8th Apollo
INTERNATIONAL
CLINICAL NUTRITION
UPDATE - 2016
Translating Evidence Based Knowledge
to Clinical Nutrition Practice
COLOMBO, SRI LANKA -13th & 14th AUGUST, 2016

Optimising the Energy and Protein in ICU

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SCOPE

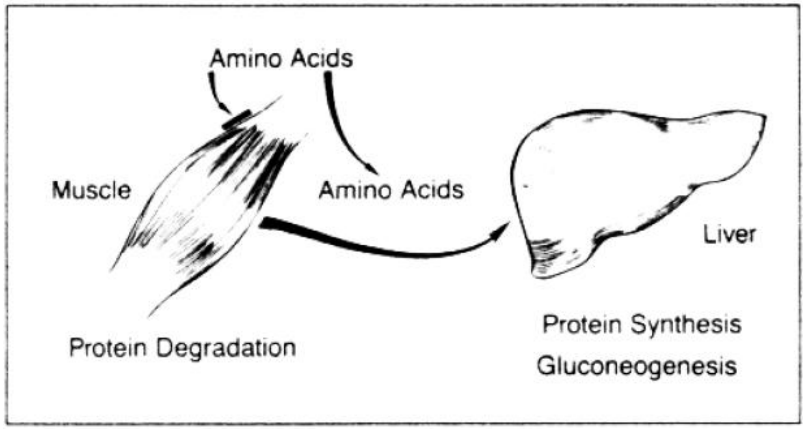
- Disclosures: Baxter; Abbot; Nestle; Bbraun; Fresenius
- The Critically ill patient challenge
- Nutrition in ICU, does it matter?
- How to make better?
- Feed interruptions and GRV
- Stuff which we just don't know…
- TTSH ICU nutrition journey
- Hypocaloric feeding (if we have time)

THE CRITICALLY ILL PATIENT

- MODs
- SIRS v CARS
- Immune Response
- Stress, Endocrine, Metabolic response
- Insulin resistance
- Fluid Balance
- CRRT
- Procedures
- Electrolytes
- Many doctors!
- Catabolism
- Low GI motility: Sedation, Vasopressors
- Malnourished??
- Acid Base
- Polypharmacy
- Gas Exchange
- Size, sex, age
- Overfeed?
- Underfeed?

ALTERED METABOLISM IN CRITICALLY ILL

- Increase endogenous glucose synthesis
- Decrease in insulin's action
- Production of inflammatory mediators i.e. TNF & IL's
- Increased in RME, protein turnover and adipose tissue lipolysis



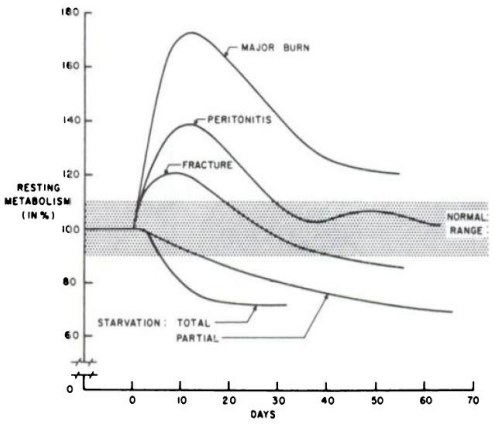


FIG. 2. Response of resting metabolism with time in man for fractures, peritonitis, and major burns as compared to partial and total starvation.

Whyte MB 2010 Am J Physiol Endocrinol Metab (298) E697 – E705
Tappy L 2007 Crit Care Med (35) S531-S534
Bozza FA 2007 Crit Care (11) 1-8
Klein S 1990 J Clin Invest (86) 1403-1408

ALTERED METABOLISM IN CRITICALLY ILL

- ESPEN 2014
- Baracos 1983 NEJM: IL1 stimulates protein loss from skeletal muscle
- 2000: Cytokines and endotoxin upregulate IL1,6, TNF receptors
- 2011: CNS Inflammation induces same muscle atrophy
- 2012 (Nature reviews clin oncology): Cytokines and eicosanoids: Energy appeal signals! Body feed thyself!

Nutrition risk assessment ICU

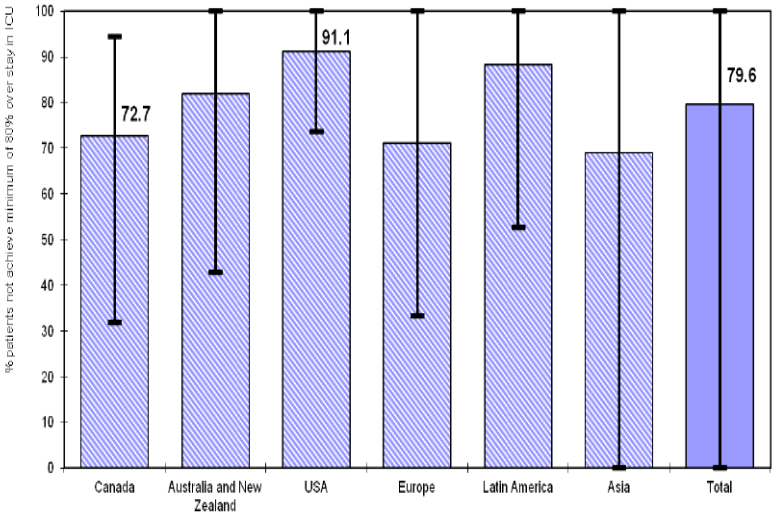
Every Critically ill patient in your ICU is at risk!!

WHAT ARE THEY GETTING IN FIRST 12-DAYS?

- Prospective, multi-institutional
- *n*= 7872 patients, > 96hrs of ICU admission
- Prescribed calories received and 60-day mortality
- Overall association of percent caloric prescription received and mortality, is statistically significant with increase calories associated with lowering mortality ($p < 0.0001$)

Optimal amount of calories for critically ill patients: Depends on how you slice the cake!*

Daren K. Heyland, MD, MSc; Naomi Cahill, RD, PhD (candidate); Andrew G. Day, MSc



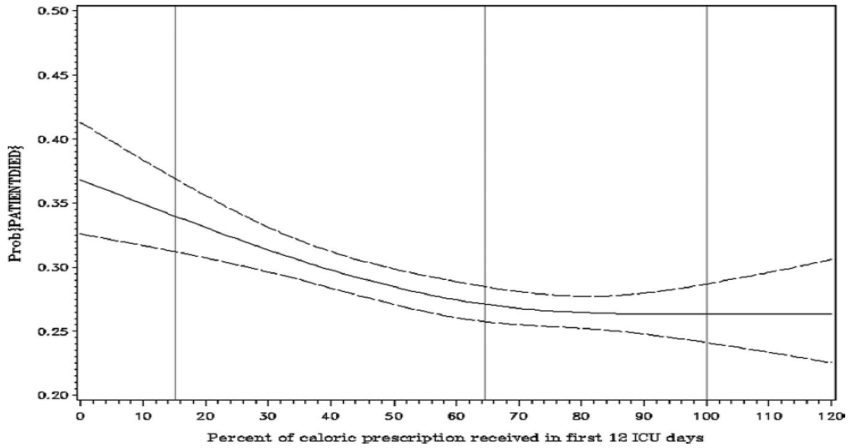
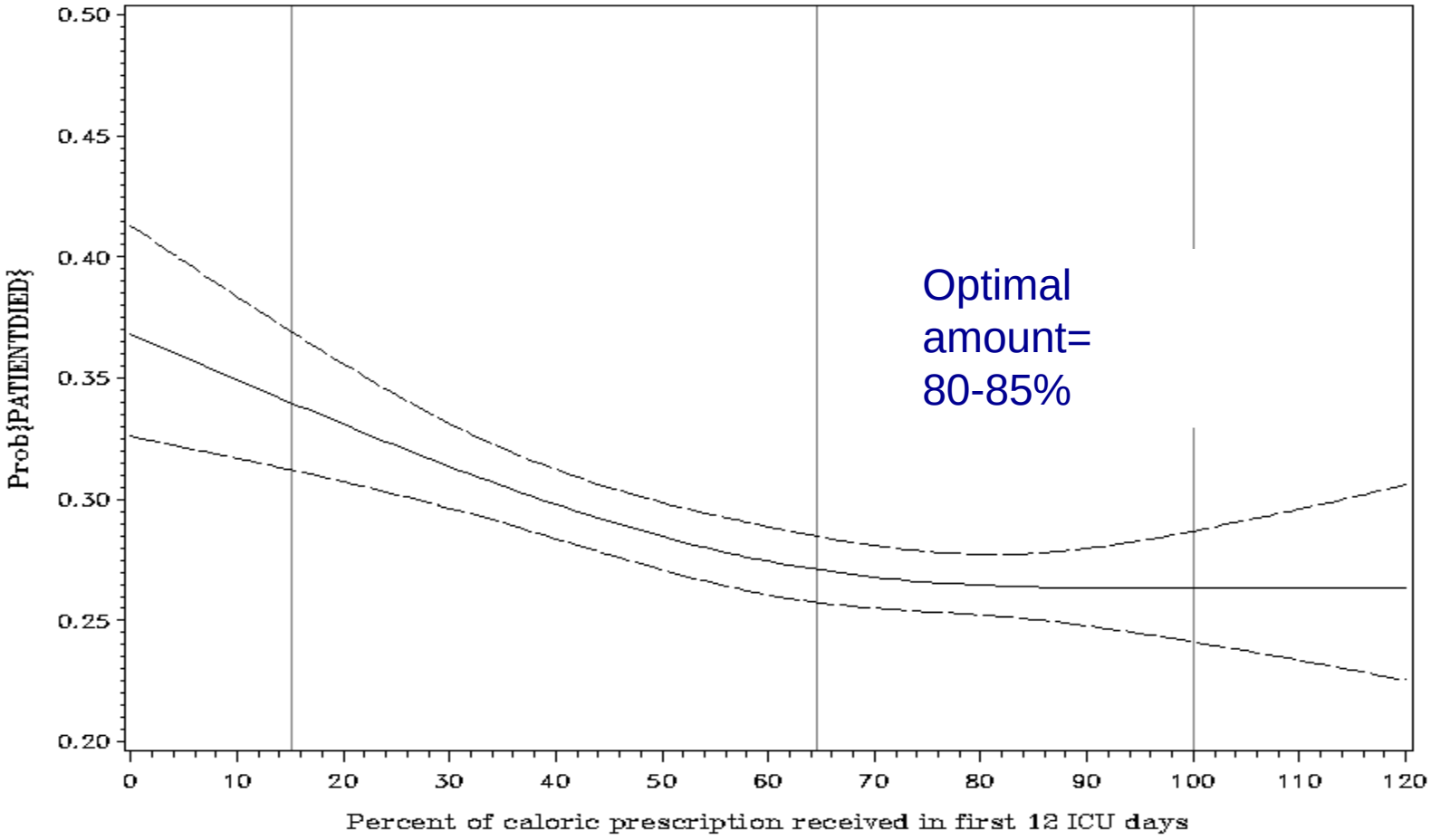


Figure 2. Association between 12-day average percentage of prescribed calories received and 60-day hospital mortality using restriction C without adjustment for covariates. The solid line is the model fit by a restricted cubic spline with knots placed at the fifth, 50th, and 95th percentiles. The dashed lines provide 95% confidence bands, and the horizontal lines provide the location of the knots. *ICU*, intensive care unit.

Heyland DK 2011 Crit Care Med (39) 2619-2626

Association Between 12-day Caloric Adequacy and 60-Day Hospital Mortality



Heyland CCM 2011

NUTRITIONAL INTAKE, OUTCOMES AND BMI

- Observational cohort study
- *n*= 2772 patients, mechanically ventilated
- Mean caloric intake 1034 kcals / 47g protein per day
- Increase of 1000 kcals / day associated with reduced mortality (adj. [OR], 0.76; 95% CI, 0.61-0.95; p = 0.014)
- Improve clinical outcomes observed in those with BMI <25 and >35

Intensive Care Med (2009) 35:1728–1737
DOI 10.1007/s00134-009-1567-4

ORIGINAL

Cathy Alberda
Leah Gramlich
Naomi Jones
Khursheed Jeejeebhoy
Andrew G. Day
Rupinder Dhaliwal
Daren K. Heyland

The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study

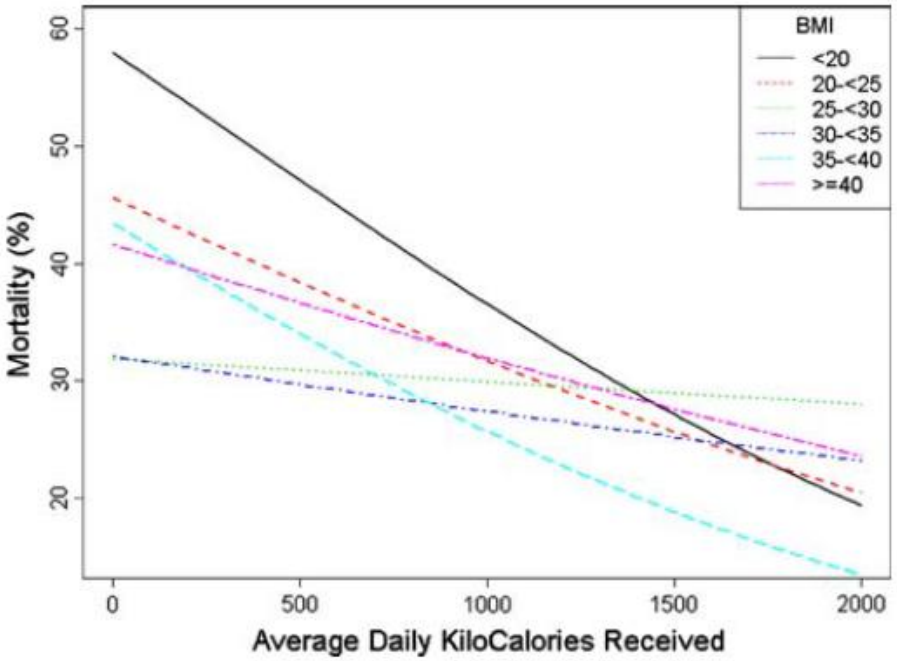
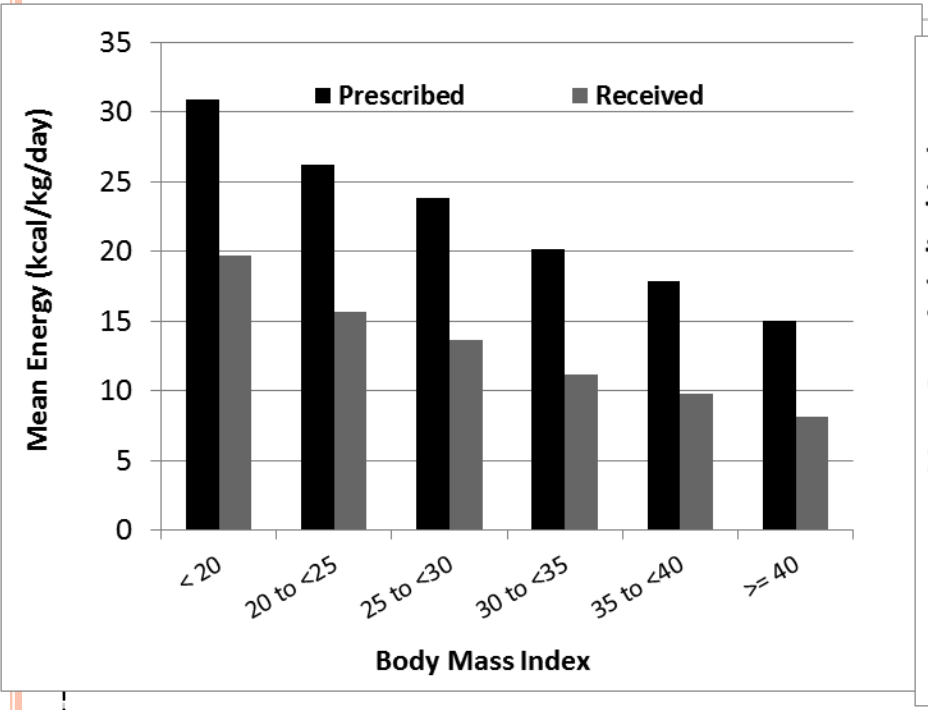
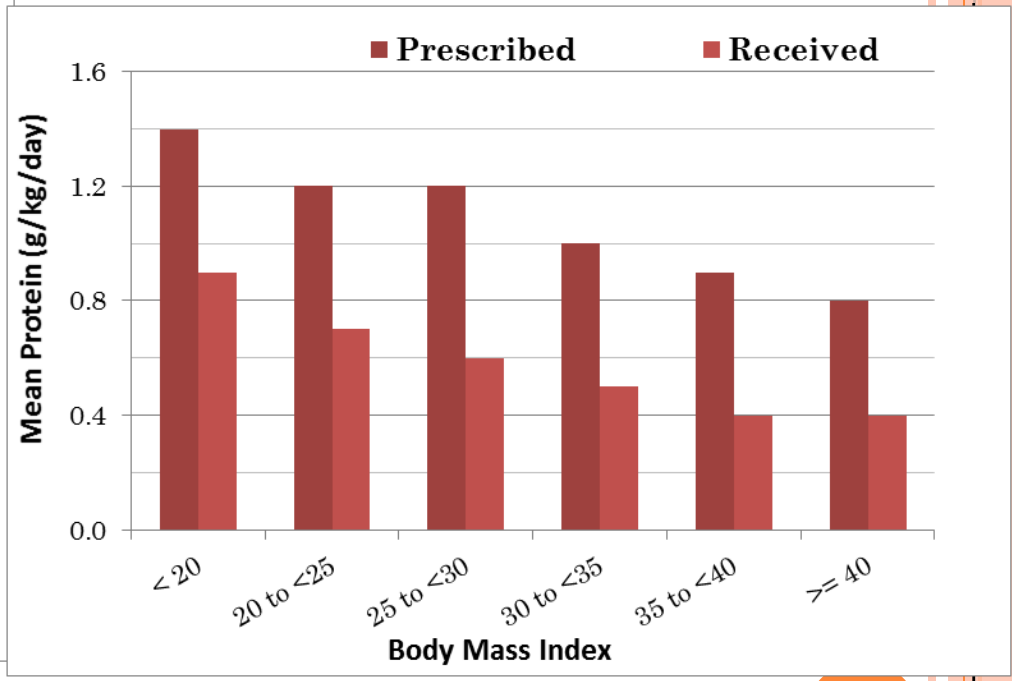


Fig. 1 The relationship between increasing calories/day and 60-day mortality by BMI. *BMI* body mass index

Alberda C 2009 Intensive Care Med (35) 1728 - 1737

- **Results**
  - Prescribed (means):
    Energy: 24 kcal/kg/day
    Protein: 1.2 g protein/kg/day
  - Received (means):
    Energy: 14 kcal/kg/day **(59.2% of target)**
    Protein: 0.6 g protein/kg/day **(56% of target)**





Calculated from Alberda C et al. *Intensive Care Med* 2009;35:1728-1737.

Dvir, Cohen, Singer. Clin Nutr 2006;25:37-44

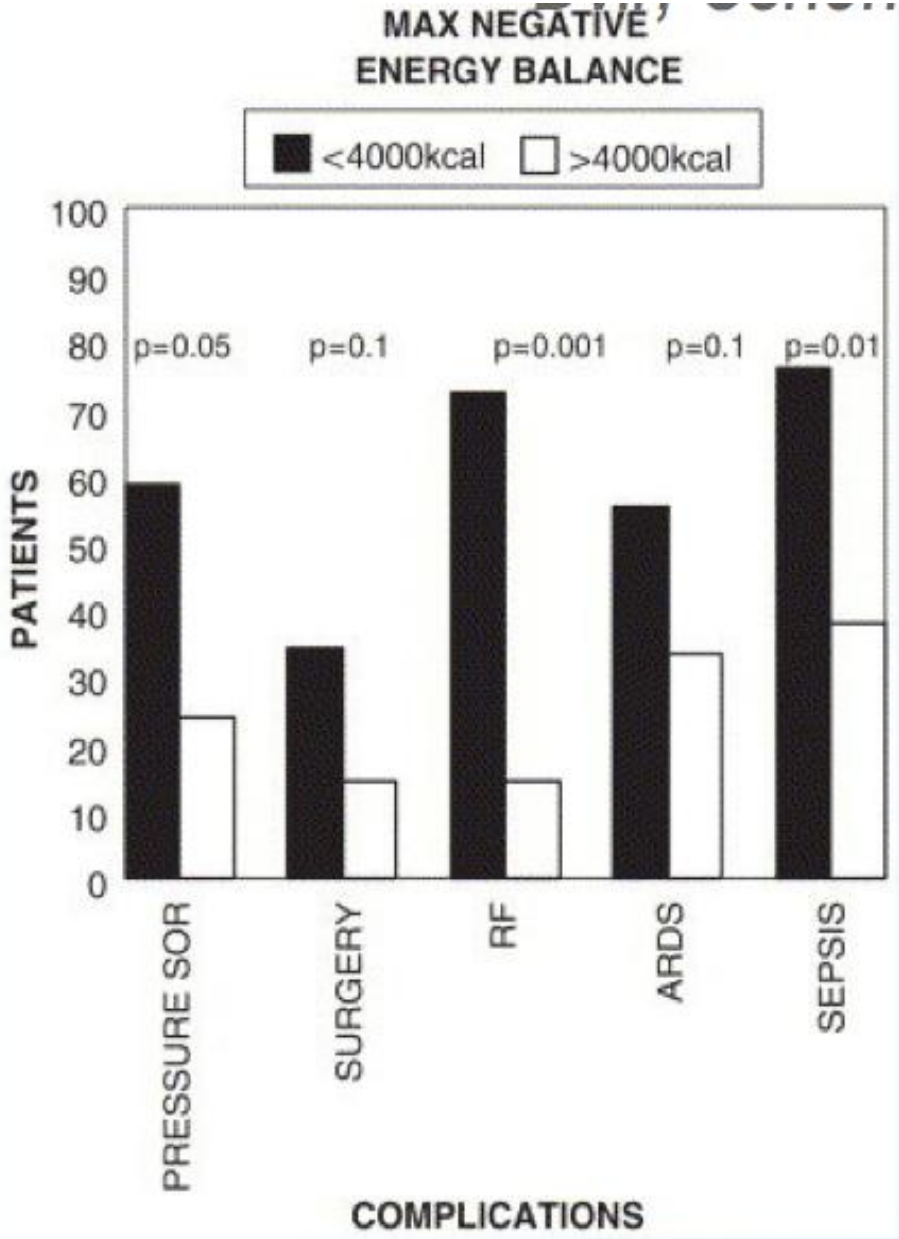


Figure 3. Complications according to cumulative energy balance above or below –4000 kcal.

