**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**

Lyvonne N Tume RN, PhD a, Frederic V Valla MD PhD b, Koen Joosten MD, PhD c, Corinne Jotterand Chaparro RD, PhD d, Lynne Latten RD e, Luise V Marino RD, PhD f, Isobel Macleod RN, MSc g, Clémence Moullet RD d, Nazima Pathan MD, PhD h, Shancy Rooze MD i, Joost van Rosmalen, PhD j, Sascha CAT Verbruggen MD, PhD c

Corresponding author: Dr Lyvonne Associate Professor in Child Health, University of Salford, Manchester UK

**\*Lyvonne N Tume RN, PhD**

Associate Professor in Child Health

Faculty of Health and Society,

University of Salford, Manchester UK

M6 6PU

And Pediatric Intensive Care Unit

Alder Hey Children’s NHS Foundation Trust

East Prescot Road,

Liverpool L12 2AP

Phone +44(0) 7710 412 142

Orchid ID 0000-0002-2547-8209

\* **Frédéric V Valla MD PhD**

Consultant in Pediatric Intensive Care

Pediatric intensive care unit, Hôpital Femme Mère Enfant,

CarMEN INSERM UMR

1060 Hospices Civils de Lyon, Lyon-Bron, France

Frederic.Valla@chuv-lyon.fr

Phone +33(0)472 129735

Orchid ID [0000-0001-5285-1104](https://orcid.org/0000-0001-5285-1104)

**\*joint first authors\***

**Koen Joosten MD, PhD**

Consultant in Pediatric Intensive Care

Intensive Care, Department of Pediatrics and Pediatric Surgery, Erasmus Medical Centre, Sophia Children’s Hospital, Rotterdam, The Netherlands

k.joosten@erasmusmc.nl

**Corinne Jotterand Chaparro RD, PhD**

Assistant Professor

Geneva School of Health Sciences, HES-SO University of Applied Sciences and Arts Western Switzerland,

Pediatric Intensive Care Unit, University Hospital of Lausanne, Switzerland.

corinne.jotterand@hesge.ch

**Lynne Latten BSc RD**

Specialist pediatric dietician

Nutrition and Dietetics, Alder Hey Children’s Hospital Liverpool, UK

Lynne.latten@alderhey.nhs.uk

**Luise V Marino RD, PhD**

Specialist pediatric dietician

Department of Dietetics/ Speech & Language Therapy, NIHR Biomedical Research Centre Southampton, University Hospital Southampton, Faculty of Environmental & Life Sciences, University of Southampton, Southampton, UK

Luise.Marino@uhs.nhs.uk

**Isobel Macleod RN, MSc**

Advanced Nurse Practitioner, PICU

Pediatric Intensive Care Unit, Royal Hospital for Children, Glasgow, UK

isobelmacleod@nhs.net

**Clémence Moullet RDMSc**

Senior Academic

Geneva School of Health Sciences, HES-SO University of Applied Sciences and Arts Western Switzerland,

Pediatric Intensive Care Unit, University Hospital of Lausanne, Switzerland.

clemence.moullet@hesge.ch

**Nazima Pathan MD, PhD**

Consultant in Pediatric Intensive Care

Department of Pediatrics, University of Cambridge, Hills Road, Cambridge, UK

np409@medschl.cam.ac.uk

**Shancy Rooze MD**

Consultant in Pediatric Intensive Care

Pediatric Intensive Care Unit, Queen Fabiola Children’s University Hospital, Brussels, Belgium

shancy.rooze@huderf.be

**Joost van Rosmalen PhD**

Assistant Professor in Biostatistics

Department of Biostatistics, Erasmus Medical Centre Rotterdam, Rotterdam, The Netherlands

j.vanrosmalen@erasmusmc.nl

**Sascha CAT Verbruggen MD, PhD**

Consultant in Pediatric Intensive Care

Intensive Care, Department of Pediatrics and Pediatric Surgery, Erasmus Medical Centre, Sophia Children’s Hospital, Rotterdam, The Netherlands;

s.verbruggen@erasmusmc.nl

Orchid ID [0000-0003-4866-9865](https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Forcid.org%2F0000-0003-4866-9865%3Flang%3Den&data=02%7C01%7Cs.verbruggen%40erasmusmc.nl%7C540d86dcda8746b40fc108d767840532%7C526638ba6af34b0fa532a1a511f4ac80%7C0%7C1%7C637091689044763324&sdata=PUKMCRQOQYGzD4R2r1TNrdMvRu9Mo00Diaw5FiCK0Dc%3D&reserved=0)

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**Take Home Message:**

There is a lack of high-quality evidence to guide nutrition in pediatric critical illness. This position statement and clinical recommendations summarises the existing evidence around 15 of the most important clinical questions, and where no evidence is available, suggests good clinical practice.**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**

**Abstract**

**Background:** Nutritional support is considered essential for the outcome of pediatric critical illness. There is a lack of methodologically sound trials to provide evidence-based guidelines leading to diverse practices in PICUs worldwide. Acknowledging these limitations, we aimed to summarize the available literature and provide practical guidance for the pediatric critical care clinicians around important clinical questions many of which are not covered by previous guidelines.

**Objective:** To provide an ESPNIC position statement and make clinical recommendations for the assessment and nutritional support in critically ill infants and children.

#### Design: The Metabolism, Endocrine and Nutrition (MEN) section of the European Society of Pediatric and Neonatal Intensive Care (ESPNIC) generated 15 clinical questions regarding different aspects of nutrition in critically ill children. After a systematic literature search, the Scottish Intercollegiate Guidelines Network (SIGN) grading system was applied to assess the quality of the evidence, conducting meta-analyses where possible, to generate statements and clinical recommendations, which were then voted on electronically. Strong consensus (>95% agreement) and consensus (>75% agreement) on these statements and recommendations was measured through modified Delphi voting rounds.

**Results:** The final 15 clinical questions generated a total of 7261 abstracts, of which 142 publications were identified relevant to develop 32 recommendations. A strong consensus was reached in 21 (66%) and consensus was reached in 11 (34%) of the recommendations. Only 11 meta-analyses could be performed on 5 questions.

**Conclusions:** We present a position statement and clinical practice recommendations. The general level of evidence of the available literature was low. We have summarised this and provided a practical guidance for the pediatric critical care clinicians around important clinical questions.

**Keywords:** Enteral nutrition; parenteral nutrition; child; pediatric; intensive care; guidelines

**Introduction**

Critical illness induces profound metabolic and endocrine changes in close interaction with the alterations in autonomic and immune systems. The metabolic and endocrine changes are characterized by catabolism, insulin resistance and shifts in substrate utilisation.1 These changes evolve during the course of illness, where the acute changes are assumed to be advantageous for survival. However, following the acute phase these changes might become harmful.1,2 Parallel to these changes, critically ill children frequently experience feeding difficulties, caused by (perceived) feed intolerance and feeding interruptions.3,4 This often leads to undernourishment with a cumulative macronutrient deficit during the course of their Pediatric Intensive Care Unit (PICU) stay.5,6 Malnutrition at PICU admission is frequent (15 to 25% prevalence rates) in developing countries; nutritional status deterioration is also an early and frequent phenomenon in this setting with almost one third of critically ill children presenting with nutritional indices decline.7-9 Muscle wasting is also a constant, intense and rapid phenomenon.10 Malnourishment and macronutrient deficits during critical illness have been associated with increased morbidity (infections, weakness, prolonged mechanical ventilation and delayed recovery) as well as increased mortality. However, overfeeding has also been shown to pose harm to critically ill children especially during the acute phase. As the metabolic and endocrine response evolves during the course of critical illness, possibly the nutritional support should also accommodate these changes and differ during the different phases of pediatric critical illness as well.

