

SIS Nov 16, 2012

# Nutrition of the Critically Ill

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**Karolinska  
Institutet**

**KAROLINSKA**  
*Universitetssjukhuset*

Jan Wernerman

Disclosure of potential conflicts of interest during the last 2 years:

Member of the Medical Advisory Boards and also invited speaker for Baxter, Danone, Fresenius-Kabi, Grifols, and Nestlé

PI for Scandinavian multi-centre study of iv glutamine supplementation

# Four issues to discuss

1. When to start?
2. What route to use?
3. How much to give?
4. Who is at risk?

16 Nov 2012

# Nutrition determinates ICU outcome

# Nutrition determinates ICU outcome?

Nutrition determinates  
ICU outcome  
in longstayers



Contents lists available at [ScienceDirect](#)

## Clinical Nutrition

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



### ESPEN Guidelines on Parenteral Nutrition: Intensive care

Pierre Singer<sup>a</sup>, Mette M. Berger<sup>b</sup>, Greet Van den Berghe<sup>c</sup>, Gianni Biolo<sup>d</sup>, Philip Calder<sup>e</sup>,  
Alastair Forbes<sup>f</sup>, Richard Griffiths<sup>g</sup>, Georg Kreyman<sup>h</sup>, Xavier Leverve<sup>i</sup>, Claude Pichard<sup>j</sup>



ESPEN Guidelines on Parenteral Nutrition: Intensive care

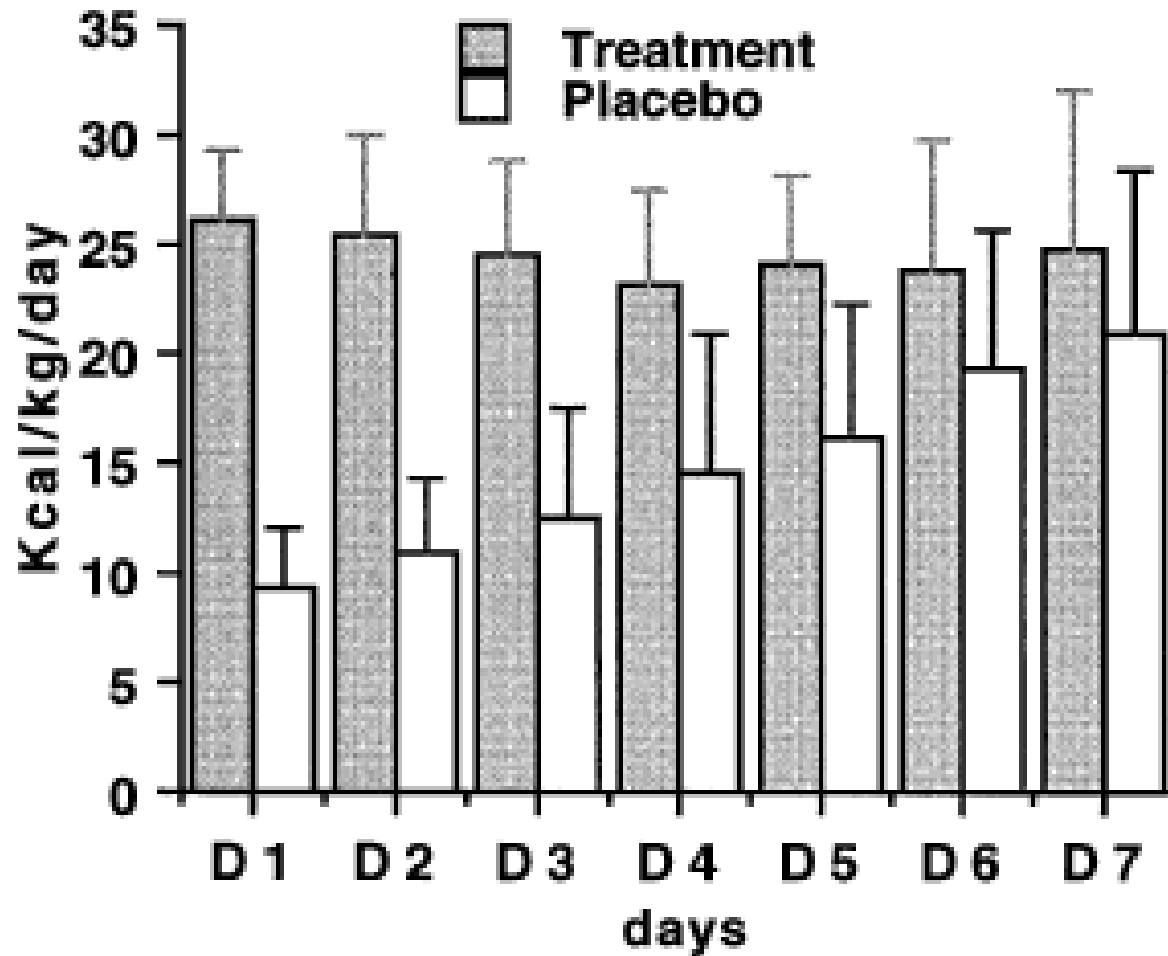
Pierre Singer<sup>a</sup>, Mette M. Berger<sup>b</sup>, Greet Van den Berghe<sup>c</sup>, Gianni Biolo<sup>d</sup>, Philip Calder<sup>e</sup>, Alastair Forbes<sup>f</sup>, Richard Griffiths<sup>g</sup>, Georg Kreyman<sup>h</sup>, Xavier Leverve<sup>i</sup>, Claude Pichard<sup>j</sup>

