3.3b Intentional Underfeeding: Hypocaloric Enteral Nutrition

Question: Does the use of hypocaloric enteral nutrition vs full feeding result in better outcomes in the critically ill adult patient?

Summary of evidence: All of the trials included in this topic resulted in similar protein intake but less caloric intake in the intervention arm (hypocaloric EN) compared to the control arm (full feeds). Trials that resulted in different levels of calories and proteins are reviewed in section 3.2 Achieving Target Dose of EN. In this section, there was one level 1 and six level 2 studies reviewed and significant heterogeneity is present in the study designs:

- Arabi 2011: Hypocaloric group aimed to receive 60-70% of calorie goals and gave protein supplements vs 90-100% of nutrition goals
- Charles 2014: Hypocaloric group aimed to receive 50% of calorie goals and 100% of protein goals vs 100% of nutrition goals
- Peake 2014 and Chapman 2018: Hypocaloric group received a 1.0 kcal/ml EN formula at 1 ml/kg IBW/hr vs a 1.5 kcal/ml EN formula provided at 1 ml/kg IBW/hr with both formulas having a comparable protein content per ml
- Arabi 2015: Hypocaloric group aimed to receive 40-60% of caloric goals and 1.2-1.5 g/kg/d protein vs 70-100% of calorie goals 1.2-1.5 g/kg/d protein
- Rugeles 2016: Hypocaloric group aimed to receive 15 kcal/kg/d and 1.7 g/kg/d protein vs 25 kcal/kg/d and 1.7 g/kg/d protein
- Rice 2018: Hypocaloric group aimed to receive 1.5 g/kg/d protein from a higher protein density formula vs 1.5 g/kg/d from a lower protein density formula with both formulas having equal caloric density.

All studies were isonitrogenous but non-isocaloric. The Arabi 2011 study also compared intensive insulin therapy to control in a 2 X 2 factorial design (refer to section 10.4 Insulin therapy for data pertaining to these groups). In previous reviews, Petros 2014 was included in this section but due to its non-isonitrogenous study design it has been moved to section 3.2 Achieving Target Dose of EN. Peake 2014 was moved to this section from section 3.2 due to its isonitrogenous study design.

Mortality: When the data from the trials were aggregated, hypocaloric enteral nutrition had no effect on overall (RR 0.95, 95% CI 0.87, 1.05, p =0.32, I^2= 0%; figure 1) or hospital mortality (RR 0.94, 95% CI 0.83, 1.06, p =0.29, I^2= 10%; figure 2). There was a trend towards a reduction in ICU mortality in the hypocaloric group (RR 0.85, 95% CI 0.67, 1.08, p =0.18, I^2= 0%; figure 3).

Infections: Hypocaloric enteral nutrition had no effect on the incidence of ICU-acquired infections (RR 1.00, 95% CI 0.82, 1.21, p=0.96, heterogeneity I^2= 47%) (figure 4).

LOS: When the data from the four studies (Arabi 2011, Charles 2014, Peake 2014, Arabi 2015) that reported results in mean and standard deviation were aggregated, hypocaloric enteral nutrition had no effect on ICU LOS (WMD 0.02, 95% CI -2.92, 2.96, p=0.99, I^2= 89%) (figure 5) or hospital LOS (-0.51, 95%CI -4.35, 3.33, p = 0.79, I^2= 85%) (figure 6).

Ventilator days: When the data from the 3 studies (Arabi 2011, Peake 2014, Arabi 2015) that reported this outcome in mean and standard deviation were aggregated, hypocaloric enteral nutrition was associated with a significant reduction in ventilator days (WMD -2.18, 95% CI -3.68, -0.67, p = 0.005, I^2= 0%) (figure 7). Rugeles et al reported mechanical ventilation duration in median and IQR and found no difference between groups (p=0.632) and Chapman et al reported the outcome as days alive and free of invasive ventilation (median and IQR) and found no difference between groups (p=NS).

