DAPEN Copenhagen, Dannmark, May 5, 2018

Critical Care Nutrition Research:
Timing of nutrition therapy during and after critical illness

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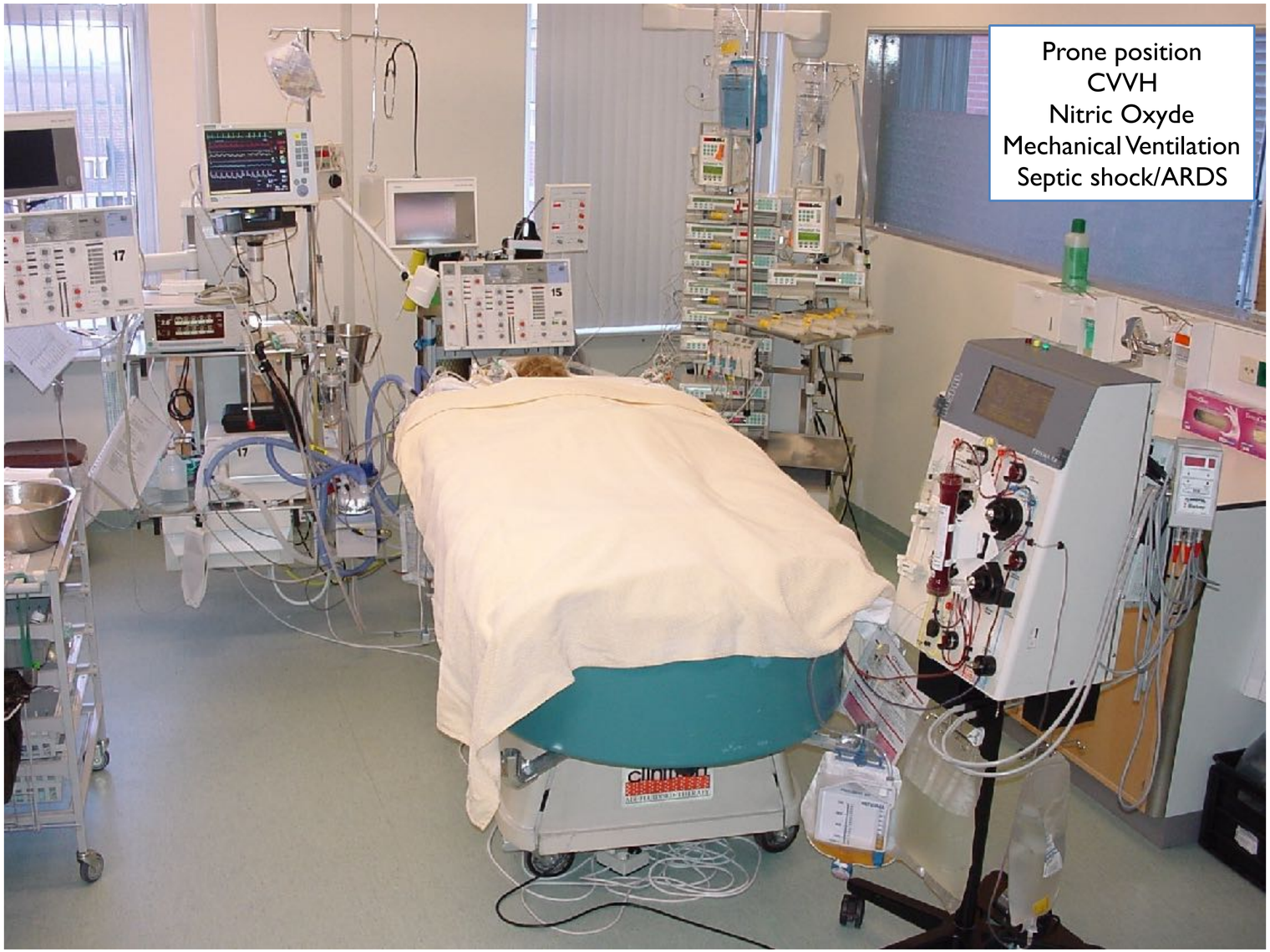
Clinical Nutrition Research, Wageningen, the Netherlands, April 26, 2018

Dr. van Zanten has received honoraria for advisory board meetings, lectures, research and travel expenses from:

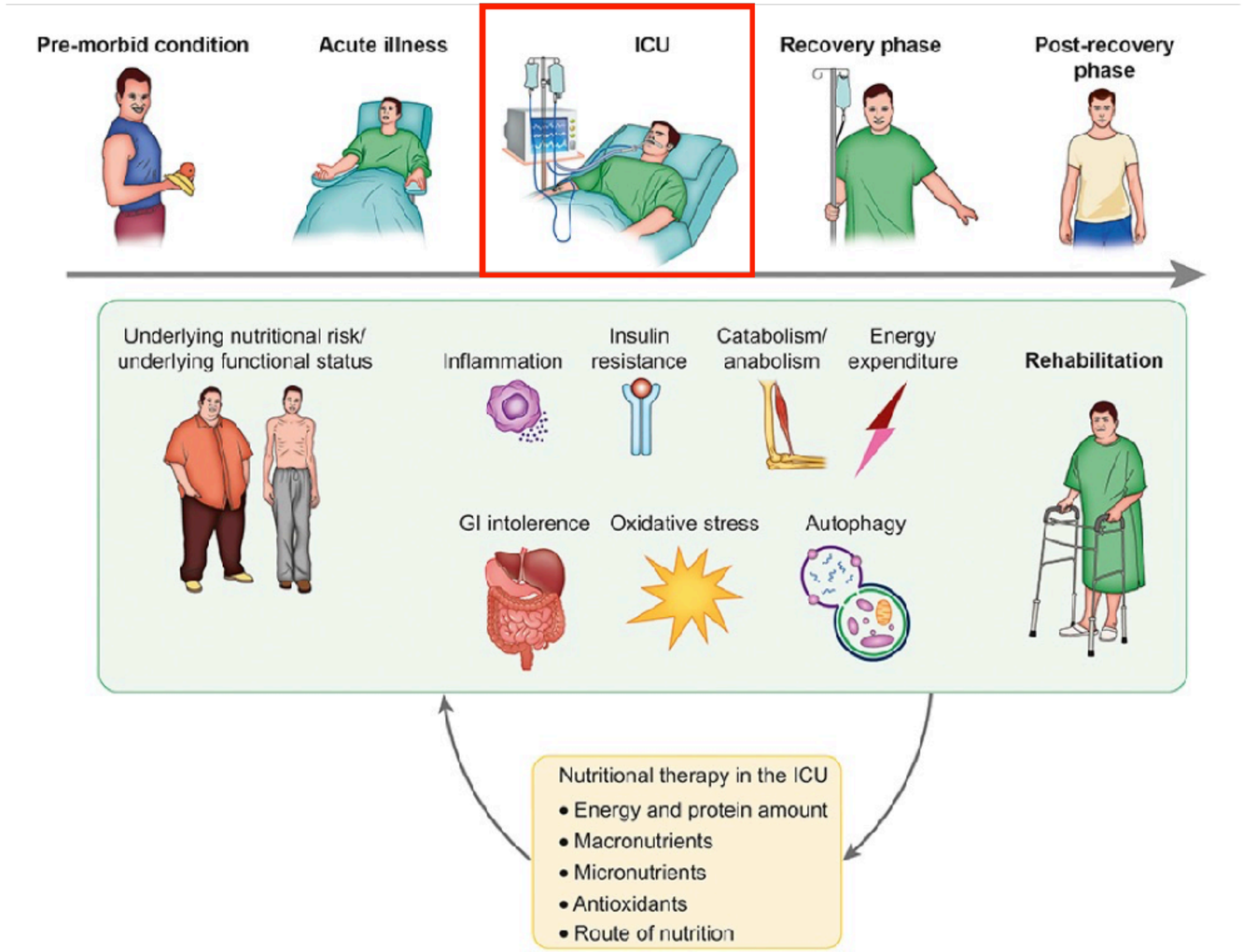
- **Abbott**
- **Baxter**
- **BBraun**
- **Cardinal Health**
- **Fresenius Kabi**
- **Lyric**
- **Nestlé-Novartis**
- **Nutricia-Danone**

ESPEN guidelines committee Critical Care Nutrition for Adults
ESICM Working Group Gastrointestinal Failure
NESPEN Executive Team
Chair Netherlands Sepsis guidelines committee

Should we feed this patient with abdominal sepsis and MODS?



Nutritional support throughout the critically ill patient journey

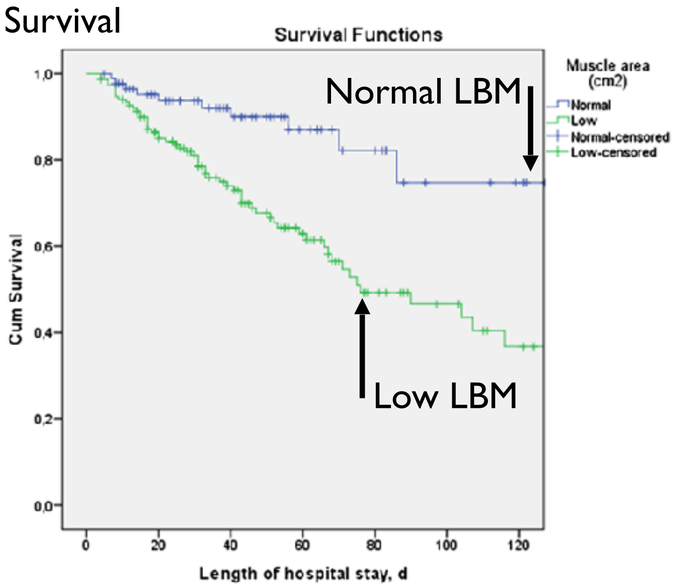


Arabi Y, ...Van Zanten AR: Intensive Care Med 2017

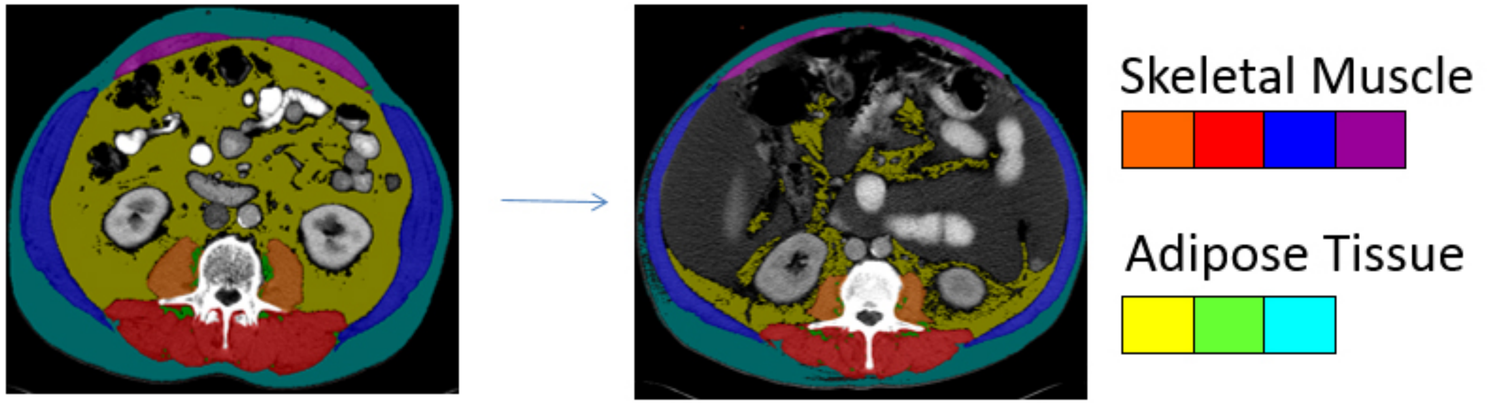
Nutritional support throughout the critically ill patient journey

Acute Phase	Days 1 - 3 of ICU admission
Chronic Phase	Days 4 - 7 of ICU admission
Recovery Phase	Week ≥2 after ICU admission
Long-term Phase	Week ≥26 after ICU admission

LBM: CT-scan and mortality

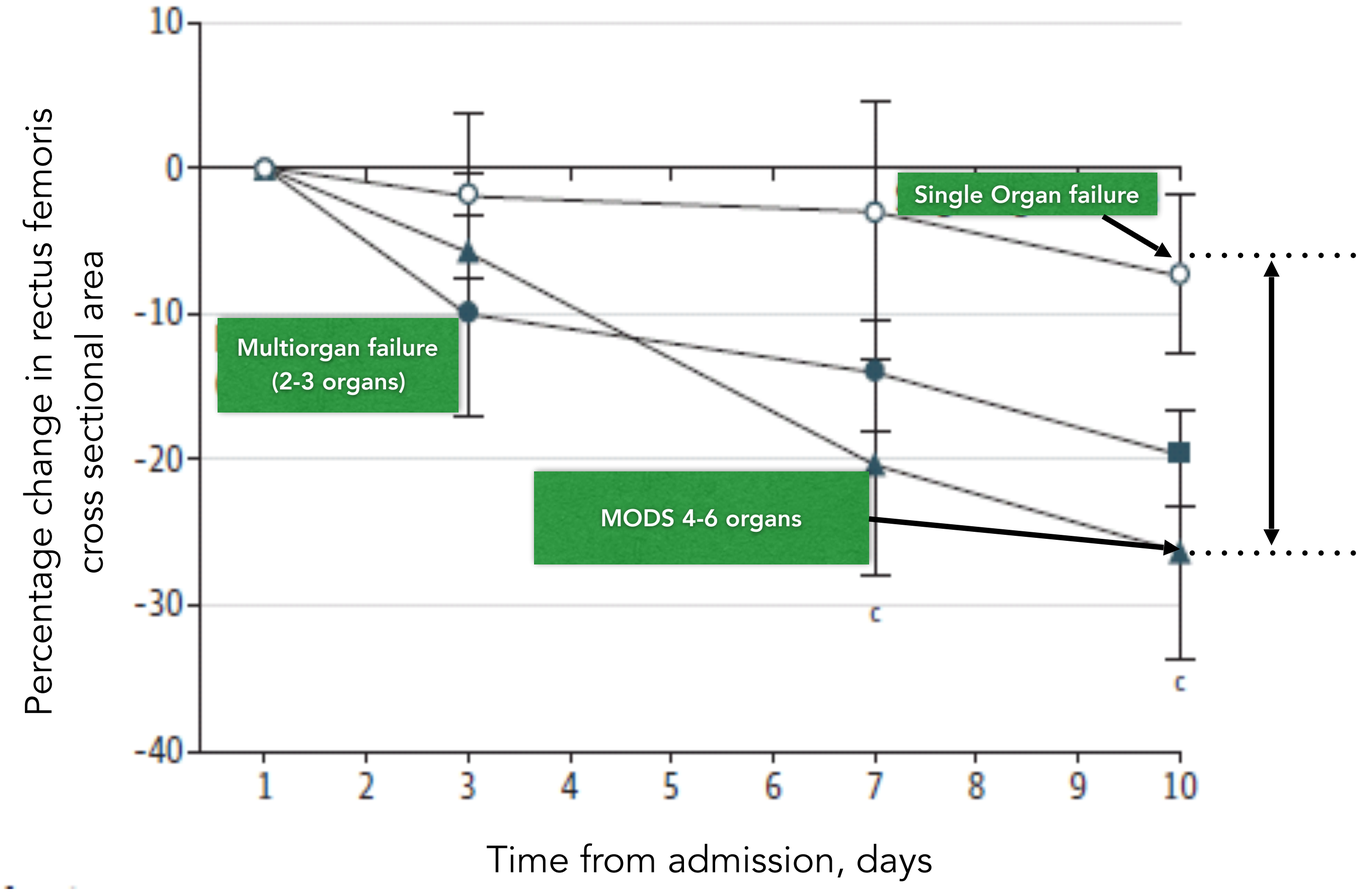


- Low skeletal muscle area, as assessed by CT scan during the early stage of critical illness, is a risk factor for mortality in mechanically ventilated critically ill patients, independent of sex and APACHE II score.
- Muscle mass is primary predictor.
- BMI is not an independent predictor of mortality when muscle area is accounted for.



Weijs et al. Critical Care 2014 18:R12

Muscle mass loss 1 kg per day



Puthucheary ZA et al., JAMA 2013

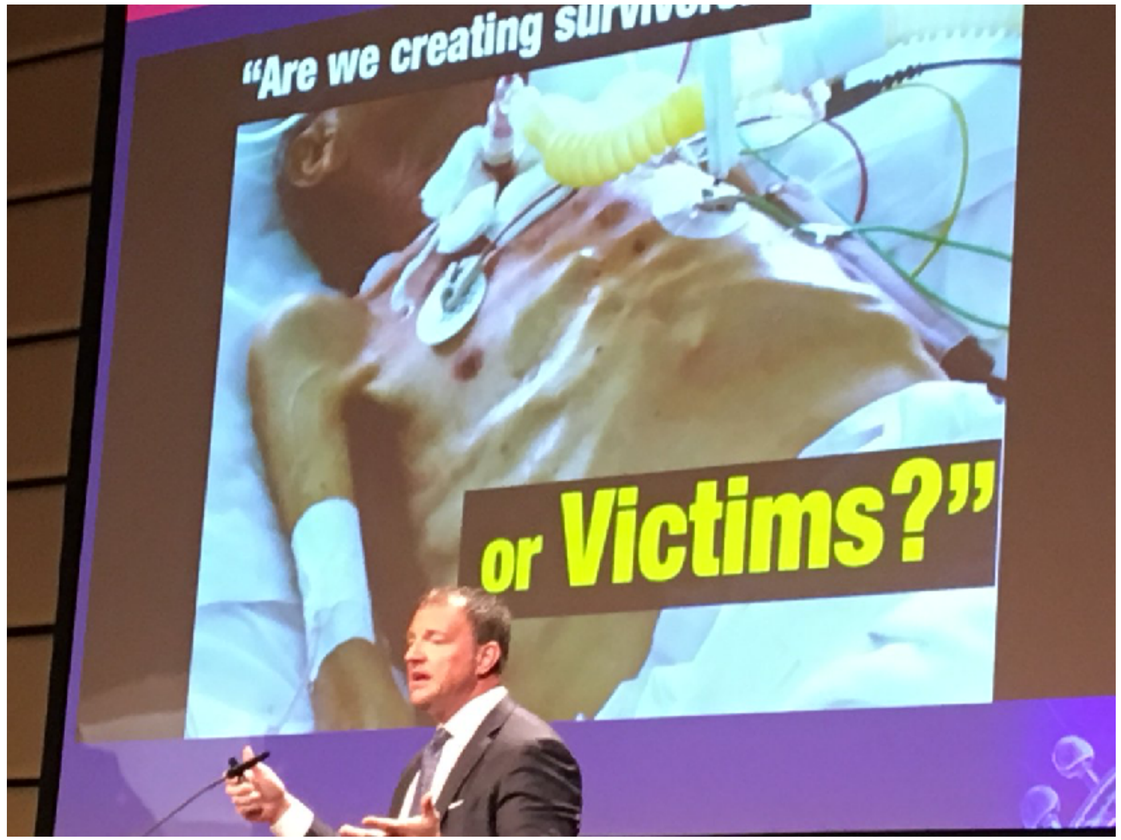
Sepsis: Survivors or Victims

33% die during first year

50% recover

17% persistent impairments

1 to 2 new functional limitations
(eg, inability to bathe or dress independently)



Prescott HC, Angus DC. JAMA. 2018;319(1):62–75.

Sepsis: long-term consequences

40% of patients are rehospitalized within 90 days of discharge.

Prescott HC, Angus DC. JAMA. 2018;319(1):62–75.

Sepsis: long-term consequences

a 3-fold increase in prevalence of moderate to severe cognitive impairment (from 6.1% before hospitalization to 16.7% after hospitalization)

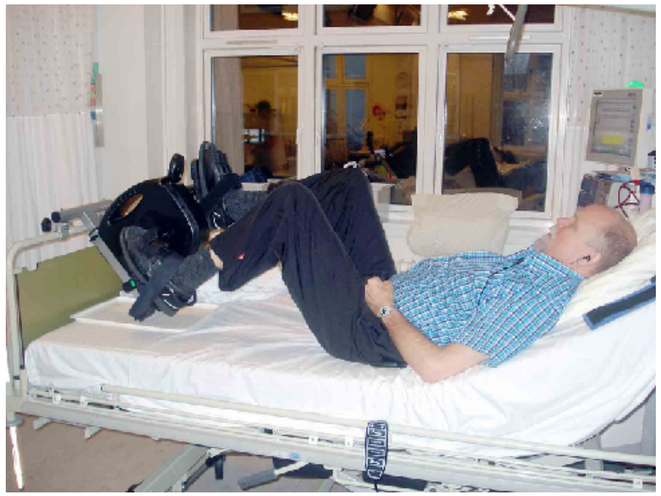
44%

Prescott HC, Angus DC. JAMA. 2018;319(1):62–75.

Sepsis: long-term consequences

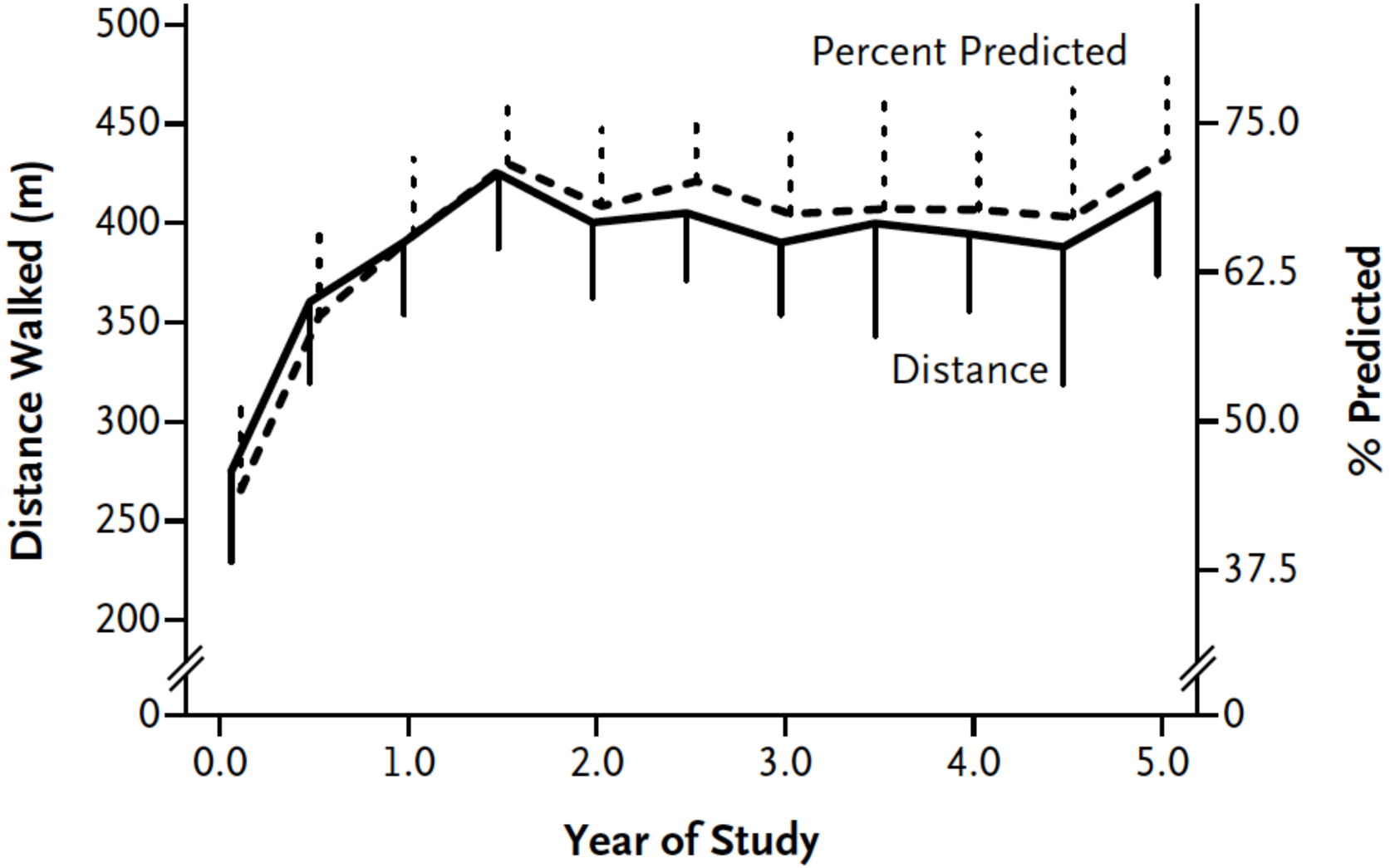
Experts recommend referral to **physical therapy** to improve exercise capacity, strength, and independent completion of activities of daily living.

Observational study involving 30,000 sepsis survivors **referral to rehabilitation within 90 days** was associated with **lower risk of 10-year mortality** compared with propensity-matched controls (adjHR, 0.94; 95% CI, 0.92-0.97, P < .001).



Prescott HC, Angus DC. JAMA. 2018;319(1):62–75.

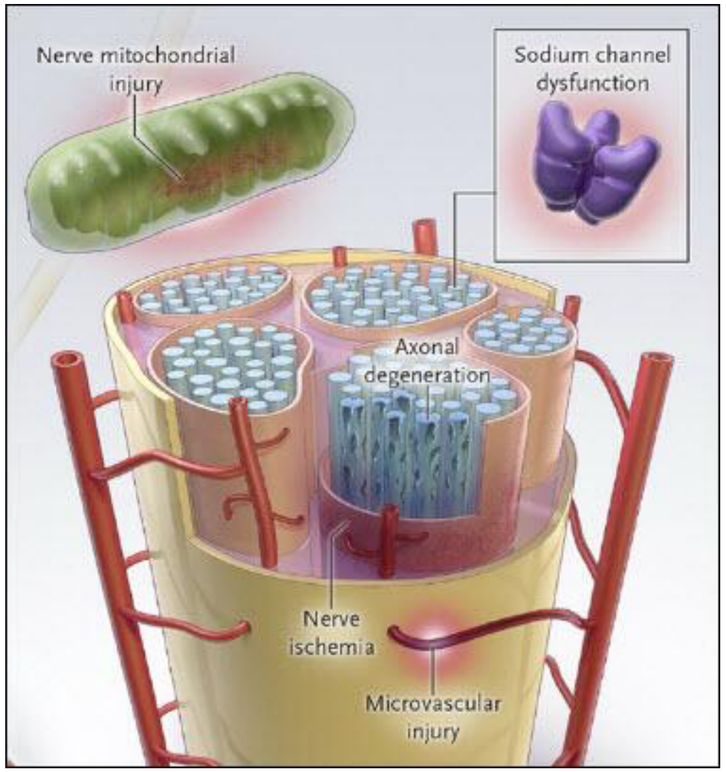
5 years after ARDS ICU treatment: ICU acquired weakness persists for years…..



Herridge MS et al NEJM 2011

Long-term consequences of ICU treatment

1. Loss of body weight
2. Loss of muscle mass
3. Loss of muscle quality
4. Loss of muscle function
5. Fat infiltration in muscles
6. VO_2 max reduced
7. Altered lactate threshold
8. Altered mitochondrial function
9. Reduced fat oxidation capacity
10. Lower age-matched survival



What is wrong with the mitochondria?

