anemia (71), respectively. Both reviews concluded that there is currently very little evidence of good quality to draw any recommendations. Until further evidence becomes available, the authors of these systematic reviews recommend use of guidelines currently endorsed by professional bodies.

In another Cochrane systematic review and metanalysis, Peña-Rosas determined the benefits and harms of rice fortification with vitamins and minerals (iron, vitamin A, zinc or folic acid) on micronutrient status and health-related outcomes in the general population (74). The authors conclude that fortification of rice with iron alone or in combination with other micronutrients may make little or no difference in the risk of having anaemia or presenting iron deficiency. Likewise, fortification of rice with iron and other micronutrients such as vitamin A or folic acid may make little or no difference in the risk of having vitamin A deficiency or on the serum folate concentration. It was also explored whether fortification of staple foods (sugar, edible oils, edible fats, maize flour or corn meal, wheat flour etc.) with vitamin A alone or in combination with other vitamins and minerals can reduce vitamin A deficiency and improve health-related outcomes in the general population (> 2 years) (75). As an overarching conclusion the authors suggest that fortification of staple food with vitamin A may increase serum retinol concentration, but it is uncertain whether the intervention reduces the risk of subclinical vitamin A deficiency.

Mihatsch and the Committee on Nutrition of ESPGHAN extensively discuss current prophylaxis practices and outcomes and provide recommendations for the prevention of Vitamin K deficiency bleeding in newborn infants (76). They provide recommendations for oral and intramuscular application and the panel recommends the latter as the preferred route.

Malnutrition including severe malnutrition

A systematic review addressed the question whether the current antibiotic recommendations from the World Health Organization (WHO) guidelines for the treatment of severe acute malnutrition (SAM) should be revisited (77). Largely based on a meta-analysis (78) of two RCTs (79, 80) on antibiotic treatment for children with uncomplicated SAM, the authors concluded that the continued use of oral amoxicillin is still justified for treating these children as outpatients. No strong evidence was found to change the current parenteral antibiotic guidelines for children with complicated SAM. The authors did note however that further clarification should be provided to harmonize different antibiotic regimens amongst different guidelines or to continue parenteral antibiotics beyond 2 days, if indicated by the clinical condition (77). The overall efficacy of these WHO guidelines for inpatient treatment of SAM was investigated in a systematic review with meta-analysis (81). This meta-analysis, based on 3933 children, concluded that the odds ratio for case fatality rate of treatment according to the WHO protocol vs (different) "conventional" protocols was 0.59 (95% CI 0.46-0.76). Children treated with conventional protocols received higher energy dense diet with less rigorous follow up.

Probiotics

Over the past 5 years, several guidelines, recommendations, and systematic reviews on the use of probiotics in children were published (82-95). Most of these were relevant to conditions of the gastrointestinal tract including the prevention of nosocomial and antibiotic-associated diarrhea; treatment of acute gastroenteritis and functional gastrointestinal disease. Importantly in the year 2020 an international group of scientists divided the genus *Lactobacillus* into groups of closely related species, which share certain physiological and metabolic properties, under new genus names (96). That was the result of the DNA-based analytical tools that showed that different species historically grouped under *Lactobacillus* are very genetically diverse. Following led to reclassification

of some of the most studied probiotics, e.g. *Lactobacillus rhamnosus* was reclassified to *Lacticaseibacillus rhamnosus* and *Lactobacillus reuteri to Limosilactobacillus reuteri.*

The use of *L. rhamnosus* GG (LGG), at more than 10^9 CFU/day, was recommended for the prevention of nosocomial diarrhoea (85). In the year 2018 two large RCTs were performed questioning the use of probiotics in the acute gastroenteritis (97, 98). Therefore ESPGHAN working group updated the recmmmendations stating that *Saccharomyces boulardii* CNCM I-745, LGG and *L. reuteri* DSM 17938 could be recommended for adjunct treatment in acute gastroenteritis (86) and *S. boulardii* and LGG for prevention of antibiotic associated diarrhea (89). *L. reuteri* DSM 17938 for the treatment of infantile colics, especially in breastfed babies (94). For other probiotics the evidence is less supportive. Safety aspects were discussed in several of these position papers and guidelines/recommendations. Overall, use of probiotics is safe although the Expert Panel of the European Paediatric Association (EPA) recommends caution with their use in premature neonates, immunocompromised patients, critically ill patients, those with a central venous catheter, cardiac valvular disease and short-gut syndrome (99). Others recommend the use of specific probiotics with a history of safe use in preterm and term infants and for the prevention of necrotizing enterocolitis (87). The use of probiotics in prevention of urinary tract infection and the treatment of constipation in children is not supported by the currently available literature (91).

Miscellaneous

In the last 5 years a number of narrative reviews, systematic-reviews, meta-analyses, consensus and position papers have been published with a view to provide recommendations for specific diseases (liver and renal diseases), pediatric conditions/symptoms (e.g. diarrhea) and miscellaneous issues related to pediatric nutrition (e.g. sugar and sweeteners consumption, dyslipidemia, fibre, early feeding, dysphagia, etc.)(100-131) Details on the characteristics of these studies and relevant recommendations can be found in Tables 1 and 3 (miscellaneous).

Discussion

In the current manuscript we provide an overview of published reports concerning guidelines, position papers from scientific societies, systematic reviews and meta-analyses published over the last 5 years (until October 2020). We identified 8 major topics and within these topics most reports were found in allergy and parenteral nutrition. Additionally, we have summarized in tables most commonly reported nutrition topics in specific diseases and the recommendations for the use of micronutrients, and some remarkable issues that were noticed will be discussed.

Collectively, we found that there is an abundance of guidelines/recommendations, but the question is how many are based on sound, new RCT, or large observational cohort studies. In 2018 the SIG of Pediatrics reported that only a limited number of large RCT's could be identified which might have an impact on the development of clinical guidelines (1). Many of the reports are based on studies of low quality or consensus statements of scientific working groups of international societies such as ESPGHAN, ESPNIC and ASPEN. On the other hand, there are some remarkable RCT's which have influenced the guidelines. In allergy, the LEAP Trial (Learning Early about Peanut Allergy) demonstrated an 11-25% absolute reduction in the risk of developing peanut allergy in high-risk infants when peanuts were introduced early in complementary feeding, between 4-11 months of age (4). In critically ill children and neonates the PEPaNIC trial showed that withholding PN for one week, while giving micronutrients, resulted in fewer new infections and reduced the duration of PICU stay as compared to initiating PN at day 1. The results of this trial had a major impact on the guidelines concerning the topic parenteral nutrition (28).

While it is recommended to withhold parenteral AA and lipids and to lower the amount of carbohydrates in the first week after admission in critically ill children and neonates, supplementation of micronutrients is recommended. Important clinical topics were addressed in the many systematic reviews, meta-analyses, and position papers we reviewed and summarized. In assessment of micronutrient status in sick children, it is important to consider the presence of acute inflammatory conditions because micronutrient measurements in plasma are than unlikely to reflect

true body status and therefore other biomarkers and assessments such as dietary assessment and functional assays have to be performed.

Concerning the topic enteral feeding one systematic review included 36 studies with quantitative information on the direct relation between maternal nutrition and breast-milk composition (44). Most evidence was found for the link between fish consumption and high docosahexaenoic acid in breast milk and dietary vitamin C and its concentration in breast milk. These findings highlight the importance of the eating of (fatty) fish not only during pregnancy but also during the lactation period.

Also of interest is a systematic review about the safety of early enteral nutrition after gastrointestinal anastomosis surgery (51). The conclusion supports to provide early (<24 hours) enteral feeding instead of a prolonged period of a nil by mouth approach.

Concerning the overview, we provided on the specific diseases, it can be concluded that the general statements about starting enteral and/or parenteral nutrition can be applied in these groups in the acute phase of disease. However, there is a need for nutritional protocols for these specific diseases after the acute phase accounting for optimal growth and development. Of interest are also studies done in oncology patients, where a systematic review including 46 studies showed both a high prevalence of undernutrition (0-65%) and overnutrition (8-78%). Undernutrition was associated with poor clinical outcomes, but reverse causation needs to be considered (132). Parental involvement in exercise and diet interventions for childhood cancer survivors showed to have positive outcomes on long-term lifestyle changes in these patients (133). Focus of future research therefore could be more on the role of parents and caregivers in relation with dietary habits, lifestyle and quality of life.

In conclusion, there is a wealth of reports in pediatric nutrition published within the last 5 years and whereas recommendations are based on many systematic reviews there is a lack on large RCT's and cohort studies to generate strong recommendations. It might be of interest to compare all these reports and identify similarities and inconsistencies in recommendations.

Statement of Authorship

Iva Hojsak: Conceptualization; Data curation; Formal analysis; Methodology; Supervision; Writing - original draft; **Michael Chourdakis:** Data curation; Formal analysis; Writing - review & editing; **Konstantinos Gerasimidis:** Data curation; Formal analysis; Writing - review & editing; **Jessie Hulst:** Data curation; Formal analysis; Writing - review & editing; **Koen Huysentruyt:** Data curation; Formal analysis; Writing - review & editing; **Jose M. Moreno-Villares:** Data curation; Formal analysis; Writing - review & editing; **Koen Joosten:** Conceptualization; Data curation; Formal analysis; Methodology; Supervision; Writing - original draft; All authors approved the submitted version of the manuscript.

