Review Article

Optimal nutrition therapy in paediatric critical care in the Asia-Pacific and Middle East: a consensus

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Background and Objectives: Current practices and available resources for nutrition therapy in paediatric intensive care units (PICUs) in the Asia Pacific-Middle East region are expected to differ from western countries. Existing guidelines for nutrition management in critically ill children may not be directly applicable in this region. This paper outlines consensus statements developed by the Asia Pacific-Middle East Consensus Working Group on Nutrition Therapy in the Paediatric Critical Care Environment. Challenges and recommendations unique to the region are described. **Methods and Study Design:** Following a systematic literature search from 2004-2014, consensus statements were developed for key areas of nutrient delivery in the PICU. This review focused on evidence applicable to the Asia Pacific-Middle East region. Quality of evidence and strength of recommendations were rated according to the Grading of Recommendation Assessment, Development and Evaluation approach. **Results:** Enteral nutrition (EN) is the preferred mode of nutritional support. Feeding algorithms that optimize EN should be encouraged and must include: assessment and monitoring of nutritional status, selection of feeding route, time to initiate and advance EN, management strategies for EN intolerance and indications for using parenteral nutrition (PN). Despite heterogeneity in nutritional status of patients, availability of resources and diversity of cultures, PICUs in the region should consider involvement of dieticians and/or nutritional support teams. **Conclusions:** Robust evidence for several aspects of optimal nutrition therapy in PICUs is lacking. Nutritional assessment must be implemented to document prevalence and impact of malnutrition. Nutritional support must be given greater priority in PICUs, with particular emphasis in optimizing EN delivery.

Key Words: Asia Pacific, children, critical care, Middle East, nutrition

INTRODUCTION

Nutrition is an important component of patient management in the paediatric intensive care unit (PICU). Critically ill infants and children may have an increased metabolic need, which predisposes them to nutritional deterioration during illness. Furthermore, the complex PICU environment often impedes nutrient delivery in this population.[1] Malnutrition is common among critically ill chil-

dren, especially in the developing world, and is associated with increased morbidity and mortality.[2-4] Failure to meet nutritional requirements, due to sub-optimal nutritional intake from critical illness, is associated with poorer outcomes, particularly in those with low nutritional reserves.[5]

The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) published clinical guidelines for nutritional support in critically ill children in 2009.[6] Newer studies have been published since then, although data from PICUs in Asia and the Middle East remain scarce. Critically ill children in these countries may face additional challenges such as higher incidence of malnutrition at baseline, and limitations of budget, inadequate training and lack of resources for nutrition therapies.

The first meeting of the Asia Pacific-Middle East Consensus Working Group on Nutrition Therapy in the Paediatric Critical Care Environment, including members from eight countries, was held in Singapore in 2014. The group reviewed the literature, audited existing PICU nutrition practices in the region, shared best practices, and identified unique clinical issues pertaining to paediatric critical care nutrition and next steps in promoting effective, evidence-based nutrition therapy in this region. We present the highlights of the proceedings of the meeting in this special report. Wherever possible, evidence-based consensus statements on specific aspects of paediatric critical care nutrition were developed. The opinions of the Working Group members do not necessarily represent the opinion of any national or international societies.

METHODS
Scope and purpose
Based on their expertise in paediatric critical care and nutrition, ten experts from Australia, India, Indonesia, Malaysia, Singapore, Thailand, the Kingdom of Saudi Arabia and the United Arab Emirates (UAE) were invited to join the Asia Pacific-Middle East Consensus Working Group on Nutrition Therapy in the Paediatric Care Environment. An international expert in paediatric critical care nutrition from outside the region was invited as the expert guide for the Working Group. The first Working Group meeting was held in Singapore on 7th and 8th June 2014. The consensus statements developed at this meeting were then further refined and finalized at the 2nd Working Group meeting in Hong Kong in April 2015.

The primary objective of the meetings and consequently this report and the consensus statements is to add a regional, updated perspective to currently available clinical guidelines on nutrition support in the paediatric intensive care environment.[6,7] The consensus statements are suggested as recommendations for paediatric patients aged 1 month to 18 years in the Asia-Pacific and Middle East region. These recommendations may not be applicable to PICUs in other regions with differing resources, and in certain subsets of paediatric patients such as premature infants or those with chronic renal and liver failure.

Evidence review
Systematic literature searches were performed on Pub-Med by the Working Group members to identify studies on paediatric critical care nutrition published from 2004-2014. Studies related to the following topics were reviewed: a) nutritional assessment and screening, b) assessment of energy requirement, c) modes of nutritional support, d) macronutrient constitution for critically ill children, and e) role of adjuncts to promote optimal nutrition in the PICU. The search terms used for each topic are listed in Supplementary Table 1. The quality of evidence and strength of recommendations were rated according to the Grading of Recommendation Assessment, Development and Evaluation (GRADE) approach.[8] A modified final grading for each recommendation was based on feasibility, safety and evidence-base for these practices. Relevant studies were collated into evidence tables for each topic, and consensus statements were developed by an iterative process at the meeting and endorsed by the entire group. Members of the Asia Pacific-Middle East region, who were not present at the meeting, reviewed the manuscript, contributed to the consensus statements and endorsed them. They have been acknowledged at the end of the manuscript.

RESULTS
Table 1 highlights the consensus statements that were developed by the Working Group. Relevant studies that were identified for each area and their key features are summarized in Tables 2-6. The development of the individual statements is discussed in greater detail below.

DISCUSSION
The Working Group found limited studies over the ten year period and evidence in paediatric critical care nutrition is unfortunately scanty. A recent survey reported that the nutritional procedures and practices followed in the PICUs in the Asia Pacific-Middle East region are significantly different from America and Europe.[9] This is mainly due to greater heterogeneity in population, genetic variations, high prevalence of malnutrition, low prioritization and lack of resources in terms of funding and qualified personnel. Our consensus manuscript can be applied to achieve best practices and improve clinical outcomes in the region. However, it is clear that the data is scarce and weak and there is need for more good quality data and larger studies. By utilizing the GRADE system, we were able to make recommendations in a uniform fashion, but the lack of evidence meant that some of these recommendations are weak.

Nutritional assessment and screening
Statement 1
Weight and height/length should be measured in all children on admission to the PICU. In addition, head circumference should be measured in children aged 0-3 years. (Strong recommendation)

Statement 2a
Within the same country, uniform reference standards should be used. International reference standards such as WHO/CDC are recommended unless robust regional data are available. (Weak recommendation)

Table 1. Summary of consensus statements NNM

#	Consensus statement	Recommendation
1	Weight and height/length should be measured in all children on admission to the PICU. In addition, head circumference should be measured in children aged 0-3 years.	Strong
2a	Within the same country, uniform reference standards should be used. International reference standards such as WHO/CDC are recommended unless robust regional data are available.	Weak
2b	Utilization of z-scores instead of percentiles is encouraged.	Moderate
3a	Indirect calorimetry (IC) remains the gold standard for estimating resting energy requirement.	Strong
3b	Resting energy requirement may be calculated based on predictive equations if IC is not available.	Weak
3c	Feeding should be introduced at 25%-50% of energy requirements and advanced slowly in severely malnourished patients and those with prolonged fasting, to avoid the risk of re-feeding syndrome.	Moderate
4	Regular reassessment of the child's nutritional status is necessary to avoid underfeeding/overfeeding.	Moderate
5	Enteral nutrition (EN) is the preferred mode of nutritional support in critically children with a functional gastrointestinal tract and no absolute contraindications to enteral feeding.	Strong
6a	Gastric feeding is recommended as the first line route for EN.	Moderate
6b	Post-pyloric (small bowel) feeding may be used when gastric route is contraindicated or not tolerated.	Weak
7a	Total parenteral nutrition (TPN) should be considered when EN is contraindicated.	Strong
7b	Supplemental PN should be used if nutritional requirements cannot be fully met by EN alone.	Weak
7c	PN should be used when EN is unable (or not anticipated to be able) to meet nutritional goal within 5-7 days in previously well children without existing malnutrition, and earlier in infants and severely malnourished patients.	Weak
8	Recommended protein intake is age-dependent with a minimum of 1.5 g/kg/day.	Moderate
9	Nutrition therapy in the PICU should be guided by a Nutrition Support Team (NST).	Moderate
10	Feeding algorithms should be encouraged in PICUs. EN feeding algorithms should include the following components: assessment and monitoring of nutritional status and intolerance, feeding routes, management strategies for feeding intolerance, and target time to initiate and advance feeding.	Moderate
11a	Nutrition should be emphasized as part of everyday patient management in the PICU.	Strong
11b	Development of national and/or regional guidelines for nutritional requirements and assessment of critically ill children should be encouraged. Education of doctors, nurses, and dieticians is crucial to increase the knowledge of healthcare professionals in the Asia-Pacific and Middle East.	Moderate

