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Strategies for Improving Enteral Nutrition Delivery in the ICU

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Critical Care Nutrition

Disclosure

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Critical Care Nutrition

Creating Clarity Out of Confusion!

Large, Negative RCTs

- EPaNIC *NEJM 2011*
- EDEN *JAMA 2012*
- PERMIT *NEJM 2015*
- NEPHROPROTECT *ICM 2015*
- EAT-ICU *ICM 2017*

Feeding: How much is enough?
[Standard presentation]

13:45	Why would fasting be a good idea during acute critical illness? *Greet Van den Berghe*
14:00	Does the ICU patient support permissive underfeeding? *Stephen McClave*
14:15	Refeeding syndrome: is it relevant? *Arthur van Zanten*
14:30	Feeding may not prevent endogenous energy supply *Olav Roovackers*

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Learning Objectives

- Identify ICU patients that benefit most from nutrition intervention.
- Describe the optimal amount of protein and calories to support positive outcomes in the ICU patient.
- Explain the evidence supporting the use of a volume-based feeding (VBF) protocol in the ICU.
- Discuss strategies for adequate EN delivery with emphasis on volume based feeding.

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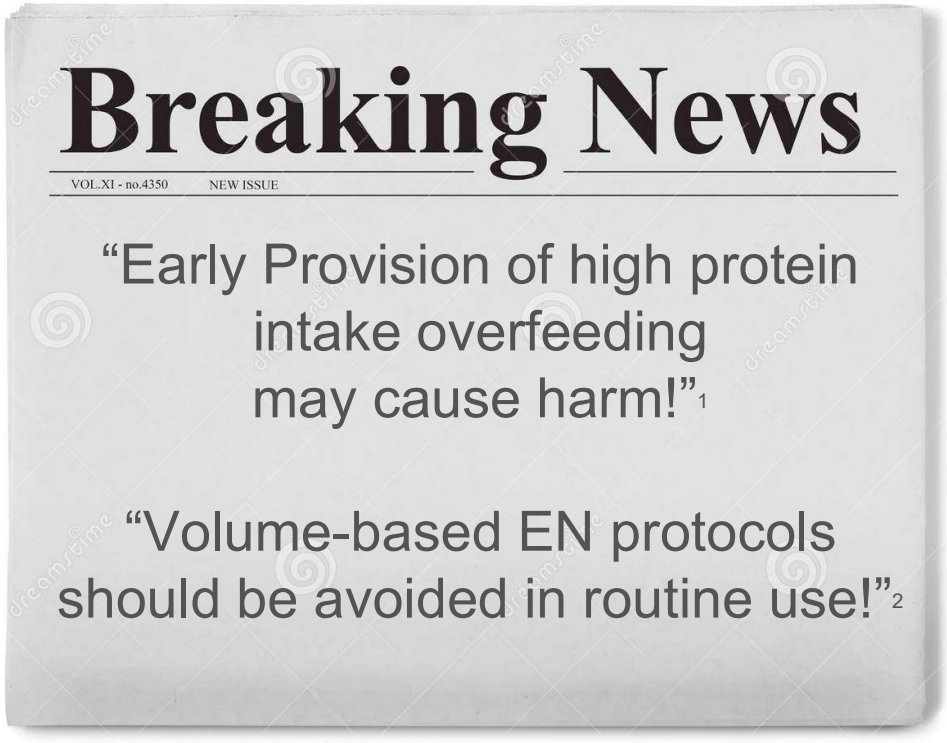

1. Koekkoek, Curr Opin Anesthesiol 2018; 31:136–143
2. Krenitsky Nutrition Issues in Gastro Aug 2018

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Slow Starts, Slow Ramp ups

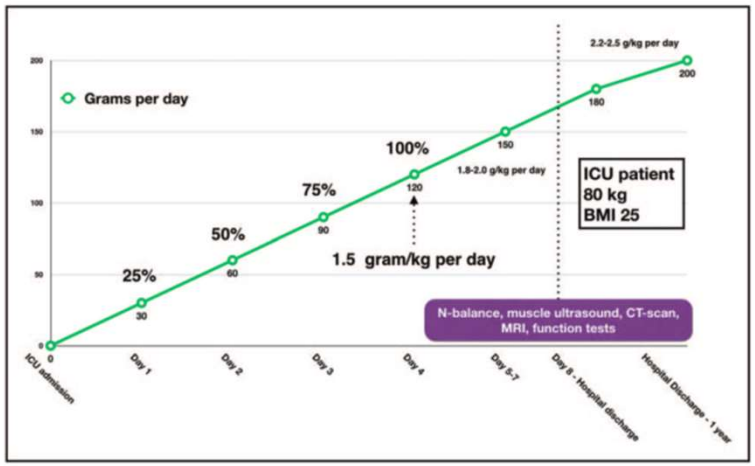

FIGURE 2. Protein targets during critical illness. In this example a weight-based equation (1.5 g/kg/day) is used to commence feeding aiming to reach target on day 4. This patient with an actual body weight of 80 kg has adaily target of 120 g of protein. Monitoring optimal protein intake after day 4 is experimental. Several strategies have been suggested such as N-balance, muscle ultrasound (m. quadriceps), CT-scan or MRI studies to estimate lean body mass, or function tests. None have been proven useful to guide protein targeting. During the post-acute phase of ICU stay higher protein intakes are associated with improved outcomes. CT, computed tomography.

DKH: setting such conservative targets will results in significantly less in the first few days. ⇨ Worse outcomes

Koekkoek, Curr Opin Anesthesiol 2018, 31:136–143

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What is the evidence driving this idea?

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Post-hoc analysis of EPANIC

Casaer, Wilmer, Hermans, *et al.*: Early Nutrition in the ICU: Less Is More

Figure 3. Time to live discharge from the intensive care unit (ICU): Relation to glucose dose as compared with protein dose. Effect size per 10% increments of target per day in cumulative glucose intake (~±28 g/d) (*yellow*) and cumulative protein intake (~±7 g/d) (*green*) in a time-to-alive ICU discharge analysis corrected for severity and type of disease. Normalized glucose target was 276.4 (±70.8) g/day and normalized protein target was 72.3 (±18.5) g/day. This target was derived from the amount of glucose and protein the patient would have received with the standard commercial parenteral (PN) preparation when receiving 100% of his calculated energy target.

Indication bias:

1) patients with longer projected stay would have been fed more aggressively; hence more protein/calories is associated with longer lengths of stay.

2) 90% of these patients are elective surgery. There would have been little effort to feed them and they would have categorically different outcomes than the longer stay patients in which there were efforts to feed

3) PN didn't start till day 3, so all the signal was from small amounts of EN?

Casaer Am J Respir Crit Care Med 2013;187:247–255

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thEy PANIC'd early: outcome differences after 2-3 days before PN started!

Table 2. Outcomes.*

Variable	Late-Initiation Group (N=2328)	Early-Initiation Group (N=2312)	P Value
Safety outcome			
Vital status — no. (%)			
Discharged live from ICU within 8 days	1750 (75.2)	1658 (71.7)	0.007
Hazard ratio (95% CI) for time to definitive weaning from ventilation	1.06 (0.99–1.12)		0.07
Duration of stay in ICU§			
Median (interquartile range) — days	3 (2–7)	4 (2–9)	0.02
Duration >3 days — no. (%)	1117 (48.0)	1185 (51.3)	0.02
Hazard ratio (95% CI) for time to discharge alive from ICU	1.06 (1.00–1.13)		0.04

Negative outcomes NOT confirmed in Swiss sPN nor Aussie early PN trial!

Cesaer NEJM 2011

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Role of timing and dose of energy received in patients with acute lung injury on mortality in the Intensive Nutrition in Acute Lung Injury Trial (INTACT): a post hoc analysis[1,2]

Carol L Braunschweig,[3] Sally Freels,[4] Patricia M Sheean,[5] Sarah J Peterson,[6] Sandra Gomez Perez,[3] Liam McKeever,[3] Omar Lateef,[7] David Gurka,[7] and Giamila Fantuzzi[3]*

- 78 patient with ALI randomized to intensive medical therapy (30 kcal/kg/day) or usual care (40-60% of target)
- Stopped early because of excess deaths in intensive group
- Post hoc analysis suggests increased death from early protein!

TABLE 3
Proportional hazards multiple regression models for hazard of death on or after 8 d for INTACT participants[1]

Independent variable	β Hat	SE	*P*	HR (95% CI)
Model 1				
Mean kcal/kg received during days 1–7[2]	0.1575	0.0441	0.0004	1.17 (1.07, 1.28)
Time-dependent mean daily kcal/kg received during days 1–7 and after day 8[2]	−0.0967	0.0471	0.04	0.91 (0.83, 1.0)
Model 2				
Mean daily g protein/kg received during days 1–7[3]	2.18	0.69	0.002	8.87 (2.3, 34.3)
Time-dependent mean daily g protein/kg received during days 1–7 and after day 8[3]	−1.89	1.00	0.06	0.15 (0.02, 1.07)

[1] Models were adjusted for age, sex, and baseline SOFA score, n = 66 (15 deaths). INTACT, Intensive Nutrition in Acute Lung Injury Trial; SOFA, Sequential Organ Failure Assessment.
[2] Mean increase of 1 kcal/kg.
[3] Mean increase of 1 g/kg.

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More Questions Than Answers!

- Randomized trials that are terminated prematurely are likely to significantly overestimate the treatment effect.
- A small study from one center has limited generalizability and should not inform practice patterns world-wide.
- Patients were moderately dosed with protein and only received approximately 82 grams/day or less than 1 gm/kg/day
- Patients were targeted to receive 30 kcal/kg/day and received approximately 85% of their prescriptions. From examination of figure 2, it appears that some patients received more than 100% of their prescription, which is already high since most guidelines recommend 20-25 kcal/kg/day.
- IMNT group rec'd more parenteral nutrition and significantly more parenteral lipids. If these are soybean based emulsions, this may explain the excess mortality.
- No mention of phosphate levels; 1/3 were malnourished- refeeding syndrome?

Heyland JPEN 2015;39:143

Timing of PROTein INtake and clinical outcomes of adult critically ill patients on prolonged mechanical VENTilation: A retrospective, single-center, study

- 455 adult critically ill patients mechanically ventilated in ICU for at least 7 days
- Divided into 3 protein intake categories, <0.8 g/kg/day, 0.8-1.2 g/kg/day and >1.2 g/kg/day
- The 6-month survival was 65.6%, 68.9% and 55.6% in the low, intermediate, and high group (p=0.21)
- Further analyzed by time

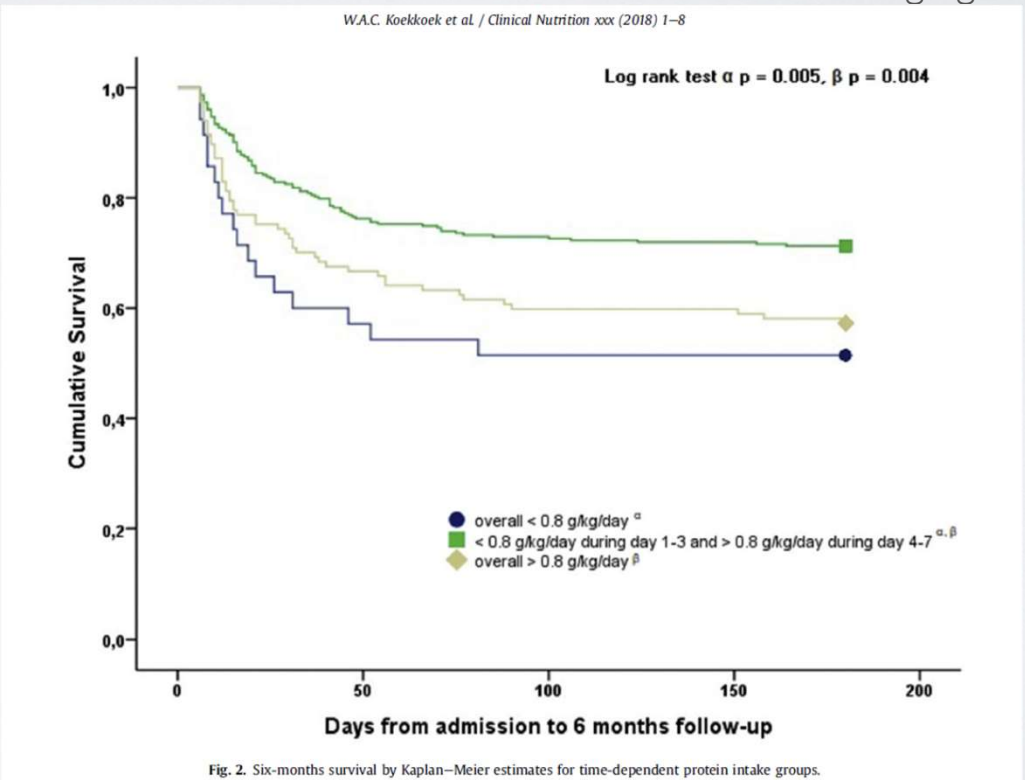

Fig. 2. Six-months survival by Kaplan–Meier estimates for time-dependent protein intake groups.

