1.0 The Use of Enteral Nutrition vs. Parenteral Nutrition

Question: Does enteral nutrition compared to parenteral nutrition result in better outcomes in the critically ill adult patient?

Summary of evidence: There were nineteen level 2 studies and one level 1 study (Woodcock et al) that were reviewed and meta-analyzed. In the Woodcock study, data from ICU patients only were abstracted and there were 11/38 patients that crossed over between EN and PN group after randomization. There have been two more recent, large RCTs, Harvey 2014 and Reignier 2017, which enrolled 2400 and 2410 patients, respectively, across 33 and 44 sites. Other more recent smaller trials included patients fasting for at least 14 days (Xi 2014), patients with moderate traumatic brain injury (Meirelles 2011) and patients with severe acute pancreatitis (Wang 2013, Sun 2013). Apriori, we considered that the harmful effect of PN may be associated with relative overfeeding and hyperglycemia. Accordingly, we conducted a subgroup analysis to determine the effect of excess calories (PN compared to EN) and higher glucose levels (across groups). The Moore 1992 study, which had been included in the 2009 summary, was reviewed again and excluded since it reports results of a meta-analysis and the individual studies have been included. Given concerns about population in the Mereilles 2011 and Wang 2013 studies not being critically ill as no mention of ventilation status and some missing data in the latter study, a sensitivity analysis was also done excluding these two studies.

Mortality: In the two largest studies (Harvey and Reignier), there were no significant differences between the parenteral group and the enteral group in 30 or 28 day mortality (P = 0.57 and 0.33, respectively) or 90 day mortality (P = 0.4 and 0.28, respectively) or hospital mortality (P = 0.44 and 0.25, respectively). However, both studies showed a trend in the reduction in ICU mortality, favoring the PN group (P = 0.13 and 0.17, respectively). When these data were aggregated with the other 16 studies reporting on mortality, there was no difference in overall mortality between the groups receiving EN or PN (RR 1.03, 95% CI 0.93, 1.14, p=0.36, heterogeneity I^2=6%, figure 1). When the trials in which the PN group were fed more calories than the EN group were aggregated, there was no effect seen (RR 1.19, 95% CI 0.86, 1.64, p = 0.30, heterogeneity I^2=31%; figure 1). Similarly, when the trials in which the PN and EN groups were fed isocalorically were aggregated, there was no effect on mortality (RR 1.03, 95% CI 0.93, 1.14, p=0.6, heterogeneity I^2=0%; figure 1). There was no difference in these subgroups (p=0.40; figure 1). In subgroup analysis comparing studies in which the PN group had higher blood sugars than the EN group to studies in which there was no difference in blood sugars, showed that increased mortality in the PN groups could not be explained by hyperglycemia (RR 0.93, 95% CI 0.30, 2.90, p=0.90, heterogeneity I^2=0%; figure 2). In a sensitivity analysis excluding Mereilles 2011, Wang 2013, there was still no difference in mortality between groups (RR 1.05, 95% CI 0.95, 1.15, p=0.32, heterogeneity I^2=7%; figure not shown). When data from the 6 studies reporting on ICU mortality were aggregated, there was no effect seen (RR 1.04, 95% CI 0.97, 1.12, p = 0.28, heterogeneity I^2=0%, figure 3). There was also no effect seen when looking at subgroups where the PN group was fed more than the EN group and where the two groups were fed isocalorically (p = 0.38 and 0.71, respectively, figure 3).

Infections: When the 12 studies which reported on patients with infectious complications were statistically aggregated, the meta-analysis showed that EN compared to PN was associated with a significant reduction in the incidence of infectious complications (RR 0.74, 95% CI 0.59, 0.91, p=0.005, heterogeneity I^2=42%; figure 4). When the trials in which the PN group were fed more calories than the EN group were aggregated, EN compared to PN was also associated with a significant reduction in the incidence of infectious complications (RR 0.58, 95% CI 0.39, 0.88, p=0.009, heterogeneity I^2=53%; figure 4). When the trials in which the PN and EN groups were fed isocalorically were aggregated, EN compared to PN had no effect on infectious complications (RR 0.94, 95% CI 0.80, 1,10, p=0.44, heterogeneity I^2=0%; figure 4). There was a significant difference in these subgroups (p=0.03; figure 4). Another subgroup analysis showed that there was a trend between the increase in infections and hyperglycemia (RR 0.79, 95% CI 0.56, 1.11, p=0.17, heterogeneity I^2=0%; figure 5). In a sensitivity analysis excluding Mereilles 2011, EN compared to PN was associated with a significant reduction in infectious complications (RR 0.66, 95% CI 0.50, 0.86, p=0.003, heterogeneity I^2=38%, figure not shown.

LOS, Ventilator days: A total of 9 studies reported on hospital length of stay (in mean and standard deviation) and when the data were aggregated, no effect was seen on hospital LOS (WMD -1.35, 95% CI -3.52, 0.82, p=0.22, heterogeneity I^2=70%; figure 6). Only 6 studies reported on ICU LOS (in mean and standard deviation) and when the data were aggregated, the use of EN was associated with a reduction in ICU LOS (WMD -2.12, 95% CI -4.20, -0.04, p=0.05, heterogeneity I^2=94%; figure 7). A total of 5 studies reported on length of mechanical ventilation (in mean and standard deviation) and when the data were aggregated, there was a trend towards a reduction in ventilator days in the EN fed group (WMD -1.23, 95% CI -2.80, 0.34, p=0.13, heterogeneity I^2=87%, figure 8).

Nutritional complications: Of the 13 studies that reported on nutritional intake, 5 found that PN was associated with a higher calorie intake (Rapp, Young, Moore, Kudsk, Woodcock {Blood sugar values in the Woodcock pertain to the entire group, not the ICU population), the remaining 8 reported no significant difference in intakes between the groups (Adams, Hadley, Cerra, Dunham, Borzotta, Kalfarantzos, Wang, Harvey). A total of 7 studies reported on hyperglycemia and in 4 of these, EN was associated with a lower incidences of hyperglycemia compared to PN (Adams p<0.001), (Borzotta p<0.05, Kalfarentzos) (Mereilles p<0.01). Three studies showed no difference in blood sugars between the groups receiving EN and PN (Moore 1989, Rapp, Harvey). Four studies showed that EN was associated with an increase in diarrhea (Cerra p<0.05, Young, Kudsk p<0.01, Harvey) while one showed an association with EN and a reduction in diarrhea (Borzotta p<0.05) and one study showed no difference (Adam).

Other Complications: EN was also associated with an increase in vomiting (Cerra p<0.05), Harvey 2014 p <0.001). One study found less favourable neurological outcome at 3 months (p =0.05) in brain injured patients (Young, p=0.05), though this significance disappeared after 6 months and 1 year. More overall nutrition related complications were noted in EN vs PN (Dunham). Seven studies reported on diarrhea. There were significant reductions in the incidence of hypoglycemia (44 patients [3.7%] vs. 74 patients [6.2%]; P = 0.006) in the parenteral group in the largest study (Harvey 2014)

Cost: Four studies reported a cost savings with the use of EN vs PN (Adams, Cerra, Borzotta and Kalfarentzos).