Other: Due to the intended study designs, the hypocaloric enteral nutrition groups received significantly fewer calories than the full feeds groups (p<0.0001) (figure 8) but received the same amount of protein (p=0.92) (figure 9).

Conclusions:

1. The use of hypocaloric enteral nutrition vs full feeds is not associated with a reduction in overall and hospital mortality but may be associated with a reduction in ICU mortality.
2. The use of hypocaloric enteral nutrition vs full feeds has no effect on ICU or hospital LOS.
3. The use of hypocaloric enteral nutrition vs full feeds has no effect on infectious complications.
4. The use of hypocaloric enteral nutrition vs full feeds may be associated with a decrease in length of ventilator support.

Note: Risk ratios, mean differences, confidence intervals and p-values indicated above were calculated using Review Manager 5.3.

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 hypocaloric vs. full feeding in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				Hypocaloric Feeds	Full Feeds	Hypocaloric Feeds	Full Feeds
1) Arabi 2011*	ICU patients ~30% brain trauma 40% Type 2 diabetes N=240 BMI (kg/m^2) Trophic feeds pts: 28.5±7.4 Full feeds pts: 28.5±8.4 Age Trophic feeds pts: 50.3±21.3 Full feeds pts: 51.9±22.1	C.Random: Yes ITT: Yes Blinding: No (9)	Underfed: 60-70% goal + protein supplements vs.90-100% goal Calories actually received 59.0% vs 71.4% Protein actually received 65.2% vs 63.7% Isonitrogenous, non-isocaloric	ICU 21/120 (18) 28 Day 22/120 (18) Hospital 36/120 (30) 180 Day 38/120 (32)	ICU 26/120 (22) 28 Day 28/120 (23) Hospital 51/120 (43) 180 Day 52/120 (43)	All Infections/1000 days 54.7 VAP/1000 vent days 14 Sepsis 53/120 (44)	All infections/1000 days 53.6 VAP/1000 vent days 10 Sepsis 56/120 (47)
2) Charles 2014	Adults admitted to surgical ICU, included operative and non-operative trauma pts, abdominal vascular liver transplant, and ortho non-trauma surgical pts. N=83	C.Random: Yes ITT: Yes Blinding: single (11)	50% of caloric goal (12.5-15 kcal/kg/d) and protein 1.5 g/kg/d vs 100% of goal calories and protein 1.5 g/kg/d. Calories received 12.3 vs 17.2 kcal/kg/d, protein 1.1 vs 1.1 g/kg/d. Isonitrogenous, non-isocaloric	Hospital 3/41 (7.3)	Hospital 4/42 (9.5)	Pts w ICU acquired 23/41 (56.1) Pneumonia 18/41 (43.9) Bloodstream 10/41 (24.4) Central Line 2/41 (4.9) UTI 6/41 (14.6) Wound 5/41 (12.2)	Pts w ICU acquired 24/42 (57.1) Pneumonia 20/42 (47.6) Bloodstream 8/42 (19.1) Central Line 2/42 (4.8) UTI 6/42 (14.3) Wound 3/42 (7.1)
3) Peake 2014	Emergency operative and non-operative and elective operative admissions N=112	C. Random: yes ITT: yes Blinding: yes (9)	Fresubin 1000 Complete 1.0kcal/ml vs Fresubin 2250 Complete 1.5kcal/ml. Goal rate of 1 ml/kg IBW/hr to a max of 100ml/hour to be achieved within 48 hours of feeding start in both groups. Comparable protein between formulas. Non-isocaloric, isonitrogenous.	ICU 9/55 (16) Hospital 14/55 (27) 28 day 18/55 (33) 90 day 20/55 (27)	ICU 6/57 (11) Hospital 10/57 (19) 28 day 11/57 (20) 90 day 11/57 (20)	NR	NR