Koekkoek Clin Nutrition 2018

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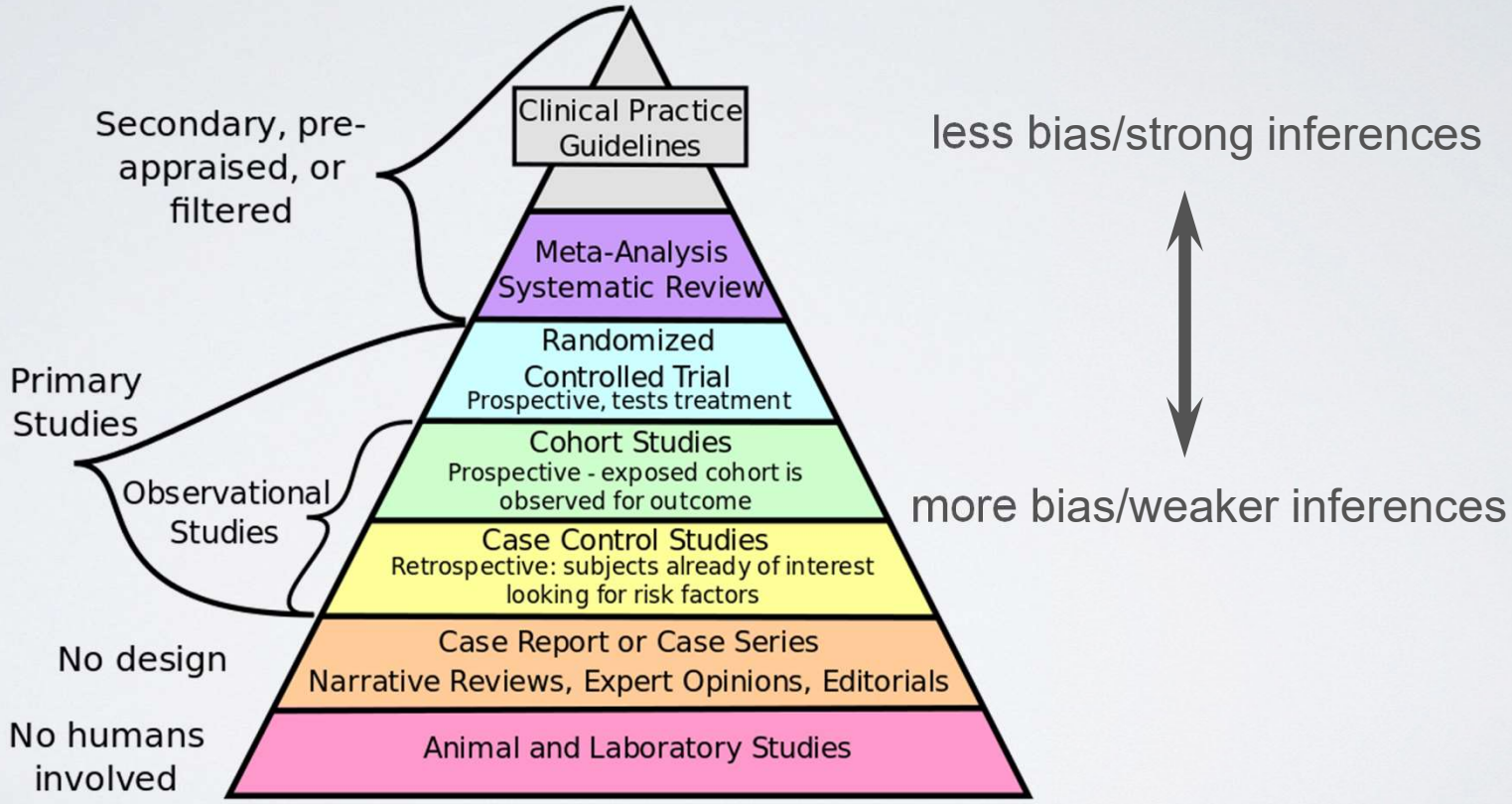
Levels of Evidence



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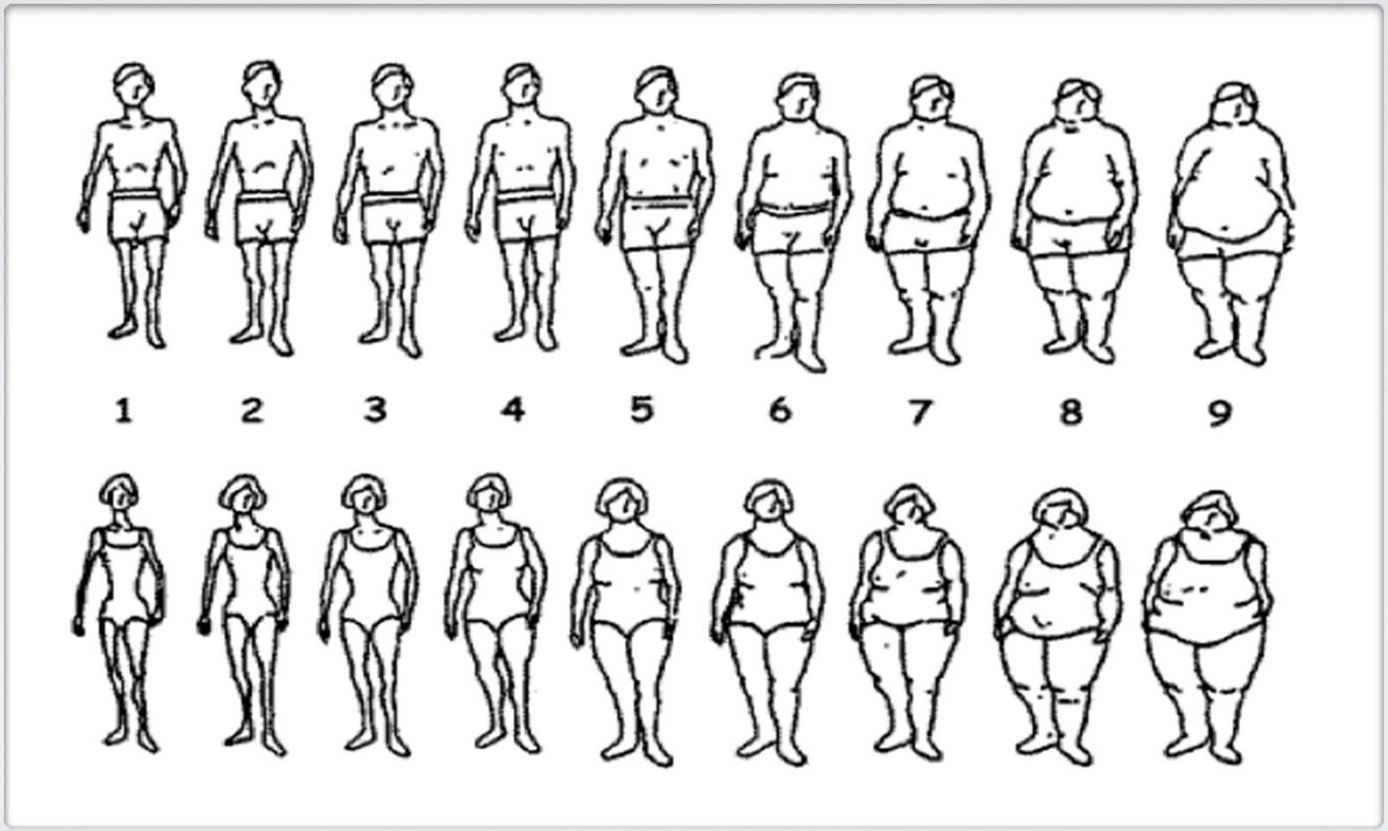
ICU Patients Are Not All Created Equal…
These recommendations were made without consideration of 'nutritional risk'!



