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Early Enteral Nutrition Is Associated With Lower Mortality in Critically Ill Children

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Abstract

Background: The purpose of this study was to examine the association of early enteral nutrition (EEN), defined as the provision of 25% of goal calories enterally over the first 48 hours of admission, with mortality and morbidity in critically ill children. *Methods*: We conducted a multicenter retrospective study of patients in 12 pediatric intensive care units (PICUs). We included patients aged 1 month to 18 years who had a PICU length of stay (LOS) of ≥96 hours for the years 2007–2008. We obtained patients' demographics, weight, Pediatric Index of Mortality–2 (PIM2) score, LOS, duration of mechanical ventilation (MV), mortality data, and nutrition intake data in the first 4 days after admission. *Results*: We identified 5105 patients (53.8% male; median age, 2.4 years). Mortality was 5.3%. EEN was achieved by 27.1% of patients. Children receiving EEN were less likely to die than those who did not (odds ratio, 0.51; 95% confidence interval, 0.34–0.76; $P = .001$ [adjusted for propensity score, PIM2 score, age, and center]). Comparing those who received EEN to those who did not, adjusted for PIM2 score, age, and center, LOS did not differ ($P = .59$), and the duration of MV for those receiving EEN tended to be longer than for those who did not, but the difference was not significant ($P = .058$). *Conclusions*: EEN is strongly associated with lower mortality in patients with PICU LOS of ≥96 hours. LOS and duration of MV are slightly longer in patients receiving EEN, but the differences are not statistically significant. (*JPEN J Parenter Enteral Nutr*. 2014;38:459-466)

Keywords

early enteral nutrition; mortality; outcomes; pediatrics; critically ill children

Clinical Relevancy Statement

Our retrospective study of a large cohort of critically ill children showed that early enteral nutrition is strongly associated with lower mortality in children who stay longer than 96 hours in the pediatric intensive care unit. Prospective randomized controlled studies are needed to further study this association.

Introduction

Malnutrition is prevalent among patients in the pediatric intensive care unit (PICU) and has been shown to worsen over the course of the PICU stay.[1,2] In critically ill children, malnutrition is associated with an increased PICU length of stay (LOS) and an increased risk-adjusted mortality.[3] The benefits of nutrition support in the critically ill patient include improved wound healing, a decreased catabolic response to injury, and improved gastrointestinal structure and function.[4,5] While data from randomized controlled trials in adults have shown the benefits of enteral nutrition (EN) in contrast to parenteral nutrition (PN),[6,7] these effects are as yet unproven in critically ill children. Multiple adult randomized controlled studies have shown the benefits of early EN in postsurgical[8] and trauma patients.[9] Randomized controlled trials in mixed adult ICU patients have

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shown that early EN decreases mortality[10] and LOS,[11] while some studies have shown increases in infectious[12] and noninfectious complications.[10,12] Adult guidelines recommend the initiation of EN in the critically ill patient.[13] In critically ill children, EN is generally recommended, but there are no recommendations on when it should be started.[14] Early EN (EEN), defined as EN that is begun within 48 hours of admission to the PICU,[13] has been shown to be feasible in critically ill children,[15] and an overall higher enteral energy intake has been associated with reduced mortality.[15] However, no data are available regarding EEN and outcomes in the PICU. The purpose of our study was to determine whether EEN is associated with lower mortality, shorter LOS, and shorter duration of mechanical ventilation (MV) in critically ill children.

Materials and Methods

This was a retrospective, multicenter study, facilitated by the National Association of Children's Hospitals and Related Institution's PICU FOCUS Group. Twelve centers participated in this study after obtaining independent institutional review board approval to ensure compliance with ethical standards. Each center participated for at least 6 of the 8 quarters during the study period (January 2007 to December 2008, but some centers were not able to participate in the first 1–2 quarters) to avoid underrepresentation of any center in the final dataset. Patients were identified from the Virtual PICU Systems (VPS LLC) database (a multisite, clinical PICU database) based on the criteria of LOS of ≥96 hours. Data were obtained retrospectively from the VPS LLC database and from a review of medical records at each participating institution by data collectors who were trained by the research coordinator from the lead institution using a standardized manual of operation. The data from the VPS LLC database were collected by the respective PICUs using a standard data dictionary. Many VPS LLC data fields are mandatory for participating institutions, but others are not.