Statement 2b

Utilization of z-scores instead of percentiles is encouraged. (Moderate recommendation)

The A.S.P.E.N. guidelines recommend that nutritional assessment on admission to the PICU is necessary to identify children at risk and to guide nutrition support in the PICU.[6,10] The Joint Commission (USA) requires assessment of nutrition risk within 24 hours of hospital admission.[11] In addition, those not at risk should also be screened if they are hospitalized for more than 7 days since malnutrition is highly prevalent in Asia; nearly half of malnourished children under age of 5 reside in this region.[12] The first step in nutrition risk assessment is to take a thorough history, with particular attention paid to acute presenting complaint, nutritional history, growth data, chronic illnesses, previous hospitalizations and surgical procedures performed. Other current methods of assessing nutritional status in critically ill children rely on a combination of objective anthropometric, dietary, biochemical and immunologic measurements (Table 2).

Anthropometry is a valuable index of nutrition status in critically ill children. However, in some clinical situations (e.g., multiple trauma, burns and surgical patients), accurate anthropometric measurement can be challenging. In addition, the use of proper equipment, accurate measurement techniques and appropriate references are necessary. Currently, the use of z-score is generally recommended.[6,10,13-15]

The use of Subjective Global Nutrition Assessment (SGNA) was considered.[16] SGNA, comprising both nutrition focused medical history-taking and physical examination, is a novel clinical approach that has been found to be useful in predicting nutrition-associated complications (Table 2). This method has been adapted successfully for use in pre-operative children in Thailand.[17] The adapted version was demonstrated to provide good correlation between malnutrition and infectious complications and longer hospital stay.[16-18] The relationship between SGNA and standard anthropometric measures was strong and significant, indicating that SGNA could also be used to identify malnutrition in critically ill children. Being a tool for nutritional assessment, SGNA may not be appropriate for rapid nutritional screening in the PICU. Recently, the paediatric nutrition screening tool (PNST) was developed to facilitate quick nutritional screening in inpatient paediatric patients, having application for wide variety of clinical diagnoses and age groups and suitable for patients needing in-depth nutritional analysis.[19] This tool was deemed as a simpler alternative to other existing nutritional screening tools such as Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP), Screening Tool Risk on Nutritional status and Growth (STRONGkids) and Paediatric Yorkhill Malnutrition Score. However, its application in the PICU patients has

Table 2. Evidence for the role of nutritional assessment

Study, year and level of evidence	Study population and design	Primary outcome measures	Main results	Comments
Vermilyea S et al (2013)[18] Level II	Prospective, single-center study of SGNA in the PICU. N=150 (age: 31 days-5 years).	Follow-up 30 days, mortality, PICU LOS	SGNA showed reasonable correlation with standard anthropometry in categorizing patients into well nourished, moderate, and severe malnourished state. Moderate inter-rater reproducibility. No difference in the groups for hospital LOS, PELOD score or severity of illness.	SGNA helped classify PICU patients into nutritional categories in this single center study. The clinical outcomes between these groups were not significantly different.
De Souza Menezes F et al (2012)[88] Level II	Prospective, single center cohort study examining the effect of nutritional status on clinical outcomes in PICU patients. N=385 [median (IQR) age: 18 (3.9-66) months. Nutritional status determined by weight-for-age and BMI z-scores, based on WHO standards.	30-day mortality, PICU LOS, length of MV.	175 (45.5%) were malnourished on admission (z score <-2). Malnutrition was associated with greater length of MV (multiple logistic regression) - OR 1.76, 95%; CI 1.08-2.88; p=0.024. No effect on mortality or LOS.	Anthropometric variables allow classification of PICU patients into relevant nutritional categories. Malnutrition was associated with prolonged MV duration.
Mehta NM et al (2012)[5] Level II	International prospective cohort study in children requiring MV longer than 48hours in PICU. N=500 (age: 1 month-18 years).	Impact of nutritional variables and PICU characteristic on 60-day mortality and acquired infection.	>30% of patients had severe malnutrition (BMI z score ≤2) on admission.	Multicenter study of 31 PICUs in 8 countries. Malnutrition is highly prevalent on admission. Energy and protein delivery is inadequate in critically ill children.
Zamberlan P et al (2011)[10] Level II	Prospective study consecutive children hospitalized for 7 days in PICU. N=90 (median age 2.9 years)	Measured fluid balance, nutrient intake and monitored anthropometric assessment weekly with evaluation of complications in PICU.	80% received EN, PN used in 10%. Average calorie and protein intake was 82 kcal/kg and 2.7 g/kg/d respectively. High prevalence of malnutrition (up to 50% of all PICU admissions) by various anthropometric variables. Significant decrease in arm circumference and triceps skinfold thickness by 7th day of hospitalization.	Consecutive patients enrolled. Malnutrition is prevalent in PICU and probably related to illness. Anthropometric deterioration is seen in this population at the end of 7 days in the PICU. No relationship between nutritional status and outcomes examined in this study.

BMI: body mass index; EN: enteral nutrition; LOS: length of stay; MV: mechanical ventilation; PICU: paediatric intensive care unit; SGNA: subjective global nutritional assessment; SD: standard deviation; WHO: World Health Organization.

Table 2. Evidence for the role of nutritional assessment (cont.)

Study, year and level of evidence	Study population and design	Primary outcome measures	Main results	Comments
Secker DJ et al (2007)[16] Level II	Prospective study, examining the validity of SGNA as a method of nutritional assessment in children undergoing major thoracic or abdominal surgery. N=175 (age: 31 days-17.9 years)	Patients classified into well nourished, moderately malnourished or severely malnourished according to SGNA. Association between nutritional status and surgical complications at 30 days.	Malnutrition as identified by the SGNA was associated with increased LOS and higher rates of infection.	Only children with major thoracic or abdominal surgery were included. SGNA is a valid tool for assessment of nutritional status in children. Helps identify groups at higher risk of post-operative complications and prolonged hospitalization.
Hulst JM et al (2006)[20] Level II	Prospective descriptive cohort study in a multidisciplinary PICU. N=105 (age: 7 days-16 years).	Association between abnormal laboratory parameters (serum urea, albumin, triglycerides and magnesium) on admission and a) clinical outcomes and b) changes in anthropometric parameters in PICU patients.	Biochemical abnormalities were prevalent on admission to the PICU, but did not predict changes in anthropometric measurement.	Abnormalities in routine nutritional laboratory parameters not predictive of changes anthropometric parameters in the PICU.

BMI: body mass index; EN: enteral nutrition; LOS: length of stay; MV: mechanical ventilation; PICU: paediatric intensive care unit; SGNA: subjective global nutritional assessment; SD: standard deviation; WHO: World Health Organization.

not been tested as yet.