RF = renal failure

CONSEQUENCES OF CALORIC DEBTS

Low caloric intake is associated with nosocomial bloodstream infections in patients in the medical intensive care unit*

Lewis Rubinson, MD; Gregory B. Diette, MD, MHS; Xiaoyan Song, MD, MHS; Roy G. Brower, MD; Jerry A. Krishnan, MD

- Prospective cohort study
- *n*= 138 patients, > 96hrs of MICU admission and NPO
- Mean caloric intake 49.4% ± 29.3% / day as per ACCP guidelines
- <25% estimated caloric intake has significantly higher risk of BSI ($p<0.05$)

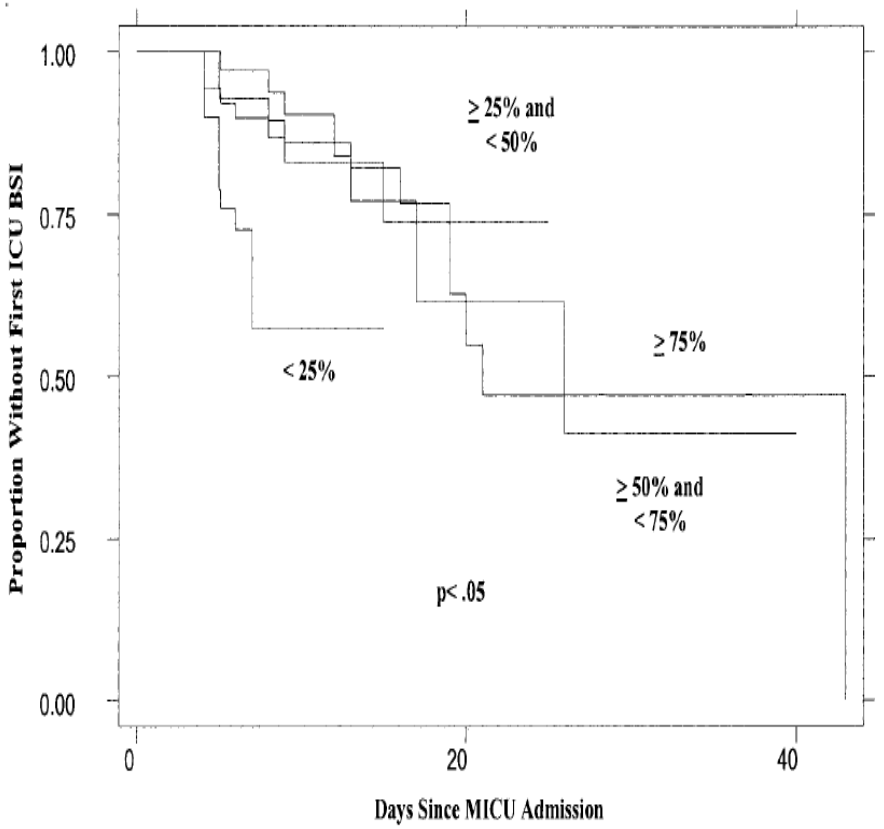


Figure 1. Kaplan-Meier curves by average daily percent of American College of Chest Physicians (ACCP)-recommended calories provided. Each Kaplan-Meier plot represents the time to first medical intensive care unit (*MICU*) bloodstream infection (*BSI*) for patients in a specific nutrition category. The 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 L 2004 Crit Care Med (32) 350 - 357

ENERGY DEFICIT AND SURVIVAL RATE

Large negative energy balance may be an independent determinant of ICU mortality

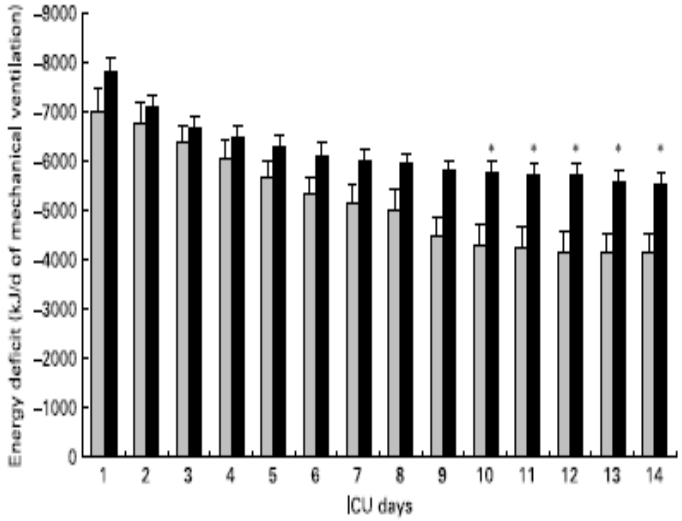


Fig. 2. Evolution of daily energy deficit of intensive care unit (ICU) survivors (□; *n* 11) and of ICU deaths (■; *n* 27) in patients requiring prolonged acute mechanical ventilation. Values are means with their standard errors depicted by vertical bars. Mean values were significantly different from those of the ICU survivors: *$P<0.05$.

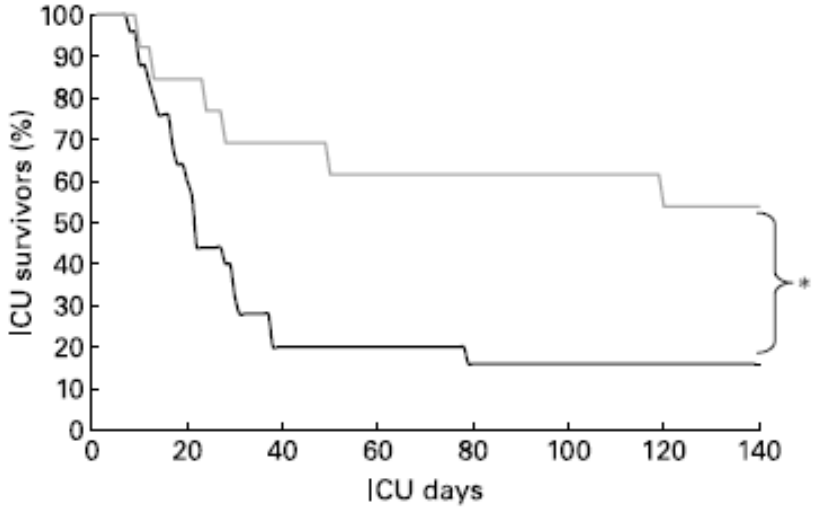


Fig. 4. Kaplan–Meier analysis of intensive care unit (ICU) survival rate in patients with mean energy deficit ≥ 5021 kJ (1200 kcal)/d of mechanical ventilation (—; *n* 25) and with mean energy deficit < 5021 kJ (1200 kcal)/d of mechanical ventilation (—; *n* 13). *Values were significantly different ($P = 0.01$; log-rank test).

Faisy C 2009 Br J Nutr (101) 1079-1087

Clinical Nutrition 31 (2012) 462–468

Contents lists available at SciVerse ScienceDirect

Clinical Nutrition

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

Original article

Provision of protein and energy in relation to measured requirements in intensive care patients

Matilde Jo Allingstrup [a,*], Negar Esmailzadeh [a], Anne Wilkens Knudsen [a], Kurt Espersen [a], Tom Hartvig Jensen [a], Jørgen Wiis [a], Anders Perner [a], Jens Kondrup [b]

[a] Department of Intensive Care 4131, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark
[b] Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen & Clinical Nutrition Unit, Copenhagen University Hospital, Rigshospitalet, Denmark

- Observational cohort study
- *n*= 113 patients, in ICU
- Low, medium and high AA groups
- **Earlier mortality observed in the group of low protein intake patients**
  (Kaplan-Meier survival probability 49% on day 10, compared to 79% and 88% in the medium and high AA groups, respectively)

Allingstrup MJ 2012 Clin Nutr (31) 462-468

Table 2
Data in groups according to ranked protein intake.

		Protein&AA provision group			*P*
		Low N = 37	Medium N = 38	High N = 38	
Distribution of patients	Period 1 (N)	17	19	20	
	Period 2 (N)	20	19	18	
Diagnoses	Severe sepsis (N)	35	33	32	
	Burns (N)	2	5	6	
Anthropometrics	Age, years	59.7 ± 17.4	62.1 ± 15.4	56.7 ± 18.5	
	Height, m	1.70 ± 0.09	1.75 ± 0.07	1.77 ± 0.09	
	Body weight, kg	70.1 ± 16.1	82.2 ± 15.6	81.1 ± 16.2	L *vs.* M: <0.01 L *vs.* H: <0.05
	BMI	24.0 ± 3.9	26.7 ± 4.7	25.9 ± 5.0	
Severity scores	APACHE II score (1st 24 h in ICU)	23.2 ± 7.4	21.9 ± 5.9	22.1 ± 6.8	
	SOFA, first score	6.78 ± 3.05	6.66 ± 3.05	7.68 ± 3.05	
	SOFA, average score in ICU	6.41 ± 3.25	6.07 ± 2.45	6.70 ± 3.56	
Blood analyses	Glucose, mmol/l	9.2 ± 2.3	9.1 ± 2.3	9.1 ± 2.2	
	Urea, mmol/l	13.5 ± 9.4	14.5 ± 9.0	15.7 ± 7.9	
Nutrition	Protein&AA provision, g/kg per day	0.79 ± 0.29	1.06 ± 0.23	1.46 ± 0.29	L *vs.* M: <0.001 L *vs.* H: <0.001 M *vs.* H: <0.001
	N loss, $Protein_{eq}$ g/kg per day	1.40 ± 0.52	1.41 ± 0.45	1.67 ± 0.47	
	N balance, $Protein_{eq}$ g/kg per day	−0.59± 0.48	−0.35± 0.41	−0.20± 0.58	L *vs.* H: <0.01
	Energy provision, kcal/kg per day	21.7 ± 6.7	24.7 ± 5.7	27.2 ± 6.7	L *vs.* H: <0.001
	Resting energy expenditure, kcal/kg per day	28.4 ± 6.2	28.1 ± 7.5	28.8 ± 7.2	
	Energy-balance, kcal/kg per day	−6.4 ± 9.1	−3.5 ± 6.3	−1.5 ± 6.9	L *vs.* H: <0.05
	Energy in Protein&AA/Energy provision, %	15.0 ± 3.3	18.1 ± 3.3	22.4 ± 3.4	L *vs.* M: <0.001 L *vs.* H: <0.001 M *vs.* H: <0.001
	Energy in $Protein_{eq}$/REE, %	20.6 ± 6.7	21.2 ± 6.6	21.2 ± 6.6	
Outcome	Length of stay in ICU, d#	5 (3–9)	10 (6–14)	10 (7–15)	L *vs.* M: <0.01 L *vs.* H: <0.01
	ICU mortality, *n* (%)	10 (27)	9 (24)	6 (16)	
	Discharged alive from ICU, *n* (%)	27 (73)	29 (76)	32 (84)	

Data are presented as *N* (%), mean ± SD, or #: median (interquartile range).
P values calculated by ANOVA with Bonferroni's test for multiple comparisons (mean ± SD) or Kruskal–Wallis with Dunn's test for multiple comparisons (median, IQR). L, Low group; M, medium group; H, high group.

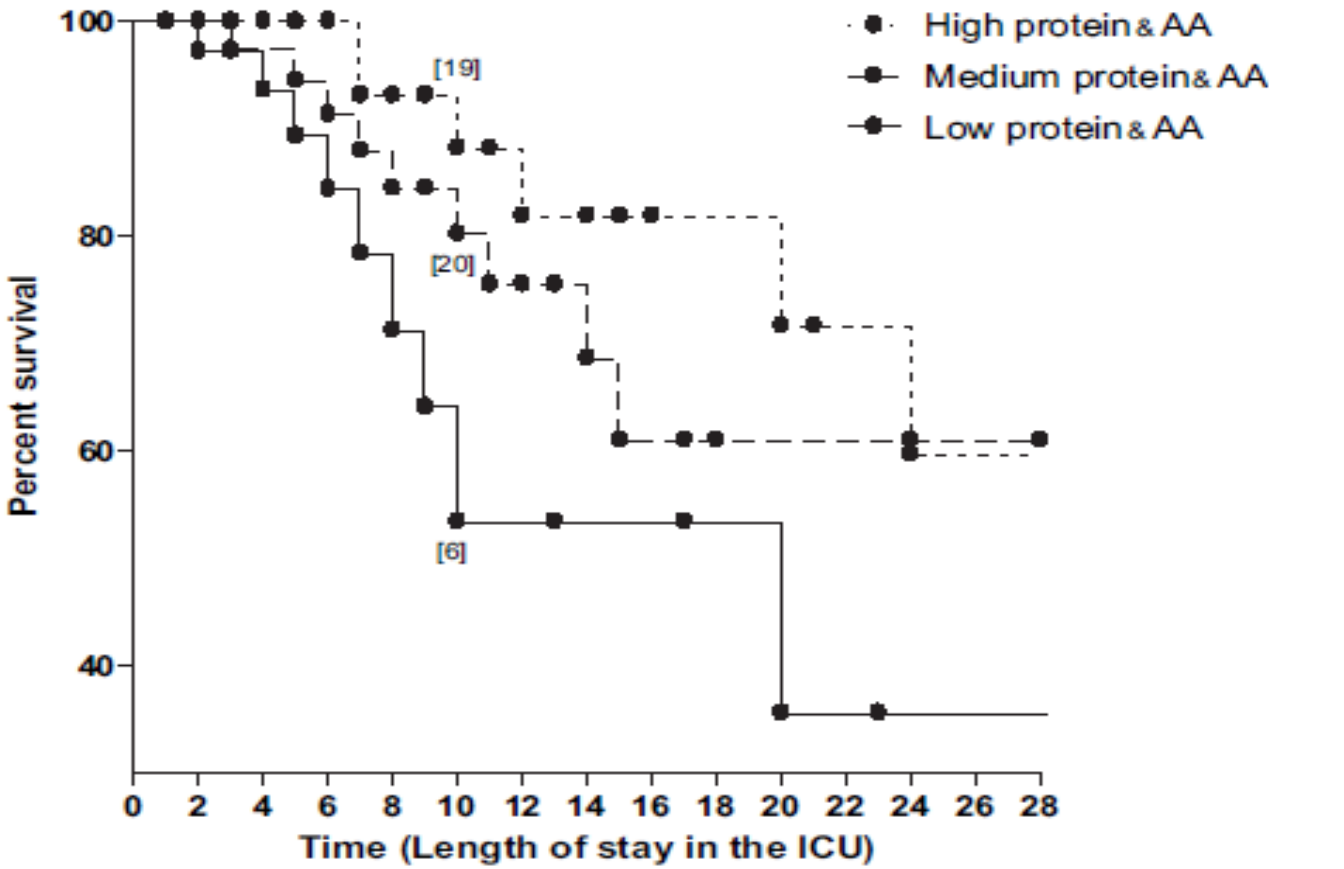
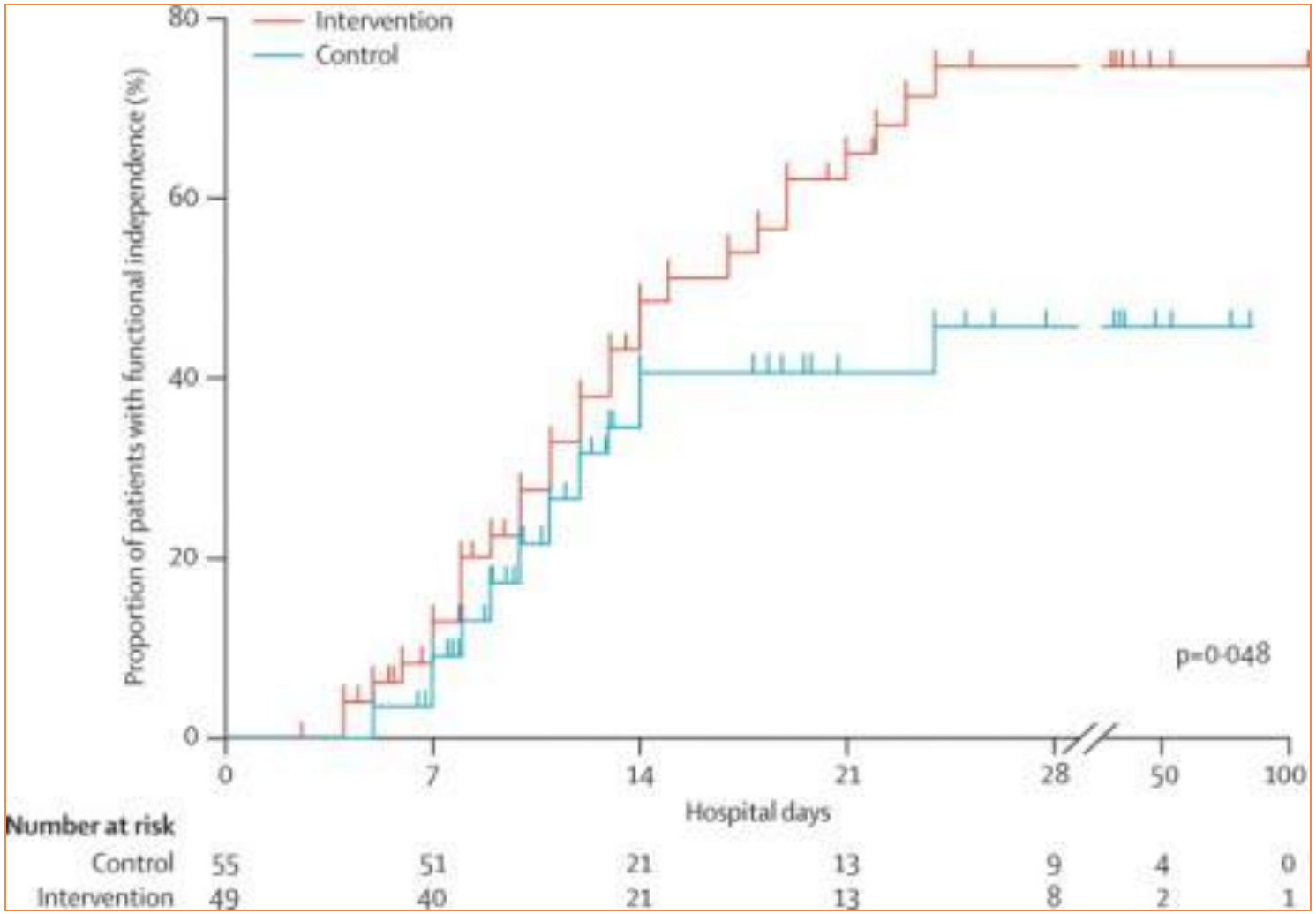


Fig. 2. 28-Day survival in the ICU. Kaplan–Meier curve that depicts 28-day survival in three groups of patients, ranked according to decreasing provision of protein during their intensive care unit stay. Initial number of patients in the three groups: Low protein&AA: 37; medium protein&AA: 38; High protein&AA: 38. The average provision of protein in the three groups were: low protein&AA: 53.8 g/day; medium protein&AA: 84.3; high protein&AA: 114.9 g/day. The square brackets indicate the number of patients remaining at risk on day 10, i.e. neither censored nor dead. The knobs indicate censoring of one or several patients. Eight patients had longer observation time than 28 days, with a maximum of 77 days. Comparison of curves for all patients: Mantel log-rank $P = 0.021$; Breslow–Gehan: $P = 0.027$. Log-rank test for trend: $P = 0.011$.

Functional independence

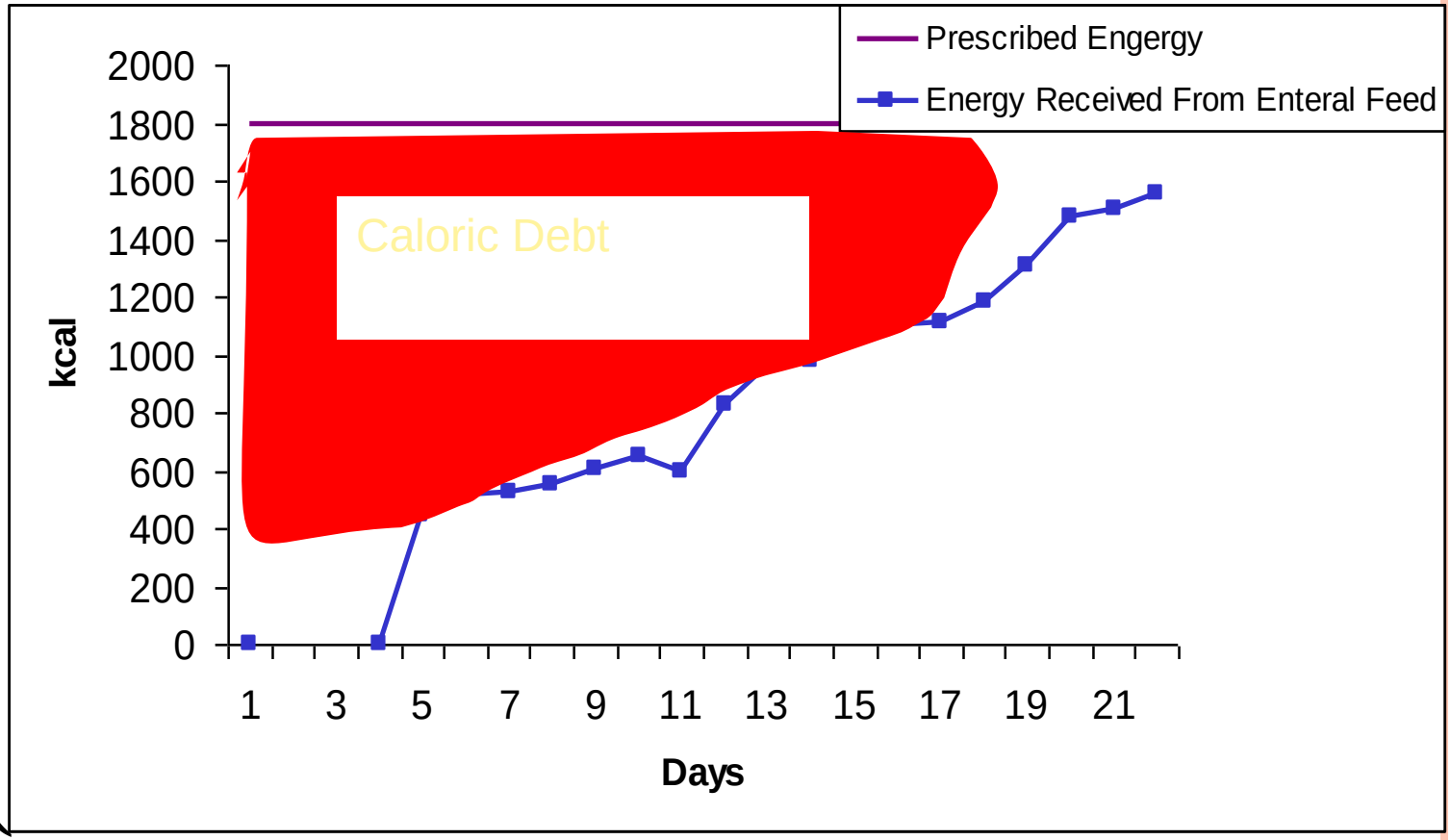
- **Early mobilization with AA / protein infusions**



Hodgson et al. Critical Care 2012 17:207
Patel BK, Pohlman AS, Chest 2014. 146(3):583-9.

Increasing Calorie Debt Associated with worse Outcomes

Adequacy of EN



- ↑ Caloric debt associated with:
  - ↑ Longer ICU stay
  - ↑ Days on mechanical ventilation
  - ↑ Complications
  - ↑ Mortality

Rubinson CCM 2004; Villet *Clin Nutr* 2005; Dvir Clin Nutr 2006; Petros Clin Nutr 2006

CAN NUTRITION BE APPLIED TO THE NEW RISK REDUCTION PROGRAMS ?

