AER 2019

AER

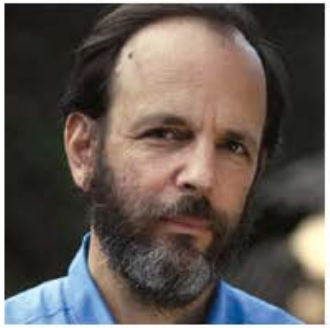
ACTUALITÉS EN RÉANIMATION

25ème AER : 19 & 20 novembre 2020

QUELLE NUTRITION A LA PHASE INITIALE ?

Jean-Charles Preiser, MD, PhD
Erasme University Hospital, Brussels

Actualités en réanimation
Lyon, 21 novembre 2019



The voice of science: let's agree to disagree

Consensus reports are the bedrock of science-based policy-making. But disagreement and arguments are more useful, says **Daniel Sarewitz**.

6 OCTOBER 2011 | VOL 478 | NATURE | 7

REAL SCIENCE DEPENDS FOR ITS **PROGRESS** ON CONTINUAL CHALLENGES TO THE CURRENT STATE OF ALWAYS-IMPERFECT **KNOWLEDGE.**

« Ou :
Ce qui était considéré comme
Vrai hier n'est plus forcément
La Vérité aujourd'hui »

Preiser *et al. Critical Care* (2015) 19:35
DOI 10.1186/s13054-015-0737-8

CRITICAL CARE

REVIEW Open Access

Metabolic and nutritional support of critically ill patients: consensus and controversies

Jean-Charles Preiser[1*], Arthur RH van Zanten[2], Mette M Berger[3], Gianni Biolo[4], Michael P Casaer[5], Gordon S Doig[6], Richard D Griffiths[7], Daren K Heyland[8], Michael Hiesmayr[9], Gaetano Iapichino[10], Alessandro Laviano[11], Claude Pichard[12], Pierre Singer[13], Greet Van den Berghe[5], Jan Wernerman[14], Paul Wischmeyer[15] and Jean-Louis Vincent[1]

Provision of Nutrients to the Acutely Ill

Introducing the "Baby Stomach" Concept

Am J Respir Crit Care Med. 2017 Jun 8.
doi: 10.1164/rccm.201705-0919ED

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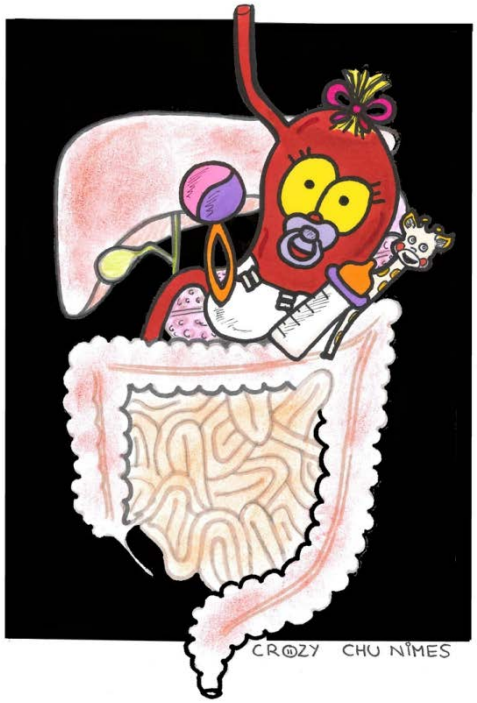
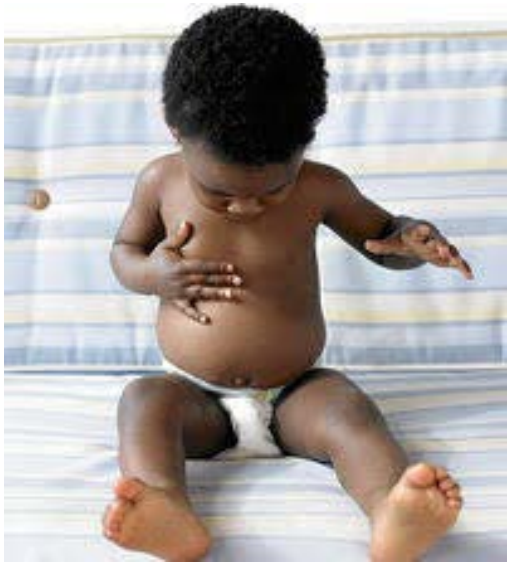
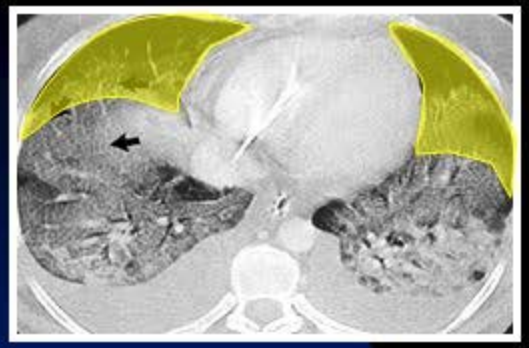
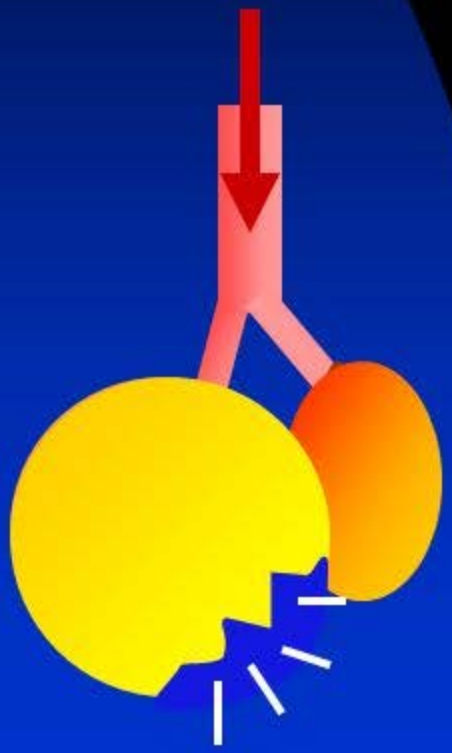








The "Baby lung"

- ARDS Lung has "normal" & unaerated / partially aerated alveoli
- "Normal" segments inflate easily
- Unaerated segments distend poorly
  - High pressure
  - Slow response
- Normal lung segments may be over-inflated when ventilated with traditional tidal volumes

ARDSnet Tidal Volume Study

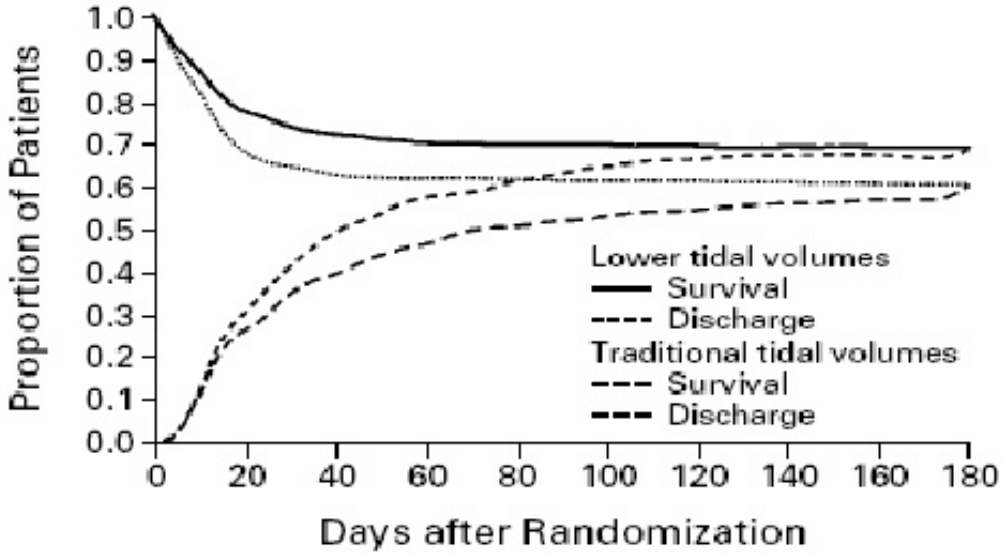
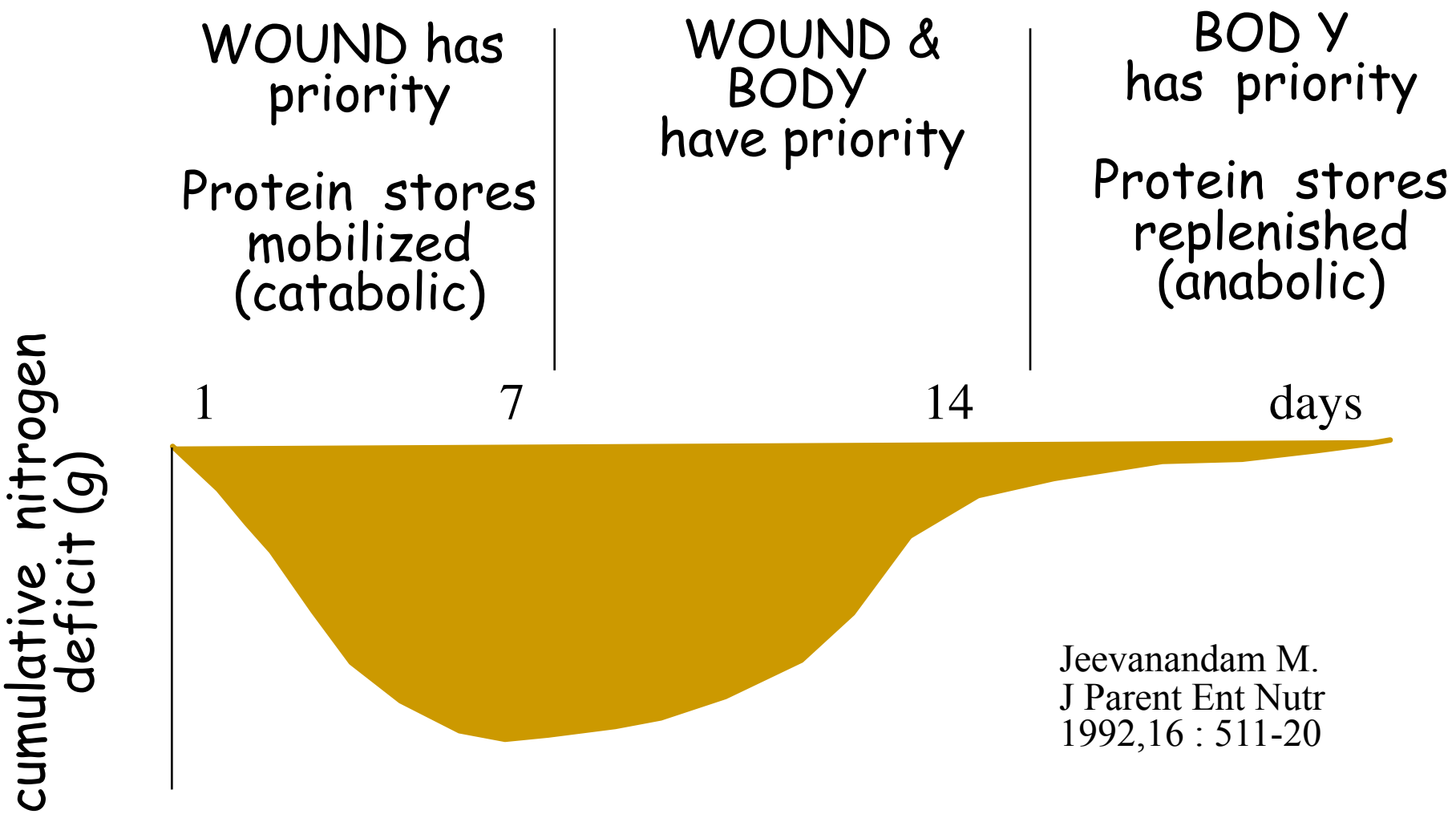
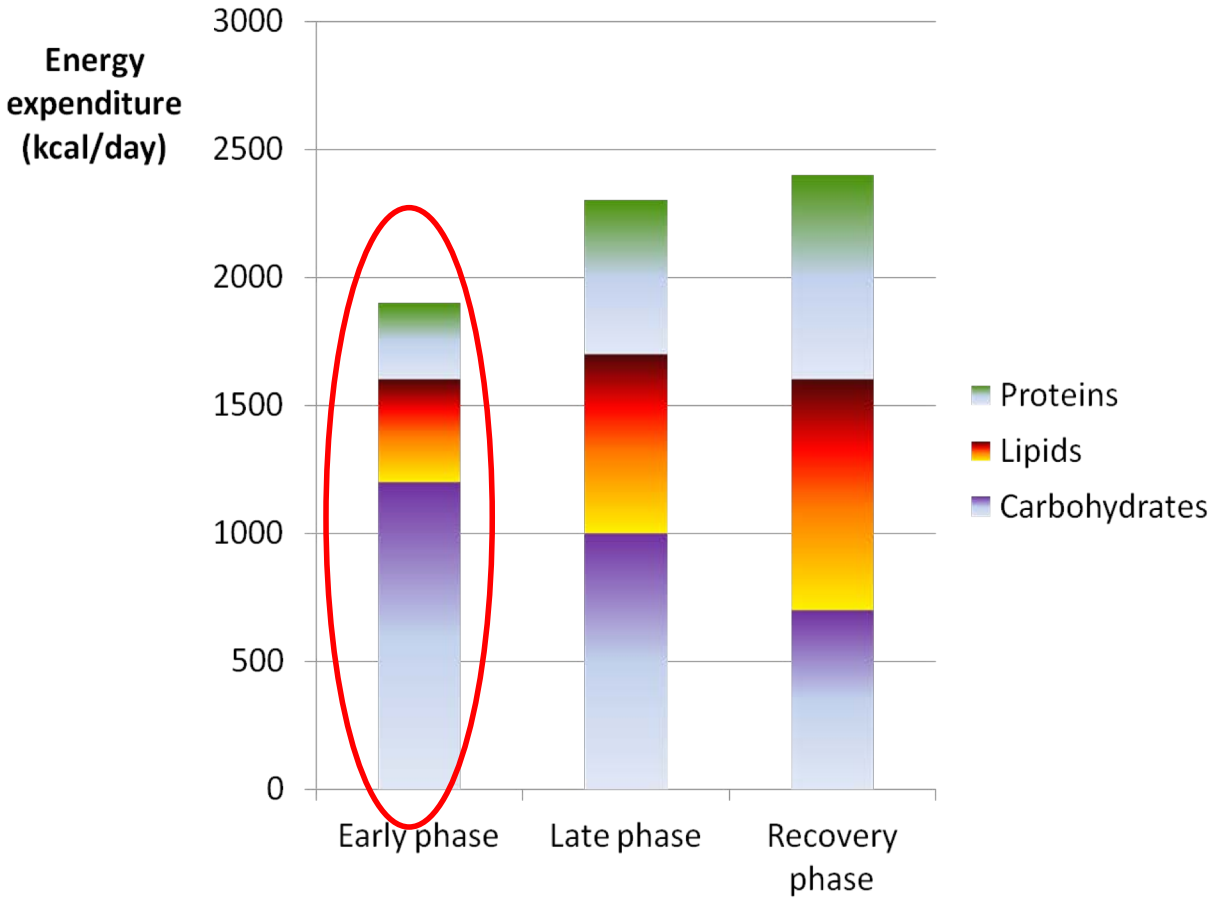


Figure 1. Probability of Survival and of Being Discharged Home and Breathing without Assistance during the First 180 Days after Randomization in Patients with Acute Lung Injury and the Acute Respiratory Distress Syndrome.

ARDSnet, NEJM 2000


WOUND has priority
Protein stores mobilized (catabolic)
WOUND & BODY have priority
BOD Y has priority
Protein stores replenished (anabolic)
1
7
14
days
cumulative nitrogen deficit (g)
Jeevanandam M.
J Parent Ent Nutr
1992,16 : 511-20

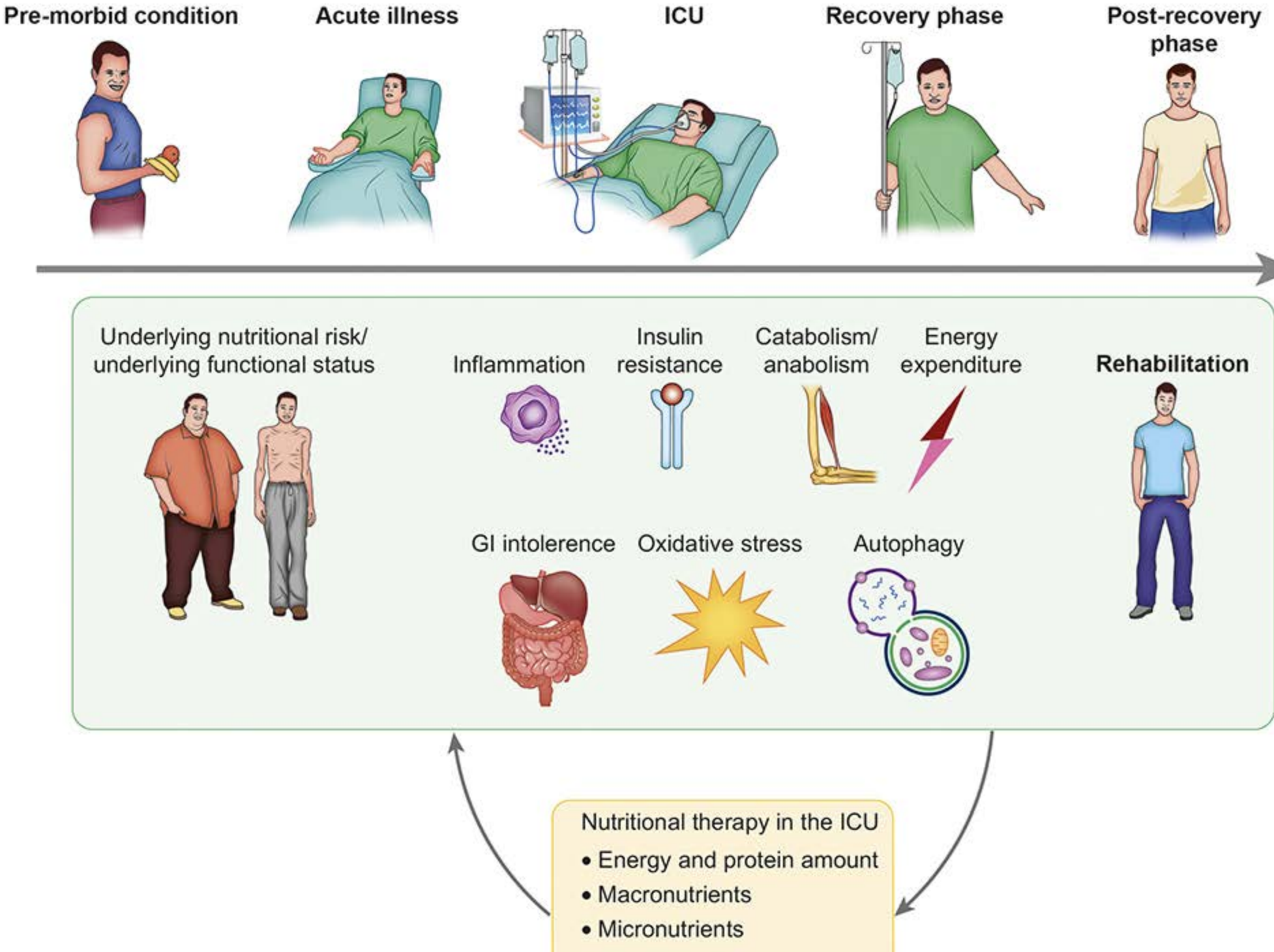
The 3 post-injury phases



British Journal of Anaesthesia Page 1 of 10
doi:10.1093/bja/aeu187

Preiser, Ichai, Orban, Groeneveld BJA

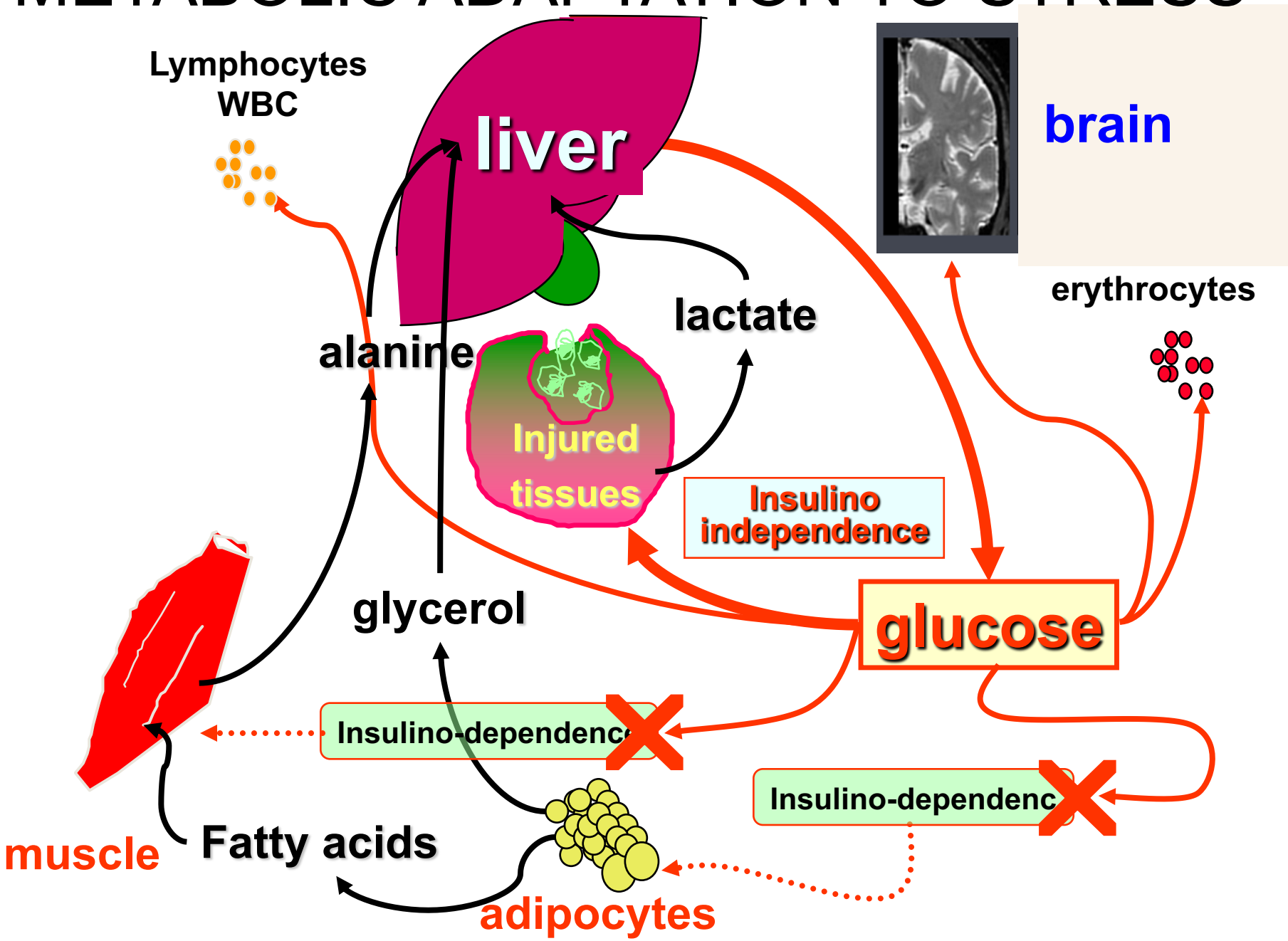
Metabolic response to the stress of critical illness


Pre-morbid condition
Acute illness
ICU
Recovery phase
Post-recovery phase
Underlying nutritional risk/ underlying functional status
Inflammation
Insulin resistance
Catabolism/ anabolism
Energy expenditure
Rehabilitation
GI intolerence
Oxidative stress
Autophagy
Nutritional therapy in the ICU
• Energy and protein amount
• Macronutrients
• Micronutrients

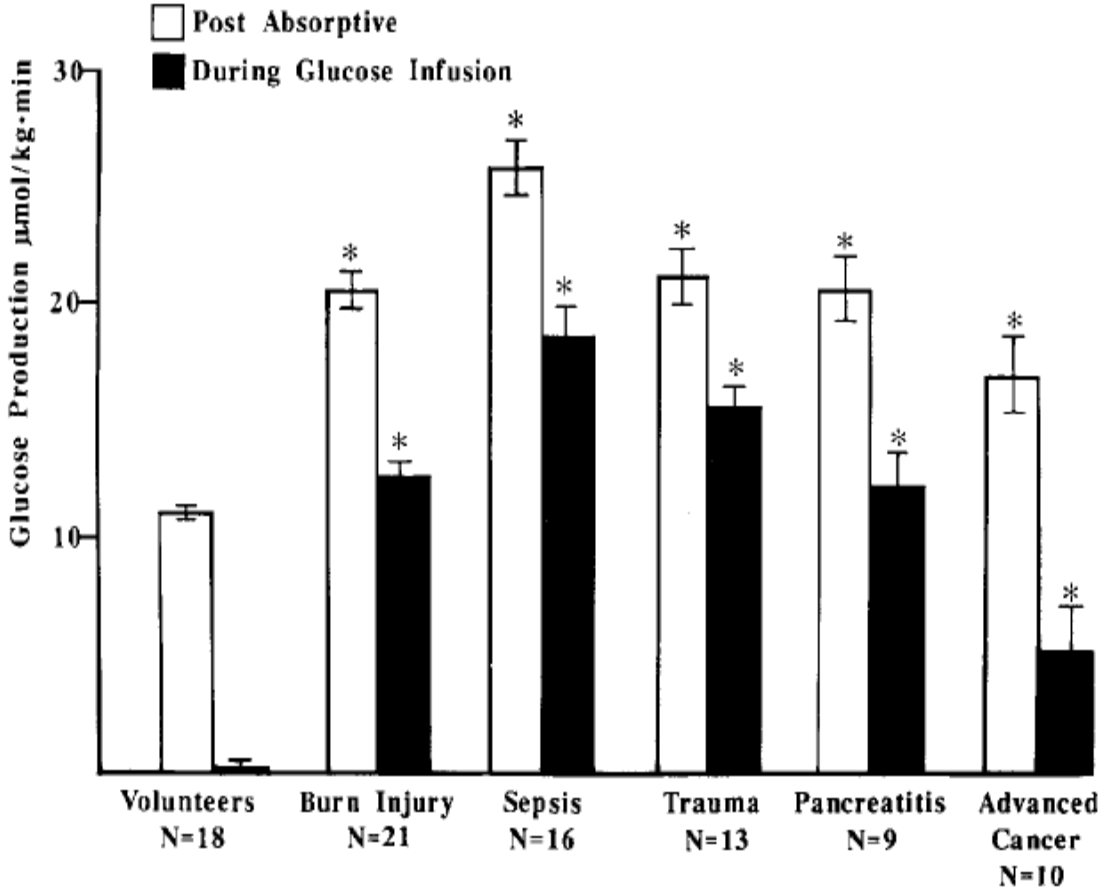
Phase aïgue / précoce
Quelques heures à 3-7 jours..

