Nutrition in critically ill

G.Ratnakar

25-09-2020

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

DOI: 10.1177/0148607115621863
jpen.sagepub.com
hosted at
online.sagepub.com
SAGE

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[†]

Clinical Nutrition 38 (2019) 48–79

Contents lists available at ScienceDirect

Clinical Nutrition

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

ESPEN Guideline

ESPEN guideline on clinical nutrition in the intensive care unit

Pierre Singer [a,*], Annika Reintam Blaser [b,c], Mette M. Berger [d], Waleed Alhazzani [e], Philip C. Calder [f], Michael P. Casaer [g], Michael Hiesmayr [h], Konstantin Mayer [i], Juan Carlos Montejo [j], Claude Pichard [k], Jean-Charles Preiser [l], Arthur R.H. van Zanten [m], Simon Oczkowski [e], Wojciech Szczeklik [n], Stephan C. Bischoff [o]

[a] *Department of General Intensive Care and Institute for Nutrition Research, Rabin Medical Center, Beilinson Hospital, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel*

[b] *Department of Anaesthesiology and Intensive Care, University of Tartu, Tartu, Estonia*

[c] *Department of Intensive Care Medicine, Lucerne Cantonal Hospital, Lucerne, Switzerland*

[d] *Service of Adult Intensive Care and Burns, Lausanne University Hospital, Lausanne, Switzerland*

[e] *Department of Medicine, Division of Critical Care and Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Canada*

[f] *Human Development and Health Academic Unit, Faculty of Medicine, University of Southampton and NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom*

[g] *Clinical Department and Laboratory of Intensive Care Medicine, Catholic University Hospitals (UZLeuven) and Catholic University Leuven, Leuven, Belgium*

[h] *Division Cardiac-, Thoracic-, Vascular Anaesthesia and Intensive Care, Medical University Vienna, Vienna, Austria*

[i] *Universitätsklinikum Gießen Medizinische, Gießen, Germany*

[j] *Servicio de Medecina Intensiva, Hospital Universitario 12 de Octobre, Madrid, Spain*

[k] *Clinical Nutrition, Geneva University Hospital, Geneva, Switzerland*

[l] *Department of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium*

[m] *Department of Intensive Care, Gelderse Vallei Hospital, Ede, the Netherlands*

[n] *Department of Intensive Care and Perioperative Medicine, Jagiellonian University Medical College, Krakow, Poland*

[o] *Department of Nutritional Medicine/Prevention, University of Hohenheim, Stuttgart, Germany*

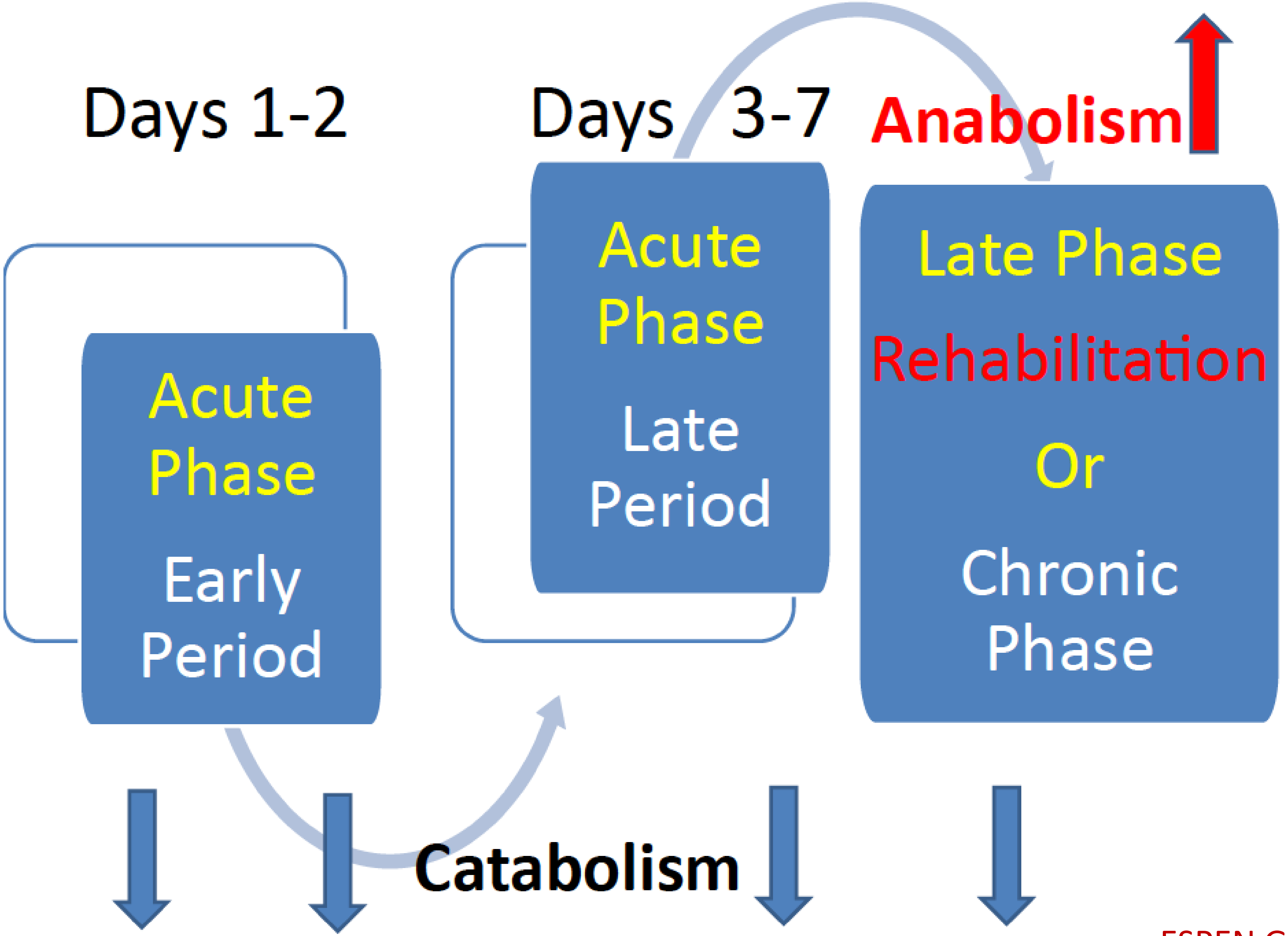
Metabolic response to critical illness

- ‘one-size fits all’ and ‘set and forget’ approaches to nutrition do not adequately address the complex metabolic, hormonal, and immunological changes that occur with critical illness

POST-SHOCK METABOLIC RESPONSE *

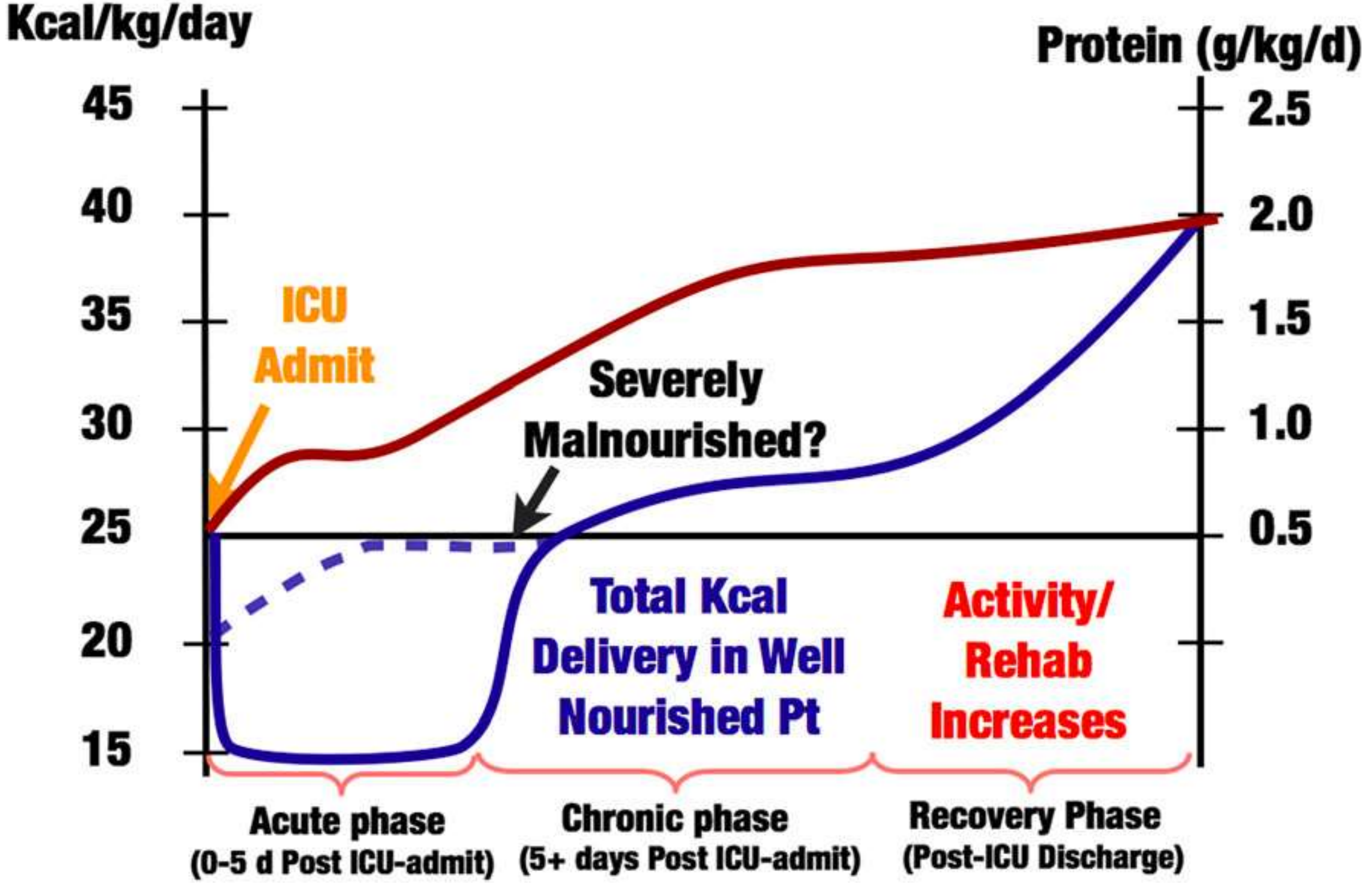
D. P. CUTHBERTSON, M.D., D.SC. GLASG.
GREIVE LECTURER IN PHYSIOLOGICAL CHEMISTRY IN THE UNIVERSITY OF GLASGOW

‘Ebb’ or early shock phase → ‘Flow’ or catabolic phase



ESPEN Guideline-2019

Targeted Nutrition Delivery in Critical Illness



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

Terminology

IBW (male) = 50 + (2.3 * (height [in inches] - 60))

IBW (female) = 45.5 + (2.3 * (height [in inches] - 60))

ABW = 0.25 * (actual body weight - IBW) + IBW

Isocaloric diet is an energy administration of around the defined target.

Hypocaloric or underfeeding is an energy administration below 70% of the defined target.

Trophic feeding is a minimal administration of nutrients having beneficial effects, such as preserving intestinal epithelium, stimulating secretion of brush border enzymes, enhancing immune function, preserving epithelial tight cell junctions, and preventing bacterial translocation.

Overfeeding is energy administration of 110% above the defined target.

Low protein diet is protein administration below 0.5 g/kg/day.

ESPN-2019 guidelines

How to define the energy expenditure (EE)?

- ESPN & ASPEN/SCCM-indirect calorimetry is better
- Weir Equation for REE: REE = (3.94 x VO2) + (1.1 x VCO2)
- If indirect calorimetry is not available, (REE= VCO2 x 8.19)

VCO2 only obtained from ventilators

- If both are not available we can use predicting equations

Lambell et al. Critical Care (2020) 24:35

TICACOS	**indirect calorimetry measurements (study group, n = 56) Vs 25 kcal/kg/day (control group, n = 56).**	**Energy (2,086 ± 460 vs. 1,480 ± 356 kcal/day, p = 0.01) Protein (76 ± 16 vs. 53 ± 16 g/day, p = 0.01) Mortality ITT(32.3% vs.31/65 patients, 47.7%, p =0.058) MV-16.1 ± 14.7 vs. 10.5 ± 8.3 days, p = 0.03 ICU stay (17.2 ± 14.6vs. 11.7 ± 8.4, p = 0.04)**
EAT-ICU trial EGDN) vs. standard nutritional	Indirect calorimetry(N=100) Vs 25 kcal/kg/day(n=99)	1877 Kcal/d Protein 1.47 g/kg/d Vs 1061 kcal/d Protein 0.50 g/kg Primary-PCS score at 6 months Secondary-mortality, rates of organ failures, serious adverse reactions or infections in the ICU, length of ICU or hospital stay, or days alive without life support at 90 days No benefit
ONCA Study	calorimetry (IC group)n=20 Vs SC group formula based (n=20)	Energy -(21.1 Å} 6.4 versus [vs] 25 kcal/kg/d, P < .01) Protein-(91% Å} 24%) vs (73% Å} 33%). ICU LOS (13 ± 8 vs 24 ± 20 days, p < 0.05)

In conclusion

- Although in above RCT targets are higher in IC method and most of patients achieved it but outcomes are poor
- It can avoid avoid under- or over delivery of energy

Equations	Parameters Used for Calculation	Accuracy Rate *
Critically Ill Patients		
25 Kcal/Kg	25 × WT	12% [91]
Harris-Benedict (1919)	M: 13.75 × WT + 5.00 × HT − 6.75 × age + 66.47 F: 9.56 × WT + 1.85 × HT − 0.67 × age + 655.09	31% [91] 32% [92]
Ireton-Jones (1997)	1925 − 10 × age + 5 × WT + (281 if M) + (292 if trauma) + (851 if burn)	37% [93]
Mifflin-St Jeor (1990)	M: 10 × WT + 6.25 × HT − 5 × age + 5 F: 10 × WT + 6.25 × HT − 5 × age − 161	18% [91] 35% [10]
Owen (1987)	M: WT × 10.2 + 879 F: WT × 7.18 + 795	12% [91]
Penn State (2003)	0.85 × HB + 175 × Tmax + 33 × Ve − 6433	43% [10]
Swinamer (1990)	945 × BSA − 6.4 × age + 108 T + 24.2 × RR + 81.7 × VT − 4349	55% [93] 45% [10]

Delsoglio, Marta et al. “Indirect Calorimetry in Clinical Practice.
” *Journal of clinical medicine* vol. 8,9 1387. 5 Sep. 2019, doi:10.3390/jcm8091387

Anorexic Patients (BMI < 16)		
Bernstein et al. (1983)	M: 11.02 × WT + 10.23 × HT − 5.8 × age − 1032 F: 7.48 × WT − 0.42 × HT − 3 × age + 844	40% [73]
Harris & Benedict (1919)	M: 13.75 × WT + 5.00 × HT − 6.75 × age + 66.47 F: 9.56 × WT + 1.85 × HT − 0.67 × age + 655.09	39% [73]
Huang et al. (2004)	10.16 × WT + 3.93 × HT − 1.44 × age + 273.82 × sex + 60.65	43% [73]
Lazzer et al. (2007)	M: 0.05 × WT + 4.65 × HT − 0.02 × age − 3.60 F: 0.04 × WT + 3.62 × HT − 2.68	39% [73]
Mifflin-St Jeor (1990)	M: 10 × WT + 6.25 × HT − 5 × age + 5 F: 10 × WT + 6.25 × HT − 5 × age − 161	40% [73]
Müller et al. (2004)	0.05 × WT + 1.01 × sex + 0.015 × age + 3.21	37% [73]
Owen (1987)	M: WT × 10.2 + 879 F: WT × 7.18 + 795	41% [73]

Delsoglio, Marta et al. “Indirect Calorimetry in Clinical Practice
” *Journal of clinical medicine* vol. 8,9 1387. 5 Sep. 2019, doi:10.3390/jcm8091387

Obese Patients (BMI > 30)		
Bernstein et al. (1983)	M: 11.02 × WT + 10.23 × HT − 5.8 × age − 1032 F: 7.48 × WT − 0.42 × HT − 3 × age + 844	16% [88] 21% [89]
Harris & Benedict (1919)	M: 13.75 × WT + 5.00 × HT − 6.75 × age + 66.47 F: 9.56 × WT + 1.85 × HT − 0.67 × age + 655.09	64% [88]
Huang et al. (2004)	10.16 × WT + 3.93 × HT − 1.44 × age + 273.82 × sex + 60.65	66% [88] 53% [89] 54% [90]
Lazzer et al. (2007)	M: 0.05 × WT + 4.65 × HT − 0.02 × age − 3.60 F: 0.04 × WT + 3.62 × HT − 2.68	58% [88] 46% [90]
Mifflin-St Jeor (1990)	M: 10 × WT + 6.25 × HT − 5 × age + 5 F: 10 × WT + 6.25 × HT − 5 × age − 161	52% [89] 56% [90]
Müller et al. (2004)	0.05 × WT + 1.10 × sex + 0.016 × age + 2.92	60% [88] 58% [89] 47% [90]
Owen (1987)	M: WT × 10.2 + 879 F: WT × 7.18 + 795	38% [73] 40% [89]

Delsoglio, Marta et al. "Indirect Calorimetry in Clinical Practice
Journal of clinical medicine vol. 8,9 1387. 5 Sep. 2019, doi:10.3390/jcm8091387

Equations	Parameters Used for Calculation	Accuracy Rate *
General Hospitalized Population		
25 kcal/kg	25 × WT	43% [10] 23% [87]
Harris & Benedict (1919)	M: 13.75 × WT + 5.00 × HT − 6.75 × age + 66.47 F: 9.56 × WT + 1.85 × HT − 0.67 × age + 655.09	43% [10] 38% [87]
Ireton-Jones (1992)	1925 − 10 × age + 5 × WT + (281 if male) + (292 if trauma) + (851 if burn)	28% [10]
Mifflin-St Jeor (1990)	M: 10 × WT + 6.25 × HT − 5 × age + 5 F: 10 × WT + 6.25 × HT − 5 × age − 161	35% [10] 32% [87]
Schofield (1985)	8.4 × WT + 4.7 × HT + 200	42% [87]

Delsoglio, Marta et al. “Indirect Calorimetry in Clinical Practice.”
Journal of clinical medicine vol. 8,9 1387. 5 Sep. 2019, doi:10.3390/jcm8091387

How to assess malnutrition?

- Weight changes are difficult to evaluate in the ICU
- weight and BMI do not accurately reflect malnutrition
- more concern is the loss of lean body mass
- critical illness associated frailty

Laboratory tools

- Albumin and isolated pre-albumin levels-not good markers

ESPN-2019 guidelines

How to assess malnutrition?

- Subjective global assessment (SGA)
- Mini-nutrition assessment (MNA)-elderly
- nutritional risk screening (NRS)
- MNA-short form (MNA-SF)
- Clinical Frailty Score
- No specific ICU nutritional score has been validated so far
- NRS,MUST scores not specifically for critically ill
- ASPEN and SCCM-recommends NRS,NUTRIC
- EPSN-not recommended any tools for assessing nutrition

TABLE 73.1 Parameters for High Nutrition Risk and Severe Acute Malnutrition		
Severe Acute Malnutrition *(At least two of following are present)*	**NRS 2002** *Total score ≥5 = High Risk*	**NUTRIC Score** *Total score ≥5 = High Risk*
Energy intake ≤50% of need for 5 days or more	Energy intake for 7 days: 1 point: <50–75% 2 points: 25–50% 3 points: 0–25%	Age (years) 0 point: <50 1 point: 50–74 2 points: >75
Weight loss: >2% in 1 week, >5% in 1 month, >7.5% in 3 months	Weight loss 1 point: >5% in 3 months 2 points: >5% in 2 months (BMI 18.5–20.5) 3 points: >5% in 1 month (BMI < 18.5)	APACHE II 0 point: <15 1 point: 15–19 2 points: 20–27 3 points: ≥28
Moderate fat loss muscle wasting and/or peripheral edema	Diagnosis 1 point: chronic condition 2 points: acute condition 3 points: head injury, BMT, ICU patient	SOFA 0 point: <6 1 point: 6–9 2 points: ≥10 No. of comorbidities 0 point: 0–1 1 point: ≥2 Days from hospital to ICU admit 0 point: 0–1 1 point: ≥1
Decreased functional status		

Washington critical care 3rd edition

- BMI <18.5 kg/m^2

Alternative 2:

2015 ESPEN definition

- Weight loss (unintentional) > 10% indefinite of time, or >5% over the last 3 months combined with either
- BMI <20 kg/m^2 if <70 years of age, or <22 kg/m^2 if ≥70 years of age or
- FFMI <15 and 17 kg/m^2 in women and men, respectively.

Thresholds for severity grading of malnutrition into Stage 1 (Moderate) and Stage 2 (Severe) malnutrition according to the recent ESPEN GLIM recommendations [23].

	Phenotype criteria			Etiology criteria	
	Weight loss (%)	Body mass index (kg/m^2)	Muscle mass[a]	Food intake, malabsorption or GI symptoms	Disease burden/ inflammation
Stage 1/Moderate Malnutrition (Requires 1 phenotypic and 1 etiologic criterion)	5–10% within the past 6 mo, or 10–20% beyond 6 mo	<20 if <70 yr, <22 if ≥70 yr Asia: <18.5 if <70 yr, <20 if ≥70 yr	Mild to moderate deficit (per validated assessment methods – see below)	Any reduction of intake below ER for >2 weeks, or moderate mal-absorption/GI symptoms[b]	Acute disease/injury[d], or chronic disease-related[e]
Stage 2/Severe Malnutrition (Requires 1 phenotypic and 1 etiologic criterion)	>10% within the past 6 mo, or >20% beyond 6 mo	<18.5 if <70 yr, <20 if ≥70 yr Asia: TBD	Severe deficit (per validated assessment methods – see below)	≤50% intake of ER for >1 week, or severe mal-absorption/GI symptoms[c]	Acute disease/injury[d], or chronic disease-related[e]

GI = gastro-intestinal, ER = energy requirements, yr = year, mo = month.