Jiroutková *et al. Critical Care* (2015) 19:448
DOI 10.1186/s13054-015-1160-x

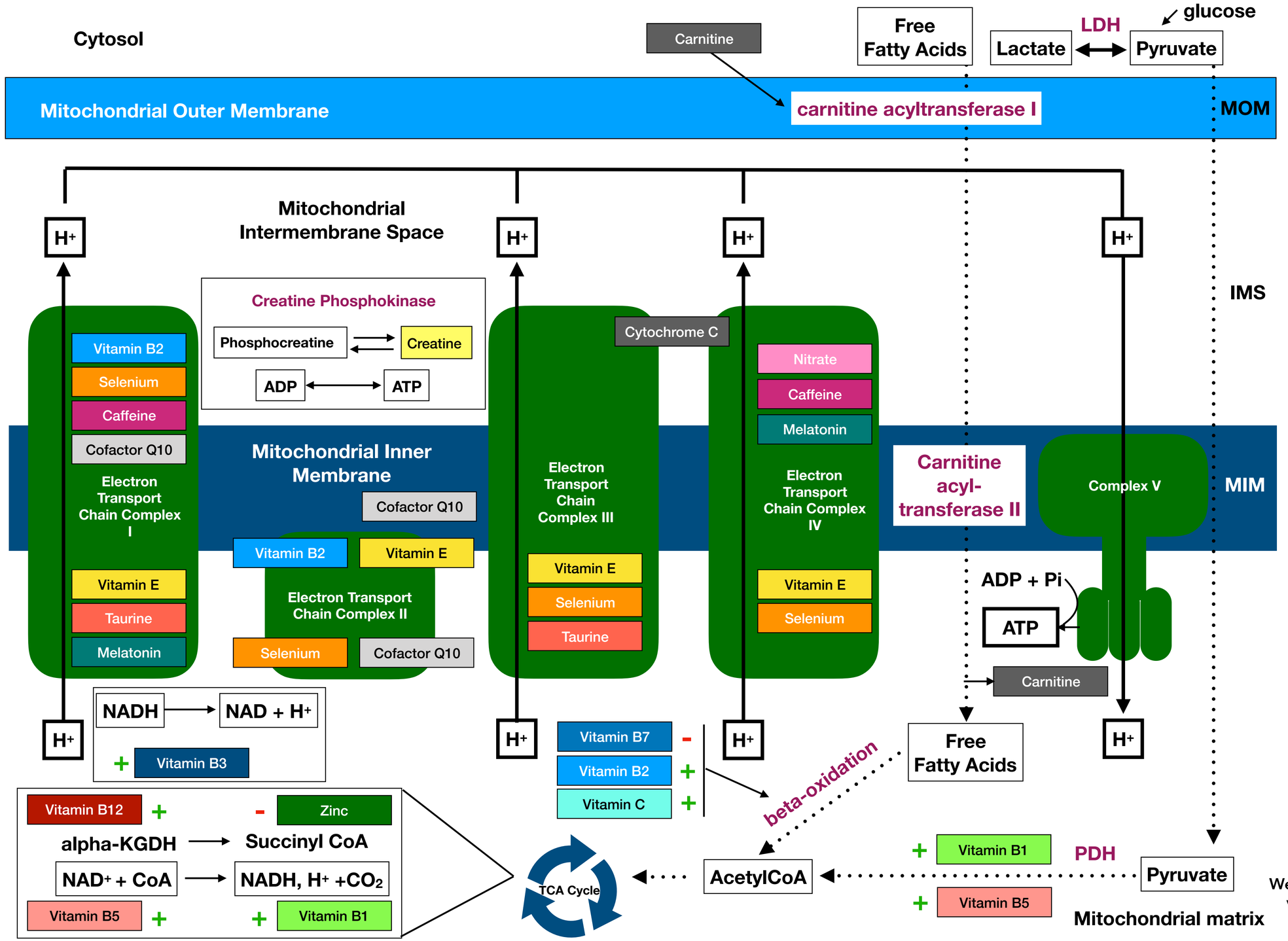
Critical Care

RESEARCH Open Access

Mitochondrial function in skeletal muscle of patients with protracted critical illness and ICU-acquired weakness

Kateřina Jiroutková[1*], Adéla Krajčová[1,2], Jakub Ziak[1], Michal Fric[4], Petr Waldauf[4], Valér Džupa[3], Jan Gojda[2], Vlasta Němcova-Fürstová[5], Jan Kovář[5], Moustafa Elkalaf[1], Jan Trnka[1] and František Duška[1,6]

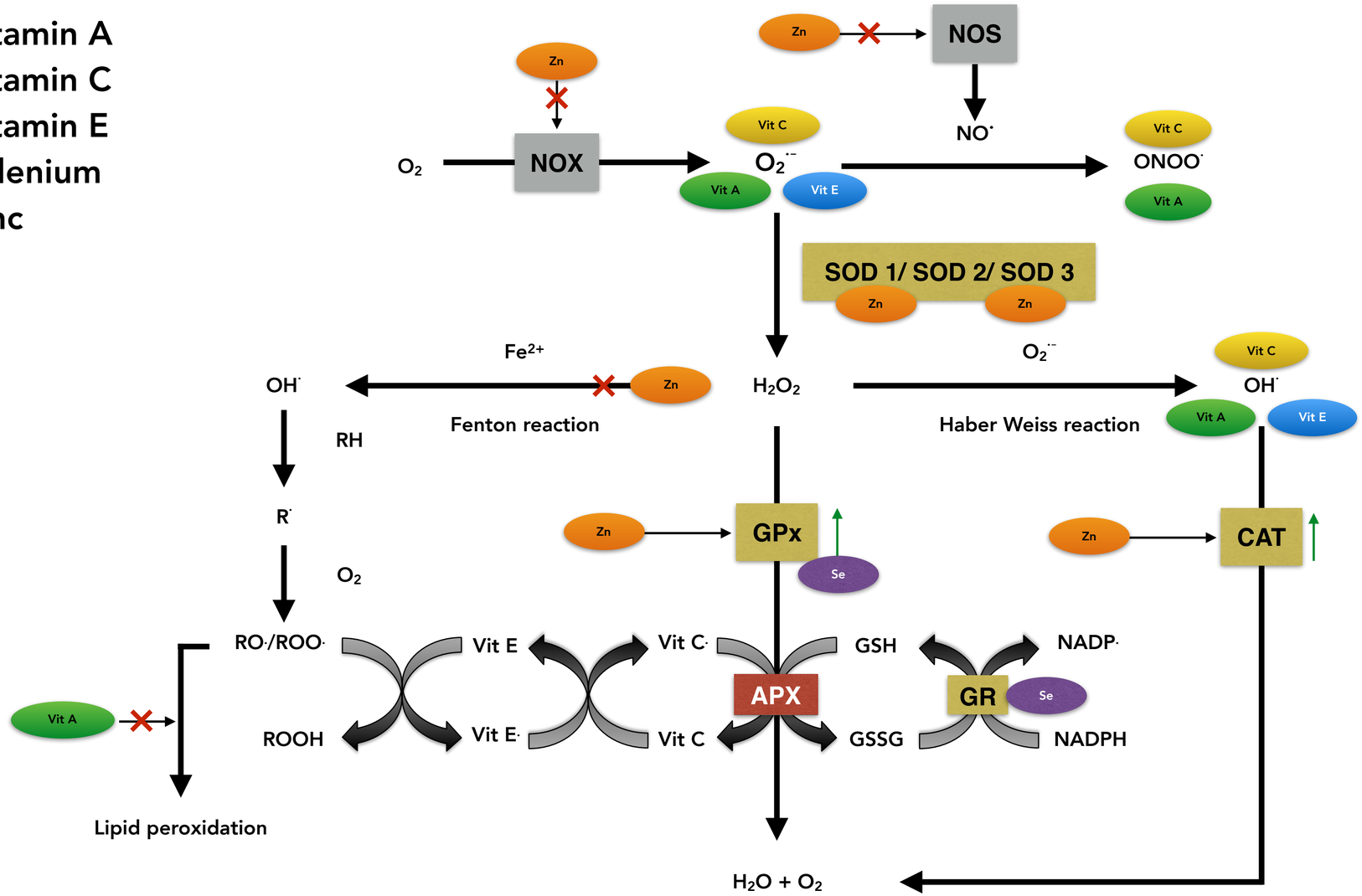
- **Compared to healthy controls, in ICU patients this group demonstrated a ~50 % reduction of the ability of skeletal muscle to synthetize ATP in mitochondria and found a depletion of complex III and IV concentrations**



Wesselink E, Koekkoek K, ... Van Zanten AR, submitted for publication

Antioxidant Network: Vitamins and trace elements

- Vit A — Vitamin A
- Vit C — Vitamin C
- Vit E — Vitamin E
- Se — Selenium
- Zn — Zinc



Koekkoek WA, van Zanten AR. Nutr Clin Pract. 2016;31(4):457-74.

Food for mitochondria: potential candidates

Mitochondrial function	Tricarboxylic acid (TCA) cycle	Boost the electron transport chain function	Boost the electron transport chain function	Mitochondrial biogenesis
• B vitamins • ascorbic acid • α-tocopherol • Selenium • Zinc • Coenzyme Q10 • Caffeine • Melatonin • Carnitine • Nitrate • Lipoic acid • Taurine • Resveratrol	• Vitamin B1 • Vitamin B5 • Vitamin B12 • Lipoic acid • Zinc	• Vitamin B1 • selenium • α-tocopherol • Coenzyme Q10 • Caffeine • Melatonin	• Carnitine	• Resveratrol • Selenium

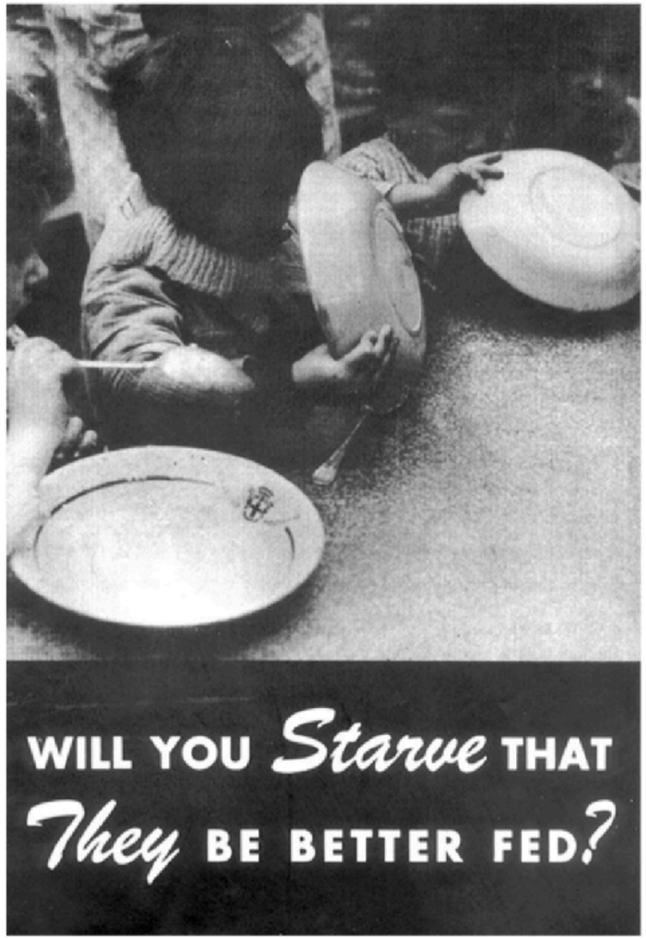
Wesselink E, Koekkoek K, …Van Zanten AR, submitted for publication

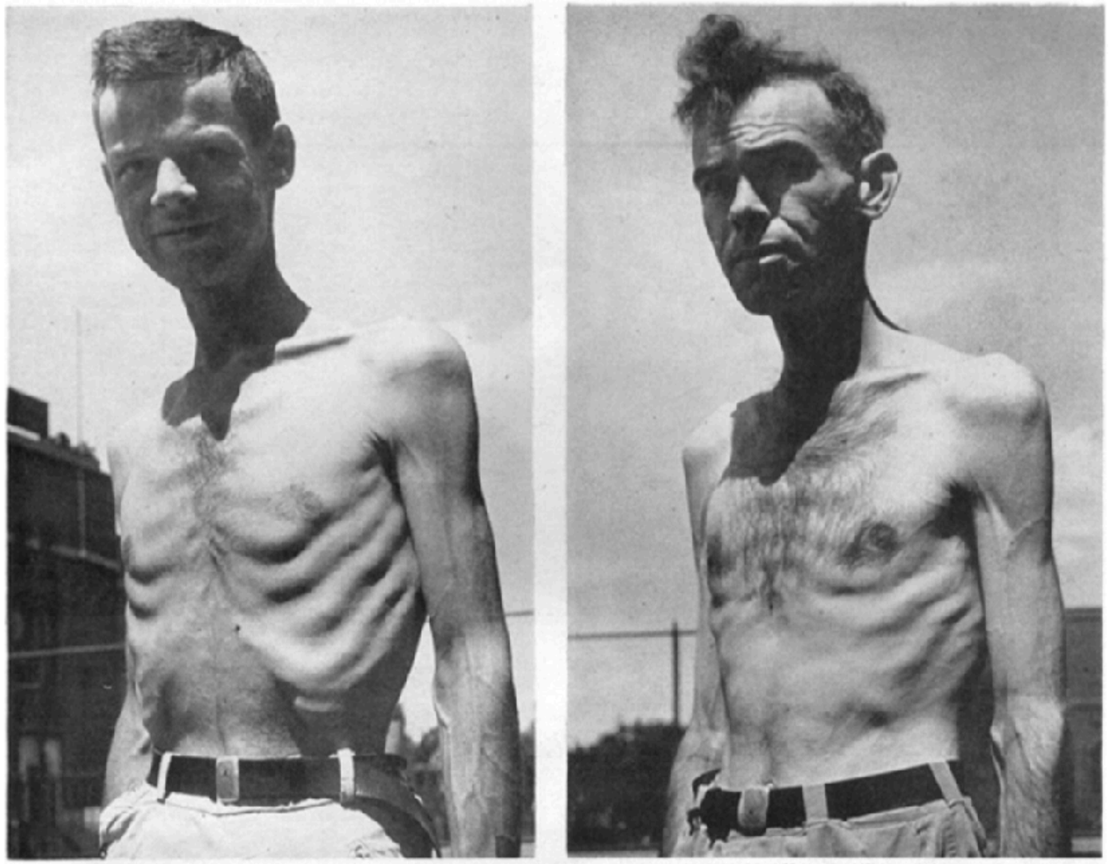
Prevention of Protein & Energy deficit essential for (functional) outcomes

Ziekenhuis Gelderse Vallei

Average ICU intake (not in Ede):	Should be (80 kg pat):
1000 kcal/day	2000 kcal/day
0.7 g proteins/kg per day	1.5 g proteins/kg per day

Tailoring nutrition therapy to illness and recovery





AFTER FIVE MONTHS OF STARVATION DIET CONSCIENTIOUS OBJECTORS SAMUEL LEGG (LEFT) AND EDWARD COWLES HAVE LOST 35 AND 30 POUNDS RESPECTIVELY

MEN STARVE IN MINNESOTA

CONSCIENTIOUS OBJECTORS VOLUNTEER FOR STRICT HUNGER TESTS TO STUDY EUROPE'S FOOD PROBLEM

Wischmeyer Critical Care 2017, 21(Suppl 3):316

Tailoring nutrition therapy to illness and recovery

Table 1 Summary of caloric needs of critically ill and healthy individuals in the context of the Minnesota Starvation Study and actual current ICU calorie delivery

		TEE/weight (kcal/kg/day)
Uehara et al., ICU study [12]		
Sepsis patients (mean age 67)		
Week 1		25 ± 5
Week 2		47 ± 6
Trauma patients (mean age 34)		
Week 1		31 ± 6
Week 2		59 ± 7
WHO calorie requirements, healthy subjects[a]		
Men		44 (range 35–53)
Women		36 (range 29–44)
Minnesota Starvation Study calorie delivery	Delivered energy (kcal/day)	Delivered energy/weight (kcal/kg/day)
Baseline period	3200	~ 50
Starvation period	~ 1800	23–30
Recovery period delivery (for recovery to occur)	~ 4000	~ 60

Starvation period:

1800 kcal/day

Recovery period:

4000 kcal/day

Actual average 1034 kcal/day delivered in critically ill patients over first 12 days of ICU stay [15]
REE resting energy expenditure, *TEE* total energy expenditure, *WHO* World Health Organization
[a]Data for a healthy 70-kg person with intermediate physical activity (1.75 physical activity level factor).
Reference: http://www.fao.org/docrep/007/y5686e/y5686e00.htm#Contents

Wischmeyer Critical Care 2017, 21(Suppl 3):316

What formula?

Equation	Bias (all)	Accuracy (all)	Accuracy among subgroups by age and body mass index			
			Younger nonobese	Younger obese	Older nonobese	Older obese
ACCP	213 to 386	35	44	34	50	12
ACCP (MAW)	−162 to −62	46	44	47	50	43
HBE	−323 to −223	34	31	45	27	35
HBE x 1.25	102 to 216	46	50	45	56	33
Faisy	72 to 149	53	65	72	37	39
Penn State	−43 to −29	67	69	70	77	53
Penn State modified	−87 to −4	–	–	–	–	74

Penn State or modified Penn State if >60 recommended by experts*

Patient Population	Predictive Equation
PSU equation for patients ≤60 years old	RMR (kcal/d) = MSJ(0.96) + Tmax(167) + VE(31) – 6212
PSU equation for patients >60 years old	RMR (kcal/d) = MSJ(0.71) + Tmax(85) + VE(64) – 3085
MSJ equation for men	RMR = 5 + (10 × Weight[kg]) + (6.25 × Height[cm]) – (5 × Age[y])
MSJ equation for women	RMR = –161 + (10 × Weight[kg]) + (6.25 × Height[cm]) – (5 × Age[y])

MSJ, Mifflin–St Jeor; PSU, Penn State University; RMR, resting metabolic rate; Tmax, maximum temperature in the past 24 hours; VE, minute ventilation (L/min).

Curr Opin Crit Care 2012, 18:174–177

*Choban JPEN 2013

What makes Penn State University equation superior?

Patient Population	Predictive Equation
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MSJ, Mifflin–St Jeor; PSU, Penn State University; RMR, resting metabolic rate; Tmax, maximum temperature in the past 24 hours; VE, minute ventilation (L/min).

$\dot{V}E$ = minute volume (in L/min)

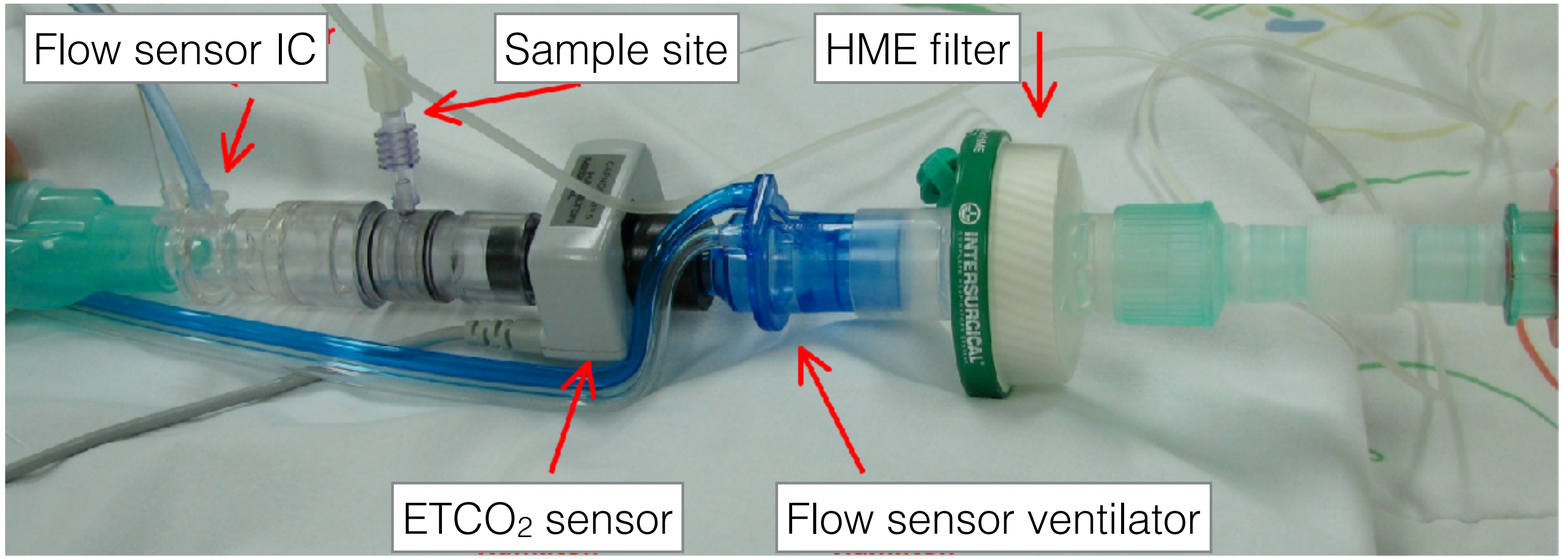
Penn State or modified Penn State if >60 recommended by experts*

MINUTE VOLUME IS A REFLECTION OF THE CO_2 PRODUCTION

Curr Opin Crit Care 2012, 18:174–177

*Choban JPEN 2013

Indirect Calorimetry



$$REE\ (kcal/\ min) = 3.9 * VO_2\ (l\ /\ min) + 1.1 * VCO_2\ (l/\ min)$$

$$\downarrow\ *1440$$

Energy Expenditure per 24 hours

DREAM-VCO_2 Study

- Indirect Calorimetry

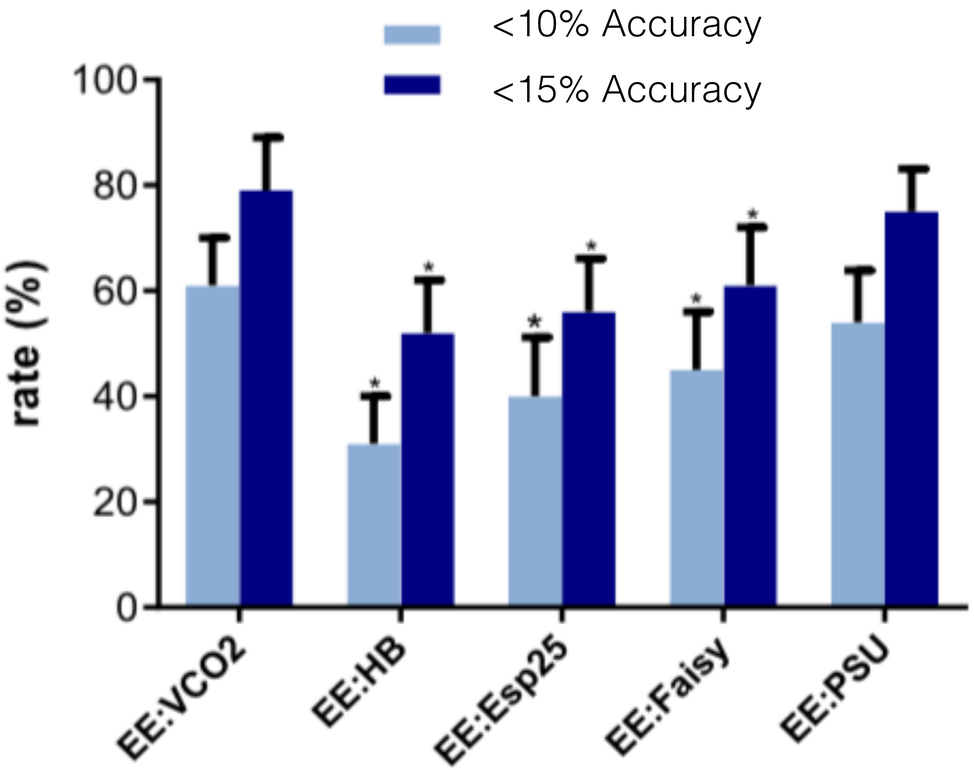
Direct R

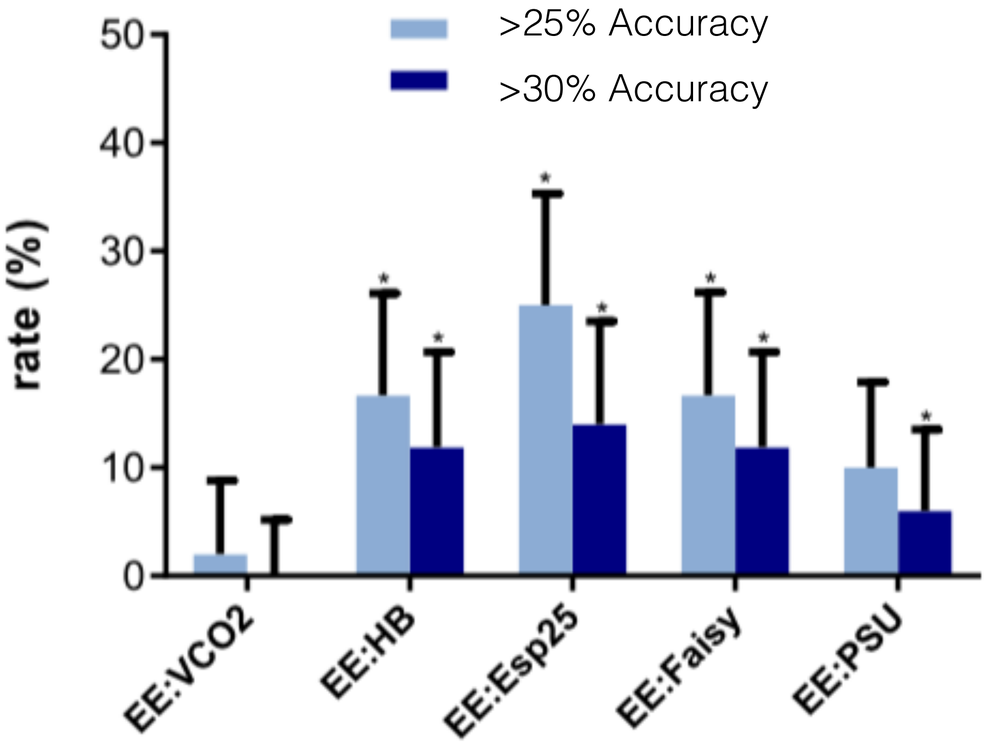
Cohort S

Metabolic Cart Compa

Ventilator VCO_2 to predict Energy Expenditure

EE= VCO_2 * 8,19 in kcal/24 h



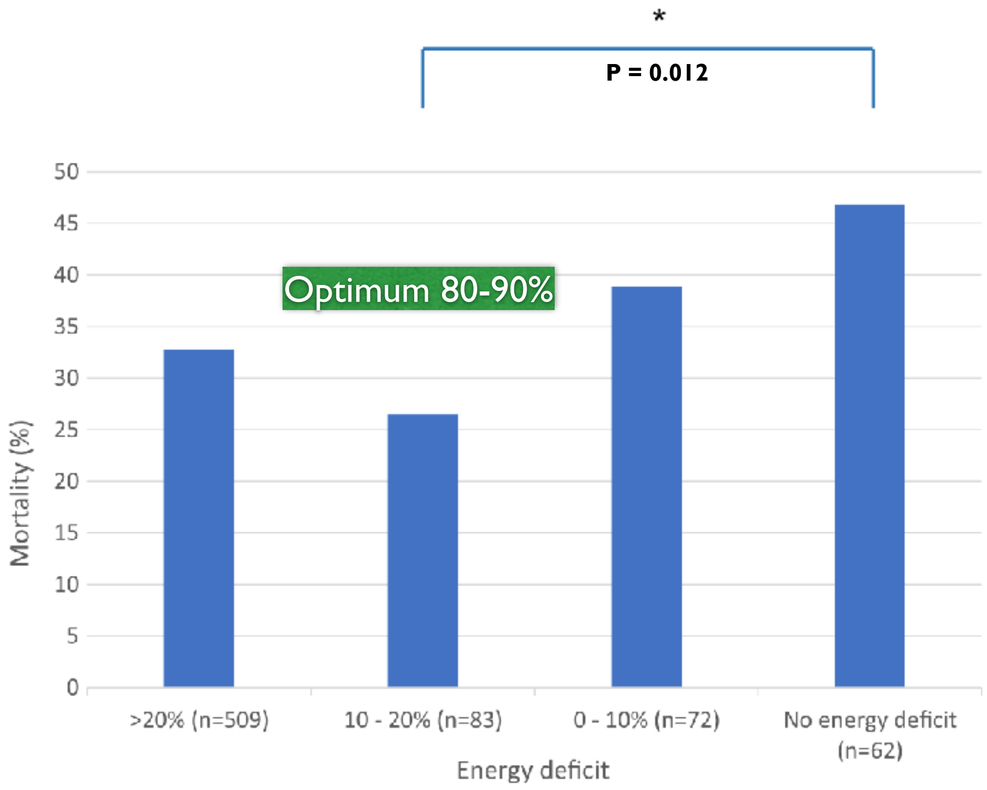


EE:Esp25, Energy expenditure calculated with the European Society for Clinical Nutrition and Metabolism guideline equation of 25 kcal/kg/day; EE:Faisy, Energy expenditure calculated with the Faisy equation; EE:HB, Energy expenditure calculated with the Harris–Benedict equation; EE:PSU, Energy expenditure calculated with the Penn State University 2003b equation; EE:VCO2, Energy expenditure from ventilator-derived volume of carbon dioxide and nutritional respiratory quotient

Stapel et al. Critical Care (2015) 19:370

Hospital mortality and cumulative energy deficit in ICU patients

during first 4 days of ICU stay for 726 non-septic ICU patients



Reference is the measured resting energy expenditure of the patient

During EN with 100% target, target achieved is typically 80-85% due to feeding interruptions

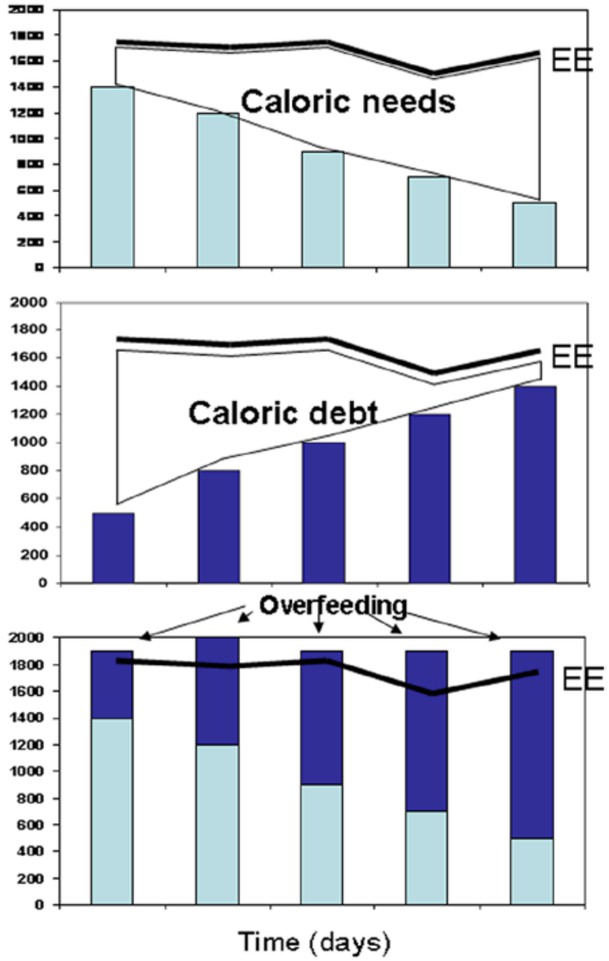
Weijs P. Crit Care 2014;18:701

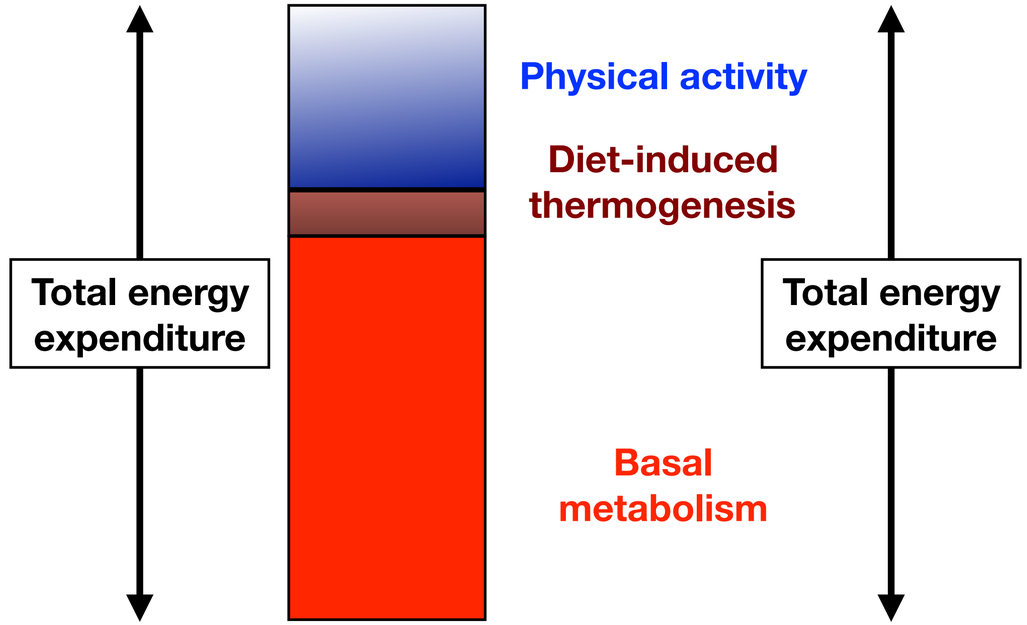
Consequences of early non-inhibitable endogenous energy production and overfeeding risk in critical illness

endogenous production

nutritional intake

total intake





Fraipont V, Preiser JC. JPEN J Parenter Enteral Nutr. 2013;37(6):705-13.

