SLACIP 2017
Asunción Paraguay
26 al 29 de Julio 2017

KK Women's and Children's Hospital
SingHealth

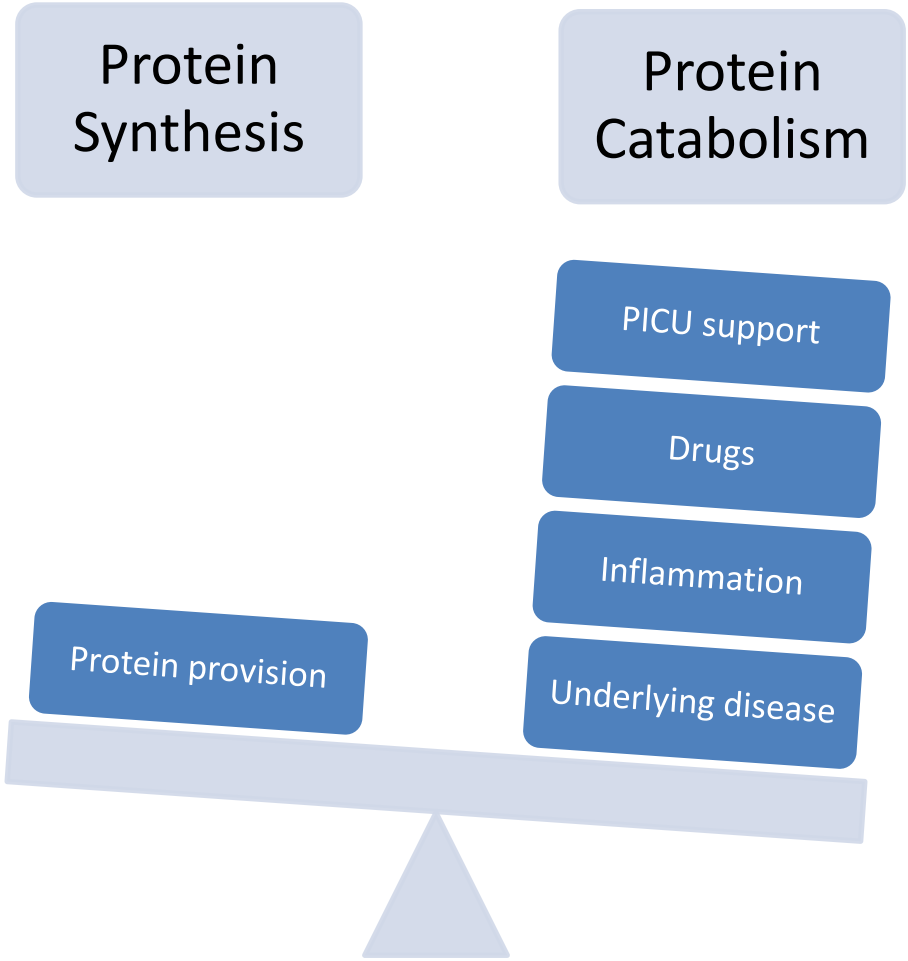
Protein Supplementation in the Pediatric Intensive Care Unit

Jan Hau Lee, MBBS, MRCPCH, MCI
Children's Intensive Care Unit
28th July 2017

Objectives

- Basis for protein supplementation
- Challenges in monitoring protein balance
- Current evidence for and against protein supplementation
- Future directions

Protein Homeostasis During Critical Illness



Coss-Bu et al. *Nutr Clin Pract* 2017

Challenges to Assessment of Protein Homeostasis in the PICU

- Traditional markers are not robust
  - BMI, skin-fold thickness
- Body composition measurements
  - Dual-energy x-ray absorptiometry, CT, MRI
- Serum biomarkers
  - Albumin, pre-albumin, plasma amino acid
- Nitrogen balance

Ong C et al. *Clin Nutr* 2014
Coss-Bu et al. *Nutr Clin Pract* 2017

A Deeper Look Into Serum Biomarkers

Review

Nutrition biomarkers and clinical outcomes in critically ill children: A critical appraisal of the literature

Chengsi Ong [a,*], Wee Meng Han [a], Judith Ju-Ming Wong [b], Jan Hau Lee [c,d]

[a] *Department of Nutrition and Dietetics, KK Women's and Children's Hospital, Singapore*
[b] *Department of Pediatric Medicine, KK Women's and Children's Hospital, Singapore*
[c] *Children's Intensive Care Unit, Department of Pediatric Subspecialties, KK Women's and Children's Hospital, Singapore*
[d] *Office of Clinical Sciences, Duke-NUS Graduate School of Medicine, Singapore*

- Adults: Prealbumin and retinol binding protein
- Children: Albumin
- Mindful of limitations of albumin

