3.2b Intentional Underfeeding: Trophic Feeds vs. Full Feeds

Question: Does the use of trophic vs. full feeding result in better outcomes in the critically ill adult patient?

Summary of evidence: There were three level 2 studies reviewed that compared trophic enteral feedings to feeding at full rate. Two studies compared starting at 10 ml/hr for the first 5-6 days to full feeds within 1-2 days (Rice 2011, Rice 2012), while in one study patients were divided into high (≥5) or low (<5) NUTRIC (Nutrition Risk in the Critically ill) score and then randomized to receive either trophic (~600 kcal/day) or full feeds (25 kcal/kg/day) for 6 days (Wang 2020). In the Rice 2012 study, the first 272 patients also received 240 mls/day of an omega-3 fatty acid supplement or control supplement (Rice 2011), refer to section 4.1 b Enteral Fish Oils for data pertaining to the omega-3 fatty acid vs. control groups. Needham et al (2013 Crit Care Med, 2013 Am J Resp Care) further analyzed the EDEN trial results (Rice 2011) with respect to patients' long term physical and cognitive performance.

Mortality: In the Wang 2020 study, the mortality data from both high and low NUTRIC Score groups was combined and when the data from all three studies were aggregated, trophic feeds had no effect on mortality (RR 1.03, 95% CI 0.85, 1.26, p=0.75, test for heterogeneity I^2 =0%; figure 1).

Infections, LOS & ventilator days: Two studies reported ventilator associated pneumonia (VAP) rates and when the data from these 2 studies were aggregated, trophic feeds had no effect on the incidence of VAP (RR 0.98, 95% CI 0.68, 1.43, p=0.94, test for heterogeneity I^2 =0%; figure 2). These two studies also reported ICU free, hospital free and ventilator free days as medians and interquartile ranges instead of means and standard deviations, hence a meta-analysis was not possible. There were no significant differences in any of these outcomes between the two groups in Rice 2011 and Rice 2012 studies. Similarly, in the Wang 2020 study, trophic feeds had no effect on ICU and hospital length of stay or duration of mechanical ventilation in patients with either high or low NUTRIC scores, when compared to full feeds.

Other: Due to the study design, all studies reported a significant difference in calories between the trophic feeds and full feeds group. Trophic feeds were also associated with better gastrointestinal tolerance i.e., significantly lower % feedings days with diarrhea and high gastric residual volumes. Trophic vs full feeds may have no effect on long-term physical or cognitive function or survival. Results from the Needham et al analyses show EDEN trial survivors had substantial physical, psychological, and cognitive impairments, reduced quality of life, and impaired return to work. Trophic vs. full feeds had no effect on physical or cognitive function at 6 and 12 months and no effect on 12-month survival yet Mental Health and mental health summary scores were higher in trophic feeding than full feeding (p=0.02 and 0.01, respectively). There was a worse 6-minute walk test (p=0.136) and 4 meter timed walk speed (p=0.125) in the trophic group.

Conclusions:

1. The use of trophic vs. full feeds has no effect on mortality in critically ill patients
2. The use of trophic vs. full feeds has no effect on VAP in critically ill patients
3. The use of trophic vs. full feeds has no effect on hospital, ICU length of stay or mechanical ventilation duration.
4. The use of trophic vs. full feeds may be associated with underfeeding but better gastrointestinal tolerance in critically ill patients.
5. The use of trophic vs. full feeds has no effect on long-term physical or cognitive function or survival but may be associated with poorer functional outcome at 12 months.

Level 1 study: *if all of the following are fulfilled: concealed randomization, blinded outcome adjudication and an intention to treat analysis.*
Level 2 study*: If any one of the above characteristics are unfulfilled.*

