



ASPEN/SCCM Pediatric Critical Care Nutrition Guideline: Protocol

Introduction

Nutritional status on admission, nutrient delivery and nutritional deterioration are important factors that may impact outcomes from pediatric critical illness.¹⁻³ Preexisting malnutrition is common in children admitted to the pediatric intensive care unit (PICU).⁴ Furthermore, imbalance between nutrient requirement and delivery, excessive nutrient losses, increased energy expenditure, decreased nutrient intake, and altered nutrient absorption or utilization during critical illness may result in nutritional deterioration during the PICU stay. Preexisting or acquired nutritional deterioration may result in altered physiologic responses and negatively influence outcomes in this group of patients.⁵ Children with certain disease characteristics may be at higher risk for worsening nutritional status with increased morbidity.⁶ A vast majority of children in the PICU with respiratory failure experience muscle atrophy. Immobilized children with respiratory failure are particularly vulnerable, incurring 1.5-7.0% muscle loss daily.⁷ Thus, careful nutritional status assessment on admission and serially during the ICU course helps early identification of vulnerable patients in whom nutritional therapies might help improve outcomes.

There continues to be interest and cumulative increase in evidence to support best practices related to nutrition in the PICU. This document represents an update to the guidelines published in 2017, as a collaborative effort between the American Society for Parenteral and Enteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM). The overarching objective of this collaborative effort is to update and summarize best practices in nutrition therapy for critically ill children, after a review and appraisal of available evidence.

Objective: The objective of this guideline will be to provide nutritional guidance for the care of patients in the Pediatric Intensive Care Unit (PICU).

Audience: This guideline is intended for dietitians, nurses, pharmacists, physicians, speech language pathologists and any other medical health professional involved in the nutritional care of PICU patients.

The Panel of Experts

The guideline is comprised of two panels of experts, a clinical expert panel and a bias panel. The current clinical panel is comprised of Nilesh M Mehta (Chair, MD), Jorge Cosbu (MD), Elizabeth Farrington (PharmD), Praveen Goday (MD), Sharon Y Irving (CRNP), Peter Johnson (PharmD), Heather Skillman (RD), and Sarah Vermilyea (RD). The interdisciplinary panel was selected and approved by the Board of Directors of ASPEN and SCCM.

A second panel, the Bias Panel of experts will be formed to perform all bias analyses and provide commentary on the direct relationship between the recommendations made and the available evidence. The Bias Panel will be comprised PhD-level researchers with a background in nutrition. The bias panel will be trained and closely overseen by the methodologist and Editor-in-Chief, Liam McKeever, PhD, RDN, who will mentor the entire process and coordinate the actions of the clinical panel and the bias panel.

Conflicts of Interest

David Church has no conflicts of interest to disclose.

Elizabeth Farrington has no conflicts of interest to disclose.

Praveen Goday has no conflicts of interest to disclose.

Peter Johnson has no conflicts of interest to disclose.

Nilesh Mehta has received funding from the NIH - NIDDK RO1DK132348-01.

Jacob Mey has no conflicts of interest to disclose.

Liam McKeever has no conflicts of interest to disclose.

Sarah Peterson has no conflicts of interest to disclose.

Heather Skillman has no conflicts of interest to disclose.

Sarah Vermilyea has no conflicts of interest to disclose.

Panel members will abstain from voting on any recommendations for which they have a conflict of interest. This includes conflicts of interest that become apparent as the guideline is being carried out. The Editor-in-Chief (L.M.) will be responsible for identifying and acting upon all known conflicts of interest.

Request for Commentary

From the time this protocol is published electronically and up to two months following electronic publication, ***we welcome and request commentary on any and every aspect of this protocol.*** We would like to hear from all key stake holders including but not limited to all levels of dietitian, physician, nurse, speech language pathologist, pharmacist, epidemiologist, methodologist, public health expert, occupational therapist, etc.... We also welcome you to show this list of PICOT questions to select patients to provide us with feedback from the patient perspective.

Timely comments from readers of this protocol are welcomed and requested. Please complete [this survey](#) to submit your feedback. We will receive comments for two months after the initial electronic posting of this protocol, so please complete the survey to submit feedback by 3/31/2024.