- ***Anorexie***
- ***Dépense énergétique limitée***
- ***Utilisation préférentielle du glucose comme substrat énergétique***

METABOLIC ADAPTATION TO STRESS



Rate of basal glucose production and endogenous production during glucose infusion in various conditions



Wolfe RR, Eur J Clin Nutr 1999

Critically ill patients are able to match their REE

Tappy L et al Crit Care Med 1998; 26: 860

3 day starvation

- **Resting metabolic rate** **1824 kcal/ day**
- **Glycemia** **7.3 mmol/L**
- **Endogenous glucose production** **360 g/ day (1360 kcal/d)**
- **Net protein balance** **-117 g/ day**

Clinical Nutrition 31 (2012) 1002–1007

Contents lists available at SciVerse ScienceDirect

Clinical Nutrition

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

Opinion paper

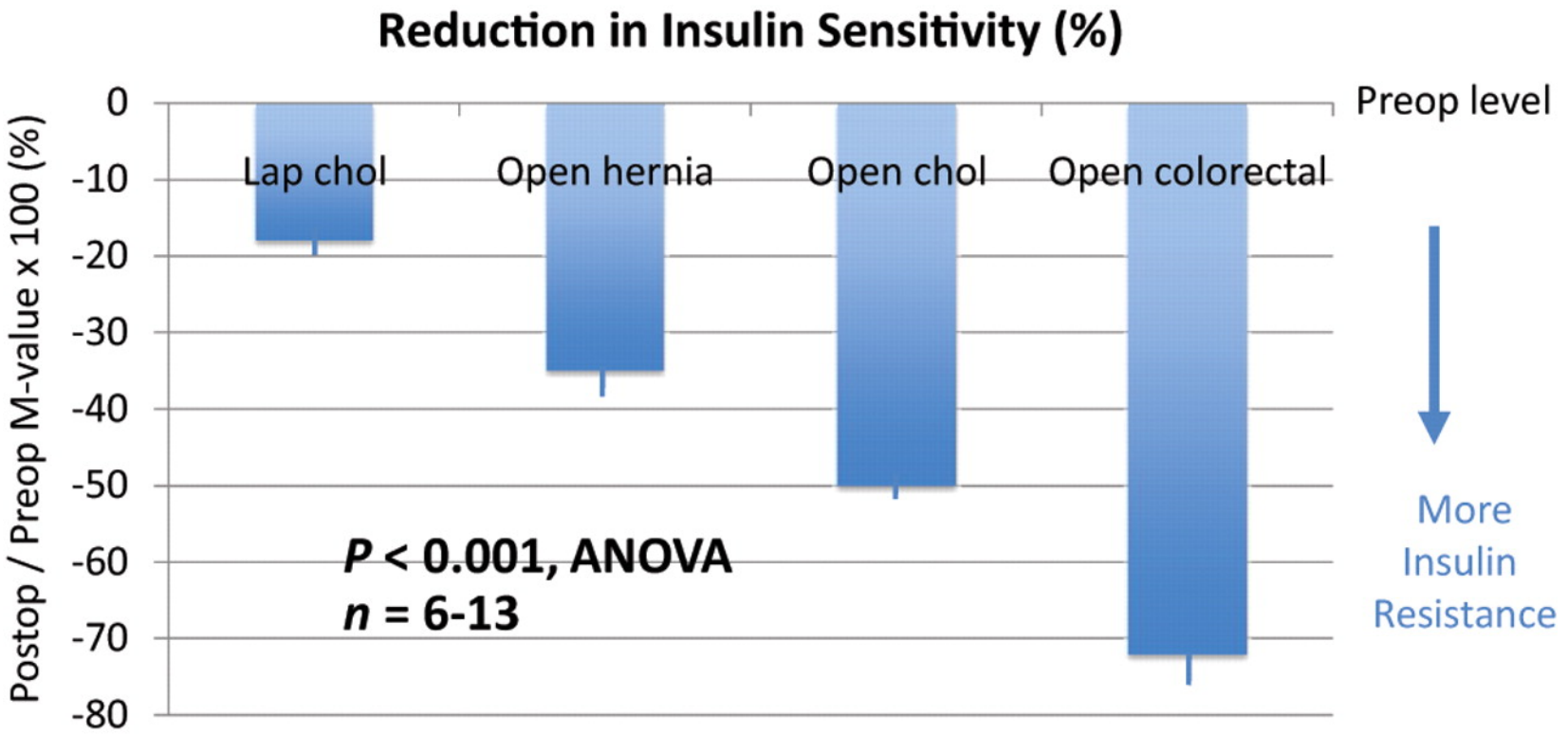
The evolutionary benefit of insulin resistance

Maarten R. Soeters [a,*], Peter B. Soeters [b,**]

[a] Department of Endocrinology and Metabolism, Academic Medical Center, University of Amsterdam, PO Box 22660, 1100 DD Amsterdam, The Netherlands
[b] Department of Surgery, Maastricht University Medical Center, Maastricht University, The Netherlands

Here we hypothesize that insulin resistance promotes glucose availability for the inflammatory response in the defense against starvation, disease and trauma and to promote growth during lactation, pregnancy, puberty and cancer, and in situations where the organism prepares itself for migration or hibernation. This mechanism is evolutionarily well preserved in multiple species, including the human organism. It is also likely that in other insulin resistance states like chronic inflammatory illnesses (chronic obstructive pulmonary disease, rheumatoid arthritis etc.), insulin resistance is initially beneficial in promoting the inflammatory response and healing and not the result of mitochondrial dysfunction.[55,56]

Figure 1. The relative change ((M-value after surgery/M-value after surgery) × 100) in insulin sensitivity after different surgical procedures and surgical approaches (open vs laparsocopic cholecystectomy).

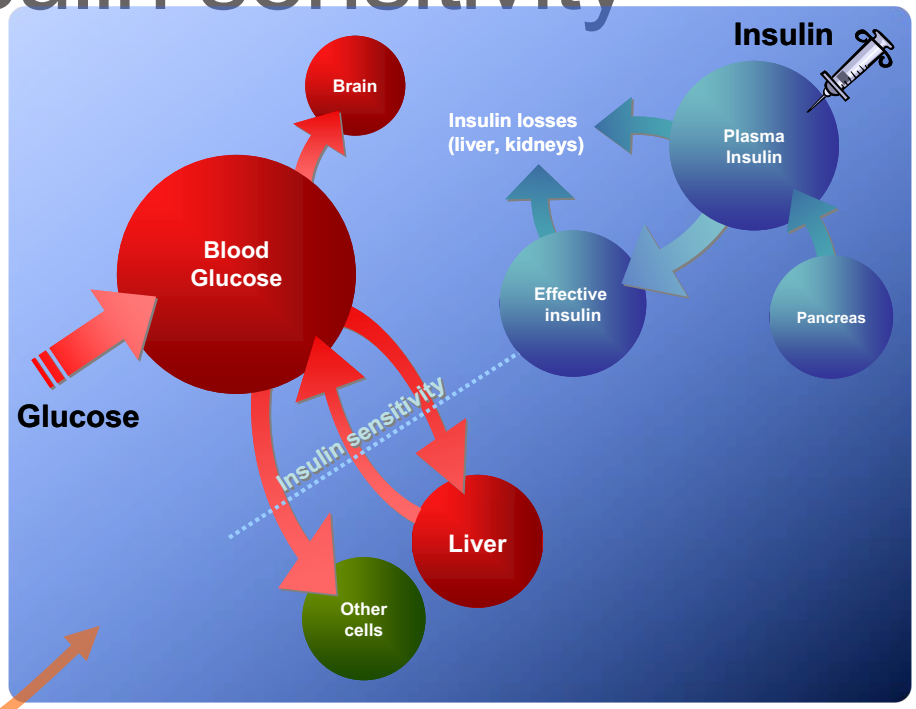


Ljungqvist O JPEN J Parenter Enteral Nutr 2012;36:389-398

JPEN JOURNAL OF PARENTERAL AND ENTERAL NUTRITION

Determination of insulin sensitivity

- Model-based approach:
  - Clinically validated in many trials (real-time BG control, retrospective clinical, and simulated trials)
  - Correlates well with euglycaemic-clamp ISI (r = 0.99)
  - Provides a means to quantify S_I and IR in critically ill patients
  - S_I identified hourly for every patient
- BG system model



Model equations

$$\dot{G} = -p_G.G - S_I.G.\frac{Q}{1+\alpha_G Q} + \frac{P(t)+EGP-CNS}{V_G(t)}$$

$$\dot{I} = -\frac{nI}{1+\alpha_I I} + \frac{u_{ex}(t)}{V_I} + e^{-(k_I u_{ex}(t))} I_B$$

$$\dot{Q} = -kQ + kI$$

Dextrose Absorption

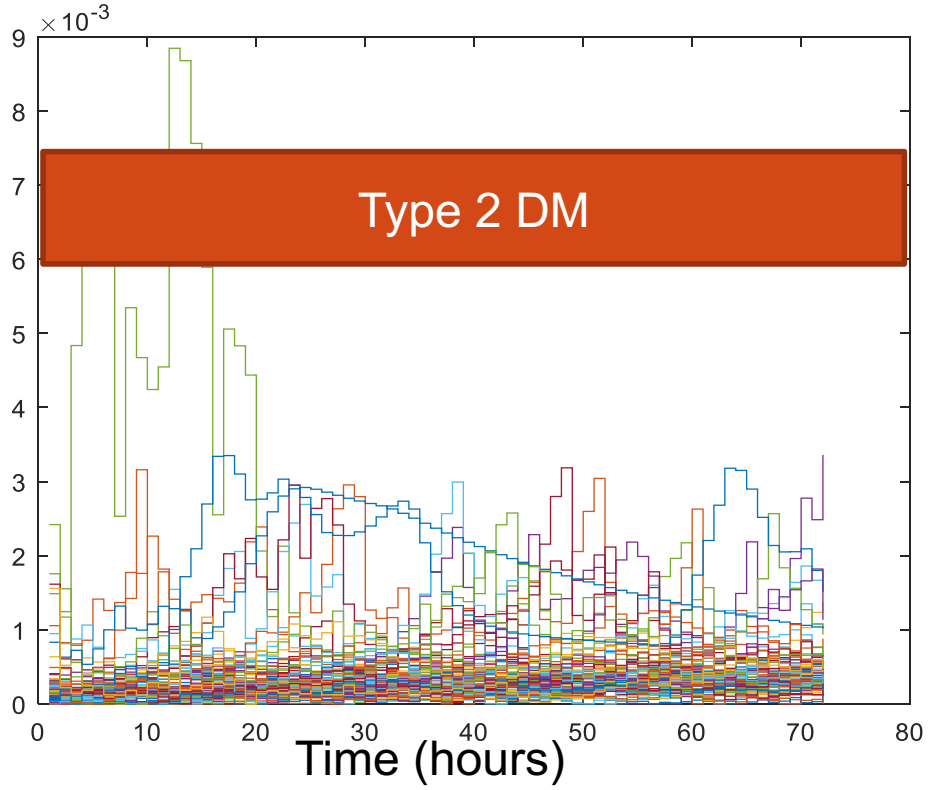
$$P(t) = \min(d_2 P_2, P_{\max})$$

$$\dot{P}_2 = -\min(d_2 P_2, P_{\max}) + d_1 P_1$$

$$\dot{P}_1 = -d_1 P_1 + D(t)$$

Individual time couse of insulin sensitivity

SI (L/mU/min)



N = 81 patients, all staying 3 days or longer form Uyttendaele et al, Critical Care 2017

PENDANT LA PHASE AIGUE

LES BESOINS CALORIQUES SONT INFERIEURS A LA DEPENSE ENERGETIQUE.

Resting energy expenditure, calorie and protein consumption in critically ill patients: a retrospective cohort study

Oren Zusman[1*], Miriam Theilla[2,3], Jonathan Cohen[2,4], Ilya Kagan[2], Itai Bendavid[2] and Pierre Singer[2,4]

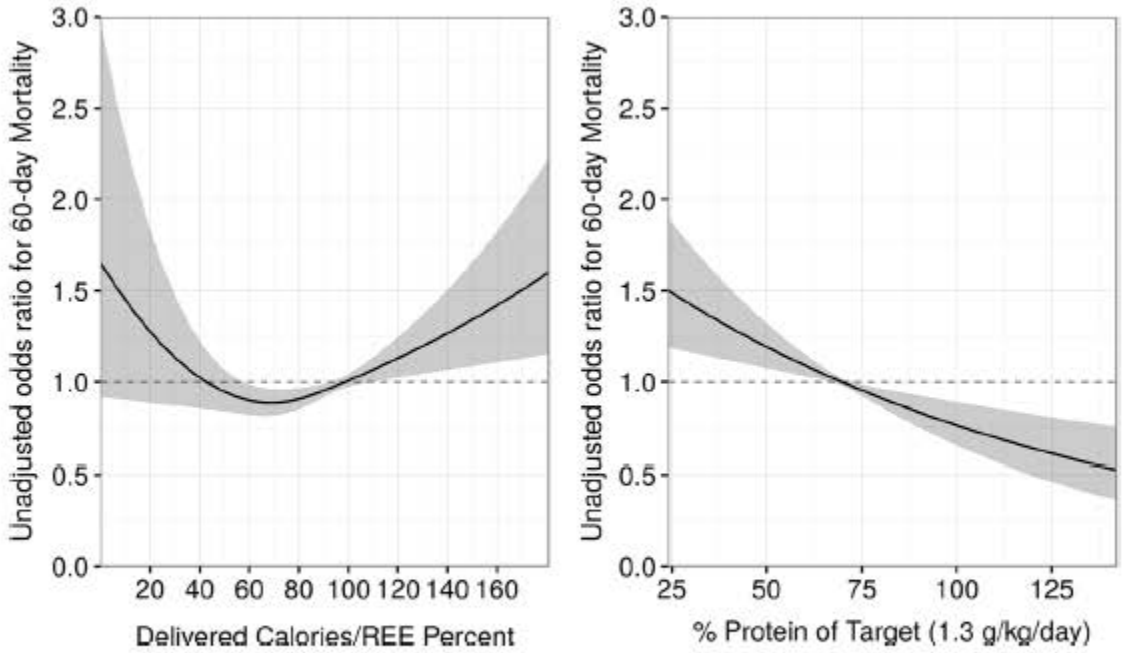


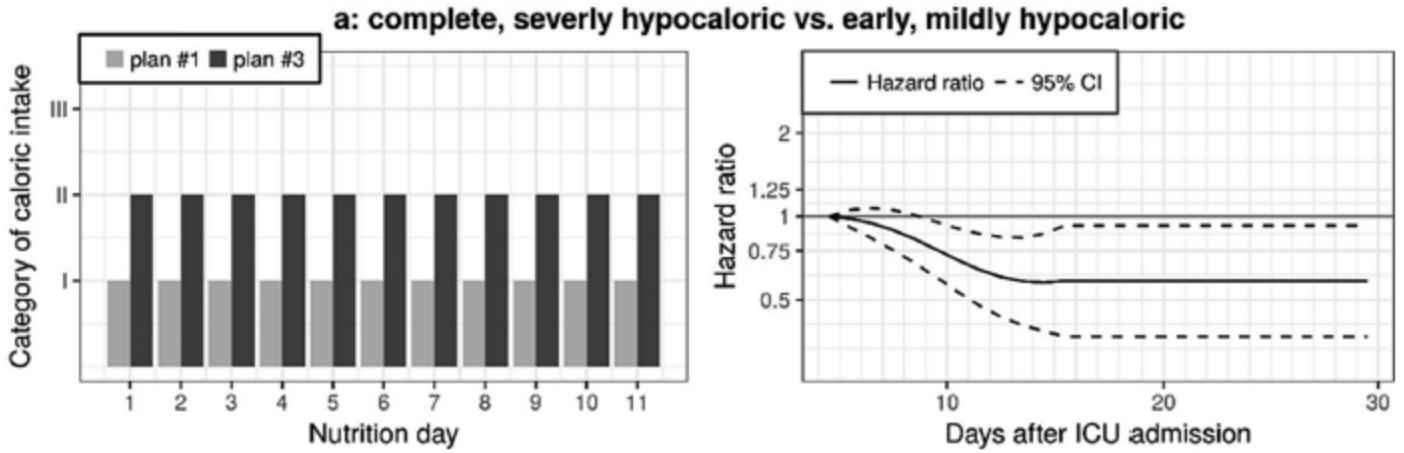
Fig. 2 Association of administered calories/resting energy expenditure (Adcal/REE) percent with 60-day mortality (*left*), and protein intake by daily requirement (1.3 g/kg/d) with 60-day mortality (*right*) by odds ratio. *REE* resting energy expenditure

N = 1,171

Calorie intake and short-term survival of critically ill patients

Wolfgang H. Hartl [a, *, 1], Andreas Bender [b, 1], Fabian Scheipl [b], David Kuppinger [a], Andrew G. Day [c], Helmut Küchenhoff [b]

Clinical Nutrition 38 (2019) 660–667

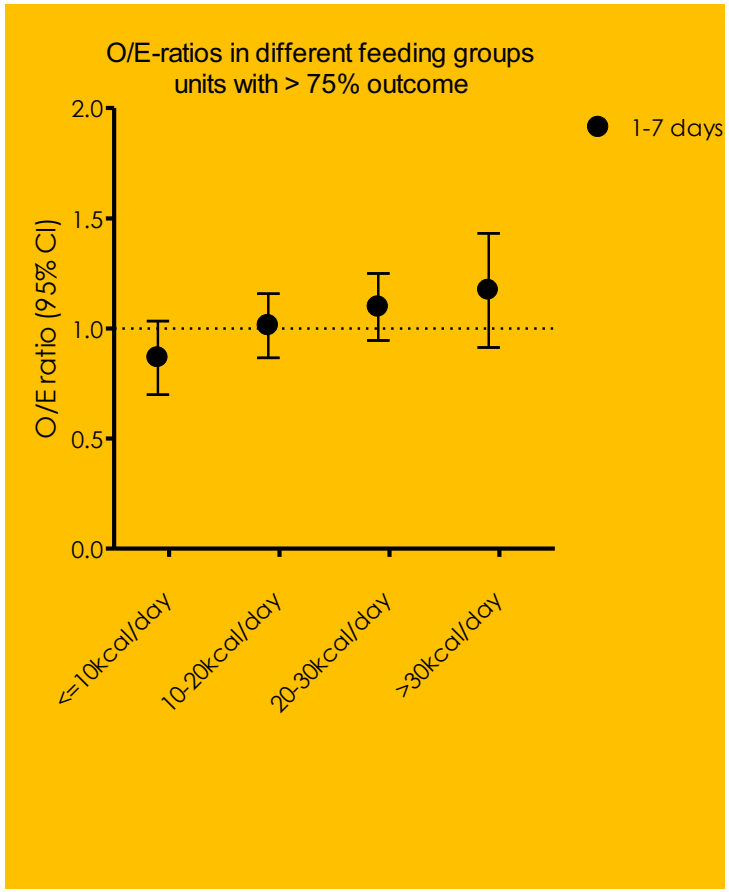


Methods: 9661 critically ill patients from 451 ICUs were extracted from an international database. We examined associations between survival time and three pragmatic nutritional categories (I: <30% of target, II: 30–70%, III: >70%) reflecting different amounts of total daily calorie intake. We compared hazard ratios for the 30-day risk of dying estimated for different hypothetical nutrition support plans (different categories of daily calorie intake during the first 11 days after ICU admission). To minimize

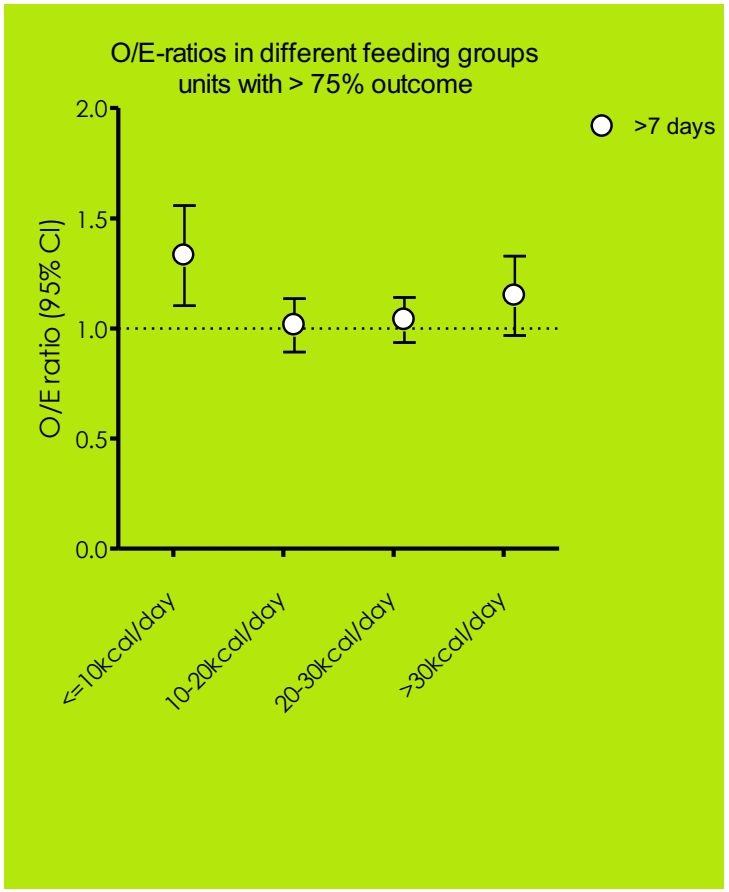
Observed/expected mortality and caloric intake

Hiesmayr et al NutritionDay 2007-2013, n= 9870

D1-D7



>D7



The pyramid of evidence-based medicine

Online version at http://www.minervamedica.it

Minerva Anestesiologica 2016 August;82(8):908-13

JOURNAL CLUB CRITIQUE

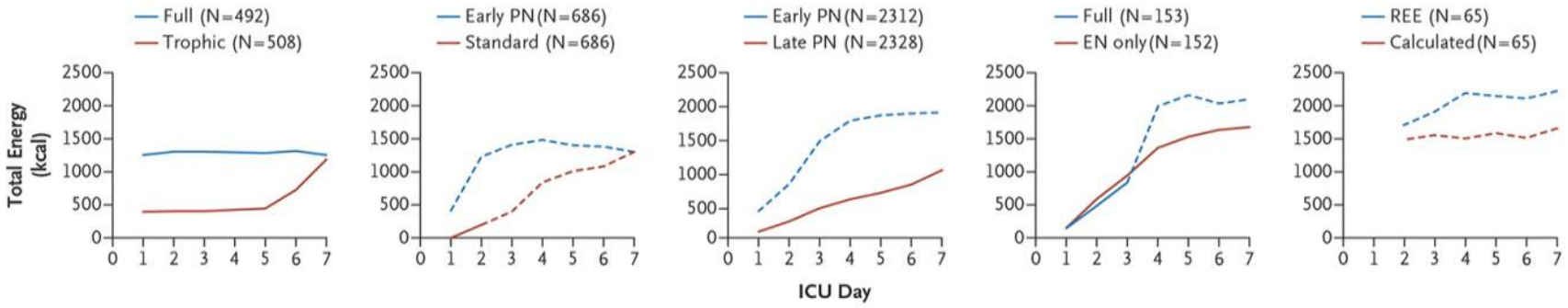
Nutrition in critically ill patients: where do we stand?