Ong C et al. *Clin Nutr* 2014

Objectives

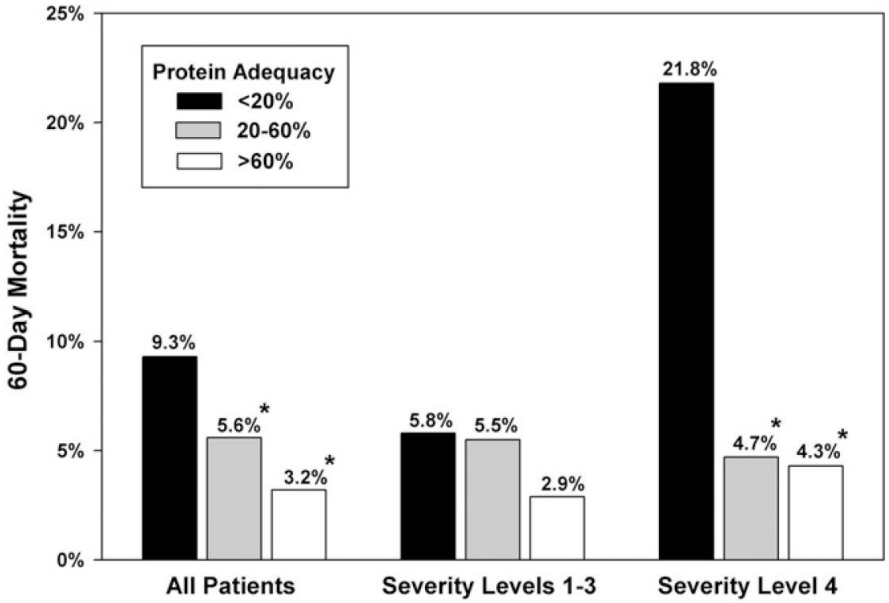
- Basis for protein supplementation
- Challenges in monitoring protein balance
- Current evidence for and against protein supplementation
- Future directions

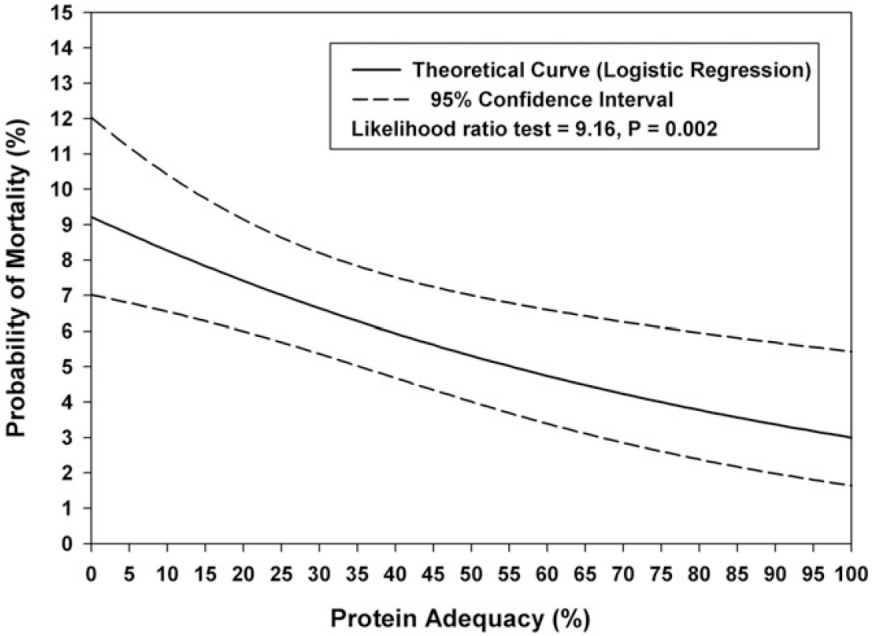
Clinical Impact of Protein Inadequacy

Adequate enteral protein intake is inversely associated with 60-d mortality in critically ill children: a multicenter, prospective, cohort study[1]

Nilesh M Mehta,[2–5] Lori J Bechard,[4,5] David Zurakowski,[3,5,6] Christopher P Duggan,[4,5] and Daren K Heyland[6]*

[2]Critical Care Medicine, Department of Anesthesiology, Perioperative and Pain Medicine, [3]Department of Anesthesiology, Perioperative and Pain Medicine, and [4]Center for Nutrition, Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; [5]Harvard Medical School, Boston, MA; and [6]Kingston General Hospital, Kingston, Canada





Metha et al. *Am J Clin Nutr 2015*

KK Women's and Children's Hospital
SingHealth

aspen LEADING THE SCIENCE AND PRACTICE OF CLINICAL NUTRITION
American Society for Parenteral and Enteral Nutrition