Although optimal nutrition is considered essential to improve outcomes in critically ill children, large well-designed randomized controlled trials (RCTs) with clinically relevant outcome measures are scarce.11,12 The limited evidence has led to a wide variation in nutritional practices worldwide, between individual clinicians, PICUs and countries.13,14 Yet the evidence is increasing, and the number of publications on nutritional support in pediatric critical illness in 2018 has doubled when compared with 2012 and tripled since 2007. In 2017 the American Society of Parenteral and Enteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM) published their guidelines for the provision of nutritional support in the PICU.15 However, several important clinical topics remained unanswered.16 For instance, term neonates (defined as >37 weeks to 44 weeks gestational age) which comprise around 32% of the PICU population, were excluded from these recommendations.17 As a multidisciplinary research group within Europe, the ESPNIC Metabolism, Endocrinology and Nutrition (MEN) section therefore felt it was timely to address unanswered clinical questions and review new evidence to produce a position statement and recommendations on artificial nutrition in critically ill children.

**Methodology**

**Selection of members**

The working group was composed of a multidisciplinary team of 11 European specialists (5 pediatric intensivists, 2 nurses and 4 dietitians) in nutritional support for critically ill children, who are members of the MEN section of the European Society of Pediatric and Neonatal Intensive Care (ESPNIC). Four members (LT/CJ/KJ/SV) were well trained and experienced in the development and methodology of systematic reviews and development of recommendations. A biostatistician (JvR) was added to the multi-disciplinary team specifically for the expertise in meta-analyses, but did not participate in development of the recommendations or the voting process.

**Question development and search strategy**

The working group met initially, in June 2017, to discuss the project, and generate 15 broad clinical questions. The systematic literature search was performed by biomedical information specialists (EK, SG, GdJ and WB; see acknowledgements) of the Erasmus Medical Centre Library (Rotterdam, The Netherlands) in four databases (Embase.com; Medline Epub (Ovid); Cochrane Central; Web of Science) and included all articles published from 1997 until May 2018 and updated in November 30 2018. Supplement file 1 describes the search terms used per question.

Inclusion and exclusion criteria were agreed by the group. Inclusion criteria were RCTs, case-control, before and after and cohort studies including critically ill term neonates and children (aged ≥37 weeks gestational age – 18 years). We only included manuscripts written in English or French, which excluded three papers, one in Russian two in Chinese. Publications describing studies in pre-term infants were excluded, unless the question specifically related to neonatal PICU patients and no evidence existed in term neonates (Question 4). In addition to reviews, animal studies, case reports, editorials, commentaries, conference abstracts and letters were excluded. Separate publications presenting outcomes from the same study population were included, but seen as one study, and the study that provided the most complete data to answer the question was included. For each of the 15 questions, key search words were defined, and specific search combinations were developed for the four databases (Supplementary file 1).

**Selection of studies**

In order to select the eligible studies, the results from each database were combined and exported to Endnote, followed by removal of duplicates and exportation to a Word document, allowing at least two working group members to separately undertake the screening of the abstracts in a standardized way. Abstracts were screened for eligibility by the group members, and those which were thought to be eligible were automatically exported as final abstract. Areas of disagreement were resolved by discussion. Abstracts that determined to be eligible by one of the two members were discussed with a third reviewer before decision of inclusion or exclusion. If eligibility criteria were met, full manuscripts were procured. Similarly, if a disagreement on the eligibility of the paper occurred, a discussion took place with a third reviewer. We also examined reference lists from included articles for suitable studies. A PRISMA diagram is shown in Supplementary file 2.

**Data extraction and assessment of study quality and evidence grading**

Data from eligible papers were extracted by two reviewers with the primary reviewer not an author on the paper. In addition, the risk of bias was assessed by two reviewers independently using the SIGN critical appraisal checklists available for each study design (<https://www.sign.ac.uk/checklists-and-notes.html>) (Supplementary file 3). Any disagreement with grading was discussed and the two lead authors (LT/FV) reviewed all the evidence grading. The classification of the literature into levels of evidence was performed according to the SIGN grading system (Supplementary file 3).

**Data analysis including meta-analyses**

In some questions, the data were combined statistically in a meta-analysis if they met the following criteria: there was more than one study, the combined studies (in one analysis) were either randomised trials or observational studies, the population and the intervention were sufficiently similar to combine and the outcomes were the same, or for continuous outcome variables, if we had data on the distribution of the variable. To perform the meta-analyses, we a priori defined clinically relevant outcome variables on which the meta-analyses would be performed. These were mortality, new infections, gastro-intestinal complications (vomiting aspiration / diarrhoea / NEC-ischemia), length of ventilation and length of stay (PICU / hospital). Anticipating a broad inconsistency of these outcome variables we chose a pragmatic meta-analysis. The risk of bias tables are presented in Supplementary File 4 For dichotomous outcomes, we used a random effects model for the relative risk of the intervention to compute a pooled relative risk and its 95% CI. The Hartung–Knapp–Sidik–Jonkman method was used to estimate the between-study variance, and a continuity correction of 0.5 was applied in case of zero cell frequencies. The heterogeneity of combined study results was assessed using the inconsistency statistic and tested using Cochran's Q test. The meta-analyses were performed using R version 3.6.1 with the package meta.

**Consensus methodology and grading of the recommendations**

Based on the results from the systematic review and meta-analyses, a first draft of recommendations was composed, including the supporting text and grade of recommendation. The classification of the grades of recommendation (A-D, Good Clinical Practice) was undertaken according to the SIGN grading system (Supplementary file 3).18 In May 2018, a second meeting took place to discuss all questions and review the evidence quality and recommendations. The group generated the position statement and a draft guideline with a total of 32 recommendations, which was followed by a round of electronic voting to gain consensus using a Delphi method in June 2018.19,20 The survey involved voting on each recommendation on 3-point scale with categories: disagree, agree and unsure. This was created and distributed via a proprietary electronic online platform hosted by the University of Southampton (<https://www.isurvey.soton.ac.uk/>) and checked by one of the authors (LM) without identifying features to ensure anonymity. In round 2, we provided the group results and asked the group to re-vote. We defined strong consensus as agreement of >95%, consensus as agreement of 75 - 95% and no consensus as agreement <75%. Feedback received during the first round of online voting was used to modify and improve the recommendations in order to reach a higher degree of consensus at the final online voting in September 2018. Any recommendations with an agreement equal to or lower than 95% were discussed at a consensus meeting which took place on 31 October 2018. Following a revised meta-analysis, a last and final meeting of a core group of 4 members took place in November 2019, which was followed by a final round of electronic voting. The AGREE reporting checklist for guideline development was followed (Supplementary File 5). The ESPNIC process for endorsement of guidelines was undertaken.