**”All patients receiving less than their targeted feeding after 2 days should be considered for supplementary PN”**

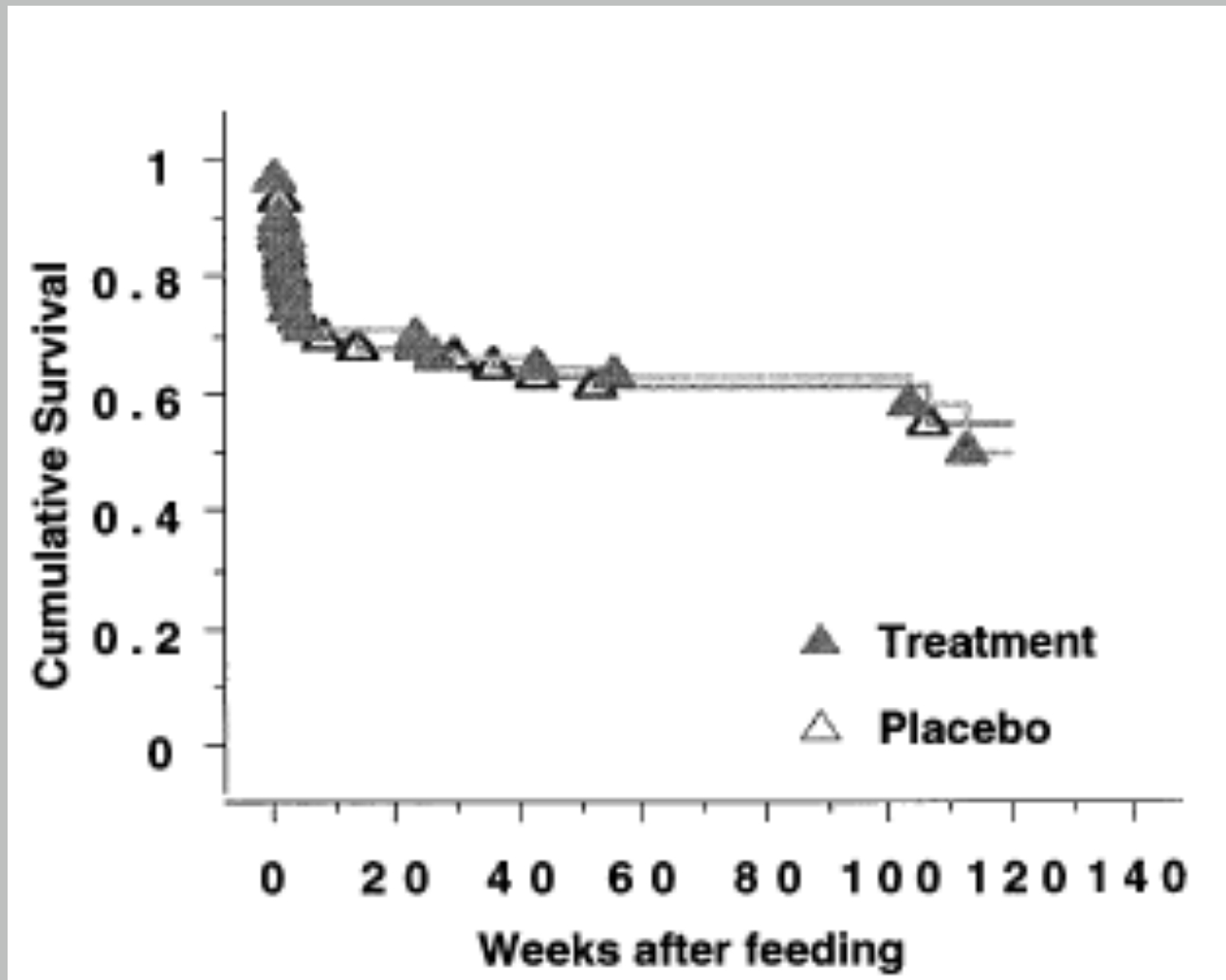
**grade C evidence**

**P. Bauer**  
**C. Charpentier**  
**C. Bouchet**  
**L. Nace**  
**F. Raffy**  
**N. Gaconnet**

## **Parenteral with enteral nutrition in the critically ill**



Bauer et al, ICM 2000;26:893-900



Bauer et al, ICM 2000;26:893-900

ORIGINAL ARTICLE

# Early versus Late Parenteral Nutrition in Critically Ill Adults

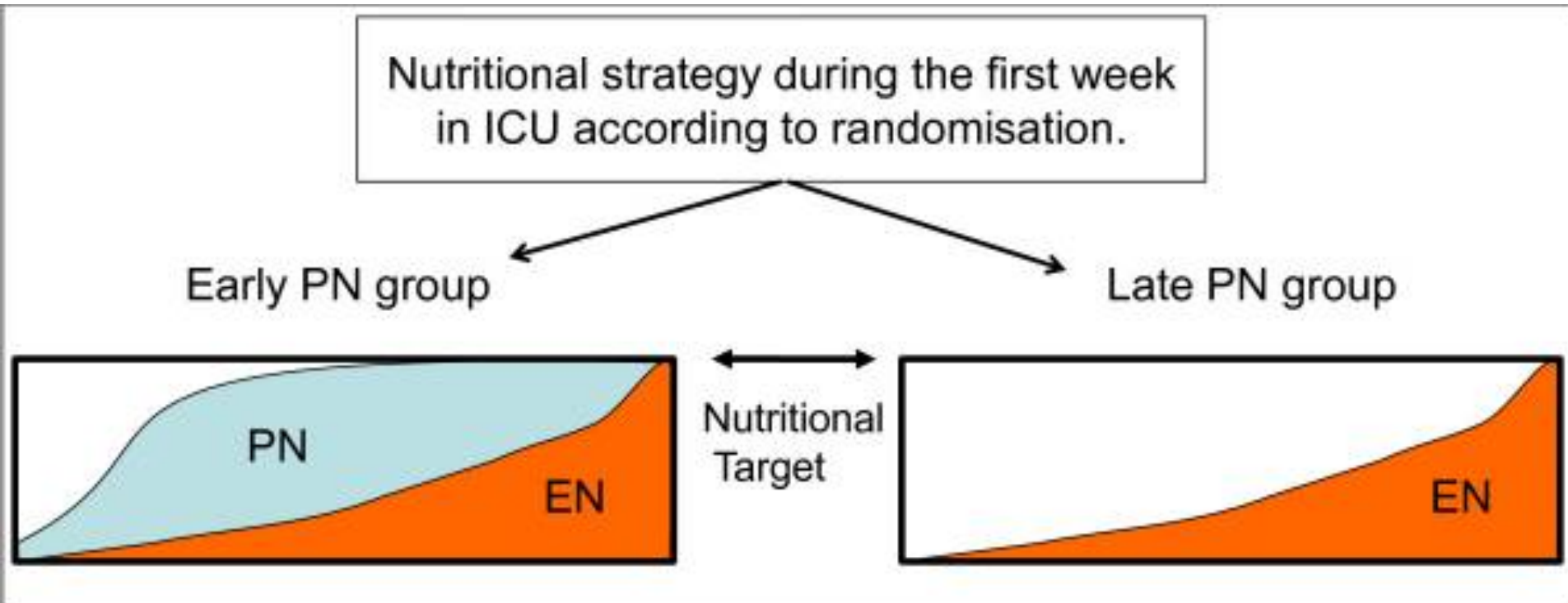
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**STUDY PROTOCOL**

**Open Access**

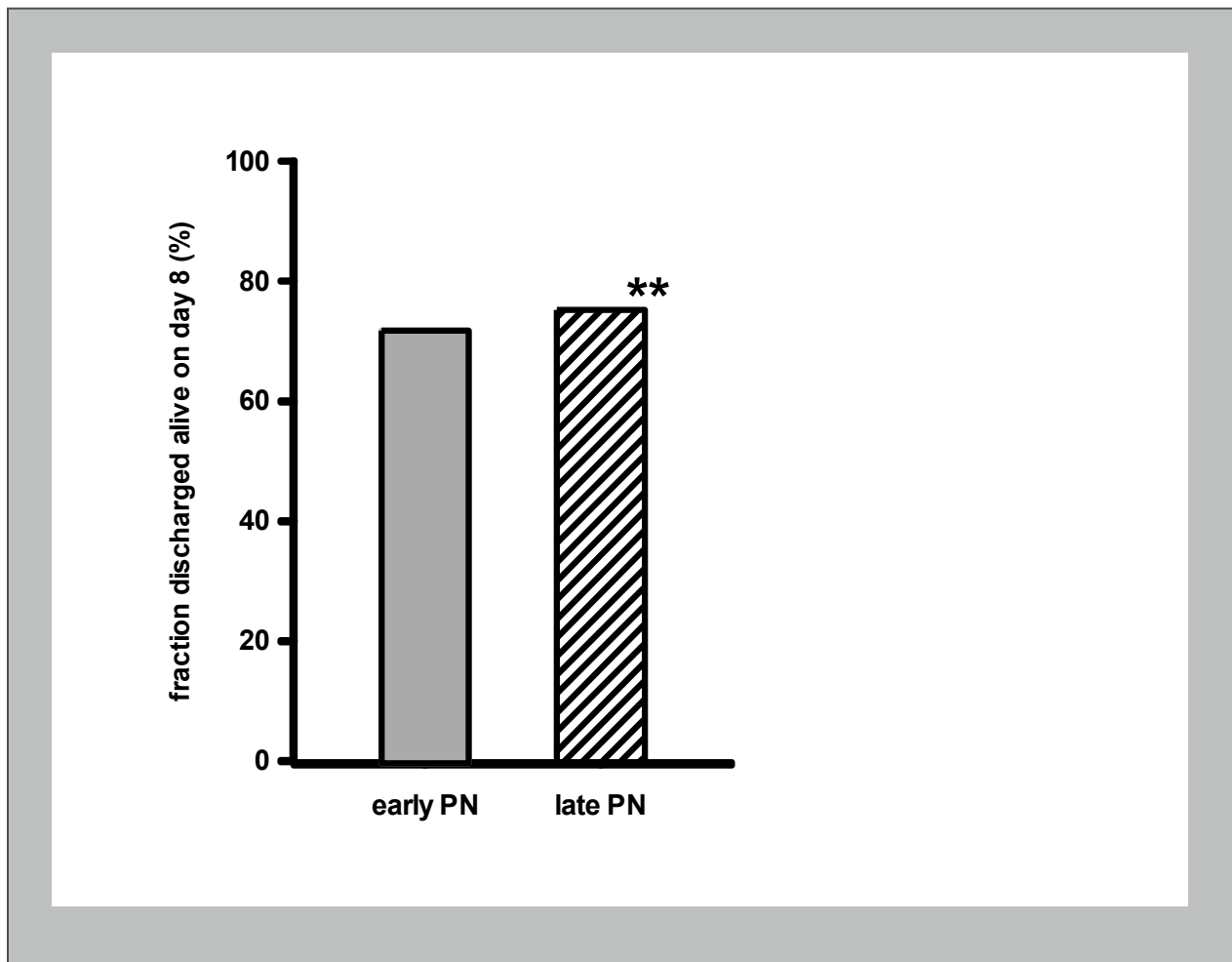
# Impact of early parenteral nutrition completing enteral nutrition in adult critically ill patients (EPaNIC trial): a study protocol and statistical analysis plan for a randomized controlled trial

Michaël P Casaer<sup>1\*</sup>, Greet Hermans<sup>2</sup>, Alexander Wilmer<sup>2</sup>, Greet Van den Berghe<sup>1</sup>



## Early versus Late Parenteral Nutrition in Critically Ill Adults

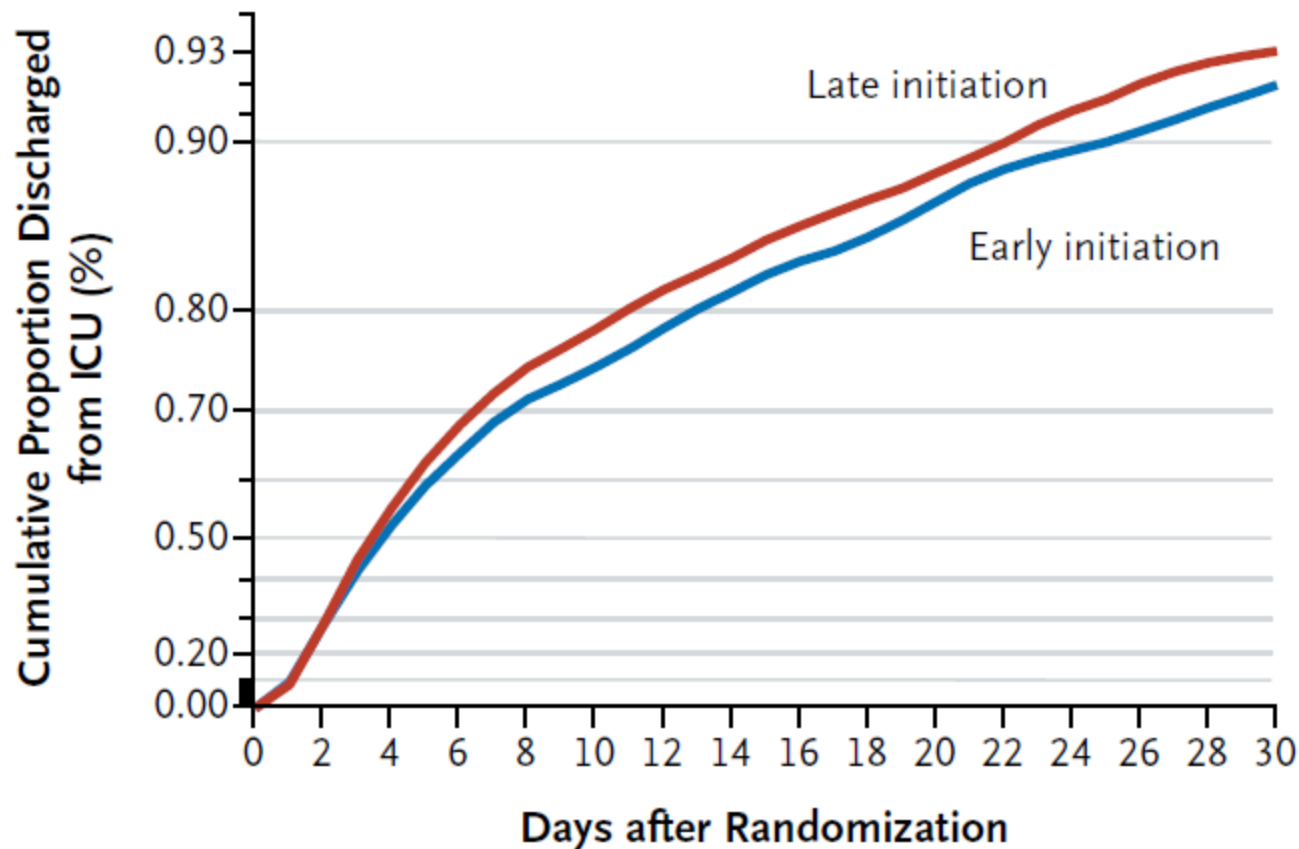
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### A Discharge from ICU