Jean-Charles PREISER *, Fabio Silvio TACCONE

TABLE I.—*A summary of the most important studies on nutrition on the critically ill patient.*

Study	Inclusion criteria	Number of patients (CTRL/intervention)	Type of intervention	Primary outcome
EPaNIC [7]	ICU admission Nutrition risk score >3	2312/2328	Early PN *vs.* late PN	Duration of ICU dependency: 4 [2-9] *vs.* 3 [2-7] P<0.02
EDEN [6]	Acute lung injury mechanical ventilation	508/492	Trophic *vs.* full feeding	Ventilator-free days 14.9 [13.9-15.8] *vs.* 15.0 [14.1-15.9] NS
SPN [8]	Patients in the ICU at day 3 expected ICU stay ≥5 days Less than 60% of target energy by EN	153/152	Supplemental PN *vs.* EN alone	Number of infections: * 100 *vs.* 114 NS
EarlyPN [9]	ICU patients ineligible for EN	686/686	Standard *vs.* early PN	60-day mortality: 22.6% *vs.* 21.5 % P=0.6
CALORIES [10]	Expected nutrition support >2 days Expected ICU stay >3 days	1191/1197	Early PN *vs.* early EN	30-day mortality: 33.1% *vs.* 34.2% P=0.57
PermiT [11]	EN within 48 hours from admission	445/440	Permissive *vs.* full EN	90-day mortality: 27.2% *vs.* 28.9% P=0.58

Recent large nutrition RCT's



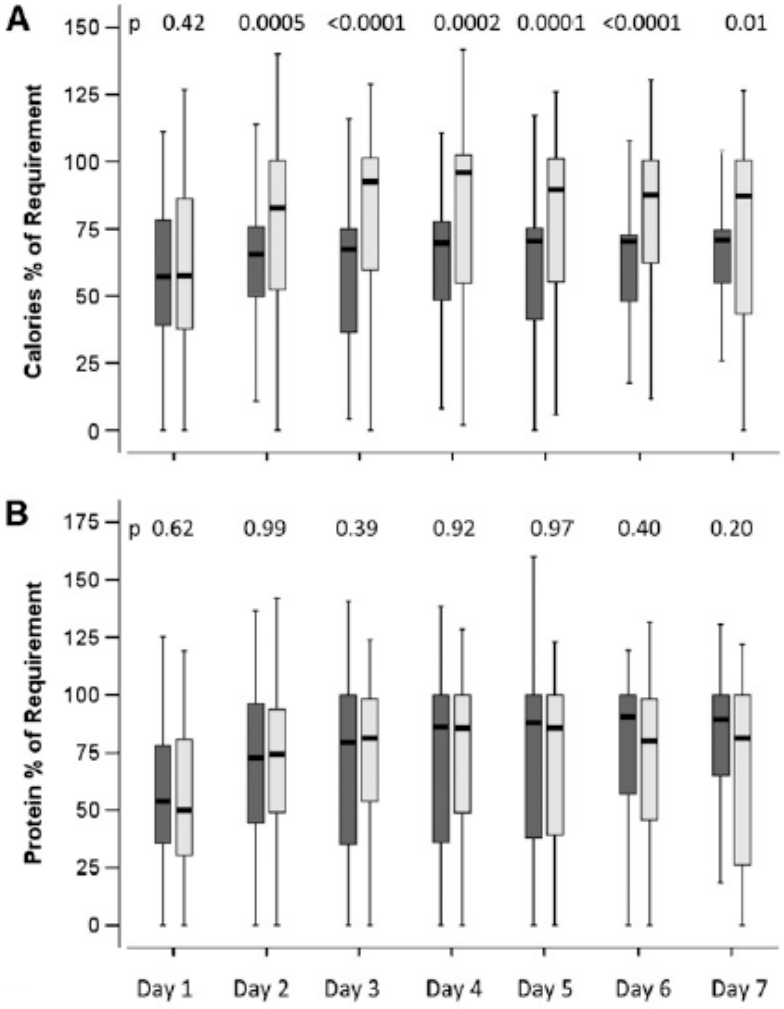
	EDEN Trial (N=1000)	Early PN Trial (N=1372)	EPaNIC Trial (N=4640)	SPN Trial (N=305)	TICACOS (N=130)
Type of Patients	Medical (acute lung injury) Eligible for EN	Mixed medical and surgical EN relatively contraindicated (short term)	Mixed medical and surgical (unselected) With nutritional risk (NRS, ≥3)	Mixed medical and surgical (on day 4) Eligible for EN but <60% target	Mixed medical and surgical
New Infections in ICU	Unaffected	Unaffected	More with early PN	Between day 9 and day 28: less with SPN From randomization to day 28: unaffected	More with REE
Duration of Mechanical Ventilation	Unaffected	Shorter with early PN	Longer with early PN	Unaffected	Longer with REE
Length of Stay in ICU	Unaffected	Unaffected	Longer with early PN	Unaffected	Longer with REE
Mortality in ICU	Unaffected	Unaffected (60-day mortality: unaffected)	Unaffected	Unaffected	Unaffected (trend toward reduced hospital mortality)

Casaer MP, Van den Berghe G. N Engl J Med 2014;370:1227-1236.

Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial[1–3]

Yaseen M Arabi, Hani M Tamim, Gousia S Dhar, Abdulaziz Al-Dawood, Muhammad Al-Sultan, Maram H Sakkijha, Salim H Kahoul, and Riette Brits

Am J Clin Nutr 2011



Design: This study had a 2 × 2 factorial, randomized, controlled design. Eligible patients were randomly assigned to permissive underfeeding or target feeding groups (caloric goal: 60–70% compared with 90–100% of calculated requirement, respectively) with either IIT or CIT (target blood glucose: 4.4–6.1 compared with 10–11.1 mmol/L, respectively).

Results: Twenty-eight-day all-cause mortality was 18.3% in the permissive underfeeding group compared with 23.3% in the target feeding group (relative risk: 0.79; 95% CI: 0.48, 1.29; $P = 0.34$). Hospital mortality was lower in the permissive underfeeding group than in the target group (30.0% compared with 42.5%, respectively; relative risk: 0.71; 95% CI: 0.50, 0.99; $P = 0.04$). No significant differences in outcomes were observed between the IIT and CIT groups.

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

Journal of Parenteral and Enteral Nutrition

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

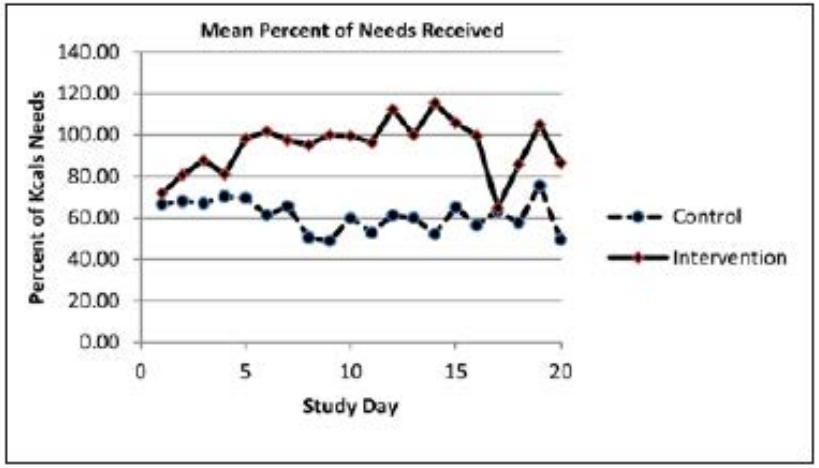


Figure 2. Mean percentage of energy needs received per day in the intensive medical nutrition therapy (Control) and standard nutrition support care (Intervention) groups.

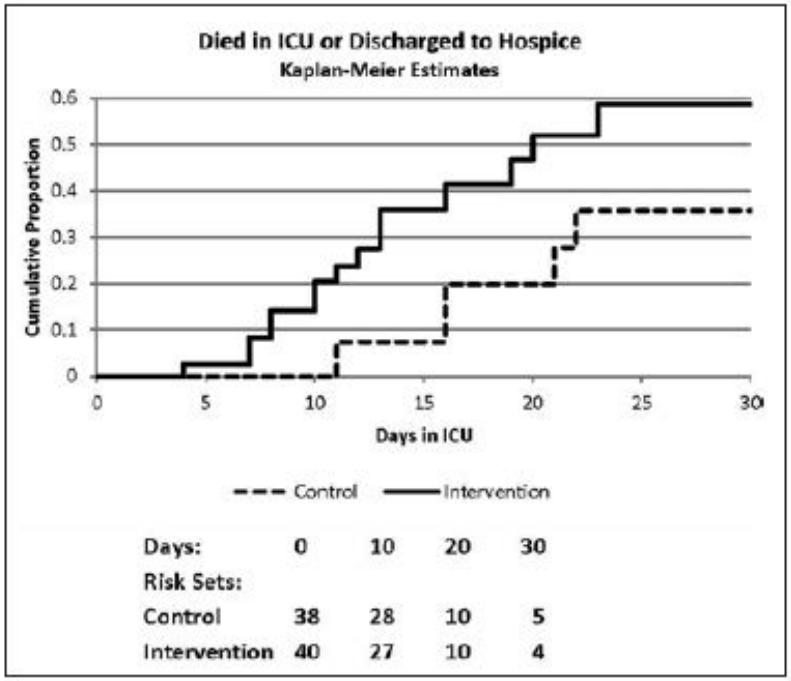


Figure 3. Kaplan-Meier estimates of time to death and log-rank test results for unadjusted comparisons between intensive medical nutrition therapy and standard nutrition support care.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early versus Late Parenteral Nutrition in Critically Ill Adults

Phi
Y
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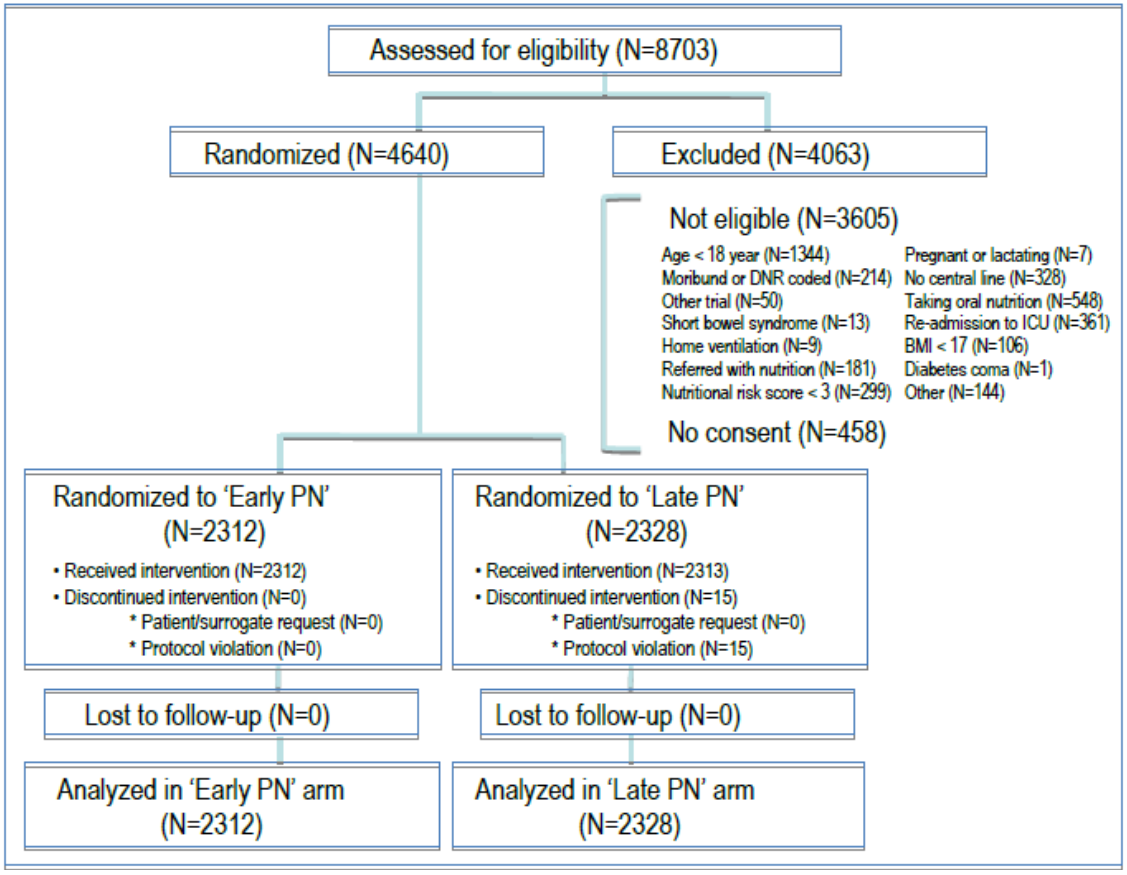
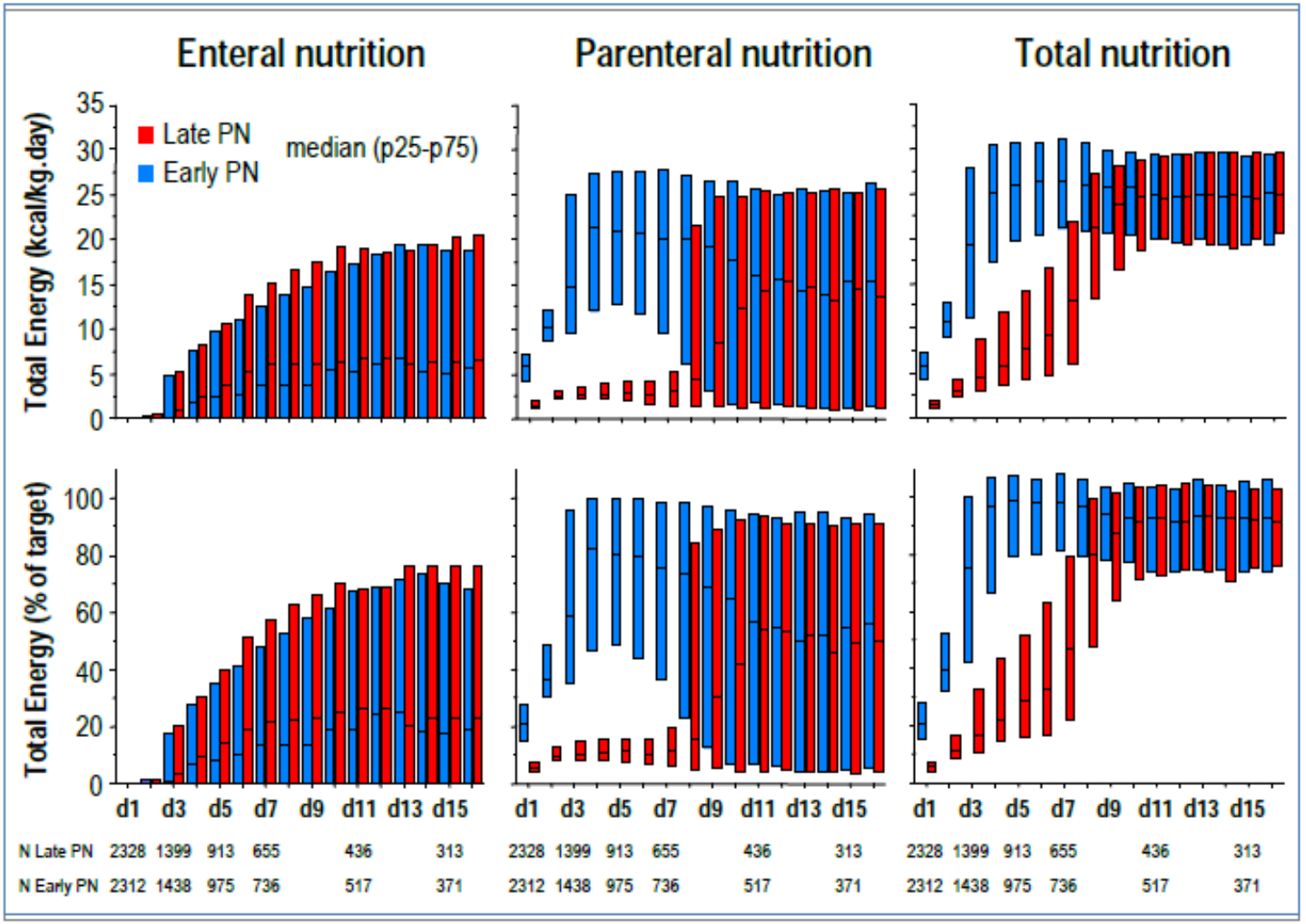
Figure 1: Consort diagram



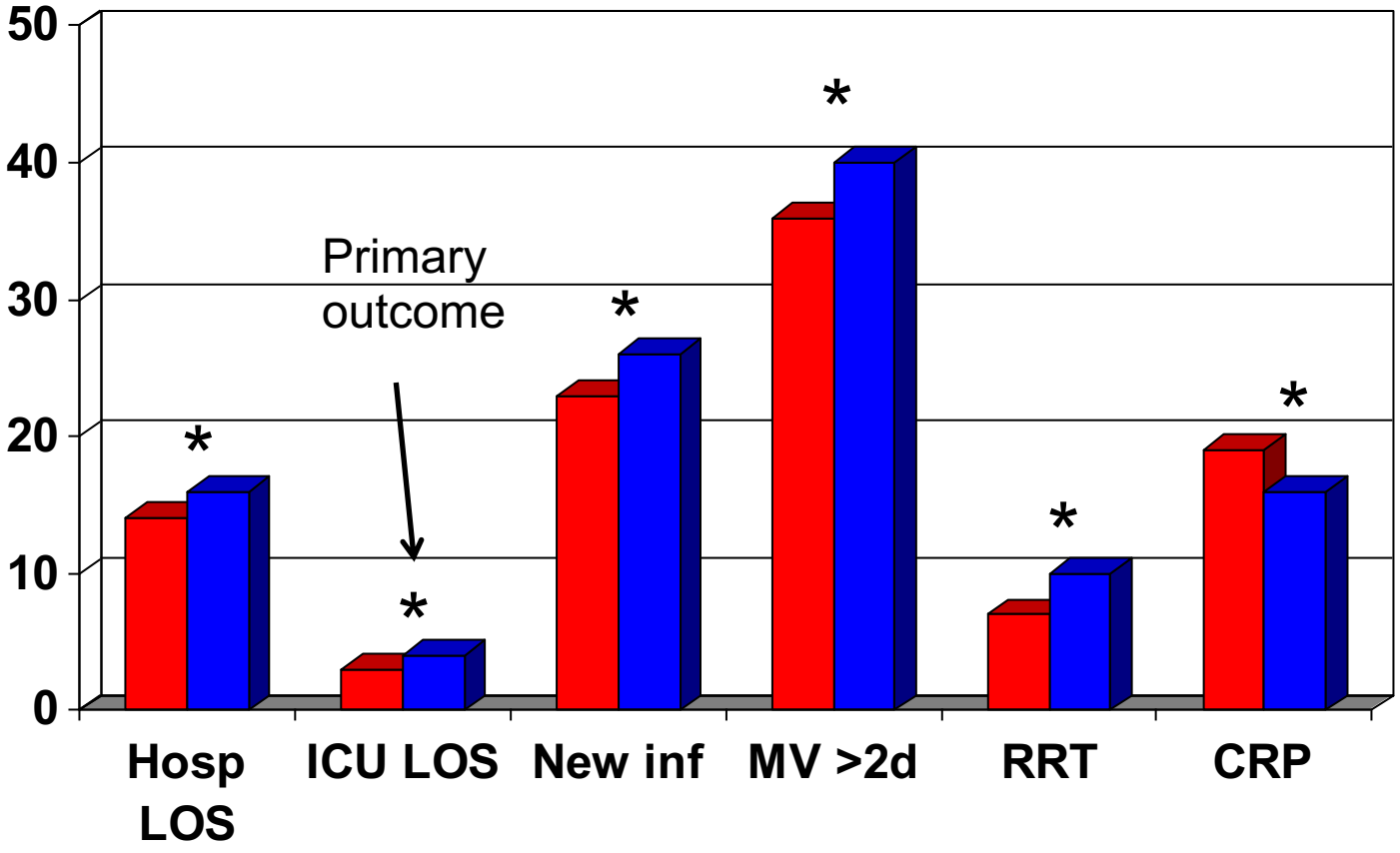
Caloric intake in the EPaNIC trial

Figure 2: Nutrition

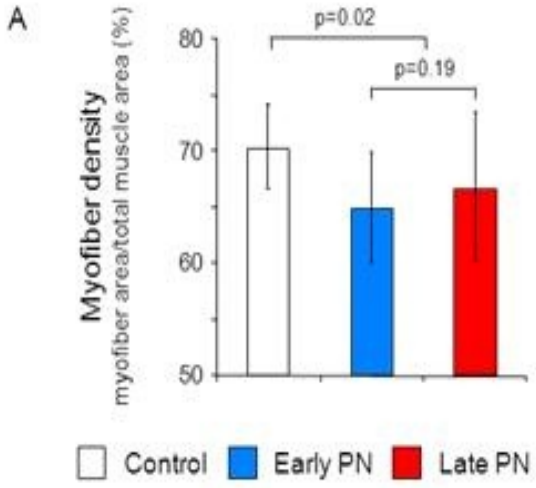


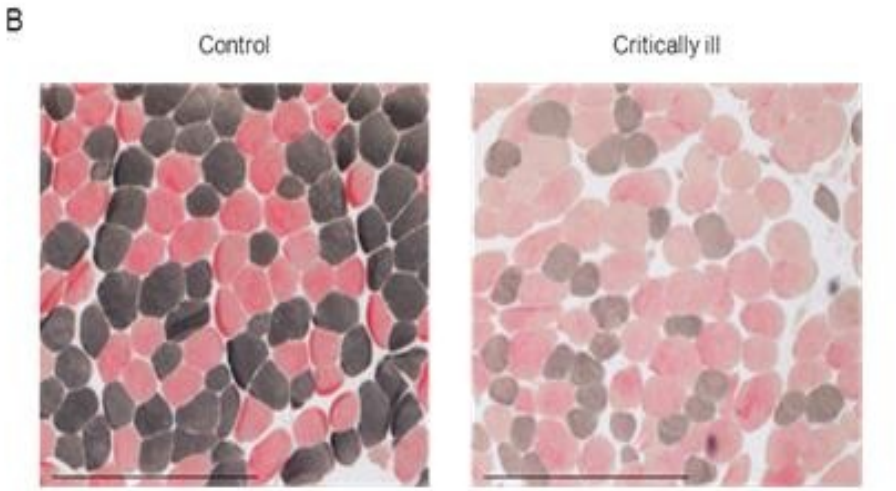
Outcomes – EPaNIC trial

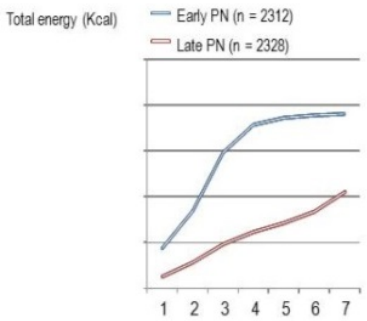
Casaer et al NEJM 2011

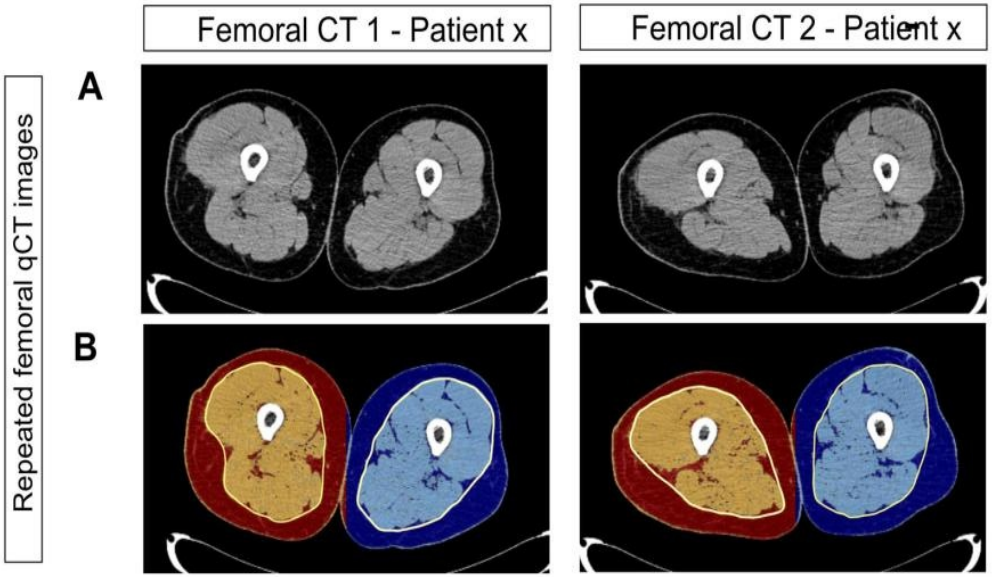


Impact of Early Parenteral Nutrition on Muscle and Adipose Tissue Compartments During Critical Illness*









Late PN **Early PN**

Supplementary Appendix.