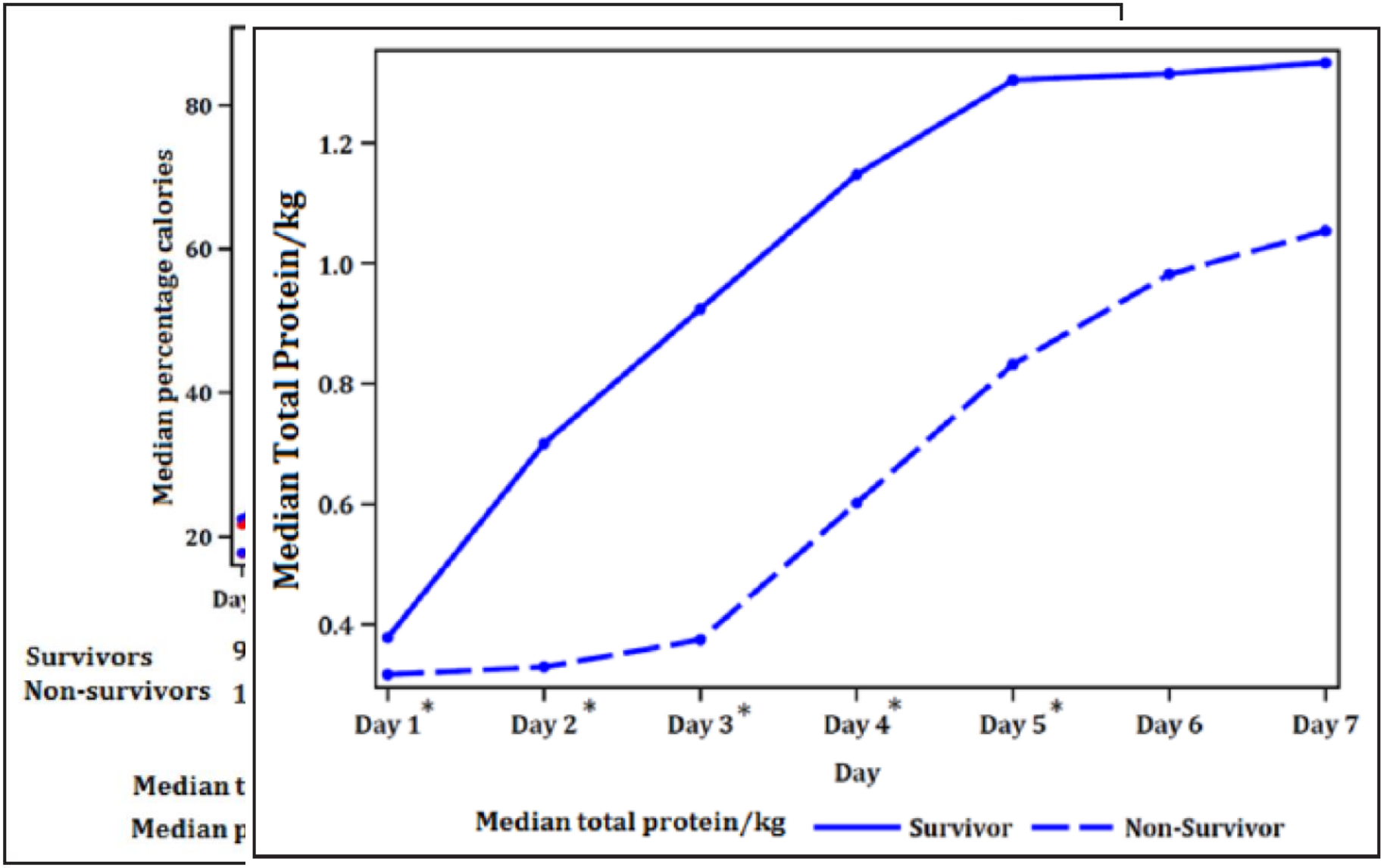
Nutrition Delivery Affects Outcomes in Pediatric Acute Respiratory Distress Syndrome

Journal of Parenteral and Enteral Nutrition
Volume XX Number X
Month 201X 1–7

DOI: 10.1177/0148607116637937
jpen.sagepub.com
hosted at
online.sagepub.com
SAGE

Judith Ju-Ming Wong, MBBCh BAO, MRCPCH[1]; Wee Meng Han, PhD[2]; Rehena Sultana, MSc[3]; Tsee Foong Loh, MBBS, MRCPCH[4]; and Jan Hau Lee, MBBS, MRCPCH, MCI[4,5]

- 109 children with ARDS
- Nutritional data over the first 7 days of ARDS
- Adequate calories: ≥ 80% of resting energy expenditure by day 3 of ARDS
- Adequate protein: ≥ 1.5 g/kg/day of protein by day 3 of ARDS
- Primary clinical outcomes: PICU mortality
- Secondary outcomes: Ventilator-free days and PICU-free days, multi-organ dysfunction and need for ECMO



Wong et al. *JPEN 2016*

KK Women's and Children's Hospital
SingHealth

Clinical Outcome	Inadequate Calories (n = 81)	Adequate Calories (n = 26)	*P* Value
PICU mortality	49 (60.5)	9 (34.6)	.003
Ventilator-free days, median (IQR)	0 (0–4)	3 (0–12)	.068
PICU-free days, median (IQR)	0 (0–15)	0 (0–17)	.687
Multiorgan dysfunction	58 (72.5)	14 (53.8)	.093
ECMO	6 (7.4)	1 (3.8)	1.000

