5.3 Strategies to Optimize Delivery and Minimize Risks of EN: Small Bowel Feeding vs. Gastric

Question: Does enteral feeding via the small bowel compared to gastric feeding result in better outcomes in the critically ill adult patient?

Summary of evidence: Twenty randomized trials that were reviewed, all except 1 (Zhu 2018) were level 2 studies. In the Taylor 1999 study, only 34% of the patients achieved small bowel access in this study (large number of protocol violations), while Minard 2000 compared outcomes in patients receiving early immune enhanced enteral nutrition via the small bowel to those receiving delayed immune enhanced enteral nutrition via the gastric route. Therefore, sensitivity analyses were conducted with and without Taylor and Minard study.

Mortality: Based on the 16 studies that reported on mortality, no significant differences between the groups were found (RR 0.97, 95% CI 0.83, 1.13, p=0.71, heterogeneity I^2=0%; figure 1). When Taylor 1999 & Minard 2000 were excluded, the mortality difference between the groups were still not significant (RR 0.98, 95% CI 0.84, 1.15, p=0.80, heterogeneity I^2=0%; figure 2).

Infections (Pneumonia): Based on the 17 studies that reported on pneumonia, the meta-analysis showed that small bowel feeding was associated with a reduction in pneumonia when compared to gastric feeding (RR 0.72, 95% CI 0.57, 0.91, p=0.006, heterogeneity I^2=26%; figure 3). When the studies by Taylor 1999 and Minard 2000 were removed from the analysis, small bowel feeding was still associated with reduction of pneumonia (RR 0.70, 95% CI 0.53, 0.93, p=0.01, heterogeneity I^2=32%; figure 4).

LOS: When all 13 studies that reported ICU LOS were aggregated, enteral feeding via the small bowel had no effect on ICU length of stay (WMD -0.56, 95% CI -3.28, 2.16, p=0.68, heterogeneity I^2=97%; figure 5). When the Minard study was excluded from the analysis, the signal did not change (WMD -1.09, 95% CI -3.88, 1.71, p=0.45, heterogeneity I^2=98%; figure 6). Based on the aggregation of the 6 studies that reported hospital LOS, enteral feeding via the small bowel had no effect on hospital length of stay (WMD 0.01, 95% CI -3.12, 3.15, p=0.99, heterogeneity I^2=7%; figure 7) when compared to gastric feeding.

Ventilator days: Based on the aggregation of the 9 studies that reported duration of ventilation, enteral feeding via the small bowel compared to gastric feeding showed a trend towards shorter duration of ventilation (WMD -1.23, 95% CI -2.79, 0.33, p=0.12, heterogeneity I^2=75%; figure 8).

Nutritional Outcomes: Many studies reported on nutritional complications, such as GI bleeds, vomiting, diarrhea, constipation and abdominal bloating. There was no difference between the 2 groups in some studies (Davies 2011, White 2009, Friedman 2015), while other reported a significant improvement in nutritional outcomes in the group fed via small bowel such as better nutrition efficiency (Hsu 2009, Acosta-Escribano 2010, Taylor 2016), calorie/protein intake & less time to reach goal (Hsu 2009), vomiting (Hsu 2009, Zhu 2018) and significantly less gastrointestinal tract colonization and high gastric residual volumes (Acosta-Escribano 2010). The studies that reported nutritional delivery generally showed better success at meeting goal targets and reaching them sooner. However, this could also be explained by the confounded nature of different gastric feeding strategies. When the data from the 6 studies that reported nutritional efficiency (% goal rate received) as a mean ± standard deviation were aggregated, small bowel feeding compared to gastric feeding was associated with a significantly greater percentage of nutritional efficiency (WMD 10.59, 95% CI 4.76, 16.41, p=0.0004, heterogeneity I^2=88%; figure 9). When the data from the 4 studies that reported the time to reach nutritional goal rate were aggregated, small bowel feeding compared to gastric feeding had no effect on the time to reach nutritional goals (WMD -3.41, 95% CI -13.45, 6.62, p=0.51, heterogeneity I^2=87%; figure 10). One study (Friedman 2015) reported a significant increase in cost when using small bowel vs gastric feeds, though the details on this calculation and the statistical significance was not reported.

Other complications: The group that had a more aggressive feeding regimen and small bowel feeding (Taylor 1999) had fewer major complications and a better neurological outcome at 3 months than the group receiving gastric feeds.

Conclusions:

Small bowel feeding, compared to gastric feeding

1) is associated with a reduction in pneumonia in critically ill patients.
2) may be associated with a reduction in duration on ventilation in critically ill patients.
3) has no effect on mortality, and ICU and hospital length of stays.
4) is associated with improved calorie and protein intake and with less time taken to reach target rate of enteral nutrition

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 small bowel feeding vs. gastric in critically ill patients

Study	Population	Methods (score)	Mortality # (%)† Small bowel	Mortality # (%)† Gastric	Pneumonia # (%)‡ Small bowel	Pneumonia # (%)‡ Gastric
1. Montecalvo 1992	Med/Surg ICU Anticipated feed >3days N=38 from 2 ICUs	C.Random: not sure ITT: no Blinding: no (8)	5/19 (26)	5/19 (26)	4/19 (21)	6/19 (32)
2. Kortbeek 1999	Trauma ISS>16 Vent >48h N=80 from 2 ICUs	C.Random: yes ITT: yes Blinding: no (11)	4/37 (11)	3/43 (7)	10/37 (27)	18/43 (42)
3. Taylor 1999	Head injured ventilated > 10 yrs N=82	C.Random: not sure ITT: yes Blinding: no (10)	**6-month** 5/41(12)	**6-month** 6/41 (15)	**Pneumonia** 18/41 (44) **Total Infections** 25/41 (61)	26/41 (63) 35/41 (85)
4. Kearns 2000	MICU Feed >3days APACHE ~21 N=44	C.Random: not sure ITT: yes Blinding: no (9)	5/21 (24)	6/23 (26)	4/21 (19)	3/23 (13)
5. Minard 2000	Trauma GCS 3-10 N=27	C.Random: not sure ITT: no Blinding: no (7)	1/12 (8)	4/15 (27)	6/12 (50)	7/15 (47)
6. Esparaza 2001	MICU MV = 98% APACHE ~25 N=54	C.Random: not sure ITT: yes Blinding: no (8)	10/27 (37)	11/27 (41)	NR	NR
7. Boivin 2001	Med/Surg/Neuro MV~98% Feed >72h APACHE~16 N=80	C.Random: not sure ITT: no Blinding: no (6)	18/39 (46)	18/39 (46)	NR	NR