PICOT Questions

Table 1 below contains the list of questions this guideline intends to answer. These are termed PICOT questions because they include the intended **P**opulation, **I**ntervention, **C**omparator or **C**ontrol, **O**utcomes, and **T**imeframe. Besides each outcome is a judgement concerning the outcome's importance. If the outcome concerns life and death, or is of utmost importance in the context of the question itself, the importance is deemed 'critical'. If the outcome is not life or death, or of utmost importance, but of unquestionable importance to

decision making, the outcome is deemed 'important, but not critical'. If the outcome is of questionable importance, it is deemed 'of limited importance'.⁸ These importance levels are then included in the decision-making process for which outcome variables will be most directive of our recommendations. At the bottom of each PICOT question will be a list of relevant co-interventions. These are additional interventions that occur as a byproduct of receiving the main intervention that provide an alternative explanation for the outcome. Most co-interventions are part of the natural sequelae of the intervention (part of the intervention package) and part of the big picture effect the PICOT is trying to address. These types of co-interventions will not be listed in the tables below, but will be captured in each study at the data extraction phase. The Co-intervention box in the tables below is reserved only for known co-interventions that are expected to differ between studies in ways that may impact the relationship between the intervention and the outcome. In most cases this box will be empty.

Table 1 PICOT Questions

General Research Question 1			
In critically ill children, how should malnutrition be detected and managed?			
PICOT 1	In critically ill children, does the use of any specific nutrition screening or assessment tool better predict nutrition status than any other screening/assessment tool?		
Outcomes			Importance
Grip Strength (beginning at age 4 years)			Important, but not Critical
Nutrition Status (Body Composition, signs and symptoms of malnutrition)			Important, but not Critical
Diagnosis of malnutrition via 2015 AND/ASPEN indicators			Important, but not Critical
Diagnosis of malnutrition via nutrition focused physical examination			Important, but not Critical
Diagnosis of malnutrition via SGNA			Important, but not Critical
Cointerventions	None	RCT's Ethical?	Yes
PICOT 2	In critically ill children with obesity, does the use of any specific nutrition screening or assessment tool better predict nutrition status than any other screening/assessment tool?		
Outcomes			Importance
Grip Strength (beginning at age 4 years)			Important, but not Critical
Nutrition Status (Body Composition, signs and symptoms of malnutrition)			Important, but not Critical
BMI calculation and definition via the CDC growth curves			Important, but not critical
Cointerventions	None	RCT's Ethical?	Yes
PICOT 3	In critically ill children, does nutrition intervention targeted at patients with a diagnosis of malnutrition or overnutrition impact clinical outcomes?		
Outcomes			Importance
PICU Mortality			Critical
Hospital Mortality			Critical
30-Day Mortality (28 day accepted)			Critical
60-Day Mortality			Critical
90-Day Mortality			Critical
NEC / intestinal ischemia			Critical
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)			Critical
Infection Rate (suspected or lab confirmed)			Important but not Critical
Wound healing			Important but not Critical
Time on Mechanical Ventilation			Important but not Critical
PICU Length of Stay			Important but not Critical
Hospital Length of Stay			Important but not Critical
Cointerventions	None	RCT's Ethical?	Yes
General Research Question 2			