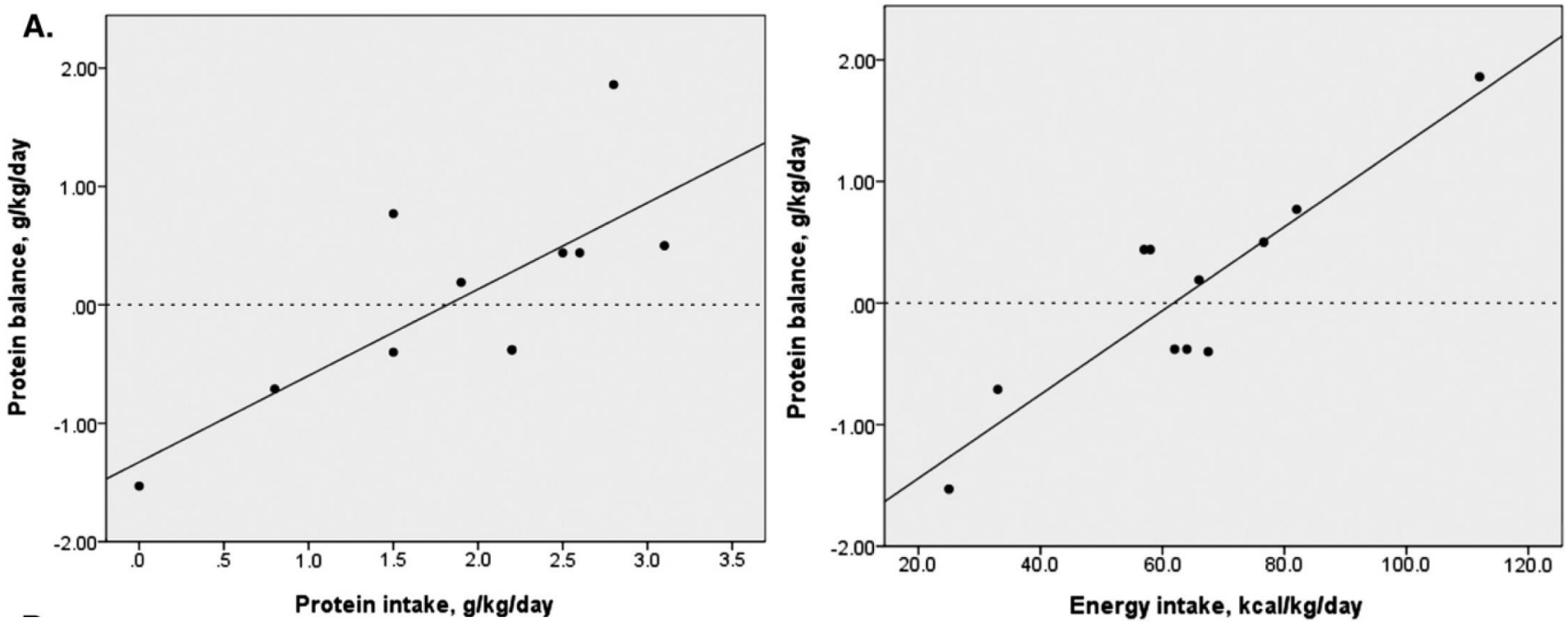
Clinical Outcome	Inadequate Protein (n = 93)	Adequate Protein (n = 14)	*P* Value
PICU mortality	56 (60.2)	2 (14.3)	.002
Ventilator-free days, median (IQR)	0 (0–4)	12.0 (3–19)	.005
PICU-free days, median (IQR)	0.0 (0–15)	0.0 (0–14)	.940
Multiorgan dysfunction	65 (70.7)	7 (50.0)	.136
ECMO	5 (5.4)	2 (14.3)	.227

After adjusting for severity illness scores, oxygenation index, presence of comorbidities, inadequate protein intake was associated with mortality

Wong et al. *JPEN 2016*

The New Power Couple

Protein + Energy



A minimum intake of **57 kcal/kg/day** and **1.5 g protein/kg/day** associated with positive protein balance

Bechard et al. *J Peds 2012*

KK Women's and Children's Hospital
SingHealth

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

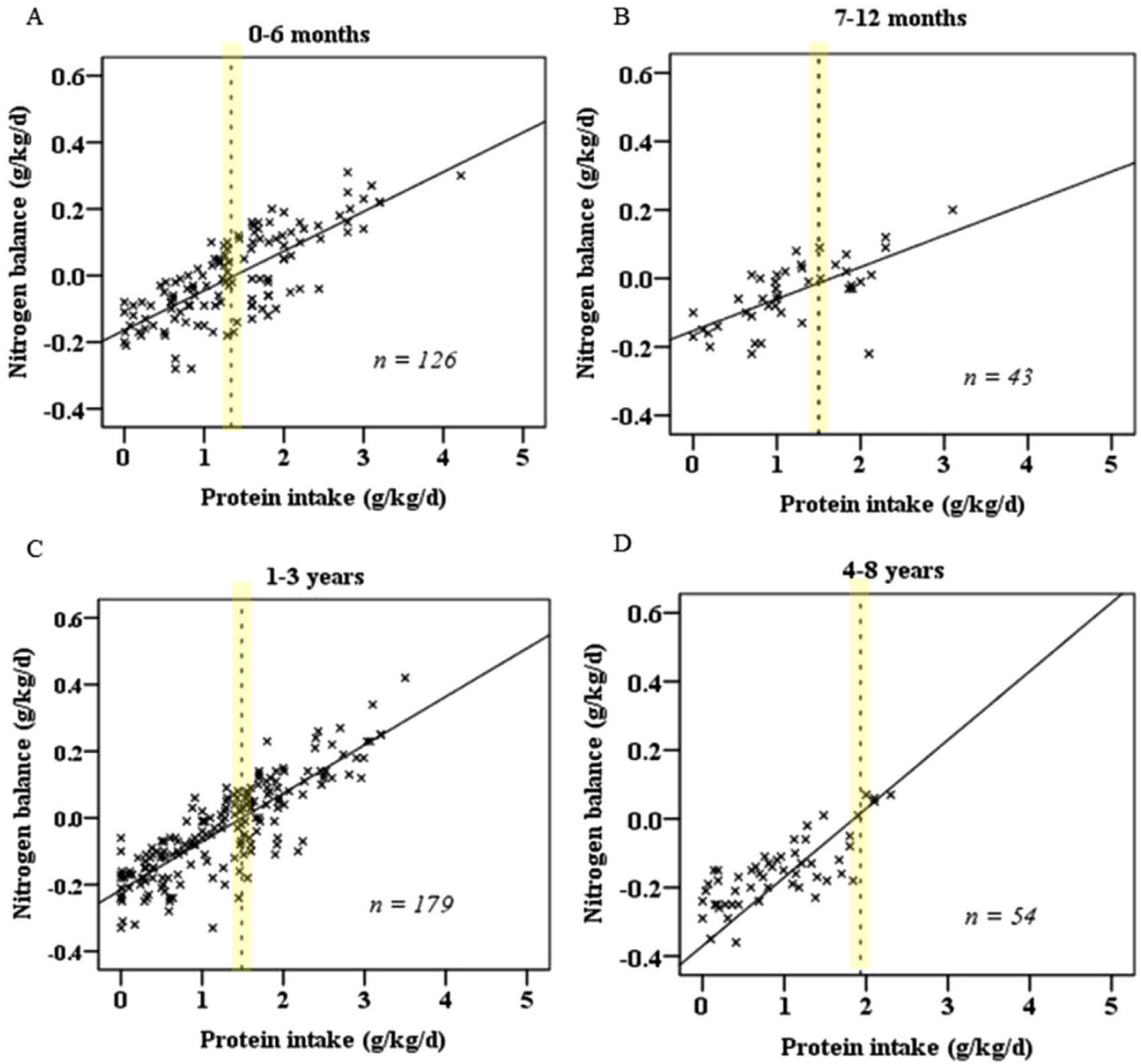
How much protein and energy are needed to equilibrate nitrogen and energy balances in ventilated critically ill children?