Conflicting results Early SPN

- **Epanic: Early PN negative effects on ICU discharge survival (no long-term survival difference) & duration of organ failure**
- **SPN trial: no differences, effect on infections questionable**
- **Anzics trial: No major outcome differences, shorter duration of MV 0.4 day and QOL significant but not relevant, 95% of patients tolerate EN within 4.1 days**

Bost *et al. Annals of Intensive Care* 2014, **4**:31
http://www.annalsofintensivecare.com/content/4/1/31

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Timing of (supplemental) parenteral nutrition in critically ill patients: a systematic review

Rianne BC Bost[1], Dave HT Tjan[1] and Arthur RH van Zanten[1,2*]

In adult ICU patients, when full EN support is not possible or fails to reach caloric targets, early administration of SPN compared with late administration (at the end of the first week after ICU admission) does not confer major benefits with respect to morbidity and mortality.

Considering that infectious morbidity and resolution of organ failure may be negatively affected through mechanisms not yet clearly understood, and acquisition costs of PN are higher compared with EN, the early administration of PN cannot be recommended.

Recent meta-analysis EN vs PN

Elke *et al. Critical Care* (2016) 20:117
DOI 10.1186/s13054-016-1298-1

Critical Care

RESEARCH Open Access

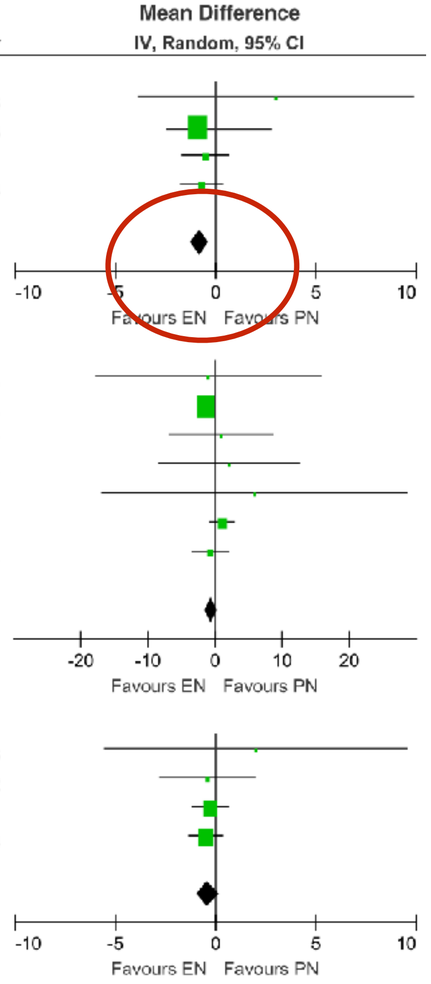
Enteral versus parenteral nutrition in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials

Gunnar Elke[1], Arthur R. H. van Zanten[2], Margot Lemieux[3], Michele McCall[4], Khursheed N. Jeejeebhoy[5], Matthias Kott[1], Xuran Jiang[3], Andrew G. Day[3] and Daren K. Heyland[3*]

Elke G, Van Zanten AR et al. Crit Care 2016;20:117

EN versus PN: LOS, duration ventilation

Study or Subgroup	EN Mean	EN SD	EN Total	PN Mean	PN SD	PN Total	Weight	Mean Difference IV, Random, 95% CI	Year
ICU LOS									
Adams	13	11	19	10	10	17	0.4%	3.00 [-3.86, 9.86]	1986
Peterson	3.7	0.8	21	4.6	1	25	68.6%	-0.90 [-1.42, -0.38]	1988
Chen	9.09	2.75	49	9.6	3.06	49	14.0%	-0.51 [-1.66, 0.64]	2011
Harvey	11.3	12.5	1197	12	13.5	1190	17.0%	-0.70 [-1.74, 0.34]	2014
Total (95% CI)	26.8		**1286**			**1281**	**100.0%**	**-0.80 [-1.23, -0.37]**	
Heterogeneity: Tau² = 0.00; Chi² = 1.60, df = 3 (P = 0.66); I² = 0%									
Test for overall effect: Z = 3.62 (P = 0.0003)									
Hospital LOS									
Adams	30	21	19	31	29	17	0.3%	-1.00 [-17.71, 15.71]	1986
Peterson	13.2	1.6	21	14.6	1.9	21	62.8%	-1.40 [-2.46, -0.34]	1988
Kudsk	20.5	19.9	51	19.6	18.8	45	1.4%	0.90 [-6.85, 8.65]	1992
Borzotta	39	23.1	28	36.9	14	21	0.8%	2.10 [-8.34, 12.54]	1994
Woodcock	33.2	43	16	27.3	18.7	18	0.2%	5.90 [-16.87, 28.67]	2001
Chen	23.32	5.6	49	22.24	3.27	49	23.6%	1.08 [-0.74, 2.90]	2011
Harvey	26.8	33.2	1186	27.5	33.9	1185	11.0%	-0.70 [-3.40, 2.00]	2014
Total (95% CI)			**1370**			**1356**	**100.0%**	**-0.67 [-1.57, 0.24]**	
Heterogeneity: Tau² = 0.05; Chi² = 6.12, df = 6 (P = 0.41); I² = 2%									
Test for overall effect: Z = 1.44 (P = 0.15)									
Mechanical ventilation									
Adams	12	11	17	10	10	13	0.6%	2.00 [-5.54, 9.54]	1986
Kudsk	2.8	4.9	51	3.2	6.7	45	6.2%	-0.40 [-2.77, 1.97]	1992
Chen	7.95	2.11	49	8.23	2.42	49	43.4%	-0.28 [-1.18, 0.62]	2011
Harvey	8.2	9.3	1197	8.7	11.5	1189	49.8%	-0.50 [-1.34, 0.34]	2014
Total (95% CI)			**1314**			**1296**	**100.0%**	**-0.38 [-0.98, 0.21]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 3 (P = 0.92); I² = 0%									
Test for overall effect: Z = 1.27 (P = 0.21)									



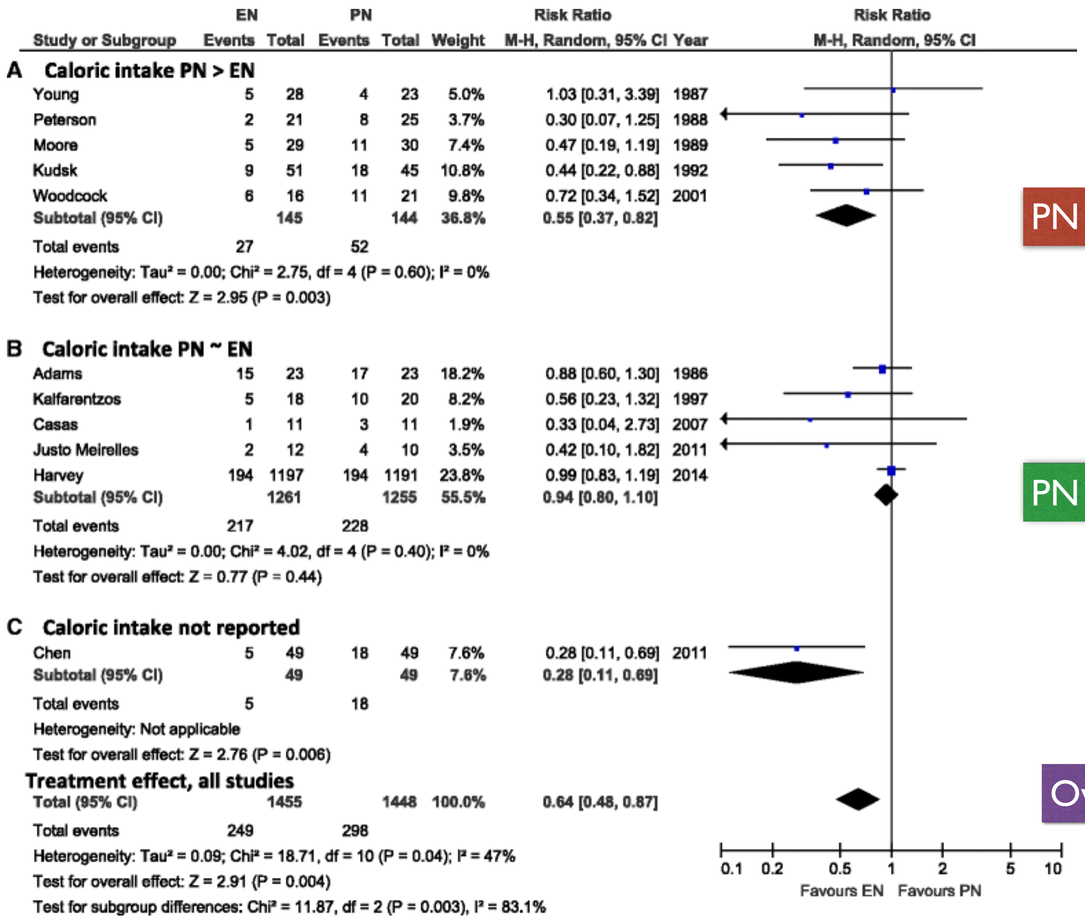
Reduction ICU LOS EN vs PN

No Reduction HLOS EN vs PN

No Reduction Duration Mechanical Ventilation

Elke G, Van Zanten AR et al. Crit Care 2016;20:117

Enteral versus parenteral nutrition in critically ill patients: and updated systematic review and meta-analysis of randomized controlled trials



PN caloric intake > EN caloric intake

PN caloric intake = EN caloric intake

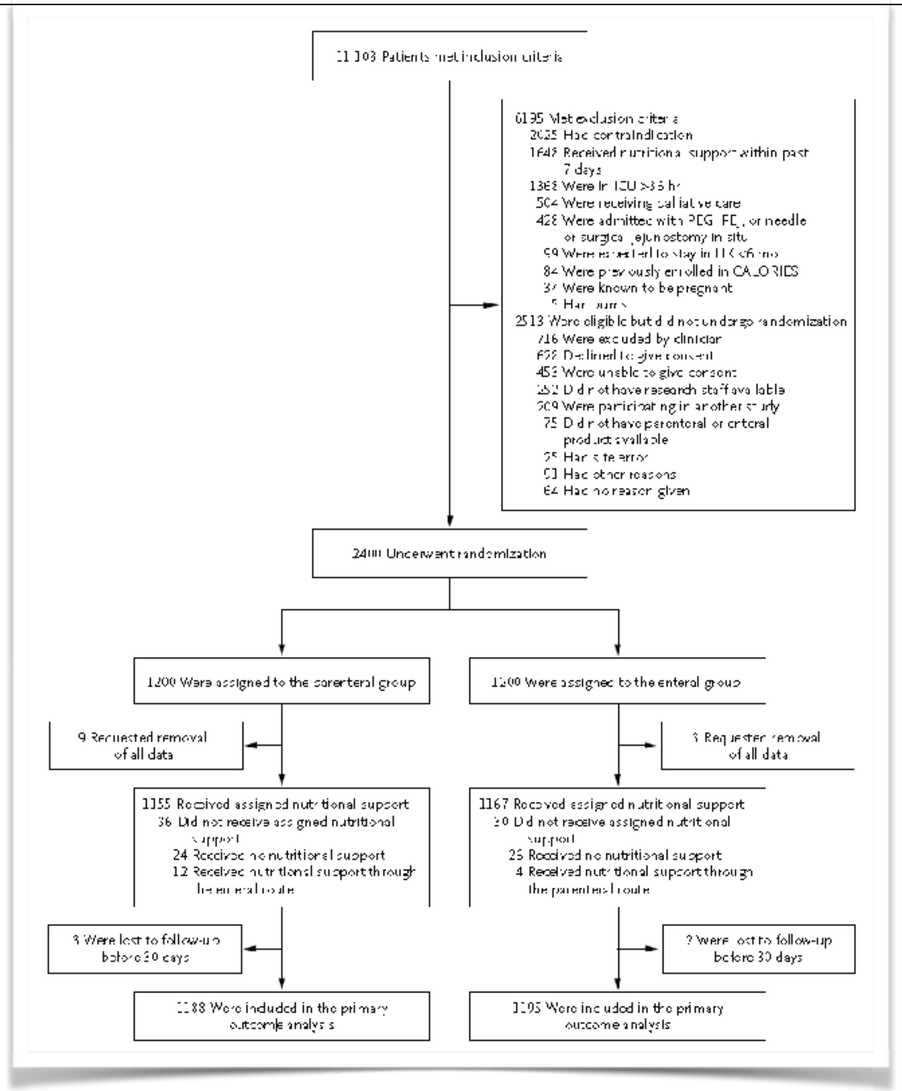
Overall EN less infections than PN

Only more infections in PN trials when caloric dose in PN group is higher

Elke G, Van Zanten AR… Heyland DK. Crit Care 2016;20:117

Calories trials: to compare EN versus PN, not SPN

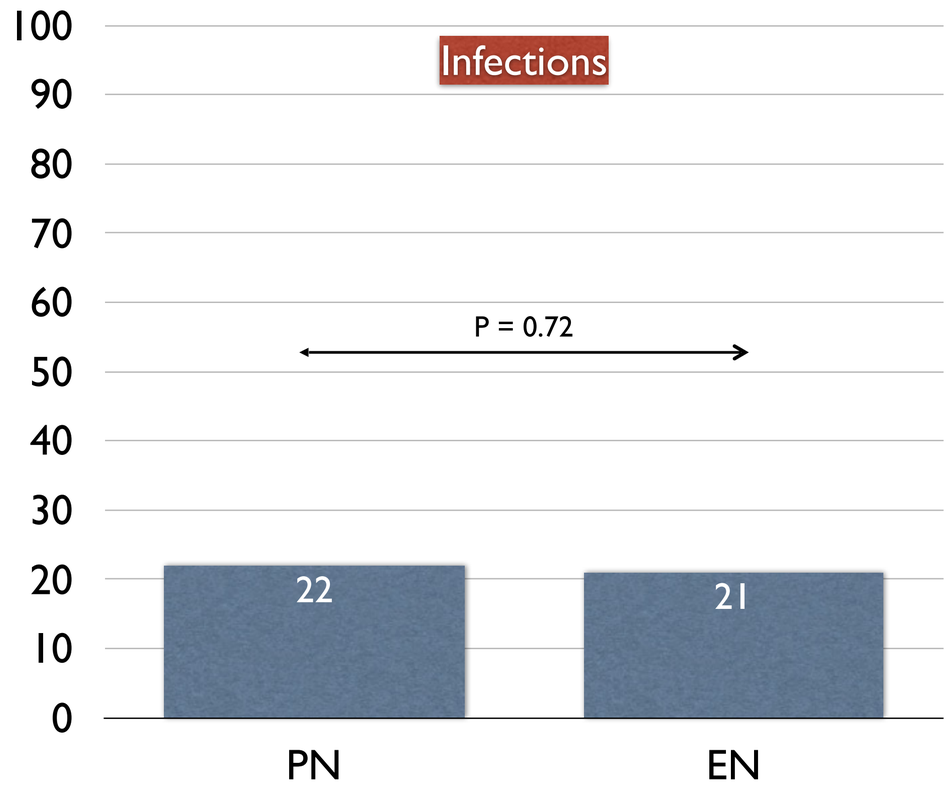
1200 PN

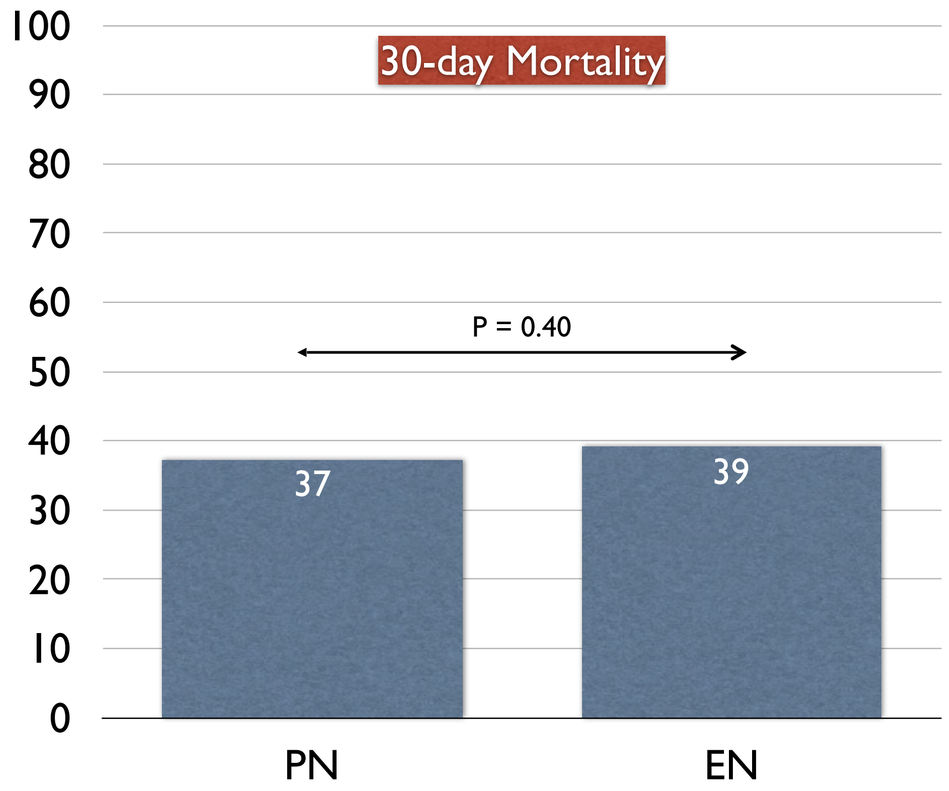


1200 EN

Harvey SE et al. NEJM 2014

Calories trial: mortality and infections

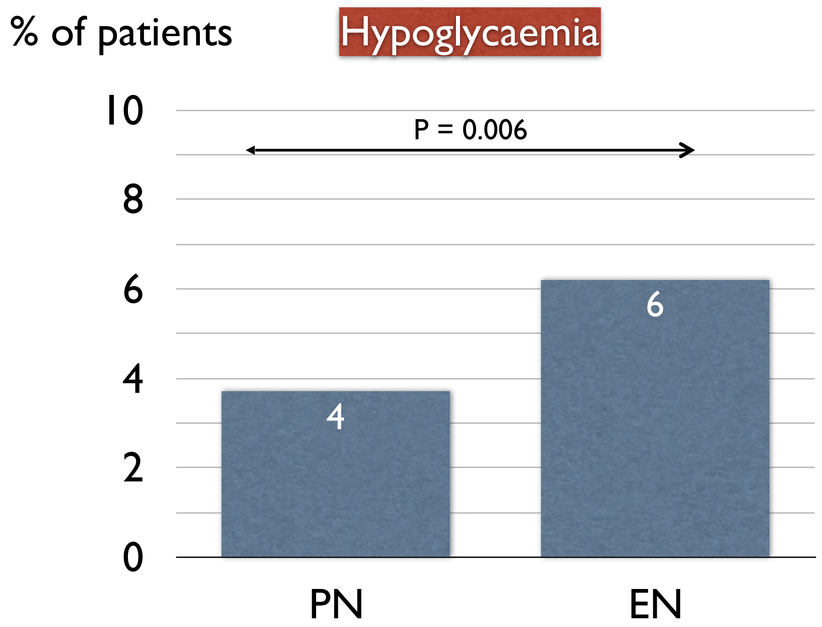


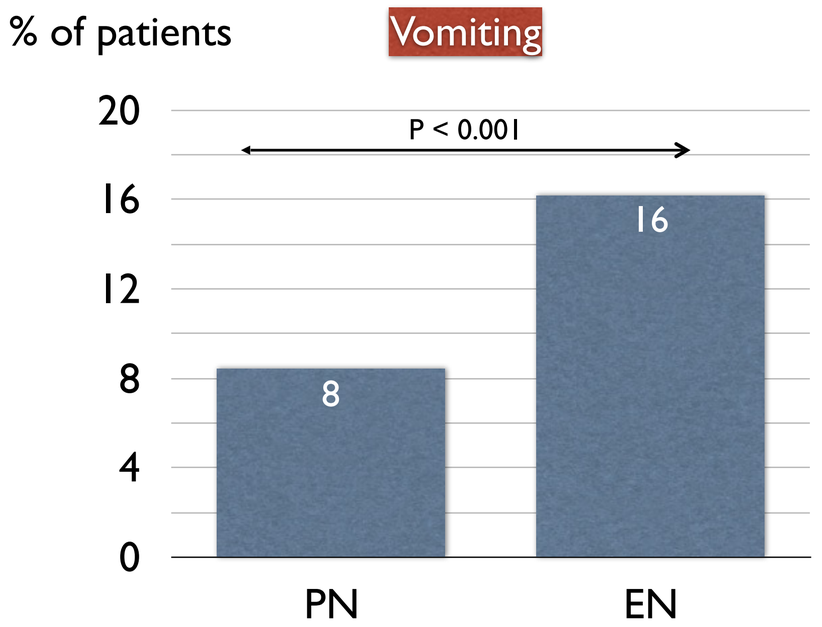


No differences in mean number of treated infectious complications (0.22 vs. 0.21; P = 0.72), 90-day mortality (442/1184 pts [37.3%] vs. 464/1188 pts [39.1%], P = 0.40), and 14 other secondary outcomes, or in rates of adverse events.

Harvey SE et al. NEJM 2014

Calories trial: EEN vs EPN

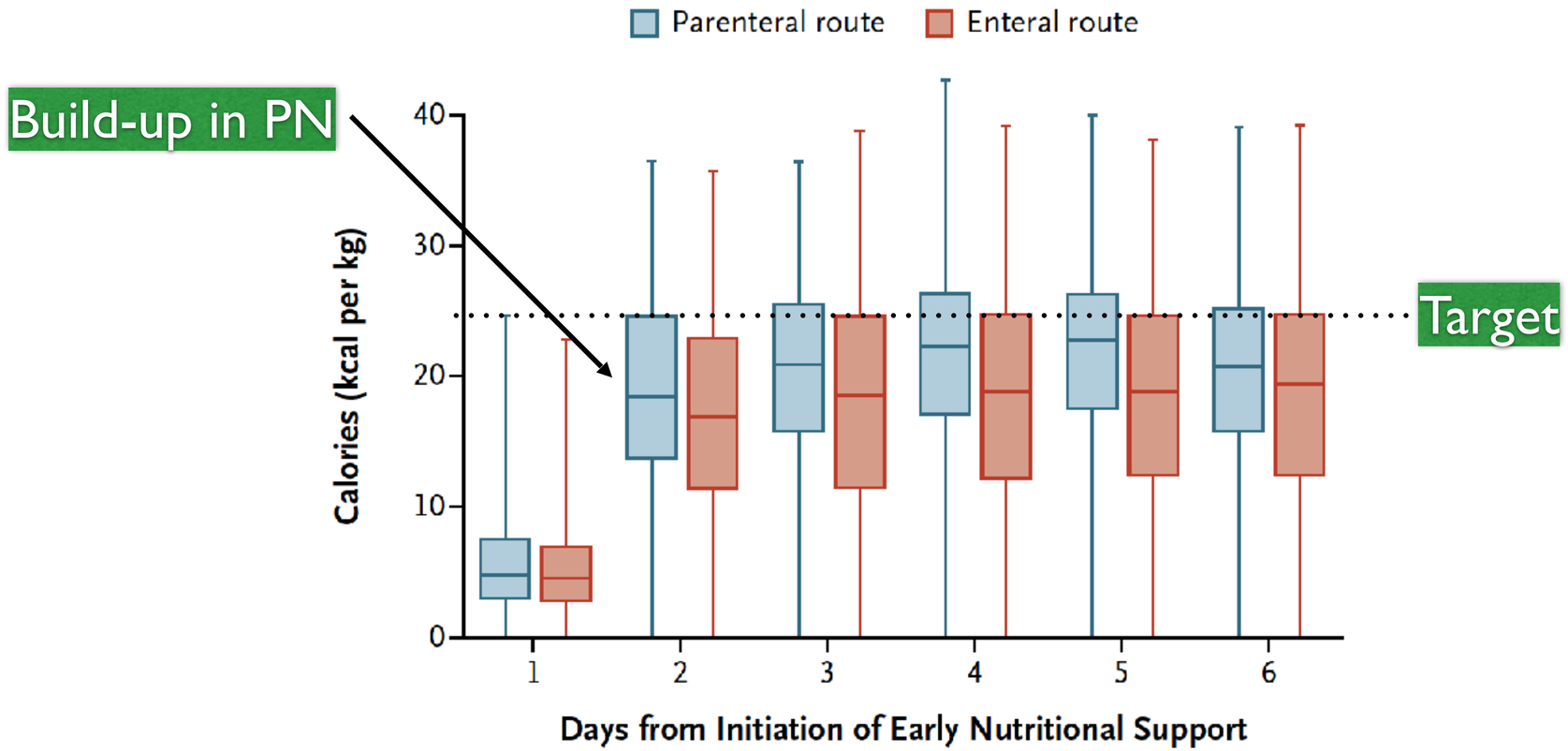




No differences in 14 other secondary outcomes, or in rates of adverse events

Harvey SE et al. NEJM 2014

Unexpected build-up in PN



PN vs. EN total protein intake 3 vs. 3 g/kg, NS
PN vs. EN total energy intake 89 vs. 74 kcal/kg, NS

Harvey SE et al. NEJM 2014

Enteral vs Parenteral nutrition in ventilated shock patients: NUTRIREA-2

	Enteral group (n=1202)	Parenteral group (n=1208)	Absolute difference estimate (95% CI)	Hazard ratio (95% CI)	p value
Primary outcome					
Day 28 mortality	443/1202 (37%)	422/1208 (35%)	2·0 (–1·9 to 5·8)	..	0·33
Secondary outcomes					
Day 90 mortality	530/1185 (45%)	507/1192 (43%)	2·2 (–1·8 to 6·2)	..	0·28
ICU mortality*	429 (33%)	405 (31%)	..	1·10 (0·96 to 1·26)	0·17
Hospital mortality*	498 (36%)	479 (34%)	..	1·08 (0·95 to 1·22)	0·25
ICU length of stay (days)	9·0 (5·0 to 16·0)	10·0 (5·0 to 17·0)	..	..	0·08
Acute-care hospital length of stay (days)	17·0 (8·0 to 32·0)	18·0 (9·0 to 33·0)	..	..	0·11
Days without vasopressor support*	20·0 (0·0 to 25·0)	21·0 (0·0 to 26·0)	..	..	0·10
Days without dialysis*	27·0 (0·0 to 28·0)	27·0 (0·0 to 28·0)	..	..	0·52
Days without mechanical ventilation*	11·0 (0·0 to 23·0)	12·0 (0·0 to 23·0)	..	..	0·54
Infections					
ICU-acquired infection*	173 (14%)	194 (16%)	..	0·89 (0·72 to 1·09)	0·25
Ventilator-associated pneumonia*	113 (9%)	118 (10%)	..	0·96 (0·74 to 1·24)	0·75
Bacteraemia*	38 (3%)	55 (5%)	..	0·69 (0·46 to 1·04)	0·08
CVC-related infection*	29 (2%)	27 (2%)	..	1·07 (0·64 to 1·81)	0·79
Urinary tract infection*	18 (2%)	16 (1%)	..	1·13 (0·58 to 2·21)	0·73
Soft-tissue infection					
Patients (n)	1/1202	6/1208	..	..	..
Other infection*	11 (1%)	21 (2%)	..	0·52 (0·25 to 1·09)	0·08
Gastrointestinal complications					
Vomiting*	406 (34%)	246 (24%)	..	1·89 (1·62 to 2·20)	<0·0001
Diarrhoea*	432 (36%)	393 (33%)	..	1·20 (1·05 to 1·37)	0·009
Bowel ischaemia*	19 (2%)	5 (<1%)	..	3·84 (1·43 to 10·3)	0·007
Acute colonic pseudo-obstruction*	11 (1%)	3 (<1%)	..	3·7 (1·03 to 13·2)	0·04

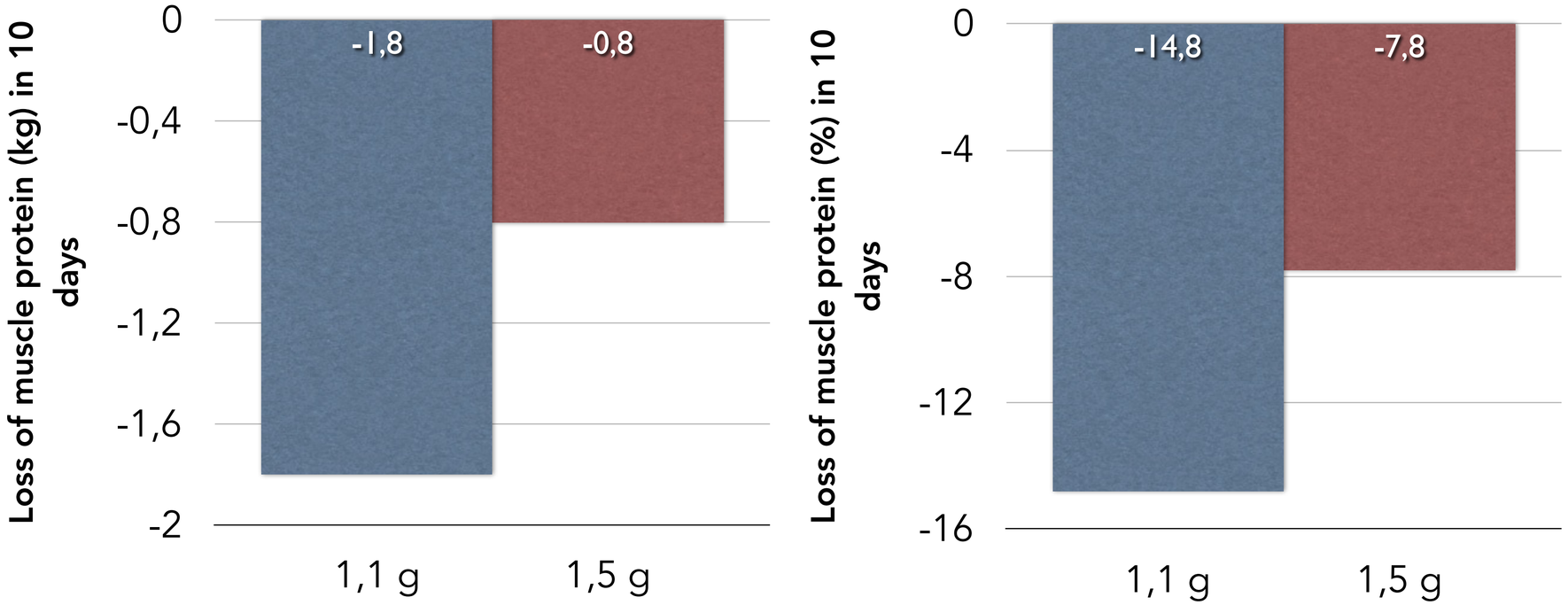
In critically ill adults with shock, early isocaloric enteral nutrition did not reduce mortality or the risk of secondary infections but was associated with a greater risk of digestive complications compared with early isocaloric parenteral nutrition.