4) Arabi 2015	Multicenter. ICU adult patients with LOS ≥72 hrs, requiring EN. N=894	C.Random: Yes ITT: no Blinding: no (8)	40-60% of calorie goals x 14 days and 1.2-1.5 g/kg/d protein achieved with EN and protein supplements vs 70-100% of calorie goals and 1.2-1.5 g/kg/d protein x 14 days. Calories received: 46.2% vs 72% adequacy. No difference in protein. Non-isocaloric, isonitrogenous.	ICU 72/448 (16.1) Hospital 108/447 (24.2) 28 day 93/447 (20.8) 90 day 121/445 (27.2) 180 day 131/438 (29.9)	ICU 85/446 (19.1) Hospital 123/445 (27.6) 28 day 97/444 (21.8) 90 day 127/440 (28.9) 180 day 140/436 (32.1)	Infections 161/448 (35.9) VAP 81/448 (18.1)	Infections 169/446 (37.9) VAP 90/446 (20.2)
5) Rugeles 2016	Single centre ICU adults expected to require EN for >96 hours N=187	C.Random: No ITT: no Blinding: double (8)	EN dosed at 15 kcal/kg, 1.7 g/kg protein for 7 days vs 25 kcal/kg, 1.7 g/kg/d protein for 7 days. Same EN formula for each group.	28 day 18/60 (30%)	28 day 16/60 (27%)	NR	NR
6) Chapman 2018	Multicentre ICU adults, mechanically ventilated, expected to receive EN beyond the calendar day N=3997	C.Random: Yes ITT: no Blinding: double (11)	Fresubin 1000 Complete 1.0 kcal/ml vs Fresubin Energy Fibre 1.5 kcal/ml. Goal rate in both groups was 1 ml/kg IBW/hr to a max of 100 ml/h to be achieved within 48h of starting EN. Protein content of formulas was comparable (55 vs 56 g/L).	Hospital 470/1981 (23.7) 28 day 455/1976 (23) 90 day 505/1966 (25.7)	Hospital 468/1967 (23.8) 28 day 450/1961 (22.9) 90 day 523/1948 (26.8)	Positive blood cultures 221/1984 (11.1)	Positive blood cultures 228/1971 (11.6) RR 1.04 (0.87-1.24)
7) Rice 2018	Multicentre ICU adults, mechanically ventilated, BMI 26-45, requiring EN for ≥ 5 days N=105	C.Random: Yes ITT: no Blinding: no (5)	Peptamen Intense VHP (1 kcal/ml, 37% protein, 29% CHO) started within 48h of randomization and advanced to reach protein goal of 1.5 g/kg IBW/d vs Replete (1 kcal/ml 25% protein, 45% CHO) also started within 48h of randomization and advanced to reach protein goal of 1.5 g/kg IBW/d	Hospital mortality or entered palliative care 7/50 Feeding protocol duration 2/50	Hospital mortality or entered palliative care 8/52 Feeding protocol duration 6/52	NR	NR