8. Day 2001	Neurological ICU APACHE ~ 48 N=25	C.Random: not sure ITT: yes Blinding: no (5)	NR	NR	0/14 (0)	2/11 (18)
9. Davies 2002	Med/surg/trauma Feed > 3days MV=90%; APACHE~21 N=73	C.Random: not sure ITT: no Blinding no (8)	4/34 (12)	5/39 (13)	2/31 (6)	1/35 (3)
10. Neumann 2002	MICU N=60	C.Random: not sure ITT: yes Blinding: no (6)	NR	NR	NR	NR
11. Montejo 2002	14 ICU APACHE ~18 Feed >5days N=101 from 11 ICUs	C.Random: not sure ITT: yes Blinding: no (6)	19/50 (38)	22/51 (43)	16/50 (32)	20/51 (39)
12. Hsu 2009	Medical ICU Anticipated feed >3days N=121	C.Random: Yes ITT: Yes Blinding: No (9)	26/59 (44)	24/62 (39)	5/59 (9)	15/62 (24)
13. White 2009	Medical ICU mechanically ventilated >24hrs N=108	C.Random: Yes ITT: Yes Blinding: No (7)	11/50 (22)	5/54 (9)	5/50 (10)	11/54 (20)
14. Acosta-Escribano 2010	Traumatic brain injury, mechanically ventilated patients in ICU required EN for >5 days N=104	C.Random: No ITT: Yes Blinding: No (9)	**30-day** 6/50 (12)	**30-day** 9/54 (17)	16/50 (32)	31/54 (57)

15. Davies 2012	Critically ill , mechanically ventilated, on narcotic infusion with elevated GRV from 17 ICUs N=181	C.Random: Yes ITT: Yes Blinding: No (11)	13/91 (14)	12/89 (13)	18/91 (20)	19/89 (21)
16. Friedman 2015	Critically ill adults withour contraindication for enteral nutrition, expected ICU LOS >48 hrs N=115	C.Random: Yes ITT: Yes Blinding: No (9)	**ICU** 20/54 (37)	**ICU** 22/61 (36)	13/54 (24)	12/61 (20)
17. Wan 2015	Mixed ICU patients. Single Centre. N=70	C.Random: Yes ITT: Yes Blinding: No (8)	NR	NR	**Aspiration pneumonia** 0/35	**Aspiration pneumonia** 10/35
18. Taylor 2016	Mechanically ventilated patients with delayed gastric emptying (vomiting or 1 episode GRV>250ml) after first line prokinetic treatment over 24h N=50	C.Random: Yes ITT: Yes Blinding: No (9)	**28-day** 4/25 (16)	**28-day** 4/25 (16)	**VAP** 2/25	**VAP** 4/25
19. Zhu 2018	Elderly (Age≥75) expected to be mechanically ventilated for >48h and required EN for ≥2 days N=141	C.Random: Yes ITT: Yes Blinding: Outcome assessors (12)	**ICU** 32/70 (45.7) **Hospital** 37/70 (52.9)	**ICU** 40/71 (56.3) **Hospital** 43/71 (60.6)	**VAP** 8/70 (11.4)	**VAP** 18/71 (25.4)
20. Liu 2019	Patients with severe craniocerebral injury N=100	C.Random: Not sure ITT: Yes Blinding: Yes (not clear who was blinded) (9)	**NR**	**NR**	**Lung infection** 4/50 (8)	**Lung infection** 11/50 (22)

Table 1. Randomized studies evaluating small bowel feeding vs. gastric in critically ill patients (continued)

Study	LOS days		Ventilator days		Nutritional Outcomes		Other	
	Small bowel	Gastric	Small bowel	Gastric	Small bowel	Gastric	Small bowel	Gastric
1. Montecalvo 1992	**ICU** 11.7 ± 8.2 (19)	**ICU** 12.3 ± 10.8 (19)	10.2 ± 7.1 (19)	11.4 ± 10.8 (19)	**Daily caloric intake (%)** 61 ± 17	46.9 ± 25.9	**GI bleeding** 7/19 (37) **Diarrhea** 12/19 (63) **Vomiting** 3/19 (16)	**GI bleeding** 6/19 (32) **Diarrhea** 9/19 (47) **Vomiting** 3/19 (16)
2. Kortbeek 1999	**ICU** 10 (3-24) **Hospital** 30 (16-47)	**ICU** 7 (3-32) **Hospital** 25 (9-88)	9 (2-13)	5 (3-15)	**Time to tolerate full feeds** 34 ± 7.1	43.8 ± 22.6	NR	NR
3. Taylor 1999	NR	NR	NR	NR	**% energy needs met (mean)** 59.2 **% nitrogen needs met (mean)** 68.7	36.8 37.9	37 % major complications 61 % had better neurological outcome at 3 months	61 % major complications 39 % had better neurological outcome at 3months
4. Kearns 2000	**ICU** 17 ± 2 (21) **Hospital** 39 ± 10 (21)	**ICU** 16 ± 2 (23) **Hospital** 43 ± 11 (23)	NR	NR	**Calories (kcal/kg/day)** 18 ± 1 **Protein (gm/kg/day)** 0.7 ± 0.1 **% REE delivered** 69 ± 7	12 ± 2 0.4 ± 0.1 47 ± 7	**Diarrhea** 3 days	**Diarrhea** 2 days