- **Malnutrition and protein wasting are independently associated with high infectious and non-infectious morbidity**
  - **Increased length of stay**
  - **Higher readmission rates**
  - **Prolonged recovery**
  - **Increased need for skilled health care resources postop and post hospitalization**

Identifying critically-ill patients who will benefit most from nutritional therapy: Further validation of the "modified NUTRIC" nutritional risk assessment tool

Rahman A, Hasan RM, Agarwala R, Martin C, Day AG, Heyland DK. Clin Nutr. 2015 Jan 28.

Critically Ill greatest risk for maluntrition!

Not enough is BAD!!

CALORIC INTAKE IN CRITICALLY ILL: How are we doing?

NICE-SUGAR STUDY

Nonprotein calories administered on days 1–14 — kcal/day		
By enteral route	624±496	623±496
By parenteral route	173±359	162±345
As intravenous glucose	93.4±88.8	87.2±93.5
Total	891±490	872±500

EN Engl J Med 2009; 360:1283-1297SUGAR Study Investigators. N Engl J Med 2009

The prevalence of iatrogenic underfeeding in the nutritionally 'at-risk' critically ill patient: Results of an international, multicenter, prospective study

Clinical Nutrition 34 (2015) 659–666

Daren K. Heyland [a, b, c, *], Rupinder Dhaliwal [a], Miao Wang [a], Andrew G. Day [a, b]

Methods: This was a prospective, multi-institutional study in 201 units from 26 countries. We included 3390 mechanically ventilated patients who remained in the unit and received artificial nutrition for at least 96 h. We report time to start of enteral nutrition and % nutrition received in various geographic regions of the world and we focus on subgroups of 'high risk' patients (those with >7 days of mechanical ventilation, body mass index of <25 or ≥35, and those with a Nutrition Risk In the Critically ill (NUTRIC) score of ≥5). We report rates of novel enteral nutrition delivery techniques and supplemental parenteral nutrition in these high risk patients.

Results: On average, enteral feedings were started 38.8 h (standard deviation: 39.6) after admission, patients received 61.2% of calories and 57.6% of protein prescribed, and 74.0% of patients failed to meet the quality metric of receiving at least 80% of energy targets. There were significant differences in nutrition outcomes across different geographic regions. There were no clinically important differences in nutrition outcomes or rates of iatrogenic underfeeding in patients in different BMI groups nor by NUTRIC score. Of all at-risk patients, 14% were ever prescribed volume-based feeds, and 15% of patients ever received supplemental parenteral nutrition.

Conclusions: Worldwide, the majority of critically ill patients, including high nutritional risk patients, fail to receive adequate nutritional intake. There is low uptake of strategies designed to optimize nutrition delivery in these patients.

INS 2014 Singapore

- SICM-NICER
- Adult Medical & Surgical ICUs
- CGH SICU, MICU
- TTSH SICU, NICU
- AH ICU
- NUH SICU, MICU
- KTPH

- Results…..

Table 2. Patient Characteristics

Number of Patients	Your Site n=86	Sister Sites n=965	All Sites n=3893
	Personal Information		
Age			
mean (range)	63.2 (19-91)	62.8 (18-97)	59.1 (16-102)
Sex			
Female	31 (36.0%)	325 (33.7%)	1391 (35.7%)
Male	55 (64.0%)	640 (66.3%)	2502 (64.3%)
	Admission Information		
Type of Admission			
Medical	48 (55.8%)	548 (56.8%)	2347 (60.3%)
Surgical Elective	1 (1.2%)	148 (15.3%)	511 (13.1%)
Surgical Emergency	37 (43.0%)	269 (27.9%)	1035 (26.6%)
BMI (kg m2)			
mean (range)	24.0 (13.6-45.7)	23.6 (9.1-64.3)	26.8 (9.1-74.7)
How was weight determined?			
Actual	47 (54.7%)	631 (66.0%)	2284 (58.9%)
Estimated	39 (45.3%)	325 (34.0%)	1594 (41.1%)

Severity of illness and Outcomes

Apache II Score mean (range)	22.5 (5-39)	22.5 (2-52)	21.3 (1-55)
SOFA score mean (range)	4.38 (0-14)	6.18 (0-18)	6.2 (0-18)
NUTRIC score mean (range)	4.22 (0-9)	4.32 (0-9)	4.07 (0-9)
Presence of ARDS Yes n/N (PCT)	3/86 (3.5%)	126/965 (13.1%)	420/3893 (10.8%)
	Outcome		
Length of Mechanical Ventilation (days, 60-day censored) median [Q1,Q3]	5.5 [3.2-8.9]	5.5 [2.9-10.6]	6.0 [2.8-12.2]
Length of Stay in ICU (days, 60-day censored) median [Q1,Q3]	7.8 [5.1-13.5]	9.2 [5.5-17.3]	10.0 [5.8-20.0]
Length of Stay in Hospital (days, 60-day censored) median [Q1,Q3]	24.5 [12.1-61.0]	27.7 [13.9-61.0]	20.7 [11.4-42.9]
Mortality (60-day censored) Yes n/N (PCT)	22/86 (25.6%)	196/965 (20.3%)	849/3893 (21.8%)

Prescription

- Weight: How measures or estimated?
- Harris Benedict with activity factor
- Schofield
- Penn State
- Weight based formula
- EN: 99% Polymeric feed, 1pt received arginine + FO formula
- <5% probiotic use
- No glutamine or Selenium supplementation

Table 5. Type of Nutrition (By Patient)

Number of Patients	Your Site n=86	Sister Sites n=965	All Sites n=3898
Type of Nutrition			
EN Only	70 (81.4%)	627 (65.0%)	2872 (73.8%)
PN Only	3 (3.5%)	84 (8.7%)	187 (4.8%)
EN+PN	10 (11.6%)	162 (16.8%)	366 (9.4%)
None	3 (3.5%)	92 (9.5%)	468 (12.0%)

Figure 3.1 Timing of Initiation of EN

Number of patients	Your Site n=86	Sister Sites n=965	All Sites n=3893
Initiation of EN			
mean (range)	61 (1-1857)	40 (0-1857)	38 (0-1857)

Table 4. Overall Performance

Number of ICU days	Your Site n=774	Sister Sites n=9100	All Sites n=37862
Adequacy of Calories from Total Nutrition (EN+PN+propofol) mean (range)	66.8%	56.2% (21.8%-94.4%)	57.7% (21.1%-94.7%)
Adequacy of Protein from Total Nutrition (EN+PN) mean (range)	64.0%	55.5% (17.5%-101%)	54.3% (14.7%-101%)
Adequacy of Calories from EN in EN Only Patients mean (range)	53.5%	50.4% (14.6%-94.3%)	51.9% (14.6%-94.3%)
Adequacy of Protein from EN in EN Only Patients mean (range)	54.5%	51.3% (16.3%-95.1%)	52.0% (16.3%-95.1%)
Received Calories from Total Nutrition(kcals, EN+PN+propofol) mean (range)	1042	897 (330-2139)	1062 (330-3298)
Received Protein from Total Nutrition (g, EN+PN) mean (range)	46	37 (11-82)	51 (11-173)
Received Calories from EN in EN only Patients (kcals) mean (range)	838	806 (197-2137)	959 (197-2669)
Received Protein from EN in EN only Patients (g) mean (range)	39	35 (10-82)	49 (10-173)

Figure 1.3 Adequacy of Calories from EN

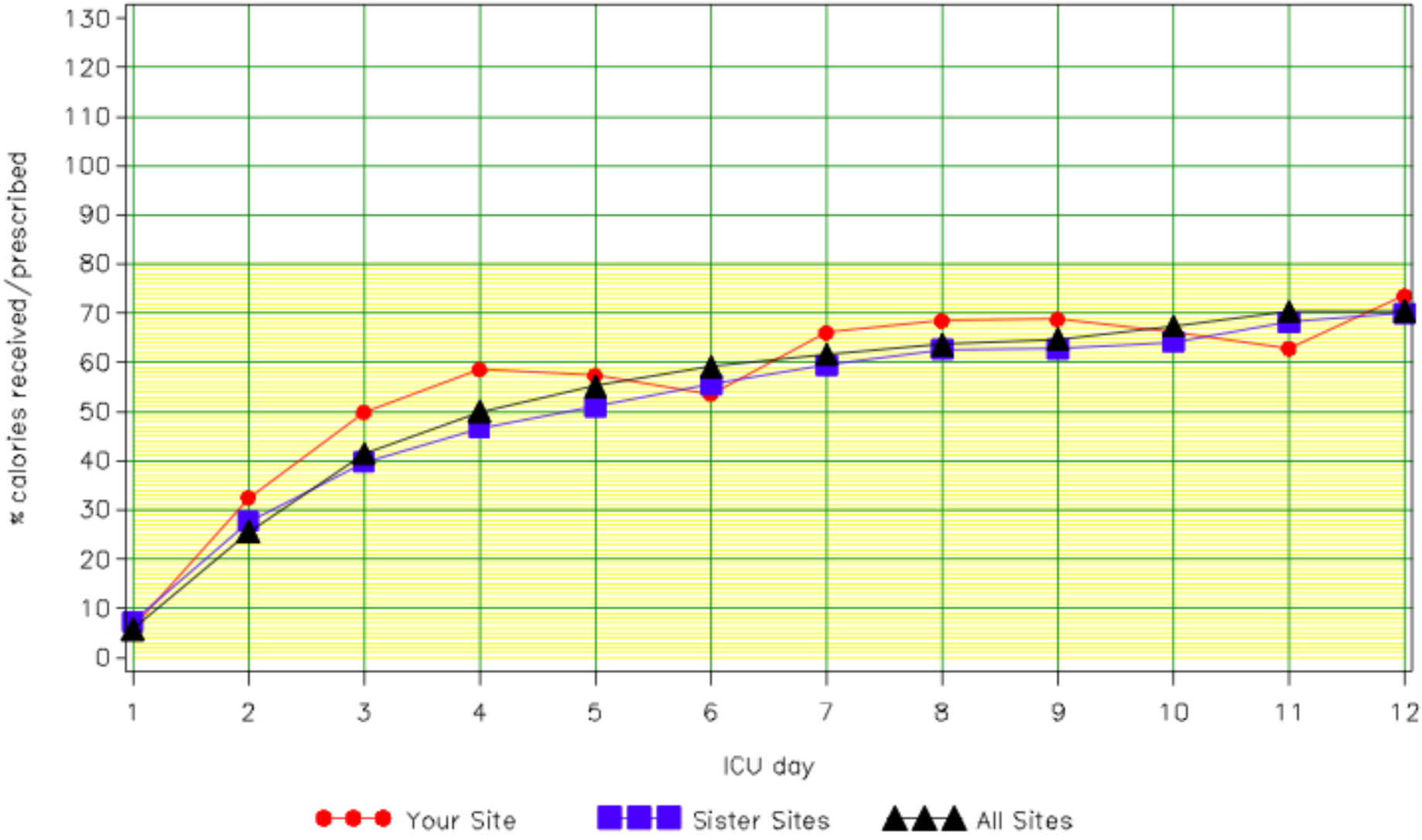


Table 9. EN Feeds Interrupted

Number of Patient-days on EN	Your Site n=564	Sister Sites n=5730	All Sites n=24026
EN Feeds Interrupted			
Yes n/N (PCT)	197/564 (34.9%)	1175/5730 (20.5%)	6828/24024 (28.4%)
Total duration of feed interruption (hours)			
median [Q1,Q3]	6.0 [4.0-10.0]	6.0 [3.0-10.0]	7.0 [3.0-12.0]
Reasons interruption			
Fasting for endotracheal extubation/intubation/trach procedure	90 (53.9%)	382 (36.0%)	1860 (31.4%)
Fasting for other bedside procedure	11 (6.6%)	262 (24.7%)	700 (11.8%)
Fasting for operating room procedure	18 (10.8%)	91 (8.6%)	877 (14.8%)
Fasting for radiology suite procedure	13 (7.8%)	83 (7.8%)	614 (10.4%)
Fasting for administration of medications	17 (10.2%)	23 (2.2%)	222 (3.8%)
Intolerance to enteral feeding - high gastric residuals	16 (9.6%)	137 (12.9%)	681 (11.5%)

GRV…. What's your unit's protocol?

Table 8. Feeding Protocols

Number of ICUs	Your Site n=1	Sister Sites n=63	All Sites n=243
Gastric Residual Volume (mls)			
mean (range)	300	265 (100-500)	301 (100-501)
Algorithms included in Protocol			
Motility agents	Yes	32 (84.2%)	134 (85.4%)
Small bowel feeding	Yes	29 (76.3%)	108 (68.8%)
Withholding for procedures	Yes	28 (73.7%)	101 (64.3%)
Head of bed elevation	Yes	36 (94.7%)	127 (80.9%)

PN Initiation indications

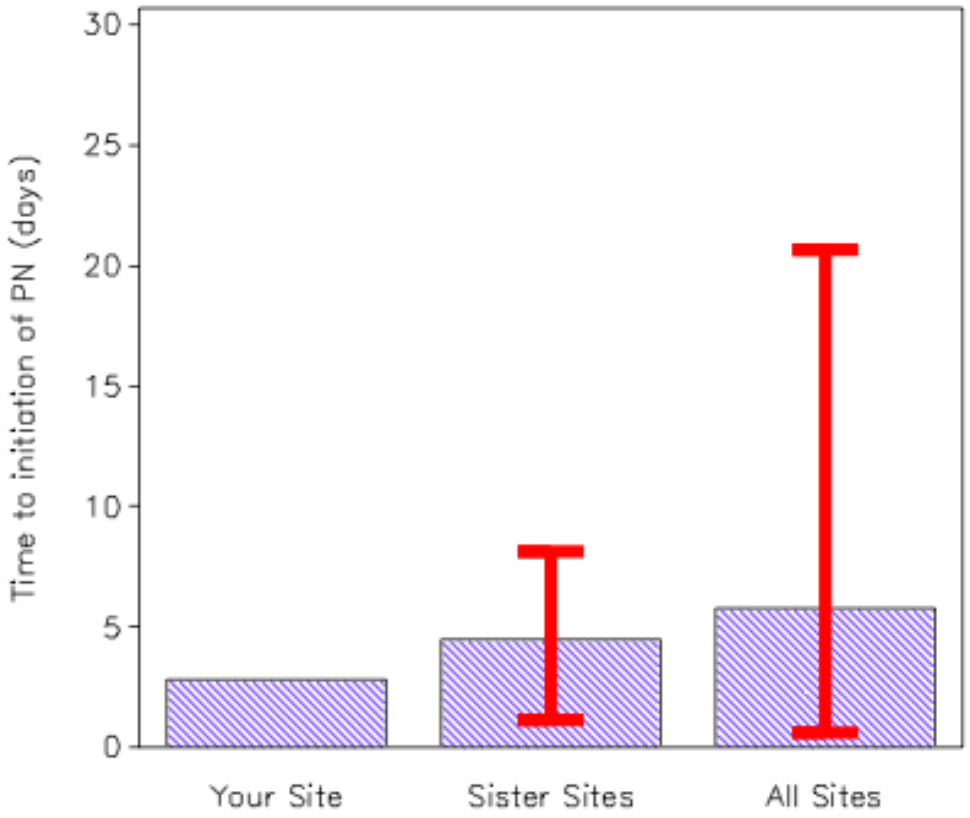
Table 10. Reason PN Initiated

Number of Patients on PN	Your Site n=13	Sister Sites n=245	All Sites n=552
Reason PN Initiated			
Other (specify)	0	44 (18.0%)	62 (11.2%)
Mechanical bowel obstruction *	0	5 (2.0%)	28 (5.1%)
Bowel ischemia *	2 (15.4%)	4 (1.6%)	21 (3.8%)
Small bowel ileus *	1 (7.7%)	8 (3.3%)	44 (8.0%)
Small bowel fistulae *	0	0	3 (0.5%)
Gastrointestinal perforation *	1 (7.7%)	10 (4.1%)	62 (11.2%)
Short gut syndrome *	0	0	3 (0.5%)
Hemodynamic instability	0	32 (13.1%)	44 (8.0%)
Proximal bowel anastomosis	0	2 (0.8%)	6 (1.1%)
Not tolerating enteral feeding	0	47 (19.2%)	99 (17.9%)
No access to small bowel	0	2 (0.8%)	13 (2.4%)
Pancreatitis	0	3 (1.2%)	10 (1.8%)
Gastrointestinal bleed	2 (15.4%)	9 (3.7%)	19 (3.4%)
Gastrointestinal surgery	7 (53.8%)	35 (14.3%)	90 (16.3%)
No clinical reason	0	44 (18.0%)	48 (8.7%)

Supplemental PN start day

Figure 5.1. Timing of Initiation of PN

Patients receiving PN after EN	Your Site	Sister Sites	All Sites
N	1	49	136



Issues Identified….

Singapore INS

- Prescribed goals OK (yes or no?) aim higher protein?
- EN adequacy poor at <55%
- EN initiation…. "Ok" or not…
- Feed Interuptions! GRV; Fasting
- Fasting guidelines? Procedures? Extubation? Who decides??
- Post extubation: when to feed? Oral? NG? Swallow test?
- Feed access: Oral; NG; Post Pyloric?

Singapore INS

- GRVs: Recent changes in units sampled; highly variable; frequency? Threshold?
- Low PN use; SPN. When to start??
- Are we happy with definition of what is adequate feeding for icu patients?
- Nutrition therapy professional access? Dietician? NST? Intensivist?
- ICU specific feeding protocol

Optimising Step 1:

How is your centre doing?

What are your issues? Barriers?

Moving Forward…

Energy Deficit
Protein Deficit

=

BAD OUTCOME!!

But will giving more fix it?...

NUTRITIONAL INTAKE, OUTCOMES AND BMI

- Observational cohort study
- *n*= 2772 patients, mechanically ventilated
- Mean caloric intake 1034 kcals / 47g protein per day
- Increase of 1000 kcals / day associated with reduced mortality (adj. [OR], 0.76; 95% CI, 0.61-0.95; p = 0.014)
- Improve clinical outcomes observed in those with BMI <25 and >35

Intensive Care Med (2009) 35:1728–1737
DOI 10.1007/s00134-009-1567-4

ORIGINAL

Cathy Alberda
Leah Gramlich
Naomi Jones
Khursheed Jeejeebhoy
Andrew G. Day
Rupinder Dhaliwal
Daren K. Heyland

The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study

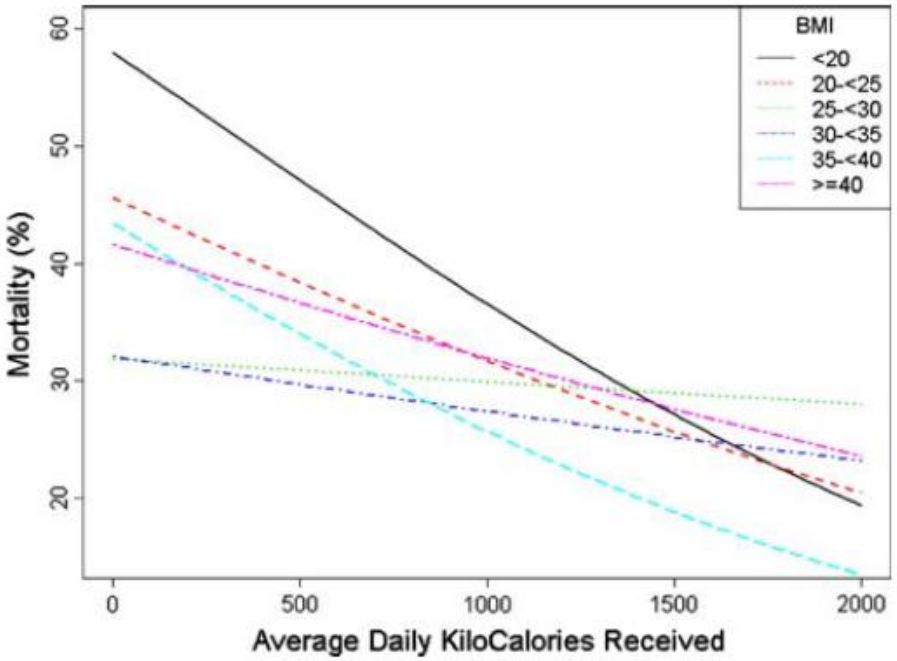


Fig. 1 The relationship between increasing calories/day and 60-day mortality by BMI. *BMI* body mass index

Alberda C 2009 Intensive Care Med (35) 1728 - 1737

OPTIMAL PROTEIN AND ENERGY NUTRITION DECREASES MORTALITY IN MECHANICALLY VENTILATED, CRITICALLY ILL PATIENTS : A PROSPECTIVE OBSERVATIONAL COHORT STUDY

- **Objective:** To investigate the effects of nutrition-targeted approach on clinical outcome.
- **Design:**
  - Prospective observational cohort study in a mixed medical-surgical ICU in a Dutch academic hospital
- **Methods:**
  - 886 consecutive mechanically ventilated patients were included
  - Nutrition was guided by indirect calorimetry and protein provision of ≥1.2 g/kg
  - Cumulative intakes were calculated for the period of mechanical ventilation

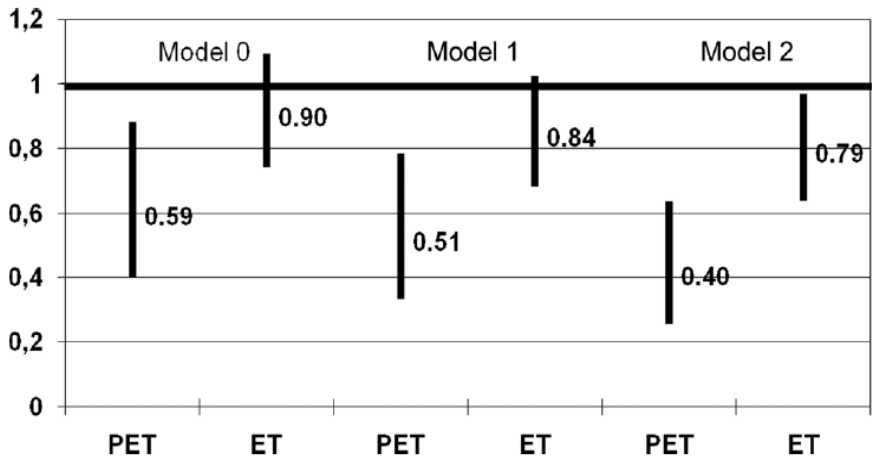
Weijs PJ, et al. *JPEN J Parenter Enteral Nutr.* 2012;36:60-68

- **Measurements:**
  - Cumulative energy and protein intakes
  - 28 day mortality

- **Results:**
  - Optimal nutritional therapy (defined as protein and energy targets reached) in mechanically ventilated ICU patients was associated with a decrease in 28-day mortality by 50%
    - Only reaching energy targets was not associated with a reduction in mortality

The 28-day mortality hazard ratio with 95% confidence interval for protein and energy target (PET) group and energy target (ET) group. Model 0 is unadjusted. Model 1 adjusted for sex, age, body mass index, diagnosis, hyperglycemic index, and APACHE II score. Model 2 additionally adjusted for time to energy target and use of parenteral nutrition.