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

Study	LOS days	Ventilator days	Other

	Hypocaloric Feeds	Full Feeds	Hypocaloric Feeds	Full Feeds	Hypocaloric Feeds / Full Feeds
1)Arabi 2011*	ICU 11.7 ±8.1 (120) Hospital 70.2 ±106.9 (120)	ICU 14.5 ±15.5 (120) Hospital 67.2 ±93.6(120)	10.6 ±7.6 (120)	13.2 ±15.2 (120)	Kcal/day 1067 ± 306 / 1252 ± 432, p=0.0002 Caloric Adequacy (%) 59 ± 16.1 / 71.4 ± 22.8, p=<0.0001 Protein adequacy (%) 65.2 ± 25.7 / 63.7 ± 25, p=0.63
2) Charles 2014	ICU 16.7 ± 2.7 (41) Hospital 35.2 ± 4.9 (41)	ICU 13.5 ± 1.1 (42) Hospital 31.0 ± 2.5 (42)	NR	NR	Kcal/d 982 ±61 / 1338 ±92 Kcal/kg/d 12.3 ±0.7 / 17.1 ±1.1 Protein g/d 86 ±6 / 83 ±6 Protein g/kg/d 1.1 ±0.1 / 1.1 ±0.1
3) Peake 2014	ICU 12.2 ± 8.3 Hospital 24 ± 17.6	ICU 12.8 ± 11.3 Hospital 33.3 ± 25.3	6.8 ± 6	8.6 ± 8.5	% Energy adequacy 83.2 ± 29 / 110.8 ± 26.8 % Protein adequacy 88.2 ± 39.1 / 82 ± 23.6
4) Arabi 2015	ICU$^+$ 15.8 ± 11.6 (444) Hospital$^+$ 48.3 ±67.5 (444)	ICU$^+$ 16.4± 12.1 (443) Hospital$^+$ 54.4±73.9 (443)	11.3±9.2 (444)$^+$	13.5±22.3 (443)$^+$	Kcal/d (p=<0.001) 835.2±297 / 1299±467 % Caloric adequacy (p=<0.001) 46±14 / 71±22 Protein g/d (p=0.29) 57±24 / 59±25 % Protein adequacy (p=0.56) 68±24 / 69±25 No. feeding intolerance (p=0.26) 67/448 (15) / 79/446 (17.7) No. Diarrhea p=0.11) 97/448 (21.7) / 117/446 (26.2)

5) Rugeles 2016	ICU 12 (7.3) Median (IQR) P=0.4132	ICU 10.5 (8.0) Median (IQR)	9 (8.3) Median (IQR) P=0.632	9 (8.3) Median (IQR)	All reported as mean and SD Calories/kg/d at 48h 12.6 + 3.4 20.5 + 5.1 P<0.0001 Calories/kg/d at 96h 12.1 + 2.6 19.2 + 4.3 P<0.0001 Protein/g/d at 48h 1.4 + 0.4 1.4 + 0.3 Protein/g/d at 96h 1.3 + 0.3 1.3 + 0.3
6) Chapman 2018	ICU free days 17.4 (0-23.1) Hospital Free days 2.9 (0-15.3)	ICU free days 17.0 (0-23) Hospital Free days 2.9 (0-15.7)	Median days alive and free of invasive ventilation (IQR) 20.0 (0-25)	Median days alive and free of invasive ventilation (IQR) 20.0 (0-25)	% of trial target rate delivered, mean and SD 81+17 (n=1971) 82+16 (n=1985) Kcal delived (kcal/kg IBW) , mean and SD 30.2+7.5 (n=1971) 21.9+5.6 (n=1985) Protein delivered (g/kg IBW) , mean and SD 1.09+0.22 (n=1971) 1.08+0.23 (n=1985) Vomiting 370/1959 (18.9) 309/1966 (15.7) Highest blood glucose 225.2 (185.6-277.4) 212.6 (174.7-261.2) Duration of study intervention 6 days (3-11) 6 days (3-11) Time to start EN 15.8h (7.7-26.3) 15.9h (7.9-28.3)
7) Rice 2018	Hospital 4.12 + 2.32 (50)	Hospital 4.17 + 2.37 (52)	NR	NR	Protein intake, g/kg IBW/d, days 1-5 1.1+0.3 1.2 +0.4, p=0.83 Calorie intake, kcal/kg IBW/d, days 1-5 12.5+3.7 18.2 +6.0, P<0.0001 Carbohydrate load, g/d, days 1-5 61 +22 126 + 48, P<0.0001 mean rate of glycemic events outside the range of >110 and _150 mg/dL between groups 2.7%; 95% CI, −6% to 11.5%; p=0.54

C.Random: concealed randomization
† presumed hospital mortality unless otherwise specified
± ( ) : mean ± Standard deviation (number)
ITT: intent to treat; NA: not available
+Data obtained from author in mean and standard deviation
‡ refers to the # of patients with infections unless specified