Reignier J et al. Lancet Published online November 8, 2017

10 kilograms of muscle mass

Effect of high protein intake on lean body mass (LBM)

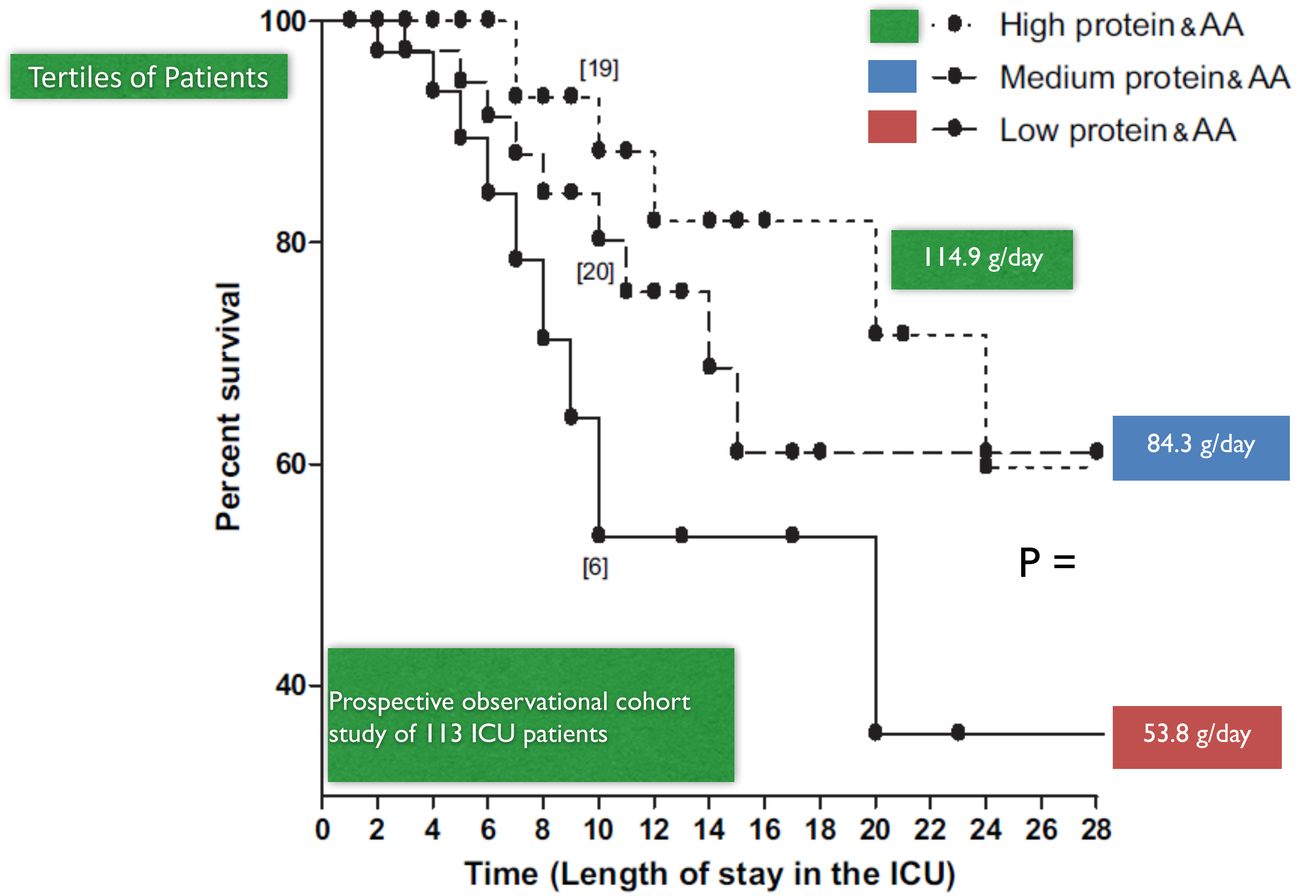
in vivo neutron activation



-1.8 kg of proteins reflects 9 kg of muscle mass

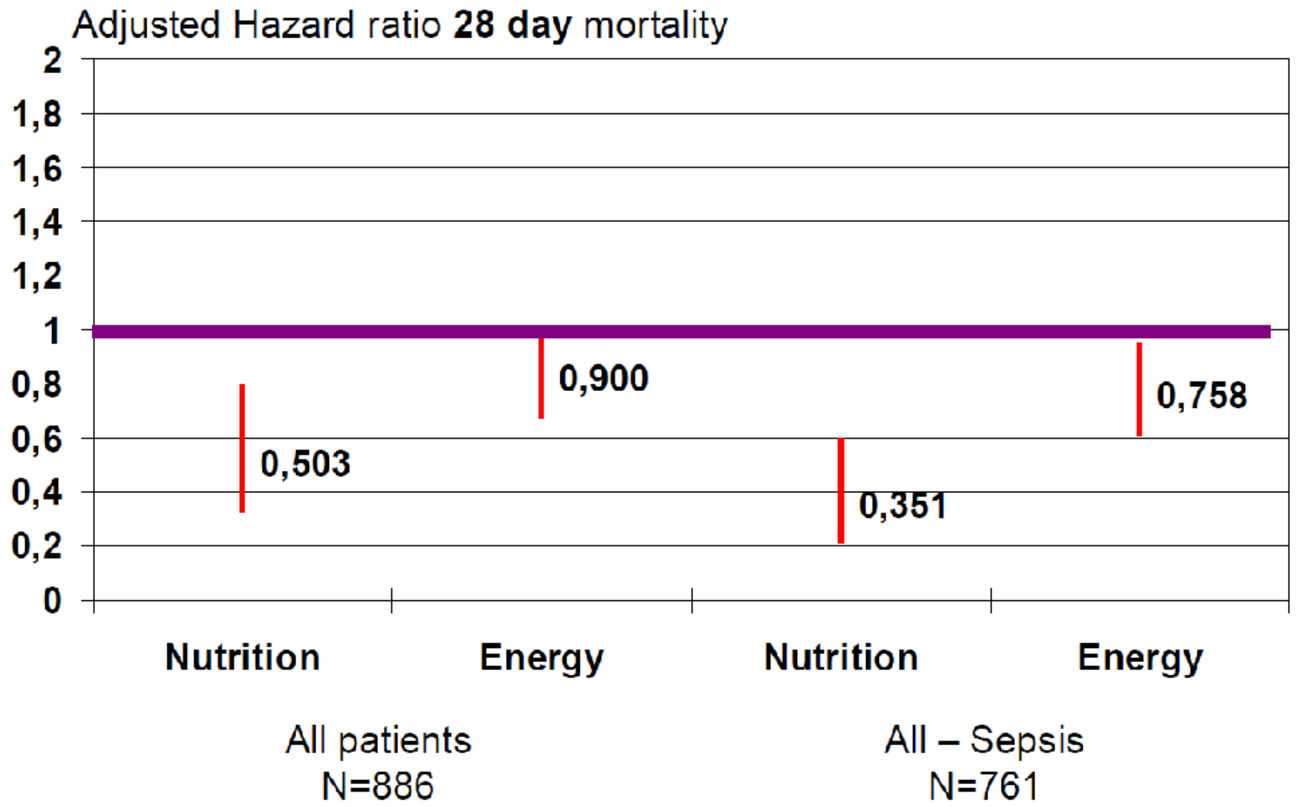
Ishibashi N et al. Crit Care Med 1998

High protein groups better survival



Allingstrup MJ J Clin Nutr 2012; 31:462-468

Reaching both protein and energy target reduces mortality

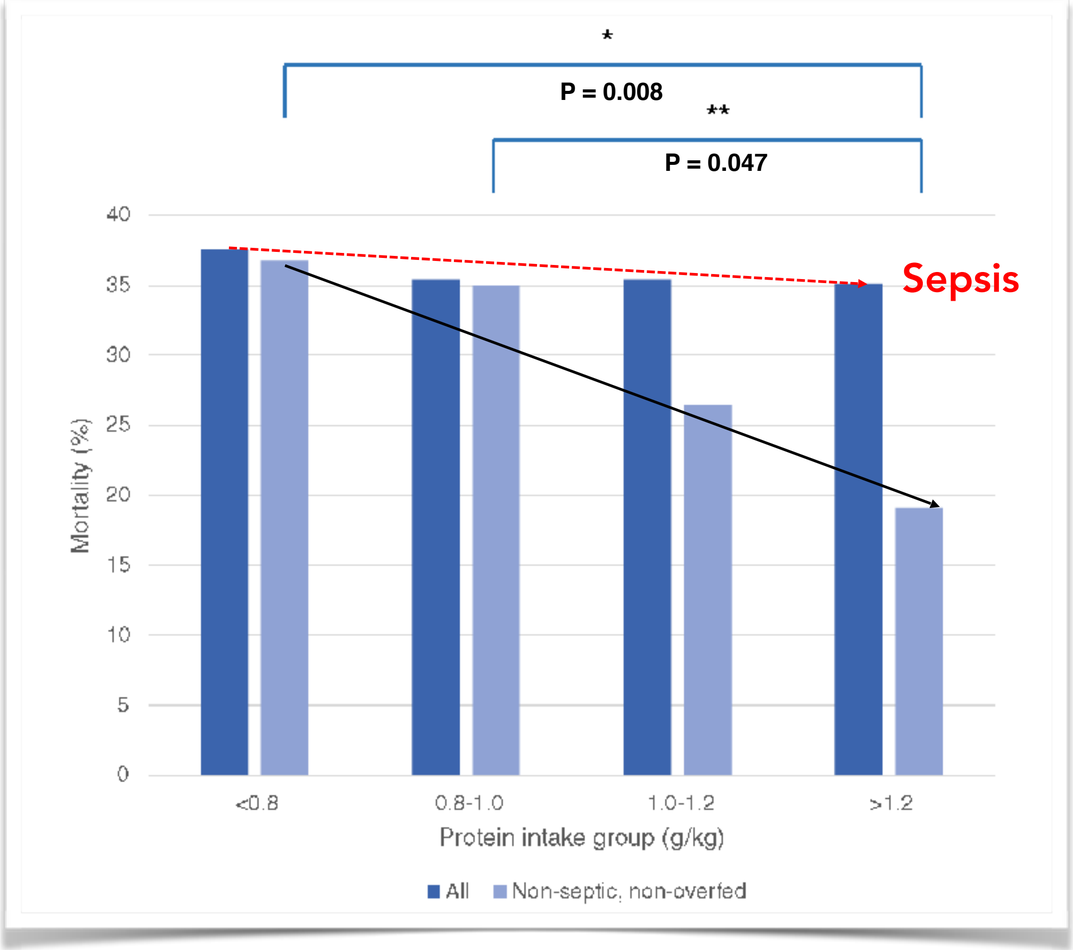


Nutrition target defined as protein and energy targets reached, is associated with a 50% decrease in 28-day mortality, only reaching energy targets is not associated with a reduction in mortality.

Weis P. JPEN. 2012;36:60-68

Hospital mortality per protein intake group

More protein intake is associated with lower in-hospital mortality



0.8 g/kg per day

1.2 g/kg per day

Weijs P. Crit Care 2014;18:701

Calories received in high and low risk patients based on NUTRIC scores and 28-day mortality

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

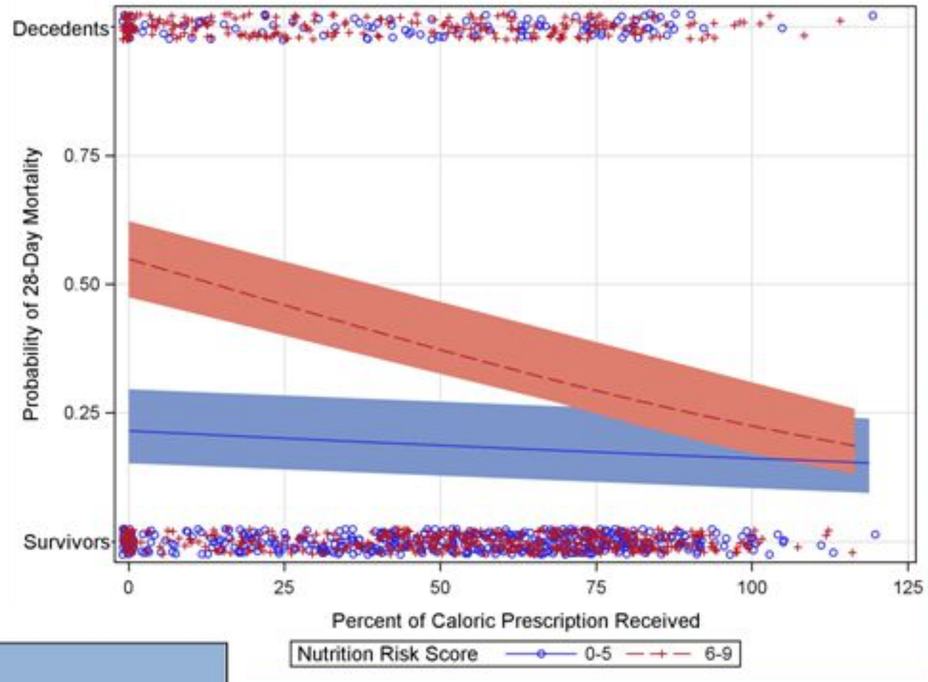


Table 2: NUTRIC Score scoring system: if IL-6 available

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.

Rahman A et al. Clin Nutr. 2016 Feb;35(1):158-62.

SPN in high-risk ICU patients

Wischmeyer *et al. Critical Care* (2017) 21:142
DOI 10.1186/s13054-017-1736-8

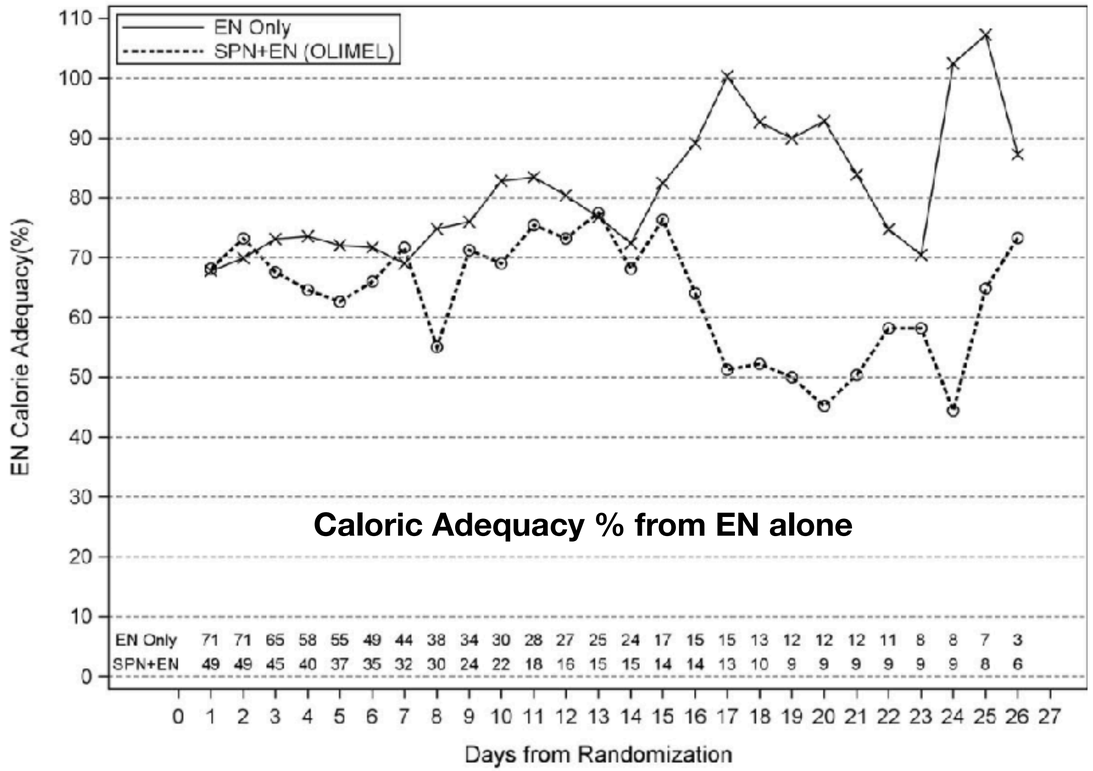
Critical Care

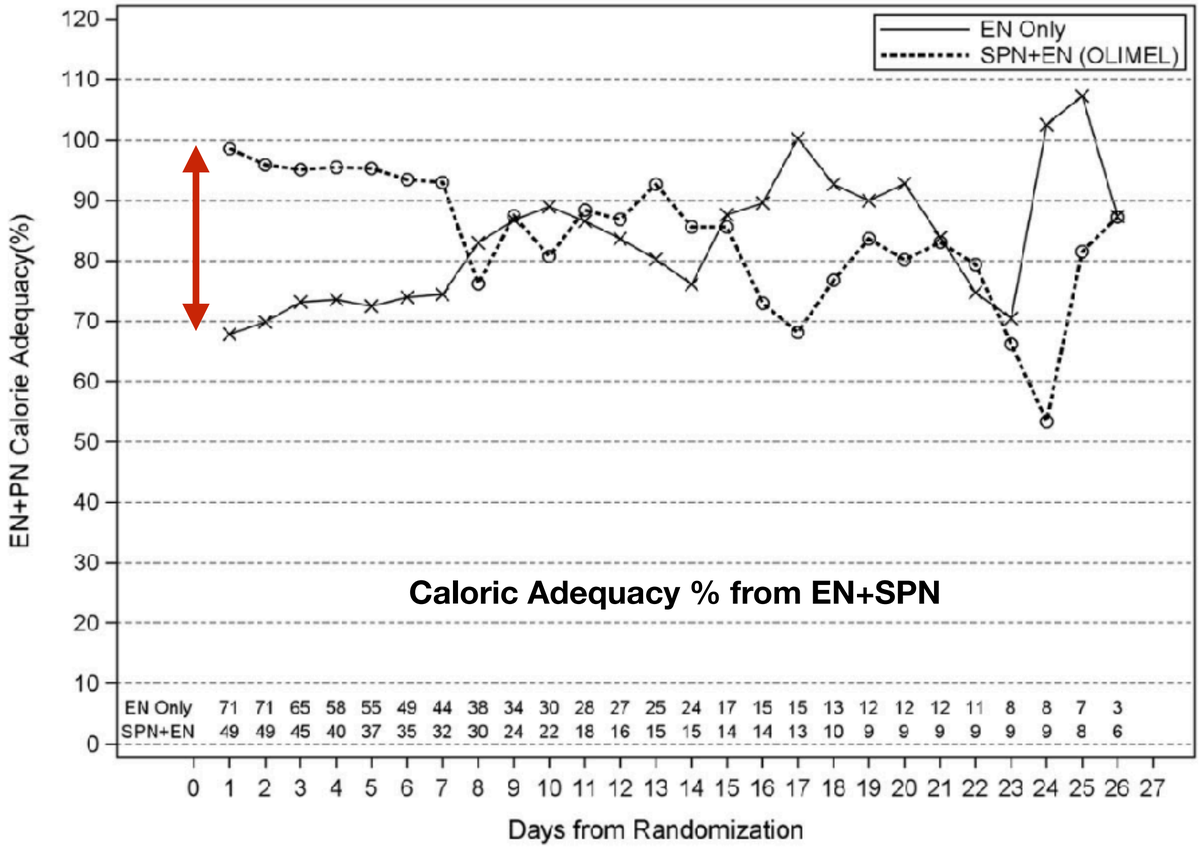
RESEARCH Open Access

A randomized trial of supplemental parenteral nutrition in underweight and overweight critically ill patients: the TOP-UP pilot trial

Paul E. Wischmeyer[1*], Michel Hasselmann[2], Christine Kummerlen[2], Rosemary Kozar[3], Demetrios James Kutsogiannis[4], Constantine J. Karvellas[5], Beth Besecker[6], David K. Evans[7], Jean-Charles Preiser[8], Leah Gramlich[9], Khursheed Jeejeebhoy[10], Rupinder Dhaliwal[11], Xuran Jiang[11], Andrew G. Day[11] and Daren K. Heyland[11,12,13]

TOP-UP pilot trial: 71 versus 49 patients





Difference in calories and proteins during first week

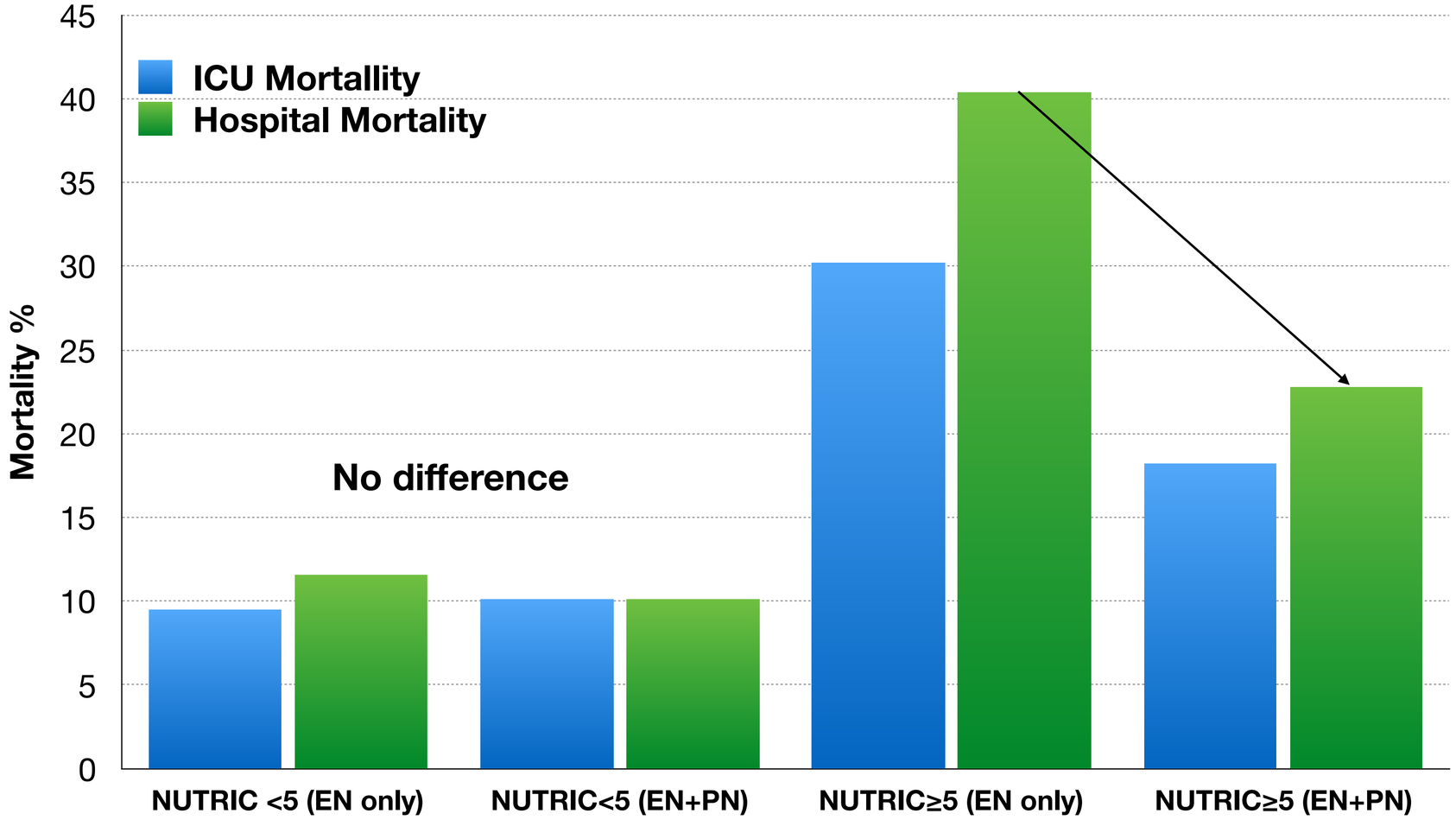
Wischmeyer et al. Critical Care (2017) 21:142

More proteins and calories (20-25%) due to SPN

Calorie prescription	1844 ± 420	1728 ± 444	−116 (−275 to 42)	0.149
Protein prescription	106 ± 30	100 ± 31	−6 (−17 to 6)	0.319
% of prescribed kcal/protein received				
EN only				
Calories first 27 days	70 ± 26	67 ± 25	−3 (−12 to 7)	0.551
Calories first 7 days	68 ± 28	68 ± 27	−1 (−11 to 9)	0.905
Protein first 27 days	66 ± 26	60 ± 23	−5 (−14 to 3)	0.231
Protein in first 7 days	63 ± 26	61 ± 25	−3 (-12 to 7)	0.566
PN + EN				
Calories first 27 days	72 ± 25	90 ± 16	18 (11 to 25)	<0.001
Calories first 7 days	69 ± 28	95 ± 13	26 (18 to 34)	<0.001
Protein first 27 days	68 ± 25	82 ± 19	13 (6 to 21)	<0.001
Protein in first 7 days	64 ± 26	86 ± 16	22 (14 to 29)	<0.001

Wischmeyer et al. Critical Care (2017) 21:142

Effect of SPN
in low and high risk ICU patients according to NUTRIC scores



Wischmeyer et al. Critical Care (2017) 21:142

Effect of SPN
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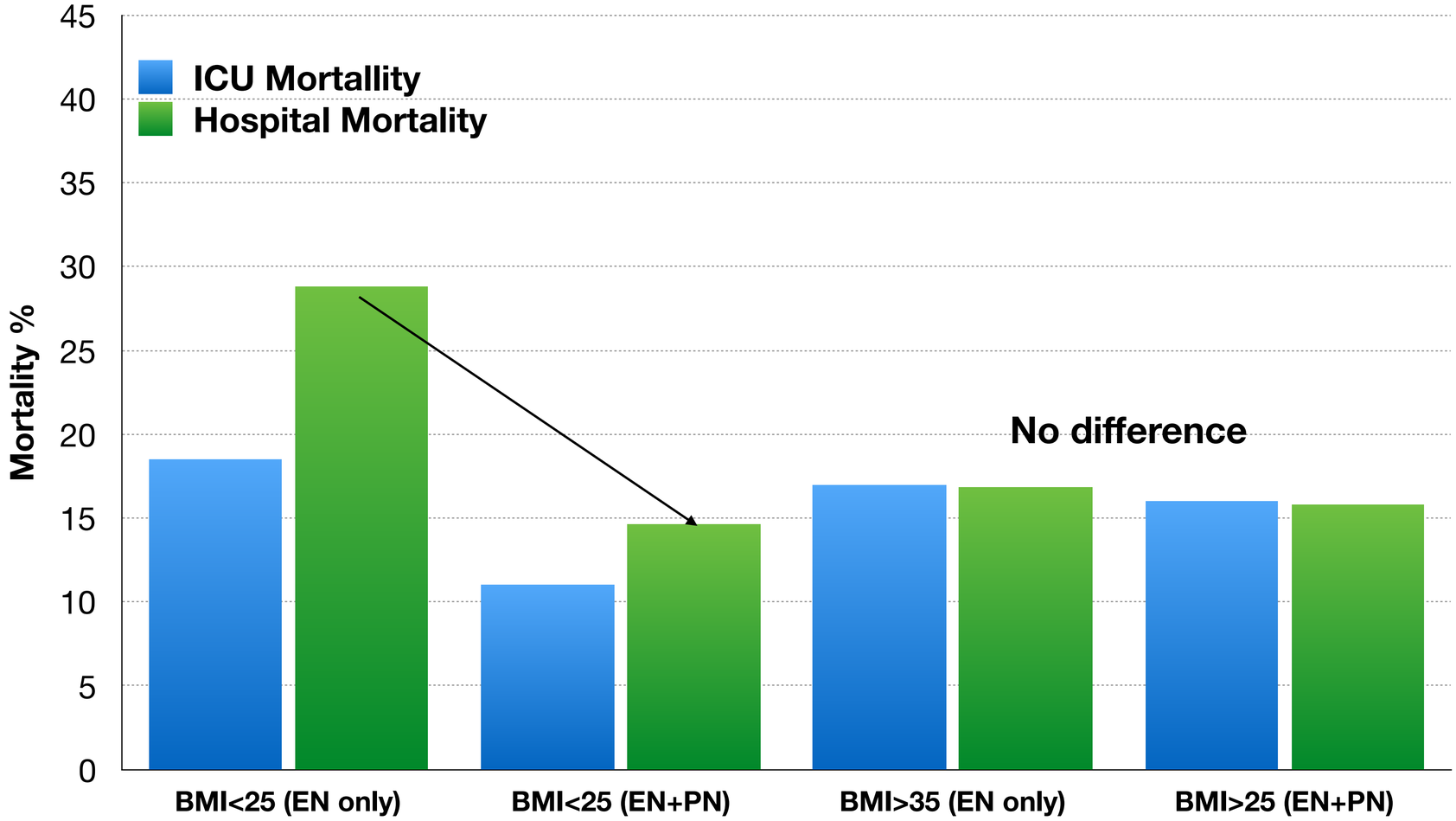