[a] For example fat free mass index (FFMI, kg/m^2) by dual-energy absorptiometry or corresponding standards using other body composition methods like bioelectrical impedance analysis (BIA), CT or MRI. When not available or by regional preference, physical exam or standard anthropometric measures like mid-arm muscle or calf circumferences may be used. Thresholds for reduced muscle mass need to be adapted to race (Asia). Functional assessments like hand-grip strength may be used as a supportive measure.

[b] Gastrointestinal symptoms of moderate degree – dysphagia, nausea, vomiting, diarrhea, constipation or abdominal pain.

[c] Gastrointestinal symptoms of severe degree – dysphagia, nausea, vomiting, diarrhea, constipation or abdominal pain.

[d] Acute disease/injury-related with severe inflammation. For example major infection, burns, trauma or closed head injury.

[e] Chronic disease-related with chronic or recurrent mild to moderate inflammation. For example malignant disease, chronic obstructive pulmonary disease, congestive heart failure, chronic renal disease or any disease with chronic or recurrent Inflammation. CRP may be used as a supportive laboratory measure.

ESPN-2019 guidelines

Muscle wasting

- Sarcopenia is defined as a decrease in muscle loss and/or function
- lean body mass evaluated by ultrasound , CT scan, bioelectric impedance or even stable isotopes
- Muscle function-handgrip dynamometer
- USG assessment of muscle glycogen

ESPN-2019 guidelines

Discussion

- Initiation: Early vs Delayed
- Trophic vs full nutrition
- EN vs PN
- Nutrition while in shock

Lack of data

- Continuous vs intermittent feeds
- Organ failure subsets
- Feeding certain subset of populations
- Chronic mal nourished
- Obese
- Which type of protein

EN vs oral diet ?

- No studies comparing EN vs oral
- Preferred in no risks of vomiting or aspiration

Initiation of nutrition

early or delayed ?

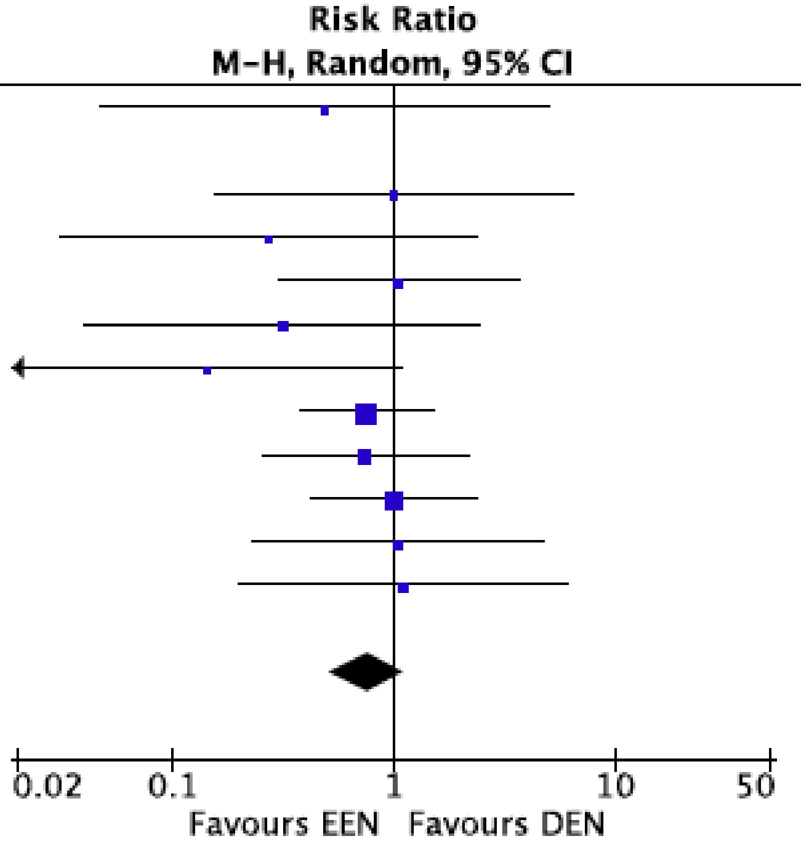
EEN vs delay nutritional intake (including delayed EN, oral diet or PN)

12 RCTs (662 patients)

a Mortality

Study or Subgroup	EEN Events	EEN Total	DEN Events	DEN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Moore 1986	1	32	2	31	2.6%	0.48 [0.05, 5.07]	1986
Chiarelli 1990	0	10	0	10		Not estimable	1990
Eyer 1993	2	19	2	19	4.2%	1.00 [0.16, 6.38]	1993
Chuntrasakul 1996	1	21	3	17	3.1%	0.27 [0.03, 2.37]	1996
Singh 1998	4	21	4	22	9.3%	1.05 [0.30, 3.66]	1998
Minard 2000	1	12	4	15	3.4%	0.31 [0.04, 2.44]	2000
Pupelis 2001	1	30	7	30	3.5%	0.14 [0.02, 1.09]	2001
Malhotra 2004	12	100	16	100	30.1%	0.75 [0.37, 1.50]	2004
Peck 2004	4	14	5	13	12.5%	0.74 [0.25, 2.18]	2004
Nguyen 2008	6	14	6	14	19.9%	1.00 [0.43, 2.35]	2008
Moses 2009	3	29	3	30	6.3%	1.03 [0.23, 4.71]	2009
Chourdakis 2012	3	34	2	25	5.0%	1.10 [0.20, 6.12]	2012
Total (95% CI)		**336**		**326**	**100.0%**	**0.76 [0.52, 1.11]**	
Total events	38		54				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.61$, df = 10 (P = 0.85); $I^2 = 0\%$
Test for overall effect: Z = 1.44 (P = 0.15)

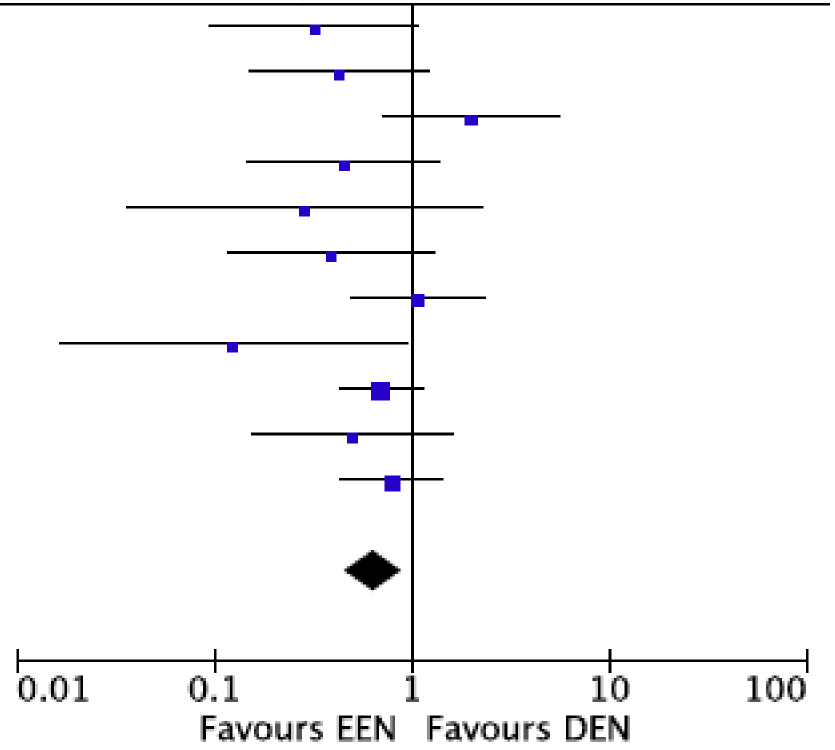


EEN vs delay nutritional intake (including delayed EN, oral diet or PN)

11 RCTs (597 patients).

b Infections

Study or Subgroup	EEN Events	EEN Total	DEN Events	DEN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year	Risk Ratio M-H, Random, 95% CI
Moore 1986	3	32	9	31	6.4%	0.32 [0.10, 1.08]	1986	
Chiarelli 1990	3	10	7	10	8.3%	0.43 [0.15, 1.20]	1990	
Eyer 1993	8	19	4	19	8.4%	2.00 [0.72, 5.53]	1993	
Hasse 1995	3	14	8	17	7.2%	0.46 [0.15, 1.40]	1995	
Watters 1997	1	13	4	15	2.5%	0.29 [0.04, 2.27]	1997	
Singh 1998	3	21	8	22	6.6%	0.39 [0.12, 1.28]	1998	
Minard 2000	6	12	7	15	12.4%	1.07 [0.49, 2.34]	2000	
Pupelis 2001	1	30	8	30	2.6%	0.13 [0.02, 0.94]	2001	
Malhotra 2004	21	100	30	100	21.3%	0.70 [0.43, 1.14]	2004	
Nguyen 2008	3	14	6	14	6.7%	0.50 [0.15, 1.61]	2008	
Chourdakis 2012	13	34	12	25	17.5%	0.80 [0.44, 1.44]	2012	
Total (95% CI)		**299**		**298**	**100.0%**	**0.64 [0.46, 0.90]**		
Total events	65		103					



Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 13.41$, df = 10 (P = 0.20); $I^2 = 25\%$
Test for overall effect: Z = 2.58 (P = 0.010)

ESPN-2019 SUPPLIMENT

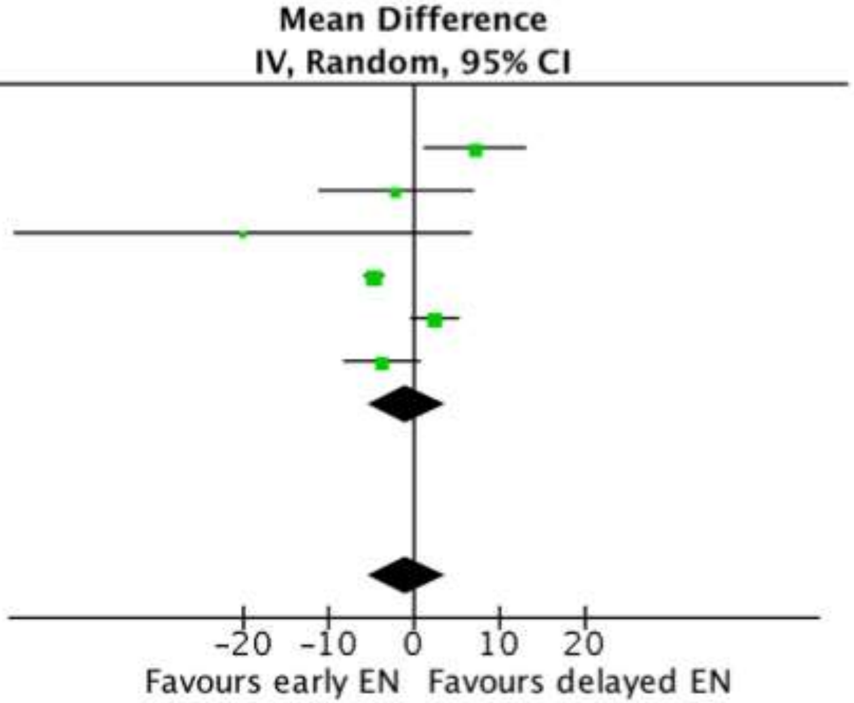
EEN vs delay nutritional intake (including delayed EN, oral diet or PN)

I., Figure 3: Intensive Care Unit Length of Stay (Includes Meta-analysis I A only)

Study or Subgroup	Early EN Mean	Early EN SD	Early EN Total	Delayed EN Mean	Delayed EN SD	Delayed EN Total	Weight	Mean Difference IV, Random, 95% CI	Year
1.3.1 ICU studies									
Minard 2000	18.5	8.8	12	11.3	6.1	15	17.5%	7.20 [1.34, 13.06]	2000
Pupelis 2001	13.9	14.6	30	16	20.5	30	12.4%	-2.10 [-11.11, 6.91]	2001
Peck 2004	40	32	14	60	38	13	2.6%	-20.00 [-46.60, 6.60]	2004
Nguyen 2008	11.3	0.8	14	15.9	1.9	14	24.5%	-4.60 [-5.68, -3.52]	2008
Moses 2009	10.5	5.2	29	8	5.6	30	22.8%	2.50 [-0.26, 5.26]	2009
Chourdakis 2012	24.8	7.6	34	28.5	8.9	25	20.2%	-3.70 [-8.02, 0.62]	2012
Subtotal (95% CI)			**133**			**127**	**100.0%**	**-0.82 [-5.31, 3.67]**	
Total (95% CI)			**133**			**127**	**100.0%**	**-0.82 [-5.31, 3.67]**	

Subtotal: Heterogeneity: $Tau^2 = 21.11$; $Chi^2 = 36.51$, df = 5 ($P < 0.00001$); $I^2 = 86\%$
Test for overall effect: Z = 0.36 (P = 0.72)

Total: Heterogeneity: $Tau^2 = 21.11$; $Chi^2 = 36.51$, df = 5 ($P < 0.00001$); $I^2 = 86\%$
Test for overall effect: Z = 0.36 (P = 0.72)
Test for subgroup differences: Not applicable

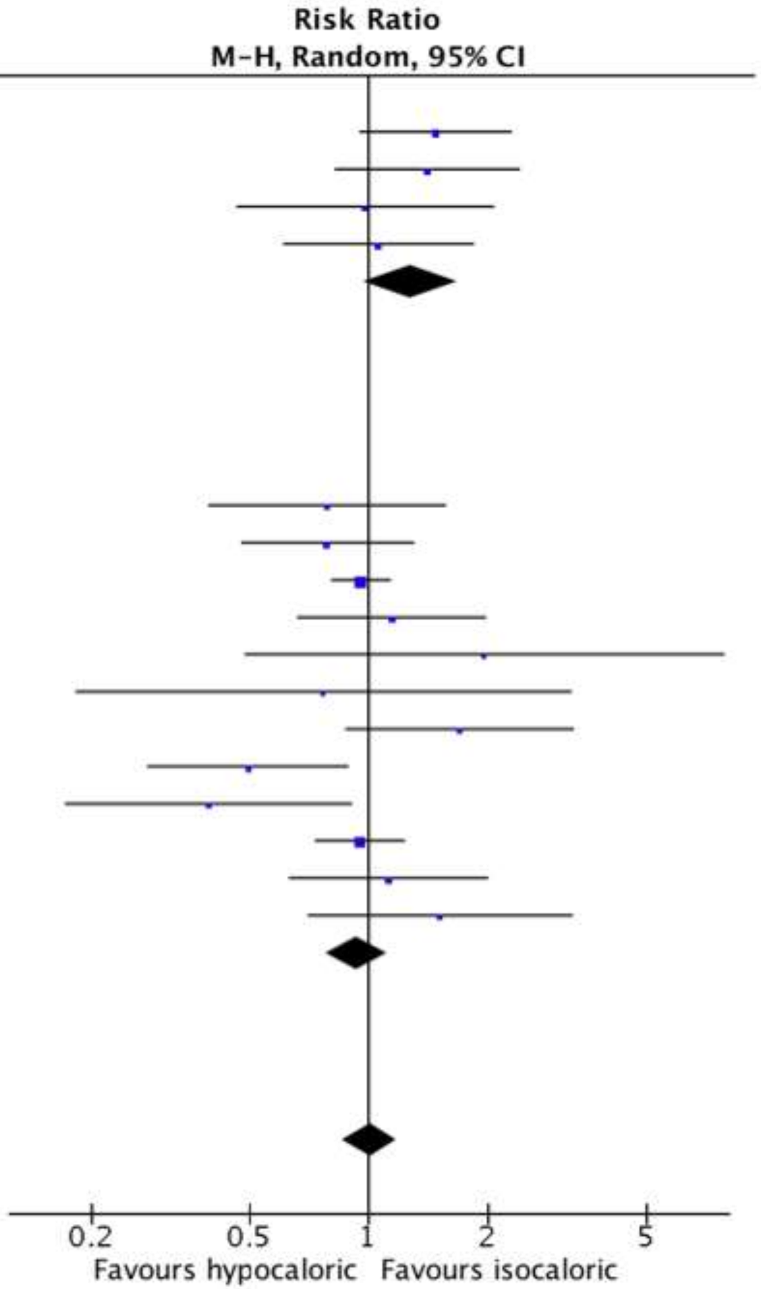


Trophic vs full nutrition

VI., Figure 1: Short-term mortality (Includes Meta-Analyses VI A and VI B)

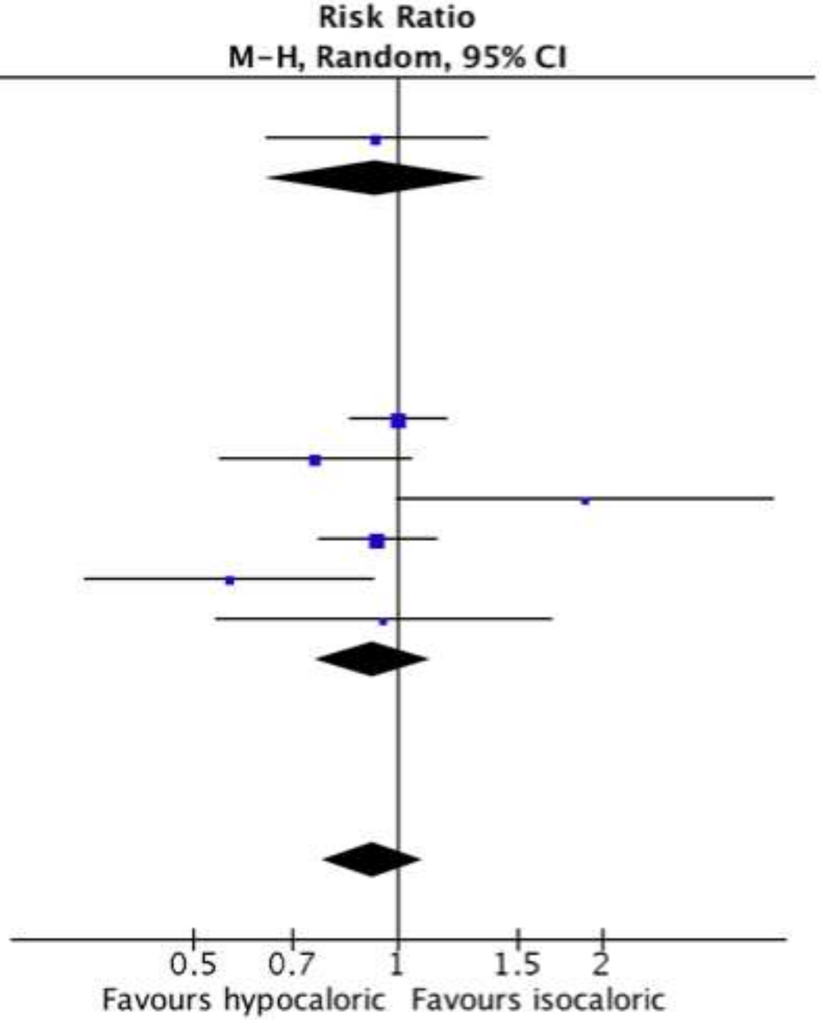
Espn-2019 supplement

Study or Subgroup	Hypocaloric nutrition Events	Hypocaloric nutrition Total	Isocaloric nutrition Events	Isocaloric nutrition Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
2.1.1 Studies using indirect calorimetry							
Singer 2011 TICACOS	31	65	21	65	8.4%	1.48 [0.96, 2.28]	2011
Heidegger 2013	28	152	20	153	6.4%	1.41 [0.83, 2.39]	2013
Petros 2016	10	46	12	54	3.7%	0.98 [0.47, 2.05]	2016
Allingstrup 2017 EAT-ICU	21	99	20	100	6.1%	1.06 [0.61, 1.83]	2017
Subtotal (95% CI)		**362**		**372**	**24.5%**	**1.28 [0.98, 1.67]**	
Total events	90		73				
Heterogeneity: Tau² = 0.00; Chi² = 1.51, df = 3 (P = 0.68); I² = 0%							
Test for overall effect: Z = 1.80 (P = 0.07)							
2.1.2 Studies without indirect calorimetry							
Desachy 2008	11	50	14	50	4.2%	0.79 [0.40, 1.56]	2008
Arabi 2011	22	120	28	120	6.9%	0.79 [0.48, 1.29]	2011
Casaer 2011 EPaNIC	242	2328	251	2312	18.7%	0.96 [0.81, 1.13]	2011
Rice 2011	22	98	20	102	6.2%	1.14 [0.67, 1.96]	2011
Rugles 2013	5	53	3	62	1.2%	1.95 [0.49, 7.78]	2013
Charles 2014	3	41	4	42	1.1%	0.77 [0.18, 3.22]	2014
Peake 2014	18	55	11	57	4.6%	1.70 [0.88, 3.26]	2014
Doig 2015	15	166	30	165	5.5%	0.50 [0.28, 0.89]	2015
Braunschweig 2015	6	38	16	40	3.1%	0.39 [0.17, 0.90]	2015
Arabi 2015 PermiT Trial	93	447	97	444	14.6%	0.95 [0.74, 1.23]	2015
Rugles 2016	18	60	16	60	5.7%	1.13 [0.64, 1.99]	2016
Wischmeyer 2017	17	73	8	52	3.6%	1.51 [0.71, 3.24]	2017
Subtotal (95% CI)		**3529**		**3506**	**75.5%**	**0.94 [0.78, 1.12]**	
Total events	472		498				
Heterogeneity: Tau² = 0.03; Chi² = 16.36, df = 11 (P = 0.13); I² = 33%							
Test for overall effect: Z = 0.73 (P = 0.47)							
Total (95% CI)		**3891**		**3878**	**100.0%**	**1.01 [0.86, 1.18]**	
Total events	562		571				
Heterogeneity: Tau² = 0.03; Chi² = 22.06, df = 15 (P = 0.11); I² = 32%							
Test for overall effect: Z = 0.09 (P = 0.93)							
Test for subgroup differences: Chi² = 3.62, df = 1 (P = 0.06), I² = 72.4%							



