Nutrition in ICU

Outline

- Therapeutic goals
- Metabolic response to critical illness
- Timing of nutrition
- Calories requirement
- Protein requirement
- Glycemic control
- Nutrition during shock
- Enteral feed intolerance
- ICU Protocol

Therapeutic goals

- Maintain weight and muscle mass
- Maintain gut integrity
- Prevent mortality
- Reduce ICU stay
- Prevent nosocomial infections

Goal of nutrition in ICU is not to feed the correct calories and protein,

it is to preserve the patient's capacity to recover

Adequacy of Nutritional Support and Its Correlation with Outcomes in Mechanically Ventilated Patients in a Respiratory ICU

BACKGROUND

- Nutritional support is frequently neglected in a busy intensive care unit (ICU) with overworked staff.
- There is a paucity of investigations on ICU nutrition from India.

OBJECTIVE

To assess the adequacy of nutritional support administered to patients requiring mechanical ventilation in the respiratory ICU of a tertiary-care institute, and its correlation with outcomes.

METHODS

Prospective cohort study

Patients ≥ 15 years, mechanically ventilated ≥ 24 h, and ICU stay ≥ 48 h

Enteral nutrition initiated as early as possible after ICU admission

Daily prescription: 30 kcal/kg and 1.2 g/kg ideal body weight, with adjustments for critical illness(es) and comorbidities

Anthropometric and laboratory parameters assessed serially

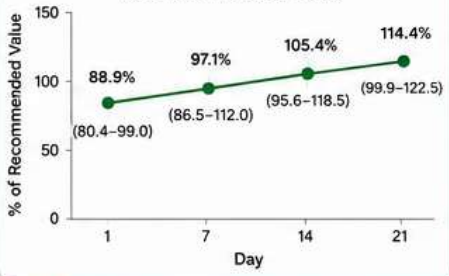
Risk factors for hospital mortality evaluated using multivariable logistic regression analysis

STUDY POPULATION

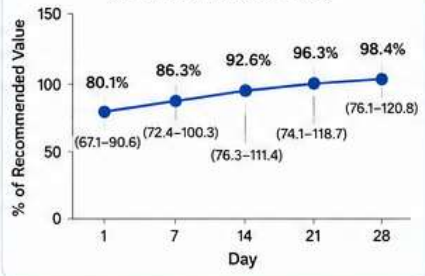
258 patients admitted to respiratory ICU during the study period → **93** patients met all inclusion criteria and were included in the analysis

RESULTS

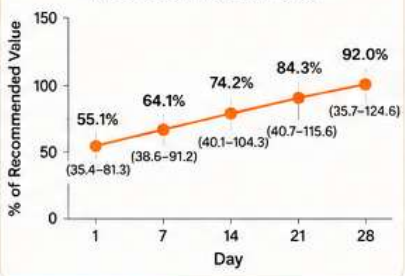
CALORIE PRESCRIPTION
(% of recommended value)



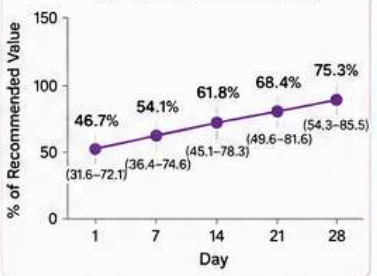
PROTEIN PRESCRIPTION
(% of recommended value)



CALORIE DELIVERY
(% of recommended value)



PROTEIN DELIVERY
(% of recommended value)



KAPLAN–MEIER ANALYSIS
Probability of Survival Stratified by Mean Calorie Delivery

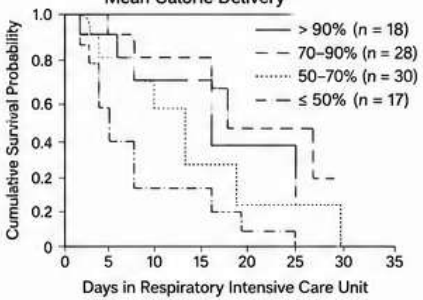


Fig. 3. Kaplan–Meier analysis of the probability of survival, stratified according to mean calorie delivery (as a percentage of the recommended value). Mean calorie delivery of 50% or less of recommended significantly reduced the probability of survival, via log-rank test.

Patients with mean calorie delivery ≤ 50% of recommended had markedly lower survival probability.

RISK FACTORS FOR HOSPITAL MORTALITY (Multivariable Logistic Regression)

Admission SOFA Score (per 1-point increase)
OR 1.30
(95% CI 1.03–1.63)

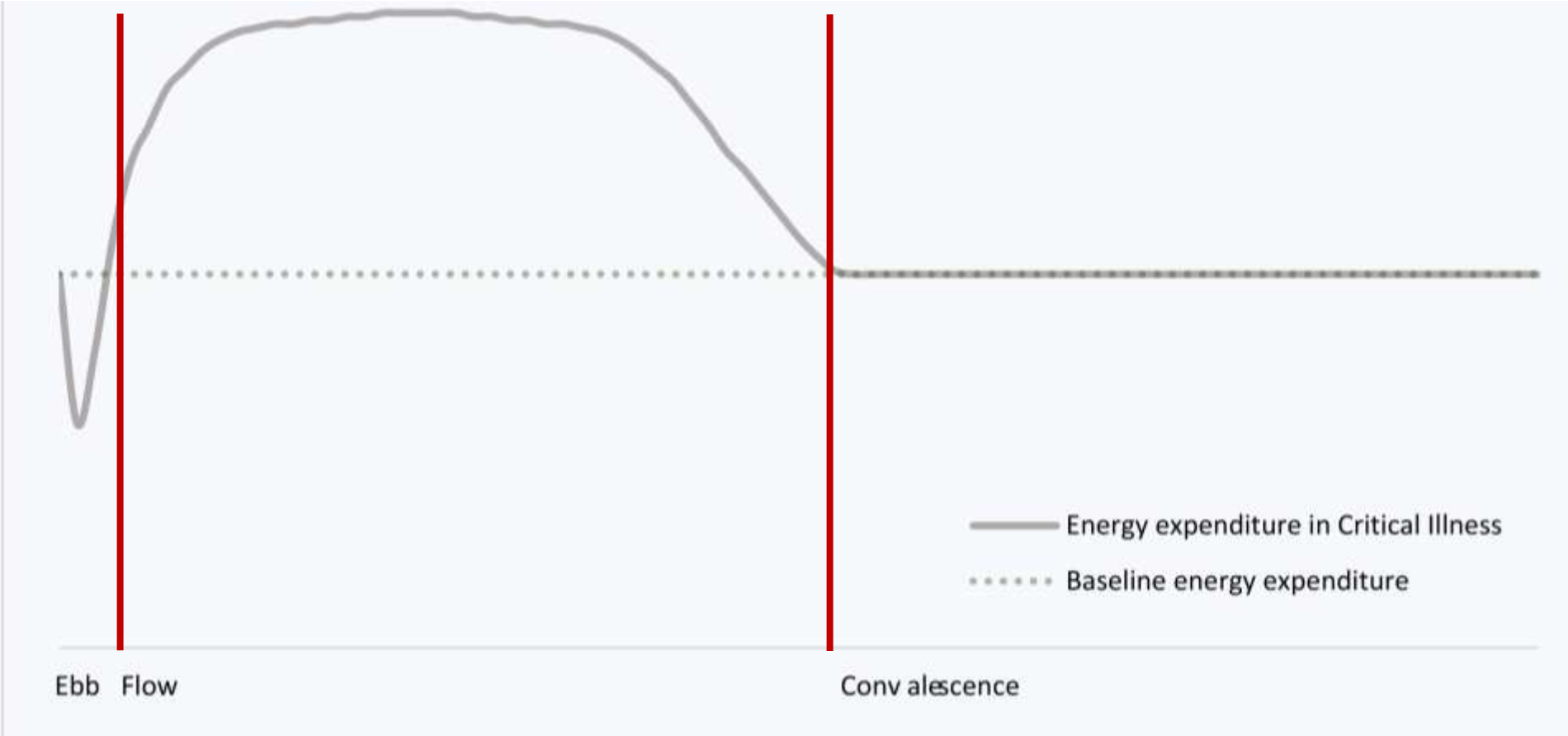
Mean Daily Calorie Delivery ≤ 50% of Recommended Value
OR 12.08
(95% CI 1.40–104.11)

KEY MESSAGE

Inadequate calorie delivery (≤ 50% of recommended) is associated with ~12 times higher odds of hospital mortality.

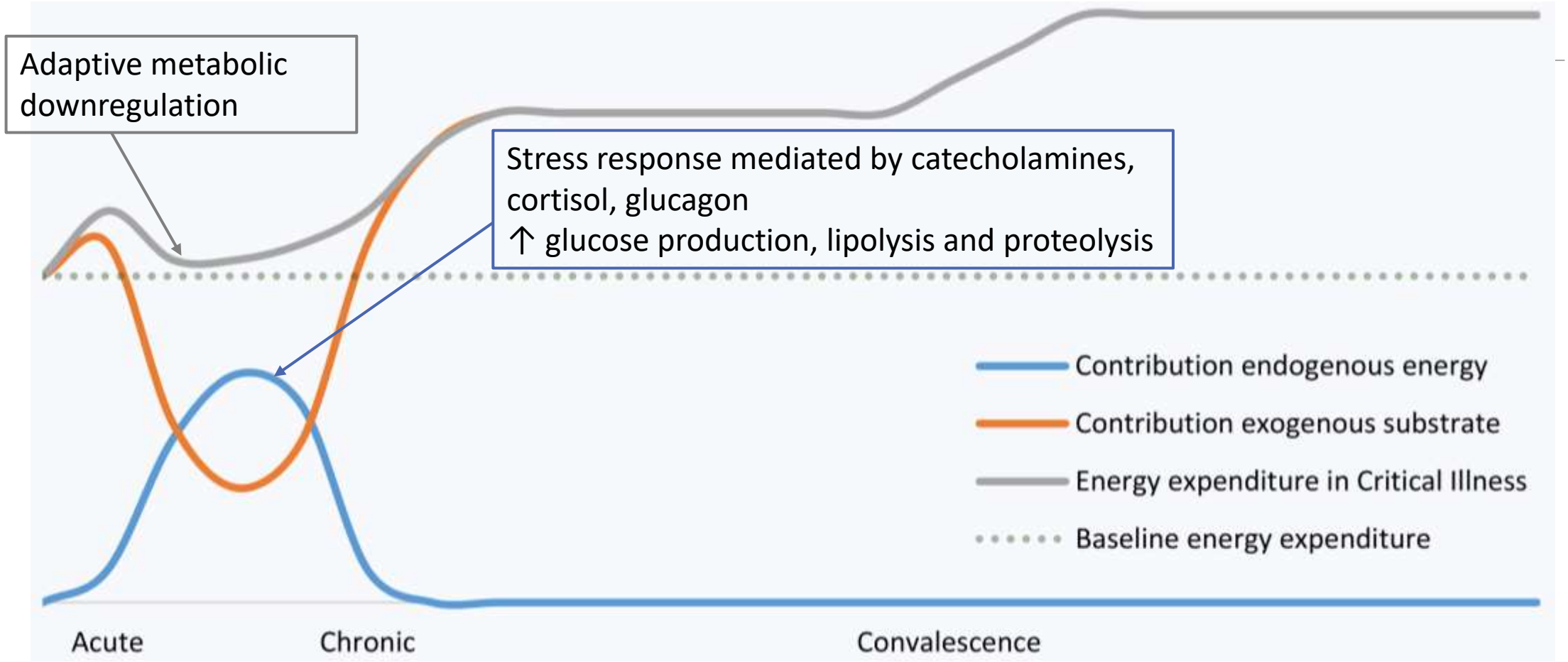
Singh N. et al. Respir Care. 2009;54:1688-96

Cuthbertson Model 1942



Recreated from: Cuthbertson DP. Post-shock metabolic response. *Lancet.* 1942

Current Model



Moonen HPFX et al. J Intensive Care. 2021;12;9:8

Enteral versus parenteral nutrition in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials

Research Question

Component	Description
Population	Critically ill aged ≥ 18, admitted in ICU
Intervention	Enteral nutrition
Comparator	Parenteral nutrition
Outcomes	Mortality, Infectious complications, ICU LoS

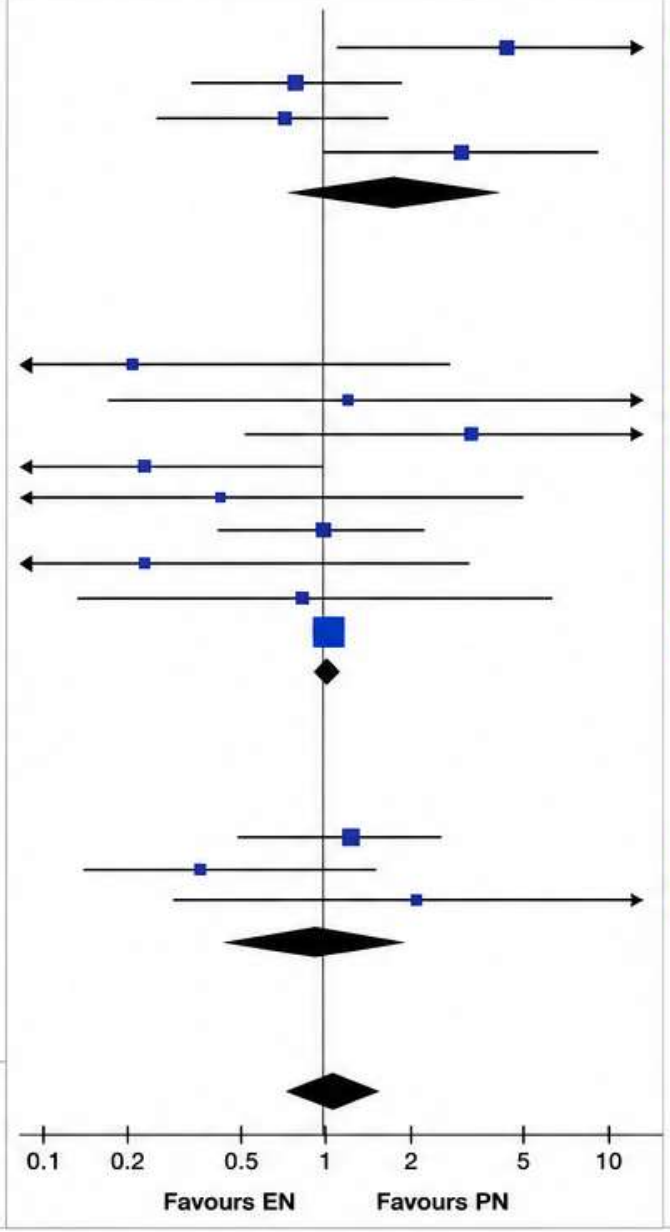
PROSPERO – Not Registered
PRISMA Checklist provided
Literature Search: Medline, Embase, Cochrane library
Analysis: 18 RCTs ; n= 3347

Elke et al. Critical Care. 2016;20:117

Enteral versus Parenteral Nutrition in Critically Ill Patients – Overall Mortality

Elke et al., Critical Care 2016;20:117 | 18 RCTs (3,347 patients); 16 trials reported mortality

Study (Year)	Design	Population (Predominant)	Events / Total EN	Events / Total PN	Weight (%)	Risk Ratio (M-H, Random, 95% CI)
A. Trials in which PN group received significantly more calories (PN > EN)						
Rapp (1983)	RCT	Mixed ICU	9 / 18	3 / 20	4.2	3.33 [1.07, 10.43]
Young (1987)	RCT	Mixed ICU	10 / 28	10 / 23	10.3	0.82 [0.42, 1.62]
Kudsk (1992)	RCT	Mixed ICU	5 / 29	11 / 45	7.4	0.80 [0.30, 1.37]
Woodcock (2001)	RCT	Mixed ICU	9 / 17	5 / 21	6.6	2.22 [0.92, 5.46]
Subtotal (95% CI)			**114**	**144**	**28.5**	**1.58 [0.75, 3.35]**
Total events		33	39	39		
Heterogeneity: Tau² = 0.27; Chi² = 5.81, df = 4 (P = 0.12); I² = 48%						
Test for overall effect: Z = 1.20 (P = 0.23)						
B. Trials in which PN and EN groups received similar calories (PN ~ EN)						
Adams (1986)	RCT	Mixed ICU	1 / 23	3 / 23	1.2	0.33 [0.04, 2.97]
Dunham (1994)	RCT	Mixed ICU	1 / 12	1 / 15	0.8	1.25 [0.09, 17.98]
Borzotta (1994)	RCT	Mixed ICU	5 / 28	1 / 21	1.3	3.75 [0.47, 29.75]
Hadfield (1996)	RCT	Surgical ICU	2 / 13	6 / 11	2.9	0.28 [0.07, 1.13]
Kalfarentzos (1997)	RCT	Surgical ICU	1 / 18	2 / 20	1.1	0.56 [0.05, 6.62]
Cerra (1998)	RCT	Mixed ICU	7 / 31	8 / 35	6.5	0.99 [0.40, 2.41]
Casas (2007)	RCT	Mixed ICU	0 / 11	1 / 11	0.7	0.20 [0.01, 3.74]
Justo Meirelles (2011)	RCT	Mixed ICU	1 / 12	1 / 10	0.8	0.83 [0.06, 11.70]
Harvey (2014)	RCT	Mixed ICU	450 / 1168	431 / 1165	55.5	1.04 [0.94, 1.16]
Subtotal (95% CI)			**1334**	**1311**	**70.8**	**1.03 [0.93, 1.14]**
Total events		468	454	454		
Heterogeneity: Tau² = 0.00; Chi² = 7.47, df = 8 (P = 0.49); I² = 0%						
Test for overall effect: Z = 0.80 (P = 0.55)						
C. Trials where caloric intake was not reported						
Chen (2011)	RCT	Medical ICU	11 / 49	10 / 49	8.6	1.10 [0.51, 2.39]
Wang (2011)	RCT	Surgical ICU	3 / 61	7 / 60	3.2	0.42 [0.11, 1.58]
Sun (2013)	RCT	Surgical ICU	2 / 30	1 / 30	1.0	2.00 [0.19, 20.50]
Subtotal (95% CI)			**140**	**139**	**12.8**	**0.92 [0.48, 1.74]**
Total events		16	18	18		
Heterogeneity: Tau² = 0.02; Chi² = 2.02, df = 2 (P = 0.36); I² = 1%						
Test for overall effect: Z = 0.37 (P = 0.71)						
Total (95% CI)			**1588**	**1579**	**100.0**	**1.04 [0.82, 1.33]**
Total events		517	511	511		
Heterogeneity: Tau² = 0.03; Chi² = 16.94, df = 15 (P = 0.32); I² = 11%						
Test for overall effect: Z = 0.32 (P = 0.75)						
Test for subgroup differences: Chi² = 1.37, df = 2 (P = 0.50); I² = 0%						



Risk of Bias (Quality Score 0–14)* A	B	C	D	E	F	G	H	Overall
+	+	?	+	+	?	+	+	High (9)
+	+	?	+	+	?	+	+	High (10)
?	+	+	?	+	?	+	+	Moderate (7)
+	+	?	+	+	−	+	+	Moderate (8)
+	?	?	+	+	?	+	+	Moderate (7)
?	?	?	?	?	−	?	+	Low (6)
+	?	+	+	+	?	+	+	Moderate (7)
?	?	?	?	?	−	?	+	Low (5)
?	?	?	?	?	?	?	+	Low (6)
+	?	+	+	+	?	+	+	Moderate (8)
?	?	?	+	+	−	?	+	Low (5)
?	?	?	?	?	?	?	+	Low (5)
+	+	+	+	+	+	+	+	High (12)
+	?	+	+	+	?	+	+	High (10)
?	?	?	?	?	?	?	+	Low (6)
?	?	?	?	?	−	?	+	Low (6)

