Published in final edited form as:

Crit Care Med. 2016 August ; 44(8): 1530–1537. doi:10.1097/CCM.0000000000001713.

Nutritional status based on Body Mass Index is associated with morbidity and mortality in mechanically ventilated critically ill children in the PICU

Lori J. Bechard, PhD, RD, LDN, Christopher Duggan, MD, MPH, Riva Touger-Decker, PhD, RD, FADA, J. Scott Parrott, PhD, Pamela Rothpletz-Puglia, EdD, RD, Laura Byham-Gray, PhD, RD, Daren Heyland, MD, and Niles M. Mehta, MD

Center for Nutrition, Boston Children's Hospital, Harvard Medical School (LJB, CD, NMM); Department of Nutritional Sciences, Rutgers University School of Health Related Professions (LJB, RTD, PRP, LBG); Department of Interdisciplinary Studies, Rutgers University School of Health Related Professions (JSP); Clinical Evaluation Research Unit, Kingston General Hospital and Queen's University (DKH); Critical Care Medicine, Department of Anesthesiology, Perioperative and Pain Medicine, Boston Children's Hospital (NMM)

Abstract

Objective—To determine the influence of admission anthropometry on clinical outcomes in mechanically ventilated children in the pediatric intensive care unit (PICU).

Design—Data from 2 multicenter cohort studies were compiled to examine the unique contribution of nutritional status, defined by BMI Z-score, to 60-day mortality, hospital-acquired infections, length of hospital stay, and ventilator free days (VFD), using multivariate analysis.

Setting—90 PICUs from 16 countries with 8 beds.

Patients—Children aged 1 month to 18 years, admitted to each participating PICU and requiring mechanical ventilation for more than 48 hours

Measurements and Main Results—Data from 1622 eligible patients, 54.8% male and mean (SD) age 4.5 (5.1) years, were analysed. Subjects were classified as underweight (17.9%), normal weight (54.2%), overweight (14.5%), and obese (13.4%) based on BMI Z-score at admission. After adjusting for severity of illness and site, the odds of 60-day mortality were higher in underweight (OR 1.53, $P<0.001$) children. The odds of hospital-acquired infections were higher in underweight (OR 1.88, $P=0.008$) and obese (OR 1.64, $P<0.001$) children. Hazard ratios for hospital discharge were lower among underweight (HR 0.71, $P<0.001$) and obese (HR 0.82,

Corresponding author: Niles M. Mehta, MD, Boston Children's Hospital, 300 Longwood Avenue, Bader 6, Boston, MA 02115.

Conflicts of Interest:

For the remaining authors none were declared.

Copyright form disclosures:

The remaining authors have disclosed that they do not have any potential conflicts of interest.

None of the authors reported a conflict of interest related to the study.

Author Responsibilities

NMM was the principal investigator for the Pediatric International Nutrition Studies. NMM, LJB, CD and DH designed the research; NMM and LJB conducted the research and data collection. LJB, CD, RTD and JSP analyzed the data and performed statistical analyses. NM and LJB had primary responsibility for the final content of the manuscript; all authors wrote the manuscript.

P=0.04) children. Underweight was associated with 1.3 (P=0.001) and 1.6 (P<0.001) fewer VFD, compared to normal weight and overweight, respectively.

Conclusions—Malnutrition is prevalent in mechanically ventilated children on admission to PICUs worldwide. Classification as underweight or obese was associated with higher risk of hospital-acquired infections and lower likelihood of hospital discharge. Underweight children had a higher risk of mortality and fewer ventilator-free days.

Keywords

pediatric intensive care unit; body mass index; malnutrition; obesity; overweight; underweight; nutritional status; mortality; hospital-acquired infections

Introduction

Children requiring mechanical ventilation may be at high risk of mortality due to their severity of illness or acquired morbidities [1–3]. Nutritional status on admission to the PICU has been associated with poor outcomes [4, 5]. Documentation of weight and height is recommended in PICU settings [6], but few studies have examined the relationships between a range of nutritional status categories (i.e. underweight, normal weight, overweight and obesity) and clinical outcomes in critically ill children [4, 7–10]. The quality of some of these studies has been limited due to retrospective design [9], single center observations, or small sample size [4, 9], and nutritional status determined by weight alone [4]. In large pediatric populations, body mass index (BMI) Z-score is a feasible assessment of nutritional status that may correlate with body composition measurements. Therefore, we aimed to determine the influence of admission nutritional status, as assessed by BMI Z-score, on important clinical outcomes in mechanically ventilated children.