Conflict of Interest Statement

Iva Hojsak reports lecture fees from BioGaia, Oktalpharma, Abela Pharm, Nestle, Nutricia, and Sandoz outside the submitted work; Konstantinos Gerasimidis reports grants, personal fees and non-financial support from Nutricia-Danone and Nestle Health Science, personal fees from Abbott, DrFalk and Baxter, grants from Mylan, outside the submitted work;

Jessie Hulst, Jose M. Moreno-Villares, Michael Chourdakis, Koen Huysentruyt and Koen Joosten have nothing to declare.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

References

1. Gerasimidis K HJ, Chourdakis M, Huysentruyt K, Koletzko B, Joosten KFM The launch of the ESPEN Special Interest Group in Paediatric Clinical Nutrition. Clin Nutr ESPEN 2017;19:45-48.

2. Eveleens RD, Gerasimidis K, Chourdakis M, Huysentruyt K, Koletzko B, Hulst JM, et al. Current clinical trials in paediatrics: Report of the ESPEN special interest group in paediatrics. Clin Nutr ESPEN. 2018;27:75-8.

3. Ierodiakonou D, Garcia-Larsen V, Logan A, Groome A, Cunha S, Chivinge J, et al. Timing of Allergenic Food Introduction to the Infant Diet and Risk of Allergic or Autoimmune Disease: A Systematic Review and Meta-analysis. JAMA. 2016;316(11):1181-92.

4. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med. 2015;372(9):803-13.

5. Fleischer DM, Sicherer S, Greenhawt M, Campbell D, Chan E, Muraro A, et al. Consensus Communication on Early Peanut Introduction and Prevention of Peanut Allergy in High-Risk Infants. Pediatr Dermatol. 2016;33(1):103-6.

6. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR, Jr., Beck LA, et al. Addendum Guidelines for the Prevention of Peanut Allergy in the United States: Summary of the National Institute of Allergy and Infectious Diseases-Sponsored Expert Panel. J Acad Nutr Diet. 2017;117(5):788-93.

7. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR, Jr., Beck LA, et al. Addendum guidelines for the prevention of peanut allergy in the United States. JAAPA. 2017;30(3):1-5.

8. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR, Jr., Beck LA, et al. Addendum Guidelines for the Prevention of Peanut Allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-Sponsored Expert Panel. J Pediatr Nurs. 2017;32:91-8.

9. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR, Jr., Beck LA, et al. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. Ann Allergy Asthma Immunol. 2017;118(2):166-73 e7.

10. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR, Jr., Beck LA, et al. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. J Allergy Clin Immunol. 2017;139(1):29-44.

11. Togias A, Cooper SF, Acebal ML, Assa'ad A, Baker JR, Jr., Beck LA, et al. Addendum Guidelines for the Prevention of Peanut Allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-Sponsored Expert Panel. Pediatr Dermatol. 2017;34(1):e1-e21.

12. Fewtrell M, Bronsky J, Campoy C, Domellof M, Embleton N, Fidler Mis N, et al. Complementary Feeding: A Position Paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2017;64(1):119-32.

13. Tham EH, Shek LP, Van Bever HP, Vichyanond P, Ebisawa M, Wong GW, et al. Early introduction of allergenic foods for the prevention of food allergy from an Asian perspective-An Asia Pacific Association of Pediatric Allergy, Respirology & Immunology (APAPARI) consensus statement. Pediatr Allergy Immunol. 2018;29(1):18-27.

14. Joffe A, Anton N, Lequier L, Vandermeer B, Tjosvold L, Larsen B, et al. Nutritional support for critically ill children. Cochrane Database Syst Rev. 2016(5):CD005144.

15. Fivez T, Kerklaan D, Mesotten D, Verbruggen S, Joosten K, Van den Berghe G. Evidence for the use of parenteral nutrition in the pediatric intensive care unit. Clin Nutr. 2017;36(1):218-23.

16. Zhu XM, Qian SY, Lu GP, Xu F, Wang Y, Liu CF, et al. Chinese guidelines for the assessment and provision of nutrition support therapy in critically ill children. World J Pediatr. 2018;14(5):419-28.

17. Mehta NM, Skillman HE, Irving SY, Coss-Bu JA, Vermilyea S, Farrington EA, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. Pediatr Crit Care Med. 2017;18(7):675-715.

18. Mehta NM, Skillman HE, Irving SY, Coss-Bu JA, Vermilyea S, Farrington EA, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient:

Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. JPEN J Parenter Enteral Nutr. 2017;41(5):706-42.

19. Tume LN, Valla FV, Joosten K, Jotterand Chaparro C, Latten L, Marino LV, et al. Nutritional support for children during critical illness: European Society of Pediatric and Neonatal Intensive Care (ESPNIC) metabolism, endocrine and nutrition section position statement and clinical recommendations. Intensive Care Med. 2020;46(3):411-25.

20. Lee JH, Rogers E, Chor YK, Samransamruajkit R, Koh PL, Miqdady M, et al. Optimal nutrition therapy in paediatric critical care in the Asia-Pacific and Middle East: a consensus. Asia Pac J Clin Nutr. 2016;25(4):676-96.

21. Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, Inwald DP, et al. Executive Summary: Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. Pediatr Crit Care Med. 2020;21(2):186-95.

22. Joosten K, Embleton N, Yan W, Senterre T, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Energy. Clin Nutr. 2018;37(6 Pt B):2309-14.

23. Mesotten D, Joosten K, van Kempen A, Verbruggen S, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Carbohydrates. Clin Nutr. 2018;37(6 Pt B):2337-43.

24. Mihatsch W, Fewtrell M, Goulet O, Molgaard C, Picaud JC, Senterre T, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Calcium, phosphorus and magnesium. Clin Nutr. 2018;37(6 Pt B):2360-5.

25. Bronsky J, Campoy C, Braegger C, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Vitamins. Clin Nutr. 2018;37(6 Pt B):2366-78.

26. van Goudoever JB, Carnielli V, Darmaun D, Sainz de Pipaon M, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Amino acids. Clin Nutr. 2018;37(6 Pt B):2315-23.

27. Lapillonne A, Fidler Mis N, Goulet O, van den Akker CHP, Wu J, Koletzko B, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids. Clin Nutr. 2018;37(6 Pt B):2324-36.

28. Fivez T, Kerklaan D, Mesotten D, Verbruggen S, Wouters PJ, Vanhorebeek I, et al. Early versus Late Parenteral Nutrition in Critically Ill Children. N Engl J Med. 2016;374(12):1111-22.

29. Farr BJ, Rice-Townsend SE, Mehta NM. Nutrition Support During Pediatric Extracorporeal Membrane Oxygenation. Nutr Clin Pract. 2018;33(6):747-53.

30. Jotterand Chaparro C, Moullet C, Taffe P, Laure Depeyre J, Perez MH, Longchamp D, et al. Estimation of Resting Energy Expenditure Using Predictive Equations in Critically Ill Children: Results of a Systematic Review. JPEN J Parenter Enteral Nutr. 2018;42(6):976-86.

31. Embleton ND, van den Akker CHP. Protein intakes to optimize outcomes for preterm infants. Semin Perinatol. 2019;43(7):151154.

32. Premakumar CM, Turner MA, Morgan C. Relationship between arginine intake in parenteral nutrition and preterm neonatal population plasma arginine concentrations: a systematic review. Nutr Rev. 2019;77(12):878-89.

33. Lapillonne A, Bronsky J, Campoy C, Embleton N, Fewtrell M, Fidler Mis N, et al. Feeding the Late and Moderately Preterm Infant: A Position Paper of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2019;69(2):259-70.

34. Quinn JM, Sparks M, Gephart SM. Discharge Criteria for the Late Preterm Infant: A Review of the Literature. Adv Neonatal Care. 2017;17(5):362-71.

35. Noble LM, Okogbule-Wonodi AC, Young MA. ABM Clinical Protocol #12: Transitioning the Breastfeeding Preterm Infant from the Neonatal Intensive Care Unit to Home, Revised 2018. Breastfeed Med. 2018;13(4):230-6.

36. Barachetti R, Villa E, Barbarini M. Weaning and complementary feeding in preterm infants: management, timing and health outcome. Pediatr Med Chir. 2017;39(4):181.

37. Guellec I, Gascoin G, Beuchee A, Boubred F, Tourneux P, Ramful D, et al. Biological Impact of Recent Guidelines on Parenteral Nutrition in Preterm Infants. J Pediatr Gastroenterol Nutr. 2015;61(6):605-9.

38. Jasani B, Simmer K, Patole SK, Rao SC. Long chain polyunsaturated fatty acid supplementation in infants born at term. Cochrane Database Syst Rev. 2017;3:CD000376.

39. Newnam KM, Bunch M. Glucose Gel as a Treatment Strategy for Transient Neonatal Hypoglycemia. Adv Neonatal Care. 2017;17(6):470-7.

40. Genoni G, Conio A, Binotti M, Manzoni P, Castagno M, Rabbone I, et al. Management and Nutrition of Neonates during the COVID-19 Pandemic: A Review of the Existing Guidelines and Recommendations. Am J Perinatol. 2020;37(S 02):S46-S53.

41. Raiten DJ, Steiber AL, Hand RK. Executive summary: evaluation of the evidence to support practice guidelines for nutritional care of preterm infants-the Pre-B Project. Am J Clin Nutr. 2016;103(2):599S-605S.

42. Raiten DJ, Steiber AL, Carlson SE, Griffin I, Anderson D, Hay WW, Jr., et al. Working group reports: evaluation of the evidence to support practice guidelines for nutritional care of preterm infants-the Pre-B Project. Am J Clin Nutr. 2016;103(2):648S-78S.