Redesigned with Chatgpt

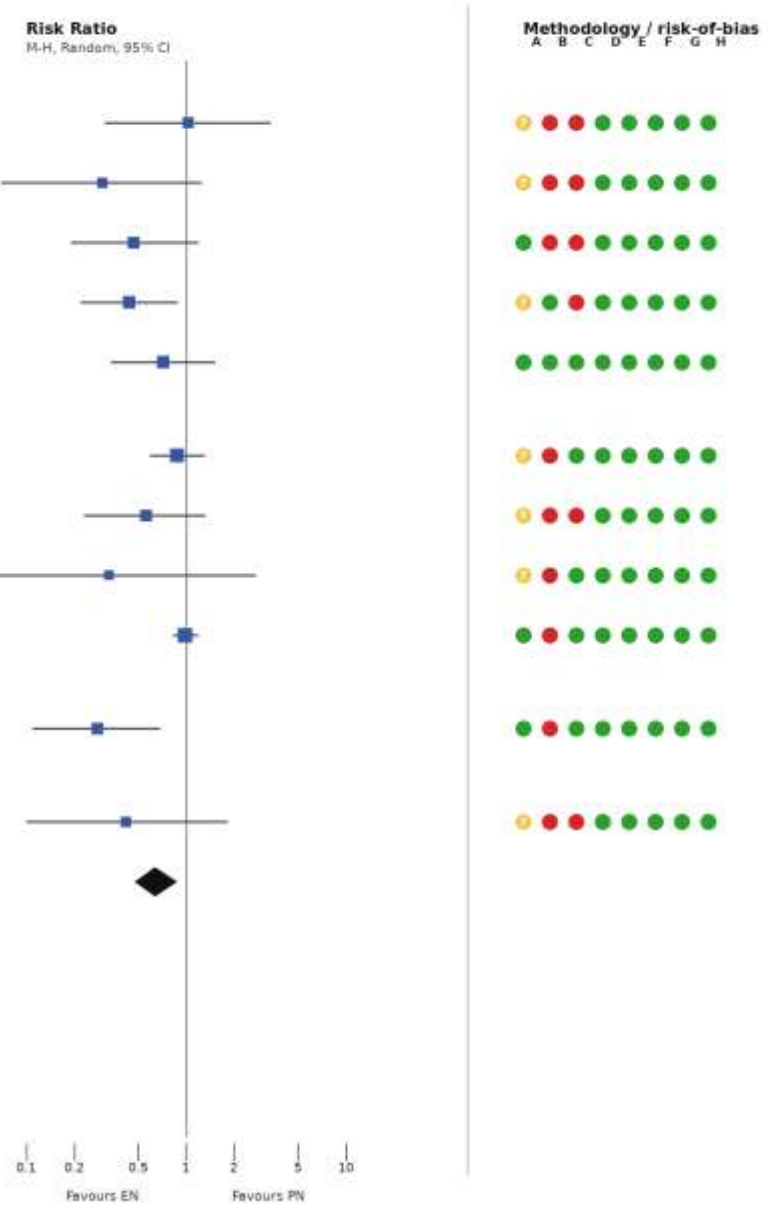
Enteral versus parenteral nutrition — infectious complications

Elke et al., Critical Care 2016;20:117 | 11 RCTs | Risk ratio (EN vs PN), M-H random effects

Study (Year)	Design	Population	EN events / total	PN events / total	Weight	RR [95% CI]
A. PN received significantly more calories than EN						
Young 1987	RCT	Surgical/trauma	5/28	4/23	5.0%	1.03 [0.31, 3.39]
Peterson 1988	RCT	Surgical/trauma	2/21	8/25	3.7%	0.30 [0.07, 1.25]
Moore 1989	RCT	Surgical/trauma	5/29	11/30	7.4%	0.47 [0.19, 1.19]
Kudsk 1992	RCT	Surgical/trauma	9/51	18/45	10.8%	0.44 [0.22, 0.88]
Woodcock 2001	RCT	Unclear	6/16	11/21	9.8%	0.72 [0.34, 1.52]
B. PN and EN received similar calories						
Adams 1986	RCT	Surgical/trauma	15/23	17/23	18.2%	0.88 [0.60, 1.30]
Kalfarentzos 1997	RCT	Unclear	5/18	10/20	8.2%	0.56 [0.23, 1.32]
Casas 2007	RCT	Unclear	1/11	3/11	1.9%	0.33 [0.04, 2.73]
Harvey 2014	RCT	Mixed	194/1197	194/1191	23.8%	0.99 [0.83, 1.19]
C. Caloric intake not reported						
Chen 2011	RCT	Medical	5/49	18/49	7.6%	0.28 [0.11, 0.69]
Additional trial contributing to overall infectious-complication estimate						
Justo Meirelles 2011	RCT	Unclear	2/12	4/10	3.5%	0.42 [0.10, 1.82]
Treatment effect, all 11 studies					**100.0%**	**0.64 [0.48, 0.87]**

Heterogeneity: $\tau^2 = 0.09$; $\chi^2 = 18.71$, df = 10 (P = 0.04); $I^2 = 47\%$

Overall effect: Z = 2.91 (P = 0.004) | Subgroup differences: $\chi^2 = 11.87$, df = 2 (P = 0.003); $I^2 = 83.1\%$



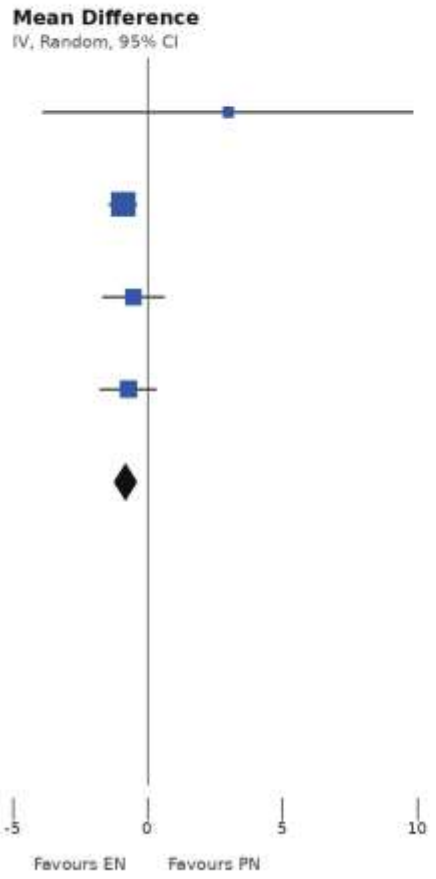
Enteral versus parenteral nutrition — ICU length of stay

Elke et al., Critical Care 2016;20:117 | 4 RCTs | Mean difference (EN − PN), inverse variance random effects

Study (Year)	Design	Population	EN mean ± SD (n)	PN mean ± SD (n)	Weight	MD [95% CI]
Adams 1986	RCT	Surgical/trauma	13 ± 11 (19)	10 ± 10 (17)	0.4%	3.00 [-3.86, 9.86]
Peterson 1988	RCT	Surgical/trauma	3.7 ± 0.8 (21)	4.6 ± 1.0 (25)	68.6%	-0.90 [-1.42, -0.38]
Chen 2011	RCT	Medical	9.09 ± 2.75 (49)	9.60 ± 3.06 (49)	14.0%	-0.51 [-1.66, 0.64]
Harvey 2014	RCT	Mixed	11.3 ± 12.5 (1197)	12.0 ± 13.5 (1190)	17.0%	-0.70 [-1.74, 0.34]
Total (95% CI)			**26.8 days (1286)**	**26.8 days (1281)**	**100.0%**	**-0.80 [-1.23, -0.37]**

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.60$, df = 3 (P = 0.66); $I^2 = 0\%$

Overall effect: Z = 3.62 (P = 0.0003)



Analysis

- Anchor study – CALORIES Trial (n = 2400)
- RoB by older system instead of RoB 2 assessment tool
- Clinical heterogeneity
- Different Calories, time of initiation

Conclusion:

- Mortality – No difference
- Infectious complications and ICU LoS – More with PN

Underfeeding versus full enteral feeding in critically ill patients with acute respiratory failure: Systematic review with meta-analysis of randomized controlled trials

Research Question

Component	Description
Population	Adult with acute respiratory failure requiring IMV
Intervention	Moderate underfeeding (46-72%)/trophic feeding (16-25%)
Comparator	Full enteral feeding, aiming to provide a substantially higher proportion of estimated energy requirements
Outcomes	Mortality, GI complications

PROSPERO –Registered
PRISMA Checklist provided
Literature Search: Medline, Embase, SCOPUS
Analysis: 5 RCTs, n = 2,432

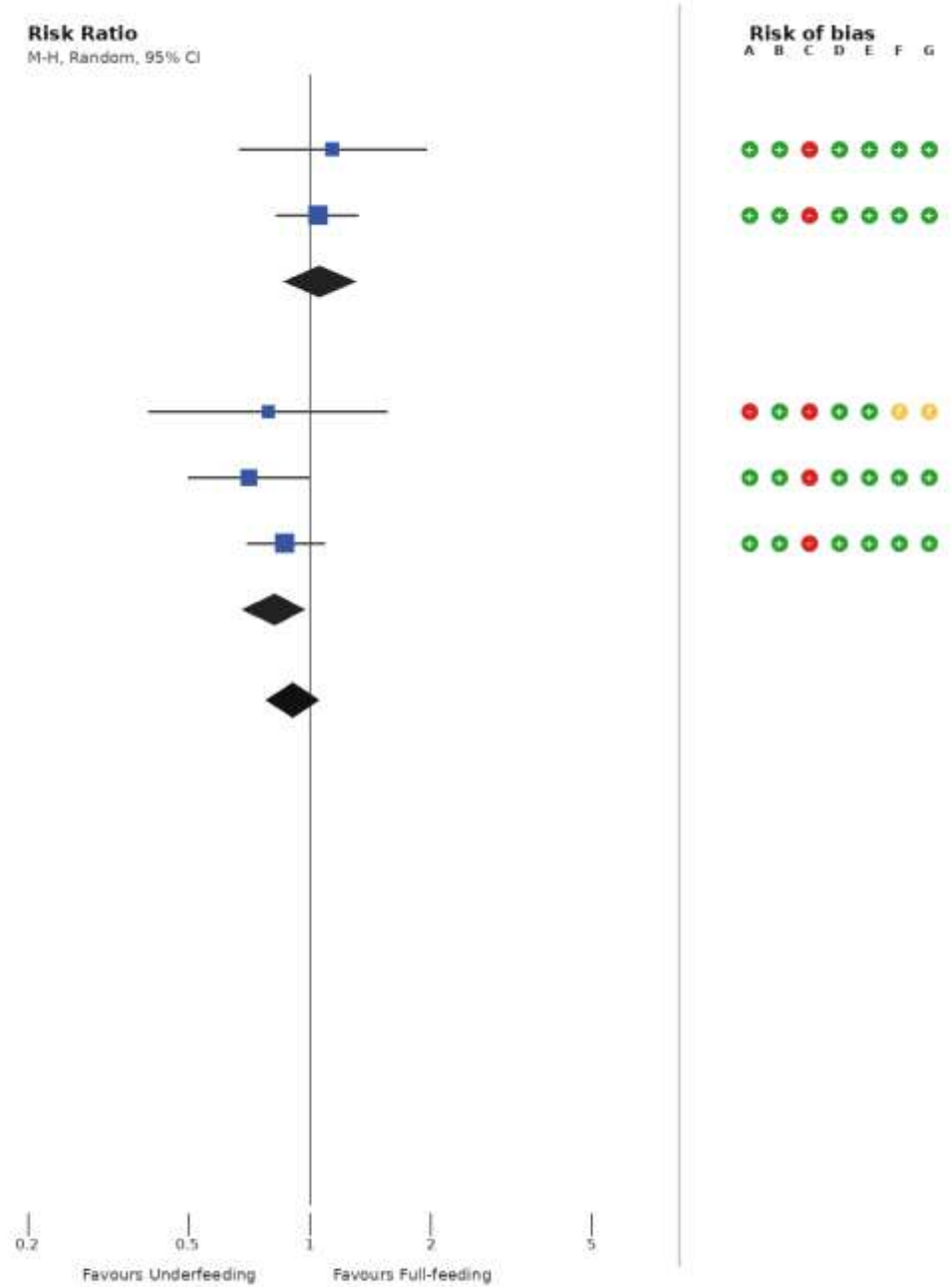
Franzosi OS et al. Nutr Hosp. 2017;34:19-29

Underfeeding versus full enteral feeding — overall mortality

Franzosi et al., Nutr Hosp 2017;34(1):19–29 | 5 RCTs | M-H random-effects RR

Study / subgroup	Design	Population	UF n/N	FF n/N	Weight	RR [95% CI]
1.1.1 Trophic feeding						
Rice 2011	RCT	Unclear	22/98	20/102	7.6%	1.14 [0.67, 1.96]
Rice 2012	RCT	Medical	118/508	109/492	34.3%	1.05 [0.83, 1.32]
Subtotal (95% CI)					**41.9%**	**1.06 [0.86, 1.31]**
Total events: 140 vs 129 | Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.77); I² = 0% | Overall Z = 0.57 (P = 0.57)						
1.1.2 Moderate feeding						
Desachy 2008	RCT	Medical	11/50	14/50	4.8%	0.79 [0.40, 1.56]
Arabi 2011	RCT	Medical	36/120	51/120	17.5%	0.71 [0.50, 1.00]
Arabi 2015	RCT	Medical	108/447	123/445	35.8%	0.87 [0.70, 1.09]
Subtotal (95% CI)					**58.1%**	**0.82 [0.68, 0.98]**
Total events: 155 vs 188 | Tau² = 0.00; Chi² = 1.06, df = 2 (P = 0.59); I² = 0% | Overall Z = 2.18 (P = 0.03)						
Total (95% CI)					**100.0%**	**0.91 [0.78, 1.06]**

Total events: 295 vs 317
Tau² = 0.00; Chi² = 4.58, df = 4 (P = 0.33); I² = 13% | Overall Z = 1.21 (P = 0.23)
Subgroup differences: Chi² = 3.42, df = 1 (P = 0.06); I² = 70.7%

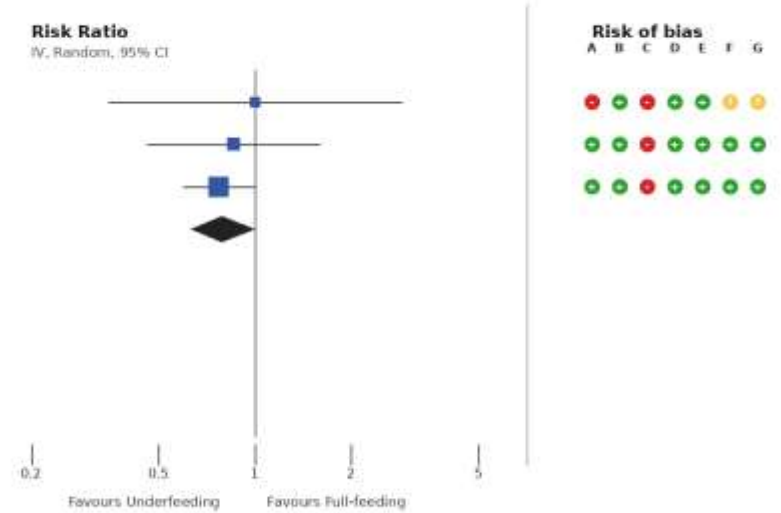


Underfeeding versus full enteral feeding — vomiting

Franzosi et al., Nutr Hosp 2017;34(1):19-29 | Figure 6 | IV random-effects RR

Study (Year)	Design	Population	log[RR]	SE	Weight	RR [95% CI]
Desachy 2008	RCT	Medical	-0.0000	0.5416	4.8%	1.00 [0.35, 2.89]
Rice 2011	RCT	Unclear	-0.1542	0.3175	13.9%	0.86 [0.46, 1.60]
Rice 2012	RCT	Medical	-0.2578	0.1315	81.3%	0.77 [0.60, 1.00]
Total (95% CI)					**100.0%**	**0.79 [0.63, 1.00]**

Tau² = 0.00; Chi² = 0.28, df = 2 (P = 0.87); I² = 0% | Overall effect P = 0.05



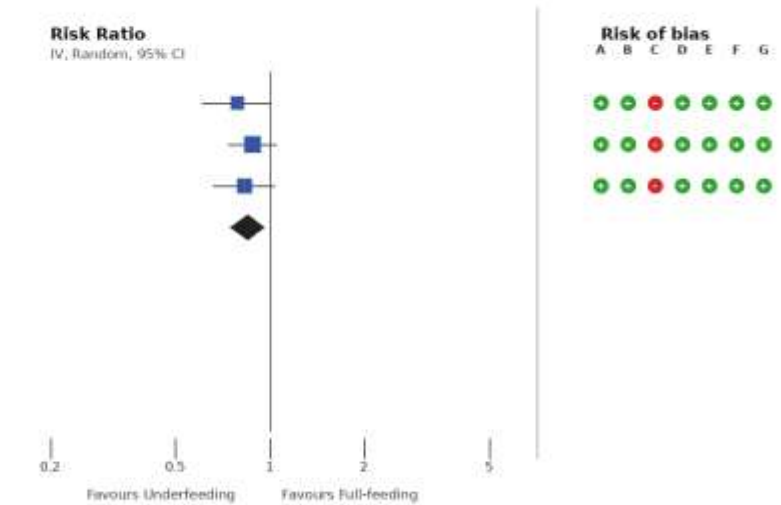
A Sequence generation | B Allocation concealment | C Performance | D Detection | E Attrition | F Selective reporting | G Otherfunding

Underfeeding versus full enteral feeding — diarrhea

Franzosi et al., Nutr Hosp 2017;34(1):19-29 | Figure 6 | IV random-effects RR

Study (Year)	Design	Population	log[RR]	SE	Weight	RR [95% CI]
Rice 2011	RCT	Unclear	-0.2325	0.1326	22.0%	0.79 [0.61, 1.01]
Rice 2012	RCT	Medical	-0.1250	0.0889	49.4%	0.88 [0.74, 1.05]
Arabi 2015	RCT	Medical	-0.1875	0.1171	28.5%	0.83 [0.66, 1.04]
Total (95% CI)					**100.0%**	**0.85 [0.75, 0.96]**

Tau² = 0.00; Chi² = 0.50, df = 2 (P = 0.78); I² = 0% | Overall effect P = 0.008



A Sequence generation | B Allocation concealment | C Performance | D Detection | E Attrition | F Selective reporting | G Otherfunding

Analysis

RCT only SRMA

Studies using supplementary PN – excluded

Focused on GI complications

Not truly Trophic vs full feeding

No RCT was blinded

Energy expenditure – variation in the formula used

Only respiratory failure patients - well suited for RICU

Continuous feeding versus intermittent feeding among mechanically ventilated patients in intensive care: Systematic review and meta-analysis of randomized controlled trials