The 28-day mortality hazard ratio



Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial

Claudia Paula Heidegger, Mette M Berger, Séverine Graf, Walter Zingg, Patrice Darmon, Michael C Costanza, Ronan Thibault, Claude Pichard

- Lancet 2013 Feb 2;381(9864):385-93

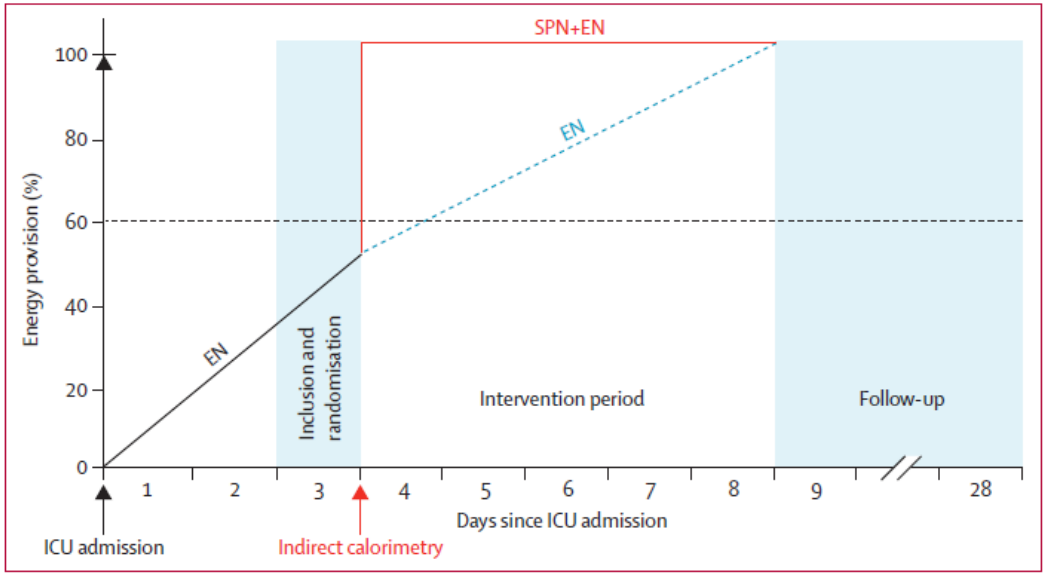
- **Objective:** Evaluate optimized energy provision by SPN for 5 days after day 3 of ICU admission, improves clinical outcome in severely ill patients whom EN alone is insufficient.
- **Design:**
  - Randomized controlled trial (N = 305) undertaken in two centers in Switzerland.

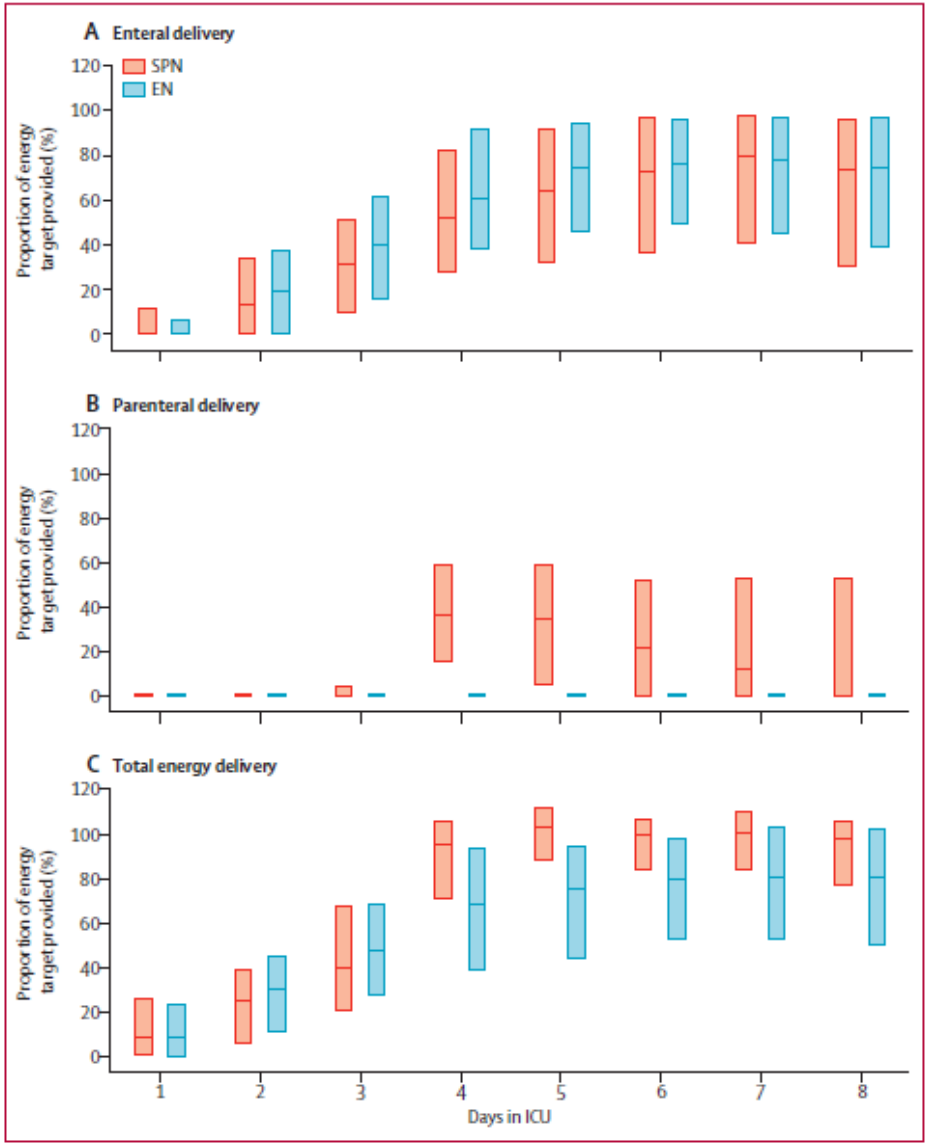
- **Measurements:**
- Energy received versus energy targets
- Nosocomial infections post day 8 till day 28

Methods:

- Supplementation for patients received less than 60% of their energy target from EN, and expected to stay for longer than 5 days, & survive for longer than 7 days
- Energy determined using IC or 25 kcal / kg IBW for women & 30 kcal / kg IBW for men
- Patients were randomly assigned to receive
  - EN + SPN or
  - Continue with EN on Day 3

Trial Design





Results

- Day 4, the mean cumulative deficit of all patients was 3999 ±1293 kcal (−4064 [1322] in the SPN group vs. −3880 [1332] in the EN group).
- Mean energy delivery between day 4 and 8:
  - SPN = 28 kcal/kg per day (SD 5) or (103% [SD 18%] of energy target
  - EN = 20 kcal/kg per day (SD 7) or (77% [27%]; p<0.0001).
- Mean protein delivery between day 4 and day 8:
  - SPN = was 1.2 g/kg per day (0.2)
  - EN = 0.8 g/kg per day (0.3)
  - SPN meeting100% [16%] vs. EN 71% [27%]; p<0.0001

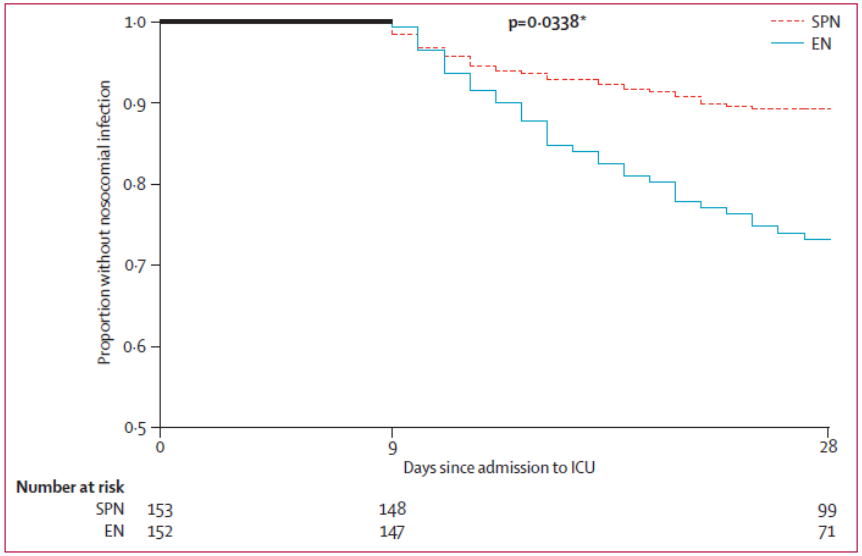


Figure 4: **Kaplan-Meier analysis of nosocomial infections**
SPN=supplemental parenteral nutrition. EN=enteral nutrition. *Statistically significant with Benjamini-Hochberg correction.

	Univariable analysis		Multivariable analysis*	
	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
Sex (women vs men)	1·02 (0·66–1·58)	0·9265	..	..
Age (1-year increase)	0·99 (0·98–1·00)	0·1934	..	..
SAPS II score (1-point increase)	1·01 (1·00–1·03)	0·0491	..	..
Body-mass index (1-kg/m² increase)	1·04 (0·99–1·08)	0·1205	..	..
Hospital (Geneva vs Lausanne)	1·18 (0·78–1·78)	0·4377	..	..
Study intervention (SPN vs EN)	0·62 (0·42–0·93)	0·0200	0·65 (0·43–0·97)	0·0338†
Admission category (surgery vs medicine)	1·01 (0·68–1·50)	0·9488	..	..
Antibiotics before day 9 (yes vs no)	1·20 (0·70–2·05)	0·5048	..	..
Infections before day 9 (yes vs no)	0·84 (0·56–1·26)	0·3958	..	..
Mechanical ventilation before day 9 (yes vs no)	1·53 (0·94–2·50)	0·0897	..	..

Univariable and multivariable Cox regression model. SAPS II=Simplified Acute Physiology II score. SPN=supplemental parenteral nutrition. EN=enteral nutrition. *Variables in the multivariable analysis were SAPS II score, hospital, study intervention, admission category, previous antibiotic use before day 9, and mechanical ventilation before day 9. †Statistically significant with Benjamini-Hochberg correction.

Table 2: **Univariable and multivariable Cox regression model for first noscomial infection during follow-up (primary endpoint)**

Results

- Adjusted probability of nosocomial infection between days 9 and 28 was significantly lower in the SPN group than in the EN group
  - SPN had nosocomial infection rates of 41 of 153 patients [27%] vs. EN with 58 of 152 patients [38%] ; hazard ratio 0.65 [95% CI 0.43–0.97]; p=0.0338; table 2, figure 4).
- Poisson regression model analysis also showed a significant reduction in the number of nosocomial infections in SPN group compared with the EN group during 28-day follow-up (−0.42, 95% CI −0.79 to −0.05; p=0.0248)
- No increase in bloodstream infections in the SPN group were noted, nor a difference in the distribution of nosocomial infections, during intervention (days 4–8) and follow-up (days 9-28)

Step 2:

How to optimise?

Should we use feeding guidelines in the ICU? A review of the evidence

GS Doig and F Simpson

NETH J CRIT CARE - VOLUME 14 - NO 2 - APRIL 2010

Effect of Evidence-Based Feeding Guidelines on Mortality of Critically Ill Adults

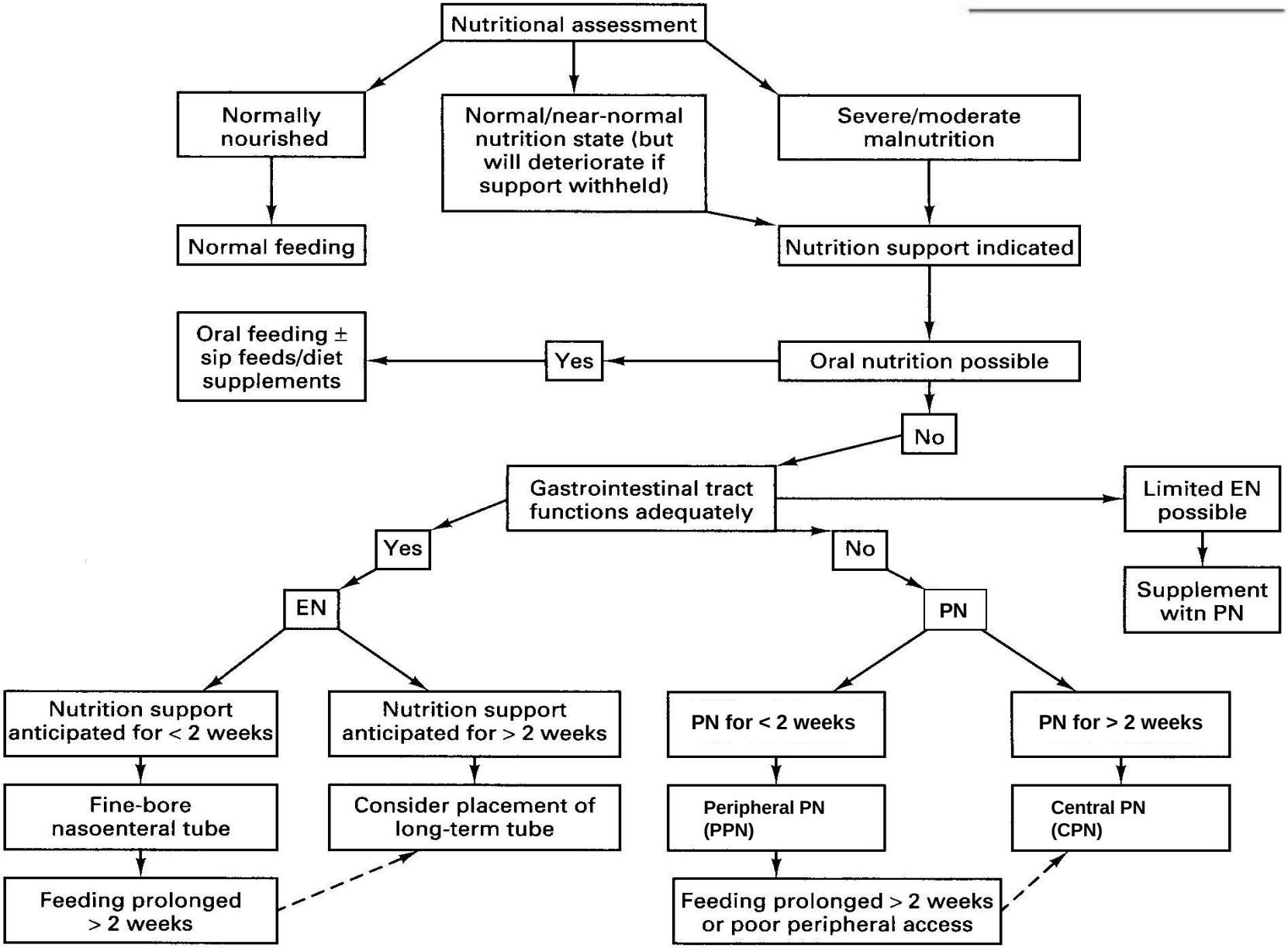
A Cluster Randomized Controlled Trial

JAMA. 2008;300(23):2731-2741

- 3 RCTs
- 1 reduced mortality, all no harm, institution of practice change.
- Multifaceted approach needed to implement change, overcome barriers.

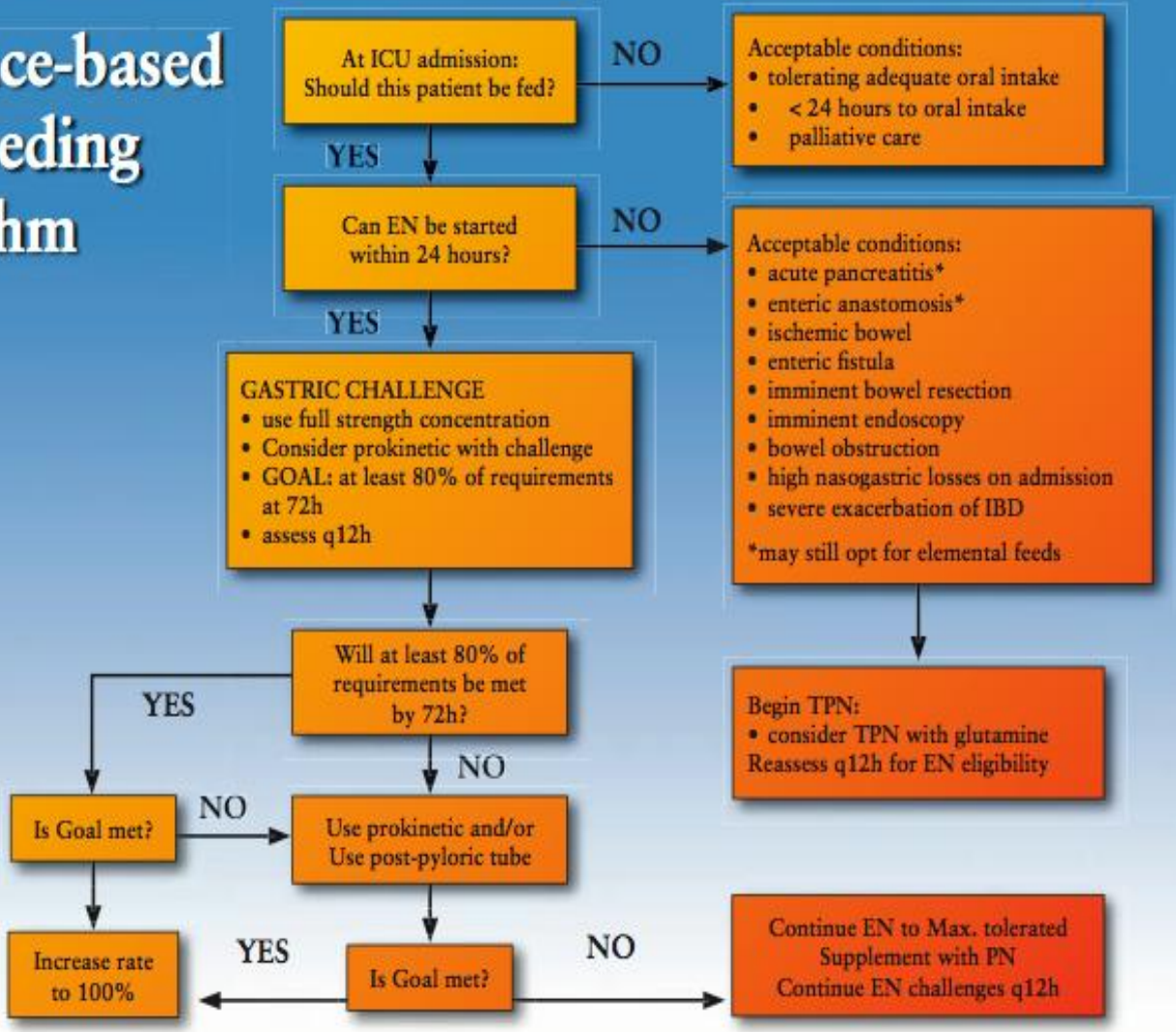
FEEDING ALGORITHM

aspen Clinical Guidelines



ICU GUIDELINES

Evidence-based ICU feeding algorithm



Evidence updated by the ANZICS CTG Feeding Investigators Group Oct 28th, 2003.
Chief Investigator: Dr. Gordon S. Doig, University of Sydney. Contact: gdoig@med.usyd.edu.au

How to optimise?
- Compliant Protocol

Clinical Guidelines

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American Society for Parenteral and Enteral Nutrition

Journal of Parenteral and Enteral Nutrition
Volume 40 Number 2
February 2016 159–211

DOI: 10.1177/0148607115621863
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Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Stephen A. McClave, MD[1*]; Beth E. Taylor, RD, DCN[2*]; Robert G. Martindale, MD, PhD[3]; Malissa M. Warren, RD[4]; Debbie R. Johnson, RN, MS[5]; Carol Braunschweig, RD, PhD[6]; Mary S. McCarthy, RN, PhD[7]; Evangelia Davanos, PharmD[8]; Todd W. Rice, MD, MSc[9]; Gail A. Cresci, RD, PhD[10]; Jane M. Gervasio, PharmD[11]; Gordon S. Sacks, PharmD[12]; Pamela R. Roberts, MD[13]; Charlene Compher, RD, PhD[14]; and the Society of Critical Care Medicine[†] and the American Society for Parenteral and Enteral Nutrition[†]

Nutrition assessment

ASPEN	ESPEN
Energy requirements Indirect calorimetry Weight-based equation Total: 25-30kcal/kg/day Protein: 1.2-2g/kg/day Requirements should be re-evaluated > 1x/week	**Energy requirements** Weight-based equation Acute/initial phase of critical illness: 20-25kcal/kg/day Anabolic/recovery phase 25-30kcal/kg/day Severe undernutrition 25-30kcal/kg/day Amount adjusted according to the progression / course of disease

ENTERAL…

Canadian Clinical Practice Guidelines

www.criticalcarenutrition.com

1.0 The Use of Enteral Nutrition vs. Parenteral Nutrition

May 2015

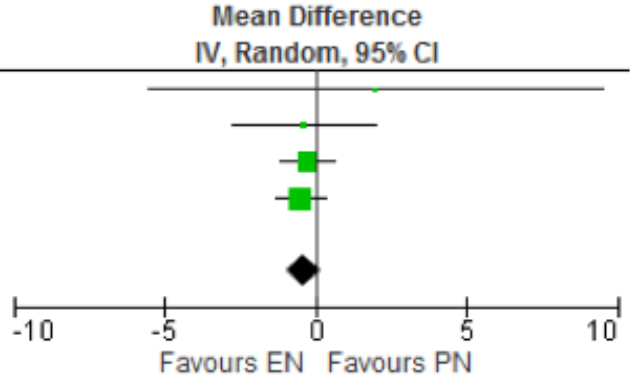
2015 Recommendation: ***Based on 16 level 2 and 1 level 1 study, when considering nutrition support for critically ill patients, we recommend the use of enteral nutrition over parenteral nutrition in patients with an intact gastrointestinal tract.***

Figure 7. Mechanical Ventilation

	EN			PN				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Adams	12	11	17	10	10	13	0.6%	2.00 [-5.54, 9.54]	1986
Kudsk	2.8	4.9	51	3.2	6.7	45	6.2%	-0.40 [-2.77, 1.97]	1992
Chen	7.95	2.11	49	8.23	2.42	49	43.4%	-0.28 [-1.18, 0.62]	2011
Harvey	8.2	9.3	1197	8.7	11.5	1189	49.8%	-0.50 [-1.34, 0.34]	2014
Total (95% CI)			**1314**			**1296**	**100.0%**	**-0.38 [-0.98, 0.21]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 3 (P = 0.92); I² = 0%

Test for overall effect: Z = 1.27 (P = 0.21)