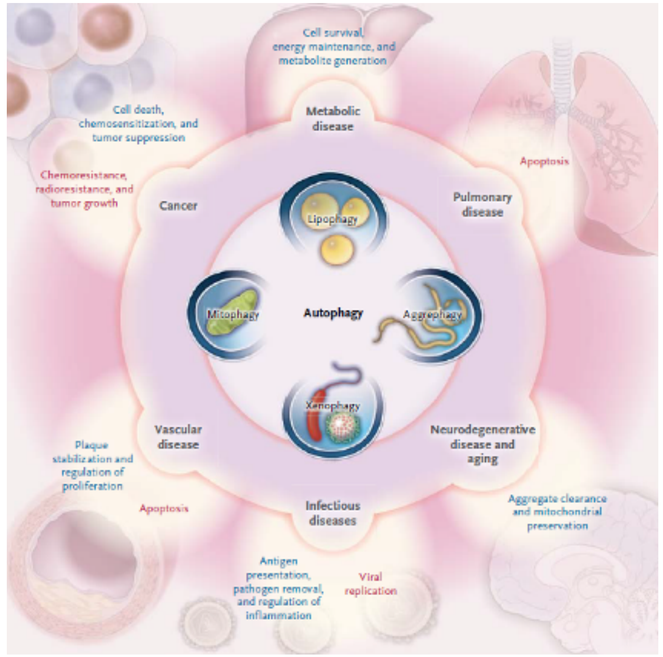
Wischmeyer et al. Critical Care (2017) 21:142

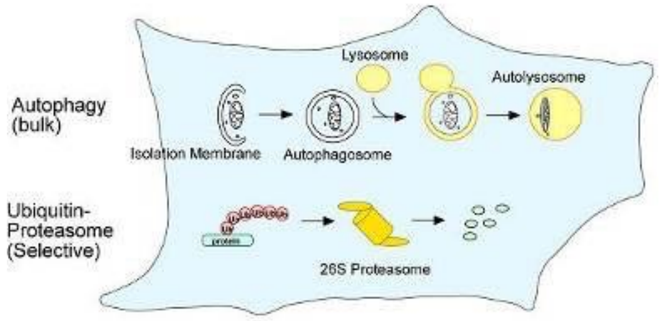
More Protein and Energy Associated With Improved Mortality in Higher Risk Patients

Outcome	Protein Intake (per 10% of Goal)		Energy Intake (per 10% of Goal)	
	Low NUTRIC Score (n = 1,217)	High NUTRIC Score (n = 1,636)	Low NUTRIC Score (n = 1,217)	High NUTRIC Score (n = 1,636)
Sample in ICU ≥ 4 d				
Mortality[a,b]	0.952 (0.895–1.011)	0.930 (0.892–0.969)[c]	0.962 (0.904–1.023)	0.927 (0.893–0.962)[c]
Adjusted[d]	0.998 (0.936–1.064)	0.934 (0.894–0.975)[c]	1.011 (0.946–1.079)	0.929 (0.893–0.966)[c]
TDA[f,g]	0.970 (0.936–1.006)	1.004 (0.967–1.043)	0.956 (0.921–0.992)[c]	0.995 (0.959–1.032)[c]
Adjusted[d]	1.013 (0.975–1.052)	1.051 (1.012–1.091)[c]	0.998 (0.958–1.039)	1.045 (1.007–1.085)[c]
Sample in ICU ≥ 12 d				
Outcome	Protein Intake (per 10% of Goal)[h]		Energy Intake (per 10% of Goal)[h]	
	Low NUTRIC Score (n = 711)	High NUTRIC Score (n = 891)	Low NUTRIC Score (n = 711)	High NUTRIC Score (n = 891)
Mortality[a,b]	1.059 (0.964–1.165)	0.913 (0.853–0.977)[e]	1.069 (0.975–1.173)	0.909 (0.854–0.967)[e]
Adjusted[d]	1.052 (0.954–1.156)	0.899 (0.84–0.963)[e]	1.067 (0.967–1.178)	0.884 (0.829–0.941)[c]
TDA [f,g]	0.963 (0.913–1.016)	1.062 (1.002–1.126)[e]	0.937 (0.888–0.989)[e]	1.048 (0.990–1.109)
Adjusted[d]	0.999 (0.946–1.056)	1.092 (1.032–1.155)[e]	0.981 (0.925–1.040)	1.091 (1.032–1.155)[e]

Compher C et al. Crit Care Med 2017; 45:156–163

Proteins and Autophagy



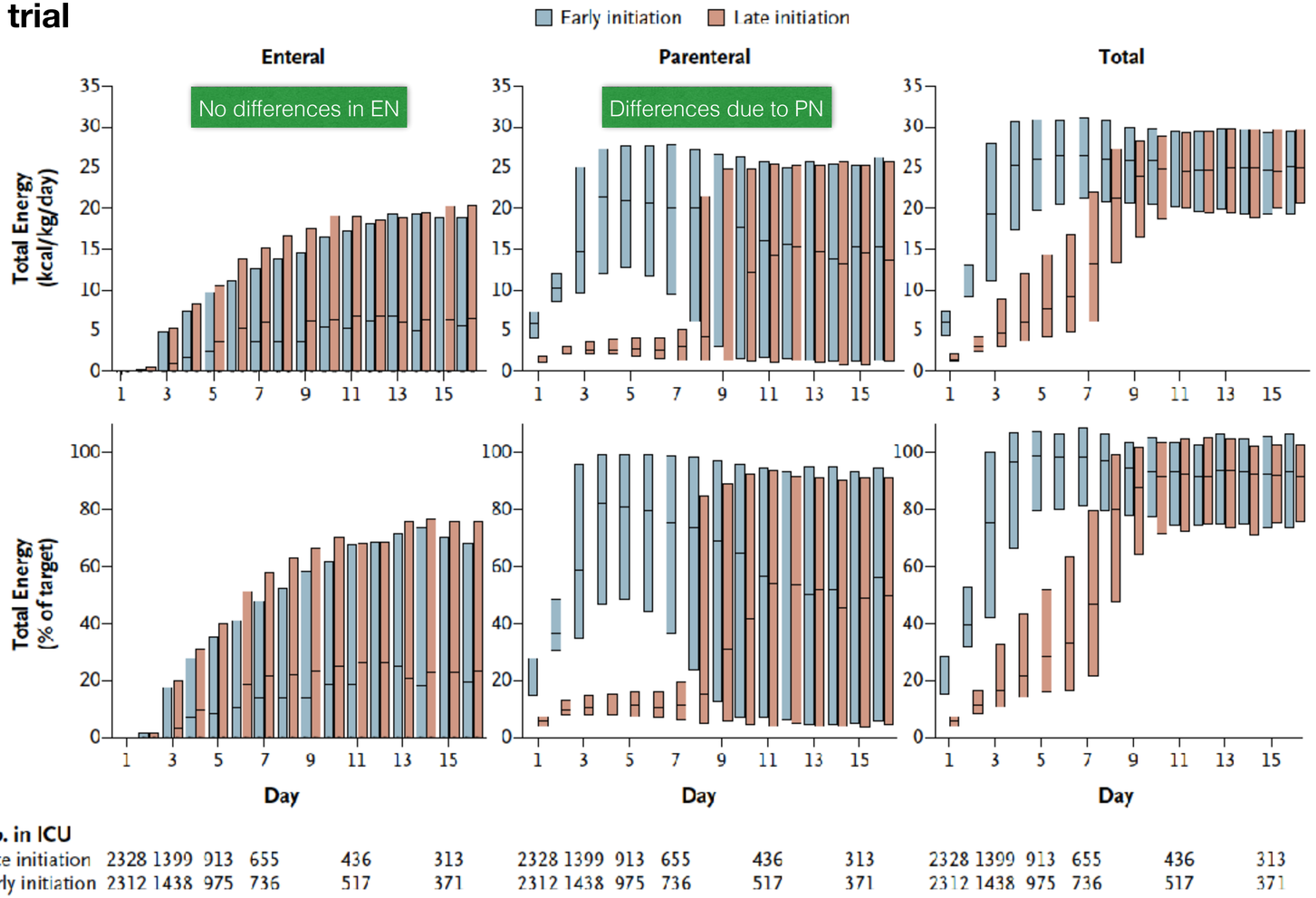


- **Method eukaryotic cells dispose damaged organelles or protein aggregates too large for proteasome ubiquitin system**
- **Involves lysosomal system for removing unfolded proteins, virus, bacteria, fat/carb, organelles**
- **Autophagy role in immunity, inflammation, infection, cancer, aging, pulmonary diseases (COPD), metabolic and neurodegenerative diseases**

AMK Choi et al NEJM 2013;368:651

Early Parenteral Nutrition but not Enteral Nutrition induced an Autophagy Deficiency Phenotype

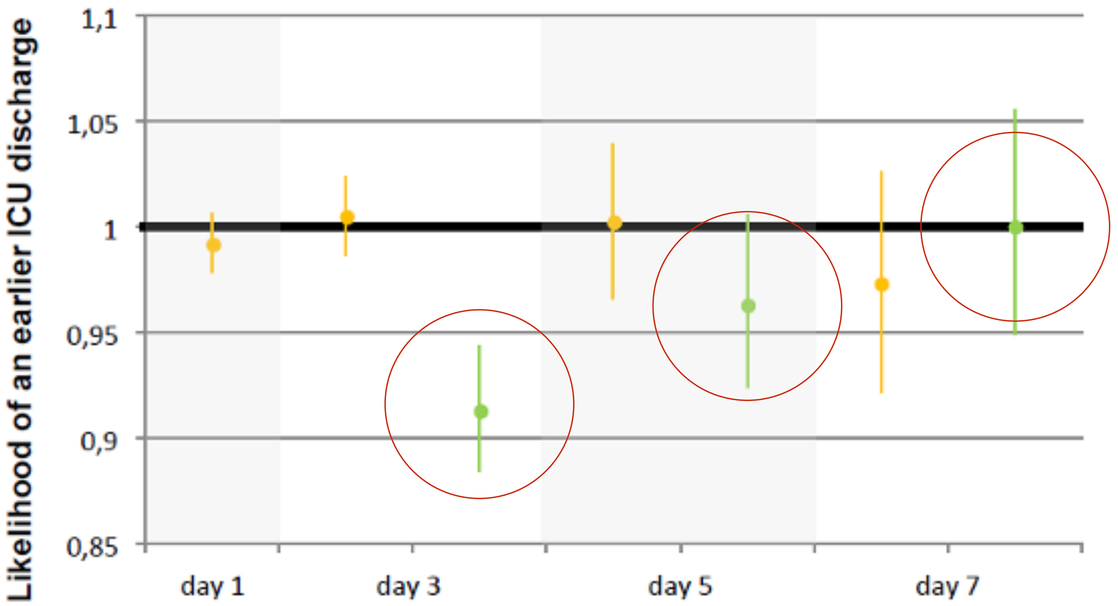
Data from the Epanic trial



Casaer MP, Van Den Berghe G. NEJM 2011;365:506

Epanic trial Suggests that early Protein administration induced Deleterious Effects, Not Glucose

Epanic trial 4600 patients randomized to early or late SPN



Glucose

HR (CI) per 10% of target increase in glucose intake (± 28 g / day)

Protein

HR (CI) per 10% of target increase in protein intake (± 7 g / day)

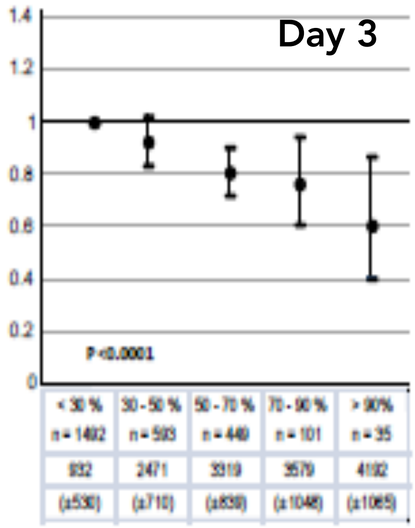
Implication: Nutrition Rx (not IV glucose load) caused adverse outcome

Casaer MP. Am J Respir Crit Care Med 2013;187:247-55.

Association Feeding/Protein intake and Mortality: Due to Autophagy Reduction?

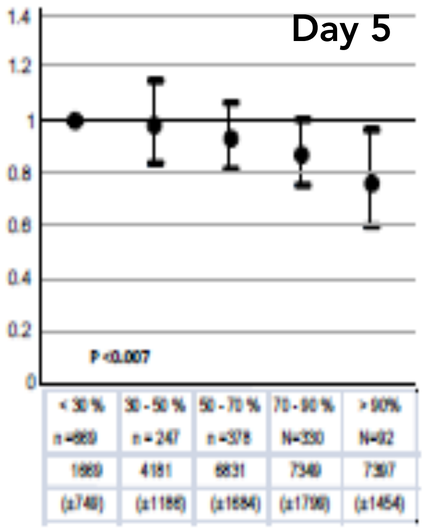
Chance of Being Discharged Alive (All pts n=4640)

Early negative effect of feeding



0% ⟶ 100%

No negative effect of feeding



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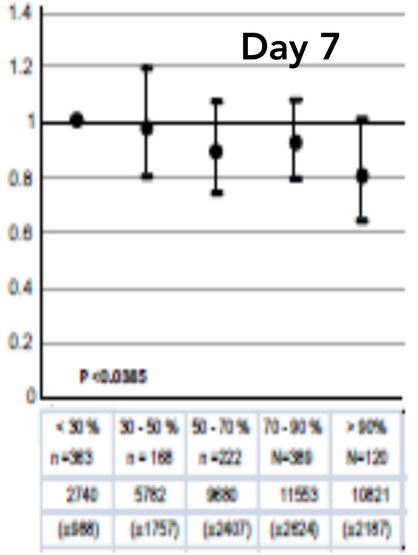
No negative effect of feeding



0% ⟶ 100%

Casaer MP. Am J Respir Crit Care Med 2013;187:247-55.

REVIEW

Ziekenhuis Gelderse Vallei

CURRENT OPINION

Preservation of autophagy should not direct nutritional therapy

Stephen A. McClave[a] *and Peter J.M. Weijs*[b]

Purpose of review
Recent reports in the literature have proposed that forced mandatory feeding should be avoided in the first week of critical illness to preserve autophagy, in order to maximize responses to oxidative stress, preserve organ function, and improve outcomes.

Recent findings
Autophagy is a well recognized physiologic process that serves a housekeeping role for the cell to eliminate large protein aggregates and as a survival mechanism in starvation for generating energy (ATP) and promoting protein synthesis to maintain cell structure. In the critical care setting, autophagy may have important roles in modulating immune function, fighting infection, and preventing organ failure. The effect of feeding on autophagy is complex, poorly understood, and difficult to predict.

Summary
The argument to withhold feeding to preserve autophagy is poorly substantiated and should not interfere with the delivery of early enteral nutrition to the critically ill patient in that first week following admission to the ICU.

Keywords
autophagy, cell death pathways, enteral nutrition, mammalian target of rapamycin signaling

Curr Opin Clin Nutr Metab Care 2015, 18:155–161

Who is right?

Early proteins No

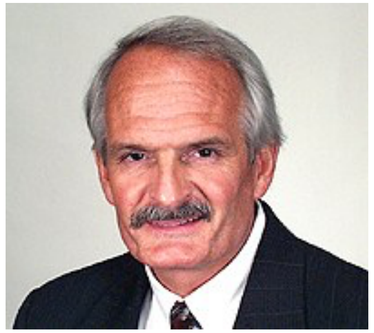
Greet vd Berghe

Michael Casaer

?

Arthur van Zanten

Early proteins yes



Stephen McClave

Peter Weijs

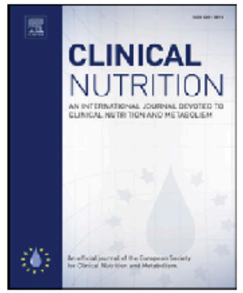
Role of timing protein intake

Clinical Nutrition xxx (2018) 1–8

Contents lists available at ScienceDirect

Clinical Nutrition

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



Original article

Timing of PROTein INtake and clinical outcomes of adult critically ill patients on prolonged mechanical VENTilation: The PROTINVENT retrospective study

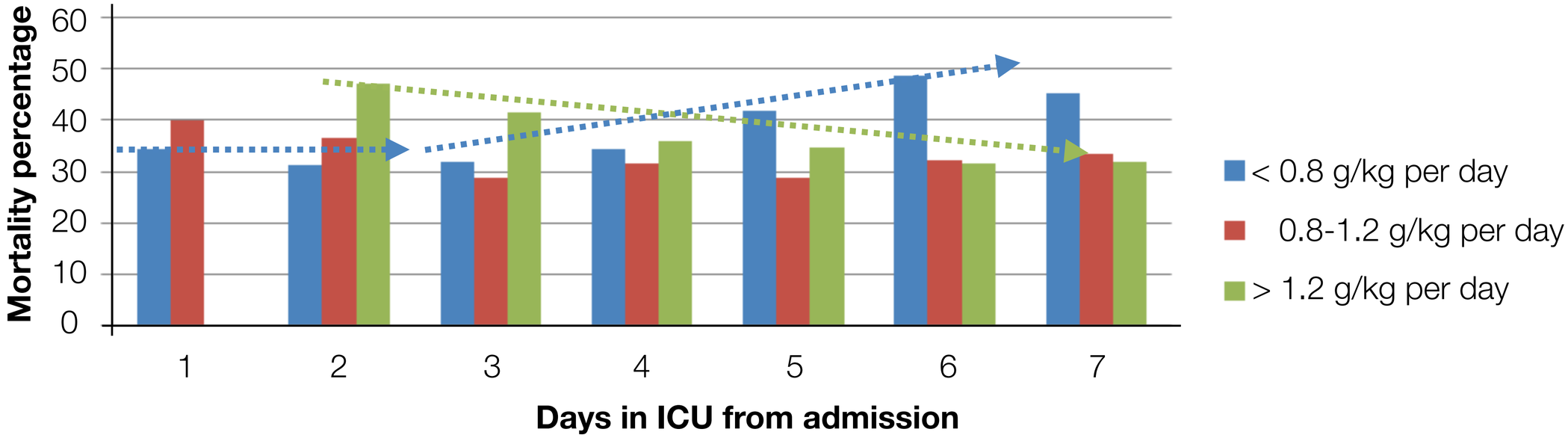
W.A.C. (Kristine) Koekkoek [a, 1], C.H. (Coralien) van Setten [a, 1], Laura E. Olthof [a], J.C.N. (Hans) Kars [b], Arthur R.H. van Zanten [a, *]

[a] *Department of Intensive Care Medicine, Gelderse Vallei Hospital, Willy Brandtlaan 10, 6716 RP, Ede, The Netherlands*
[b] *Department of Information Technology and Datawarehouse, Gelderse Vallei Hospital, Willy Brandtlaan 10, 6716 RP, Ede, The Netherlands*

Koekkoek WA, Van Setten C, Van Zanten AR. Clin Nutr. 2018 Feb 17. pii: S0261-5614(18)30075-X.

PROTINVENT retrospective study in 456 patients: Role of timing protein intake

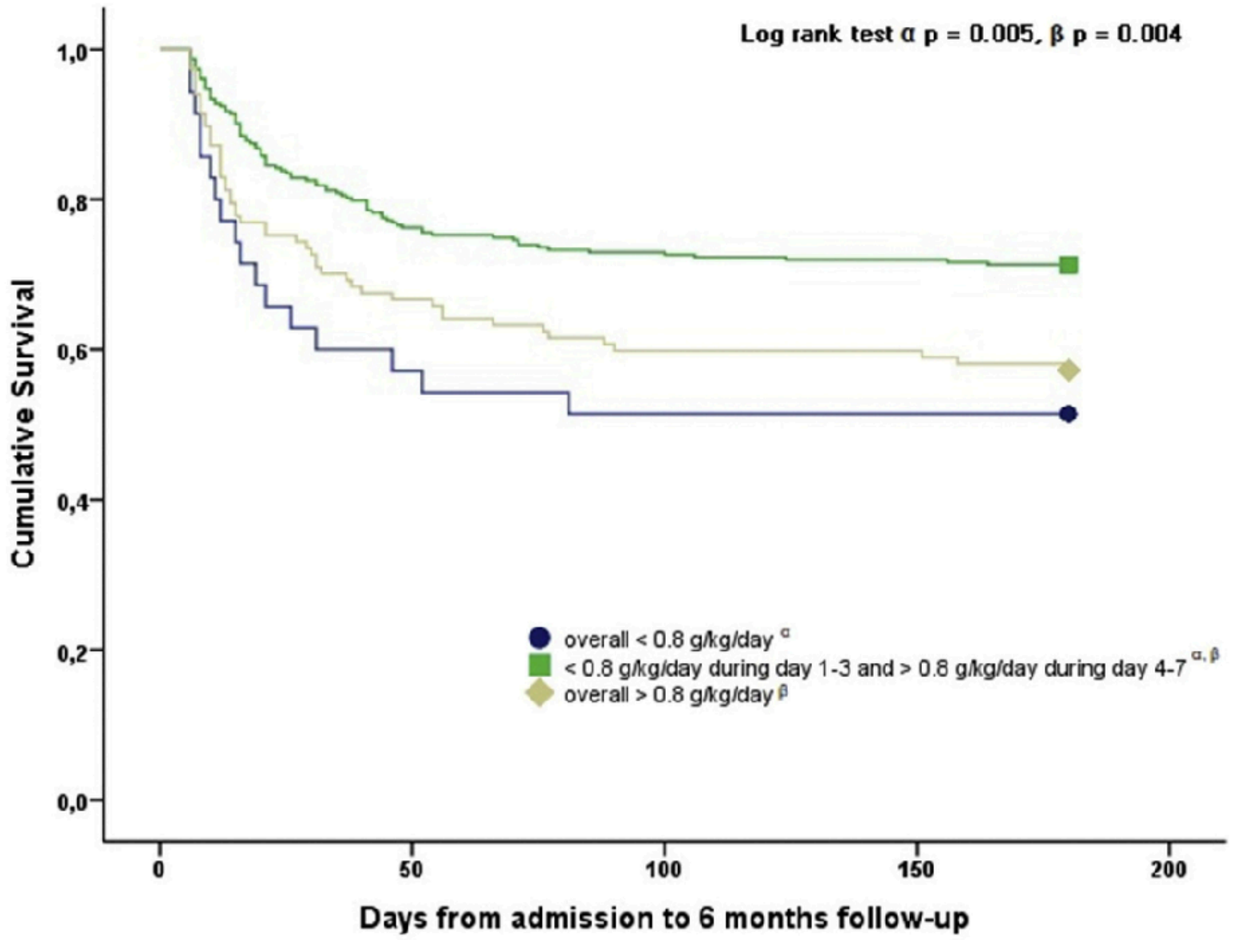
PROTein INtake and clinical outcome in adult critically ill patients on prolonged mechanical VENTilation:
n=456; 2011-2015, Mechanical Ventilation > 7 days; Primary endpoint 6 month mortality



Early (< 3 days) high protein intake associated with higher mortality, after day 3 high intake is better. Is low to high intake after 3 days better?

Van Setten C, Koekkoek WA, Olthof L, Van Zanten AR submitted

Effect on protein intake (day 1-3) and (day 4-7) & 6-month mortality



A time-dependent effect of protein intake in critically ill patients is observed.

A gradual increase from low protein intake during the first 2 days of ICU stay to intermediate on day 3-5 and high protein intake from day 6 is associated with lower 6-month mortality.

In addition, overall low protein intake is associated with the highest 6-month, ICU and hospital mortality and should be avoided.

Koekkoek WA, Van Setten C, Van Zanten AR. Clin Nutr. 2018 Feb 17. pii: S0261-5614(18)30075-X.

Who is right?

Early proteins No

Greet vd Berghe

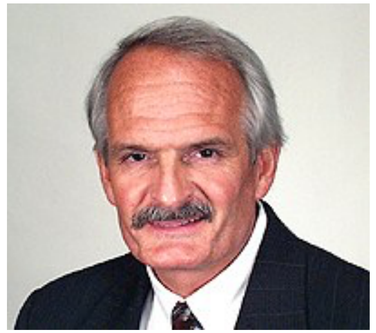
Michael Casaer

Both?

Arthur van Zanten

First 3 days low, after d3 high better during first week

Early proteins yes



Stephen McClave

Peter Weijs

Big scientific debate on this study

2014 Harry M. Vars Award

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

Intensive Nutrition in Acute Lung Injury: A Clinical Trial (INTACT)

Carol A. Braunschweig, PhD, RD[1]; Patricia M. Sheean, PhD, RD[2]; Sarah J. Peterson, MS, RD[3]; Sandra Gomez Perez, MS, RD[4]; Sally Freels, PhD[5]; Omar Lateef, DO[6]; David Gurka, MD, PhD[6]; and Giamila Fantuzzi, PhD[1]

Journal of Parenteral and Enteral Nutrition
Volume 39 Number 1
January 2015 13–20

DOI: 10.1177/0148607114528541
jpen.sagepub.com
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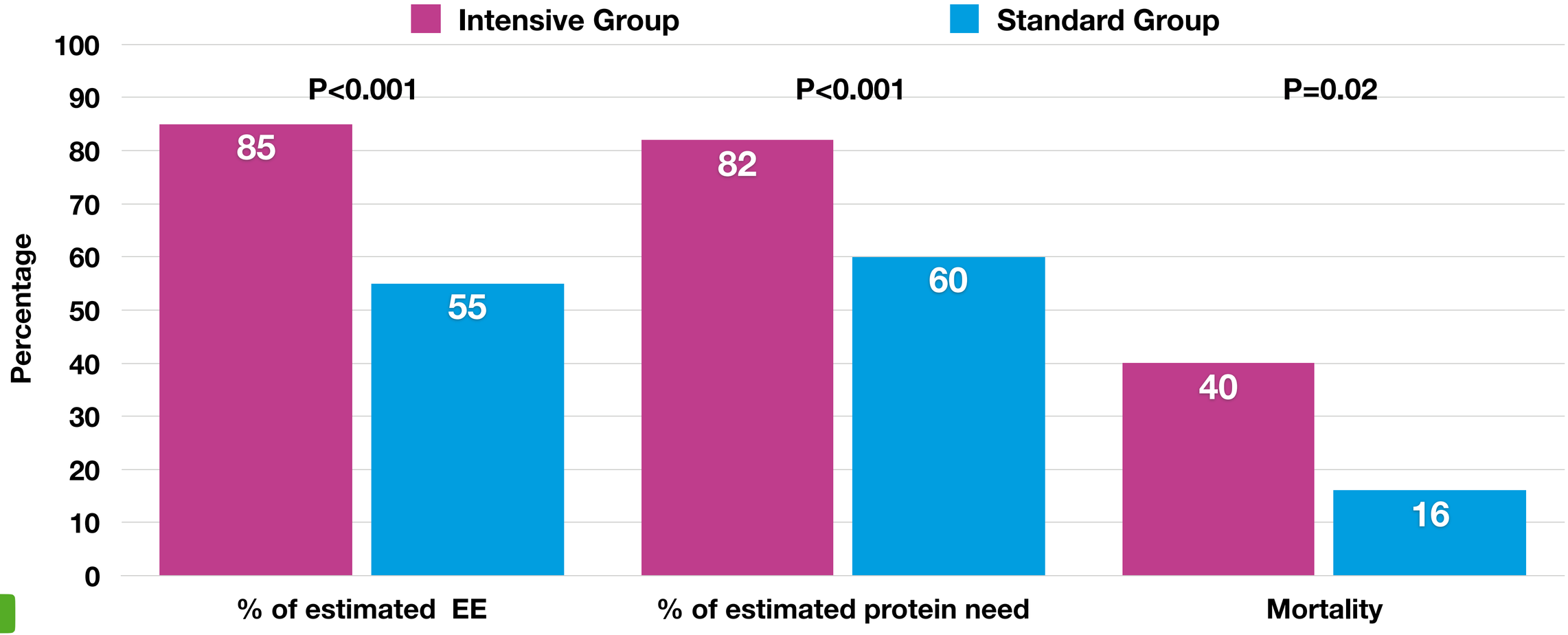
online.sagepub.com
SAGE

INTACT trial, stopped early (n = 78)

Intensive medical nutrition therapy (IMNT; 30 kcal/kg/day) from acute lung injury diagnosis to hospital discharge



Braunschweig CA, et al. JPEN J Parenter Enteral Nutr. 2015;39:13–20.