43. Pasek T. Clinical Practice Guidelines for the Use of Human Milk and Breastfeeding for the Hospitalized Infant/Child Beyond Immediate Neonatal Care. J Pediatr Nurs. 2019;49:106-7.

44. Bravi F, Wiens F, Decarli A, Dal Pont A, Agostoni C, Ferraroni M. Impact of maternal nutrition on breast-milk composition: a systematic review. Am J Clin Nutr. 2016;104(3):646-62.

45. Kang K, Sotunde OF, Weiler HA. Effects of Milk and Milk-Product Consumption on Growth among Children and Adolescents Aged 6-18 Years: A Meta-Analysis of Randomized Controlled Trials. Adv Nutr. 2019;10(2):250-61.

46. de Lamas C, de Castro MJ, Gil-Campos M, Gil A, Couce ML, Leis R. Effects of Dairy Product Consumption on Height and Bone Mineral Content in Children: A Systematic Review of Controlled Trials. Adv Nutr. 2019;10(suppl_2):S88-S96.

47. Hojsak I, Bronsky J, Campoy C, Domellof M, Embleton N, Fidler Mis N, et al. Young Child Formula: A Position Paper by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2018;66(1):177-85.

48. Shivakumar N, Jackson AA, Courtney-Martin G, Elango R, Ghosh S, Hodgkinson S, et al. Protein Quality Assessment of Follow-up Formula for Young Children and Ready-to-Use Therapeutic Foods: Recommendations by the FAO Expert Working Group in 2017. J Nutr. 2020;150(2):195-201.

49. Broekaert IJ, Falconer J, Bronsky J, Gottrand F, Dall'Oglio L, Goto E, et al. The Use of Jejunal Tube Feeding in Children: A Position Paper by the Gastroenterology and Nutrition Committees of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition 2019. J Pediatr Gastroenterol Nutr. 2019;69(2):239-58.

50. Morse J, Baird R, Muchantef K, Levesque D, Morinville V, Puligandla PS. Gastrojejunostomy tube complications - A single center experience and systematic review. J Pediatr Surg. 2017;52(5):726-33.

51. Braungart S, Siminas S. Early Enteral Nutrition Following Gastrointestinal Surgery in Children: A Systematic Review of the Literature. Ann Surg. 2020;272(2):377-83.

52. Mihatsch WA, Braegger C, Bronsky J, Cai W, Campoy C, Carnielli V, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition. Clin Nutr. 2018;37(6 Pt B):2303-5.

53. Hill S, Ksiazyk J, Prell C, Tabbers M, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Home parenteral nutrition. Clin Nutr. 2018;37(6 Pt B):2401-8.

54. Domellof M, Szitanyi P, Simchowitz V, Franz A, Mimouni F, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Iron and trace minerals. Clin Nutr. 2018;37(6 Pt B):2354-9.

55. Jochum F, Moltu SJ, Senterre T, Nomayo A, Goulet O, Iacobelli S, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Fluid and electrolytes. Clin Nutr. 2018;37(6 Pt B):2344-53.

56. Puntis J, Hojsak I, Ksiazyk J, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Organisational aspects. Clin Nutr. 2018;37(6 Pt B):2392-400.

57. Kolacek S, Puntis JWL, Hojsak I, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Venous access. Clin Nutr. 2018;37(6 Pt B):2379-91.

58. Mihatsch W, Shamir R, van Goudoever JB, Fewtrell M, Lapillonne A, Lohner S, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Guideline development process for the updated guidelines. Clin Nutr. 2018;37(6 Pt B):2306-8.

59. Riskin A, Picaud JC, Shamir R, nutrition EEECwgopp. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Standard versus individualized parenteral nutrition. Clin Nutr. 2018;37(6 Pt B):2409-17.

60. Hartman C, Shamir R, Simchowitz V, Lohner S, Cai W, Decsi T, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Complications. Clin Nutr. 2018;37(6 Pt B):2418-29.

61. www.nice.org.uk/guidance/ng154. NpnNgPF.

62. National Clinical Practice Guideline. Guideline on the Use of Parenteral Nutrition in Neonatal and Paediatric Units. Irish Society for Clinical Nutrition & Metabolism.

63. Zemrani B, McCallum Z, Bines JE. Trace Element Provision in Parenteral Nutrition in Children: One Size Does Not Fit All. Nutrients. 2018;10(11).

64. Ares G, Hunter CJ. Central venous access in children: indications, devices, and risks. Curr Opin Pediatr. 2017;29(3):340-6.

65. Baskin KM, Mermel LA, Saad TF, Journeycake JM, Schaefer CM, Modi BP, et al. Evidence-Based Strategies and Recommendations for Preservation of Central Venous Access in Children. JPEN J Parenter Enteral Nutr. 2019;43(5):591-614.

66. Phua AI, Hon KY, Holt A, O'Callaghan M, Bihari S. Candida catheter-related bloodstream infection in patients on home parenteral nutrition - Rates, risk factors, outcomes, and management. Clin Nutr ESPEN. 2019;31:1-9.

67. Barco S, Atema JJ, Coppens M, Serlie MJ, Middeldorp S. Anticoagulants for the prevention and treatment of catheter-related thrombosis in adults and children on parenteral nutrition: a systematic review and critical appraisal. Blood Transfus. 2017;15(4):369-77.

68. Brett NR, Gharibeh N, Weiler HA. Effect of Vitamin D Supplementation, Food Fortification, or Bolus Injection on Vitamin D Status in Children Aged 2-18 Years: A Meta-Analysis. Adv Nutr. 2018;9(4):454-64.

69. Grossman Z, Hadjipanayis A, Stiris T, Del Torso S, Mercier JC, Valiulis A, et al. Vitamin D in European children-statement from the European Academy of Paediatrics (EAP). Eur J Pediatr. 2017;176(6):829-31.

70. Haq A, Wimalawansa SJ, Pludowski P, Anouti FA. Clinical practice guidelines for vitamin D in the United Arab Emirates. J Steroid Biochem Mol Biol. 2018;175:4-11.

71. Soe HHK, Abas AB, Than NN, Ni H, Singh J, Said A, et al. Vitamin D supplementation for sickle cell disease. Cochrane Database Syst Rev. 2020;5:CD010858.

72. Gerasimidis K, Bronsky J, Catchpole A, Embleton N, Fewtrell M, Hojsak I, et al. Assessment and Interpretation of Vitamin and Trace Element Status in Sick Children: A Position Paper From the European Society for Paediatric Gastroenterology Hepatology, and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2020;70(6):873-81.

73. Jagannath VA, Thaker V, Chang AB, Price AI. Vitamin K supplementation for cystic fibrosis. Cochrane Database Syst Rev. 2020;6:CD008482.

74. Pena-Rosas JP, Mithra P, Unnikrishnan B, Kumar N, De-Regil LM, Nair NS, et al. Fortification of rice with vitamins and minerals for addressing micronutrient malnutrition. Cochrane Database Syst Rev. 2019;2019(10).

75. Hombali AS, Solon JA, Venkatesh BT, Nair NS, Pena-Rosas JP. Fortification of staple foods with vitamin A for vitamin A deficiency. Cochrane Database Syst Rev. 2019;5:CD010068.

76. Mihatsch WA, Braegger C, Bronsky J, Campoy C, Domellof M, Fewtrell M, et al. Prevention of Vitamin K Deficiency Bleeding in Newborn Infants: A Position Paper by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr. 2016;63(1):123-9.

77. Williams PCM, Berkley JA. Guidelines for the treatment of severe acute malnutrition: a systematic review of the evidence for antimicrobial therapy. Paediatrics and international child health. 2018;38(sup1):S32-s49.

78. Million M, Lagier JC, Raoult D. Meta-analysis on efficacy of amoxicillin in uncomplicated severe acute malnutrition. Microbial pathogenesis. 2017;106:76-7.

79. Isanaka S, Langendorf C, Berthé F, Gnegne S, Li N, Ousmane N, et al. Routine Amoxicillin for Uncomplicated Severe Acute Malnutrition in Children. N Engl J Med. 2016;374(5):444-53.

80. Trehan I, Goldbach HS, LaGrone LN, Meuli GJ, Wang RJ, Maleta KM, et al. Antibiotics as part of the management of severe acute malnutrition. N Engl J Med. 2013;368(5):425-35.

81. Hossain M, Chisti MJ, Hossain MI, Mahfuz M, Islam MM, Ahmed T. Efficacy of World Health Organization guideline in facility-based reduction of mortality in severely malnourished children from low and middle income countries: A systematic review and meta-analysis. Journal of paediatrics and child health. 2017;53(5):474-9.

82. Hojsak I, Fabiano V, Pop TL, Goulet O, Zuccotti GV, Cokugras FC, et al. More research is needed on the use of probiotics for critically ill patients. Acta Paediatr. 2019;108(1):181.

83. Laursen RP, Hojsak I. Probiotics for respiratory tract infections in children attending day care centers-a systematic review. Eur J Pediatr. 2018;177(7):979-94.

84. van den Akker CHP, van Goudoever JB, Szajewska H, Embleton ND, Hojsak I, Reid D, et al. Probiotics for Preterm Infants: A Strain-Specific Systematic Review and Network Meta-analysis. J Pediatr Gastroenterol Nutr. 2018;67(1):103-22.

85. Hojsak I, Szajewska H, Canani RB, Guarino A, Indrio F, Kolacek S, et al. Probiotics for the Prevention of Nosocomial Diarrhea in Children. J Pediatr Gastroenterol Nutr. 2018;66(1):3-9.