Materials and Methods

The sample was a combined cohort of subjects enrolled in the Pediatric International Nutrition Studies (PINS) 1 and 2. Study methods have been previously described [11] and were the identical for two surveys [12]. Site investigators in participating PICUs with 8 or more beds collected demographic, clinical, and nutritional data on consecutively admitted mechanically ventilated children aged 1 month to 18 years with an expected stay of 3 or more days. Patients were excluded if they were enrolled in another nutritional study, were receiving palliative care at end of life or if they had achieved full oral feeding and were not dependent on any artificial feeding (EN or PN) by Day 3. The dietitian recorded details of nutrient intake daily for the duration of PICU stay, up to 10 days. Severity of illness was classified as mild, moderate, or severe based on the tertile of the lowest severity score recorded (PRISM, PRISM III or PIM2) [11].

Nutritional status on admission was defined by BMI Z-score using the most recent internationally relevant growth standards and references [13, 14]. The Z-scores were calculated using the World Health Organization (WHO) AnthroPlus® software [15]. Subjects were categorized as underweight (BMI Z-score < -2), normal weight (BMI Z-score

-2 and -1), overweight (BMI Z-score > 1 and < 2), or obese (BMI Z-score > 2) [13, 16, 17].

During a 60-day follow up period, the 4 primary outcomes, a) mortality, b) hospital-acquired infections, c) mechanical ventilation days, and d) hospital length of stay, were recorded for each subject. Hospital acquired infections were defined as those that were diagnosed at least 48 hours after admission to the PICU and during the PICU or hospital stay up to 60 days. Ventilator free days were calculated as the difference between 28 days and the total number of days mechanical ventilation was required [18]. For subjects who died or received 28 or more days of mechanical ventilation, zero ventilator free days were recorded. All data were de-identified and entered into a web-based remote data capture system by site investigators, with cross-checks and confirmation by the coordinating site (Boston Children's Hospital) [11].

Data analysis

Descriptive statistics are reported for demographic (age, sex, PICU country/region), anthropomorphic/clinical (BMI Z-scores, PICU number of beds, admission category, diagnosis category, illness severity), and outcome variables (infection incidence, mortality and ventilator free days), and nutrition status groups were compared using bivariate analyses across a range of variables, including study year, to identify potential confounders. A Kaplan Meier time to event analysis was used to describe length of hospital stay among only those subjects who survived, to avoid the competing effect of mortality on the outcome.

To account for the clustering effect of data within the geographic location of PICUs, generalized estimating equations (GEE) were used to model the probability of the dichotomous (presence of infection, mortality) and continuous (ventilator-free days) outcomes among the four nutritional status categories. Based on the bivariate analyses of the clinical and demographic characteristics, all variables significant at $p < 0.1$ were considered for inclusion in the multivariate models [19]. Regardless of significance, nutritional status category, as the primary independent variable, was retained in the final regression models with the best fit for predicting each respective outcome. Since they are important factors for outcomes in this population, age, sex, and PICU location were also retained in the final models. In addition, two outcomes that showed a significant relationship with nutritional status, acquired infection and length of hospital stay, were added to the multivariate model of ventilator free days. The distribution of ventilator free days (VFD) was bimodal, therefore a two-step approach to the analysis was conducted using 1) a logistic regression GEE model to categorically evaluate subjects with zero vs. any number of VFD, and 2) a multiple linear regression GEE to model the results of subjects with one or more VFD among the four nutritional status categories. A hierarchical Cox proportional hazards regression model was constructed to determine if nutritional status category significantly influenced days until hospital discharge, while controlling for PICU location and the same set of covariates as in the GEE models.

Ethics

The institutional review boards of Boston Children's Hospital and the Rutgers Biomedical and Health Sciences approved this investigation. Each participating site obtained local IRB approval or waiver.

Results

Of the 1769 eligible subjects in the combined cohort of the first (n=524) and second international study (n=1245), data from 1622 subjects were analyzed (Figure 1). Weights were measured in 91% of the cohort and estimated in the remaining 9% of the cohort. Measured heights were available in 72% of the cohort on admission, and estimated in 28% of subjects. Subject characteristics are shown in Table 1. In the combined cohort, 54.2% (n = 879) of subjects were classified as normal weight, 17.9% (n = 291) were underweight, 14.5% (n = 235) were overweight, and 13.4% (n = 217) were obese. There were no significant differences in age, sex, weight-for-age Z-score, height-for-age Z-score, BMI-for-age Z-score, length of hospital stay, or 60-day mortality between the two cohorts.