Inclusion and Exclusion Criteria

Patients who were admitted between January 1, 2007, and December 31, 2008, and had a LOS in the PICU of ≥96 hours were eligible for inclusion in the study. Patients who were at least 30 days and less than 18 years of age at PICU admission were included in the study. Patients who were transferred from another PICU were excluded.

Data From the VPS LLC Database

Data obtained from the VPS LLC database included weight, LOS, duration of MV, PICU mortality, age, sex, primary diagnosis category, patient type (scheduled [defined as PICU reservation made at least 12 hours before admission] vs unscheduled), operative status, trauma status, and Pediatric Index of Mortality–2 (PIM2) score. The PIM2 is a validated scoring system used to estimate the likelihood of mortality (range, 0%–100%) for a patient admitted to the PICU.[16] The PIM2 was a mandatory data field in the VPS LLC database during the study period and was the only mandatory severity of illness measure during the study period. Of the 12 participating centers, only 11 reported trauma status, and only 9 reported the duration of MV. Neither trauma status nor the duration of MV were mandatory data fields in the VPS LLC database during the study period, but centers that chose to include these fields were required to complete them for every patient entered into the database.

Data From Medical Records

Medical record data included the composition and quantity of EN and PN from which caloric intake was calculated. Calories were determined for each 24-hour period from admission for a total of 96 hours. Caloric intake from glucose in standard intravenous (IV) fluids was not included, but caloric intake from lipid-based medications (ie, propofol) was included. Goal calories were determined using the World Health Organization's (WHO) equation for the calculation of resting energy expenditure (REE).[17] For the purposes of this study, EEN was defined as the delivery of 25% of cumulative goal calories for the first 48 hours via the enteral route within the first 48 hours of PICU admission. Nutrition intake data were gathered on only the first 4 days of PICU admission. Malnourished patients, based on a weight-for-age Z score of less than –2.0, were excluded in some analyses to demonstrate that the findings did not reflect premorbid status.

Sample Size

Because mortality is low in North American PICUs,[18,19] sample size estimates were based on the aim of demonstrating a LOS of 1 day shorter in patients who received EEN. Because no previous data were available regarding what proportion of patients had been given EEN, it was estimated that 10%–15% of critically ill patients would have received EEN. Based on this information, sample size estimates were calculated using a 2-tailed α of .05 and power of .8. This yielded sample size estimates ranging from 3948–5590 patients.

Statistical Methods

Descriptive variables were analyzed using Mann-Whitney tests for continuous variables with a skewed distribution or by the χ^2 test of proportions for categorical variables. The associations between EEN and LOS and between EEN and duration of MV were analyzed using Mann-Whitney tests (because of the skewed distributions of LOS and duration of MV). Statistical

analysis with an adjustment for possible confounding was performed by an analysis of covariance using log-transformed LOS or duration of MV. The association between EEN and mortality was compared using χ^2 tests of proportion. Logistic regression analysis was performed to adjust for possible confounding. We assessed for trends in mortality based on the proportion of goal calories achieved by EN at the 48-hour and 96-hour mark using the Cochran-Armitage trend test. *P* values of less than .05 were considered statistically significant for all comparisons. All statistical comparisons were conducted using SAS version 9.1 (SAS Institute Inc, Cary, NC). All major comparisons were adjusted for the risk of mortality as determined by the PIM2 to account for differences in the severity of illness, for age due to confounding by age, and for center to account for inherent differences between centers. In an additional analysis, to address the possibility that sicker patients were less likely to be given EEN, a propensity score was calculated for each patient by using logistic regression to derive the probability of receiving EEN based on the VPS LLC variables described above.[20] The probability of EEN (propensity score) was then added as a covariate in the analysis of mortality.