Post-hoc analysis INTACT trial

- Higher overall energy intake, higher mortality (OR: 1.14, 95% CI: 1.02, 1.27).
- Patients enrolled for at least 8 days (n = 66), higher early energy intake significantly increased the HR for mortality (HR: 1.17, 95% CI: 1.07, 1.28), higher late energy intake was significantly protective (HR: 0.91, 95% CI: 0.83, 1.0).
- Results were similar for early but not late protein (g/kg) exposure (early-exposure HR: 8.9, 95% CI: 2.3, 34.3; late-exposure HR: 0.15, 95% CI: 0.02, 1.1).
- Threshold analyses indicated early mean intakes >18 kcal/kg significantly increased subsequent mortality.

Braunschweig CA, et al. Am J Clin Nutr 2017;105:411–6.

Intensive Care Med (2017) 43:1637–1647
DOI 10.1007/s00134-017-4880-3

SEVEN-DAY PROFILE PUBLICATION

Early goal-directed nutrition versus standard of care in adult intensive care patients: the single-centre, randomised, outcome assessor-blinded EAT-ICU trial

Matilde Jo Allingstrup[1], Jens Kondrup[2], Jørgen Wiis[1], Casper Claudius[1], Ulf Gøttrup Pedersen[1], Rikke Hein-Rasmussen[1], Mads Rye Bjerregaard[1], Morten Steensen[1], Tom Hartvig Jensen[1], Theis Lange[3,4], Martin Bruun Madsen[1], Morten Hylander Møller[1] and Anders Perner[1*]

Methods EAT-ICU study

- Acutely admitted, mechanically ventilated ICU patients expected to stay longer than 3 days in the ICU.
- Early goal-directed nutrition (EGDN) group
  - indirect calorimetry
  - 24-h urinary urea aiming at covering 100% of requirements from the first full trial day using enteral and parenteral nutrition.
- Standard of care group
  - 25 kcal/kg/day by enteral nutrition.
  - If not met by day 7, supplemented with parenteral nutrition.
- Primary outcome: physical component summary (PCS) score of SF-36 at 6 months.

Allingstrup MJ et al. Intensive Care Med (2017) 43:1637–1647

Baseline characteristics

Variable	Early goal-directed nutrition (*N* = 100)	Standard of care (*N* = 99)
Age, years	63 (51–72)	68 (52–75)
Male sex, no. (%)	65 (65%)	59 (60%)
Actual body weight, kg	78 (67–90)	80 (70–90)
BMI[a], kg/m^2	22 (20–26)	22 (20–25)
Source of ICU admission, no. (%)		
Emergency department	31 (31%)	30 (30%)
General ward	45 (45%)	38 (38%)
Operating or recovery room	6 (6%)	12 (12%)
Other ICU[b]	10 (10%)	11 (11%)
Other hospital	8 (8%)	8 (8%)
Admission type, no. (%)		
Medical	52 (52%)	43 (43%)
Emergency surgery	43 (43%)	53 (54%)
Elective surgery	5 (5%)	3 (3%)
Diagnoses and procedures, no. (%)		
Haematologic malignancy[c]	13 (13%)	12 (12%)
Multiple trauma	8 (8%)	10 (10%)
Severe sepsis	47 (47%)	47 (47%)
Dialysis on admission	6 (6%)	5 (5%)
Mechanical ventilation	100 (100%)	99 (100%)
Days in hospital before ICU admission, days	0.9 (0.2–4.1)	1.1 (0.2–4.8)
Time from ICU admission to randomisation, h	14 (10–20)	13 (7–20)
Nutrition given in ICU prior to randomisation		
Energy, kcal/day	140 (24–260)	122 (30–275)
Protein, g/day	0 (0–0)	0 (0–0)
SAPS II[d]	47 (37–54)	48 (39–59)
SOFA score[e]	8 (6–11)	8 (5–10)

- 5 years age difference
- low BMI
- 11% other ICU
- otherwise well balanced

Allingstrup MJ et al. Intensive Care Med (2017) 43:1637–1647

Nutrition characteristics in ICU after randomisation

Variable	Early goal-directed nutrition (*N* = 100)	Standard of care (*N* = 99)
Measured[a] energy requirement, kcal/day	2069 (1816–2380)	1887 (1674–2244)
Calculated[b] energy requirement, kcal/day	1950 (1750–2125)	1875 (1650–2100)
Energy intake, kcal/day	1877 (1567–2254)	1061 (745–1470)
Energy balance[c], kcal/day	−66 (−157 to −6)	−787 (−1223 to −333)
Measured[d] protein requirement, g/kg/day	1.63 (1.36–2.05)	1.16 (0.89–1.62)
Protein intake, g/kg/day	1.47 (1.13–1.69)	0.50 (0.29–0.69)
Protein balance[c], g/kg/day	−0.28 (−0.76 to 0.11)	−0.69 (−1.02 to −0.38)
Plasma urea, mmol/l	13.5 (8.7–21.9)	9.0 (5.6–14.4)
24-h urinary urea, mmol/day	516 (368–760)	320 (175–482)

Allingstrup MJ et al. Intensive Care Med (2017) 43:1637–1647

Primary and secondary outcomes

Primary outcome measure	Early goal-directed nutrition (*N* = 100)	Standard of care (*N* = 99)	Adjusted mean difference (95% CI)	*p* value
PCS score at 6 months adjusted for presence of haematologic malignancy, mean (SD)	22.9 (21.8)	23.0 (22.3)	−0.0[a] (−5.9 to 5.8)	0.99

Secondary outcome measures	Early goal-directed nutrition (*N* = 100)	Standard of care (*N* = 99)	Relative risk or mean difference (95% CI)	*p* value
Vital status, no. (%)				
Dead at day 28	20 (20%)	21 (21%)	0.94 (0.55–1.63)	0.83
Dead at day 90	30 (30%)	32 (32%)	0.93 (0.61–1.40)	0.72
Dead at 6 months	37 (37%)	34 (34%)	1.08 (0.74–1.57)	0.70
Length of stay among 6-month survivors, median days (IQR)				
ICU	7 (5–22)	7 (4–11)	NA	0.21
Hospital	30 (12–53)	34 (14–53)	NA	1.00
Percentage of days alive without life support at day 90, median (IQR)				
RRT	100% (97–100)	100% (97–100)	NA	0.64
Mechanical ventilation	86% (39–96)	92% (56–96)	NA	0.27
Inotrope/vasopressor support	96% (82–98)	96% (84–98)	NA	0.67
Time to new organ failure, mean days (SD)	5.4 (0.4)	5.9 (0.5)	NA	0.33[b]
New organ failure in ICU, no. (%)	81 (81%)	77 (78%)	1.04 (0.90–1.20)	0.57
Time to death, mean days (SD)	60 (13)	91 (24)	NA	0.51[c]
New use of RRT in ICU, no. (%)	22 (22%)	17 (17%)	1.28 (0.73–2.26)	0.39
Time to any infection, mean days (SD)	20 (1)	51 (9)	NA	0.80[b]
Nosocomial infections, no. (%)				
Any	19 (19%)	12 (12%)	1.57 (0.80–3.05)	0.18[d]

Allingstrup MJ et al. Intensive Care Med (2017) 43:1637–1647

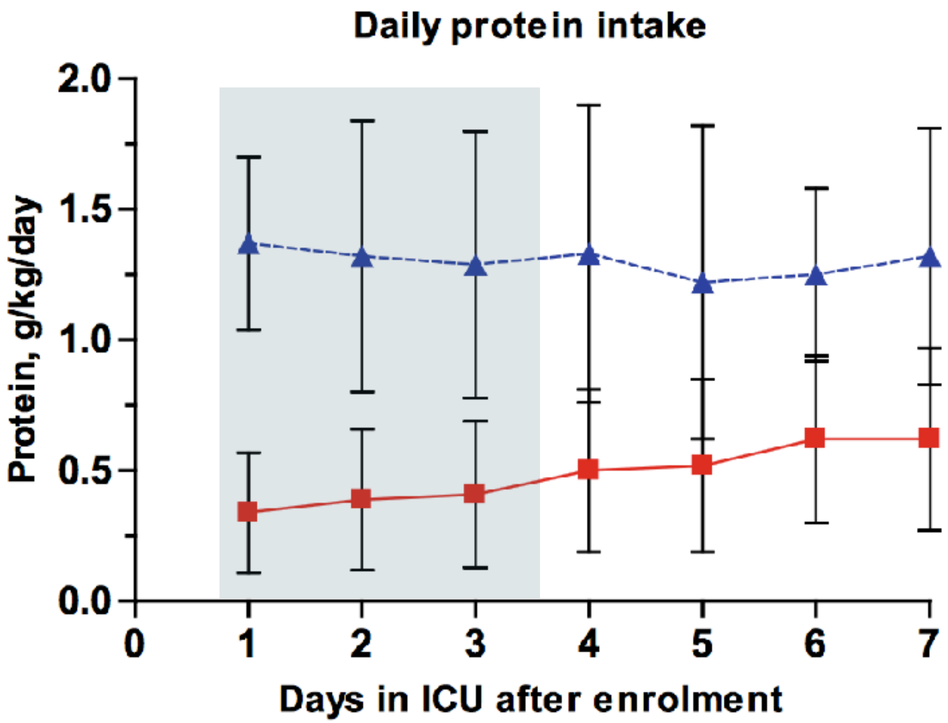
EGDN induces more hyperglycemia and insulin use

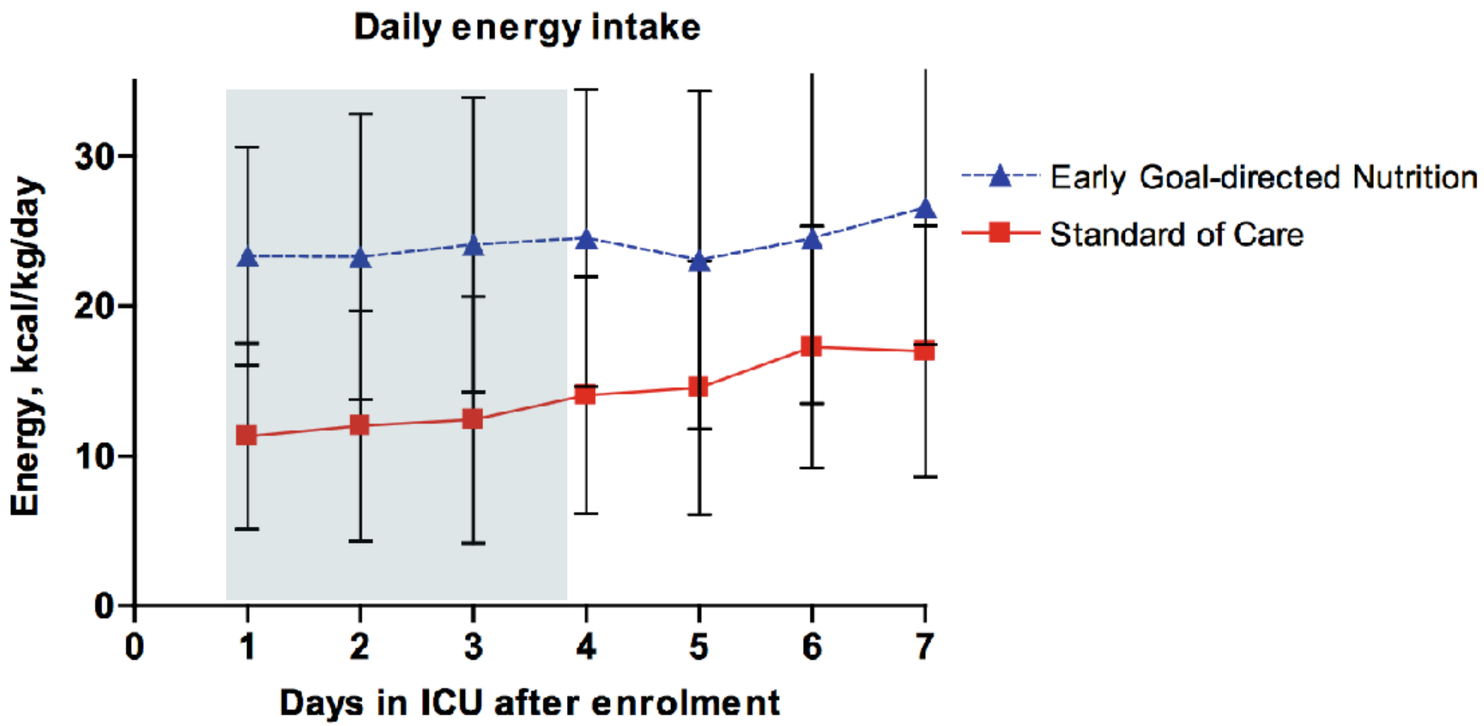
Secondary outcome measures	Early goal-directed nutrition (*N* = 100)	Standard of care (*N* = 99)	Relative risk or mean difference (95% CI)	*p* value
Cumulative insulin dose in ICU, median IU (IQR)[g]	86 (2–530)	0 (0–39)	262 (71–453)	0.008
No. of patients (%) with at least one episode of				
Blood glucose ≤2.2 mmol/l	2 (2%)	1 (1%)	NA	–[e]
Blood glucose ≥15 mmol/l	52 (52%)	25 (25%)	2.06 (1.40–3.03)	0.0001

- **Protein balance improved from –0.69 to –0.28 in the EGDN group, i.e. by 0.41 g/kg/day.**
- **Plasma urea also increased, (assuming Vd of 60% of weight), increase in plasma urea nitrogen matches the apparent increase in protein balance**
- **This indicates that no net protein gain was obtained with the extra supply of protein.**
- **Reduction of protein load at a plasma urea above 20 mmol/l may explain why no increased in RRT was observed.**

Allingstrup MJ et al. Intensive Care Med (2017) 43:1637–1647

Additional protein and energy by SPN



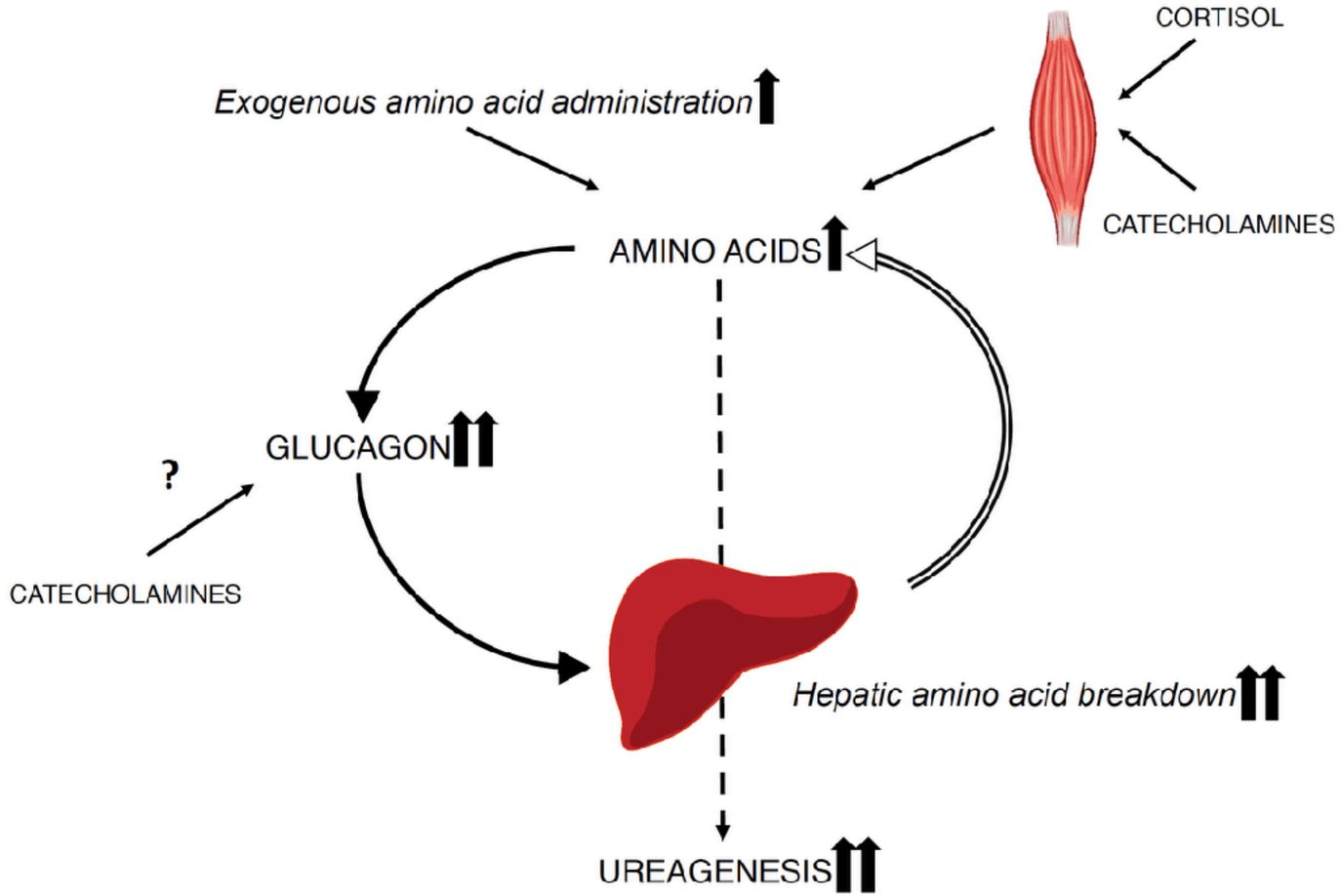


Period of autophagy suppression

Period of endogenous energy production

Allingstrup MJ et al. Intensive Care Med (2017) 43:1637–1647

Glucagon and amino acid supplementation interaction



Thiese SE, Gunst J, Vd Berghe G, submitted for publication

Role of Refeeding Hypophosphatemia

Clinical Nutrition xxx (2017) 1–9

Contents lists available at ScienceDirect

Clinical Nutrition

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

Original article

Impact of caloric intake in critically ill patients with, and without, refeeding syndrome: A retrospective study

Laura E. Olthof [a], W.A.C. Kristine Koekkoek [b], Coralien van Setten [a], Johannes C.N. Kars [c], Dick van Blokland [a], Arthur R.H. van Zanten [a, *]

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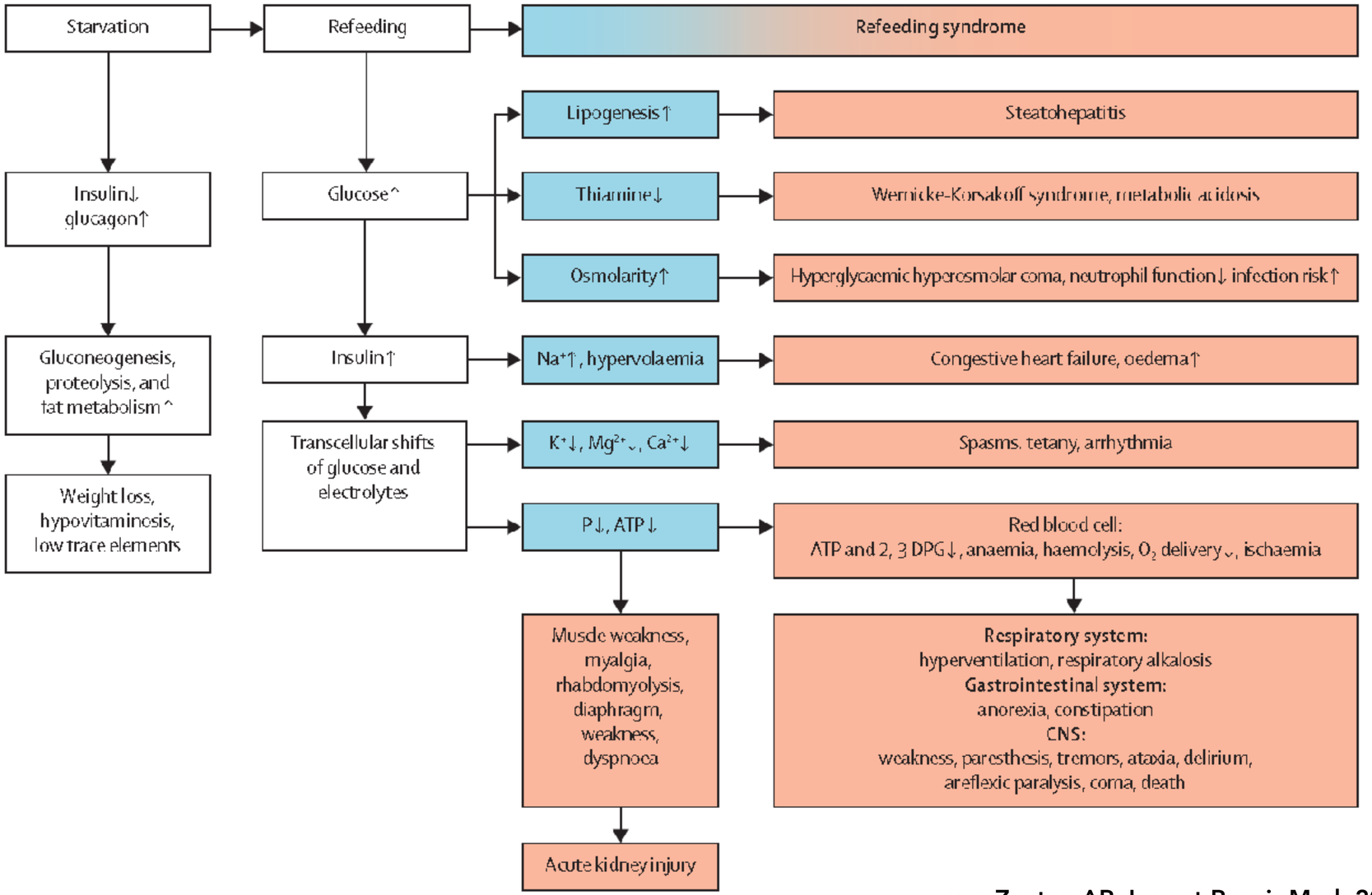
Olthof L, Koekkoek K, ..Van Zanten AR
Clin Nutr 2017 http://dx.doi.org/10.1016/j.clnu.2017.08.001

Refeeding Syndrome



van Zanten AR. Lancet Respir Med. 2015 Dec;3(12):904-5.

Patients at risk of developing refeeding problems: useful in the ICU?

NICE criteria (UK)

Patient has one or more of the following:

- BMI < 16 kg/m^2
- Unintentional weight loss >15% within the last 3-6 months
- Little or no nutritional intake for more than 10 days
- Low levels of phosphate, potassium or magnesium prior to feeding

Or patient has 2 or more of the following:

- BMI < 18.5 kg/m^2
- Unintentional weight loss >10% within the last 3-6 months
- Littel or no nutritional intake for more than 5 days
- A history of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics

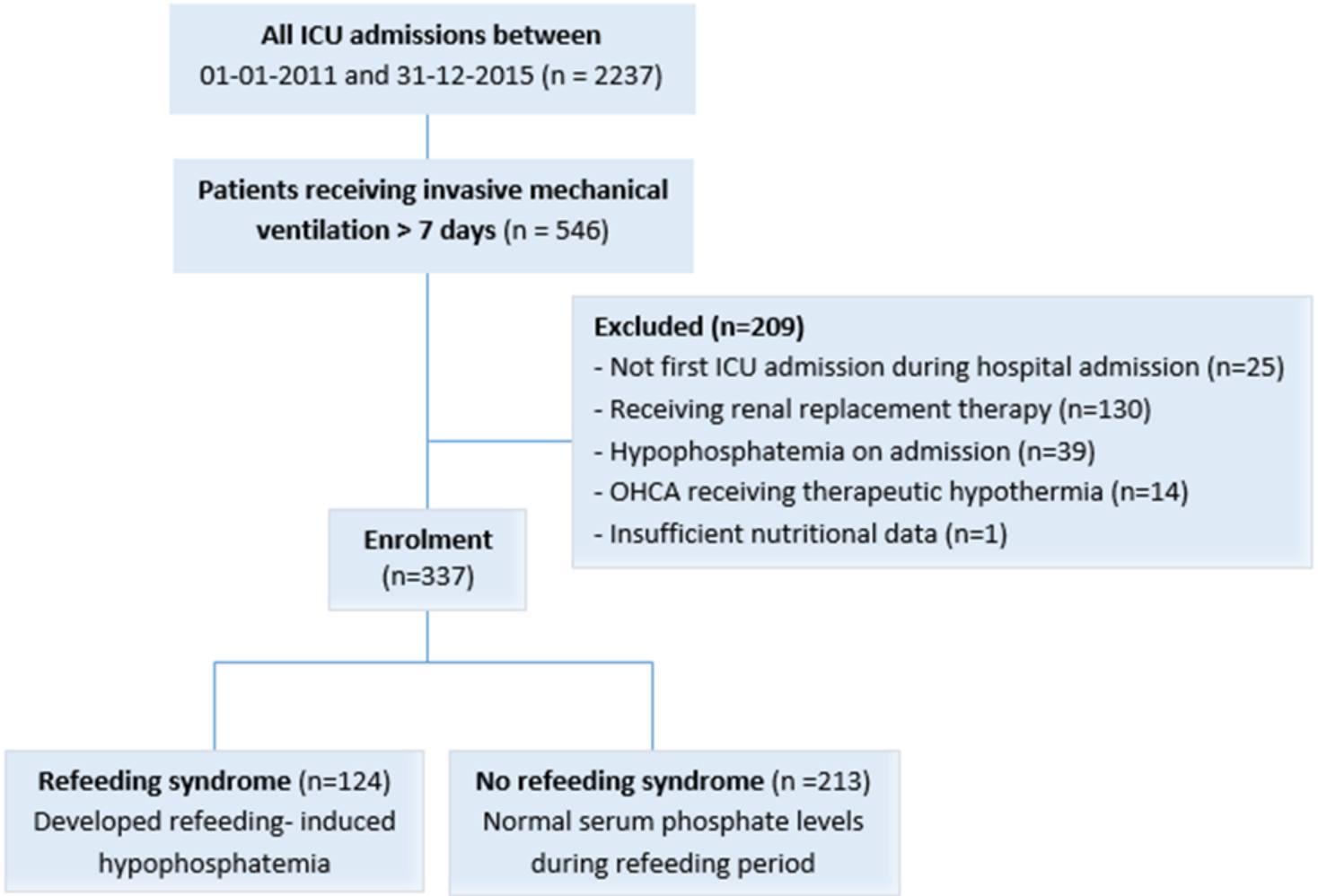
Practice guidelines recommend:
start feeding at 50% of energy target during first 3 days

Koekkoek WAC, Van Zanten ARH.
Curr Opin Clin Nutr Metab Care. 2018 Mar;21(2):130-137.

Is refeeding syndrome relevant during critical illness?

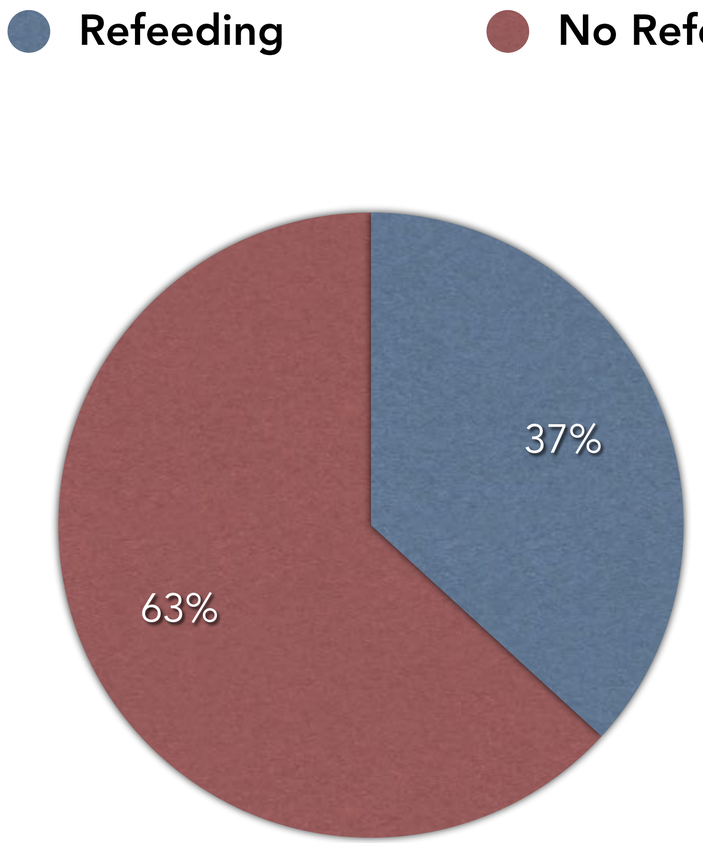
Diagnosis:
serum phosphate level below 0·65 mmol/l within 72h after start nutritional support. Change >0·16 mmol/l decrease from any previous level.

Exclusion:
Patients with other major causes of hypophosphataemia: ongoing dialysis, recent parathyroidectomy, or treatment for hyperphosphataemia.