Overall 60-day mortality in the combined cohort was 6.8% (n = 111). The incidence of one or more acquired infections was 14.7% (n = 237), ventilator associated pneumonia 8.3% (n = 134), urinary tract infections 5.0% (n = 80), and catheter related blood stream infections 4.3% (n = 68). The relationships between nutritional status and the risks of mortality and infections are shown in Table 2. When controlling for the covariates, underweight subjects were 1.53 times more likely to die during the 60-day study period than normal weight subjects (95% CI 1.24–1.89, $P < 0.001$). The odds of 60-day mortality were not significantly higher among overweight and obese subjects compared to normal weight subjects. Compared to normal weight subjects, the likelihood of acquiring an infection during PICU stay was significantly higher for underweight (OR 1.88, 95% CI 1.18–3.01, $P = 0.008$) and obese subjects (OR 1.64, 95% CI 1.33 – 2.03, $P < 0.001$). The odds of acquired infections were not significantly higher among overweight subjects compared to normal weight subjects.

The proportional hazards model explained length of hospital stay significantly among survivors in this cohort. The Kaplan Meier curve for hospital length of stay (up to 60 days) for survivors in the nutritional status groups is shown in Figure 2 ($\chi^2 = 121.6$, $P < 0.001$). For each additional day in the hospital, underweight subjects had a 29% (HR 0.71, 95% CI 0.60–0.84, $P < 0.001$) lower chance of being discharged and obese subjects had an 18% (HR 0.82, 95% CI 0.68–0.99, $P = 0.04$) lower chance of being discharged than those who were normal weight, after controlling for the covariates.

Of the 98% of subjects (n = 1593) with available data for VFD, 17% (n = 264) had zero VFD. The logistic regression GEE model showed that underweight subjects were 40% less likely (OR 0.60, 95% CI 0.53–0.69, $P < 0.001$), obese subjects were 51% less likely (OR 0.49, 95% CI 0.43–0.54, $P < 0.001$), and overweight subjects were 19% less likely (OR 0.81, 95% CI 0.76–0.86, $P < 0.001$), respectively, to have one or more VFD compared to normal weight subjects. To further model the relationship between nutritional status category and VFD, data from the 82% (n=1329) of subjects in the cohort who had one or more VFD were

included in a linear regression GEE, with PICU country/region as the second level predictor. Nutritional status category was a significant contributor to the model predicting one or more VFD ($\chi^2 = 20.4$, $P < 0.001$), when controlling for age, sex, study year, admission category, diagnosis category, illness severity, and PICU size. Underweight was significantly associated with 1.3 fewer VFDs than normal weight (95% CI -2.1 to -0.6 , $P = 0.001$), 1.6 fewer days than overweight (95% CI -2.4 to -0.9 , $P < 0.001$), and 1.2 fewer days than obese (95% CI -1.9 to -0.6 , $P < 0.001$). Compared to normal weight subjects, there were no significant differences in VFD among overweight and obese subjects.

Discussion

Suboptimal nutritional status (underweight, overweight or obesity) was documented in nearly half (46%) the cohort of over 1600 mechanically ventilated children on admission to the PICU. Being underweight was associated with significantly higher odds of 60-day mortality and hospital-acquired infections. Obesity was significantly associated with longer hospital stay among survivors. To our knowledge, this is the largest prospective pediatric critical care cohort demonstrating an association between BMI at admission and important clinical outcomes. Our results highlight the prevalence of malnutrition in PICUs and the importance of anthropometry to allow early interventions to be targeted in high-risk critically ill children.

Underweight status has been shown to predict outcomes in a variety of critically ill pediatric populations [20–22]. In a recent study of PICU admissions at a tertiary referral center in the U.K., mean weight for age was significantly lower than that of the national reference population [10]. Mortality risk was highest in children who were underweight (WFA Z-score < -3) or overweight (WFA Z-score $> +3$) in this cohort. Similarly, a prospective cohort study of children admitted to a Brazilian PICU, malnutrition was significantly associated with duration of mechanical ventilation [23]. In a cohort of children admitted to an Indian PICU, malnutrition was associated with increased risk of acquired infections and length of stay [7]. In children with congenital heart defects underweight is a significant predictor of lengthier hospital stay [22, 24, 25]. Other researchers have demonstrated associations between pediatric undernutrition and higher risk for pressure ulcers [26], and respiratory infections [27, 28], all of which may contribute to morbidity and mortality. While associations such as these do not imply causality; the impact of being underweight on pediatric outcomes may have biologic plausibility. Underweight could be a symptom of an underlying disease or reason for admission that relates to mortality risk [29]. Underweight children may also have impaired immune function that could limit their defence against exposure to infections common in hospitals [30]. Furthermore, critically ill children are at risk of further nutritional deterioration during their illness course due to disease or barriers to nutrient delivery in the intensive care unit.