Quality of Life (QOL) Outcomes: In a second publication (Harvey 2016), quality of life from the Harvey 2014 study was reported. In the trial, the EuroQol 5-dimension (5-level version) questionnaire (EQ-5D-5L) and a Health Services Questionnaire (to evaluate health and nutrition related quality of life (QOL)) were completed at 90 days post randomization and 1 year post-randomization with survivors. At 90 days and 1 year post randomization, Harvey et al found that health components from the EQ-5D-5L questionnaire were similar between groups. The results for nutrition related QOL were reported on a scale from 1 (worst possible satisfaction) to 7 (best possible satisfaction). At 90 days post-randomization, there was no difference in the mean response between the PN (mean (SD) of 5.2 (1.6, n=405)) and EN groups (5.1 (1.7, n=378)) (mean difference 0.10, 95% CI, -0.14, 0.33, p=0.43) (data not shown in table). At 1 year, there was also no significant difference (5.3 (1.6) in the PN group (n=338) vs 5.4 (1.6) in the EN group (n=322), mean difference -0.10, 95% CI,-0.35, 0.14, p=0.41) (data not shown in table).

Conclusions:

1) The use of EN compared to PN has no effect on mortality in critically ill patients.
2) The use of EN compared to PN is associated with a reduction in the number of infectious complications in the critically ill in trials where patients in the PN group received more calories than in the EN group.
3) The use of EN compared to PN may be associated with a reduction in ICU LOS and ventilator days, but it has no effect on hospital LOS. Significant heterogeneity limits the inferences from these aggregated analyses.
4) The use of EN compared to PN may not be associated with an improvement in calories due to underfeeding in both groups
5) The use of EN may be associated with increased episodes of vomiting.
6) There is no difference between EN and PN in terms of patient reported outcomes

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 EN vs PN in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)† EN	PN	Infections # (%)‡ EN	PN
1. Rapp 1983	Head Injured patients N=38 (<Ideal weight) Single-centre	C.Random: not sure ITT: no Blinding: no (4)	EN vs PN	9/18 (50)	3/20 (15)	NR	NR
2. Adams 1986	Trauma patients undergoing laporotomy N=46 36/46 ICU patients Single-centre	C.Random: not sure ITT: yes Blinding: no (8)	EN vs PN	1/23 (4)	3/23 (13)	15/23 (65)	17/23 (74)
3. Young 1987	Brain injured patients N=58 (N=51 randomized) Single-centre	C.Random: not sure ITT: no Blinding: no (6)	EN vs PN	10/28 (36)	10/23 (43)	5/28 (18)	4/23 (17)
4. Peterson 1988	Critically ill patients with abdominal trauma N=59 Single-centre	C.Random: not sure ITT: no Blinding: no (5)	EN vs PN	NR	NR	2/21 (10)	8/25 (32)
5. Cerra 1988	ICU patients post sepsis N=70 (hypermetabolic patients) Single-centre	C.Random: not sure ITT: no Blinding: no (2)	EN vs PN	ICU 7/31 (22)	ICU 8/35 (23)	NR	NR
6. Moore 1989	Abdominal trauma patients N=75 Single-centre	C.Random: yes ITT: no Blinding: no (10)	EN vs PN	NR	NR	5/29 (17)	11/30 (37)
7. Kudsk 1992	Abdominal trauma N=98 Single-centre	C.Random: not sure ITT: no Blinding: single (10)	EN vs PN	ICU 1/51 (2)	ICU 1/45 (2)	9/51 (16)	18/45 (40)

8. Dunham 1994	Blunt trauma N=38 Single-centre	C.Random: not sure ITT: no Blinding: no (8)	EN vs PN	1/12 (7)	1/15 (8)	NR	NR
9. Borzotta 1994	Closed head injury N=59 Single-centre	C.Random: not sure ITT: no Blinding: no (6)	EN vs PN	5/28 (18)	1/21 (5)	51/28 per group	39/21 per group
10. Hadfield 1995	ICU patients, mainly cardiac bypass N=24 Single-centre	C.Random: not sure ITT: no Blinding: no (7)	EN vs PN	ICU 2/13 (15)	ICU 6/11 (55)	NR	NR
11. Kalfarentzos 1997	Severe acute pancreatitis N=38 Single-centre	C.Random: not sure ITT: no Blinding: single (9)	EN vs PN	ICU 1/18 (6)	ICU 2/20 (10)	5/18 (28)	10/20 (50)
12. Woodcock 2001	Patients needing nutrition support N=562 ICU patients N=38 (all degrees of malnutirition) Single-centre	C.Random: yes ITT: yes Blinding: single (12)	EN vs PN	9/17 (53)	5/21 (24)	6/16 (38)	11/21 (52)
13. Casas 2007	Severe acute pancreatitis; ICU≥72 hrs N=22 Single-centre	C.Random: no/unsure ITT: Yes Blinding: No (8)	EN vs PN	Hospital 0/11 (0)	Hospital 2/11 (18)	1/11 (9)	3/11 (27)
14. Chen 2011	Elderly Patients in respiratory intensive care unit N=147 Single-centre	C.Random: Yes ITT: Yes Blinding: No (7)	EN vs PN	20-day 11/49 (22)	20-day 10/49 (20)	5/49 (10)	18/49 (37)

15. Meirelles 2011	Adult patients with moderate traumatic brain injury N=22 Single-centre	C.Random: No ITT: No Blinding: No (5)	EN vs PN	Unspecified 1/12 (8.3)	Unspecified 1/10 (10)	Total infectious complications 2/12 (16.7) Pneumonia (cases) 2/12 (16.7) Sepsis (cases) 0	Total infectious complications 4/10 (40) Pneumonia (cases) 2/10 (20) Sepsis (cases) 2/10 (20)
16. Wang 2013	Patients 18-45 years with severe acute pancreatitis N=183 Single-centre	C.Random: No ITT: No Blinding: Double (7)	EN vs PN	Hospital 3/61 (5)	Hospital 7/60 (12)	Pancreatic sepsis 13/61 (21) MODS 15/61 (24.6)	Pancreatic sepsis 24/60 (40) MODS 22/60 (36.7)
17. Sun 2013	Severe acute pancreatitis admitted to surgical ICU N=60 Single-centre	C.Random: No ITT: No Blinding: No (6)	EN vs PN	Hospital 2/30 (7)	Hospital 1/30 (3)	Pancreatic 3/30 (10) MODS 5/30 (17) SIRS 12/30 (40)	Pancreatic 10/30 (33) MODS 13/30 (43) SIRS 22/30 (73)
18. Harvey 2014	Adult patients admitted to a general ICU N=2400 Multi-centre	C.Random: Yes ITT: Yes Blinding: No (8)	EN vs PN	ICU 352/1197 (29.4) Hospital 450/1186 (37.9) 30-day 409/1195 (34.2) 90-day 464/1188 (39.1)	ICU 317/1190 (26.6) Hospital 431/1185 (36.4) 30-day 393/1188 (33.1) 90-day 442/1184 (37.3)	Total infectious complications 194/1197 (16.2)** Infectious complications per pt 0.21 +/- 0.5 Pneumonia 143/1197 (11.9) Bloodstream inf 21/1197 (1.8) Surgical inf 12/1197 (1.0)	Total infectious complications 194/1191 (16.3)** Infectious complications per pt 0.22 +/- 0.6 Pneumonia 135/1191 (11.3) Bloodstream inf 27/1191 (2.9) Surgical inf 10/1191 (0.8)
19. Xi 2014	ICU pts fasting at least 14 days, eligible for EN. Single Centre. N=45	C.Random: No ITT: Yes Blinding: No (7)	EN vs PN	28-day 0/22	28-day 0/23	Positive blood cultures 4/22 Sepsis 4/22 (17)	Positive blood cultures 0/23 Sepsis 5/23 (23)