* 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. Overall Mortality

Study or Subgroup	Hypocaloric Events	Hypocaloric Total	Normocaloric Events	Normocaloric Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Arabi 2011	36	120	51	120	7.4%	0.71 [0.50, 1.00]	2011
Charles	3	41	4	42	0.4%	0.77 [0.18, 3.22]	2014
Peake	14	55	10	57	1.7%	1.45 [0.70, 2.99]	2014
Arabi 2015	108	447	123	445	17.5%	0.87 [0.70, 1.09]	2015
Rugeles	16	60	16	60	2.5%	1.00 [0.55, 1.81]	2016
Rice	7	50	8	52	1.0%	0.91 [0.36, 2.32]	2018
Chapman	470	1981	468	1967	69.6%	1.00 [0.89, 1.12]	2018
Total (95% CI)		**2754**		**2743**	**100.0%**	**0.95 [0.87, 1.05]**	
Total events	654		680				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.57$, df = 6 (P = 0.47); $I^2 = 0\%$
Test for overall effect: Z = 0.99 (P = 0.32)

Risk Ratio
M-H, Random, 95% CI

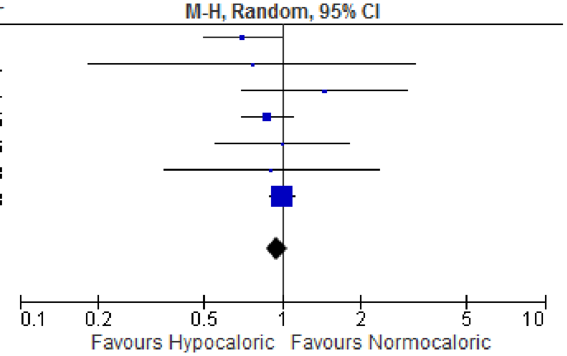

Figure 2: Hospital Mortality

Study or Subgroup	Hypocaloric Events	Hypocaloric Total	Normocaloric Events	Normocaloric Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Arabi 2011	36	120	51	120	11.0%	0.71 [0.50, 1.00]	2011
Charles	3	41	4	42	0.7%	0.77 [0.18, 3.22]	2014
Peake	14	55	10	57	2.7%	1.45 [0.70, 2.99]	2014
Arabi 2015	108	447	123	445	23.4%	0.87 [0.70, 1.09]	2015
Chapman	470	1981	468	1967	60.7%	1.00 [0.89, 1.12]	2018
Rice	7	50	8	52	1.6%	0.91 [0.36, 2.32]	2018
Total (95% CI)		**2694**		**2683**	**100.0%**	**0.94 [0.83, 1.06]**	
Total events	638		664				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.55$, df = 5 (P = 0.35); $I^2 = 10\%$
Test for overall effect: Z = 1.07 (P = 0.29)

Risk Ratio
M-H, Random, 95% CI

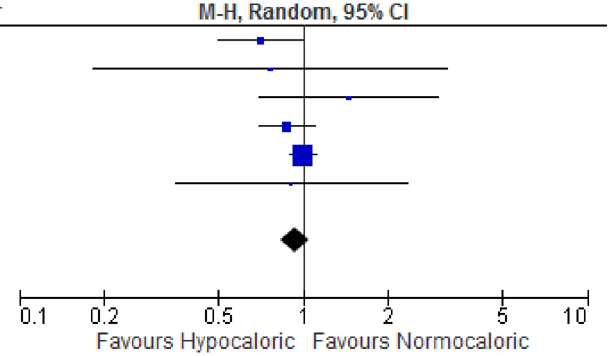

Figure 3: ICU Mortality

Study or Subgroup	Hypocaloric Events	Hypocaloric Total	Normocaloric Events	Normocaloric Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Arabi 2011	21	120	26	120	21.4%	0.81 [0.48, 1.35]	2011
Peake	9	55	6	57	6.1%	1.55 [0.59, 4.08]	2014
Arabi 2015	72	448	85	446	70.1%	0.84 [0.63, 1.12]	2015
Rice	2	50	6	52	2.4%	0.35 [0.07, 1.64]	2018
Total (95% CI)		**673**		**675**	**100.0%**	**0.85 [0.67, 1.08]**	
Total events	104		123				