VI., Figure 2: Long-term mortality (Includes Meta-Analyses VI A and VI B)

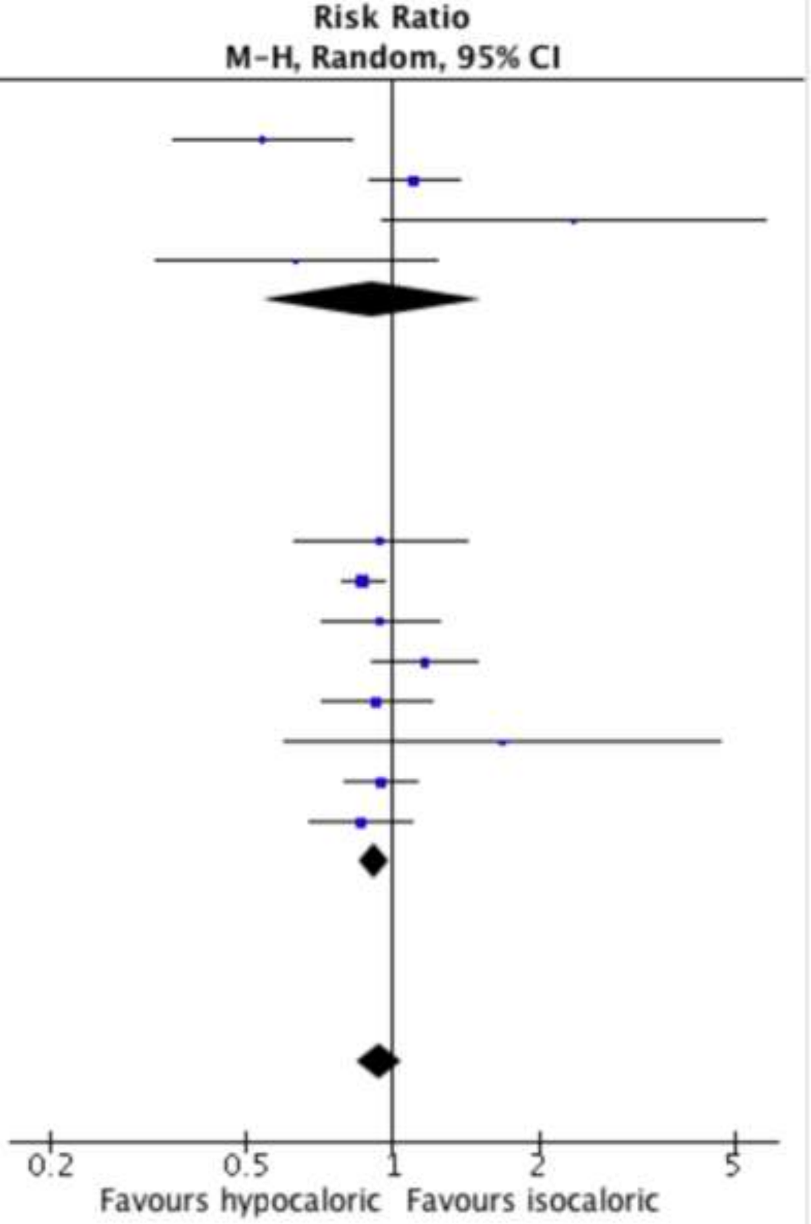
	Hypocaloric nutrition		Isocaloric nutrition			Risk Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
2.2.1 Studies using indirect calorimetry							
Allingstrup 2017	34	99	37	100	12.9%	0.93 [0.64, 1.35]	2017
Subtotal (95% CI)		**99**		**100**	**12.9%**	**0.93 [0.64, 1.35]**	
Total events	34		37				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.39 (P = 0.70)							
2.2.2 Studies without indirect calorimetry							
Casaer 2011	257	2328	255	2312	26.6%	1.00 [0.85, 1.18]	2011
Arabi 2011	39	116	53	119	15.2%	0.75 [0.55, 1.04]	2011
Peake 2014	20	55	11	57	5.8%	1.88 [1.00, 3.56]	2014
Arabi 2015	131	438	140	436	23.8%	0.93 [0.76, 1.14]	2015
Doig 2015	21	166	37	165	8.8%	0.56 [0.35, 0.92]	2015
Wischmeyer 2017	20	73	15	52	7.0%	0.95 [0.54, 1.67]	2017
Subtotal (95% CI)		**3176**		**3141**	**87.1%**	**0.91 [0.75, 1.11]**	
Total events	488		511				
Heterogeneity: Tau² = 0.03; Chi² = 11.10, df = 5 (P = 0.05); I² = 55%							
Test for overall effect: Z = 0.89 (P = 0.38)							
Total (95% CI)		**3275**		**3241**	**100.0%**	**0.92 [0.78, 1.08]**	
Total events	522		548				
Heterogeneity: Tau² = 0.02; Chi² = 11.10, df = 6 (P = 0.09); I² = 46%							
Test for overall effect: Z = 1.01 (P = 0.31)							
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%							



Espn-2019 supplement

VI., Figure 3: Infections (Includes Meta-Analyses VI A and VI B)

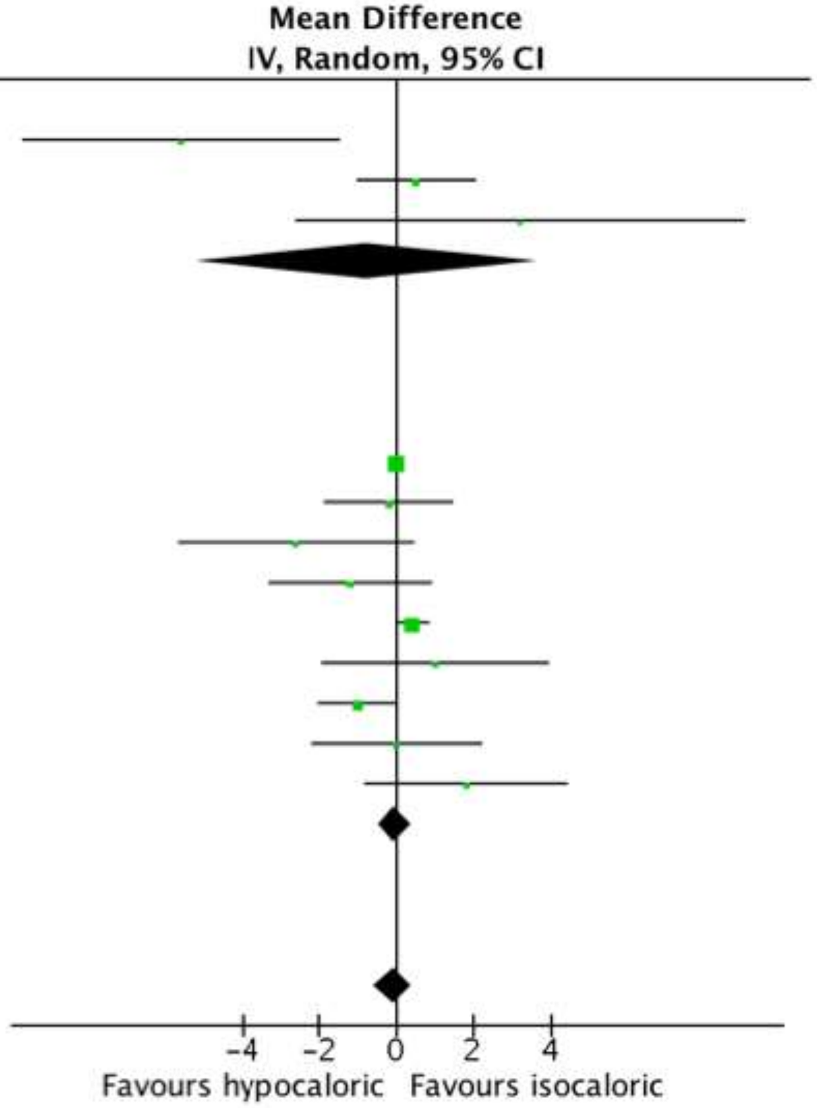
Study or Subgroup	Hypocaloric nutrition Events	Hypocaloric nutrition Total	Isocaloric nutrition Events	Isocaloric nutrition Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
2.5.1 Studies using indirect calorimetry							
Singer 2011	20	65	37	65	5.2%	0.54 [0.35, 0.82]	2011
Heidegger 2013	85	152	77	153	12.0%	1.11 [0.90, 1.37]	2013
Petros 2016	12	46	6	54	1.4%	2.35 [0.96, 5.76]	2016
Allingstrup 2017	12	99	19	100	2.4%	0.64 [0.33, 1.24]	2017
Subtotal (95% CI)		**362**		**372**	**21.0%**	**0.91 [0.54, 1.54]**	
Total events	129		139				
Heterogeneity: Tau² = 0.20; Chi² = 14.29, df = 3 (P = 0.003); I² = 79%							
Test for overall effect: Z = 0.35 (P = 0.73)							
2.5.2 Studies without indirect calorimetry							
Rice 2011	30	98	33	102	5.4%	0.95 [0.63, 1.42]	2011
Casaer 2011	531	2328	605	2312	18.3%	0.87 [0.79, 0.96]	2011
Arabi 2011	53	120	56	120	9.1%	0.95 [0.72, 1.25]	2011
Rice 2012 EDEN Trial	111	508	92	492	10.4%	1.17 [0.91, 1.50]	2012
Charles 2014	29	41	32	42	9.8%	0.93 [0.72, 1.20]	2014
Braunschweig 2015	8	38	5	40	1.1%	1.68 [0.60, 4.70]	2015
Arabi 2015	161	448	169	446	14.2%	0.95 [0.80, 1.13]	2015
Wischmeyer 2017	46	73	38	52	10.6%	0.86 [0.68, 1.10]	2017
Subtotal (95% CI)		**3654**		**3606**	**79.0%**	**0.92 [0.86, 0.99]**	
Total events	969		1030				
Heterogeneity: Tau² = 0.00; Chi² = 6.50, df = 7 (P = 0.48); I² = 0%							
Test for overall effect: Z = 2.33 (P = 0.02)							
Total (95% CI)		**4016**		**3978**	**100.0%**	**0.94 [0.84, 1.05]**	
Total events	1098		1169				
Heterogeneity: Tau² = 0.01; Chi² = 20.97, df = 11 (P = 0.03); I² = 48%							
Test for overall effect: Z = 1.07 (P = 0.29)							
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.98), I² = 0%							



Espn-2019 supplement

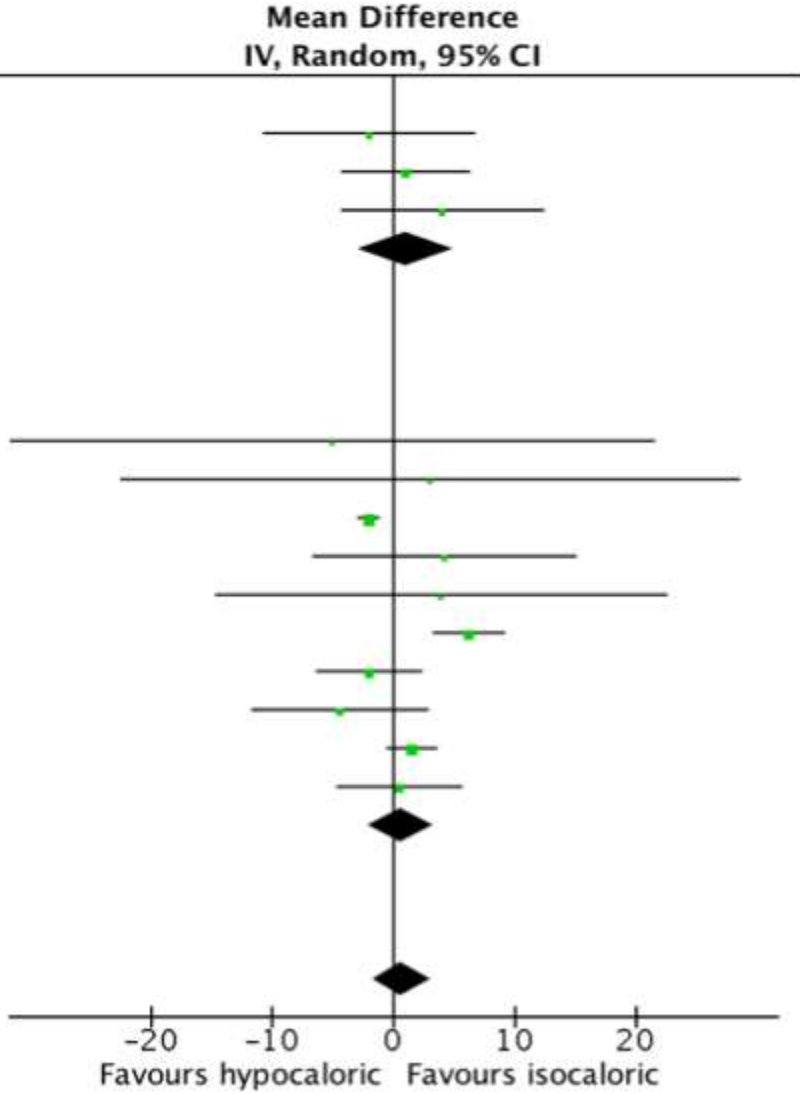
VI., Figure 4: Duration of mechanical ventilation

Study or Subgroup	Hypocaloric nutrition Mean	SD	Total	Isocaloric nutrition Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
2.3.1 Studies using indirect calorimetry									
Singer 2011	10.5	8.3	65	16.1	14.7	65	1.3%	-5.60 [-9.70, -1.50]	2011
Heidegger 2013	6.9	6.7	152	6.4	6.8	153	7.6%	0.50 [-1.02, 2.02]	2013
Petros 2016	10.6	17.6	46	7.4	10.3	54	0.7%	3.20 [-2.58, 8.98]	2016
Subtotal (95% CI)			**263**			**272**	**9.7%**	**-0.78 [-5.19, 3.63]**	
Heterogeneity: $Tau^2 = 11.33$; $Chi^2 = 8.75$, df = 2 (P = 0.01); $I^2 = 77\%$									
Test for overall effect: Z = 0.35 (P = 0.73)									
2.3.2 Studies without indirect calorimetry									
Casaer 2011	2	3	2328	2	3	2312	28.9%	0.00 [-0.17, 0.17]	2011
Rice 2011	5.5	5.4	98	5.7	6.4	102	6.8%	-0.20 [-1.84, 1.44]	2011
Arabi 2011	10.6	7.6	120	13.2	15.2	120	2.3%	-2.60 [-5.64, 0.44]	2011
Rugles 2013	8.5	4.6	40	9.7	4.9	40	4.6%	-1.20 [-3.28, 0.88]	2013
Doig 2015	7.86	2.1	166	7.45	1.6	165	24.9%	0.41 [0.01, 0.81]	2015
Braunschweig 2015	7	8.1	38	6	4.4	40	2.5%	1.00 [-1.91, 3.91]	2015
Arabi 2015	9	7.4	448	10	8.1	446	12.9%	-1.00 [-2.02, 0.02]	2015
Rugles 2016	9	6.1	60	9	6.1	60	4.2%	0.00 [-2.18, 2.18]	2016
Wischmeyer 2017	8.3	7	73	6.5	7.6	52	3.1%	1.80 [-0.82, 4.42]	2017
Subtotal (95% CI)			**3371**			**3337**	**90.3%**	**-0.04 [-0.46, 0.38]**	
Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 13.96$, df = 8 (P = 0.08); $I^2 = 43\%$									
Test for overall effect: Z = 0.17 (P = 0.86)									
Total (95% CI)			**3634**			**3609**	**100.0%**	**-0.09 [-0.58, 0.39]**	
Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 22.71$, df = 11 (P = 0.02); $I^2 = 52\%$									
Test for overall effect: Z = 0.37 (P = 0.71)									
Test for subgroup differences: $Chi^2 = 0.11$, df = 1 (P = 0.74), $I^2 = 0\%$									



VI., Figure 5: Length of hospital stay

Study or Subgroup	Hypocaloric nutrition Mean	Hypocaloric nutrition SD	Hypocaloric nutrition Total	Isocaloric nutrition Mean	Isocaloric nutrition SD	Isocaloric nutrition Total	Weight	Mean Difference IV, Random, 95% CI	Year
2.4.1 Studies using indirect calorimetry									
Singer 2011	31.8	27.3	65	33.8	22.9	65	5.1%	-2.00 [-10.66, 6.66]	2011
Heidegger 2013	32	23	152	31	23	153	9.4%	1.00 [-4.16, 6.16]	2013
Allingstrup 2017	34	28.9	99	30	30.4	100	5.5%	4.00 [-4.24, 12.24]	2017
Subtotal (95% CI)			**316**			**318**	**20.0%**	**1.06 [-2.84, 4.97]**	
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.97$, df = 2 (P = 0.62); $I^2 = 0\%$									
Test for overall effect: Z = 0.53 (P = 0.59)									
2.4.2 Studies without indirect calorimetry									
Desachy 2008	51	75	50	56	59	50	0.7%	-5.00 [-31.45, 21.45]	2008
Arabi 2011	70.2	106.9	120	67.2	93.6	120	0.8%	3.00 [-22.42, 28.42]	2011
Casaer 2011	14	13.3	2328	16	14.8	2312	17.2%	-2.00 [-2.81, -1.19]	2011
Charles 2014	35.2	31.4	41	31	16.2	42	3.7%	4.20 [-6.59, 14.99]	2014
Peake 2014	34.5	49.4	55	30.6	50.6	57	1.4%	3.90 [-14.62, 22.42]	2014
Doig 2015	27.9	15.1	166	21.7	11.5	165	13.8%	6.20 [3.31, 9.09]	2015
Arabi 2015	28	28.9	448	30	36.3	446	11.0%	-2.00 [-6.30, 2.30]	2015
Braunschweig 2015	22.8	14.3	38	27.2	18.2	40	6.5%	-4.40 [-11.64, 2.84]	2015
Rugles 2016	12	5.4	60	10.5	5.9	60	15.5%	1.50 [-0.52, 3.52]	2016
Wischmeyer 2017	24	16.5	73	23.5	12.7	52	9.5%	0.50 [-4.62, 5.62]	2017
Subtotal (95% CI)			**3379**			**3344**	**80.0%**	**0.60 [-2.14, 3.34]**	
Heterogeneity: $Tau^2 = 9.28$; $Chi^2 = 38.27$, df = 9 (P < 0.0001); $I^2 = 76\%$									
Test for overall effect: Z = 0.43 (P = 0.67)									
Total (95% CI)			**3695**			**3662**	**100.0%**	**0.70 [-1.63, 3.02]**	
Heterogeneity: $Tau^2 = 7.98$; $Chi^2 = 40.31$, df = 12 (P < 0.0001); $I^2 = 70\%$									
Test for overall effect: Z = 0.59 (P = 0.56)									
Test for subgroup differences: $Chi^2 = 0.04$, df = 1 (P = 0.85), $I^2 = 0\%$									



ONLINE FIRST

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

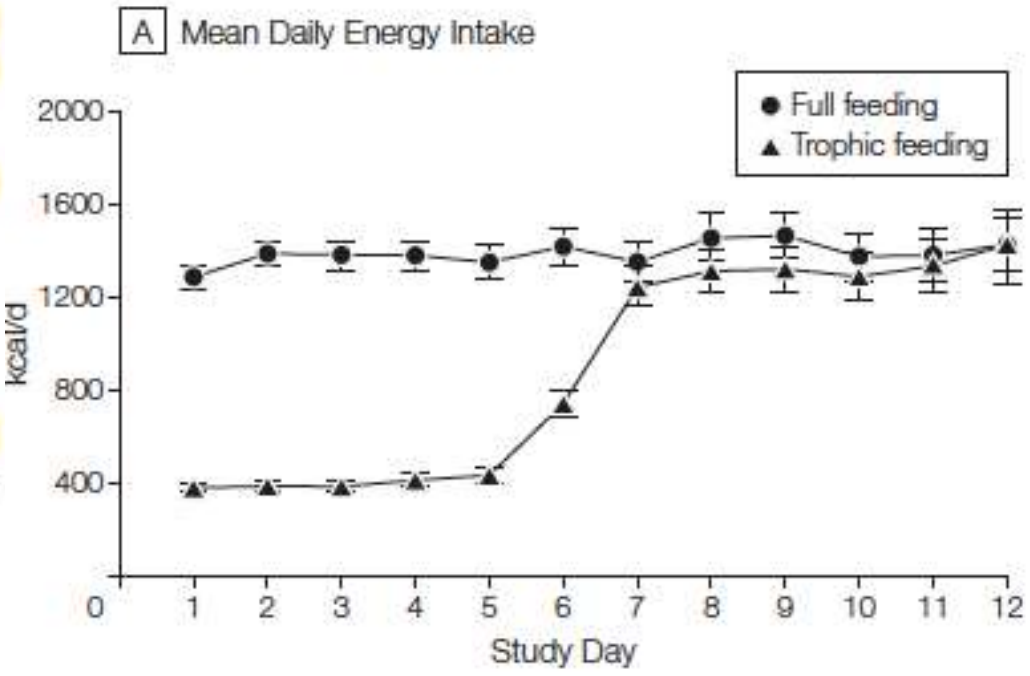
The EDEN Randomized Trial

Objective To determine if initial lower-volume trophic enteral feeding would increase ventilator-free days and decrease gastrointestinal intolerances compared with initial full enteral feeding.

