Is there a place for TPN in ICU's in 2004?

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A sound alarm was heard…

Intensive Care Med (2003) 29:867–869
DOI 10.1007/s00134-003-1744-9

EDITORIAL

Paul E. Marik
Michael Pinsky

Death by parenteral nutrition

Death by parenteral nutrition

.. A poison or toxin is « a substance that through its chemical action usually kills, injures or impairs an organism ». Based on this definition, in the critically ill, TPN meets all the criteria of a poison/toxin…

..The adverse sequelae associated with TPN result from the combined detrimental effects of not directly feeding the bowel, as well as the metabolic, immunological, endocrine and infective complications associated with infusing a synthetic « nutrient cocktail » into a patient systemic venous system.

Adverse effects of gut starvation

Table 3.1 Adverse effects of gut starvation

Target	Effects
Gut barrier (epithelial cell junction)	Increased permeability to macromolecules and micro-organisms (bacteria, fungi)
Enterocytes	Increased adherence of bacteria
Intestinal flora	Overgrowth of pathogens
Sub-mucosal immune system	Atrophy of Peyer's patches Decreased production of immunoglobulin A

Proceedings of the Nutrition Society (2001), **60**, 399–402
DOI:10.1079/PNS2001103

Enteral and parenteral nutrition: evidence-based approach

Khursheed N. Jeejeebhoy
University of Toronto and St Michael's Hospital, Toronto, Ontario M5B 1W8, Canada

Table 1. Total parenteral nutrition (TPN) and intestinal atrophy in human subjects

Reference	Outcome
Guedon *et al.* (1986)	No atrophy after 21 d of NPO
Rossi *et al.* (1993)	Atrophy after 9 months of NPO
Pironi *et al.* (1994)	Atrophy after 2–3 months of TPN
Sedman *et al.* (1995)	No atrophy with TPN *v.* enteral for ≥10 d
Groos *et al.* (1996)	Atrophy after 7–12 weeks of TPN

NPO, nil per os (nothing fed by mouth).

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EDITORIAL

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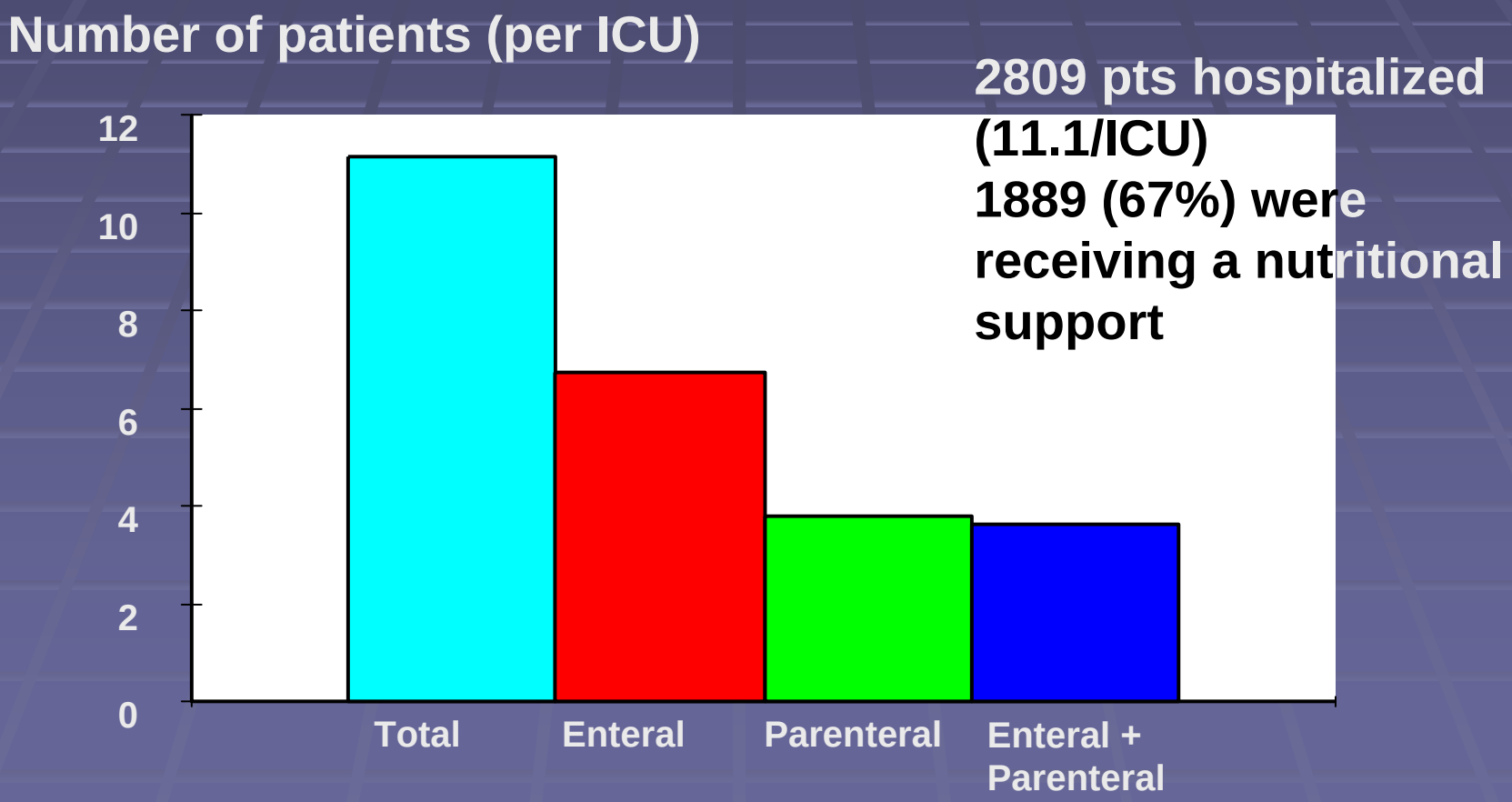
Death by parenteral nutrition

- 54 references :
  - Animal experiments : 23
  - Non-ICU (scheduled surgery, oncology, pancreatitis) : 11
  - Reviews, meta-analyses, expert opinion : 10
  - **Original ICU : 4**
  - Others (dictionary, historical reports) : 3
  - In vitro : 2
  - Abstract : 1

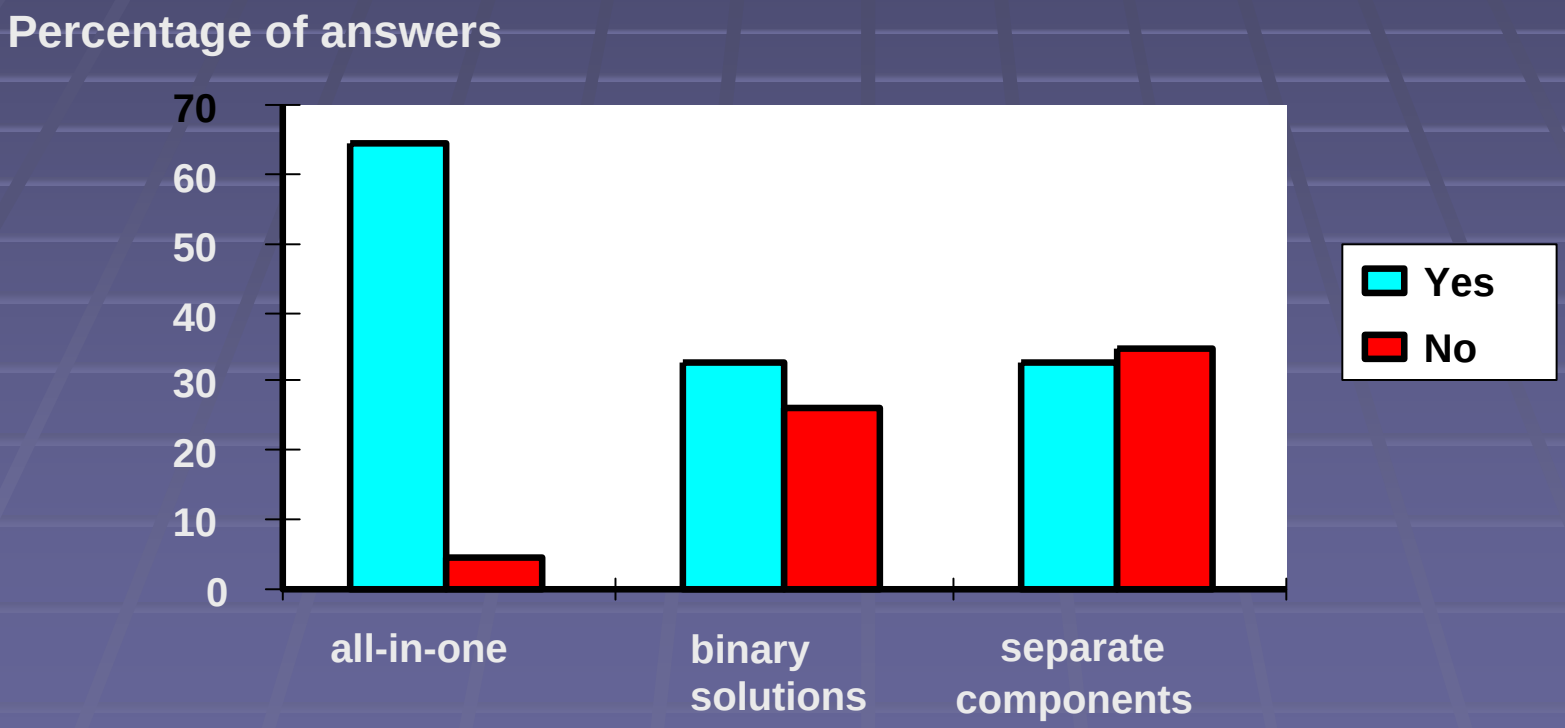
Current nutritional support

Preiser et al Intensive Care Med 1999;25:95



Current practice of parenteral nutrition

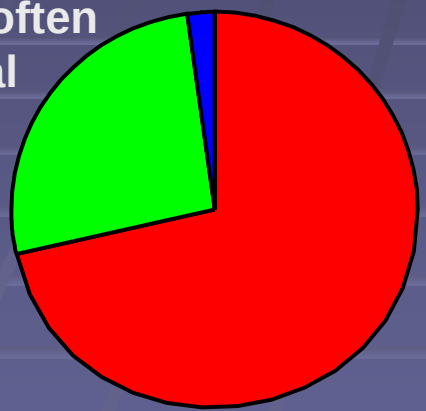
Type of solutions : ready-to-use weapons



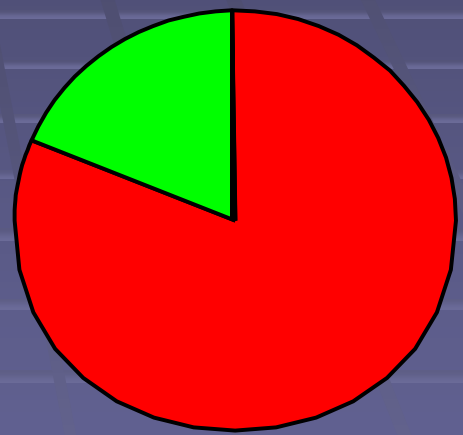
Current practice of parenteral nutrition

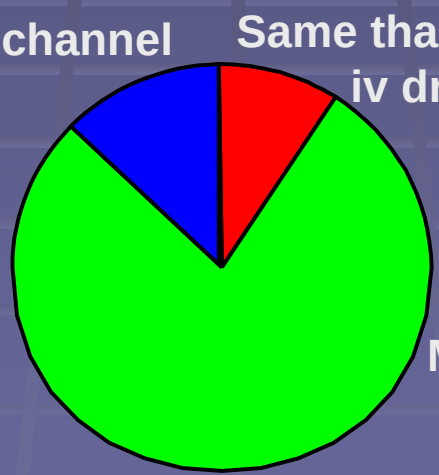
System of administration : a criminal organisation?

Which line do you use?



Do you use filters?





Which type of central line?