Research Question

Component	Description
Population	Adult critically ill requiring IMV and on EN
Intervention	Continuous EN
Comparator	Intermittent/bolus EN
Outcomes	Mortality, GI complications

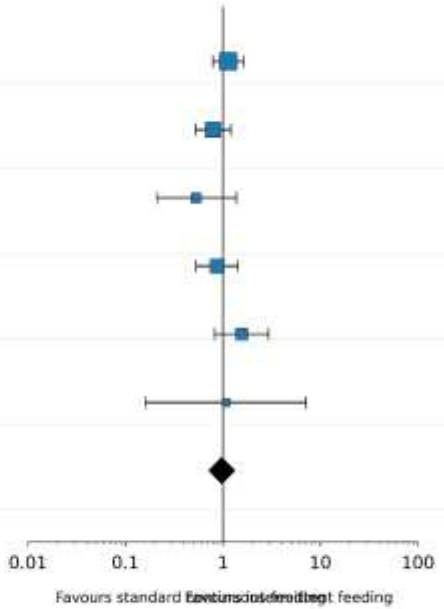
PROSPERO –Registered
PRISMA Checklist provided
Literature Search: MEDLINE, EMBASE and CENTRAL
Analysis: 8 RCTs, n = 993

Panwar R. et al. Clinical Nutrition. 2025;51:40–49

Standard continuous feeding versus intermittent gastric feeding — all-cause mortality

Reconstruction of the published mortality forest plot (Panwar et al., Clinical Nutrition 2025)

Study / subgroup	Design	Population	Standard feeding Events / Total	Intermittent feeding Events / Total	Weight	Risk ratio RR [95% CI]	Forest plot	RoB 2 D1	D2	D3	D4	D5	Overall
Hrdy et al., 2025	RCT	Predominantly Medical	46 / 148	40 / 146	34.2%	1.13 [0.79, 1.62]		✓	△	✓	✓	△	△
Lee et al., 2022	RCT	Predominantly Medical	21 / 50	26 / 49	26.2%	0.79 [0.52, 1.20]		✓	△	✓	✓	△	△
MacLeod et al., 2007	RCT	Predominantly Surgical / Trauma	6 / 81	11 / 79	5.9%	0.53 [0.21, 1.37]		✓	△	✓	✓	△	△
McNelly et al., 2020	RCT	Mixed	19 / 59	23 / 62	19.8%	0.87 [0.53, 1.42]		✓	△	✓	✓	△	△
Panwar et al., 2024	RCT	Mixed medical-surgical	18 / 59	12 / 61	12.4%	1.55 [0.82, 2.93]		✓	△	✓	✓	△	△
Ren et al., 2021	RCT	Unclear	2 / 30	2 / 32	1.5%	1.07 [0.16, 7.10]		✓	△	✓	✓	△	△
Total (HKSJ[a])			**112 / 427**	**114 / 429**	**100.0%**	**0.97 [0.72, 1.32]**							



Total events: 112 vs 114
Test for overall effect: Z = 0.23, p = 0.82
Test for subgroup differences: Not applicable
Heterogeneity: τ^2 (DL) = 0.01; χ^2 = 5.49, df = 5 (p = 0.36); I^2 = 9%

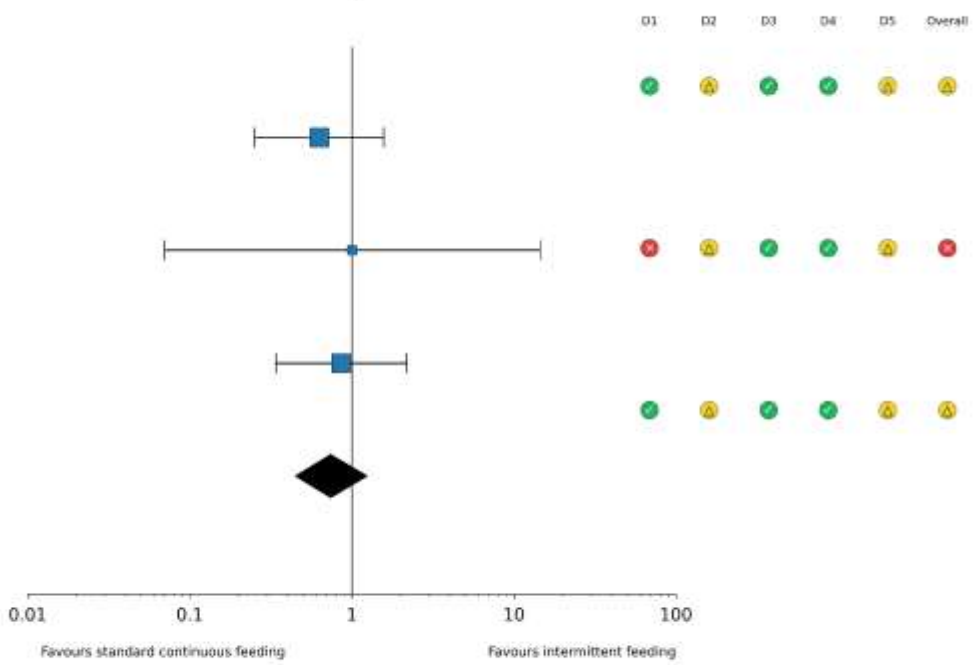
Risk-of-bias judgement

✓ low △ some concerns ✗ high

Standard continuous vs intermittent feeding — Vomiting

Corrected reconstruction of the published Figure 4 — Panwar et al., Clinical Nutrition 2025

Study / subgroup	Design	Population	Standard feeding Events / Total	Intermittent feeding Events / Total	Weight	Risk ratio M-H, random, 95% CI
Hrdy et al., 2025	RCT	Predominantly Medical	7 / 148	11 / 146	47.9%	0.63 [0.25, 1.57]
Kadamani et al., 2013	non-RCT	Unclear	1 / 15	1 / 15	5.7%	1.00 [0.07, 14.55]
Lee et al., 2022	RCT	Predominantly Medical	7 / 50	8 / 49	46.4%	0.86 [0.34, 2.18]
Total (HKSJ[a])			**213**	**210**	**100.0%**	**0.74 [0.45, 1.24]**



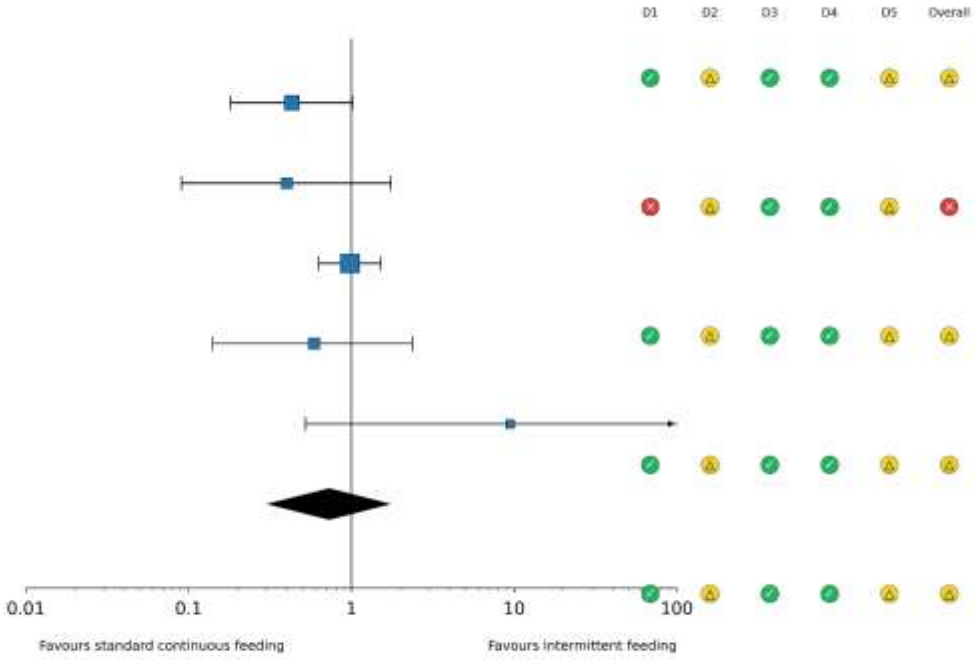
Total events: 15 vs 20
Test for overall effect: T = 2.48, df = 2 (p = 0.13)
Test for subgroup differences: Not applicable
Heterogeneity: τ^2 (DL) = 0.00; χ^2 = 0.27, df = 2 (p = 0.87); I^2 = 0%

Standard continuous vs intermittent feeding — Diarrhoea

Corrected reconstruction of the published Figure 4 — Panwar et al., Clinical Nutrition 2025

Study / subgroup	Design	Population	Standard feeding Events / Total	Intermittent feeding Events / Total	Weight	Risk ratio M-H, random, 95% CI
Hrdy et al., 2025	RCT	Predominantly Medical	7 / 148	16 / 146	25.2%	0.43 [0.18, 1.02]
Kadamani et al., 2013	non-RCT	Unclear	2 / 15	5 / 15	11.1%	0.40 [0.09, 1.75]
Lee et al., 2022	RCT	Predominantly Medical	22 / 50	22 / 49	48.5%	0.98 [0.63, 1.52]
MacLeod et al., 2007	RCT	Predominantly Surgical / Trauma	3 / 81	5 / 79	12.1%	0.59 [0.14, 2.37]
McNelly et al., 2020	RCT	Mixed	4 / 59	0 / 62	3.2%	9.45 [0.52, 171.79]
Total (HKSJ[a])			**353**	**351**	**100.0%**	**0.73 [0.31, 1.70]**

Total events: 38 vs 48
Test for overall effect: T = 1.04, df = 4 (p = 0.36)
Test for subgroup differences: Not applicable
Heterogeneity: τ^2 (REML) = 0.10; χ^2 = 6.63, df = 4 (p = 0.16); I^2 = 27%



Analysis

Most trials were underpowered

Clinical heterogeneity

Intermittent feeding – heterogenous (q8h to q4h)

Conclusion:

No difference in any outcome

Timing of enteral nutrition

frontiers | Frontiers in Nutrition

Optimal timing of enteral nutrition initiation in critically ill patients: a network meta-analysis

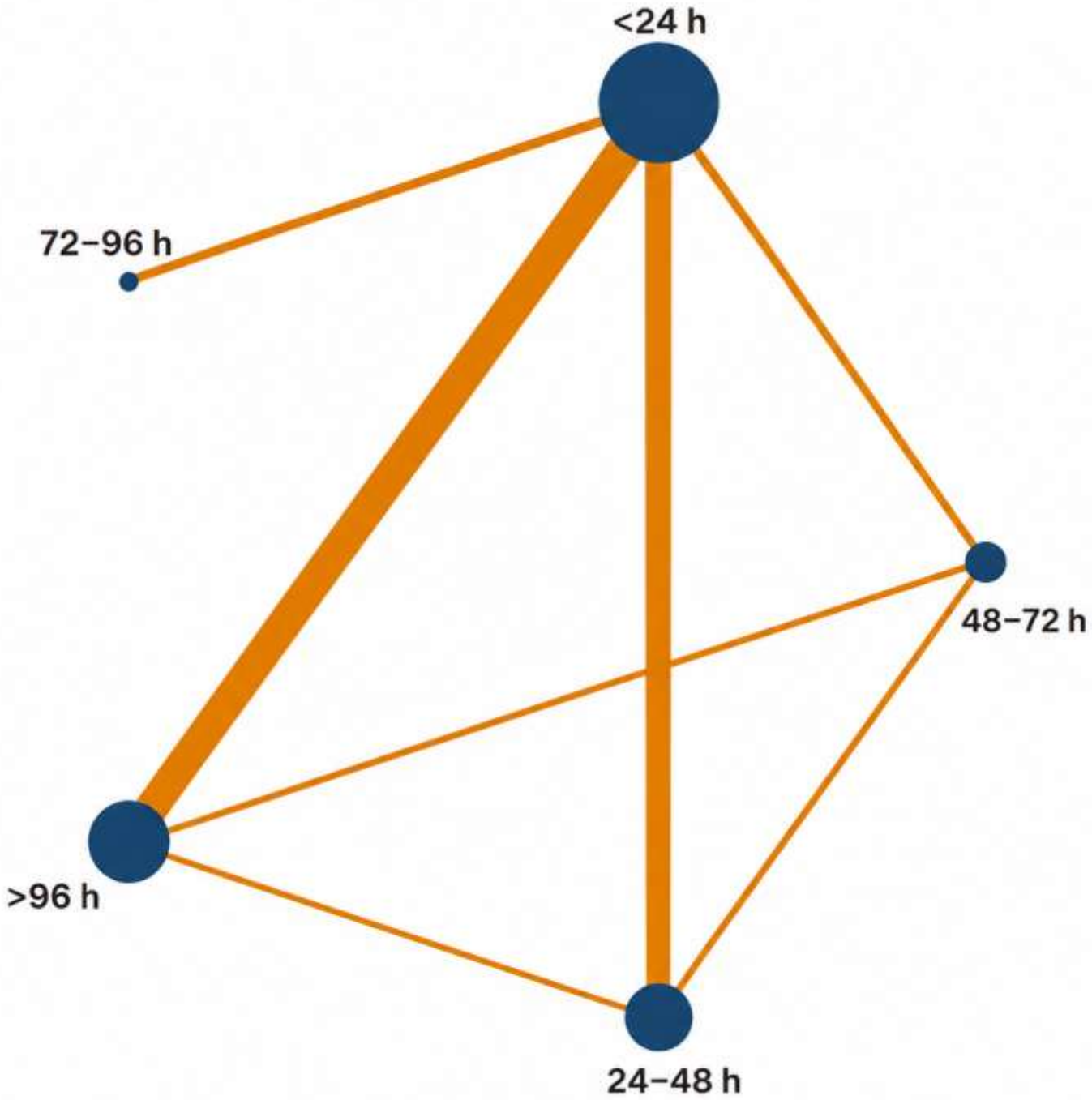
Research Question

Component	Description
Population	Critically ill admitted in ICU
Intervention	Initiation of enteral nutrition at different time windows
Comparator	≤ 24hrs, 24-48hrs, 48-72hrs, 72-96hrs, > 96hrs
Outcomes	Mortality, ICU LoS

PROSPERO Registered and PRISMA-NMA Checklist provided
Literature Search: Pubmed, Embase, Cochrane library, web of science
Analysis: 15 RCTs ; n= 903

Dai M et al. Front Nutr. 2026; 6;13:1722626.

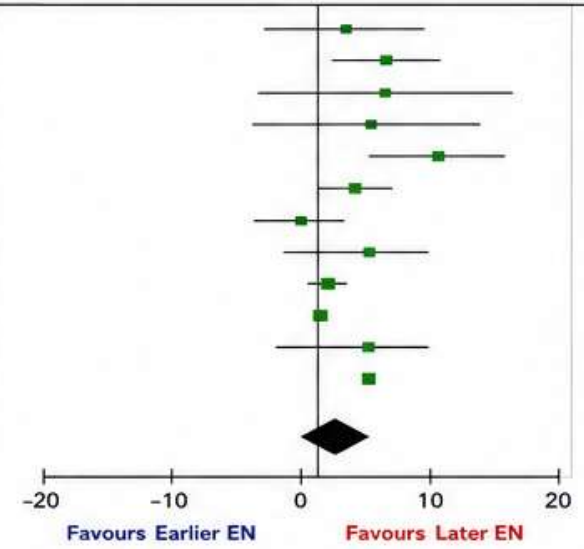
Network Plot



No mortality benefit

B. ICU LENGTH OF STAY (days): Earlier EN initiation vs Later EN initiation

Study (Year)	Design	Population (Predominant)	Mean (SD), days		Weight (%)	Mean Difference (IV, Random, 95% CI)	Risk of Bias (RoB 2) Domains					
			Earlier EN	Later EN			D1	D2	D3	D4	D5	Overall
Chourdakis, M 2012	RCT	Abdominal surgery	24.8 (6.8)	23.7 (7.6)	12.6	1.10 (-2.76, 4.96)	+	?	+	?	+	Some concerns
Eerahm, EH 2002	RCT	Multiple organ failure	11.9 (7.5)	8.7 (3.7)	9.2	3.20 (1.04, 5.36)	+	!	+	+	+	Low
Kopman, L 1999	RCT	Blunt trauma	15.8 (12.7)	12.7 (9.7)	8.7	3.10 (-3.18, 9.38)	+	+	+	!	+	Low
Mirand, 2000	RCT	Blunt trauma	15.0 (8.3)	12.6 (10.5)	10.2	2.40 (-3.08, 7.88)	!	!	+	−	!	High
Nguyen, NQ 2008	RCT	Mechanically ventilated	19.5 (10.0)	13.1 (5.5)	10.7	6.40 (2.53, 10.27)	+	+	+	+	+	Low
Pock, M 2004	RCT	Traumatic brain injury	8.9 (4.1)	7.0 (2.5)	11.8	1.90 (0.30, 3.50)	+	+	+	!	+	Some concerns
Stein, J 2002	RCT	Blunt trauma	12.0 (4.6)	12.9 (5.8)	12.9	-0.90 (-3.29, 1.49)	+	+	+	+	+	Low
Te, AS 2001	RCT	Critically ill patients	6.8 (5.7)	4.4 (8.6)	7.5	2.40 (-1.53, 6.33)	+	+	!	−	+	Some concerns
Waters, JH 1987	RCT	Abdominal surgery	5.2 (1.7)	4.7 (1.8)	13.4	0.50 (-0.41, 1.41)	+	!	+	−	+	High
Wang, J 2023	RCT	Critically ill patients	2.2 (0.7)	2.0 (0.6)	13.2	0.20 (-0.03, 0.43)	+	+	+	+	+	Low
Yu, AB 2021	RCT	Critically ill patients	6.8 (5.7)	4.4 (8.6)	7.5	2.40 (-1.53, 6.33)	+	+	+	+	+	Low
Sun, JX 2013	RCT	Septic shock	9.4 (1.7)	7.0 (1.2)	12.4	2.40 (1.90, 2.90)	+	+	!	−	+	Some concerns
Total (95% CI)			**684**	**689**	**100.0**	**0.74 (-1.08, 2.55)**						



Heterogeneity: $Tau^2 = 5.93$; $Chi^2 = 68.62$, df = 11 ($P < 0.00001$); $I^2 = 84\%$
Test for overall effect: $Z = 0.80$ ($P = 0.43$)

Definition of comparison: "Earlier EN" refers to EN initiation within ≤48 hours of ICU admission (i.e., <24 h or 24–48 h).
"Later EN" refers to EN initiation >48 hours (i.e., 48–72 h, 72–96 h or >96 h).

