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Strategies for Improving Enteral Nutrition Delivery in the ICU

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Critical Care Nutrition

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Disclosure

Financial Support for this presentation was provided by Nestlé Health Science. The views expressed herein are those of the presenter and do not necessarily represent Nestlé's views. The material herein is accurate as of the date it was presented, and is for educational purposes only and is not intended as a substitute for medical advice.

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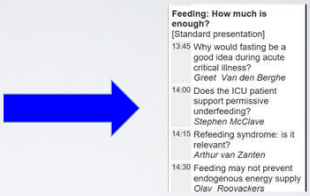
Creating Clarity Out of Confusion!

Large, Negative RCTs

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



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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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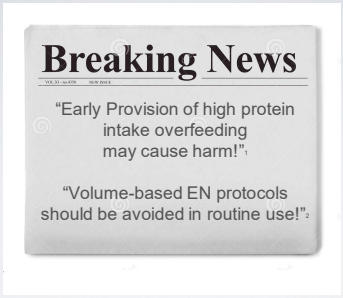

1. Koekkoek, Curr Opin Anesthesiol 2018; 31:136–143
2. Krenitsky Nutrition Issues in Gastro Aug 2018

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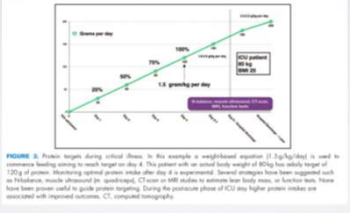
Slow Starts, Slow Ramp ups



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

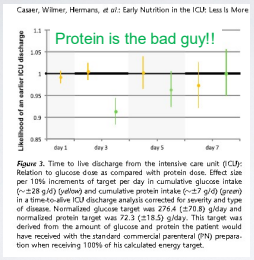

Figure 3. Time to live discharge from the intensive care unit (ICU): Relation to glucose dose as compared with protein dose. Effect size per 10% increments of target per day in cumulative glucose intake (~±28 g/d) (yellow) and cumulative protein intake (~±7 g/d) (green) in a time-to-alive ICU discharge 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.[a]

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,[1]* Sally Freels,[2] Patricia M Sheean,[1] Sarah J Peterson,[1] Sandra Gomez Perez,[1] Liam McKeever,[1] Omar Lateef,[1] David Gurka,[1] and Giamila Fantuzzi[1]

- 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[3]	−0.0967	0.0471	0.04	0.91 (0.83, 1.0)
Model 2				
Mean daily g protein/kg received during days 1–7[4]	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

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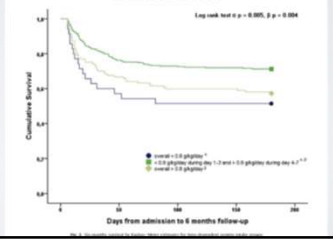
Timing of PROTein INtake and clinical outcomes of adult critically ill patients on prolonged mechanical VENTilation: A retrospective, single-center, study

- 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



Koekkoek Clin Nutrition 2018

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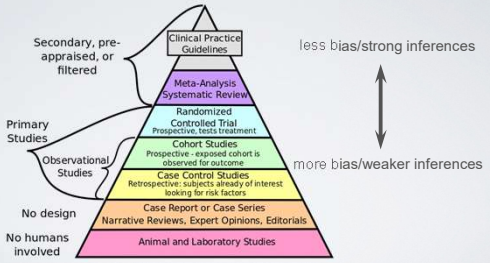
Levels of Evidence



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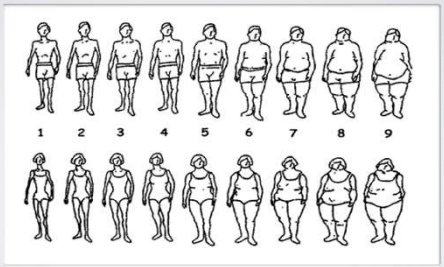
ICU Patients Are Not All Created Equal…
These recommendations were made without consideration of 'nutritional risk'!