20. Reignier 2017	Mechanically ventilated ICU pts receiving vasopressor support for shock. Multi-centre. N=2410	C.Random: Yes ITT: Yes Blinding: No (11)	EN vs PN	ICU 429/1202 (33) Hospital 498/1202 (36) 28-day 443/1202 (37) 90-day 530/1185 (45)	ICU 405/1208 (31) Hospital 479/1208 (34) 28-day 422/1208 (35) 90-day 507/1192 (43)	ICU acquired 173/1202 (14)	ICU acquired 194/1208 (16)

C.Random: concealed randomization
* median/mean values, no standard deviation hence not included in meta-analysis
‡ refers to the # of patients with infections unless specified
** data on ICU patients/infections obtained directly from author

ITT: intent to treat
NR: not reported
† presumed hospital mortality unless otherwise specified

± ( ) : mean ± Standard deviation (number)
reported data pertaining to ICU patients only
NS = not statistically significant

Table 1. Randomized studies evaluating EN vs. PN in critically ill patients (continued)

Study	LOS days		Ventilator days		Cost		Other
	EN	PN	EN	PN	EN	PN	EN PN
1. Rapp 1983	Hospital 49.4*	Hospital 52.6*	10.3*	10.4*	NR	NR	Mean Calorie Intake (kcals) in study 685 1750 p=0.001 Nitrogen Intake (gms) 4.0 10.2 p=0.002 N balance/24hrs, p=0.002 -17.6 -10.9 Hyperglycemia no difference between groups
2. Adams 1986	ICU 13 ± 11 (19) Hospital 30 ± 21 (19)	ICU 10 ± 10 (17) Hospital 31 ± 29 (17)	12 ± 11 (17)	10 ± 10 (13)	$1346/day	$3729/day	Calorie Intake (kcals) in study 2088 2572 p=NS Caloric adequacy 73% 89% N balance/24 hrs -8.7±6.8 -4.1±4.6 Hyperglycemia (pt days) 24/242 (10) 49/220 (22) p<0.001 Line Problems 13/9 9/7 Diarrhea (days/pt) 3.5 3.8
3. Young 1987	NR	NR	NR	NR	NR	NR	Calories ÷ BEE x 1.75 59% ± 5.13% 75.6% ± 4.26% p=0.02 Protein Intake (gm/kg/day) 0.91 ± 0.09 1.35 ± 0.12 p=0.004 Favourable Neurological Outcome (3 months) 17.9 % 43.5 % Diarrhea 23/28 (82) 13/23 (57)

4. Peterson 1988	ICU 3.7 ± 0.8 (21) Hospital 13. 2 ± 1.6 (21)	ICU 4.6 ± 1.0 (25) Hospital 14.6 ± 1.9 (24)	NR	NR	NR	NR	Day 5 Calorie Intake (kcals) 2204 ± 173 2548 ± 85 P=0.04 Day 5 Nitrogen Intake (gms) 12.6 ± 1.0 14.8 ± 0.6
5. Cerra 1988	NR	NR	NR	NR	$228 ± 59 /day	$330 ± 61 /day	NON PROTEIN Calorie Intake 1684 ± 573 2000 ± 20 p=NS Protein g/d 80±26 88±20 N-balance/d -3.4±10 0.4±3.8 MOSF 7/31 (23) 7/35 (20) Diarrhea 25/31 (81) 9/35 (26) Vomiting 10/31 (32) 10/35 (6)
6. Moore 1989	NR	NR	NR	NR	NR	NR	Non-protein Calorie Intake, day 5 1847 ± 123 2261 ± 60 p=0.01 Nitrogen intake, day 5, p=0.01 12.4±0.8 15.4±0.4 N balance, day 5, p=NS -0.3±0.1 0.1±0.8 Blood Sugars no difference between the groups Non-septic Complications 6/29 (21) 7/30 (23)
7. Kudsk 1992	Hospital 20.5 ± 19.9 (51)	Hospital 19.6 ± 18.8 (45)	2.8 ± 4.9 (51)	3.2 ± 6.7 (45)	NR	NR	NON PROTEIN Calorie Intake (kcal/kg/day) 15.7 ± 4.2 19.1 ± 3.3 p<0.05 Diarrhea 11/51 (22) 7/45 (16)

8. Dunham 1994	NR	NR	NR	NR	NR	NR	Calorie Intake no difference between the groups Protein Intake no difference between the groups Nutrition-related Complications 3/12 (25) 2/15 (13)
9. Borzotta 1994	Hospital (assumed) 39 ± 23.1	Hospital (assumed) 36.9 ± 14	NR	NR	$121,941	$112,450	Calorie Intake no difference between the groups Placement Complications 3/28 (11) 0/21 (0) Aspiration 3/28 (11) 0/21 (0) Hyperglycemia 12/28 (44) 16/21 (76) P=<0.05 Diarrhea 30% 62%
10. Hadfield 1995	NR	NR	NR	NR	NR	NR	
11. Kalfarentzos 1997	ICU 11 (5-21)* Hospital 40 (25-83)*	ICU 12 (5-24)* Hospital 39 (22-73)*	15 (6-16)*	11 (7-31)*	£70/day savings	NR	Non-protein Calorie Intake (kcal/kg/day) 24.1 24.5 p=NS Protein Intake (gm/kg/day) 1.43 1.45 p=NS Hyperglycemia 4/18 (22) 9/20 (45) P=NR
12. Woodcock 2001	33.2 ± 43 (16)	27.3 ± 18.7 (18)	NR	NR	NR	NR	% Target Intake Achieved 54.1% 96.7% p<0.001 < 80% Target Intake 62.5% 6.3% p<0.001

13. Casas 2007	Hospital 30.2 (average)	Hospital 30.7 (average)	NR	NR	NR	NR	Kcal/kg/d, p=ns, n=11 in both groups 20.09±1.83 20.8±1.68 P=NS Nitrogen g/kg/d, p<0.005 0.148±0.016 0.186±0.009
14. Chen 2011	ICU 9.09 ± 2.75 Hospital 23.32 ± 5.6	ICU 9.60 ± 3.06 Hospital 22.24 ± 3.27	7.95 ± 2.11	8.23 ± 2.42	NR	NR	Non-infectious Complications 10/49 (20) 21/49 (43) Gastric Residuals 6/49 (12) 0/49 (0) Diarrhea 6/49 (12) 8/49 (16)
15. Meirelles 2011	ICU 14 (5-26)	ICU 14 (6-24)	NR	NR	NR	NR	Kcal over 5 days 5958 +/- 3619 6586 +/- 1052 P=0.34 Mean daily N-balance, p=0.34 -4.6g/day -5.9g/day Blood Glucose (mg/dl) 102.4 (91.6 – 113.2) 134.4 (122.6-146.2) p < 0.0111
16. Wang 2013	NR	NR	NR	NR	NR	NR	NR
17. Sun 2013	ICU 9 (5-14)	ICU 12 (8-21)	*NR*	NR	NR	NR	NR
18. Harvey 2014	ICU 11.3 ± 12,5 (1197) Hospital 26.8 ± 33.2 (1186)	ICU 12 ± 13.5 (1190) Hospital 27.5 ± 33.9 (1185)	8.2 ± 9.3 (1197)	8.7 ± 11,5 (1189)	NR	NR	Vomiting 1/1197 (0.1) 1/1197 (0.1) Aspiration/Regurgitation 4/1197 (0.3) 2/1191 (0.2) Diarrhea 250/1197 (21) 192/1191 (16.2) Total kcal received during intervention period (kcal/kg) 74 ± 44 89 ± 44 P=NR Total protein received during intervention period (g/kg) 3 ± 2 3 ± 2
19. Xi 2014	ICU 8.52 ± 3.6 (22) Hospital 20.43 ± 10.49 (22)	ICU 20.33 ± 4.47 (23) Hospital 38.76 ± 15.04 (23)	2.96 ± 1.74 (22)	8.62 ± 3.6 (23)	Hospital cost x $\$10^4$ 1.45 ±0.25	Hospital cost x $\$10^4$ 3.47 ± 0.69	NR