Design, Setting, and Participants The EDEN study, a randomized, open-label, multicenter trial conducted from January 2, 2008, through April 12, 2011. Participants were 1000 adults within 48 hours of developing acute lung injury requiring mechanical ventilation whose physicians intended to start enteral nutrition at 44 hospitals in the National Heart, Lung, and Blood Institute ARDS Clinical Trials Network.

Interventions Participants were randomized to receive either trophic or full enteral feeding for the first 6 days. After day 6, the care of all patients who were still receiving mechanical ventilation was managed according to the full feeding protocol.

Main Outcome Measures Ventilator-free days to study day 28.



- Full enteral vs trophic for 6 days
- N=1000

Table 2. Clinical Outcomes

Outcome	Trophic Feeding (n = 508)	Full Feeding (n = 492)	*P* Value
Ventilator-free days, No. (95% CI)	14.9 (13.9-15.8)	15.0 (14.1-15.9)	.89
Failure-free days, No. (95% CI)			
Cardiovascular	19.1 (18.2-20.0)	18.9 (18.1-19.8)	.75
Renal	20.0 (19.0-20/9)	19.4 (18.4-20.5)	.43
Hepatic	22.0 (21.2-22.9)	22.6 (21.8-23.5)	.37
Coagulation	22.3 (21.4-23.1)	23.1 (22.3-23.9)	.16
ICU-free days, No. (95% CI)	14.4 (13.5-15.3)	14.7 (13.8-15.6)	.67
60-d mortality, No. (%) [95% CI]	118 (23.2) [19.6-26.9]	109 (22.2) [18.5-25.8]	.77
Development of infections, No. (%) [95% CI]			
VAP	37 (7.3) [5.0-9.5]	33 (6.7) [4.5-8.9]	.72
Clostridium difficile colitis	15 (3.0) [1.5-4.4]	13 (2.6) [1.2-4.1]	.77
Bacteremia, No. (%)	59 (11.6) [8.8-14.4]	46 (9.3) [6.8-11.9]	.24

Abbreviations: ICU, intensive care unit; VAP, ventilator-associated pneumonia.

- Full-feeding group used more prokinetic agents,
- Vomiting (2.2% vs 1.7% of patient feeding days; P=.05),
- Elevated gastric residual volumes (4.9% vs 2.2% of feeding days;P.001)
- Constipation (3.1% vs 2.1% of feeding days; P=.003)

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*

METHODS

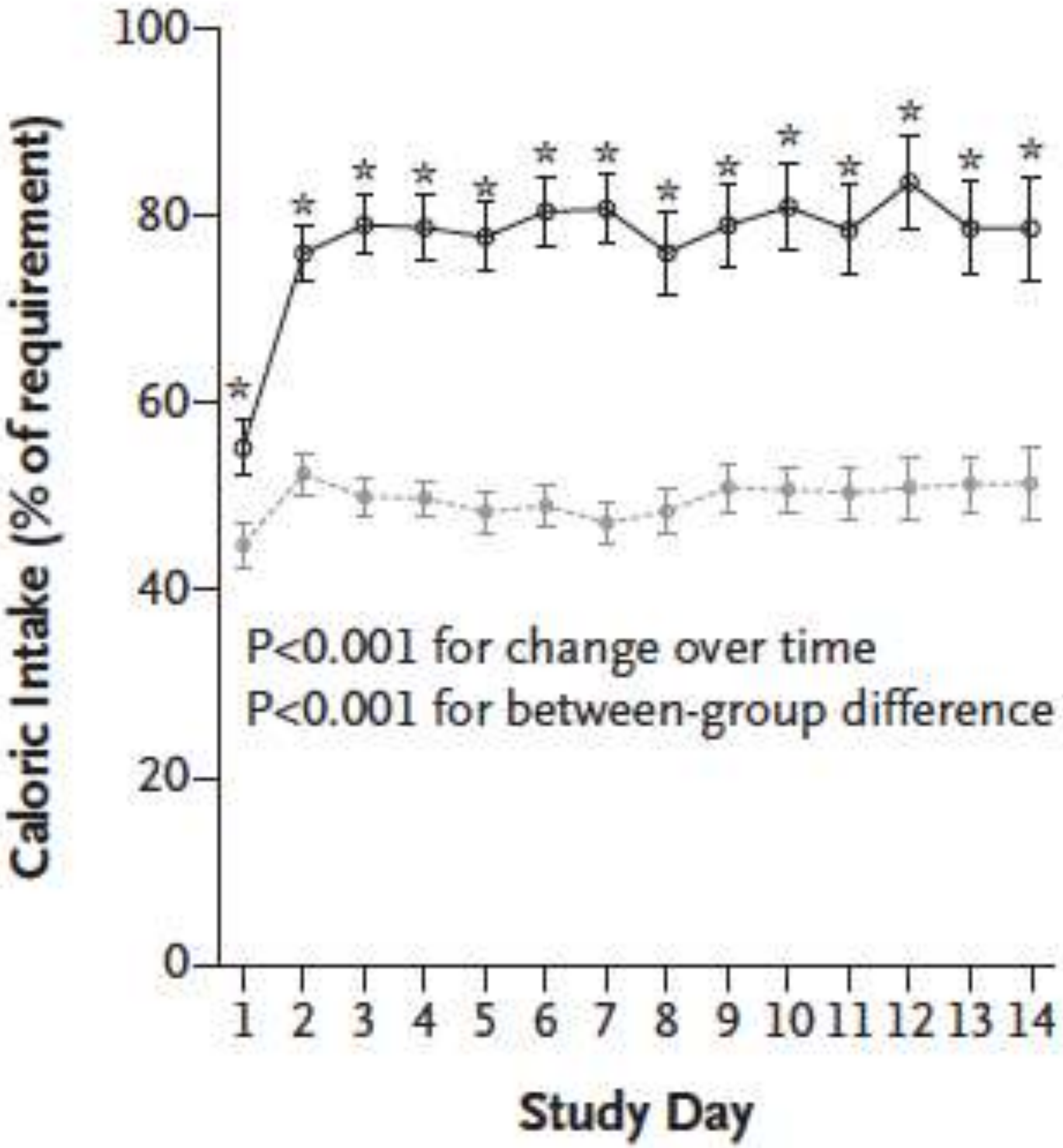
At seven centers, we randomly assigned 894 critically ill adults with a medical, surgical, or trauma admission category to permissive underfeeding (40 to 60% of calculated caloric requirements) or standard enteral feeding (70 to 100%) for up to 14 days while maintaining a similar protein intake in the two groups. The primary outcome was 90-day mortality.

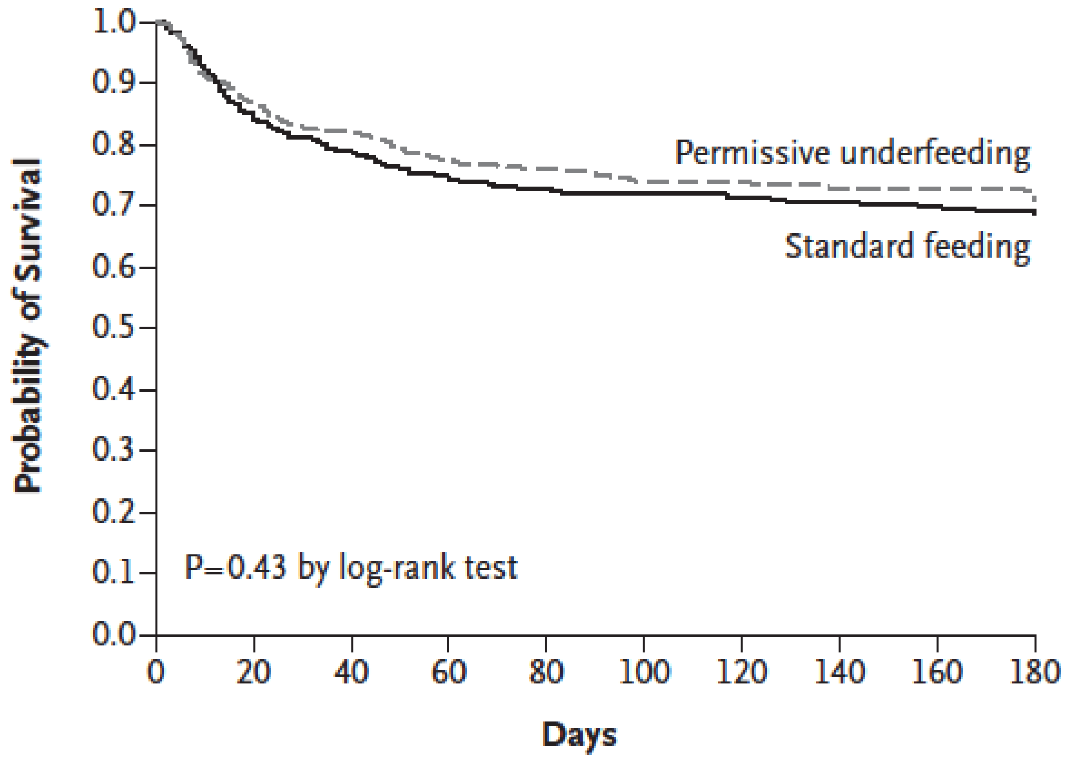
Admission category — no. (%)		
Medical	336 (75.0)	335 (75.1)
Surgical	19 (4.2)	12 (2.7)
Nonoperative trauma	93 (20.8)	99 (22.2)
Severe sepsis at admission — no. (%)	159 (35.5)	133 (29.8)
Traumatic brain injury — no. (%)	55 (12.3)	63 (14.1)
APACHE II score‡	21.0±7.9	21.0±8.2
SOFA score§	9.9±3.5	9.8±3.5
Mechanical ventilation — no. (%)	436 (97.3)	429 (96.2)
Vasopressor therapy — no. (%)	255 (56.9)	243 (54.5)

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†
Caloric source for duration of intervention — kcal/day			
Enteral	740±294	1198±470	<0.001‡
Propofol	63±88	65±89	0.84†
Intravenous dextrose	32±59	35±60	0.23†
Parenteral nutrition	3±32	5±59	0.38†
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†
Parenteral protein	0.2±2.6	0.2±2.7	0.79†

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†
Parenteral protein	0.2±2.6	0.2±2.7	0.79†
Duration of intervention — days	9.1±4.6	9.4±4.4	0.36†
Cointerventions during study period			
Insulin			
Use — no. (%)	205 (45.8)	235 (52.7)	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†
Fluid balance — ml/day	490±1408	688±1196	<0.001†

A





No. at Risk

	0	20	40	60	80	100	120	140	160	180
Standard feeding	446	380	352	334	325	322	319	315	312	308
Permissive underfeeding	448	390	368	346	340	331	330	326	326	324

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
Duration of mechanical ventilation — days				
Median	9	10		0.49†
Interquartile range	5–15	5–16		
Days free from mechanical ventilation				
Median	77	75		0.48†
Interquartile range	0–84	0–84		
ICU length of stay — days				
Median	13	13		0.46†
Interquartile range	8–21	8–20		
ICU-free days				
Median	72	71		0.28†
Interquartile range	0–81	0–79		
Hospital length of stay — days				
Median	28	30		0.24†
Interquartile range	15–54	14–63		

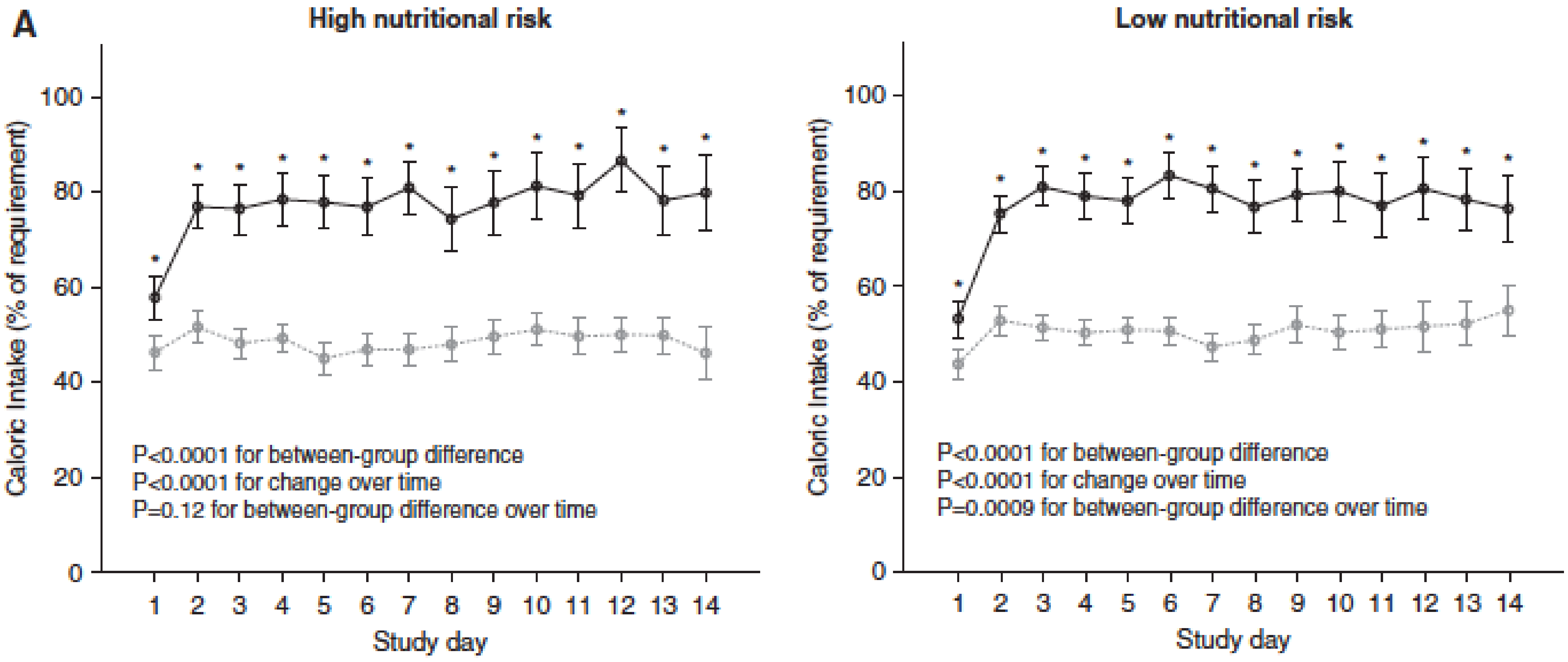
Outcome	Permissive Underfeeding (N=448)	Standard Feeding (N=446)	Relative Risk (95% CI)	P Value
Hypoglycemia — no. (%)	6 (1.3)	7 (1.6)	0.85 (0.29–2.52)	0.77
Hypokalemia — no. (%)	101 (22.5)	91 (20.4)	1.10 (0.86–1.42)	0.44
Hypomagnesemia — no. (%)	127 (28.3)	131 (29.4)	0.97 (0.79–1.19)	0.74
Hypophosphatemia — no. (%)	267 (59.6)	261 (58.5)	1.01 (0.91–1.14)	0.74
Transfusion of packed red cells — no. (%)	141 (31.5)	142 (31.8)	0.99 (0.82–1.20)	0.91
Incident renal-replacement therapy — no./total no. (%)	29/406 (7.1)	45/396 (11.4)	0.63 (0.40–0.98)	0.04
ICU-associated infection — no. (%)	161 (35.9)	169 (37.9)	0.95 (0.80–1.13)	0.54
Urinary tract infection — no. (%)	45 (10.0)	48 (10.8)	0.93 (0.64–1.37)	0.73
Catheter-related infection — no. (%)	11 (2.5)	19 (4.3)	0.58 (0.28–1.20)	0.13
Ventilator-associated pneumonia — no. (%)	81 (18.1)	90 (20.2)	0.90 (0.68–1.17)	0.43
ICU-associated severe sepsis or septic shock — no. (%)	61 (13.6)	58 (13.0)	1.05 (0.75–1.46)	0.79
Feeding intolerance — no. (%)	67 (15.0)	79 (17.7)	0.84 (0.63–1.14)	0.26
Diarrhea — no. (%)	97 (21.7)	117 (26.2)	0.83 (0.65–1.04)	0.11

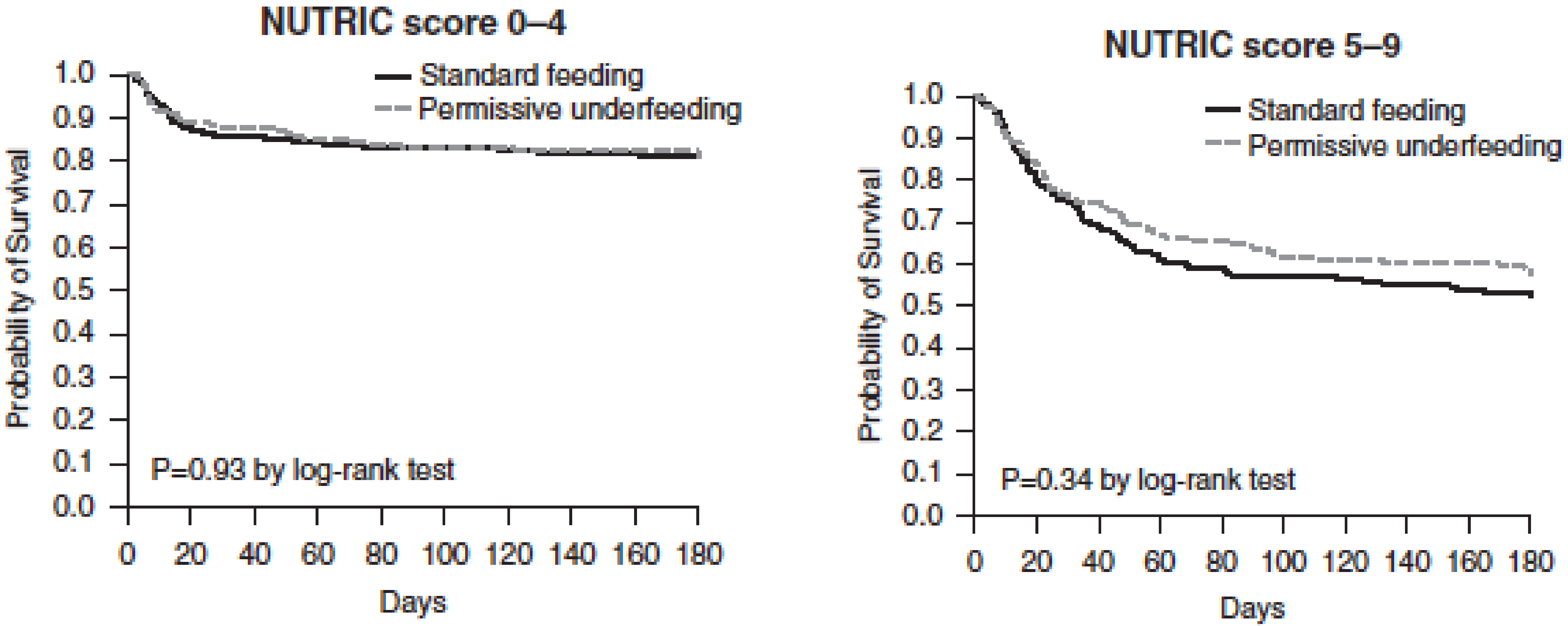
Permissive Underfeeding or Standard Enteral Feeding in High– and Low–Nutritional-Risk Critically Ill Adults

Post Hoc Analysis of the PermiT Trial

Yaseen M. Arabi[1], Abdulaziz S. Aldawood[1], Hasan M. Al-Dorzi[1], Hani M. Tamim[1,2], Samir H. Haddad[1], Gwynne Jones[3]

High nutritional ris= score 5–9 vs low nutritional risk=score 0–4




NUTRIC score 0–4
Standard feeding
Permissive underfeeding
Probability of Survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
P=0.93 by log-rank test
0
20
40
60
80
100
120
140
160
180
Days
NUTRIC score 5–9
Standard feeding
Permissive underfeeding
Probability of Survival
P=0.34 by log-rank test
Days