Olthof L, Koekkoek K, ..Van Zanten AR
Clin Nutr 2017 http://dx.doi.org/10.1016/j.clnu.2017.08.001

Refeeding syndrome in critically ill patients is common



Olthof L, Koekkoek K, ..Van Zanten AR
Clin Nutr 2017 http://dx.doi.org/10.1016/j.clnu.2017.08.001

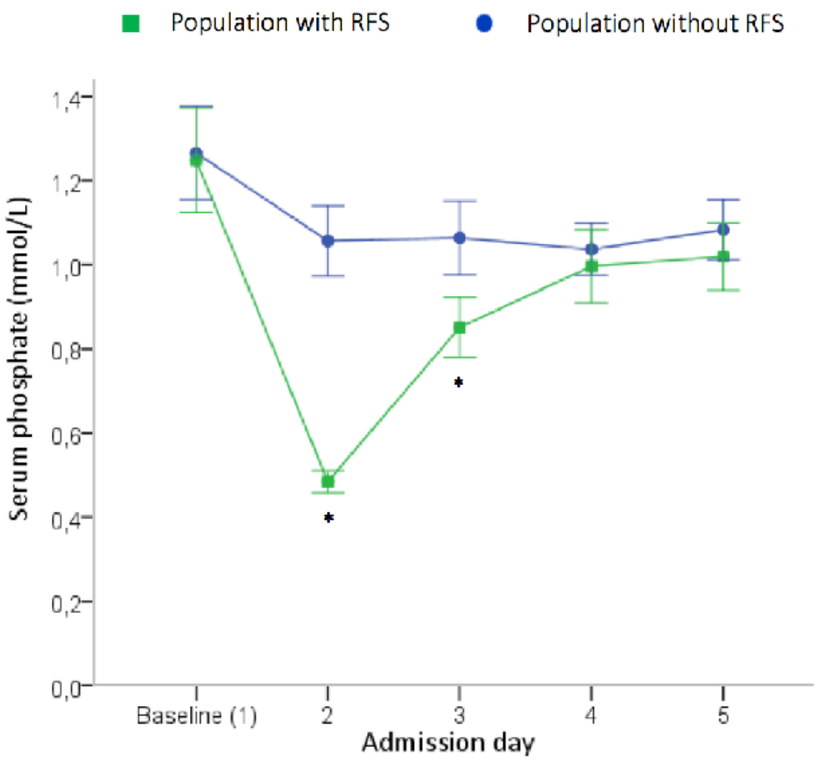
Baseline characteristics

		Total	*RFS (n=124)*	*No RFS (n=213)*	*P value*
Age (years)	mean (SD)	66.5 (13.4)	66.4 (13.2)	66.6 (13.6)	0.94
Gender, female	N (%)	126 (37.4%)	50 (40.3%)	76 (35.7%)	0.39
BMI on admission kg/m					
Mean		27.0 (5.6)	26.6 (5.7)	27.2 (5.5)	0.31
<18.5		14 (4.2%)	8 (6.5%)	6 (2.8%)	0.11
APACHE II-score [a]	mean (SD)	21.6(6.5)	21.3 (5.8)	21.7 (6.9)	0.56
SOFA score [b]	mean (SD)	6.9 (2.8)	6.6 (2.7)	7.1 (2.9)	0.17
Baseline blood test	median [IQR]				
Leukocytes ($x10^9$)		14.6 [8,4]	14.1 [9,2]	12.6 [8,7]	0.12
Creatinine (µmol/L)		88.5 [59]	86.0 [44]	90.5 [67]	0.50
CRP (mg/L)		131.0 [217]	117.0 [209]	145.0 [227]	0.10
Bilirubin (mmol/L)		8.5 [7]	9.0 [8]	8.0 [7]	0.48
Albumin (g/L)		27.0 [12]	28.0 [12]	26.0 [11]	0.10
Highest glucose		7.5 [2.3]	7.5 [2,2]	7.5 [2.5]	0.62
first 24 hours (mmol/L)					
Baseline electrolytes					
Sodium (mmol/L)	mean (SD)	138,0 (5.9)	138.4 (5.5)	137.7 (6.1)	0.34
Potassium (mmol/L)	mean (SD)	3.8 (0.7)	3.7 (0.6)	3.8 (0.7)	*0.016**
Magnesium (mmol/L)	mean (SD)	0.75 (0.21)	0.71 (0.21)	0.77 (0.21)	*0.013**
Phosphate (mmol/L)	median [IQR]	1.17 [0.56]	1.14 [0.42]	1.20 [0.63]	0.320
Sepsis on admission, yes	N (%)	158 (46.9%)	66 (53.2%)	92 (43.2%)	0.075

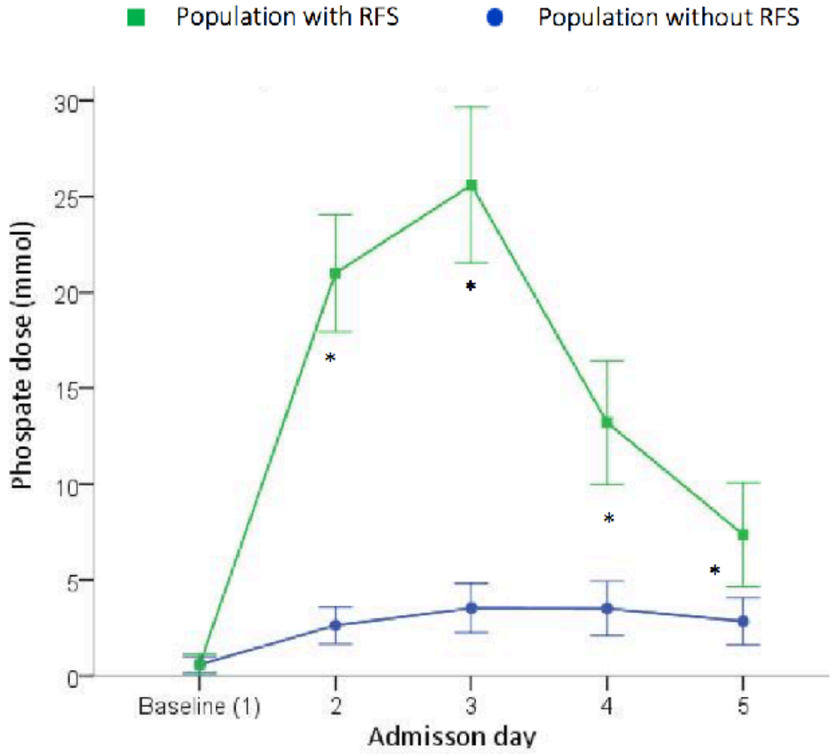
Olthof L, Koekkoek K, ..Van Zanten AR
Clin Nutr 2017 http://dx.doi.org/10.1016/j.clnu.2017.08.001

Phosphate levels and supplementation in RFS patients

n=337



Phosphate level

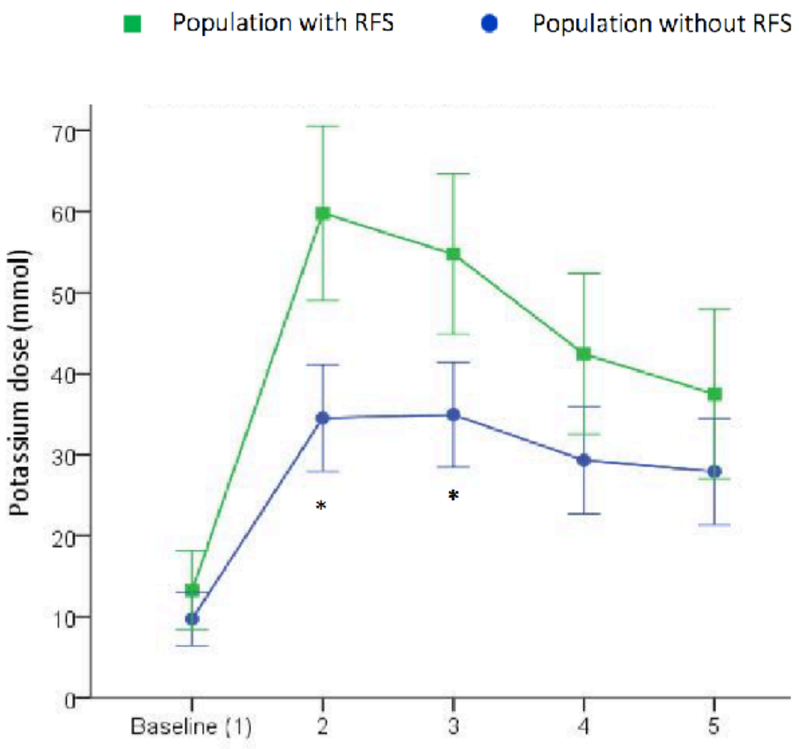


Phosphate supplementation

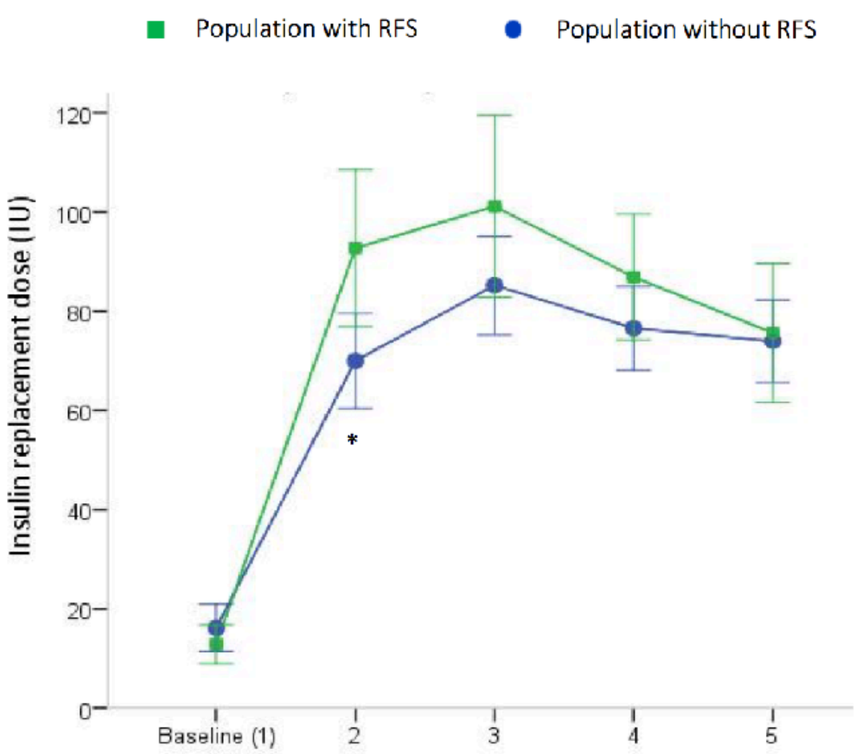
Olthof L, Koekkoek K, ..Van Zanten AR
Clin Nutr 2017 http://dx.doi.org/10.1016/j.clnu.2017.08.001

Potassium and insuline supplementation in RFS patients

n=337



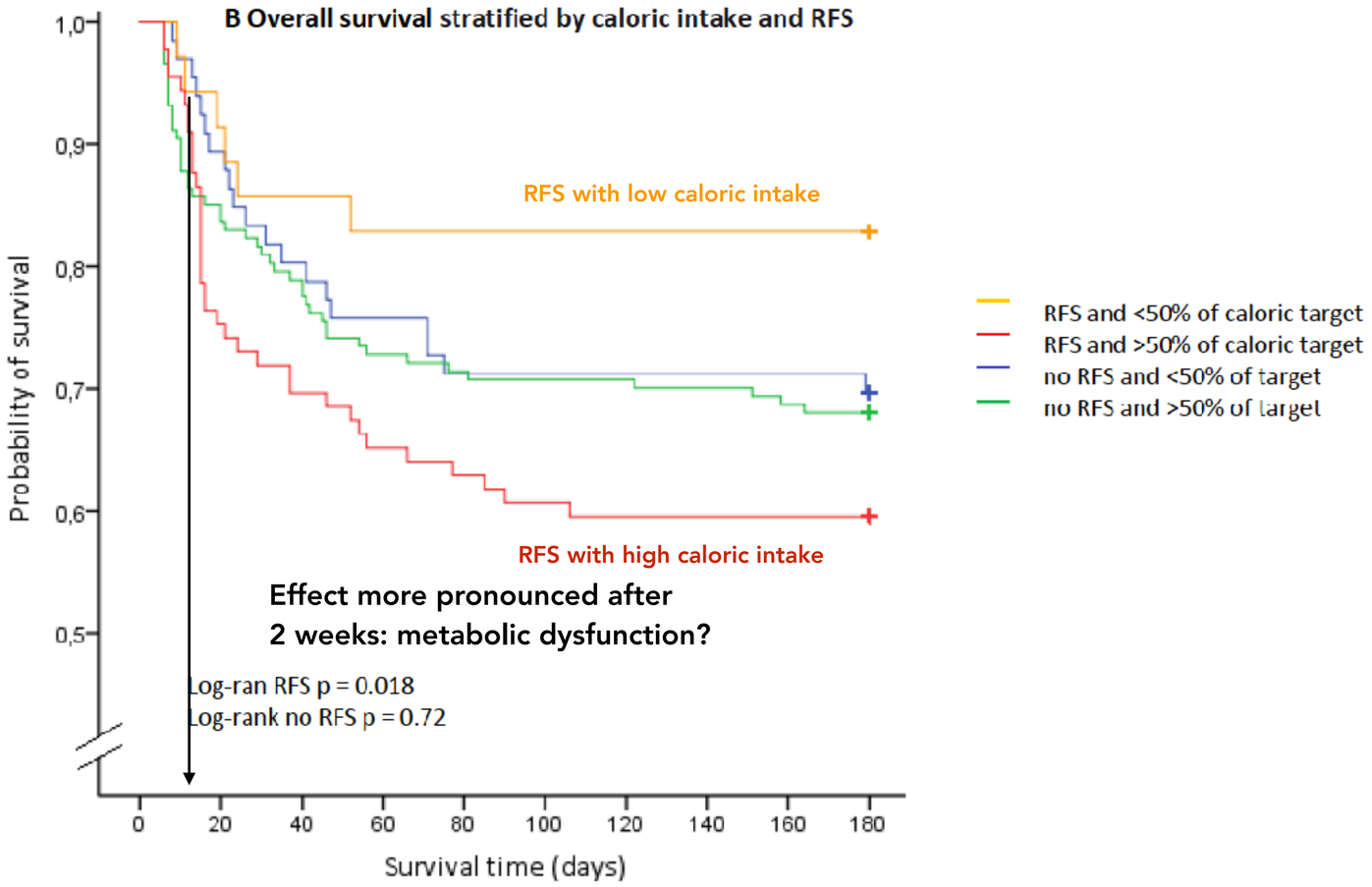
Potassium supplementation



Insulin supplementation

Olthof L, Koekkoek K, ..Van Zanten AR
Clin Nutr 2017 http://dx.doi.org/10.1016/j.clnu.2017.08.001

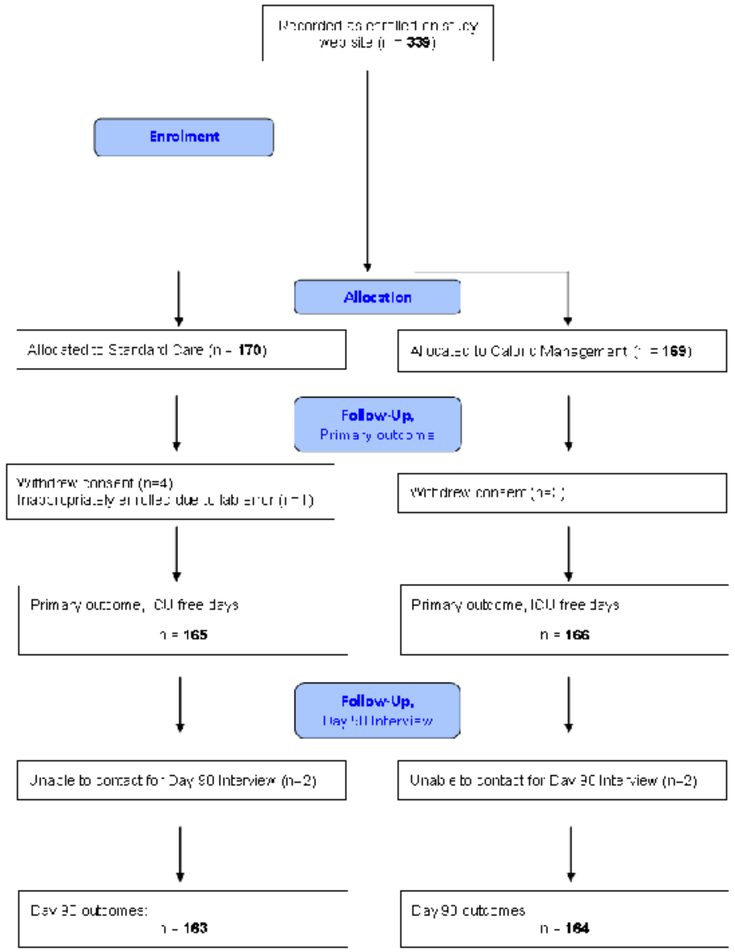
ICU patients with and without refeeding syndrome



Lower caloric intake is associated with better 6-month survival only in refeeding syndrome patients and not in those patients without RFS

Olthof L, Koekkoek K, ..Van Zanten AR
Clin Nutr 2017 http://dx.doi.org/10.1016/j.clnu.2017.08.001

Refeeding Syndrome the “only” RCT



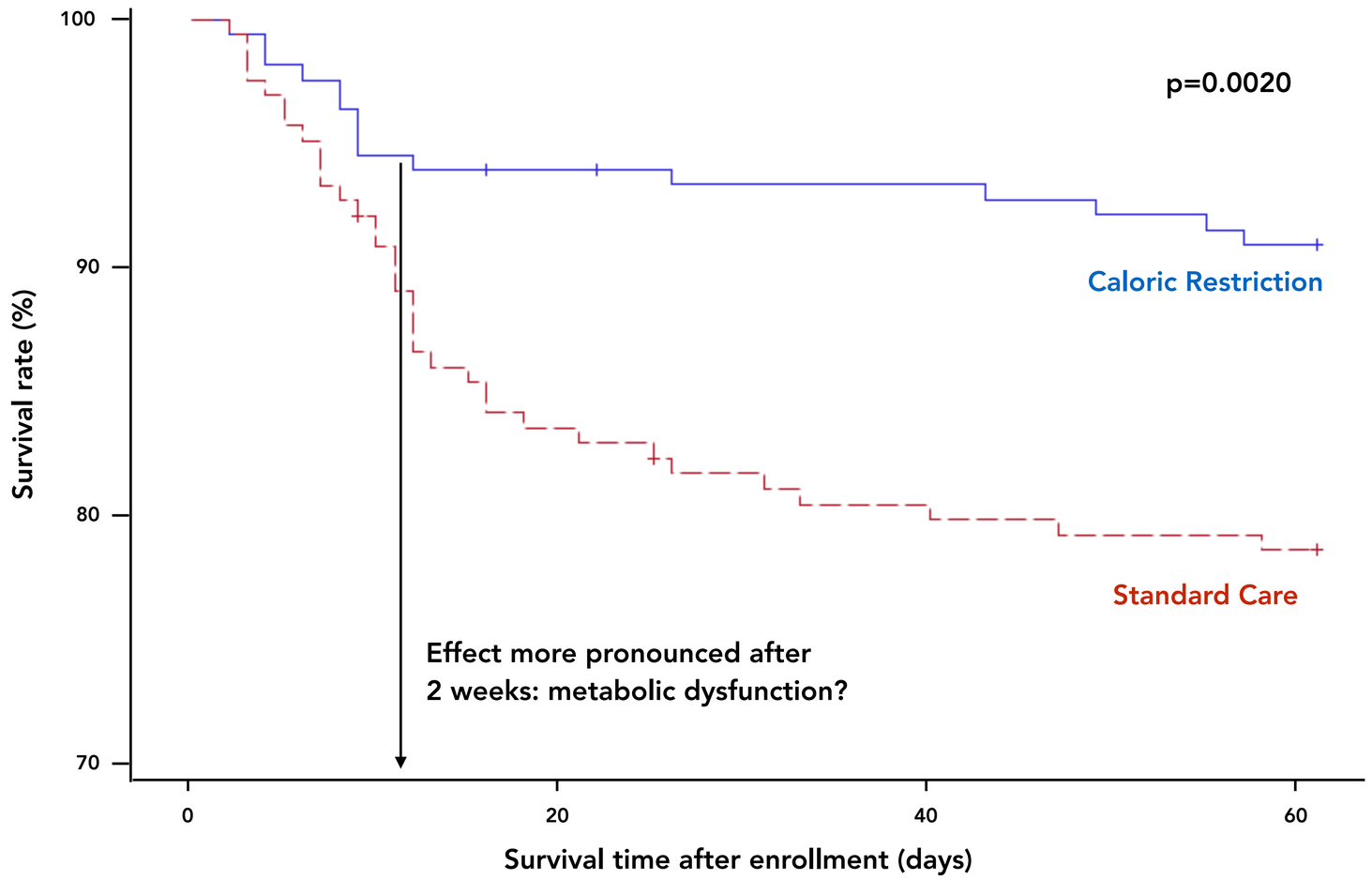
Inclusion:
serum phosphate level decreased to below 0·65 mmol per litre within 72 hours of commencing nutritional support.
Change required to be greater than 0·16 mmol per litre decrease from any previous level.

Exclusion:
Patients with other major causes of hypophosphataemia, such as ongoing dialysis, recent parathyroidectomy, or treatment for hyperphosphataemia were excluded from enrolment.

Caloric Management Protocol reduced energy intake to 20 kilocal/h for at least 2 days.
After 2 days, if phosphate levels did not need to be supplemented, energy intake returned to normal.

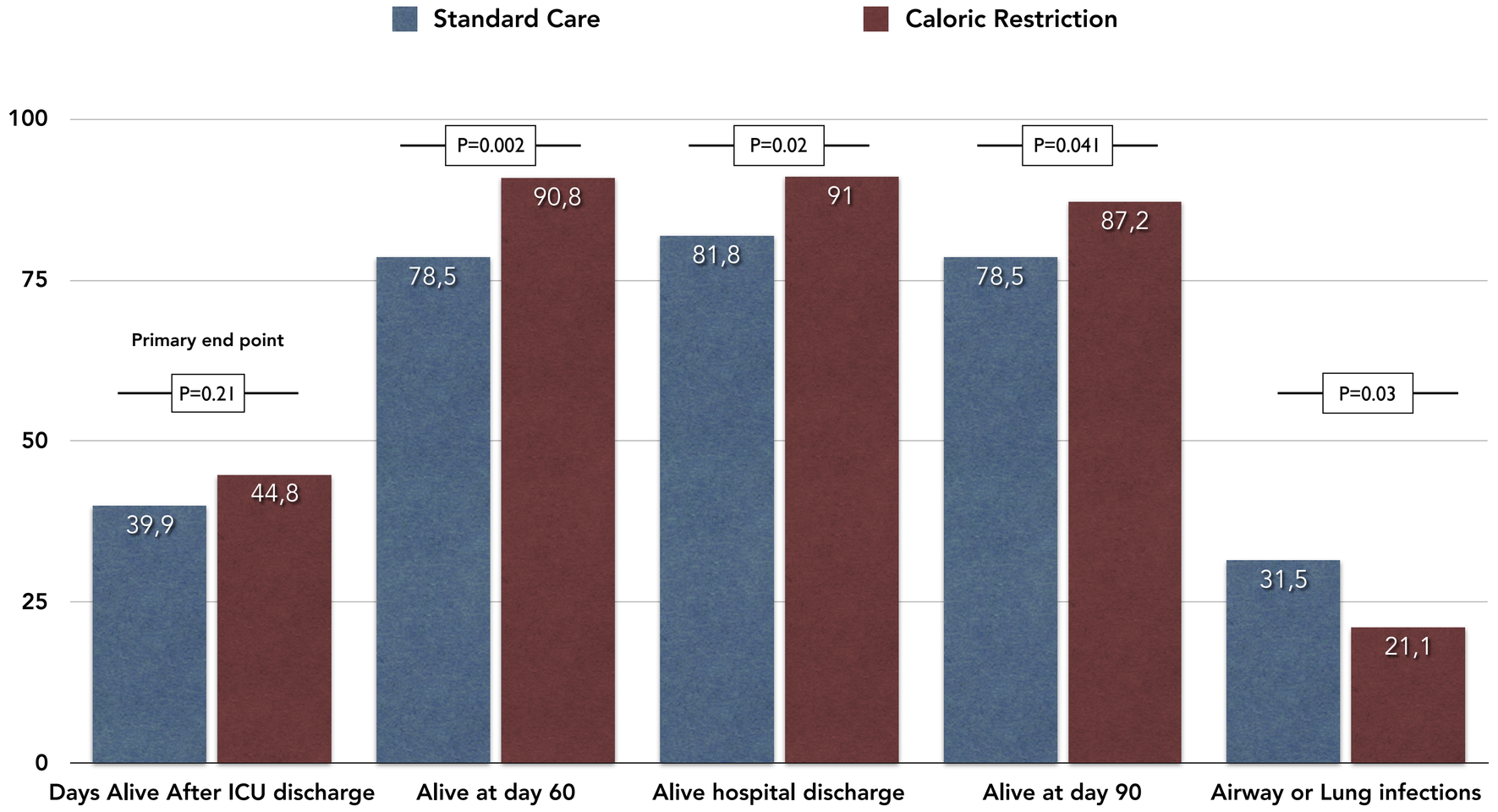
Doig GS, et al. Lancet Respir Med. 2015.

Caloric restriction and survival after inclusion



Doig GS, et al. Lancet Respir Med. 2015.

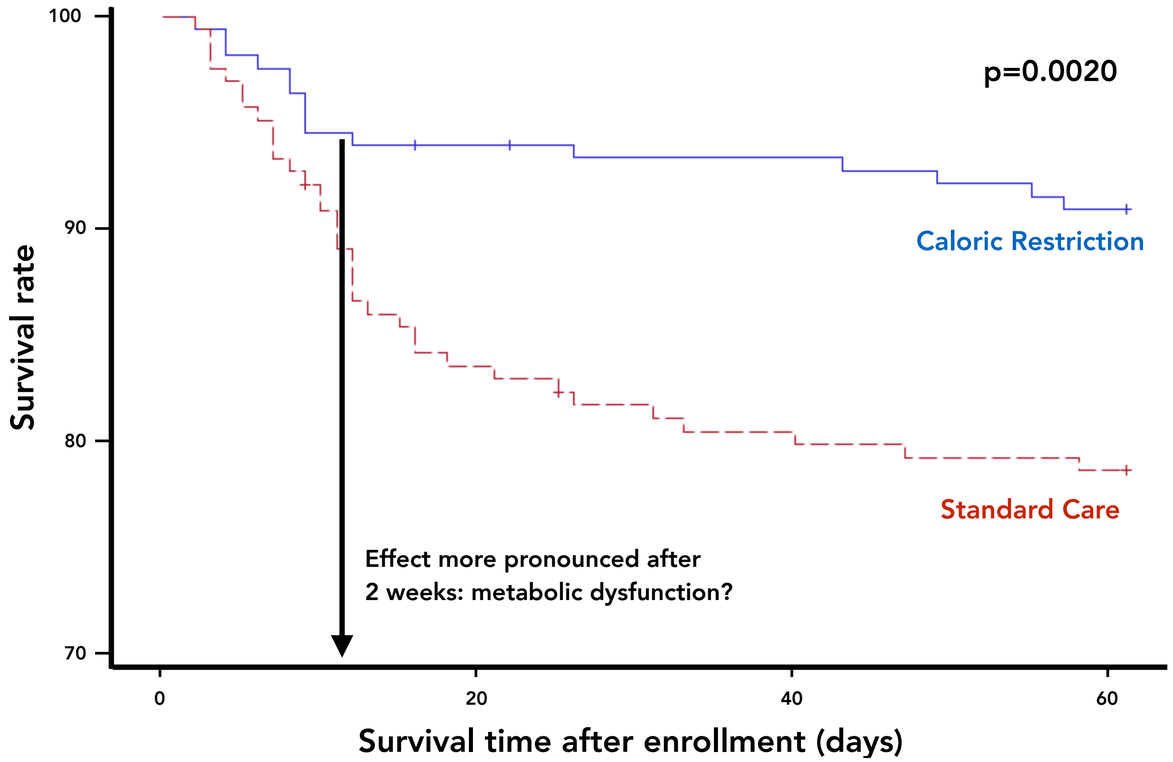
Caloric restriction during treatment for refeeding syndrome



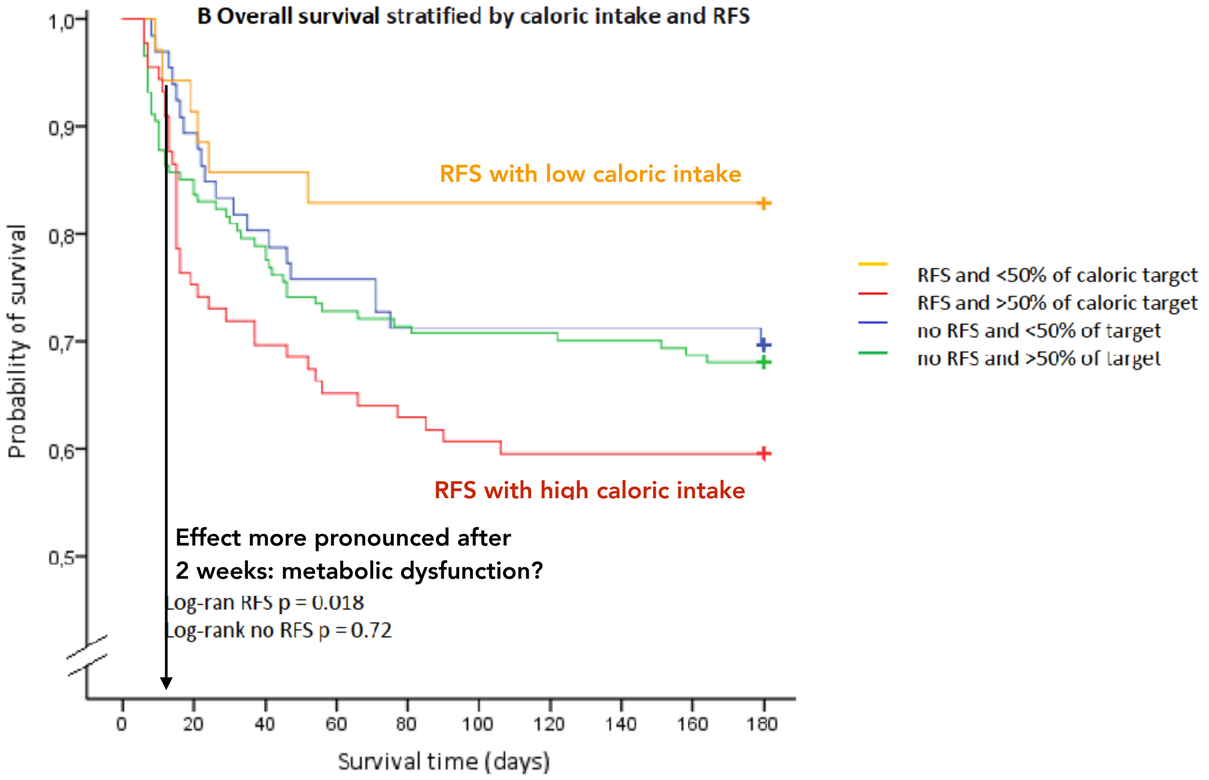
Doig GS, et al. Lancet Respir Med. 2015.