Heterogeneity: Tau² = 0.00; Chi² = 2.83, df = 3 (P = 0.42); I² = 0%
Test for overall effect: Z = 1.34 (P = 0.18)

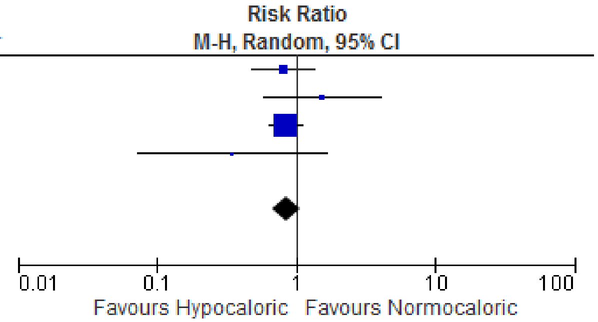

Figure 4: Infectious complications

Study or Subgroup	Trophic Events	Trophic Total	Full Events	Full Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Charles	12	46	6	54	4.5%	2.35 [0.96, 5.76]	2014
Arabi 2015	161	448	169	446	48.0%	0.95 [0.80, 1.13]	2015
Chapman	221	1984	228	1971	47.5%	0.96 [0.81, 1.15]	2018
Total (95% CI)		**2478**		**2471**	**100.0%**	**1.00 [0.82, 1.21]**	
Total events	394		403				

Heterogeneity: Tau² = 0.01; Chi² = 3.80, df = 2 (P = 0.15); I² = 47%
Test for overall effect: Z = 0.05 (P = 0.96)

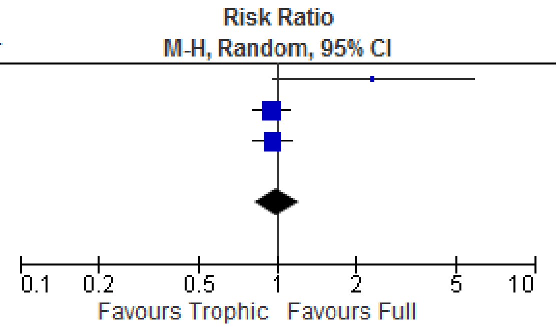

Figure 5. ICU LOS

Study or Subgroup	Hypocaloric Events	Hypocaloric Total	Normocaloric Events	Normocaloric Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Arabi 2011	36	120	51	120	7.4%	0.71 [0.50, 1.00]	2011
Charles	3	41	4	42	0.4%	0.77 [0.18, 3.22]	2014
Peake	14	55	10	57	1.7%	1.45 [0.70, 2.99]	2014
Arabi 2015	108	447	123	445	17.5%	0.87 [0.70, 1.09]	2015
Rugeles	16	60	16	60	2.5%	1.00 [0.55, 1.81]	2016
Rice	7	50	8	52	1.0%	0.91 [0.36, 2.32]	2018
Chapman	470	1981	468	1967	69.6%	1.00 [0.89, 1.12]	2018
Total (95% CI)		**2754**		**2743**	**100.0%**	**0.95 [0.87, 1.05]**	
Total events	654		680				

Heterogeneity: Tau² = 0.00; Chi² = 5.57, df = 6 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.99 (P = 0.32)