Previous studies have utilized weight for age Z-scores to classify patients according to their nutritional status. This is probably due to the lack of available heights in PICUs. Despite the prospective nature of our study, measured heights were substituted by estimated values in 28% of the cohort. However, weight alone may be misleading as a marker of nutrition, especially in the PICU population where fluid shifts are commonly present during the acute

phase of illness. Weight for height or BMI may provide a better index of nutritional status and were recently recommended as primary indicators of nutritional status and growth in children [31]. Lean body mass may be a better predictor of outcomes compared to weight alone [32]. Skeletal muscle mass loss, or sarcopenia, has been shown to predict a variety of outcomes in critically ill adults [33]. Anthropometric measurements such as mid-arm circumference, triceps skinfold thickness, mid-arm muscle circumference, mid-arm muscle area have been used to describe fat and lean stores and their relation to outcomes in mechanically ventilated children [8]. However, accurate measurements require expertise and experience. Despite its limitations, BMI can be easily determined by weight and height measurement and may be a better indicator than body weight for evaluating the proportion of fat mass relative to lean mass in children [34].

The relationship between obesity and pediatric critical care outcomes remains unclear. In a single center retrospective study of mechanically ventilated children, overweight, obese or severely obese children did not have any significant difference in mortality, length of stay or duration of MV, when compared to patients with normal weight [35]. In children admitted for status asthmaticus, obesity was a significant predictor of PICU stay [36]. Pediatric cohorts with critical illness, cancer, solid organ and stem cell transplantation have a mortality association with obesity [37]. In our current study, children who were obese or underweight had significantly longer hospital stays but their odds of acquiring an infection were not higher. The nature of the impact of obesity on outcomes may depend on the individual patient and illness type. Excess fat stores may affect ventilatory status, potentially increasing dependence on respiratory support [38]. Patients who are obese may also be at greater risk for complications related to skin integrity such as pressure sores, which could delay hospital discharge [39]. Existing studies have used heterogeneous methods to classify subjects as obese or obese and a uniform definition might help clarify some of these associations in future investigations.

As a PICU outcome, ventilator-free days accounts for the impact of ventilator time and mortality within a defined time period, with larger numbers indicating reduced morbidity and zero indicating mortality or extended ventilator time [18]. The analysis of ventilator days unadjusted for mortality could potentially yield ambiguous results, since fewer days on ventilation would suggest a positive outcome even if resulting from death. In our cohort, the bimodal distribution of the outcome was appropriate for the two-step analysis approach. The odds of at least one ventilator-free day were lower among underweight, overweight, and obese patients compared to normal weight patients. Underweight patients had at least 1.2 fewer ventilator-free days compared to all other categories of nutritional status. Other studies using weight-for-age as the nutritional status marker have failed to demonstrate significant relationships between nutritional status and days on mechanical ventilation [35, 36, 40].

Malnutrition detected on admission to the PICU may represent a variety of etiologies, often related to the underlying disease and comorbidities. In Table 3 we describe the relationship between comorbidities and nutritional status for our cohort. Children with congenital heart disease had the highest incidence of underweight, followed by those admitted with other cardiac diseases and respiratory illness. On the other hand, children admitted with existing renal and endocrine illness had high prevalence of obesity. Pre-existing conditions may

impede nutritional status by decreased intake, absorption or assimilation of nutrients. Therapies aimed at alleviating the underlying conditions along with attention to optimal nutrient intake for individual patients may be important in reversing or in some cases preventing nutritional deterioration during prolonged critical illness. Our results suggest that simple anthropometric variables might allow effective screening of patients at risk of poor outcomes. The associations reported in our study strengthen the argument for resource allocation to the further nutritional assessment of flagged patients and targeted interventions for critically ill children with existing malnutrition. Future studies examining targeted strategies and their impact on outcomes in malnourished children in the PICU are desirable.