Routine laboratory parameters linked to nutritional status in critically ill children include albumin, pre-albumin, retinol binding protein, urea, and triglycerides.[3,20] However, markers such as albumin can be confounded by albumin infusion, dehydration, sepsis, trauma, inflammatory reaction or liver disease. As such, most members of the Working Group do not recommend that serum biomarkers such as albumin be used to assess nutritional status in the PICU population.

Overall, the Working Group urges centers in the Asia Pacific-Middle East region to encourage routine screening for malnutrition, develop and disseminate best anthropometric techniques, ensure regular assessments for long-stay patients, make anthropometric equipment and resources available, and use uniform reference guides and z-scores to classify nutritional status. The group stressed the importance to educate PICU personnel on the need for accurate nutritional assessment.

Assessment of energy requirement
Statement 3a
Indirect calorimetry (IC) remains the gold standard for estimating resting energy requirement. (Strong recommendation)

Statement 3b
Resting energy requirement may be calculated based on predictive equations if IC is not available. (Weak recommendation)

Statement 3c
Feeding should be introduced at 25%-50% of energy requirements and advanced slowly in severely malnourished patients and those with prolonged fasting, to avoid the risk of re-feeding syndrome. (Moderate recommendation)

Statement 4
Regular reassessment of the child's nutritional status is necessary to avoid underfeeding/overfeeding. (Moderate recommendation)
Because of the limited availability of indirect calorimetry (IC) in the region, estimation of energy requirement using predictive equations is a common practice in many hospitals. However, predictive equations do not always accurately predict energy expenditure in critically ill children (Table 3).[21-28] The Schofield equation is the most commonly used formula in many studies, with some demonstrating that this equation has good performance for predicting energy expenditure in critically ill children.[29-31] However, other studies showed poor agreement between predicted energy expenditure using the Schofield formula and measured energy expenditure.[22,23,25-28] There is no correlation between severity of illness score and measured energy expenditure.[21] Stress factors should be used only after careful consideration to avoid overfeeding. Cumulative energy imbalances due to unintended suboptimal nutrient delivery may impact clinical outcomes. In the absence of IC, regular nutritional assessment may help avoid cumulative underfeeding or overfeeding.

Modes of nutritional support
Statement 5
Enteral nutrition (EN) is the preferred mode of nutritional support in critically children with a functional gastrointestinal tract and no absolute contraindications to enteral feeding. (Strong recommendation)

Statement 6a
Gastric feeding is recommended as the first line route for EN. (Moderate recommendation)

Statement 6b
Post-pyloric (small bowel) feeding may be used when gastric route is contraindicated or not tolerated. (Weak recommendation)

Statement 7a
Total parenteral nutrition (PN) should be considered when EN is contraindicated. (Strong recommendation)

Statement 7b
Supplemental PN should be used if nutritional requirements cannot be fully met by EN alone. (Weak recommendation)

Statement 7c
PN should be used when EN is unable (or not anticipated to be able) to meet nutritional goal within 5-7 days in previously well children without existing malnutrition, and earlier in infants and severely malnourished patients. (Weak recommendation)
Prolonged fasting during critical illness is not recommended. Efforts to optimize EN such as early initiation and avoiding interruptions to EN should be encouraged. Trophic feeding may provide some of the benefits of EN in patients who do not tolerate full EN.

There is a lack of randomized controlled trials that compare the use of enteral nutrition (EN) vs parenteral nutrition (PN) in children. There are distinct advantages to using the gut for feeding whenever possible. In critically ill children, EN is preferred over PN because it is more physiological, promotes intestinal trophism, stimulates the immune system, and reduces the incidence of bacterial translocation and sepsis. In addition, EN is associated with fewer complications and costs less than PN.[32-34] Early EN (within first 24 hours) is therefore encouraged whenever possible.[35-38] PICUs that utilized protocols for the initiation and advancement of EN had a lower prevalence of acquired infection and mortality rate.[5,39-41] Absolute contraindications for starting EN are intestinal obstruction, gut failure secondary to massive resection, or congenital defects. Relative contraindications include hemodynamic instability and severe septic shock.

Gastric feeding is well tolerated by most critically ill infants and children.[38,42,43] The Working Group members agreed that gastric feeding should be the route of choice for EN in all children in the PICU. There is a lack of evidence to support the preference of continuous over bolus feeding or vice versa. Several Working Group members felt that continuous feeding may be preferable at the start of the feed, because it may be better tolerated and easier to implement in older children. Because of differences in

Table 3. Evidence tables for methods for assessment of energy requirement

Study	Study population and design	Primary outcome measures	Main results	Comments
Mehta et al (2014)[89] Level II	2 center study examining the accuracy of a new simplified equation for estimating REE, using VCO_2 measurements. Derivation dataset N=72; Validation dataset N=94 (age <18 years).	Accuracy of a simplified equation for predicting REE using carbon dioxide elimination (VCO_2) values, i.e. REE (kcal/day)=5.534*VCO_2(L/min)*1440.	The simplified equation was superior to the standard equation in estimating REE. Mean bias in relation to measured REE was -0.65% (range -14.4 to 13.1%). Diagnostic accuracy for classifying subjects as hypometabolic or hypermetabolic was 84%. Mean bias of agreement between measured and Schofield equation-estimated REE was -0.1% (range 40.5 to 40.7%).	Bedside VCO_2 measurement is now available in most PICUs. In the absence of IC, bedside VCO_2 values could provide valuable continuous metabolic information. Due to a fixed RQ assumed for the simplified equation, there is inherent error in the prediction when actual RQ is higher or lower than 0.89.
Smallwood at al (2012)[26] Level III	Prospective study in mechanically ventilated children – examining the accuracy of shorter steady state criteria for IC tests. N=34.	Examination of the agreement of REE with IC testing by 5-minute steady state (SS5) versus 4-minute (SS4) and 3-minute (SS3) protocols as well as the Schofield prediction equation.	Steady state was achieved in 56%, 69% and 93% tests using SS5, SS4 and SS3 protocols respectively. Mean bias (limits of agreement) for REE was 2.8 (-47 to 65), 5.8 (-71 to 72), and -127 (-418 to 1176) kcal/d using SS4, SS3, and Schofield, respectively. Schofield equation overestimated measured REE by an average of 25%, with wide limits of agreement (-85% to 142%). In mechanically ventilated children, 4-minute and 3-minute SS protocols allowed REE measurements to be obtained in most patients with reasonable accuracy.	Shorter IC tests may be feasible. However, the effect of variables such as temperature, specific clinical conditions, BMI, timing of test, use of muscle relaxants, sedatives on the accuracy of shortened IC needs to be determined.
Meyer et al (2012)[29] Level II	Prospective observational study and development of new equations for estimating REE. N=175 (age: newborn-16 years).	Three formulas with an R^2 >0.8 were developed and compared with commonly used equations (Schofield, Food and Agriculture Organization/WHO/United Nations University, and White equation).	All formulas performed similarly. Schofield equation performed better than other predictive methods in predicting EE in these patients. None of the predictive equations, including the new equations, predicted EE within a clinically accepted range.	Large number (369) of energy expenditure measurements. Mixed cases of patients included.
Botran M et al (2011)[21] Level III	Prospective PICU observational study in children on MV with FiO_2 ≤60%, only receiving intravenous glucose infusions (nil-by-mouth). Identify relationship between EE and biochemical or anthropometric nutritional status or severity scales in critically ill children. N=46 (age: 1 month-16 years).	EE measured by IC.	No correlation was found between EE and anthropometric and biochemical nutritional status and clinical severity in critically ill children. Recommend EE to be measured individually in each critically ill child using IC.	Results mimic previous studies, making a case for measured REE in the PICU population. Small sample size Predominantly surgical patients in the cohort. Broad but skewed age range with almost 75% of children ≤2 years.