MD < 0 favours Earlier EN (shorter ICU stay)
MD > 0 favours Later EN

D1: Randomization process; D2: Deviations from intended interventions; D3: Missing outcome data; D4: Measurement of the outcome; D5: Selection of the reported result

+ Low risk ? Some concerns − High risk

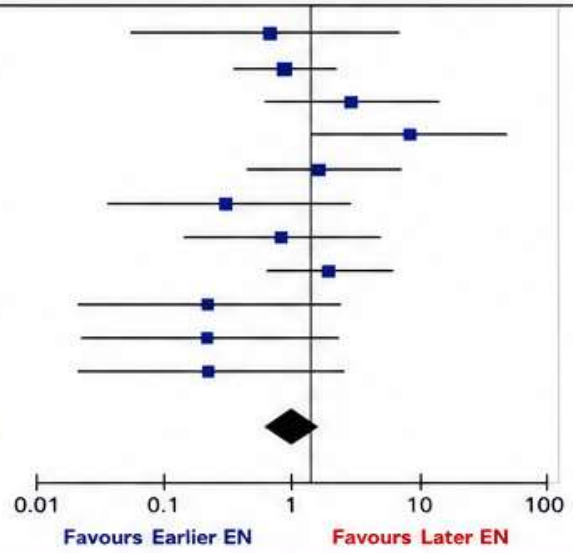
Similar ICU LoS

A. MORTALITY: Earlier EN initiation vs Later EN initiation

Study (Year)	Design	Population (Predominant)	Events / Total: Earlier EN	Events / Total: Later EN	Weight (%)	Risk Ratio (M-H, Random, 95% CI)	Risk of Bias (RoB 2) Domains: D1	D2	D3	D4	D5	Overall
Chourdakis, M 2012	RCT	Abdominal surgery	2 / 25	3 / 25	3.2	0.67 (0.12, 3.69)	+	?	+	?	+	Some concerns
Eerahm, EH 2002	RCT	Multiple organ failure	15 / 75	20 / 75	27.5	0.75 (0.42, 1.33)	+	!	+	+	+	Low
Mauder, KJ 2011	RCT	Blunt trauma	9 / 27	6 / 29	7.9	1.61 (0.66, 3.94)	+	+	+	!	+	Low
Mirand, 2000	RCT	Blunt trauma	12 / 14	6 / 16	8.4	3.31 (1.04, 10.54)	!	!	+	−	!	High
Nguyen, NQ 2008	RCT	Mechanically ventilated	6 / 14	6 / 14	8.2	1.00 (0.40, 2.49)	+	+	+	+	+	Low
Patel, JJ 2019	RCT	Multiple organ failure	2 / 15	5 / 16	5.1	0.35 (0.08, 1.59)	!	−	+	−	+	High
Pock, M 2004	RCT	Traumatic brain injury	7 / 15	10 / 15	13.7	0.74 (0.25, 2.16)	+	+	+	!	+	Some concerns
Stein, J 2002	RCT	Blunt trauma	12 / 40	10 / 40	13.7	1.20 (0.59, 2.44)	+	+	+	+	+	Low
Sun, JX 2013	RCT	Septic shock	2 / 30	7 / 30	7.7	0.29 (0.06, 1.31)	+	+	!	−	+	Some concerns
Watson, J 1987	RCT	Abdominal surgery	2 / 19	7 / 19	6.1	0.29 (0.07, 1.20)	+	!	+	−	+	High
Wang, J 2023	RCT	Critically ill patients	2 / 75	7 / 77	7.5	0.29 (0.06, 1.30)	+	+	+	+	+	Low
Total (95% CI)			**347**	**357**	**100.0**	**0.80 (0.59, 1.08)**						
Total events		79	87									

Heterogeneity: $Tau^2 = 10.80$; $Chi^2 = 10.69$, df = 10 (P = 0.37); $I^2 = 7\%$

Test for overall effect: Z = 1.48 (P = 0.14)



Definition of comparison: "Earlier EN" refers to EN initiation within ≤48 hours of ICU admission (i.e., <24 h or 24–48 h).
"Later EN" refers to EN initiation >48 hours (i.e., 48–72 h, 72–96 h or >96 h).

RR < 1 favours Earlier EN (lower mortality)
RR > 1 favours Later EN

Initiation timings and Outcomes

A. Mortality

<24 h				
1.20 (0.59,2.45)	24–48 h			
0.44 (0.09,2.01)	0.88 (0.31,2.50)	48–72 h		
1.06 (0.50,2.26)	0.83 (0.11,6.08)	0.94 (0.13,6.99)	72–96 h	
1.00 (0.16,6.38)	0.67 (0.29,1.56)	0.76 (0.32,1.83)	0.81 (0.12,5.44)	>96 h

B. ICU Length of stay (days)

<24 h				
-1.69 (-4.69,1.31)	24–48 h			
-5.69 (-12.17,0.79)	1.99 (-2.07,6.05)	48–72 h		
0.30 (-2.44,3.04)	3.59 (-2.53,9.71)	1.60 (-4.40,7.60)	72–96 h	
1.90 (-3.44,7.24)	3.22 (-0.82,7.26)	1.23 (-2.68,5.15)	-0.37 (-6.39,5.66)	>96 h

SUCRA Ranking for mortality by EN initiation timing

Mortality	
EN timing	SUCRA Ranking
< 24 hours	51.7%
24 – 48 hours	**67%**
48 – 72 hours	55.4%
72 – 96 hours	49.8%
> 96 hours	26.1%

ICU length of stay	
EN timing	SUCRA Ranking
< 24 hours	41.3%
24 – 48 hours	12.3%
48 – 72 hours	49.4%
72 – 96 hours	71.8%
> 96 hours	**75.2%**

Interpretation

Mortality – No benefit

ICU – No benefit

SUCRA RANKING

Mortality: 24 – 48 hours

ICU LoS: > 96 hours

No statistically significant difference

5 EN initiation windows instead to just early vs delayed

Restricted inclusion to RCTs

No global or loop inconsistency in NMA

Large proportion of surgical patients

ICU LoS: competing risk with early mortality not accounted

Calories

HOW THE EVIDENCE EVOLVED

JAMA EDEN Trial: Initial Trophic vs Full Enteral Feeding in Acute Lung Injury

The EDEN Randomized Trial (ARDS Network)

OBJECTIVE: To determine whether initial lower-volume trophic enteral feeding improves ventilator-free days compared with initial full enteral feeding in mechanically ventilated patients with acute lung injury.

- **Design:** Multicenter, randomized, open-label trial
- **Setting:** 44 hospitals in the ARDS Network (2008–2011)
- **Participants:** 1,000 adults with acute lung injury within 48 h of meeting inclusion criteria
- **Randomization:** 1:1

INTERVENTION: FIRST 6 DAYS (RANDOMIZED PERIOD)

TROPHIC ENTERAL FEEDING (n = 508)

Start at **20 kcal/hour**
≈ 480 kcal/day (prescribed)
≈ 400 kcal/day (delivered)
≈ 25% of calculated calorie target

VS.

FULL ENTERAL FEEDING (n = 492)

Start at **25 mL/hour**
Increase by **25 mL/hour** every 6 hours as tolerated
Target: 25–30 kcal/kg/day (non-protein energy)

(standardized protocol), then reattempt.

DAY 7 ONWARD (FOR PATIENTS STILL ON MECHANICAL VENTILATION)

Trophic group switches to full-feeding protocol (advance by 25 mL/hour every 6 h as tolerated to reach target)

Both groups managed according to the **full-feeding protocol** until extubation or death

Full group continues full-feeding protocol

Baseline
Similar between groups (age ~50 yr; ~70% male; mean APACHE II score ~14; ~75% direct ALI)

Primary Outcome
Ventilator-free days (VFDs) through day 28 (alive and free of mechanical ventilation)

Key Secondary Outcome
60-day all-cause mortality (and gastrointestinal intolerance, infections, organ failure–free days)

PRIMARY OUTCOMES

	TROPHIC	FULL	Difference
VENTILATOR-FREE DAYS through day 28, Mean (95% CI)	14.9 days	15.0 days	−0.1 days
60-DAY MORTALITY % (95% CI)	23.2%	22.2%	1.0%

No significant difference

No significant difference

SELECTED SECONDARY OUTCOMES (FIRST 6 DAYS)

Outcome (% of patient feeding days)	Trophic (n = 508)	Full (n = 492)	*P* Value
Vomiting	1.7%	2.2%	0.05
Elevated gastric residual volume (GRV >400 mL)	2.2%	4.9%	<0.001
Constipation	2.1%	3.1%	0.003

Full-feeding group had higher mean plasma glucose and greater insulin requirements during the first 6 days.

First paradigm shift: Early full feeding was not better

Rice TW et al. JAMA. 2012;307(8):795-803

The NEW ENGLAND JOURNAL of MEDICINE

PERMiT Trial: Permissive Underfeeding vs Standard Enteral Feeding in Critically Ill Adults

Arabi YM, et al. N Engl J Med 2015;372:2398-408.

BACKGROUND: The appropriate caloric goal for critically ill adults is unclear. This trial evaluated whether a moderate delivery of nonprotein calories (permissive underfeeding) is non-inferior to standard feeding on 90-day mortality, while maintaining similar protein intake in both groups.

- **Design:** Multicenter, randomized controlled trial
- **Setting:** 7 ICUs in Saudi Arabia and Canada
- **Participants:** 894 critically ill adults (medical, surgical or trauma)
- **Randomization:** 1:1

INTERVENTION: UP TO 14 DAYS OF ENTERAL FEEDING

Target 40–60% of calculated caloric requirements (nonprotein calories)

PROTEIN TARGET
Similar to standard group (~1.2–1.5 g/kg/day of actual body weight)

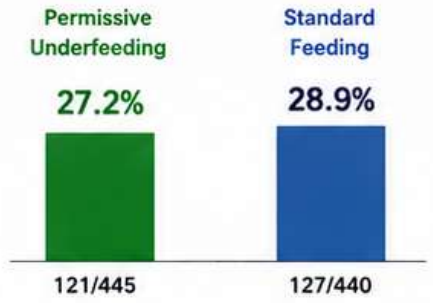
VS.

Target 70–100% of calculated caloric requirements (nonprotein calories)

PROTEIN TARGET
Similar to permissive group (~1.2–1.5 g/kg/day of actual body weight)

Both groups:
Same enteral formulas. Advancement as tolerated to reach assigned calorie targets. Parenteral nutrition was avoided during the first 7 days and used only if needed thereafter.

PRIMARY OUTCOME



Relative Risk 0.94
(95% CI, 0.76–1.16)
P = 0.58

No significant difference

ACTUAL INTAKE DURING INTERVENTION (MEAN ± SD)

46 ± 14% of caloric requirements

71 ± 22% of caloric requirements

P < 0.001

P = 0.29

Second paradigm shift: Lower target calories did not affect mortality

KEY SECONDARY OUTCOMES

Outcome	Permissive Underfeeding (n = 445)	Standard Feeding (n = 440)	Relative Risk (95% CI)	P Value
Feeding intolerance (high gastric residual volume, vomiting, or abdominal distension)	18.7%	17.5%	1.07 (0.86–1.34)	0.54
Diarrhea	17.8%	16.7%	1.07 (0.86–1.34)	0.54
ICU-acquired infection	41.3%	44.1%	0.94 (0.80–1.10)	0.44
ICU length of stay (days)	6 (3–11)	6 (3–11)	—	0.76
Hospital length of stay (days)	16 (8–28)	17 (9–30)	—	0.60

Calorie Requirement Estimation

Indirect Calorimetry

- Gold standard, limited availability
- Measures O2 consumption and CO2 production represents real-time energy metabolism

$$\text{REE (kcal/day)} = (3.941 \times VO_2\ [\text{L/min}] + 1.106 \times VCO_2\ [\text{L/min}]) \times 1{,}440$$

Equation	Equation Formula (Calculation of REE)	Patient Population	Sample Size (No.)	Accuracy Rate*
Harris-Benedict (1919)	Male: $66.4730 + (13.7516 \times W) + (5.0033 \times H) - (6.7550 \times A)$ Female: $655.0955 + (9.5634 \times W) + (1.8496 \times H) - (4.6756 \times A)$	ICU patients, 18 years and older	85	31.76%
		Patients under mechanical ventilation (BMI < 30)	76	No factor applied: 0% 1.3 factor: 21% 1.6 factor: 51%
ACCP recommendation	25 × weight - If BMI 16–25 kg/m^2 use usual body W - If BMI > 25 kg/m^2 use ideal body W - If BMI < 16 kg/m^2 use existing body weight for the first 7–10 days, then use IBW	ICU patients under mechanical ventilation	927	12%
Mifflin	Male: $(9.99 \times W) + (6.25 \times H) - (4.92 \times A) + 5$ Female: $(9.99 \times W) + (6.25 \times H) - (4.92 \times A) - 161$	ICU patients under mechanical ventilation	927	17.8%
		Medical and surgical patients who underwent IC	395	No factor applied: 35% 1.1 factor: 58%
Swinamer	$(945 \times BSA) - (6.4 \times A) + (108 \times T) + (24.2 \times RR) + (817 \times V_T) - 4,349$	Patients under mechanical ventilation (BMI < 30)	76	55%
		Ventilated patients	141	45%
Ireton-Jones (1992)	1,925 – (10 × A) + (5 × W) + (281 if male) + (292 if trauma present) + (851 if burns present)	Patients under mechanical ventilation (BMI < 30)	76	28%
		Medical, surgical, and trauma patients under mechanical ventilation	47	60%
Ireton-Jones (1997)	(5 × W) – (11 × A) + (244 if male) + (239 if trauma present) + (840 if burns present) + 1,784	Medical, surgical, and trauma patients under mechanical ventilation	47	36%
Penn State (1998)	$(1.1 \times \text{value of HBE}) + (140 \times T_{max}) + (32 \times V_E) - 5,340$	Patients under mechanical ventilation (BMI < 30)	76	39%
		Medical, surgical, and trauma patients under mechanical ventilation	47	68%
Penn State (2003)	$(0.85 \times \text{value of HBE}) + (175 \times T_{max}) + (33 \times V_E) - 6,433$	Ventilated patients	141	43%
		Medical, surgical, and trauma patients under mechanical ventilation	47	72%

nutrients

Effects of Energy Delivery Guided by Indirect Calorimetry in Critically Ill Patients: A Systematic Review and Meta-Analysis

Component	Study
Population	Critically ill adults
Intervention	Calorie delivery guided by Indirect calorimetry
Comparator	Energy delivery based on predictive equations
Primary outcome	ICU mortality
Secondary outcomes	Nosocomial pneumonia, bowel ischemia, hospital LOS,

PROSPERO – NOT Registered, OSF Registered
PRISMA Checklist provided
Literature Search: MEDLINE, Cochrane
Analysis: 9 RCTs ; n= 1178

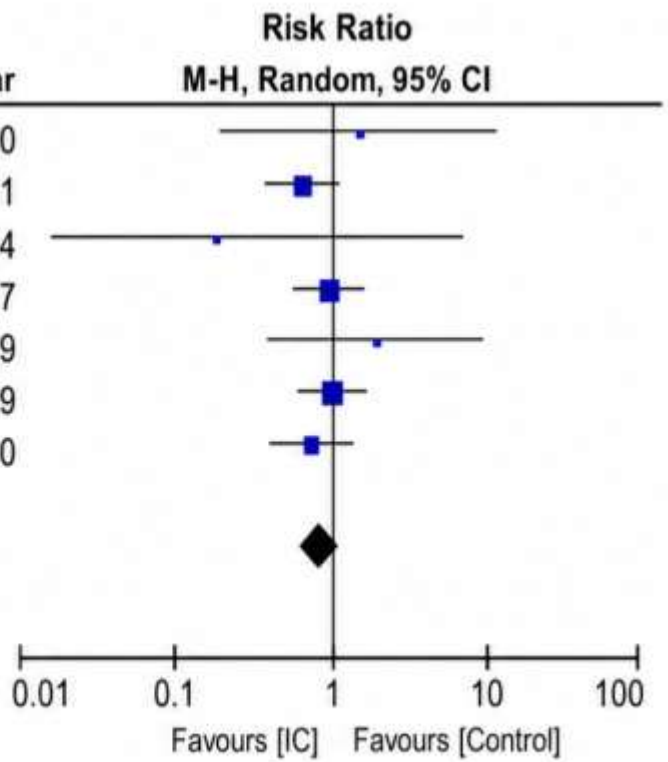
Watanabe S. et al. Nutrients. 2024; 11;16:1452

No difference in 90-day mortality

Study or Subgroup	IC Events	IC Total	Equation Events	Equation Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Jeffrey 1990	3	26	2	23	1.5%	1.33 [0.24, 7.26]	1990
Singer 2011	21	65	31	65	23.5%	0.68 [0.44, 1.05]	2011
Arfsar 2014	0	22	2	28	0.5%	0.25 [0.01, 5.00]	2014
Allingstrup 2017	30	100	32	98	26.0%	0.93 [0.61, 1.40]	2017
Gonzalez-Granda 2019	5	20	3	20	2.7%	1.67 [0.46, 6.06]	2019
Azevedo 2019	26	57	29	63	29.2%	0.99 [0.67, 1.46]	2019
Singer 2020	22	200	29	200	16.5%	0.76 [0.45, 1.27]	2020
Total (95% CI)		**490**		**498**	**100.0%**	**0.86 [0.70, 1.06]**	
Total events	107		128				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.94$, df = 6 (P = 0.68); $I^2 = 0\%$

Test for overall effect: Z = 1.38 (P = 0.17)



Clinical Nutrition

Higher versus lower enteral calorie delivery and gastrointestinal dysfunction in critical illness: A systematic review and meta-analysis

Component	Study
Population	Critically ill adults
Intervention	Higher calorie EN (1673 ± 468 kcal/day)
Comparator	Lower calorie EN (1121 ± 312 kcal/day)
Primary outcome	Gastric residual volume
Secondary outcomes	Nausea/vomiting

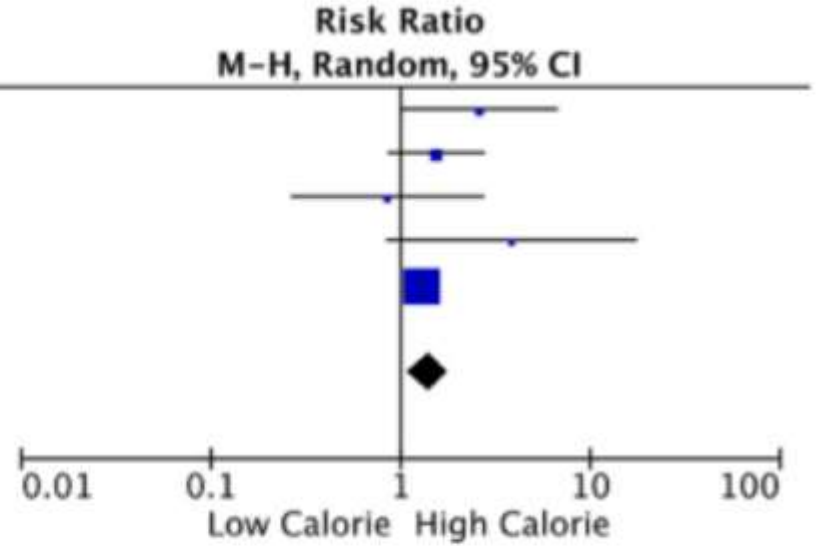
PROSPERO –Registered
PRISMA Checklist provided
Literature Search: MEDLINE, Cochrane
Analysis: 13 RCTs ; n= 6824

Murthy TA et al. Clin Nutr. 2022;41:2185-2194

Study or Subgroup	High Calorie Events	Total	Low Calorie Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Desachy 2008	13	50	5	50	6.5%	2.60 [1.00, 6.75]
McNelly 2020	21	62	13	59	14.8%	1.54 [0.85, 2.78]
Petros 2016	5	54	5	46	4.4%	0.85 [0.26, 2.76]
Rice 2011	8	102	2	98	2.7%	3.84 [0.84, 17.65]
TARGET investigators 2018*	855	1971	668	1986	71.7%	1.29 [1.19, 1.40]
Total (95% CI)		**2239**		**2239**	**100.0%**	**1.40 [1.09, 1.80]**
Total events	902		693			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 4.83$, df = 4 (P = 0.31); $I^2 = 17\%$

Test for overall effect: Z = 2.60 (P = 0.009)



*TARGET study includes re-analysed data for the purpose of this meta-analysis.