No Mortality Difference

Figure 3. Studies comparing EN vs PN: Infectious complications

Study or Subgroup	EN Events	EN Total	PN Events	PN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.1.1 Infections (PN>EN kcal)							
Young	5	28	4	23	5.0%	1.03 [0.31, 3.39]	1987
Peterson	2	21	8	25	3.7%	0.30 [0.07, 1.25]	1988
Moore	5	29	11	30	7.4%	0.47 [0.19, 1.19]	1989
Kudsk	9	51	18	45	10.8%	0.44 [0.22, 0.88]	1992
Woodcock	6	16	11	21	9.8%	0.72 [0.34, 1.52]	2001
Chen	5	49	18	49	7.6%	0.28 [0.11, 0.69]	2011
Subtotal (95% CI)		**194**		**193**	**44.5%**	**0.49 [0.34, 0.71]**	
Total events	32		70				
Heterogeneity: Tau² = 0.00; Chi² = 4.60, df = 5 (P = 0.47); I² = 0%							
Test for overall effect: Z = 3.81 (P = 0.0001)							
1.1.2 Infections (PN~EN kcal)							
Adams	15	23	17	23	18.2%	0.88 [0.60, 1.30]	1986
Kalfarentzos	5	18	10	20	8.2%	0.56 [0.23, 1.32]	1997
Casas	1	11	3	11	1.9%	0.33 [0.04, 2.73]	2007
Meirelles	2	12	4	10	3.5%	0.42 [0.10, 1.82]	2011
Harvey	194	1197	194	1191	23.8%	0.99 [0.83, 1.19]	2014
Subtotal (95% CI)		**1261**		**1255**	**55.5%**	**0.94 [0.80, 1.10]**	
Total events	217		228				
Heterogeneity: Tau² = 0.00; Chi² = 4.02, df = 4 (P = 0.40); I² = 0%							
Test for overall effect: Z = 0.77 (P = 0.44)							
Total (95% CI)		**1455**		**1448**	**100.0%**	**0.64 [0.48, 0.87]**	
Total events	249		298				
Heterogeneity: Tau² = 0.09; Chi² = 18.71, df = 10 (P = 0.04); I² = 47%							
Test for overall effect: Z = 2.91 (P = 0.004)							
Test for subgroup differences: Chi² = 10.08, df = 1 (P = 0.001), I² = 90.1%							

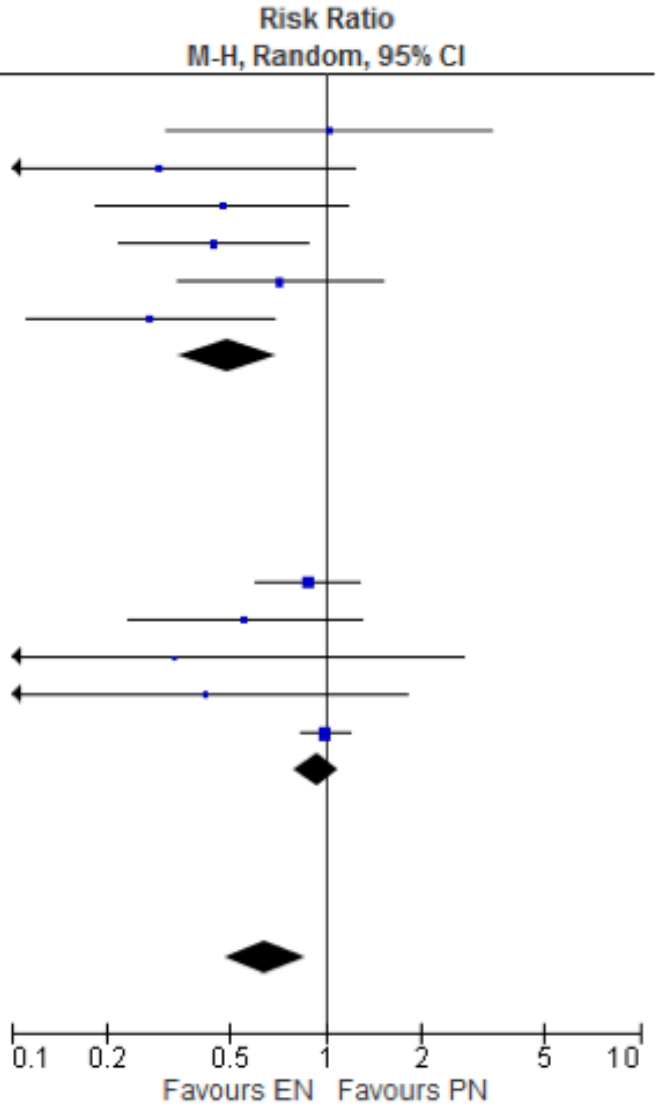


Figure 5. Hospital LOS

Study or Subgroup	EN Mean	EN SD	EN Total	PN Mean	PN SD	PN Total	Weight	Mean Difference IV, Random, 95% CI	Year
Adams	30	21	19	31	29	17	0.3%	-1.00 [-17.71, 15.71]	1986
Peterson	13.2	1.6	21	14.6	1.9	21	62.8%	-1.40 [-2.46, -0.34]	1988
Kudsk	20.5	19.9	51	19.6	18.8	45	1.4%	0.90 [-6.85, 8.65]	1992
Borzotta	39	23.1	28	36.9	14	21	0.8%	2.10 [-8.34, 12.54]	1994
Woodcock	33.2	43	16	27.3	18.7	18	0.2%	5.90 [-16.87, 28.67]	2001
Chen	23.32	5.6	49	22.24	3.27	49	23.6%	1.08 [-0.74, 2.90]	2011
Harvey	26.8	33.2	1186	27.5	33.9	1185	11.0%	-0.70 [-3.40, 2.00]	2014
Total (95% CI)			**1370**			**1356**	**100.0%**	**-0.67 [-1.57, 0.24]**	

Heterogeneity: Tau² = 0.05; Chi² = 6.12, df = 6 (P = 0.41); I² = 2%
Test for overall effect: Z = 1.44 (P = 0.15)

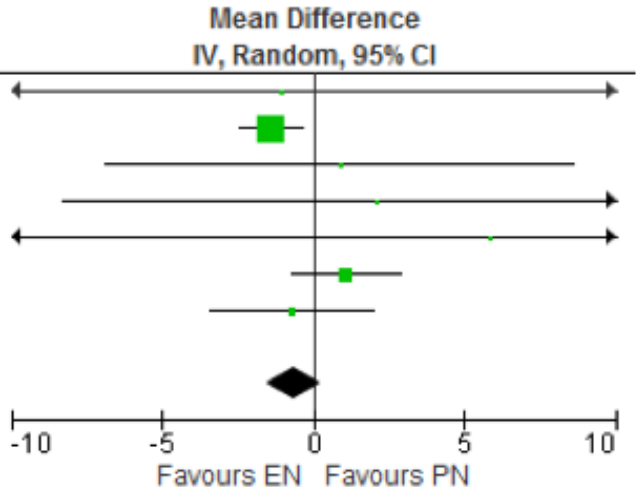
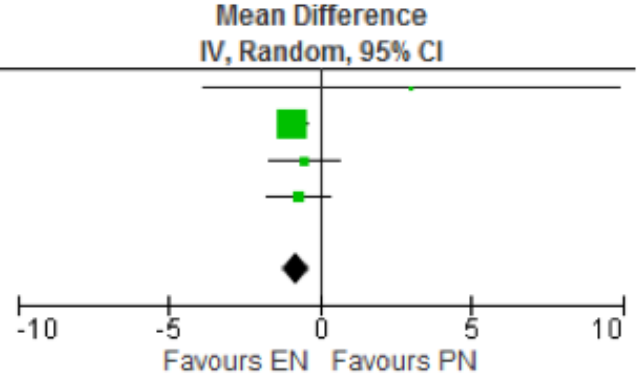


Figure 6. ICU LOS

Study or Subgroup	EN Mean	EN SD	EN Total	PN Mean	PN SD	PN Total	Weight	Mean Difference IV, Random, 95% CI	Year
Adams	13	11	19	10	10	17	0.4%	3.00 [-3.86, 9.86]	1986
Peterson	3.7	0.8	21	4.6	1	25	68.6%	-0.90 [-1.42, -0.38]	1988
Chen	9.09	2.75	49	9.6	3.06	49	14.0%	-0.51 [-1.66, 0.64]	2011
Harvey	11.3	12.5	1197	12	13.5	1190	17.0%	-0.70 [-1.74, 0.34]	2014
Total (95% CI)			**1286**			**1281**	**100.0%**	**-0.80 [-1.23, -0.37]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.60, df = 3 (P = 0.66); I² = 0%
Test for overall effect: Z = 3.62 (P = 0.0003)



- Direct evidence (RCTs in Trauma patients), indirect evidence (RCTs in upper GI Sx), observational studies and physiology supports *the benefits of early EN for trauma patients*
  - Significant reduction in mortality, VAP and severity of MODs
- EN should begin within 24 h of injury, as soon as shock is stabilised:
  - Shock Index ≤ 1 (Heart rate / SBP) for one hour or
  - SBP > 100 mmHg without need for *increasing* doses of vasoactive agents for one hour.

Stable shock is not defined by weaning or removing all vasoactive agents.

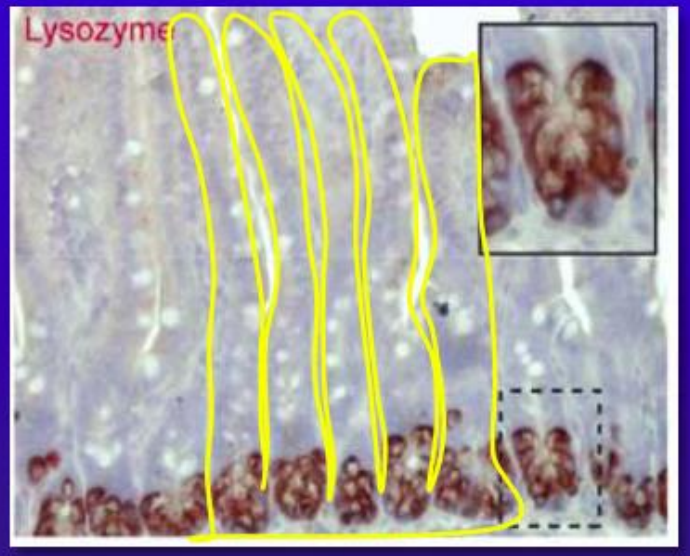
The Eastern Association for the Surgery of Trauma. Nutritional Support: Timing (Early versus Delayed Enteral Feedings). J Trauma. 57(3):660-679.

Doig GS, Heighes PT, Simpson F and Sweetman EA. Early enteral nutrition reduces mortality in trauma patients requiring intensive care: A meta-analysis of randomised controlled trials. *Injury* 2011;42(1):50-56

www.EvidenceBased.net

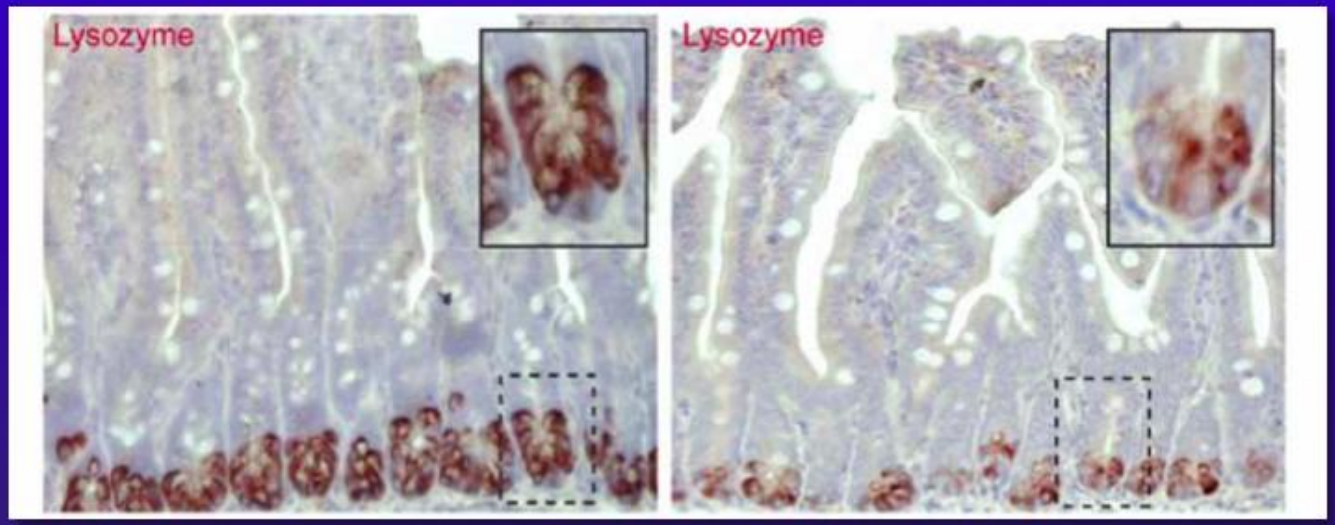
The gut as the motor of MODs: Paneth cells

- Highly specialized epithelial cells located in the crypts of the small intestine.
- Paneth cells are the main producers of antimicrobial proteins in the gut.
- 'Sense' bacterial cells and secrete granules containing antimicrobial peptides.
  - Lysozyme , α-defensins plus others
- Play a crucial role in preventing bacterial translocation in situations of physical intestinal barrier loss.



Vaishnava S, Behrendt CL, Ismail AS, Eckmann L, Hooper LV: Paneth cells directly sense gut commensals and maintain homeostasis at the intestinal host-microbial interface. *Proc Natl Acad Sci* U S A 2008, 105:20858–20863

- Fasting led to a significant reduction in lysozyme ($P<0.01$ by quantitative western blot assay and quantitative PCR for lysozyme mRNA).



- Increase in bacterial translocation as indicated by a 2-fold increase in CFUs cultured from mesenteric lymph node tissue ($p < 0.01$).

Hodin CM, Lenaerts K, Grootjans J, de Haan JJ, Hadfoune M, Verheyen FK, Kiyama H, Keineman E and Buurman WA. Starvation compromises Paneth Cells. Am J Path 2011;179:2885-2893.

EN

- Preferred Route always in functioning GIT
- Reduction in Gut origin sepsis
- Trauma; GI Sx; Open Abdomen
- If delayed, start slow and consider semi polypeptide feeds to “feed the gut mucousa”
- Use it or Lose it!!

How to optimise?

- Compliant Protocol
- EN

PN

When to start?

ASPEN	ESPEN
When to start? X low nutrition risk, first 7 days High nutrition risk – as soon as possible, if EN is not feasible **Supplemental PN** After 7-10 days If unable to meet >60% of energy and protein requirements by EN alone In both high and low risk patients	**When to start?** 24-48H, if EN is contraindicated or not tolerated **Supplemental PN** If unable to meet energy requirements by EN alone after 2 days Care not to exceed requirements **Access** Usually central PN needed to cover nutritional needs fully PPN can be considered for supplementary PN

Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial

Claudia Paula Heidegger, Mette M Berger, Séverine Graf, Walter Zingg, Patrice Darmon, Michael C Costanza, Ronan Thibault, Claude Pichard

- Lancet 2013 Feb 2;381(9864):385-93

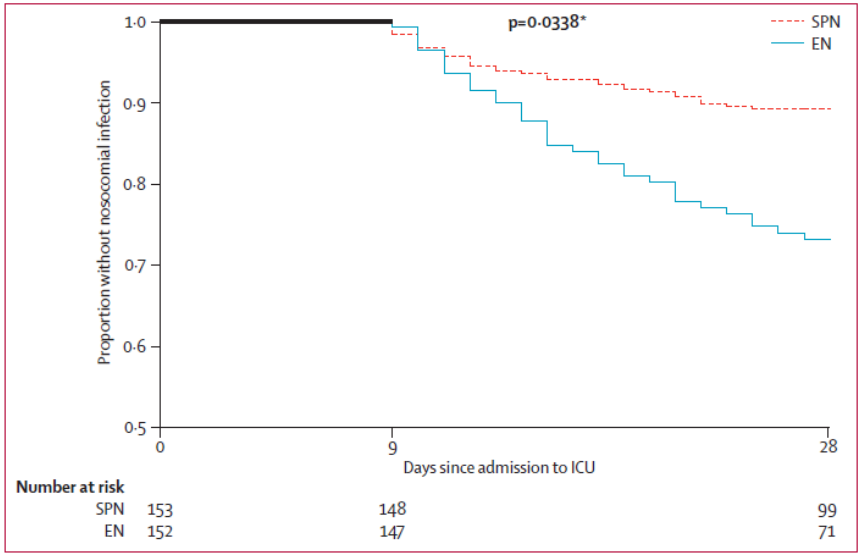


Figure 4: **Kaplan-Meier analysis of nosocomial infections**
SPN=supplemental parenteral nutrition. EN=enteral nutrition. *Statistically significant with Benjamini-Hochberg correction.

	Univariable analysis		Multivariable analysis*	
	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
Sex (women vs men)	1·02 (0·66–1·58)	0·9265	..	..
Age (1-year increase)	0·99 (0·98–1·00)	0·1934	..	..
SAPS II score (1-point increase)	1·01 (1·00–1·03)	0·0491	..	..
Body-mass index (1-kg/m² increase)	1·04 (0·99–1·08)	0·1205	..	..
Hospital (Geneva vs Lausanne)	1·18 (0·78–1·78)	0·4377	..	..
Study intervention (SPN vs EN)	0·62 (0·42–0·93)	0·0200	0·65 (0·43–0·97)	0·0338†
Admission category (surgery vs medicine)	1·01 (0·68–1·50)	0·9488	..	..
Antibiotics before day 9 (yes vs no)	1·20 (0·70–2·05)	0·5048	..	..
Infections before day 9 (yes vs no)	0·84 (0·56–1·26)	0·3958	..	..
Mechanical ventilation before day 9 (yes vs no)	1·53 (0·94–2·50)	0·0897	..	..

Univariable and multivariable Cox regression model. SAPS II=Simplified Acute Physiology II score. SPN=supplemental parenteral nutrition. EN=enteral nutrition. *Variables in the multivariable analysis were SAPS II score, hospital, study intervention, admission category, previous antibiotic use before day 9, and mechanical ventilation before day 9. †Statistically significant with Benjamini-Hochberg correction.

Table 2: **Univariable and multivariable Cox regression model for first noscomial infection during follow-up (primary endpoint)**

Results

- Adjusted probability of nosocomial infection between days 9 and 28 was significantly lower in the SPN group than in the EN group
  - SPN had nosocomial infection rates of 41 of 153 patients [27%] vs. EN with 58 of 152 patients [38%] ; hazard ratio 0.65 [95% CI 0.43–0.97]; p=0.0338; table 2, figure 4).
- Poisson regression model analysis also showed a significant reduction in the number of nosocomial infections in SPN group compared with the EN group during 28-day follow-up (−0.42, 95% CI −0.79 to −0.05; p=0.0248)
- No increase in bloodstream infections in the SPN group were noted, nor a difference in the distribution of nosocomial infections, during intervention (days 4–8) and follow-up (days 9-28)

Early Parenteral Nutrition in Critically Ill Patients With Short-term Relative Contraindications to Early Enteral Nutrition

A Randomized Controlled Trial

Gordon S. Doig, PhD
Fiona Simpson, MND
Elizabeth A. Sweetman, MHM
Simon R. Finfer, FCICM
D. Jamie Cooper, FCICM
Philippa T. Heighes, MN
Andrew R. Davies, FCICM
Michael O'Leary, FCICM
Tom Solano, FCICM
Sandra Peake, FCICM
for the Early PN Investigators of the ANZICS Clinical Trials Group

JAMA. 2013;309(20):2130-2138
Published online May 20, 2013. doi:10.1001/jama.2013.5124

Importance Systematic reviews suggest adult patients in intensive care units (ICUs) with relative contraindications to early enteral nutrition (EN) may benefit from parenteral nutrition (PN) provided within 24 hours of ICU admission.

Objective To determine whether providing early PN to critically ill adults with relative contraindications to early EN alters outcomes.

Design, Setting, and Participants Multicenter, randomized, single-blind clinical trial conducted between October 2006 and June 2011 in ICUs of 31 community and tertiary hospitals in Australia and New Zealand. Participants were critically ill adults with relative contraindications to early EN who were expected to remain in the ICU longer than 2 days.

Interventions Random allocation to pragmatic standard care or early PN.

Main Outcomes and Measures Day-60 mortality; quality of life, infections, and body composition.

Results A total of 1372 patients were randomized (686 to standard care, 686 to early PN). Of 682 patients receiving standard care, 199 patients (29.2%) initially commenced EN, 186 patients (27.3%) initially commenced PN, and 278 patients (40.8%) remained unfed. Time to EN or PN in patients receiving standard care was 2.8 days (95% CI, 2.3 to 3.4). Patients receiving early PN commenced PN a mean of 44 minutes after enrollment (95% CI, 36 to 55). Day-60 mortality did not differ significantly (22.8% for standard care vs 21.5% for early PN; risk difference, −1.26%; 95% CI, −6.6 to 4.1; $P=.60$). Early PN patients rated day-60 quality of life (RAND-36 General Health Status) statistically, but not clinically meaningfully, higher (45.5 for standard care vs 49.8 for early PN; mean difference, 4.3; 95% CI, 0.95 to 7.58; $P=.01$). Early PN patients required fewer days of invasive ventilation (7.73 vs 7.26 days per 10 patient × ICU days, risk difference, −0.47; 95% CI, −0.82 to −0.11; $P=.01$) and, based on Subjective Global Assessment, experienced less muscle wasting (0.43 vs 0.27 score increase per week; mean difference, −0.16; 95% CI, −0.28 to −0.038; $P=.01$) and fat loss (0.44 vs 0.31 score increase per week; mean difference, −0.13; 95% CI, −0.25 to −0.01; $P=.04$).

Conclusions and Relevance The provision of early PN to critically ill adults with relative contraindications to early EN, compared with standard care, did not result in a difference in day-60 mortality. The early PN strategy resulted in significantly fewer days of invasive ventilation but not significantly shorter ICU or hospital stays.

Muscle mass preservation; Economic analysis savings (USD 3000/pt)

How to optimise?

- Compliant Protocol
- EN
- EN + PN

Feeding interuptions

- Audit: how much interuptions per icu stay?
- Why not reach 80% prescribed?
- Fasting
- GRV
- ?? Feed intolerance criteria
- System issues? Eg availability?