EE: energy expenditure; FiO_2: fraction of inspired oxygen; GCS: Glasgow Coma Scale; IC: indirect calorimetry; MEE: measured energy expenditure; MV: mechanical ventilation/mechanically ventilated; PICU: paediatric intensive care unit; REE: resting energy expenditure; RQ: respiratory quotient; SS: steady-state; TPN: total parenteral nutrition; WHO: World Health Organization.

Table 3. Evidence tables for methods for assessment of energy requirement (cont.)

Study	Study population and design	Primary outcome measures	Main results	Comments
Mehta et al (2011)[24] Level III	Prospective cohort study. N=33 (age: 0.1-25.8 years).	Comparison of accuracy of standard equations (Schofield, Harris-Benedict, WHO) for estimating REE in relation to measured REE by IC.	High incidence (72%) of metabolic instability and alterations in REE with predominance of hypometabolism. Physicians failed to accurately predict the true metabolic state in 62% of patients. Overestimation of EE by standard equations resulting in overfeeding in 83% cases. Cumulative energy excess of up to 8,000 kcal/week, especially in children <1 year of age. RQ was not an accurate indicator of adequacy or excess of energy intake.	Inaccuracy of standard equations and indiscriminate use of stress factors contributed to overfeeding in critically ill children. The study did not evaluate serial REE measurements in the cohort. Single center study with a small sample size.
Mehta et al (2009)[25] Level IV	Retrospective cohort study to measure EE. N=14 (age: 1.6 months-32 years).	REE from IC compared with estimated REE from standard equations and total energy intake. Equations used: Schofield, Harris Benedict, WHO. Stress factors applied based on illness, fever, inflammation, hypermetabolic features.	Lack of correlation between metabolic status (hypo- or hypermetabolic) and PRISM3, age, BMI and initial diagnosis. Poor agreement between measured REE and estimated EE using Schofield, Harris Benedict and WHO equations (mean bias of 72.3±446 kcal/d; limits of agreement -801.9 to 946.5). Use of equations resulted in under or overfeeding. Mean MREE: EEE ratio of 0.94 (range 0.43-1.53).	Small sample size with a wide age range. The study introduces the concept of targeted IC in high risk patients – to address limited resources in most centers. This approach may prevent cumulative excesses or deficit in energy balance.
Sy et al (2008)[27] Level III	Prospective observational study Hemodynamically stable patients with major diagnoses of sepsis, pneumonia and acute lung injury. N=31 (age: 1 month-20 years).	Compared bicarbonate rate of appearance based EE with actual intake received by critically ill children, energy intake recommended by 2001 WHO publication and Schofield equation mediated calculation.	The 2001 WHO and Schofield predictive equations overestimated and underestimated, respectively, energy requirements compared with those obtained by bicarbonate dilution kinetics. Bicarbonate kinetics allows accurate determination of energy needs in critically ill children.	Single center, small sample size. Limited practical application because bicarbonate dilution kinetics is unavailable for bedside use.

EE: energy expenditure; FiO$_2$: fraction of inspired oxygen; GCS: Glasgow Coma Scale; IC: indirect calorimetry; MEE: measured energy expenditure; MV: mechanical ventilation/mechanically ventilated; PICU: paediatric intensive care unit; REE: resting energy expenditure; RQ: respiratory quotient; SS: steady-state; TPN: total parenteral nutrition; WHO: World Health Organization.

Table 3. Evidence tables for methods for assessment of energy requirement (cont.)

Study	Study population and design	Primary outcome measures	Main results	Comments
van der Kuip et al (2004)[28] Level III	Prospective study. N=14 (age: 0-18 years).	Validity and reliability of energy expenditure measurements with a short Douglas bag protocol compared with the standard metabolic monitor.	Both the metabolic monitor and Douglas bag showed significant bias compared with Schofield equations (3.39±1.64 MJ/day) of -7% ($p<0.01$) and -5% ($p<0.05$), respectively, with wide limits of agreement: metabolic monitor vs Schofield: -37%±22%, Douglas bag vs Schofield: -37%±26%. The Douglas bag method compared favourably to the metabolic monitor where Schofield equations failed to predict individual energy expenditure.	Small sample size. Douglas bag method is an old concept, low cost, short and simple. Currently not widely available. Could be used routinely to tailor nutritional assessment in critically ill children.
Vazquez Martinez et al (2004)[31] Level II	Prospective study. N=43 children (mean age 4.21+3.67 years).	Comparison of predicted EE (by anthropometric equations) with continuous IC. Prediction of EE (PEE) using actual and ideal weight was done using: Harris benedict, Caldwell-Kennedy, Schofield, Food and agriculture/WHO/United nation union, Maffies, Fleisch, Kleiber, Dreyer and Hunter equations.	Most of the predictive equations overestimated MEE during the early post injury period. MEE and PEE differed significantly ($p<0.05$) except for Caldwell-Kennedy and Fleisch equations. Caldwell-Kennedy equation was best predictor of EE (bias, 38 kcal/day; precision, ±179 kcal/day).	Predictive equations are inaccurate in predicting EE in MV critically ill children. IC is preferred whenever available. The results suggest that EE is overestimated when equations are used. Small sample group.

EE: energy expenditure; FiO_2: fraction of inspired oxygen; GCS: Glasgow Coma Scale; IC: indirect calorimetry; MEE: measured energy expenditure; MV: mechanical ventilation/mechanically ventilated; PICU: paediatric intensive care unit; REE: resting energy expenditure; RQ: respiratory quotient; SS: steady-state; TPN: total parenteral nutrition; WHO: World Health Organization.

local practice, the Working Group recommends starting feeds according to current local practice and resources, in order to encourage EN. Trophic feeding, also termed as 'minimal enteral nutrition', is recommended in certain subset of PICU patients such as those with duct-dependent systemic circulation to balance the risk and benefits of advancement of feeds. In children who do not tolerate gastric feeding, trans-pyloric feeding may be considered. Local healthcare structures should determine the personnel and method used for insertion of trans-pyloric feeding tubes.

In some critically ill children in whom enteral feeding is not possible at all (e.g., total intestinal failure), PN is the only method for ensuring an adequate supply of nutrients (Table 4). PN may also be initiated when EN alone is anticipated to be insufficient to provide energy goals within 5 days in infants and malnourished children.[44] In patients in whom EN alone cannot meet nutrition demands, the combination of PN and EN may be useful during first 72 hours of critical illness.[45-49] Prudent use of PN is necessary, because its use has been associated with higher mortality, increased risks of infection, hepatic injury, atrophy of intestinal mucosa and hyperglycaemia.[32,40,50-52]

In the Working Group's opinion, central lines are preferred over peripheral lines for the provision of PN. However, peripheral PN can be used temporarily while waiting for central lines to be established. Care must be taken to limit osmolality (<1000 mOSm/L) of the PN if peripheral access is utilized.[53] In addition, the clinician must be cognisant of the risk of central-line associated blood stream infection that is associated with the use of PN with central lines.[40,51,52] All children on PN need to be monitored for appropriate growth and side effects of this therapy. Anthropometry and pertinent laboratory data (e.g., complete blood count, glucose level, electrolytes, liver function tests and triglyceride levels) should be monitored regularly along-with fluid intake and output.

Gastric residual volume (GRV) is often used to define feeding intolerance in this region. However, evidence guiding this practice is lacking and the use of GRV may lead to unnecessary feed interruptions. Most Working Group members felt strongly that GRV should always be interpreted in the context of other signs of intolerance (e.g., abdominal distension and vomiting). In children, there is no evidence that monitoring GRV prevents aspiration and in adults, monitoring GRV did not reduce aspiration or vomiting.[54] To the best of our knowledge, there is no published evidence with regard to the optimal methods for the management of feed intolerance. In the members' opinion, the top three preferred methods were: (1) stopping the feed and restarting at the previously tolerated rate; (2) use of prokinetic agents and (3) post-pyloric feeding if other methods remain unsuccessful after 24-48 hours.