5. Minard 2000	**ICU** 18.5 ± 8.8 (12) **Hospital** 30 ± 14.7 (12)	**ICU** 11.3 ± 6.1 (12) **Hospital** 21.3 ± 14.7 (12)	15.1 ± 7.5 (12)	10.4 ± 6.1 (15)	**Time feeding initiated (hours)** 33 ± 15 84 ± 41 **Avg kcals/ day** 1509 ± 45 1174 ± 425 **Days fed** 13 ± 3.7 8 ± 4.5 **# patients with > 50 % goal for ≥ 5 days** 10/12 (83) 7/15 (47)	**Diarrhea** 11/12 (92) **Vomiting** 1/12 (8)	**Diarrhea** 8/15 (53) **Vomiting** 3/15 (20)
6. Esparaza 2001	NR	NR	NR	NR	**Feed days (average)** 3.6 4.1 **Average daily % of goal** 66 64	NR	NR
7. Boivin 2001	NR	NR	NR	NR	**Time of placement** 304 minutes 13 minutes **Time to goal rate achieved and maintained for 4 hours** 33 hours 32 hours	NR	NR
8. Day 2001	NR	NR	NR	NR	**Calories and protein received** were significantly higher only on days 2 and 3 in the gastric group. No difference between the groups on Days 1, 4-10. **Replaced tubes** 16/14 9/11	**Diarrhea** 7/14 (50)	**Diarrhea** 5/11 (45)
9. Davies 2002	**ICU** 13.9 ± 1.8 (34)	**ICU** 10.4 ± 1.2 (39)	NR	NR	**Time to reach target rate** 23.2 ± 3.9 23.0 ± 3.4 **Time to start feeds** 81.2 ± 13.4 54.5 ± 4.9	**GI bleeding** 3/31 (10) **Diarrhea** 4/31 (13)	**GI bleeding** 0/35 (0) **Diarrhea** 3/35 (9)
10. Neumann 2002	NR	NR	NR	NR	**Time from initial attempt to start of feeding** 27.0 ± 22.6 11.2 ± 11.0 **Time to reach goal rate (from initial placement attempt)** 43 ± 24.1 28.8 ± 15.9 **Time to reach goal rate (from successful tube placement)** 17.3 ± 15.7 17.0 ± 11.9	**Aspiration** 1/30 (3)	**Aspiration** 0/30 (0)

11. Montejo 2002	**ICU** 15 ± 10 (50)	**ICU** 18 ± 16 (50)	NR	NR	**High gastric residuals** 1/50 (2) 25/51 (49) **Caloric intake (mean)** 1286 ± 344 1237 ± 342 **Volume ratio at day 7 (%)** 80 ± 28 75 ± 30	**Diarrhea** 7/50 (14) **Vomiting** 4/50 (8)	**Diarrhea** 7/51 (14) **Vomiting** 2/51 (4)
12. Hsu 2009	**ICU** 18.20 ± 11.80 **Hospital** 36.0 ± 24.2	**ICU** 18.20 ± 11.20 **Hospital** 31.7 ± 21.1	28.5 ± 24.9 (59)	23.8 ± 18.2 (62)	**Mean % of daily goal calorie fed** 95 ± 5 83 ± 6 **Caloric intake (kcal/day)** 1658 ± 118 1426 ±110 **Protein (grams/day)** 67.9 (4.9) 58.8 (4.9)	**Vomiting** 1/59 (2) **GI bleeding** 7/59 (12) **Time to reach goal** 32.4 (27.1) hrs	**Vomiting** 8/62 (13) **GI bleeding** 9/62 (15) **Time to reach goal** 54.5 (51.4) hrs
13. White 2009	**ICU** 5.3 (2.73-9.89) 7.12 ± 6.00 (51)*	**ICU** 5.02 (1.98-9.99) 9.10 ± 10.55 (55)*	3.93 (2.3-8.38) 5.73 ± 5.29 (51)*	3.92 (1.5-8.54) 7.68 ± 9.81 (55)*	**Caloric intake (median, IQR)** 1463 (1232-1804) 1588 (913-1832) **Protein intake (median, IQR)** 63 (50-78) 69 (45-87)	**Time to reach goal** 4.1 (3.4-5.0) hrs	**Time to reach goal** 4.3 (4.0-5.0)
14. Acosta-Escribano 2010	**ICU** 16 ± 9 (50) **Hospital** 38 ± 24 (50)	**ICU** 18 ± 7 (54) **Hospital** 41 ± 28 (54)	7.3 ± 4 (50)	8.9 ± 4 (54)	**Nutritional efficiency (%)** 92 ± 7 84 ± 15	**High GRVs** 3/50 (6) **GIT complications** 7/50 (14)	**High GRVs** 15/54 (28) **GIT complications** 27/54 (47)
15. Davies 2012	**ICU** 10 (7-15) 12.5 ± 8.6 (91)* **Hospital** 20 (11-33) 28.8 ± 26.1 (91)*	**ICU** 11 (7-16) 12.7 ± 9.8 (89)* **Hospital** 24 (15-32) 27.4 ± 21.1 (89)*	8 (6-12) 9.8 ± 6.2 (91)*	8 (5-14) 9.7 ± 6.3 (89)*	**Nutritional efficiency (%)** 72 71 p=0.66 **Caloric intake (mean)** 1497 ± 521 1444 ± 485	**Major haemorrhage** 2/91 (2) **Minor haemorrhage** 12/91 (13) Vomiting 30/91 (33) **Aspiration** 5/91 (5) **Diarrhea** 26/91 (29) **Abdom distention** 16/91 (18)	**Major haemorrhage** 2/89 (2) **Minor haemorrhage** 3/89 (3) **Vomiting** 30/89 (30) **Aspiration** 4/89 (5) **Diarrhea** 26/89 (30) **Abdom distention** 18/89 (20)