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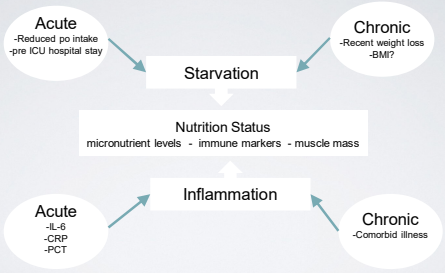
A Conceptual Model for Nutrition Risk Assessment in the Critically Ill



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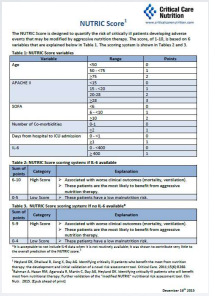
Calculating the NUTRIC Score



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

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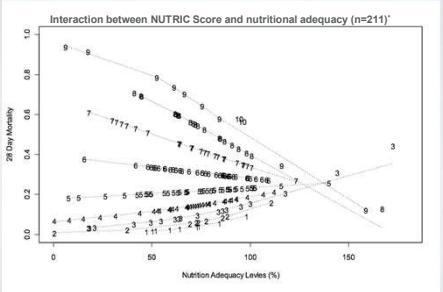
The Validation of the NUTrition Risk in the Critically Ill Score (NUTRIC Score)



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

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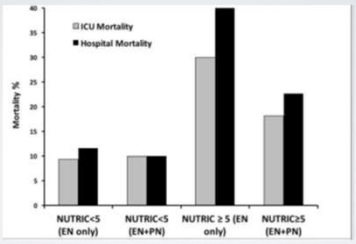
Results of TOP UP Pilot Trial

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?

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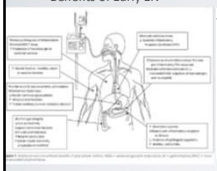
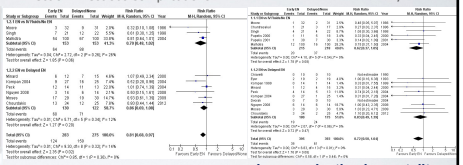
RCTs Level of Evidence for Early EN supported by our understanding of underlying pathophysiology!

Nutritional and Non-Nutritional Benefits of Early EN



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)

www.criticalcarenutrition.com

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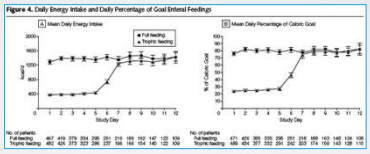
Initial Trophic vs. Full EN in Patients with Acute Lung Injury

The EDEN randomized trial



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

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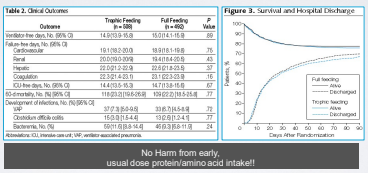
Initial Tropic vs. Full EN in Patients with Acute Lung Injury

The EDEN randomized trial



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

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

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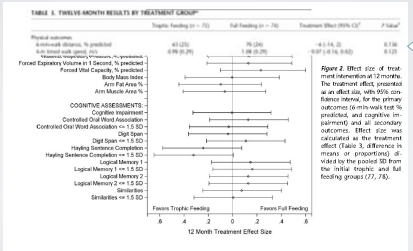
Physical and Cognitive Performance of Patients with Acute Lung Injury 1 Year after Initial Trophic versus Full Enteral Feeding

EDEN Trial Follow-up



Trend towards improvement with full feeds!

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Critical Care Nutrition

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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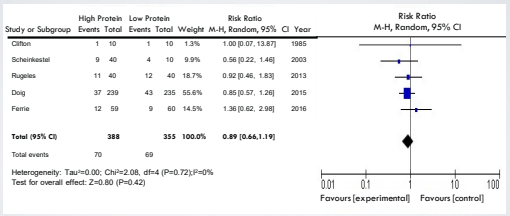
Critical Care Nutrition

Systematic Review of RCTs of High vs. Low Dose Protein



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Critical Care Nutrition

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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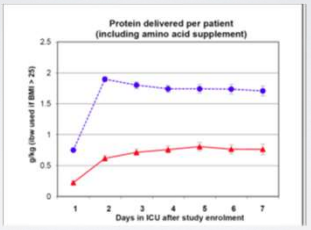
Critical Care Nutrition

The Nephroprotect Study



Doig Int Care Med 2015

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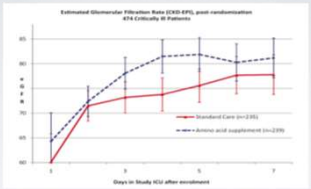
Critical Care Nutrition

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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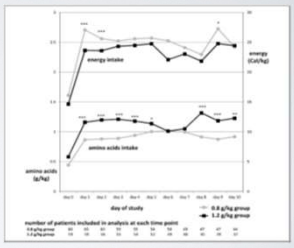
Critical Care Nutrition

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

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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), cm²	5.8 (1.9)	6.8 (2.1)	.02*

No impact on LOS or mortality

Ferrie JPEN 2016

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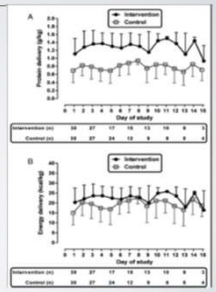
What is the evidence that exogenously administered amino acids/protein favorably impacts muscle mass and function?