20. Reignier 2017	ICU 9.0 (5.0-16.0) 13.7±16.1** N=1201 Hospital 17.0 (8.0-32.0) 25.1±28.4** N=1202	ICU 10.0 (5.0-17.0) 13.7±13.9** N=1207 Hospital 18.0 (9.0-33.0) 25.9±27.0** N=1208	10.7±14.4** N=1201	10.9±12.6** N=1207	NR	NR	Diarrhea 432/1202 (36) 393/1208 (33) Kcal/kg/d 17.8 ± 5.5 19.6 ± 5.3 P<0.0001 Protein g/kg/d 0.7 ± 0.2 0.8 ± 0.2 P<0.0001

C.Random: concealed randomization
* median/mean values, no standard deviation hence not included in meta-analysis
‡ refers to the # of patients with infections unless specified
** data obtained directly from authors
ITT: intent to treat
NR: not reported
† presumed hospital mortality unless otherwise specified
± ( ) : mean ± Standard deviation (number)
reported data pertaining to ICU patients only
NS = not statistically significant

Table 2. Quality of Life (QOL) Outcomes

Study	QOL outcomes			
	EN	PN	EN	PN
18. Harvey 2014	N=544	N=558	N=473	N=467
	EQ-5D-5L components at 90 days post-randomization		EQ-5D-5L components at 1 year post-randomization	
	Mobility: No problems		Mobility: No problems	
	168	170	172	166
	Mobility: Slight problems		Mobility: Slight problems	
	108	118	90	93
	Mobility: Moderate problems		Mobility: Moderate problems	
	142	135	99	114
	Mobility: Severe problems		Mobility: Severe problems	
	76	75	80	65
	Mobility: Extreme problems		Mobility: Extreme problems	
	50	60	32	29
	Self-care: No problems		Self-care: No problems	
	293	299	287	280
	Self-care: slight problems		Self-care: slight problems	
	113	106	71	87
	Self-care: Moderate problems		Self-care: Moderate problems	
	72	85	71	60
	Self-care: Severe problems		Self-care: Severe problems	
	29	31	24	20
	Self-care: Extreme problems		Self-care: Extreme problems	
	37	37	20	20
	Usual Activities: No problems		Usual Activities: No problems	

		119	131		163	151
	Usual Activities: Slight problems	131	123	Usual Activities: Slight problems	104	110
	Usual Activities: Moderate problems	130	140	Usual Activities: Moderate problems	99	103
	Usual Activities: Severe problems	67	74	Usual Activities: Severe problems	62	65
	Usual Activities: Extreme problems	97	90	Usual Activities: Extreme problems	45	38
	Pain/discomfort: No problems	178	173	Pain/discomfort: No problems	159	145
	Pain/discomfort: Slight problems	163	150	Pain/discomfort: Slight problems	136	139
	Pain/discomfort: Moderate problems	133	162	Pain/discomfort: Moderate problems	125	111
	Pain/discomfort: Severe problems	54	56	Pain/discomfort: Severe problems	54	42
	Pain/discomfort: Extreme problems	16	17	Pain/discomfort: Extreme problems	11	18
	Anxiety/depression: No problems	239	242	Anxiety/depression: No problems	235	218
	Anxiety/depression: Slight problems	142	158	Anxiety/depression: Slight problems	91	109
	Anxiety/depression: Moderate problems	114	111	Anxiety/depression: Moderate problems	95	95
	Anxiety/depression: Severe problems	35	28	Anxiety/depression: Severe problems	41	30
	Anxiety/depression: Extreme problems	14	19	Anxiety/depression: Extreme problems	11	15
		N=1197	N=1191		N=1197	N=1191
	EQ-5D-5L Utility Score (survivors), mean (SD)	0.654 (0.283)	0.655 (0.282)	EQ-5D-5L Utility Score (survivors), mean (SD)	0.683 (0.292)	0.684 (0.285)
	QALYs	0.050 (0.049)	0.051 (0.048)	QALYs	0.335 (0.332)	0.348 (0.333)
	P=0.46			P=0.35		

Note: Only studies reporting on these outcomes are shown in this table.

Figure 1. Studies comparing EN vs PN: Overall Mortality

Study or Subgroup	EN Events	EN Total	PN Events	PN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.2.1 Mortality (PN>EN kcal)							
Rapp	9	18	3	20	0.6%	3.33 [1.07, 10.43]	1983
Young	10	28	10	23	1.8%	0.82 [0.42, 1.62]	1987
Kudsk	1	51	1	45	0.1%	0.88 [0.06, 13.70]	1992
Woodcock	9	17	5	21	1.1%	2.22 [0.92, 5.40]	2001
Chen	11	49	10	49	1.5%	1.10 [0.51, 2.35]	2011
Reignier	498	1202	479	1208	47.9%	1.04 [0.95, 1.15]	2017
Subtotal (95% CI)		**1365**		**1366**	**53.0%**	**1.19 [0.86, 1.64]**	
Total events	538		508				
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 7.22$, df = 5 (P = 0.20); $I^2 = 31\%$							
Test for overall effect: Z = 1.04 (P = 0.30)							
1.2.2 Mortality (PN~EN kcal)							
Adams	1	23	3	23	0.2%	0.33 [0.04, 2.97]	1986
Borzotta	5	28	1	21	0.2%	3.75 [0.47, 29.75]	1994
Dunham	1	12	1	15	0.1%	1.25 [0.09, 17.98]	1994
Hadfield	2	13	6	11	0.4%	0.28 [0.07, 1.13]	1995
Kalfarentzos	1	18	2	20	0.2%	0.56 [0.05, 5.62]	1997
Cerra	7	31	8	35	1.1%	0.99 [0.40, 2.41]	1998
Casas	0	11	2	11	0.1%	0.20 [0.01, 3.74]	2007
Justo Meirelles	1	12	1	10	0.1%	0.83 [0.06, 11.70]	2011
Wang	3	61	7	60	0.5%	0.42 [0.11, 1.55]	2013
Sun	2	30	1	30	0.2%	2.00 [0.19, 20.90]	2013
Xi	0	22	0	23		Not estimable	2014
Harvey	450	1186	431	1185	43.9%	1.04 [0.94, 1.16]	2014
Subtotal (95% CI)		**1447**		**1444**	**47.0%**	**1.03 [0.93, 1.14]**	
Total events	473		463				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 9.59$, df = 10 (P = 0.48); $I^2 = 0\%$							
Test for overall effect: Z = 0.52 (P = 0.60)							
Total (95% CI)		**2812**		**2810**	**100.0%**	**1.04 [0.95, 1.14]**	
Total events	1011		971				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 16.94$, df = 16 (P = 0.39); $I^2 = 6\%$							
Test for overall effect: Z = 0.91 (P = 0.36)							
Test for subgroup differences: $Chi^2 = 0.69$, df = 1 (P = 0.40), $I^2 = 0\%$							