Macronutrient constitution for critically ill children
Statement 8
Recommended protein intake is age-dependent with a minimum of 1.5 g/kg/day. (Moderate recommendation)
In critically ill children, carbohydrate is utilized poorly, with fat being used preferentially for oxidation.[55] There

are few evidence-based data for recommendations for carbohydrate and fat in this population[1] but it seems reasonable to aim for approximately 50-60% energy from carbohydrate and 30-40% energy from fat.

Protein requirements in critically ill children are higher than their healthier counterparts.[6] An increased protein intake cannot reverse protein breakdown, but can improve nitrogen balance by enhancing protein synthesis.[5] The A.S.P.E.N. guidelines for protein requirements for injured children are: 0-2 years: 2-3 g/kg/day; 2-13 years: 1.5-2 g/kg/day; and 13-18 years: 1.5 g/kg/day.[1] There is a complex interplay between energy intake and protein balance in critically ill children (Table 5). A systematic review of 9 studies in PICU demonstrated that a minimum of 57 kcal/kg/day and 1.5 g protein/kg/day is required for positive protein balance in infants with bronchiolitis, although parenterally fed hypermetabolic patients required up to 2.8 g protein/kg/day to achieve this.[13]

Lipid emulsions provide a dense source of energy and essential fatty acids in PN. However, the use of lipid emulsion is associated with cholestasis [PN-associated cholestasis and PN- associated liver disease (PNALD)]. Doses of intravenous (IV) soy-bean based lipid emulsion of more than 1 g/kg/day have been associated with increased risk of PNALD.[56,57] Hence, soy based sparing lipid emulsion (i.e., omega 6 fatty acid-reducing strategy) has been used. Unfortunately, large well-designed prospective randomised controlled trials (RCT) to test the ability of fish oil emulsion to prevent or treat cholestasis are lacking, but parenteral fish-oil-based fat emulsions are safe and may be effective in the treatment of PNALD.[57,58]

Lipid formulations in use in Asia and the Middle East include Intralipid (100% soy based), Clinoleic (80% olive oil/20% soybean oil mix), SMOF (soy, MCT, olive and fish oils) and Omegaven (100% fish oil). There is growing interest in the use of omega-3 fatty acid lipid emulsions to prevent complications of intestinal failure associated liver disease (IFALD) and in critical illness. A recent systematic review in children concluded that the use of omega-3 fatty acids resulted in improved biochemical indices of IFALD, but no difference in mortality.[59] Few studies have examined other clinical outcomes such as length of hospital or intensive care stay, need for transplantation or growth.[59] An RCT on infants undergoing open heart surgery assessed the effects of a lipid emulsion containing omega-3 fatty acids, given before and after surgery, on cytokine production and length of stay. Tumor necrosis factor (TNF)-α was significantly lower in the treatment group compared with the control group, and was associated with a shorter length of hospital stay.[60] In contrast to the use of fish oil in critically ill adults,[61] more evidence is needed before firm recommendations can be made with regard to which paediatric populations would benefit from fish-oil containing lipids.

Obesity and issues of over- and underfeeding
The prevalence of obesity is increasing worldwide, although in some regions of Asia, the incidence of obesity is lower than in western countries.[62] The impact of pre-existing obesity on outcomes in critically ill children remains ill-defined. In an international multicenter study of 500 PICU patients, 13.2% of patients were obese on ad-

Table 4. Evidence for enteral nutrition

Study	Study population and design	Primary outcome measures	Main results	Comments
Abdul Manaf et al (2013)[91] Level III	Cross-sectional study. N=53 (age: median 10.2 months; interquartile range 5.1-50.5 months).	Time EN was initiated, delivery method, volume and rate of feeding, type of EN product used, number of feeding interruptions and reasons for it.	EN initiated within 21 hrs of admission. Interruptions in 66% patients. Overall duration of feeding interruption was 20% of feeding time. Reasons for interruption: medical procedures (55%), non-gastrointestinal complications (27%). Feeding initiation time, referral to dietician, frequency and duration of feeding interruptions positively associated with cumulative energy and protein deficits.	Substantial inadequacy of energy and protein delivery, feeding interruption and delay in feeding initiation. Malnutrition prevalent upon admission.
de Menezes et al (2013)[49] Level II	Prospective study. N=207 (age: 2.6-58.3 months).	To identify factors associated with the non-attainment of estimated energy requirements. The outcome variable was whether 90% of the estimated basal metabolic rate was maintained for at least half the ICU stay.	Satisfactory energy intake was reached by 20.8% of patients; mean time: 5.07±2.48 days. Heart disease (OR 3.62, 95% CI 1.03-12.68, p=0.045) was an independent risk factor for non-attainment of satisfactory energy intake. PN (OR 0.34, 95% CI, 0.15-0.77, p=0.001) was a protective factor against insufficient energy intake.	Study demonstrated non-satisfactory energy intake in nearly a quarter of patients and long duration to achieve adequate feeds. Patients with heart disease had higher chance of not attaining satisfactory energy intake compared with subjects without heart disease, while PN and malnutrition were protective factors.
Wakeham et al (2013)[92] Level III	Retrospective study. N=1,349 (age: 30 days-18 years)	To describe early documentation of caloric requirement in critically ill children and its effect on daily energy and route of nutrition.	47.7% patients had documented caloric requirement in medical record. These patients had higher total daily energy intake, more likely to be fed EN during first 4 days of PICU admission than those without documented caloric requirement (p<0.001 for all comparisons).	Caloric requirements were entered by registered dietician in almost all cases. Highlights the advantages of including nutrition during daily rounds, involvement of dieticians and overall higher awareness/documentation of nutritional needs.
Willis et al (2008)[93] Level IV	Retrospective study. N=34 infants.	Examine feeding tolerance in infants receiving prostaglandin (PGE$_1$). Clinical and radiographic information, feeding type, delivery and caloric density determined.	Only one patient with intolerance.	Small scale study. Illustrates safety of enteral feeding in patients receiving prostaglandins.
Gurgueira et al (2005)[39] Level IV	Historical cohort observational study. N=323 (age: 0-23 months).	Effect of PN and EN on PICU mortality before and after a continuous education program in nutrition support that led to implementation of NST.	EN use in medical patients increased progressively from 25% before intervention to 67% after NST, and PN use decreased from 73% to 69% (p=0.0001 for both), with significant reduction in-PICU mortality (p<0.001). Risk of death was 83% lower in patients who received EN for >50% of LOS (OR, 0.17; CI, 0.066-0.412; p<0.0001).	Single center study, demonstrates significant increase in EN and decrease in PN use after implementation of NST. Independent predictive factor for risk of death during hospitalization in PICU was patients receiving EN for >50% LOS.

EN: enteral nutrition; IC: indirect calorimetry; LOS: length of stay; NST: nutrition support team; PGE$_1$: prostaglandin E1; PN: parenteral nutrition; PICU: pediatric intensive care unit; TGA: transposition of great arteries.