- In post hoc subgroup analyses, we compared late initiation of parenteral nutrition with early initiation in patients for whom early enteral nutrition was surgically contraindicated (517 patients who had undergone complicated pulmonary, esophageal, abdominal, or pelvic surgery and who had a mean APACHE II score of 27±11).
- Together, these high-risk subgroups predictably received a median of 0 kcal (interquartile range, 0 to 163) per day of enteral nutrition by day 7. Among these patients, the rate of infection was lower in the late-initiation group (29.9%) than in the early initiation group (40.2%, P = 0.01).
- In the late-initiation group, there was a relative increase of 20% in the likelihood of earlier discharge alive from the ICU (hazard ratio, 1.20; 95% CI, 1.00 to 1.44; P = 0.05; P = 0.11 for interaction)

Early versus Late Parenteral Nutrition in Critically Ill Children

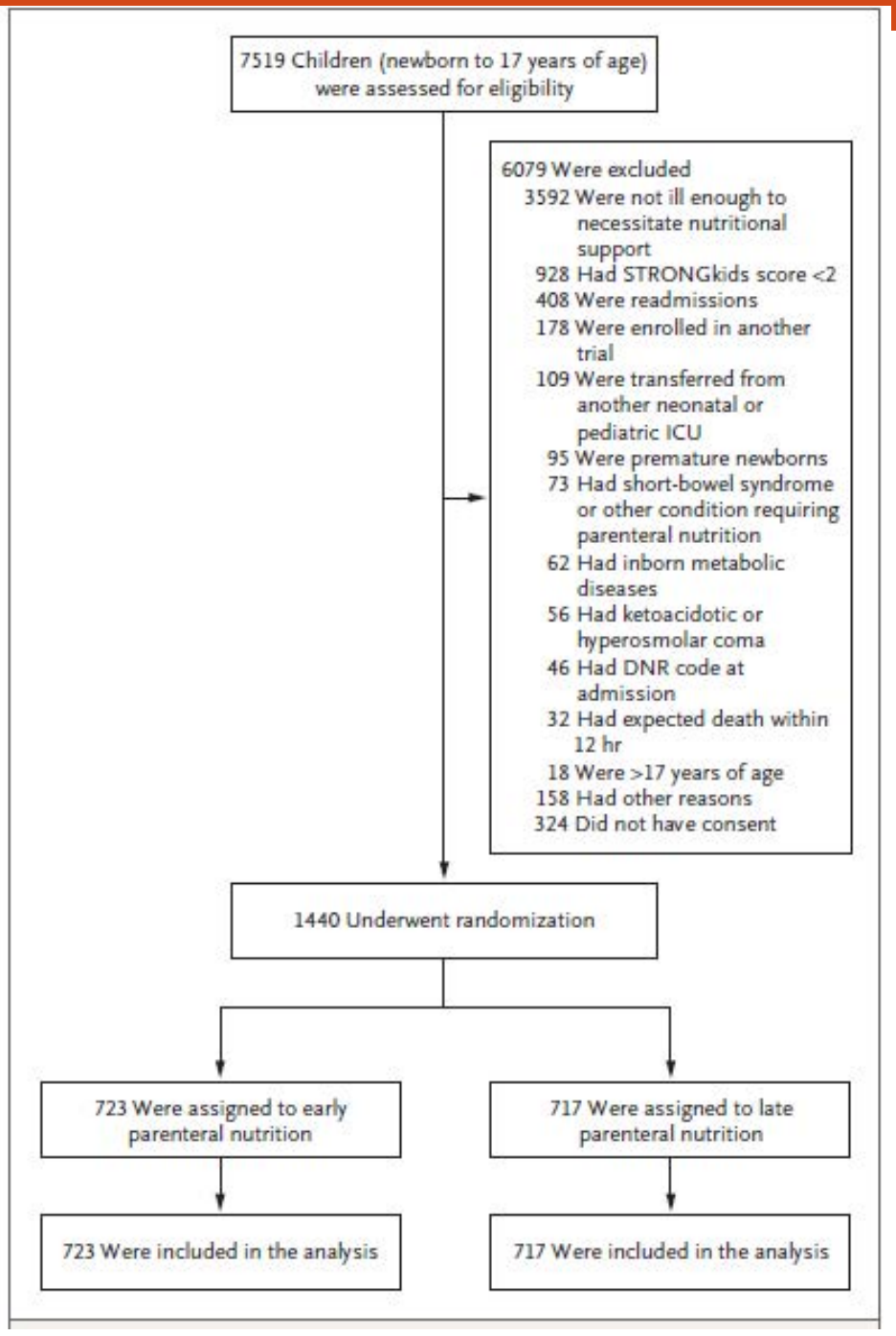
Tom Fivez, M.D., Dorian Kerklaan, M.D., Dieter Mesotten, M.D., Ph.D.,

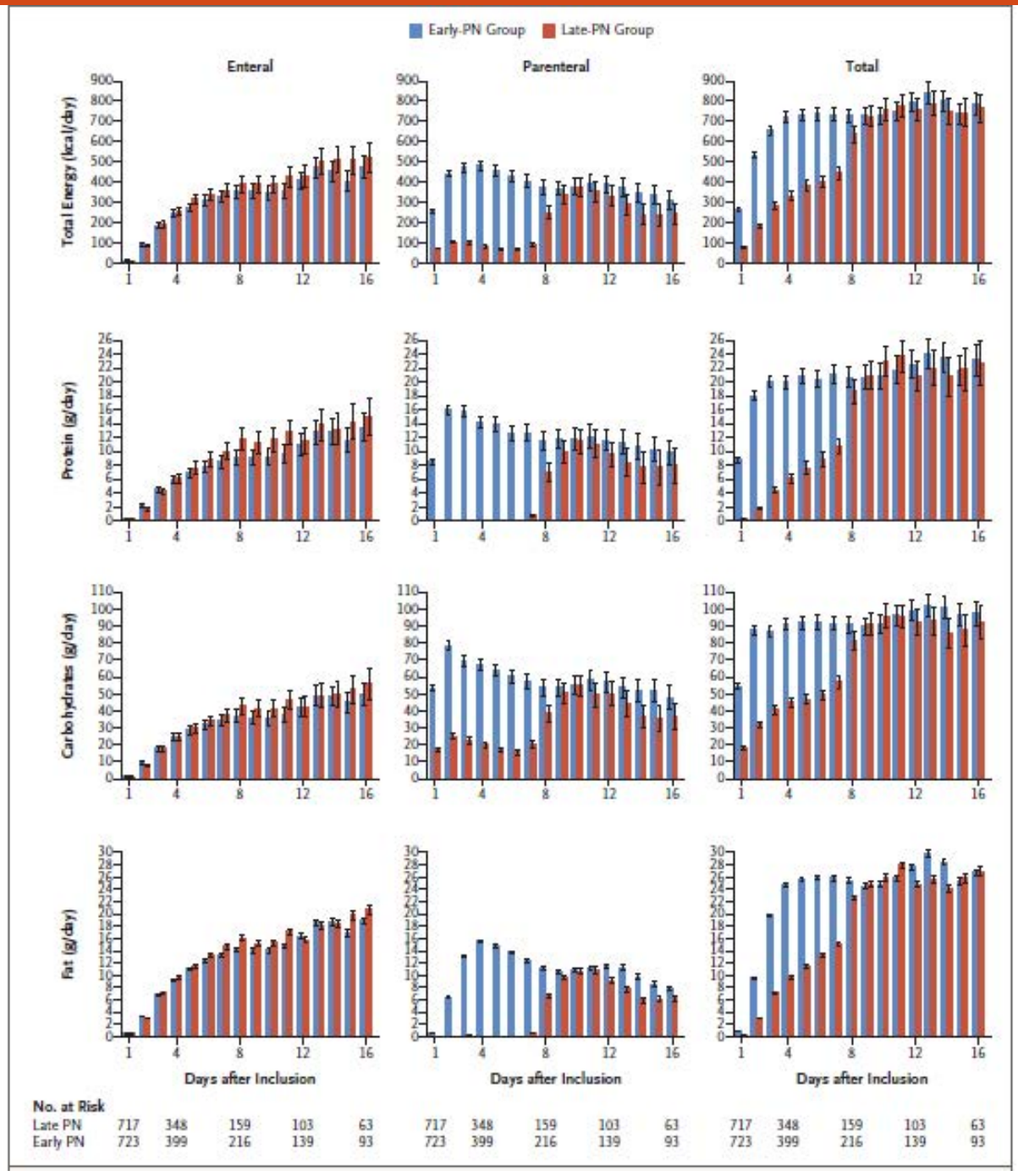
This article was published on March 15, 2016, at NEJM.org.

DOI: 10.1056/NEJMoa1514762

METHODS

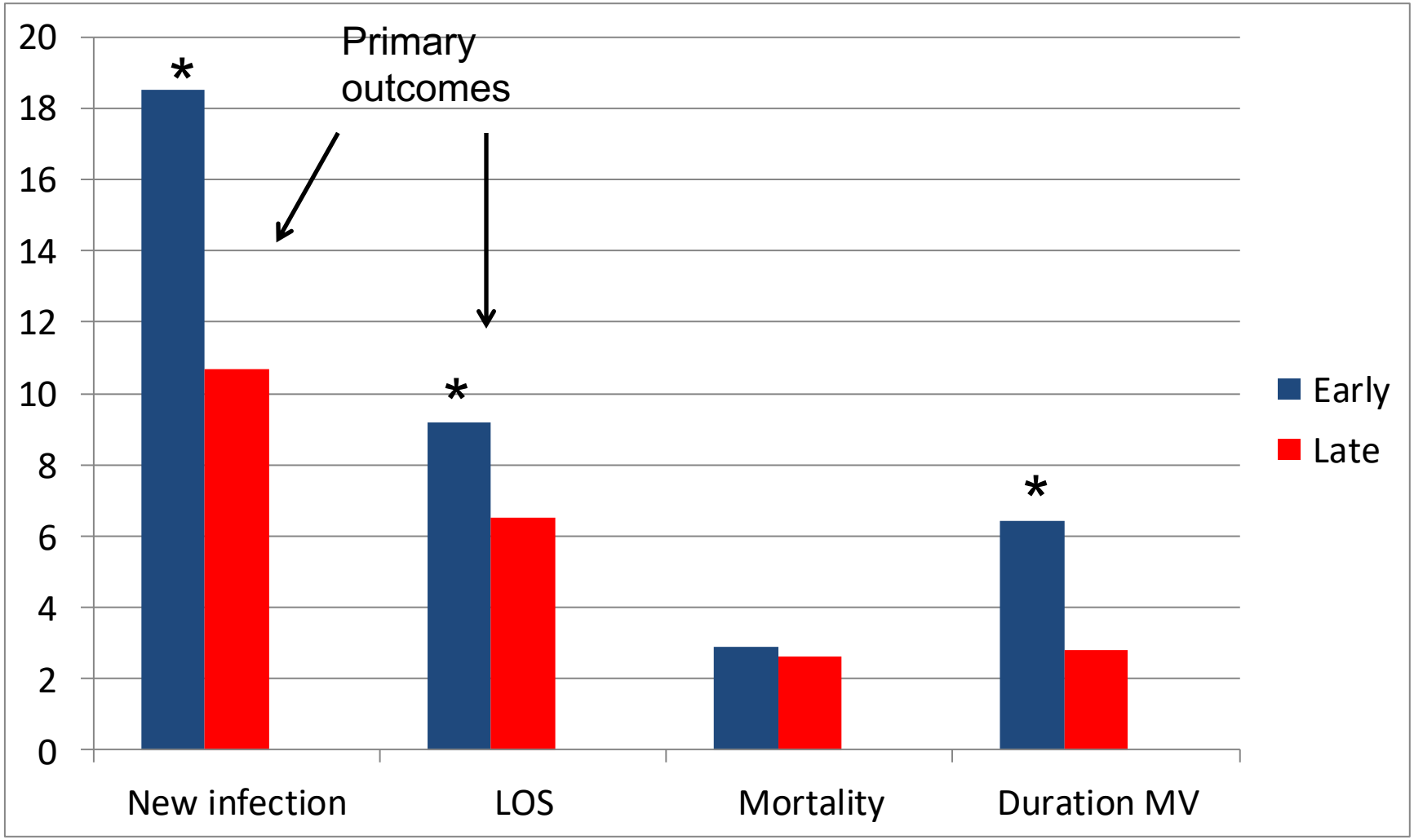
We conducted a multicenter, randomized, controlled trial involving 1440 critically ill children to investigate whether withholding parenteral nutrition for 1 week (i.e., providing late parenteral nutrition) in the pediatric intensive care unit (ICU) is clinically superior to providing early parenteral nutrition. Fluid loading was similar in the two groups. The two primary end points were new infection acquired during the ICU stay and the adjusted duration of ICU dependency, as assessed by the number of days in the ICU and as time to discharge alive from ICU. For the 723 patients receiving early parenteral nutrition, parenteral nutrition was initiated within 24 hours after ICU admission, whereas for the 717 patients receiving late parenteral nutrition, parenteral nutrition was not provided until the morning of the 8th day in the ICU. In both groups, enteral nutrition was attempted early and intravenous micronutrients were provided.


7519 Children (newborn to 17 years of age) were assessed for eligibility
6079 Were excluded
3592 Were not ill enough to necessitate nutritional support
928 Had STRONGkids score <2
408 Were readmissions
178 Were enrolled in another trial
109 Were transferred from another neonatal or pediatric ICU
95 Were premature newborns
73 Had short-bowel syndrome or other condition requiring parenteral nutrition
62 Had inborn metabolic diseases
56 Had ketoacidotic or hyperosmolar coma
46 Had DNR code at admission
32 Had expected death within 12 hr
18 Were >17 years of age
158 Had other reasons
324 Did not have consent
1440 Underwent randomization
723 Were assigned to early parenteral nutrition
717 Were assigned to late parenteral nutrition
723 Were included in the analysis
717 Were included in the analysis


Early-PN Group
Late-PN Group
Enteral
Parenteral
Total
Total Energy (kcal/day)
Protein (g/day)
Carbohydrates (g/day)
Fat (g/day)
Days after Inclusion
No. at Risk
Late PN 717 348 159 103 63 717 348 159 103 63 717 348 159 103 63
Early PN 723 399 216 139 93 723 399 216 139 93 723 399 216 139 93

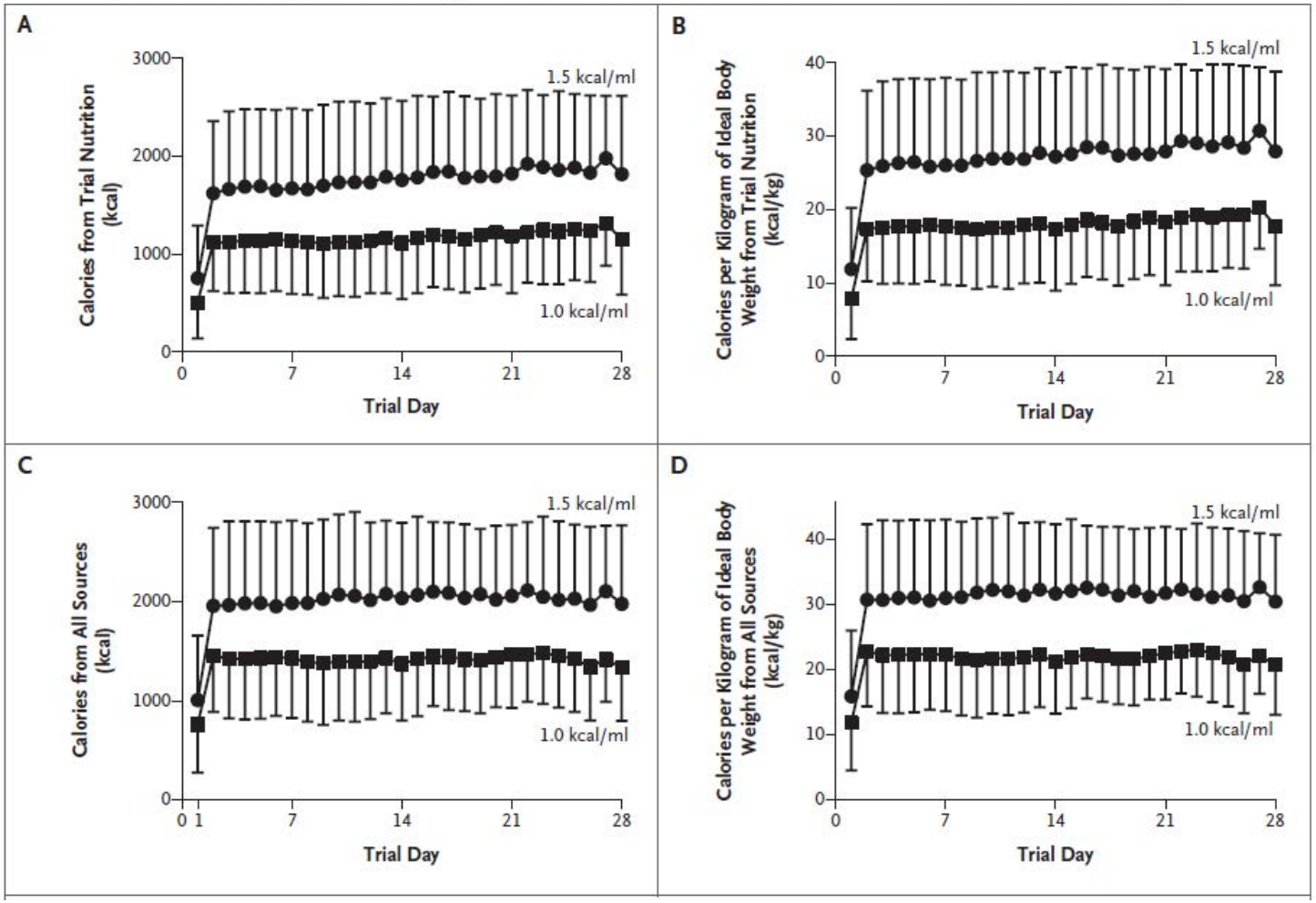
Outcomes – PEPaNIC trial

Fivez et al NEJM 2016



Energy-Dense versus Routine Enteral Nutrition in the Critically Ill

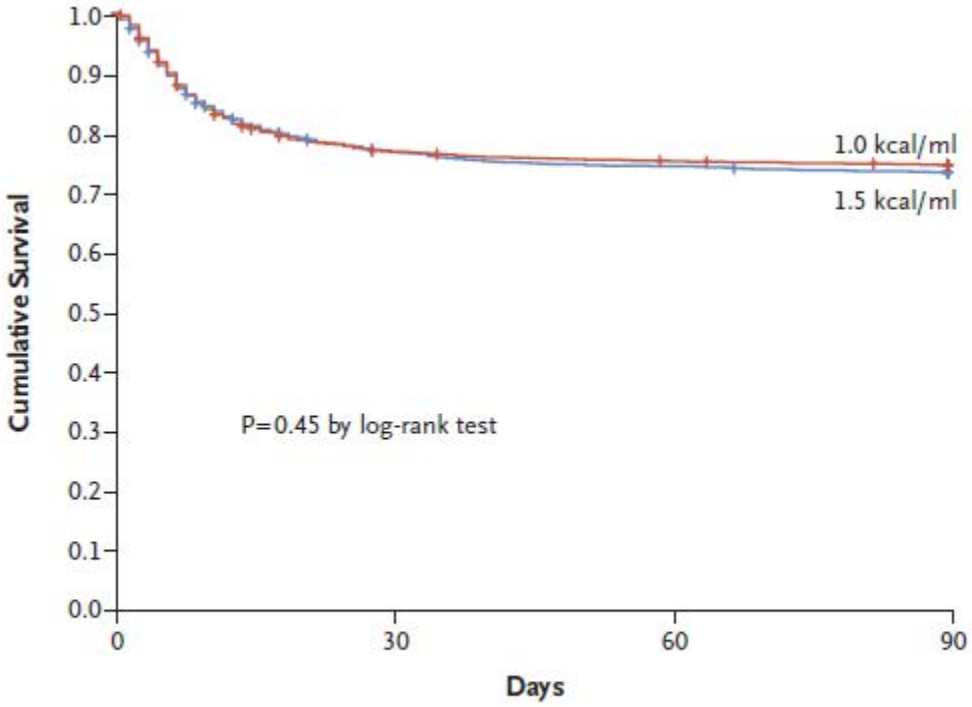
The TARGET Investigators, for the ANZICS Clinical Trials Group*



Energy-Dense versus Routine Enteral Nutrition in the Critically Ill

The TARGET Investigators, for the ANZICS Clinical Trials Group*

A Survival



No. at Risk				
1.5 kcal/ml	1971	1495	1445	1425
1.0 kcal/ml	1985	1512	1477	1461

The pyramid of evidence-based medicine

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 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

Infectious complications

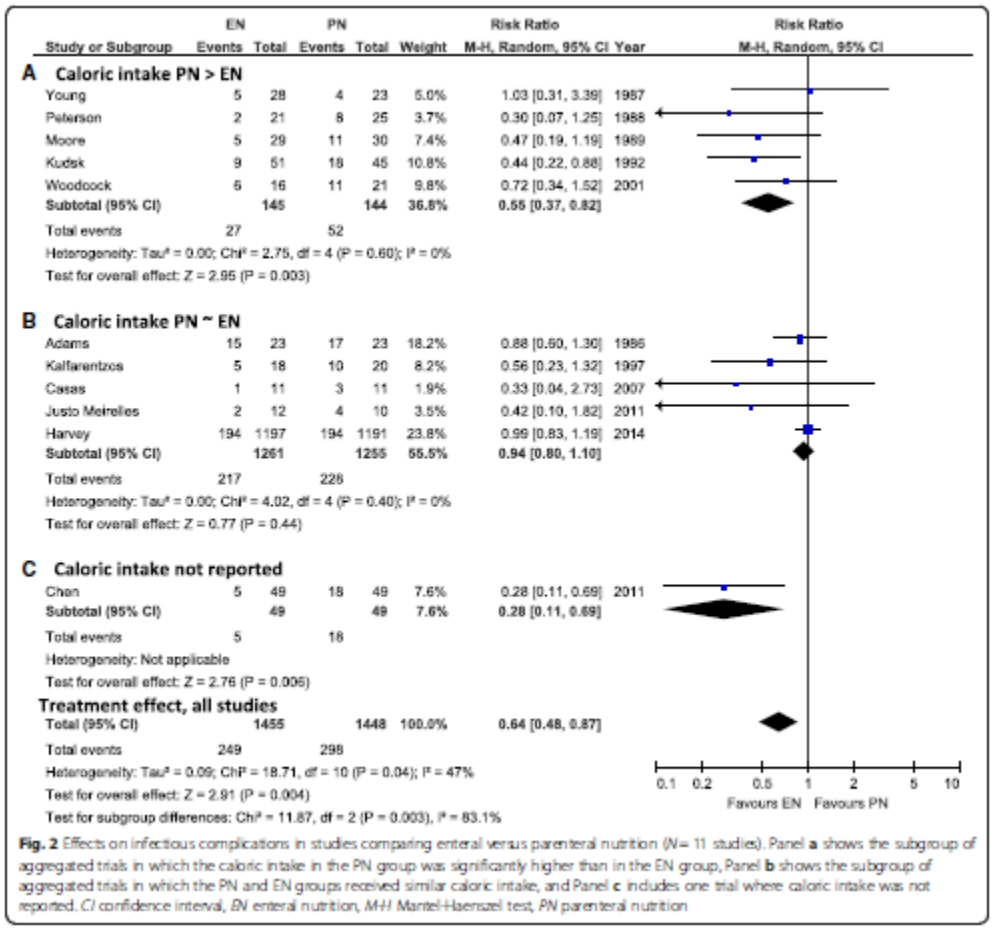


Fig. 2 Effects on infectious complications in studies comparing enteral versus parenteral nutrition (*N* = 11 studies). Panel **a** shows the subgroup of aggregated trials in which the caloric intake in the PN group was significantly higher than in the EN group, Panel **b** shows the subgroup of aggregated trials in which the PN and EN groups received similar caloric intake, and Panel **c** includes one trial where caloric intake was not reported. *CI* confidence interval, *EN* enteral nutrition, *M-H* Mantel-Haenszel test, *PN* parenteral nutrition

WHY COULD HIGH CALORIC INTAKE BE DETRIMENTAL DURING THE ACUTE / EARLY PHASE?