Fig. 2. Forest plot showing the impact of higher calorie delivery on gastric residual volume ≥300 ml in critically ill patients.

Study or Subgroup	High calorie Events	Total	Low calorie Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Desachy 2008	6	50	6	50	13.8%	1.00 [0.35, 2.89]
Kompan 2004	1	27	9	25	5.0%	0.10 [0.01, 0.75]
Minard 2000	1	12	3	15	4.4%	0.42 [0.05, 3.51]
Mousavian 2020	2	29	0	29	2.4%	5.00 [0.25, 99.82]
Qiu 2017	2	71	6	73	7.6%	0.34 [0.07, 1.64]
Rice 2011	2	102	2	98	5.3%	0.96 [0.14, 6.69]
Rice 2012	11	492	9	508	17.8%	1.26 [0.53, 3.02]
TARGET investigators 2018	370	1971	309	1986	43.7%	1.21 [1.05, 1.38]
Total (95% CI)		**2754**		**2784**	**100.0%**	**0.93 [0.58, 1.49]**
Total events	395		344			

Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 10.28$, df = 7 (P = 0.17); $I^2 = 32\%$

Test for overall effect: Z = 0.31 (P = 0.76)

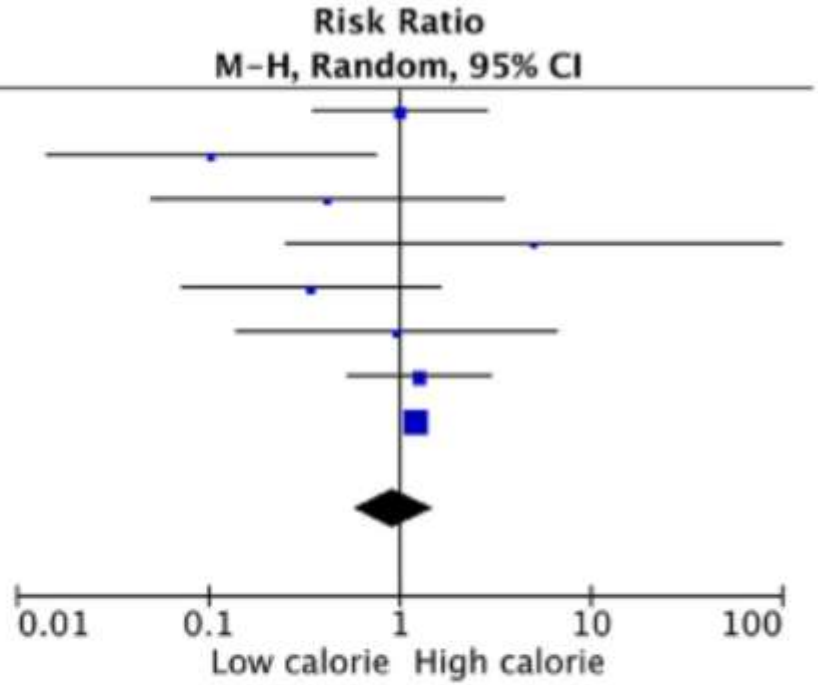


Fig. 3. Forest plot showing the impact of higher calorie delivery on vomiting or regurgitation in critically ill patients.

Study or Subgroup	High calorie Events	Total	Low calorie Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Arabi 2015	127	446	120	448	9.9%	1.06 [0.86, 1.31]
Desachy 2008	12	50	9	50	0.8%	1.33 [0.62, 2.88]
Peake 2014	28	57	25	55	2.9%	1.08 [0.73, 1.60]
TARGET investigators 2018	929	1971	779	1986	86.4%	1.20 [1.12, 1.29]
Total (95% CI)		**2524**		**2539**	**100.0%**	**1.18 [1.11, 1.27]**
Total events	1096		933			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.45$, df = 3 ($P = 0.69$); $I^2 = 0\%$

Test for overall effect: $Z = 4.96$ ($P < 0.00001$)

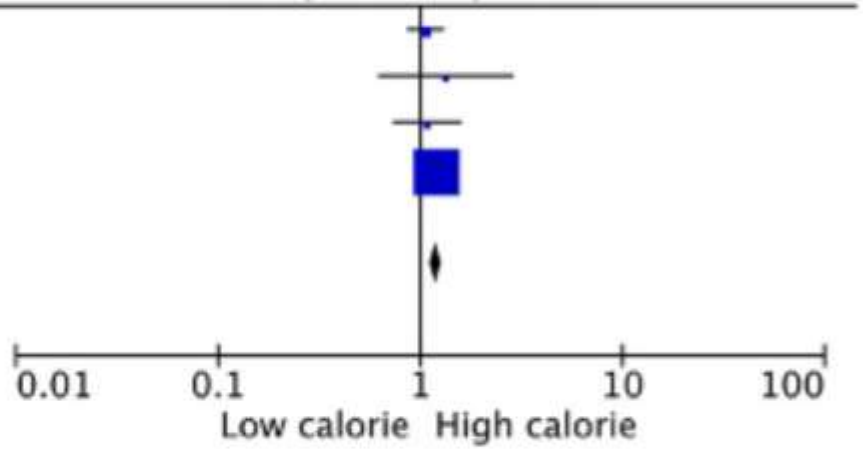


Fig. 4. Forest plot showing the impact of higher calorie delivery on administration of prokinetics in critically ill patients.

Summary of Part One

- Acute, chronic and convalescence phase of nutrition in critically ill
- EN vs PN:
  - No difference in mortality, more infections with PN
- Underfeeding EN vs full feeding EN:
  - Lower mortality, vomiting, diarrhea with 46-72% of target EE (2017)
- Continuous vs intermittent EN:
  - No difference in mortality or GI complications
- Time of EN Initiation:
  - No difference in mortality or ICU LoS

Summary of Part One

- EDEN Trial
  - ARDS patients with Trophic feeding (10ml/hr aka 20kcal/hr) vs full feeding (25ml/hr and increased to target 25-30 kcal/IBW) for first 6 days
  - Cumulative balance on day 7 – Trophic feeding group (0.4 Lit) vs Full feeding group (2.1Lit)
- Indirect calorimetry vs Predictive equations:
  - No difference in mortality
- Higher vs lower enteral calorie delivery:
  - RR for GRV > 300ml = 1.40 (1.09 – 1.80) and RR for prokinetic use = 1.18 (1.11 – 1.27)

Efficacy of permissive underfeeding for critically ill patients: an updated systematic review and trial sequential meta-analysis

Component	Study
Population	Critically ill adults with APACHE ≥ 10
Intervention	Permissive underfeeding (<70% of target or < 20 Kcal/kg/day)
Comparator	Isocaloric feeding (>70% or > 20Kcal/kg/day)
Primary outcome	Overall mortality
Secondary outcome	ICU mortality, ICU LoS

PROSPERO –Registered
PICOS framework, PRISMA Checklist given
Literature Search: Pubmed, Embase, Cochrane
Analysis: 23 RCTs ; n= 11444

Yue H. et al. J Intensive Care. 2024;12:4.

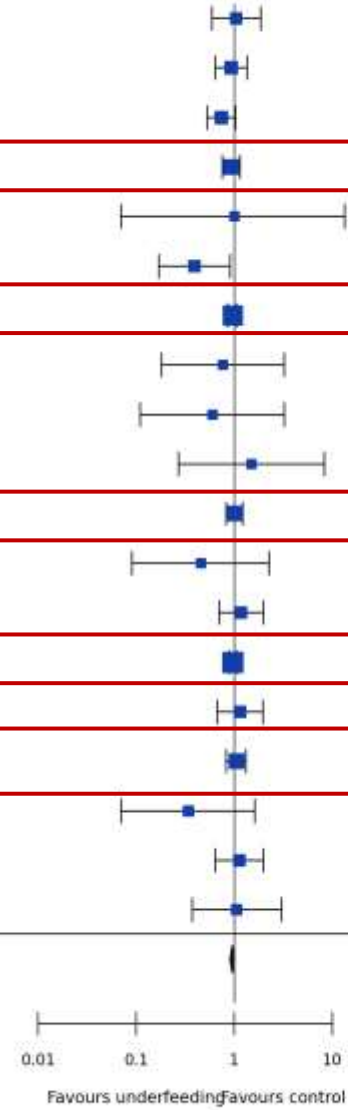
Permissive Underfeeding vs Control — Overall Mortality

Yue et al., Journal of Intensive Care 2024;12:4 | 19 RCTs | 11,181 participants

Study (Year)	Design	Study population	ICU / setting	Permissive underfeeding Events	Permissive underfeeding Total	Control Events	Control Total	Weight	Risk Ratio M-H, 95% CI	Risk of Bias (ROB 2) A	B	C	D	E	Overall
Aljada et al 2019	RCT	Critically ill adults	Medical-surgical ICU	16	46	15	45	0.9%	1.04 [0.59, 1.85]	!	!	+	−	+	−
Allingstrup et al 2017	RCT	Acutely admitted, mechanically ventilated adults	Mixed adult ICU	34	99	37	100	2.1%	0.93 [0.64, 1.35]	+	+	+	+	+	+
Arabi et al 2011	RCT	Critically ill adults	Medical-surgical ICU	38	116	52	117	2.9%	0.74 [0.53, 1.03]	+	!	+	−	+	−
Arabi et al 2015	RCT	Critically ill adults	Medical / surgical / trauma ICUs	131	438	140	436	8.0%	0.93 [0.76, 1.14]	+	+	+	+	+	+
Berg et al 2013	RCT	Traumatic brain injury / intracranial bleeding	Neurosurgical ICU	1	8	1	8	0.1%	1.00 [0.07, 13.37]	!	!	+	−	+	−
Braunschweig et al 2014	RCT	Acute lung injury	Medical / surgical ICUs	6	38	16	40	0.9%	0.39 [0.17, 0.90]	+	!	+	−	+	−
Chapman et al 2018	RCT	Mechanically ventilated critically ill adults	46 ICUs, Australia / New Zealand	505	1966	523	1948	29.8%	0.96 [0.86, 1.06]	+	+	+	!	+	!
Charles et al 2014	RCT	Surgical ICU patients requiring nutrition support	Surgical ICU	3	41	4	42	0.2%	0.77 [0.18, 3.22]	+	!	+	+	+	!
McCowen et al 2000	RCT	Critically ill adults receiving TPN	ICU	2	21	3	19	0.2%	0.60 [0.11, 3.23]	!	!	+	−	+	−
Mousavian et al 2020	RCT	Neurosurgical / neurocritical patients	Trauma / stroke / neurosurgery ICUs	3	29	2	29	0.1%	1.50 [0.27, 8.33]	!	!	+	+	+	!
Needham et al 2013	RCT	Acute lung injury, mechanically ventilated adults	ARDS Clinical Trials Network ICUs	145	481	141	470	8.1%	1.00 [0.83, 1.22]	+	!	+	+	+	!
Owais et al 2014	RCT	Patients requiring short-term parenteral nutrition	Hospital-based critical care population	2	24	4	22	0.2%	0.46 [0.09, 2.26]	!	!	+	+	+	−
Petros et al 2014	RCT	Critically ill adults requiring artificial nutrition	Medical ICU	18	46	18	54	0.9%	1.17 [0.70, 1.98]	+	!	+	!	+	!
Reignier et al 2023	RCT	Ventilated adults with shock	ICU	628	1521	648	1515	36.8%	0.97 [0.89, 1.05]	+	!	+	+	+	!
Rice et al 2011	RCT	Mechanically ventilated acute respiratory failure	Medical / surgical ICUs	22	98	20	102	1.1%	1.14 [0.67, 1.96]	+	!	+	!	+	!
Rice et al 2012	RCT	Acute lung injury requiring mechanical ventilation	44 ARDS Network hospitals / ICUs	118	508	109	492	6.3%	1.05 [0.83, 1.32]	!	!	+	!	+	!
Rice et al 2018	RCT	Overweight / obese mechanically ventilated adults	Medical ICUs	2	52	6	53	0.3%	0.34 [0.07, 1.61]	!	!	+	!	+	!
Rugeles et al 2016	RCT	Adult ICU patients requiring enteral nutrition >96 h	ICU	18	60	16	60	0.9%	1.13 [0.64, 1.99]	+	+	+	!	+	!
Sun et al 2021	RCT	Adults with sepsis receiving enteral nutrition	ICU	5	18	5	19	0.3%	1.06 [0.37, 3.04]	+	!	+	−	+	−
Total (95% CI)				**1697**	**5610**	**1760**	**5571**	**100.0%**	**0.96 [0.91, 1.01]**						
Total events				1697		1760									

Heterogeneity: $\chi^2 = 12.41$, df = 18 (P = 0.83); $I^2 = 0\%$

Test for overall effect: Z = 1.52 (P = 0.13)



ROB 2: + Low risk ! Some concerns − High risk

A Randomization B Deviations C Missing data D Outcome measurement E Reported result

Population/setting labels verified against the original study reports/journal sources where available.

Source: Yue et al. 2024; Figure 3 + Table S2; individual trial reports.

Permissive underfeeding vs isocaloric feeding – ICU Mortality

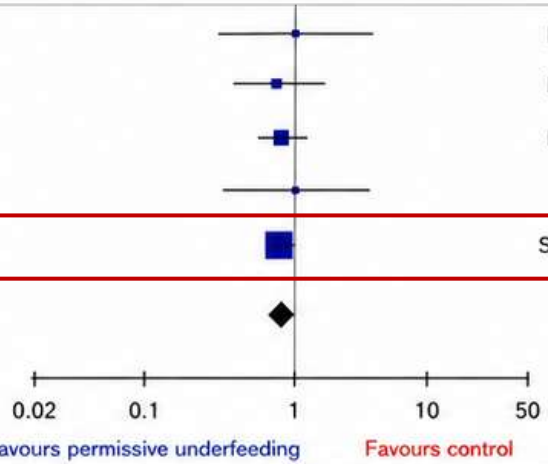
Yue et al., Journal of Intensive Care 2021;9:7 | 5 RCTs (4,361 patients)

A. Original analysis (all 5 studies)

Study or Subgroup	Permissive underfeeding Events	Permissive underfeeding Total	Control (isocaloric feeding) Events	Control (isocaloric feeding) Total	Weight (%)	Risk Ratio M-H, Fixed, 95% CI	Type of Population	Setting (ICU)	Risk of Bias (RoB 2) D1	D2	D3	D4	D5	Overall
Aljada et al 2019	9	46	9	45	1.5	0.98 [0.43, 2.24]	Mixed medical–surgical	Mixed	+	+	!	+	!	Some concerns
Arabi et al 2011	21	120	26	120	4.1	0.81 [0.48, 1.35]	Mixed medical–surgical	Mixed	+	+	!	!	!	Some concerns
Arabi et al 2015 (PermiT)	72	448	85	446	13.6	0.84 [0.63, 1.12]	Mixed medical–surgical	Mixed	+	+	+	+	+	Low
Petros et al 2014	10	46	12	54	1.8	0.98 [0.47, 2.05]	Cardiac surgery	Cardiac ICU	+	+	!	!	!	Some concerns
Reignier et al 2023 (NUTRIREA–3)	450	1521	495	1515	79.1	0.91 [0.81, 1.01]	Shock (medical–surgical)	Mixed	+	+	+	+	+	Low
Total (95% CI)		**2181**		**2180**	**100.0**	**0.90 [0.81, 0.99]**								
Total events	562		627											

Heterogeneity: Chi² = 0.46, df = 4 (*P* = 0.98); I^2 = 0%

Test for overall effect: Z = 2.25 (*P* = 0.02)

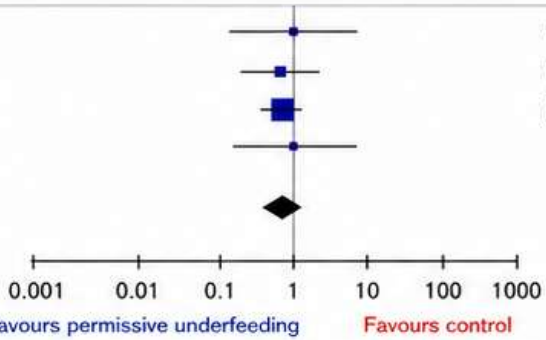


B. Sensitivity analysis (NUTRIREA–3 excluded)

Study or Subgroup	Permissive underfeeding Events	Permissive underfeeding Total	Control (isocaloric feeding) Events	Control (isocaloric feeding) Total	Weight (%)	Risk Ratio M-H, Fixed, 95% CI	Type of Population	Setting (ICU)	Risk of Bias (RoB 2) D1	D2	D3	D4	D5	Overall
Aljada et al 2019	9	46	9	45	9.4	0.98 [0.43, 2.24]	Mixed medical–surgical	Mixed	+	+	!	+	!	Some concerns
Arabi et al 2011	21	120	26	120	24.2	0.81 [0.48, 1.35]	Mixed medical–surgical	Mixed	+	+	!	!	!	Some concerns
Arabi et al 2015 (PermiT)	72	448	85	446	59.9	0.84 [0.63, 1.12]	Mixed medical–surgical	Mixed	+	+	+	+	+	Low
Petros et al 2014	10	46	12	54	6.5	0.98 [0.47, 2.05]	Cardiac surgery	Cardiac ICU	+	+	!	!	!	Some concerns
Total (95% CI)		**660**		**665**	**100.0**	**0.86 [0.68, 1.08]**								
Total events	112		132											

Heterogeneity: Chi² = 0.28, df = 3 (*P* = 0.96); I^2 = 0%

Test for overall effect: Z = 1.33 (*P* = 0.18)



RoB 2 domains:

D1 Randomization process
D2 Deviations from intended interventions
D3 Missing outcome data
D4 Measurement of the outcome
D5 Selection of the reported result

+ Low risk
! Some concerns
− High risk

Notes:

- Risk Ratio (RR) < 1 favours permissive underfeeding.
- Fixed–effect Mantel–Haenszel model used (I^2 = 0%).
- NUTRIREA–3 (Reignier et al, 2023) is the anchor trial excluded in the sensitivity analysis.

Type of population legend:

- Mixed medical–surgical: general ICU population with mixed diagnoses
- Cardiac surgery: patients after cardiac surgery
- Shock (medical–surgical): patients with shock (septic/circulatory)

Analysis

- No difference in overall mortality with underfeeding vs full feeding
- Lower ICU mortality with underfeeding
  - Robustness reduced by sensitivity analysis and TSA
- Protein intake – not accounted
- No difference in ICU LoS and infectious complications

Calories: How many and when?

ICU phase	Calorie target	Practical approach
First 7 days	≤70% of estimated EE	To be adjusted as per tolerance and clinical characteristics of each patient Aggressive feeding in first week may be avoided
Day 8 onwards	80–100% of estimated EE	Increase as per clinical status Correct accumulated deficit

Estimated EE = 25 – 30 Kcal/kg/day by IBW

Protein

ACUTE SKELETAL MUSCLE WASTING IN CRITICAL ILLNESS

Puthucheary ZA, et al. JAMA. 2013;310(15):1591–1600.