Caloric restriction (<500 kcal/day) and <50% of caloric intake during Refeeding Hypphophataemia is associated with lower mortality

Doig RCT



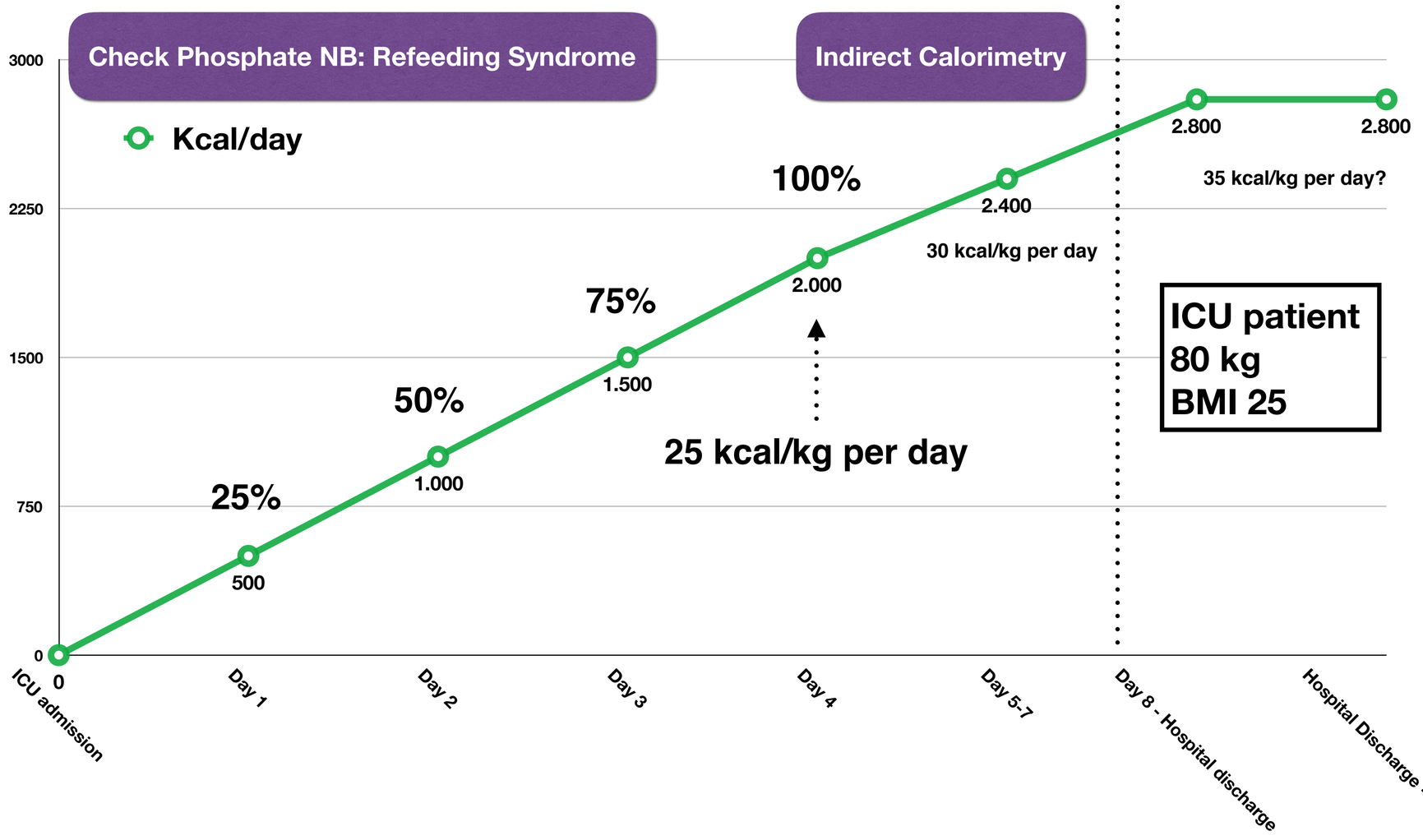
Olthof Retrospective study



Mortality separation after 2 weeks suggesting metabolic effect and not effect of electrolyte abnormalities

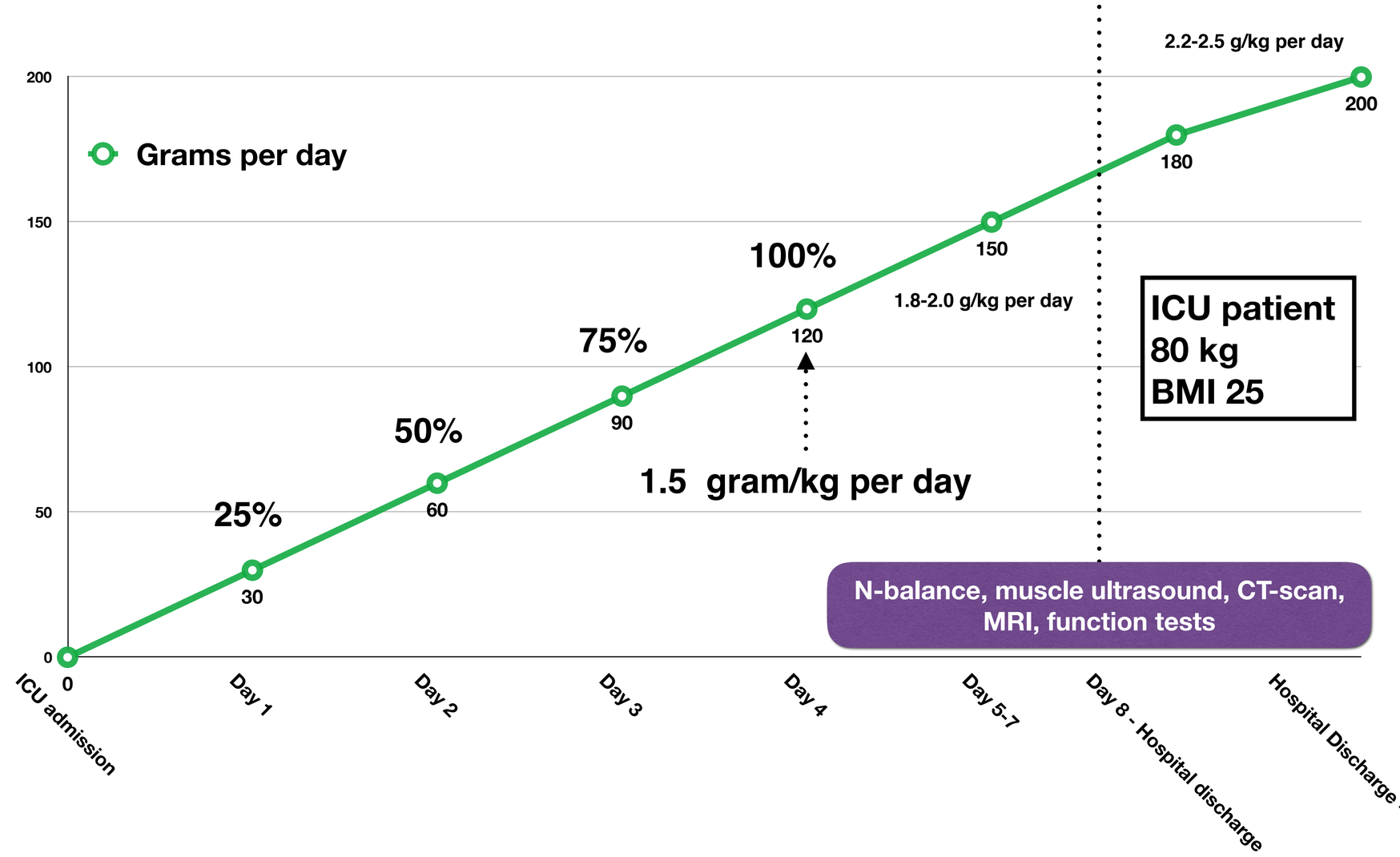
Doig GS, et al. Lancet Respir Med. 2015.
Olthof L, Koekkoek K, ..Van Zanten AR Clin Nutr 2017

Energy targets in ICU patients



Koekkoek KWAC, van Zanten ARH. Curr Opin Anaesthesiol. 2018

Protein targets in ICU patients



Koekkoek KWAC, van Zanten ARH. Curr Opin Anaesthesiol. 2018

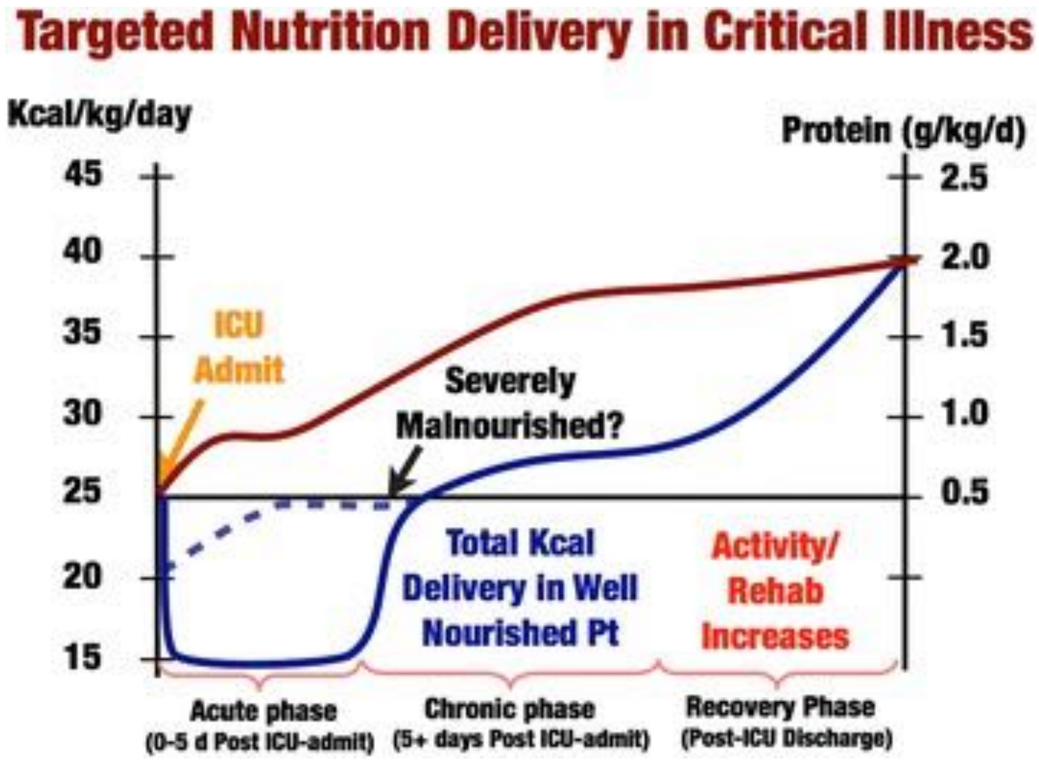
Tailoring nutrition therapy to illness and recovery

Protein intake:

- Day 1-5: increasing up to 1.2 g/kg bw
- Day 5 =>: increasing from 1.2 to 2.0 g/kg/day

Energy intake

- Day 1-5: 15 kcal/kg bw (malnourished (20 – 25)
- Day 5 till discharge: increasing to 27.5 kcal/kg bw
- Post ICU discharge: increasing 27.5 to 40 kcal/kg bw



Do we have the enteral feeds to meet the protein targets without overfeeding the patient in the ICU?

Wischmeyer Critical Care 2017, 21(Suppl 3):316

Very high intact-protein formula successfully provides protein intake according to nutritional recommendations in critically ill patients: a double-blind randomized trial

Arthur R.H. van Zanten, MD, PhD; Laurent Petit, MD, PhD; Jan De Waele, MD, PhD; Hans Kieft, MD, PhD, Janneke de Wilde, PhD; Peter van Horssen, PhD; Marianne Klebach, MSc; Zandrie Hofman, MSc

Submitted

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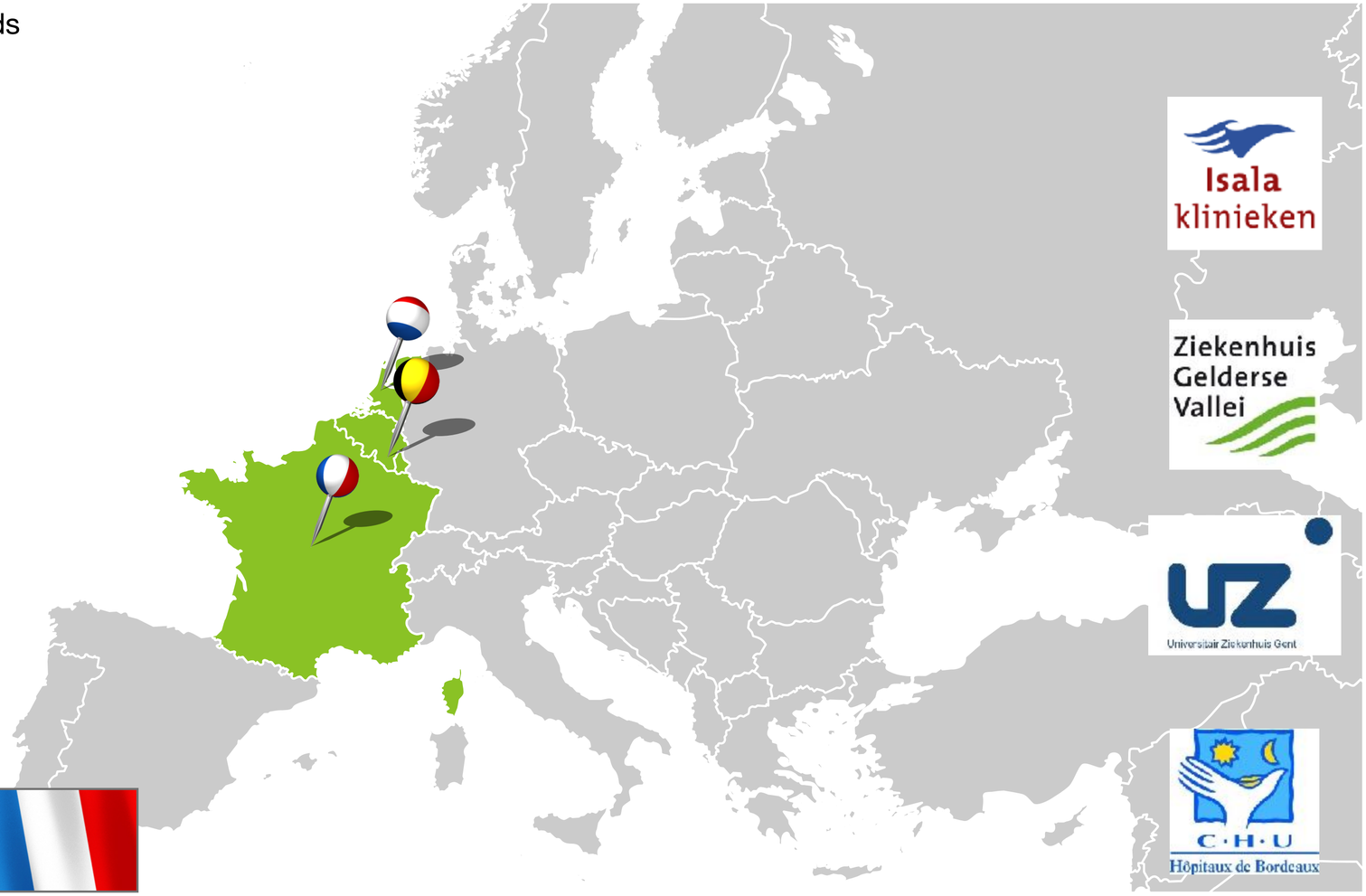

Van Zanten AR et al 2018 submitted

Study products and feeding regimen

	New very high intact- protein (VHPF)		Standard high intact- protein * (SHPF)	
	Per 100 ml	% of energy	Per 100 ml	% of energy
Energy	125 kcal		125 kcal	
Protein**	10 g	32 %	6.3 g	20 %
Carbohydrate	10.3 g	33 %	14.2 g	45 %
Fat	4.9 g	35%	4.9 g	35%

* : Nutrison Protein Plus (Nutricia, Zoetermeer),
** : intact protein sources: 35% whey, 25% casein, 20% soy and 20% pea

Feeding regimen recommended in protocol: Start enteral feeding with 20 ml/hour, Assess Gastric Residual Volume (GRV) and increase enteral feeding with 20 ml/hour every 6 hour, Target 25 kcal/kg bw per day, If BMI > 30 kcal/m², the Ideal Body Weight (IBW) was defined: 30 x height²

Van Zanten AR et al 2018 submitted

Patient characteristics

		SHPF (standard) (N = 22)	VHPF (new) (N = 22)
Sex (Male)	n (%)	13 (59.1%)	9 (40.9%)
Sex (Female)	n (%)	9 (40.9%)	13 (59.1%)
Age (years)	Mean (sd)	60.8 (15.2)	63.9 (13.3)
Body weight (kg)	Mean (sd)	91.2 (20.7)	84.9 (18.3)
BMI (kg/m^2)	Mean (sd)	30.7 (8.4)	30.3 (4.1)
Type of patient			
• Medical	n (%)	9 (40.9%)	8 (36.4%)
• Surgical	n (%)	10 (45.5%)	11 (50.0%)
• Surgical non-trauma	n (%)	4 (18.2%)	4 (18.2%)
• Surgical trauma*	n (%)	6 (27.3%)	7 (31.8%)
• Trauma	n (%)	9 (40.9%)	10 (45.5%)
• Trauma non-surgical	n (%)	3 (13.6%)	3 (13.6%)
SOFA score from screening	Median (Q1-Q3)	9 (7-11)	10 (9-11)
APACHE II score at baseline	Median (Q1-Q3)	24 (18-27)	25 (21-28)
Predicted mortality (%)	Mean (sd)	48.4 (18.7)	52.6 (17.7)
Adjusted predicted mortality (%)	Mean (sd)	38.7 (19.8)	42.7 (20.3)

*surgical trauma patients were included in both the surgical and trauma subgroup of patients

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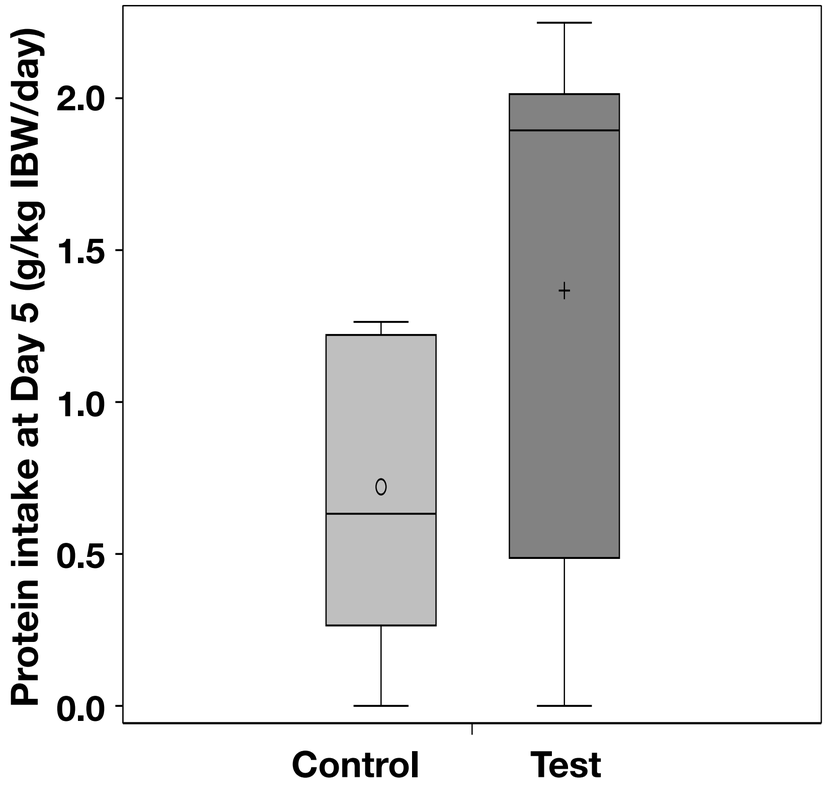
Protein intake at day 5



		SHPF (N = 22)	VHPF (N = 22)	p-value
Protein g/kg ABW	Mean (SD) Median (Q1-Q3)	0.68 (0.47) 0.6 (0.3-1.2)	1.32 (0.80) 1.6 (0.4-2.0)	
	LS mean (95% CI)	**0.76** (0.49, 1.03)	**1.49** (1.21, 1.78)	<0.001
Protein g/kg IBW	Mean (SD) Median (Q1-Q3)	0.72 (0.47) 0.6 (0.3-1.2)	1.37 (0.82) 1.9 (0.5-2.0)	
	LS mean (95% CI)	**0.80** (0.52, 1.07)	**1.54** (1.26, 1.83)	<0.001

VHPF: Statistically significant higher protein intake at day 5

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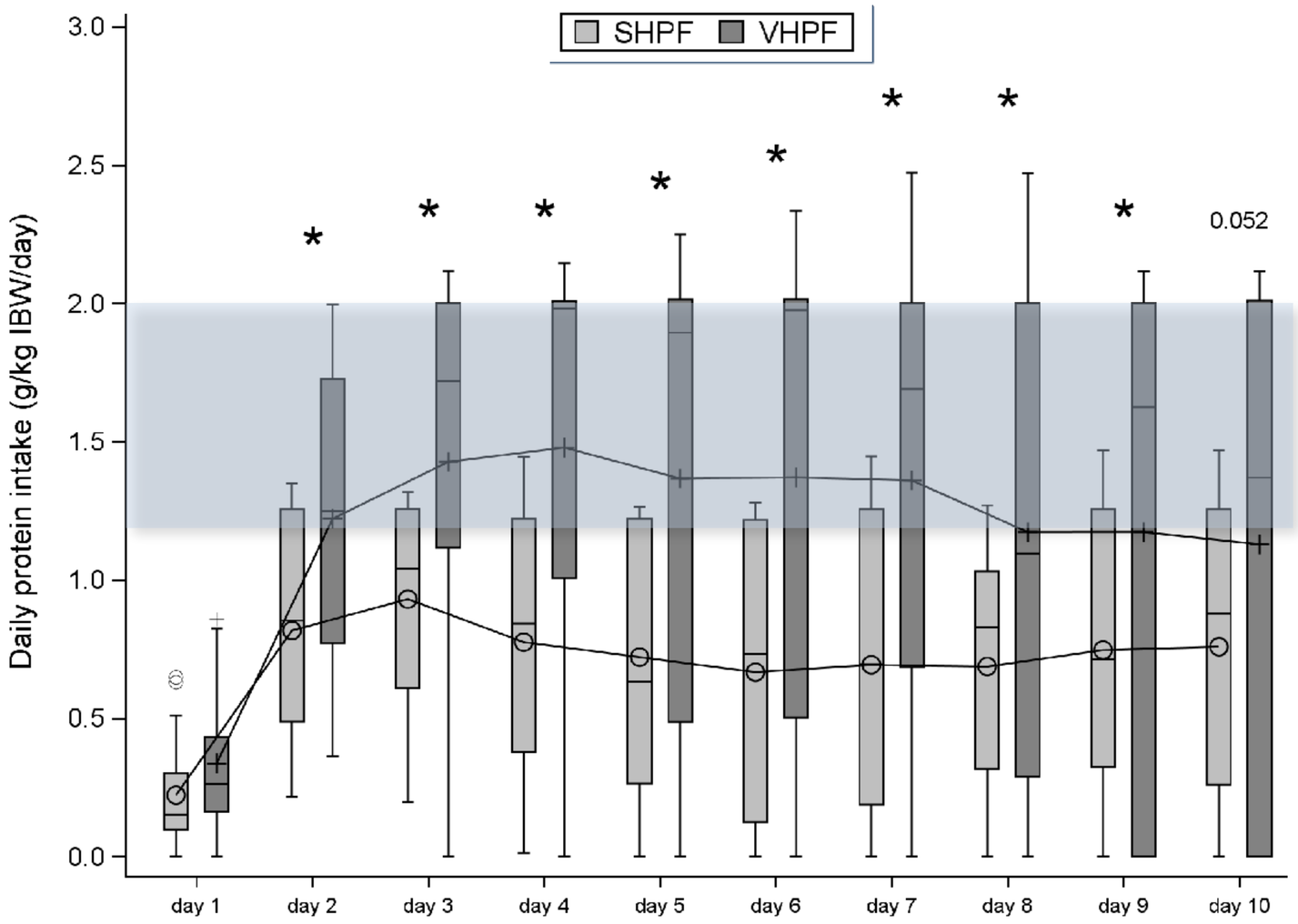
Protein intake day 1 - 10



Recommended protein intake range

VHPF: Statistically significant higher protein intake from day 1 - 10

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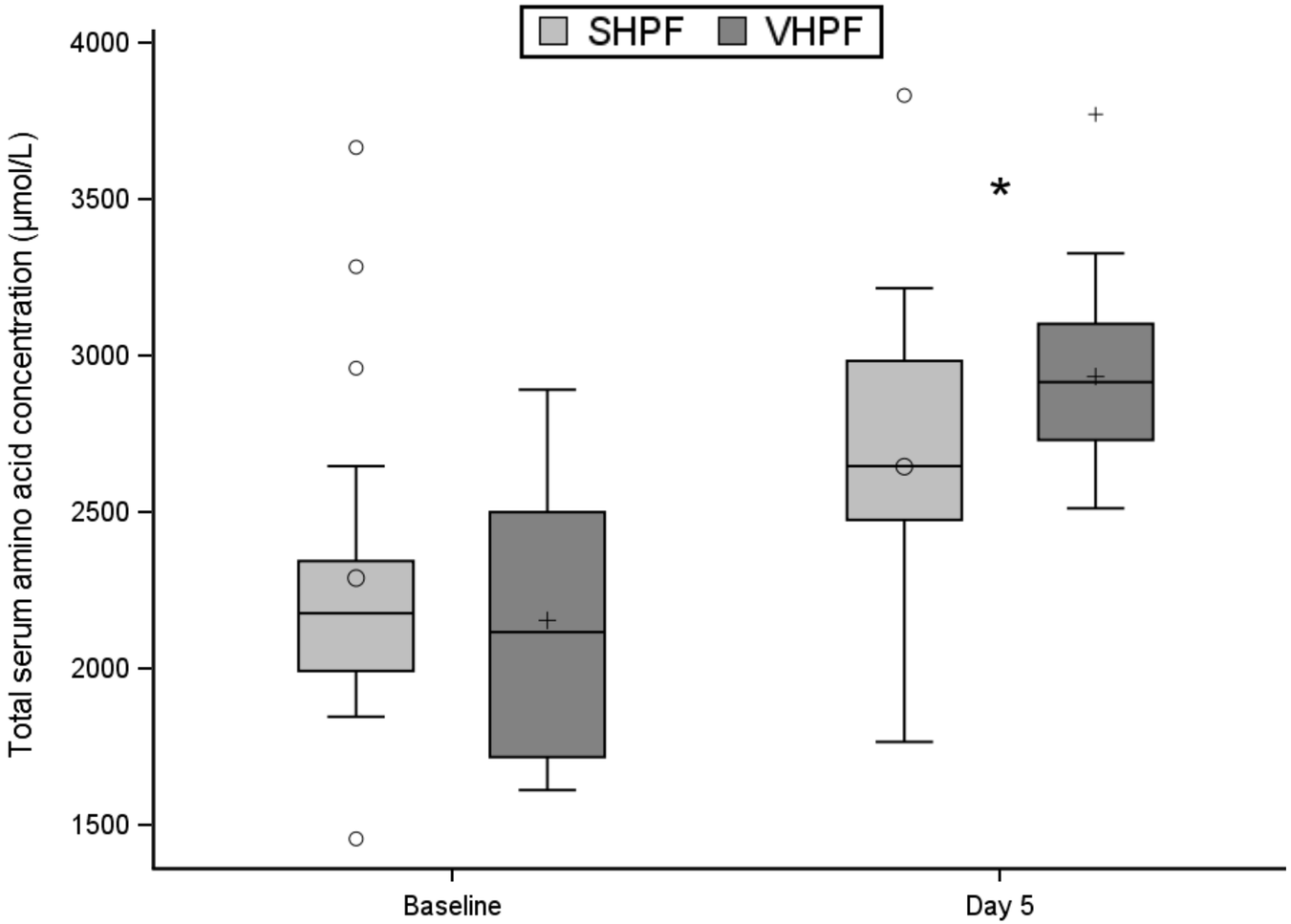
Plasma amino acid concentrations at baseline and day 5



VHPF: Statistically significant higher concentrations of plasma amino acids

*** : Statistically significant higher amino acid concentration at Day 5 (p=0.031)**

*** : Statistically significant within-group increase from baseline (both p <0.001)**

*** : Significantly higher increase from baseline compared to control (p=0.031)**

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Ziekenhuis Gelderse Vallei

Conclusions

- Feeding is essential for severely ill patients
- Early aggressive feeding energy and proteins has negative effects
- Refeeding syndrome is real in ICU patients and warrants caloric restriction
- Gradual progression of both calories and proteins is best
- After 5 days higher protein intake is pivotal
- We have new enteral feeds to achieve the targets
- Attention to feeding after ICU discharge on general wards and after hospital discharge is important
- Combining exercise and nutrition therapy may improve functional outcomes and potentially circumvent problems of mitochondrial dysfunction

Timing nutrition during and after critical illness is essential