WE NEED TO OPEN THE ENGINE!!

- **Overfeeding**
- **Autophagy**
- **Refeeding**

- **Overfeeding**
- Autophagy
- Refeeding

Ziegler et al N Engl J Med. 2009;361:1088

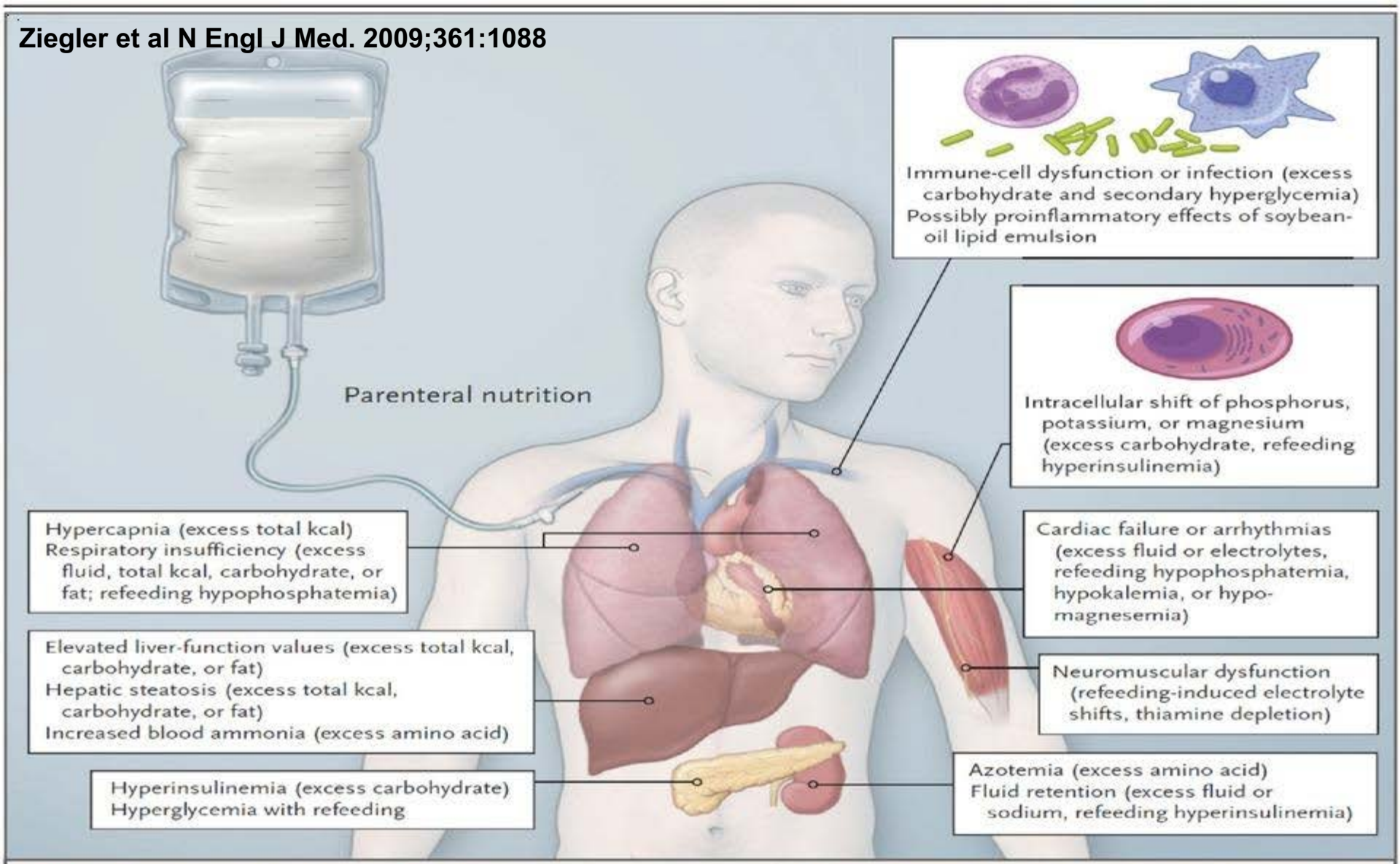
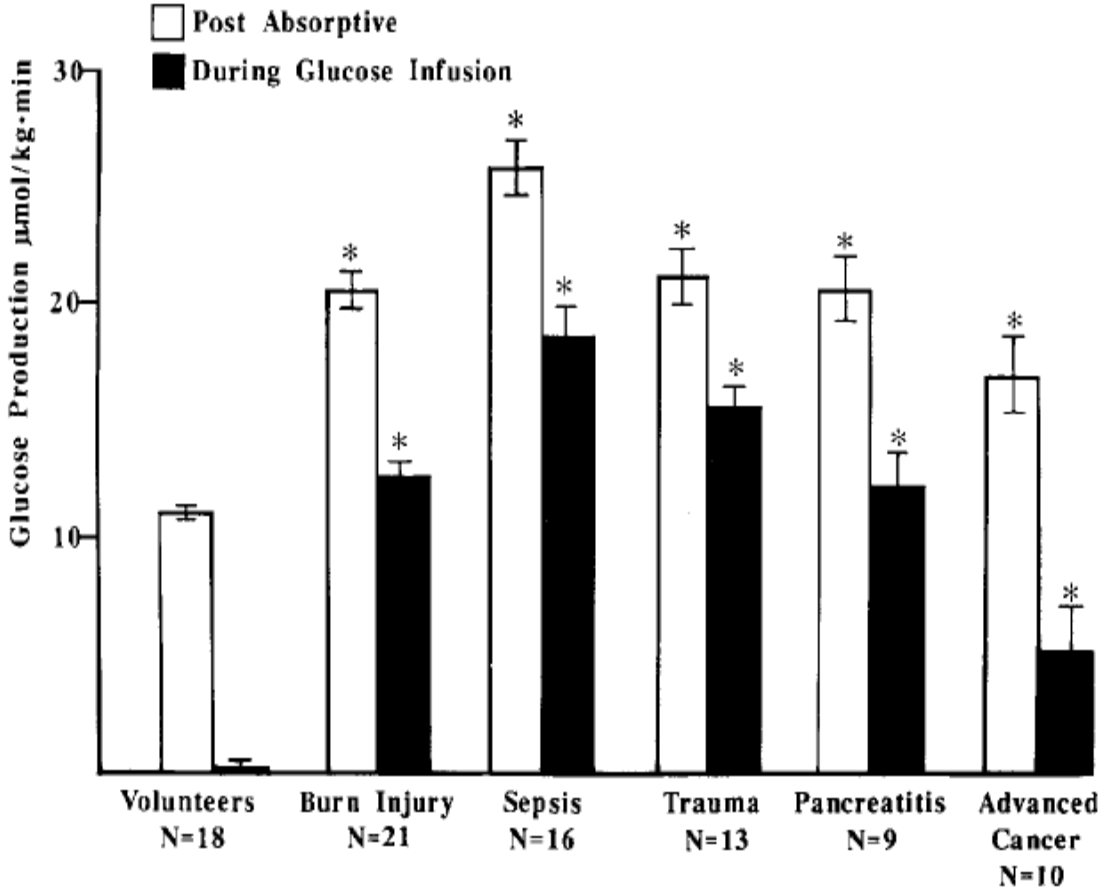


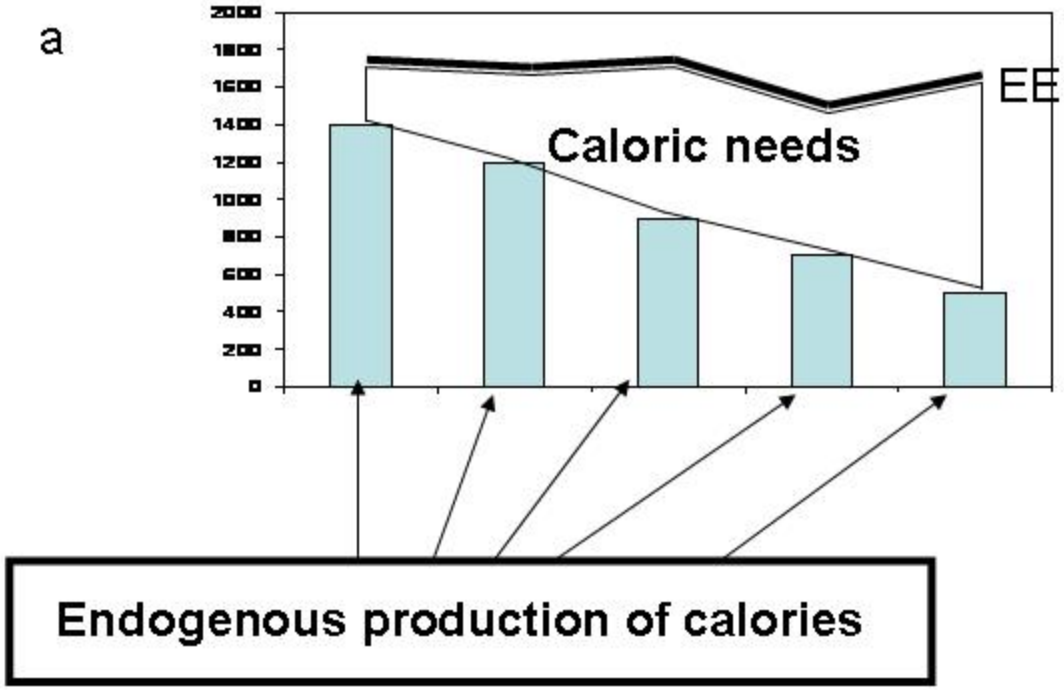
Figure 1. Potential Metabolic and Clinical Consequences of Overfeeding and the Refeeding Syndrome during Administration of Central Venous Parenteral Nutrition in Patients with Critical Illness.

Hypertriglyceridemia can occur with excess administration of carbohydrates or fat emulsion; excess administration of specific electrolytes in a variety of clinical conditions (e.g., acute kidney injury) can lead to elevated blood levels, whereas inadequate administration, especially during refeeding, can lead to decreased blood levels. Inadequate energy provision in relation to the dose of amino acids can contribute to azotemia.

Rate of basal glucose production and endogenous production during glucose infusion in various conditions

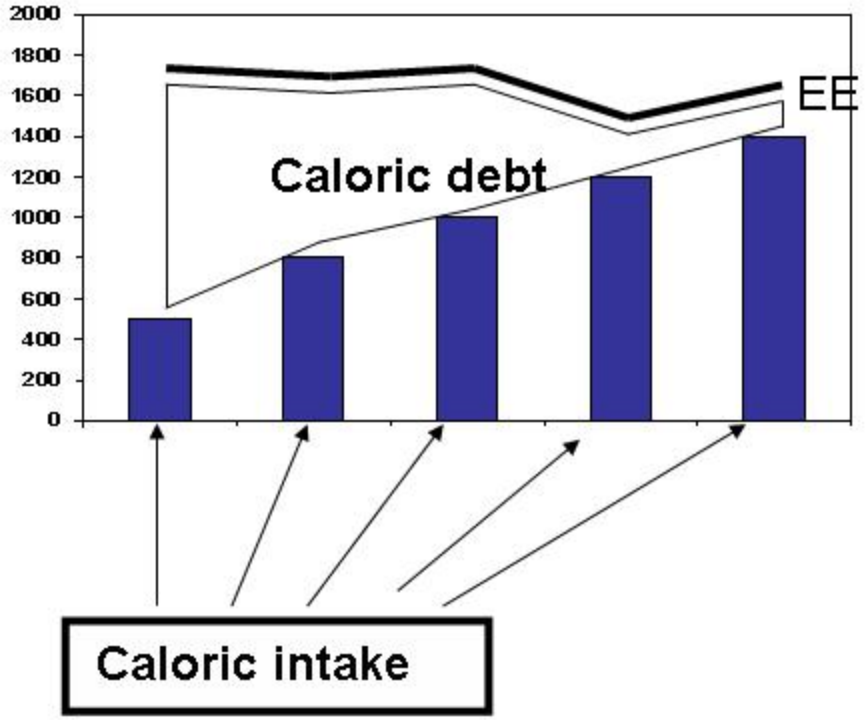


Wolfe RR, Eur J Clin Nutr 1999

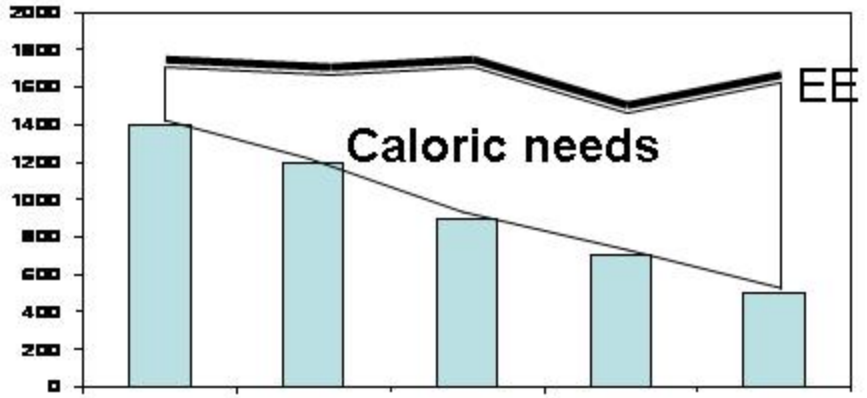


Energy estimation and measurement in critically ill patients.
Fraipont V, Preiser JC. JPEN J Parenter Enteral Nutr. 2013 Nov-Dec;37(6):705-13

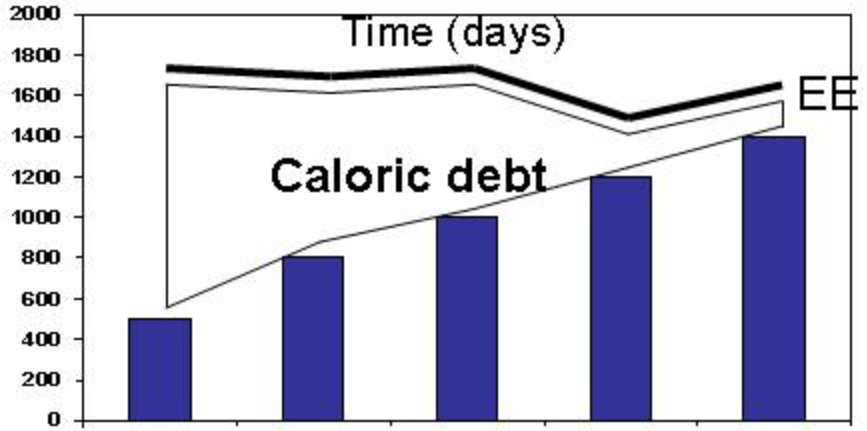
b


2000
1800
1600
1400
1200
1000
800
600
400
200
0
EE
Caloric debt
Caloric intake

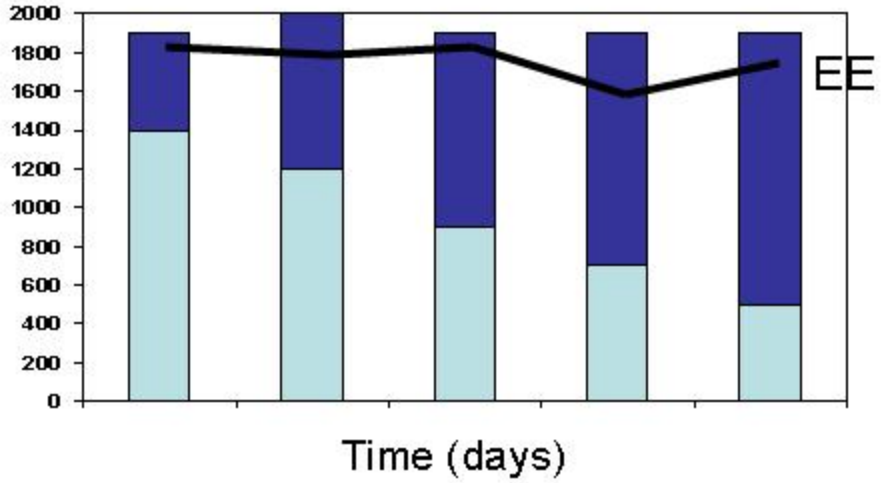
a

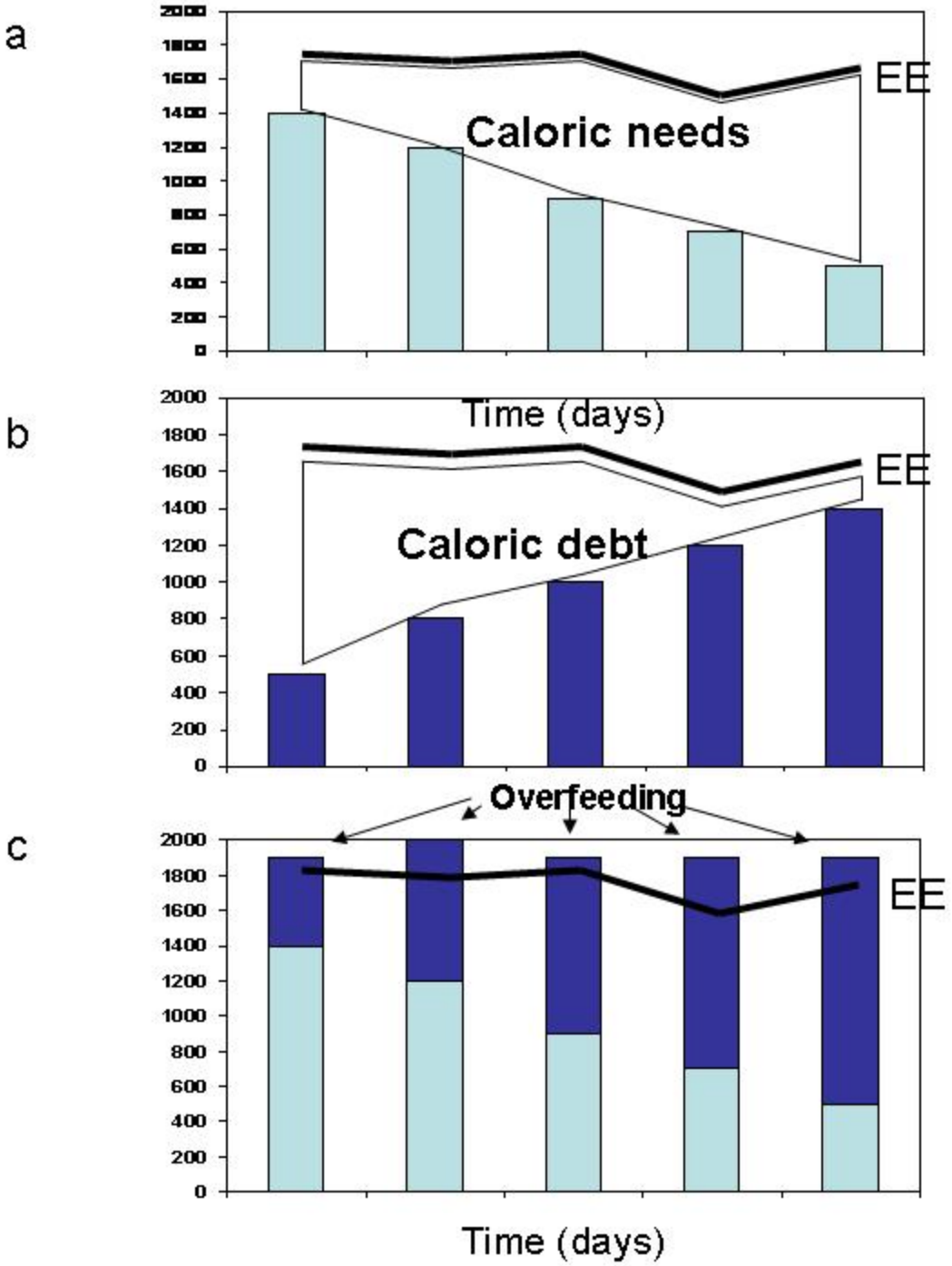


b



c




a
EE
Caloric needs
b
Time (days)
EE
Caloric debt
Overfeeding
c
EE
Time (days)