86. Szajewska H, Guarino A, Hojsak I, Indrio F, Kolacek S, Orel R, et al. Use of Probiotics for the Management of Acute Gastroenteritis in Children: An Update. J Pediatr Gastroenterol Nutr. 2020;71(2):261-9.

87. van den Akker CHP, van Goudoever JB, Shamir R, Domellof M, Embleton ND, Hojsak I, et al. Probiotics and Preterm Infants: A Position Paper by the European Society for Paediatric Gastroenterology Hepatology and Nutrition Committee on Nutrition and the European Society for Paediatric Gastroenterology Hepatology and Nutrition Working Group for Probiotics and Prebiotics. J Pediatr Gastroenterol Nutr. 2020;70(5):664-80.

88. Kolacek S, Hojsak I, Berni Canani R, Guarino A, Indrio F, Orel R, et al. Commercial Probiotic Products: A Call for Improved Quality Control. A Position Paper by the ESPGHAN Working Group for Probiotics and Prebiotics. J Pediatr Gastroenterol Nutr. 2017;65(1):117-24.

89. Szajewska H, Canani RB, Guarino A, Hojsak I, Indrio F, Kolacek S, et al. Probiotics for the Prevention of Antibiotic-Associated Diarrhea in Children. J Pediatr Gastroenterol Nutr. 2016;62(3):495-506.

90. Wojtyniak K, Szajewska H. Systematic review: probiotics for functional constipation in children. Eur J Pediatr. 2017;176(9):1155-62.

91. Hosseini M, Yousefifard M, Ataei N, Oraii A, Mirzay Razaz J, Izadi A. The efficacy of probiotics in prevention of urinary tract infection in children: A systematic review and meta-analysis. J Pediatr Urol. 2017;13(6):581-91.

92. Cameron D, Hock QS, Kadim M, Mohan N, Ryoo E, Sandhu B, et al. Probiotics for gastrointestinal disorders: Proposed recommendations for children of the Asia-Pacific region. World J Gastroenterol. 2017;23(45):7952-64.

93. Dryl R, Szajewska H. Probiotics for management of infantile colic: a systematic review of randomized controlled trials. Arch Med Sci. 2018;14(5):1137-43.

94. Sung V, D'Amico F, Cabana MD, Chau K, Koren G, Savino F, et al. Lactobacillus reuteri to Treat Infant Colic: A Meta-analysis. Pediatrics. 2018;141(1).

95. Trivic I, Niseteo T, Jadresin O, Hojsak I. Use of probiotics in the treatment of functional abdominal pain in children-systematic review and meta-analysis. Eur J Pediatr. 2020.

96. Zheng J, Wittouck S, Salvetti E, Franz C, Harris HMB, Mattarelli P, et al. A taxonomic note on the genus Lactobacillus: Description of 23 novel genera, emended description of the genus Lactobacillus Beijerinck 1901, and union of Lactobacillaceae and Leuconostocaceae. Int J Syst Evol Microbiol. 2020;70(4):2782-858.

97. Schnadower D, Tarr PI, Casper TC, Gorelick MH, Dean JM, O'Connell KJ, et al. Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children. N Engl J Med. 2018;379(21):2002-14.

98. Freedman SB, Williamson-Urquhart S, Farion KJ, Gouin S, Willan AR, Poonai N, et al. Multicenter Trial of a Combination Probiotic for Children with Gastroenteritis. N Engl J Med. 2018;379(21):2015-26.

99. Hojsak I, Fabiano V, Pop TL, Goulet O, Zuccotti GV, Cokugras FC, et al. Guidance on the use of probiotics in clinical practice in children with selected clinical conditions and in specific vulnerable groups. Acta Paediatr. 2018;107(6):927-37.

100. Lo Vecchio A, Vandenplas Y, Benninga M, Broekaert I, Falconer J, Gottrand F, et al. An international consensus report on a new algorithm for the management of infant diarrhoea. Acta Paediatr. 2016;105(8):e384-9.

101. Guarino A, Guandalini S, Lo Vecchio A. Probiotics for Prevention and Treatment of Diarrhea. Journal of clinical gastroenterology. 2015;49 Suppl 1:S37-45.

102. Society CP. Dehydration and diarrhea. Paediatr Child Health. 2003;8(7):459-68.

103. Jonckheer J, Vergaelen K, Spapen H, Malbrain MLNG, De Waele E. Modification of Nutrition Therapy During Continuous Renal Replacement Therapy in Critically Ill Pediatric Patients: A Narrative Review and Recommendations. Nutrition in Clinical Practice. 2019;34(1):37-47.

104. Bes DF, Fernández MC, Malla I, Repetto HA, Buamsch D, López S, et al. Management of cirrhotic ascites in children. Review and recommendations. Part 1: Pathophysiology, diagnostic evaluation, hospitalization criteria, treatment, nutritional management. Archivos argentinos de pediatria. 2017;115(4):385-90.

105. D'Alò GL, De Crescenzo F, Minozzi S, Morgano GP, Mitrova Z, Scattoni ML, et al. Equity, acceptability and feasibility of using polyunsaturated fatty acids in children and adolescents with autism spectrum disorder: a rapid systematic review. Health and Quality of Life Outcomes. 2020;18(1):101.

106. Te Morenga L, Montez JM. Health effects of saturated and trans-fatty acid intake in children and adolescents: Systematic review and meta-analysis. PloS one. 2017;12(11):e0186672.

107. Jacobson TA, Maki KC, Orringer CE, Jones PH, Kris-Etherton P, Sikand G, et al. National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia: Part 2. Journal of clinical lipidology. 2015;9(6 Suppl):S1-122.e1.

108. Rhee EJ, Kim HC, Kim JH, Lee EY, Kim BJ, Kim EM, et al. 2018 Guidelines for the management of dyslipidemia in Korea. The Korean journal of internal medicine. 2019;34(5):1171.

109. Gupta P, Shah D, Kumar P, Bedi N, Mittal HG, Mishra K, et al. Indian Academy of Pediatrics Guidelines on the Fast and Junk Foods, Sugar Sweetened Beverages, Fruit Juices, and Energy Drinks. Indian pediatrics. 2019;56(10):849-63.

110. Abdel Rahman A, Jomaa L, Kahale LA, Adair P, Pine C. Effectiveness of behavioral interventions to reduce the intake of sugar-sweetened beverages in children and adolescents: a systematic review and meta-analysis. Nutrition Reviews. 2018;76(2):88-107.

111. Dereń K, Weghuber D, Caroli M, Koletzko B, Thivel D, Frelut ML, et al. Consumption of Sugar-Sweetened Beverages in Paediatric Age: A Position Paper of the European Academy of Paediatrics and the European Childhood Obesity Group. Annals of Nutrition and Metabolism. 2019;74(4):296-302.

112. Baker-Smith CM, de Ferranti SD, Cochran WJ. The Use of Nonnutritive Sweeteners in Children. Pediatrics. 2019;144(5):e20192765.

113. Heyman MB, Abrams SA. Fruit Juice in Infants, Children, and Adolescents: Current Recommendations. Pediatrics. 2017;139(6):e20170967.

114. Stephen AM, Champ MMJ, Cloran SJ, Fleith M, van Lieshout L, Mejborn H, et al. Dietary fibre in Europe: current state of knowledge on definitions, sources, recommendations, intakes and relationships to health. Nutrition Research Reviews. 2017;30(2):149-90.

115. Hill ID, Fasano A, Guandalini S, Hoffenberg E, Levy J, Reilly N, et al. NASPGHAN Clinical Report on the Diagnosis and Treatment of Gluten-related Disorders. J Pediatr Gastroenterol Nutr. 2016;63(1):156-65.

116. Noronha JC, Braunstein CR, Blanco Mejia S, Khan TA, Kendall CWC, Wolever TMS, et al. The Effect of Small Doses of Fructose and Its Epimers on Glycemic Control: A Systematic Review and Meta-Analysis of Controlled Feeding Trials. Nutrients. 2018;10(11).

117. Barends C, Weenen H, Warren J, Hetherington MM, de Graaf C, de Vries JHM. A systematic review of practices to promote vegetable acceptance in the first three years of life. Appetite. 2019;137:174-97.

118. Koletzko B, Godfrey KM, Poston L, Szajewska H, van Goudoever JB, de Waard M, et al. Nutrition During Pregnancy, Lactation and Early Childhood and its Implications for Maternal and Long-Term Child Health: The Early Nutrition Project Recommendations. Annals of Nutrition and Metabolism. 2019;74(2):93-106.

119. Zalewski BM, Patro B, Veldhorst M, Kouwenhoven S, Crespo Escobar P, Calvo Lerma J, et al. Nutrition of infants and young children (one to three years) and its effect on later health: A systematic review of current recommendations (EarlyNutrition project). Critical Reviews in Food Science and Nutrition. 2017;57(3):489-500.

120. Mennella JA, Reiter AR, Daniels LM. Vegetable and Fruit Acceptance during Infancy: Impact of Ontogeny, Genetics, and Early Experiences. Advances in Nutrition. 2016;7(1):211S-9S.

121. de Waard M, Brands B, Kouwenhoven SMP, Lerma JC, Crespo-Escobar P, Koletzko B, et al. Optimal nutrition in lactating women and its effect on later health of offspring: A systematic review of current evidence and recommendations (EarlyNutrition project). Crit Rev Food Sci Nutr. 2017;57(18):4003-16.