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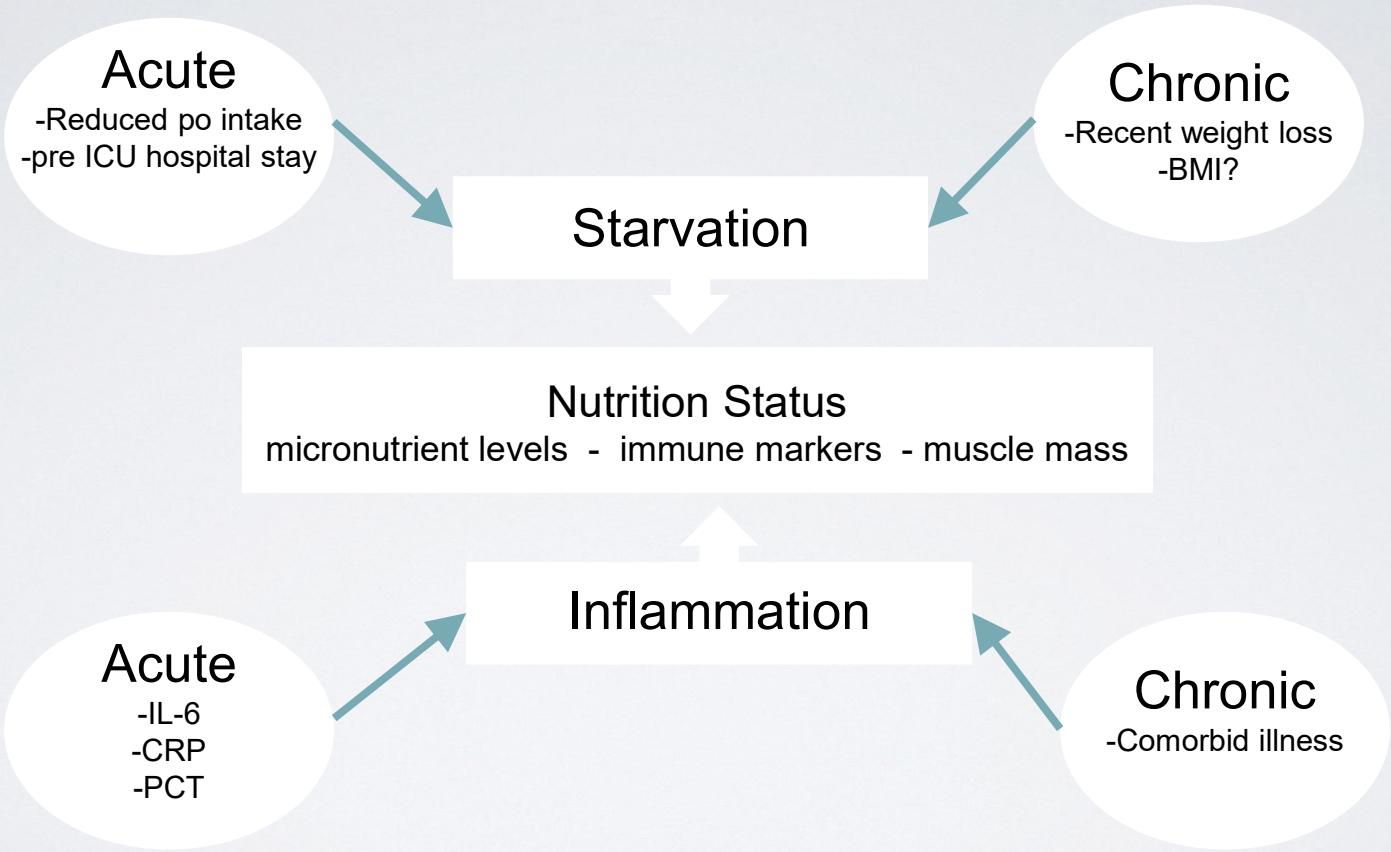
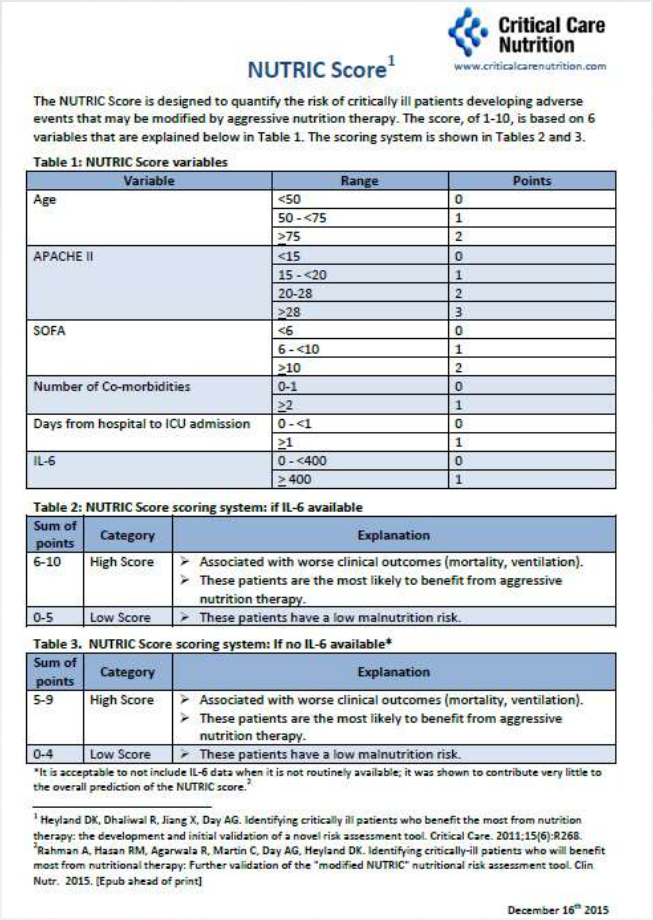
A Conceptual Model for Nutrition Risk Assessment in the Critically Ill



Calculating the NUTRIC Score



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www.criticalcarenutrition.com

NUTRIC Score[1]

The NUTRIC Score is designed to quantify the risk of critically ill patients developing adverse events that may be modified by aggressive nutrition therapy. The score, of 1-10, is based on 6 variables that are explained below in Table 1. The scoring system is shown in Tables 2 and 3.

Table 1: NUTRIC Score variables

Variable	Range	Points
Age	<50	0
	50 - <75	1
	≥75	2
APACHE II	<15	0
	15 - <20	1
	20-28	2
	≥28	3
SOFA	<6	0
	6 - <10	1
	≥10	2
Number of Co-morbidities	0-1	0
	≥2	1
Days from hospital to ICU admission	0 - <1	0
	≥1	1
IL-6	0 - <400	0
	≥ 400	1

Table 2: NUTRIC Score scoring system: if IL-6 available

Sum of points	Category	Explanation
6-10	High Score	➢ Associated with worse clinical outcomes (mortality, ventilation). ➢ These patients are the most likely to benefit from aggressive nutrition therapy.
0-5	Low Score	➢ These patients have a low malnutrition risk.

Table 3. NUTRIC Score scoring system: If no IL-6 available*

Sum of points	Category	Explanation
5-9	High Score	➢ Associated with worse clinical outcomes (mortality, ventilation). ➢ These patients are the most likely to benefit from aggressive nutrition therapy.
0-4	Low Score	➢ These patients have a low malnutrition risk.

*It is acceptable to not include IL-6 data when it is not routinely available; it was shown to contribute very little to the overall prediction of the NUTRIC score.[2]

[1] Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Critical Care. 2011;15(6):R268.
[2]Rahman A, Hasan RM, Agarwala R, Martin C, Day AG, Heyland DK. Identifying critically-ill patients who will benefit most from nutritional therapy: Further validation of the "modified NUTRIC" nutritional risk assessment tool. Clin Nutr. 2015. [Epub ahead of print]

December 16th 2015

https://www.criticalcarenutrition.com/resources/nutric-score

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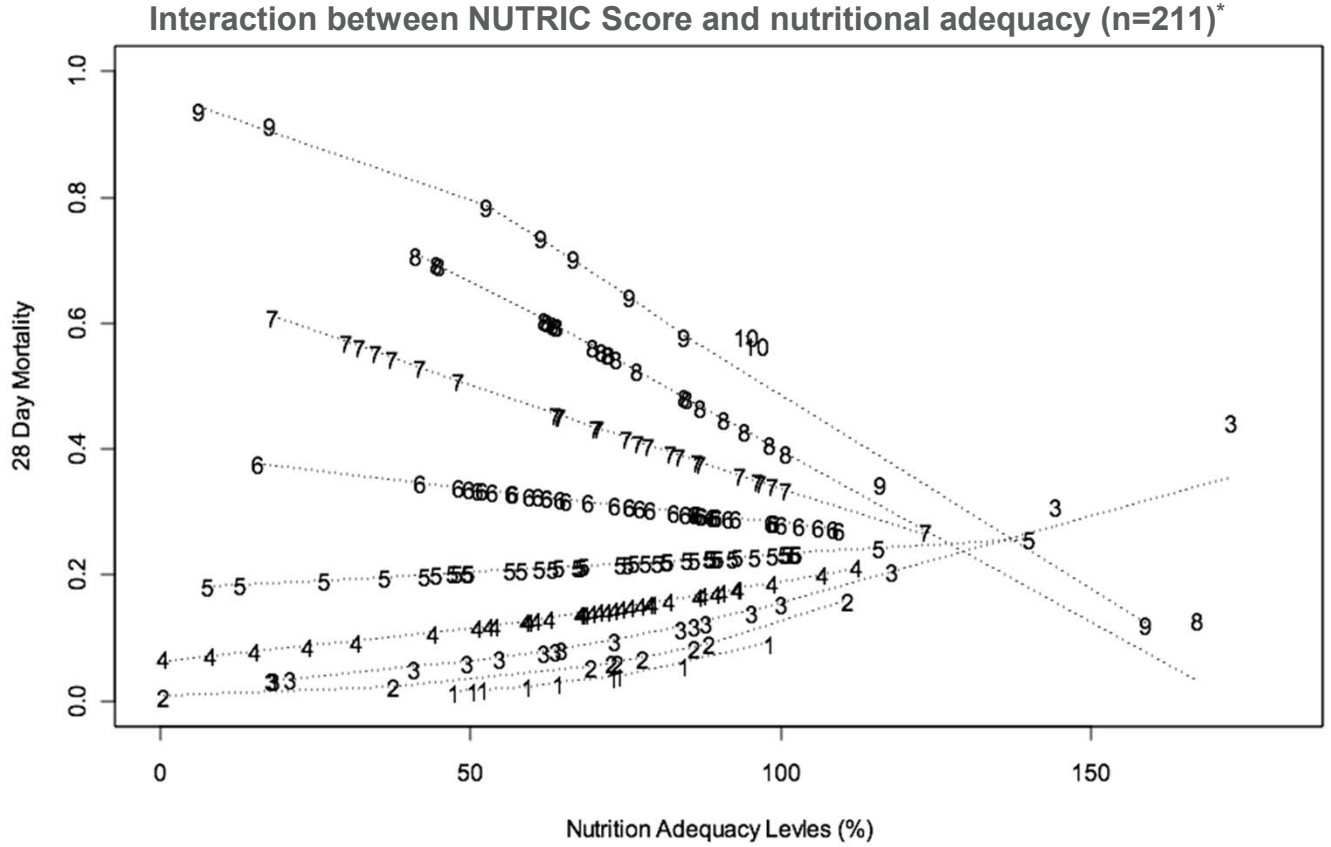
The Validation of the NUTrition Risk in the Critically Ill Score (NUTRIC Score)



Heyland
Critical Care 2011, 15:R28

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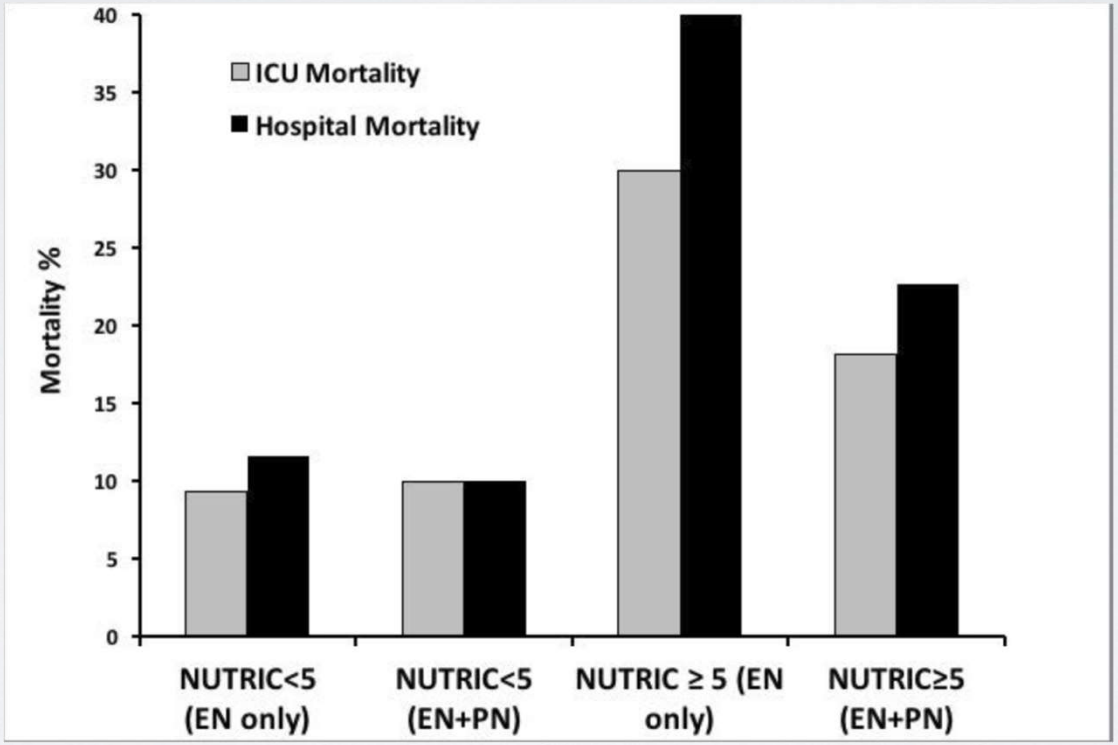
The Validation of the NUTrition Risk in the Critically Ill Score (NUTRIC Score)

- Validated in 3 separate databases including the INS Dataset involving over 200 ICU's worldwide [1,2,3]
- Validated without IL-6 levels (modified NUTRIC) [2]
- Independently validated in Brazilian, Portuguese, and Asian populations [4,5,6,7]
- Not validated in post hoc analysis of the PERMIT trial [8]
  - RCT of different caloric intake (protein more important)
  - Underpowered, very wide confidence intervals

1.Heyland Critical Care 2011, 15:R28
2.Rahman, Clinical Nutrition 2013
3.Compher, CCM, 2017
4.Rosa, Marcadenti Clinical Nutrition ESPEN 2016
5.Mendes J Crit Care 2017
6.Mukhopadhyah Clinical Nutrition 2016
7.Lee Clin Nutrition 2017
8.Arabi AmJRCCM 2016

Results of TOP UP Pilot Trial

A RCT of supplemental PN in low and high BMI ICU patients



Post-hoc subgroup analysis

Wischmeyer Critical Care 2017

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On the other hand, What is the evidence supporting early, optimal protein dosing in the ICU?