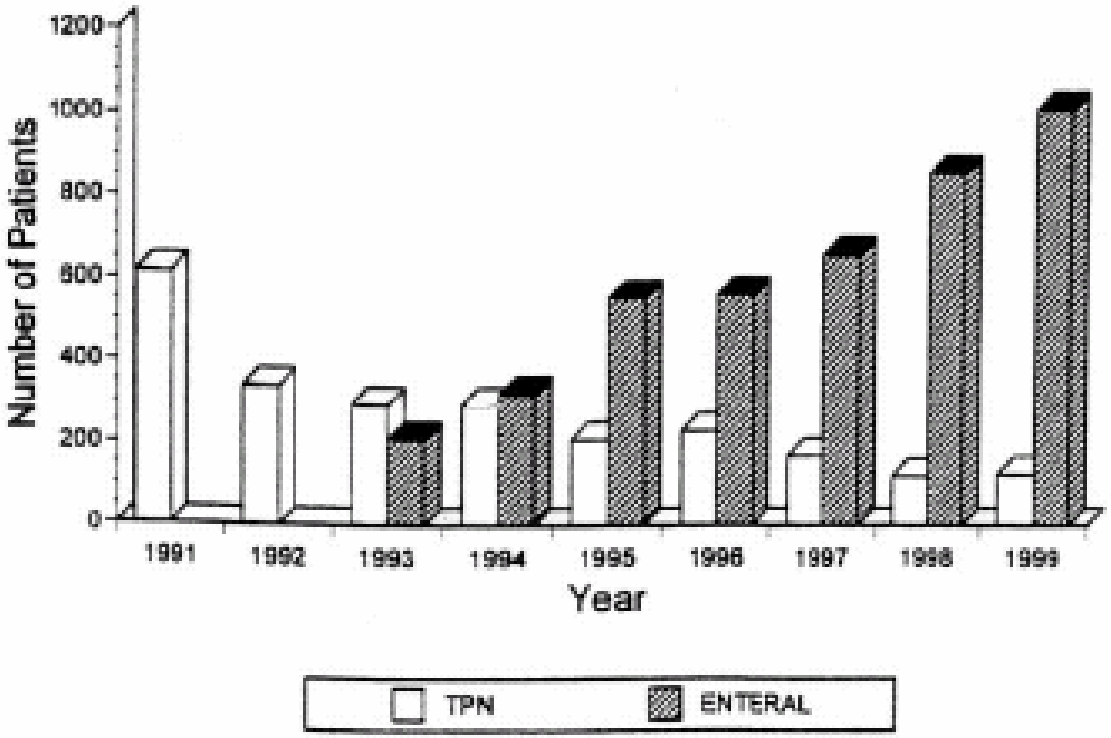


Fig. 1 As TPN use decreased, enteral feeding become the standard of care when a functional GI tract exists. Reprinted with permission from the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N) from the following: Nutrition in Clinical Practice (2000) 15:174–180, (Fig. 1.). A.S.P.E.N. does not endorse the use of this material in any form other than its entirety

The trial of TPN
vs
EN and Standard Care

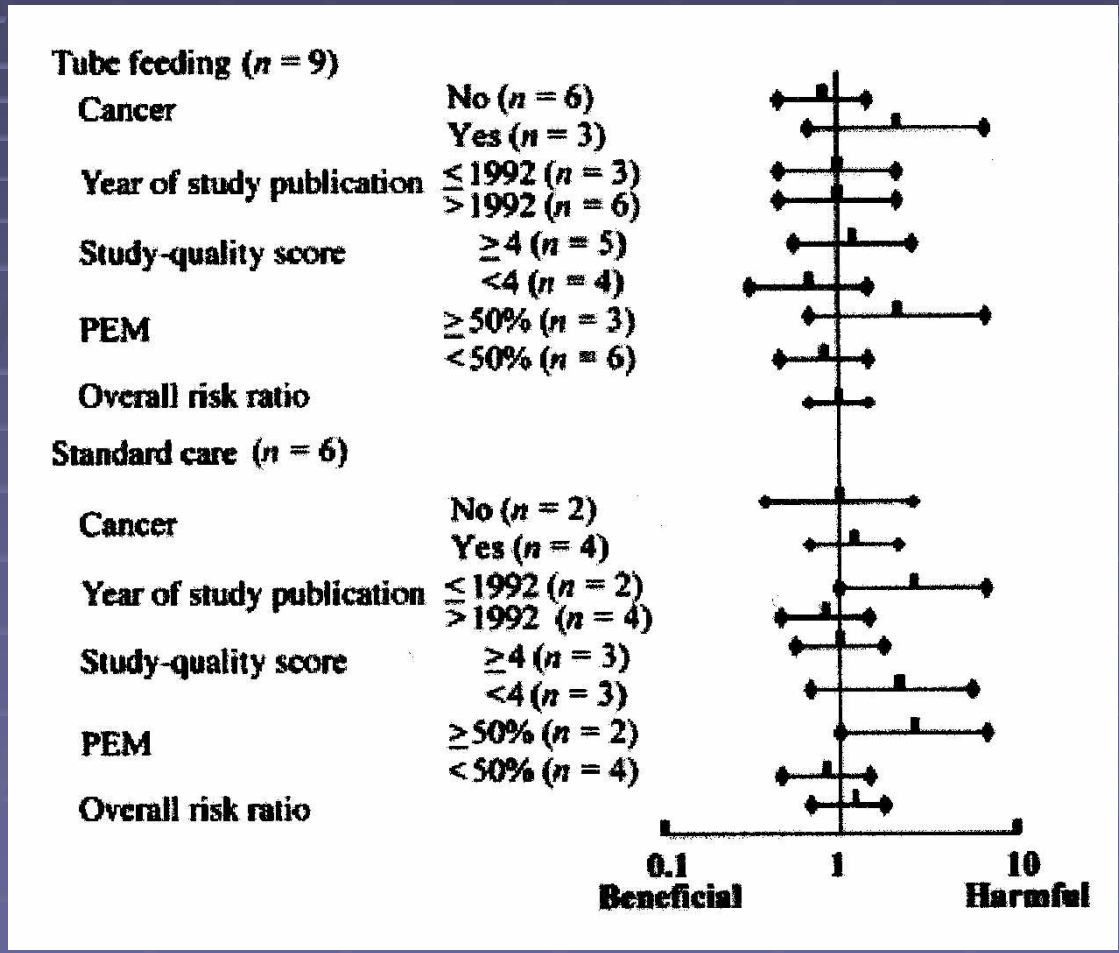
Meta-analysis

27 studies

1828 patients

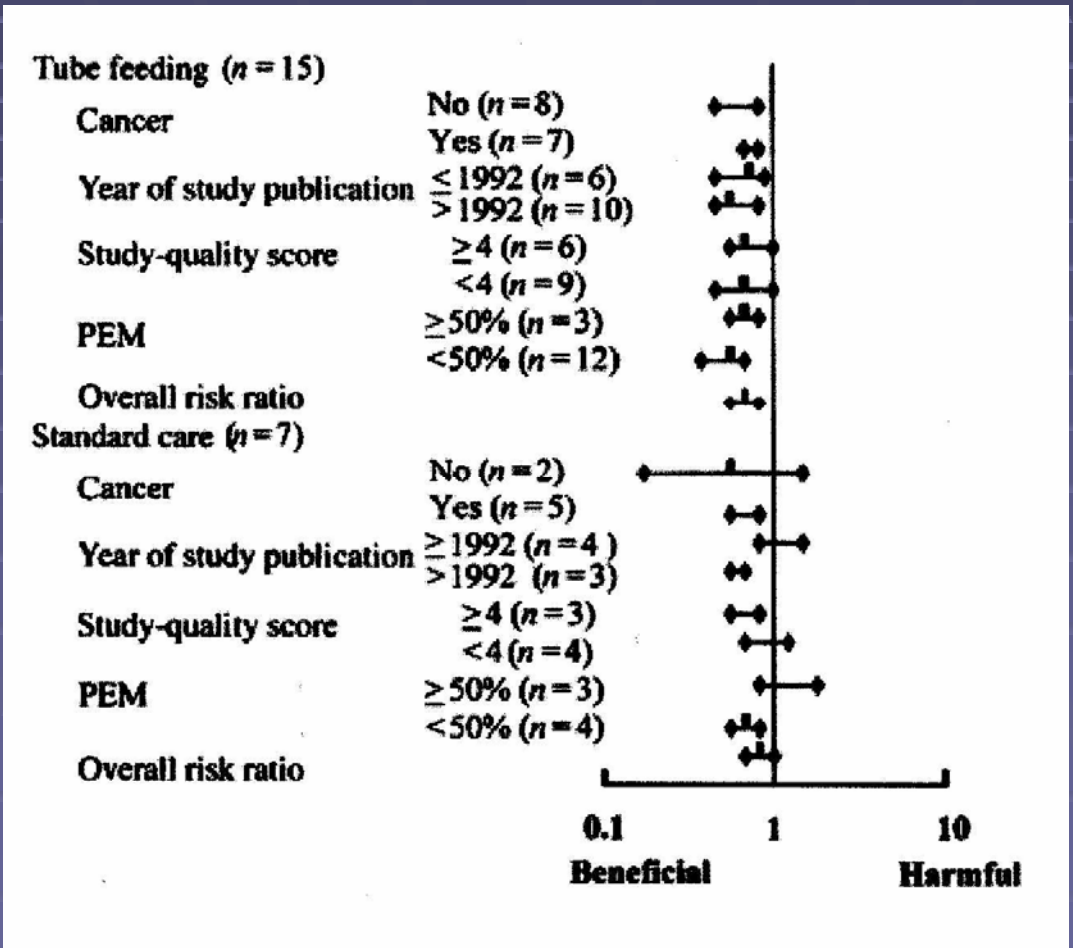
Braunschweig et al Am J Clin Nutr 2001

Mortality
Effects of TPN vs



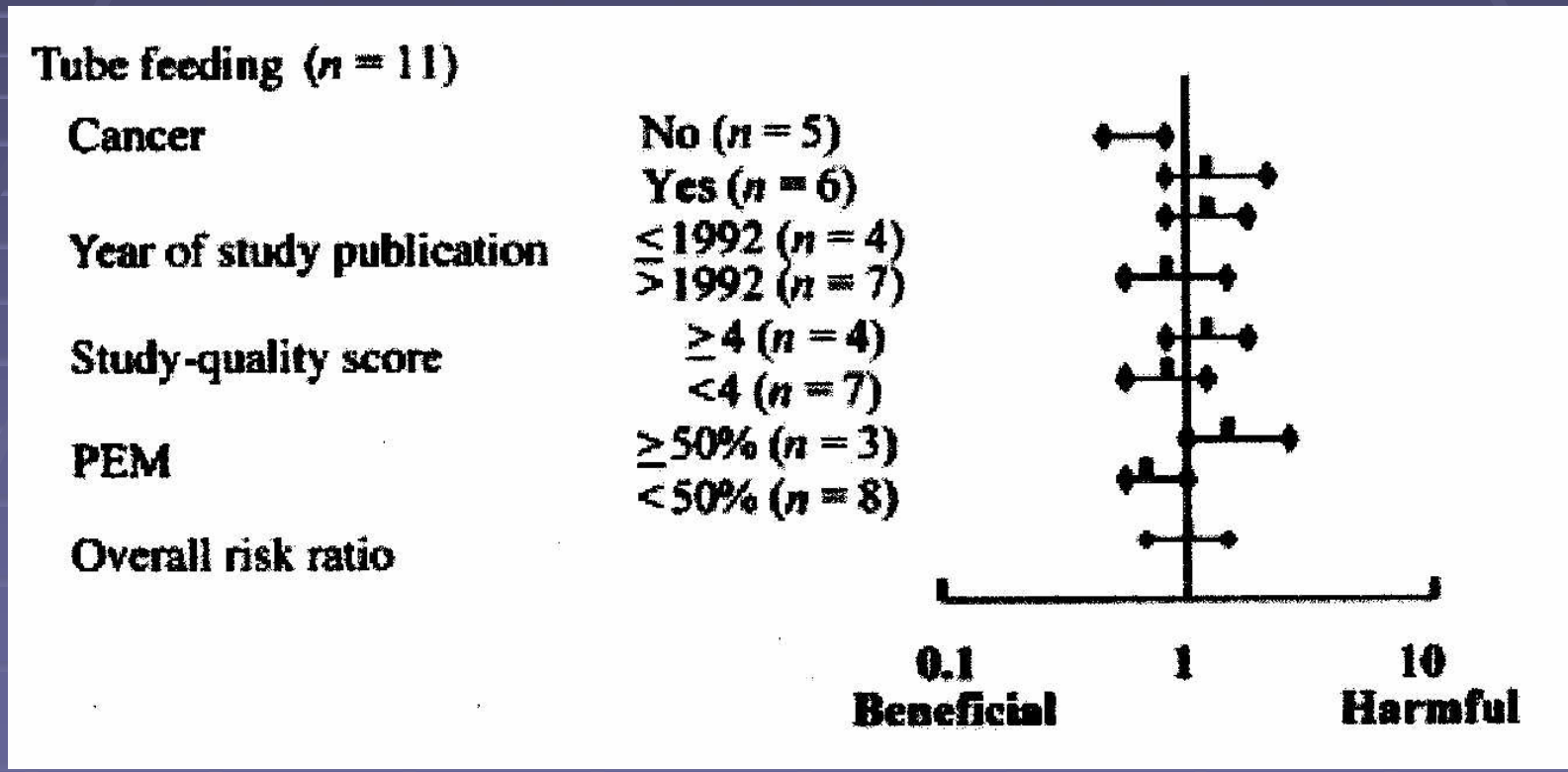
Braunschweig et al Am J Clin Nutr 2001

Infection rate Effects of TPN vs



Braunschweig et al Am J Clin Nutr 2001

Other complications Effects of TPN vs



Braunschweig et al Am J Clin Nutr 2001

Intensive Care Med (2003) 29:1861–1864
DOI 10.1007/s00134-003-2006-6

EDITORIAL

Is parenteral nutrition guilty?

Peter Varga
Richard Griffiths
René Chiolero
Gérard Nitenberg
Xavier Leverve
Marek Pertkiewicz
Erich Roth
Jan Wernerman
Claude Pichard
Jean-Charles Preiser

- 24 references
  - **Original ICU : 10**
  - Reviews, meta-analyses, expert opinions : 7
  - Non-ICU : 3
  - Animal : 1

What’s the matter?