**Results**

A total of 7261 abstracts were screened. Subsequently 142 publications were reviewed, and data were extracted (Supplementary file 2) and included in the development of 32 recommendations (Table 1). The general level of evidence was low: out of the 142 publications, 5 (3.5%) were graded 1+ according to the SIGN grading system, 27 (18.9%) were graded 1-, six (4.2%) were graded 2++, 20 (14.0%) were graded 2+, 82 (58.0%) were graded 2-, one (0.7%) was graded 3 and one (0.7%) was graded 4. Furthermore, the data were suitable for meta-analysis for only 11 (sub)questions, all of which had dichotomous outcome measures. All forest plots of the meta-analyses have been provided in supplement file 6. Overall, heterogeneity of the studies suitable for meta-analysis varied with *I2* 0-91% (p-value 0.13-0.83), and two meta-analyses with a *I2* of higher than 50%, 53% and 55% respectively for the impact of gastric versus post-pyloric feeding on aspiration and intermittent versus continuous feeding on diarrhoea. The pooled relative risk showed a significant difference between groups in only 1 out of these 11 meta-analyses. Enteral feeding versus no enteral feeding in children on hemodynamic support resulted in a lower risk of mortality (RR 0.41 [95%CI 0.20 - 0.86]). Accordingly, the grading of the 32 recommendations were as follows: five recommendations were graded as B, five as C, 12 as D and 10 were GCP.

A strong consensus was reached in 21 (66%) and consensus was reached in 11 (34%) of the recommendations. A detailed discussion of the clinical questions, the recommendations with evidence grading, and level of consensus achieved in presented in Supplementary file 7 with a full reference list. The table of evidence is presented in Supplementary file 8. A summary of all recommendations is shown in Table 1. A summary of comparisons between our recommendations and those presented by ASPEN/SCCM is shown in Table 2.

**Discussion**

This position statement with clinical recommendations provides new guidance based on new evidence, as well as reinforcing most of the existing 2017 ASPEN Guidelines. These ASPEN PICU nutrition guidelines published in 2017, were based on a literature search from January 1995 to March 2016 and consisted of 17 recommendations. These ESPNIC clinical recommendations are based on an updated literature search until November 2018. Both the American (ASPEN) and our European guidelines provide expert opinion which is essential in this setting where limited data is available. Our recommendations are predominantly consistent with the ASPEN guideline recommendations (Table 2) which helps assist in the uptake and implementation of guidelines into practice.161 Implementation of evidence into clinical practice remains problematic, in 2017 a European survey of 59 PICUs found that 69% of PICUs still had no local feeding guidelines.13 Additionally, this position statement generated new clinical guidance as half of our clinical questions differed from the ASPEN guidelines. These included guidance on feeding neonates with arterial umbilical arterial catheters; the type of enteral formula to be used; the amount or type of each macronutrient to provide; the value of gastric residual volume to assess feeding tolerance; the use of prokinetics to enhance feeding tolerance and the use of feeding protocols to improve outcomes. Furthermore, these new ESPNIC recommendations covered in more detail the indications for enteral nutrition in various subgroups of patients in clinicians are in general uncertain on how to progress feeding (i.e. term neonates and children on hemodynamic support and after cardiac surgery).13 In addition, our position statement provides a different stand on two recommendations as compared with the ASPEN guidelines, based on new available research. In contrast with the ASPEN guidelines we recommend to consider withholding parenteral nutrition during the first week in neonates and children, independent of their nutritional state.8,15,150 Furthermore, there was also strong consensus in our working group that there is insufficient evidence to recommend a protein/amino acid intake of 1.5 gr/kg/day or higher during the acute phase of disease to benefit clinical outcomse.15 The intake of 1.5 gr/kg/day or higher has shown to prevent cumulative negative protein balance.96,97 However, future research should consider that the exact threshold is unknown, and might overestimate protein/amino acid requirements during acute critical illness, thus further work should therefore also investigate low protein/amino acid intakes during that phase.131

Overall, as expected, the general level of evidence was low, and the meta-analyses provided little value because of the heterogeneity in interventions and outcomes, population and the type of study designs (few RCTs). This resulted in few studies able to be pooled for this analysis. Despite these limitations, we formulated 32 recommendations which can guide PICU healthcare professionals. There are a few key messages to be taken from our position statement. Although hardly any methodologically sound studies exist, recent developments have shown that nutritional interventions in our PICUs are capable of impacting on the short and long-term outcome in critically ill children.92,152 Despite the lack of effect shown of protocols on mortality and NEC in the meta-analysis, as the level of this evidence was low, all individual studies did show positive effect on other variables such as time to initiate feeding and achievement of energy goals, but it was not possible to pool these in a meta-analysis. Therefore, despite this, we still recommend PICUs use feeding protocols which provide guidance on the assessment of nutritional status, and the start and advancement of feeding. A final key messages from this position statement is to encourage the enteral feeding of critically ill neonates and children early wherever possible, unless clear contraindications exist. Although starting early EN is recommended, no evidence exists to support high nutritional intake during the acute phase of critical illness and withholding supplemental PN during the first week in PICU may be considered when enteral nutrition is insufficient.

**Limitations**

We acknowledge that these clinical recommendations are based at times on sparse pediatric evidence. Moreover, for many questions and clinical recommendations we could not be age-specific, although the (patho)physiology of nutritional and metabolic changes during critical illness is age-dependent. For instance, the recommendations specifically for neonates were partially based upon studies in preterm neonates as no evidence existed in term neonates. The threshold of >37 weeks in our recommendations is recognized as rigid and we cannot exclude that some of our recommendations also apply for late preterm (>34 weeks) or early term (>36 weeks) neonates. Similarly, the same arguments can be raised for adolescents, where for certain (older) adolescents, recommendations from adult guidelines might be suitable. However, the mean age in adult ICUs is 60.9 years 162 and it therefore cannot be assumed that critically ill young adults are similar in their (patho)physiologic response to nutritional and metabolic changes to elderly patients. We further acknowledge that, as a priori anticipated, pragmatic meta-analyses were required due to the inconsistencies in the outcome variables. Another limitation is that our consensus voting was based only on the views of our study team of 11 experts. Finally, as already elaborated on in our discussion, aside from several novel features our recommendations have an overlap with the American (ASPEN) guidelines published in 2017. A future collaboration between the American and European societies might improve upcoming guidelines and help implement the recommendations worldwide. Despite these limitations, this work has provided an updated summary of the existing evidence, including questions around term neonates, which are not dealt with by other recommendations or guidelines, yet comprise a significant amount of the European PICU population.

**Conclusion**

This ESPNIC position statement with recommendations provide a ‘best-available-evidence’ guide for clinicians working in PICU to provide nutritional support in this setting. The lack of methodologically sound trials and the heterogeneous character of studies available were important barriers in the generation of these recommendations. Many recommendations are based on expert consensus and have a low level of evidence. Nonetheless, our recommendations support the use of a formal nutritional assessment and a feeding protocol in all PICUs.

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**References**

1. Joosten KF, Kerklaan D, Verbruggen SC. Nutritional support and the role of the stress response in critically ill children. Curr Opin Clin Nutr Metab Care 2016;19:226-33.