RCTs Level of Evidence for Early EN supported by our understanding of underlying pathophysiology!

Nutritional and Non-Nutritional Benefits of Early EN

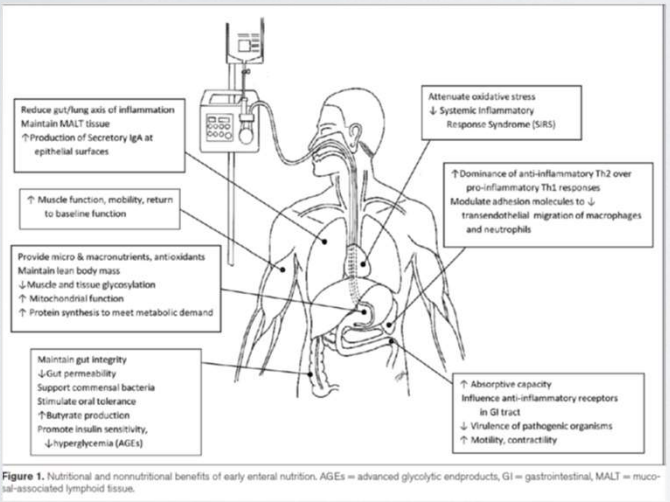
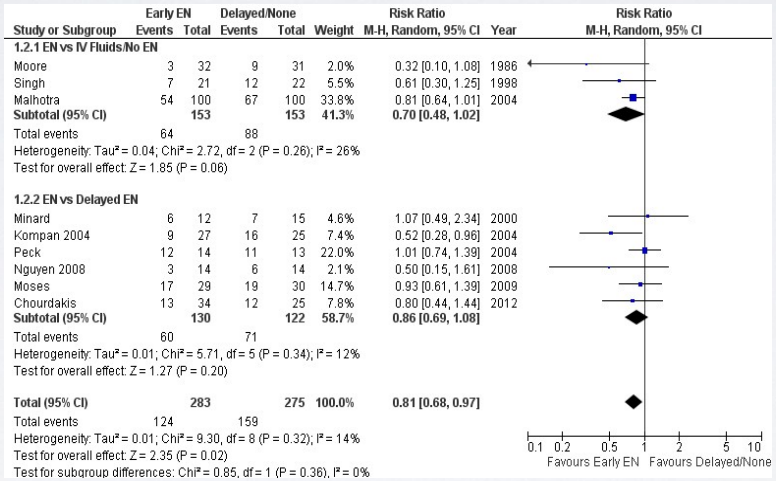


Figure 1. Nutritional and nonnutritional benefits of early enteral nutrition. AGEs = advanced glycolytic endproducts, GI = gastrointestinal, MALT = mucosal-associated lymphoid tissue.

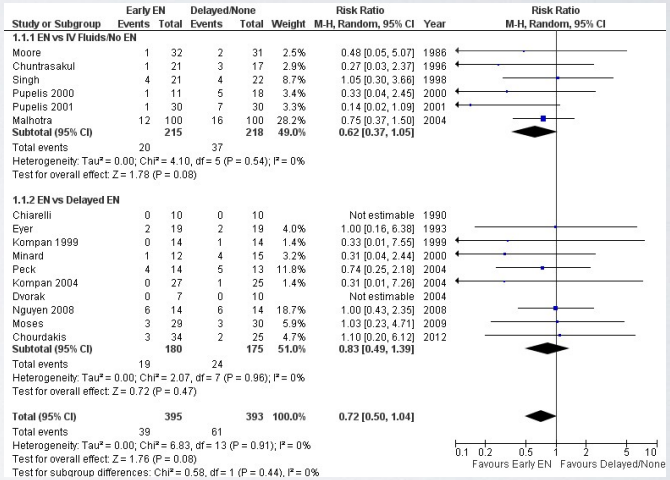
McClave CCM 2014

Early vs. Delayed EN: Effect on Infectious Complications



Significant reduction in infection: RR 0.81 (0.68, 0.97)

Early vs. Delayed EN: Effect on Mortality



Large reduction in mortality: RR 0.72 (0.50, 1.04)

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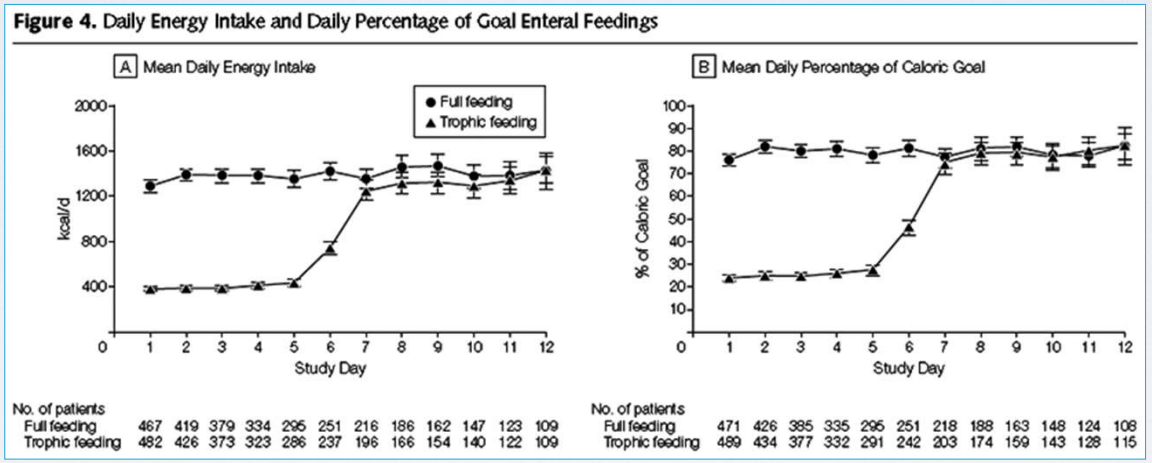
Initial Trophic vs. Full EN in Patients with Acute Lung Injury

The EDEN randomized trial



Rice TW, et al. *JAMA*. 2012;307(8):795-803.

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Initial Tropic vs. Full EN in Patients with Acute Lung Injury

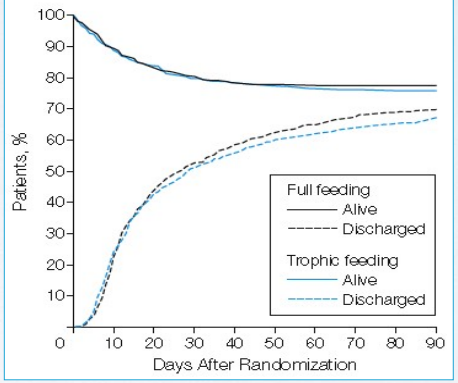
The EDEN randomized trial

Table 2. Clinical Outcomes

Outcome	Trophic Feeding (n = 508)	Full Feeding (n = 492)	*P* Value
Ventilator-free days, No. (95% CI)	14.9 (13.9-15.8)	15.0 (14.1-15.9)	.89
Failure-free days, No. (95% CI)			
Cardiovascular	19.1 (18.2-20.0)	18.9 (18.1-19.8)	.75
Renal	20.0 (19.0-20/9)	19.4 (18.4-20.5)	.43
Hepatic	22.0 (21.2-22.9)	22.6 (21.8-23.5)	.37
Coagulation	22.3 (21.4-23.1)	23.1 (22.3-23.9)	.16
ICU-free days, No. (95% CI)	14.4 (13.5-15.3)	14.7 (13.8-15.6)	.67
60-d mortality, No. (%) [95% CI]	118 (23.2) [19.6-26.9]	109 (22.2) [18.5-25.8]	.77
Development of infections, No. (%) [95% CI]			
VAP	37 (7.3) [5.0-9.5]	33 (6.7) [4.5-8.9]	.72
Clostridium difficile colitis	15 (3.0) [1.5-4.4]	13 (2.6) [1.2-4.1]	.77
Bacteremia, No. (%)	59 (11.6) [8.8-14.4]	46 (9.3) [6.8-11.9]	.24

Abbreviations: ICU, intensive care unit; VAP, ventilator-associated pneumonia.

Figure 3. Survival and Hospital Discharge



No Harm from early,
usual dose protein/amino acid intake!!

Rice TW, et al. *JAMA*. 2012;307(8):795-803.

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Physical and Cognitive Performance of Patients with Acute Lung Injury 1 Year after Initial Trophic versus Full Enteral Feeding

EDEN Trial Follow-up

Dale M. Needham[1,2,3], Victor D. Dinglas[1,2], Peter E. Morris[4], James C. Jackson[5], Catherine L. Hough[6], Pedro A. Mendez-Tellez[1,7], Amy W. Wozniak[1,8], Elizabeth Colantuoni[1,8], E. Wesley Ely[5,9], Todd W. Rice[5], and Ramona O. Hopkins[10,11]; for the NIH NHLBI ARDS Network

TABLE 3. TWELVE-MONTH RESULTS BY TREATMENT GROUP*

	Trophic Feeding ($n = 75$)	Full Feeding ($n = 74$)	Treatment Effect (95% CI)†	*P* Value†
Physical outcomes				
6-min-walk distance, % predicted	63 (25)	70 (24)	−6 (−14, 2)	0.136
4-m timed walk speed, m/s	0.98 (0.29)	1.08 (0.29)	−0.07 (−0.16, 0.02)	0.125

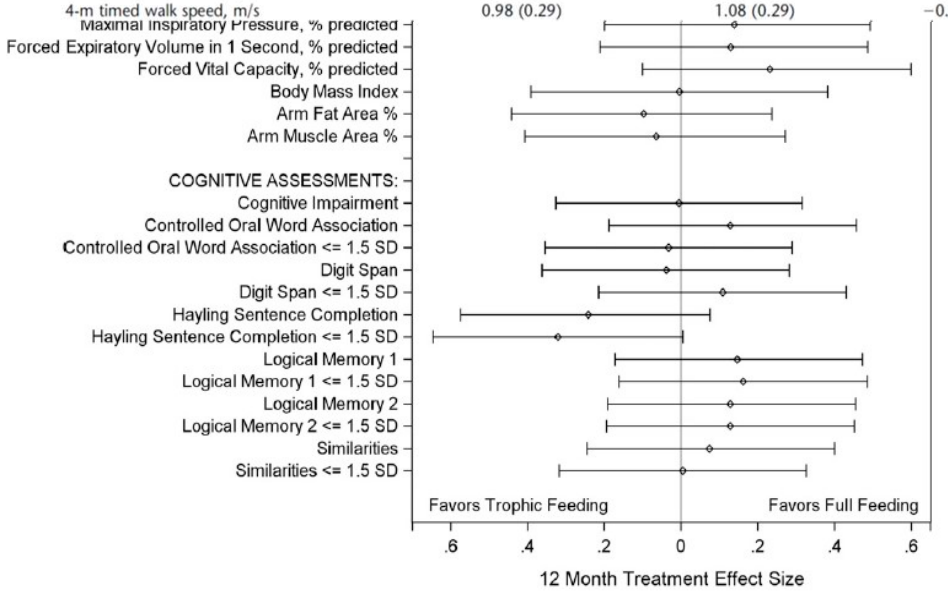

Figure 2. Effect size of treatment intervention at 12 months. The treatment effect, presented as an effect size, with 95% confidence interval, for the primary outcomes (6-min-walk test % predicted, and cognitive impairment) and all secondary outcomes. Effect size was calculated as the treatment effect (Table 3, difference in means or proportions) divided by the pooled SD from the initial trophic and full feeding groups (*77*, *78*).