- 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

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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

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]

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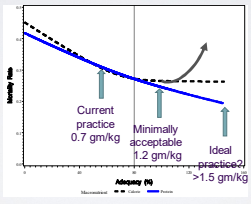
Rate of Mortality Relative to Adequacy of Protein and Energy Intake Delivered



TIACOS ICM 2011
INTACT JPEN 2014

Heyland JPEN 2015

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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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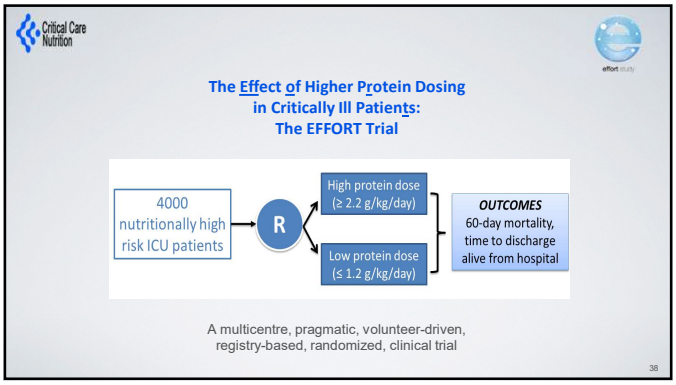

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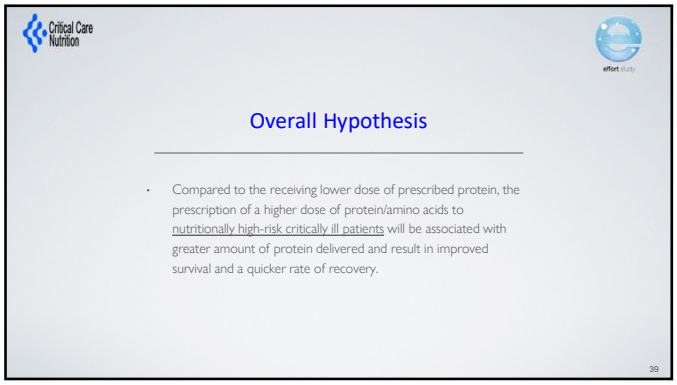

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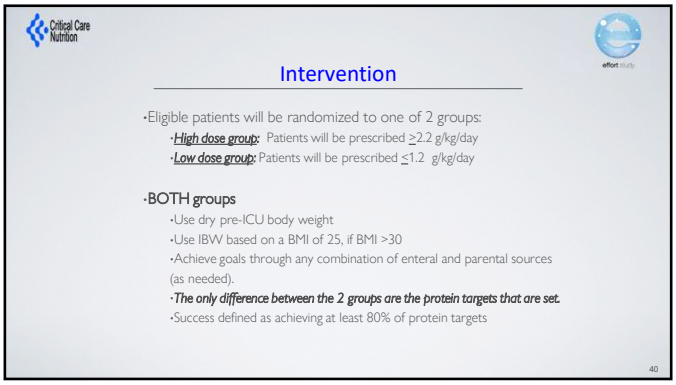

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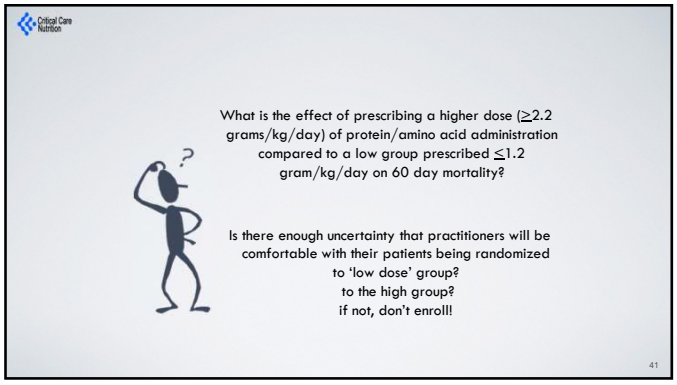

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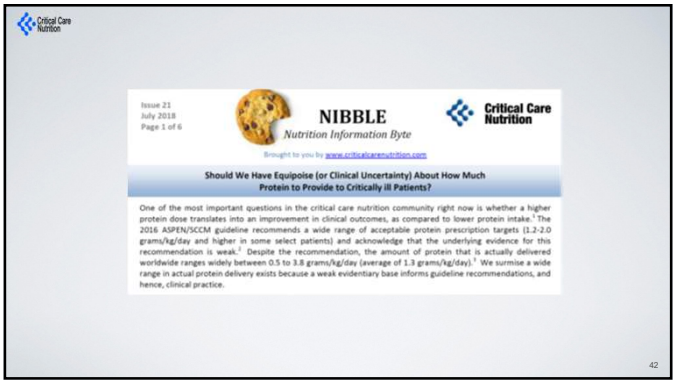