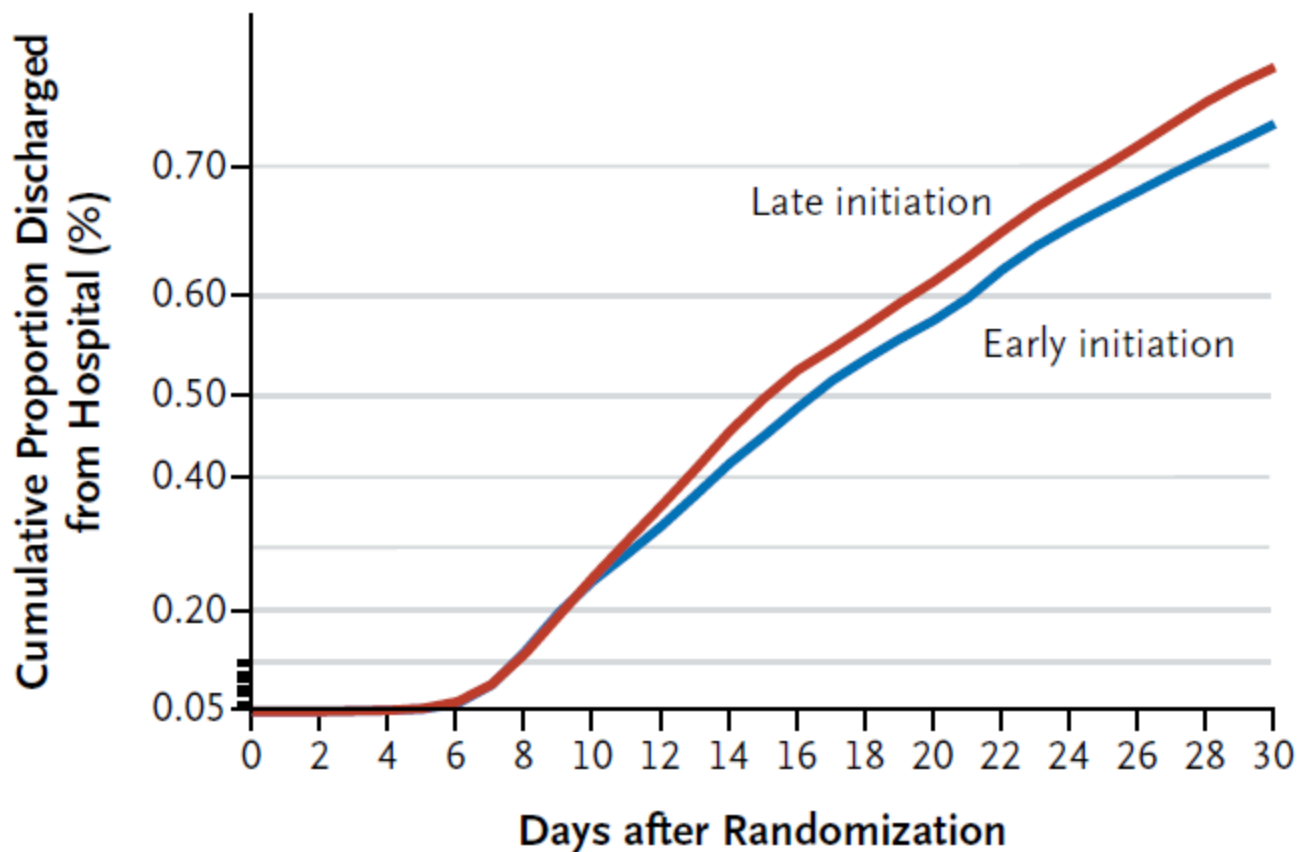
#### No. at Risk

Late initiation	2328	574	291	122
Early initiation	2312	646	342	147

Early versus Late Parenteral Nutrition  
in Critically Ill Adults

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### C Discharge from Hospital



**No. at Risk**

Late initiation	2328	2084	1061	508
Early initiation	2312	2059	1159	574

## Early versus Late Parenteral Nutrition in Critically Ill Adults

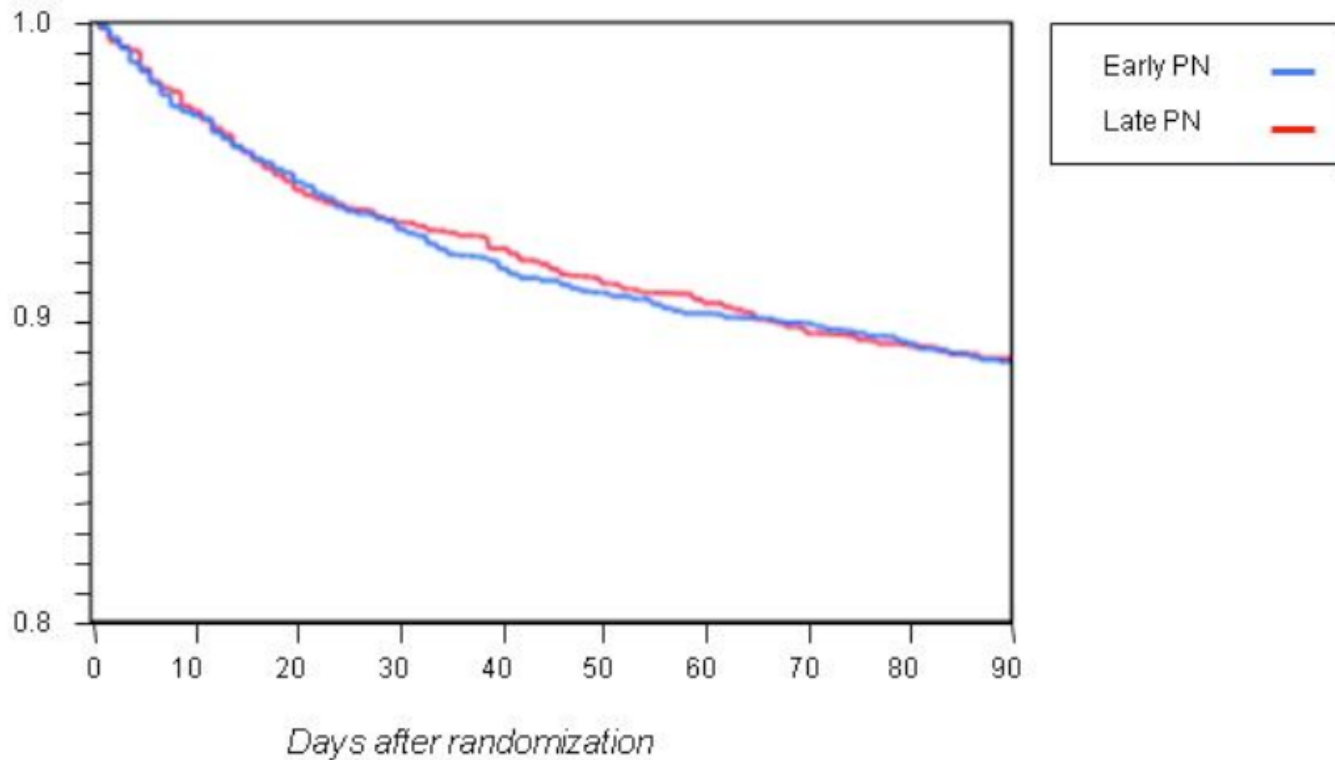
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### Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

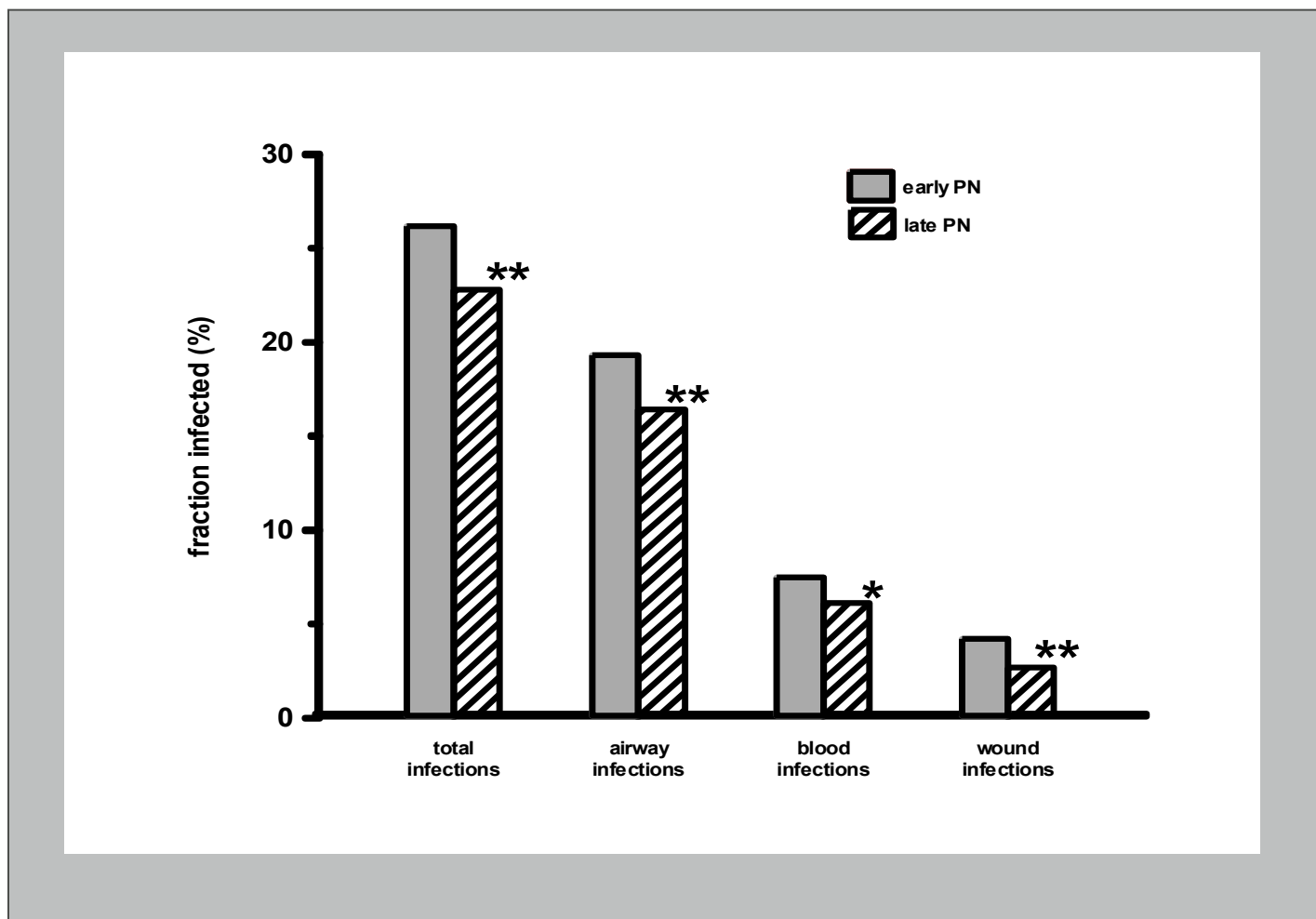
Supplement to: Caser MP, Mesotten D, Hermans G, et al. Early versus late parenteral nutrition in critically ill adults. *N Engl J Med* 2011;365:506-17. DOI: 10.1056/NEJMa110262.