- TPN as the first-line nutrition support
- Early TPN when early EN not tolerated
- TPN in each case of contra-indication to EN
- TPN when EN impossible or not sufficient

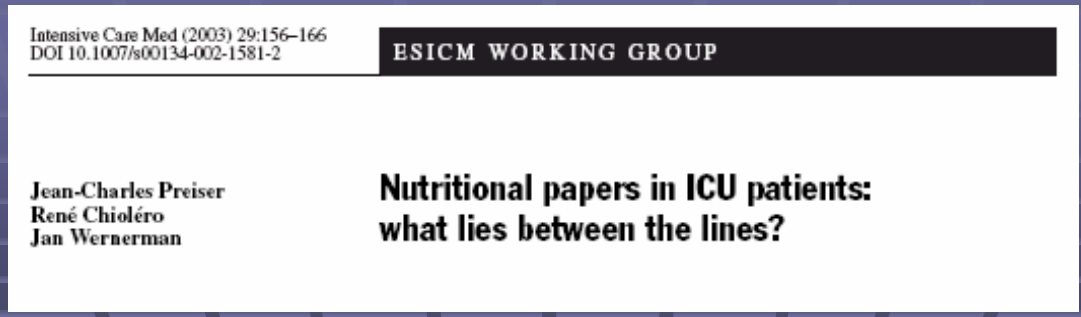
- NO
- NO
- NO
- **YES**

Methodological assessment criteria

Table 1 Methodological quality assessment criteria

Criterion	Score 0	Score 1	Score 2
Randomization	Not applicable	Not concealed or not sure	Concealed randomization
Analysis	Other	Not applicable	Intention to treat
Blinding	Not blinded	Single blind	Double blind
Patient selection	Selected patients or unable to tell	Consecutive eligible patients	Not applicable
Comparability of groups at baseline	No or not sure	Yes	Not applicable
Extent of follow-up	<100%	100%	Not applicable
Treatment protocol	Poorly described	Reproducibly described	Not applicable
Cointerventions[a]	Not described	Described but not equal or not sure	Well described and all equal
Outcomes	Not described	Partially described	Objectively defined

[a] The extent to which antibiotics, nutritional support, ventilation, oxygen, and transfusions were applied equally across groups



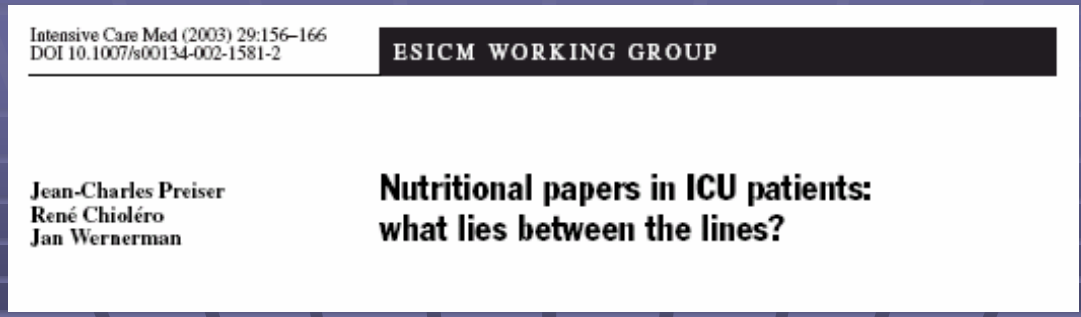
Intensive Care Med (2003) 29:156–166
DOI 10.1007/s00134-002-1581-2

ESICM WORKING GROUP

Jean-Charles Preiser
René Chioléro
Jan Wernerman

Nutritional papers in ICU patients: what lies between the lines?

- **Clinical considerations : widely scattered**
  - Outcome variables
  - Type and size of study populations
  - Time and route of administration
- **Energy supply and nutrients : very variable**
- **Methodological aspects : generally poor**
  - Working hypothesis, study design and power calculation
  - Management and clinical safety
  - Control population



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Nutritional papers in ICU patients: what lies between the lines?

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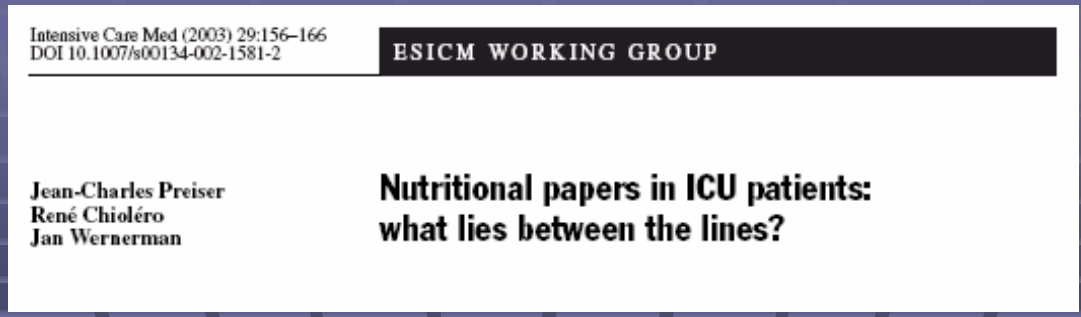
  - Outcome variables

Table 4 List of parameters used as end points in a selection of nutritional studies of ICU patients

Variables	References
General variables	
Mortality (28 days, 6-month, ICU, hospital)	Griffiths [2], Herndon [43], Sandström [31]*, Van den Berghe [3], Powell-Tuck [44]*
Rate of discharge from hospital	Bower [41]
Length of stay (ICU, hospital)	Van den Berghe [3], Powell-Tuck [44]*, Atkinson [36], Bauer [15], Galban [45], Houdijk [46]
Septic morbidity (total or classified by locations: wound infections, catheter infection, nosocomial pneumonia, urinary tract infections)	Bower [41], Galban [45], Kudsk [9], Bozzetti [47]*, Caparros [48]
Immune function: lymphocyte count, immune cell responsiveness, plasma concentrations of inflammatory markers/mediators (CRP, TNF, IL-1, IL-2, IL-6, IL-8, NO metabolites)	Herndon [49]
Rate of organ dysfunctions (severity scores, number of failing organs, number of episodes of organ failures, rate of requirement of dialysis/haemofiltration, duration of mechanical ventilation, PaO_2/FIO_2 ratio)	Bower [41], Gadek [50]
Cost-effectiveness (cost of nutritional support versus cost of complications, and treatment of the complications, cost of hospital stay)	Griffiths [2], Jones [11], Senkal [51]
Nutritional, metabolic and intestinal variables	
Nitrogen balance	Singh [52], Vente [53]
Energy expenditure	Cerra [54]
Nutritional markers plasma concentrations (albumin, pre-albumin, retinol-binding protein, transthyretin)	Kudsk [55]
Absorption, metabolic/biochemical fate of specialised nutrients	Houdijk [46],Preiser [56, 57]
Biological effects of specialised nutrients	Preiser [56, 57]
Fatty acid composition (plasma or membrane)	Bower [41]
Amino acid plasma/tissue concentrations	Bower [41], Gamrin [58]
Gut barrier function	Kompan [59], Tremel [60], Hadfield [61]
Gastrointestinal motility/incidence of diarrhoea	Bosscha [62], Heimburger [63]

* denotes a study including ICU patients, but also other patients



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  - Type and size of study populations
  - Time and route of administration
- **Energy supply and nutrients : very variable**

INCREASED RISK OF INFECTION WITH HYPOCALORIC REGIMEN

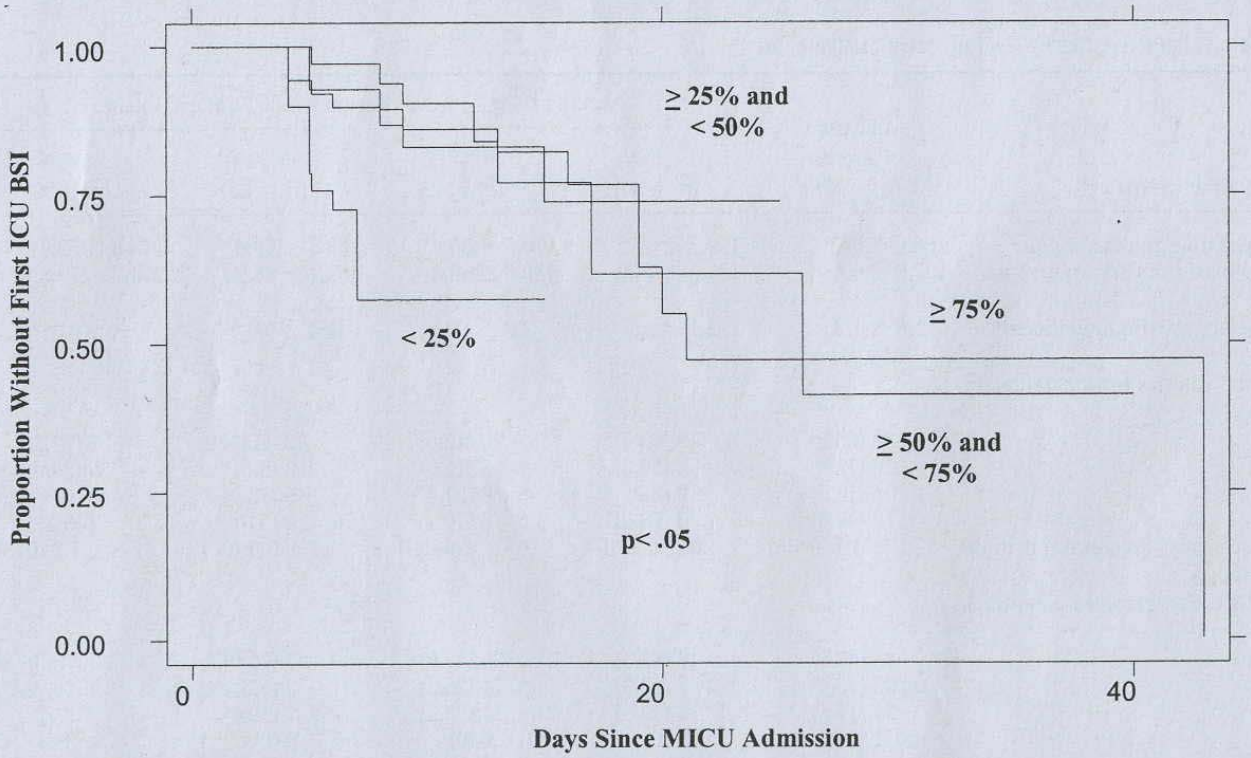


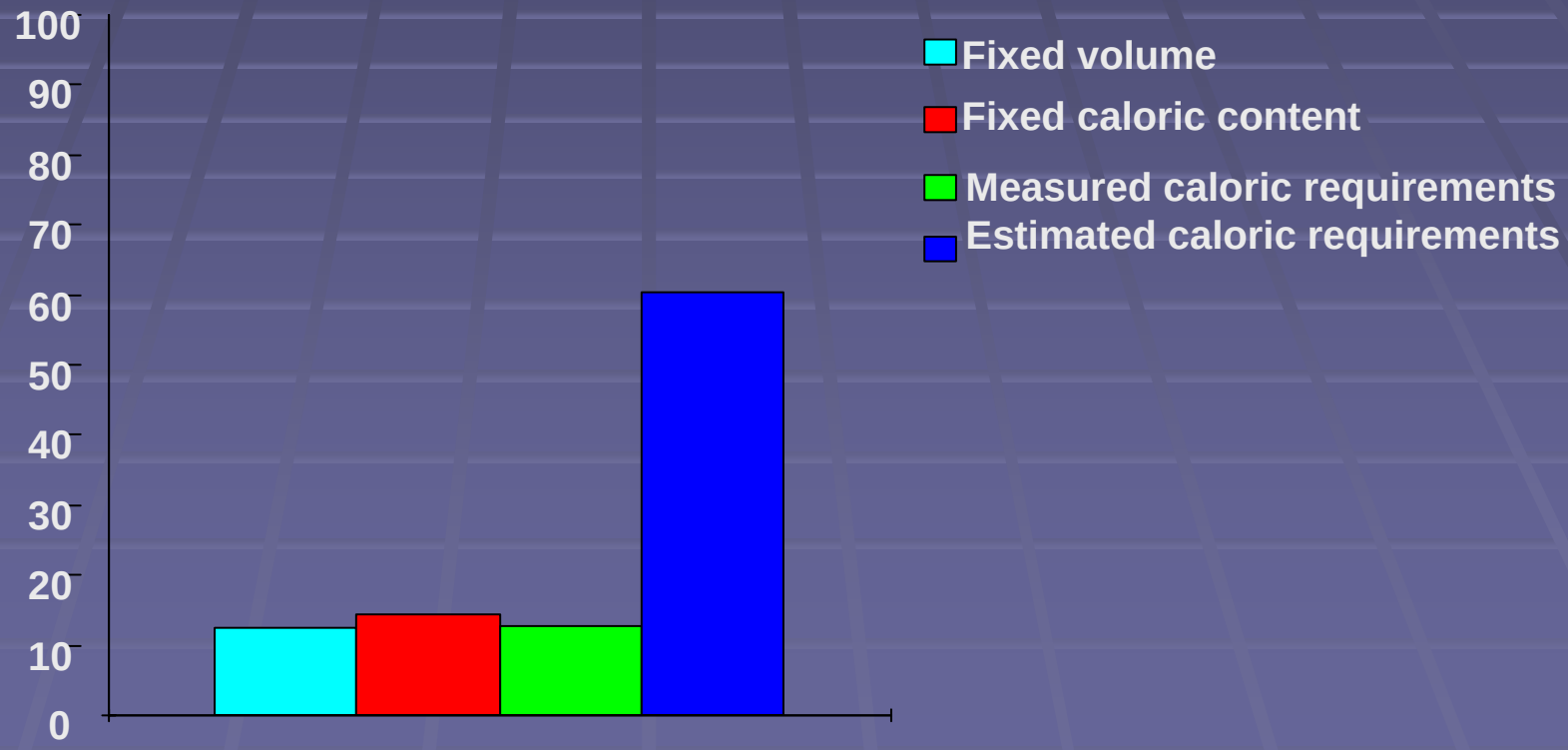
Figure 1. Kaplan-Meier curves by average daily percent of American College of Chest Physicians (ACCP)-recommended calories provided. Each Kaplan-Meier plot represents the time to first medical intensive care unit (*MICU*) bloodstream infection (*BSI*) for patients in a specific nutrition category. The categories are based on the average daily percent of ACCP-recommended calories and are lagged 2 days prior to outcome or date of censoring (see Methods). The categories are <25%, 25–49%, 50–74%, and ≥75%. The *p* values were determined by log-rank testing.