Trend towards improvement with full feeds!

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Appropriate protein provision in critical illness: a systematic and narrative review[1–3]

L John Hoffer and Bruce R Bistrian

Results: The limited amount and poor quality of the evidence preclude conclusions or clinical recommendations but strongly suggest that 2.0–2.5 g protein substrate · kg normal body weight^{-1} · d^{-1} is safe and could be optimum for most critically ill patients. At the

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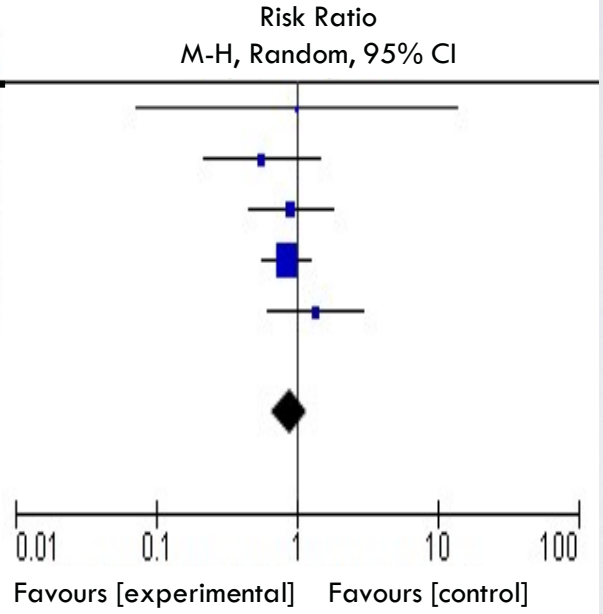
Systematic Review of RCTs of High vs. Low Dose Protein

Study or Subgroup	High Protein Events	Total	Low Protein Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Clifton	1	10	1	10	1.3%	1.00 [0.07, 13.87]	1985
Scheinkestel	9	40	4	10	9.9%	0.56 [0.22, 1.46]	2003
Rugeles	11	40	12	40	18.7%	0.92 [0.46, 1.83]	2013
Doig	37	239	43	235	55.6%	0.85 [0.57, 1.26]	2015
Ferrie	12	59	9	60	14.5%	1.36 [0.62, 2.98]	2016
Total (95% CI)		**388**		**355**	**100.0%**	**0.89 [0.66,1.19]**	
Total events	70		69				

Heterogeneity: Tau^2=0.00; Chi^2=2.08, df=4 (P=0.72);I^2=0%
Test for overall effect: Z=0.80 (P=0.42)



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Impact on Clinical Outcomes: RCT Level of Evidence?

The Nephroprotect Study

- RCT short-term daily IV aa on kidney function in critical illness, compared to standard care.
- Unblinded
- All patients expected to remain 48 hrs; excluded patients with AKI
- Max protein intake total of 2.0 gm/kg/day (IBW)
- More patient in Intervention group with:
  - Higher APACHE II severity of illness scores (20.2 ± 6.8 vs. 21.7 ± 7.6, P = 0.02)
  - pre-existing renal dysfunction (29/235 vs. 44/239, P = 0.07)

Doig Int Care Med 2015

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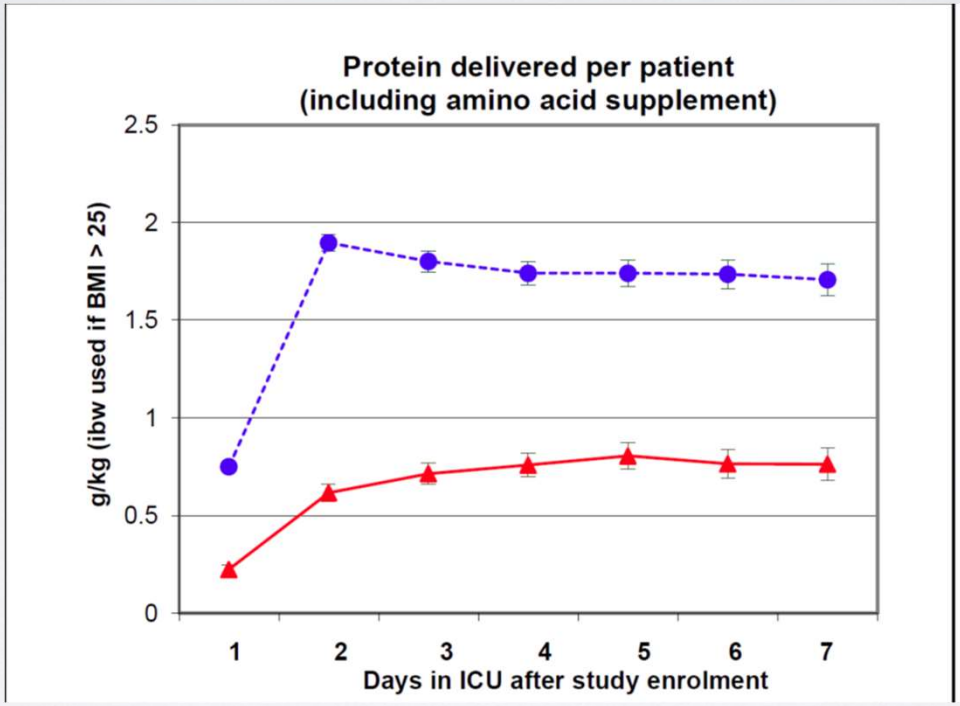
The Nephroprotect Study



Doig Int Care Med 2015

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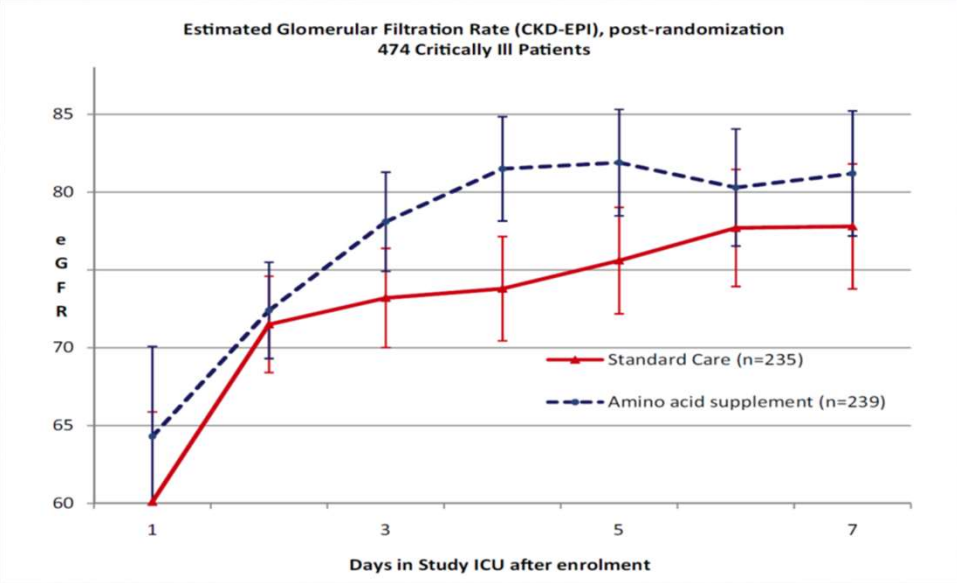
The Nephroprotect Study



P=0.004

No Harm from early,
high dose protein/aa intake!!

- No difference in any other renal or clinical outcome
- No impact on survival or HRQOL

Doig Int Care Med 2015

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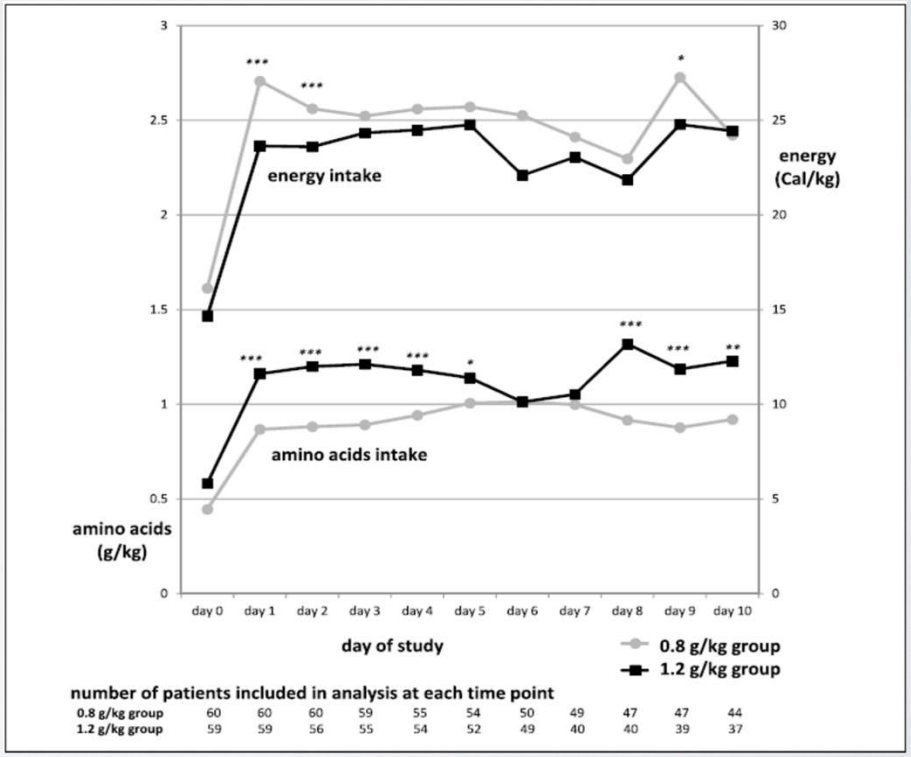
What is the evidence that exogenously administered amino acids/protein favorably impacts muscle mass and function?

- RCT of 119 ICU patients requiring PN
- Randomized to 0.8 gram/kg/day vs. 1.2 grams/kg/day IV aa



Ferrie JPEN 2016

Critical Care Nutrition

What is the evidence that exogenously administered amino acids/protein favorably impacts muscle mass and function?

Table 4. Intention-to-Treat Analysis Comparing Outcomes (0.8 g/kg vs 1.2 g/kg Amino Acids).