Our study has several limitations that must be recognized. Despite the multinational participation, only medium sized PICU sites were eligible and sites in the U.S. and Europe dominate these data. African and many Asian centers, where malnutrition may be even more prevalent, were not adequately represented. Although we included mechanically ventilated children in an attempt to enroll sick children, we acknowledge that a fraction of the cohort was on this support following elective surgeries. Lack of accuracy of measurements due to variability in measurement techniques is an important limitation to anthropometric studies. Weights could be influenced by volume depletion or dehydration. Critically ill children frequently have alterations in fluid balance that lead to erroneous, sometimes inflated, weight measurements [41]. These fluctuations from usual body weight may lead to invalid BMI Z-scores and misrepresentations in the distribution of nutritional status. In addition, accurate measurement of weight and particularly height may not be feasible in all critically ill patients. The prospective nature of the study allowed us to make best efforts to obtain these measurements. In cases where these were deemed unsafe or not feasible, dietitians at the enrolling sites used best estimates for these variables. Subgroup analyses of subjects that only included those with measured weight and height showed similar associations between BMI Z scores categories and clinical outcomes, including mortality, hospital-acquired infection, ventilator-free days and hospital length of stay. A small number of patients with implausible BMI z scores were removed from the final analysis. Furthermore, BMI reflects only one aspect of nutritional assessment in children. An in- depth nutritional status assessment must involve dietary and recent growth history, physical examination and biochemical markers. Composite screening tools that incorporate some of these elements are available for hospitalized children but have not been validated in the PICU population. Our study was also limited by the cross-sectional nature of the data collection. The prevalence of admission disease categories and severity of illness could be related to time, site or region. We attempted to address many of these limitations with the prospective study design and a large sample of patients from PICUs in regions across the world, and limiting the participation to sites with 8 or more beds. Training on the use of our standardized data entry form, prospective data recording by experienced dietitians, in a majority of centers, and rigorous built-in and manual crosschecks for missing or erroneous data points, were incorporated in the study design. This helped provide a high percentage of complete and reliable data. The data were strengthened by the diversity and size of the sample, which enhances the generalizability of our observations to PICUs with similar characteristics.

Conclusions

In a large cohort of mechanically ventilated children, we recorded a high prevalence of malnutrition; and have demonstrated significant associations between nutritional status on admission to the PICU and important clinical outcomes. Underweight status predicted a higher risk-adjusted mortality, likelihood of hospital discharge, and hospital-acquired infections. Abnormal nutritional status negatively impacted ventilator-free days in this cohort. Nutritional status must be determined on all children in the PICU. Malnourished children (both underweight and obese) must be flagged on admission in order to target optimal nutritional strategies aimed at preventing further nutritional deterioration. Future studies must examine the role of targeted nutritional interventions in this cohort and their impact on improving clinical outcomes.

Acknowledgments

Source of Funding:

This study was partly supported by the Jean Hankin Epidemiology grant from the Academy of Nutrition and Dietetics (LJB), NIH K24 DK 104676 (CD), and an unrestricted grant from the Division of Critical Care Medicine at Boston Children's Hospital (NMM).

Dr. Mehta served as a board member for American Society of Parenteral and Enteral Nutrition (A.S.P.E.N.), received book royalties from McGraw Hill (Editor of the textbook -Pediatric Critical Care Nutrition), and received support for the international study (Unrestricted one time institutional grant - Division of Critical Care Medicine). Dr. Bechard's institution received grant support from the Academy of Nutrition and Dietetics Foundation. Dr. Duggan received royalties from UpToDate, Inc. (chapter royalties) and Peoples Medical Publishing House USA, Inc. (book royalties). He received support for article research from the National Institutes of Health (NIH). His institution received grant support from the NIDDK (K24 DK104676, the NIH, and the Gates Foundation. Dr. Byham-Gray is employed by Rutgers University and received royalties from Springer Publications (Chief Editor, Nutrition in Kidney Disease). Her institution received grant support from the NIDDK and AHRQ (two federal grants).

We are grateful for the valuable contributions of the site investigators and data collectors of the 2009 and 2011 Pediatric International Nutrition Studies. The analysis for the current paper was conducted while LJB was a PhD student at Rutgers University School of Health Related Professions, Department of Nutritional Sciences.