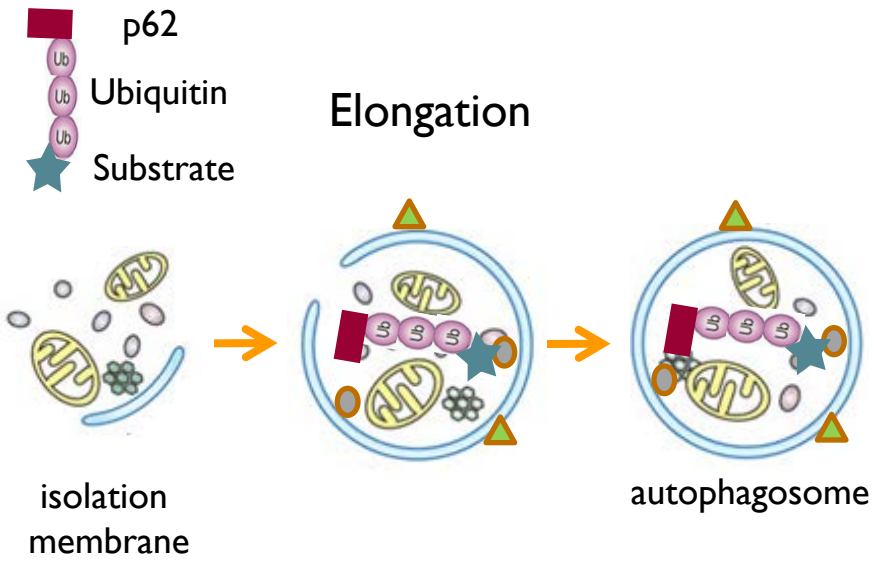
- Overfeeding
- **Autophagy**
- Refeeding

Damage removal : Autophagy

isolation membrane

Atg factors (Atg1)
Beclin1
PI3K class III

Damage removal : Autophagy

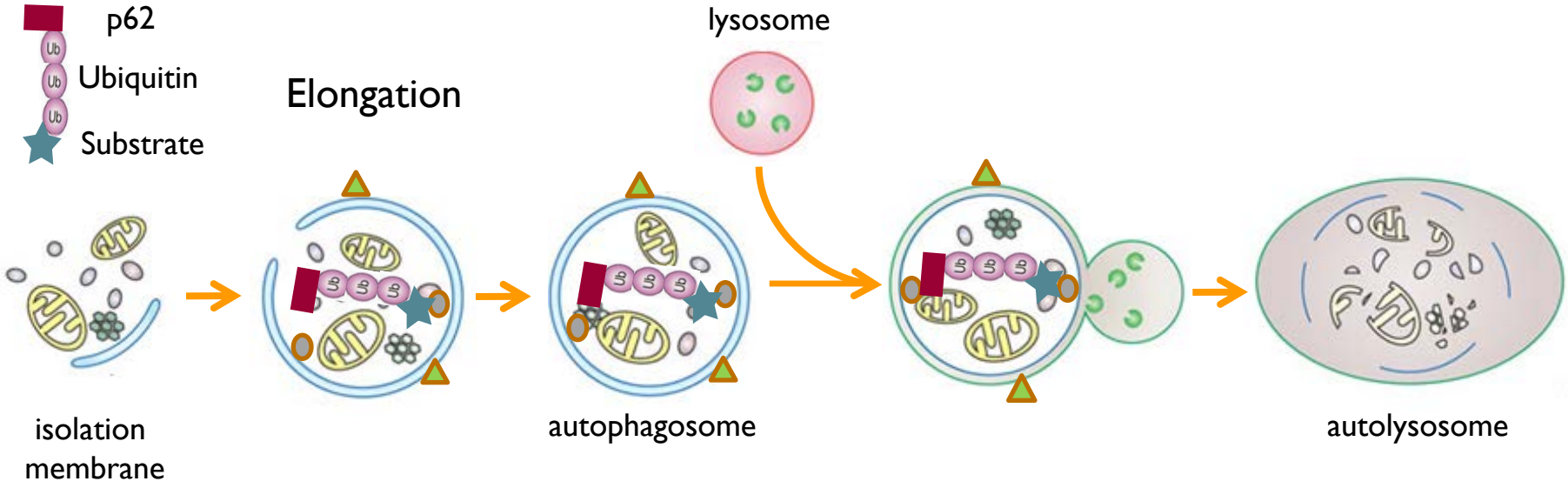


Atg factors (Atg1)
Beclin1
PI3K class III

Atg12
Atg5 → Atg12-5/16
Atg16

Atg8 → Atg8-PE
(LC3-I) (LC3-II)

Damage removal : Autophagy



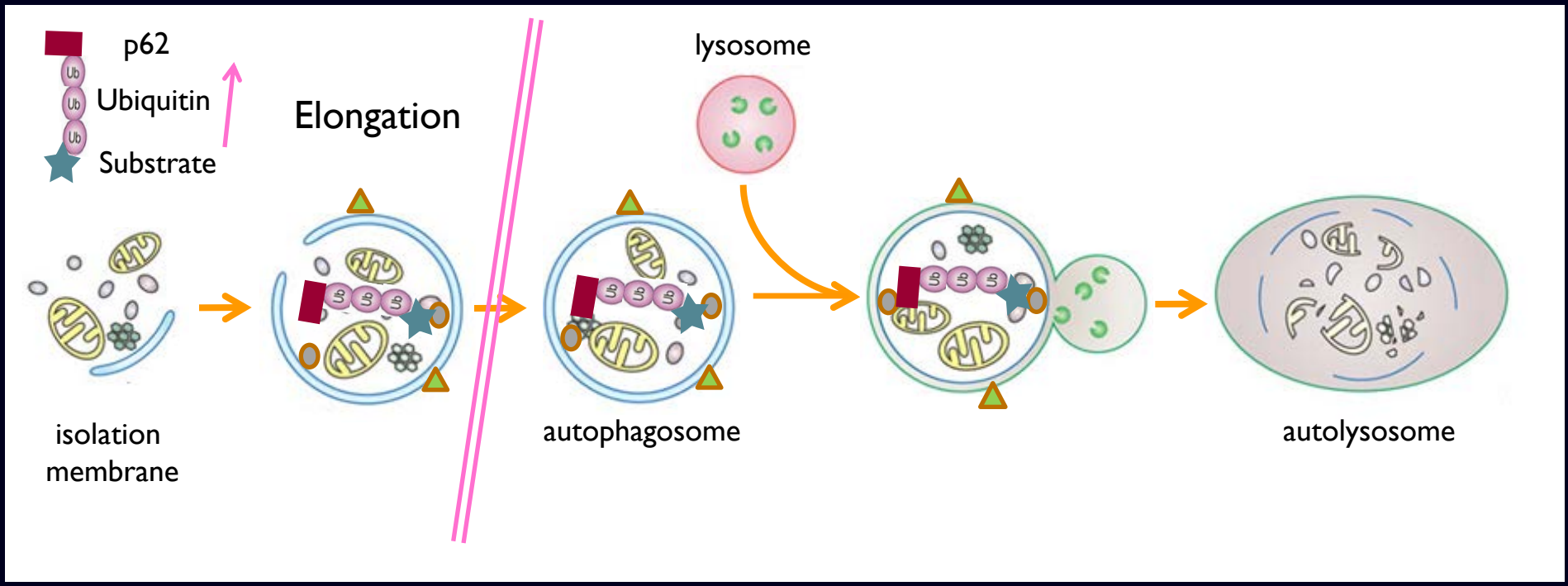
Atg factors (Atg1)
Beclin1
PI3K class III

Atg12
Atg5 → Atg12-5/16
Atg16

Atg8 → Atg8-PE
(LC3-I) (LC3-II)

M.P.C., K.U.Leuven

Damage removal : Autophagy



Atg factors (Atg1)
Beclin1
PI3K class III

Atg12
Atg5 → Atg12-5/16
Atg16

Atg8 (LC3-I) → Atg8-PE (LC3-II)

LC3-II / LC3-I ↓

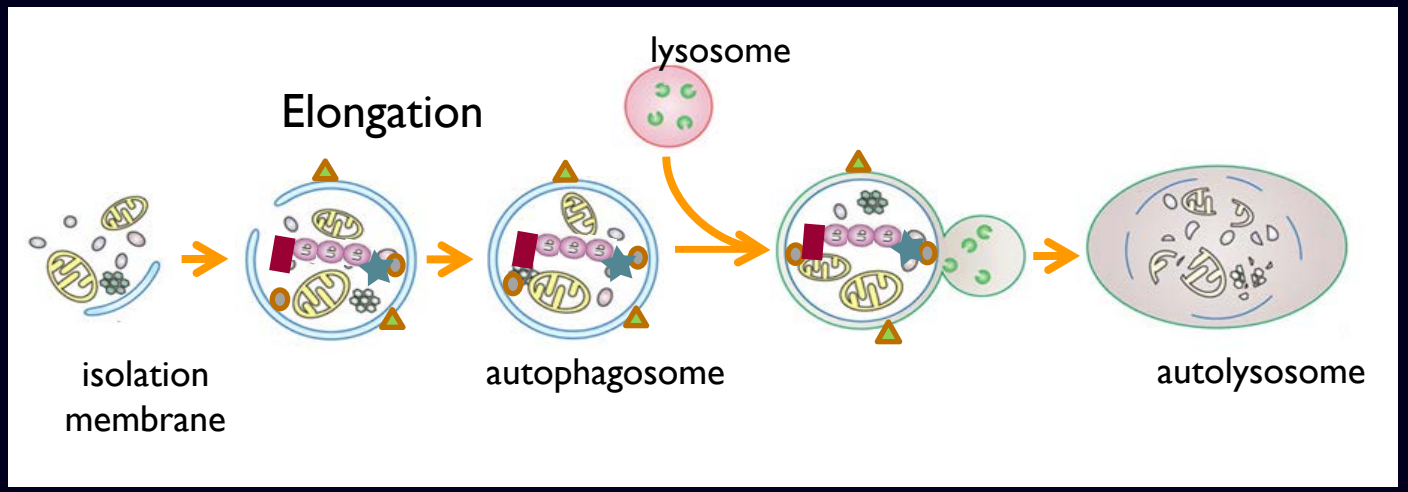
Masiero E et al. Cell Metab 200

Activators of autophagy ?

Fasting

Cellular stress

Hypoxia



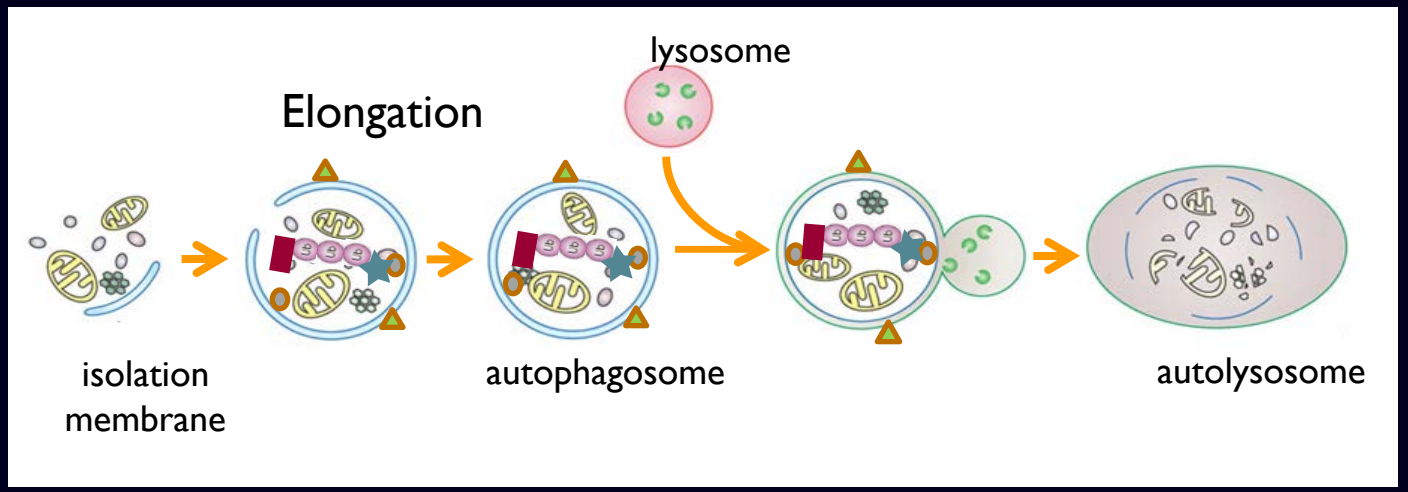
M.P.C., K.U.Leuven

Suppressors of autophagy ?

Nutrients

Growth Factors

Insulin



M.P.C., K.U.Leuven

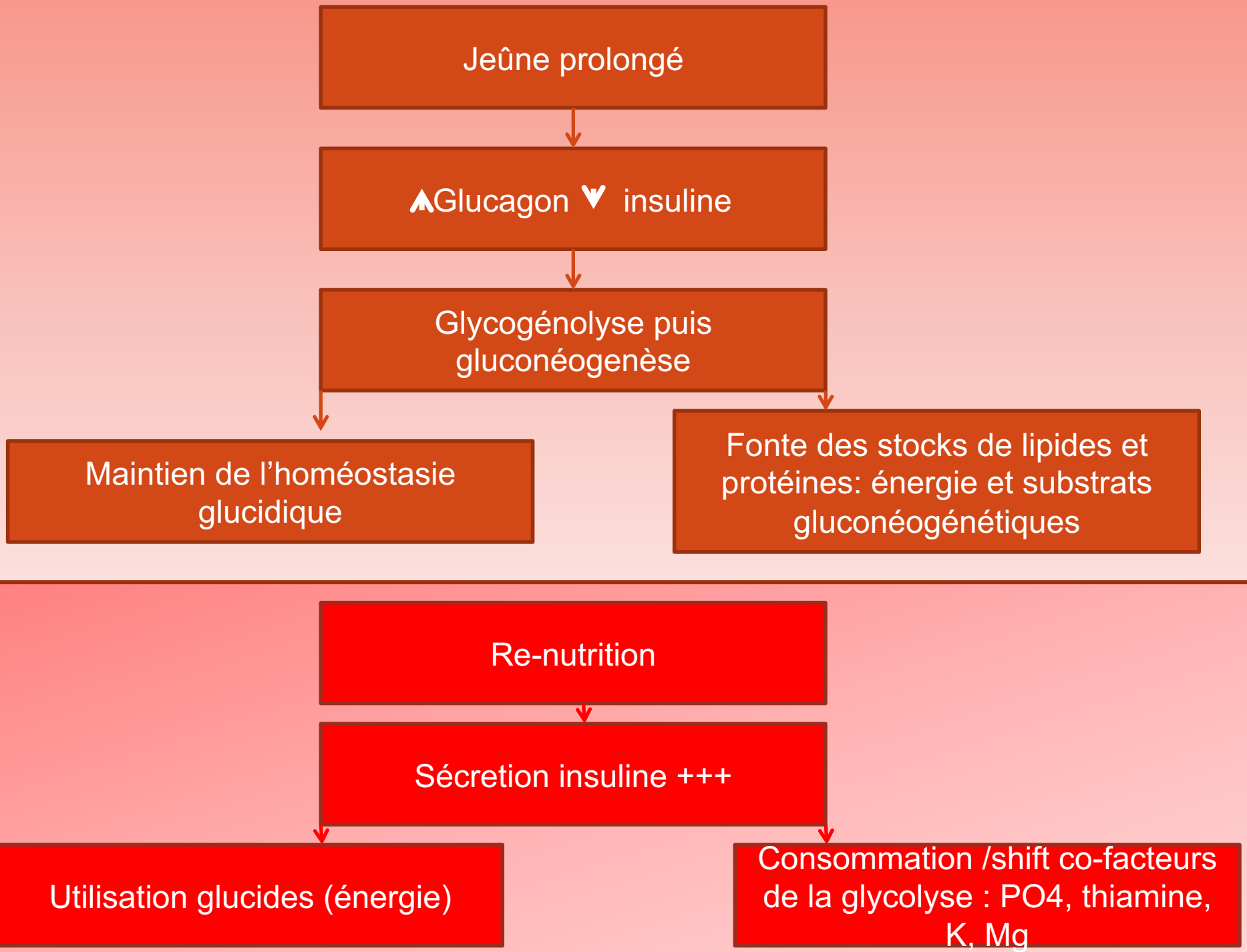
- Overfeeding
- Autophagy
- **Refeeding**

Refeeding : tout un spectre!

Refeeding hypophosphatemia

Refeeding syndrome

Le plus Fréquent en SI


Jeûne prolongé
▲Glucagon ▼ insuline
Glycogénolyse puis gluconéogenèse
Maintien de l'homéostasie glucidique
Fonte des stocks de lipides et protéines: énergie et substrats gluconéogénétiques
Re-nutrition
Sécretion insuline +++
Utilisation glucides (énergie)
Consommation /shift co-facteurs de la glycolyse : PO4, thiamine, K, Mg

In clinical practice, in case of refeeding syndrome….

- **Hypophosphatemia**
- **Hypokaliemia**
- **Hypomagnesemia**
- **Thiamin deficiency**

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, *]

Clinical Nutrition 37 (2018) 1609–1617

defined as the occurrence of new onset hypophosphatemia within 72 h of the start of nutritional support. Outcomes of patients who developed RFS were compared with patients that did not.

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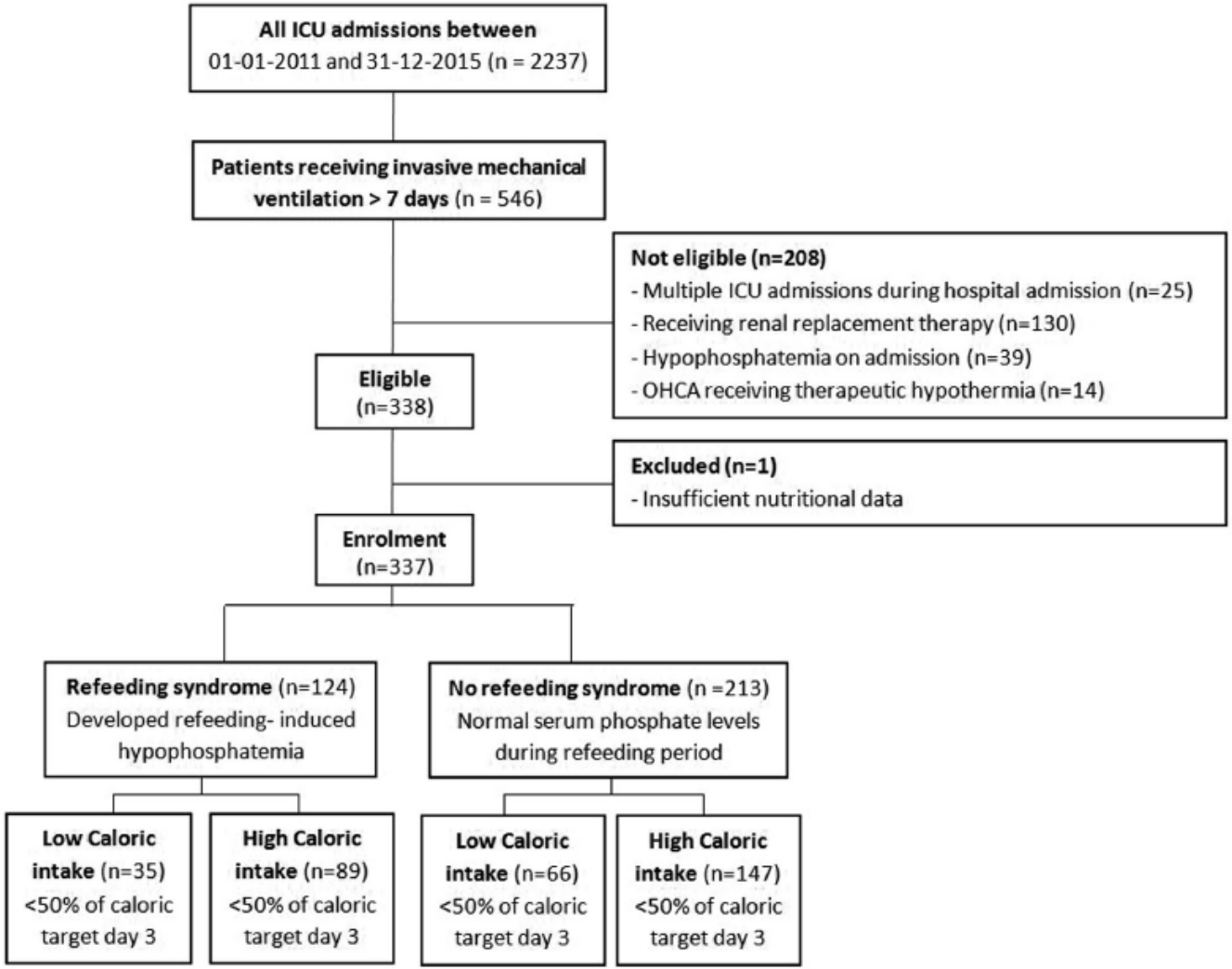
Laura E. Olthof [a], W.A.C. Kristine Koekkoek [b], Coralien van Setten [a], Johannes C.N. Kars [c], Dick van Blokland [a], Arthur R.H. van Zanten [a, *]

Clinical Nutrition 37 (2018) 1609–1617



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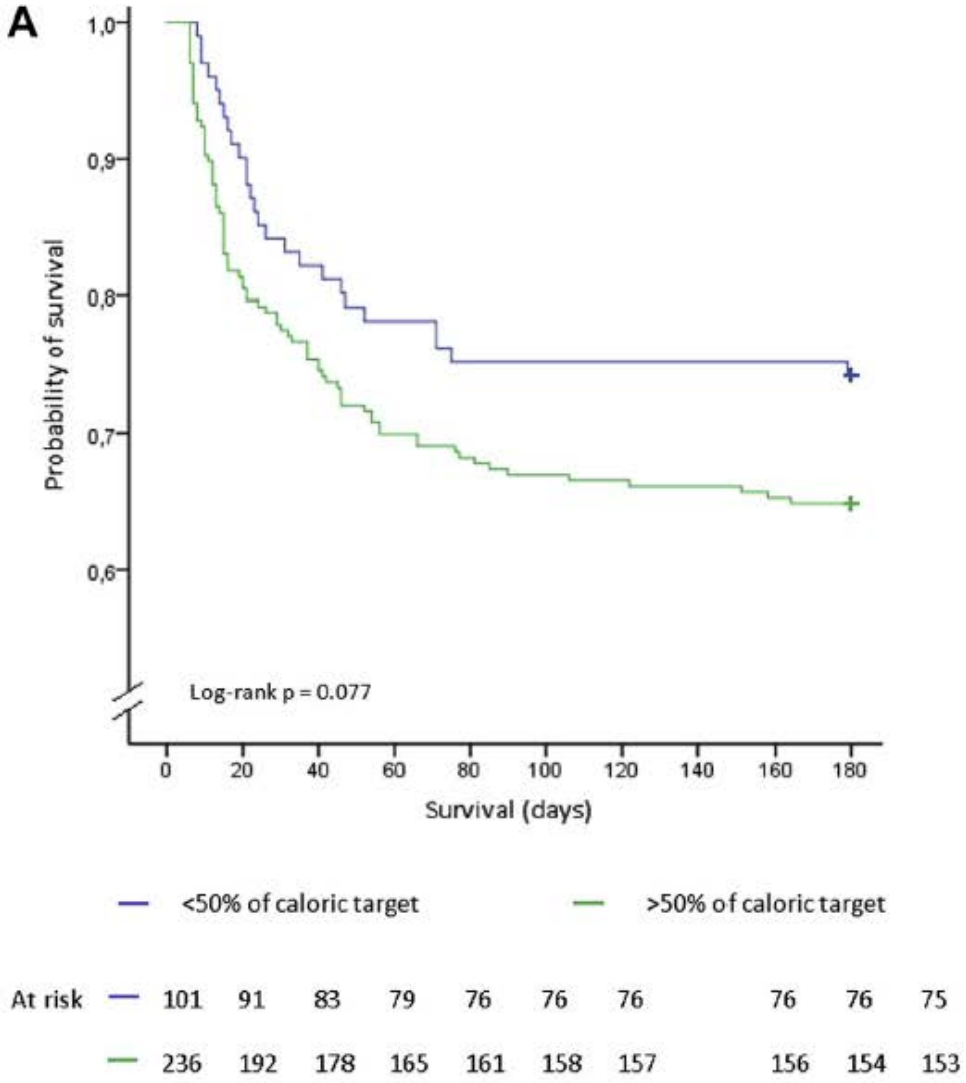