Rubinson et al Crit Care Med 2004 (feb)

Current practice of parenteral nutrition

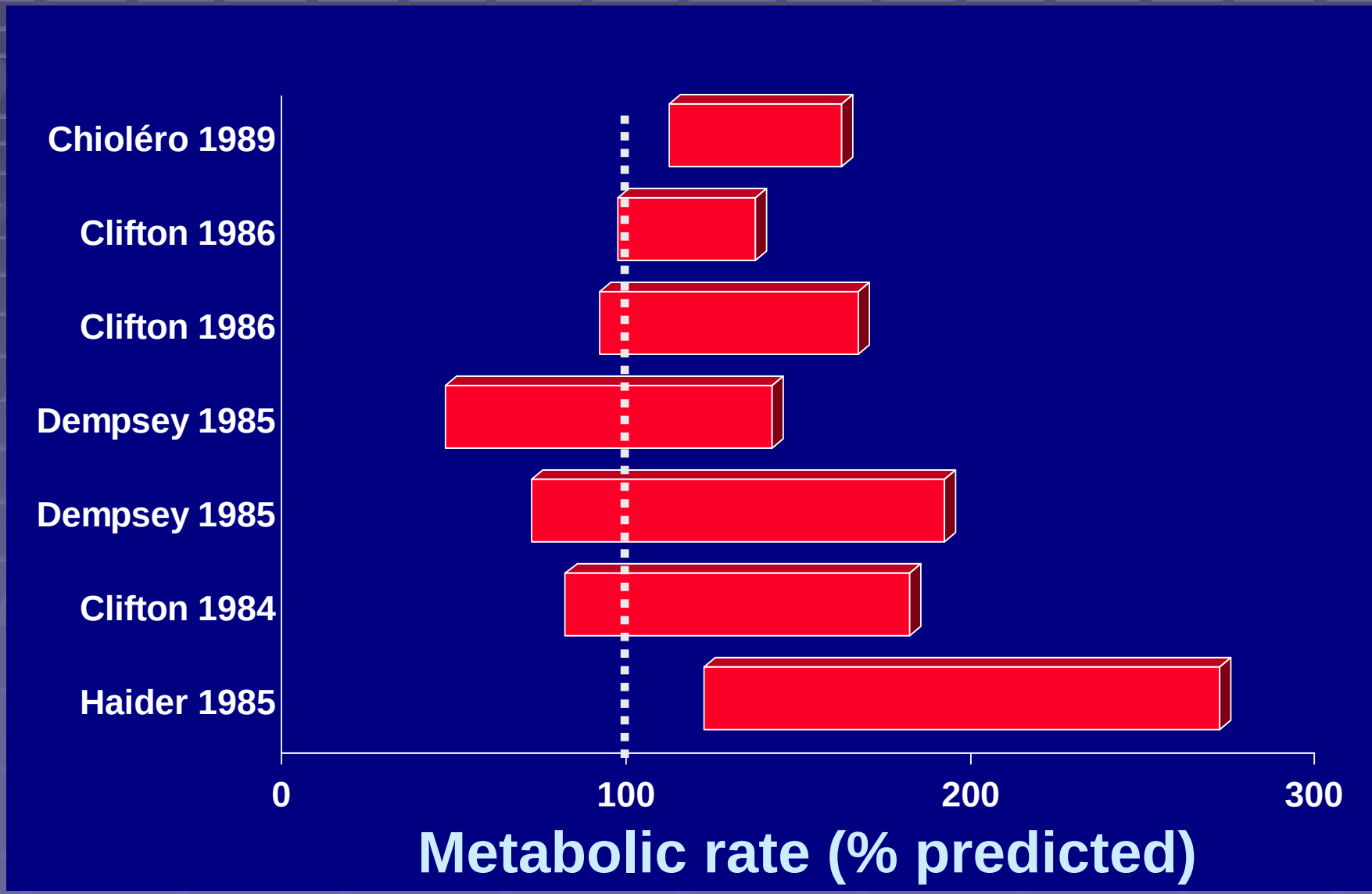
Initiating TPN

Which criteria do you use to prescribe the amount of TPN?



Preiser et al Intensive Care Med 1999;25:95

Metabolic rate in severe brain injury



Klinische Ernährung

Intensiv Care Unit: Energieverbrauch

Autoren	Jahr	RU (%)	EV (kcal)
Nach Operationen und schweren Traumen			
Swinamer et al.	1987	+47	2342
Behrendt et al.	1991	+56	2330
Adolph et al.	1987	+54	2620
Frankenfield et al.	1994	+55	2750
Sepsis nach Operation/Trauma			
Giovannini et al.	1983	+45	2140
Shangraw et al.	1989	+48	2950
Frankenfield et al.	1994	+91c	3390
Multiorganversagen			
Forsberg et al.	1991	+41d	2080
	1991	+26e	1860
Müller et al.	1995	31 kcal/kg/Tag	

Klinische Ernährung

Intensiv Care Unit: Energiebedarf II

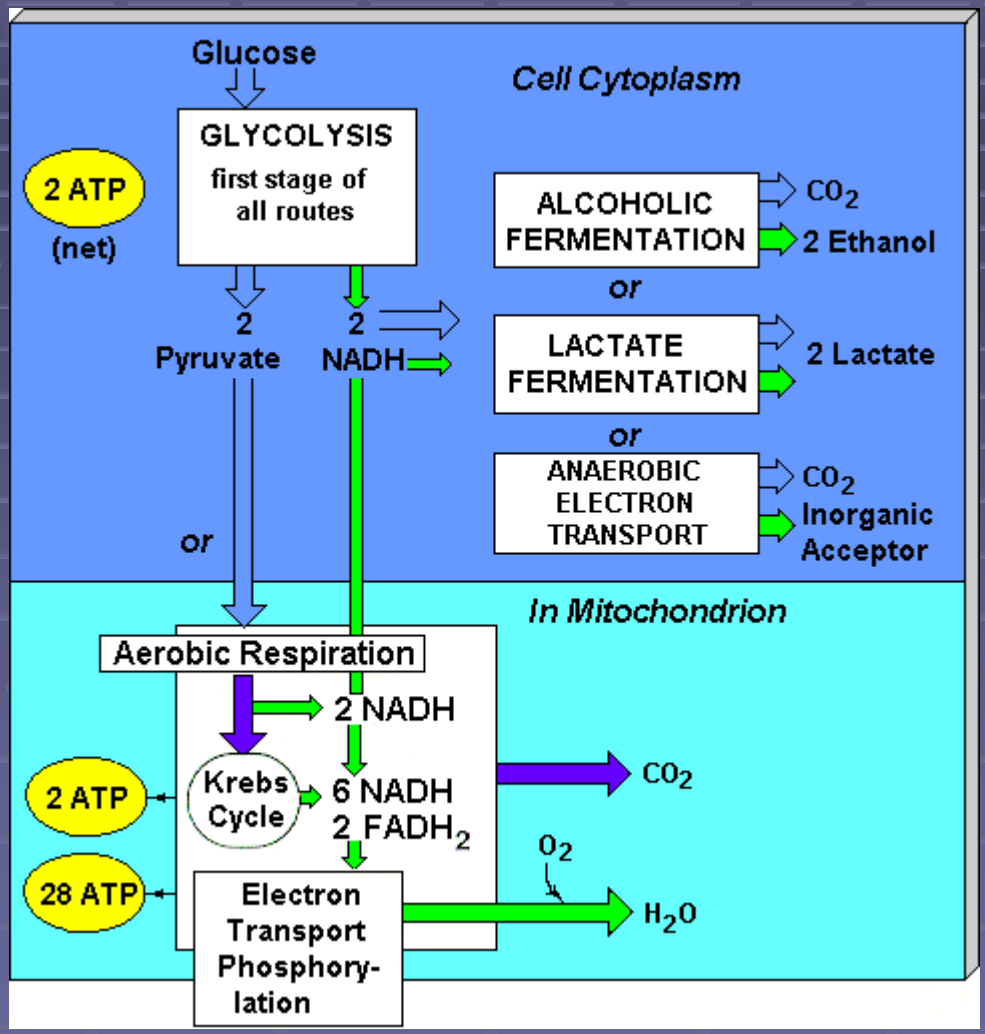
Internistische Patienten

Autor/Jahr	Erkrankung	RU(%)	EV (kcal)
Barot et al. 1982	Entzündliche Darmerkranunge[a]	+23	1290[a]
Dickerson et al. 1991	Pankreatitis Pankreatitis mit Sepsis	+12 +20	1560[b] 1900[b]
Schneeweiß 1991	ANV mit Sepsis	+33	1500[b]
Kreymann 1992	Schwere Infektion Sepsis Septischer Schock	+55 +25 + 2	2300[c] 1855[c] 1484[c]

Substrate utilization in energy metabolism

1. **Endogenous substrates**

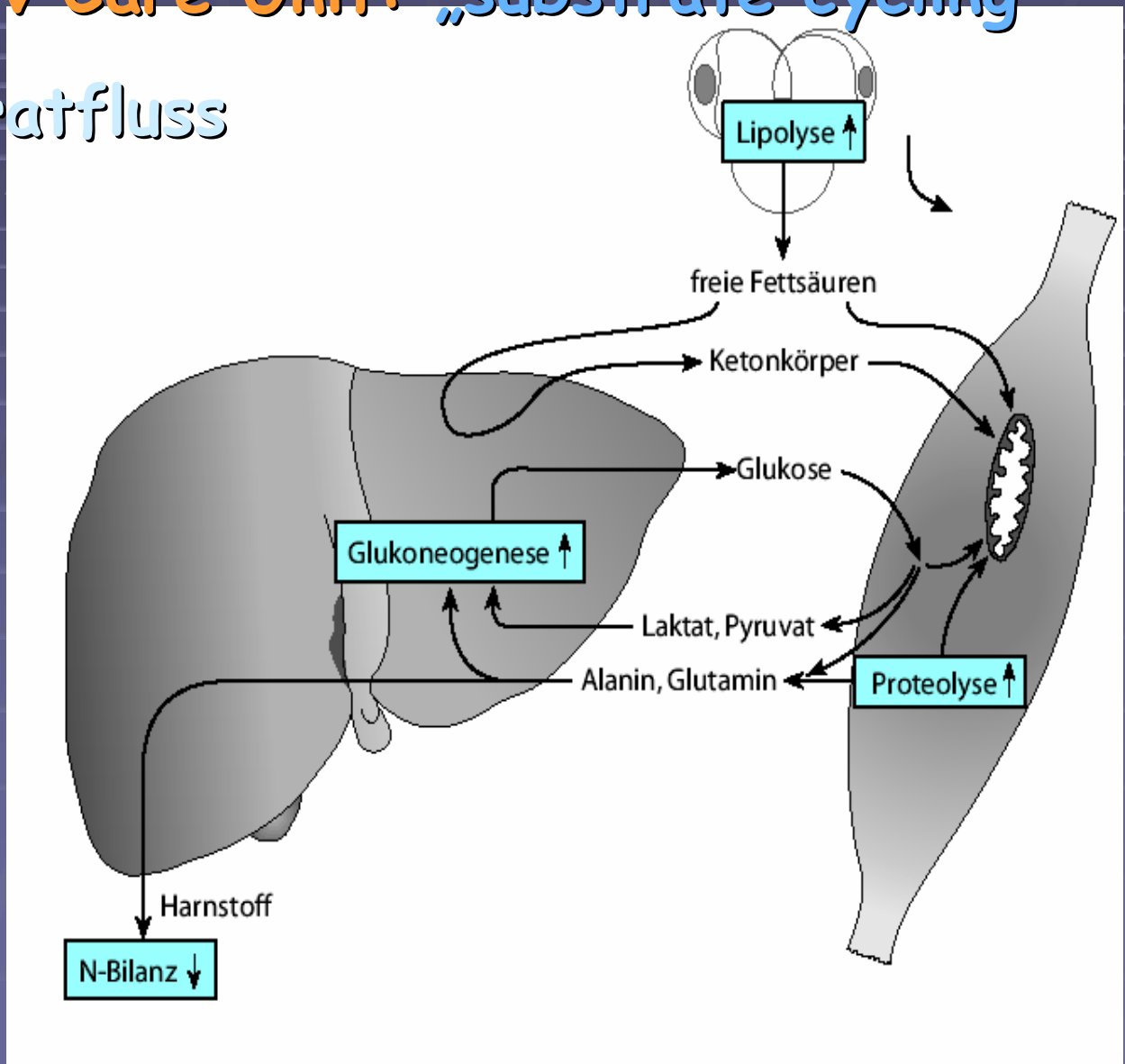
- Substrate mobilisation from body stores
  Glycogen, proteins, fatty acids
- Interorgan substrate exchanges
  Glucose, lactate, glutamine, glycerol, amino acids