References

1. Pollack MM, Patel KM, Ruttimann UE. PRISM III: an updated Pediatric Risk of Mortality score. *Critical Care Medicine*. 1996; 24(5):743–752. [PubMed: 8706448]
2. Slater A, Shann F, Pearson G. PIM2: a revised version of the Paediatric Index of Mortality. *Intensive Care Med*. 2003; 29(2):278–285. [PubMed: 12541154]
3. Gupta S, Boville BM, Blanton R, Lukasiewicz G, Wincek J, Bai C, Forbes ML. A multicentered prospective analysis of diagnosis, risk factors, and outcomes associated with pediatric ventilator-associated pneumonia. *Pediatr Crit Care Med*. 2015; 16(3):e65–e73. [PubMed: 25607739]
4. Numa A, McAweeney J, Williams G, Awad J, Ravindranathan H. Extremes of weight centile are associated with increased risk of mortality in pediatric intensive care. *Crit Care*. 2011; 15(2):R106. [PubMed: 21453507]
5. Mello MJG, Albuquerque MFPM, Alencar Ximenes RA, Lacerda HR, Ferraz EJS, Byington R, Barbosa MTS. Factors associated with time to acquisition of bloodstream infection in a pediatric intensive care unit. *Infection Control and Hospital Epidemiology*. 2010; 31(3):249–255. [PubMed: 20102276]
6. Mehta NM, Compher C, A.S.P.E.N. Board of Directors. A.S.P.E.N. clinical guidelines: nutrition support of the critically ill child. *Journal of Parenteral and Enteral Nutrition*. 2009; 33(3):260–276. [PubMed: 19398612]

7. Bagri NK, Jose B, Shah SK, Bhutia TD, Kabra SK, Lodha R. Impact of Malnutrition on the Outcome of Critically Ill Children. *Indian journal of pediatrics*. 2015
8. Briassoulis G, Zavras N, Hatzis T. Malnutrition, nutritional indices, and early enteral feeding in critically ill children. *Nutrition*. 2001; 17(7–8):548–557. [PubMed: 11448572]
9. Delgado AF, Okay TS, Leone C, Nichols B, Del Negro GM, Vaz FA. Hospital malnutrition and inflammatory response in critically ill children and adolescents admitted to a tertiary intensive care unit. *Clinics (Sao Paulo)*. 2008; 63(3):357–362. [PubMed: 18568246]
10. Prince NJ, Brown KL, Mebrahtu TF, Parslow RC, Peters MJ. Weight-for-age distribution and case-mix adjusted outcomes of 14,307 paediatric intensive care admissions. *Intensive Care Med*. 2014; 40(8):1132–1139. [PubMed: 25034475]
11. Mehta NM, Bechard LJ, Cahill N, Wang M, Day A, Duggan CP, Heyland DK. Nutritional practices and their relationship to clinical outcomes in critically ill children--an international multicenter cohort study*. *Crit Care Med*. 2012; 40(7):2204–2211. [PubMed: 22564954]
12. Mehta NM, Bechard LJ, Zurakowski D, Duggan CP, Heyland DK. Adequate enteral protein intake is inversely associated with 60-d mortality in critically ill children: a multicenter, prospective, cohort study. *The American journal of clinical nutrition*. 2015
13. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bulletin of the World Health Organization*. 2007; 85:660–667. [PubMed: 18026621]
14. World Health Organization. Geneva, Switzerland: World Health Organization; 2006. WHO Child Growth Standards: Methods and development: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age.
15. World Health Organization. Geneva: WHO; 2009. WHO AnthroPlus for personal computers manual: software for assessing growth of the world's children and adolescents.
16. World Health Organization. Geneva: WHO; 2008. Training Course on Child Growth Assessment.
17. Rolland-Cachera MF. Childhood obesity: current definitions and recommendations for their use. *Int J Pediatr Obes*. 2011; 6(5–6):325–331. [PubMed: 21916784]
18. Schoenfeld DA, Bernard GR. Statistical evaluation of ventilator-free days as an efficacy measure in clinical trials of treatments for acute respiratory distress syndrome. *Critical Care Medicine*. 2002; 30(8):1772–1777. [PubMed: 12163791]
19. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. *Source Code Biol Med*. 2008; 3:17. [PubMed: 19087314]
20. Chisti MJ, Pietroni MA, Smith JH, Bardhan PK, Salam MA. Predictors of death in under-five children with diarrhoea admitted to a critical care ward in an urban hospital in Bangladesh. *Acta Paediatr*. 2011; 100(12):e275–e279. [PubMed: 21627690]
21. Mattos SS, Neves JR, Costa MC, Hatem TP, Luna CF. An index for evaluating results in paediatric cardiac intensive care. *Cardiol Young*. 2006; 16(4):369–377. [PubMed: 16839429]
22. Wallace MC, Jaggars J, Li JS, Jacobs ML, Jacobs JP, Benjamin DK, O'Brien SM, Peterson ED, Smith PB, Pasquali SK. Center variation in patient age and weight at Fontan operation and impact on postoperative outcomes. *Ann Thorac Surg*. 2011; 91(5):1445–1452. [PubMed: 21524453]
23. de Souza Menezes F, Leite HP, Koch Nogueira PC. Malnutrition as an independent predictor of clinical outcome in critically ill children. *Nutrition*. 2012; 28(3):267–270. [PubMed: 21872433]
24. Anderson JB, Beekman RH 3rd, Border WL, Kalkwarf HJ, Khoury PR, Uzark K, Eggesbø P, Marino BS. Lower weight-for-age z score adversely affects hospital length of stay after the bidirectional Glenn procedure in 100 infants with a single ventricle. *J Thorac Cardiovasc Surg*. 2009; 138(2):397–404. e391. [PubMed: 19619784]
25. Anderson JB, Kalkwarf HJ, Kehl JE, Eggesbø P, Marino BS. Low weight-for-age z-score and infection risk after the Fontan procedure. *Ann Thorac Surg*. 2011; 91(5):1460–1466. [PubMed: 21377649]
26. Brito PA, de Vasconcelos Generoso S, Correia MI. Prevalence of pressure ulcers in hospitals in Brazil and association with nutritional status--a multicenter, cross-sectional study. *Nutrition*. 2013; 29(4):646–649. [PubMed: 23466049]