Results

We identified 5105 patients from 12 centers who met the inclusion criteria. Each center collected data for at least 6 quarters from 2007 and 2008, and 8 centers collected data for all 8 quarters of 2007 and 2008. The number of patients from each center was related to the size of the PICU at the center and the number of quarters that the center participated in the study. The median age of patients was 2.4 years (interquartile range [IQR], 0.5–9.8), and 53.8% were male. Of the 5105 patients, 1386 (27.1%) (range, 15.6%–45.1%) received EEN. Patients who received EEN were significantly younger than those who did not (median, 0.7 years; IQR, 0.3–2.9 vs median, 4.0 years; IQR, 0.8–11.6, respectively; $P < .0001$). Sex did not differ between those who received EEN and those who did not. The PIM2 risk of mortality was significantly lower in those who received EEN than in those who did not (median, 1.2%; IQR, 0.8–3.9 vs median, 1.6%; IQR, 0.8–4.6, respectively; $P < .0001$). When stratified by quartiles of the PIM2 score, EEN was achieved by 31.4% of patients in the lowest quartile, 28.0% in the second quartile, 27.2% in the third quartile, and 22.0% of patients in the highest quartile. Nine of the 12 centers reported data on the duration of MV; patients who were mechanically ventilated were more likely to receive EEN than patients who were not mechanically ventilated (Table 1). Patients with a primary diagnosis in the respiratory category were more likely to receive EEN than patients with a primary diagnosis in other major diagnostic categories (Table 1). Scheduled patients, postoperative patients, post-bypass patients, and trauma patients were less likely to receive EEN (Table 1).

Mortality

Of 5105 patients, 273 (5.3%) died during their PICU admission. Patients who received EEN were less likely to die than those who did not (2.5% vs 6.4%, respectively; odds ratio [OR], 0.38; 95% confidence interval [CI], 0.26–0.54; $P < .001$). To address the concern that sicker patients were less likely to be given EEN, propensity testing was conducted. Adding the propensity score to the analysis, patients who received EEN were less likely to die than those who did not (OR, 0.51; 95% CI, 0.34–0.76; $P = .001$ [adjusted for propensity score, PIM2 score, age, and center]) (Table 2). These findings were not altered by excluding malnourished patients or by including only mechanically ventilated patients (Table 2). Excluding patients who received any PN in the first 48 hours of admission, patients who received EEN were less likely to die than those who did not (OR, 0.63; 95% CI, 0.41–0.96; $P = .032$ [n = 4344; adjusted for propensity score, PIM2 score, age, and center]). Patients who received EEN were less likely to die in the first 30 days of PICU admission (OR, 0.46; 95% CI, 0.29–0.74; $P < .002$ [adjusted for propensity score, PIM2 score, age, and center]) or the first 60 days of PICU admission (OR, 0.51; 95% CI, 0.33–0.78; $P < .002$ [adjusted for propensity score, PIM2 score, age, and center]) than those who did not receive EEN. When stratified by quartiles of the PIM2 score, patients in the second and fourth quartiles who received EEN were less likely to die than those who did not (OR, 0.37; 95% CI, 0.15–0.95; $P = .039$ vs OR, 0.53; 95% CI, 0.30–0.95; $P = .033$, respectively [both adjusted for propensity score, PIM2 score, age, and center]).

Trend in Mortality

An increasing proportion of EN relative to goal calories at 48 hours was associated with significantly decreased mortality ($P < .0001$ [unadjusted and adjusted for propensity score, PIM2 score, age, and center]) (Table 3). This trend of decreasing mortality associated with an increasing proportion of EN continued at 96 hours ($P < .0001$ [unadjusted and adjusted for propensity score, PIM2 score, age, and center]) (Table 4).

Length of Stay

Although the unadjusted LOS for those who received EEN was significantly longer than for those who did not (median, 7.95 days; IQR, 5.69–12.97 vs median, 7.65 days; IQR, 5.27–13.22, respectively; $P = .037$), the difference in LOS was not significant when adjusted for PIM2 score, age, and center ($P = .59$). These findings were not altered by excluding malnourished patients and patients who died or by including only mechanically ventilated patients (Table 5).

Table 1. Characteristics of Study Sample.

Characteristic	Received EEN, n (%)	Did Not Receive EEN, n (%)	χ^2 (*P* Value)
Mechanically ventilated (n = 3079 for 9 centers that reported data on duration of mechanical ventilation)			<.001
Yes	689 (31.7)	1484 (68.3)	
No	223 (24.6)	683 (75.4)	
Patient type[a] (n = 5105)			<.001
Scheduled	294 (22.8)	994 (77.2)	
Unscheduled	1092 (28.6)	2725 (71.4)	
Operative status (n = 5105)			<.001
Preoperative	108 (28.4)	272 (71.6)	
Postoperative	345 (19.5)	1425 (80.5)	
Nonoperative	933 (31.6)	2022 (68.4)	
Post-bypass status (n = 5105)			<.001
Yes	45 (10.5)	383 (89.5)	
No	1341 (28.7)	3336 (71.3)	
Trauma status (n = 4811 for 11 centers that reported trauma status)			<.001
Yes	43 (11.9)	318 (88.1)	
No	1297 (29.1)	3153 (70.9)	
Primary diagnostic category (n = 5105)			<.001
Respiratory	780 (45.2)	944 (54.8)	
Cardiovascular	177 (19.5)	733 (80.5)	
Neurological	85 (19.9)	342 (80.1)	
Injury/poisoning	53 (12.7)	365 (87.3)	
Gastrointestinal	15 (5.2)	274 (94.8)	
Infectious	62 (21.5)	226 (78.5)	
Oncological	24 (9.2)	237 (90.8)	
All others	190 (24.1)	598 (75.9)	