Outcomes	High–Nutritional-Risk Group (*n* = 378) Permissive Underfeeding (*n* = 189)	Standard Feeding (*n* = 189)	Adjusted Odds Ratio or Correlation Coefficient (95% CI)	*P* Value	Low–Nutritional-Risk Group (*n* = 516) Permissive Underfeeding (*n* = 259)	Standard Feeding (*n* = 257)	Adjusted Odds Ratio or Correlation Coefficient (95% CI)	*P* Value	*P* Value for Interaction
28-d mortality, n (%)	56/189 (29.6)	59/189 (31.2)	0.93 (0.60 to 1.44)	0.74	37/258 (14.3)	38/255 (14.9)	0.93 (0.56 to 1.53)	0.76	0.93
90-d mortality, n (%)	75/189 (39.7)	83/189 (43.9)	0.84 (0.56 to 1.27)	0.40	46/256 (18.0)	44/251 (17.5)	1.01 (0.64 to 1.61)	0.96	0.53
180-d mortality, n (%)	81/188 (43.1)	90/189 (47.6)	0.86 (0.57 to 1.29)	0.45	50/250 (20.0)	50/247 (20.2)	0.96 (0.61 to 1.50)	0.85	0.60
ICU mortality, n (%)	43/189 (22.8)	51/189 (27.0)	0.80 (0.50 to 1.27)	0.34	29/259 (11.2)	34/257 (13.2)	0.82 (0.48 to 1.39)	0.46	0.91
Hospital mortality, n (%)	67/188 (35.6)	80/189 (42.3)	0.73 (0.48 to 1.11)	0.14	41/259 (15.8)	43/256 (16.8)	0.90 (0.56 to 1.45)	0.67	0.50
ICU LOS, d, median (Q1 to Q3)	13.0 (8.0 to 21.0)	14 (9.0 to 22.0)	−1.4 (−4.0 to 1.3)	0.30	13.0 (7.0 to 20.0)	13.0 (8.0 to 19.0)	−0.04 (−1.9 to 1.8)	0.96	0.39
Hospital LOS, d, median (Q1 to Q3)	29.0 (16.0 to 52.5)	35.0 (17.0 to 62.0)	−8.5 (−21.5 to 4.4)	0.20	27.0 (14.0 to 55.0)	27.0 (13.0 to 65.0)	−5.2 (−18.2 to 7.9)	0.44	0.72
Ventilation duration, d, median (Q1 to Q3)	9.0 (6.0 to 16.0)	10.0 (5.0 to 17.0)	−1.9 (−4.7 to 0.9)	0.18	9.0 (5.0 to 14.0)	9.0 (5.0 to 15.0)	−2.6 (−5.9 to 0.7)	0.13	0.72
PRBC transfusions, n (%)	81/189 (42.9)	82/189 (43.4)	1.02 (0.67 to 1.53)	0.94	60/259 (23.2)	60/257 (23.4)	0.97 (0.64 to 1.47)	0.89	0.90
Cumulative PRBC transfusion over 14 d, units, mean ± SD	0.17 ± 0.37	0.15 ± 0.25	0.01 (−0.05 to 0.08)	0.72	0.10 ± 0.20	0.10 ± 0.30	−0.02 (−0.06 to 0.02)	0.41	0.46
Hypoglycemia, n (%)	6/189 (3.2)	5/189 (2.7)	1.22 (0.37 to 4.09)	0.75	0/259 (0.0)	2/257 (0.80)	NA	NA	NA
Hypokalemia, n (%)	44/189 (23.3)	50/189 (26.5)	0.80 (0.49 to 1.28)	0.34	57/259 (22.0)	41/257(16.0)	1.48 (0.95 to 2.32)	0.08	0.06
Hypomagnesemia, n (%)	44/189 (23.3)	59/189 (31.2)	0.67 (0.42 to 1.06)	0.08	83/259 (32.1)	72/257 (28.0)	1.21 (0.83 to 1.77)	0.32	0.05
Hypophosphatemia, n (%)	108/189 (57.1)	99/189 (52.4)	1.16 (0.76 to 1.75)	0.49	159/259 (61.4)	162/257 (63.0)	0.96 (0.67 to 1.37)	0.81	0.46
Incident renal-replacement therapy, n (%)	22/153 (14.4)	35/148 (23.7)	0.45 (0.23 to 0.89)	0.02	7/253 (2.8)	10/248 (4.0)	0.55 (0.18 to 1.66)	0.29	0.61
Healthcare-associated infections, n (%)	66/189 (34.9)	73/189 (38.6)	0.85 (0.56 to 1.30)	0.46	95/259 (36.7)	96/257 (37.4)	0.99 (0.69 to 1.41)	0.94	0.60
Urinary tract infection, n (%)	28/189 (14.8)	25/189 (13.2)	1.12 (0.63 to 2.02)	0.70	17/259 (6.6)	23/257 (9.0)	0.72 (0.37 to 1.37)	0.31	0.36
Catheter-related bloodstream infection, n (%)	2/189 (1.1)	8/189 (4.2)	0.24 (0.05 to 1.16)	0.08	9/259 (3.5)	11/257 (4.3)	0.81 (0.33 to 1.98)	0.64	0.19
Ventilator-associated pneumonia, n (%)	25/189 (13.2)	33/189 (17.5)	0.72 (0.41 to 1.27)	0.25	56/259 (21.6)	57/257 (22.2)	0.99 (0.65 to 1.51)	0.95	0.41
ICU-associated severe sepsis or septic shock, n (%)	1/189 (0.5)	1/189 (0.5)	1.7 (0.09 to 33.17)	0.73	2/259 (0.8)	1/257 (0.4)	1.99 (0.18 to 22.11)	0.57	0.73
Feeding intolerance, n (%)	36/189 (19.1)	37/189 (19.6)	0.97 (0.58 to 1.61)	0.90	31/259 (12.0)	42/257 (16.3)	0.71 (0.43 to 1.17)	0.18	0.34
Diarrhea, n (%)	55/189 (29.1)	66/189 (34.9)	0.77 (0.50 to 1.18)	0.23	42/259 (16.2)	51/257 (19.8)	0.75 (0.48 to 1.18)	0.22	0.86

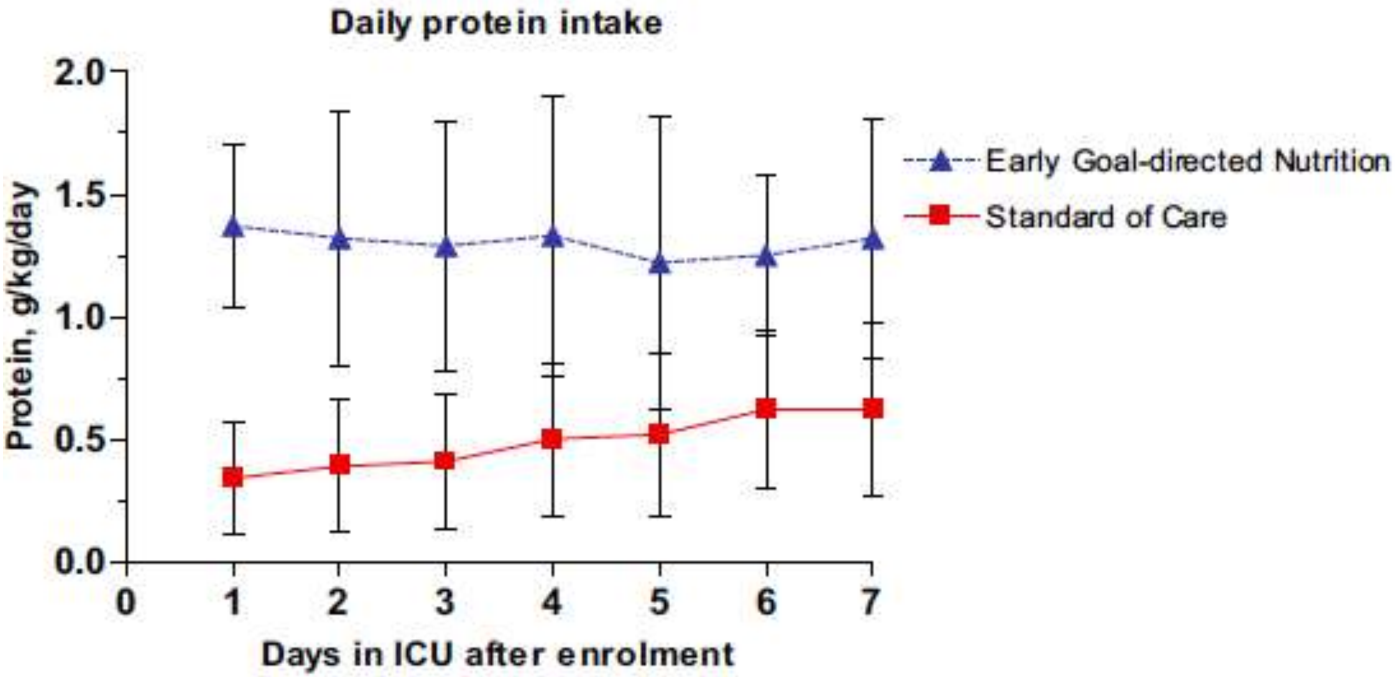
Early goal-directed nutrition versus standard of care in adult intensive care patients: the single-centre, randomised, outcome assessor-blinded EAT-ICU trial

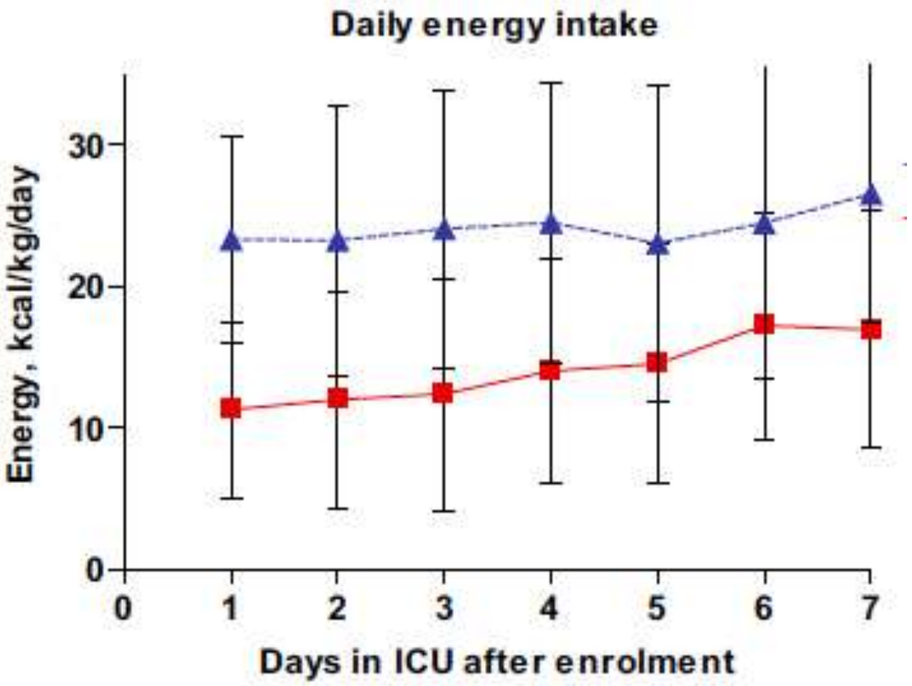
Matilde Jo Allingstrup[1], Jens Kondrup[2], Jørgen Wiis[1], Casper Claudius[1], Ulf Gøttrup Pedersen[1],

Methods: We randomised acutely admitted, mechanically ventilated ICU patients expected to stay longer than 3 days in the ICU. In the EGDN group we estimated nutritional requirements by indirect calorimetry and 24-h urinary urea aiming at covering 100% of requirements from the first full trial day using enteral and parenteral nutrition. In the standard of care group we aimed at providing 25 kcal/kg/day by enteral nutrition. If this was not met by day 7, patients were supplemented with parenteral nutrition. The primary outcome was physical component summary (PCS) score of SF-36 at 6 months. We performed multiple imputation for data of the non-responders.

Admission type, no. (%)		
Medical	52 (52%)	43 (43%)
Emergency surgery	43 (43%)	53 (54%)
Elective surgery	5 (5%)	3 (3%)
Diagnoses and procedures, no. (%)		
Haematologic malignancy[c]	13 (13%)	12 (12%)
Multiple trauma	8 (8%)	10 (10%)
Severe sepsis	47 (47%)	47 (47%)
Dialysis on admission	6 (6%)	5 (5%)
Mechanical ventilation	100 (100%)	99 (100%)
Days in hospital before ICU admission, days	0.9 (0.2–4.1)	1.1 (0.2–4.8)
Time from ICU admission to randomisation, h	14 (10–20)	13 (7–20)

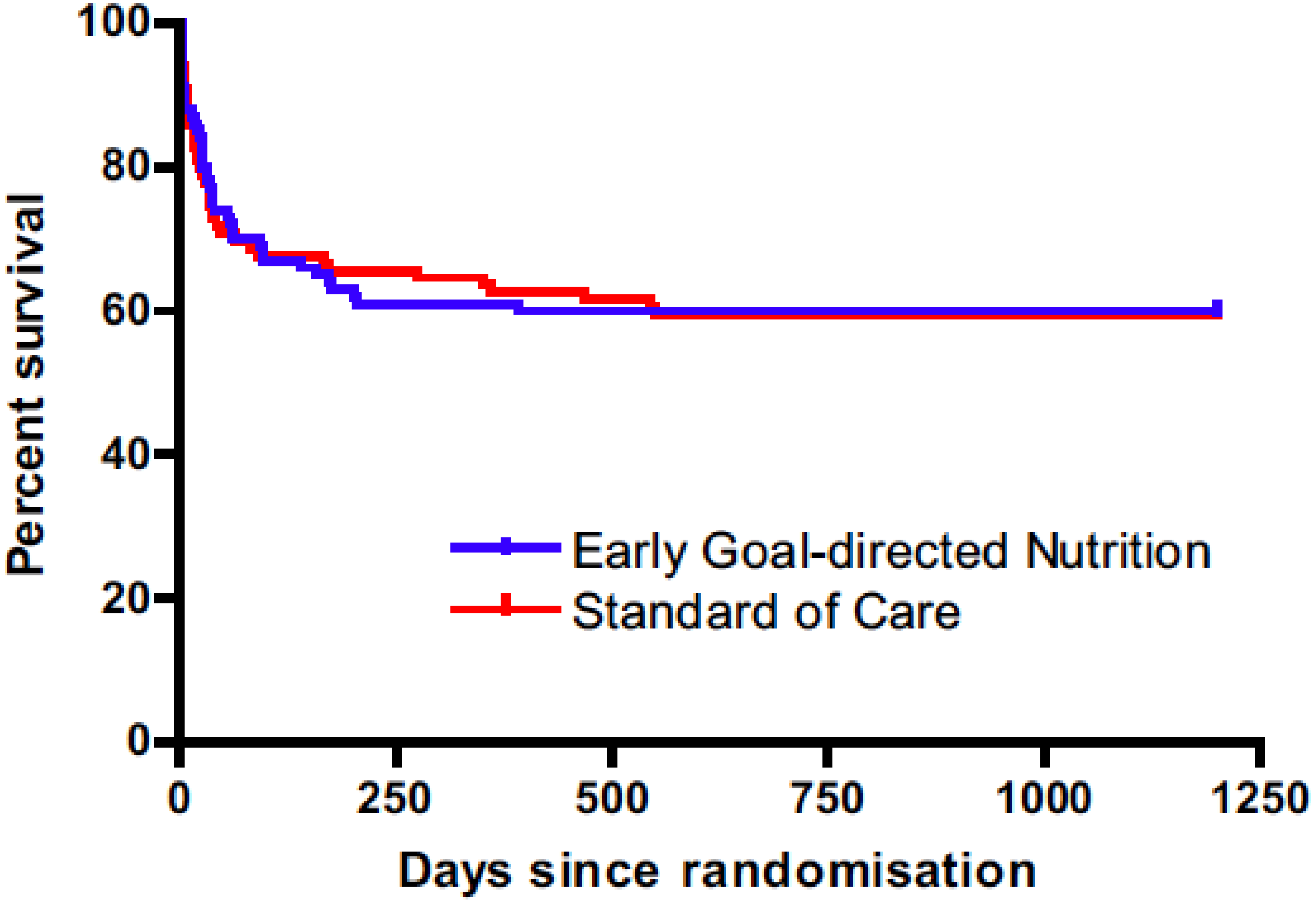
Variable	Early goal-directed nutrition ($N = 100$)	Standard of care ($N = 99$)
Measured[a] energy requirement, kcal/day	2069 (1816–2380)	1887 (1674–2244)
Calculated[b] energy requirement, kcal/day	1950 (1750–2125)	1875 (1650–2100)
Energy intake, kcal/day	1877 (1567–2254)	1061 (745–1470)
Energy balance[c], kcal/day	−66 (−157 to −6)	−787 (−1223 to −333)
Measured[d] protein requirement, g/kg/day	1.63 (1.36–2.05)	1.16 (0.89–1.62)
Protein intake, g/kg/day	1.47 (1.13–1.69)	0.50 (0.29–0.69)





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

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



No. at risk

EGDN	100	38	10
Std. of Care	99	41	8

In conclusion

- Early full feeding also increases the risk of refeeding
- Too low intake, below 50%, may lead to severe calorie debt and empty the energy reserves, reduce lean body mass and may increase infectious complications
- Optimal amount appeared to be between 70 and 100% of measured EE

EN vs PN ?

EN vs PN – summary of evidences

- No benefit in mortality.
- Increase in number of infectious complication with use of PN
- EN associated with significant reduction in ICU days compared to PN
- But no difference in hospital length of stay or ventilator days
- EN associated with increased vomiting

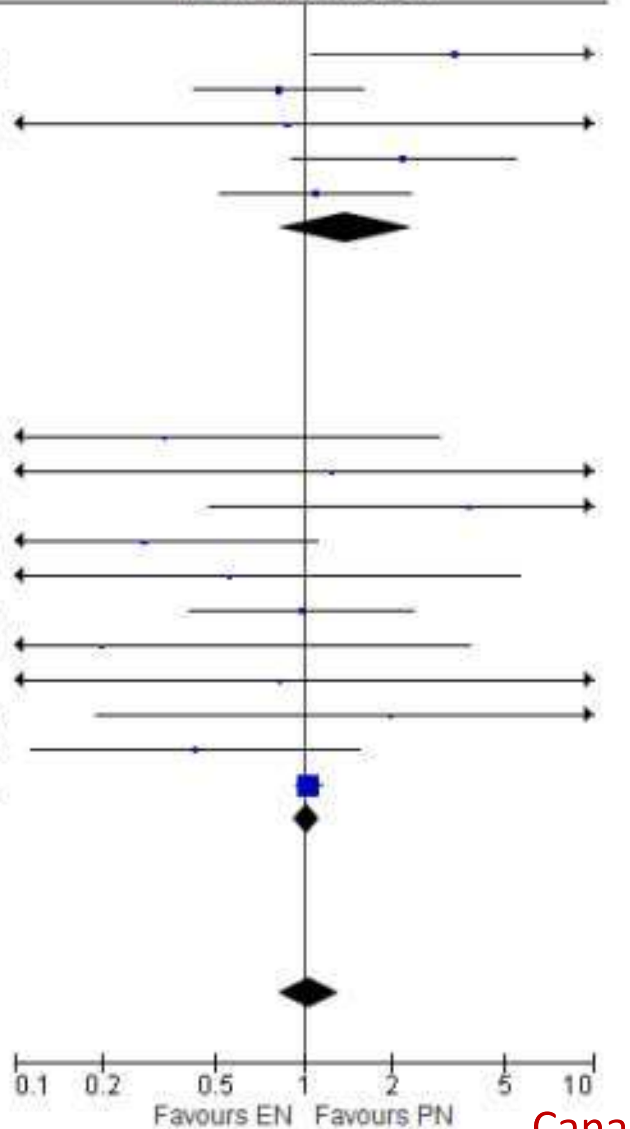
CANADIAN CLINICAL PRACTICE GUIDELINE 2015

EN vs PN mortality

Figure 1. Studies comparing EN vs PN: Mortality

Study or Subgroup	EN Events	EN Total	PN Events	PN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.2.1 Mortality (PN>EN kcal)							
Rapp	9	18	3	20	4.2%	3.33 [1.07, 10.43]	1983
Young	10	28	10	23	10.3%	0.82 [0.42, 1.62]	1987
Kudsk	1	51	1	45	0.8%	0.88 [0.06, 13.70]	1992
Woodcock	9	17	5	21	6.6%	2.22 [0.92, 5.40]	2001
Chen	11	49	10	49	8.6%	1.10 [0.51, 2.35]	2011
Subtotal (95% CI)		**163**		**158**	**30.4%**	**1.40 [0.82, 2.38]**	
Total events	40		29				
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 6.07$, df = 4 (P = 0.19); $I^2 = 34\%$							
Test for overall effect: Z = 1.24 (P = 0.22)							
1.2.2 Mortality (PN~EN kcal)							
Adams	1	23	3	23	1.2%	0.33 [0.04, 2.97]	1986
Dunham	1	12	1	15	0.8%	1.25 [0.09, 17.98]	1994
Borzotta	5	28	1	21	1.3%	3.75 [0.47, 29.75]	1994
Hadfield	2	13	6	11	2.9%	0.28 [0.07, 1.13]	1995
Kalfarentzos	1	18	2	20	1.1%	0.56 [0.05, 5.62]	1997
Cerra	7	31	8	35	6.5%	0.99 [0.40, 2.41]	1998
Casas	0	11	2	11	0.7%	0.20 [0.01, 3.74]	2007
Meirelles	1	12	1	10	0.8%	0.83 [0.06, 11.70]	2011
Sun	2	30	1	30	1.0%	2.00 [0.19, 20.90]	2013
Wang	3	61	7	60	3.2%	0.42 [0.11, 1.55]	2013
Harvey	450	1186	431	1185	50.0%	1.04 [0.94, 1.16]	2014
Subtotal (95% CI)		**1425**		**1421**	**69.6%**	**1.03 [0.93, 1.14]**	
Total events	473		463				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 9.59$, df = 10 (P = 0.48); $I^2 = 0\%$							
Test for overall effect: Z = 0.52 (P = 0.60)							
Total (95% CI)		**1588**		**1579**	**100.0%**	**1.04 [0.82, 1.33]**	
Total events	513		492				
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 16.94$, df = 15 (P = 0.32); $I^2 = 11\%$							
Test for overall effect: Z = 0.32 (P = 0.75)							
Test for subgroup differences: $Chi^2 = 1.24$, df = 1 (P = 0.27), $I^2 = 19.5\%$							