27. Akiyama N, Segawa T, Ida H, Mezawa H, Noya M, Tamez S, Urashima M. Bimodal effects of obesity ratio on disease duration of respiratory syncytial virus infection in children. *Allergol Int*. 2011; 60(3):305–308. [PubMed: 21430434]
28. Caulfield LE, de Onis M, Blossner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. *The American journal of clinical nutrition*. 2004; 80(1):193–198. [PubMed: 15213048]
29. Joosten KFM, Hulst JM. Malnutrition in pediatric hospital patients: Current issues. *Nutrition*. 2011; 27(2):133–137. [PubMed: 20708380]
30. Reid M, Badaloo A, Forrester T, Morlese JF, Heird WC, Jahoor F. The acute-phase protein response to infection in edematous and nonedematous protein-energy malnutrition. *The American journal of clinical nutrition*. 2002; 76(6):1409–1415. [PubMed: 12450910]
31. Becker PJ, Nieman Carney L, Corkins MR, Monczka J, Smith E, Smith SE, Spear BA, White JV. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition). *Journal of the Academy of Nutrition and Dietetics*. 2014; 114(12):1988–2000. [PubMed: 25458748]
32. Martin L, Birdsell L, Macdonald N, Reiman T, Clandinin MT, McCargar LJ, Murphy R, Ghosh S, Sawyer MB, Baracos VE. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2013; 31(12):1539–1547. [PubMed: 23530101]
33. Moisey LL, Mourtzakis M, Cotton BA, Premji T, Heyland DK, Wade CE, Bulger E, Kozar RA. Nutrition, Rehabilitation Investigators C. Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. *Crit Care*. 2013; 17(5):R206. [PubMed: 24050662]
34. Dietz WH, Bellizzi MC. Introduction: the use of body mass index to assess obesity in children. *The American journal of clinical nutrition*. 1999; 70(1):123S–125S. [PubMed: 10419414]
35. Goh VL, Wakeham MK, Brazauskas R, Mikhailov TA, Goday PS. Obesity is not associated with increased mortality and morbidity in critically ill children. *Journal of Parenteral and Enteral Nutrition*. 2013; 37:102–108. [PubMed: 22457419]
36. Carroll CL, Bhandari A, Zucker AR, Schramm CM. Childhood obesity increases duration of therapy during severe asthma exacerbations. *Pediatr Crit Care Med*. 2006; 7(6):527–531. [PubMed: 17006390]
37. Bechard LJ, Rothpletz-Puglia P, Touger-Decker R, Duggan C, Mehta NM. Influence of obesity on clinical outcomes in hospitalized children: a systematic review. *JAMA pediatrics*. 2013; 167(5):476–482. [PubMed: 23478891]
38. Tait AR, Voepel-Lewis T, Burke C, Kostrzewa A, Lewis I. Incidence and risk factors for perioperative adverse respiratory events in children who are obese. *Anesthesiology*. 2008; 108(3):375–380. [PubMed: 18292674]
39. Schindler CA, Mikhailov TA, Kuhn EM, Christopher J, Conway P, Ridling D, Scott AM, Simpson VS. Protecting fragile skin: nursing interventions to decrease development of pressure ulcers in pediatric intensive care. *American journal of critical care : an official publication, American Association of Critical-Care Nurses*. 2011; 20(1):26–34. quiz 35.
40. Brown CV, Neville AL, Salim A, Rhee P, Cologne K, Demetriades D. The impact of obesity on severely injured children and adolescents. *J Pediatr Surg*. 2006; 41(1):88–91. [PubMed: 16410114]
41. Hazle MA, Gajarski RJ, Yu S, Donohue J, Blatt NB. Fluid overload in infants following congenital heart surgery. *Pediatr Crit Care Med*. 2013; 14(1):44–49. [PubMed: 23249789]

Figure 1.
Final sample of an international cohort of mechanically ventilated children.