Table 5. Evidence for nutrient intake

Study	Study population and design	Primary outcome measures	Main results	Comments
Botran et al (2011)[94] Level II	Unblinded RCT 73% post cardiac surgery to compare protein-enriched EN formula (PE) vs standard (S) formula (over 5 days. N=41 (median age: 7 months).	Nitrogen balance (NB) Nutritional markers	Positive NB achieved on day 5 in the PE group (median 0.5 g/kg/day) but remained negative in the S group (median–0.4 g/kg/day) ($p<0.09$). Significantly higher retinol binding protein on day 1 and day 5 in PE formula group.	No adverse effects or hyperproteinemia detected in protein-enriched diet group Insufficient protein in standard diet.
de Betue et al (2011)[95] Level II	Blinded RCT in children admitted to PICU with respiratory failure to compare protein and energy- enriched (PE) EN formula vs S formula over 5 days. N=18 (mean age: 2.9±1.7 months).	Whole body protein balance. First pass splanchnic phenylalanine extraction (SPE_{Phe}).	Protein balance was significantly higher with PE-formula than with S-formula (PE-formula: 0.73±0.5 vs S-formula: 0.02±0.6 g/kg/24 hr) ($p=0.026$). SPE_{Phe} was not statistically different between groups.	Increasing protein and energy intakes promotes protein anabolism. Both energy and protein increased so unable to distinguish effect of protein vs energy.
van Waardenburg et al (2009)[96] Level II	Blinded RCT in children admitted to PICU with RSV to compare PE EN formula vs S formula over 5 days. N=18 (mean age: 2.7±0.5 months and 3.0±0.6 for PE and S-group respectively).	Nutrient delivery, energy and NB. Plasma amino acid concentrations. Tolerance and safety.	Cumulative NB (cNB) and energy balance (cEB) significantly higher in the PE-formula group vs S-formula group (cNB: 866±113 vs 296±71 mg/kg; cEB:151±31 and 26±17 kcal/kg, both $p<0.01$) Essential amino acid levels significantly higher in PE-formula group vs S-formula group. Both formulas were well tolerated but GRV were significantly higher in PE vs the S group (9.8±2.7 and 4.7±2.4 mL/24 hr respectively).	Early administration of protein and energy enriched formula well tolerated in critically ill children, improves energy and nitrogen balance. Both energy and protein increased so unable to distinguish effect of protein vs energy. The impact of optimizing protein balance on significant clinical outcomes needs to be examined.

EN: enteral nutrition; NB: Nitrogen balance; PE: protein enriched; RCT: randomized controlled trial; S: standard.

mission (BMI z score >+2).[5] In another study of 316 paediatric trauma patients admitted to a PICU, 54 (17%) were obese (BMI>95th percentile) and they had more complications including sepsis, wound infection and longer ICU stay than their lean counterparts.[63] In contrast, another study showed no difference in mortality, length of mechanical ventilation and length of stay in obese and normal-weight critically ill children.[64]

Energy requirements are often derived from standard equations that have been shown to be inaccurate in critical illness and can significantly underestimate or overestimate true energy requirements. This can result in underfeeding or overfeeding during the PICU stay, with significant morbidity associated with each scenario.[6] One study reported overfeeding on 69% of days over a 14-day study period of 98 critically ill children.[65] In a group of long-term PICU patients with median length of stay 44 days, targeted for IC, the incidence of overfeeding was as high as 83% with cumulative energy excess of up to 8,000 kcal/week.[25] Overfeeding has important adverse effects during critical illness as it can increase carbon dioxide production, impede ventilator weaning, increase length of stay and cause fatty deposition in the liver.[66,67] On the other hand, underfeeding of critically ill children has also been reported in a number of studies.[5,15,65] Underfeeding causes protein-energy malnutrition in critically ill children: 17.1% of paediatric patients are malnourished on admission to PICU and further energy deficits in these patients significantly increases mortality, quantity of care and physiologic instability.[5,68,69]

The Working Group members advise that clinicians should be aware of causes of under- and overfeeding so that at-risk children can be identified promptly. Causes of underfeeding include: (i) inability to predict the hypermetabolic stress response [underestimating energy expenditure (EE)]; (ii) inaccurate estimation of EE; (iii) delay in detection of deteriorating nutritional status; (iv) failure to deliver prescribed nutrients. Causes of overfeeding include: (i) failure to recognize the hypometabolic phase of metabolic stress response (overestimating EE); (ii) reliance on standardized formulae/equations for energy expenditure, which are frequently inaccurate; (iii) inaccurate weights, confusion about which weight to use for obese patients; (iv) over-estimating the degree of metabolic stress in the era of modern anaesthesia and surgery.

Use of prokinetic agents

Abnormal gastric motility is common in critically ill patients and prevents achievement of nutritional goals. Delayed gastric emptying may manifest as large GRV and may increase the risk of aspiration of gastric contents. Feed intolerance may be alleviated with prokinetic drugs, although their role in the treatment of feed intolerance is still unclear. Several agents (e.g., erythromycin, metoclopramide and domperidone) have been used alone or in combination, with variable results.[70-73] The use of such medications is not risk-free; there is evidence for the risk of long QT syndrome in patients using domperidone.[74]

In agreement with the A.S.P.E.N. guidelines on paediatric nutrition,[6] the Working Group agreed that there is insufficient evidence to recommend the use of prokinetic medications or motility agents for EN intolerance or to facilitate enteral access device placement. Other novel drugs (e.g., methylnaltrexone, mitemcinal, ghrelin agonists and dexloxiglumide) may have potential advantages, but require further research to prove their efficacy and safety before they can be recommended.

Role of pre-biotic, probiotic and synbiotic organisms in supporting nutritional well-being

Probiotics are viable bacteria or yeast microorganisms that can benefit patients when added as dietary supplements.[75] Prebiotics are fermentable soluble dietary fibers, such as inulin and fructooligosaccharides, which stimulate the growth or activity of beneficial bacteria in the gut, thereby improving host health. Synbiotic formulations contain both products. Data on their beneficial effects in adult ICU populations have been inconsistent due to the use of different probiotics, dosages and protocols.[76-78]

Few studies examining the beneficial effects of these agents in critically ill children have been published since the A.S.P.E.N. guidelines in 2009. The tolerability and safety of synbiotics was demonstrated in critically ill children, and their inclusion in the enteral formula resulted in an increase in faecal bacterial groups previously reported to have beneficial effects.[79] In another study, probiotic use in critically ill children was associated with a reduction in candidemia and candiduria.[80] Nevertheless, there is still not enough evidence to recommend the use of prebiotics, probiotics, or synbiotics in critically ill children.

Evidence in the topics of obesity, over- and underfeeding in critically ill children and the role of prokinetic agents, pre-biotic, probiotic and symbiotic organisms in the PICU is scant and further studies are required. The Work Group did not find enough evidence to make consensus statements on these adjuncts.

Role of adjuncts to promote optimal nutrition in the PICU in the region
Statement 9
Nutrition therapy in the PICU should be guided by a Nutrition Support Team (NST). (Moderate recommendation)

Statement 10
Feeding algorithms should be encouraged in PICUs. EN feeding algorithms should include the following components: assessment and monitoring of nutritional status and intolerance, feeding routes, management strategies for feeding intolerance, and target time to initiate and advance feeding. (Moderate recommendation)

Role of dieticians and nutrition support team

The incidence of the availability of dedicated dieticians and NSTs and the use of feeding protocols within PICUs in Asia Pacific and Middle East is not well described. The Working Group agreed that routine participation of dieticians in PICU practice is helpful. If a dedicated PICU dietician is available, he/she should participate in daily bedside PICU rounds. An alternative approach would be to have dieticians review PICU patients few times a week. If resource limitations prevent the employment of full-time dieticians, workflow in the PICU should be tailored to allow regular adequate discussion of nutrition for each

patient.

A NST usually consists of a physician specialized in gastroenterology or nutrition, and a dietician; pharmacists or nurses may also be included. NSTs can potentially advise on the following aspects of care: nutritional status assessment at admission and during PICU stay, estimation of nutritional requirements, route of administration of nutrition, on the use of insulin, and establishing a day-to-day nutritional prescription.[81] NSTs can also facilitate teaching of residents and provide knowledge updates for clinical staff.[39]

Two studies have demonstrated a positive effect of NST in the PICU (Table 6).[39,82] Improvement in nutrition was demonstrated by progressively increased EN and decreased PN use, without any increase in adverse gastrointestinal events. Nutritional targets were reached earlier, although there were no differences in clinical outcome parameters (length of ICU stay, ventilator days and mortality).