EEN, early enteral nutrition.
[a]A scheduled admission means that the pediatric intensive care unit (PICU) reservation was made at least 12 hours before the upcoming admission. Unscheduled means the PICU reservation was made less than 12 hours before the upcoming PICU admission.

Table 2. Effect of EEN on Mortality.

Patient Group	EEN vs Not (Unadjusted), OR (95% CI)	EEN vs Not (Adjusted[a]), OR (95% CI)
No exclusions (n = 5105)	0.38 (0.26–0.54)	0.51 (0.34–0.76)
Excluding malnourished patients (n = 3667)	0.29 (0.18–0.48)	0.44 (0.25–0.76)
Mechanically ventilated patients only (n = 2173)	0.40 (0.26–0.62)	0.59 (0.36–0.96)

CI, confidence interval; EEN, early enteral nutrition; OR, odds ratio.
[a]Adjusted for propensity score, Pediatric Index of Mortality–2 score, age, and center.

Table 3. Effect of Increased Proportion of EN at 48 Hours on Mortality.

Patient Group Based on % of EN Goal Received by 48 Hours	Died, n (%)	Survived, n (%)	Unadjusted OR (95% CI)[b]	Adjusted[a] OR (95% CI)[b]
Did not receive EN by 48 hours	208 (7.04)	2747 (92.96)	—	—
Received <25% of EN goal for 48 hours	30 (3.93)	734 (96.07)	0.54 (0.37–0.80)	0.53 (0.35–0.81)
Received 25%–100% of EN goal for 48 hours	22 (2.43)	885 (97.57)	0.33 (0.21–0.51)	0.42 (0.26–0.67)
Received >100% of EN goal for 48 hours	13 (2.71)	466 (97.29)	0.37 (0.21–0.65)	0.50 (0.27–0.93)
Total	273 (5.35)	4832 (94.65)		

CI, confidence interval; EN, enteral nutrition; OR, odds ratio.
[a]Adjusted for propensity score, Pediatric Index of Mortality–2 score, age, and center.
[b]Comparison to "did not receive EN by 48 hours."

Table 4. Effect of Increased Proportion of EN at 96 Hours on Mortality.

Patient Group Based on % of EN Goal Received by 96 Hours	Died, n (%)	Survived, n (%)	Unadjusted OR (95% CI)[b]	Adjusted[a] OR (95% CI)[b]
Did not receive EN by 96 hours	162 (7.83)	1907 (92.17)	—	—
Received <25% of EN goal for 96 hours	54 (6.26)	809 (93.74)	0.79 (0.57–1.08)	0.64 (0.45–0.91)
Received 25%–100% of EN goal for 96 hours	38 (2.71)	1363 (97.29)	0.33 (0.23–0.47)	0.34 (0.23–0.50)
Received >100% of EN goal for 96 hours	19 (2.46)	753 (97.54)	0.30 (0.18–0.48)	0.37 (0.21–0.63)
Total	273 (5.35)	4832 (94.65)		

CI, confidence interval; EN, enteral nutrition; OR, odds ratio.
[a]Adjusted for propensity score, Pediatric Index of Mortality–2 score, age, and center.
[b]Comparison to "did not receive EN by 96 hours."

Table 5. Association Between EEN and LOS.