Figure 2. Cumulative percentage of subjects remaining hospitalized over the 60 day study period, according to nutritional status category, N=1510.

Table 1

Characteristics of an international cohort of mechanically ventilated children, (N =1622, unless specified otherwise)

Variable	Mean (SD) or n (%)
Age (years)	4.5 (5.1)
Weight (kg)	19.5 (19.8)
Height (cm)	94.9 (36.5)
BMI (kg/m ²)	17.1 (4.4)
BMI Z-score	-0.14 (2.01)
Nutritional status	
Underweight	291 (18)
Overweight	235 (15)
Obese	217 (13)
Normal	879 (54)
Admission Type	
Elective Surgery	440 (27)
Emergency Surgery	206 (13)
Medical	976 (60)
Diagnosis Category	
Congenital Heart Disease	242 (15)
Hematology/Oncology	41 (3)
Infectious Disease	92 (6)
Miscellaneous	220 (14)
Neurology	203 (13)
Other Cardiac	68 (4)
Renal, Endocrine	18 (1)
Respiratory	628 (39)
Trauma/Orthopedic	110 (7)
Severity of Illness * (n=1444)	
Mild	505 (35)
Moderate	521 (36)
Severe	418 (29)
Mortality	111 (7)
Infection (1 or more episodes) (n=1607)	
VAP	134 (8)
UTI	80 (5)
CRBSI	68 (4)
PICU length of stay among survivors in days, Median (95% CI), (n=1510)	10 (6, 19)
Hospital stay among survivors in days, median (IQR) (n=1510)	20 (10, 39)
Ventilator free days, median (IQR) (n=1593)	21 (13, 24)
Country/Region	
USA	873 (54)

Variable	Mean (SD) or n (%)
Europe ¹	372 (23)
South America ²	186 (11)
Canada	90 (5)
Oceania ³	93 (6)
Singapore	8 (1)

Note.

* Categorized by tertile of lowest entered score (PRISM, PRISM III, PIM).

VAP = Ventilator Associated Pneumonia, UTI = Urinary Tract Infection, CRBSI = Catheter Related Blood Stream Infection.

¹Europe included United Kingdom, Ireland, Spain, Switzerland, Italy, and Russia.

²South America included Argentina, Peru, Chile, Brazil, and Venezuela.

³Oceania included Australia, New Zealand.

Table 2

Clinical outcomes risk in critically ill children in PICUs

Mortality^a	OR	95% CI	P
Underweight	1.53	1.24–1.89	<0.001
Overweight	1.44	0.94–2.19	0.09
Obese	1.55	0.87–2.76	0.14
Infections			
Underweight	1.88	1.18–3.01	0.008
Overweight	1.42	0.99–2.05	0.06
Obese	1.64	1.33–2.03	<0.001

GEE model controlling for location, age, sex, study year, admission category, diagnosis category, PICU size, infections^a, length of stay^a, and illness severity. n=1430.

Referent category = normal weight.

Table 3

Clinical and Demographic Characteristics among Nutritional Status Categories

<i>Characteristic</i>	<i>Underweight</i>		<i>Normal weight</i>		<i>Overweight</i>		<i>Obese</i>		χ^2	<i>P</i>
	<i>N</i>	<i>n</i>	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>		
<i>Diagnosis Category</i>									134.7	<0.001
Respiratory	628	108	338	53.8	85	13.5	97	15.4		
Congenital Heart Disease	242	91	129	53.3	17	7.0	5	2.1		
Neurology	203	21	102	50.2	43	21.2	37	18.2		
Trauma/Orthopedic	110	10	63	57.3	25	22.7	12	10.9		
Infectious Disease	92	12	47	51.1	16	17.4	17	18.5		
Other Cardiac	68	13	36	52.9	10	14.7	9	13.2		
Hematology/Oncology	41	6	25	61.0	6	14.6	4	9.8		
Gastrointestinal	34	10	3	8.8	2	5.9	3	8.8		
Renal, Endocrine	18	1	9	50.0	1	5.6	7	38.9		
Miscellaneous	411	29	130	59.1	32	14.5	29	13.2		

Note. Chi-square analysis row statistics for nutritional status categories in each categorical variable.