16. Friedman 2015	**ICU** 10 (7-21) (54)	**ICU** 12 (8-20) (61)	4 (2-11) (54)	7 (3-13) (61)	**NR**	**Cost, US$** 1163 **Diarrhea** 15/54 (28) **Vomiting** 14/54 (26) **Constipation** 9/54 (17)	**Cost, US$** 467 **Diarrhea** 11/61 (18), p=0.306 **Vomiting** 18/61, p=0.826 **Constipation** 14/61 (23), p=0.544
17. Wan 2015	**ICU** 12.2 ± 0.7 (35)	**ICU** 17.1 ± 1.0 (35)	5.2 ± 0.3 (35)	8.5 ± 0.5 (35)	**NR**	**Cost** 5203 ± 247 **Diarrhea** 9/35 **Reflux** 1/35	**Cost** 7786 ± 555, P <0.01 **Diarrhea** 9/35 **Reflux** 14/35, P <0.01
18. Taylor 2016	**ICU-free days** 10 (0-16) **ICU** 14.24±8.97(25)*	**ICU-free days** 11 (0-19) **ICU** 14.00±8.41(25)*	**Ventilator-free days** 21 (16-25) **Ventilator days** 8.28±5.01 (25)*	**Ventilator-free days** 20 (13-25) **Ventilator days** 10±6.95 (25)*	**Area under the curve of feed goal** 432 (253-464)%. 350 (213-381)% p=0.026	**Diarrhea** 0/25 **Vomiting** 3/25	**Diarrhea** 2/25 **Vomiting** 5/25
19. Zhu 2018	**ICU** 402.14±272.59h (70)* (16.76±11.36 d) **Hospital** 21.06 ±12.81 (70)*	**ICU** 461.96 ±394.56h (71)* (19.25±16.44 d) **Hospital** 21.97±20.18 (71)*	290.20±211.40h (70)* (12.09±8.81d)	362.42±374.35h (71)* (15.10±15.60d)	**Achieve energy goal by EN in the first 7 days** 40/70 (57.1) 32/71 (45.1) p=0.15	**Vomiting** 12/70 (17.1) **Diarrhea** 6/70 (8.57) **Abdominal distension** 18/70 (25.7) **Abdominal pain** 4/70 (5.71)	**Vomiting** 29/71 (41.4) **Diarrhea** 4/71 (5.63) **Abdominal distension** 33/71 (46.5) **Abdominal pain** 3/71 (4.22)
20. Liu 2019	**ICU** 12.96±4.11 (50)	**ICU** 15.83±4.72 (50)	**NR**	**NR**	**NR**	**Aspiration** 1/50 (2) **Regurgitation** 3/50 (6) **GI bleed** 5/50 (10) **Diarrhea** 8/50 (16) **Vomiting/ GRV>150 ml** 0	**Aspiration** 7/50 (40) **Regurgitation** 10/50 (20) **GI bleed** 6/50 (12) **Diarrhea** 11/50 (22) **Vomiting/ GRV>150 ml** 6/50 (22)

C.Random: concealed randomization
ITT: intent to treat
† presumed ICU mortality unless otherwise specified
‡ refers to the # of patients with infections unless specified
* Data obtained from author

± ( ) : mean ± Standard deviation (number)
(-) : median (range)
NR: not reported

Figure 1. Mortality

Study or Subgroup	Small Bowel Events	Small Bowel Total	Gastric Events	Gastric Total	Weight	Risk Ratio M-H, Random, 95% CI
Montecalvo 1992	5	19	5	19	2.1%	1.00 [0.35, 2.90]
Kortbeek 1999	4	37	3	43	1.2%	1.55 [0.37, 6.48]
Taylor 1999	5	41	6	41	2.0%	0.83 [0.28, 2.52]
Kearns 2000	5	21	6	23	2.3%	0.91 [0.33, 2.55]
Minard 2000	1	12	4	15	0.6%	0.31 [0.04, 2.44]
Esparaza 2001	10	27	11	27	5.4%	0.91 [0.47, 1.78]
Boivin 2001	18	39	18	39	10.5%	1.00 [0.62, 1.62]
Davies 2002	4	34	5	39	1.6%	0.92 [0.27, 3.14]
Montejo 2002	19	50	22	51	10.8%	0.88 [0.55, 1.42]
Hsu 2009	26	59	24	62	13.4%	1.14 [0.74, 1.74]
White 2009	11	51	5	57	2.5%	2.46 [0.92, 6.60]
Acosta-Escribano 2010	6	50	9	54	2.6%	0.72 [0.28, 1.88]
Davies 2012	13	91	12	89	4.6%	1.06 [0.51, 2.19]
Friedman 2015	20	54	22	61	10.4%	1.03 [0.63, 1.66]
Taylor 2016	4	25	4	25	1.5%	1.00 [0.28, 3.56]
Zhu 2018	37	70	43	71	28.7%	0.87 [0.65, 1.17]
Total (95% CI)		680		716	100.0%	0.97 [0.83, 1.13]
Total events	188		199			

Heterogeneity: Tau² = 0.00; Chi² = 6.87, df = 15 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.38 (P = 0.71)

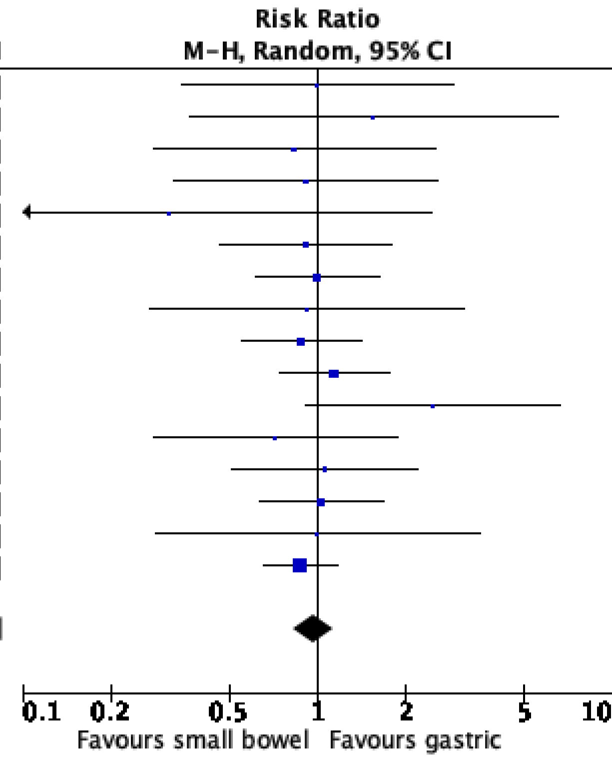


Figure 2. Mortality (excluding Taylor 1999 and Minard 2000)

	Small Bowel		Gastric			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Montecalvo 1992	5	19	5	19	2.2%	1.00 [0.35, 2.90]	1992
Kortbeek 1999	4	37	3	43	1.2%	1.55 [0.37, 6.48]	1999
Kearns 2000	5	21	6	23	2.3%	0.91 [0.33, 2.55]	2000
Esparaza 2001	10	27	11	27	5.5%	0.91 [0.47, 1.78]	2001
Boivin 2001	18	39	18	39	10.8%	1.00 [0.62, 1.62]	2001
Montejo 2002	19	50	22	51	11.0%	0.88 [0.55, 1.42]	2002
Davies 2002	4	34	5	39	1.6%	0.92 [0.27, 3.14]	2002
Hsu 2009	26	59	24	62	13.7%	1.14 [0.74, 1.74]	2009
Acosta-Escribano 2010	6	50	9	54	2.7%	0.72 [0.28, 1.88]	2010
White 2009	11	51	5	57	2.5%	2.46 [0.92, 6.60]	2010
Davies 2012	13	91	12	89	4.7%	1.06 [0.51, 2.19]	2012
Friedman 2015	20	54	22	61	10.7%	1.03 [0.63, 1.66]	2015
Taylor 2016	4	25	4	25	1.5%	1.00 [0.28, 3.56]	2016
Zhu 2018	37	70	43	71	29.5%	0.87 [0.65, 1.17]	2018
Total (95% CI)		627		660	100.0%	0.98 [0.84, 1.15]	
Total events	182		189				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.66$, df = 13 (P = 0.96); $I^2 = 0\%$
Test for overall effect: Z = 0.25 (P = 0.80)