Corinne Jotterand Chaparro [a, 1], Jocelyne Laure Depeyre [a, 1], David Longchamp [b], Marie-Hélène Perez [b], Patrick Taffé [c], Jacques Cotting [b, *]

[a] Department of Nutrition and Dietetics, School of Health Professions, University of Applied Sciences Western Switzerland (HES-SO), Rue des Caroubiers 25, 1227 Carouge, Geneva, Switzerland
[b] Paediatric Intensive Care Unit, Medico-Surgical Department of Paediatrics, Lausanne University Hospital (CHUV), Rue du Bugnon 46, 1011 Lausanne, Switzerland
[c] Institute for Social and Preventive Medicine (IUMSP), Biopôle 2, Route de la Corniche 10, 1010 Lausanne, Switzerland

- 74 children [median: 21 (4-35) months]
  - 54 patients had surgical diagnoses
- 402 measurements of total urinary nitrogen and resting energy expenditure

Chaparro et al. *Nutr Clin 2016*



Nitrogen balance was achieved with **1.5** (95% CI: 1.4 – 1.6) g/kg/day

Energy balance was achieved with **58** (95% CI: 53 – 63) kcal/kg/day

Chaparro et al. *Nutr Clin 2016*

KK Women's and Children's Hospital
SingHealth

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 24, 2016 VOL. 374 NO. 12

Early versus Late Parenteral Nutrition in Critically Ill Children

Tom Fivez, M.D., Dorian Kerklaan, M.D., Dieter Mesotten, M.D., Ph.D., Sascha Verbruggen, M.D., Ph.D., Pieter J. Wouters, M.Sc., Ilse Vanhorebeek, Ph.D., Yves Debaveye, M.D., Ph.D., Dirk Vlasselaers, M.D., Ph.D., Lars Desmet, M.D., Michael P. Casaer, M.D., Ph.D., Gonzalo Garcia Guerra, M.D., Jan Hanot, M.D., Ari Joffe, M.D., Dick Tibboel, M.D., Ph.D., Koen Joosten, M.D., Ph.D., and Greet Van den Berghe, M.D., Ph.D.

- RCT across 3 sites involving 1440 critically ill children
- Early PN (within 24 hours of PICU admission) vs. Late PN (8th day of PICU stay)
- No difference in mortality between the groups
- Late PN group
  - Reduced risk of nosocomial infection
  - Shorter duration of mechanical ventilation
  - Higher chance to discharge from PICU earlier