2. Joosten KFM, Eveleens RD, Verbruggen S. Nutritional support in the recovery phase of critically ill children. Curr Opin Clin Nutr Metab Care 2018.

3. Keehn A, O'Brien C, Mazurak V, et al. Epidemiology of interruptions to nutrition support in critically ill children in the pediatric intensive care unit. JPEN J Parenter Enteral Nutr 2015;39:211-7.

4. Leong AY, Cartwright KR, Guerra GG, Joffe AR, Mazurak VC, Larsen BM. A Canadian survey of perceived barriers to initiation and continuation of enteral feeding in PICUs. Pediatr Crit Care Med 2014;15:e49-55.

5. Hulst J, Joosten K, Zimmermann L, et al. Malnutrition in critically ill children: from admission to 6 months after discharge. Clin Nutr 2004;23:223-32.

6. Hulst JM, van Goudoever JB, Zimmermann LJ, et al. The effect of cumulative energy and protein deficiency on anthropometric parameters in a pediatric ICU population. Clin Nutr 2004;23:1381-9.

7. Prince NJ, Brown KL, Mebrahtu TF, Parslow RC, Peters MJ. Weight-for-age distribution and case-mix adjusted outcomes of 14,307 pediatric intensive care admissions. Intensive Care Med 2014;40:1132-9.

8. van Puffelen EH, J M; Vanhorebeek, I; Dulfer, K; Van den Berghe, G; Verbruggen, S C A T; Joosten, K F M. Outcomes of delaying parenteral nutrition for 1 week vs initiation within 24 hours among undernourished children in pediatric intensive care. JAMA Network Open 2018;1:e182668.

9. van Puffelen E, Hulst JM, Vanhorebeek I, et al. Effect of late versus early initiation of parenteral nutrition on weight deterioration during PICU stay: Secondary analysis of the PEPaNIC randomised controlled trial. Clin Nutr 2019.

10. Valla FV, Young DK, Rabilloud M, et al. Thigh Ultrasound Monitoring Identifies Decreases in Quadriceps Femoris Thickness as a Frequent Observation in Critically Ill Children. Pediatr Crit Care Med 2017;18:e339-e47.

11. Joffe A, Anton N, Lequier L, et al. Nutritional support for critically ill children. Cochrane Database Syst Rev 2009:CD005144.

12. 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;36:218-23.

13. Tume LN, Balmaks R, da Cruz E, et al. Enteral Feeding Practices in Infants With Congenital Heart Disease Across European PICUs: A European Society of Pediatric and Neonatal Intensive Care Survey. Pediatr Crit Care Med 2018;19:137-44.

14. Kerklaan D, Fivez T, Mehta NM, et al. Worldwide Survey of Nutritional Practices in PICUs. Pediatr Crit Care Med 2016;17:10-8.

15. Mehta NM, Skillman HE, Irving SY, 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;18:675-715.

16. Valla FV, Gaillard Le Roux B, Tume LN. Pediatric Intensive Care Nutrition Guidelines 2017: Key Questions Remain Unanswered. JPEN J Parenter Enteral Nutr 2018;42:9.

17. <http://www.picanet.org.uk/Audit/Annual-Reporting/PICANet_2017_Annual_Report_Tables_and_Figures_FINAL_v2.0.pdf> Accessed PICANET, 2018. (Accessed November 2019, 2018, at <http://www.picanet.org.uk/Audit/Annual-Reporting/PICANet_2017_Annual_Report_Tables_and_Figures_FINAL_v2.0.pdf> )

18. Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ 2001;323:334-6.

19. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. J Adv Nurs 2000;32:1008-15.

20. Keeney S, Hasson F, McKenna HP. A critical review of the Delphi technique as a research methodology for nursing. Int J Nurs Stud 2001;38:195-200.

21. Wakita M, Fukatsu A, Amagai T. Nutrition assessment as a predictor of clinical outcomes for infants with cardiac surgery: using the prognostic nutritional index. Nutr Clin Pract 2011;26:192-8.

22. Vermilyea S, Slicker J, El-Chammas K, et al. Subjective global nutritional assessment in critically ill children. JPEN J Parenter Enteral Nutr 2013;37:659-66.

23. Valla FV, Ford-Chessel C, Meyer R, et al. A training program for anthropometric measurements by a dedicated nutrition support team improves nutritional status assessment of the critically ill child. Pediatr Crit Care Med 2015;16:e82-8.

24. Irving SY, Seiple S, Nagle M, Falk S, Mascarenhas M, Srinivasan V. Perceived barriers to anthropometric measurements in critically ill children. Am J Crit Care 2015;24:e99-e107.

25. Valla FV, Berthiller J, Gaillard-Le-Roux B, et al. Faltering growth in the critically ill child: prevalence, risk factors, and impaired outcome. Eur J Pediatr 2018;177:345-53.

26. Grippa RB, Silva PS, Barbosa E, Bresolin NL, Mehta NM, Moreno YM. Nutritional status as a predictor of duration of mechanical ventilation in critically ill children. Nutrition 2017;33:91-5.

27. Sotoudeh M, Khalili M, Azizian M, Imani B. PREVALENCE OF MALNUTRITION BASED ON UNDER WEIGHT INPATIENTS IN PEDIATRIC INTENSIVE CARE UNIT. International Journal Of Pharmacy & Technology 2016;8:12333-40.

28. Bechard LJ, Duggan C, Touger-Decker R, et al. Nutritional Status Based on Body Mass Index Is Associated With Morbidity and Mortality in Mechanically Ventilated Critically Ill Children in the PICU. Crit Care Med 2016;44:1530-7.

29. Radman M, Mack R, Barnoya J, et al. The effect of preoperative nutritional status on postoperative outcomes in children undergoing surgery for congenital heart defects in San Francisco (UCSF) and Guatemala City (UNICAR). J Thorac Cardiovasc Surg 2014;147:442-50.

30. Anton-Martin P, Papacostas M, Lee E, Nakonezny PA, Green ML. Underweight Status Is an Independent Predictor of In-Hospital Mortality in Pediatric Patients on Extracorporeal Membrane Oxygenation. JPEN J Parenter Enteral Nutr 2018;42:104-11.

31. Leite HP, de Lima LF, de Oliveira Iglesias SB, Pacheco JC, de Carvalho WB. Malnutrition may worsen the prognosis of critically ill children with hyperglycemia and hypoglycemia. JPEN J Parenter Enteral Nutr 2013;37:335-41.

32. Zamberlan P, Leone C, Tannuri U, Carvalho WB, Delgado AF. Nutritional risk and anthropometric evaluation in pediatric liver transplantation. Clinics (Sao Paulo) 2012;67:1387-92.

33. de Souza Menezes F, Leite HP, Koch Nogueira PC. Malnutrition as an independent predictor of clinical outcome in critically ill children. Nutrition 2012;28:267-70.

34. Castillo A, Santiago MJ, Lopez-Herce J, et al. Nutritional status and clinical outcome of children on continuous renal replacement therapy: a prospective observational study. BMC Nephrol 2012;13:125.

35. Numa A, McAweeney J, Williams G, Awad J, Ravindranathan H. Extremes of weight centile are associated with increased risk of mortality in pediatric intensive care. Crit Care 2011;15:R106.