Table 1. Randomized studies evaluating trophic vs. full feeding in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				Trophic Feeds	Full Feeds	Trophic Feeds	Full Feeds
1) Rice 2011	Mechanically ventilated with acute respiratory failure N=200	C.Random: Yes ITT: Yes Blinding: No (10)	Underfed: 10ml/hr for first 5 days vs. full feed: increased by 25 mls q6h, received 74.8% target. Non isocaloric, non-isonitrogenous	**Hospital** 22/98 (22)	**Hospital** 20/102 (17)	30/98 (31) **VAP** 14/98 (14)	33/102 (32) **VAP** 18/102 (18)
2) Rice 2012**	Acute Lung Injury patients from 44 ICUs N=1000	C.Random: Yes ITT: Yes Blinding: No (12)	Underfed 10ml/hr ~400kcal/day x 6 days vs. Full feed: ~1300kcal/day, 90% reached goal in 1.3 days; 25ml/hr advanced q6h Non isocaloric, non isonitrogenous	**60 Day** 118/508 (23)	**60 Day** 109/492 (27)	**VAP** 37/508 (7)	**VAP** 33/492 (7)
3) Wang 2020	Mechanically ventilated with high (≥5) and low NUTRIC (<5) risk scores N=150	C.Random: No ITT: Yes Blinding: No (8)	Underfed 600 kcal/day for 6 days vs. Full feed: 25 kcal/kg/day for 6 days Non isocaloric, non isonitrogenous	**Hospital** High NUTRIC 11/56 (19.6%) Low NUTRIC 4/20 (20%) **28 day** High NUTRIC 6/56 (10.7%) Low NUTRIC 1/20 (5%)	**Hospital** High NUTRIC 12/50 (16%) Low NUTRIC 6/24 (25%) **28 day** High NUTRIC 8/50 (16%) Low NUTRIC 3/24 (12.5%)	NR	NR

Table 1. Randomized studies evaluating trophic vs. full feeding in critically ill patients (continued)

Study	LOS days		Ventilator days		Other	
	Trophic Feeds	Full Feeds	Trophic Feeds	Full Feeds	Trophic Feeds	Full Feeds
1) Rice 2011	**ICU-free Days** 21.0 (6.5-24) **Hospital-free Days** 12.0 (0-21)	**ICU-free Days** 21.0 (9.3-24) **Hospital-free Days** 16.5 (0-21)	**Vent-free Days** 23 (10.5-26)	**Vent-free Days** 23 (9.3-26)	**Kcal/day** 300 ± 149	1481 ± 686, p<0.001 **Diarrhea (% feeding days)** 19% 24%, p 0.08 **High Gastric Residuals (% feeding days)** 2% 8%, p<0.001
2) Rice 2012	**ICU-free Days** 14.4 (13.5-15.3)	**ICU-free Days** 14.7 (13.8-15.6)	**Vent-free Days** 14.9 (13.9-15.8)	**Vent-free Days** 15.0 (14.9-15.8)	**Kcal/day** 400 (25) **Time to goal rate (days)** 6.7 ± 1.8 **Diarrhea (% feeding days)** 16.5% **High Gastric Residuals (% feeding days)** 2.2% **Vomiting (% feeding days)** 1.7% **Quality of Life, Physical function – SF-36** 55 (33) **Quality of Life, mental health – SF-36** 67 (25) **Quality of Life, mental health summary-SF-36** 46 (15) **Mini Mental Score** 25 (2) **6 min walk test @ 12 months** 63 (25) **4 min timed walk speed** 0.98 (0.29) **Hand grip strength** 82 (27)	1300 (82), p=0.001 1.3 ± 1.2, p=0.001 18.7%, p=0.16 4.9%, p<0.001 2.2%, p=0.05 55(31), p=0.54 63 (26), p=0.02 43 (15), p=0.01 26 (2), p=0.45 70 (24), p=0.136 1.08 (0.29), p=0.125 85 (26), p=0.462

3) Wang 2020	**ICU, days** High NUTRIC 15.54 ±13.17 Low NUTRIC 14.35 ± 12.30 **Hospital** High NUTRIC 33.16 ± 20.74 Low NUTRIC 32.40 ± 28.38	**ICU, days** High NUTRIC 16.88 ±11.44 Low NUTRIC 11.81 ± 8.68 **Hospital** High NUTRIC 36.44 ± 26.84 Low NUTRIC 28.17 ± 18.27	**Ventilation, days** High NUTRIC 21.52 ± 19.46 Low NUTRIC 19.45 ± 19.23	**Ventilation, days** High NUTRIC 24.46 ± 25.12 Low NUTRIC 21.0 ± 18.86	**Kcal/day** High NUTRIC 614.6 ± 109.5 1260.2 ± 305.2 Low NUTRIC 645.2 ± 173.3 1350.5 ± 334.1 **Protein intake g/day** High NUTRIC 27.9 ± 12.4 50.4 ± 15.8 Low NUTRIC 30.2 ± 17.0 54.3 ± 14.4

C.Random: concealed randomization
† presumed hospital mortality unless otherwise specified
± ( ) : mean ± Standard deviation (number)
VAP: ventilator associated pneumonia
ITT: intent to treat; NA: not available
‡ refers to the # of patients with infections unless specified
ICU: intensive care unit
* Data shown here for underfed group and full fed groups include patients randomized to the intensive insulin and conventional insulin therapy within these 2 groups. Refer to the intensive insulin therapy section for data on intensive insulin vs. conventional groups.
** Includes 272 patients that also randomized to an experimental arm of omega 3fatty acids arm.