Risk Ratio
M-H, Random, 95% CI

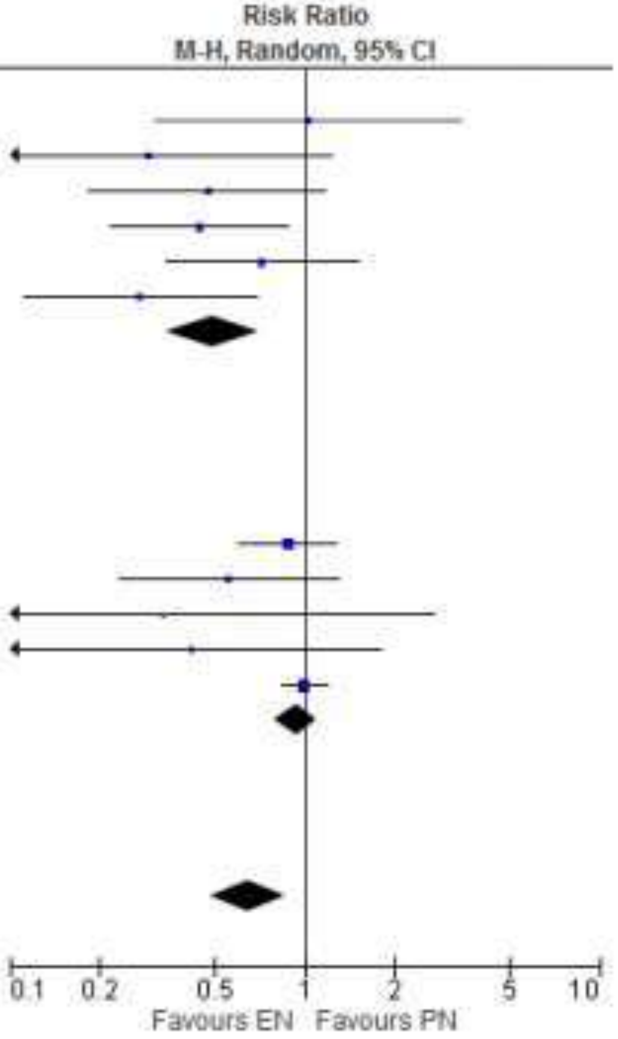


Canadian-2015 guidelines

Infectious complication EN vs PN

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%							

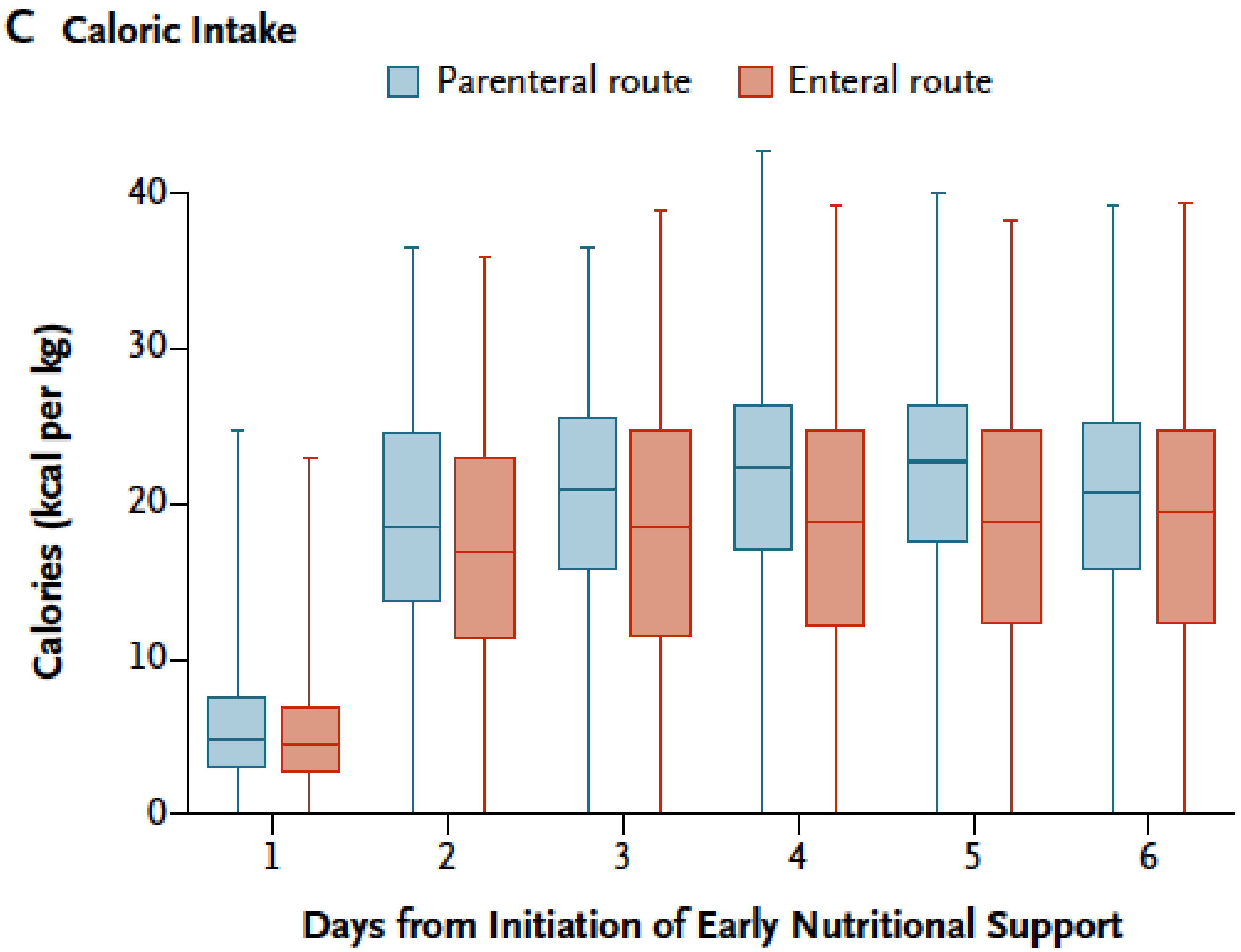


Canadian-2015 guidelines

Trial of the Route of Early Nutritional Support in Critically Ill Adults

Sheila E. Harvey, Ph.D., Francesca Parrott, M.Sci., David A. Harrison, Ph.D., Danielle E. Bear, M.Res., Ella Segaran, M.Sc., Richard Beale, M.B., B.S., Geoff Bellingan, M.D., Richard Leonard, M.B., B.Chir., Michael G. Mythen, M.D., and Kathryn M. Rowan, Ph.D., for the CALORIES Trial Investigators*

- Pragmatic, randomized trial
- EN vs PN with in 36 hrs x5
- N=2388



Outcome	Parenteral Group (N=1191)	Enteral Group (N=1197)	Absolute Difference between Groups (95% CI)	Relative Risk (95% CI)	P Value
Primary outcome: death within 30 days — no./total no. (%)	393/1188 (33.1)	409/1195 (34.2)	1.15 (−2.65 to 4.94)†	0.97 (0.86 to 1.08)‡	0.57§
Secondary outcomes					
No. of days alive and free of specified organ support up to 30 days¶					
Free of advanced respiratory support	14.3±12.1	14.3±12.2	0.04 (−0.94 to 1.01)		0.94
Free of advanced cardiovascular support	18.9±13.5	18.5±13.6	0.41 (−0.63 to 1.53)		0.44
Free of renal support	19.1±13.9	18.8±14.0	0.26 (−0.85 to 1.47)		0.66
Free of neurologic support	19.2±13.8	18.9±14.0	0.34 (−0.81 to 1.36)		0.57
Free of gastrointestinal support	13.0±11.7	13.2±11.8	−0.12 (−1.05 to 0.80)		0.81
No. of treated infectious complications per patient‖	0.22±0.60	0.21±0.56	0.01 (−0.04 to 0.06)		0.72
Noninfectious complications — no./total no. (%)					

Outcome	Parenteral Group (N=1191)	Enteral Group (N=1197)	Absolute Difference between Groups (95% CI)	Relative Risk (95% CI)	P Value
Noninfectious complications — no./total no. (%)					
Episodes of hypoglycemia	44/1191 (3.7)**	74/1197 (6.2)††	2.49 (0.75 to 4.22)†		0.006§
Elevated liver enzymes	212/1191 (17.8)	179/1197 (15.0)	−2.85 (−5.81 to 0.12)†		0.07§
Nausea requiring treatment	44/1191 (3.7)	53/1197 (4.4)	0.73 (−0.85 to 2.32)†		0.41§
Abdominal distention	78/1191 (6.5)	99/1197 (8.3)	1.72 (−0.38 to 3.82)†		0.12§
Vomiting	100/1191 (8.4)	194/1197 (16.2)	7.81 (5.20 to 10.43)†		<0.001§
New or substantially worsened pressure ulcers	181/1190 (15.2)	179/1195 (15.0)	−0.23 (−3.10 to 2.64)†		0.91§
Median no. of days in the ICU (IQR)‡‡	8.1 (4.0–15.8)	7.3 (3.9–14.3)			0.15
Median no. of days in acute care hospital (IQR)§§	17 (8–34)	16 (8–33)			0.32
Death — no./total no. (%)¶¶					
In the ICU	317/1190 (26.6)	352/1197 (29.4)		0.91 (0.80 to 1.03)	0.13§
In acute care hospital	431/1185 (36.4)	450/1186 (37.9)		0.96 (0.86 to 1.06)	0.44§
By 90 days	442/1184 (37.3)	464/1188 (39.1)		0.96 (0.86 to 1.06)	0.40§

What if early EN is contraindicated?

Should we start PN?

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

A Randomized Controlled Trial

- Standard care vs early PN
- Standard care-EN,PN, at =2,8 days
- Early PN-44 min after enrollment
- Multicenter study
- n=1372

Source of admission to ICU, No. (%)[b]		
Operating room	430 (63.0)	464 (68.1)
Other hospital	91 (13.3)	70 (10.3)
Emergency department	88 (12.9)	70 (10.3)
Hospital ward	71 (10.4)	72 (10.6)
Transfer from ICU	2 (0.3)	5 (0.7)
ICU readmission	0	0

Table 2. Mortality, Quality of Life, and Length of Stay

	Standard Care (n = 680)[a]	Early PN (n = 678)[a]	Risk Difference, % (95% CI)	Odds Ratio (95% CI)	*P* Value
Deaths before study day 60, No. (%)	155 (22.8)	146 (21.5)	−1.26 (−6.6 to 4.1)	0.93 (0.71 to 1.21)	.60
Covariate-adjusted deaths before study day 60[b]			0.04 (−4.2 to 4.3)	1.00 (0.76 to 1.31)	>.99
Quality of life and physical function, mean (SD)[c]	**(n = 525)**	**(n = 532)**	**Difference (95% CI)**		
RAND-36 general health status[d]	45.5 (26.8) (n = 516)	49.8 (27.6) (n = 525)	4.3 (0.95 to 7.58)		.01
ECOG performance status[e]	1.53 (1.1) (n = 516)	1.51 (1.1) (n = 525)	−0.02 (−0.15 to 0.11)		.70
RAND-36 physical function[f]	40.7 (29.6) (n = 513)	42.5 (30.8) (n = 524)	1.8 (−1.85 to 5.52)		.33
Discharge status and length of stay	**(n = 682)**	**(n = 681)**	**Difference (95% CI)**		
ICU stay, mean (95% CI), d	9.3 (8.9 to 9.7)	8.6 (8.2 to 9.0)	−0.75 (−1.47 to 0.04)		.06
Deaths before ICU discharge, No. (%)	100 (14.66)	81 (11.89)	−2.77% (−8.08% to 2.52%)		.15
Hospital stay, mean (95% CI), d	24.7 (23.7 to 25.8)	25.4 (24.4 to 26.6)	0.7 (−1.4 to 3.1)		.50
Deaths before hospital discharge, No. (%)	151 (22.1)	140 (20.6)	−1.58% (−6.91% to 3.69%)		.51

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; ECOG, Eastern Collaborative Oncology Group; ICU, intensive care unit; PN, parenteral nutrition.
[a] Five patients (2 standard care, 3 early PN) who were alive at hospital discharge prior to day 60 could not be contacted on study day 60 to determine vital status. These patients were considered “missing at random” for the intention-to-treat primary and adjusted primary outcome analysis.
[b] Covariate model controlled for confounding due to age, gender, body mass index, APACHE II score, chronic liver disease, chronic respiratory disease, and source of admission.
[c] Responses available for analysis as reported by survivors at day-60 interview.
[d] Scored on a scale from 0 to 100, with higher scores indicating better general health status.
[e] Scores range from 0 to 4, with lower scores indicating fewer physical limitations.
[f] Scored on a scale from 0 to 100, with higher scores indicating better physical function.

Table 3. Clinically Significant Organ Failure and Concomitant Interventions, Adjusted for Time at Risk (ICU Stay)[a]

	Mean (95% CI), Days per 10 Patient × ICU Days		Mean Difference (95% CI), Days per 10 Patient × ICU Days	*P* Value[b]
	Standard Care (n = 682)	Early PN (n = 681)		
Organ system failures[c]				
Renal	1.66 (1.51 to 1.82)	1.65 (1.51 to 1.81)	−0.01 (−0.28 to 0.33)	.98
Pulmonary	8.51 (8.34 to 8.69)	8.54 (8.37 to 8.71)	0.03 (−0.31 to 0.37)	.88
Hepatic	1.14 (1.09 to 1.20)	1.08 (1.03 to 1.14)	−0.06 (−0.16 to 0.06)	.15
Coagulation	2.23 (2.09 to 2.38)	1.89 (1.78 to 2.02)	−0.34 (−0.57 to −0.08)	.01
Cardiovascular	1.16 (1.05 to 1.27)	0.99 (0.89 to 1.09)	−0.17 (−0.34 to 0.04)	.11
MODs	4.04 (3.85 to 4.25)	3.93 (3.74 to 4.13)	−0.11 (−0.48 to 0.29)	.59
No. of organ failures[d]	1.47 (1.44 to 1.51)	1.42 (1.39 to 1.46)	−0.05 (−0.12 to 0.02)	.12
Concomitant therapies and tertiary outcomes				
Renal replacement therapy	0.99 (0.82 to 1.81)	0.80 (0.67 to 0.96)	−0.19 (−0.42 to 0.16)	.25
Invasive mechanical ventilation	7.73 (7.55 to 7.92)	7.26 (7.09 to 7.44)	−0.47 (−0.82 to −0.11)	.01
Pressure ulcer treatment[e]	0.87 (0.74 to 1.02)	0.78 (0.67 to 0.92)	−0.09 (−0.30 to 0.22)	.54
Low serum albumin (<2.5 g/dL)	5.47 (5.28 to 5.67)	5.76 (5.56 to 5.97)	0.29 (−0.10 to 0.71)	.15
Systemic antibiotic use	7.95 (7.78 to 8.12)	8.05 (7.88 to 8.22)	0.10 (−0.23 to 0.45)	.55
Witnessed aspiration[f]	1.59 (0.98 to 2.54)	1.96 (1.21 to 3.13)	0.37 (−0.80 to 3.45)	.66
With new pulmonary infiltrates[f]	0.48 (0.20 to 1.15)	0.71 (0.30 to 1.72)	0.23 (−0.36 to 0.37)	.65

Abbreviations: ICU, intensive care unit; MODs, multiple organ dysfunction syndrome; PN, parenteral nutrition.
[a] These measures are reported as crude counts, not adjusted for time at risk (ICU stay), in eTable 5.
[b] *P* values from negative binomial model, controlled for duration of risk (ICU stay).
[c] Organ failure was defined using the following measures: renal failure, creatinine >2.0 mg/dL; pulmonary failure, PaO_2:FiO_2 ratio <301; hepatic failure, total bilirubin >2.0 mg/dL; coagulation failure, platelets <81 x10^9/L; cardiovascular failure, systolic blood pressure <90 mm Hg, not fluid responsive; MODs, ≥2 organ system failures on the same day.
[d] Per patient per ICU day.
[e] Treatment for stage 1 or greater.
[f] Events per 1000 patient × ICU days.

Table 4. New Infections During Study

Patients With New Infections[a]	No. (%) Standard Care (n = 682)	No. (%) Early PN (n = 681)	Risk Difference (Exact 95% CI)	Exact P Value[b]
Catheter[c]	32 (4.69)	31 (4.55)	−0.14 (−5.45 to 5.12)	>.99
Catheter tip[c]	28 (4.11)	26 (3.82)	−0.29 (−5.60 to 5.01)	.89
Surgical wound	27 (3.96)	22 (3.23)	−0.73 (−6.04 to 4.57)	.56
Bloodstream	33 (4.84)	39 (5.73)	0.89 (−4.43 to 6.18)	.47
Abdominal	3 (0.44)	6 (0.88)	0.44 (−4.89 to 5.74)	.34
Clinically significant UTI	1 (0.15)	2 (0.29)	0.15 (−5.16 to 5.45)	.62
Airway or lung[d]	123 (18.04)	101 (14.83)	−3.20 (−8.52 to 2.08)	.12
CPIS-probable pneumonia[e]	96 (14.08)	81 (11.89)	−2.18 (−7.50 to 3.11)	.26
CPIS-confirmed pneumonia[f]	45 (6.60)	43 (6.31)	−0.28 (−5.60 to 5.01)	.91
Any major infection[g]	78 (11.4)	74 (10.9)	−0.57 (−5.89 to 4.72)	.80

Parenteral Nutrition

When should we start?

- EpaNIC
- N=4640,RCT
- Supplemental PN
- Day 1 vs day 8

Early versus Late Parenteral Nutrition in Critically Ill Adults

Michael P. Casaer, M.D., Dieter Mesotten, M.D., Ph.D.,

Variable	Late-Initiation Group (N=2328)	Early-Initiation Group (N=2312)	P Value
Safety outcome			
Vital status — no. (%)			
Discharged live from ICU within 8 days	1750 (75.2)	1658 (71.7)	0.007
Death			
In ICU	141 (6.1)	146 (6.3)	0.76
In hospital	242 (10.4)	251 (10.9)	0.63
Within 90 days after enrollment†	257 (11.2)	255 (11.2)	1.00
Nutrition-related complication — no. (%)	423 (18.2)	434 (18.8)	0.62
Hypoglycemia during intervention — no. (%)‡	81 (3.5)	45 (1.9)	0.001
Primary outcome			
Duration of stay in ICU§			
Median (interquartile range) — days	3 (2–7)	4 (2–9)	0.02
Duration >3 days — no. (%)	1117 (48.0)	1185 (51.3)	0.02
Hazard ratio (95% CI) for time to discharge alive from ICU	1.06 (1.00–1.13)		0.04

Primary outcome			
Duration of stay in ICU§			
Median (interquartile range) — days	3 (2–7)	4 (2–9)	0.02
Duration >3 days — no. (%)	1117 (48.0)	1185 (51.3)	0.02
Hazard ratio (95% CI) for time to discharge alive from ICU	1.06 (1.00–1.13)		0.04
Secondary outcome			
New infection — no. (%)			
Any	531 (22.8)	605 (26.2)	0.008
Airway or lung	381 (16.4)	447 (19.3)	0.009
Bloodstream	142 (6.1)	174 (7.5)	0.05
Wound	64 (2.7)	98 (4.2)	0.006
Urinary tract	60 (2.6)	72 (3.1)	0.28
Inflammation			
Median peak C-reactive protein level during ICU stay (interquartile range) — mg/liter	190.6 (100.8–263.2)	159.7 (84.3–243.5)	<0.001
Mechanical ventilation			
Median duration (interquartile range) — days	2 (1–5)	2 (1–5)	0.02
Duration >2 days — no. (%)	846 (36.3)	930 (40.2)	0.006
Hazard ratio (95% CI) for time to definitive weaning from ventilation	1.06 (0.99–1.12)		0.07
Tracheostomy — no. (%)	134 (5.8)	162 (7.0)	0.08

Variable	Late-Initiation Group (N=2328)	Early-Initiation Group (N=2312)	P Value
Kidney failure			
Modified RIFLE category — no. (%)¶	104 (4.6)	131 (5.8)	0.06
Renal-replacement therapy — no. (%)	201 (8.6)	205 (8.9)	0.77
Median duration of renal-replacement therapy (interquartile range) — days	7 (3–16)	10 (5–23)	0.008
Duration of hospital stay			
Median (interquartile range) — days	14 (9–27)	16 (9–29)	0.004
Duration >15 days — no. (%)	1060 (45.5)	1159 (50.1)	0.001
Hazard ratio (95% CI) for time to discharge alive from hospital	1.06 (1.00–1.13)		0.04
Functional status at hospital discharge			
Distance on 6-min walk test			
No. of patients evaluated	624	603	
Distance (interquartile range) — m	277 (210–345)	283 (205–336)	0.57
Activities of daily living			
No. of patients evaluated	1060	996	
Independent in all activities — no. (%)	779 (73.5)	752 (75.5)	0.31
Mean total incremental health care cost (interquartile range) — €‖	16,863 (8,793–17,774)	17,973 (8,749–18,677)	0.04

In conclusion-in early initiation group

- Fewer discharges
- Long ICU LOS
- More new infections
- More inflammation
- More time on vent
- More renal failure
- Cost more money

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.)