36. Botran M, Lopez-Herce J, Mencia S, et al. Relationship between energy expenditure, nutritional status and clinical severity before starting enteral nutrition in critically ill children. Br J Nutr 2011;105:731-7.

37. Srinivasan V, Nadkarni VM, Helfaer MA, Carey SM, Berg RA, American Heart Association National Registry of Cardiopulmonary Resuscitation I. Childhood obesity and survival after in-hospital pediatric cardiopulmonary resuscitation. Pediatrics 2010;125:e481-8.

38. Anderson JB, Beekman RH, 3rd, Border WL, et al. Lower weight-for-age z score adversely affects hospital length of stay after the bidirectional Glenn procedure in 100 infants with a single ventricle. J Thorac Cardiovasc Surg 2009;138:397-404 e1.

39. Eskedal LT, Hagemo PS, Seem E, et al. Impaired weight gain predicts risk of late death after surgery for congenital heart defects. Arch Dis Child 2008;93:495-501.

40. Kelleher DK, Laussen P, Teixeira-Pinto A, Duggan C. Growth and correlates of nutritional status among infants with hypoplastic left heart syndrome (HLHS) after stage 1 Norwood procedure. Nutrition 2006;22:237-44.

41. Hulst JM, van Goudoever JB, Zimmermann LJ, Tibboel D, Joosten KF. The role of initial monitoring of routine biochemical nutritional markers in critically ill children. J Nutr Biochem 2006;17:57-62.

42. Fivez T, Hendrickx A, Van Herpe T, et al. An Analysis of Reliability and Accuracy of Muscle Thickness Ultrasonography in Critically Ill Children and Adults. JPEN J Parenter Enteral Nutr 2016;40:944-9.

43. Briassoulis G, Zavras N, Hatzis T. Malnutrition, nutritional indices, and early enteral feeding in critically ill children. Nutrition 2001;17:548-57.

44. Davis ET, Xie L, Levenbrown Y. Impact of Obesity on Outcomes in Critically Ill Children. JPEN J Parenter Enteral Nutr 2017:148607117725043.

45. Ross PA, Newth CJ, Leung D, Wetzel RC, Khemani RG. Obesity and Mortality Risk in Critically Ill Children. Pediatrics 2016;137:e20152035.

46. Ward SL, Gildengorin V, Valentine SL, et al. Impact of Weight Extremes on Clinical Outcomes in Pediatric Acute Respiratory Distress Syndrome. Crit Care Med 2016;44:2052-9.

47. Goh VL, Wakeham MK, Brazauskas R, Mikhailov TA, Goday PS. Obesity is not associated with increased mortality and morbidity in critically ill children. JPEN J Parenter Enteral Nutr 2013;37:102-8.

48. Abdul Manaf Z, Kassim N, Hamzaid NH, Razali NH. Delivery of enteral nutrition for critically ill children. Nutr Diet 2013;70:120-5.

49. Ang B, Han WM, Wong JJM, Lee AN, Chan YH, Lee JH. Impact of a nurse-led feeding protocol in a pediatric intensive care unit. Proc Singap Healthc 2016;25:35-42.

50. Braudis NJ, Curley MA, Beaupre K, et al. Enteral feeding algorithm for infants with hypoplastic left heart syndrome poststage I palliation. Pediatr Crit Care Med 2009;10:460-6.

51. Canarie MF, Barry S, Carroll CL, et al. Risk Factors for Delayed Enteral Nutrition in Critically Ill Children. Pediatr Crit Care Med 2015;16:e283-9.

52. Carpenito KR, Prusinski R, Kirchner K, et al. Results of a Feeding Protocol in Patients Undergoing the Hybrid Procedure. Pediatr Cardiol 2016;37:852-9.

53. Lee H, Koh SO, Kim H, Sohn MH, Kim KE, Kim KW. Avoidable causes of delayed enteral nutrition in critically ill children. J Korean Med Sci 2013;28:1055-9.

54. Mikhailov TA, Kuhn EM, Manzi J, et al. Early enteral nutrition is associated with lower mortality in critically ill children. JPEN J Parenter Enteral Nutr 2014;38:459-66.

55. Tripathi S, Kaur H, Varayil JE, Hurt RT. Effects of enteral nutrition on clinical outcomes among mechanically ventilated and sedated patients in the pediatric intensive care unit. Signa Vitae 2015;10.

56. Mikhailov TA, Gertz SJ, Kuhn EM, Scanlon MC, Rice TB, Goday PS. Early Enteral Nutrition Is Associated With Significantly Lower Hospital Charges in Critically Ill Children. JPEN J Parenter Enteral Nutr 2018;42:920-5.

57. Bagci S, Keles E, Girgin F, et al. Early initiated feeding versus early reached target enteral nutrition in critically ill children: An observational study in pediatric intensive care units in Turkey. J Paediatr Child Health 2018;54:480-6.

58. Balakrishnan B, Flynn-O'Brien KT, Simpson PM, Dasgupta M, Hanson SJ. Enteral Nutrition Initiation in Children Admitted to Pediatric Intensive Care Units After Traumatic Brain Injury. Neurocrit Care 2019;30:193-200.

59. Malakouti A, Sookplung P, Siriussawakul A, et al. Nutrition support and deficiencies in children with severe traumatic brain injury. Pediatr Crit Care Med 2012;13:e18-24.

60. Fayazi SA, M. Zahraei Fard, S. Farokh Payam, H. Ahmadie Batvandy, Z. Comparing Two Methods of Enteral Nutrition in Terms of their Complications and the Time Needed to Reach Goal Calorie in Children Hospitalized in ICU. Int J Pediatr 2016;4:2119-30.

61. Gurgueira GL, Leite HP, Taddei JA, de Carvalho WB. Outcomes in a pediatric intensive care unit before and after the implementation of a nutrition support team. JPEN J Parenter Enteral Nutr 2005;29:176-85.

62. Hamilton S, McAleer DM, Ariagno K, et al. A stepwise enteral nutrition algorithm for critically ill children helps achieve nutrient delivery goals\*. Pediatr Crit Care Med 2014;15:583-9.

63. Mara J, Gentles E, Alfheeaid HA, et al. An evaluation of enteral nutrition practices and nutritional provision in children during the entire length of stay in critical care. BMC Pediatr 2014;14:186.

64. Meyer R, Harrison S, Sargent S, Ramnarayan P, Habibi P, Labadarios D. The impact of enteral feeding protocols on nutritional support in critically ill children. J Hum Nutr Diet 2009;22:428-36.

65. Petrillo-Albarano T, Pettignano R, Asfaw M, Easley K. Use of a feeding protocol to improve nutritional support through early, aggressive, enteral nutrition in the pediatric intensive care unit. Pediatr Crit Care Med 2006;7:340-4.

66. Yoshimura S, Miyazu M, Yoshizawa S, et al. Efficacy of an enteral feeding protocol for providing nutritional support after pediatric cardiac surgery. Anaesth Intensive Care 2015;43:587-93.

67. Hanekamp MN, Spoel M, Sharman-Koendjbiharie M, et al. Gut hormone profiles in critically ill neonates on extracorporeal membrane oxygenation. J Pediatr Gastroenterol Nutr 2005;40:175-9.