Patient Group	LOS in Those Who Received EEN, Median (IQR)	LOS in Those Who Did Not Receive EEN, Median (IQR)	Unadjusted *P* Value	Adjusted[a] *P* Value
All patients (n = 5105)	7.95 (5.69–12.97)	7.65 (5.27–13.22)	.037	.59
Excluding malnourished patients and patients who died (n = 3468)	7.86 (5.69–12.33)	7.26 (5.13–12.12)	.087	.62
Mechanically ventilated patients only (n = 2173)	9.07 (5.99–15.15)	8.92 (5.90–16.50)	.765	.92
Mechanically ventilated patients only excluding malnourished patients and patients who died (n = 1391)	8.78 (5.95–14.76)	8.64 (5.82–15.77)	.751	.78

EEN, early enteral nutrition; IQR, interquartile range; LOS, length of stay.
[a]Adjusted for Pediatric Index of Mortality–2 score, age, and center.

Duration of MV

The unadjusted duration of MV for those who received EEN was significantly longer than the duration of MV for those who did not (median, 6.29 days; IQR, 3.92–9.92 vs median, 5.51 days; IQR, 2.99–10.26, respectively; $P = .0027$). The difference was not statistically significant after adjustment for PIM2 score, age, and center ($P = .058$) for the entire group but was significant after excluding malnourished patients and patients who died (Table 6).

Discussion

We have shown that EEN in critically ill children is associated with a significantly lower mortality rate during their PICU admission (adjusted for severity of illness, age, and inherent differences between participating centers). These data cannot be used to determine the cause and effect but only to infer a strong association. We have also shown that EEN is not associated with LOS and duration of MV. As has been shown previously, the rates of achieving EEN are poor, with only about one quarter of our patients achieving that goal.[1] EEN was more likely to be achieved in younger children and patients with a lower severity of illness as measured by the PIM2. Furthermore, sicker patients were less likely to receive EEN. Whether EN was contraindicated in sicker patients or whether providers were biased against administering EN in sicker patients cannot be determined from the data available in this study.

EEN was less likely to be achieved postoperatively, in scheduled patients, in trauma patients, and after cardiopulmonary bypass. It was more likely to be achieved in patients who were mechanically ventilated. This may reflect postoperative ileus or impending extubation postoperatively. Patients after cardiac surgery may be less likely to be promptly fed potentially because of hemodynamic concerns. It is somewhat surprising that children who were mechanically ventilated were more likely to be fed earlier than children who were not. The reasons for this are less clear. Patients in the respiratory diagnostic category were the most likely to achieve EEN, while patients in the gastrointestinal, trauma, and oncological diagnostic categories were the least likely to achieve EEN. The lack of EEN in patients admitted with gastrointestinal diagnoses is not surprising as the underlying pathology of these patients may serve as relative or absolute contraindications to EN. PN is commonly used in the pediatric oncology population, with 25% of all PN used in children's hospitals being administered to children with oncological diagnoses.[21] Patients with oncological diagnoses may have nausea and vomiting,

Table 6. Association Between EEN and Duration of MV.

Patient Group	Duration of MV in Those Who Received EEN, Median (IQR)	Duration of MV in Those Who Did Not Receive EEN, Median (IQR)	Unadjusted *P* Value	Adjusted[a] *P* Value
All mechanically ventilated patients (n = 2173)	6.29 (3.92–9.92)	5.51 (2.99–10.26)	.0027	.058
All mechanically ventilated patients excluding malnourished patients and patients who died (n = 1391)	6.14 (3.92–9.53)	5.07 (2.74–9.60)	.0006	.023

EEN, early enteral nutrition; IQR, interquartile range; MV, mechanical ventilation.
[a]Adjusted for Pediatric Index of Mortality–2 score, age, and center.

oral mucositis, and gastrointestinal graft-vs-host disease that may make EN more difficult.[22] The causes for these variations should be explored prospectively.

The relationship between EEN and survival remained significant even after excluding patients who were malnourished at admission and correcting for severity of illness, age, and individual center. Increasing amounts of EN from 25%–100% achieved within 48 hours appeared to confer more survival benefits, with no further benefit beyond 100% of the predicted REE. Higher energy and protein intakes have been correlated with the achievement of positive protein balance in children receiving MV in the PICU.[23] We did not specifically study protein intake in our patients. Within our dataset, we were unable to investigate the additional causes for the increased mortality in the children not receiving EEN.