### Kaplan-Meier survival Plot



## Early versus Late Parenteral Nutrition in Critically Ill Adults

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## Online-table 6. Subgroup Analysis

	Primary outcome		Safety outcome	
	time to alive discharge from ICU		discharged alive from ICU within 8 days	
	HR (95% CI)	interaction P Value	OR (95% CI)	interaction P Value
Overall (N=4640)	1.063 (1.002-1.128)	NA	1.271 (1.080-1.495)	NA
<b>A priori defined subgroups</b>				
BMI (<25 OR ≥40) (N=1989)	1.045 (0.956-1.143)	0.5725	1.239 (0.985-1.560)	0.7985
<b>NRS ≥5 (N=863)</b>	<b>1.059 (0.916-1.224)</b>	<b>0.8454</b>	<b>1.222 (0.887-1.685)</b>	<b>0.7898</b>
Cardiac surgery (N=2818)	1.047 (0.971-1.129)	0.8616	1.232 (0.963-1.599)	0.7445
<b>Sepsis admission (N=1015)</b>	<b>0.991 (0.866-1.134)</b>	<b>0.3198</b>	<b>1.068 (0.820-1.439)</b>	<b>0.2701</b>
<b>Post-hoc defined subgroup</b>				
<b>Surgical contraindication for EN* (N = 517)</b>	<b>1.198 (0.999 -1.437)</b>	<b>0.1197</b>	<b>1.749 (1.141 - 2.683)</b>	<b>0.1348</b>

## Early versus Late Parenteral Nutrition in Critically Ill Adults

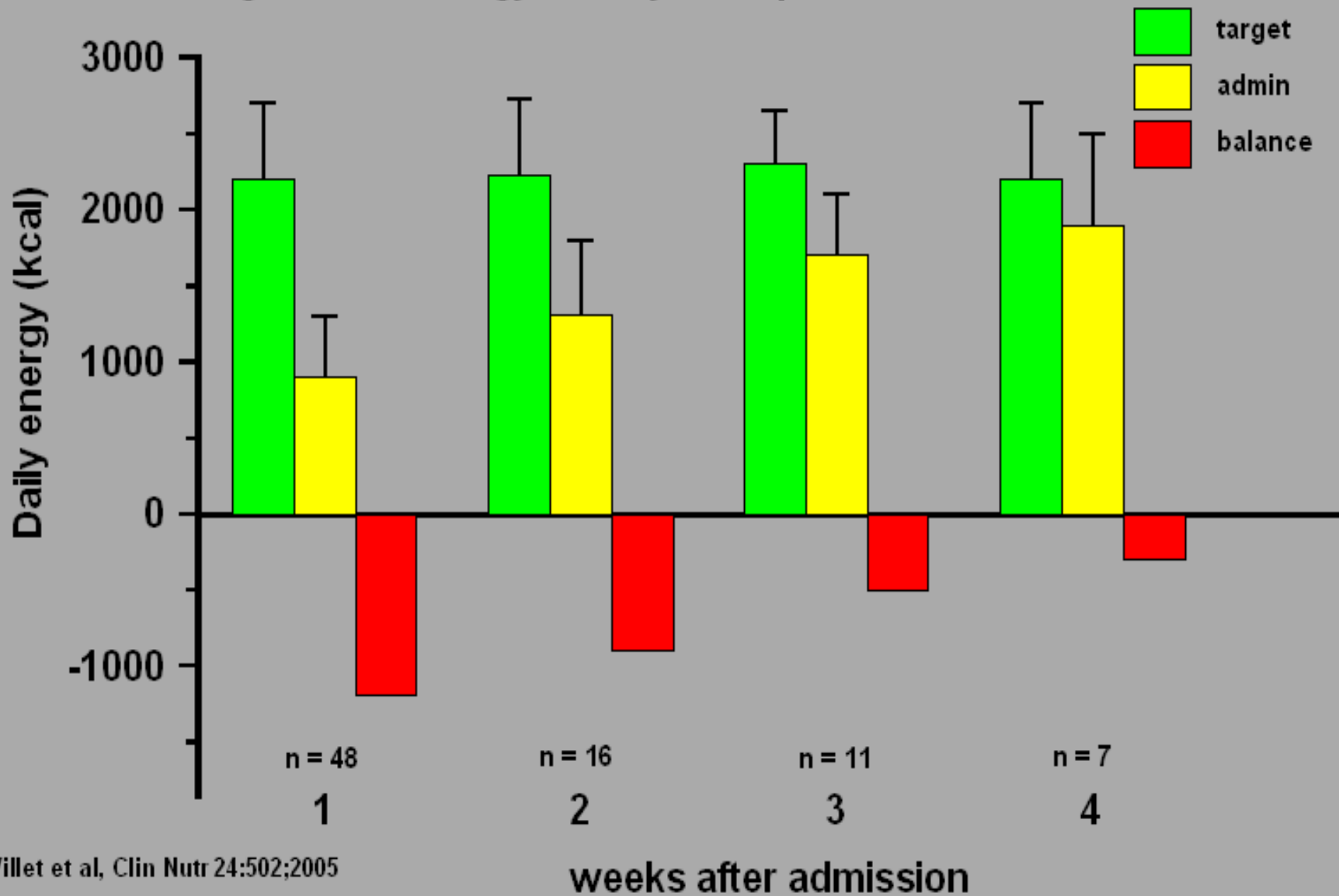
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# Comments

1. Broad inclusions
2. Over-representation of cardiac surgery
3. High energy supply (ESPEN Guidelines)
4. High initial glucose supply
5. No glutamin or selenium

There are a number of examples that a cumulated energy deficit is associated with a higher mortality and morbidity

### Progression of energy delivery in ICU patients over time



# Cumulated energy deficit v. infections

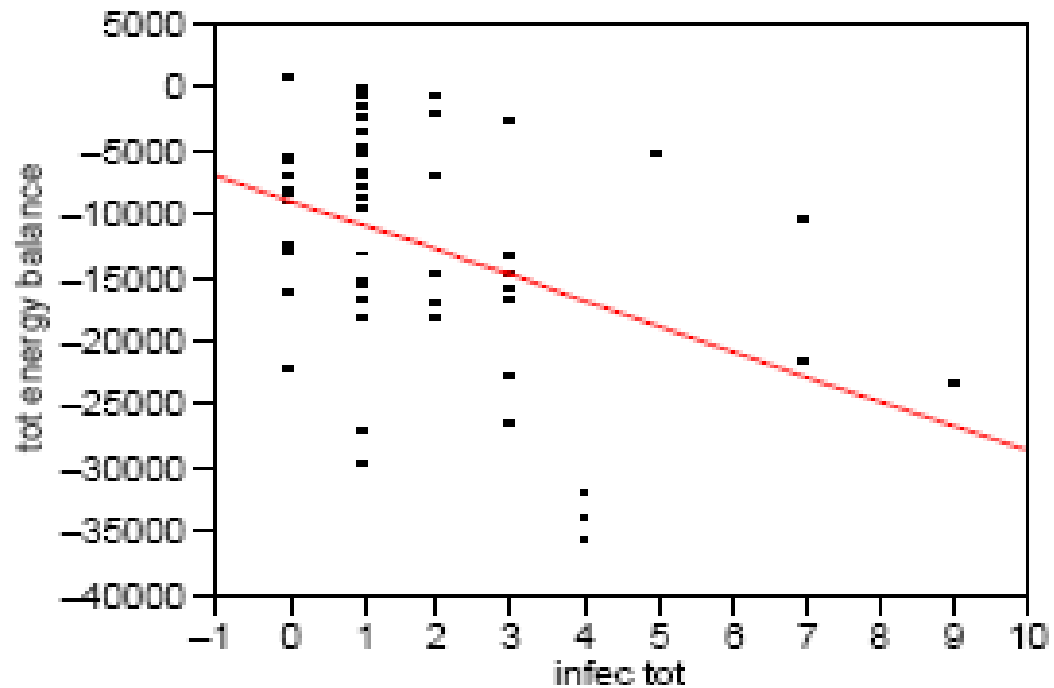
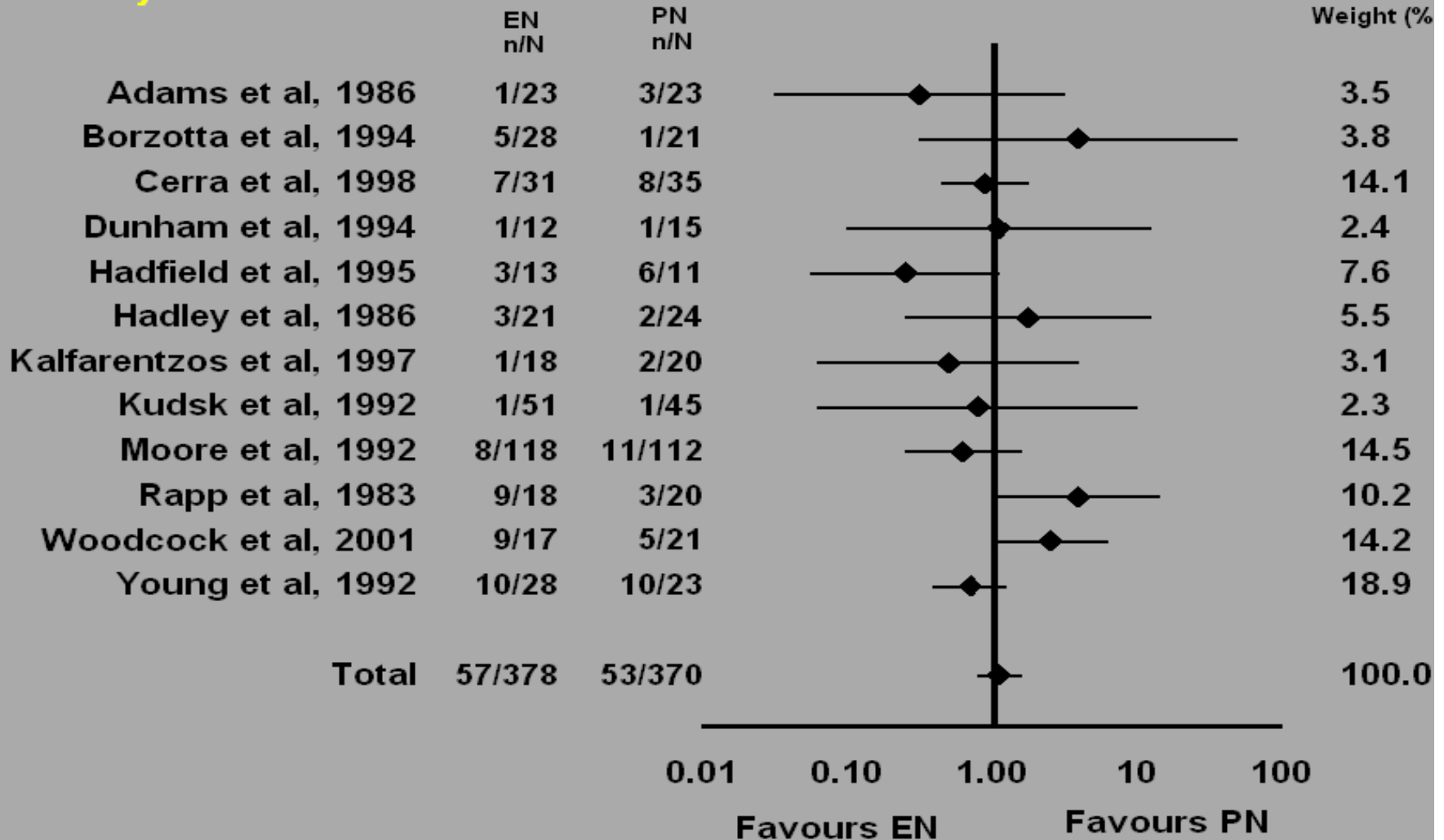