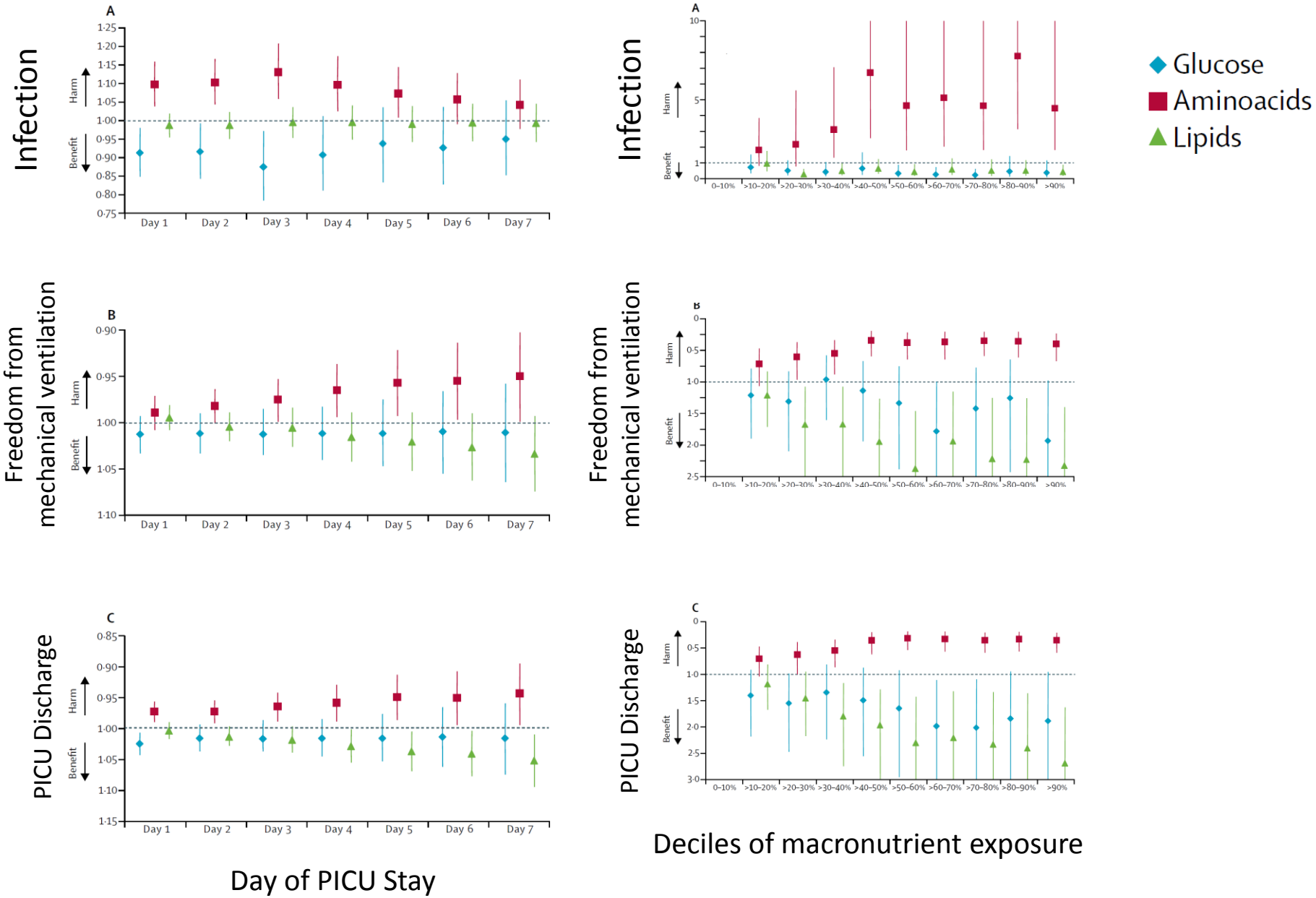
Fivez et al. *NEJM 2016*

Effect of early supplemental parenteral nutrition in the paediatric ICU: a preplanned observational study of post-randomisation treatments in the PEPaNIC trial

Ilse Vanhorebeek, Sascha Verbruggen, Michaël P Casaer, Jan Gunst, Pieter J Wouters, Jan Hanot, Gonzalo Garcia Guerra, Dirk Vlasselaers, Koen Joosten, Greet Van den Berghe

- Examined the doses of glucose, lipids and amino acids
- Analysis focused on first 7 days of PICU admission
- Adjusted for appropriate covariates
  - Diagnostic groups
  - Age
  - Severity of illness scores
  - Risk of malnutrition
  - Site