Intensive Care Med (2010) 36:1386–1393
DOI 10.1007/s00134-010-1856-y

ORIGINAL

J. C. Montejo
E. Miñambres
L. Bordejé
A. Mesejo
J. Acosta
A. Heras
M. Ferré
F. Fernandez-Ortega
C. I. Vaquerizo
R. Manzanedo

Gastric residual volume during enteral nutrition in ICU patients: the REGANE study

- 329 intubated patients; 28 Spanish ICUs
- 200ml vs 500ml 6hrly GRV
- Diet volume ratio better in 500ml grp with no increase in any adverse events
- 500ml GRV 6hrly: Safe

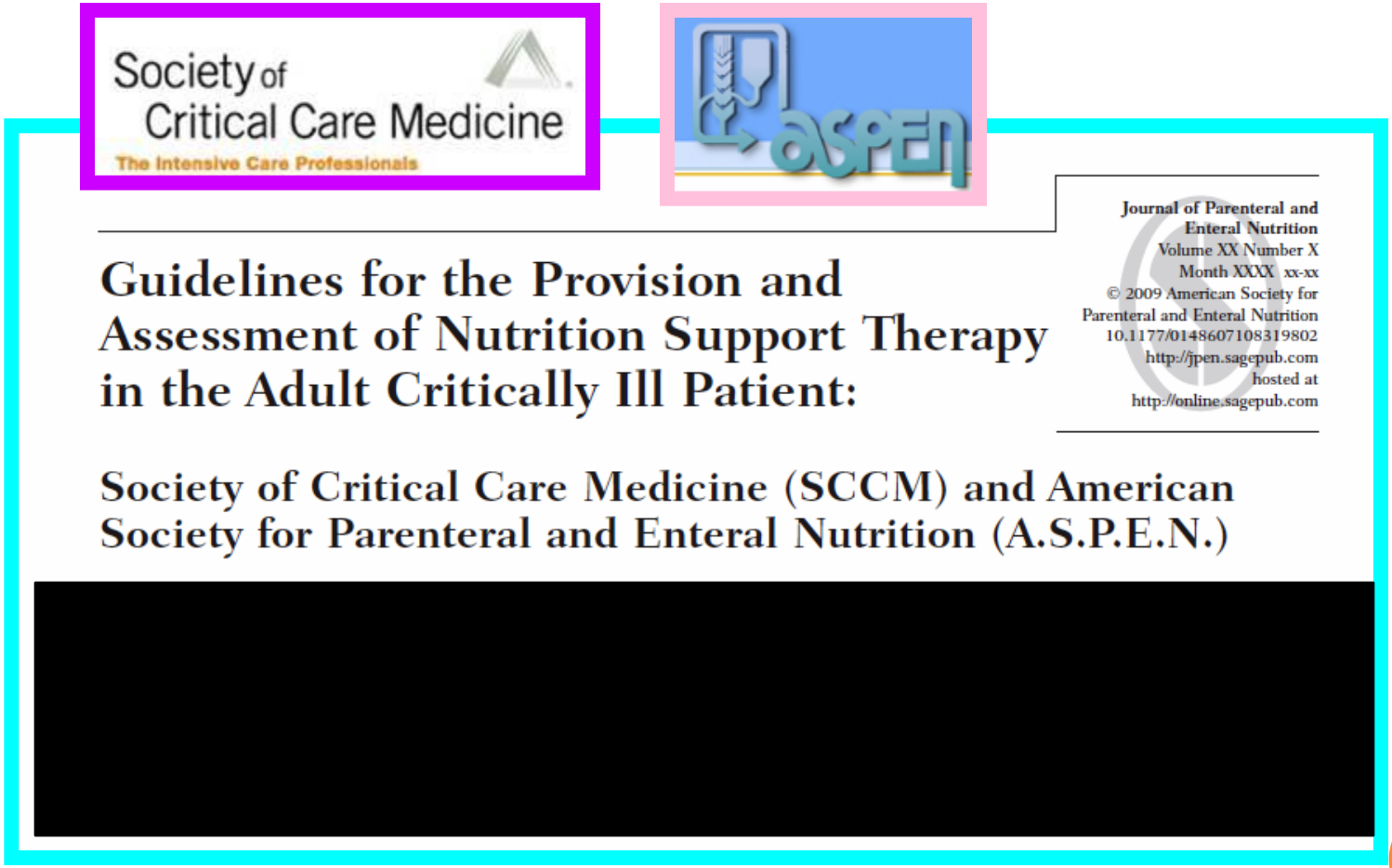
Effect of Not Monitoring Residual Gastric Volume on Risk of Ventilator-Associated Pneumonia in Adults Receiving Mechanical Ventilation and Early Enteral Feeding

A Randomized Controlled Trial

JAMA, January 16, 2013—Vol 309, No. 3

- 9 French ICUs, 449 Ventilated pts
- 250ml 6hrly vs no GRV monitoring
- Higher %age of study arm achieved 100% target
- No increased VAP or any adverse outcomes

SCCM/ASPEN Guidelines 2015



D2. Patients should be monitored for tolerance of EN (determined by patient complaints of pain and/or distention, physical exam, passage of flatus and stool, abdominal radiographs). (Grade: E) Inappropriate cessation of EN should be avoided. (Grade: E) Holding EN for gastric residual volumes <500 mL in the absence of other signs of intolerance should be avoided. (Grade: B) The time period that a patient is made nil per os (NPO) prior to, during, and immediately following the time of diagnostic tests or procedures should be minimized to prevent inadequate delivery of nutrients and prolonged periods of ileus. Ileus may be propagated by NPO status. (Grade: C)

Canadian 2015 CPG

5.1 Strategies to Optimize Delivery and Minimize Risks of EN: Feeding Protocols **May 2015**

2015 Recommendation: ***Based on 2 level 2 studies and 3 cluster randomized controlled trials, a feeding protocol should be considered that incorporates strategies to optimize delivery of enteral nutrition in critically ill adult patients.***

2015 Discussion: The committee noted the addition of 1 new trial in traumatic brain injury/hemorrhagic stroke patients (Zavetailo 2010) and 1 large cluster trial (Heyland 2012) to the existing studies of the implementation of a feeding protocol in critically ill patients. The components of the protocols varied slightly in the studies and some also utilized nursing education, however all resulted in an improvement in nutrition goals being met and earlier time to start of enteral nutrition. The committee noted the lack of an improvement in clinical outcomes other than the Martin 2004 trial. Given the improvement seen in enteral nutrition delivery in all the trials, the favourable safety, feasibility considerations and low cost, the committee decided that feeding protocols should be considered The following components of feeding protocols have been used in these trials and should be considered: early EN, EN over PN, higher target rates/volume based feeding, initial use of semi-elemental solutions then transitioning to polymeric, empiric use of protein supplements, initiating motility agents at the time of starting EN and tolerating a higher GRV threshold (300 mls vs 250 mls).

5.2 Strategies to Optimize Delivery and Minimize Risks of EN: Motility Agents **May 2015**

There were no new randomized controlled trials since the 2009 and 2013 updates and hence there are no changes to the following Summary of Evidence.

Recommendation: ***Based on 1 level 1 study and 5 level 2 studies, in critically ill patients who experience feed intolerance (high gastric residuals, emesis), we recommend the use of a promotility agent. Given the safety concerns associated with erythromycin, the recommendation is made for metoclopramide. There are insufficient data to make a recommendation about the use of combined use of metoclopramide and erythromycin.***

How to optimise?

- Compliant Protocol
- EN
- EN + PN
- Eliminate Interuptions

How much is optimal? Prescribe??

Indirect Calorimetry

- Regarded as gold standard for assessment
- Difficulties in ICU pts
- TICACOS ICM 2011 Singer et al : IC directed vs 25 kcal/kg/day. EN or EN + PN. Improved hospital mortality in matched measured EE grp. Trend.
- Await multi centre trial
- Continuos? Repeated? When? How to do it?? (discussion?)
- Protocol adherance; ICU dietician: KEY

Nutrition assessment

ASPEN	ESPEN
Energy requirements Indirect calorimetry Weight-based equation Total: 25-30kcal/kg/day Protein: 1.2-2g/kg/day Requirements should be re-evaluated > 1x/week	**Energy requirements** Weight-based equation Acute/initial phase of critical illness: 20-25kcal/kg/day Anabolic/recovery phase 25-30kcal/kg/day Severe undernutrition 25-30kcal/kg/day Amount adjusted according to the progression / course of disease

How to optimise?

- Compliant Protocol
- EN
- EN + PN
- Eliminate Interuptions
- Review prescription, achieved/prescribed

We really don’t know….
What do we do then?

Guidelines

Table 1
Summary of commonly used nutrition practice guidelines for use in critical care.

Guideline	Features	Comment
Canadian clinical practice guidelines [16].	First published in 2003. Updated every 12–18 months Only use RCTs to derive recommendations. Develops recommendations from the RCTs based on consensus opinion from topic experts with standardised procedures.	The development method leads to high grade recommendations. Non-randomised studies are excluded from recommendations, potentially limiting pragmatic advice to aid clinical practice.
European Society of Parenteral and Enteral Nutrition (ESPEN) guidelines [10].	Various clinical topic guidelines available. Enteral ICU guidelines developed in 2006. Parenteral guidelines developed in 2009. Use observational and RCTs to derive guidelines. Develops recommendations based on consensus opinion from topic experts.	Guidelines are more encompassing and provide real advice to clinicians accounting for small but clinically useful research.
Society of Critical Care Medicine and the American Society of Parenteral and Enteral Nutrition (ASPEN) [44].	Developed in 2009. RCTs used to derive recommendations using a grade of evidence system.	These recommendations are controversial as they conflict in some areas with the European and Canadian guidelines Methods in which they were formulated have been questioned and may not be as objective as the available alternatives.

Review

Nutrition therapy in critically ill patients- a review of current evidence for clinicians

Emma Ridley [a, b, *], Dashiell Gantner [a, c, d], Vincent Pellegrino [c]

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]

Table 2 Areas of consensus (ICU patients with a more than 4-day length of stay)

	Consensus
Early enteral feeding	Consider in each patient without absolute contraindication; prevents mucosal atrophy
Risks of overfeeding	Early phase
Estimation of energy expenditure	Requires indirect calorimetry – cannot be predicted by equations
Arginine	Not recommended in sepsis; beneficial in perioperative patients outside the ICU
Vitamins, trace elements	Mandatory, in nutritional doses; particularly true in parenteral nutrition

Table 1 Areas of uncertainty – opposing views

Topic/area	One viewpoint	Opposing view
Optimal caloric intake	Early match of EE.	Less than EE during the early phase.
Supplemental PN	When EN provision is less than 60% in early course of ICU stay not contraindicated.	Not before day 8 in patients with a body mass index of at least 17.
Optimal protein intake	Equal to nitrogen losses, up to 1.5 g/kg per day.	Less than nitrogen losses.
Re-feeding syndrome	Slowly increase nutritional support to prevent re-feeding syndrome consequences even if this results in increased energy deficit.	Early nutritional support improves outcome also in malnourished patients; re-feeding syndrome consequences should be monitored and immediately treated if necessary.
Role of indirect calorimetry	Yes (patients staying more than 4 days).	No.
Autophagy	Provision of nutrients should be reduced so as not to reduce autophagy capacity as early nutrients provoke a phenotype of suppressed autophagy in human and animal experiments, with functional consequences that impair recovery.	Although experimentally autophagy may be reduced in early critical illness, pharmacological autophagy activation remains to be tested clinically.
Antioxidants	Supplement in case of low levels of antioxidants.	Use pharmacological dosages.
Glutamine	In all patients on PN.	High-dose glutamine increases mortality in critically ill patients, regardless of route of administration.
Omega-3 lipid formulations	Use continuous enteral administration and avoid bolus administration.	Not beneficial in acute respiratory distress syndrome.
High-dose selenium 800 to 4,000 μg/day	High-dose trials (1,000 μg) show greater improvement than low-dose trials.	Potential for toxicity. In selenium-replete populations, 800 to 1,000 μg may be ineffective.
Probiotics	Safe. Avoid use in pancreatitis patients with multiple organ dysfunction syndrome.	May be harmful in ICU patients when given post-pyloric with fiber.
Monitoring GRV	Accept GRV of 250 up to 500 mL per 6 hours.	Abandon GRV monitoring in medical patients and consider in surgical patients.

EE, energy expenditure; EN, enteral nutrition; GRV, gastric residual volume; PN, parenteral nutrition.

How to optimise?

- Compliant Protocol
- EN
- EN + PN
- Eliminate Interuptions
- Review prescription, achieved/prescribed
- Guidelines; Updates; CME;

How to optimise?

- TTSH ICU story….

CPIP PROJECT IMPROVING NUTRITION DELIVERY IN MICU

Ng Puay Shi
Senior Dietitian
Tan Tock Seng Hospital

International Nutrition Survey 2013

Feeding adequacy

Alert!

Only 50% of energy and protein requirement met throughout ICU stay

Early feeding

88% met the guideline of feed initiation within 24 - 48hr of ICU admission

Interruption to feeding

Alert!

Incidence 24%

Long duration of interruption

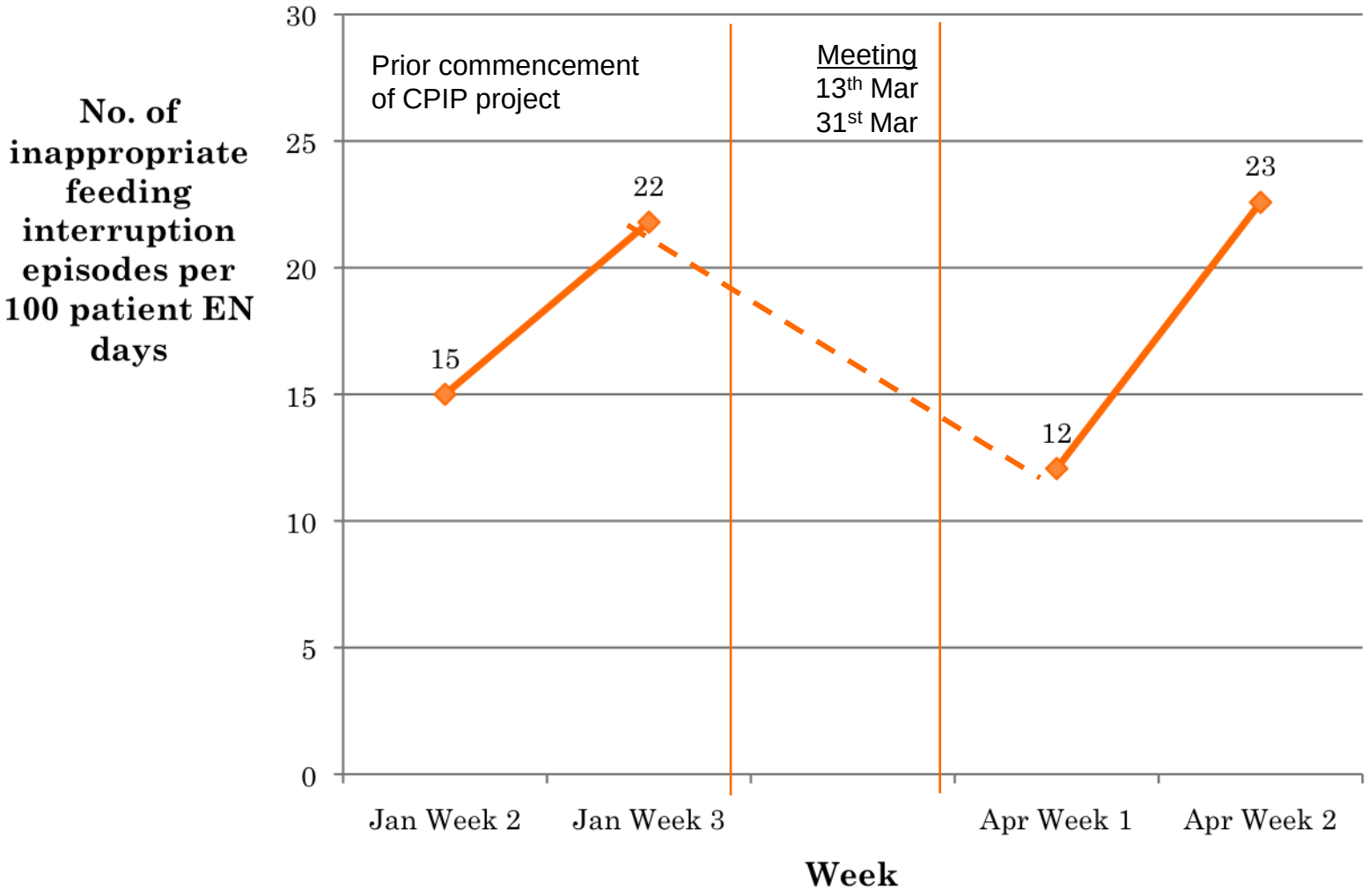
Top 3 reasons for feed interruption		
1st	2nd	3rd
Intubation/extubation 12 ± 14h	High GRV 7 ± 18h	Unknown 6 ± 24h

MISSION STATEMENT

To reduce the no. of inappropriate feeding interruption episodes* per 100 patient enteral feeding days from 18 to 0 in MICU patients in 6 months

*as defined by withholding of feeds when aspirates <250ml; extended period of fasting prior extubation (>2hr); stopping of feeds for standard procedures as stated in protocol; unstated reasons for feed interruption

Run Chart



Raw data	7 GRV 2 extubation	17 GRV		6 GRV 1 extubation	11 GRV 1 extubation 2 procedure

EVIDENCE OF PROBLEM WORTH SOLVING

- Consequences of frequent feeding interruption
  - Decreases nutrition delivery

- International guidelines from ASPEN, ESPEN, Canadian Critical Care Nutrition and vast evidence from various journals

  - Underfeeding is detrimental
  - Increases infectious complications, length of mechanical ventilation and mortality

TEAM MEMBERS

- Ng Puay Shi, Nutrition and Dietetics (Team leader)
- Dr Jonathan Tan, Dept of Anesthesiology, Snr Consultant, SICU Director
- Dr Sennen Lew, Dept of Respiratory Medicine, Consultant
- Lorraine Tan, MICU Nurse Clinician
- Durghasri, MICU Staff Nurse
- Glen Brian, MICU Enrolled Nurse

Project Mentor

- Dr Tan Hui Ling
- Jayachandran Balachandran

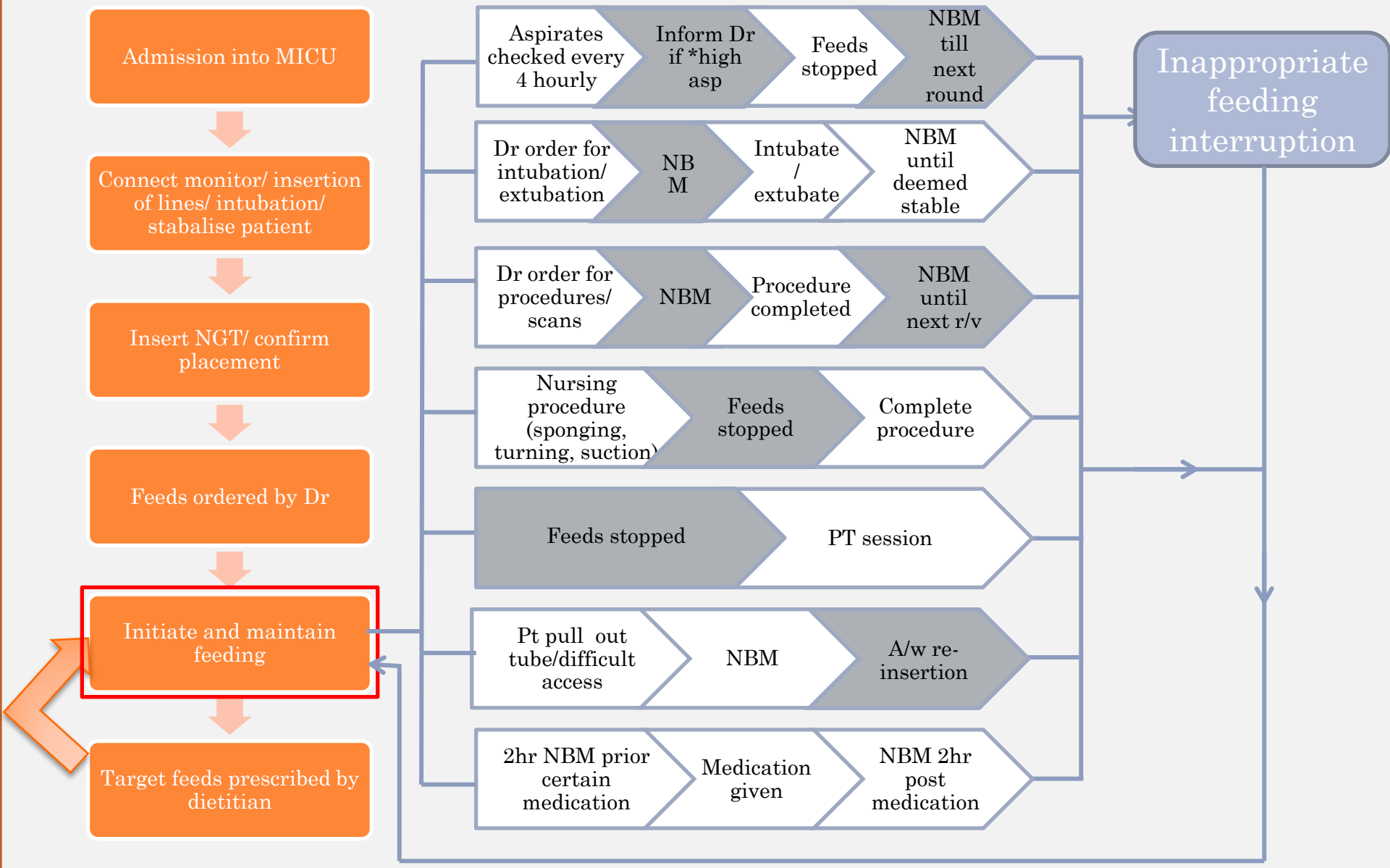
Support and sponsor

- Dr Lim Yen Peng, Head of Nutrition and Dietetics (Sponsor)
- Dr Benjamin Ho, MICU Director
- ICU Committee

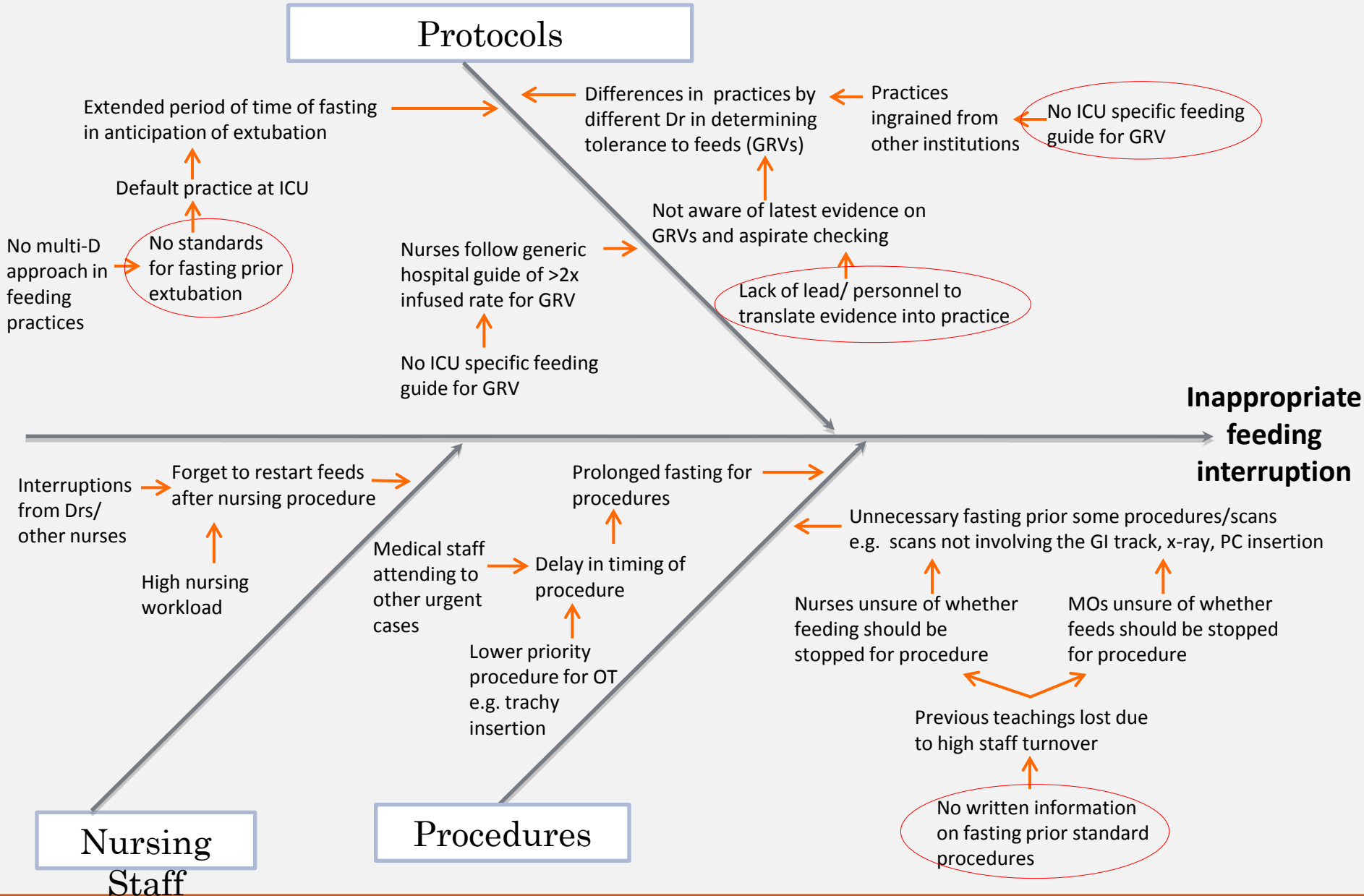
MEASURES AND COUNTER MEASURE

- Primary measure (process)
  - Incidence of inappropriate feeding interruption per 100 patient enteral nutrition days in MICU patients
- Secondary measures (outcome)
  - Percent energy and protein requirement met
- Counter measure
  - Ventilator associated pneumonia rates