So, why would EEN be beneficial in the PICU setting? Animal studies have shown that starvation after injury for as short a period as 12 hours depletes tissue antioxidant systems, whereas early feeding after injury helps maintain antioxidant levels.[24,25] EEN may protect the liver from injury after hemorrhages and the kidney from damage after rhabdomyolysis.[26,27] Immediate postoperative EN improves protein synthesis,[28,29] which is necessary for wound healing.[29,30] Finally, EEN has been shown to prevent gut atrophy and loss of villi and to maintain intestinal barrier function.[31,32] Loss of gut barrier function has been proposed as a major contributor to the systemic inflammatory response that ultimately leads to multiple organ failure. Sepsis syndrome also results from bacterial translocation in which intestinal bacteria and/or lipopolysaccharides (LPS) are thought to enter the portal bloodstream and serve as a trigger for inflammatory cytokine production, systemic immunoinflammatory responses, and septic complications in critically ill patients. Thus, the provision of EEN results in the preservation of gut-associated lymphoid tissue, gut barrier function, and the ability to detoxify LPS.[14,33] Specifically, intestinal alkaline phosphatase has been shown to be maintained by EN, and this serves to neutralize LPS.[32]

We have shown that EEN in critically ill children is associated with a significantly lower mortality rate after adjusting for severity of illness, inherent variation between participating centers, age of the patients, and propensity score. The PICU LOS did not differ between the 2 groups. This is similar to several adult studies that have shown no difference in ICU and hospital LOS with EEN.[34-37] In addition, after adjustments for the risk of mortality, center, and age of the patients, we found no differences in the duration of MV in the 2 groups, except when patients who died and malnourished patients were excluded. Similarly, several adult interventional studies have found no differences in the duration of MV with EEN.[35,38,39]

Our study has all the limitations of a retrospective study, in particular, the inability to demonstrate causality and the inability to determine why certain patients were or were not given sufficient EN to meet our definition of EEN. However, the usual limitations of registry data were addressed using VPS LLC's standard operating procedure, which has been previously described.[40] Furthermore, ongoing measurement of within-center interrater reliability is a requirement for data submission and remains greater than 97% (VPS LLC, personal communication, 2012). Sampling bias was minimized through the use of strict inclusion and exclusion criteria, comprehensive methods to verify data completeness, and a large sample size. However, it is possible that the existing VPS LLC data elements failed to capture unmeasured confounders of outcomes.

Our study has other limitations related to the retrospective design. First, we chose not to include caloric intake from glucose in IV fluids because the additional time required to collect such data would have been prohibitive, and our focus was the effect of EN on outcomes. Second, it was beyond the scope of this study to determine whether dehydration or fluid overload led to inaccurate admission weights and thereby misclassification by weight. Finally, because the VPS LLC database includes data from the PICU stay only, the definition of mortality was limited to death occurring during the PICU stay. While it is unlikely that many patients died after leaving the PICU, this could not be verified. It is possible that some participating centers transferred patients to another PICU, either at their own institution or at another institution, and data for their course at that subsequent PICU were not available.

We used the WHO equation to calculate caloric needs. Ideally, we would have measured REE on all our patients, but this was not possible in a retrospective study. Thus, we cannot adequately explore the relationship between energy deficits and outcomes in our study. However, most PICUs use a variety

of methods including equations to calculate caloric needs. There are now robust data suggesting that no equation accurately predicts REE in critically ill children.[41,42] Furthermore, we did not specifically study protein intake in this study, so we cannot evaluate the relationship between protein intake and outcomes in our patients. However, this would be an appropriate direction for future studies.

We used the PIM2 for risk adjustment of severity of illness instead of the Pediatric Risk of Mortality III (PRISM III) scores. The PRISM III may have been better suited to our study because it uses data captured during the first 12 hours of PICU admission as opposed to the PIM2, which uses data from only the first hour of PICU admission. However, the PRISM III score was not obtained at some of the centers that participated in this study and was therefore not available for use.

For this study, we chose a population that would benefit from EEN by including all patients who spent at least 4 days in the PICU. This resulted in a population that is somewhat skewed compared with the norm for PICU patients, as evidenced by the higher mortality and the large proportion of malnourished patients in our study population. While EEN may confer benefits to all children admitted to the PICU, it may be much more difficult to ascertain those benefits in children who have a LOS shorter than 4 days. While it is clear from our study that less sick children are more likely to receive EEN, achievement of EEN confers a significant survival advantage at the highest levels of illness severity. This outcome is seen in all children who spend at least 4 days in the PICU. Future work is necessary to understand the physiological mechanism of the benefits of EEN and to identify and eliminate barriers to EEN among nonfed critically ill children.

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