Vanhorebeek et al. *Lancet Respir Med 2017*



Vanhorebeek et al. *Lancet Respir Med 2017*

	n*	Glucose		Aminoacids		Lipids	
		Early PN	Late PN	Early PN	Late PN	Early PN	Late PN
Total dose†							
Day 1	1440	58·2% (33·8–81·1)	16·8% (11·4–24·6)	62·8% (0–99·6)	0% (0–0)	0% (0–0)	0% (0–0)
Day 2	1188	68·4% (44·2–86·4)	19·2% (14·3–31·6)	81·0% (37·4–109·2)	0% (0–7·0)	12·0% (4·6–46·1)	0% (0–11·7)
Day 3	924	60·9% (41·7–77·6)	19·8% (14·6–31·0)	77·3% (47·8–99·5)	1·4% (0–15·9)	34·4% (20·8–64·1)	2·7% (0–28·4)
Day 4	747	58·7% (40·1–72·9)	20·9% (14·7–31·5)	75·0% (48·9–90·8)	3·7% (0–23·2)	49·5% (34·2–79·1)	7·3% (0–40·4)
Day 5	611	56·6% (39·5–71·0)	21·8% (14·9–32·6)	73·3% (50·9–88·6)	6·0% (0–28·8)	57·2% (42·1–87·2)	11·7% (0–45·1)
Day 6	517	55·2% (39·3–71·6)	24·4% (16·1–35·2)	73·6% (53·1–85·6)	9·9% (1·1–34·5)	64·0% (45·8–92·9)	18·6% (1·6–50·1)
Day 7	443	54·2% (39·0–70·3)	25·8% (16·3–35·5)	72·6% (55·0–85·4)	14·3% (1·9–37·9)	68·3% (48·0–100·3)	24·3% (3·2–54·4)
Enteral dose							
Day 1	1440	0% (0-0)	0% (0–0)	0% (0–0)	0% (0–0)	0% (0–0)	0% (0–0)
Day 2	1188	0% (0–3·5)	0% (0–4·9)	0% (0–3·8)	0% (0–4·9)	0% (0–7·4)	0% (0–10·4)
Day 3	924	0% (0–8·8)	1·2% (0–9·4)	0% (0–11·7)	1·1% (0–13·4)	0% (0–22·2)	2·1% (0–26·5)
Day 4	747	1·8% (0–14·1)	2·6% (0–16·4)	2·5% (0–19·7)	3·2% (0–21·2)	4·3% (0–34·4)	6·8% (0–39·0)
Day 5	611	3·3% (0–18·4)	4·4% (0–18·8)	4·6% (0–27·5)	5·5% (0–28·3)	8·9% (0–44·2)	10·3% (0–45·1)
Day 6	517	4·2% (0–19·3)	7·0% (0·9–22·7)	6·2% (0–30·7)	8·1% (1·0–34·4)	10·4% (0–46·0)	16·6% (1·5–50·1)
Day 7	443	4·8% (0–21·1)	9·2% (0·9–24·2)	7·2% (0–32·1)	12·9% (1·0–37·6)	12·9% (0–49·5)	23·5% (2·1–54·4)
Parenteral dose							
Day 1	1440	56·6% (32·0–79·7)	16·3% (10·7–23·6)	59·7% (0–99·4)	0% (0–0)	0% (0–0)	0% (0–0)
Day 2	1188	63·9% (34·5–81·3)	16·9% (12·5–23·4)	75·1% (22·4–107·6)	0% (0–0)	4·7% (0–29·1)	0% (0–0)
Day 3	924	55·3% (29·4–71·8)	15·1% (11·2–20·2)	67·2% (22·4–94·7)	0% (0–0)	21·6% (4·2–39·5)	0% (0–0)
Day 4	747	47·8% (25·5–68·7)	13·4% (10·3–18·9)	65·2% (21·4–85·3)	0% (0–0)	35·2% (9·2–49·7)	0% (0–0)
Day 5	611	42·6% (22·5–66·8)	12·8% (9·4–17·4)	62·1% (20·6–80·7)	0% (0–0)	37·9% (10·0–54·1)	0% (0–0)
Day 6	517	39·6% (20·9–67·0)	12·1% (8·1–16·9)	62·0% (23·2–77·7)	0% (0–0)	40·9% (11·2–60·9)	0% (0–0)
Day 7	443	38·2% (19·3–66·1)	11·8% (7·7–16·2)	57·4% (22·2–75·4)	0% (0–0)	40·4% (11·7–65·6)	0% (0–0)

Vanhorebeek et al. *Lancet Respir Med 2017*

Take Home Messages from PEPaNIC trial

- Limitations of the study
  - > 55% of the patients in early PN group were discharged by day 4
  - > 77% of patients in the late PN group were discharged by day 8 without having received any PN
- The pre-planned analysis did not take into account which group the patient came from
- Delaying PN with early initiation and stepwise advancement of EN seems sensible in most patient
- Nutrition prescription needs to be individualized

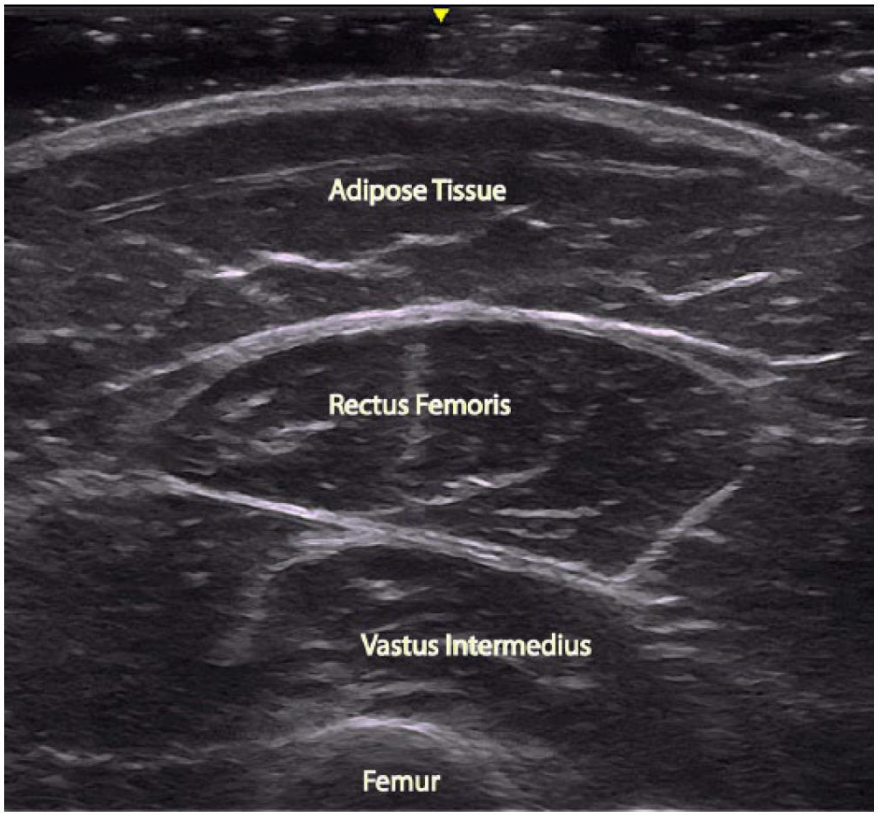
Metha. *NEJM 2016*
Ong and Lee. Lancet Resp Med 2017