Figure 1. Mortality

Study or Subgroup	Trophic Events	Trophic Total	Full Events	Full Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Rice 2011	22	98	20	102	13.7%	1.14 [0.67, 1.96]	2011
Rice 2012	118	508	109	492	75.5%	1.05 [0.83, 1.32]	2012
Wang 2020	15	76	18	74	10.8%	0.81 [0.44, 1.49]	2020
Total (95% CI)		**682**		**668**	**100.0%**	**1.03 [0.85, 1.26]**	
Total events	155		147				

Heterogeneity: Tau² = 0.00; Chi² = 0.77, df = 2 (P = 0.68); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.75)

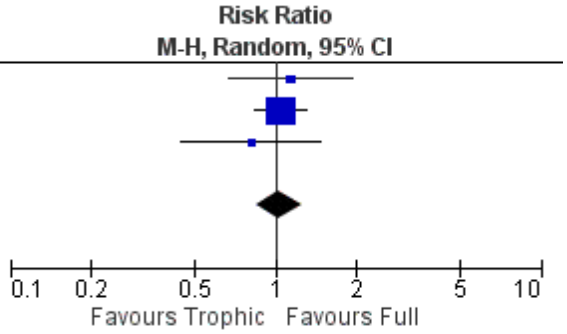
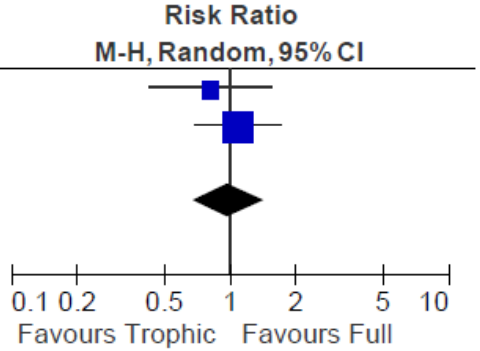


Figure 2. Ventilator Associated Pneumonia

Study or Subgroup	Trophic Events	Trophic Total	Full Events	Full Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Rice 2011	14	98	18	102	33.3%	0.81 [0.43, 1.54]	2011
Rice 2012	37	508	33	492	66.7%	1.09 [0.69, 1.71]	2012
Total (95% CI)		**606**		**594**	**100.0%**	**0.98 [0.68, 1.43]**	
Total events	51		51				

Heterogeneity: Tau² = 0.00; Chi² = 0.54, df = 1 (P = 0.46); I² = 0%
Test for overall effect: Z = 0.08 (P = 0.94)



References

Included Studies

1. Rice TW, Mogan S, Hays MA, Bernard GR, Jensen GL, Wheeler AP. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. Crit Care Med. 2011;39(5):967-974. doi:10.1097/CCM.0b013e31820a905a
2. Rice TW, Wheeler AP, Thompson BT, Steingrub J, Hite RD, Moss M, Morris A, Dong N, Rock P, National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. JAMA. 2012 Feb 22;307(8):795-803. doi:10.1001/jama.2012.137
3. Needham DM, Dinglas VD, Bienvenu OJ, Colantuoni E, Wozniak AW, Rice TW, Hopkins RO; NIH NHLBI ARDS Network. One year outcomes in patients with acute lung injury randomised to initial trophic or full enteral feeding: prospective follow-up of EDEN randomised trial. BMJ. 2013 Mar 19;346:f1532.
4. Needham DM, Dinglas VD, Morris PE, Jackson JC, Hough CL, Mendez-Tellez PA, Wozniak AW, Colantuoni E, Ely EW, Rice TW, Hopkins RO; NIH NHLBI ARDS Network. Physical and cognitive performance of patients with acute lung injury 1 year after initial trophic versus full enteral feeding. EDEN trial follow-up. Am J Respir Crit Care Med. 2013 Sep 1;188(5):567-76.
5. Wang CY, Fu PK, Chao WC, Wang WN, Chen CH, Huang YC. Full Versus Trophic Feeds in Critically Ill Adults with High and Low Nutritional Risk Scores: A Randomized Controlled Trial. Nutrients. 2020;12(11):3518. Published 2020 Nov 15. doi:10.3390/nu12113518

Excluded Studies	**Reason**
Bastarache JA, Ware LB, Girard TD, Wheeler AP, Rice TW. Markers of inflammation and coagulation may be modulated by enteral feeding strategy. JPEN J Parenter Enteral Nutr. 2012 Nov;36(6):732-40	Secondary analysis of Rice