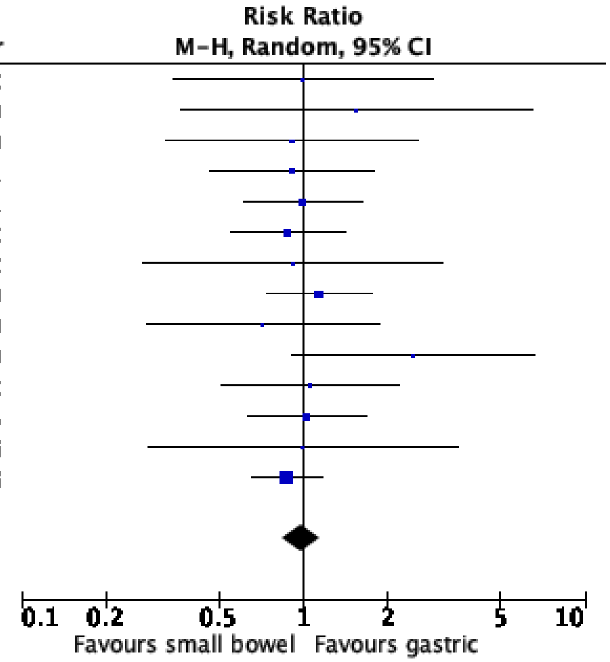


Figure 3. Pneumonia

Study or Subgroup	Small Bowel Events	Small Bowel Total	Gastric Events	Gastric Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Montecalvo 1992	4	19	6	19	3.8%	0.67 [0.22, 1.99]	1992
Kortbeek 1999	10	37	18	43	8.6%	0.65 [0.34, 1.22]	1999
Taylor 1999	18	41	26	41	13.8%	0.69 [0.46, 1.05]	1999
Kearns 2000	4	21	3	23	2.5%	1.46 [0.37, 5.78]	2000
Minard 2000	6	12	7	15	6.5%	1.07 [0.49, 2.34]	2000
Day 2001	0	14	2	11	0.6%	0.16 [0.01, 3.03]	2001
Davies 2002	2	31	1	35	0.9%	2.26 [0.22, 23.71]	2002
Montejo 2002	16	50	20	51	10.8%	0.82 [0.48, 1.39]	2002
Hsu 2009	5	59	15	62	4.8%	0.35 [0.14, 0.90]	2009
White 2009	11	57	5	51	4.5%	1.97 [0.73, 5.28]	2010
Acosta-Escribano 2010	16	50	31	54	12.4%	0.56 [0.35, 0.89]	2010
Davies 2012	18	91	19	89	9.8%	0.93 [0.52, 1.65]	2012
Friedman 2015	13	54	12	61	7.7%	1.22 [0.61, 2.45]	2015
Wan 2015	0	35	10	35	0.7%	0.05 [0.00, 0.78]	2015
Taylor 2016	2	25	4	25	1.9%	0.50 [0.10, 2.49]	2016
Zhu 2018	8	70	18	71	6.7%	0.45 [0.21, 0.97]	2018
Liu 2019	4	50	11	50	3.9%	0.36 [0.12, 1.07]	2019
Total (95% CI)		716		736	100.0%	0.72 [0.57, 0.91]	
Total events	137		208				

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 21.72$, df = 16 (P = 0.15); $I^2 = 26\%$
Test for overall effect: Z = 2.77 (P = 0.006)

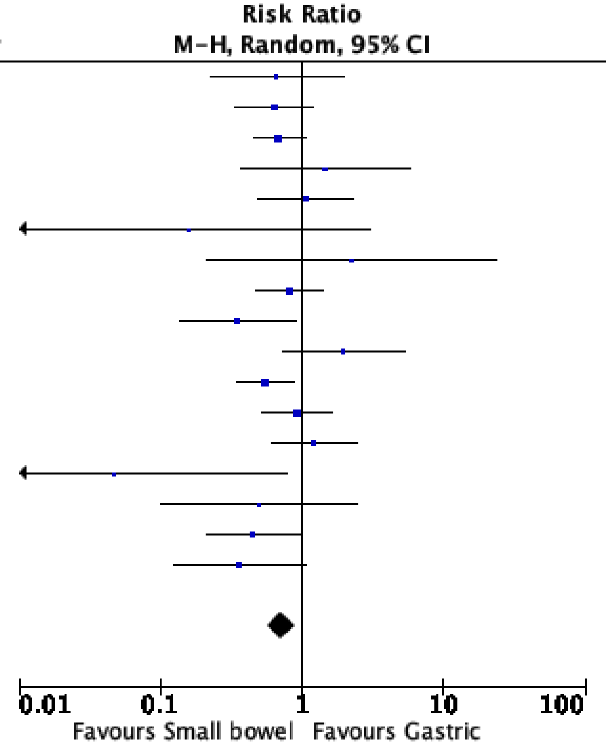


Figure 4. Pneumonia (excluding Taylor 1999 and Minard 2000)

	Small Bowel		Gastric			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Montecalvo 1992	4	19	6	19	5.1%	0.67 [0.22, 1.99]	1992
Kortbeek 1999	10	37	18	43	10.7%	0.65 [0.34, 1.22]	1999
Kearns 2000	4	21	3	23	3.5%	1.46 [0.37, 5.78]	2000
Day 2001	0	14	2	11	0.9%	0.16 [0.01, 3.03]	2001
Davies 2002	2	31	1	35	1.3%	2.26 [0.22, 23.71]	2002
Montejo 2002	16	50	20	51	12.8%	0.82 [0.48, 1.39]	2002
Hsu 2009	5	59	15	62	6.4%	0.35 [0.14, 0.90]	2009
White 2009	11	57	5	51	6.0%	1.97 [0.73, 5.28]	2010
Acosta-Escribano 2010	16	50	31	54	14.3%	0.56 [0.35, 0.89]	2010
Davies 2012	18	91	19	89	11.8%	0.93 [0.52, 1.65]	2012
Friedman 2015	13	54	12	61	9.6%	1.22 [0.61, 2.45]	2015
Wan 2015	0	35	10	35	1.0%	0.05 [0.00, 0.78]	2015
Taylor 2016	2	25	4	25	2.7%	0.50 [0.10, 2.49]	2016
Zhu 2018	8	70	18	71	8.6%	0.45 [0.21, 0.97]	2018
Liu 2019	4	50	11	50	5.3%	0.36 [0.12, 1.07]	2019
Total (95% CI)		663		680	100.0%	0.70 [0.53, 0.93]	
Total events	113		175				