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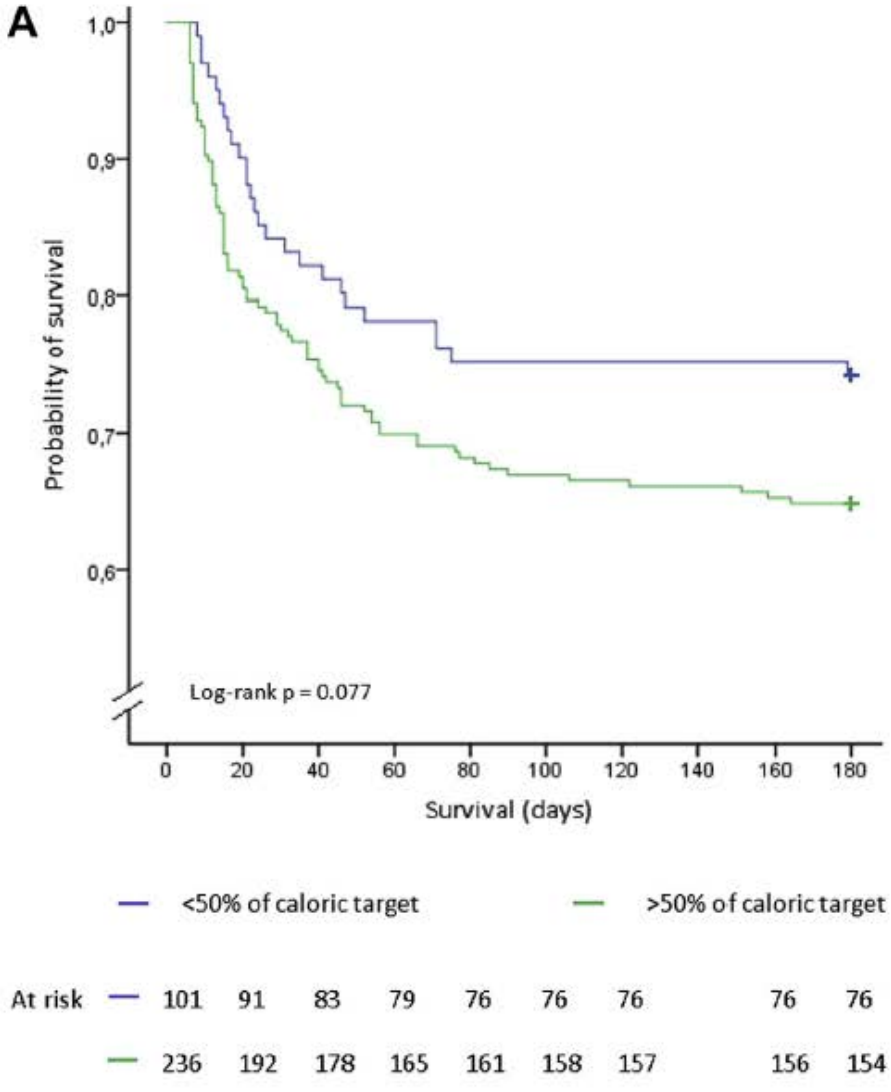

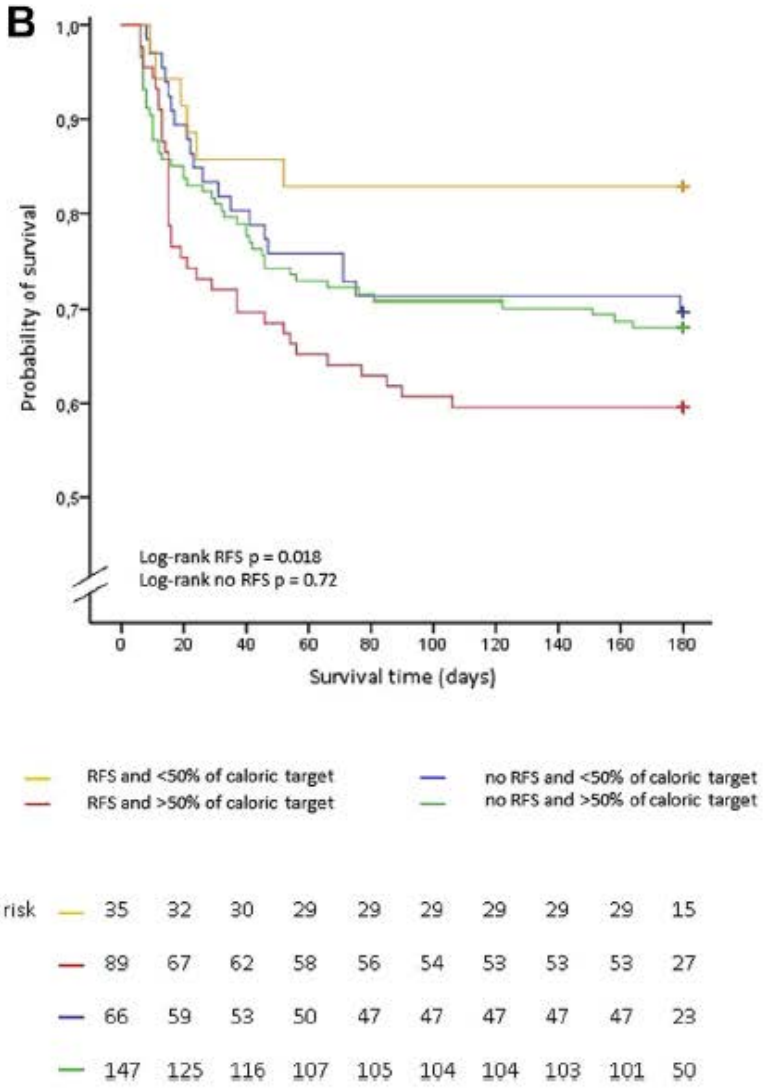

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

*Gordon S Doig, Fiona Simpson, Philippa T Heighes, Rinaldo Bellomo, Douglas Chesher, Ian D Caterson, Michael C Reade, Peter W J Harrigan, for the Refeeding Syndrome Trial Investigators Group**

Lancet Respir Med 2015; 3: 943–52

We screened critically ill adults (aged ≥18 years) for eligibility and enrolled them if their serum phosphate concentration decreased to below 0·65 mmol/L within 72 h after starting nutritional support in a participating ICU. To account for within-participant biological variation of serum phosphate concentrations, this change needed to be greater than a 0·16 mmol/L decrease from any concentration previously recorded during the patient's ICU stay. We excluded patients with other major causes of hypophosphataemia—such as ongoing dialysis, recent parathyroidectomy, or treatment for hyperphosphataemia—from enrolment. The appendix reports the complete eligibility and exclusion criteria.

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

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- Standard care

- Intervention

  - Reduce support to 20 kcal/h
  - Replace phosphate (protocol)
  - Thiamine (at least 100 mg IV/d)
  - other B-group vitamins
  - monitoring of K, Mg

  - Gradual return to normal intake protocol (40 – 60 kcal/h, 80 – 100%) unless P drop < 0.71 mmol/l

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

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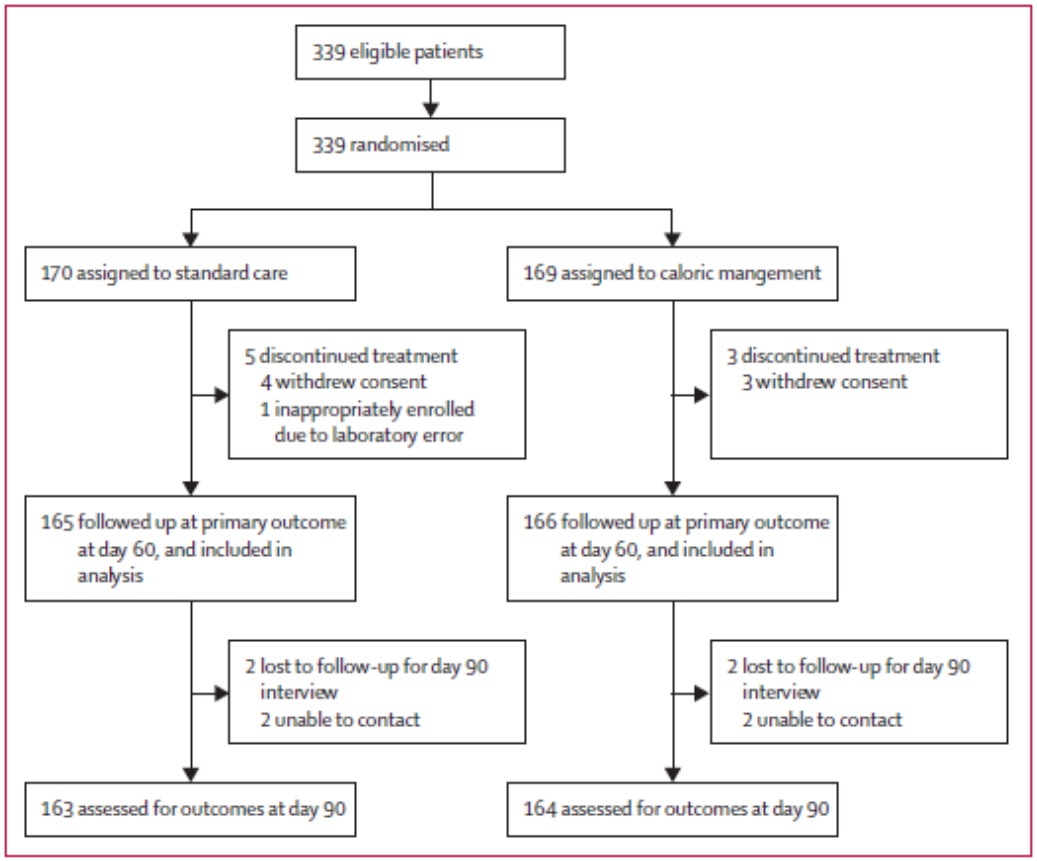

Figure 1: **Trial profile**
ICU=intensive care unit.

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

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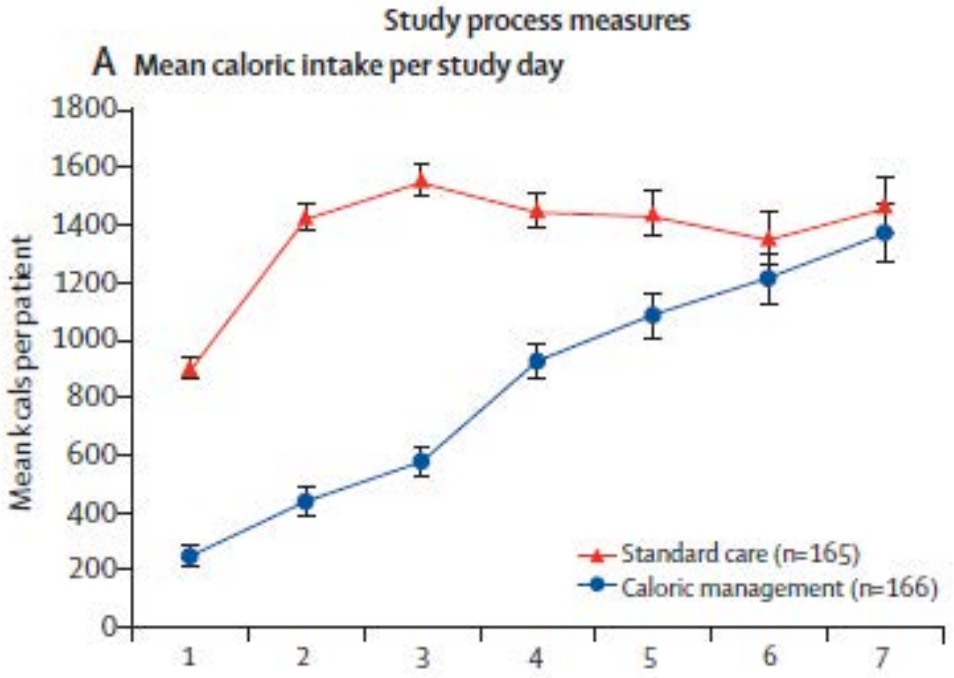

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Lancet Respir Med 2015; 3: 943–52

	Standard care (n=165 patients)	Caloric management (n=166 patients)	Risk difference (95% CI)	p value
Vital status (% alive)				
ICU discharge status	150/165 (91%)	157/166 (95%)	3·7% (–5·3 to 12·7)	0·20
Hospital discharge status	135/165 (82%)	151/166 (91%)	9·2% (0·7 to 17·7)	0·017
Day 60 status	128/163 (79%)*	149/164 (91%)*	12·3% (3·9 to 20·7)	0·002
Day 90 status	128/163 (79%)*	143/164 (87%)*	8·7% (0·04 to 17·0)	0·041
Length of stay (days)				
ICU	10·0 (9·2 to 10·9)	11·4 (10·5 to 12·4)	1·4 (–0·42 to 3·5)	0·14
Hospital	21·7 (20·0 to 23·5)	27·9 (25·7 to 30·3)	6·2 (2·0 to 11·2)	0·003
Quality of life and physical function scores† (n responses available for analysis)				
RAND-36 general health	53·4 (22·6; n=124/128)	46·0 (26·0 n=136/143)	–7·5 (–13·4 to –1·5)	0·014
ECOG performance status	1·3 (1·0; n=125/128)	1·5 (1·1; n=135/143)	0·18 (–0·08 to 0·43)	0·18
RAND-36 physical function	47·3 (35·0; n=123/128)	40·9 (33·4; n=135/143)	–6·4 (–14·8 to 2·0)	0·13

Data are n/N (%), mean (95% CI), and mean (SD), unless otherwise stated. ICU=intensive care unit. RAND=the RAND Corporation.[13] ECOG=Eastern Collaborative Oncology Group. *Four patients could not be contacted after hospital discharge (two in the standard care and two in the caloric management group). †Reported by survivors at day 90 interview.

Table 2: **Vital status, length of stay, and quality of life interviews**

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

*Gordon S Doig, Fiona Simpson, Philippa T Heighes, Rinaldo Bellomo, Douglas Chesher, Ian D Caterson, Michael C Reade, Peter W J Harrigan, for the Refeeding Syndrome Trial Investigators Group**

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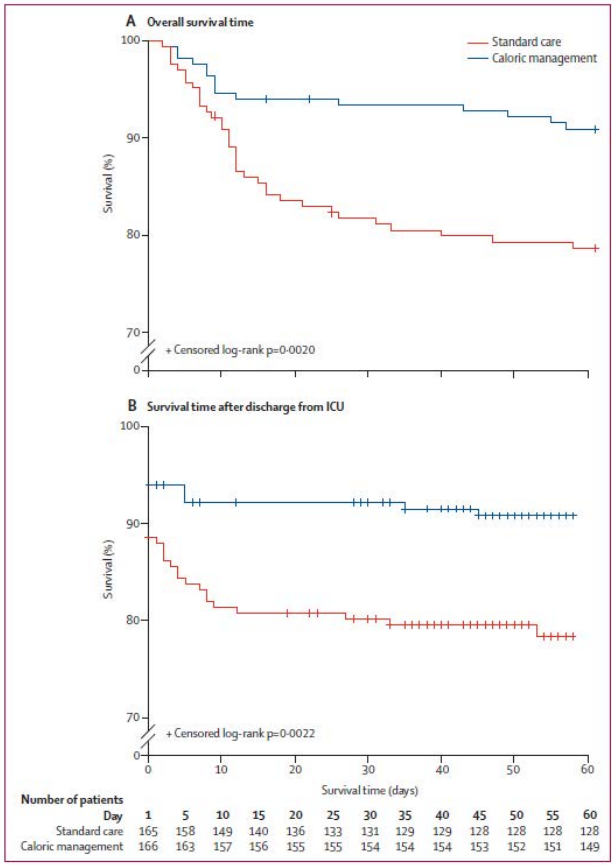
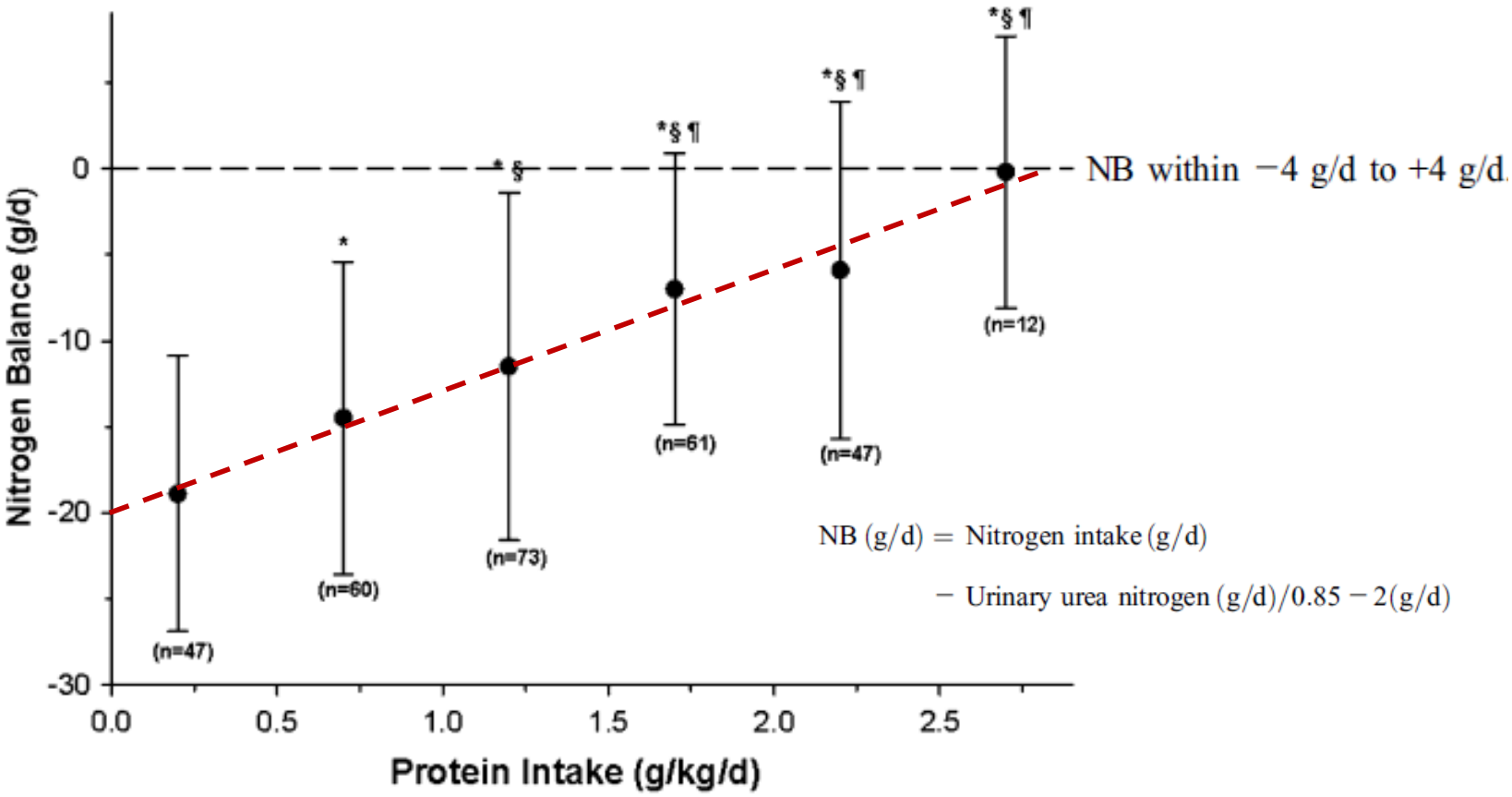


Figure 3: **Kaplan-Meier plot at 60-day follow-up after enrolment**
ICU=intensive care unit.

WHAT ABOUT PROTEIN INTAKES?

A reappraisal of nitrogen requirements for patients with critical illness and trauma



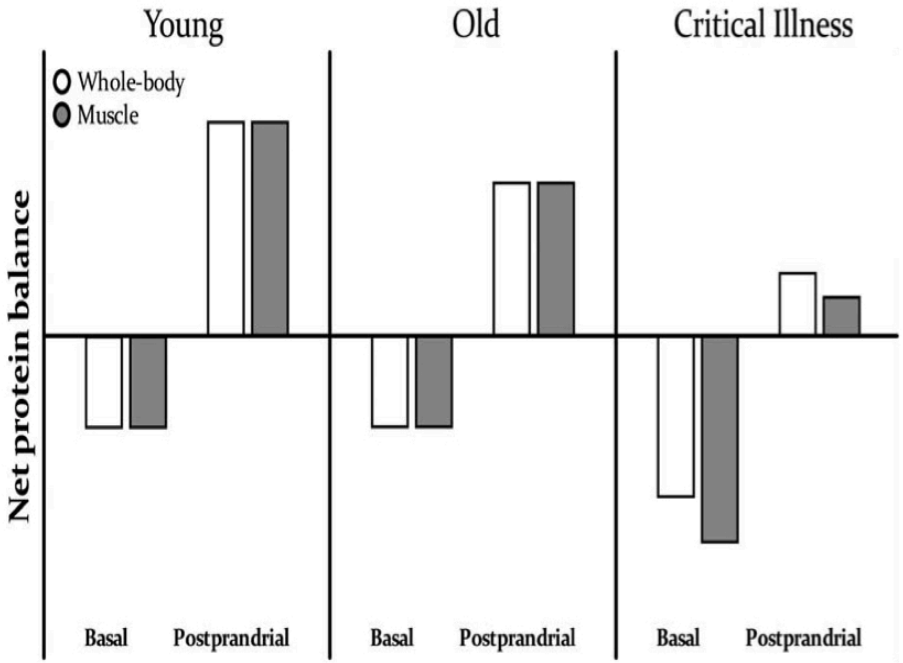
Dickerson et al. 2012

IV aminoacid therapy for kidney function

Doig Intensive Care Med 2015;41:1197

- ***Objective:***
  - To determine whether IV AA therapy preserves kidney function in patients at risk of AKI
- ***Intervention:***
  - Random allocation to receive a daily supplement up to 100g AA or standard
- ***Main outcome:***
  - Duration of renal dysfunction
- ***Results :***
  - 474 patients (235 standard, 239 AA) – no difference in duration of renal dysfunction / transient improvement in GFR

Critical Illness is Associated With Anabolic Resistance



Curr Opin Crit Care 2018, 24:(

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*]

Intensive Care Med (2017) 43:1637–1647

Table 2. Nutrition characteristics in ICU after randomisation [a]

Variable	Early Goal-directed Nutrition (N=100)	Standard of Care (N=99)
Measured [b] energy requirement, kcal/day	2069 (1816 - 2380)	1887 (1674 - 2244)
Calculated [c] energy requirement, kcal/day	1950 (1750 - 2125)	1875 (1650 - 2100)
Energy intake, kcal/day	1877 (1567 - 2254)	1061 (745 - 1470)
Energy balance [d], kcal/day	-66 (-157 - -6)	-787 (-1223 - -333)
Measured [e] 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 [d], g/kg/day	-0.28 (-0.76 - 0.11)	-0.69 (-1.02 - -0.38)
P-urea, mmol/l	13.5 (8.7 – 21.9)	9.0 (5.6 – 14.4)
24-hour urinary urea, mmol/day	516 (368 – 760)	320 (175 – 482)

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

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www.thelancet.com/respiratory **Vol 5 June 2017**

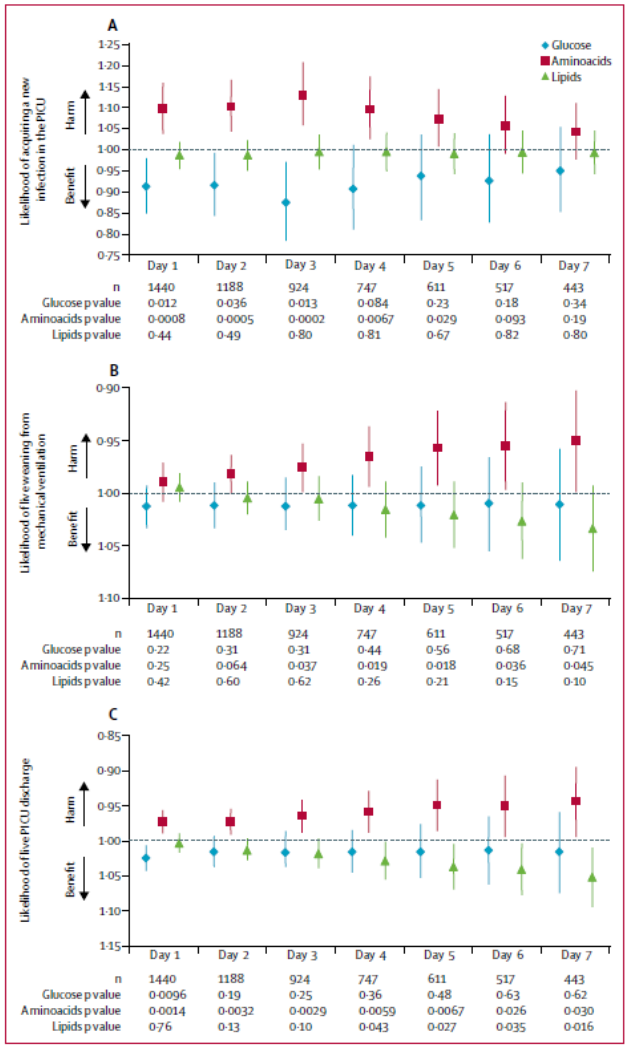

***Figure 2*: Association of average total macronutrient doses with clinical outcome**

PICU=paediatric intensive care unit. For each of the first 7 days in the PICU, associations of average daily total doses of the individual macronutrients up to that day with likelihood of (A) acquiring a new infection in the PICU, (B) live weaning from mechanical ventilation, and (C) live PICU discharge are shown as hazard ratios and 95 % CIs per 10% added, with macronutrients entered as continuous variables. These data were obtained after adjustment for type of illness, age group, severity of risk of malnutrition, severity of illness, and treatment centre. A hazard ratio higher than 1 indicates a detrimental effect for likelihood of acquiring a new infection, but a beneficial effect for likelihood of live weaning from mechanical ventilation and of live PICU discharge, and vice versa for a hazard ratio less than 1. n indicates the number of patients still in the PICU on the day of analysis. Harm by increasing doses was observed irrespective of baseline risk factors as analysed by interaction p value.