68. Hanekamp MN, Spoel M, Sharman-Koendjbiharie I, Peters JW, Albers MJ, Tibboel D. Routine enteral nutrition in neonates on extracorporeal membrane oxygenation. Pediatr Crit Care Med 2005;6:275-9.

69. Piena M, Albers MJ, Van Haard PM, Gischler S, Tibboel D. Introduction of enteral feeding in neonates on extracorporeal membrane oxygenation after evaluation of intestinal permeability changes. J Pediatr Surg 1998;33:30-4.

70. Wertheim HF, Albers MJ, Piena-Spoel M, Tibboel D. The incidence of septic complications in newborns on extracorporeal membrane oxygenation is not affected by feeding route. J Pediatr Surg 2001;36:1485-9.

71. Ong EG, Eaton S, Wade AM, et al. Randomized clinical trial of glutamine-supplemented versus standard parenteral nutrition in infants with surgical gastrointestinal disease. Br J Surg 2012;99:929-38.

72. Pettignano R, Heard M, Davis R, Labuz M, Hart M. Total enteral nutrition versus total parenteral nutrition during pediatric extracorporeal membrane oxygenation. Crit Care Med 1998;26:358-63.

73. López-Herce J, Mencía S, Sánchez C, Santiago MJ, Bustinza A, Vigil D. Postpyloric enteral nutrition in the critically ill child with shock: A prospective observational study. Nutrition Journal 2008;7.

74. Iannucci GJ, Oster ME, Mahle WT. Necrotising enterocolitis in infants with congenital heart disease: the role of enteral feeds. Cardiol Young 2013;23:553-9.

75. King W, Petrillo T, Pettignano R. Enteral nutrition and cardiovascular medications in the pediatric intensive care unit. JPEN J Parenter Enteral Nutr 2004;28:334-8.

76. Panchal AK, Manzi J, Connolly S, et al. Safety of Enteral Feedings in Critically Ill Children Receiving Vasoactive Agents. JPEN J Parenter Enteral Nutr 2016;40:236-41.

77. del Castillo SL, McCulley ME, Khemani RG, et al. Reducing the incidence of necrotizing enterocolitis in neonates with hypoplastic left heart syndrome with the introduction of an enteral feed protocol. Pediatr Crit Care Med 2010;11:373-7.

78. Jeffries HE, Wells WJ, Starnes VA, Wetzel RC, Moromisato DY. Gastrointestinal morbidity after Norwood palliation for hypoplastic left heart syndrome. Ann Thorac Surg 2006;81:982-7.

79. Luce WA, Schwartz RM, Beauseau W, et al. Necrotizing enterocolitis in neonates undergoing the hybrid approach to complex congenital heart disease. Pediatr Crit Care Med 2011;12:46-51.

80. Manuri L, Morelli S, Agati S, et al. Early hybrid approach and enteral feeding algorithm could reduce the incidence of necrotising enterocolitis in neonates with ductus-dependent systemic circulation. Cardiol Young 2017;27:154-60.

81. Natarajan G, Reddy Anne S, Aggarwal S. Enteral feeding of neonates with congenital heart disease. Neonatology 2010;98:330-6.

82. Sánchez C, López-Herce J, Carrillo A, Bustinza A, Sancho L, Vigil D. Transpyloric enteral feeding in the postoperative of cardiac surgery in children. Journal of Pediatric Surgery 2006;41:1096-102.

83. Sahu MK, Singal A, Menon R, et al. Early enteral nutrition therapy in congenital cardiac repair postoperatively: A randomized, controlled pilot study. Ann Card Anaesth 2016;19:653-61.

84. Typpo KV, Larmonier CB, Deschenes J, Redford D, Kiela PR, Ghishan FK. Clinical characteristics associated with postoperative intestinal epithelial barrier dysfunction in children with congenital heart disease. Pediatr Crit Care Med 2015;16:37-44.

85. Davey AM, Wagner CL, Cox C, Kendig JW. Feeding premature infants while low umbilical artery catheters are in place: a prospective, randomized trial. J Pediatr 1994;124:795-9.

86. Barrington KJ. Umbilical artery catheters in the newborn: effects of position of the catheter tip. Cochrane Database Syst Rev 2000:CD000505.

87. Willis L, Thureen P, Kaufman J, Wymore E, Skillman H, da Cruz E. Enteral feeding in prostaglandin-dependent neonates: is it a safe practice? J Pediatr 2008;153:867-9.

88. Lucron H, Chipaux M, Bosser G, et al. [Complications of prostaglandin E1 treatment of congenital heart disease in pediatric medical intensive care]

Complications du traitement par prostaglandines E1 des cardiopathies congenitales en reanimation medicale pediatrique. Arch Mal Coeur Vaiss 2005;98:524-30.

89. Becker KC, Hornik CP, Cotten CM, et al. Necrotizing enterocolitis in infants with ductal-dependent congenital heart disease. Am J Perinatol 2015;32:633-8.

90. Havranek T, Johanboeke P, Madramootoo C, Carver JD. Umbilical artery catheters do not affect intestinal blood flow responses to minimal enteral feedings. J Perinatol 2007;27:375-9.

91. Larsen BMK, Beggs MR, Leong AY, Kang SH, Persad R, Garcia Guerra G. Can energy intake alter clinical and hospital outcomes in PICU? Clin Nutr ESPEN 2018;24:41-6.

92. Fivez T, Kerklaan D, Mesotten D, et al. Early versus Late Parenteral Nutrition in Critically Ill Children. N Engl J Med 2016;374:1111-22.

93. Joosten KF, Verhoeven JJ, Hazelzet JA. Energy expenditure and substrate utilization in mechanically ventilated children. Nutrition 1999;15:444-8.

94. Dylewski M, Wibbenmeyer L, Bessey PQ, et al. Nutrition Outcomes. Journal of Burn Care & Research 2013;34:371-5.

95. Coss-Bu JA, Jefferson LS, Walding D, David Y, Smith EO, Klish WJ. Resting energy expenditure and nitrogen balance in critically ill pediatric patients on mechanical ventilation. Nutrition 1998;14:649-52.

96. Jotterand Chaparro C, Laure Depeyre J, Longchamp D, Perez MH, Taffe P, Cotting J. How much protein and energy are needed to equilibrate nitrogen and energy balances in ventilated critically ill children? Clin Nutr 2016;35:460-7.

97. Bechard LJ, Parrott JS, Mehta NM. Systematic review of the influence of energy and protein intake on protein balance in critically ill children. J Pediatr 2012;161:333-9 e1.

98. de Betue CT, van Waardenburg DA, Deutz NE, et al. Increased protein-energy intake promotes anabolism in critically ill infants with viral bronchiolitis: a double-blind randomised controlled trial. Arch Dis Child 2011;96:817-22.

99. van Waardenburg DA, de Betue CT, Goudoever JB, Zimmermann LJ, Joosten KF. Critically ill infants benefit from early administration of protein and energy-enriched formula: a randomized controlled trial. Clin Nutr 2009;28:249-55.

100. Coss-Bu JA, Klish WJ, Walding D, Stein F, Smith EO, Jefferson LS. Energy metabolism, nitrogen balance, and substrate utilization in critically ill children. Am J Clin Nutr 2001;74:664-9.