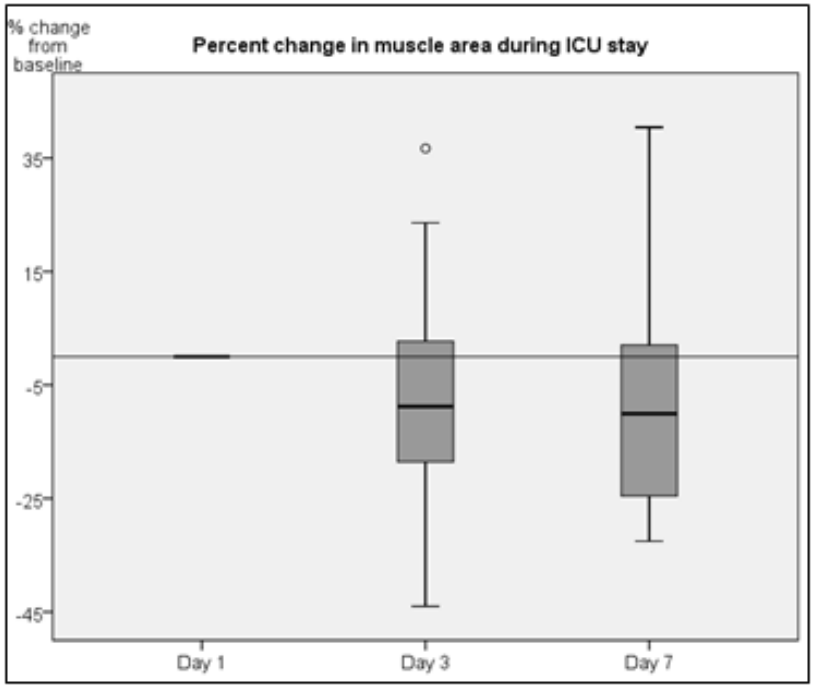
KK Women's and Children's Hospital
SingHealth

Objectives

- Basis for protein supplementation
- Challenges in monitoring protein balance
- Current evidence for and against protein supplementation
- Future directions

Muscle Ultrasound: Novel Biomarker





Ong et al. *J Parenter Enteral Nutrition* 2017

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition

Journal of Parenteral and Enteral Nutrition
Volume XX Number X
Month 201X 1–37

DOI: 10.1177/0148607117711387
journals.sagepub.com/home/pen
SAGE

Nilesh M. Mehta, MD[1]; Heather E. Skillman, MS, RD, CSP, CNSC[2]; Sharon Y. Irving, PhD, CRNP, FCCM, FAAN[3]; Jorge A. Coss-Bu, MD[4]; Sarah Verhulyea, MS, RD, CSP, LD, CNSC[5]; Elizabeth Anne Farrington, PharmD, FCCP, FCCM, FPPAG, BCPS[6]; Liam McKeever, MS, RDN[7]; Amber M. Hall, MS[8]; Praveen S. Goday, MBBS, CNSC[9]; and Carol Braunschweig, PhD, RD[10]

1. A minimum protein intake of 1.5 g/kg/day
2. Optimal protein dose associated with improved clinical outcomes is not known
3. Provide protein early in the course of critical illness

Q3A: What is the minimum recommended protein requirement for critically ill children? *R3A*: On the basis of evidence from RCTs and as supported by observational cohort studies, we recommend a minimum protein intake of 1.5 g/kg/d. Protein intake higher than this threshold has been shown to prevent cumulative negative protein balance in RCTs. In critically ill infants and young children, the optimal protein intake required to attain a positive protein balance may be much higher than this minimum threshold. Negative protein balance may result in loss of lean muscle mass, which has been associated with poor outcomes in critically ill patients. Based on a large observational study, higher protein intake may be associated with lower 90-d mortality in mechanically ventilated children.	Quality of evidence: moderate GRADE recommendation: strong
Q3B: What is the optimal protein delivery strategy in the PICU? *R3B*: On the basis of results of randomized trials, we suggest provision of protein early in the course of critical illness to attain protein delivery goals and promote positive nitrogen balance. Delivery of a higher proportion of the protein goal has been associated with positive clinical outcomes in observational studies.	Quality of evidence: moderate GRADE recommendation: weak
Q3C: How should protein delivery goals be determined in critically ill children? *R3C*: The optimal protein dose associated with improved clinical outcomes is not known. We do not recommend the use of RDA values to guide protein prescription in critically ill children. These values were developed for healthy children and often underestimate the protein needs during critical illness.	Quality of evidence: moderate GRADE recommendation: strong

KK Women's and Children's Hospital
SingHealth

Conclusion

- We need to be mindful of caloric and protein provision in critically ill children
- Too much and too little can be bad
- Future studies will need to focus on novel biomarkers for protein balance and address the issue of the clinical impact of protein supplementation

SLACIP 2017
Asunción Paraguay
26 al 29 de Julio 2017

Thank you

lee.jan.hau@singhealth.com.sg

Singapore
WFPICCS 2018

9th Congress of the World Federation of Pediatric Intensive & Critical Care Societies

9-13 June, 2018 | Singapore