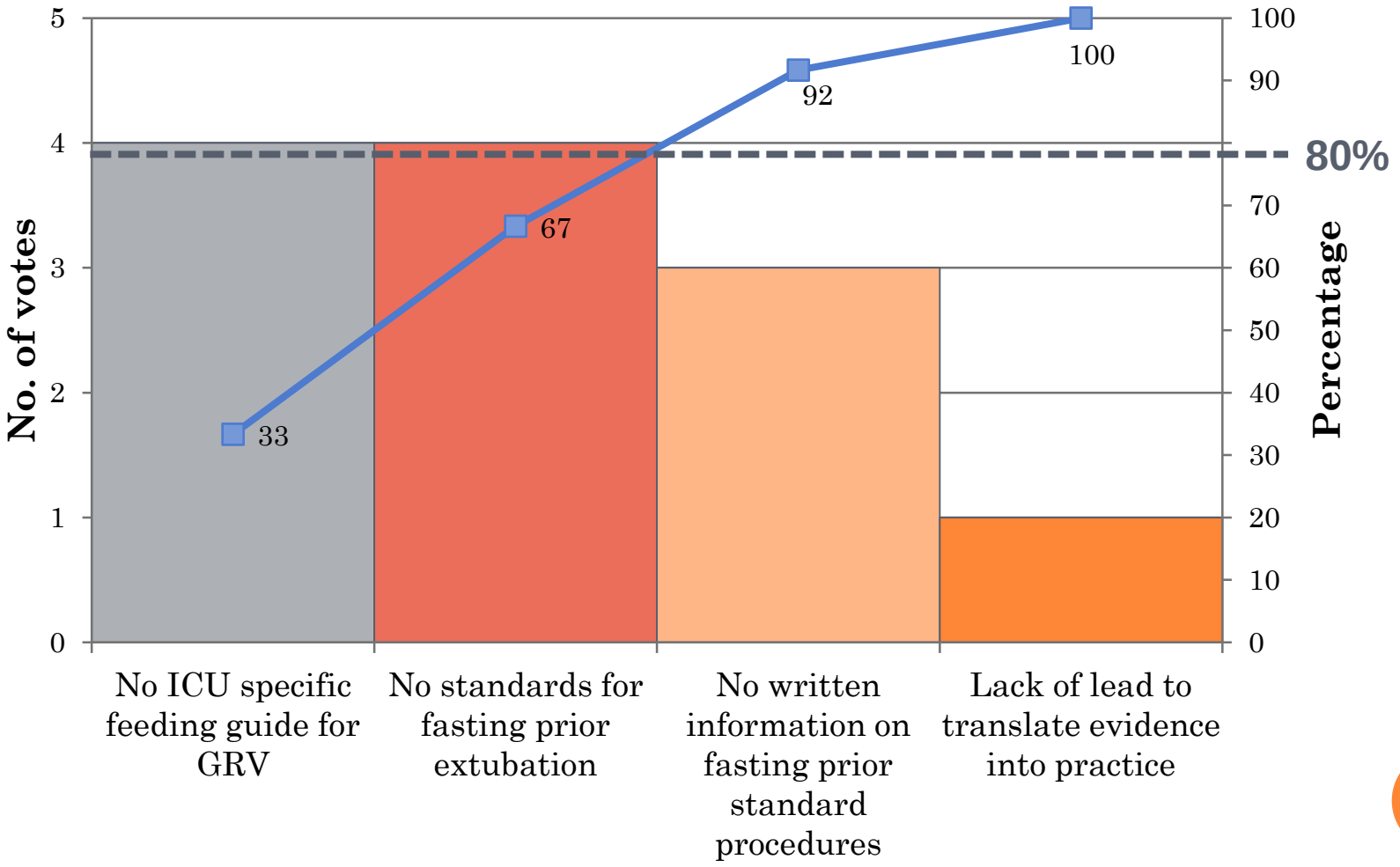
FLOW CHART


Admission into MICU
Connect monitor/ insertion of lines/ intubation/ stabalise patient
Insert NGT/ confirm placement
Feeds ordered by Dr
Initiate and maintain feeding
Target feeds prescribed by dietitian
Aspirates checked every 4 hourly
Inform Dr if *high asp
Feeds stopped
NBM till next round
Dr order for intubation/ extubation
NBM
Intubate / extubate
NBM until deemed stable
Dr order for procedures/ scans
NBM
Procedure completed
NBM until next r/v
Nursing procedure (sponging, turning, suction)
Feeds stopped
Complete procedure
Feeds stopped
PT session
Pt pull out tube/difficult access
NBM
A/w re-insertion
2hr NBM prior certain medication
Medication given
NBM 2hr post medication
Inappropriate feeding interruption

FISHBONE DIAGRAM



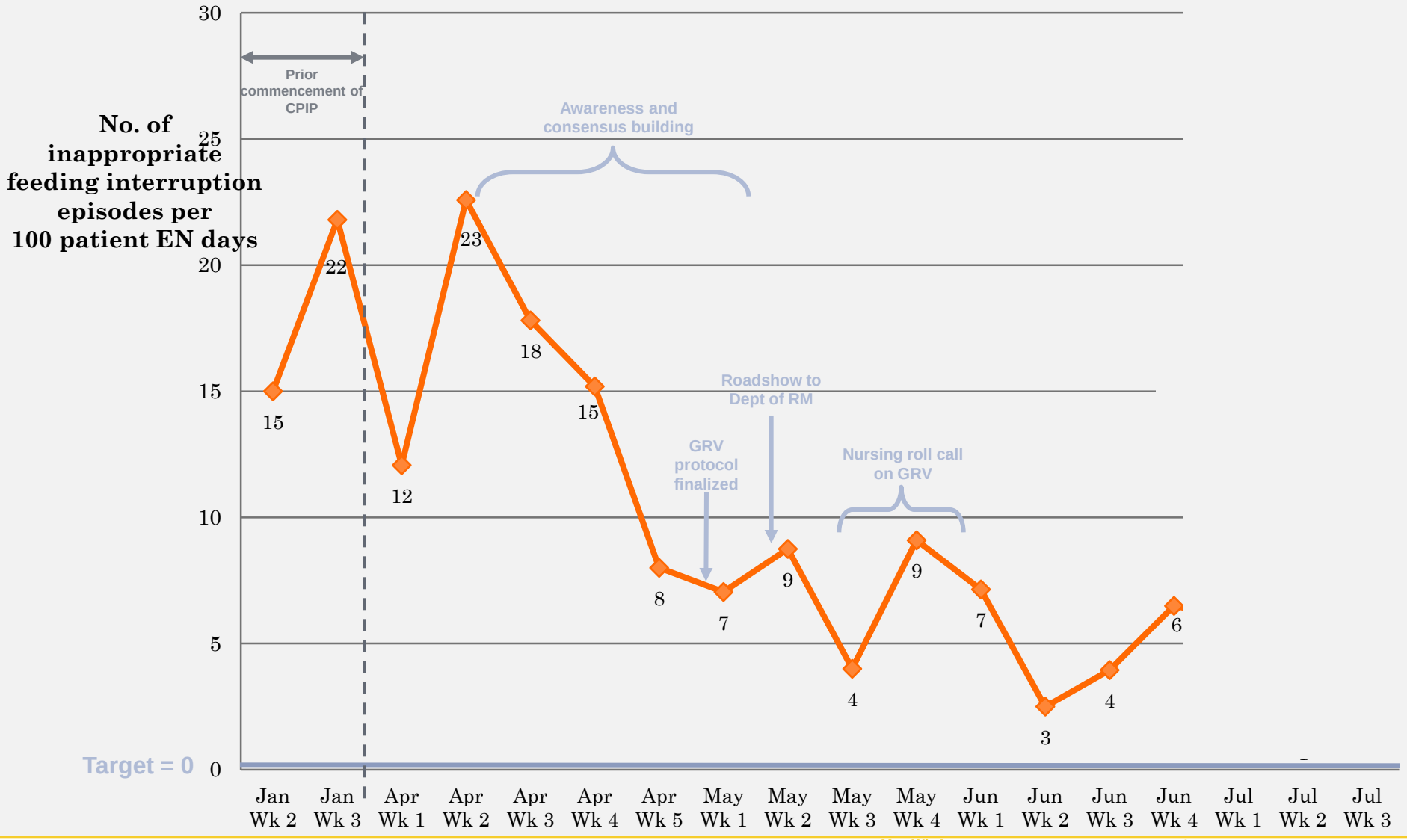
PARETO CHART



INTERVENTIONS

Cause / Problem	Intervention	Date of implementation
No ICU specific feeding guide for GRV	Awareness and consensus building with key stakeholders	13 Apr – 7 May
	GRV protocol finalized	8 May
	Roadshow to consultants from Dept of Respiratory Medicine - Poll on preferred practice regarding feeding standards	14 May
	Roll call to nurses for 2 weeks - Feeding protocol made available at bedside	20 May – 3 Jun

Run Chart



Raw data

Jan Wk 2
7 GRV
2 extubation

Jan Wk 3
17 GRV

Apr Wk 1
6 GRV
1 extubation

Apr Wk 2
11 GRV
1 extubation
2 procedure

Apr Wk 3
12 GRV
1 procedure

Apr Wk 4
6 GRV
3 extubation
2 procedure
1 nil reasons

Apr Wk 5
3 GRV
1 procedure

May Wk 1
1 GRV
2 extubation

May Wk 2
1 GRV
2 extubation
3 procedure

May Wk 3
2 extubation
1 nil reasons

May Wk 4
1 GRV
1 extubation
3 forget to restart

Jun Wk 1
1 GRV
1 extubation
1 procedure
1 supply run out
1 forget to restart

Jun Wk 2
1 extubation
1 procedure

Jun Wk 3
1 GRV
1 extubation
1 procedure

Jun Wk 4
1 GRV
1 extubation
1 procedure
1 medication

PDSA CYCLE – GRV

- Data from run chart: reduction in inappropriate feeding interruption from GRV

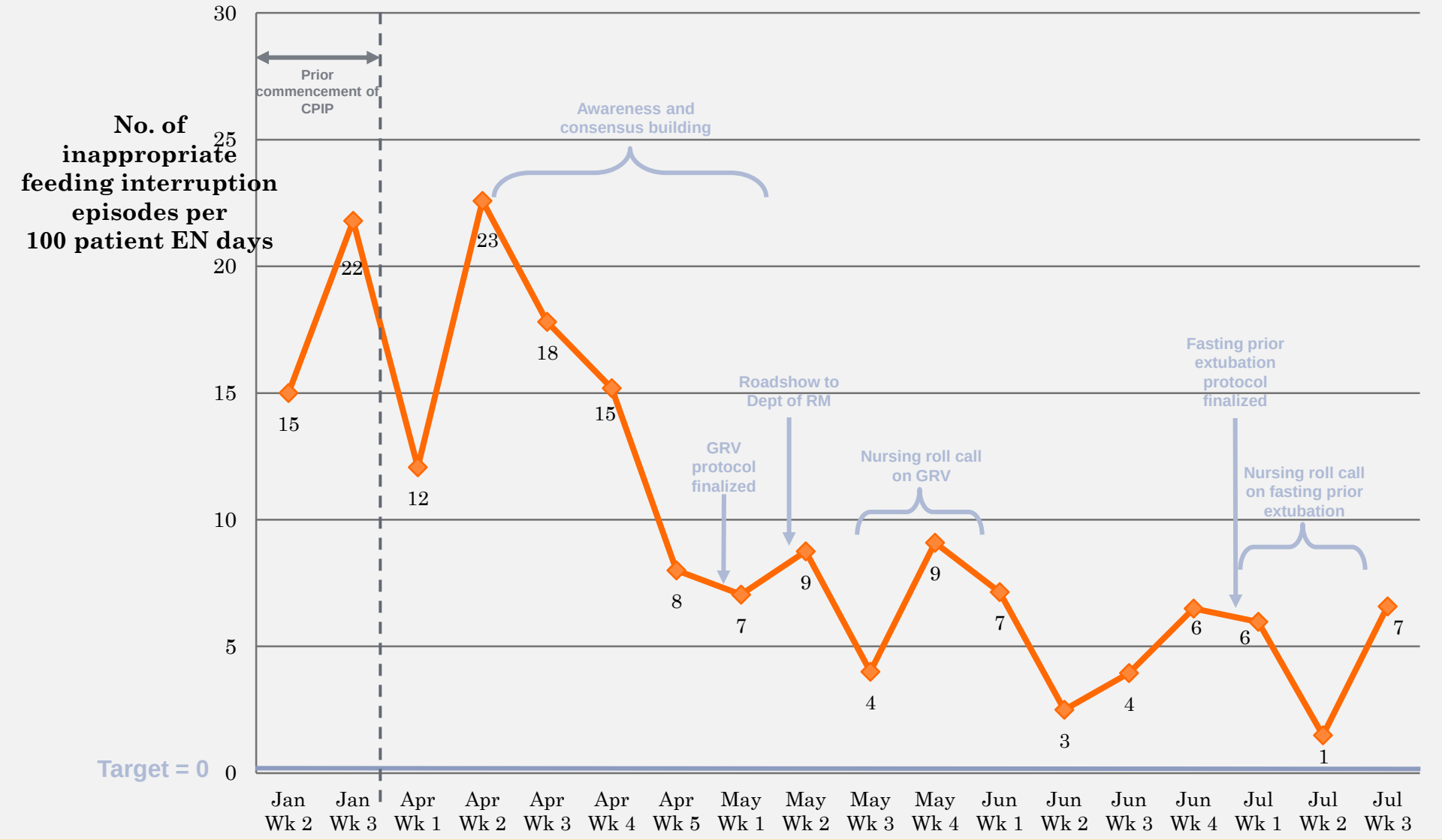
- Feedback from nurses
  - Better workflow and use of time, less troublesome
  - Initially not comfortable
  - Some MOs not aware of protocol
  - AN not sure if they need to inform SN first before escalating feeds
  - 1 not aware of protocol (on leave)

- Reinforced protocol at subsequent nurses roll call to ensure all nurses captured
- Reinforced to nurses that they are the gatekeepers – their duty to highlight to MOs re the GRV protocol

INTERVENTIONS

Cause / Problem	Intervention	Date of implementation
Lack of standardisation in NBM duration pre/post extubation	Roadshow to consultants from Dept of Respiratory Medicine - Consensus obtained re fasting prior extubation	14 May
	Protocol on fasting prior extubation rolled out	30 Jun
	Roll call to nursing re protocol	30 Jun – 14 Jul

Run Chart



Raw data

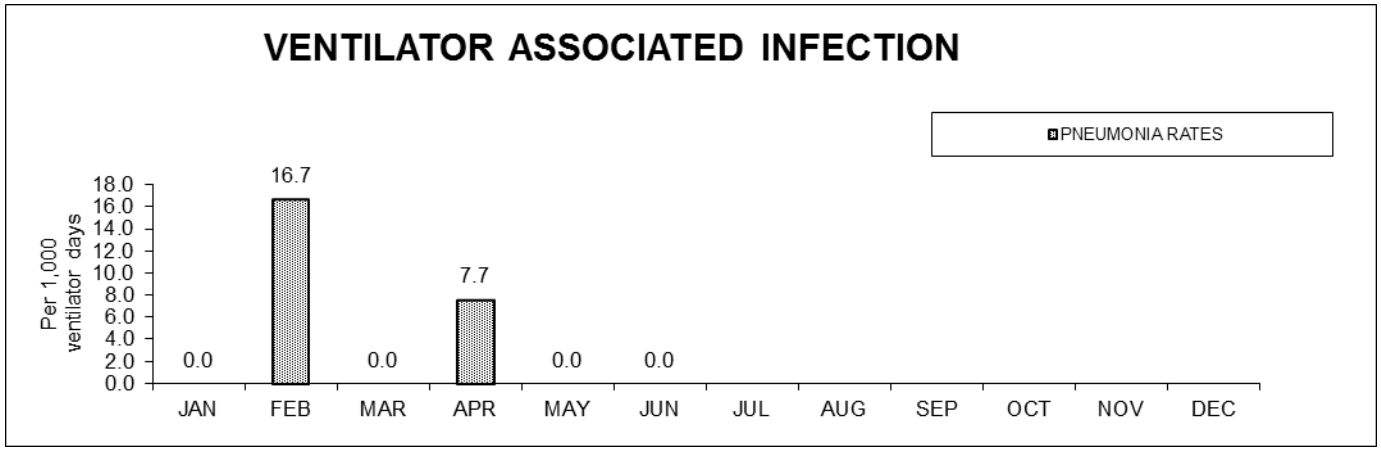
Jan Wk 2	Jan Wk 3	Apr Wk 1	Apr Wk 2	Apr Wk 3	Apr Wk 4	Apr Wk 5	May Wk 1	May Wk 2	May Wk 3	May Wk 4	Jun Wk 1	Jun Wk 2	Jun Wk 3	Jun Wk 4	Jul Wk 1	Jul Wk 2	Jul Wk 3
7 GRV 2 extubation	17 GRV	6 GRV 1 extubation	11 GRV 1 extubation 2 procedure	12 GRV 1 procedure	6 GRV 3 extubation 2 procedure 1 nil reasons	3 GRV 1 procedure	1 GRV 2 extubation	1 GRV 2 extubation 3 procedure	2 extubation 1 nil reasons	1 GRV 1 extubation 3 forget to restart	1 GRV 1 extubation 1 procedure 1 supply run out 1 forget to restart	1 extubation 1 procedure	1 GRV 1 extubation 1 procedure	1 GRV 1 extubation 1 procedure 1 medication	1 extubation 3 medication	1 procedure	3 extubation 2 procedures

PDSA CYCLE – FASTING PRIOR EXTUBATION

- Data from run chart
  - Inappropriate feeding interruption due to GRV has been eliminated as shown by the last 3 data points
  - Inappropriate feeding interruption in anticipation of extubation still exist
- Feedback from nurses
  - Some of the newer MOs not aware
- Feedback from MICU consultant
  - New rotation of MOs, need some time impart medical knowledge before introducing new protocol on fasting prior extubation
  - To be reinforced to the MOs again

COUNTER MEASURE

DEVICE ASSOCIATED INFECTION RATES IN MICU 2015

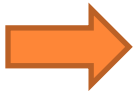


	JAN	FEB	MAR	APR	MAY	JUN
PNEUMONIA RATES	0.0	16.7	0.0	7.7	0.0	0.0

COST SAVINGS

Secondary measure

Baseline data
On average, patients meeting 54% energy requirement
58% protein requirement



Current data
On average, patients meeting 80% energy requirement
83% protein requirement

Improvement in nutrition delivery translates to:

- Projected reduction in ventilator free days by 3.5 day

  = savings of ~$791 per patient

  (Average cost of ventilation per patient per day = ~$226)

- Projected lower odds of mortality by 24% (OR=0.76)

LESSONS LEARNED

- Preparatory work important to start the mind-set change
- Engaging the key stakeholders to get buy-in to improve feeding practices
- Platform to allow stakeholders air their view and have a say in shaping the feeding practices in MICU
- Empowering nursing to take up gatekeeping role
- Working with people outside the immediate improvement area e.g. nursing educators

Conclusion

- Nutrition debt = poor outcome; slow lingering death
- Start within 48hrs, advance to goal within 2 days.
- EN vs PN vs EN + PN : Risk assessment
- 25kcal/kg/day ; 1.2-2g protein /day is key
- Monitor! Dietician; Nutrition champion
- Its as important as antibiotics within 1st hour.
- Start your audit and own journey today.

Conclusion

- Many aspects of optimising calories and proteins discussed in more detail in programme
- Kitchen feeds?
- What we use in Singapore?

- Discussion…

WWW.SINGSPEN.ORG.SG
WWW.SICM.ORG.SG
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Special groups

Obese pt

- Assessment: focus on central adiposity, metabolic syndrome, sarcopenia, BMI > 40, SIRS, other co-morbids
- Initiation similar to general population
- High protein, hypocaloric feeding
  - 65-70% target energy req (measured by IC) or
  - 11-14kcal/kg/day ACTUAL BW (BMI 30-50) or
  - 22-25kcal/kg/day IDEAL BW (BMI > 50)
  - Protein 2g/kg/day IBW (BMI 30-40); 2.5g/kg/day IBW (BMI >40)
- EN with low caloric density + reduced NPC:N
- Additional monitoring for hyperglycaemia, hypercapnia, fluid overload, hepatic fat accumulation
- Thiamine supplementation in pts with prev bariatric surgery
- Assessment for micronutrient deficiencies

Hypocaloric feeding?
Intentional?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults

Yaseen M. Arabi, M.D., Abdulaziz S. Aldawood, M.D., Samir H. Haddad, M.D., Hasan M. Al-Dorzi, M.D., Hani M. Tamim, M.P.H., Ph.D., Gwynne Jones, M.D., Sangeeta Mehta, M.D., Lauralyn McIntyre, M.D., Othman Solaiman, M.D., Maram H. Sakkijha, R.D., Musharaf Sadat, M.B., B.S., and Lara Afesh, M.S.N., for the PermiT Trial Group*

BACKGROUND - TROPHIC ENTERAL FEEDING

- Trophic enteral nutrition (10 mL/hr) resulted in clinical outcomes in mechanically ventilated patients with acute respiratory failure similar to those of early full-energy enteral nutrition but with fewer episodes of gastrointestinal intolerance

Rice TW, Mogan S, Hays MA, Bernard GR, Jensen GL, Wheeler AP. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. Crit Care Med 2011; 39: 967-74.

Rice TW, Wheeler AP, Thompson BT, et al. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. JAMA 2012; 307: 795-803.

BACKGROUND – A ROLE FOR PERMISSIVE UNDERFEEDING?

- Reviews of the existing evidence recommend a level of protein intake during early critical illness that is sufficient to satisfy full protein requirements,[1] regardless of the simultaneous caloric intake.[2]
- Such findings prompt the question of whether moderate caloric restriction while protein intake is preserved would improve the outcomes in critically ill adults

1. Weijs P, Cynober L, DeLegge M, Kreymann G, Wernerman J, Wolfe RR. Proteins and amino acids are fundamental to optimal nutrition support in critically ill patients. Crit Care 2014; 18: 591
2. Singer P, Hiesmayr M, Biolo G, et al. Pragmatic approach to nutrition in the ICU: expert opinion regarding which calorie protein target. Clin Nutr 2014; 33: 246-51

BACKGROUND – A ROLE FOR PERMISSIVE UNDERFEEDING?