METHODOLOGY

STUDY DESIGN
Prospective observational cohort study

SETTING
2 hospitals (UK): University teaching & community

DURATION
Aug 2009 – Apr 2011

SAMPLE
63 critically ill patients

INCLUSION CRITERIA

- Age ≥18 years
- Intubated within 24 h and anticipated >48 h
- Expected ICU stay >7 days
- Anticipated to survive ICU stay

TWO GROUPS (COMPARISONS)

FASTED HEALTHY CONTROLS
(n = 8)
For protein synthesis comparison

CRITICALLY ILL PATIENTS
(n = 63)
Assessed serially during ICU stay

BASELINE CHARACTERISTICS (n = 63)

DEMOGRAPHICS & SEVERITY	
Mean age (years)	55
Male sex	60%
Mean APACHE II score	24
Mean/Median BMI (kg/m²)	28 (median)
Median ICU stay (days)	16
Median IMV duration (days)	10

ADMISSION DIAGNOSIS	% of patients
Sepsis	49%
Trauma	25%
Cardiogenic shock	10%
Acute liver failure (ALF)	8%
Intracranial hemorrhage (ICH)	8%
Other / Miscelleneous	—

COMORBIDITIES & OTHER TREATMENTS	
Hypertension (HTN)	19%
Ischemic heart disease (IHD)	15%
Diabetes mellitus (DM)	13%
Chronic obstructive pulmonary disease (COPD)	14%

Renal replacement therapy (RRT) during ICU stay — 30%

MEASUREMENTS & ASSESSMENTS

Muscle mass (primary measure)
Rectus femoris cross-sectional area (CSA) by ultrasound on days 1, 3, 7 and 10

Muscle structure (subset)
Fiber CSA and protein:DNA ratio by biopsy on days 1 and 7

Protein kinetics (subset)
Muscle protein synthesis (fractional synthetic rate) and leg protein breakdown

Signaling pathways (subset)
Intracellular anabolic and catabolic signaling (separate mechanistic subset)

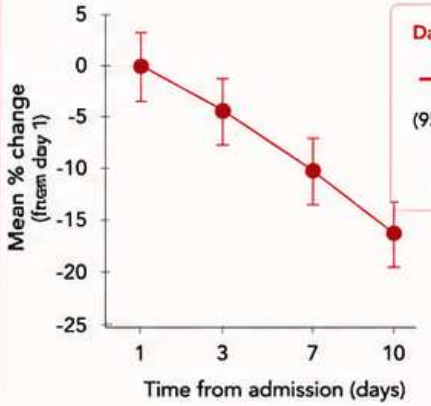
CSA = cross-sectional area; ICU = intensive care unit; IMV = invasive mechanical ventilation; ALF = acute liver failure; ICH = intracanial hemorrhage; RRT = renal replacement therapy; HTN = hypertension; IHD = ischemic heart disease; DM = diabetes mellitus; COPD = chronic obstructive pulmonary disease; BMI = body mass index; Phe = phenylalanine

RESULTS

PRIMARY OUTCOMES (Co-primary)

1. SKELETAL MUSCLE WASTING

Change in rectus femoris CSA over the first 10 days



Day 10 change
−17.7%
(95% CI, −20.9 to −4.8)
P < .001

2. PATHOPHYSIOLOGY OF MUSCLE METABOLISM

Muscle protein synthesis (fractional synthetic rate, %/h)

Fasted controls	Patients Day 1	Patients Day 7	Fed controls
0.039%/h (95% CI, 0.029–0.048)	0.035%/h (95% CI, 0.022–0.047)	0.076%/h (95% CI, 0.032–0.120)	0.065%/h (95% CI, 0.049–0.080)

Day 1 vs fasted controls: *P* = .57 | Day 7 vs fed controls: *P* = .30

Leg protein breakdown (μmol Phe/min/IBW × 100)

Day 1		Day 7	
8.5 (95% CI, 4.7–12.3)	⟷	10.6 (95% CI, 6.8–14.4)	*P* = .40 (no significant change)

KEY SECONDARY OUTCOMES

Change in muscle fiber CSA (days 1 to 7)
−17.5%
(95% CI, 5.8 to 29.3)

Change in protein:DNA ratio (days 1 to 7)
−29.5%
(95% CI, 13.4 to 45.6)

Multiorgan failure vs single organ failure (rectus femoris CSA) Day 7 change
−15.7% vs −3.0%
P < .001

Myofiber necrosis present
20 of 37 patients (54.1%)

Wasting evident as early as day 3 (−8.7% vs −1.8%; *P* = .03)

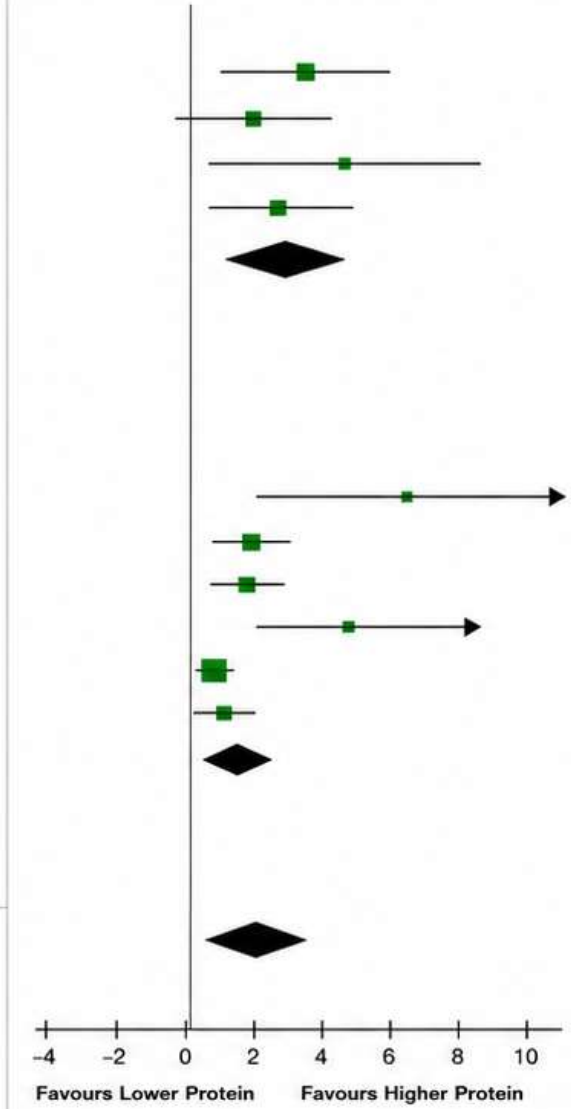
KEY TAKE-HOME MESSAGE

Critically ill patients lose skeletal muscle rapidly—about 12.5% by day 7 and 17.7% by day 10—driven by early suppression of protein synthesis and persistent protein breakdown, with greater loss in those with multiorgan failure.

Higher versus Lower Protein Nutrition on Handgrip Strength in Critically Ill Patients

Mohamed et al., Nutrients 2025;17:2613 | 5 RCTs (632 patients)

Study (Year)	Design	Population (Predominant)	Events / Total		Weight (%)	Mean Difference (kg) (IV, Random, 95% CI)	Risk of Bias (Quality Score 0–14)*								
			High Protein	Low Protein			A	B	C	D	E	F	G	H	Overall
A. High protein provided as ≥1.8–2.2 g/kg/day versus lower protein (≈1.2–1.5 g/kg/day)															
Chen (2011)	RCT	Medical ICU	11 / 49	10 / 49	15.6	1.50 [0.39, 2.61]	+	+	?	+	+	?	+	+	High (10)
Wang (2011)	RCT	Surgical ICU	3 / 61	7 / 60	10.1	0.90 [−0.11, 1.91]	+	+	?	+	+	?	+	+	Low (6)
Sun (2013)	RCT	Surgical ICU	2 / 30	1 / 30	6.2	2.00 [0.19, 3.81]	+	+	?	+	+	?	+	+	Low (6)
Cerra (1998)	RCT	Mixed ICU	7 / 31	8 / 35	11.7	0.99 [0.40, 2.41]	+	+	?	+	+	−	+	+	Moderate (8)
Subtotal (95% CI)			**171**	**174**	**43.6**	**1.34 [0.63, 2.05]**									
Total events		23	23	26											
Heterogeneity: Tau² = 0.10; Chi² = 4.73, df = 3 (P = 0.19); I² = 37%															
Test for overall effect: Z = 3.69 (P = 0.0002)															
B. High protein provided as ~1.5–1.7 g/kg/day versus lower protein (≈0.8–1.0 g/kg/day)															
Rapp (1983)	RCT	Mixed ICU	9 / 18	3 / 20	6.8	3.33 [1.07, 10.43]	+	+	?	+	+	?	+	+	High (9)
Young (1987)	RCT	Mixed ICU	10 / 28	10 / 23	9.4	0.82 [0.42, 1.62]	+	+	?	+	+	?	+	+	High (10)
Kudsk (1992)	RCT	Mixed ICU	5 / 29	11 / 45	10.2	0.80 [0.30, 1.37]	?	+	?	±	+	−	±	?	Moderate (7)
Woodcock (2001)	RCT	Mixed ICU	9 / 17	5 / 21	7.7	2.22 [0.92, 5.46]	?	±	?	±	?	−	±	±	Moderate (8)
Fetterplace (2018)	RCT	Mixed ICU	27 / 102	14 / 100	12.3	0.40 [0.08, 0.72]	+	+	+	+	+	−	±	+	High (12)
Azevedo (2019)	RCT	Mixed ICU	15 / 29	12 / 29	9.9	0.50 [0.01, 0.99]	+	?	+	+	+	+	+	+	Low (6)
Subtotal (95% CI)			**223**	**238**	**56.4**	**0.80 [0.32, 1.28]**									
Total events		75	65	65											
Heterogeneity: Tau² = 0.08; Chi² = 11.30, df = 5 (P = 0.05); I² = 56%															
Test for overall effect: Z = 3.28 (P = 0.001)															
Total (95% CI)			**394**	**412**	**100.0**	**1.04 [0.34, 1.74]**									
Total events		98	91	91											
Heterogeneity: Tau² = 0.10; Chi² = 18.75, df = 9 (P = 0.03); I² = 52%															
Test for overall effect: Z = 2.91 (P = 0.004)															
Test for subgroup differences: Chi² = 1.28, df = 1 (P = 0.26); I² = 21%															



*** Risk of Bias domains** (Cochrane RoB 2)

- **A** Randomisation process
- **B** Deviations from intended interventions
- **C** Missing outcome data
- **D** Measurement of the outcome
- **E** Selection of the reported result
- **F** Overall bias
- **G** Other bias
- **H** Recruitment bias

+ Low risk
? Some concerns
− High risk

EN = Enteral nutrition; PN = Parenteral nutrition; RCT = Randomised controlled trial; ICU = Intensive care unit; CI = Confidence interval; IV = Inverse variance

Impact of High-Protein Enteral Nutrition on Muscle Preservation in Mechanically Ventilated Patients with Severe Pneumonia: A Randomized Controlled Trial

Liu et al., Journal of Health, Population and Nutrition (2024) 43:152

STUDY AIM

To assess the effects of enteral nutrition with different protein concentrations on muscle mass in severe pneumonia patients, providing insights for enteral nutrition practice in ICUs.

STUDY DESIGN

Single-center, randomized controlled trial

June 1, 2022 – February 1, 2023

ICU, Dazhou Central Hospital, China

STUDY POPULATION

- Severe pneumonia patients admitted to ICU
- Age ≥18 years
- Expected to stay in ICU ≥96 hours

Total randomized: 120 patients

BASELINE CHARACTERISTICS (Overall Cohort, n = 120)

Mean age (years)	55
Sex (Male/Female)	72 / 48
Male (%)	60%
Ideal body weight (IBW) (kg)	58.83 ± 8.31
Body mass index (BMI) (kg/m²)	24.78 ± 3.41
SOFA score at admission	7.34 ± 2.11

METHODOLOGY

Assessed for eligibility (n = 343)

Excluded (n = 211)
- Did not meet inclusion criteria (n=81)
- Refused / not participating (n=53)
- History of neurological or neuromuscular diseases (n=22)
- Lower limb injury (n=24)
- Severe kidney dysfunction (n=39)
- Gastrointestinal diseases (n=15)
- Concurrent malignant tumors (n=27)
- Others (n=36)
- Pregnant (n=5)

Randomized (n = 120)

High-Protein Group (n = 60)

Standard-Protein Group (n = 60)

Follow-up & Assessments on Day 1, Day 5, Day 10
- Quadriceps thickness (QMT) by ultrasound
- Rectus muscle thickness (RMT) by ultrasound
- Diaphragm thickness (DMT) by ultrasound
- Nutritional status: Prealbumin, Albumin
- Adverse events: diarrhea, constipation, others

Analysis

Autoregressive of order 1 model (AR(1)) for repeated measures; group × time interaction

INTERVENTION (ENTERAL NUTRITION)

High-Protein Group	Standard-Protein Group
Protein target: 1.8 g/kg/day	Protein target: 1.2 g/kg/day
Energy target: 25–30 kcal/kg/day	Energy target: 25–30 kcal/kg/day
Delivered via enteral nutrition (continuous infusion)	Delivered via enteral nutrition (continuous infusion)

Nutrition provided from Day 1 to Day 10 of ICU admission

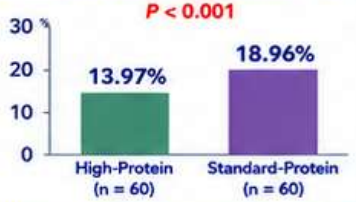
PRIMARY RESULT: QUADRICEPS MUSCLE THICKNESS (QMT)

Change in QMT by Day 10 (compared to Day 1 baseline)

High-Protein Group (n = 60)	Standard-Protein Group (n = 60)
−0.315 cm (95% CI, −0.340 to −0.289)	−0.429 cm (95% CI, −0.455 to −0.404)

Quadriceps Atrophy Rate (%) by Day 10

P < 0.001



The high-protein group had a significantly lower rate of quadriceps atrophy.

SECONDARY RESULT: DIAPHRAGM MUSCLE THICKNESS (DMT)

Change in DMT by Day 10 (compared to Day 1 baseline)

High-Protein Group	Standard-Protein Group
Atrophy rate: 33.76 ± 5.09%	Atrophy rate: 33.41 ± 4.53%

No significant difference between groups (P = 0.317).

OUTCOMES (Change by Day 10 vs Day 1 baseline)

Rectus Muscle Thickness (RMT)	Diaphragm Muscle Thickness (DMT)	Quadriceps Muscle Thickness (QMT)
High-Protein Group: −0.315 cm (95% CI, −0.340 to −0.289)	High-Protein Group: −0.315 cm (95% CI, −0.340 to −0.289)	High-Protein Group: −0.315 cm (95% CI, −0.340 to −0.289)
Standard-Protein Group: −0.429 cm (95% CI, −0.455 to −0.404)	Standard-Protein Group: −0.429 cm (95% CI, −0.455 to −0.404)	Standard-Protein Group: −0.429 cm (95% CI, −0.455 to −0.404)
P < 0.001	*P* = 0.317	*P* < 0.001

Both groups experienced enteral nutritional intolerance: diarrhea, constipation and other adverse events.

INTERPRETATION

In mechanically ventilated severe pneumonia patients, high-protein enteral nutrition (1.8 g/kg/day) significantly improved preservation of quadriceps muscle mass compared with standard protein (1.2 g/kg/day), without increasing adverse events.

Higher protein intake appears beneficial for limb muscle preservation in the early ICU phase.

STRENGTHS

- ✓ Randomized controlled design
- ✓ Repeated measurements with ultrasound (QMT, RMT, DMT) on Days 1, 5 and 10
- ✓ Homogeneous ICU population (severe pneumonia, mechanically ventilated)
- ✓ Relevant clinical outcomes
- ✓ Good protocol adherence and safety monitoring

LIMITATIONS

- Single-center study; results may not be generalizable
- Sample size relatively small (n = 120)
- Short follow-up duration (10 days only)
- Did not evaluate long-term functional outcomes (e.g., weaning success, ICU mortality)
- Potential confounding factors despite randomization

CONCLUSION

High-protein enteral nutrition (1.8 g/kg/day) significantly reduced quadriceps muscle loss and demonstrated good safety in mechanically ventilated patients with severe pneumonia, suggesting its suitability for widespread clinical application.

Higher Versus Lower Protein Delivery in Critically Ill: A Systematic Review and Bayesian Meta-Analysis

Research Question

Component	Description
Population	Critically ill (admitted to ICU or control group mortality > 5%)
Intervention	Higher protein (Mean across studies: 1.5 ± 0.6 gm/kg/day)
Comparator	Lower protein (Mean across studies: 0.9 ± 0.4 gm/kg/day)
Outcomes	Mortality, infections, mechanical ventilation duration

PROSPERO Registered and PRISMA Checklist provided
Literature Search: MEDLINE, Embase, CENTRAL
Analysis: 22 RCTs ; n= 4164

Heuts S et al. Crit Care Med. 2025:1;53:e645-e655

Strengths

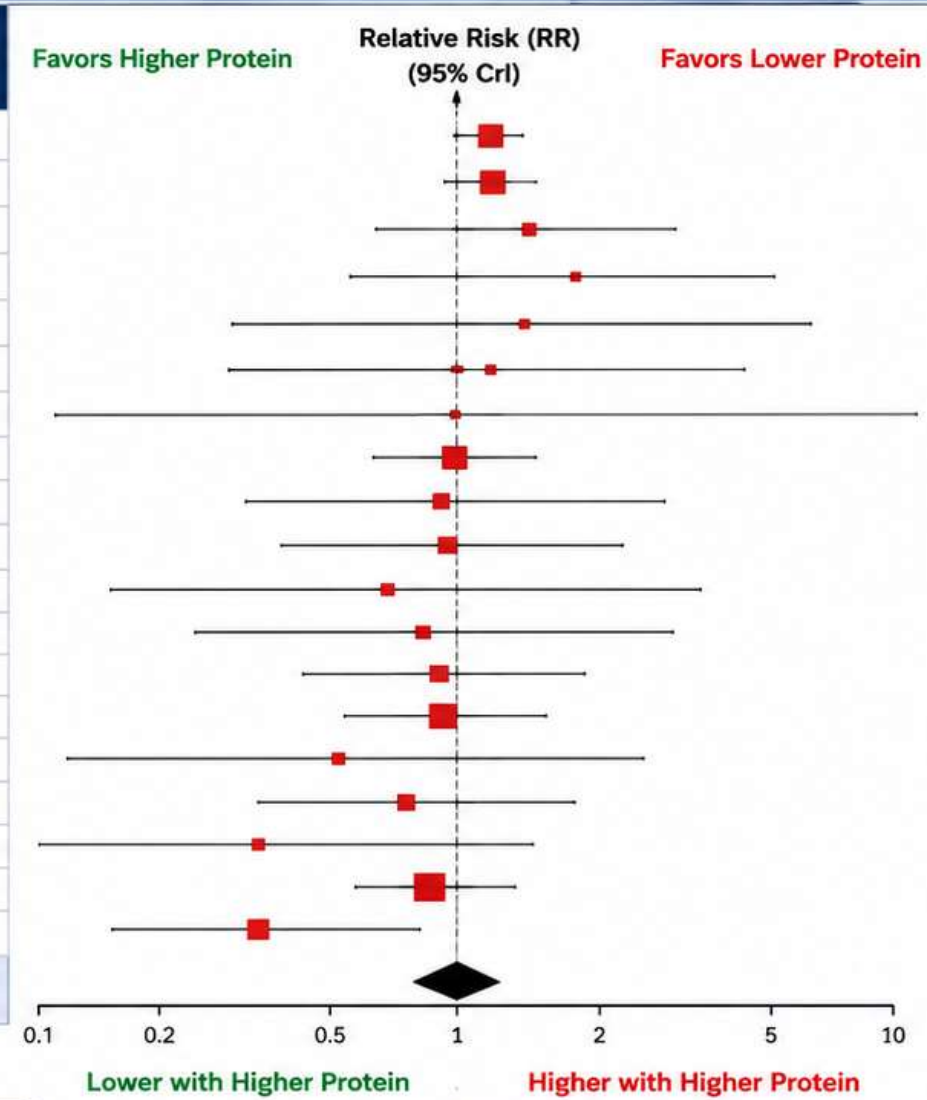
MCIDs

- Proposed MCIDs for each outcome based on published literature

Outcome	Effect measure	MCID		Rationale
		Beneficial	Harmful	
Mortality	Relative Risk (RR)	RR < 0.90	RR > 1.11	Arbitrary, investigator defined
Infections	RR	RR < 0.90	RR > 1.11	Based on analysis by Lee et al.
IMV Duration	Mean Difference (MD)	−1.0 day	+1.0 day	Derived from PRECISe trial protocol
Quality of life	Standardized Mean Difference (SMD)	+0.156	−0.156	