Outcome Measures	0.8 g/kg Amino Acids (n = 60)	1.2 g/kg Amino Acids (n = 59)	*P* Value Between Groups
Handgrip strength on discharge from ICU, mean (SD), kg	15.8 (10.3)	18.5 (10.4)	.054
% Expected value	45	51	
Handgrip strength at study day 7, mean (SD), kg	18.5 (11.8)	221.1 (10.1)	.025*
% Expected value	52	62	
Sum of 3 muscle sites on ultrasound at study day 7, mean (SD), cm	7.9 (1.1)	8.4 (1.0)	.02*
Forearm muscle thickness on ultrasound at study day 7, mean (SD), cm	2.8 (0.4)	3.2 (0.4)	<.0001***
Biceps muscle thickness on ultrasound at study day 7, mean (SD), cm	2.4 (0.4)	2.5 (0.6)	.21
Thigh muscle area on ultrasound at study day 7, mean (SD), cm^2	5.8 (1.9)	6.8 (2.1)	.02*

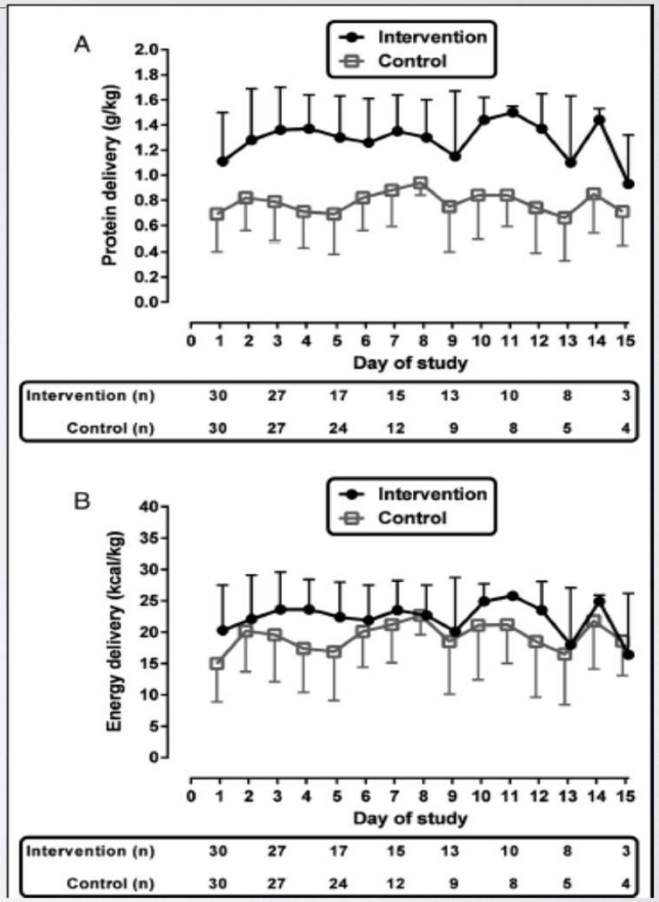
No impact on LOS or mortality

Ferrie JPEN 2016

Critical Care Nutrition

What is the evidence that exogenously administered amino acids/protein favorably impacts muscle mass and function?

- Pilot RCT of Volume-based feeds and protein supplements vs. standard nutrition
- 60 patients
- Adjusted for baseline QMLT, greater protein intake was associated with less QMLT loss at discharge with a mean attenuated loss of 0.22 cm (95% CI, 0.06 –0.38; P = .01), controlling for patient age severity of illness (APACHE III score), BMI, and admission diagnosis
- No change in LOS or mortality or muscle function



Fetterplace JPEN 2018

Critical Care Nutrition

What is the evidence that exogenously administered amino acids/protein favorably impacts clinical outcomes?

2015 Premier Research Paper

Clinical Outcomes Related to Protein Delivery in a Critically Ill Population: A Multicenter, Multinational Observation Study

Journal of Parenteral and Enteral Nutrition
Volume XX Number X
Month 201X 1–8

DOI: 10.1177/0148607115583675
jpen.sagepub.com
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online.sagepub.com

Michele Nicolo, MS, RD, CNSC[1]; Daren K. Heyland, MD, MSc, FRCPC[2];
Jesse Chittams, MS[3]; Therese Sammarco, BA[3];
and Charlene Compher, PhD, RD, CNSC, LDN, FADA, FASPEN[3]

Critical Care Nutrition

Impact of Protein Intake on 60-day Mortality

Data from 2828 patients from 2013 International Nutrition Survey

Variable	Patients in ICU ≥ 4 d 60-Day Mortality, Odds Ratio (95% CI)	
	Adjusted[1]	Adjusted[2]
Protein Intake (Delivery ≥ 80% of prescribed vs. < 80%)	0.61 (0.47, 0.818)	0.66 (0.50, 0.88)
Energy Intake (Delivery ≥ 80% vs. < 80% of Prescribed)	0.71 (0.56, 0.89)	0.88 (0.70, 1.11)

[1] Adjusted for BMI, Gender, Admission Type, Age, Evaluable Days, APACHE II Score, SOFA Score
[2] Adjusted for all in model 1 plus for calories and protein. Adjustment for protein intake is to control for energy intake and adjustment for energy intake is to control for protein intake.

Nicolo JPEN 2015

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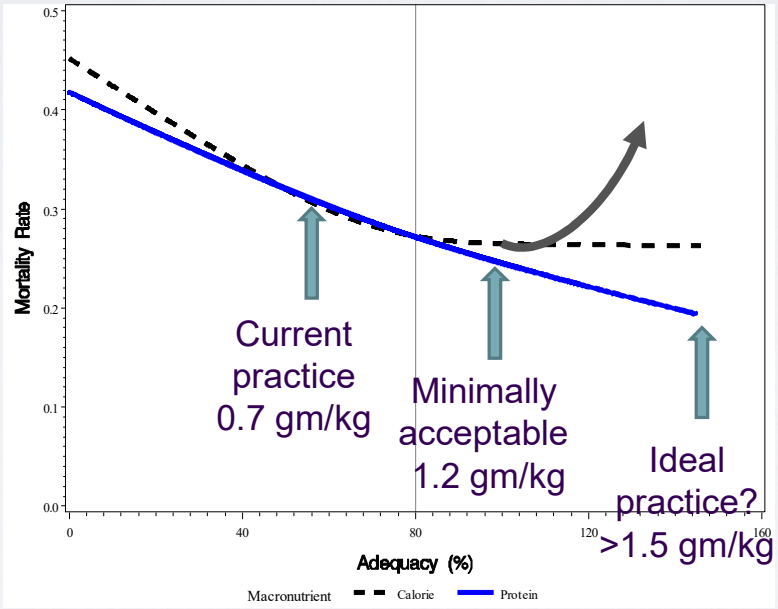
Rate of Mortality Relative to Adequacy of Protein and Energy Intake Delivered



TIACOS ICM 2011
INTACT JPEN 2014

Heyland JPEN 2015

RCTs do not suggest any evidence of harm and observational studies suggest increased protein intake associated with…

- Reduced mortality[1]
- Quicker Time-to-discharge-alive[1]
- Greater preservation of muscle [2,3]
- Reduced infection [4]

- Increased mortality[5]
- Slower time-to-discharge-alive from ICU[6]
- Greater loss of muscle mass and increased weakness[7,8]

1 Nicolo JPEN 2015
2 Ferrie JPEN 2016
3 Fetterplace JPEN 2018
4 Heyland JPEN 2010

5 Braunschweig Am J Clin Nutr 2017
6 Casaer Am J Respir Crit Care Med 2013
7 Puthucheary JAMA 2013
8 Hermans Lancet Respir 2013

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So how do we put this all together?

Agree: We need more research!

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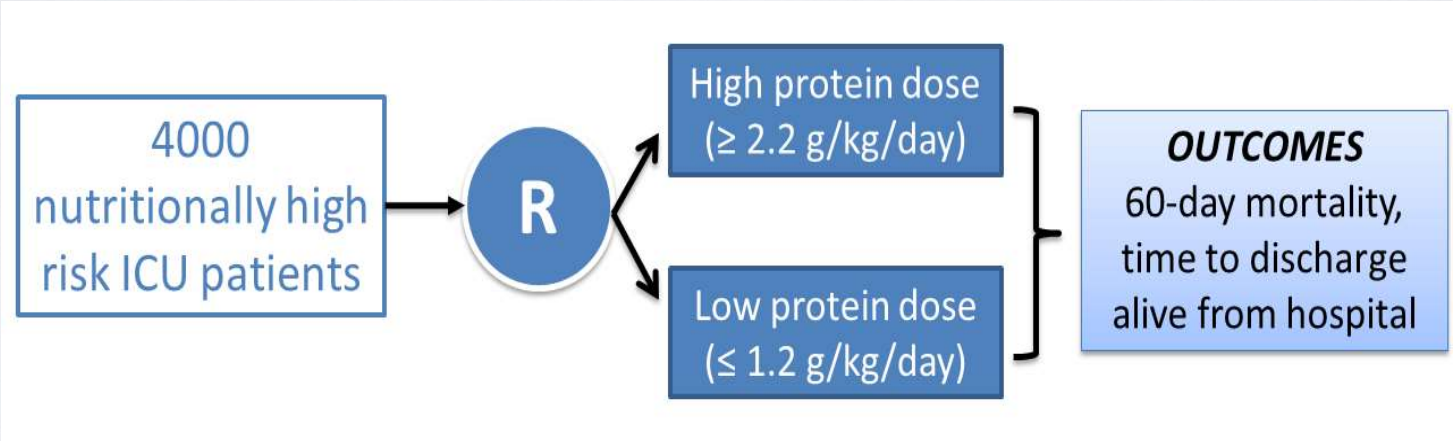
effort study

The Effect of Higher Protein Dosing in Critically Ill Patients: The EFFORT Trial



A multicentre, pragmatic, volunteer-driven, registry-based, randomized, clinical trial

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Overall Hypothesis

- Compared to the receiving lower dose of prescribed protein, the prescription of a higher dose of protein/amino acids to nutritionally high-risk critically ill patients will be associated with greater amount of protein delivered and result in improved survival and a quicker rate of recovery.

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Intervention

- Eligible patients will be randomized to one of 2 groups:
  - *High dose group:* Patients will be prescribed ≥2.2 g/kg/day
  - *Low dose group:* Patients will be prescribed ≤1.2 g/kg/day

- BOTH groups
  - Use dry pre-ICU body weight
  - Use IBW based on a BMI of 25, if BMI >30
  - Achieve goals through any combination of enteral and parental sources (as needed).
  - *The only difference between the 2 groups are the protein targets that are set.*
  - Success defined as achieving at least 80% of protein targets

What is the effect of prescribing a higher dose ($\geq$2.2 grams/kg/day) of protein/amino acid administration compared to a low group prescribed $\leq$1.2 gram/kg/day on 60 day mortality?

Is there enough uncertainty that practitioners will be comfortable with their patients being randomized
to 'low dose' group?
to the high group?
if not, don't enroll!

Issue 21
July 2018
Page 1 of 6

NIBBLE

Nutrition Information Byte

Critical Care Nutrition

Brought to you by www.criticalcarenutrition.com

Should We Have Equipoise (or Clinical Uncertainty) About How Much Protein to Provide to Critically ill Patients?

One of the most important questions in the critical care nutrition community right now is whether a higher protein dose translates into an improvement in clinical outcomes, as compared to lower protein intake.[1] The 2016 ASPEN/SCCM guideline recommends a wide range of acceptable protein prescription targets (1.2-2.0 grams/kg/day and higher in some select patients) and acknowledge that the underlying evidence for this recommendation is weak.[2] Despite the recommendation, the amount of protein that is actually delivered worldwide ranges widely between 0.5 to 3.8 grams/kg/day (average of 1.3 grams/kg/day).[3] We surmise a wide range in actual protein delivery exists because a weak evidentiary base informs guideline recommendations, and hence, clinical practice.

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Table 1. What does the evidence say about protein dose in critically ill patients?