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

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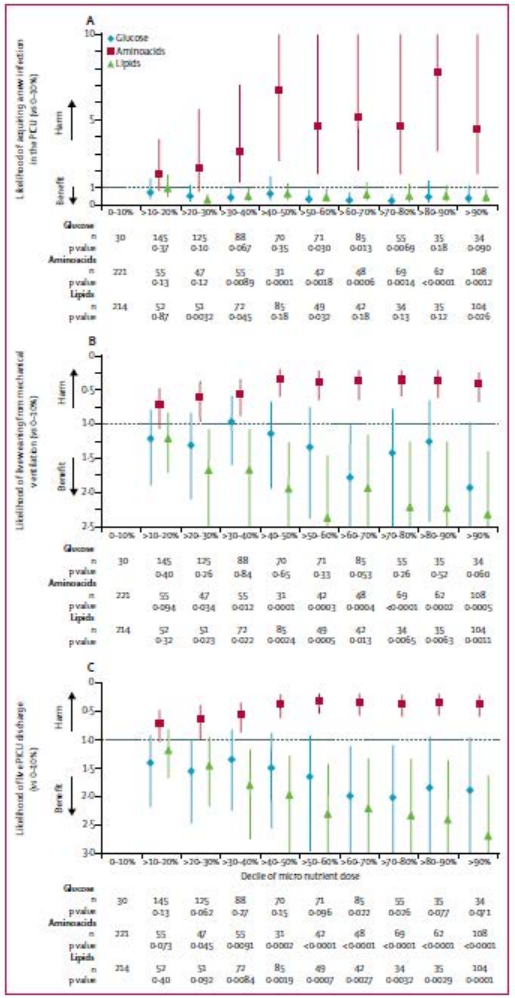
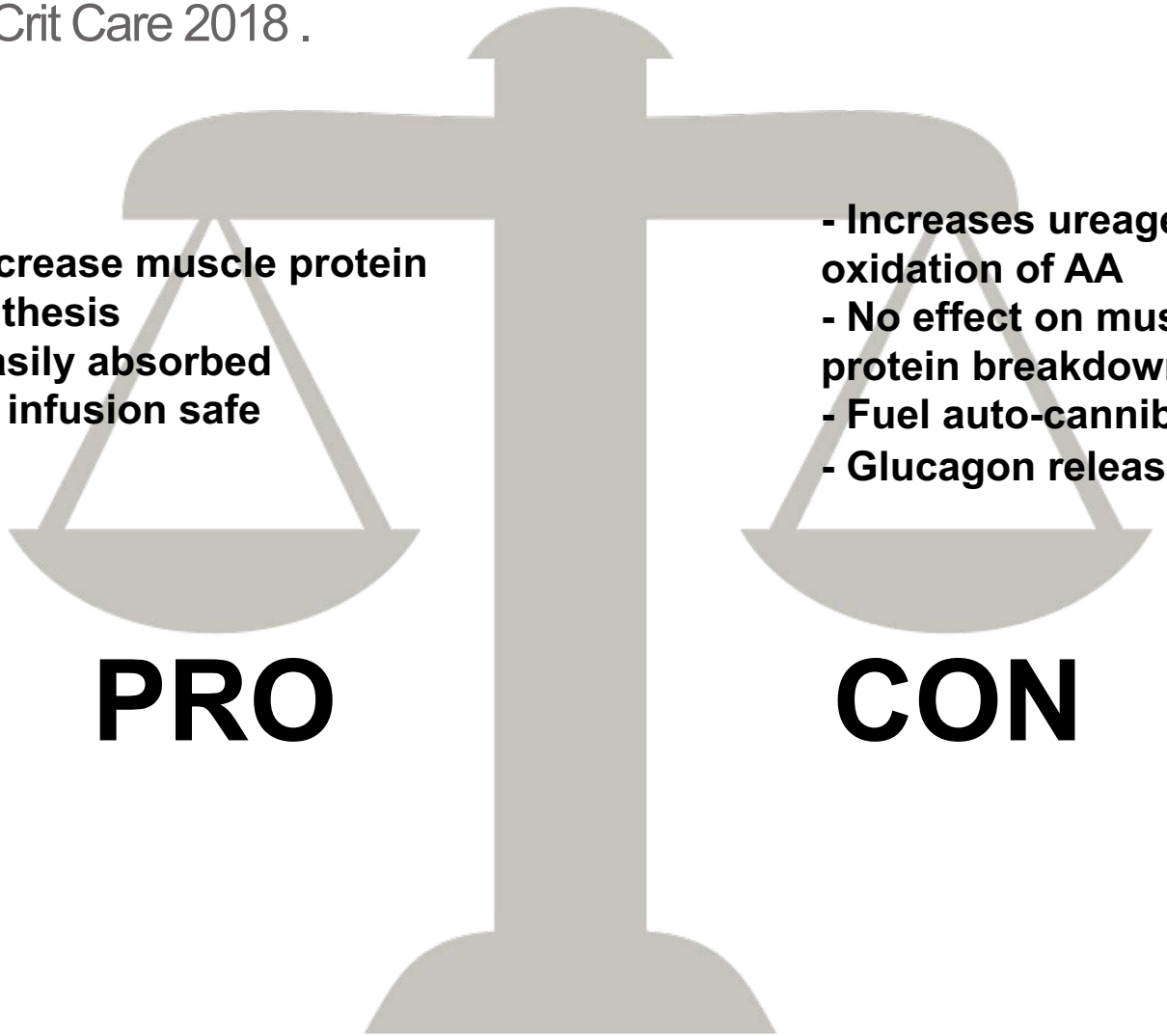


***Figure 3*: Dose relationship between average total macronutrient administration up to day 4 by decile and clinical outcome**

PICU=paediatric intensive care unit. Average daily total doses up to day 4 of each macronutrient were split up in deciles, with doses above 90% combined in a single class. The associations of the classes of average daily total doses of the individual macronutrients up to day 4 with (A) likelihood of acquiring a new infection in the PICU, (B) live weaning from mechanical ventilation, and (C) live PICU discharge are shown as hazard ratios and corresponding 95% CIs, compared with the reference class of 0–10%. These data were obtained after adjustment for type of illness, age group, severity of risk of malnutrition, severity of illness, and treatment centre. A hazard ratio higher than 1 indicates a detrimental effect for likelihood of acquiring a new infection, but a beneficial effect for likelihood of live weaning from mechanical ventilation and of live PICU discharge, and vice versa for a hazard ratio less than 1. The y-axis has been cut to better visualise the dose response. Full-scale figures are given in the appendix.

‘High protein intake during the early phase of critical illness: yes or no?’

JC Preiser, Crit Care 2018 .



- Increase muscle protein synthesis
- Easily absorbed
- IV infusion safe

PRO

- Increases ureagenesis and oxidation of AA
- No effect on muscle protein breakdown
- Fuel auto-cannibalism
- Glucagon release

CON

Provision of Nutrients to the Acutely Ill

Introducing the "Baby Stomach" Concept

Am J Respir Crit Care Med. 2017 Jun 8.
doi: 10.1164/rccm.201705-0919ED

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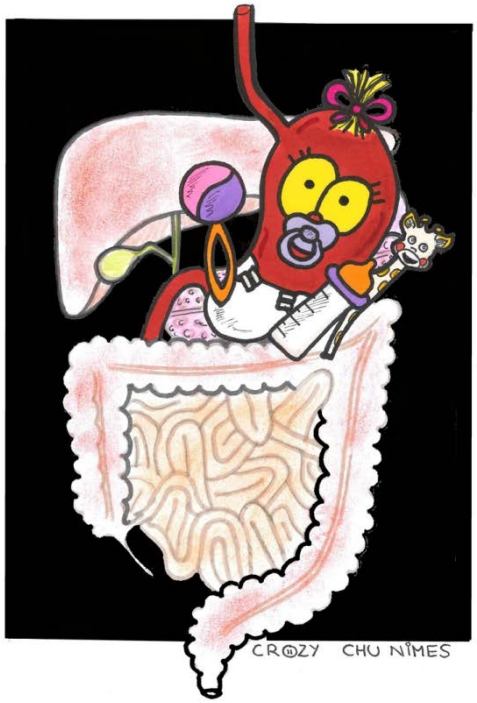

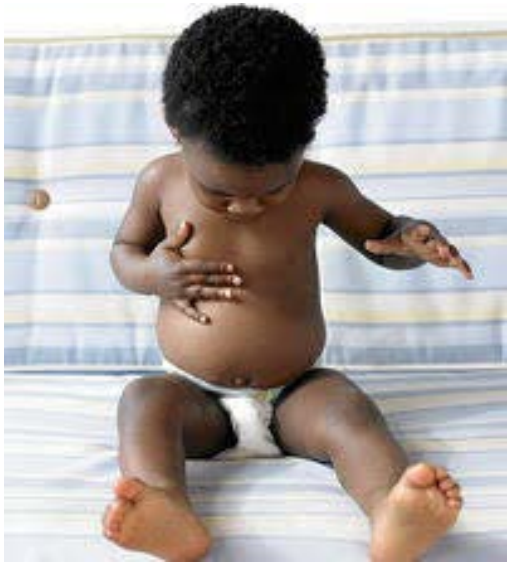

Intensive Care Med
DOI 10.1007/s00134-015-4156-8

EDITORIAL

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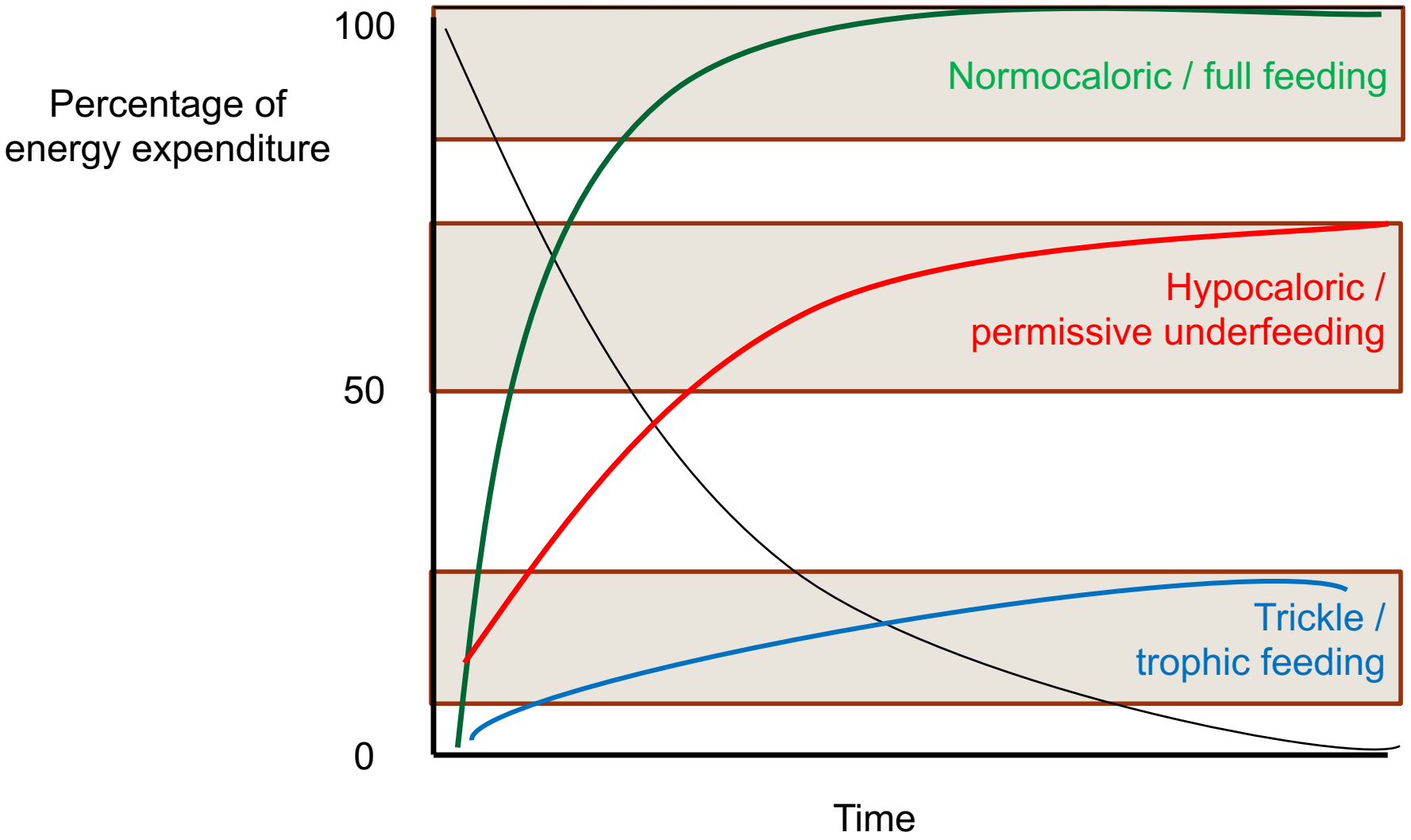
Be early for enteral, no rush for calories!



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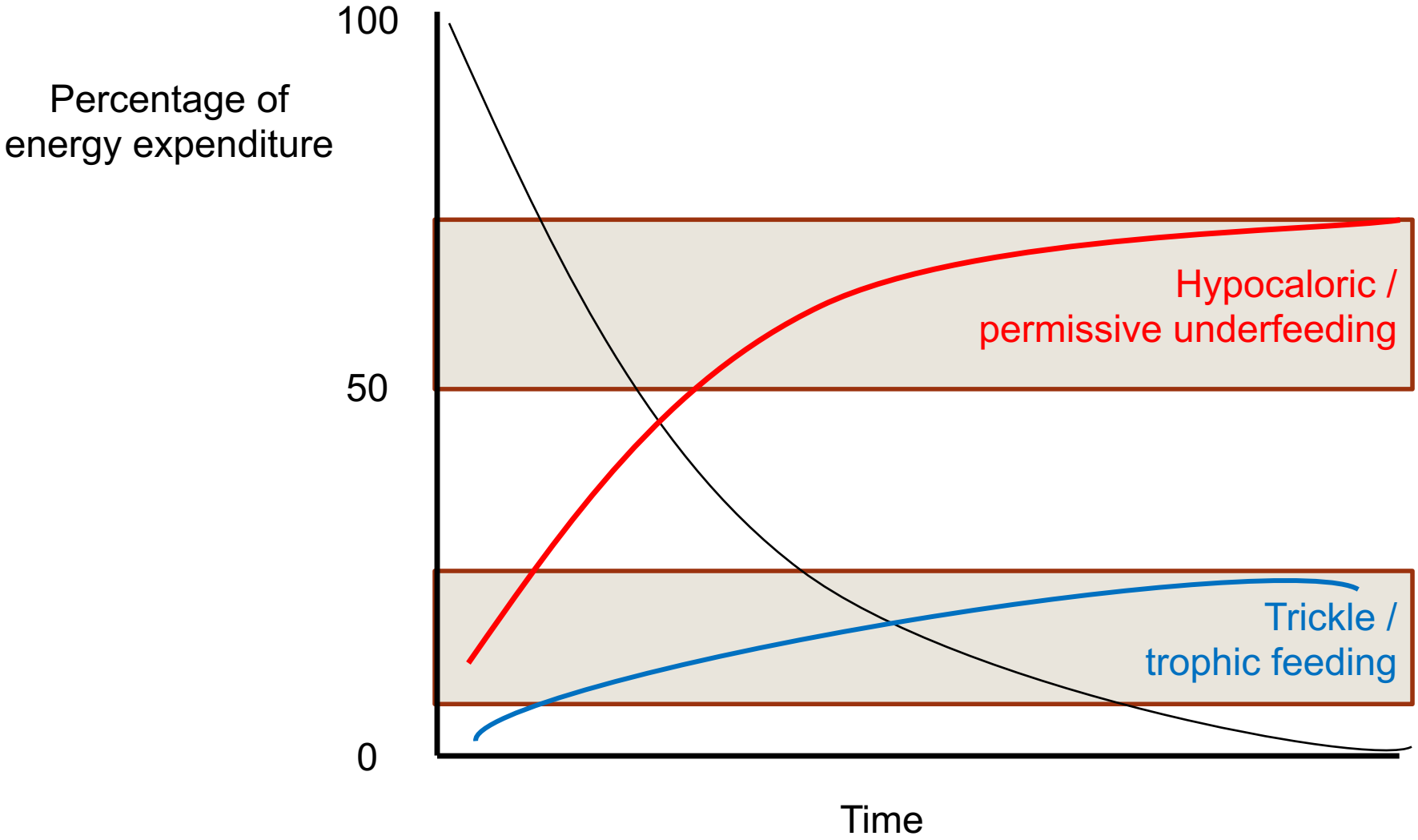
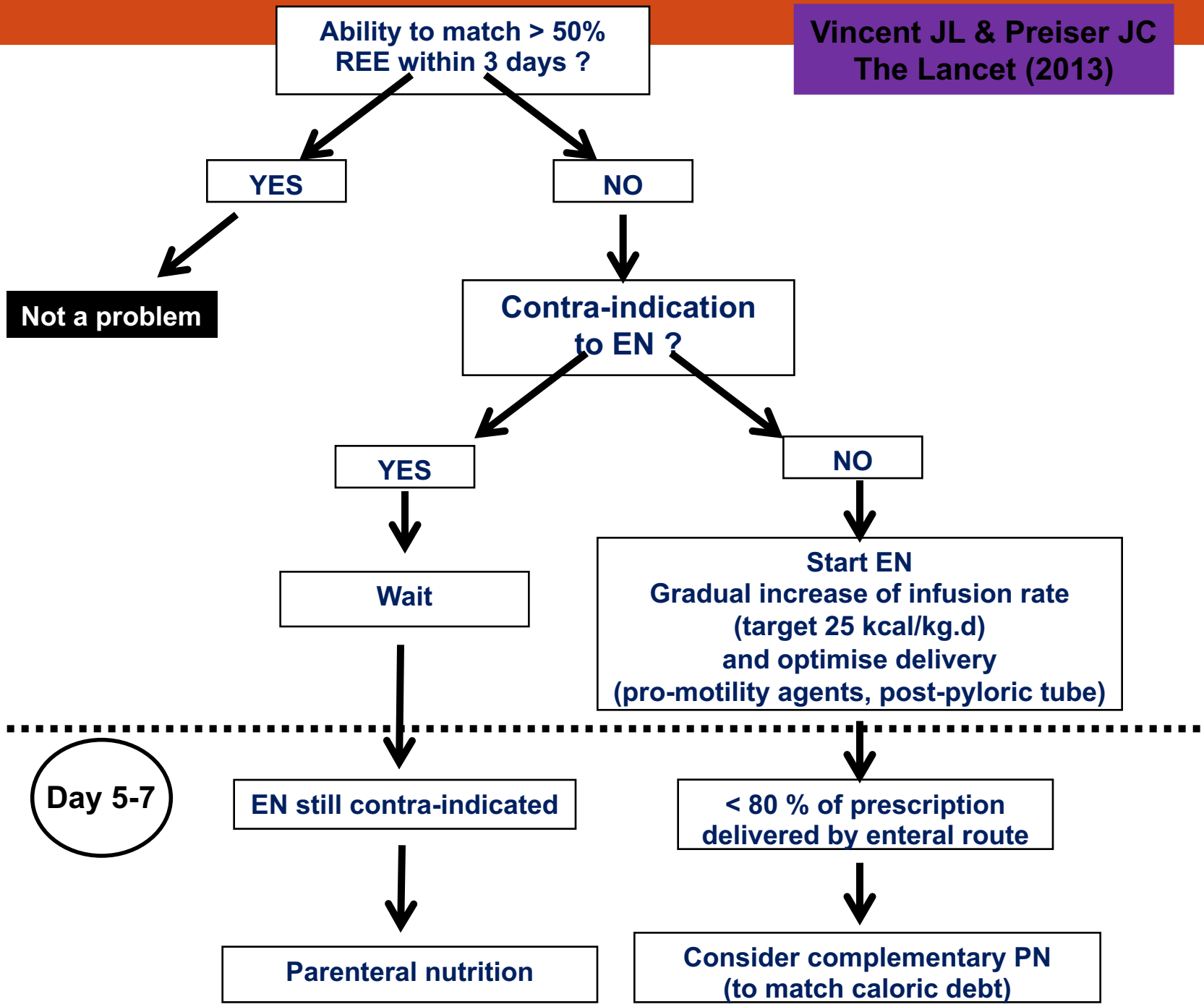
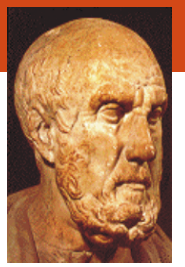


Permissive underfeeding is no longer abusive nor insulting!

Vincent JL & Preiser JC
The Lancet (2013)





Hippocrate (470-377 av. JC)
« Que ta nourriture soit ton médicament! »

Primum non nocere… avec une nutrition inadéquate: apports excessifs à la phase aïgue, insuffisants en phase tardive

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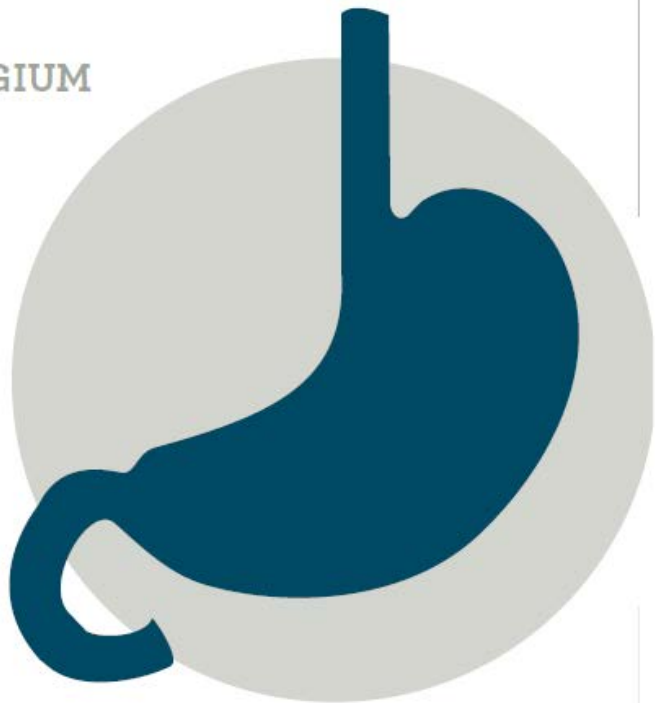

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