What are the energy and protein requirements for critically ill children and how should these be determined?			
PICOT 4	In critically ill children, does intensive nutrition therapy designed to meet resting energy expenditure (through IC or equation) vs standard care improve clinical outcomes?		
Outcomes			Importance
PICU Mortality			Critical
Hospital Mortality			Critical
30-Day Mortality (28 day accepted)			Critical
60-Day Mortality			Critical
90-Day Mortality			Critical
NEC / intestinal ischemia			Critical
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)			Critical
Infection Rate (suspected or lab confirmed)			Important but not Critical
Wound healing			Important but not Critical
Time on Mechanical Ventilation			Important but not Critical
PICU Length of Stay			Important but not Critical
Hospital Length of Stay			Important but not Critical
Cointerventions	Early Mobility in the ICU Route – use of PN versus EN to achieve energy goals.	RCT's Ethical?	Yes
PICOT 5	In critically ill children, does nutrition therapy designed to deliver higher protein dose vs standard care improve clinical outcomes?		
Outcomes			Importance
PICU Mortality			Critical
Hospital Mortality			Critical
30-Day Mortality (28 day accepted)			Critical
60-Day Mortality			Critical
90-Day Mortality			Critical
NEC / intestinal ischemia			Critical
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)			Critical
Infection Rate (suspected or lab confirmed)			Important but not Critical
Wound healing			Important but not Critical
Time on Mechanical Ventilation			Important but not Critical
PICU Length of Stay			Important but not Critical
Hospital Length of Stay			Important but not Critical
Nutrition Status (Body Composition, signs and symptoms of malnutrition)			Important, but not Critical
Grip Strength			Important but not Critical
Cointerventions	Early Mobility in the ICU PN vs EN	RCT's Ethical?	Yes
PICOT 6	In critically ill children, does energy dosing based on measured value by indirect calorimetry vs equation estimated dosing improve clinical outcomes?		
Outcomes			Importance
PICU Mortality			Critical
Hospital Mortality			Critical
30-Day Mortality (28 day accepted)			Critical
60-Day Mortality			Critical
90-Day Mortality			Critical
NEC / intestinal ischemia			Critical
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)			Critical
Infection Rate (suspected or lab confirmed)			Important but not Critical
Wound healing			Important but not Critical
Time on Mechanical Ventilation			Important but not Critical
PICU Length of Stay			Important but not Critical
Hospital Length of Stay			Important but not Critical

Cointerventions	None	RCT's Ethical?	Yes
PICOT 7	In critically ill children who do not have access to IC, does energy dosing according to more specific equations vs age-based kcal/kg dosing improve clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28 day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
PICOT 8	In critically ill children, does the use of an algorithm-based feeding guideline to reach target goals vs no algorithm improve nutrition delivery and/or clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28 day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Critical	
Protein Received (g, g/kg, % Goal)		Critical	
Volume Received (mL, % Goal Volume)		Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
General Research Question 3			
Does timing of initiation of enteral nutrition impact clinical outcomes?			
PICOT 9	In critically ill children, does the introduction of early EN (≤ 48 hrs) vs no early EN improve clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28 day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	

Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
PICOT 10	In critically ill children who require hemodynamic support (vasoactive medications, ECMO), does initiating early EN vs later EN (once hemodynamic stability is achieved) support impact clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28 day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
PICOT 11	In critically ill children, does a continuous gastric feeding strategy vs intermittent bolus gastric feeding strategy impact delivery and/or clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28-day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
General Research Question 4			
What is the best way to monitor for and/or manage EN tolerance?			
PICOT 12	In critically ill children, does routine checking of Gastric Residual Volume (GRV) to guide enteral feeding vs no GRV checking improve clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28 day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	

NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cost Effectiveness		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
PICOT 13	In critically ill children, does gastric feeding compared to post-pyloric feeding impact nutrition delivery, tolerance, and/or clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28-day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Nutrition Status (via measures of body composition and weight)		Important but not Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cost Effectiveness		Important but not Critical	
Cointerventions	Prokinetics, Use of specialized tubes/techniques to ensure proper and expedited tube placement	RCT's Ethical?	Yes
PICOT 14	In critically ill children, does the provision of non-standard formulas (e.g., those with custom energy density macronutrient type, and/or composition, immune enhancement) vs standard formulas impact tolerance or clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28 day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Nutrition Status (via measures of body composition and weight)		Important but not Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	

Hospital Length of Stay		Important but not Critical	
Cost Effectiveness		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
General Research Question 6			
How and when should parenteral nutrition be administered in critically ill children?			
PICOT 15	In critically ill children with contraindications to use of EN or inability to advance EN, does initiating PN earlier in care (<7 days after admission) vs later impact clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28-day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Nutrition Status (via measures of body composition and weight)		Important but not Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cost Effectiveness		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
PICOT 16	In critically ill children, does provision of omega-6-reduced lipid emulsions vs 100% soy-based emulsions impact clinical outcomes?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28-day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Long term liver function (ALT/AST/ Bilirubin)		Critical	
Nutrition Status (via measures of body composition and weight)		Important but not Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cost Effectiveness		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes
General Research Question 7			
What is the role of a dietitian or nutrition support team in the management of critically ill children?			