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 20.62$, df = 14 ($P = 0.11$); $I^2 = 32\%$
Test for overall effect: $Z = 2.48$ ($P = 0.01$)

Risk Ratio
M-H, Random, 95% CI

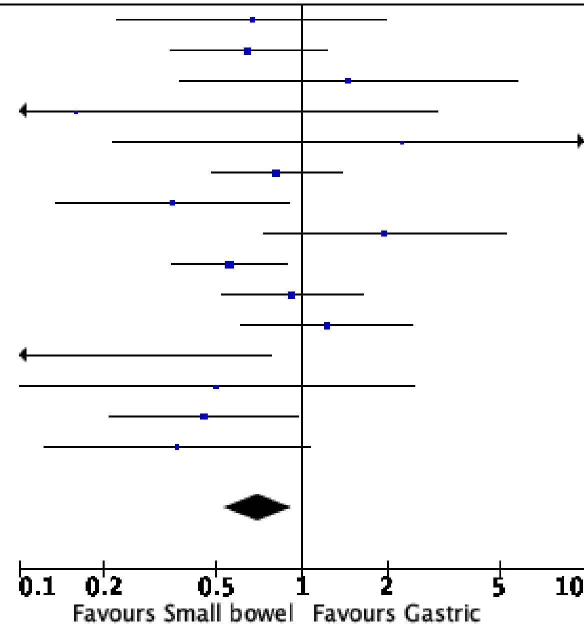


Figure 5. ICU LOS

	Small Bowel			Gastric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Montecalvo 1992	11.7	8.2	19	12.3	10.8	19	6.2%	−0.60 [−6.70, 5.50]	1992
Kearns 2000	17	2	21	16	2	23	8.8%	1.00 [−0.18, 2.18]	2000
Minard 2000	18.5	8.8	12	11.3	6.1	15	6.3%	7.20 [1.34, 13.06]	2000
Davies 2002	13.9	1.8	34	10.4	1.2	39	8.9%	3.50 [2.79, 4.21]	2002
Montejo 2002	15	10	50	18	16	51	6.7%	−3.00 [−8.19, 2.19]	2002
Hsu 2009	18.2	11.8	59	18.2	11.2	62	7.4%	0.00 [−4.10, 4.10]	2009
White 2009	7.12	6	51	9.1	10.55	55	7.9%	−1.98 [−5.22, 1.26]	2010
Acosta−Escribano 2010	16	9	50	18	7	54	8.0%	−2.00 [−5.12, 1.12]	2010
Davies 2012	12.5	8.6	91	12.7	9.8	89	8.2%	−0.20 [−2.90, 2.50]	2012
Wan 2015	12.2	0.7	35	17.1	1	35	8.9%	−4.90 [−5.30, −4.50]	2015
Taylor 2016	14.24	8.97	25	14	8.41	25	7.0%	0.24 [−4.58, 5.06]	2016
Zhu 2018	16.76	11.36	70	19.25	16.44	71	7.1%	−2.49 [−7.15, 2.17]	2018
Liu 2019	12.96	4.11	50	15.83	4.72	50	8.6%	−2.87 [−4.60, −1.14]	2019
Total (95% CI)			567			588	100.0%	−0.56 [−3.28, 2.16]	

Heterogeneity: $Tau^2 = 21.54$; $Chi^2 = 457.87$, df = 12 ($P < 0.00001$); $I^2 = 97\%$
Test for overall effect: Z = 0.41 (P = 0.68)

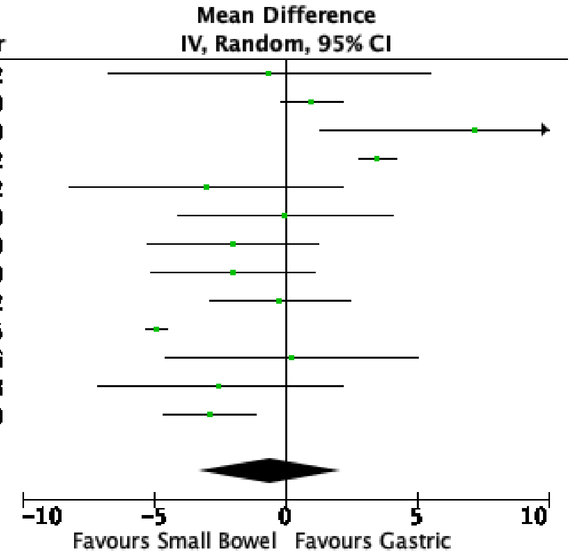


Figure 6. ICU LOS (excluding Minard)

	Small Bowel			Gastric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Montecalvo 1992	11.7	8.2	19	12.3	10.8	19	6.6%	-0.60 [-6.70, 5.50]	1992
Kearns 2000	17	2	21	16	2	23	9.4%	1.00 [-0.18, 2.18]	2000
Davies 2002	13.9	1.8	34	10.4	1.2	39	9.5%	3.50 [2.79, 4.21]	2002
Montejo 2002	15	10	50	18	16	51	7.2%	-3.00 [-8.19, 2.19]	2002
Hsu 2009	18.2	11.8	59	18.2	11.2	62	7.9%	0.00 [-4.10, 4.10]	2009
White 2009	7.12	6	51	9.1	10.55	55	8.5%	-1.98 [-5.22, 1.26]	2010
Acosta-Escribano 2010	16	9	50	18	7	54	8.5%	-2.00 [-5.12, 1.12]	2010
Davies 2012	12.5	8.6	91	12.7	9.8	89	8.8%	-0.20 [-2.90, 2.50]	2012
Wan 2015	12.2	0.7	35	17.1	1	35	9.5%	-4.90 [-5.30, -4.50]	2015
Taylor 2016	14.24	8.97	25	14	8.41	25	7.4%	0.24 [-4.58, 5.06]	2016
Zhu 2018	16.76	11.36	70	19.25	16.44	71	7.5%	-2.49 [-7.15, 2.17]	2018
Liu 2019	12.96	4.11	50	15.83	4.72	50	9.2%	-2.87 [-4.60, -1.14]	2019
Total (95% CI)			555			573	100.0%	-1.09 [-3.88, 1.71]	