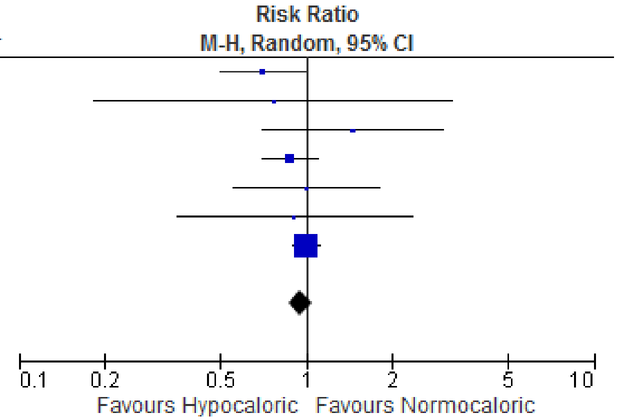

Figure 6. Hospital LOS

Study or Subgroup	Hypocaloric Mean	Hypocaloric SD	Hypocaloric Total	Normocaloric Mean	Normocaloric SD	Normocaloric Total	Weight	Mean Difference IV, Random, 95% CI	Year
Arabi 2011	70.2	106.9	120	67.2	93.6	120	2.1%	3.00 [-22.42, 28.42]	2011
Charles	35.2	4.9	41	31	2.5	42	35.1%	4.20 [2.52, 5.88]	2014
Peake	24	17.6	55	33.3	25.3	57	14.2%	-9.30 [-17.35, -1.25]	2014
Arabi 2015	48.3	67.5	444	54.4	73.9	443	11.7%	-6.10 [-15.42, 3.22]	2015
Rice	4.12	2.32	50	4.17	2.37	52	36.9%	-0.05 [-0.96, 0.86]	2018
Total (95% CI)			**710**			**714**	**100.0%**	**-0.51 [-4.35, 3.33]**	

Heterogeneity: Tau² = 10.19; Chi² = 27.27, df = 4 (P < 0.0001); I² = 85%
Test for overall effect: Z = 0.26 (P = 0.79)

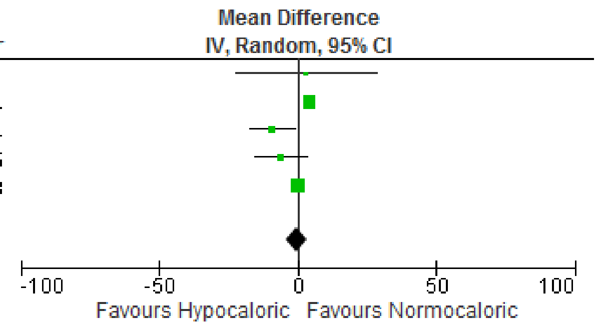

Figure 7. Ventilator Days

	Hypocaloric			Normocaloric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Arabi 2011	10.6	7.6	120	13.2	15.2	120	24.5%	-2.60 [-5.64, 0.44]	2011
Peake	6.8	6	55	8.6	8.5	57	30.7%	-1.80 [-4.52, 0.92]	2014
Arabi 2015	11.3	9.2	444	13.5	22.3	443	44.9%	-2.20 [-4.45, 0.05]	2015
Total (95% CI)			**619**			**620**	**100.0%**	**-2.18 [-3.68, -0.67]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 2.83 (P = 0.005)

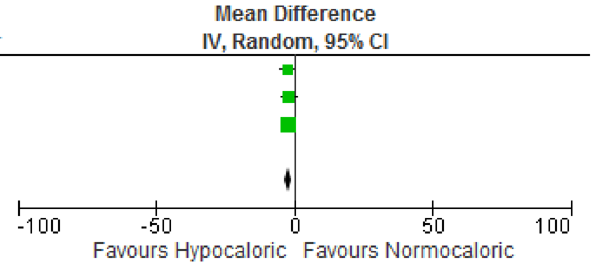

Figure 8. Caloric Adequacy

	Hypocaloric			Normocaloric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Arabi 2011	59	16.1	120	71.4	22.8	120	35.2%	-12.40 [-17.39, -7.41]	2011
Peake	83.2	29	55	110.8	26.8	57	26.7%	-27.60 [-37.95, -17.25]	2014
Arabi 2015	46	14	448	71	22	446	38.0%	-25.00 [-27.42, -22.58]	2015
Total (95% CI)			**623**			**623**	**100.0%**	**-21.26 [-30.79, -11.72]**	