122. D'Auria E, Bergamini M, Staiano A, Banderali G, Pendezza E, Penagini F, et al. Baby-led weaning: what a systematic review of the literature adds on. Italian journal of pediatrics. 2018;44(1):49.

123. Lau C. Development of infant oral feeding skills: what do we know?1–3. The American Journal of Clinical Nutrition. 2016;103(2):616S-21S.

124. O'Donoghue CR, Nottingham EE. Dysphagia Management in the Schools: Past, Present, and Future. Seminars in speech and language. 2017;38(2):126-34.

125. Jadcherla S. Dysphagia in the high-risk infant: potential factors and mechanisms1–3. The American Journal of Clinical Nutrition. 2016;103(2):622S-8S.

126. Meyer R, Foong R-XM, Thapar N, Kritas S, Shah N. Systematic review of the impact of feed protein type and degree of hydrolysis on gastric emptying in children. BMC Gastroenterology. 2015;15(1):137.

127. Harrison SE, Greenhouse D. Dietary and Nutrition Recommendations in Pediatric Primary Care: A Call to Action. Southern medical journal. 2018;111(1):12-7.

128. Gordon M, Biagioli E, Sorrenti M, Lingua C, Moja L, Banks SSC, et al. Dietary modifications for infantile colic. Cochrane Database of Systematic Reviews. 2018(10).

129. Agnoli C, Baroni L, Bertini I, Ciappellano S, Fabbri A, Papa M, et al. Position paper on vegetarian diets from the working group of the Italian Society of Human Nutrition. Nutrition, metabolism, and cardiovascular diseases : NMCD. 2017;27(12):1037-52.

130. Lemale J, Mas E, Jung C, Bellaiche M, Tounian P. Vegan diet in children and adolescents. Recommendations from the French-speaking Pediatric Hepatology, Gastroenterology and Nutrition Group (GFHGNP). Archives de Pédiatrie. 2019;26(7):442-50.

131. Oba J, Carvalho WB, Silva CA, Delgado AF. Gastrointestinal manifestations and nutritional therapy during COVID-19 pandemic: a practical guide for pediatricians. Einstein (Sao Paulo, Brazil). 2020;18:eRW5774.

132. Iniesta RR, Paciarotti I, Brougham MF, McKenzie JM, Wilson DC. Effects of pediatric cancer and its treatment on nutritional status: a systematic review. Nutr Rev. 2015;73(5):276-95.

133. Raber M, Swartz MC, Santa Maria D, O'Connor T, Baranowski T, Li R, et al. Parental involvement in exercise and diet interventions for childhood cancer survivors: a systematic review. Pediatr Res. 2016;80(3):338-46.

134. Karpen HE. Nutrition in the Cardiac Newborns: Evidence-based Nutrition Guidelines for Cardiac Newborns. Clin Perinatol. 2016;43(1):131-45.

135. Mangili G, Garzoli E, Sadou Y. Feeding dysfunctions and failure to thrive in neonates with congenital heart diseases. Pediatr Med Chir. 2018;40(1).

136. Zhang J, Cui YQ, Ma Md ZM, Luo Y, Chen XX, Li J. Energy and Protein Requirements in Children Undergoing Cardiopulmonary Bypass Surgery: Current Problems and Future Direction. JPEN J Parenter Enteral Nutr. 2019;43(1):54-62.

137. Castellani C, Duff AJA, Bell SC, Heijerman HGM, Munck A, Ratjen F, et al. ECFS best practice guidelines: the 2018 revision. J Cyst Fibros. 2018;17(2):153-78.

138. Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al. Highlights of the ESPEN-ESPGHAN-ECFS Guidelines on Nutrition Care for Infants and Children With Cystic Fibrosis. J Pediatr Gastroenterol Nutr. 2016;63(6):671-5.

139. Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al. ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with cystic fibrosis. Clin Nutr. 2016;35(3):557-77.

140. Lahiri T, Hempstead SE, Brady C, Cannon CL, Clark K, Condren ME, et al. Clinical Practice Guidelines From the Cystic Fibrosis Foundation for Preschoolers With Cystic Fibrosis. Pediatrics. 2016;137(4).

141. Smart CE, Annan F, Higgins LA, Jelleryd E, Lopez M, Acerini CL. ISPAD Clinical Practice Consensus Guidelines 2018: Nutritional management in children and adolescents with diabetes. Pediatr Diabetes. 2018;19 Suppl 27:136-54.

142. Sundberg F, Barnard K, Cato A, de Beaufort C, DiMeglio LA, Dooley G, et al. ISPAD Guidelines. Managing diabetes in preschool children. Pediatr Diabetes. 2017;18(7):499-517.

143. Chiang JL, Maahs DM, Garvey KC, Hood KK, Laffel LM, Weinzimer SA, et al. Type 1 Diabetes in Children and Adolescents: A Position Statement by the American Diabetes Association. Diabetes Care. 2018;41(9):2026-44.

144. Krishnan U, Mousa H, Dall'Oglio L, Homaira N, Rosen R, Faure C, et al. ESPGHAN-NASPGHAN Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children With Esophageal Atresia-Tracheoesophageal Fistula. J Pediatr Gastroenterol Nutr. 2016;63(5):550-70.

145. Miele E, Shamir R, Aloi M, Assa A, Braegger C, Bronsky J, et al. Nutrition in Pediatric Inflammatory Bowel Disease: A Position Paper on Behalf of the Porto Inflammatory Bowel Disease Group of the European Society of Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr. 2018;66(4):687-708.

146. Fritz J, Walia C, Elkadri A, Pipkorn R, Dunn RK, Sieracki R, et al. A Systematic Review of Micronutrient Deficiencies in Pediatric Inflammatory Bowel Disease. Inflamm Bowel Dis. 2019;25(3):445-59.

147. Narula N, Dhillon A, Zhang D, Sherlock ME, Tondeur M, Zachos M. Enteral nutritional therapy for induction of remission in Crohn's disease. Cochrane Database Syst Rev. 2018;4:CD000542.

148. Penagini F, Dilillo D, Borsani B, Cococcioni L, Galli E, Bedogni G, et al. Nutrition in Pediatric Inflammatory Bowel Disease: From Etiology to Treatment. A Systematic Review. Nutrients. 2016;8(6).

149. Merritt RJ, Cohran V, Raphael BP, Sentongo T, Volpert D, Warner BW, et al. Intestinal Rehabilitation Programs in the Management of Pediatric Intestinal Failure and Short Bowel Syndrome. J Pediatr Gastroenterol Nutr. 2017;65(5):588-96.

150. Gondolesi GE, Pattin F, Nikkoupur H. Management of intestinal failure in middle-income countries, for children and adults. Curr Opin Organ Transplant. 2018;23(2):212-8.

151. Jurecki E, Ueda K, Frazier D, Rohr F, Thompson A, Hussa C, et al. Nutrition management guideline for propionic acidemia: An evidence- and consensus-based approach. Mol Genet Metab. 2019;126(4):341-54.

152. Singh RH, Cunningham AC, Mofidi S, Douglas TD, Frazier DM, Hook DG, et al. Updated, web-based nutrition management guideline for PKU: An evidence and consensus based approach. Mol Genet Metab. 2016;118(2):72-83.

153. Couce ML, de Castro MJ, de Lamas C, Leis R. Effects of LC-PUFA Supplementation in Patients with Phenylketonuria: A Systematic Review of Controlled Trials. Nutrients. 2019;11(7).

154. Haberle J, Burlina A, Chakrapani A, Dixon M, Karall D, Lindner M, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders: First revision. J Inherit Metab Dis. 2019;42(6):1192-230.

155. Kishnani PS, Goldstein J, Austin SL, Arn P, Bachrach B, Bali DS, et al. Diagnosis and management of glycogen storage diseases type VI and IX: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2019;21(4):772-89.

156. Panera N, Barbaro B, Della Corte C, Mosca A, Nobili V, Alisi A. A review of the pathogenic and therapeutic role of nutrition in pediatric nonalcoholic fatty liver disease. Nutr Res. 2018;58:1-16.

157. Gibson PS, Lang S, Dhawan A, Fitzpatrick E, Blumfield ML, Truby H, et al. Systematic Review: Nutrition and Physical Activity in the Management of Paediatric Nonalcoholic Fatty Liver Disease. J Pediatr Gastroenterol Nutr. 2017;65(2):141-9.

158. Vos MB, Abrams SH, Barlow SE, Caprio S, Daniels SR, Kohli R, et al. NASPGHAN Clinical Practice Guideline for the Diagnosis and Treatment of Nonalcoholic Fatty Liver Disease in Children: Recommendations from the Expert Committee on NAFLD (ECON) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). J Pediatr Gastroenterol Nutr. 2017;64(2):319-34.

159. Romano C, van Wynckel M, Hulst J, Broekaert I, Bronsky J, Dall'Oglio L, et al. European Society for Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children With Neurological Impairment. J Pediatr Gastroenterol Nutr. 2017;65(2):242-64.

160. van der Louw E, van den Hurk D, Neal E, Leiendecker B, Fitzsimmon G, Dority L, et al. Ketogenic diet guidelines for infants with refractory epilepsy. Eur J Paediatr Neurol. 2016;20(6):798-809.

161. Theodoridis X, Grammatikopoulou MG, Petalidou A, Stamouli EM, Fotiadou I, Gkiouras K, et al. Nutrition Interventions in Pediatric Pancreatitis: Guidelines We Can Trust. J Pediatr Gastroenterol Nutr. 2019;69(1):120-5.