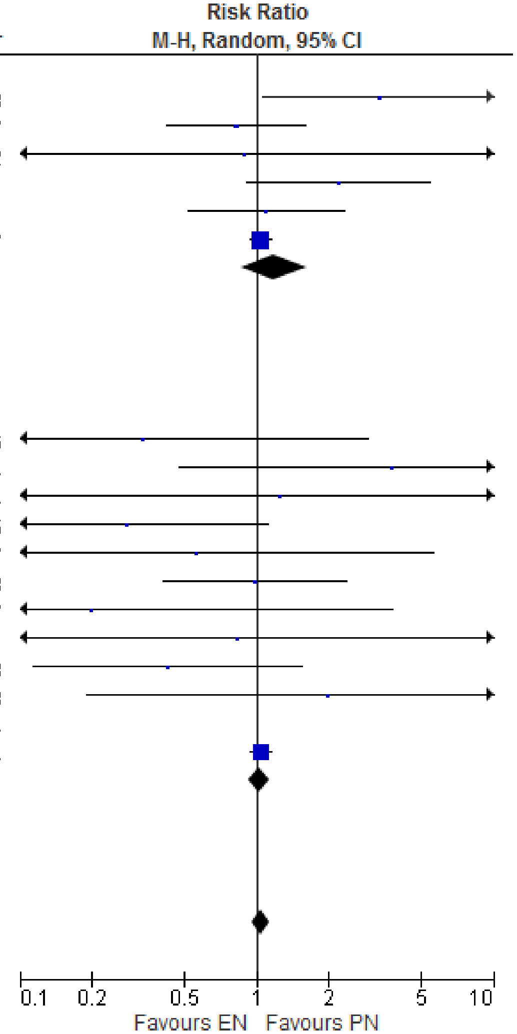

Figure 2. Overall mortality in studies with hyperglycemia where the PN group had higher blood sugars than the EN group

Study or Subgroup	EN Events	EN Total	PN Events	PN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Adams	1	23	3	23	27.1%	0.33 [0.04, 2.97]	1986
Borzotta	5	28	1	21	30.2%	3.75 [0.47, 29.75]	1994
Kalfarentzos	1	18	2	20	24.2%	0.56 [0.05, 5.62]	1997
Meirelles	1	12	1	10	18.6%	0.83 [0.06, 11.70]	2011
Total (95% CI)		**81**		**74**	**100.0%**	**0.93 [0.30, 2.90]**	
Total events	8		7				

Heterogeneity: Tau² = 0.00; Chi² = 2.81, df = 3 (P = 0.42); I² = 0%
Test for overall effect: Z = 0.13 (P = 0.90)

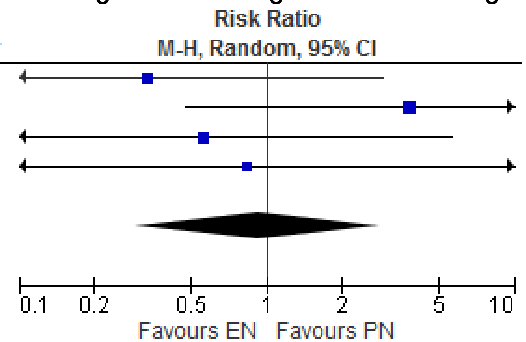

Figure 3. ICU Mortality

Study or Subgroup	EN Events	EN Total	PN Events	PN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.19.1 Mortality (PN>EN kcal)							
Kudsk	1	51	1	45	0.1%	0.88 [0.06, 13.70]	1992
Reignier	498	1202	479	1208	53.4%	1.04 [0.95, 1.15]	2017
Subtotal (95% CI)		**1253**		**1253**	**53.5%**	**1.04 [0.95, 1.15]**	
Total events	499		480				
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.90); I² = 0%							
Test for overall effect: Z = 0.89 (P = 0.38)							
1.19.2 Mortality (PN~EN kcal)							
Hadfield	2	13	6	11	0.3%	0.28 [0.07, 1.13]	1995
Kalfarentzos	1	18	2	20	0.1%	0.56 [0.05, 5.62]	1997
Cerra	7	31	8	35	0.6%	0.99 [0.40, 2.41]	1998
Harvey	450	1186	431	1185	45.6%	1.04 [0.94, 1.16]	2014
Subtotal (95% CI)		**1248**		**1251**	**46.5%**	**0.93 [0.63, 1.36]**	
Total events	460		447				
Heterogeneity: Tau² = 0.05; Chi² = 3.70, df = 3 (P = 0.30); I² = 19%							
Test for overall effect: Z = 0.38 (P = 0.71)							
Total (95% CI)		**2501**		**2504**	**100.0%**	**1.04 [0.97, 1.12]**	
Total events	959		927				

Heterogeneity: Tau² = 0.00; Chi² = 3.74, df = 5 (P = 0.59); I² = 0%
Test for overall effect: Z = 1.07 (P = 0.28)
Test for subgroup differences: Chi² = 0.34, df = 1 (P = 0.56), I² = 0%

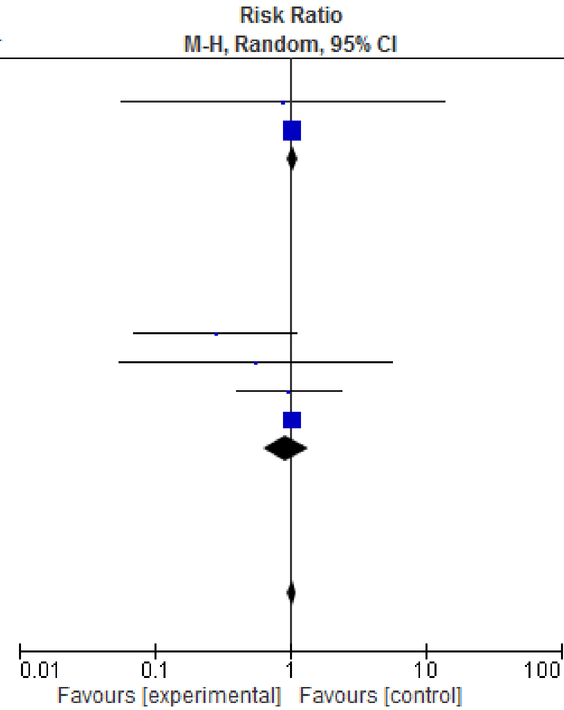

Figure 4. Studies comparing EN vs PN: Infectious complications

Study or Subgroup	EN Events	EN Total	PN Events	PN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.1.1 Infections (PN>EN kcal)							
Young	5	28	4	23	2.9%	1.03 [0.31, 3.39]	1987
Peterson	2	21	8	25	2.1%	0.30 [0.07, 1.25]	1988
Moore	5	29	11	30	4.6%	0.47 [0.19, 1.19]	1989
Kudsk	9	51	18	45	7.3%	0.44 [0.22, 0.88]	1992
Woodcock	6	16	11	21	6.4%	0.72 [0.34, 1.52]	2001
Chen	5	49	18	49	4.7%	0.28 [0.11, 0.69]	2011
Reignier	173	1202	194	1208	24.2%	0.90 [0.74, 1.08]	2017
Subtotal (95% CI)		**1396**		**1401**	**52.2%**	**0.58 [0.39, 0.88]**	
Total events	205		264				
Heterogeneity: Tau² = 0.14; Chi² = 12.77, df = 6 (P = 0.05); I² = 53%							
Test for overall effect: Z = 2.60 (P = 0.009)							
1.1.2 Infections (PN~EN kcal)							
Adams	15	23	17	23	15.2%	0.88 [0.60, 1.30]	1986
Kalfarentzos	5	18	10	20	5.1%	0.56 [0.23, 1.32]	1997
Casas	1	11	3	11	1.0%	0.33 [0.04, 2.73]	2007
Justo Meirelles	2	12	4	10	2.0%	0.42 [0.10, 1.82]	2011
Harvey	194	1197	194	1191	24.5%	0.99 [0.83, 1.19]	2014
Subtotal (95% CI)		**1261**		**1255**	**47.8%**	**0.94 [0.80, 1.10]**	
Total events	217		228				
Heterogeneity: Tau² = 0.00; Chi² = 4.02, df = 4 (P = 0.40); I² = 0%							
Test for overall effect: Z = 0.77 (P = 0.44)							
Total (95% CI)		**2657**		**2656**	**100.0%**	**0.74 [0.59, 0.91]**	
Total events	422		492				
Heterogeneity: Tau² = 0.04; Chi² = 18.91, df = 11 (P = 0.06); I² = 42%							
Test for overall effect: Z = 2.79 (P = 0.005)							
Test for subgroup differences: Chi² = 4.53, df = 1 (P = 0.03), I² = 77.9%							