A survey of 111 European PICUs showed that NSTs were available in 73% of PICUs,[83] but the proportion of PICUs with NSTs is likely to be much lower in Asia-Pacific and Middle East. The Working Group felt that, although NSTs may improve the delivery of nutrition in PICU, there is still insufficient evidence to show that this translates to better clinical outcomes.

Role of Feeding Protocols

EN protocols/guidelines/algorithms usually include nutritional assessment, indications and contraindications to enteral feeding, initiation and progression of feeding, type of feeding (continuous or bolus) and definitions of feeding intolerance.[2]

There is low-level evidence of positive impact of EN protocols on nutrient delivery in critically ill children (Table 6). In one study, use of an enteral feeding protocol in the PICU appeared to optimize EN intake and enhance gastrointestinal tolerance.[84] Deployment of clinical practice guideline was related to significant reduction in the use of short-term PN across several clinical disciplines and the hospital costs and charges.[44] A large international multicenter cohort study of 31 PICUs (including only 1 PICU from Asia) on nutritional practices and their relationship to clinical outcomes in critically ill children concluded that PICUs that utilized protocols for the initiation and advancement of EN had a lower prevalence of acquired infections, reduced GI and infective complications, and improved timeliness of feed initiation and achievement of goal feeds.[5] When nutrition algorithms and bedside nutrient delivery practices from the same study were evaluated, only 9 used EN algorithms, all of which defined advancement and EN intolerance.[85] Recommendations in the algorithms were variable and not in agreement with published guidelines. However, the use of EN protocols was not associated with increased energy delivery in this study and the investigators were unable to assess compliance of the respective institutions with their algorithms.

Our Working Group's literature review identified several studies have shown that EN protocols improve nutrition delivery and reduce gastrointestinal and infective complications, but there is still no high-level evidence to support that EN protocol improves clinical outcomes.

Regional challenges to optimal nutrition practice in critically ill children

Statement 11a
Nutrition should be emphasized as part of everyday patient management in the PICU. (Strong recommendation)

Statement 11b
Development of national and/or regional guidelines for nutritional requirements and assessment of critically ill children should be encouraged. Education of doctors, nurses, and dieticians is crucial to increase the knowledge of healthcare professionals in the Asia-Pacific and Middle East. (Moderate recommendation)

Challenges to providing optimal nutrition in PICUs in the Asia Pacific and Middle East are mainly due to resource limitations and the low priority often accorded to nutritional support. Some of the unique challenges brought up by Working Group members are highlighted below:

1. Hospital-acquired malnutrition: Malnutrition is very common in children in developing countries,[4] and is often observed in PICU. It places an additional burden on them, thus adversely affecting the outcomes of the PICU.

2. Nutritional assessment: Accurate, comprehensive methods of assessment of nutritional status in critically ill children are lacking. The existing methods that are in use are not only insensitive, but also produce variable results.

3. Suboptimal therapeutic nutrition: Critically ill children in the PICU usually suffer from high catabolic stress and REE. They often also have lower nutritional reserves than adults, with significant nutritional loss from wounds, drains, specimen collection, or dialysis.

4. With the added burden of poor gut function, fluid constraints, and frequent feeding delays caused by procedures and investigations, the significance of adequate and timely nutritional support in these children is underestimated. Few centers have NSTs, hence accurate knowledge of their nutritional status and timely provision of appropriate nutrition is often lacking.

5. Lack of guidelines: The existing World Health Organization (WHO) guidelines address the treatment of severe malnutrition in children, but are not applicable to critically ill children suffering from severe malnutrition.[86]

6. Ready-to-use food: Although WHO guidelines recommend use of micronutrient mixes and ready-to-use food,[87] these products are not readily available for use in hospitals. The potential role of regionally developed food sources, formulae or recipes for cost-effective nutritional support in the PICU should be explored.

7. Glucose levels: Glucose is an essential component of nutrition, particularly for the brain, red blood cells, renal medulla and for repair of injured tissues, but there is lack of high quality data on the amount of glucose to be added to PN supplements, and on the optimal blood glucose range for critically ill children. Total PN is advisable in cases where EN cannot meet energy requirements, but in young patients, PN feeding may

Table 6. Evidence table for role of adjuncts

Study	Study population and design	Primary outcome measures	Main results	Comments
Martinez et al (2014)[85] Level III	International (31 PICUs) prospective cohort study of children requiring MV>48 hrs in PICU. N=524 (age 1 month to 18 years).	Use and composition of nutrition guidelines and comparison of components with national recommendations based on expert consensus.	EN algorithms were available in nine centers; all defined advancement and EN intolerance; 7/9 defined intolerance by GRV; 3/9 recommended nutrition screening and fasting guidelines.	Few elements were in agreement with the A.S.P.E.N. and ESPGHAN guidelines. EN algorithms used in minority of centers.
Wong et al (2014)[2] Level II	Systematic review of effect of EN protocols on important clinical outcomes in PICU. Included RCT and observational studies that involved EN protocols in children admitted to PICU>24 hrs. N=1,564 (age- 1 day-16 years).	PICU or hospital mortality, PICU or hospital length of stay, duration of mechanical ventilation, gastrointestinal complications and infective complications.	Total of 9 studies included. Low-level evidence that use of EN protocols was associated with reduction in GI and infective complications and improved timeliness of feed initiation and achievement of goal feeds.	Majority of studies did not mention details on severity of illness, case mix of patients, timing of nutrition intervention. Protocol heterogeneity present among different studies.
Hamilton et al (2014)[97] Level III	Prospective audit of nutritional outcomes following implementation of EN algorithm in children with PICU stay >24 hrs, compared with pre-implementation phase cohort N=160 (median age (IQR): pre-intervention cohort 6.5 (1.5, 15) years and post-intervention cohort 7.4 (2.2, 12.9) years.	Total and avoidable interruptions to EN; Time to initiate EN after PICU admission; Time to reach prescribed energy goal; PN use in patients with EN interruption.	Significant decrease in number of avoidable episodes of EN interruption (3 vs 51, $p<0.0001$) in post-intervention cohort. Median time to reach energy goal decreased from 4 days to 1 day ($p<0.0001$), with higher proportion of patients reaching this goal (99% vs 61%, $p=0.01$).	Significant improvements reported in time to initiating EN and achieving goals with implementation of the algorithm. Single center study. Need to be validated in other centers. Differences in patient case type pre- and post-implementation.
Gentles et al (2014)[98] Level IV	Audit of nutritional intake and EN practices before (period A) and after (period B) 690 introduction of enteral feeding practice guidelines and participation of dieticians in daily ward rounds in a PICU. N=130.	Increase in nutrition delivery to critically ill children in the PICU.	69% patients in period A and 83% patients in period B received EN support within 24 hrs of PICU admission ($p=0.153$). BMR energy requirements achieved in 27% of patients in period A vs 48.9% in period B, $p<0.001$. In patients admitted for nonsurgical reasons, median energy, protein, and micronutrient intake improved significantly.	Compliance to feeding practice guidelines not assessed. Patients on PN excluded. Not possible to explore whether it was the use of the EN guidelines, participation of the dieticians, or their combined effect that improved nutritional intake.
Mehta et al (2012)[5] Level II	International multicenter prospective cohort study in children requiring MV>48 hours. N=500 (age: 1 month to 18 years).	Variables associated with achieving optimal EN intake, and relationship between adequacy of energy intake (in relation to prescribed goal) and clinical outcomes (mortality and infectious complications).	10 PICUs used EN guidelines or protocols. Patients admitted to units that utilized a feeding protocol had a lower prevalence of acquired infections (OR 0.18 [0.05, 0.64], $p=0.008$).	Heterogeneous groups of patients as multi-center study. Observational study, thus cannot make definitive causal inferences form findings.