Figure 2 Relation between the progressive negative energy balance and the number of infectious complications.

There is no evidence for a mortality difference between patients randomised to either enteral or parenteral nutrition, but there may be a morbidity difference

## Mortality



Heyland et al, JPEN 27:355-373 (2003)

# Indirect evidence

1. Malnutrition is dangerous
2. Energy deficit is dangerous
3. EN & PN carries equal mortality

## Current practice in nutritional support and its association with mortality in septic patients—Results from a national, prospective, multicenter study\*

Gunnar Elke, MD; Dirk Schädler, MD; Christoph Engel, MD; Holger Bogatsch; Inez Frerichs, MD; Maximilian Ragaller, MD; Jens Scholz, MD; Frank M. Brunkhorst, MD; Markus Löffler, MD; Konrad Reinhart, MD; Norbert Weiler, MD; for the German Competence Network Sepsis (SepNet)

***Conclusions:* Patients with severe sepsis or septic shock in German intensive care units received preferentially parenteral or mixed nutrition. The use of parenteral nutrition was associated with an increased risk of death. (Crit Care Med 2008; 36:1762–1767)**

Table 4. Independent predictors for mortality

Variable	Univariate		Multivariate <sup>a</sup>	
	OR	<i>p</i> Value	OR	95% CI
Enteral nutrition	0.68	.065	1.13	0.84–1.51
Parenteral nutrition	1.97	.003	2.09	1.29–3.37
APACHE II	1.07	<.0001	1.05	1.02–1.09
Renal dysfunction <sup>b</sup>	2.91	<.0001	2.07	1.30–3.31
Insulin dose (IU/24 hrs)	1.00	.338		
Serum glucose concentration (mg/dL)	1.00	.145		
Age	1.01	.051	1.01	0.99–1.02
Gender	0.90	.609		
Mechanical ventilation	2.88	.083		
Septic shock	1.85	.004	1.54	0.97–2.44

Elke et al, CCM 2008;36:1762

**ONLINE FIRST**

# Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury

## The EDEN Randomized Trial

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The National Heart, Lung, and Blood  
Institute Acute Respiratory Distress  
Syndrome (ARDS) Clinical Trials  
Network\*

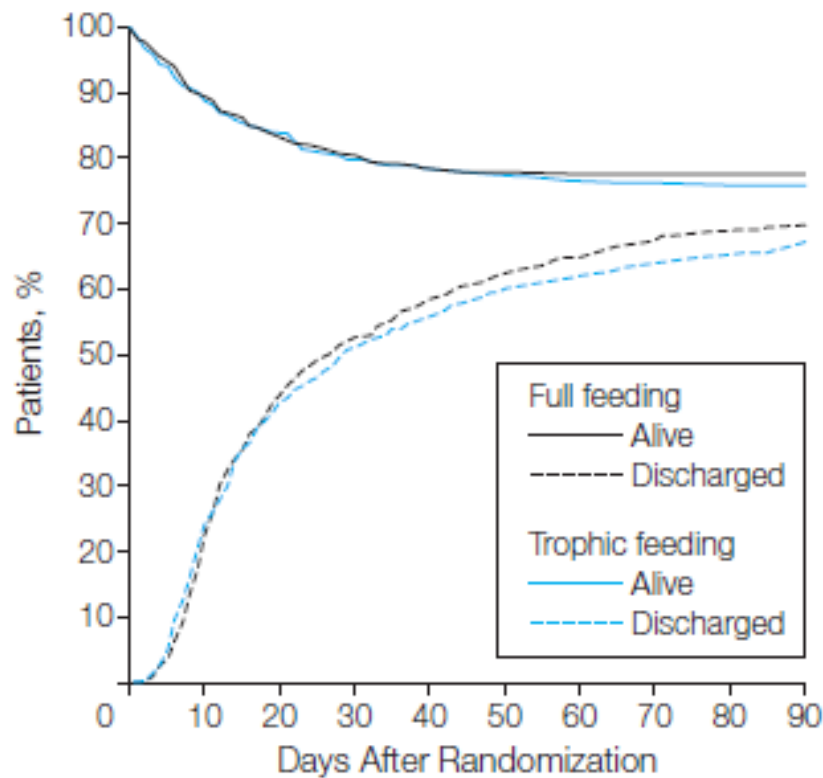
*JAMA*. 2012;307(8):795-803

Published online February 5, 2012. doi:10.1001/jama.2012.137

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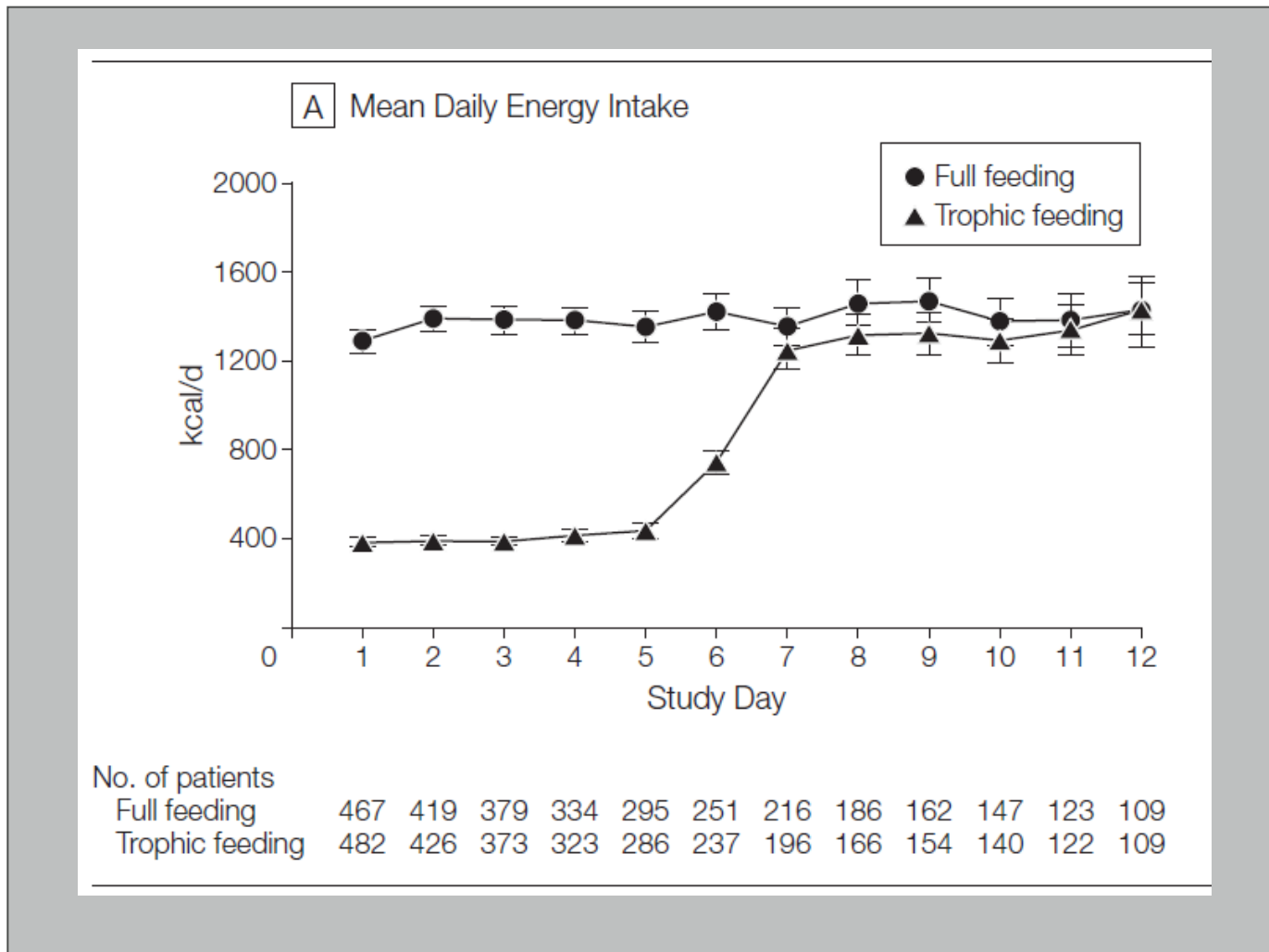
The EDEN Randomized Trial

**Figure 3.** Survival and Hospital Discharge



# Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury

The EDEN Randomized Trial



# **SUPPLEMENTAL PARENTERAL NUTRITION (SPN) IN INTENSIVE CARE UNIT (ICU) PATIENTS FOR OPTIMAL ENERGY COVERAGE: IMPROVED CLINICAL OUTCOME**