Glucose
Cell Cytoplasm
GLYCOLYSIS
first stage of all routes
2 ATP
(net)
2
Pyruvate
2
NADH
ALCOHOLIC FERMENTATION
CO_2
2 Ethanol
or
LACTATE FERMENTATION
2 Lactate
or
ANAEROBIC ELECTRON TRANSPORT
CO_2
Inorganic Acceptor
or
In Mitochondrion
Aerobic Respiration
2 NADH
Krebs Cycle
6 NADH
2 $FADH_2$
CO_2
2 ATP
28 ATP
O_2
Electron Transport Phosphory-lation
H_2O

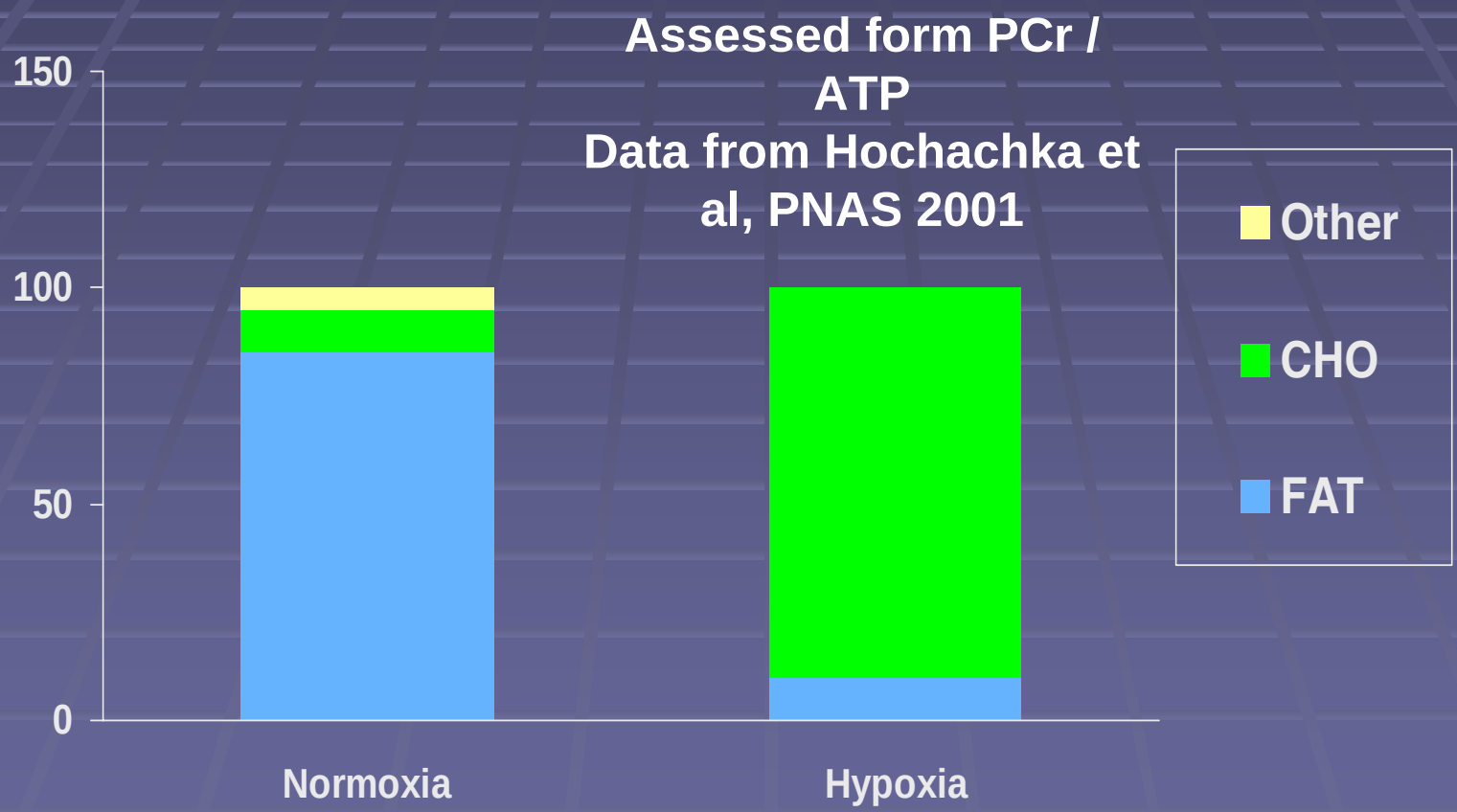
Klinische Ernährung

Intensiv Care Unit: „substrate cycling"

Substratfluss



Myocardium metabolism in normoxic and hypoxic condition



Hormonal regulation of the use of macro-nutrients

Macronutrient	Anabolic	Catabolic
Protein	Insulin Growth hormone Insulin-like growth factor-I Testosterone Catecholamines	Cortisol Glucagon Catecholamines
Carbohydrate	Insulin	Cortisol Glucagon Growth hormone Catecholamines
Lipid	Insulin	Catecholamines

Substrate utilization in energy metabolism

1. **Endogenous substrates**
   - Substrate mobilisation from body stores
     Glycogen, proteins, fatty acids
   - Interorgan substrate exchanges
     Glucose, lactate, glutamine, glycerol, amino acids
2. **Exogenous substrates**
   - Carbohydrates, fat, proteins

Appropriateness of TPN

- Criteria :
  - Type of nutrients and other components
  - Amount
  - Infusion rate

Type of nutrients

- Carbohydrates
  - Glucose : 4 kcal/g
  - Maximum 4 mg/kg.min (maximal oxidation rate)
  - ! osmolarity

Type of nutrients

- Lipids
  - Fatty acids : 9 kcal/g
  - Low osmolarity
  - Potential pharmacological effects