A.S.P.E.N.: American Society of Parenteral Enteral Nutrition; BMR: Basal metabolic rate; EAR: estimated average requirement; EN: enteral nutrition; ESPGHAN: European Society for Paediatric Gastroenterology, Hepatology, and Nutrition; GI: gastrointestinal; HLHS: hypoplastic left heart syndrome; LOS: length of stay; MV: mechanical ventilation; NEC: necrotizing colitis; REE: resting energy expenditure; SOCI: sustained optimal caloric intake.

Table 6. Evidence table for role of adjuncts (cont.)

Study	Study population and design	Primary outcome measures	Main results	Comments
Tume et al (2010)[100] Level III	Prospective observational study in a tertiary PICU over 1 month of patents who stayed >24 hrs and had no contraindications to EN N=47 (median age: 10 months, IQR: 0.03-168)	Compare actual calorie intake with estimated caloric requirements. Influence of feeding guideline adherence on improved nutritional intake.	Only 35% adhered to the feeding guidelines and if feeding guidelines were followed, this resulted in a significantly higher delivery of the child's estimated requirements (75% vs 38%, p=0.004).	Use of feeding guidelines improved calorie delivery. Units should develop own evidence-based guidelines Short period of study. Outcomes of patients (e.g., LOS, MV, mortality) not studied. Lack of a control group.
Meyer et al (2009)[101] Level III	Prospective audit on all MV patients admitted in PICU for >24 hrs over four time periods over 9 yrs. Feeding algorithms and protocols were introduced after each audit. N=353 (mean age (SD): 3.5(4.3), 3.2 (4.2), 3.3 (4.3), 3.2 (4.1) for the four time periods).	Time taken to initiate nutritional support Proportion of patients fed via the EN vs PN Proportion of children reaching 50% and 70% of EAR by day 3.	Time to initiate nutrition support was reduced from 15 h in 1st period to 4.5 h in the last period. Patients on PN feed was reduced from 11% to 4%. Patients receiving a daily energy provision of 50% and 70% of the EAR by day 3 increased (from 6% to 21% for 70% of EAR).	Feeding protocol improve nutritional practices but protocol need to be monitored through audit. Used EAR for energy to assess adequacy of delivery of energy, first two audits did not collect reasons for not feeding. Absence of severity of disease scores.
Braudis et al (2009)[102] Level IV	Prospective case series of infants with HLHS following stage I palliation on enteral feeding algorithm versus historical controls N=63 (median age: 1 and 2 days for control and case groups respectively)	Safety and efficacy of enteral feeding algorithm.	Median PN duration was significantly lower in the study group (51 vs 116 hrs; p=0.03). Median time to achieve recommended daily allowance of calories was significantly reduced in the study group (9 vs 13 days; p=0.01). No incidence of NEC in the study group (11% in the control group). No difference in hospital LOS.	Use of EN feeding algorithm is safe and effective. Retrospective control group.
Lambe et al (2007)[81] Level IV	Retrospective study. Study aim was to determine the impact of NST intervention in PICU. N=82 (age: 7 days-2 years)	Caloric and protein intake and nutritional parameters were compared in 82 children in 2000 and 2003, before and after the introduction of NST.	No difference in parameters before and after introduction of NST: cumulative caloric deficits (19±15.7 vs 20.7±14.8 kcal/kg day); cumulative protein deficits (0.26±0.31 vs 0.22±0.20 g/kg day), time to achieve a SOCI (7 vs 7 days).	No significant differences with and without NST. Retrospective study. Results not applicable to all ICU patients as in this study a small age group was included REE could not be measured in this study.
Petrillo-Albarano et al (2006)[84] Level IV	Retrospective study medical patients before institution of feeding protocol and prospective review after feeding protocol. N=184 (mean age: 29.7 months and 55.9 months before and after feeding protocol respectively).	Time to goal feedings; GI complications.	Goal nutrition was achieved earlier in the protocol group (18.5 vs 57.8 hours, p<0.0001). Reduction in patient vomiting (20% to 11%) and a reduction in constipation (51% to 33%).	Retrospective study. Significant improvements reported in time to initiating EN and achieving goals with implementation of the algorithm.

A.S.P.E.N.: American Society of Parenteral Enteral Nutrition; BMR: Basal metabolic rate; EAR: estimated average requirement; EN: enteral nutrition; ESPGHAN: European Society for Paediatric Gastroenterology, Hepatology, and Nutrition; GI: gastrointestinal; HLHS: hypoplastic left heart syndrome; LOS: length of stay; MV: mechanical ventilation; NEC: necrotizing colitis; REE: resting energy expenditure; SOCI: sustained optimal caloric intake.

result in essential fatty acid deficiency. At present, there are no commercially available lipid for mulations that are suitable for critically ill children. Moreover, PN compounding facilities are not available in all centers in the region. Hence, efforts to optimize EN are critical in this region.

8. Use of prokinetics: The safety and use of prokinetics requires more well-designed studies in children.

9. There is a paucity of nutritional education in the curricula of medical and nursing schools. As a result, the basic level of awareness and scientific knowledge of the role of nutrition during critical illness remains low.

Conclusions and future steps

Nutritional support is given low priority in care of the critically ill child. There is an urgent need for enhanced advocacy for nutrition support and NSTs in every tertiary paediatric hospital. Optimal nutrition support should be emphasized as a part of everyday patient management and clinical practice through improved education of doctors, nurses and dieticians in the PICU. Most PICUs in the Asia-Pacific and Middle East region lack feeding protocols, or when available, they are not aligned with existing national or international guidelines. It is thus crucial that guidelines on nutrition therapy are developed and implemented at a national level so as to reduce heterogeneity in practice. Such guidelines should also be adapted to the needs of specialized populations such as critically-ill children with severe malnutrition. Clinical data are always required to support evidence-based guidelines, and more well-designed studies are required to support many aspects that are discussed in this report. These include investigations in energy requirements and utilization by severely malnourished critically ill children, and development of comprehensive and sensitive nutrition assessment tools for the PICU. Finally, the objective of advancing nutrition therapy in the PICU cannot be achieved without a comprehensive improvement in nutritional education across the spectrum of healthcare professionals.

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Review Article

Optimal nutrition therapy in paediatric critical care in the Asia-Pacific and Middle East: a consensus

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亚太和中东地区儿科重症监护的最佳营养治疗共识

背景与目的：亚太中东地区儿科重症监护病房（PICU）营养治疗的现状和可用资源与西方国家不同。现有的对危重症儿童营养管理的指南可能不能直接用于这一地区。本文概述了亚太中东共识工作组制定的儿科重症监护环境下营养治疗的共识声明，描述了这一地区独特的挑战和建议。**方法与研究设计**：系统检索了2004-2014 年间的文献，形成了 PICU 营养应用关键领域的共识声明。本综述重点关注适用于亚太中东地区的证据。推荐的证据和强度的质量是根据推荐评估、制定和评价方法的分级评分的。**结果**：肠内营养（EN）是首选的营养支持模式、应鼓励最优化 EN，其必须包括：评估和检测营养状态、给食途径的选择、开始和增加 EN 的时间、EN 不耐受的管理策略和使用肠外营养的适应症。因为存在患者营养状态的异质性、资源的可用性和文化的多样性，这个地区的 PICU 应该考虑营养师和/或营养团队的参与。**结论**：PICU 最佳营养治疗几个方面强有力的证据是不足的。营养评估必须落实到患病率的记录和营养不良的影响。PICU 必须优先考虑营养支持，尤其强调最优化 EN 的应用。

关键词：亚太地区、儿童、重症监护、中东、营养