Heterogeneity: $Tau^2 = 21.25$; $Chi^2 = 447.42$, df = 11 ($P < 0.00001$); $I^2 = 98\%$
Test for overall effect: Z = 0.76 (P = 0.45)

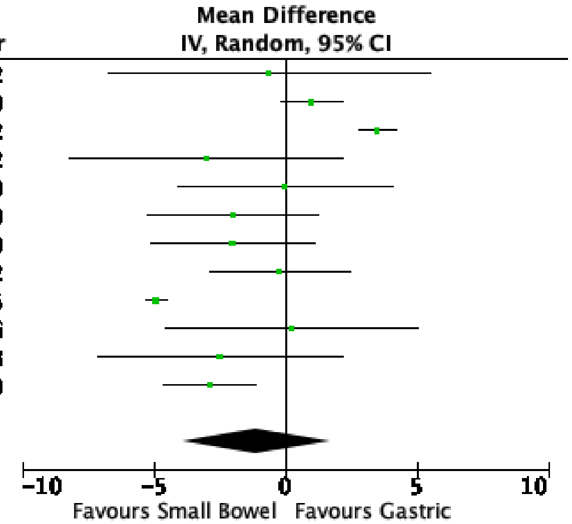


Figure 7. Hospital LOS

Study or Subgroup	Small Bowel Mean	Small Bowel SD	Small Bowel Total	Gastric Mean	Gastric SD	Gastric Total	Weight	Mean Difference IV, Random, 95% CI	Year
Minard 2000	30	14.7	12	21.3	14.7	12	6.9%	8.70 [-3.06, 20.46]	2000
Kearns 2000	39	10	21	43	11	23	23.0%	-4.00 [-10.21, 2.21]	2000
Hsu 2009	36	24.2	59	31.7	21.1	62	14.0%	4.30 [-3.81, 12.41]	2009
Acosta-Escribano 2010	38	24	50	41	28	54	9.4%	-3.00 [-13.00, 7.00]	2010
Davies 2012	28.8	26.1	91	27.4	21.1	89	18.8%	1.40 [-5.53, 8.33]	2012
Zhu 2018	21.06	12.81	70	21.97	20.18	71	27.8%	-0.91 [-6.48, 4.66]	2018
Total (95% CI)			303			311	100.0%	0.01 [-3.12, 3.15]	

Heterogeneity: $Tau^2 = 1.12$; $Chi^2 = 5.38$, df = 5 ($P = 0.37$); $I^2 = 7\%$
Test for overall effect: $Z = 0.01$ ($P = 0.99$)

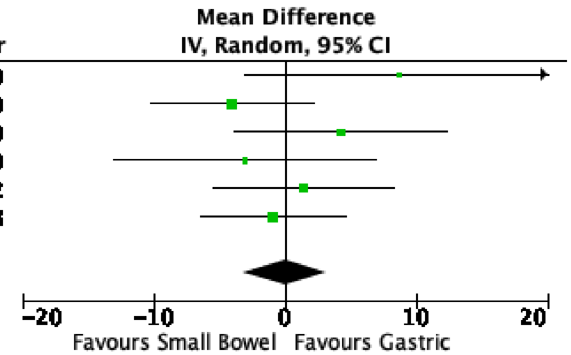


Figure 8. Duration of ventilation

Study or Subgroup	Small Bowel Mean	Small Bowel SD	Small Bowel Total	Gastric Mean	Gastric SD	Gastric Total	Weight	Mean Difference IV, Random, 95% CI
Montecalvo 1992	10.2	7.1	19	11.4	10.8	19	5.4%	-1.20 [-7.01, 4.61]
Minard 2000	15.1	7.5	12	10.4	6.1	15	6.2%	4.70 [-0.55, 9.95]
Hsu 2009	28.5	24.9	59	23.8	18.2	62	3.4%	4.70 [-3.10, 12.50]
White 2009	5.73	5.29	51	7.68	9.81	55	11.9%	-1.95 [-4.92, 1.02]
Acosta-Escribano 2010	7.3	4	50	8.9	4	54	17.3%	-1.60 [-3.14, -0.06]
Davies 2012	9.8	6.2	91	9.7	6.3	89	16.2%	0.10 [-1.73, 1.93]
Wan 2015	5.2	0.3	35	8.5	0.5	35	20.8%	-3.30 [-3.49, -3.11]
Taylor 2016	8.28	5.01	25	10	6.95	25	10.6%	-1.72 [-5.08, 1.64]
Zhu 2018	12.09	8.81	70	15.1	15.6	71	8.4%	-3.01 [-7.18, 1.16]
Total (95% CI)			412			425	100.0%	-1.23 [-2.79, 0.33]

Heterogeneity: $Tau^2 = 3.04$; $Chi^2 = 32.25$, df = 8 ($P < 0.0001$); $I^2 = 75\%$
Test for overall effect: $Z = 1.54$ ($P = 0.12$)

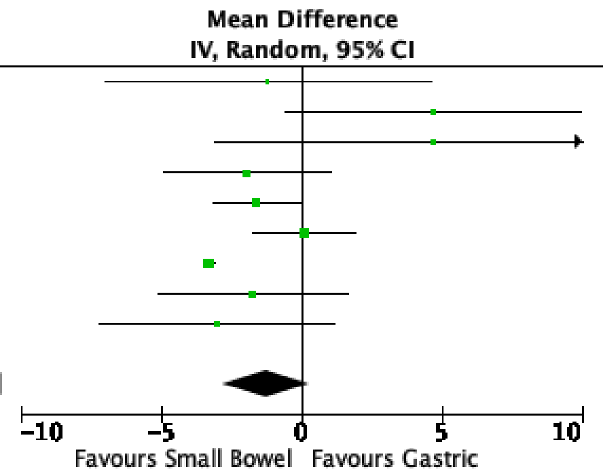


Figure 9. Nutritional efficiency (%)