Adequately nourished critically ill patients

- No PN within the first 7 days
- Associated with unnecessary costs
- < 7 days of an ICU stay associated with harm,or at best no benefit,interms of survival and ICU length of stay

Severely malnourished

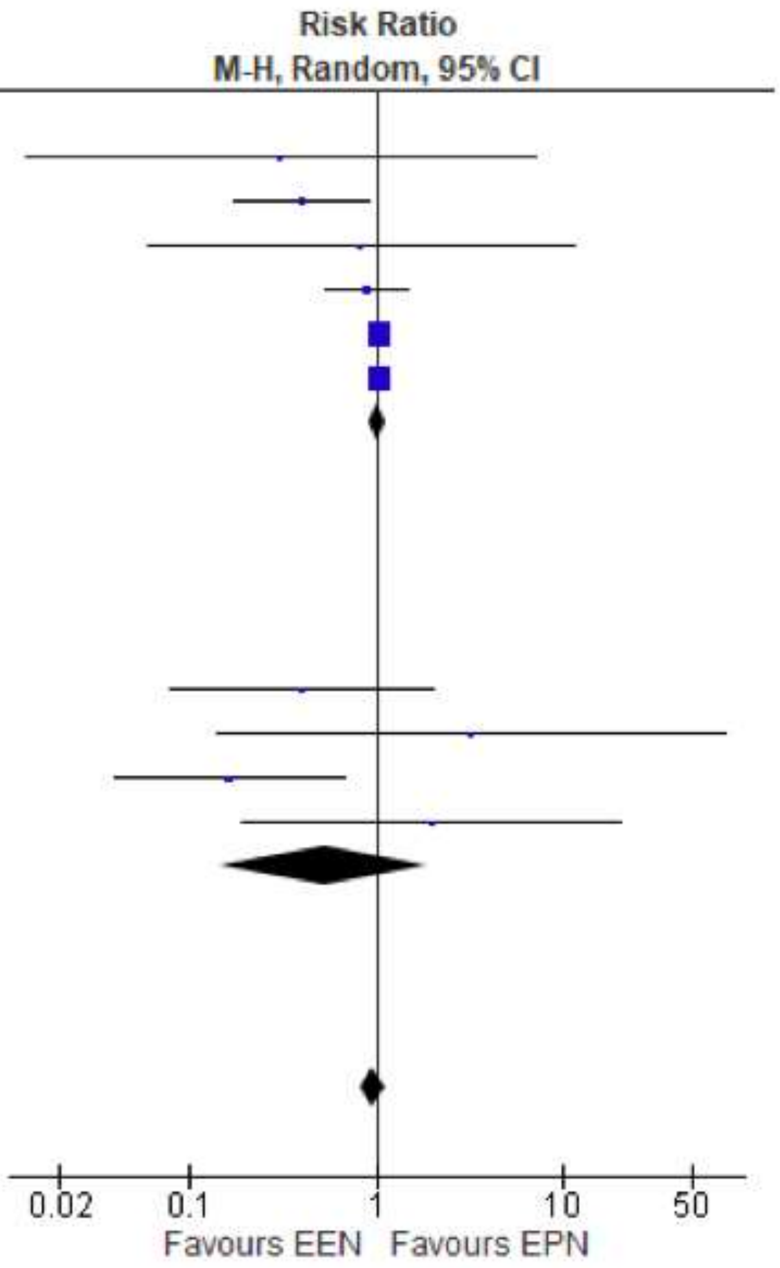
- may be benefit from earlier PN

Early EN vs Early PN ?

II, Figure 1: Mortality (Includes Meta-analyses II A and II B)

ESPN-2019 guidelines

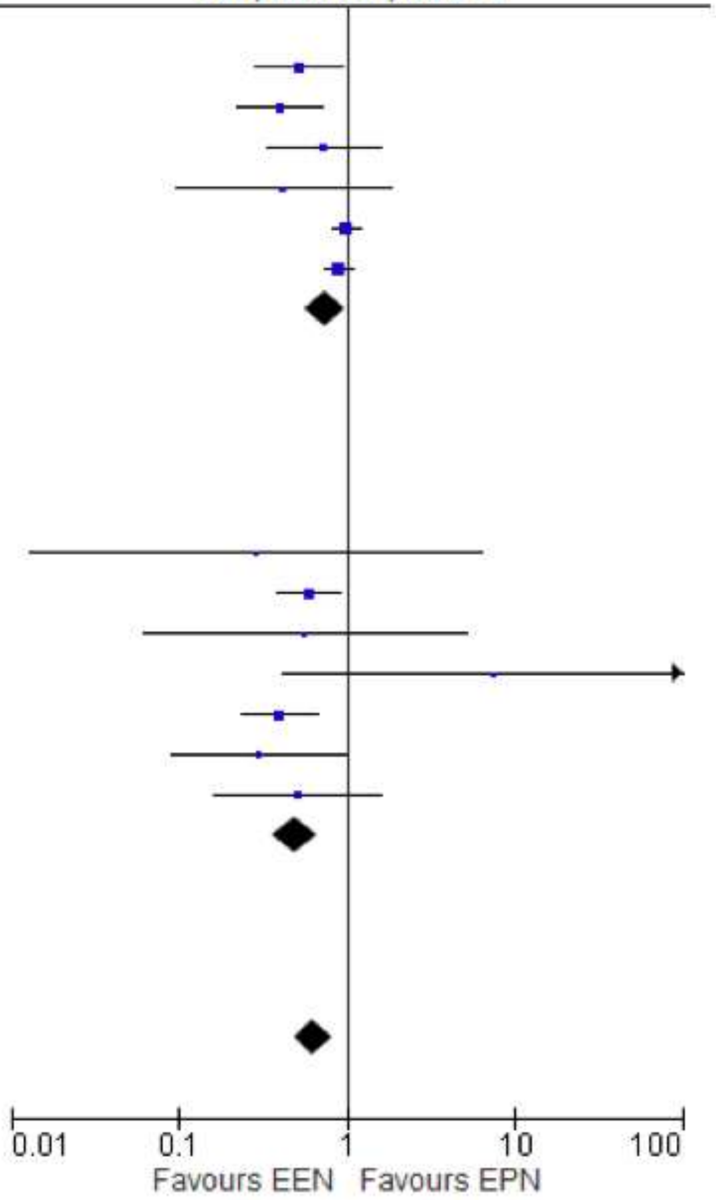
Study or Subgroup	EEN Events	EEN Total	EPN Events	EPN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.1.1 ICU studies							
Kompan 2004	0	27	1	25	0.3%	0.31 [0.01, 7.26]	2004
Lam 2008	6	41	15	41	3.5%	0.40 [0.17, 0.93]	2008
Justo Meirelles 2011	1	12	1	10	0.4%	0.83 [0.06, 11.70]	2011
Altintas 2011	13	30	20	41	8.3%	0.89 [0.53, 1.49]	2011
Harvey 2014 CALORIES Trial	450	1186	431	1185	41.8%	1.04 [0.94, 1.16]	2014
Reignier 2017 NUTRIREA-2	498	1202	479	1208	42.9%	1.04 [0.95, 1.15]	2017
Subtotal (95% CI)		**2498**		**2510**	**97.0%**	**1.03 [0.93, 1.13]**	
Total events	968		947				
Heterogeneity: Tau² = 0.00; Chi² = 5.89, df = 5 (P = 0.32); I² = 15%							
Test for overall effect: Z = 0.52 (P = 0.60)							
1.1.2 Studies with unclear proportion of ICU patients							
Bozzetti 2001	2	159	5	158	1.0%	0.40 [0.08, 2.02]	2001
Eckerwall 2006	1	23	0	25	0.3%	3.25 [0.14, 76.01]	2006
Petrov 2006	2	35	12	34	1.3%	0.16 [0.04, 0.67]	2006
Sun 2013	2	30	1	30	0.5%	2.00 [0.19, 20.90]	2013
Subtotal (95% CI)		**247**		**247**	**3.0%**	**0.53 [0.15, 1.91]**	
Total events	7		18				
Heterogeneity: Tau² = 0.68; Chi² = 5.06, df = 3 (P = 0.17); I² = 41%							
Test for overall effect: Z = 0.98 (P = 0.33)							
Total (95% CI)		**2745**		**2757**	**100.0%**	**0.97 [0.82, 1.14]**	
Total events	975		965				
Heterogeneity: Tau² = 0.01; Chi² = 14.62, df = 9 (P = 0.10); I² = 38%							
Test for overall effect: Z = 0.42 (P = 0.68)							
Test for subgroup differences: Chi² = 1.02, df = 1 (P = 0.31), I² = 2.1%							



II., Figure 2: Infectious complications (Includes Meta-analyses II A and II B)

Study or Subgroup	EEN Events	EEN Total	EPN Events	EPN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
2.1.1 ICU studies							
Kompan 2004	9	27	16	25	9.5%	0.52 [0.28, 0.96]	2004
Lam 2008	10	41	25	41	9.8%	0.40 [0.22, 0.72]	2008
Altintas 2011	7	30	13	41	7.0%	0.74 [0.33, 1.62]	2011
Justo Meirelles 2011	2	12	4	10	2.7%	0.42 [0.10, 1.82]	2011
Harvey 2014	194	1197	194	1191	18.3%	0.99 [0.83, 1.19]	2014
Reignier 2017	173	1202	194	1208	18.2%	0.90 [0.74, 1.08]	2017
Subtotal (95% CI)		**2509**		**2516**	**65.6%**	**0.75 [0.57, 0.98]**	
Total events	395		446				
Heterogeneity: Tau² = 0.05; Chi² = 12.66, df = 5 (P = 0.03); I² = 61%							
Test for overall effect: Z = 2.14 (P = 0.03)							
2.1.2 Studies with unclear proportion of ICU patients							
Aiko 2001	0	13	1	11	0.7%	0.29 [0.01, 6.38]	2001
Bozzetti 2001	25	159	42	158	12.7%	0.59 [0.38, 0.92]	2001
Gupta 2003	1	8	2	9	1.3%	0.56 [0.06, 5.09]	2003
Eckerwall 2006	3	23	0	25	0.8%	7.58 [0.41, 139.32]	2006
Petrov 2006	11	35	27	34	11.1%	0.40 [0.24, 0.66]	2006
Sun 2013	3	30	10	30	3.8%	0.30 [0.09, 0.98]	2013
Boelens 2014	4	61	8	62	4.1%	0.51 [0.16, 1.60]	2014
Subtotal (95% CI)		**329**		**329**	**34.4%**	**0.50 [0.37, 0.67]**	
Total events	47		90				
Heterogeneity: Tau² = 0.00; Chi² = 5.66, df = 6 (P = 0.46); I² = 0%							
Test for overall effect: Z = 4.49 (P < 0.00001)							
Total (95% CI)		**2838**		**2845**	**100.0%**	**0.63 [0.49, 0.82]**	
Total events	442		536				
Heterogeneity: Tau² = 0.09; Chi² = 29.81, df = 12 (P = 0.003); I² = 60%							
Test for overall effect: Z = 3.50 (P = 0.0005)							
Test for subgroup differences: Chi² = 3.92, df = 1 (P = 0.05), I² = 74.5%							

Risk Ratio
M-H, Random, 95% CI

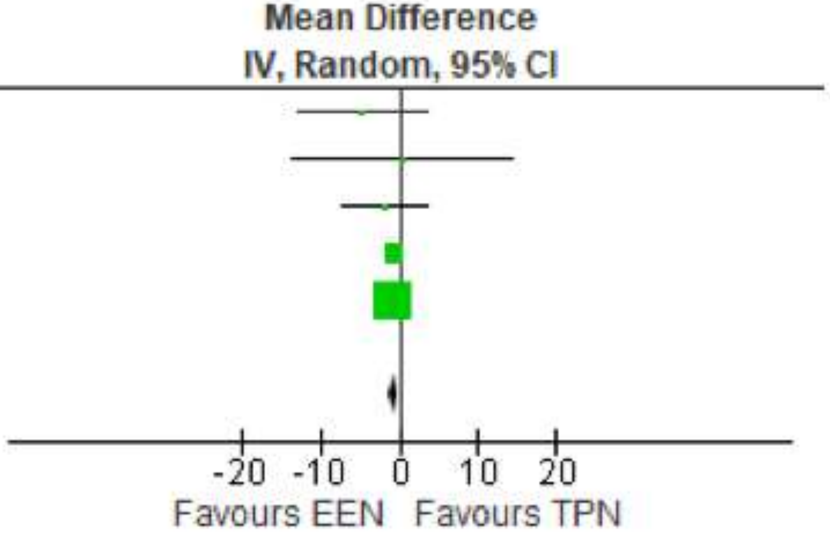


early EN vs early PN ?

II., Figure 3: Intensive Care Unit Length of Stay (Includes Meta-analysis II A only)

Study or Subgroup	EEN Mean	EEN SD	EEN Total	EPN Mean	EPN SD	EPN Total	Weight	Mean Difference IV, Random, 95% CI	Year
Kompan 2004	15.9	9.7	27	20.6	18.5	25	0.5%	-4.70 [-12.82, 3.42]	2004
Justo Meirelles 2011	15	17.6	12	14.7	15.5	10	0.2%	0.30 [-13.54, 14.14]	2011
Altintas 2011	15.3	10.1	30	17	13	41	1.1%	-1.70 [-7.08, 3.68]	2011
Harvey 2014	11.3	12.5	1197	12	13.5	1190	29.5%	-0.70 [-1.74, 0.34]	2014
Reignier 2017	10	8.2	1202	10.7	8.9	1208	68.8%	-0.70 [-1.38, -0.02]	2017
Total (95% CI)			**2468**			**2474**	**100.0%**	**-0.73 [-1.30, -0.16]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.07, df = 4 (P = 0.90); I² = 0%
Test for overall effect: Z = 2.52 (P = 0.01)



ESPN-2019 guidelines

early EN vs early PN ?

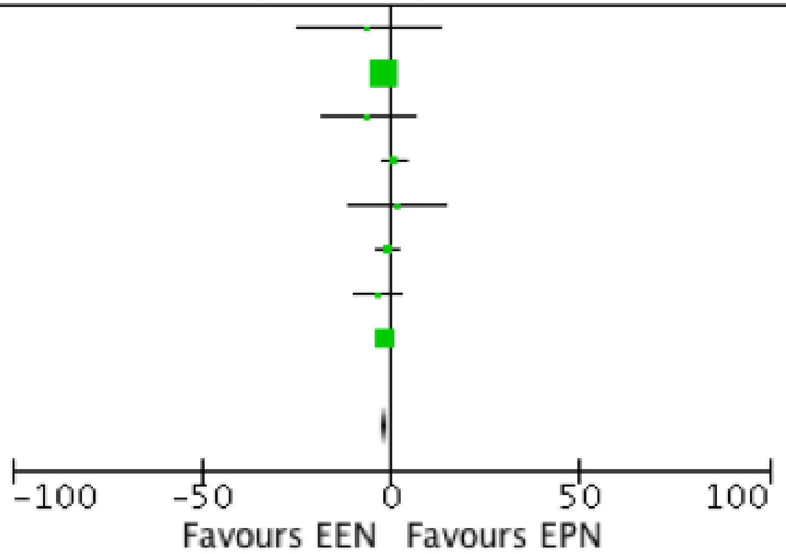
II., Figure 4: Hospital Length of Stay (Includes Meta-analyses II A and II B)

Study or Subgroup	EEN Mean	EEN SD	EEN Total	EPN Mean	EPN SD	EPN Total	Weight	Mean Difference IV, Random, 95% CI	Year
Aiko 2001	34	14.4	13	40	29.8	11	0.2%	-6.00 [-25.27, 13.27]	2001
Bozzetti 2001	13.4	4.1	159	15	5.6	158	52.8%	-1.60 [-2.68, -0.52]	2001
Gupta 2003	8.3	8.9	8	14.3	16.6	9	0.4%	-6.00 [-18.48, 6.48]	2003
Eckerwall 2006	10	5.5	23	9	6.3	25	5.5%	1.00 [-2.34, 4.34]	2006
Altintas 2011	32.9	30.2	30	31	22.3	41	0.4%	1.90 [-10.88, 14.68]	2011
Harvey 2014	26.8	33.2	1197	27.5	33.9	1191	8.5%	-0.70 [-3.39, 1.99]	2014
Boelens 2014	13.5	17.2	61	16.7	18.1	62	1.6%	-3.20 [-9.44, 3.04]	2014
Reignier 2017	19	17.8	1202	20	17.8	1208	30.6%	-1.00 [-2.42, 0.42]	2017
Total (95% CI)			**2693**			**2705**	**100.0%**	**-1.23 [-2.02, -0.45]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.82$, $df = 7$ ($P = 0.80$); $I^2 = 0\%$

Test for overall effect: $Z = 3.07$ ($P = 0.002$)

Mean Difference IV, Random, 95% CI



Intermittent vs continuous

ESPN-2019 guidelines

Intermittent vs continuous ?

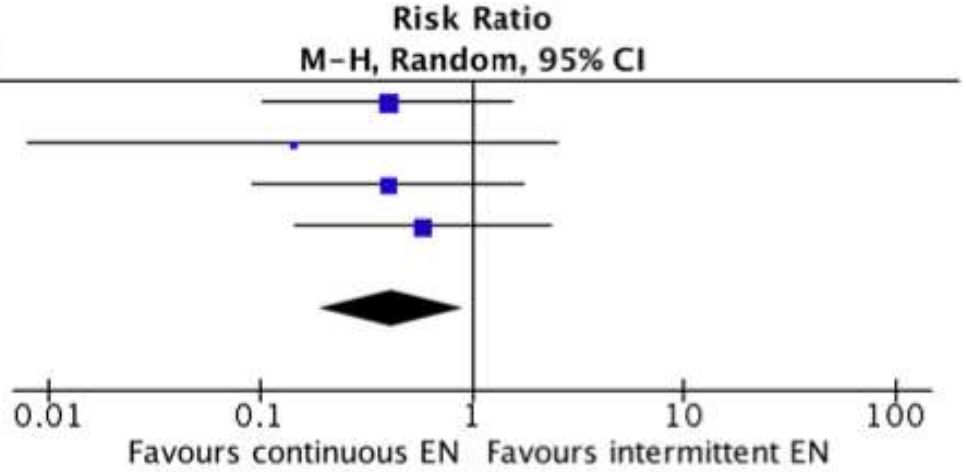
Intermittent vs continuous

III., Figure 1: Diarrhea

	Continuous EN		Intermittent EN			Risk Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Steevens 2002	2	9	5	9	33.3%	0.40 [0.10, 1.55]	2002
Serpa 2006	0	14	3	14	7.4%	0.14 [0.01, 2.53]	2006
Kadami 2014	2	15	5	15	28.1%	0.40 [0.09, 1.75]	2014
MacLeod 2017	3	81	5	79	31.3%	0.59 [0.14, 2.37]	2017
Total (95% CI)		**119**		**117**	**100.0%**	**0.42 [0.19, 0.91]**	
Total events	7		18				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.77$, df = 3 (P = 0.86); $I^2 = 0\%$

Test for overall effect: Z = 2.19 (P = 0.03)

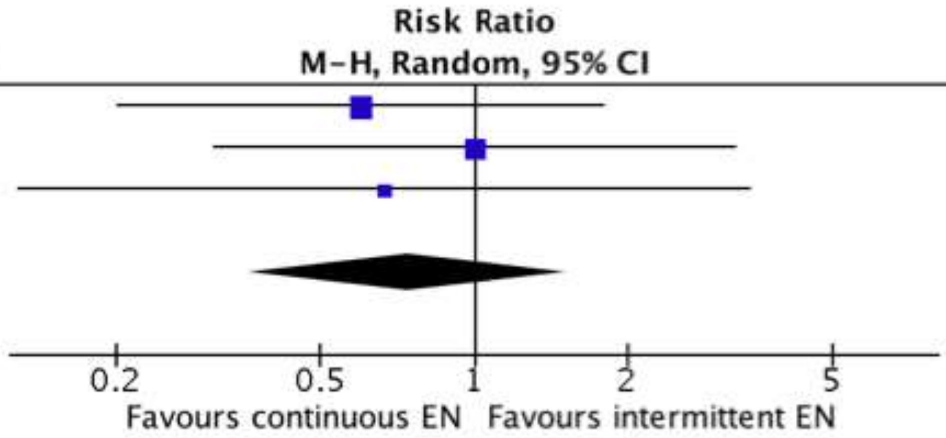


Intermittent vs continuous

III., Figure 2: High Gastric Residual Volumes

Study or Subgroup	Continuous EN Events	Continuous EN Total	Intermittent EN Events	Intermittent EN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Steevens 2002	3	9	5	9	43.2%	0.60 [0.20, 1.79]	2002
Serpa 2006	4	14	4	14	37.6%	1.00 [0.31, 3.23]	2006
Kadami 2014	2	15	3	15	19.2%	0.67 [0.13, 3.44]	2014
Total (95% CI)		**38**		**38**	**100.0%**	**0.74 [0.36, 1.52]**	
Total events	9		12				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.41$, df = 2 (P = 0.81); $I^2 = 0\%$
Test for overall effect: Z = 0.81 (P = 0.42)



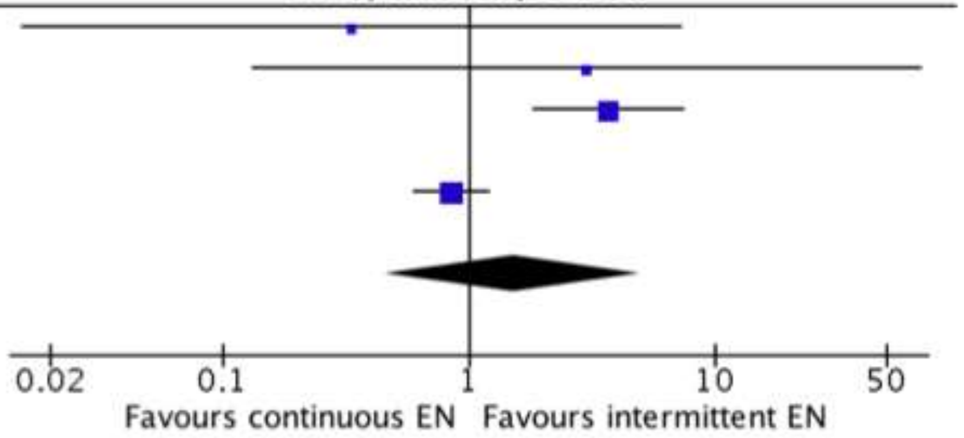
Intermittent vs continuous

III., Figure 3: Aspiration or pneumonia

	Continuous EN		Intermittent EN			Risk Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Steevens 2002	0	9	1	9	11.2%	0.33 [0.02, 7.24]	2002
Serpa 2006	1	14	0	14	11.0%	3.00 [0.13, 67.91]	2006
Chen 2006	26	51	8	58	37.0%	3.70 [1.84, 7.42]	2006
Kadami 2014	0	15	0	15		Not estimable	2014
MacLeod 2017	33	81	38	79	40.8%	0.85 [0.60, 1.20]	2017
Total (95% CI)		**170**		**175**	**100.0%**	**1.51 [0.45, 5.03]**	
Total events	60		47				

Heterogeneity: $Tau^2 = 0.89$; $Chi^2 = 15.44$, df = 3 (P = 0.001); $I^2 = 81\%$
Test for overall effect: Z = 0.67 (P = 0.50)

Risk Ratio
M-H, Random, 95% CI



Gastric vs post pyloric feeding ?