PICOT 17	In critically ill children, does use of a dedicated multidisciplinary nutrition support team vs no dedicated multidisciplinary nutrition support team improve clinical outcomes and/or the achievement of nutrition goals?		
Outcomes		Importance	
PICU Mortality		Critical	
Hospital Mortality		Critical	
30-Day Mortality (28-day accepted)		Critical	
60-Day Mortality		Critical	
90-Day Mortality		Critical	
NEC / intestinal ischemia		Critical	
Functional outcomes (e.g. Functional Status Scale/ Pediatric QOL)		Critical	
Nutrition Status (via measures of body composition and weight)		Important but not Critical	
Infection Rate (suspected or lab confirmed)		Important but not Critical	
Energy Received (kcal, kcal/kg, % Goal)		Important but not Critical	
Protein Received (g, g/kg, % Goal)		Important but not Critical	
Volume Received (mL, % Goal Volume)		Important but not Critical	
Wound healing		Important but not Critical	
Time on Mechanical Ventilation		Important but not Critical	
PICU Length of Stay		Important but not Critical	
Hospital Length of Stay		Important but not Critical	
Cost Effectiveness		Important but not Critical	
Cointerventions	None	RCT's Ethical?	Yes

Methods:

The Search Strategy

The PubMed/MEDLINE database will be searched from 2001 to present. The search strategy aims to identify relevant literature on nutritional support in pediatric critical care. We utilized a combination of Medical Subject Headings (MeSH) and text words, categorized by nutrition-related and critical illness-related terms, as well as inclusion/exclusion criteria. Analogous search strategies will be created for the EMBASE, Cochrane Central, and CINAHL databases.

MeSH Terms:

Nutrition-Related: "Nutritional Support"[Mesh], "Malnutrition"[Mesh], "Nutrition Assessment"[Mesh], "Energy Intake"[Mesh], "Energy Metabolism"[MeSH], "Dietary Proteins"[Mesh], "Fat Emulsions, Intravenous"[Mesh], "Nutritional Status"[MeSH], "Mass Screening"[MeSH], "Nutrition Disorders"[MeSH].

Critical Illness-Related: "Critical Illness"[Mesh], "Intensive Care Units, Pediatric"[Mesh], "Critical Care" [MeSH].

Pediatric Population-Related: "Pediatrics"[Mesh], "Infant"[Mesh], "Adolescent"[Mesh], "Young Adult"[Mesh], "Child"[Mesh].

Inclusion: "Humans" [MeSH].

Text Words (Title/Abstract):

Nutrition-Related: malnutrition, malnourished, inadequate, "nutritional assessment", "malnutrition screening", "energy needs", "energy requirement", "caloric requirement", "energy expenditure", kcal*, kilocalorie*, calori*, "kcal/kg", "kcal/kg", "protein needs", "protein requirement", "amino acid requirement", "protein intake", "estimated protein", "estimated amino acid", "lipid emulsions", "SMOF", "soy", "soya", "MOLE", "SOLE", "fish oil", "SO-ILE", "intralipid", "enteral nutrition", "enteral feeding", "enterally fed", tubefeed*, "tube-feeding", "tube feeding", "j-tube", "g-tube", "jejunal feeding", "gastric feeding", "parenteral nutrition", "parenteral feeding", "parenteral feed", "parenterally fed", "IV feeding", "intravenous feeding", "IV fed", "intravenously fed".

Critical Illness-Related: "critical illness", "Critically Ill", "ICU", PICU, "intensive care".

Inclusionary Terms: Randomized Control Trials [Filter]

Exclusionary Text Terms: Adult, elderly, geriatric, senescen*

The text-based portion of the search is restricted to the non-MEDLINE database, but to address the potential for miscataloged terms, a secondary text-based search of the MEDLINE PubMed database will also be run, restricted to text-terms found in the title or abstract of the citation.

This search will be further restricted to randomized control trials with the exception that a specialized search for pre-planned subanalysis of randomized control trials will also be run using the following terms: "subgroup", "sub-analysis", "post hoc", "secondary analysis".