162. Abu-El-Haija M, Uc A, Werlin SL, Freeman AJ, Georgieva M, Jojkic-Pavkov D, et al. Nutritional Considerations in Pediatric Pancreatitis: A Position Paper from the NASPGHAN Pancreas Committee and ESPGHAN Cystic Fibrosis/Pancreas Working Group. J Pediatr Gastroenterol Nutr. 2018;67(1):131-43.

163. Parniczky A, Abu-El-Haija M, Husain S, Lowe M, Oracz G, Sahin-Toth M, et al. EPC/HPSG evidence-based guidelines for the management of pediatric pancreatitis. Pancreatology. 2018;18(2):146-60.

164. Abu-El-Haija M, Kumar S, Quiros JA, Balakrishnan K, Barth B, Bitton S, et al. Management of Acute Pancreatitis in the Pediatric Population: A Clinical Report From the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Pancreas Committee. J Pediatr Gastroenterol Nutr. 2018;66(1):159-76.

165. Freeman AJ, Maqbool A, Bellin MD, Goldschneider KR, Grover AS, Hartzell C, et al. Medical Management of Chronic Pancreatitis in Children: A Position Paper by the NASPGHAN Pancreas Committee. J Pediatr Gastroenterol Nutr. 2020.

Table 1. Overview of disease-specific guidelines, recommendations and systematic reviews with meta-analyses published in the last 5 years.

Disease/disorder	Reference	Description
Cardiac	Karpen (2016) (134)	Review showing that neonates with congenital heart disease (CHD) are at increased risk of developing NEC, particularly the preterm population. Standardized feeding protocols may affect both incidence of NEC and growth failure in infants with CHD.
	Mangili et al (2018) (135)	Review stating that there is a lack of standardized feeding protocols and caloric goals about how to feed neonates with CHD. Eating difficulties may persist even after discharge because these patients require nutritional support through nasogastric tubes or percutaneous endoscopic gastrostomies.
	Zhang (2019) (136)	Review to examine the nutrition conditions in perioperative children with CHD and the main problems in nutrition management in the cardiac intensive care unit

Cystic fibrosis	Castellani et al (2018) (137)	A revision of the best practice guidelines of the European Society of Cystic Fibrosis addressing key aspects of CF care. It is endorsed by the CF Network in ERN LUNG and CF Europe and is expected to be useful to clinical teams both in countries where CF care is developing and those with established CF centres. Nutritional topics discussed are goals, assessment and monitoring of nutritional status; assessment and treatment of exocrine pancreatic insufficiency; preventive and interventional nutritional care; and screening for diabetes mellitus and CF bone disease.
	Wilschanski et al (2016) (138)	Summary of the ESPEN-ESPGHAN-ECFS Guidelines (139) on nutrition care for infants and children with CF. Highlighted recommendations are presented in some practical tables.
	Turck et al (2016) (139)	ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with cystic fibrosis – both general and specific. Specific guidelines include assessment and monitoring of nutritional status, feeding newly diagnosed infants, nutrition counselling, energy intake, sodium supplementation, micronutrient supplementation and monitoring, PERT, malnutrition, CF-related complications (bone disease, diabetes and liver disease)

	Lahiri et al (2016) (140)	Clinical practice guidelines from the American Cystic Fibrosis Foundation specifically for preschoolers (2 to 5 year of age). It includes 22 comprehensive evidence-based and consensus recommendations on nutritional care: nutritional status assessment, nutritional intake, nutritional therapy, PERT, vitamin supplementation and routine monitoring. It also provides a nutritional algorithm including consideration of G-tube.
Diarrhea (acute)	Lo Vecchio A et al (100)	Algorithm by the ESPGHAN and ESPID of management of an infant with acute diarrhoea should include: 1) screening dehydration with validated clinical tools 2) rehydration interventions and early refeeding 3) agents to reduce the severity and duration of the diarrhoea. Lactose should always be withdrawn.
	Guarino A et al (101)	Systematic review showing moderate clinical benefit of some probiotic strains (LGG and S. boulardii) in the treatment of acute diarrhoea
Diabetes mellitus type 1	Smart et al (2018)(141) Sundberg et al (2017) (142)	The International Society for Pediatric and Adolescent Diabetes (ISPAD) published the last guidelines on nutritional management in children and adolescents with

		diabetes. Although most recommendations are based in low grade evidence (C-E), they emphasized the implementation of individualized meal plans with prandial insulin adjustments, the importance of meal-time routines with limitations on snacking and enhanced the role of carbohydrate counting as well as the use of glycemic index to benefit glycemic control.
	Chiang et al (2018) (143)	In the same direction of ISPAD are the recommendations on Nutrition therapy from the American Diabetes Association
Esophageal atresia	Krishnan et al (2016) (144)	The GI working group of International Network on Esophageal Atresia (with members from ESPGHAN/NASPGHAN) developed uniform evidence-based guidelines for the management of GI complications in children with EA.
IBD	Miele et al (2018)(145)	Position paper on nutrition in IBD by ESPGHAN Porto IBD group; covers nutritional assessment; macronutrients need; trace elements, minerals, and vitamins; nutrition as a primary therapy of pediatric IBD; probiotics and prebiotics; specific dietary restrictions; and dietary compounds and the risk of IBD
	Fritz et al (2019) (146)	Systematic review on micronutrient deficiency in children with IBD and provides evidence-based guidelines for nutritional surveillance

	Narula et al (2018)(147)	An update of a previously published Cochrane review on the role of enteral nutrition for remission induction in Crohn's disease in adults and children
	Penagini et al (2016) (148)	Systematic review on the role of nutrition (etiology and therapy) in pediatric IBD
Intestinal failure	Merritt et al (2017)(149)	NASPGHAN practice guidelines summarizes recommendations for the intestinal rehabilitation programs for intestinal failure and short bowel syndrome
	Gondolesi et al (2018) (150)	A systematic review on the current differences in management of intestinal failure patients in middle income countries from Latin America and Asia
Liver/renal	Bes DF et al Arch (104)	Recommendations of this review were based on cirrhotic ascites pathophysiology and suggested preferred approach for the diagnosis and therapeutic aspects as well as preventive care. Nutritional assessment is considered critical. Because it plays an important role to post-transplantation outcome
	Jonckheer J et al (103)	This review stated that recommendations on nutrition for children on chronic RRT are not evidence-based and further research needed in this field. Caloric prescription should be adapted accordingly. Fatty acid from olive oil seems to have anti-inflammatory effects. Frequent monitoring of electrolytes is needed. Elements such as thiamine, pyridoxin, folic acid, ascorbic C and selenium that are removed

		during the effluent should be supplemented which will be based on patients' condition
Metabolic disease	Jurecki et al (2019) (151)	Guidelines by the Southeast Regional Genetics Network (SERN) and Genetic Metabolic Dietitians International (GMDI) on the management Propionic Acidemia. Only the recommendation to use human breast milk as source of intact protein with careful monitoring for infants has a fair strength of evidence, while other were weak or by consensus, although clinical practice makes mandatory its implementation.
	Singh et al (2016) (152)	Guidelines by the Southeast Regional Genetics Network (SERN) and Genetic Metabolic Dietitians International (GMDI) on the management of Phenylketonuria (PKU). It is recommended to meet the individual's recommended Phenylalanine intake (for anabolism and maintaining an appropriate blood PHE concentration) by adjusting intact protein intake.
	Couce et al (2019) (153)	DHA supplementation in PKU patients from 2 weeks to 47 years of age improves DHA status and decreases visual evoked potential P100 wave latency in PKU children from 1 to 11 years old. Neurocognitive data are inconclusive.
	Häberle et al (2019) (154)	An updated guideline of group of experts on the management of urea cycle

		disorders in currently in its first revision.
	Kishnani et al (2019) (155)	A guideline on the management of Glycogen storage disease VI and IX was published by the American College of Medical Genetics and Genomics. It includes the delivery of each macronutrient within the diet and the roles of cornstarch.
NAFLD	Panera et al (2018) (156)	Systematic review on pathophysiology, the role of nutrition as a cause and therapeutic target and the role/evidence of nutritional supplements in paediatric NAFLD.
	Gibson et al (2017)(157)	Systematic review (RCT's on nutritional and lifestyle modifications only) focusing on histology, liver fat assessed by MRI and change in liver enzymes as primary outcome measures for NAFLD. They conclude that Vit. E may be an option in biopsy-proven NASH or poor compliance with lifestyle modifications. Probiotic or omega-3 fatty acid supplementation may be a possible intervention. There is a lack of RCT's assessing the impact of physical activity.
	Vos et al (2017)(158)	Guidelines from NASPGHAN for the diagnosis and management on paediatric NAFLD. Topics addressed were epidemiology and evolution of NAFLD, screening, diagnosis, follow up and management