Fatty acid composition

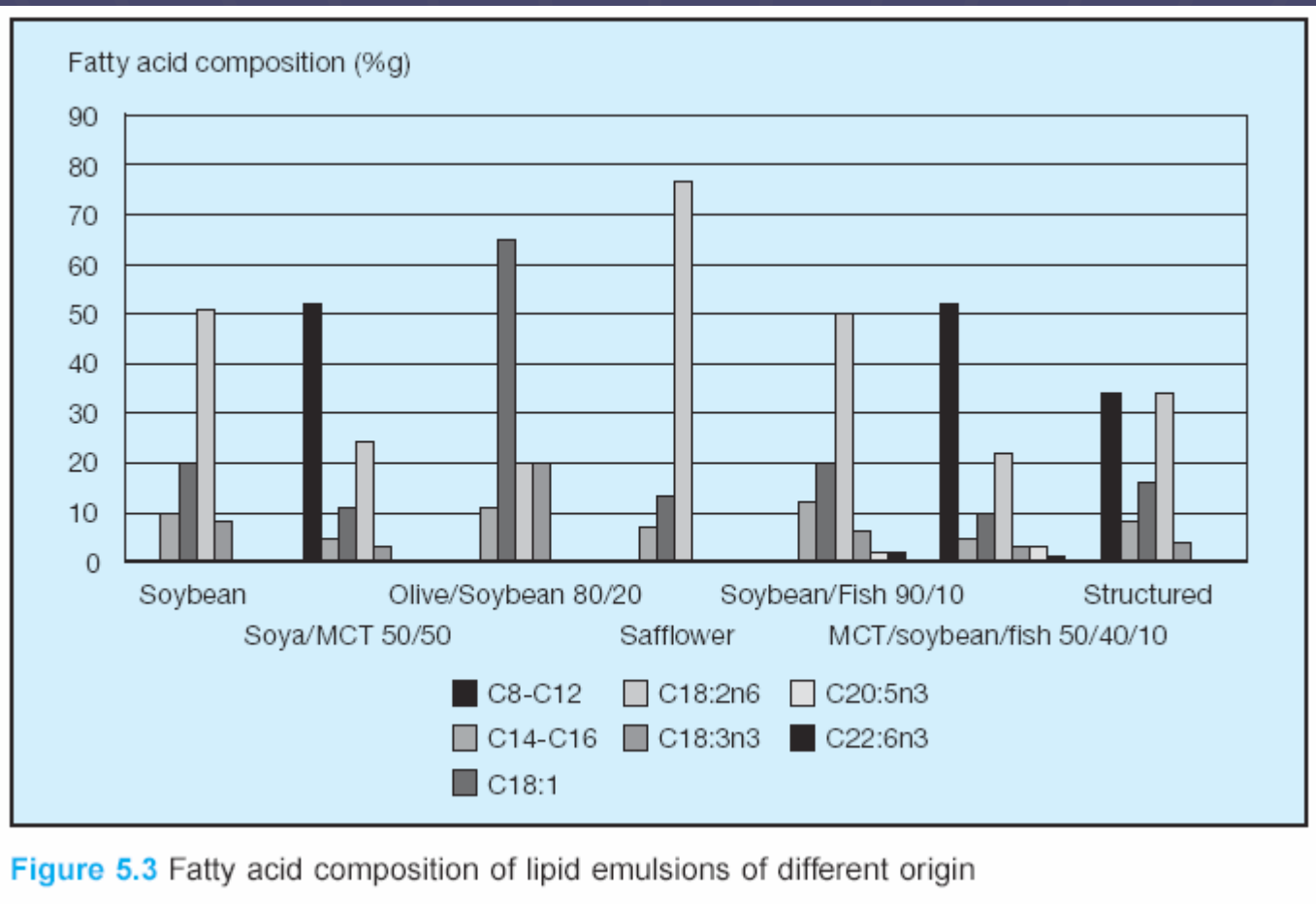


Figure 5.3 Fatty acid composition of lipid emulsions of different origin

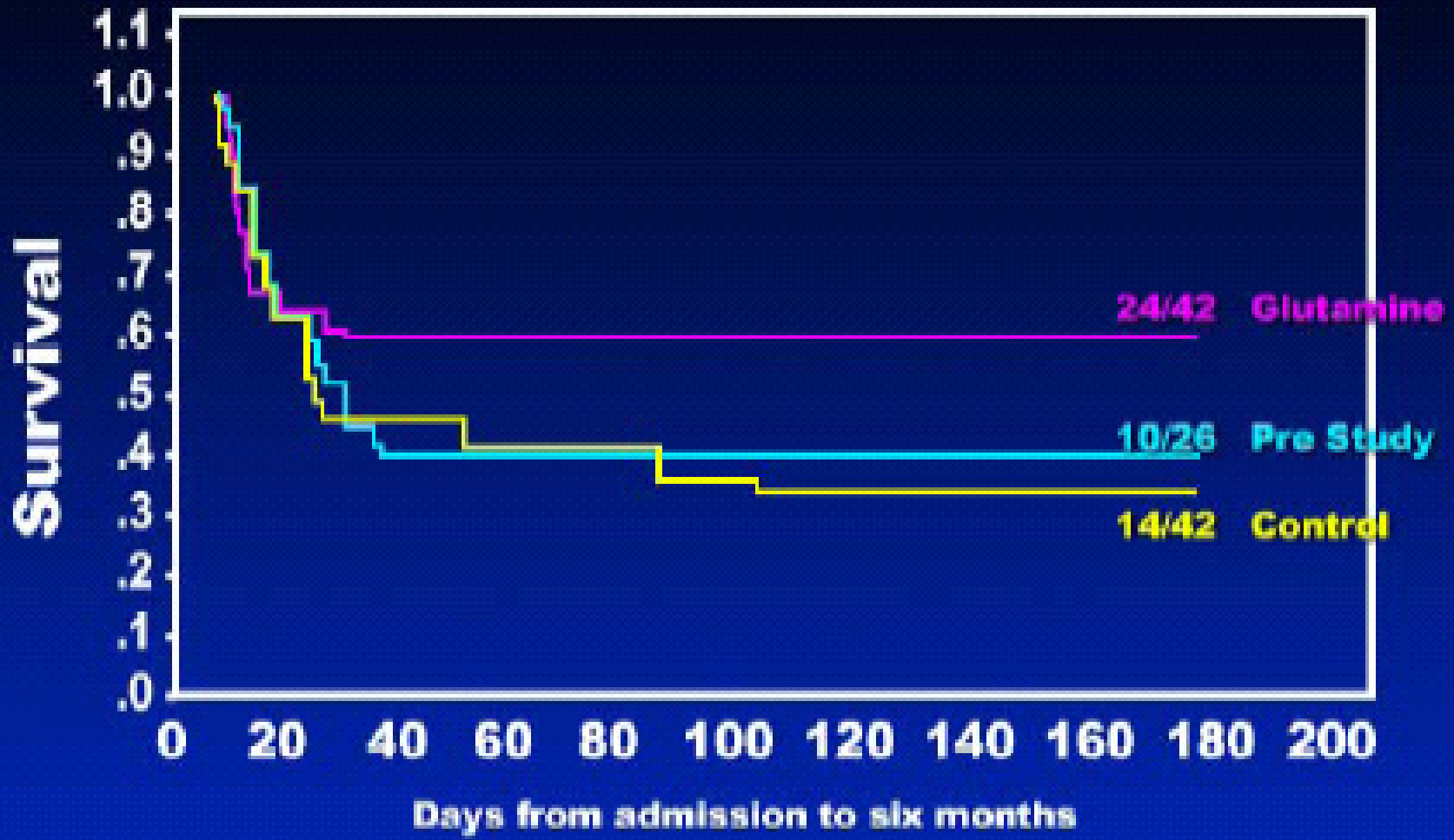
Type of nutrients

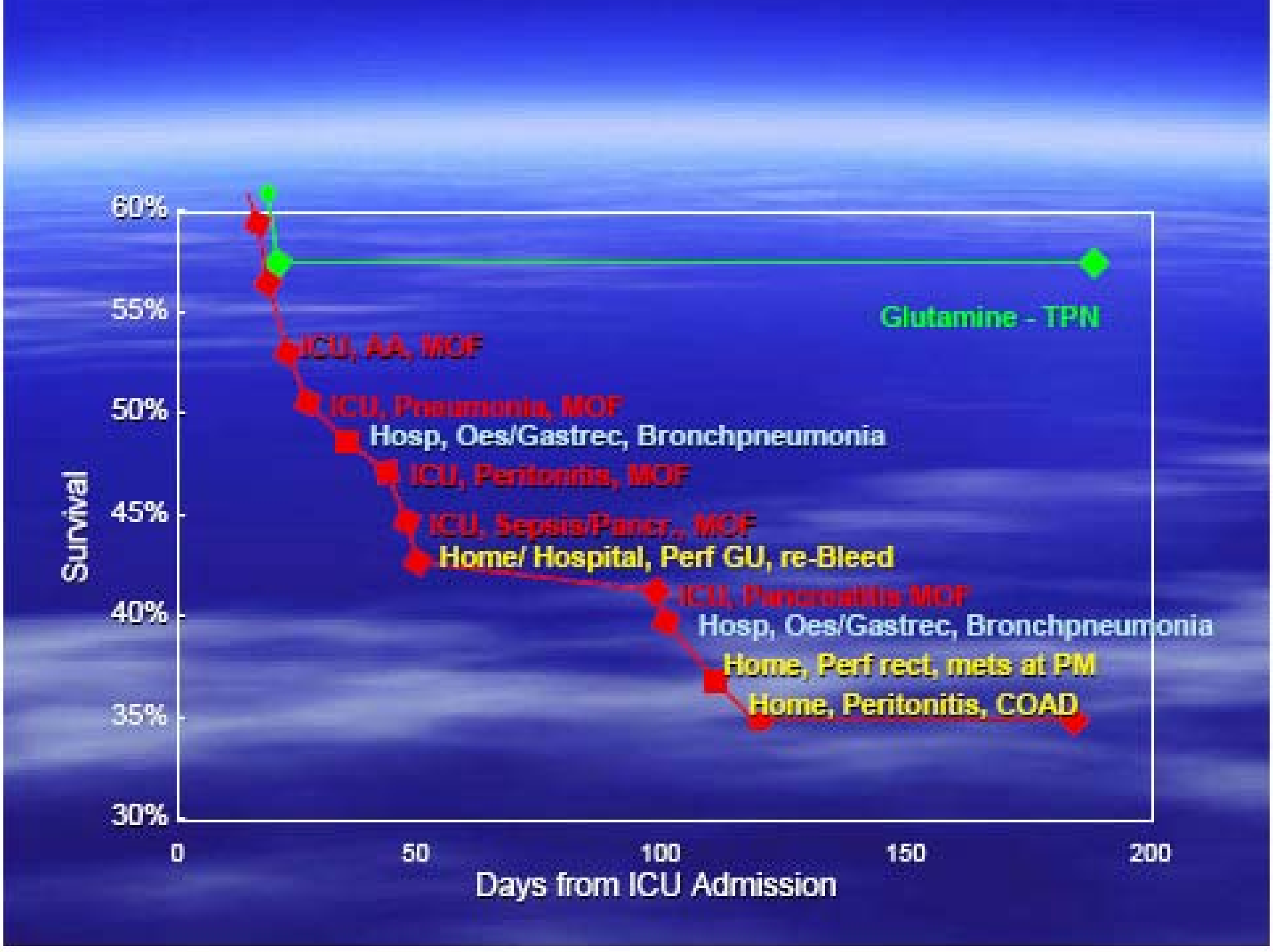
- Lipids
  - Potential limitations :
    - Decreased clearance (VLDL)
    - Maximal infusion rate 1 mg/kg/min
    - Increased peroxidation
    - PL/TG ratio

Type of nutrients

- Proteins
  - Essential aminoacids
  - Glutamine

Survival to Six Months -TPN




60%
55%
50%
45%
40%
35%
30%
Survival
0
50
100
150
200
Days from ICU Admission
Glutamine - TPN
ICU, AA, MOF
ICU, Pneumonia, MOF
Hosp, Oes/Gastrec, Bronchpneumonia
ICU, Peritonitis, MOF
ICU, Sepsis/Pancr., MOF
Home/ Hospital, Perf GU, re-Bleed
ICU, Pancreatitis MOF
Hosp, Oes/Gastrec, Bronchpneumonia
Home, Perf rect, mets at PM
Home, Peritonitis, COAD

GLUTAMINE :
A life-saving nutrient, but why??

FATE OF GLUTAMINE DURING CRITICAL ILLNESS

SKELETAL MUSCLE

↓ **intracellular glutamine levels**
↑ ***glutamine efflux***
↓ ***glutamine synthesis***

Glutamine

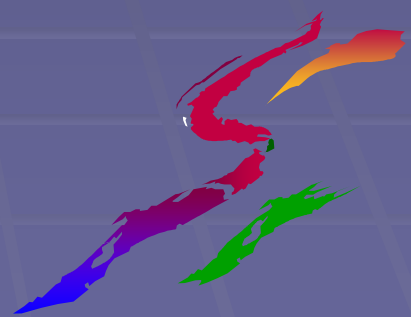
GUT MUCOSA
IMMUNE SYSTEM
KIDNEY
WOUND TISSUE

Cell division – synthesis of nucleotides
Gluconeogenesis
Glutathione
Ammonium (urea cycle)

POSSIBLE BENEFICIAL EFFECTS OF GLUTAMINE SUPPLEMENTATION

Preiser and Wernerman Crit Care Med 2003; 31:2555

- Metabolic
  - Protein synthesis
  - C / N transporter
  - Gluconeogenesis
  - Ammoniagenesis
- Immunologic
  - Replication
  - T-cells function
  - IgA synthesis
  - HLA-DR on CD14
- Gut protection
  - Replication
  - Maintenance of GALT
- Anti-oxidant
  - Glutathione
  - Taurine



Current recommendations

- Energy
  - Women : 20-25 kcal/kg/d
  - Men 25-30 kcal/kg/d
  - Carbohydrate/Lipid ratio : 60-70/30-40%
- Nitrogen
  - 1.0-1.5 g/kcal/d proteins
  - Non protein calories/nitrogen ratio : 100-150
  - Supplemental glutamine
- Vitamins (including liposolubles)
- Trace elements

RESULTS OF INAPPROPRIATE USE OF TPN (I)

- Smirniotis et al ICM 1998;24:1029
  - 21 pts with ARDS randomised to LCT or MCT/LCT
  - Lipids 12 g/h ~ 2.5 ±mg/kg.min
  - Increased MPAP (25 ± 5 to 33 ± 4 mmHg), decreased PaO2/FiO2 (240 ± 30 to 180 ± 35) and Qva/Qt (24 ± 5 to 37 ± 6%) ONLY in the LCT group.

RESULTS OF INAPPROPRIATE USE OF TPN (II)

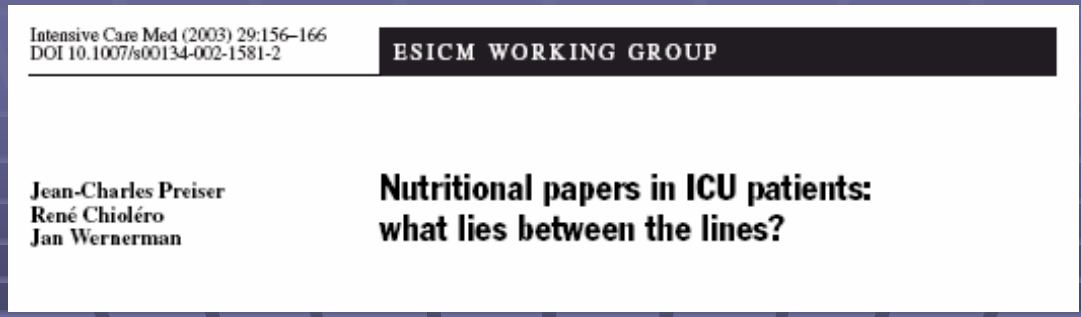
- Masclans et al ICM 1998;24:918
  - 21 pt with ARDS randomised to LCT, LCT/MCT or placebo
  - Lipids 2 mg/kg.min over 12 hours
  - Increases in T°, CO and DO2, decrease in PvO2 ONLY in the LCT group

METABOLIC COMPLICATIONS

Type	Risk factors	Prevention	Treatment	Complication
Hyperglycaemia	Rate of glucose infusion > 4 mg/kg.min	Provide calories as a dextrose + lipids mixture Check glycaemia every 4 hours	Reduce glucose supply (2–4 mg/kg.min) Intensive insulin therapy	
Hypoglycaemia	Abrupt withdrawal of dextrose administration Excessive insulin therapy	Check glycaemia every 4 hours	Re-infuse dextrose solution	Coma
Hypertriglyceridaemia	Excessive lipid supply (>4–6 g/kg.day)	Check plasma triglycerides 1–2 times /week		Macrophage activation syndrome
Cholestasis	Absence of oral alimentation Sepsis	Check liver tests 2–3 times/week	Interrupt TPN Re-start oral nutrition as soon as possible	
Steatosis	High caloric supply	Avoid excessive caloric supply. Check liver tests 2–3 times/week	Interrupt TPN	Hepatic failure
Acalculous cholecystitis	Fasting Intraluminal microbial overgrowth	Check liver tests 2–3 times/week		

FOLLOW-UP OF TPN

Variable	Minimal frequency
Glycaemia	2–3/day
Triglycerides	1/week
Electrolytes (Na, K, Cl, Ca, P, Mg)	1/week
Total proteins	1/week
Liver function tests (bilirubin, transaminases, alkaline phosphatases, gamma-glutamyltransferase)	1/week



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Intensive Care Med (2004) 30:1666–1671
DOI 10.1007/s00134-004-2345-y

BRIEF REPORT

Rupinder Dhaliwal
Brian Jurewitsch
Darlene Harrietha
Daren K. Heyland

Combination enteral and parenteral nutrition in critically ill patients: harmful or beneficial? A systematic review of the evidence

Effects of combined PN + EN on mortality

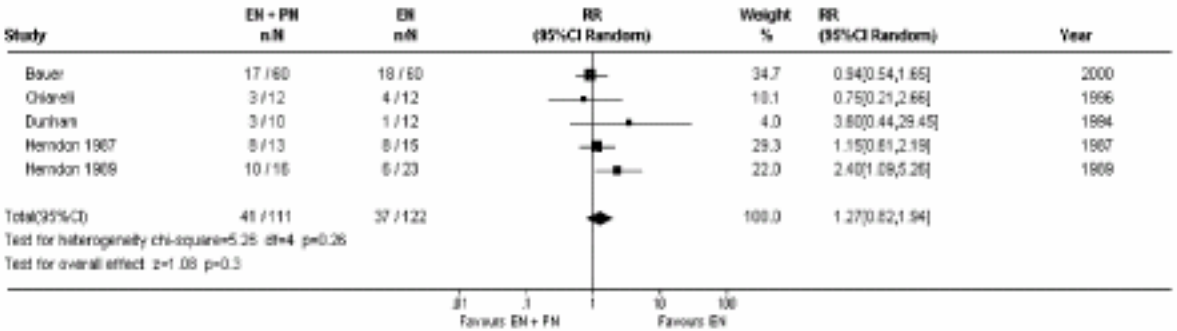


Fig. 1 Effect of combination EN + PN on mortality [13, 14, 15, 16, 17]. *EN* Enteral nutrition; *PN* parenteral nutrition; *EN + PN* combination enteral nutrition and parenteral nutrition; *n* number of persons who died in the group; *N* total number of persons in the group; *RR* relative risk; *CI* confidence intervals. (Reprinted with permission from the American Society for Parenteral and Enteral Nutrition from the *Journal of Parenteral and Enteral Nutrition, Canadian Clinical Practice Guidelines for Nutrition Support in Mechanically Ventilated, Critically Ill Adult Patients, Vol. 27; no, 5, pp355-378, Fig. 8; Sept. 2003*; the American Society for Parenteral and Enteral Nutrition does not endorse the use of this material in any form other than its entirety