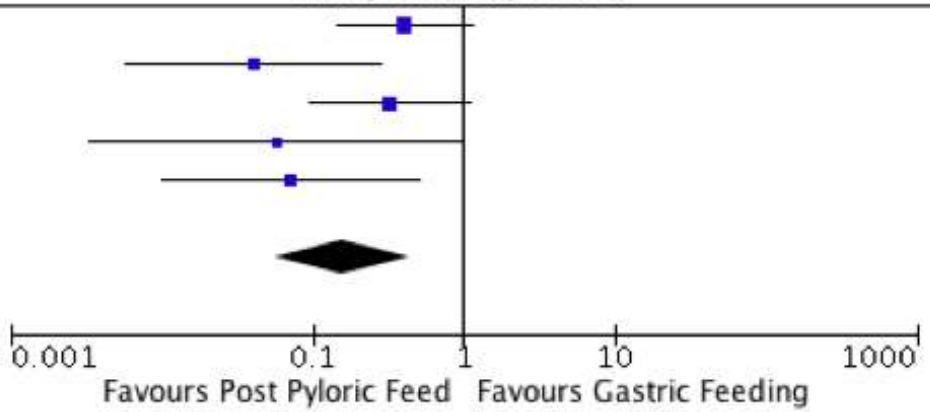
Gastric vs post pyloric feeding

IV. Figure. Feeding Intolerance (5 RCTs, n=521)

	Post Pyloric Feeding		Gastric Feeding			Risk Ratio		Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**	**M-H, Random, 95% CI**
Davies 2002	4	31	11	35	29.8%	0.41 [0.15, 1.16]	2002	
Montejo 2002	1	50	25	51	16.8%	0.04 [0.01, 0.29]	2002	
Acosta-Escribano 2010	3	50	10	54	26.6%	0.32 [0.09, 1.11]	2010	
Davies 2012	0	91	8	89	10.1%	0.06 [0.00, 0.98]	2012	
Wan 2015	1	35	14	35	16.7%	0.07 [0.01, 0.51]	2015	
Total (95% CI)		**257**		**264**	**100.0%**	**0.16 [0.06, 0.45]**		
Total events	9		68					

Heterogeneity: $Tau^2 = 0.65$; $Chi^2 = 7.94$, df = 4 (P = 0.09); $I^2 = 50\%$

Test for overall effect: Z = 3.48 (P = 0.0005)



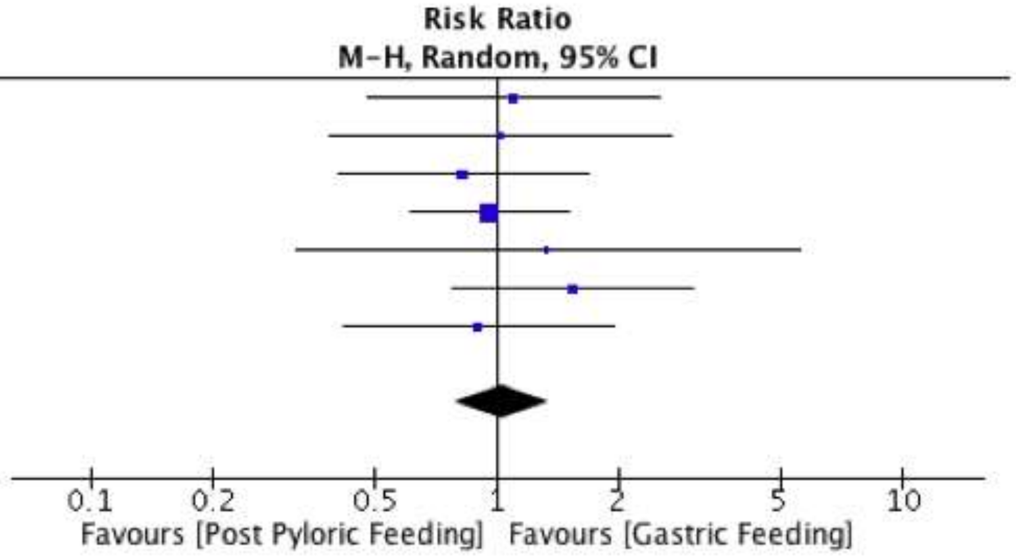
Gastric vs post pyloric feeding

IV. Figure. Diarrhea (7 RCTs, n=692)

Study or Subgroup	Post Pyloric Feeding Events	Post Pyloric Feeding Total	Gastric Feeding Events	Gastric Feeding Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Day 2001	7	14	5	11	10.5%	1.10 [0.48, 2.53]	2001
Montejo 2002	7	50	7	51	7.7%	1.02 [0.39, 2.70]	2002
Hsu 2009	11	59	14	62	14.7%	0.83 [0.41, 1.67]	2009
Davies 2012	26	91	27	91	35.6%	0.96 [0.61, 1.52]	2012
Singh 2012	4	39	3	39	3.6%	1.33 [0.32, 5.57]	2012
Friedman 2015	15	54	11	61	15.5%	1.54 [0.78, 3.06]	2015
Wan 2015	9	35	10	35	12.4%	0.90 [0.42, 1.94]	2015
Total (95% CI)		**342**		**350**	**100.0%**	**1.03 [0.79, 1.36]**	
Total events	79		77				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.05$, df = 6 (P = 0.91); $I^2 = 0\%$

Test for overall effect: Z = 0.25 (P = 0.80)



Gastric vs post pyloric feeding

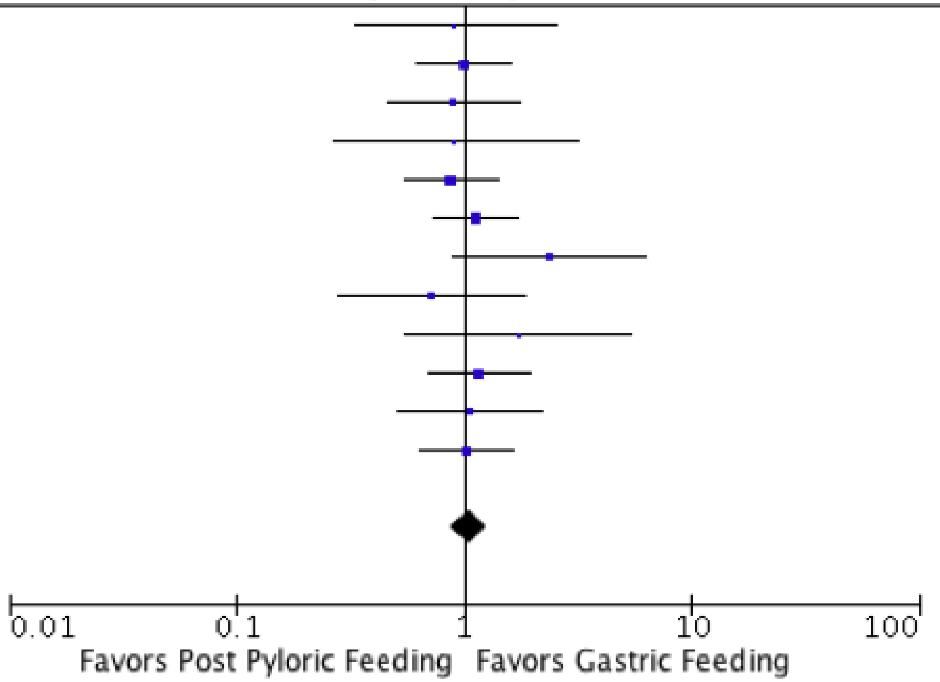
IV. Figure. Mortality (12 RCTs, n=1148)

Study or Subgroup	Post Pyloric Feeding Events	Post Pyloric Feeding Total	Gastric Feeding Events	Gastric Feeding Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kearns 2000	5	21	6	23	3.0%	0.91 [0.33, 2.55]	2000
Boivin 2001	18	39	18	39	14.0%	1.00 [0.62, 1.62]	2001
Esparza 2001	10	27	11	27	7.2%	0.91 [0.47, 1.78]	2001
Davies 2002	4	34	5	39	2.1%	0.92 [0.27, 3.14]	2002
Montejo 2002	19	50	22	51	14.3%	0.88 [0.55, 1.42]	2002
Hsu 2009	26	59	24	62	17.8%	1.14 [0.74, 1.74]	2009
White 2009	11	50	5	54	3.3%	2.38 [0.89, 6.36]	2009
Acosta-Escribano 2010	6	50	9	54	3.5%	0.72 [0.28, 1.88]	2010
Singh 2012	7	39	4	39	2.4%	1.75 [0.56, 5.50]	2012
Huang 2012	20	48	17	48	12.5%	1.18 [0.71, 1.96]	2012
Davies 2012	13	91	12	89	6.1%	1.06 [0.51, 2.19]	2012
Friedman 2015	20	54	22	61	13.8%	1.03 [0.63, 1.66]	2015
Total (95% CI)		**562**		**586**	**100.0%**	**1.05 [0.88, 1.26]**	
Total events	159		155				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.22$, df = 11 (P = 0.92); $I^2 = 0\%$

Test for overall effect: Z = 0.57 (P = 0.57)

Risk Ratio
M-H, Random, 95% CI

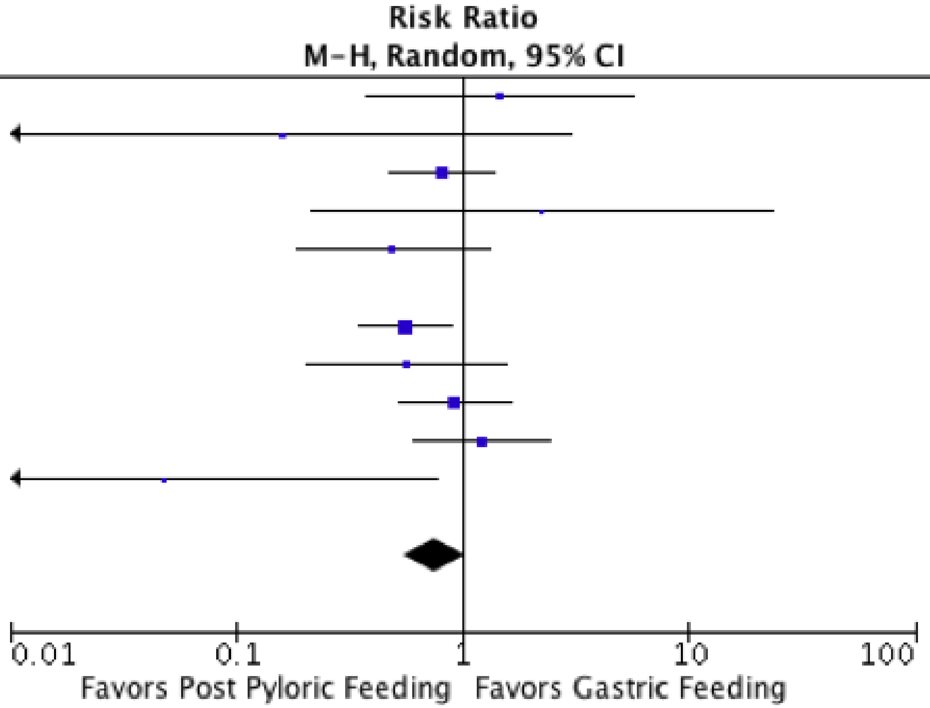


Gastric vs post pyloric feeding

IV. Figure. Pneumonia Outcome (11 RCTs, n=1031)

	Post Pyloric Feeding		Gastric Feeding			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Kearns 2000	4	21	3	23	4.7%	1.46 [0.37, 5.78]	2000
Day 2001	0	14	2	11	1.1%	0.16 [0.01, 3.03]	2001
Montejo 2002	16	50	20	51	19.9%	0.82 [0.48, 1.39]	2002
Davies 2002	2	31	1	35	1.7%	2.26 [0.22, 23.71]	2002
White 2009	5	50	11	54	8.3%	0.49 [0.18, 1.31]	2009
Hsu 2009	0	59	0	62		Not estimable	2009
Acosta-Escribano 2010	16	50	31	54	22.9%	0.56 [0.35, 0.89]	2010
Huang 2012	5	50	9	51	7.9%	0.57 [0.20, 1.57]	2012
Davies 2012	18	91	19	89	18.1%	0.93 [0.52, 1.65]	2012
Friedman 2015	13	54	12	61	14.2%	1.22 [0.61, 2.45]	2015
Wan 2015	0	35	10	35	1.2%	0.05 [0.00, 0.78]	2015
Total (95% CI)		**505**		**526**	**100.0%**	**0.75 [0.55, 1.03]**	
Total events	79		118				

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 11.86$, df = 9 (P = 0.22); $I^2 = 24\%$
Test for overall effect: Z = 1.80 (P = 0.07)



ESPN-2019 guidelines

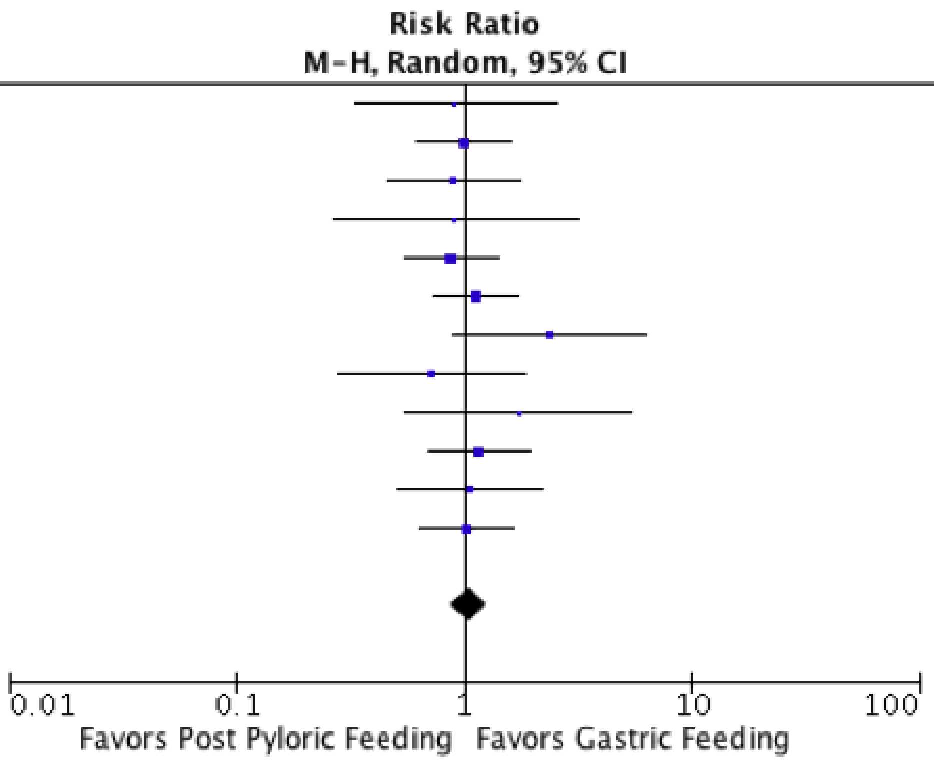
Gastric vs post pyloric feeding

IV. Figure. Mortality (12 RCTs, n=1148)

	Post Pyloric Feeding		Gastric Feeding			Risk Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Kearns 2000	5	21	6	23	3.0%	0.91 [0.33, 2.55]	2000
Boivin 2001	18	39	18	39	14.0%	1.00 [0.62, 1.62]	2001
Esparza 2001	10	27	11	27	7.2%	0.91 [0.47, 1.78]	2001
Davies 2002	4	34	5	39	2.1%	0.92 [0.27, 3.14]	2002
Montejo 2002	19	50	22	51	14.3%	0.88 [0.55, 1.42]	2002
Hsu 2009	26	59	24	62	17.8%	1.14 [0.74, 1.74]	2009
White 2009	11	50	5	54	3.3%	2.38 [0.89, 6.36]	2009
Acosta-Escribano 2010	6	50	9	54	3.5%	0.72 [0.28, 1.88]	2010
Singh 2012	7	39	4	39	2.4%	1.75 [0.56, 5.50]	2012
Huang 2012	20	48	17	48	12.5%	1.18 [0.71, 1.96]	2012
Davies 2012	13	91	12	89	6.1%	1.06 [0.51, 2.19]	2012
Friedman 2015	20	54	22	61	13.8%	1.03 [0.63, 1.66]	2015
Total (95% CI)		**562**		**586**	**100.0%**	**1.05 [0.88, 1.26]**	
Total events	159		155				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.22$, df = 11 (P = 0.92); $I^2 = 0\%$

Test for overall effect: Z = 0.57 (P = 0.57)



ESPN-2019 guidelines

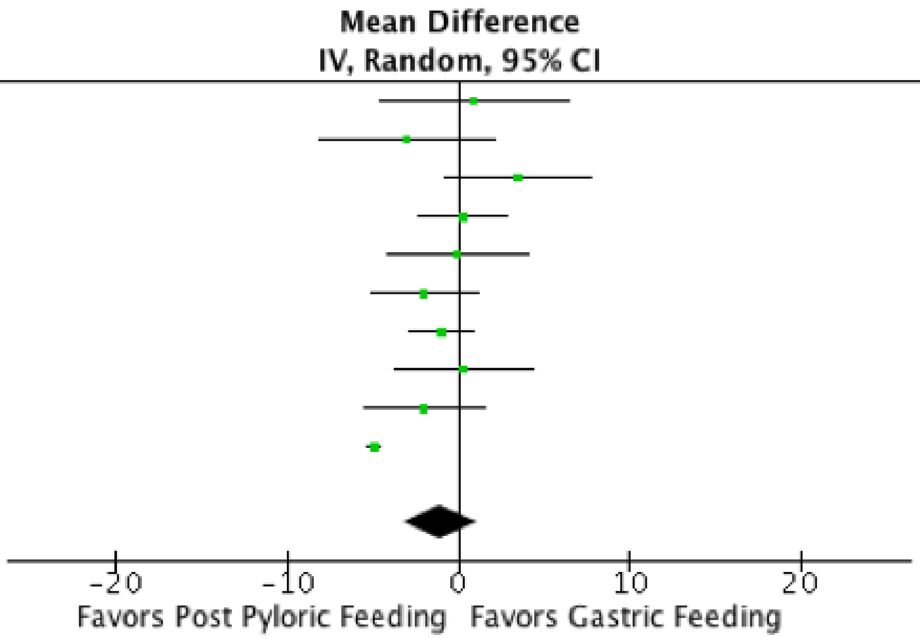
Gastric vs post pyloric feeding

IV. Figure. ICU Length of stay (10 RCTs, n=1013)

Study or Subgroup	Post Pyloric Feeding Mean	SD	Total	Gastric Feeding Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Kearns 2000	17	9	21	16	9.6	23	7.2%	1.00 [-4.50, 6.50]	2000
Montejo 2002	15	10	50	18	16	51	7.6%	-3.00 [-8.19, 2.19]	2002
Davies 2002	13.9	10.5	34	10.4	7.5	39	8.9%	3.50 [-0.74, 7.74]	2002
White 2009	5.3	7.16	50	5.02	5.93	54	11.5%	0.28 [-2.26, 2.82]	2009
Hsu 2009	18.2	11.8	59	18.2	11.2	62	9.1%	0.00 [-4.10, 4.10]	2009
Acosta-Escribano 2010	16	9	50	18	7	54	10.6%	-2.00 [-5.12, 1.12]	2010
Davies 2012	10	6	91	11	6.7	89	12.4%	-1.00 [-2.86, 0.86]	2012
Huang 2012	17.2	11.4	50	16.9	9.1	51	9.2%	0.30 [-3.73, 4.33]	2012
Friedman 2015	10	10.37	54	12	8.88	61	9.9%	-2.00 [-5.55, 1.55]	2015
Wan 2015	12.2	0.7	35	17.1	1	35	13.6%	-4.90 [-5.30, -4.50]	2015
Total (95% CI)			**494**			**519**	**100.0%**	**-0.99 [-3.12, 1.15]**	

Heterogeneity: $Tau^2 = 8.64$; $Chi^2 = 62.72$, $df = 9$ ($P < 0.00001$); $I^2 = 86\%$

Test for overall effect: $Z = 0.91$ ($P = 0.36$)



ESPN-2019 guidelines

In conclusion

- Postpyloric EN has been associated with a decrease in VAP, but this benefit did not translate into decreases in length of ventilation, ICU or hospital stay, or mortality
- Duodenal vs jejunal are not differentiated
- Post pyloric feeding is better in patients with a high risk for aspiration

(Inability to protect the airway, mechanical ventilation, age >70 years, reduced level of consciousness, poor oral care, inadequate nurse:patient ratio, supine positioning, neurologic deficits, gastroesophageal reflux, transport out of the ICU, and use of bolus intermittent EN)