Neurological impairment/Epilepsy	Romano et al (2017) (159)	Guidelines from ESPGHAN for the evaluation and treatment of gastrointestinal and nutritional complications in children with neurological impairment. Topics addressed are nutritional status assessment, nutrient requirements, oropharyngeal dysfunction, GERD, gastric and jejunal tube feeding, fundoplication.
	Van der Louw et al (2016) (160)	International consensus statement regarding the clinical management of the ketogenic diet in infants. The recommendations include patient selection, pre-ketogenic diet counseling and evaluation, specific nutritional requirements, preferred initiation, monitoring of adverse effects at initiation and follow-up, evaluation, and ketogenic diet discontinuation.
Oncology	Iniesta et al (2015)(132)	Systematic review gathering the results from 46 studies. Prevalence of undernutrition ranged from 0% to 65% and overnutrition from 8% to 78%. In six of the studies, undernutrition was associated with poor clinical outcomes.
	Raber et al (2016) (133)	Systematic review of the literature reviewing the parental involvement in exercise and diet interventions for childhood cancer survivors. It was found that direct parental involvement showed positive outcomes on long-term lifestyle changes in

		these patients.
Pancreatitis	Theodoridis et al (2019) (161)	Systematic review and appraisal of guidelines for the medical nutrition therapy of pediatric pancreatitis. The joint ESPGHAN/NASPGHAN recommendations demonstrated the highest quality based on the AGREE II tool
	Abu-El-Haija et al (2018) (162)	Joint ESPGHAN/NASPGHAN guidelines for timing, monitoring, modality and composition of nutrition in acute and chronic pediatric pancreatitis. Nearly all recommendations were based on low quality evidence
	Parniczky et al (2018) (163)	Joint EPC/HPSG guidelines for diagnosing and treating acute, acute recurrent and chronic pediatric pancreatitis.
	Abu-El-Haija et al (2018)(164)	NASPGHAN guidelines for diagnosis, treatment and follow up of acute pediatric pancreatitis
	Freeman et al (2020) (165)	NASPGHAN guidelines for diagnosis, treatment and follow up of chronic pediatric pancreatitis

CHD - congenital heart disease; ; CF - cystic fibrosis; IBD- inflammatory bowel disease; NEC - necrotizing enterocolitis; ECFS - European Society of Cystic Fibrosis; EPC - European Pancreatic Club; ESPEN - European Society for Clinical Nutrition and Metabolism; ESPGHAN - European Society of Gastroenterology, Hepatology and Nutrition; ESPID – European Society for Paediatric Diseases; HPSG – Hungarian Pancreatic Study Group; ISPAD -

International Society for Pediatric and Adolescent Diabetes; NASPGHAN - North American Society For Pediatric Gastroenterology, Hepatology & Nutrition;

PKU – phenylketonuria; RCT - randomized controlled trials; RRT – renal replacement therapy;

Table 2. Guidelines, recommendations and systematic reviews with meta-analyses on micronutrients in paediatric patients and healthy children.

Study	Nutrient	Population	Objective	Inclusions	Conclusions
Gerasimidis et al (2020)(72)	Vitamins and Trace Elements	Children	Present the various micronutrient assessment methods and critically discuss pitfalls with interpretation of their results	Societal Position Paper-ESPGHAN	A multimodal approach, including clinical examination, dietary assessment, and laboratory biomarkers is proposed as the optimal way to ascertain the micronutrient status of individual patients. In the presence of acute inflammatory conditions, micronutrient measurements in plasma should be replaced by biomarkers not affected by systemic inflammatory response or delayed until inflammatory state is resolved.
Jagannath et al (2020) (73)	Vitamin K	Cystic fibrosis	Effects of vitamin K supplementation in people with	RCT of all preparations of vitamin K supplement	There is very low-quality evidence of any effect of vitamin K on outcomes in

			cystic fibrosis to decrease deficiency-related coagulopathy, increase bone mineral density, decrease risk of fractures and improve quality of life in people with cystic fbrosis	compared to either no supplementation or placebo	people with cystic fibrosis. While there is no evidence of harm, recommendations by national cystic fibrosis guidelines should be followed
Soeet al (2020) (71)	Vitamin D	Sickle cell anaemia	To investigate the effects of vitamin D supplementation in people with sickle cell anaemia on general health, musculoskeletal health, respiratory health and the safety of vitamin D supplementation	RCTs and quasi-RCTs comparing oral administration of any form of vitamin D supplementation at any dose and for any duration to another type or dose of vitamin D or placebo or no supplementation in	Current evidence presented is not of sufficient quality to guide clinical practice. Clinicians should consider the relevant existing guidelines for vitamin D supplementation and dietary reference intakes for calcium and vitamin D

				people with sickle cell anaemia	
Peña-Rosas et al (2019) (74)	Rice fortification with iron, vitamin A, zinc or folic acid	General population (>2 years)	To determine the benefits and harms of rice fortification with vitamins and minerals (iron, vitamin A, zinc or folic acid) on micronutrient status and health-related outcomes in the general population.	RCTs and quasi-RCTs and controlled before-and-after studies. Rice fortification vs unfortified rice or no intervention.	Fortification of rice with iron alone or in combination with other micronutrients may make little or no difference in the risk of having anaemia or presenting iron deficiency. Fortification of rice with iron and other micronutrients such as vitamin A or folic acid may make little or no difference in the risk of having vitamin A deficiency or on the serum folate concentration. There is limited

					evidence on any adverse effects of rice
Hombali et al (2019) (75)	Fortification of staple foods with vitamin A	General population (> 2 years)	To assess the effects of fortifying staple foods with vitamin A for reducing vitamin A deficiency and improving health-related outcomes in the general population older than two years of age	RCTs; Fortification of staple foods (sugar, edible oils, edible fats, maize flour or corn meal, wheat flour etc) with vitamin A alone or in combination with other vitamins and minerals	Fortifying staple foods with vitamin A alone may make little or no difference to serum retinol concentrations or the risk of subclinical vitamin A deficiency. In comparison with provision of unfortified foods, provision of staple foods fortified with vitamin A plus other micronutrients may not increase serum retinol concentration but probably reduces the risk of subclinical vitamin A

					deficiency. Compared to no intervention, staple foods fortified with vitamin A plus other micronutrients may increase serum retinol concentration, although it is uncertain whether the intervention reduces the risk of subclinical vitamin A deficiency as the certainty of the evidence has been assessed as very low
Brett et al (2018) (68)	Vitamin D	Children 2-18 years	Investigate the effect of vitamin D interventions (fortified foods, supplements, bolus injections) on vitamin D status in children 2–18 y of age	Meta-analyses of RCTs	The serum 25(OH)D response to vitamin D intake differs based on baseline status, dietary intakes, and delivery mode, but not age, sex, or latitude.

Grossman et al (2017) (69)	Vitamin D	Children	Statement from the European Academy in Paediatrics	Opinion statement	No justification for routine screening for vitamin D deficiency in healthy children. Evaluation of vitamin D status in children belonging to high-risk groups. All infants up to 1 year of age should receive an oral supplementation of 400 IU/day of vitamin D
Haq et al (2018) (70)	Vitamin D	People in United Arabic Emirates	Provide clinical practice guidelines for people from the Gulf area	Review	Different intakes are recommended for different age groups, premature infants, during pregnancy, obese and people with dark skin colour
Mihatsch et al (2016) (76)	Vitamin K	Newborns & infants	Describe the prevalence, discuss current prophylaxis practices and outcomes, and provide recommendations for the prevention of VKDB in healthy	Societal Position Paper-ESPGHAN	Healthy newborn infants should either receive 1 mg of vitamin K1 by intramuscular injection at birth; or 3 × 2 mg vitamin K1 orally at birth, at 4 to 6 days and at 4 to 6 weeks; or 2 mg

			term newborns and infants.		vitamin K1 orally at birth, and a weekly dose of 1 mg orally for 3 months. Intramuscular application is the preferred route

ESPGHAN - European Society of Gastroenterology, Hepatology and Nutrition; RCT - randomized controlled trials; VKDB - Vitamin K Deficiency Bleeding;

Table 3. Guidelines, recommendations and systematic reviews with meta-analyses published in the last 5 years on miscellaneous nutrients/components and situations of paediatric nutrition.

Study	Nutrient /Component /Condition	Population	Objective	Type of study	Conclusions
D'Alò et al (2020) (105)	PUFA	Children and adolescents with autism spectrum disorder (ASD)	Impact on equity, acceptability and feasibility for developing a pilot recommendation for PUFAs in children and adolescents with autism spectrum disorder	Systematic review	Evidence of the effectiveness of PUFAs therapy in children and adolescents with ASD are limited. PUFAs are not expected to have either negative or positive impacts on equity. Overall, the implementation of PUFAs is likely to be feasible and acceptable
Te Morenga (2017) et al (106)	SFA and TFA	Children, adolescents and young adults between 2-19 years old	Health effects of reducing SFA and TFA intake in free-living children, adolescents and young adults between 2-19 years old	Systematic Review and meta-analysis	Restriction of SFA intake lead to a significant reduction in levels of total and LDL cholesterol as well as diastolic blood pressure. Growth and development seem not to be affected by these restrictions.

Jacobson et al (2015) (107)	Dyslipidaemia	Children, adult women, older patients, patients infected with HIV, patients with rheumatoid arthritis, and patients with residual risk despite statin and lifestyle therapies	Management of dyslipidaemia in clinical practice	Consensus paper by the National Lipid Association	Diet and lifestyle interventions can be effective in lowering LDL-C in children and adolescents. Children older than 8 years are potential candidates for pharmacologic lipid lowering treatment but there is inadequate evidence regarding treatment goals.
Rhee et al (2019) (108)	Dyslipidaemia	Adults, children and specific patient groups	Management of dyslipidaemia in clinical practice	Guidelines by the Korean Association of Internal Medicine and the Korean Society of Lipid and Atherosclerosis	Screening test is not recommended for Children < 9 years. Statin therapy should not be immediately initiated even in diagnosis of dyslipidaemia. Pharmacologic therapy is not recommended for children under 10 years but only lifestyle and dietary interventions.