Heterogeneity: Tau² = 60.67; Chi² = 20.66, df = 2 (P < 0.0001); I² = 90%
Test for overall effect: Z = 4.37 (P < 0.0001)

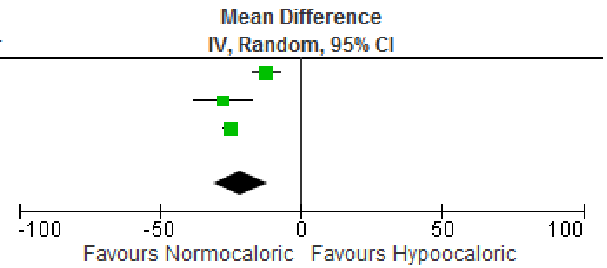

Figure 9. Protein Adequacy

	Hypocaloric			Normocaloric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Arabi 2011	65.2	25.7	120	63.7	25	120	19.0%	1.50 [-4.91, 7.91]	2011
Peake	88.2	39.1	55	82	23.6	57	5.4%	6.20 [-5.81, 18.21]	2014
Arabi 2015	68	24	448	69	25	446	75.6%	-1.00 [-4.21, 2.21]	2015
Total (95% CI)			**623**			**623**	**100.0%**	**-0.14 [-2.93, 2.66]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.60, df = 2 (P = 0.45); I² = 0%
Test for overall effect: Z = 0.10 (P = 0.92)

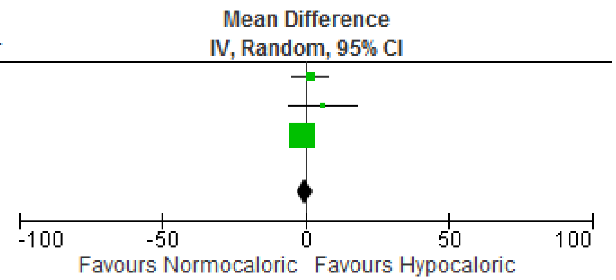

Table 2. Excluded Articles

#	Reason excluded	Reference
1	Not critically ill pts	Owais AE, Kabir SI, Mcnaught C, Gatt M, MacFie J. A single-blinded randomised clinical trial of permissive underfeeding in patients requiring parenteral nutrition. Clin Nutr. 2014 Dec;33(6):997-1001.
2	Abstract	Theodorakopoulou M, Diamantakis A, Kontogiorgi M, Chrysanthopoulou E, Christodoulopoulou T, Frantzeskaki F, Lygnos M, Apostolopoulou O, Armaganidis A. Permissive underfeeding of mechanically ventilated septic ICU Patients. Intensive Care Medicine Experimental. Conference: 29th Annual Congress of the European Society of Intensive Care Medicine, ESICM 2016.
3	Post-hoc analysis	Arabi YM, Aldawood AS, Al-Dorzi HM, Tamim HM, Haddad SH, Jones G, McIntyre L, Solaiman O, Sakkijha MH, Sadat M, Mundekkadan S, Kumar A, Bagshaw SM, Mehta S; PermiT trial group. Permissive Underfeeding or Standard Enteral Feeding in High- and Low-Nutritional-Risk Critically Ill Adults. Post Hoc Analysis of the PermiT Trial. Am J Respir Crit Care Med. 2017 Mar 1;195(5):652-662.
4	Abstract	Ochoa J, Huhmann M, Files DC, Drover J, Bernard A, Ziegler T, Kress J, Ham K.R, Grathwol D, Kulkarni H, Rice T. Hypocaloric high-protein enteral nutrition improves glucose management in critically ill patients. JPEN. 2017:41(2);289-90.
5	Meta-analysis	Chelkeba L, Mojtahedzadeh M, Mekonnen Z. Effect of Calories Delivered on Clinical Outcomes in Critically Ill Patients: Systemic Review and Meta-analysis. Indian J Crit Care Med. 2017 Jun;21(6):376-390.