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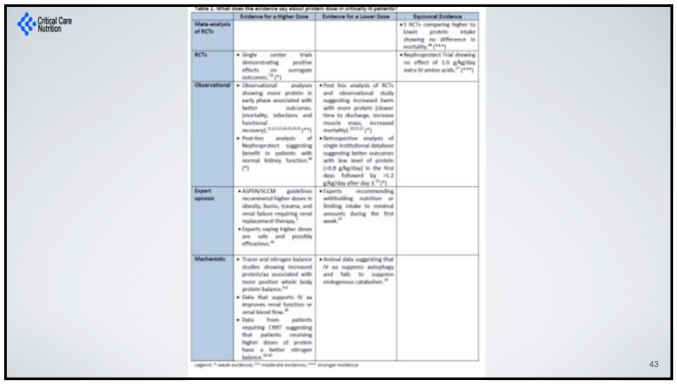

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Study Population

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.)

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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

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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

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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[1]; John Muscedere, MD[1,2]; Henry T. Stelfox, MD, PhD[1,2,3]; Tricia Bray, RN, MN[1]; Teddie Tanguay, RN, NP, MN[1]; 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

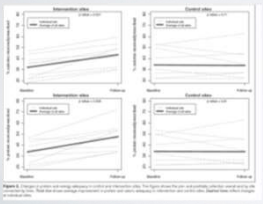

TABLE 4. Clinical Outcomes Between Groups and Across Time (All Patients – $n = 1,059$)

Variable	Intervention Baseline	Intervention Follow-Up	Control Baseline	Control Follow-Up	p^*
n	270	252	270	267	
ICU mortality (%)	47 (17.4)	35 (13.9)	49 (18.1)	42 (15.7)	0.07
Died within 60 d of ICU admission (%)	70 (25.9)	66 (27.0)	65 (24.1)	62 (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, 9.0)	3.1 (1.4, 8.4)	3.0 (1.4, 7.3)	0.07
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 (10, 27.7)	13.6 (7.1, 26.6)	0.73

*p value 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

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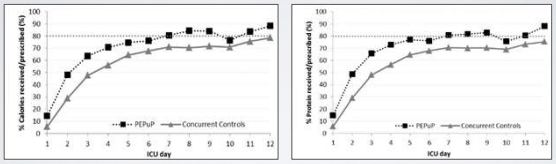
Results of the Canadian PEP uP Collaborative

Results of 2013 International Nutrition Survey (INS)



Heyland JPEN 2015

Nestlé provided partial funding and product for this project

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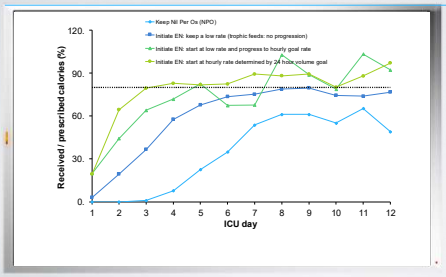
Results of the Canadian PEP uP Collaborative

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[1,3]

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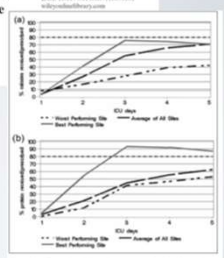

Figure 2. Enteral nutrition adequacy over the first 5 days in best, worst, and average Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol (PEP uP) sites (a) The

Nestlé provided partial funding and product for this project

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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.

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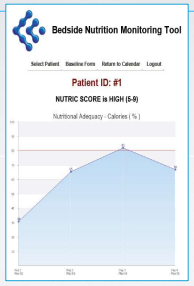
Need to Monitor Daily Success!



See www.criticalcarenutrition.com for monitoring tool

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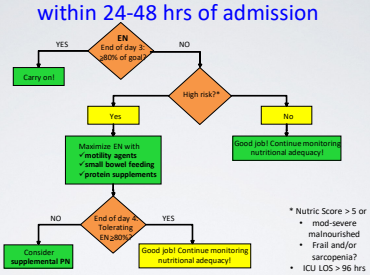
Start PEP uP Protocol in all patients within 24-48 hrs of admission



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

Heyland, Right here, Right now!

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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!

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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

Visit MyCE at MyCEeducation.com
Offering CE to dietitians and nurses

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