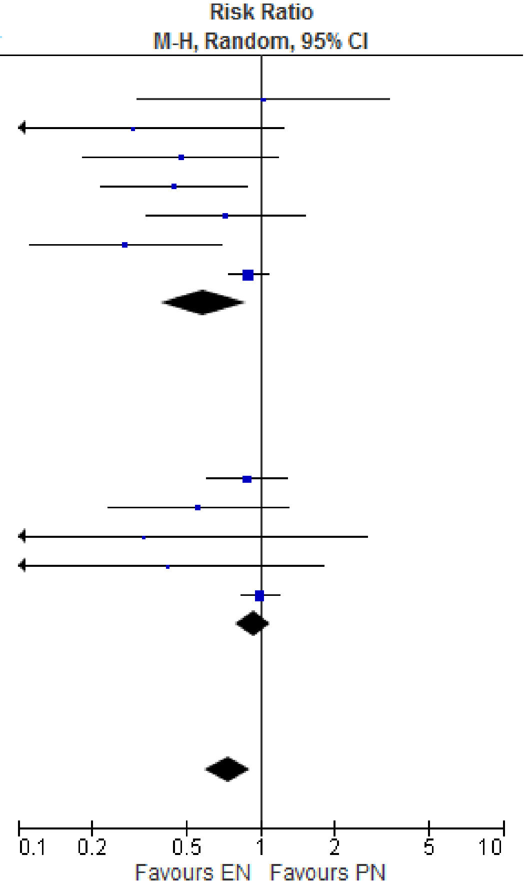

Figure 5. Infections in studies with hyperglycemia where the PN group had higher blood sugars than the EN group

Study or Subgroup	EN Events	EN Total	PN Events	PN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Adams	15	23	17	23	79.0%	0.88 [0.60, 1.30]	1986
Kalfarentzos	5	18	10	20	15.7%	0.56 [0.23, 1.32]	1997
Meirelles	2	12	4	10	5.4%	0.42 [0.10, 1.82]	2011
Total (95% CI)		**53**		**53**	**100.0%**	**0.79 [0.56, 1.11]**	
Total events	22		31				

Heterogeneity: Tau² = 0.00; Chi² = 1.98, df = 2 (P = 0.37); I² = 0%
Test for overall effect: Z = 1.36 (P = 0.17)

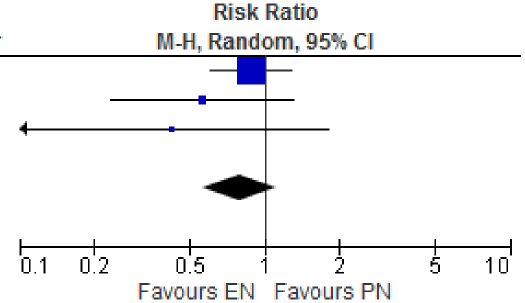

Figure 6. Hospital LOS

Study or Subgroup	EN Mean	EN SD	EN Total	PN Mean	PN SD	PN Total	Weight	Mean Difference IV, Random, 95% CI	Year
1.3.1 Hospital LOS (PN>EN kcal)									
Peterson	13.2	1.6	21	14.6	1.9	21	23.3%	-1.40 [-2.46, -0.34]	1988
Kudsk	20.5	19.9	51	19.6	18.8	45	5.9%	0.90 [-6.85, 8.65]	1992
Woodcock	33.2	43	16	27.3	18.7	18	0.9%	5.90 [-16.87, 28.67]	2001
Chen	23.32	5.6	49	22.24	3.27	49	21.0%	1.08 [-0.74, 2.90]	2011
Reignier	25.1	28.4	1202	25.9	27	1208	19.6%	-0.80 [-3.01, 1.41]	2017
Subtotal (95% CI)			**1339**			**1341**	**70.7%**	**-0.47 [-1.75, 0.81]**	
Heterogeneity: Tau² = 0.63; Chi² = 5.84, df = 4 (P = 0.21); I² = 32%									
Test for overall effect: Z = 0.72 (P = 0.47)									
1.3.2 Hospital LOS (PN~EN kcal)									
Adams	30	21	19	31	29	17	1.6%	-1.00 [-17.71, 15.71]	1986
Borzotta	39	23.1	28	36.9	14	21	3.7%	2.10 [-8.34, 12.54]	1994
Harvey	26.8	33.2	1186	27.5	33.9	1185	17.8%	-0.70 [-3.40, 2.00]	2014
Xi	20.43	10.49	22	38.76	15.04	23	6.2%	-18.33 [-25.88, -10.78]	2014
Subtotal (95% CI)			**1255**			**1246**	**29.3%**	**-4.90 [-14.93, 5.12]**	
Heterogeneity: Tau² = 80.86; Chi² = 19.37, df = 3 (P = 0.0002); I² = 85%									
Test for overall effect: Z = 0.96 (P = 0.34)									
Total (95% CI)			**2594**			**2587**	**100.0%**	**-1.35 [-3.52, 0.82]**	

Heterogeneity: Tau² = 4.96; Chi² = 26.79, df = 8 (P = 0.0008); I² = 70%
Test for overall effect: Z = 1.22 (P = 0.22)
Test for subgroup differences: Chi² = 0.74, df = 1 (P = 0.39), I² = 0%