For PICOT Questions 1 and 2, which assess the validity of specific nutrition screening and assessment tools, we will search for validation studies using our screening/assessment based terms with a filter composed of the following terms:

"Validation Study" [Publication Type], "Validation", "Confirmatory Studies", "Reproducibility of Results"[Mesh], "Predictive Value of Tests"[Mesh], "Sensitivity and Specificity"[Mesh], "Validation"[Title/Abstract], "Confirmatory"[Title/Abstract], "Criterion Validity", "Content Validity", "Construct Validity", "Face Validity"

Data Acquisition

Training: Twenty-five citations will be uploaded into Rayyan for the team calibration test. Using their PICOT questions and inclusion criteria, the team will individually screen the 25 studies and determine if they meet inclusion criteria. If the team achieves less than 75% overall percent agreement, the discrepancies will be discussed, 25 new citations will be uploaded, and the group will try again. This will continue until they achieve ≥ 75 overall percent agreement, at which time, they will be permitted to move onto to official citation screening in Covidence.

Screening: All citations will be uploaded into Covidence for screening. For any given article, all steps below will be performed in duplicate (by two reviewers) and discrepancies will be adjudicated by a third reviewer. First, citation titles and abstracts will be screened for relevance to our PICOT questions. Then, a full text review will be performed for any citations that were

deemed relevant in the previous phase of review. Articles that meet our inclusion criteria will be moved forward to the final phase of data extraction.

Inclusion/Exclusion Criteria/Study Design Selection

The patient populations included in these guidelines are children < or =18 years of age, with medical, surgical, and cardiac diagnoses, who are admitted to the pediatric intensive care unit (PICU) with an expected length of stay (LOS) >2–3 days. These guidelines are not intended for neonates (less than 30 days of age) or adult patients (> 18 years of age). Neonates are physiologically different from older infants and children and have different macro and micronutrient requirements; therefore, these guidelines do not include them. These guidelines are not intended for patients with specific diagnoses, such as burn injuries. These guidelines are directed toward generalized patient populations, but, like any other management strategy in the PICU, nutrition therapy should be tailored to the individual patient.

For each question, we will restrict the study design most able to answer that specific question. The decision will be made as follows (Figure 2). If randomized control trials (RCT) are available, we will restrict to RCT's and their a priori planned sub analyses, provided their randomization structure is preserved. If RCT's are not available, but are ethically feasible, we will call for RCT's and include high quality quasi-experimental designs, defined as those designs that have a true control group and demonstrable baseline similarity between groups. If RCT's are not ethically feasible, we will ask ourselves if there are known confounders in the exposure/outcome relationship that cannot be completely managed through adjustment. If the answer is no, then we will restrict to prospective cohort studies that adjust for the known confounder and high quality quasi-experimental designs. If the answer is yes, we will restrict to only include high-quality quasi-experimental designs. To be considered a high-quality quasi-experimental design, the study must have a true control group and demonstrate similarity between the two groups compared. Co-interventions will be permitted only if they can be reasonably assumed to be similar between groups.