*C.-P. Heidegger<sup>1</sup>, S. Graf<sup>2</sup>, R. Thibault<sup>2</sup>, P. Darmon<sup>2</sup>, M. Berger<sup>3</sup>, C. Pichard<sup>2</sup>*

<sup>1</sup>Geneva University Hospitals, Division of Intensive Care, Geneva, Switzerland, <sup>2</sup>Geneva University Hospitals, Clinical Nutrition Unit, Geneva, Switzerland,

<sup>3</sup>University Hospital Lausanne, Lausanne, Switzerland

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<sup>3</sup>University Hospital Lausanne, Lausanne, Switzerland

N=275	Coefficient	95% CI	p
New Infection	-0.27	-0.50 to -0.04	0.019
AB	-3.4	-5.71 to -1.04	0.005
AB free days	3.48	0.94 to 6.01	0.007
Hours of mechanical ventilation	-87.4	-131 to -43.8	< 0.001
LOS	-2.70	-4.72 to -0.69	0.009

[EN group vs. SPN group and clinical outcome]

*C.-P. Heidegger<sup>1</sup>, S. Graf<sup>2</sup>, R. Thibault<sup>2</sup>, P. Darmon<sup>2</sup>, M. Berger<sup>3</sup>, C. Pichard<sup>2</sup>*

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<sup>3</sup>University Hospital Lausanne, Lausanne, Switzerland

# Comments

1. Narrow inclusions (10%)
2. MOF patients
3. High energy supply (ESPEN Guidelines)
4. Indirect calorimetry (200-300 kcal lower)
5. Not yet published



THE UNIVERSITY OF  
**SYDNEY**



**Statistical Analysis Plan for a multi-centre randomised controlled trial:  
Early parenteral nutrition vs. standard care in patients not expected to  
be fed within 24 h of ICU admission.**

Gordon S. Doig,<sup>1</sup> Fiona Simpson,<sup>2</sup> Elizabeth A. Sweetman<sup>2</sup> and Philippa T. Heighes<sup>3</sup>  
on behalf of the Early PN Trial Management Committee.

*The Early PN Trial*

# Possible conclusion today

1. Early enteral nutrition is recommended
2. Parenteral supplementation may wait
3. Over-nutrition is not a good idea

16 Nov 2012

# Three unsolved issues

1. How much nutrition to give (kcal)?
2. What should be the protein (amino acid) content?
3. How to identify patients at a nutritional risk?

16 Nov 2012



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Nutrition

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<http://intl.elsevierhealth.com/journals/clnu>

ESPEN GUIDELINES

## ESPEN Guidelines on Enteral Nutrition: Intensive care ☆

K.G. Kreymann<sup>a,\*</sup>, M.M. Berger<sup>b</sup>, N.E.P. Deutz<sup>c</sup>, M. Hiesmayr<sup>d</sup>, P. Jolliet<sup>e</sup>,  
G. Kazandjiev<sup>f</sup>, G. Nitenberg<sup>g</sup>, G. van den Berghe<sup>h</sup>, J. Wernerman<sup>i</sup>,  
DGEM: ☆ ☆ C. Ebner, W. Hartl, C. Heymann, C. Spies



ESPEN GUIDELINES

**ESPEN Guidelines on Enteral Nutrition:  
Intensive care** ☆

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No general amount can be recommended as EN therapy has to be adjusted to the progression/ course of the disease and to gut tolerance.

Exogenous energy supply:

- during the acute and initial phase of critical illness: in excess of 20–25 kcal/kg BW/day may be associated with a less favourable outcome. C
- during the anabolic recovery phase, the aim should be to provide 25–30 kcal/kg BW/day. C



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**”In the absence of indirect calorimetry, ICU-patients should receive 25 kcal/kg/day increasing to target over the next 2-3 days”**

**grade C evidence**

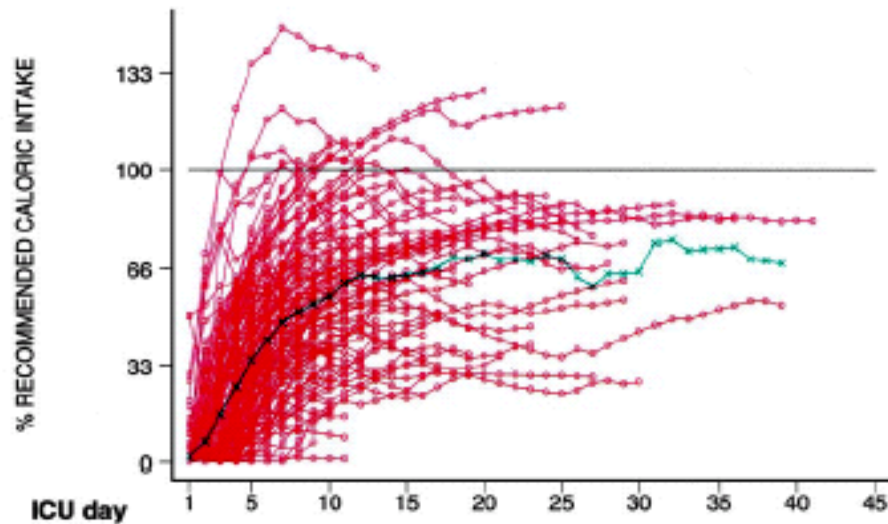
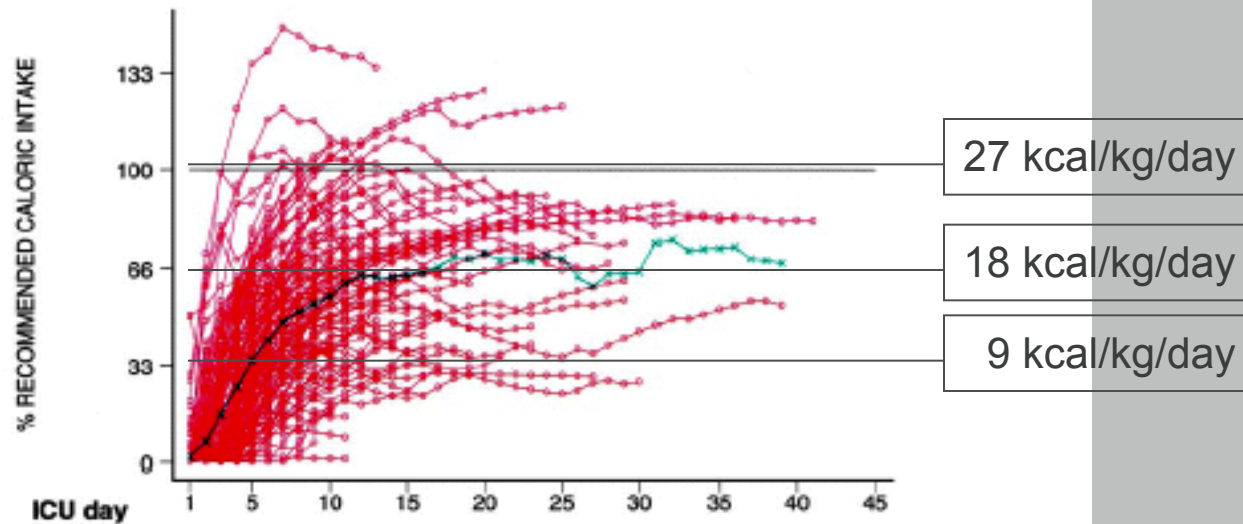


FIGURE 1. The cumulative average caloric intake since ICU admission for each of 187 participants (○) is shown. For example, a participant's cumulative average caloric intake for ICU day 5 is the mean for days 1 to 5. Similarly, a participant's cumulative average caloric intake for ICU day 10 is the mean caloric intake for ICU days 1 to 10. The last cumulative average caloric intake for each participant thus represents the average caloric intake from nutritional support over all ICU days for that participant. The mean caloric intake for each ICU day (x) for all participants in the ICU is also shown. The horizontal line at caloric intake represents 100% of the target caloric intake recommended by ACCP guidelines.

Krishnan et al. Chest124:297 (2003)