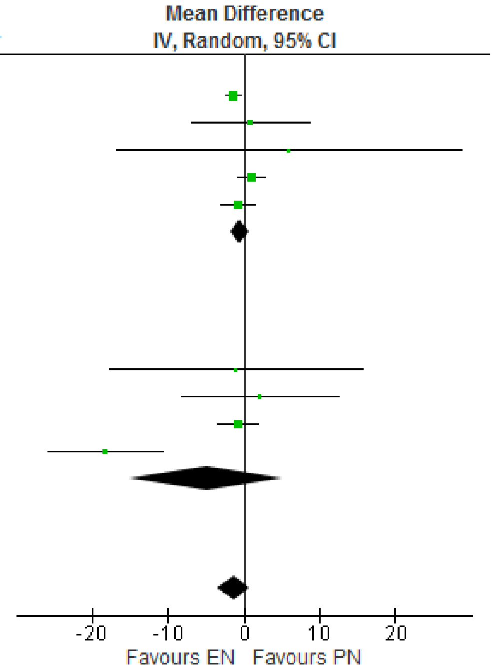

Figure 7. ICU LOS

	EN			PN				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
1.6.1 ICU LOS (PN>EN)									
Peterson	3.7	0.8	21	4.6	1	25	20.1%	-0.90 [-1.42, -0.38]	1988
Chen	9.09	2.75	49	9.6	3.06	49	19.1%	-0.51 [-1.66, 0.64]	2011
Reignier	13.7	16.1	1201	13.7	13.9	1207	19.0%	0.00 [-1.20, 1.20]	2017
Subtotal (95% CI)			**1271**			**1281**	**58.2%**	**-0.72 [-1.16, -0.28]**	
Heterogeneity: Tau² = 0.00; Chi² = 1.97, df = 2 (P = 0.37); I² = 0%									
Test for overall effect: Z = 3.21 (P = 0.001)									
1.6.2 ICU LOS (PN~EN kcal)									
Adams	13	11	19	10	10	17	6.3%	3.00 [-3.86, 9.86]	1986
Xi	8.52	3.6	22	20.33	4.47	23	16.1%	-11.81 [-14.18, -9.44]	2014
Harvey	11.3	12.5	1197	12	13.5	1190	19.3%	-0.70 [-1.74, 0.34]	2014
Subtotal (95% CI)			**1238**			**1230**	**41.8%**	**-3.50 [-12.23, 5.24]**	
Heterogeneity: Tau² = 55.42; Chi² = 73.31, df = 2 (P < 0.00001); I² = 97%									
Test for overall effect: Z = 0.78 (P = 0.43)									
Total (95% CI)			**2509**			**2511**	**100.0%**	**-2.12 [-4.20, -0.04]**	
Heterogeneity: Tau² = 5.54; Chi² = 85.27, df = 5 (P < 0.00001); I² = 94%									
Test for overall effect: Z = 2.00 (P = 0.05)									
Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0%									

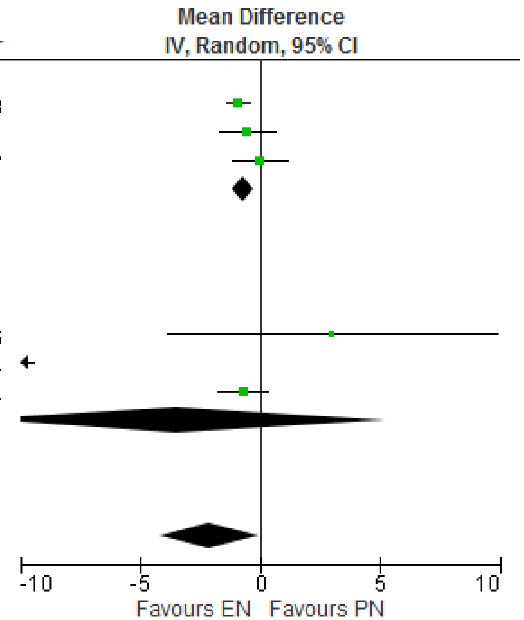

Figure 8. Mechanical Ventilation

	EN			PN				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**Year**
Adams	12	11	17	10	10	13	3.6%	2.00 [-5.54, 9.54]	1986
Kudsk	2.8	4.9	51	3.2	6.7	45	15.0%	-0.40 [-2.77, 1.97]	1992
Chen	7.95	2.11	49	8.23	2.42	49	21.2%	-0.28 [-1.18, 0.62]	2011
Harvey	8.2	9.3	1197	8.7	11.5	1189	21.4%	-0.50 [-1.34, 0.34]	2014
Xi	2.96	1.74	22	8.62	3.6	23	18.2%	-5.66 [-7.30, -4.02]	2014
Reignier	10.7	14.4	1201	10.9	12.6	1207	20.6%	-0.20 [-1.28, 0.88]	2017
Total (95% CI)			**2537**			**2526**	**100.0%**	**-1.23 [-2.80, 0.34]**	
Heterogeneity: Tau² = 2.81; Chi² = 37.28, df = 5 (P < 0.00001); I² = 87%									
Test for overall effect: Z = 1.53 (P = 0.13)									

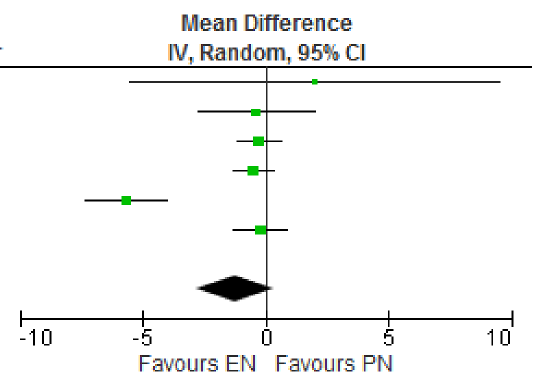

Table 3. Excluded Articles

#	Reason Excluded	Citation
1	Cancer patients, not ICU patients	Lim ST, Choa RG, Lam KH, Wong J, Ong GB. Total parenteral nutrition versus gastrostomy in the preoperative preparation of patients with carcinoma of the oesophagus. Br J Surg. 1981 Feb;68(2):69-72.
2	Cancer patients, not ICU patients	Sako K, Loré JM, Kaufman S, Razack MS, Bakamjian V, Reese P. Parenteral hyperalimentation in surgical patients with head and neck cancer: a randomized study. J Surg Oncol. 1981;16(4):391-402.
3	Unclear if ICU patients	Bauer E, Graber R, Brodike R et al. Ernahrungsphysiologische, immunologische und klinische parameter bei prospektiv randomisierten patienten unter enteraler oder parenteraler ernahrungstherapie nach dickdarmoperationen. Infusionstherapie 1984;11:165-167.
4	Patients not critically ill	Quayle AR, Mangnall D, Clark RG. A comparison of immediate post-operative enteral and parenteral nutrition in patients with gastric carcinoma. Clin Nutr 1984;3:35-39.
5	Not likely ICU patients	Seri S, Aquilio E. Effects of early nutritional support in patients with abdominal trauma. It J Surg Sci 1984;14:223-7.
6	Elective surgery patients	Wiedeck H, Merkle N, Herfarth Ch, Grunert A. Postoperative enteral nutrition following resection of the colon. Anaesthesist 1984;33:63-67.
7	Elective surgery patients	Costalat G, Vernhet J. Nutrition enterale postoperatoire precoce par catheter jejunal en chirurgie digestive lourde. Comparison avec la nutrition parenterale exclusive. Chirurgie 1985 ;111 :708-714.
8	Elective surgery patients	Bower RH, Talamini MA, Sax HC. Postoperative enteral vs parenteral nutrition: A randomized controlled trial. Arch Surg 1986;121:1040-5.
9	Elective surgery patients	Fletcher JP, Little JM. A comparison of parenteral nutrition and early postoperative enteral feeding on the nitrogen balance after major surgery. Surgery 1986;100:21-4.
10	Pseudo-randomized	Hadley MN, Grahm TW, Harrington T. Nutritional support and neurotrauma: A critical review of early nutrition in forty-five acute head injury patients. Neurosurgery 1986;19:367-73.
11	No significant outcomes	Young B, Ott L, Haack D. Effect of total parenteral nutrition upon intracranial pressure in severe head injury. J Neurosurg 1987;67:76-80.
12	Not ICU patients	Greenberg GR, Fleming CR, Jeejeebhoy KN, Rosenberg IH, Sales D, Tremaine WJ. Controlled trial of bowel rest and nutritional support in the management of Crohn's disease. Gut. 1988 Oct;29(10):1309-15.
13	Elective surgery patients	Hamaoui E, Lefkowitz R, Olender L et al. Enteral nutrition in the early postoperative period: A new semi-elemental formula versus total parenteral nutrition. JPEN:J Parenter Enteral Nutr 1990;14:501-7.
14	Meta-analysis	Moore FA, Feliciano DV, Andrassy RJ et al. Early enteral feeding, compared with parenteral, reduces postoperative septic complications: The results of a meta-analysis. Ann Surg 1992;216:172-83.
15	Elective surgery patients	Von Meyenfeldt MF, Meijerink WJ, Rouflart MM, Builmaassen MT, Soeters PB.C. Perioperative nutritional support: a randomised clinical trial. lin Nutr. 1992 Aug;11(4):180-6.
16	Cancer patients, not ICU patients	González-Huix F, Fernández-Bañares F, Esteve-Comas M, Abad-Lacruz A, Cabré E, Acero D, Figa M, Guilera M, Humbert P, de León R, et al. Enteral versus parenteral nutrition as adjunct therapy in acute ulcerative colitis.Am J Gastroenterol. 1993 Feb;88(2):227-32.
17	Elective surgery	Iovinelli G, Marsili I, Varrassi G. Nutrition support after total laryngectomy. JPEN J Parenter Enteral Nutr. 1993 Sep-Oct;17(5):445-8.