	Evidence for a Higher Dose	Evidence for a Lower Dose	Equivocal Evidence
Meta-analysis of RCTs			• 5 RCTs comparing higher to lower protein intake showing no difference in mortality.[36] (***)
RCTs	• Single center trials demonstrating positive effects on surrogate outcomes.[7,8] (*)		• Nephroprotect Trial showing no effect of 1.0 g/kg/day extra IV amino acids.[17] (***)
Observational	• Observational analyses showing more protein in early phase associated with better outcomes. (mortality, infections and functional recovery).[11,12,13,14,15,14,15] (**) • Post-hoc analysis of Nephroprotect suggesting benefit in patients with normal kidney function.[35] (*)	• Post hoc analysis of RCTs and observational study suggesting increased harm with more protein (slower time to discharge, increase muscle mass, increased mortality).[19,21,22] (*) • Retrospective analysis of single institutional database suggesting better outcomes with low level of protein (<0.8 g/kg/day) in the first days followed by >1.2 g/kg/day after day 3.[23] (*)	
Expert opinion	• ASPEN/SCCM guidelines recommend higher doses in obesity, burns, trauma, and renal failure requiring renal replacement therapy.[2] • Experts saying higher doses are safe and possibly efficacious.[16]	• Experts recommending withholding nutrition or limiting intake to minimal amounts during the first week.[37]	
Mechanistic	• Tracer and nitrogen balance studies showing increased protein/aa associated with more positive whole body protein balance.[5,6] • Data that supports IV aa improves renal function or renal blood flow.[25] • Data from patients requiring CRRT suggesting that patients receiving higher doses of protein have a better nitrogen balance.[26-30]	• Animal data suggesting that IV aa suppress autophagy and fails to suppress endogenous catabolism.[24]	

Legend: *-weak evidence; ** moderate evidence; *** stronger evidence

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effort study

Study Population

Inclusion Criteria	Exclusion Criteria	Rationale for Exclusion
1. >18 years old 2. Nutritionally "high-risk" (meeting one of the below criteria) a. Low (≤25) or High BMI (≥35) b. Moderate to severe malnutrition (as defined by local assessments) c. Frailty (Clinical Frailty Scale, 5 or more from proxy) d. Sarcopenia – (SARC-F score of 4 or more from proxy) e. From point of screening, projected duration of mechanical ventilation >4 days) 3. Requiring mechanical ventilation with actual or expected total duration of mechanical ventilation >48 hours	1. >96 continuous hours of mechanical ventilation before screening	Intervention is likely most effective when delivered early
	2. Expected death or withdrawal of life-sustaining treatments within 7 days from screening	Patients unlikely to receive benefit
	3. Pregnant	Unknown effects on fetus
	4. The responsible clinician feels that the patient either needs low or high protein	Uncertainty doesn't exist; patient safety issues
	5. Patient requires parenteral nutrition only and site does not have products to reach the high protein dose group	Site will be unable to reach high protein dose prescription

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I see no reason to change practice at the moment…

Clinical Guidelines

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Journal of Parenteral and Enteral Nutrition
Volume 40 Number 2
February 2016 159–211

DOI: 10.1177/0148607115621863

C4. We suggest that sufficient (high-dose) protein should be provided. Protein requirements are expected to be in the range of 1.2–2.0 g/kg actual body weight per day and may likely be even higher in burn or multitrauma patients (see sections M and P).

[Quality of Evidence: Very Low]

M1a. We suggest that, similar to other critically ill patients, early enteral feeding with a high protein polymeric diet be initiated in the immediate posttrauma period (within 24–48 hours of injury) once the patient is hemodynamically stable.

[Quality of Evidence: Very Low]

My recommendation: Aim on the low side (1.2-1.5) for first few days-week then increase after wards but achieve 80% of your prescription!

Target 20-25 kcal/kg but only achieve 40-80% of goal in first week

Careful control of blood glucose (<10 mmol/L) and monitoring of phosphate

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…but we need more data! Join the EFFORT!

For more information on the EFFORT Trial
See www.criticalcarenutrition.com

Or contact:

Daren Heyland
Dkh2@queensu.ca

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Optimizing Nutrition Therapy: A practical approach

Critical Care Nutrition

The PEP uP Protocol!

The Efficacy of Enhanced Protein-Energy Provision via the Enteral Route in Critically Ill Patients:

- Different feeding options based on hemodynamic stability and suitability for high volume intragastric feeds.
- In select patients, we start the EN immediately at goal rate, not at 25 mL/hr.
- We target a 24 hour volume of EN rather than an hourly rate and provide the nurse with the latitude to increase the hourly rate to make up the 24 hour volume.
- Start with a very high protein solution; semi elemental solution then progress to polymeric
- Motility agents and protein supplements are started immediately, rather than started when there is a problem
- Tolerate higher GRV threshold (300 mL or more)

A Major Paradigm Shift in How we Feed Enterally

Heyland Crit Care 2010

see www.criticalcarenutrition.com for more information on PEP uP tools

Critical Care Nutrition

Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol in Critically Ill Patients: Results of a Cluster Randomized Trial

Daren K. Heyland, MD, MSc[1,2,3]; Lauren Murch, MSc[1]; Naomi Cahill, RD, PhD[1,2]; Michele McCall, RD, MSc[4]; John Muscedere, MD[1,3]; Henry T. Stelfox, MD, PhD[5,6,7]; Tricia Bray, RN, MN[8]; Teddie Tanguay, RN, NP, MN[9]; Xuran Jiang, MSc[1]; Andrew G. Day, MSc[1]

- Resulted in a significant improvement in nutrition delivery (12-14% increase with no overfeeding)
- No change in clinical outcomes (not powered to do so)
- Observed a 4% reduction in mortality from baseline in PEP uP group

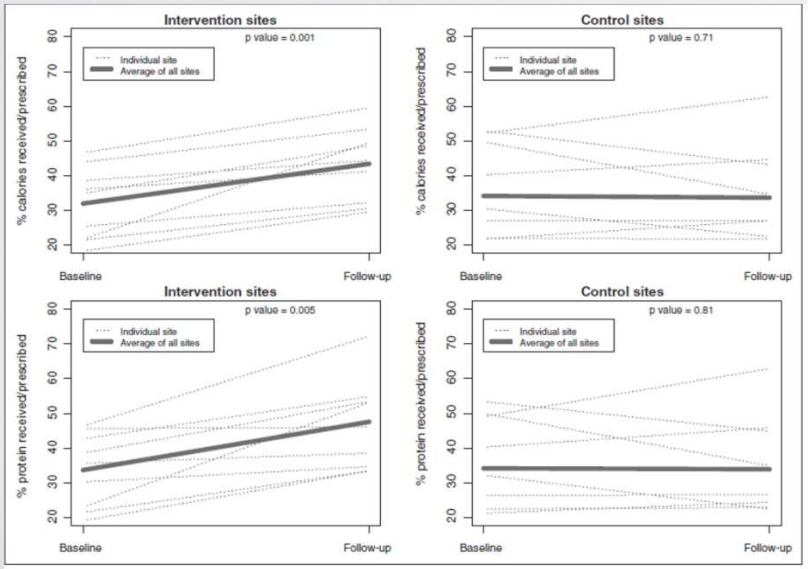


Figure 2. Changes in protein and energy adequacy in control and intervention sites. This figure shows the pre- and postdata collection overall and by site connected by lines. *Thick line* shows average improvement in protein and caloric adequacy in intervention and control sites. *Dashed lines* reflect changes at individual sites.

TABLE 4. Clinical Outcomes Between Groups and Across Time (All Patients – *n* = 1,059)

Variable	Intervention		Control		*p*[a]
	Baseline	Follow-Up	Baseline	Follow-Up	
n	270	252	270	267	
ICU mortality (%)	47 (17.4)	35 (13.9)	49 (18.1)	42 (15.7)	0.57
Died within 60 d of ICU admission (%)	70 (25.9)	68 (27.0)	65 (24.1)	63 (23.6)	0.53
Length of stay among 60-d survivors					
Days on mechanical ventilation	3.7 (1.6, 9.1)	4.3 (1.3, 9.9)	3.1 (1.4, 8.4)	3.0 (1.4, 7.3)	0.57
Days in ICU	6.1 (3.4, 11.4)	7.2 (3.4, 11.1)	6.4 (3.3, 12.6)	5.7 (2.8, 11.8)	0.35
Days in hospital	14.2 (8.1, 29.8)	13.5 (8.1, 28.4)	16.7 (7.5, 27.7)	13.8 (7.1, 26.6)	0.73

[a]*p* values test against the null hypothesis that the mean within ICU change is the same in both arms.

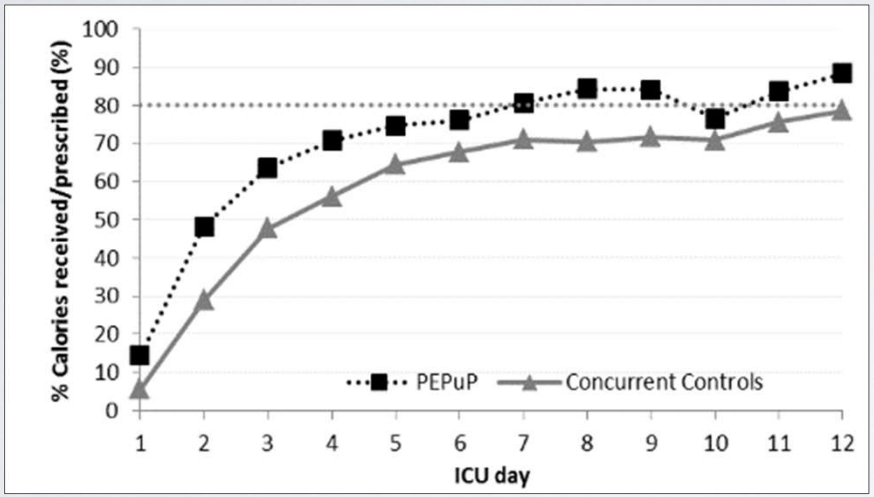
Heyland CCM 2013

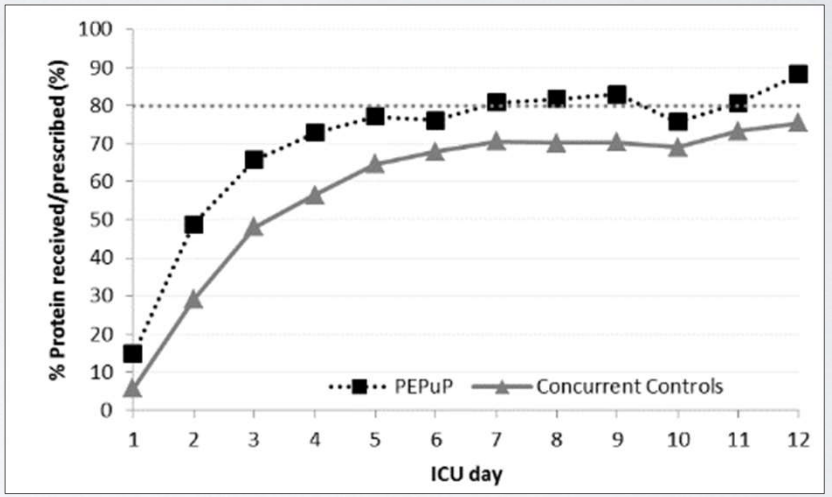
Nestlé provided partial funding for this trial

Critical Care Nutrition

Results of the Canadian PEP uP Collaborative

Results of 2013 International Nutrition Survey (INS)