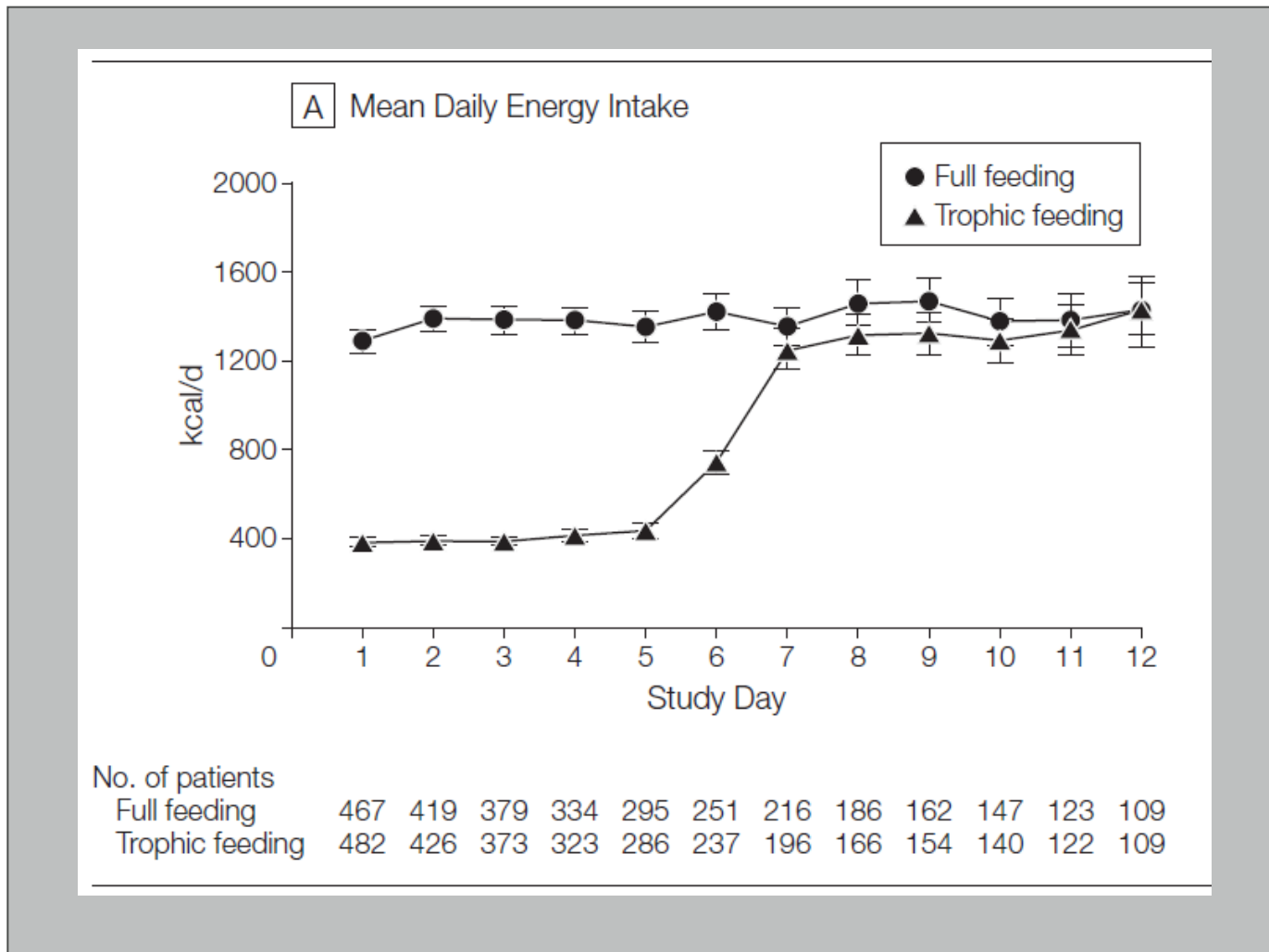
<b># Participants</b>	187	186	95	45	26	16	5	3	1	0
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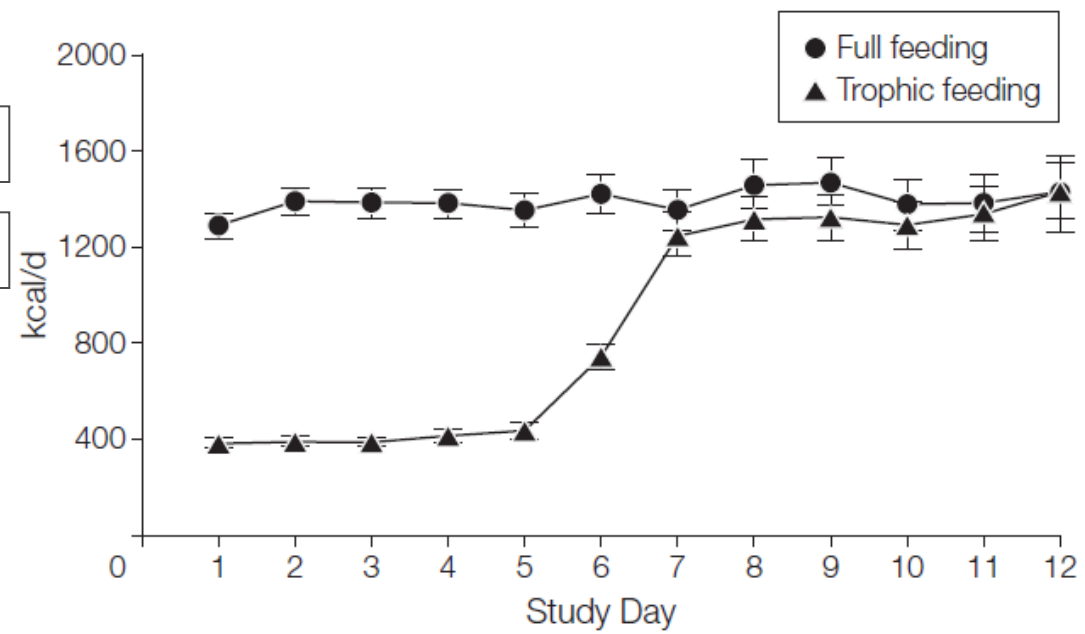
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The EDEN Randomized Trial

18 kcal/kg/d

14 kcal/kg/d

A Mean Daily Energy Intake



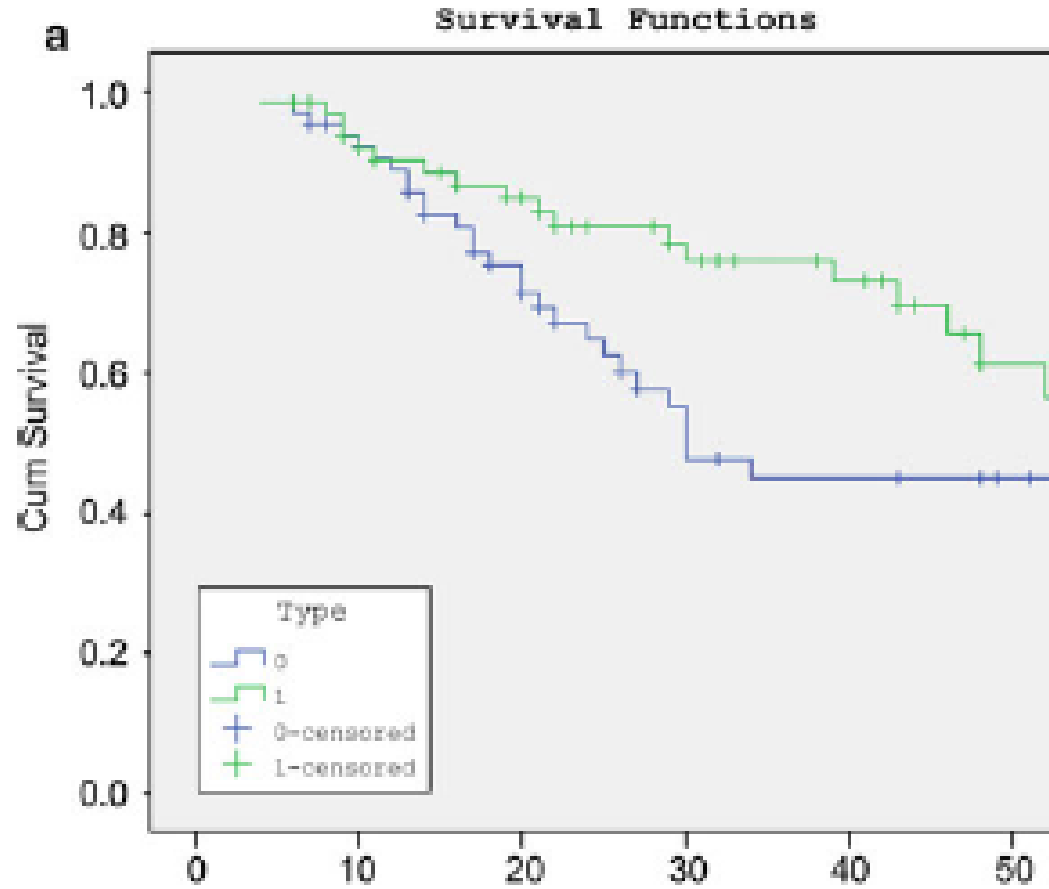
No. of patients	1	2	3	4	5	6	7	8	9	10	11	12
Full feeding	467	419	379	334	295	251	216	186	162	147	123	109
Trophic feeding	482	426	373	323	286	237	196	166	154	140	122	109

Pierre Singer  
Ronit Anbar  
Jonathan Cohen  
Haim Shapiro  
Michal Shalita-Chesner  
Shaul Lev  
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Miryam Theilla  
Sigal Frishman  
Zecharia Madar

**The tight calorie control study (TICACOS):  
a prospective, randomized, controlled pilot  
study of nutritional support in critically ill  
patients**

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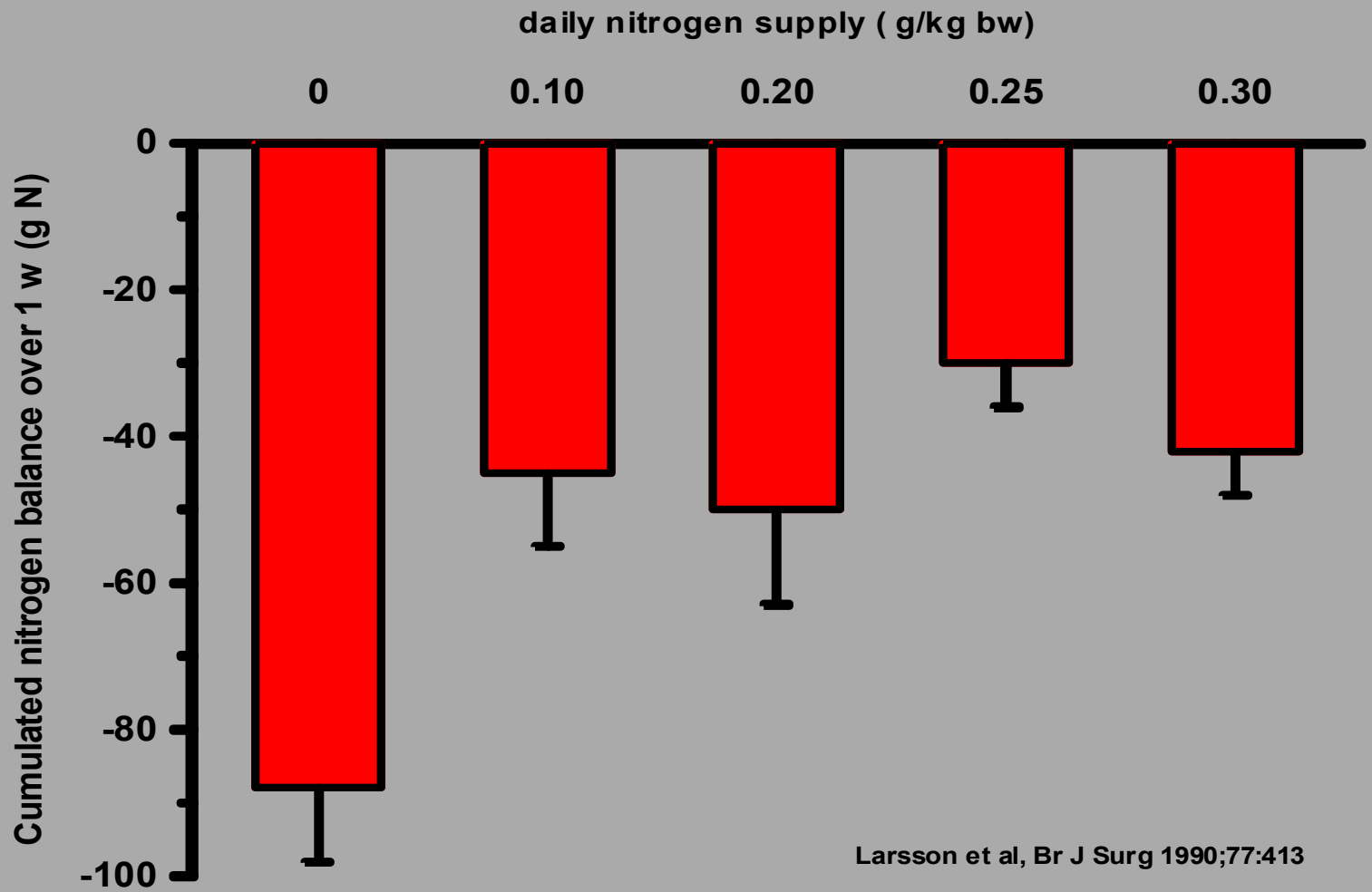