- Single-center, randomized controlled trial of moderate caloric intake (60 to 70% of estimated caloric requirement) vs standard caloric intake (90 to 100%), with maintenance of full targeted protein intake in both groups
  - lower caloric intake was associated with a reduction in hospital mortality

Arabi YM, Tamim HM, Dhar GS, et al. Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial. Am J Clin Nutr 2011; 93: 569-77

STUDY METHODOLOGY

Permissive Underfeeding versus Target Enteral Feeding in Adult Critically Ill Patients (PermiT)

- Unblinded randomized controlled trial conducted at seven tertiary care centers in Saudi Arabia and Canada

Recruitment by Center		
King Abdulaziz Medical City, Riyadh, Saudi Arabia - no. (%)	305 (68.1)	307 (68.9)
King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia - no. (%)	26 (5.8)	28 (6.3)
Mount Sinai Hospital, Toronto, Canada- no. (%)	46 (10.3)	42 (9.4)
Ottawa General Hospital, Ottawa, Canada- no. (%)	48 (10.7)	47 (10.6)
Ottawa Civic Hospital, Ottawa, Canada- no. (%)	18 (4.0)	18 (4.0)
Health Sciences Centre, Manitoba, Canada- no. (%)	3 (0.7)	2 (0.5)
University of Alberta Hospital, Edmonton, Canada- no. (%)	2 (0.5)	2 (0.5)

INCLUSION AND EXCLUSION

Inclusion Criteria (All the following)

- Age 18-80 years
- Admission to an intensive care unit (ICU)
- Commencement of enteral feeding within 48 hours of ICU admission
- Expected to remain in ICU ≥72 hours

Exclusion criteria (Any of the following)

- Lack of commitment to ongoing life support
- Brain death
- A pre-existing condition with expected six-month mortality >50%
- Post cardiac arrest
- Use of total parenteral nutrition
- Previous enrollment in this study
- Pregnancy
- Liver transplantation
- Burns
- Receipt of high-dose vasopressors (norepinephrine >0.4 µg/ kg/min, epinephrine >0.4 µg/kg/min, dopamine >20 µg/kg/min, phenylephrine >300 µg/min, vasopressin >0.04 unit/min, or 50% of these doses for patients who received two or more vasopressors)

INTERVENTION

Estimation of patient's standard caloric requirements

BMI < 30

- Equation developed by investigators at Pennsylvania State University (the Penn State equation)

BMI > 30

- 1992 Ireton-Jones equation

INTERVENTION

Caloric Goal

- **40 to 60%** of caloric requirements in the permissive underfeeding group
- **70 to 100%** of caloric requirements in the standard feeding group

Time

- Continued for up to 14 days or until ICU discharge, initiation of oral feeding, death, or withholding of nutrition as part of palliation

INTERVENTION

Protein

- Protein ***1.2 to 1.5 g per kilogram per day***
- To ensure that enteral protein in the permissive-underfeeding group would be similar to those in the standard-feeding group
  - Supplemental protein administered in the permissive-underfeeding group, eliminating the confounding effect of reduced protein intake.

INTERVENTION

Volume

- Volume delivery similar in both groups.
- Enteral normal saline or water given to minimize the differences in delivered enteral volume at a dose of 2 ml per kilogram every 4 hours

Glucose

- Target blood glucose level of 4.4 to 10 mmol per liter

Multivitamins

- Recommended daily enteral multivitamins for all patients

OUTCOMES

Primary outcome

- 90-day all-cause mortality

Secondary outcome

- Mortality in the ICU, 28-day mortality, in-hospital mortality, 180-day mortality, and serial SOFA scores

Tertiary outcome

- Days free from mechanical ventilation, ICU-free days, hospital length of stay
- Hypoglycemia, hypokalemia, hypomagnesemia, hypophosphatemia
- Transfusions of packed red cells
- ICU-associated infections
- Feeding intolerance (vomiting, abdominal distention, or a gastric residual volume of more than 200 ml) and diarrhea.

RESULTS

- Patients in the permissive underfeeding group had a lower caloric intake than did patients in the standard feeding group

Table 2. Study Interventions and Cointerventions.*

Variable	Permissive Underfeeding (N=448)	Standard Feeding (N=446)	P Value
Calculated caloric requirement — kcal/day	1822±377	1842±370	0.51†
Caloric target for the trial — kcal/day	1036±262	1826±375	<0.001†
Daily caloric intake for duration of intervention			
No. of kilocalories	835±297	1299±467	<0.001‡
Percent of requirement	46±14	71±22	<0.001†

- Average caloric intake during the intervention period was 46% versus 71% of daily requirements ($P<0.001$).

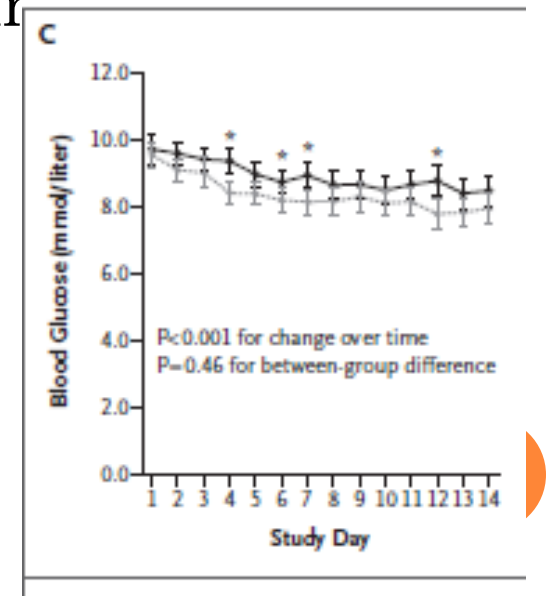
RESULTS

- Protein intake did not differ significantly between the two groups

Calculated protein requirement — g/day	85±21	88±23	0.18†
Daily protein intake for duration of intervention			
No. of grams	[illegible]	[illegible]	0.29†
Percent of requirement	68±24	69±25	0.56†
Protein source — g/day			
Main enteral formula	30±13	54±22	<0.001†
Supplemental enteral protein	27±16	6±10	<0.001†

- Patients in the permissive underfeedir group had lower glucose levels, required less insulin

Cointerventions during study period			
Insulin			
Use — no. (%)	[illegible]	[illegible]	0.04
Dose — units/day	15±27	22±40	0.02†
Enteral formulas on day 1 — no./total no. (%)‖			
Without a specific disease indication	263/441 (59.6)	240/443 (54.2)	0.10
With a specific disease indication	178/441 (40.4)	203/443 (45.8)	
Prokinetics — no. (%)¶	120 (26.8)	127 (28.5)	0.57
Blood glucose — mmol/liter	9.1±5.3	9.4±5.0	0.04†



MORTALITY – PRIMARY AND SECONDARY OUTCOME

- The 90-day mortality (primary end point) was ***27.2%*** in the permissive underfeeding group and ***28.9%*** in the standard-feeding group (relative risk 0.94; 95% confidence interval [CI] 0.76 to 1.16; P = 0.58)

Table 3. Outcomes in the Permissive-Underfeeding and Standard-Feeding Groups.*

Outcome	Permissive Underfeeding (N=448)	Standard Feeding (N=446)	Relative Risk (95% CI)	P Value
Death by 90 days — no./total no. (%)	121/445 (27.2)	127/440 (28.9)	0.94 (0.76–1.16)	0.58
Death in the ICU — no. (%)	72 (16.1)	85 (19.1)	0.84 (0.63–1.12)	0.24
Death by 28 days — no./total no. (%)	93/447 (20.8)	97/444 (21.8)	0.95 (0.74–1.23)	0.7
Death in the hospital — no./total no. (%)	108/447 (24.2)	123/445 (27.6)	0.87 (0.70–1.09)	0.24
Death by 180 days — no./total no. (%)	131/438 (29.9)	140/436 (32.1)	0.93 (0.76–1.14)	0.48

MORTALITY – PRIMARY AND SECONDARY OUTCOME

- Kaplan–Meier survival estimates showed ***no significant difference*** in the probability of survival between the two groups

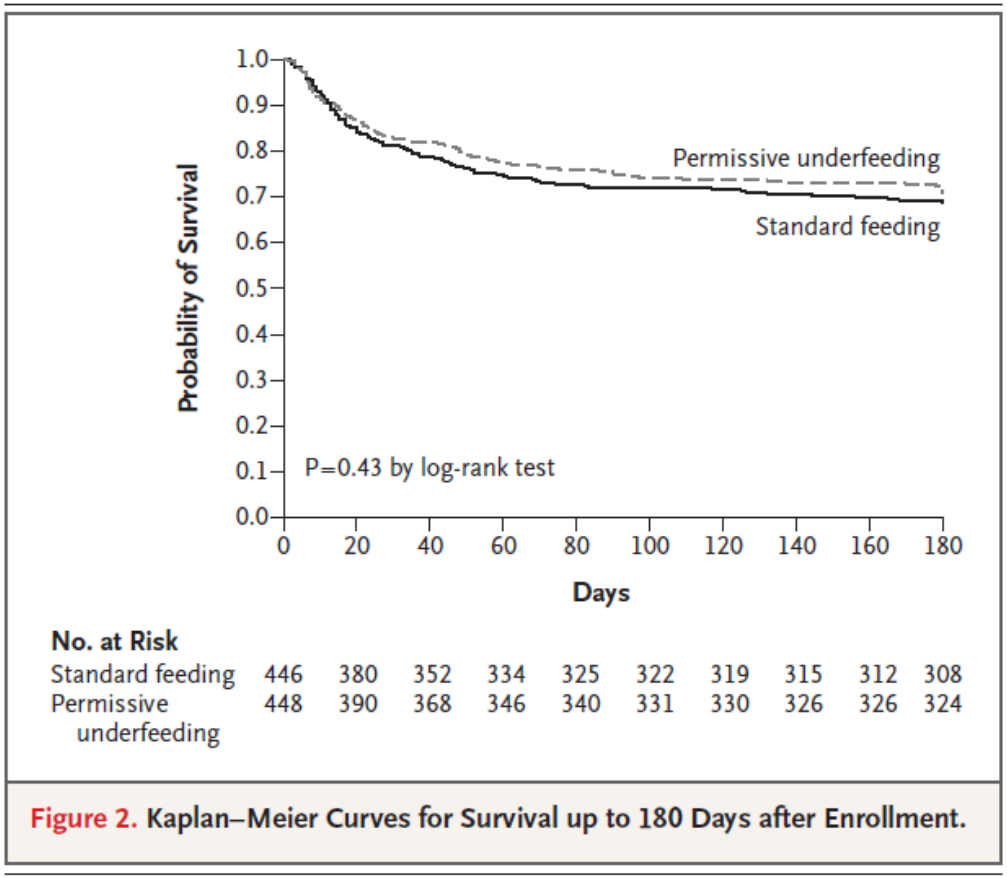


Figure 2. Kaplan–Meier Curves for Survival up to 180 Days after Enrollment.

MORTALITY – PRIMARY AND SECONDARY OUTCOME

Table S9: 90-day mortality by subgroups. RR: relative risk. CI: confidence interval.

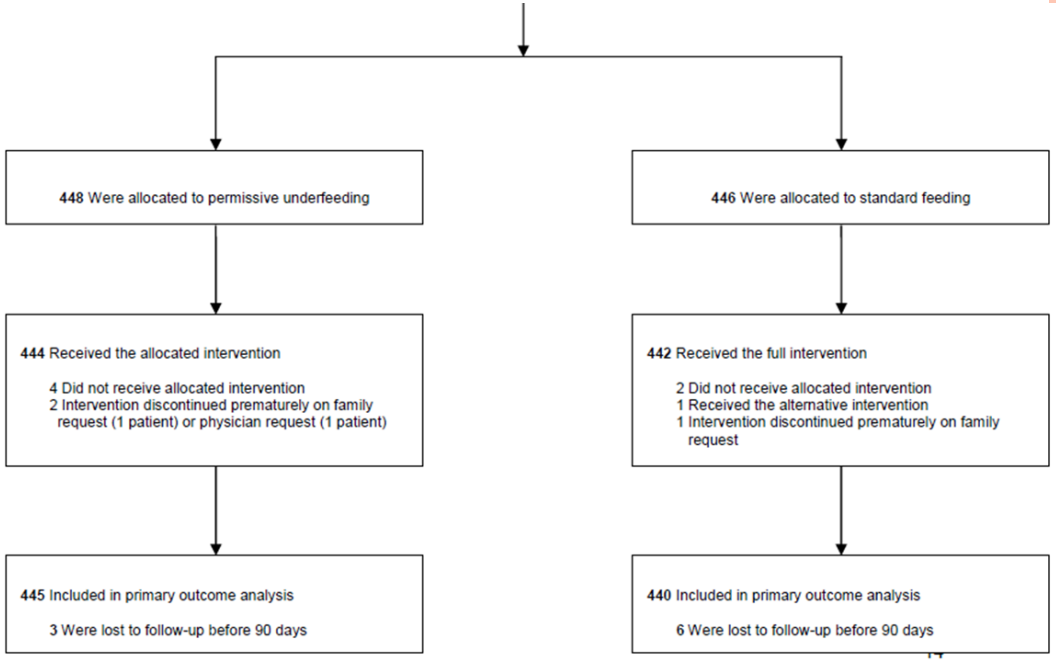
Variables	Permissive Underfeeding n=448	Standard Feeding n=446	RR (95% CI)	P-value	P-value for Interaction
Non-surgical admission	119/426 (27.9)	125/428 (29.2)	0.96 (0.77, 1.18)	0.68	0.67
Surgical admission	2/19 (10.5)	2/12 (16.7)	0.63 (0.10, 3.90)	0.61	
Diabetic	48/158 (30.4)	52/153 (33.9)	0.90 (0.65, 1.24)	0.5	0.68
Non-diabetic	73/287 (25.4)	75/287 (26.1)	0.97 (0.74, 1.28)	0.85	
APACHE II≤18	27/180 (15.0)	28/183 (15.3)	0.98 (0.60, 1.60)	0.94	0.76
APACHE II>18	93/263 (35.4)	97/253 (38.3)	0.92 (0.74, 1.16)	0.48	
Admitted with severe sepsis	59/159 (37.1)	52/133 (39.1)	0.95 (0.71, 1.27)	0.72	0.82
Admitted with no severe sepsis	62/286 (21.7)	75/307 (24.4)	0.89 (0.66, 1.19)	0.43	
Traumatic brain injury	8/55 (14.6)	9/63 (14.3)	1.02 (0.42, 2.46)	0.97	0.81
No traumatic brain injury	113/390 (29.0)	118/377 (31.3)	0.93 (0.75, 1.15)	0.48	
Vasopressors	72/254 (28.4)	75/242 (31.0)	0.91 (0.70, 1.20)	0.52	0.75
No vasopressors	49/191 (25.7)	52/198 (26.3)	0.98 (0.70, 1.37)	0.89	
Randomization blood glucose ≤9.2 mmol/L	51/210 (24.3)	51/214 (23.8)	1.02 (0.73, 1.43)	0.91	0.34
Randomization blood glucose >9.2 mmol/L	65/229 (28.8)	74/217 (34.1)	0.83 (0.63, 1.1)	0.19	

DISCUSSION

Strengths of study

- Multi-centre study, adequate randomisation
- Baseline characteristics of both groups similar
- Objective measures (mortality) used as outcome

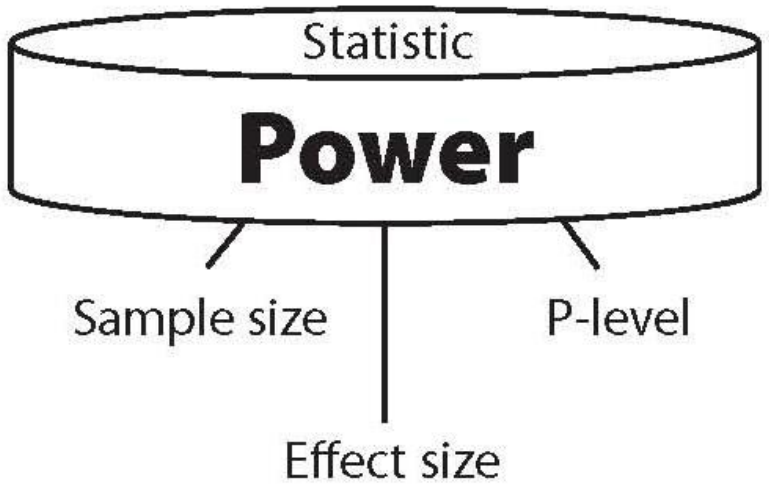
- Analysis based on intention to treat
- ***Low*** proportion of patients who did not receive allocated intervention
- ***Low*** loss to follow up



DISCUSSION

Limitations

- Not blinded
- Possible treatment bias as investigators not blinded
- Study was powered to detect an absolute risk reduction of 8 percentage points in 90-day mortality → cannot rule out a smaller treatment effect
- Limited generalizability
  - Only applicable to patients fed within 48h ICU adm



DISCUSSION

Limitations

- Only 14% of the patients who were admitted to the ICU and screened were included in the study
- Blinding of the intervention was not possible
- The target caloric intake was not reached in some patients, particularly in the standard-feeding group.

Table 2. Study Interventions and Cointerventions.*

Variable	Permissive Underfeeding (N=448)	Standard Feeding (N=446)	P Value
Calculated caloric requirement — kcal/day	1822±377	1842±370	0.51†
Caloric target for the trial — kcal/day	1036±262	1826±375	<0.001†
Daily caloric intake for duration of intervention			
No. of kilocalories	835±297	1299±467	<0.001‡
Percent of requirement	46±14	71±22	<0.001†

DISCUSSION - MORTALITY

- Permissive underfeeding for critically ill adults had ***no significant effect on mortality***, as compared with full enteral feeding
  - ***Did not*** reproduce effects of earlier trial which showed that lower caloric intake was associated with a reduction in hospital mortality[1]

1. Arabi YM, Tamim HM, Dhar GS, et al. Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial. Am J Clin Nutr 2011; 93: 569-77

CONCLUSION

In conclusion, enteral feeding to provide a moderate amount of calories to critically ill adults

in the presence of full protein intake was

not associated with lower mortality

than a strategy aimed at providing a full amount of calories.

INTEGRATING THE RESULTS OF THE PERMIT STUDY IN OUR CLINICAL PRACTICE GUIDELINES

- The results **lack generalizability**

- **WE MUST NOT literally apply permissive underfeeding to all our patients.**

Below is the rationale:

- Subjects were **all fed within 48 hours** of ICU admission. Hence, their accumulated caloric debt were minimized.
- In the permissive underfed group, patients were fed 11 kcal /kg (835 kcal/day). If this strategy was used on patients who were NBM for a few days, the caloric dept would be huge.
- There is evidence that a caloric debt of > 10,000kcal will increase the risk of mortality.[1]

Fed at 24th hr of admission	NBM	835	835	835	835	835	835	835	835	9.4 kcal/kg
Caloric debt	1822	987	987	987	987	987	987	987	987	9718 kcal
Fed at 96th hr of admission	NBM	NBM	NBM	NBM	835	835	835	835	835	4.7 kcal/kg
Caloric debt	1822	1822	1822	1822	987	987	987	987	987	12223 kcal

Villet, Stéphane, et al. "Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients." *Clinical Nutrition* 24.4 (2005): 502-509

INTEGRATING THE RESULTS OF THE PERMIT STUDY IN OUR CLINICAL PRACTICE GUIDELINES

Who were these patients studied in the PERMIT study?

- mostly medical, young (mean age = 51 years), and well-nourished (mean body mass index = 29.3) were recruited
- **Possible that permissive underfeeding could increase mortality in nutritionally high risk patients (e.g. low BMI, elderly - not well represented in this study)**

Heyland DK. Should We PERMIT Systematic Underfeeding in All Intensive Care Unit Patients? Integrating the Results of the PERMIT Study in Our Clinical Practice Guidelines. JPEN 2015 Jul 6. [Epub ahead of print]

How generalizable are the results?

They screened > 6400 patients to enroll almost 900, so studied patients represent a select sample from the overall ICU patient population

Moreover, 70% of patients were recruited from 1 site in Saudi Arabia.

These factors limit the generalizability of the results to other practice settings worldwide

Recruitment by Center		
King Abdulaziz Medical City, Riyadh, Saudi Arabia - no. (%)	305 (68.1)	307 (68.9)
King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia - no. (%)	26 (5.8)	28 (6.3)
Mount Sinai Hospital, Toronto, Canada- no. (%)	46 (10.3)	42 (9.4)
Ottawa General Hospital, Ottawa, Canada- no. (%)	48 (10.7)	47 (10.6)
Ottawa Civic Hospital, Ottawa, Canada- no. (%)	18 (4.0)	18 (4.0)
Health Sciences Centre, Manitoba, Canada- no. (%)	3 (0.7)	2 (0.5)
University of Alberta Hospital, Edmonton, Canada- no. (%)	2 (0.5)	2 (0.5)

Integrating the Results of the PERMIT Study in Our Clinical Practice Guidelines

- Studies show that ICU patients only receive 60% of caloric target (i.e. we are "unwillingly" doing permissive under feeding)
  - In PERMIT Trial
  - The protein intake achieved (mean = 0.7 g/kg/day in both groups) was far below the recommended intake of 1.2–1.5 g/kg/day

Calculated protein requirement — g/day	85±21	88±23	0.18†
Daily protein intake for duration of intervention			
No. of grams	57±24	59±25	0.29†
Percent of requirement	68±24	69±25	0.56†
Protein source — g/day			
Main enteral formula	30±13	54±22	<0.001†
Supplemental enteral protein	27±16	6±10	<0.001†

RECOMMENDATIONS

- This paper demonstrated **the importance of providing enough protein**
- A huge multi-centered cohort study[1] showed that every additional 30g of protein and every 1000 kcal reduce the adjusted odds of mortality by **24%** (OR, 0.76; 95% CI, 0.65–0.87; P < .001) and **39%** (OR, 0.61; 95% CI, 0.48–0.77; P < .001) respectively
- In this RCT by Arabi et al, the **"detrimental effects of underfeeding" is compensated by the adequate protein provision**
- Since most ICU patients are underfed (international studies showed that ICU patients only receive 60% of caloric target)[2], **we must do our best to provide adequate protein**.

1. Elke G, Wang M, Weiler N, Day AG, Heyland DK. Close to recommended caloric and protein intake by enteral nutrition is associated with better clinical outcome of critically ill septic patients: secondary analysis of a large international nutrition database. *Crit Care*. 2014;18:R29.
2. Heyland, Daren K., Naomi Cahill, and Andrew G. Day. "Optimal amount of calories for critically ill patients: Depends on how you slice the cake!*." *Critical care medicine* 39.12 (2011): 2619-2626.

RECOMMENDATIONS

- We should **still feed to requirements**
- This trial showed **no benefit nor harm** when patients were fed to requirements.
- However, a large RCT conducted by Rice et al.[1] showed that patients who are fed to requirements tends to be discharged home as opposed to nursing facilities.
- This is further supported by a large cohort study published this year,[2] showing feeding to requirements is associated with improved functional status and quality of life.
- Aside to mortality outcome, we **MUST ALSO CONSIDER the quality of life post ICU**

1. Rice, Todd W., et al. "A randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure." *Critical care medicine* 39.5 (2011): 967
2. Wei X, Day AG, Ouellette Kuntz H, Heyland DK. The association between nutritional adequacy and long term outcomes in critically ill patients requiring prolonged mechanical ventilation: a multicentre cohort study. *Critical Care Medicine* 2015. [Epub ahead of print]