	patients	
18	Duplicate of 1992 study	Kudsk KA. Gut mucosal nutritional support - Enteral nutrition as primary therapy after multiple system trauma. Gut 1994;35:S52-S54.
19	Elective surgery patients	Wicks C, Somasundaram S, Bjarnason I et al. Comparison of enteral feeding and total parenteral nutrition after liver transplantation. Lancet 1994;344:837-40.
20	Elective surgery patients	Baigrie RJ, Devitt PG, Watkin DS. Enteral versus parenteral nutrition after oesophagogastric surgery: a prospective randomized comparison. Aust N Z J Surg. 1996 Oct;66(10):668-70.
21	Not a RCT, not ICU patients	Hernandez-Aranda JC, Gallo-Chico B, Ramirez-Barba EJ. Nutritional support in severe acute pancreatitis. Controlled clinical trial. Nutr Hosp 1996;11:160-6.
22	No significant outcomes	Suchner U, Senftleben U, Eckart T et al. Enteral versus parenteral nutrition: Effects on gastrointestinal function and metabolism. Nutrition 1996;12:13-22.
23	Not ICU patients	Georgiannos SN, Renaut AJ, Goode AW. Short-term restorative nutrition in malnourished patients: Pro's and con's of intravenous and enteral alimentation using compositionally matched nutrients. Int Surg 1997;82:301-306.
24	Cancer patients, not ICU patients	Gianotti L, Braga M, Vignali A, Balzano G, Zerbi A, Bisagni P, Di Carlo V. Effect of route of delivery and formulation of postoperative nutritional support in patients undergoing major operations for malignant neoplasms. Arch Surg. 1997 Nov;132(11):1222-9.
25	Not ICU pts	McClave SA, Greene LM, Snider HL, Makk LJ, Cheadle WG, Owens NA, Dukes LG, Goldsmith LJ. Comparison of the safety of early enteral vs parenteral nutrition in mild acute pancreatitis. JPEN J Parenter Enteral Nutr. 1997 Jan-Feb;21(1):14-20.
26	Cancer patients, not ICU patients	Reynolds JV, Kanwar S, Welsh FK, Windsor AC, Murchan P, Barclay GR, Guillou PJ. Does the route of feeding modify gut barrier function and clinical outcome in patients after major upper gastrointestinal surgery? JPEN J Parenter Enteral Nutr. 1997 Jul-Aug;21(4):196-201.
27	Cancer patients, not ICU patients	Sand J, Luostarinen M, Matikainen M. Enteral or parenteral feeding after total gastrectomy: prospective randomised pilot study. Eur J Surg. 1997 Oct;163(10):761-6.
28	Cancer patients, not ICU patients	Shirabe K, Matsumata T, Shimada M, Takenaka K, Kawahara N, Yamamoto K, Nishizaki T, Sugimachi K. A comparison of parenteral hyperalimentation and early enteral feeding regarding systemic immunity after major hepatic resection--the results of a randomized prospective study.Hepatogastroenterology. 1997 Jan-Feb;44(13):205-9.
29	Elective surgery patients	Braga M, Gianotti L, Vignali A, Cestari A, Bisagni P, Di C, V. Artificial nutrition after major abdominal surgery: Impact of route of administration and composition of the diet. Crit Care Med 1998;26:24-30.
30	Not ICU patients	Windsor ACJ, Kanwar S, Li AGK et al. Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. Gut 1998;42:431-5.
31	Elective surgery patients	Oláh A, Pardavi G, Belágyi T. [Early jejunal feeding in acute pancreatitis: prevention of septic complications and multiorgan failure][Article in Hungarian] Magy Seb. 2000 Feb;53(1):7-12.
32	Elective surgery patients	Bozzetti F, Braga M, Gianotti L, Gavazzi C, Mariani L. Postoperative enteral versus parenteral nutrition in malnourished patients with gastrointestinal cancer: A randomised multicentre trial. Lancet 2001;358:1487-92.
33	Elective surgery patients	Braga M, Gianotti L, Gentilini O, Parisi V, Salis C, Di C, V. Early postoperative enteral nutrition improves gut oxygenation and reduces costs compared with total parenteral nutrition. Crit Care Med 2001;29:242-8.

34	Meta-analysis	Braunschweig CL, Levy P, Sheean PM, Wang X. Enteral compared with parenteral nutrition: A meta-analysis. Am J Clin Nutr 2001;74:534-42.
35	Meta-analysis	Heyland DK Montalvo M, MacDonald S et al. Total parenteral nutrition in the surgical patient: a meta-analysis. Can J Surg 2001;44(2):102-111.
36	Elective surgery patients	Pacelli F, Bossola M, Papa V et al. Enteral vs parenteral nutrition after major abdominal surgery: An even match. Arch Surg 2001;136:933-6.
37	Not ICU patients	Abou-Assi S. Craig K, O'Keefe SJ. Hypocaloric jejunal feeding is better than total parenteral nutrition in acute pancreatitis : results of a randomized comparative study. Am J Gastroenterology 2002;97(9):2255-2262.
38	Not Randomized	Huang YC, Yen CE, Cheng CH, Jih KS, Kan MN. Nutritional status of mechanically ventilated critically ill patients: comparison of different types of nutritional support. Clin Nutr 2002:101-7.
39	Pseudo-randomized	Olah A, Pardavi G, Belagyi T, Nagy A, Issekutz A, Mohamed GE. Early nasojejunal feeding in acute pancreatitis is associated with a lower complication rate. Nutrition 2002;18(3):259-62.
40	Elective surgery patients	Rayes N, Hansen S, Seehofer D, Müller AR, Serke S, Bengmark S, Neuhaus P. Early enteral supply of fiber and Lactobacilli versus conventional nutrition: a controlled trial in patients with major abdominal surgery. Nutrition. 2002 Jul-Aug;18(7-8):609-15.
41	Not ICU patients	Gupta R, Patel K, Calder PC, Yaqoob P, Primrose JN, Johnson CD. A randomised clinical trial to assess the effect of total enteral and total parenteral nutritional support on metabolic, inflammatory and oxidative markers in patients with predicted severe acute pancreatitis (APACHE II > or =6). Pancreatology. 2003;3(5):406-13.
42	No clinical outcomes	Zhao G, Wang CY, Wang F, Xiong JX. Clinical study on nutrition support in patients with severe acute pancreatitis. World journal of gastroenterology: WJG 2003;9(9):2105-8.
43	Not ICU patients	Louie BE, Noseworthy T, Hailey D, Gramlich LM, Jacobs P, Warnock GL. 2004 MacLean-Mueller prize enteral or parenteral nutrition for severe pancreatitis: a randomized controlled trial and health technology assessment. Can J Surg. 2005 Aug;48(4):298-306.
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