101. Briassoulis G, Tsorva A, Zavras N, Hatzis T. Influence of an aggressive early enteral nutrition protocol on nitrogen balance in critically ill children. J Nutr Biochem 2002;13:560.

102. Mehta NM, Bechard LJ, Cahill N, et al. Nutritional practices and their relationship to clinical outcomes in critically ill children--an international multicenter cohort study\*. Crit Care Med 2012;40:2204-11.

103. Mtaweh H, Smith R, Kochanek PM, et al. Energy expenditure in children after severe traumatic brain injury. Pediatr Crit Care Med 2014;15:242-9.

104. De Wit B, Meyer R, Desai A, Macrae D, Pathan N. Challenge of predicting resting energy expenditure in children undergoing surgery for congenital heart disease. Pediatr Crit Care Med 2010;11:496-501.

105. Sy J, Gourishankar A, Gordon WE, et al. Bicarbonate kinetics and predicted energy expenditure in critically ill children. Am J Clin Nutr 2008;88:340-7.

106. Framson CM, LeLeiko NS, Dallal GE, Roubenoff R, Snelling LK, Dwyer JT. Energy expenditure in critically ill children. Pediatr Crit Care Med 2007;8:264-7.

107. Havalad S, Quaid MA, Sapiega V. Energy expenditure in children with severe head injury: lack of agreement between measured and estimated energy expenditure. Nutr Clin Pract 2006;21:175-81.

108. van der Kuip M, de Meer K, Oosterveld MJ, Lafeber HN, Gemke RJ. Simple and accurate assessment of energy expenditure in ventilated pediatric intensive care patients. Clin Nutr 2004;23:657-63.

109. Vazquez Martinez JL, Martinez-Romillo PD, Diez Sebastian J, Ruza Tarrio F. Predicted versus measured energy expenditure by continuous, online indirect calorimetry in ventilated, critically ill children during the early postinjury period. Pediatr Crit Care Med 2004;5:19-27.

110. Hardy CM, Dwyer J, Snelling LK, Dallal GE, Adelson JW. Pitfalls in predicting resting energy requirements in critically ill children: a comparison of predictive methods to indirect calorimetry. Nutr Clin Pract 2002;17:182-9.

111. White MS, Shepherd RW, McEniery JA. Energy expenditure in 100 ventilated, critically ill children: improving the accuracy of predictive equations. Crit Care Med 2000;28:2307-12.

112. Briassoulis G, Venkataraman S, Thompson AE. Energy expenditure in critically ill children. Crit Care Med 2000;28:1166-72.

113. Verhoeven JJ, Hazelzet JA, van der Voort E, Joosten KF. Comparison of measured and predicted energy expenditure in mechanically ventilated children. Intensive Care Med 1998;24:464-8.

114. Jotterand Chaparro C, Moullet C, Taffe P, 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;42:976-86.

115. Mehta NM, Smallwood CD, Joosten KF, Hulst JM, Tasker RC, Duggan CP. Accuracy of a simplified equation for energy expenditure based on bedside volumetric carbon dioxide elimination measurement--a two-center study. Clin Nutr 2015;34:151-5.

116. Meyer R, Kulinskaya E, Briassoulis G, et al. The challenge of developing a new predictive formula to estimate energy requirements in ventilated critically ill children. Nutr Clin Pract 2012;27:669-76.

117. Lopez-Herce Cid J, Sanchez Sanchez C, Mencia Bartolome S, Santiago Lozano MJ, Carrillo Alvarez A, Bellon Cano JM. [Energy expenditure in critically ill children: correlation with clinical characteristics, caloric intake, and predictive equations]

Consumo calorico en el nino critico: relacion con las caracteristicas clinicas, el aporte calorico y las formulas teoricas de calculo de las necesidades. An Pediatr (Barc) 2007;66:229-39.

118. Taylor RM, Cheeseman P, Preedy V, Baker AJ, Grimble G. Can energy expenditure be predicted in critically ill children? Pediatr Crit Care Med 2003;4:176-80.

119. Verbruggen SC, de Betue CT, Schierbeek H, et al. Reducing glucose infusion safely prevents hyperglycemia in post-surgical children. Clin Nutr 2011;30:786-92.

120. de Betue CT, Verbruggen SC, Schierbeek H, et al. Does a reduced glucose intake prevent hyperglycemia in children early after cardiac surgery? a randomized controlled crossover study. Crit Care 2012;16:R176.

121. Larsen BM, Goonewardene, L. A.,Joffe, A. R.,Van Aerde, J. E.,Field, C. J.,Olstad, D. L.,Clandinin, M. T. Pre-treatment with an intravenous lipid emulsion containing fish oil (eicosapentaenoic and docosahexaenoic acid) decreases inflammatory markers after open-heart surgery in infants: a randomized, controlled trial. Clin Nutr 2012;31:322-9.

122. Geukers VG, Dijsselhof ME, Jansen NJ, et al. The effect of short-term high versus normal protein intake on whole-body protein synthesis and balance in children following cardiac surgery: a randomized double-blind controlled clinical trial. Nutr J 2015;14:72.

123. Botran M, Lopez-Herce J, Mencia S, Urbano J, Solana MJ, Garcia A. Enteral nutrition in the critically ill child: comparison of standard and protein-enriched diets. J Pediatr 2011;159:27-32 e1.

124. Verbruggen SC, Coss-Bu J, Wu M, et al. Current recommended parenteral protein intakes do not support protein synthesis in critically ill septic, insulin-resistant adolescents with tight glucose control. Crit Care Med 2011;39:2518-25.

125. Hauschild DB, Oliveira LDA, Farias MS, et al. Enteral Protein Supplementation in Critically Ill Children: A Randomized Controlled Pilot and Feasibility Study. JPEN J Parenter Enteral Nutr 2019;43:281-9.

126. Kyle UG, Akcan-Arikan A, Silva JC, Goldsworthy M, Shekerdemian LS, Coss-Bu JA. Protein Feeding in Pediatric Acute Kidney Injury Is Not Associated With a Delay in Renal Recovery. J Ren Nutr 2017;27:8-15.

127. Wong JJ, Han WM, Sultana R, Loh TF, Lee JH. Nutrition Delivery Affects Outcomes in Pediatric Acute Respiratory Distress Syndrome. JPEN J Parenter Enteral Nutr 2017;41:1007-13.

128. Mehta NM, Bechard LJ, Zurakowski D, Duggan CP, Heyland DK. Adequate enteral protein intake is inversely associated with 60-d mortality in critically ill children: a multicenter, prospective, cohort study. Am J Clin Nutr 2015;102:199-206.

129. Merhar SL, Meinzen-Derr J, Sprague J, et al. Safety and Tolerability of Enteral Protein Supplementation for Infants With Brain Injury. Nutr Clin Pract 2015;30:546-50.

130. de Betue CT, Joosten KF, Deutz NE, Vreugdenhil AC, van Waardenburg DA. Arginine appearance and nitric oxide synthesis in critically ill infants can be increased with a protein-energy-enriched enteral formula. Am J Clin Nutr 2013;98:907-16.

131. Vanhorebeek I, Verbruggen S, Casaer MP, et al. Effect of early supplemental parenteral nutrition in the pediatric ICU: a preplanned observational study of post-randomisation treatments in the PEPaNIC trial. Lancet Respir Med 2017;5:475-83.