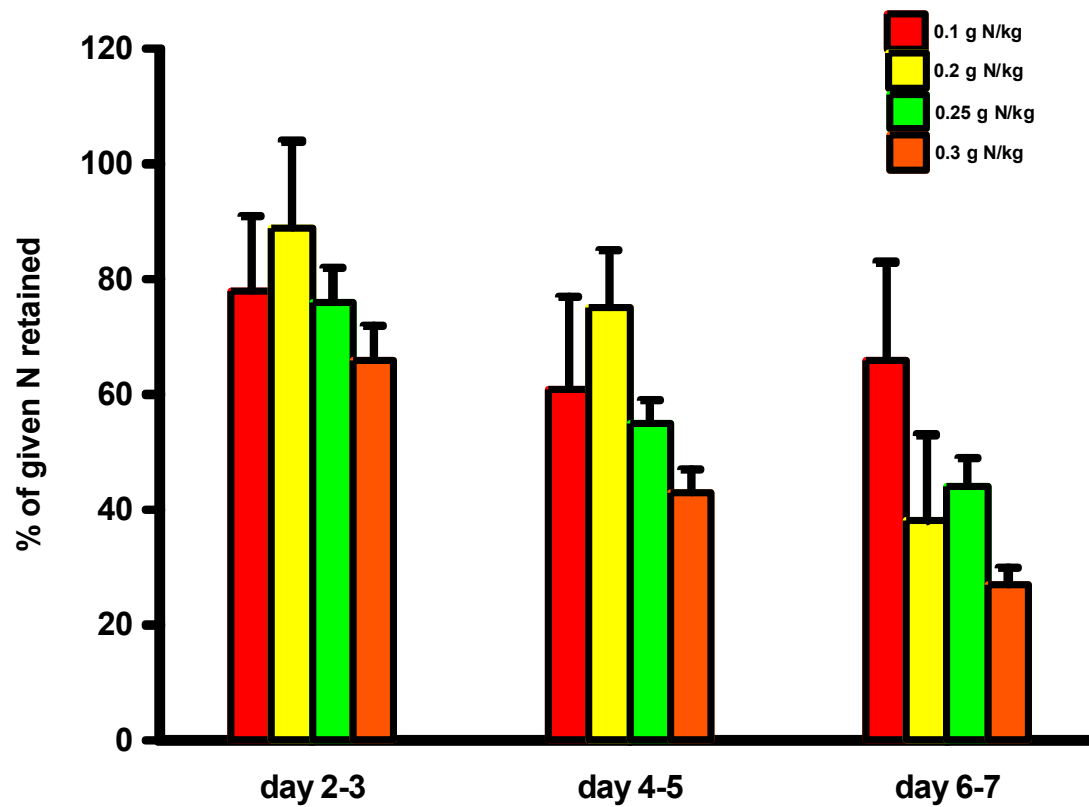
## ESPEN Guidelines on Parenteral Nutrition: Intensive care

Pierre Singer<sup>a</sup>, Mette M. Berger<sup>b</sup>, Greet Van den Berghe<sup>c</sup>, Gianni Biolo<sup>d</sup>, Philip Calder<sup>e</sup>, Alastair Forbes<sup>f</sup>, Richard Griffiths<sup>g</sup>, Georg Kreyman<sup>h</sup>, Xavier Leverve<sup>i</sup>, Claude Pichard<sup>j</sup>

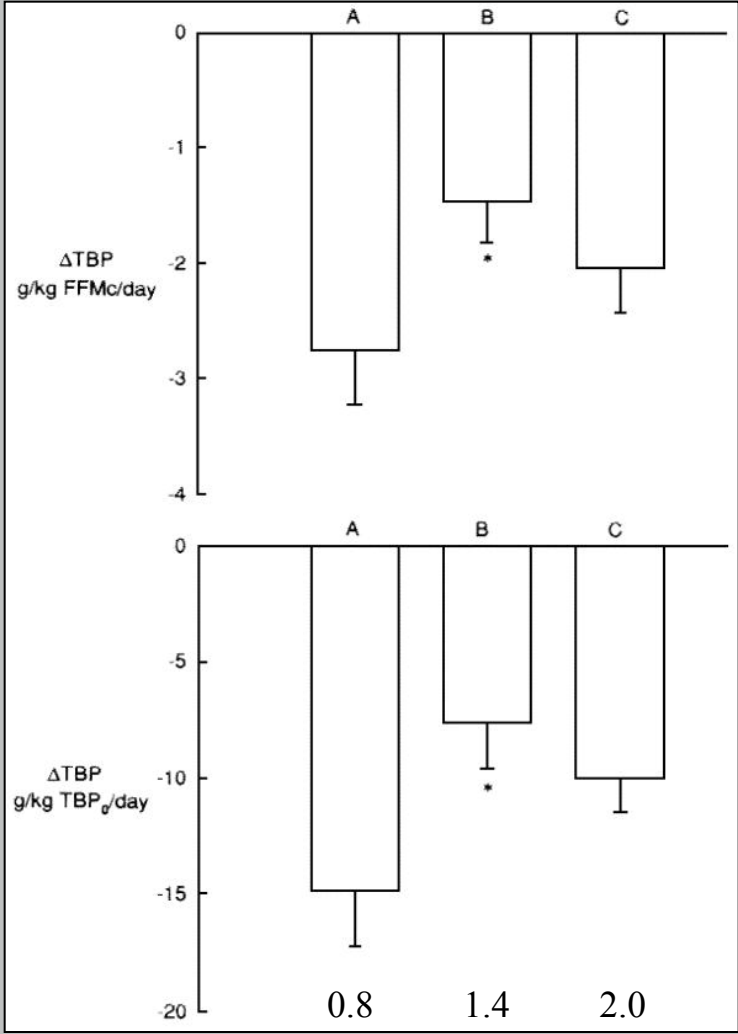
### **15. How much should be administered to meet protein requirements?**

***Recommendation: When PN is indicated, a balanced amino acid mixture should be infused at approximately 1.3–1.5 g/kg ideal body weight per day in conjunction with an adequate energy supply (Grade B)***





Larsson et al, Br J Surg, 1990;77:413-6



Ishibashi et al, CCM 1998;26:1529-35

# Appropriate protein provision in critical illness: a systematic and narrative review<sup>1-3</sup>

*L John Hoffer and Bruce R Bistrian*

*Am J Clin Nutr* 2012;96:591–600.

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

SPECIAL ARTICLE

# ESPEN Guidelines for Nutrition Screening 2002

J. KONDRUP,\* S. P. ALLISON,† M. ELIA,‡ B. VELLAS,¶ M. PLAUTH§

**Table 2** Final screening

Impaired nutritional status		Severity of disease (≈ increase in requirements)	
Absent Score 0	Normal nutritional status	Absent Score 0	Normal nutritional requirements
Mild Score 1	Wt loss > 5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week	Mild Score 1	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*. <i>Chronic hemodialysis, diabetes, oncology</i>
Moderate Score 2	Wt loss > 5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week	Moderate Score 2	Major abdominal surgery* Stroke* <i>Severe pneumonia, hematologic malignancy</i>
Severe Score 3	Wt loss > 5% in 1 mth (> 15% in 3 mths) or BMI < 18.5 + impaired general condition or Food intake 0–25% of normal requirement in preceding week in preceding week.	Severe Score 3	Head injury* Bone marrow transplantation* <i>Intensive care patients (APACHE &gt; 10).</i>
Score:	+	Score:	= Total score
Age	if ≥ 70 years: add 1 to total score above		= age-adjusted total score
<p>Score ≥ 3: the patient is nutritionally at-risk and a nutritional care plan is initiated                      Score &lt; 3: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.</p>			

SPECIAL ARTICLE

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J. KONDRUP,\* S. P. ALLISON,† M. ELIA,‡ B. VELLAS,¶ M. PLAUTH§

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<b>Absent Score 0</b>	Normal nutritional status
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SPECIAL ARTICLE

## ESPEN Guidelines for Nutrition Screening 2002

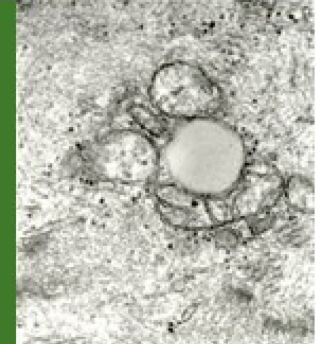
J. KONDRUP,\* S. P. ALLISON,† M. ELIA,‡ B. VELLAS,¶ M. PLAUTH§

### Severity of disease ( $\approx$ increase in requirements)

Absent Score 0	Normal nutritional requirements
Mild Score 1	Hip fracture* Chronic patients, in particular with acute complications: cirrhosis*, COPD*. <i>Chronic hemodialysis, diabetes, oncology</i>
Moderate Score 2	Major abdominal surgery* Stroke* <i>Severe pneumonia, hematologic malignancy</i>
Severe Score 3	Head injury* Bone marrow transplantation* <i>Intensive care patients (APACHE &gt; 10).</i>



## Home of the research group in ICU Metabolism and Nutrition at Karolinska Institutet and Karolinska University Hospital



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What do we do

What have we done

Our lab

Tracer site

**Our research is dedicated to the metabolic and nutritional problems of critically ill patients treated in the ICU.**

We are a small research group dedicated to the metabolic and nutritional problems of critically ill patients in the intensive care unit (ICU).

### Latest news/meetings



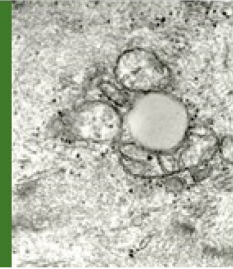
Program for our weekly wednesday research meeting can be found **here!**



Jonathan Grip will present his poster at the **ESCIM** meeting in Barcelona next week on wednesday.



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# Thank you for listening