Higher vs. Lower Protein Delivery in Critically Ill Patients – Mortality (Bayesian Hierarchical Random-Effects Model)

Study (Year)	Higher Protein		Lower Protein		Relative Risk (RR) (95% CI)	Weight (%)	Type of Patients	Risk of Bias (RoB 2.0)
	Events	Total	Events	Total				
Heyland 2023	279	603	231	597	1.14 (0.97–1.34)	15.3	Mixed	+
Bels 2024	233	1118	193	1116	1.15 (0.94–1.41)	14.0	Mixed	+
Ferrerie 2015	77	78	56	78	1.36 (0.62–2.98)	3.0	Mixed	!
Bukhari 2020	107	276	62	242	1.72 (0.54–5.50)	1.5	Medical	!
Salle 1990	12	29	8	22	1.44 (0.26–7.86)	0.7	Surgical	–
Singer 2008	77	409	64	390	1.13 (0.27–4.76)	1.0	Mixed	+
Clifton 1985	1	38	1	40	1.00 (0.07–13.87)	0.2	Surgical	–
Azevedo 2019	74	208	78	215	0.99 (0.67–1.46)	7.0	Mixed	+
Nakamura 2020	34	107	36	110	0.95 (0.33–2.76)	2.3	Mixed	!
Mesejo 2003	20	56	18	41	0.95 (0.41–2.22)	2.1	Medical	!
van Zanten 2018	11	65	18	66	0.67 (0.12–3.61)	0.8	Mixed	!
Fetterplace 2018	16	125	21	125	0.80 (0.24–2.68)	1.6	Mixed	!
Chapple 2020	6	31	8	28	0.87 (0.44–1.72)	2.3	Mixed	!
Carteron 2021	38	201	44	197	0.90 (0.53–1.57)	4.5	Mixed	!
Dresen 2021	12	72	24	68	0.50 (0.10–2.44)	1.0	Mixed	!
Zhou 2006	11	32	16	31	0.73 (0.33–1.81)	1.8	Surgical	–
Danielis 2019	6	42	18	43	0.32 (0.07–1.34)	0.9	Mixed	–
Doig 2015	13	53	13	52	0.85 (0.57–1.26)	5.4	Mixed	+
Wang 2024	6	33	14	33	0.42 (0.18–0.95)	1.6	Mixed	!
Pooled (Bayesian RE Model)	**1052**	**3513**	**958**	**3490**	**1.01 (0.84–1.16)**	**100.0**	–	–



Total patients: 7,003 (Higher 3,513; Lower 3,490)
Total events: 2,010 (Higher 1,052; Lower 958)
Bayesian hierarchical random-effects model with vague priors
Between-study heterogeneity (τ): mean = 0.10 (SD 0.06)
Median RR = 1.01; 95% CrI = 0.84–1.16

Risk of Bias (RoB 2.0)
- + Low risk
- ! Some concerns
- – High risk

Interpretation (Bayesian)
- *P*(any benefit, RR<1.00) = 43.6%
- *P*(any harm, RR>1.00) = 56.4%
- *P*(RR<0.95) = 22.9%; *P*(RR>1.05) = 32.4%
- *P*(RR<0.90) = 10.1%; *P*(RR>1.10) = 10.3%

TARGET PROTEIN TRIAL

Augmented Enteral Protein During Critical Illness (The TARGET Protein Randomized Clinical Trial)

Summers MJ et al. JAMA. 2025;334(4);319-328.

METHODOLOGY

Design:
Cluster randomized, crossover, open-label trial

Setting:
8 ICUs in Australia and New Zealand

Participants:
Critically ill adults receiving enteral nutrition

Reodomiment:
May 23, 2022 – Aug 23, 2023
Each ICU used both formulas sequentially for 3 months over a 12-month period.

KEY EXCLUSION CRITERIA

- Age < 18 years
- Expected ICU stay < 72 hours
- Pregnancy or breastfeeding
- Severe chronic liver disease (Child-Pugh C)
- Intestinal obstruction, short bowel syndrome
- Allergy to study formula components
- Decision to withhold or withdraw life-sustaining treatment
- Participation in another interventional trial

INTERVENTION (Days 0–14)

	AUGMENTED PROTEIN (High protein formula)	USUAL PROTEIN (Standard protein formula)
Protein content	100 g protein/L	63 g protein/L
Calorie content	Isocaloric with usual protein (~1.0 kcal/mL)	Isocaloric with augmented protein (~1.0 kcal/mL)
EN delivery	Continuous infusion via feeding pump Target rate: 80 mL/h (1.0 kcal/mL)	Target rate: 80 mL/h (1.0 kcal/mL)
Duration of intervention	First 14 days of ICU admission (enteral nutrition commenced early as per ICU practice)	

CALORIE REQUIREMENT

Calculated as 25–30 kcal/kg/day using Ideal Body Weight (IBW)

IBW calculated by the Devine formula:

- Men: 50 kg + 2.3 kg for each inch > 5 feet
- Women: 45.5 kg + 2.3 kg for each inch > 5 feet

(1 inch = 2.54 cm)

PROTEIN CALCULATION

Protein delivered and analyzed as g/kg/day based on **Ideal Body Weight (IBW)**

BASELINE CHARACTERISTICS

Characteristic	Augmented Protein Group (n=1681)	Usual Protein Group (n=1716)
Age, median (IQR), years	61 (48–71)	61 (49–70)
Male sex, n (%)	1068 (63.5)	1089 (63.4)
BMI, median (IQR), kg/m²	27.3 (23.6–31.6)	27.4 (23.7–31.5)
Medical diagnosis at ICU admission, n (%)		
• Sepsis	1008 (59.9)	1010 (58.8)
• Pneumonia	508 (30.2)	524 (30.5)
• Abdominal source	85 (5.1)	86 (5.0)
• Other	80 (4.8)	96 (5.6)
Acute respiratory failure, n (%)	1527 (90.8)	1556 (90.7)
Septic shock, n (%)	1351 (80.4)	1376 (80.2)
FiO_2 requirement at inclusion, median (IQR)	0.60 (0.40–0.80)	0.60 (0.40–0.80)
APACHE II score, median (IQR)	23 (18–29)	23 (18–29)

NUTRITION DELIVERED DURING INTERVENTION (DAYS 0–14)

Calories Delivered

Mean ± SD kcal/kg/day

Augmented Protein
25.6 ± 3.9
(~98% of target)

Usual Protein
25.4 ± 4.1
(~97% of target)

Protein Delivered

Mean ± SD g/kg/day

Augmented Protein
1.22 ± 0.20
(~100% of target)

Usual Protein
0.78 ± 0.18
(~95% of target)

Parenteral Nutrition (PN)

Received PN during trial (Days 0–14)

Augmented Protein: 46 (2.7%)

Usual Protein: 58 (3.4%)

PRIMARY OUTCOMES

Primary Outcome 1

Days Alive and Free from Hospital at Day 90 (all patients)

Median (IQR) days

Augmented Protein (n=1681)	Usual Protein (n=1716)
62 (0–77)	64 (0–77)

Adjusted between-group median difference
−1.97 days
(95% CI, −7.24 to 3.30)
P = .46

Primary Outcome 2

All-Cause Mortality at Day 90

Alive at day 90, n (%)

Augmented Protein (n=1681)	Usual Protein (n=1716)
1221 (72.6%)	1269 (74.0%)

Risk ratio 0.99
(95% CI, 0.95–1.03)
P = .81

GASTROINTESTINAL COMPLICATIONS During ICU Stay

Outcome	Risk Ratio (95% CI) Augmented vs Usual Protein	P Value
Vomiting	0.77 (0.67–0.89)	<0.001
Diarrhoea	0.83 (0.73–0.94)	0.004
Bowel ischaemia	0.50 (0.26–0.95)	0.030
Liver dysfunction	0.92 (0.86–0.99)	0.032
Large gastric residual volume (≥400 mL)	1.02 (0.86–1.21)	0.82

(Hazard/Risk ratios <1 favour augmented protein)

KEY SECONDARY OUTCOMES

Days free of hospital at Day 90 (in survivors):
Between-group difference
0.01 days (95% CI, −1.94 to 1.96)

Duration of invasive ventilation:
Mean difference 6.8 hours
(95% CI, −3.0 to 16.5)

ICU length of stay (time to live ICU discharge):
HR 0.93 (95% CI, 0.88–1.00)

Hospital length of stay (time to live hospital discharge):
HR 0.96 (95% CI, 0.90–1.02)

New kidney replacement therapy:
RR 0.97 (95% CI, 0.81–1.16)

Tracheostomy insertion:
RR 1.15 (95% CI, 0.66–2.01)

Discharge destination:
No significant differences

COMPLETION OF INTERVENTION (Days 0–14)

Completed full 14 days of intervention

Augmented Protein (n=1681)	Usual Protein (n=1716)
1512 (89.9%)	1539 (89.7%)

Did not complete 14 days
Reason for discontinuation, n (%)

	Augmented Protein (n=169)	Usual Protein (n=177)
Extubation	70 (41.4%)	77 (43.5%)
Switched to oral intake	38 (22.5%)	42 (23.7%)
Death	40 (23.7%)	40 (22.6%)
Other*	21 (12.4%)	18 (10.2%)

* Other: transfer out of ICU, intolerance, protocol deviation, other clinical reasons.
Percentages may not total 100 due to rounding.

NUTRITIONAL PROTOCOL AFTER DAY 14

After day 14, all patients received nutrition according to local ICU practice with no study formula restrictions. Clinicians were encouraged to meet estimated energy needs (≈ 25–30 kcal/kg/day) and protein needs (≈ 1.2–2.0 g/kg/day) as tolerated.

STRENGTHS

- Large, multicenter, cluster randomized crossover trial.
- High protocol adherence and data completeness.
- Isocaloric formulas – isolates effect of protein content.
- Robust statistical analyses adjusting for period effects.

LIMITATIONS

- Cluster design with only 8 ICUs – potential for residual confounding.
- Open-label design – performance bias possible.
- First 14 days only – long-term nutrition effects not assessed.
- Results may not generalize to parenteral nutrition or patients not receiving enteral feeding.

ABBREVIATIONS

APACHE II = Acute Physiology and Chronic Health Evaluation II; CI = confidence interval; FiO_2 = fraction of inspired oxygen; HR = hazard ratio; ICU = intensive care unit; IQR = interquartile range; RR = risk ratio; SD = standard deviation.

Glycemic Control

ORIGINAL ARTICLE | CRITICAL CARE REVIEWS MEETING 2024

A Patient-Level Meta-Analysis of Intensive Glucose Control in Critically Ill Adults

Research Question

Component	Description
Population	Critically ill adults admitted in ICU (medical + surgical)
Intervention	Intensive glycemic control (≤ 120 mg/dl)
Comparator	Conventional glycemic control (140 - 180mg/dl)
Outcomes	In-hospital mortality (censored at 90 days), IMV duration, Vasopressor requirement, RRT
Safety Outcome	Severe hypoglycemia (< 40mg/dl)
Time	Duration of ICU stay

Excluded: CCU, Stroke units

Adigbli D. et al.*NEJM Evid*. 2024;3:EVIDoa240082

In-hospital mortality: No difference

Outcome	No. of Trials	IGC (n)	CGC (n)	Effect Estimate	95% CI / CrI	P value
One-stage IPD (Model 1 – primary – mixed effect)	20	7059	7049	**RR 1.02**	0.96–1.07	0.52
One-stage (Model 2 – adjusted)	20	5683	5677	RR 1.02	0.95–1.09	—
One-stage (Model 3 – hospital random effect)	20	7059	7049	RR 1.02	0.97–1.08	—
One-stage (Model 4 – adjusted + hospital effect)	20	5683	5677	RR 1.02	0.95–1.10	—

More hypoglycemia in IGC

Outcome	No. of Trials	IGC (n)	CGC (n)	Effect Estimate	95% CI
Survival at 90 days	20	7060	7048	HR 1.03	0.97–1.10
Mechanical ventilation (proportion)	18	6785	6777	RR 1.00	0.97–1.04
Time to cessation of MV	18	6238	6191	HR 1.00	0.96–1.04
Severe Hypoglycemia (<40)	**20**	**933 (13.3%)**	**277 (3.9%)**	**RR 3.38**	**2.99–3.83**
Time to cessation of vasopressors	13	4115	4094	HR 0.96	0.91–1.00
New renal replacement therapy	11	4373	4394	RR 1.08	0.96–1.22
Time to cessation of RRT	9	403	370	HR 0.93	0.79–1.10

Timing in Shock

nutrients

Early Enteral Nutrition for Patients with Sepsis or Septic Shock: A Systematic Review and Meta-Analysis

Research Question

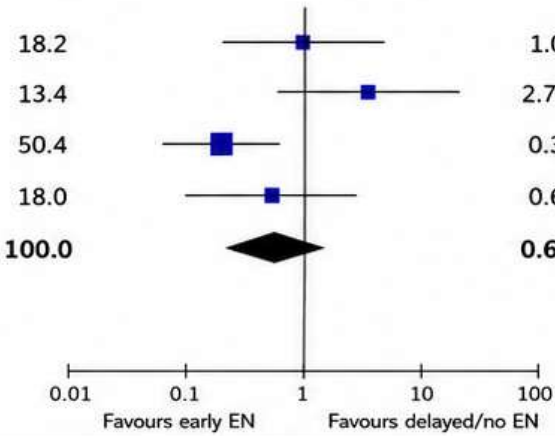
Component	Description
Population	ICU admission for ≥ 48 hours with sepsis or septic shock
Intervention	Initiation of early enteral nutrition (EEN) in ≤ 48 hours
Comparator	No enteral nutrition or delayed enteral nutrition (> 48 hours)
Outcomes	Mortality, duration of mechanical ventilation, feed intolerance

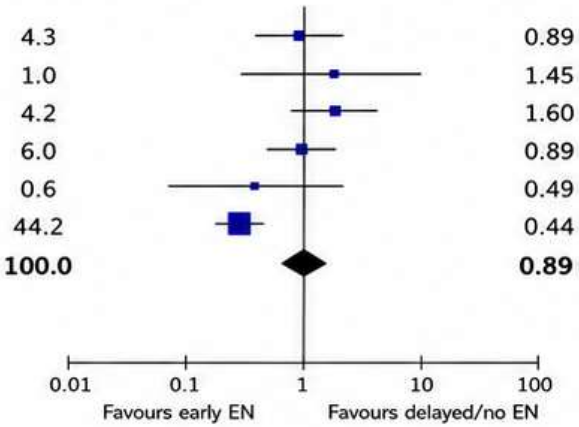
PROSPERO Registered and PRISMA Checklist provided
Literature Search: Medline, Embase, Central
Analysis: 5 RCTs ; n= 442, Non-RCT: 10, n=3724, Total=4166

Grillo-Ardila CF et al. Nutrients. 2024;16:1560

Early enteral nutrition (within 48 h) vs delayed/ no enteral nutrition – In-hospital mortality

Study or Subgroup	Study design	ICU type	Early enteral nutrition Events	Early enteral nutrition Total	Delayed/ no enteral nutrition Events	Delayed/ no enteral nutrition Total	Weight (%)	Odds Ratio M–H, Fixed, 95% CI	Pooled Odds Ratio M–H, Fixed, 95% CI	Risk of bias (overall)	Risk of bias domains D1	D2	D3	D4	D5	Overall
1.1 Randomized controlled trials (RCTs)																
Beale 2008	RCT	Mixed	16	27	17	28	18.2		1.05 (0.31–3.53)	Some concerns	+	!	!	+	!	!
Kaur 2005	RCT	Mixed	7	27	4	26	13.4		2.73 (0.74–10.16)	Some concerns	+	!	!	+	!	!
Malhotra 2004	RCT	Surgical	16	55	44	82	50.4		0.39 (0.19–0.78)	Some concerns	+	!	!	+	!	!
Patel 2019	RCT	Medical	12	25	14	25	18.0		0.69 (0.24–1.98)	Some concerns	+	!	!	+	!	!
Subtotal (95% CI)				**134**		**161**	**100.0**		**0.69 (0.39–1.23)**							
Total events			51		79											
Heterogeneity: Chi² = 1.61, df = 3 (P = 0.65); I² = 0%																
Test for overall effect: Z = 1.25 (P = 0.21)																
1.2 Non-randomized studies (NRSs)																
Wang 2021	NRS	Mixed	17	818	19	818	4.3		0.89 (0.45–1.73)	Serious / High	−	−	−	−	−	−
Kopp 2018	NRS	Mixed	10	68	3	28	1.0		1.45 (0.38–5.50)	Serious / High	−	−	−	−	−	−
Murphy 2023	NRS	Mixed	16	110	21	218	4.2		1.60 (0.81–3.18)	Serious / High	−	−	−	−	−	−
Ondr-Westys 2022	NRS	Mixed	161	526	32	100	6.0		0.89 (0.55–1.43)	Serious / High	−	−	−	−	−	−
Patel 2014	NRS	Mixed	13	37	5	9	0.6		0.49 (0.16–1.53)	Serious / High	−	−	−	−	−	−
Slone 2016	NRS	Mixed	137	877	63	211	44.2		0.44 (0.31–0.62)	Serious / High	−	−	−	−	−	−
Subtotal (95% CI)				**2,742**		**1,606**	**100.0**		**0.89 (0.69–1.13)**		−	−	−	−	−	−
Total events			465		204											
Heterogeneity: Chi² = 6.55, df = 6 (P = 0.36); I² = 8%																
Test for overall effect: Z = 0.97 (P = 0.33)																





Risk of bias domains
D1: Bias arising from the randomization process (for RCTs) or confounding (for NRSs)
D2: Bias due to deviations from intended interventions
D3: Bias due to missing outcome data
D4: Bias in measurement of the outcome
D5: Bias in selection of the reported result

+ Low risk
! Some concerns / Moderate risk
− Serious / High risk

EN: Enteral Nutrition; EN: Enteral Nutrition
RCT: Randomized Controlled Trial; NRS: Non-randomized Study
M–H: Mantel–Haenszel; CI: Confidence Interval

Analysis

Mortality – No benefit

Mechanical ventilation – No benefit

Feed intolerance – No benefit

Most studies are non-RCT

48 hours – no a single standardized intervention

Clinical heterogeneity

Nutrirea 2 and 3 excluded

NUTRIREA-3 TRIAL

Low vs Standard Calorie and Protein Feeding in Ventilated Adults with Shock

Reignier J et al. Lancet Respir Med 2023; 11: 602–12.