Effects of combined PN + EN on infectious complications

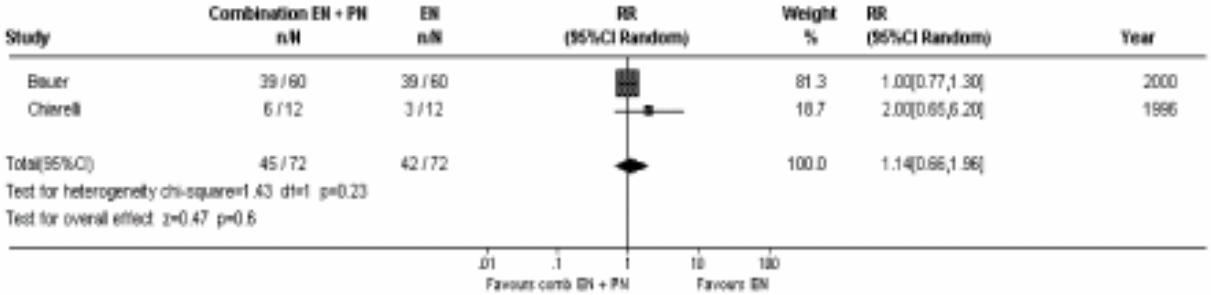


Fig. 2 Effect of combination EN + PN on infectious complications. *EN* Enteral nutrition; *PN* parenteral nutrition; *EN + PN* combination enteral nutrition and parenteral nutrition; *n* number of persons with infectious complications in the group; *N* total number of persons in the group; *RR* relative risk; *CI* confidence intervals

Increasing caloric supply with combined nutrition

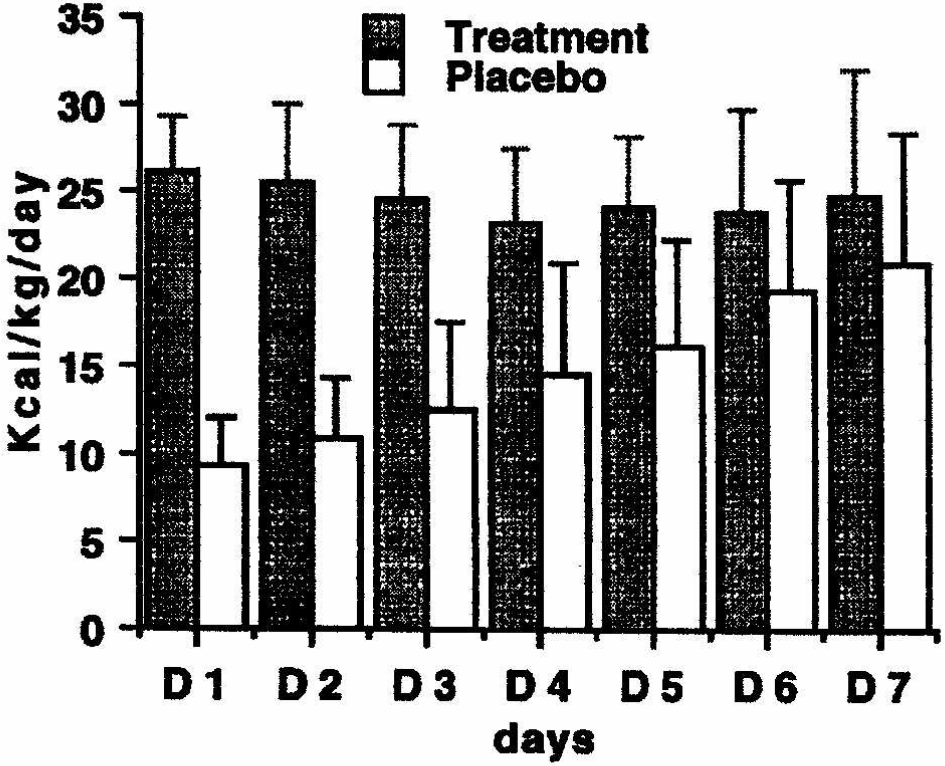


Fig. 1 Effective caloric intake delivered in treatment group (enteral nutrition + parenteral nutrition) and placebo group (enteral nutrition + placebo). $P < 0.0001$ (analysis of variance)

Bauer et al Intensive Care Med 2000

Effects of combined nutritional support on survival

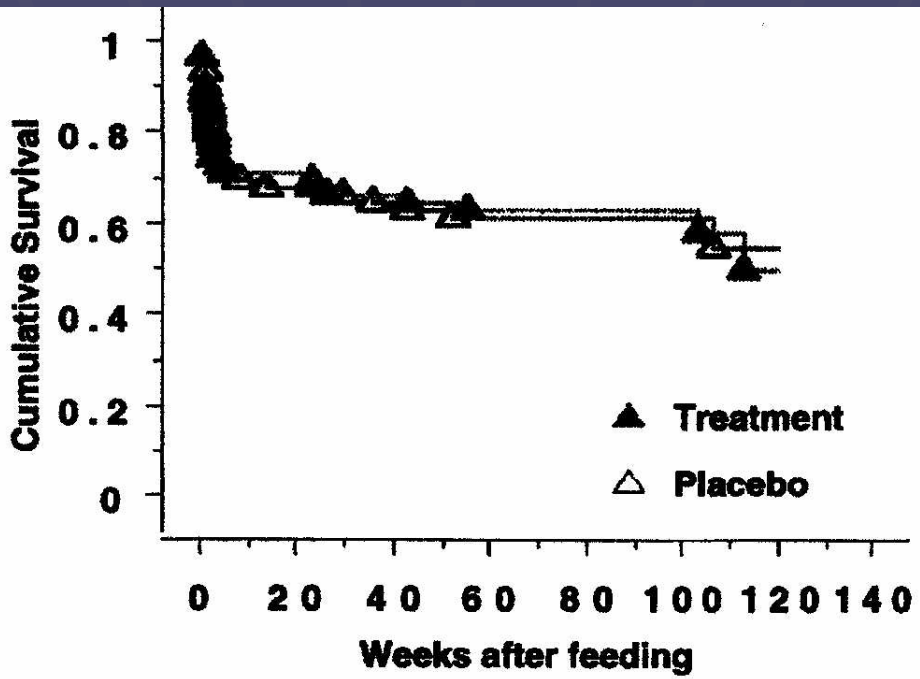


Fig. 2 Kaplan-Meyer estimates of cumulative survival in treatment group (enteral nutrition + parenteral nutrition) and placebo group (enteral nutrition + placebo). The estimated mean survival was 61.9 ± 5.7 weeks in the treatment group (24/60 patients died) and 58.5 ± 5.6 weeks in the placebo group (24/patients died). Differences between groups were not significant ($P = 0.94$ by the log-rank test)

What are we looking to?

Table 3 Studies on the effect of combination EN + PN on nutritional intake (both interventions began at the same time) (*EN* enteral nutrition, *PN* parenteral nutrition, *BEE* basal energy expenditure, *GI* gastrointestinal)

	Herndon et al. [13]	Herndon et al. [14]	Dunham et al. [15]	Chiarelli et al. [16]	Bauer et al. [17]
Intervention					
Design	EN + PN vs. EN	EN + PN vs. EN	EN + PN vs. EN	EN + PN vs. EN	EN + PN vs. EN + placebo
Timing	Upon return of GI function	upon return of GI function	Within 24–48 h admission	Both groups received PN within 24–36 h of enrollment for 4 days before experimental group received EN	Within 24–48 h of admission
Duration	10 days	2 weeks	1 week	2 weeks	4–7 days
Calories					
Calories prescribed	25 kcal/kg per day +40 kcal/% TSBA	25 kcal/kg per day +40 kcal/% TSBA	1.3 ×BEE	Energy according to catabolic rate	25 kcal/kg per day
Calories received		N/A[a]			
EN + PN	3431±336 kcal/day[b] 3977±304 kcal/day[c]		1154±904 to 2218±335 kcal/day[d]	31±6 kcal/kg per day	24.6±4.9 kcal/kg per day
EN alone	2159±196 kcal/day[b] 3036±337 kcal/day[c]		1065±435 to 1931±353 kcal/day[d]	33±9 kcal/kg per day	14.2±6.5 kcal/kg per day
p	<0.05[b] <0.05[c]		NS	NS	<0.0001

[a] Calorie intake reported as survivors vs. nonsurvivors only; text reports EN + PN group received more calories than the EN group
[b] 0–3 days
[c] 4–7 days
[d] 1–7 days

Characteristics of selected studies comparing EN + PN with EN

Table 2 Randomized studies evaluating combined EN + PN in critically ill patients. Maximal score: 14 (for methodological quality assessment criteria see Table 1) (*EN* enteral nutrition, *PN* parenteral nutrition, *TBSA* total burn surface area)

	Herndon et al. [13]	Herndon et al. [14]	Dunham et al. [15]	Chiarelli et al. [16]	Bauer et al. [17]
Population	Burns >50% TBSA (*n*=28)	Burns >50% TBSA (*n*=39)	Blunt trauma (*n*=37)	ICU patients medical and surgical (*n*=24)	ICU patients (*n*=120)
Methods					
Concealed randomization	Not sure	Not sure	Not sure	Not sure	Not sure
Intent to treat	Yes	Yes	No	Yes	Yes
Blinding	No	No	No	No	Double
Score	6	7	8	8	12
Mortality					
EN + PN	8/13 (62%)	10/16 (63%)	3/10 (30%)	3/12 (25%)	17/60 (28%)
EN	8/15 (53%)	6/23 (26%)	1/12 (8%)	4/12 (33%)	18/60 (30%)
Infections[a]					
EN + PN	NA	NA	NA	6/12 (50%)	39/60 (65%)
EN	NA	NA	NA	3/12 (25%)	39/60 (65%)
Length of stay (days)					
EN + PN	NA	NA	NA	37±13 hospital	31.2±18.5 hospital; 16.9±11.8 ICU
EN	NA	NA	NA	41±23 hospital	33.7±27.7 hospital; 17.3±12.8 ICU

[a] Number of patients with infections

Methodological assessment criteria

Table 1 Methodological quality assessment criteria

Criterion	Score 0	Score 1	Score 2
Randomization	Not applicable	Not concealed or not sure	Concealed randomization
Analysis	Other	Not applicable	Intention to treat
Blinding	Not blinded	Single blind	Double blind
Patient selection	Selected patients or unable to tell	Consecutive eligible patients	Not applicable
Comparability of groups at baseline	No or not sure	Yes	Not applicable
Extent of follow-up	<100%	100%	Not applicable
Treatment protocol	Poorly described	Reproducibly described	Not applicable
Cointerventions[a]	Not described	Described but not equal or not sure	Well described and all equal
Outcomes	Not described	Partially described	Objectively defined

[a] The extent to which antibiotics, nutritional support, ventilation, oxygen, and transfusions were applied equally across groups

Do we have compelling evidence for detrimental effects of combined nutritional support?

Do we have compelling evidence for detrimental effects of combined nutritional support?

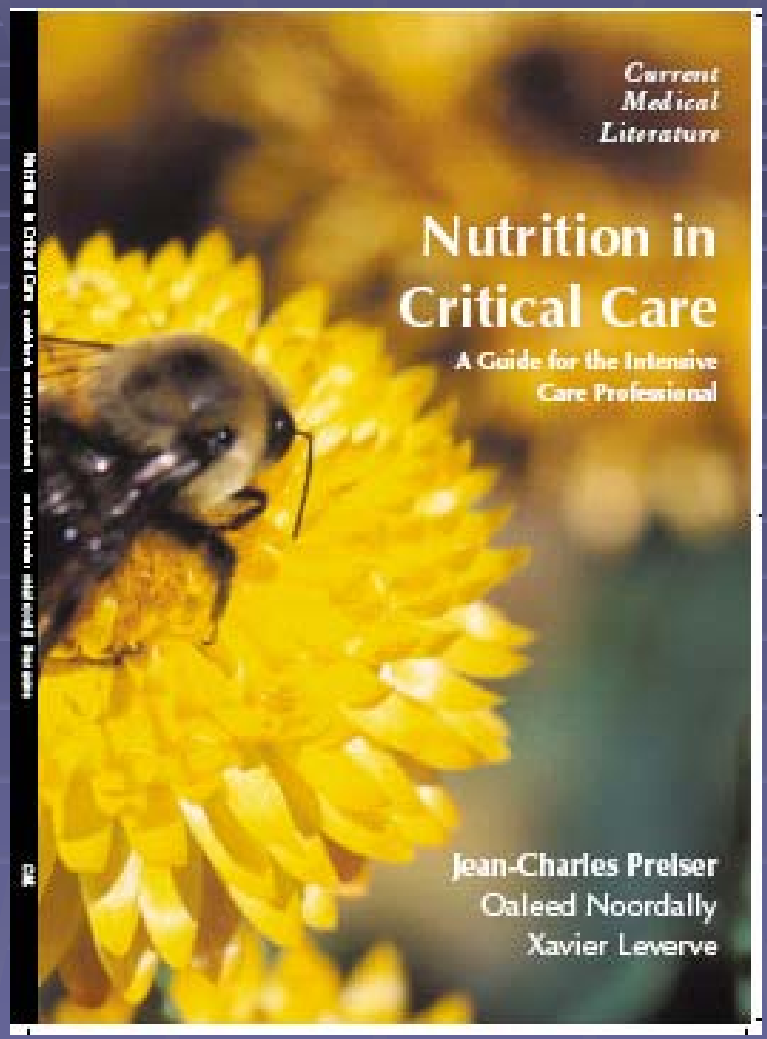
NO!