Gupta et al (2019) (109)	Sugar	Indian children and adolescents	Effects of junk foods, fast foods, sugar-sweetened beverages and carbonated drinks and formulation of recommendations	Guidelines by the Indian Academy of Pediatrics	Consumption of these foods and beverages is associated with higher energy and free sugar intake and is associated with higher body mass index and obesity. Caffeinated drinks may be linked to cardiac and sleep disturbances. Major recommendations suggest intake of whole fruits, limitation of sweetened beverages and ban on sale of these foods in school canteens
Dereń et al (2019) (111)	Sugar	Infants, children and adolescents	Inform health-care professionals, parents, teachers and care-givers, stakeholders and governing bodies about the risks of sweet- sweetened beverages in childhood and adolescence	Position Paper by the European Academy of Paediatrics and the European Childhood Obesity Group	Sweet-sweetened beverages consumption by children and adolescents should be limited. Consumption of water and other non-sweetened beverages should be promoted.

Abdel Rahman et al (2018) (110)	Sugar	Children 4-16 years old	Effects of educational and behavioural interventions to reduce sweet-sweetened beverages consumption and health outcomes in children	Systematic review and Meta-analysis	Behavioural interventions conducted in schools are possibly better than no intervention in reducing sweet-sweetened beverages consumption, although the evidence is modest.
Baker-Smith et al (2019) (112)	Sweeteners	Children and adolescents	Examination of the safety of non-nutritive sweetener (NNS) use in the paediatric population as well as their benefits and/or adverse effects that paediatricians may use when discussing with families	Recommendations by the American Academy of Paediatrics	Current FDA-approved NNSs include saccharin, aspartame, acesulfame potassium, sucralose, neotame, stevia, and advantame. NNSs can promote slight weight reduction in children, bu data are limited. Health care providers should remain alert. There are no absolute contraindications to use of NNSs in children, except for aspartame and neotame in cases of phenylketonuria.

Heyman et al (2017) (113)	Fruit Juice	Children and adolescents	Benefits and detrimental effects of fruit juices in infants, children and adolescents	Recommendations by the American Academy of Paediatrics	Fruit juices do not offer nutritional benefits for infants compare to whole fruits for infants and children and there is not essential role in a healthy, balanced diet of children. Excessive consumption of fruit juices can be linked to malnutrition, diarrhoea, abdominal pain as well as tooth impairments.
Stephen et al (2017) (114)	Fibre	European population	Investigation of how countries in Europe describe dietary fibre, what they recommend in terms of dietary fibre to the public and how intakes may vary	Review	In Europe intakes do not reach recommendations and very few countries provide appropriate guidance on the fibre intake. Moreover, research gaps were identified.

Hill et al (2016) (115)	Gluten	Infants and children	Comparison of clinical manifestations of gluten-related disorders. Description of the initial tests how the diagnosis of each condition is confirmed and discussion of these conditions treatment.	NASPGHAN Clinical Report	Overlapping of gluten-related disorders symptoms makes differentiation difficult for the clinicians. Tests for IgA and IgG antibodies against gliadin (AGA), endomysium (EMA), tissue transglutaminase (tTG) and deamidated gliadin peptides (DGPs) are available, with the tTG-IgA antibody to be described as the most cost-effective. The complete exclusion of dietary gluten for life for Celiac disease and elimination for the other gluten-related disorders are reported as the best approach for these conditions.
Noronha et al (2018) (116)	Fructose	People of all ages	Assessment of the impact of small doses of fructose and its epimers on glycaemic control	Systematic review and meta-analysis	Long term improvement on glycaemic control can be observed but further research with RCTs is needed.
Barends C et al	Early eating	Infants and children	Promotion of vegetable	Systematic review	Early introduction of vegetables, variety in

(2019) (117)		up to 3 years old	acceptance in infants for the first 3 years of life		type of vegetable daily as well as repeated exposure to the same vegetable in a few days pattern are the most promising strategies.
Koletzko et al (2019) (118)	Early eating	Women before pregnancy, pregnant and breastfeeding women, infants, and young children	Promotion of the optimized nutrition during pregnancy, lactation, infancy and early childhood and its long-term effects on both maternal child health	Recommendations by the Early Nutrition Project Group	Exclusive or even partial breastfeeding should be promoted. Non breastfed infants should receive an infant protein-rich formula (or after 6 months for breastfed infants). Cow milk or other animal milks are not suggested in the first year of life. Complementary foods can be introduced after 17 weeks and not later than 26 weeks. Dietary sugar and sugar beverages should be avoided in infancy and early childhood.
Zalewski et al (2017) (119)	Early eating	Infants and children up to 3 years old	Summarization of the nutrition recommendations in infancy and early childhood with	Recommendations by the Early Nutrition Project	Several fields of nutrition need further elucidations. Major gaps were identified in long-term effects as well as recordings of

			emphasis of long-term effects on child health	Group	children's dietary habits.
Mennella et al (2016) (120)	Early eating	Young Children	Introduction of vegetables and fruits in infancy	Review	Early exposure to nutritious foods and flavours may maximize the likelihood of following healthier diets. Fruits and vegetables should be part of the family's diet pattern.
De Waard et al (2017) (121)	Early eating	Lactating women	Summarization of current evidence on nutrition and/or supplements in lactating women with emphasis on long-term effects in offspring's health	Recommendations by the Early Nutrition Project Group	PUFA supplementation during lactation may protect the offspring from overweight/obesity and/or hypertension. Further research is needed regarding vitamin, mineral and probiotics supplementation during lactation.
D'Auria et al (2018) (122)	Baby-led weaning	Infants, young Children	Examination of the current evidence regarding Baby-led weaning in order to assess its	Systematic review	There is insufficient evidence for baby-led-weaning approach and its energy and nutrient in take adequacy. Baby-led-weaning

			safety		could be associated with lower risk of choking and nutrients deficiency, but, these further investigation and RCTs are required.
Lau et al (2016) (123)	Oral Feeding	Infants	Examination of the evidence on the development of oral feeding skills in very low birth weight infants	Review	Oral feeding in infants has led to special assessment scales that can help clinicians to identify feeding difficulties in infants and act accordingly.
O'Donoghue et al (2017) (124)	Dysphagia	Children in School	Examination of interventions in schools that can benefit children dysphagia	Review	Speech language pathologists should ensure equitable access to services related dysphagia for all school children that need them.
Jadcherla et al (2016) (125)	Dysphagia	Infants	Examination of current evidence related to neonatal dysphagia and opportunities to improve feeding.	Review	The fact that there is not a single symptom or sign or test to provide a definitive diagnosis and clinicians need to be aware and coordinate with interdisciplinary teams to manage dysphagia.

Meyer et al(2016) (126)	Gastric emptying	Children up to 16 years old	Comparison of Gastric emptying of breast milk to casein and whey formulas and to hydrolysed whey or casein formulas	Systematic review	Breast milk appears to empty faster than formula milk. Moreover, whole protein formula milk and whey feeds present fast gastric emptying. However, different production methodologies and compositions of feeds lead to inconsistent conclusions.
Harrison et al (2018) (127)	Primary care	Children and adolescents	How to incorporate diet and nutrition advise for children in primary care and formulation of recommendations	Review	Primary care clinicians can assess, counsel and intervene in nutrition and diet of children in order to prevent weight gain and other impairments related to nutrition.
Gordon M et al (2018) (128)	Colic	Infants <4 months of age	Assessment of the impact of dietary modifications in order to reduce colic incidence	Cochrane Systematic Review	There is insufficient evidence to conclude if nutritional modifications are useful or detrimental in reducing infant colic.
Agnoli et al (2017) (129)	Vegetarianism	Vegetarian populations	Investigation of the adequacy of vegetarian diets and recommendations for	Position Paper from the Working Group of the Italian	Vegetarians should supplement their diets with reliable sources of vitamin B12 (fortified foods or supplements). They should be

			vegetarians	Society of Human Nutrition	encouraged to consume more proteins than the general population and foods that are rich sources of calcium, iron, zinc and n-3 fatty acids.
Lemale et al (2019) (130)	Veganism	Children and adolescents	Investigation of the adequacy of vegan diets and formulation of recommendations for vegan children	Recommendations by the French-speaking Pediatric Hepatology, Gastroenterology and Nutrition Group	Vegan diets do not provide all the micronutrient requirements and nutritional deficiencies can be observed. Dietary monitoring is essential. Supplementation of vitamins B12 and D are always necessary, while iron, calcium, docosahexaenoic acid, and zinc should be supplemented in cases of deficiency.
Oba et al (2020) (131)	COVID-19	Children and adolescents	Guidance regarding manifestations of gastrointestinal involvement in children and adolescents	Review	Children and adolescents with nausea, vomiting or diarrhoea should be seriously suspected for COVID-19 infection. Children with inflammatory bowel disease or chronic

			with COVID-19		liver disease are not at greater risk of COVID-19 infection. Nutritional support is important in treatment of paediatric patients, particularly in severe or critical cases of COVID-19.

AGA - antibodies against gliadin; ASD - autism spectrum disorder; DGP - deamidated gliadin peptides; EMA – endomysium antibodies; FDA - Food and Drug Administration; HIV - human immunodeficiency virus; LDL - low-density lipoprotein; NASPGHAN - North American Society For Pediatric Gastroenterology, Hepatology & Nutrition; NNS - non-nutritive sweetener; PUFA - polyunsaturated fatty acids; SFA - saturated fatty acids; TFA - trans-fatty acids; TTG - tissue transglutaminase;