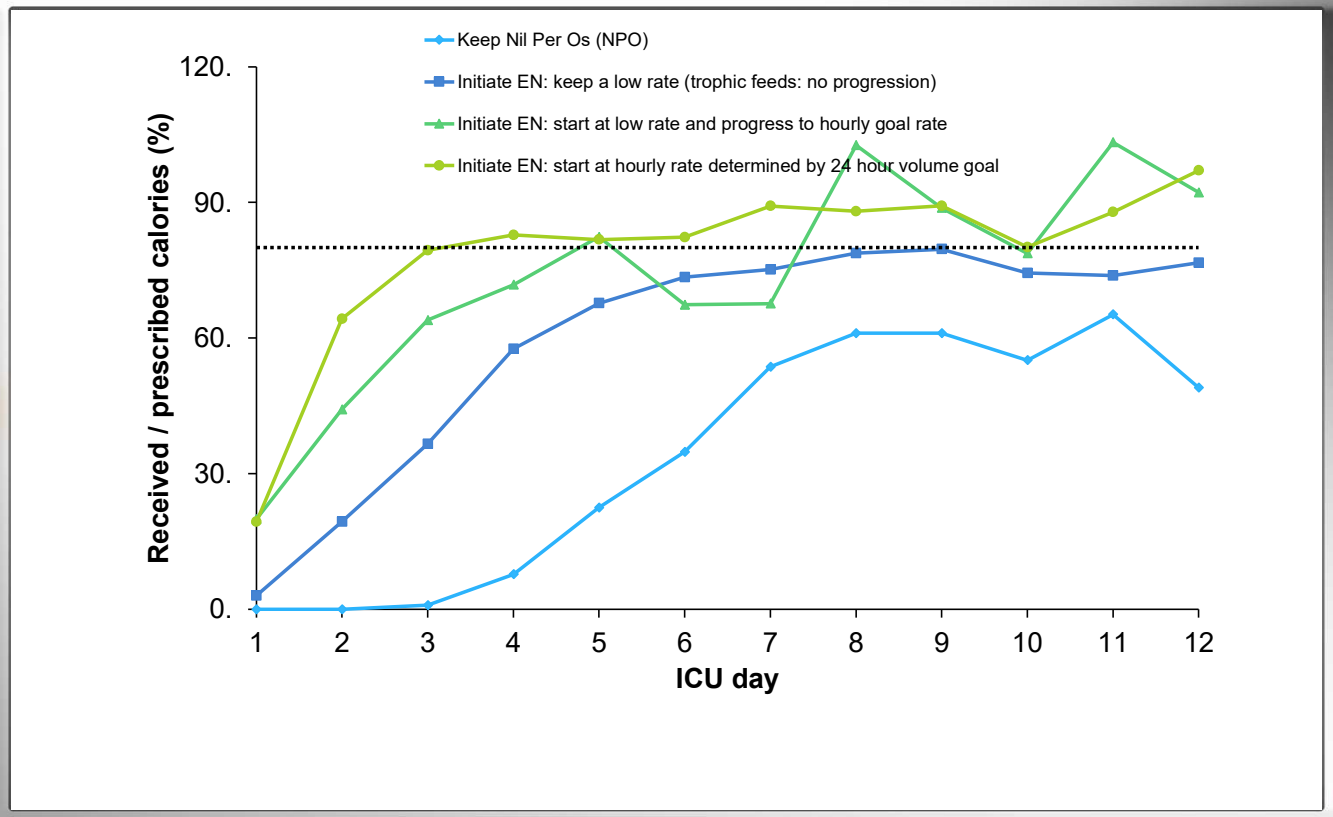
Heyland JPEN 2015

Nestlé provided partial funding and product for this project

Critical Care Nutrition

Results of the Canadian PEP uP Collaborative

Proportion of Prescribed Energy From EN According to Initial EN Delivery Strategy



Heyland JPEN 2015

Nestlé provided partial funding and product for this project

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Original Communication

What Is "Best Achievable" Practice in Implementing the Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol in Intensive Care Units in the United States? Results of a Multicenter, Quality Improvement Collaborative

Daren K. Heyland, MD, MSc[1,2,3]; Margot Lemieux, RD[1]; Lin Shu, MS, RD[4]; Kristen Quisenberry, RD, LD, CNSC[5]; and Andrew G. Day, MSc[1,2]

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xxx 2017 1–10

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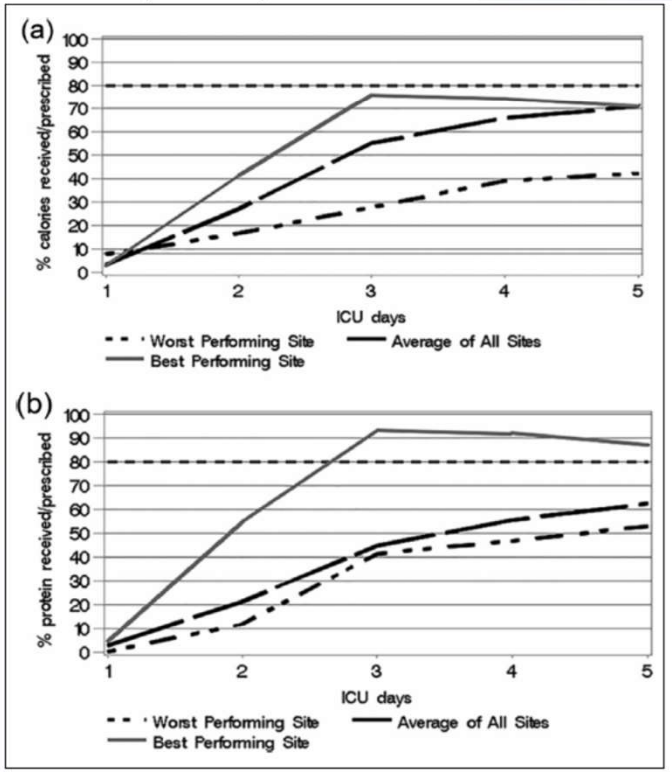


Figure 2. Enteral nutrition adequacy over the first 5 days in best, worst, and average Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol (PEP uP) sites. (a) The

Nestlé provided partial funding and product for this project

Critical Care Nutrition

Need to Monitor Daily Success!

Please report this % on rounds as part of the GI systems report

Adequacy of nutrition support
=
24 hour volume of EN received

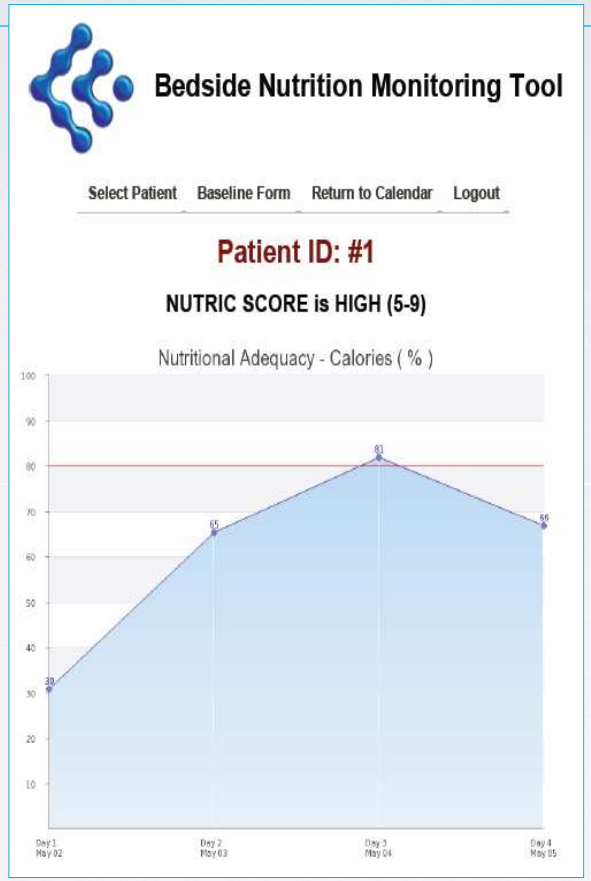
Volume prescribed to meet caloric requirements in 24 hours

When performance is measured, performance improves.

When performance is measured and reported back, the rate of improvement accelerates.

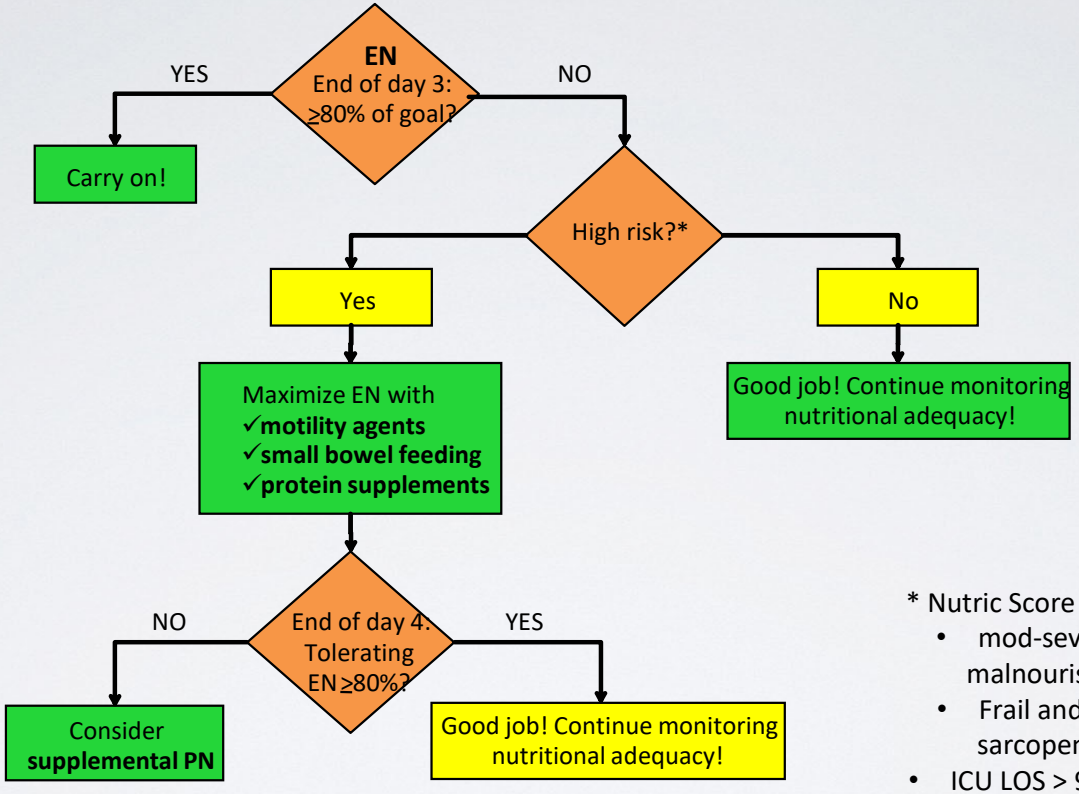
Critical Care Nutrition

Need to Monitor Daily Success!



See www.criticalcarenutrition.com for monitoring tool

Start PEP uP Protocol in all patients within 24-48 hrs of admission



* Nutric Score > 5 or
  - mod-severe malnourished
  - Frail and/or sarcopenia?
- ICU LOS > 96 hrs

Heyland, Right here, Right now!

Critical Care Nutrition

Conclusions

- Early enteral feeds is still standard of care.
- The burden of evidence suggests that early, optimal (>80%), dosed at 1.2-2.0 grams/kg/day is suggestive of best clinical outcomes.
- Glucose and phosphate important variables to measure a patients response to nutrition support; no other validated monitoring variables.
- Probably nutritionally high-risk patients will benefit the most from macronutrients; It's important to monitor adequacy of intake in high-risk patients!
- Tools and strategies exist to identify high risk patients that benefit from clinical nutrition support and to optimize nutrition intake
- Protein more important that calories in acute phase
- Need more research to prove these points- Join the EFFORT trial!

Critical Care Nutrition

QUESTIONS?

Nutrition-related resources and tools are available from the Nestlé Nutrition Institute at
nestlenutrition-institute.org

Access QI project nutrition-related resources and tools at
https://www.enactnutrition.com/act.aspx

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Offering CE to dietitians and nurses