How can we optimise the use of nutritional support?

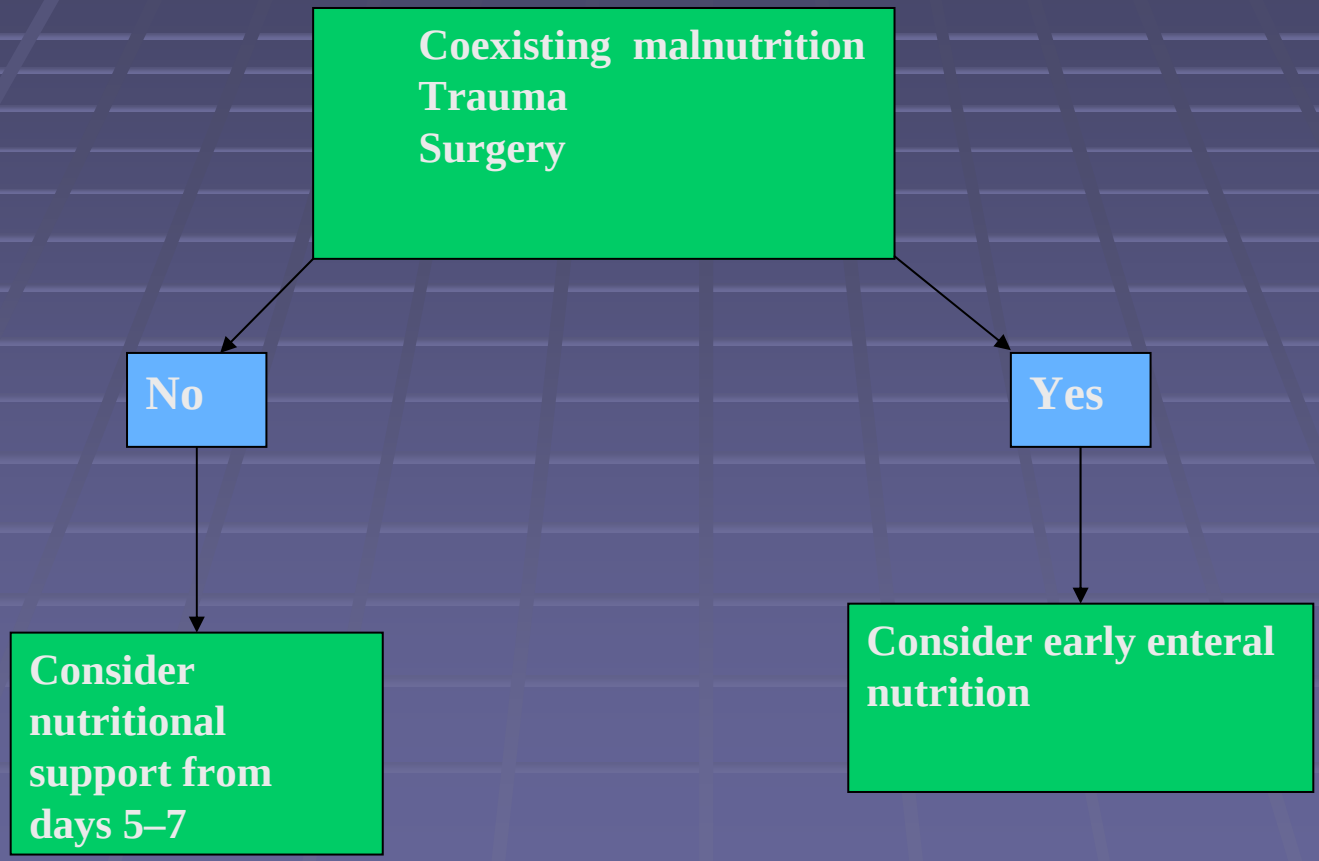
- Standardisation
  - Available guidelines
  - Local factors

Current algorithms of integrated nutritional support

- Two examples


Current
Medical
Literature
Nutrition in
Critical Care
A Guide for the Intensive
Care Professional
Jean-Charles Preiser
Oaleed Noordally
Xavier Leverve

Suggested algorithm for implementation of nutritional support



Canadian algorithm

Martin et al CMAJ 2004;170:197 (online)

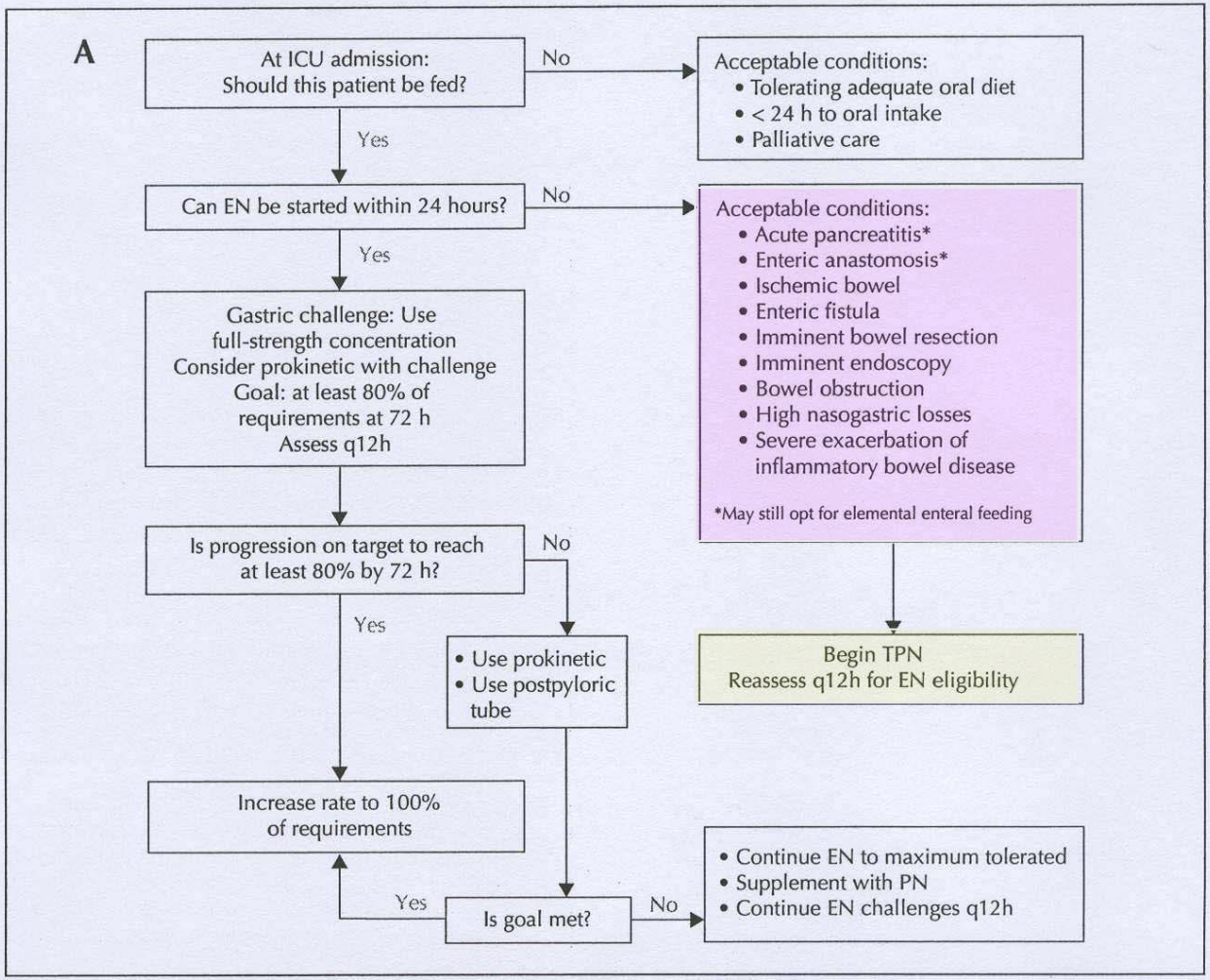


Fig. 1: Algorithms A, B and C (depicted on this page and the next one) for critical-care nutritional support, developed in 1996[17] and used in the intervention hospitals to guide selection and management and assist in the assessment of diarrhea associated with tube feeding and tolerance to tube feeding. ICU = intensive care unit, EN = enteral nutrition, TPN = total parenteral nutrition, PN = parenteral nutrition, *C.* = *Clostridium*.

Canadian algorithm

Martin et al CMAJ 2004;170:197 (online)

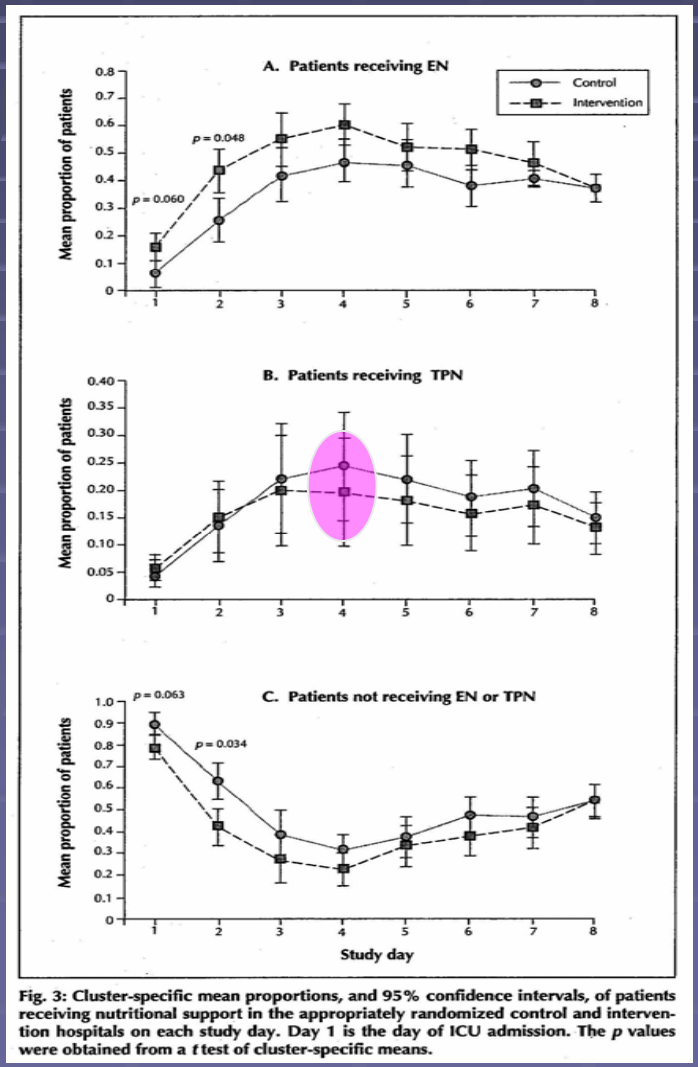


Fig. 3: Cluster-specific mean proportions, and 95% confidence intervals, of patients receiving nutritional support in the appropriately randomized control and intervention hospitals on each study day. Day 1 is the day of ICU admission. The *p* values were obtained from a *t* test of cluster-specific means.

Canadian algorithm

Martin et al CMAJ 2004;170:197 (online)

Table 4: Primary outcomes in the randomized phase

	Appropriately randomized hospitals							
	Actual values			Design effect*		All 14 hospitals; actual values		
Outcome	Control	Intervention	*p* value	C_1	C_2	Control	Intervention	*p* value
Hospital mortality rate, %	37	27	0.058	1.79	1.65	37	24	0.047
Mean hospital stay, d	35	25	0.003	20.33	63.29	34.3	25.4	0.006
Mean ICU stay, d	11.8	10.9	0.7	9.16	86.63	11.7	10.8	0.65

*The design effect is the ratio of the total number of subjects required with cluster randomization to the number required with simple randomization. For example, if 100 patients were required per group to obtain statistical significance in a mortality-rate difference in a simple randomized trial, 179 and 165 patients per group would be required in a cluster-randomized trial. The design effects for hospital and ICU stay were obtained with the method of Rao and Scott[22] for the appropriately randomized hospitals.

TPN CAN BE TOXIC…

- When used inappropriately
  - In patients
    - non-malnourished
    - able to eat or to tolerate EN
  - Too early
  - Too fast / too much
  - Unbalanced composition
  - Poor management of complications

IS PN GUILTY?

- No proof of toxicity of PN
- PN is « often » necessary in critically ill surgical patients
- All routes of feeding should be used in ICU patients