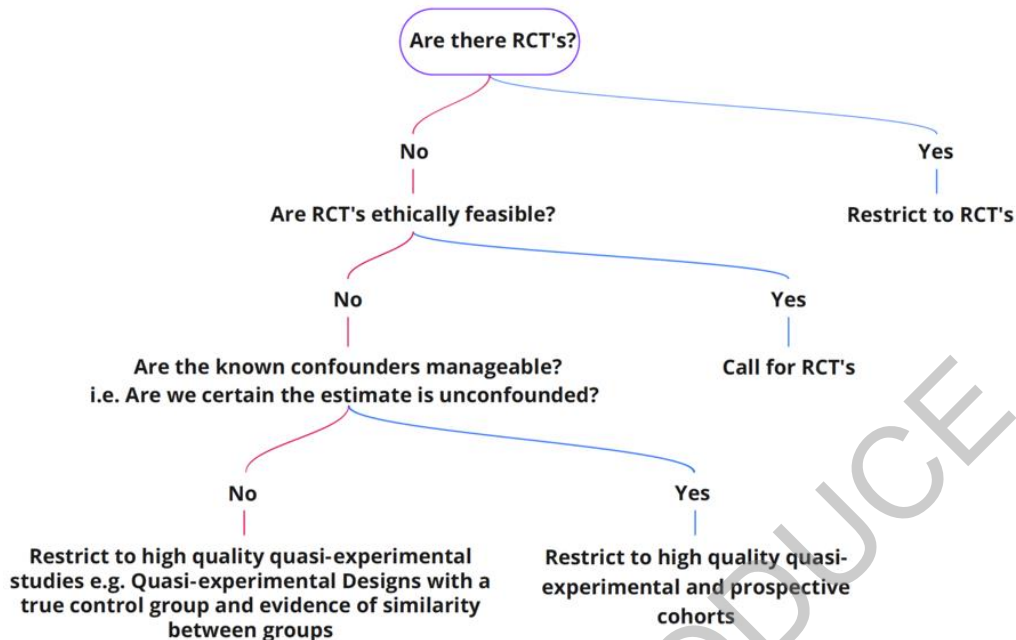


Figure 1: Decision Tree for Study Design Inclusion

Bias Analysis

Study quality will be assessed according to its methodologic vulnerability to bias using different tools for different study types. For RCT's, the Risk of Bias 2 (ROB2)⁹ tool will be used. For quasi-experimental studies, the Risk of Bias in Non-randomized Study Interventions (ROBINS-I)¹⁰ tool will be used. For prospective cohort studies, the Newcastle-Ottawa scale¹¹ will be used. For RCT's the Clinical Panel will create a list of potential co-interventions to consider in the bias assessment. For prospective cohorts, they will determine a list of confounders that require adequate adjustment. These lists will be handed to the Bias Panel who will perform the official bias analysis. All bias analyses will be performed in duplicate. The results of all bias analyses will be published as part of the supplement for this guideline and discussed as strengths and limitations in the body of the guideline.

Quality of Evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system will be used to assess the quality of our evidence in regard to its ability to answer our PICOT questions. This will be used to rate the quality of evidence for each outcome across all studies. The Clinical Panel will then determine which outcomes are most critical and this will be used to inform the overall quality of the evidence for each PICOT question. All data will be tabulated and presented in the supplement as a Summary of Findings Table.

Statistical Analysis

Wherever three or more studies exist with interventions, comparators, outcomes, and populations similar enough to justify conflation, Forest Plots will be created with summary statistics using a random effects model to account for the minor population differences between hospitals. All forest plots will utilize a Knapp-Hartung adjustment.^{12, 13} Heterogeneity

will be assessed using the I^2 statistic. If the I^2 is greater than 0.5, we will perform sub-analyses as an attempt to explain the heterogeneity. Publication bias will be assessed through funnel plots and Egger tests wherever ≥ 10 studies are available for conflation into a forest plot.

Formulation of Recommendations

Recommendations will be formulated using the GRADE Criteria. The GRADE process separates the body of evidence quality rating from the strength of the recommendation permitting a benefits and harms analysis. Evidence quality will be listed underneath each recommendation. Recommendations will be labeled as strong or weak based upon the balance of potential benefit and harm. Where the recommendation is strong, we will use the term “recommend” regarding our guideline recommendation. Where the recommendation strength is weak, we will use the term “suggest”.

Wherever possible, these recommendations will be based upon the data analyzed. Where inadequate data is present to guide a recommendation, the clinical panel will formulate a consensus of expert opinions using a modified Delphi technique. Briefly, the clinical panel will meet to discuss the various potential benefits and harms of the intervention in question. Based on this conversation, the chair will formulate recommendations for each PICOT question. This will be sent out to the clinical panel, who will either agree with the wording of the recommendation or return it with comments. These responses will be deidentified and returned to the chair. If each expert opinion recommendation has $<70\%$ agreement, the chair will alter the questions to be more agreeable to the panel and send them out again. This process will repeat until $\geq 70\%$ agreement is achieved. The process will then start over with an external panel of at least 8 outside experts who will receive the current state of the recommendations from the chair and send back de-identified responses. When the external panel has $\geq 70\%$ agreement on each expert opinion recommendation, the recommendation will be considered finalized. The external panel will have at least 1 patient representative to ensure input from this often-neglected stakeholder.

Review

Upon completion, a draft of the guideline will be sent to both the ASPEN Clinical Practice Committee and the ASPEN Pediatric Section for review. It will also be sent to external reviewers through the Journal of Parenteral and Enteral Nutrition for Review and independent reviewers designated by the Society for Pediatric Critical Care Medicine?

Updates

This guideline will be updated every 5 years.

Conclusion

Involvement of all key stakeholders is crucial to the success and generalizability of any guideline. We need your expertise to help make this guideline the best it can be. Please send us your comments and concerns and we will consider them carefully in the next iteration of this protocol.

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