132. Zhang H, Gu Y, Mi Y, Jin Y, Fu W, Latour JM. High-energy nutrition in pediatric cardiac critical care patients: a randomized controlled trial. Nurs Crit Care 2018.

133. Eveleens RD, Dungen DK, Verbruggen S, Hulst JM, Joosten KFM. Weight improvement with the use of protein and energy enriched nutritional formula in infants with a prolonged PICU stay. J Hum Nutr Diet 2018.

134. Vidigal MV, Leite HP, Nogueira PC. Factors associated with peptide-based formula prescription in a pediatric intensive care unit. J Pediatr Gastroenterol Nutr 2012;54:620-3.

135. Barbosa E, Moreira EA, Goes JE, Faintuch J. Pilot study with a glutamine-supplemented enteral formula in critically ill infants. Rev Hosp Clin Fac Med Sao Paulo 1999;54:21-4.

136. Briassoulis G, Filippou O, Hatzi E, Papassotiriou I, Hatzis T. Early enteral administration of immunonutrition in critically ill children: results of a blinded randomized controlled clinical trial. Nutrition 2005;21:799-807.

137. Carcillo JA, Dean JM, Holubkov R, et al. The randomized comparative pediatric critical illness stress-induced immune suppression (CRISIS) prevention trial. Pediatr Crit Care Med 2012;13:165-73.

138. Carcillo JA, Dean JM, Holubkov R, et al. Interaction Between 2 Nutraceutical Treatments and Host Immune Status in the Pediatric Critical Illness Stress-Induced Immune Suppression Comparative Effectiveness Trial. JPEN J Parenter Enteral Nutr 2017;41:1325-35.

139. Jacobs BR, Nadkarni V, Goldstein B, et al. Nutritional immunomodulation in critically ill children with acute lung injury: feasibility and impact on circulating biomarkers. Pediatr Crit Care Med 2013;14:e45-56.

140. Jordan I, Balaguer M, Esteban ME, et al. Glutamine effects on heat shock protein 70 and interleukines 6 and 10: Randomized trial of glutamine supplementation versus standard parenteral nutrition in critically ill children. Clin Nutr 2016;35:34-40.

141. McNally JD, Nama N, O'Hearn K, et al. Vitamin D deficiency in critically ill children: a systematic review and meta-analysis. Crit Care 2017;21:287.

142. Cvijanovich NZ, King JC, Flori HR, Gildengorin G, Vinks AA, Wong HR. Safety and Dose Escalation Study of Intravenous Zinc Supplementation in Pediatric Critical Illness. JPEN J Parenter Enteral Nutr 2016;40:860-8.

143. Horn D, Chaboyer W. Gastric feeding in critically ill children: a randomized controlled trial. Am J Crit Care 2003;12:461-8.

144. Meert KL, Daphtary KM, Metheny NA. Gastric vs small-bowel feeding in critically ill children receiving mechanical ventilation: a randomized controlled trial. Chest 2004;126:872-8.

145. Sonmez Duzkaya D, Yildiz S. Effect of two different feeding methods on preventing ventilator associated pneumonia in the pediatric intensive care unit (PICU): A randomised controlled study. Aust Crit Care 2016;29:139-45.

146. Horn D, Chaboyer W, Schluter PJ. Gastric residual volumes in critically ill pediatric patients: a comparison of feeding regimens. Aust Crit Care 2004;17:98-100, 2-3.

147. Kamat P, Favaloro-Sabatier J, Rogers K, Stockwell JA. Use of methylene blue spectrophotometry to detect subclinical aspiration in enterally fed intubated pediatric patients. Pediatr Crit Care Med 2008;9:299-303.

148. Tume LN, Bickerdike A, Latten L, et al. Routine gastric residual volume measurement and energy target achievement in the PICU: a comparison study. Eur J Pediatr 2017;176:1637-44.

149. Gharpure V, Meert KL, Sarnaik AP. Efficacy of erythromycin for postpyloric placement of feeding tubes in critically ill children: a randomized, double-blind, placebo controlled study. JPEN J Parenter Enteral Nutr 2001;25:160-5.

150. van Puffelen E, Vanhorebeek I, Joosten KFM, Wouters PJ, Van den Berghe G, Verbruggen S. Early versus late parenteral nutrition in critically ill, term neonates: a preplanned secondary subgroup analysis of the PEPaNIC multicentre, randomised controlled trial. Lancet Child Adolesc Health 2018;2:505-15.

151. van Puffelen E, Hulst JM, Vanhorebeek I, et al. Outcomes of Delaying Parenteral Nutrition for 1 Week vs Initiation Within 24 Hours Among Undernourished Children in Pediatric Intensive Care: A Subanalysis of the PEPaNIC Randomized Clinical Trial. JAMA Netw Open 2018;1:e182668.

152. Verstraete S, Verbruggen SC, Hordijk JA, et al. Long-term developmental effects of withholding parenteral nutrition for 1 week in the pediatric intensive care unit: a 2-year follow-up of the PEPaNIC international, randomised, controlled trial. Lancet Respir Med 2019;7:141-53.

153. Kyle UG, Lucas LA, Mackey G, et al. Implementation of Nutrition Support Guidelines May Affect Energy and Protein Intake in the Pediatric Intensive Care Unit. J Acad Nutr Diet 2016;116:844-51 e4.

154. Brown A-M, Forbes ML, Vitale VS, Tirodker UH, Zeller R. Effects of a Gastric Feeding Protocol on Efficiency of Enteral Nutrition in Critically Ill Infants and Children. ICAN: Infant, Child, & Adolescent Nutrition 2012;4:175-80.

155. Wong JJ, Ong C, Han WM, Lee JH. Protocol-driven enteral nutrition in critically ill children: a systematic review. JPEN J Parenter Enteral Nutr 2014;38:29-39.

156. Gentles E, Mara J, Diamantidi K, et al. Delivery of enteral nutrition after the introduction of practice guidelines and participation of dietitians in pediatric critical care clinical teams. J Acad Nutr Diet 2014;114:1974-80 e3.

157. Kaufman J, Vichayavilas P, Rannie M, et al. Improved nutrition delivery and nutrition status in critically ill children with heart disease. Pediatrics 2015;135:e717-25.

158. Geukers V, Neef M, Dijsselhof M, Sauerwein H, Bos A. Effect of a nurse-driven feeding algorithm and the institution of a nutritional support team on energy and macronutrient intake in critically ill children2012.

159. Simsic JM, Carpenito KR, Kirchner K, et al. Reducing variation in feeding newborns with congenital heart disease. Congenit Heart Dis 2017;12:275-81.

160. Furlong-Dillard J, Neary A, Marietta J, et al. Evaluating the Impact of a Feeding Protocol in Neonates before and after Biventricular Cardiac Surgery. Pediatric quality & safety 2018;3:e080.

161. van Puffelen E, Jacobs A, Verdoorn CJM, et al. International survey of De-implementation of initiating parenteral nutrition early in Pediatric intensive care units. BMC Health Serv Res 2019;19:379.

162. UK Intensive Care National Audit and Research centre. Key statistics from the Case Mix Programme — adult, general critical care units 2015-2016. http://www.icnarc.org.uk [accessed December 2019]