STUDY DESIGN

- Pragmatic, multicentre, randomised, controlled, open-label, parallel-group trial
- 61 ICUs in France
- Randomisation 1:1 (stratified by centre)
- Study period: Jul 5, 2018 – Dec 8, 2020
- ClinicalTrials.gov: NCT03573739

POPULATION

- Adults ≥18 years
- Invasive mechanical ventilation
- Vasopressor support for shock

3044 patients randomised

Low group: 1521

Standard group: 1515

BASELINE CHARACTERISTICS

	Low group (n=1521)	Standard group (n=1515)
Medical diagnosis at ICU admission, n (%)		
• Sepsis	908 (59.7)	911 (60.1)
• Pneumonia	384 (25.3)	384 (26.0)
• Abdominal source	151 (9.9)	152 (10.0)
• Other	78 (5.1)	58 (3.8)
Acute respiratory failure, n (%)	1372 (90.2)	1361 (89.9)
Septic shock, n (%)	1290 (84.8)	1290 (85.4)
FiO_2 requirement at inclusion, median (IQR)	0.60 (0.40–0.80)	0.60 (0.40–0.80)

INTERVENTION (during first 7 ICU days)

	LOW CALORIE–PROTEIN (n=1521)	STANDARD CALORIE–PROTEIN (n=1515)
Calories	6 kcal/kg/day (target)	25 kcal/kg/day (target)
Protein	0.2–0.4 g/kg/day (target)	1.0–1.3 g/kg/day (target)

Early nutrition started within 24 h after intubation

NUTRITION DELIVERED DURING INTERVENTION PERIOD (DAYS 0–7)

CALORIES DELIVERED

(mean ± SD kcal/day)

Low group	Standard group
881 ± 264 kcal/day (~59% of target)	1631 ± 420 kcal/day (~87% of target)

PROTEIN DELIVERED

(mean ± SD g/kg/day)

Low group	Standard group
0.36 ± 0.16 g/kg/day (~100% of target)	1.07 ± 0.32 g/kg/day (~100% of target)

PRIMARY OUTCOMES

1. TIME TO READINESS FOR ICU DISCHARGE

(Primary co-primary outcome)

Median (IQR)

Low group	Standard group
8.0 days (5.0–14.0)	9.0 days (5.0–17.0)

Hazard Ratio 1.12 (95% CI 1.02–1.22)
p = 0.015

2. ALL-CAUSE MORTALITY AT DAY 90

(Primary co-primary outcome)

n (%)

Low group	Standard group
628/1521 (41.3%)	648/1515 (42.8%)

Absolute difference −1.5%
(95% CI −5.0 to 2.0)
p = 0.41

GASTROINTESTINAL COMPLICATIONS

	Hazard Ratio (95% CI) Low group vs Standard group
Vomiting	0.77 (0.67–0.89) p < 0.001
Diarrhoea	0.83 (0.73–0.94) p = 0.004
Bowel ischaemia	0.50 (0.26–0.95) p = 0.030
Liver dysfunction	0.92 (0.86–0.99) p = 0.032
Large gastric residual volume (≥400 mL)	1.02 (0.86–1.21) p = 0.82

OTHER KEY RESULTS

- **Secondary infections:** HR 0.85 (95% CI 0.71–1.01); p = 0.06
- **Duration of invasive mechanical ventilation:** Median 7.0 days (5.0–12.0) vs 8.0 days (5.0–14.0); p = 0.02
- **ICU length of stay:** Median 9.0 days (6.0–17.0) vs 10.0 days (6.0–20.0); p = 0.02
- **Hospital length of stay:** Median 24.0 days (14.0–40.0) vs 26.0 days (15.0–43.0); p = 0.06

CONCLUSION

In ventilated adults with shock, early calorie and protein restriction (6 kcal/kg/day and 0.2–0.4 g/kg/day protein) compared with standard targets (25 kcal/kg/day and 1.0–1.3 g/kg/day protein) **did not reduce 90-day mortality but resulted in faster recovery and fewer gastrointestinal complications.**

LIMITATIONS

- Open-label design (performance bias possible).
- Conducted in French ICUs – generalisability to other settings may be limited.
- Nutrition delivered via enteral route only; findings may not apply to parenteral nutrition.
- Targets applied for only first 7 ICU days; long-term nutritional strategy not assessed.

STRENGTHS

- Large, multicentre randomised controlled trial in a well-defined population with shock and mechanical ventilation.
- High adherence to protocol with clear difference in calorie and protein delivery between groups.
- Clinically relevant primary outcomes (time to ICU discharge, 90-day mortality).
- Comprehensive assessment of GI complications and safety.

Abbreviations: CI = confidence interval; FiO_2 = fraction of inspired oxygen; g = gram; HR = hazard ratio; ICU = intensive care unit; IQR = interquartile range; kcal = kilocalorie; MD = mean difference; SD = standard deviation.

Differences in effect of early enteral nutrition on mortality among ventilated adults with shock requiring low-, medium-, and high-dose noradrenaline: A propensity-matched analysis

Component	Study
Population	ICU admission + IMV + shock requiring vasopressors
Intervention	EN in first 48 hours vs No EN in first 48 hours
Subgroups	Low, medium and high norepinephrine dose
Primary outcome	28-day mortality
Secondary outcomes	Nosocomial pneumonia, bowel ischemia, hospital LOS,
Design	Retrospective observational cohort

Shock Category	Noradrenaline dose
Low	< 0.1 µg/kg/min
Medium	0.1 – 0.3 µg/kg/min
High	> 0.3 µg/kg/min

Ohbe H et al. Clin Nutr. 2020;39:460-46

EEN safe in low in medium dose noradrenaline

Outcome	EEN	LEN	Risk difference (95% CI)	Odds ratio (95% CI)
28-day mortality				
Low	945 (16) (n = 5969)	2240 (19) (n = 11,938)	−2.9 (−4.5 to −1.3)	0.84 (0.77–0.93)
Medium	479 (22) (n = 2162)	1252 (29) (n = 4324)	−6.8 (−9.6 to −4.0)	0.77 (0.68–0.86)
High	169 (35) (n = 477)	351 (37) (n = 954)	−1.4 (−7.4 to 4.7)	0.96 (0.81–1.14)
Nosocomial pneumonia				
Low	614 (10)	1073 (9.0)	1.3 (0.2–2.4)	1.14 (1.02–1.28)
Medium	212 (9.8)	384 (8.9)	0.9 (−1.0 to 2.8)	1.10 (0.90–1.35)
High	43 (9.0)	76 (8.0)	1.0 (−2.4 to 4.5)	1.13 (0.79–1.62)
Bowel ischemia				
Low	13 (0.2)	32 (0.3)	−0.1 (−0.2 to 0.1)	0.81 (0.40–1.65)
Medium	7 (0.3)	15 (0.3)	−0.02 (−0.4 to 0.3)	0.93 (0.33–2.66)
High	1 (0.2)	3 (0.3)	−0.1 (−0.6 to 0.4)	0.67 (0.07–6.19)
Length of hospital stay[a]				
Low	43 (27–71)	41 (25–67)	1.0 (−2.5 to 4.6)	1.01 (0.96–1.08)
Medium	47 (29–78)	46 (28–72)	3.7 (−0.9 to 8.3)	1.06 (0.99–1.15)
High	49 (32–81)	51 (34–77)	0.9 (−9.5 to 11)	1.01 (0.87–1.18)
Length of MV[a]				
Low	9 (5–20)	8 (4–19)	−0.4 (−3.2 to 2.5)	0.98 (0.83–1.15)
Medium	10 (5–24)	9 (5–20)	1.4 (−1.5 to 4.3)	1.07 (0.93–1.24)
High	11 (6–24)	9 (5–22)	4.6 (−2.5 to 12)	1.23 (0.90–1.67)

Analysis

- Early EN in patients which shock requiring noradrenaline < 0.3 mcg/kg/min had lower mortality
- No difference in bowel ischemia, LoS, IMV duration

Micronutrients

Why are they important

- Energy production
- Immune function
- Wound healing
- Hematopoiesis
- Neuromuscular functions
- Endocrine regulation

Bergur MM. et al. Clin Nutr. 2025;50:75

Micronutrient	DRI/day (age 31–70 y)	EN: High requirements	EN: 1500 kcal
Chromium	20–35 µg	200 µg	35–150 µg
Copper	0.9 mg	Same as C	1–3 mg
Fluoride	3–5 mg (AI)	3–4 mg	0–3 mg
Iodine	150 µg	Same as C	150–300 µg
Iron	8 mg (18 mg F, 19–50 y)	30 mg	18–30 mg
Manganese	1.8–2.3 mg	Same as C	2–3 mg
Molybdenum	45 µg	250 µg	50–250 µg
Selenium	55 µg	200 µg	50–150 µg
Zinc	8–11 mg	20 mg	10–20 mg
Vitamin A	700–900 µg	1500 µg	900–1500 µg
Vitamin D3	15–20 µg	30 µg	25 µg
Vitamin E	15 mg	40 mg	15 mg
Vitamin K2	90–120 µg	Same as C	120 µg

Bergur MM. et al. Clin Nutr. 2025;50:75

Micronutrient	DRI/day (age 31–70 y)	EN: High requirements	EN: 1500 kcal
Vitamin B1	1.1–1.2 mg	100 mg	1.5 mg
Vitamin B2	1.1–1.3 mg	10 mg	1.2 mg
Vitamin B3	11–16 mg	40 mg	18 mg
Vitamin B5	5 mg	7.5 mg	5 mg
Vitamin B6	1.5–1.7 mg	7.5 mg	1.5 mg
Vitamin B7	30 µg (AI)	75 µg	30 µg
Vitamin B9	400 µg DFE	500 µg	330–400 µg DFE
Vitamin B12	2.4 µg	7.5 µg	>2.5 µg
Vitamin C	75–90 mg	200 mg	100 mg

Bergur MM. et al. Clin Nutr. 2025;50:75

Special Situations

EVIDENCE IN MOST SITUATIONS IN INSUFFICIENT, MOST RECOMMENDATIONS ARE BASED ON OBSERVATIONAL DATA AND EXPERT CONSENSUS

Renal disease in critical illness

Category	Protein	Calories (kcal/kg/day)
AKI/AKI-on-CKD/CKD NOT on RRT	1.0 - 1.3 g/kg/day	20 - 25 - initially; increase till 30
intermittent HD	1.3 - 1.5 g/kg/day	20 - 25 - initially; increase till 30
CRRT	1.5 - 1.7 g/kg/day	20 - 25 - initially; increase till 30

Sabatino A et al. *Clin Nutr.* 2024;43:2238-2254

Liver disease in critical illness

Category	Protein	Calories	Evidence
Cirrhosis	1.2–1.5 g/kg/day	30–35 kcal/kg/day	Observational + expert consensus
Cirrhosis + malnutrition	1.5 g/kg/day	30–35 kcal/kg/day	Observational + expert consensus
NASH/MASLD	1.2–1.5 g/kg/day	30–35 kcal/kg/day	RCT + observational + expert consensus
Obese liver disease	2.0–2.5 g/kg IBW/day	25 kcal/kg IBW/day	Expert consensus

Plauth M et al. Clin Nutr. 2019;38:485-521

Obesity in critical illness

Recommendation	ESPEN 2023	ASPEN/SCCM 2016
Energy — IC unavailable	Does not specify the kcal/kg	BMI 30–50: 11–14 kcal/kg/day - Actual BW BMI >50: 22–25 kcal/kg/day - IBW
Protein	1.3 g/kg/day × adjusted BW	BMI 30–40: 2.0 g/kg/day IBW; BMI ≥40: up to 2.5 g/kg/day IBW
Weight calculation	Adjusted BW IBW + 0.20 × (Actual BW − IBW) or IBW + 0.25 x (Actual BW – IBW)	Actual BW for energy; IBW for protein. Avoid adjusted BW Male = 50 + 0.91 × [height (cm) − 152.4] Female = 45.5 + 0.91 × [height (cm) − 152.4]
Evidence	Expert consensus	Expert consensus

McClave SA et al. JPEN J Parenter Enteral Nutr. 2016;40:159-211
Singer P et al. Clin Nutr. 2023;42:1671-1689

Pregnancy in critical illness

Category	1st trimester	2nd trimester	3rd trimester
Normal EE	Nonpregnant EE	T1 + 340 kcal/day	T1 + 452 kcal/day
Energy targets reported in critical illness	Variable, few studies used same calories as normal pregnancy requirement. Some studies used 35 kcal/kg/day, with one escalating to 55–61 kcal/kg/day		
Protein targets reported in critical illness	1.0–1.1 g/kg/day	1.0–1.1 g/kg/day	1.0–1.1 g/kg/day

Extremely weak evidence base: 24 included studies: 12 case reports, 7 case series, 1 RCT, rest observational/cross-sectional/cohort evidence.

Dear DE et al. J Hum Nutr Diet. 2026;39:e70315

RF feeds in RICU

Feed	Composition (For 1 litre)	Calories(kcal)	Protein(g)	Na(mmol)	K (mmol)	PO_4^{3-}(mmol)
A-1	Milk – 1 L ; SMP – 70 g Sugar – 60 g ; Refined oil – 40 g	1330	57	44	32	53.4
A-2	Soyabean refined oil – 75 g Refined oil – 40 g ; Rice – 25 g Protein supplement – 30 g Sugar – 60 g	1116	43	1.83	33.7	14.30
A-3	Whey protein supplement – 100 g Coconut oil – 40 g ; Sugar – 60 g Water – 1 L	1251	45	5.74	6.96	5.81

Feed	Composition (For 1 litre)	Calories (kcal)	Protein (g)	Na (mmol)	K (mmol)	PO_4^3 (mmol)
Puralbumen Feed	Puralbumen powder – 100 g Soya atta – 25 g ; Rice flour – 25 g Besan – 40 g ; Sugar – 100 g Water – 750 ml ; Refined oil – 60 ml	1349	85	1.8	22.8	9.2
Khichdi	Dal – 60 g ; Rice – 40 g Refined oil – 10 g ; Salt – 3 g ; Vegetable – 100 g	450	18	51	25.5	10
Special Khichdi	Dal – 60 g ; Rice atta – 10 g Refined oil – 8 g ; Salt – 3 g Vegetable – 100 g Puralbumen powder – 15 g	568	26	51	25	9.2
Dialysis (500 mL)	SMP – 35 g ; Soya atta – 35 g Besan – 50 g ; Rice – 35 g Sugar – 180 g ; Refined oil – 60 g	1484	39	10.4	29	23.2

Nutrient (1 Lit)	A-1	A-2	A-3	Dialysis 1 500 mL	Dialysis 2 500 mL	Khichdi	Special Khichdi
Vitamin A (µg)	660	300	—	~275*	—	≥75*	≥224*
Vitamin D (µg)	10.7	**54.4***	0	**40.9***	—	2.4*	6.1*
Vitamin E (mg)	2.5*	1.8*	0.75*	2.1*	—	0.72*	0.33*
Vitamin K1 (µg)	3.9*	46.2*	0.033*	24.5*	—	25.4*	21.0*
Vitamin B1 (mg)	0.52*	0.45*	0.025*	0.55*	—	0.29*	0.23*
Vitamin B2 (mg)	1.92*	0.23*	0.025*	0.61*	—	0.087*	0.059*
Vitamin B3 (mg)	1.40*	2.01*	0.84*	2.63*	—	1.93*	1.17*
Vitamin B5 (mg)	**5.96***	1.63*	0.28*	3.05*	—	0.99*	0.67*
Vitamin B6 (mg)	0.70*	0.35*	0.058*	0.48*	—	0.19*	0.13*
Biotin / B7 (µg)	**34.7***	0.70*	0.30*	8.4*	—	0.43*	0.20*
Folate / B9 (µg)	123*	226*	4.65*	244*	—	68.4*	54.5*
Vitamin C (mg)	35.2*	0	0	7.6*	—	0	0

RICU Nutrition Protocol

Nutritional goals

Calories: 25-30 kcal/kg/day

Protein: 1.2-2.0 g/kg/day

Ideal body weight (IBW) should be used for all calculations.

IBW to be calculated by Devine's Formula

Male:

$$\boxed{IBW = 50 + 0.905 \times (Height - 152.4)}$$

Female:

$$\boxed{IBW = 45.5 + 0.905 \times (Height - 152.4)}$$

Special situations

Renal failure

- Use standard recommendation for protein, i.e., 1.2-2.0 g/kg/day.
- If on renal replacement therapy (RRT), increase protein intake, up to a maximum of 2.5 g/kg/day.

Liver disease

- Use standard recommendation for protein, i.e., 1.2-2.0 g/kg/day.
- DO NOT RESTRICT PROTEIN IN LIVER FAILURE AND HEPATIC ENCEPHALOPATHY.

Obesity

- Calories – 15-20 Kcal/IBW, Patients with BMI ≥40 should be provided a higher protein intake of 2.5 g/kg/day

General Instructions and RT placement

- Head end elevation - 30-45°
- Chlorhexidine (0.2%) mouth wash q12h
- Nasogastric (NG) tube is preferred over orogastric tube
- NG tube of size 16F is preferable
- Confirm enteral tube placement by auscultation before initiating feeds.
- Enteral tubes should NOT be changed/replaced routinely unless they malfunction, or sinusitis develops.

Timing and Volume

Initiation

- Start enteral feeding within the first 24 hours of ICU admission.
- Absence of bowel sounds should not delay initiation of enteral feeding.
- Septic shock, enteral feeding initiated as soon as resuscitation is complete, and the patient is hemodynamically stable on steady dose of vasopressors.

Administration

- 250-300ml q4h to q6h
- After every feed, flush the tube with 50 ml of water

Monitoring

- Tolerance of enteral feeding should be monitored daily.
- Signs of gastrointestinal intolerance include abdominal discomfort, vomiting or regurgitation of feeds, abdominal distension, diminished bowel sounds, or diarrhea.
- Gastric residual volume (GRV) to be done in selected patients with feed intolerance
- NPO orders should not extend beyond 6 hours unless indicated.

Feed intolerance

- Abdominal distension, vomiting, or feed regurgitation

GRV monitoring:

- In selected patients with feed intolerance
- Checked before every feed and feeds withheld if GRV is >500 mL
- If GRV > 500ml, 50% of the aspirated feed should be returned through the NG tube.

Prokinetics:

- Metoclopramide 10 mg IV q8h
- No improvement in 24 hours, consider erythromycin 200 mg IV q12h
- Taper/discontinue the prokinetics once patient tolerates feeds well for >48 hours

Diarrhea

- Do not stop enteral nutrition
- Establish the etiology and manage accordingly
- Osmotic: oral supplements of potassium or phosphate
- Infective: Clostridium difficile, cytomegalovirus
- Drugs: antibiotics, laxatives
- Try to switch to a lactose-free feed or a curd-based diet.
- Consider probiotics in patients with suspected antibiotic-associated diarrhea