Study or Subgroup	Small Bowel Mean	Small Bowel SD	Small Bowel Total	Gastric Mean	Gastric SD	Gastric Total	Weight	Mean Difference IV, Random, 95% CI	Year
Montecalvo 1992	61	17	19	46.9	25.9	19	9.7%	14.10 [0.17, 28.03]	1992
Kearns 2000	69	7	21	47	7	23	19.7%	22.00 [17.86, 26.14]	2000
Montejo 2002	80	28	50	75	30	51	12.0%	5.00 [-6.31, 16.31]	2002
Hsu 2009	95	5	59	83	6	62	21.3%	12.00 [10.04, 13.96]	2009
Acosta-Escribano 2010	92	7	50	84	15	54	19.4%	8.00 [3.55, 12.45]	2010
Davies 2012	72	21	91	71	19	89	17.9%	1.00 [-4.85, 6.85]	2012
Total (95% CI)			290			298	100.0%	10.59 [4.76, 16.41]	

Heterogeneity: $Tau^2 = 40.41$; $Chi^2 = 40.66$, df = 5 ($P < 0.00001$); $I^2 = 88\%$
Test for overall effect: Z = 3.56 (P = 0.0004)

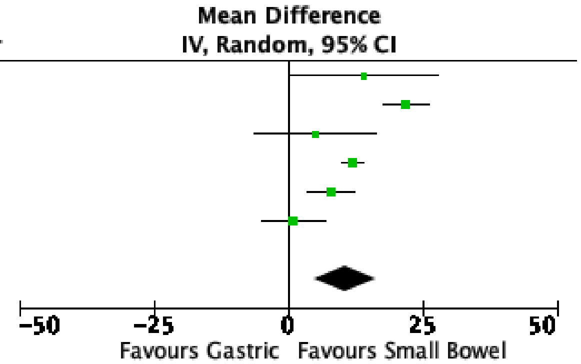
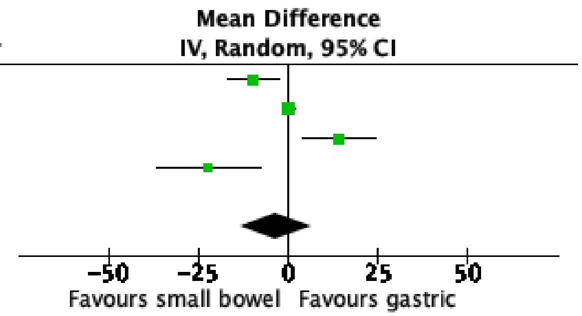


Figure 10. Time to reach EN target

Study or Subgroup	Small Bowel Mean	Small Bowel SD	Small Bowel Total	Gastric Mean	Gastric SD	Gastric Total	Weight	Mean Difference IV, Random, 95% CI	Year
Kortbeek 1999	34	7.1	37	43.8	22.6	43	26.9%	-9.80 [-16.93, -2.67]	1999
Davies 2002	23.2	3.9	31	23	3.4	35	30.8%	0.20 [-1.58, 1.98]	2002
Neumann 2002	43	24.1	30	28.8	15.9	30	23.4%	14.20 [3.87, 24.53]	2002
Hsu 2009	32.4	27.1	59	54.5	51.4	62	18.8%	-22.10 [-36.64, -7.56]	2009
Total (95% CI)			157			170	100.0%	-3.41 [-13.45, 6.62]	

Heterogeneity: $Tau^2 = 84.16$; $Chi^2 = 23.32$, df = 3 ($P < 0.0001$); $I^2 = 87\%$
Test for overall effect: Z = 0.67 (P = 0.51)



Included Studies

1. Montecalvo MA, Steger KA, Farber HW et al. Nutritional outcome and pneumonia in critical care patients randomized to gastric versus jejunal tube feedings. The Critical Care Research Team. Crit Care Med. 20:1377-87, 1992.
2. Kortbeek JB, Haigh PI, Doig C. Duodenal versus gastric feeding in ventilated blunt trauma patients: a randomized controlled trial. J Trauma 1999;46:992-6.
3. Taylor SJ, Fettes SB, Jewkes C, Nelson RJ. Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. Crit Care Med 1999;27:2525-31.
4. Kearns LJ, Chin D, Mueller L, Wallace K, Jensen WA, Kirsch CM. The incidence of ventilator-associated pneumonia and success in nutrient delivery with gastric versus small intestinal feeding: A randomized clinical trial. Crit Care Med 2000;28:1742-6.
5. Minard G, Kudsk KA, Melton S, Patton JH, Tolley EA. Early versus delayed feeding with an immune-enhancing diet in patients with severe head injuries. JPEN J Parenter Enteral Nutr 2000;24:145-9.
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11. Montejo JC, Grau T, Acosta J et al. Multicenter, prospective, randomized, single-blind study comparing the efficacy and gastrointestinal complications of early jejunal feeding with early gastric feeding in critically ill patients. Crit Care Med 2002;30:796-800.
12. Hsu CW, Sun SF, Lin SL, Kang SP, Chu KA, Lin CH, Huang HH. Duodenal versus gastric feeding in medical intensive care unit patients: a prospective, randomized, clinical study. Crit Care Med. 2009 Jun;37(6):1866-72.
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14. Acosta-Escribano J, Fernández-Vivas M, Grau Carmona T, et al. Gastric versus transpyloric feeding in severe traumatic brain injury: a prospective, randomized trial. Intensive Care Med. 2010;36(9):1532-1539. doi:10.1007/s00134-010-1908-3
15. Davies AR, Morrison SS, Bailey MJ, Bellomo R, Cooper DJ, Doig GS, Finfer SR, Heyland DK; ENTERIC Study Investigators; ANZICS Clinical Trials Group. A multicenter, randomized controlled trial comparing early nasojejunal with nasogastric nutrition in critical illness. Crit Care Med. 2012 Aug;40(8):2342-8.
16. Friedman G, Flávia Couto CL, Becker M. Randomized study to compare nasojejunal with nasogastric nutrition in critically ill patients without prior evidence of altered gastric emptying. Indian J Crit Care Med. 2015 Feb;19(2):71-5.
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Excluded Articles

#	Reason excluded	Citation
1	Pseudo-randomized	Grahm TW, Zadrozny DB, Harrington T. The benefits of early jejunal hyperalimentation in the head-injured patient. Neurosurgery 1989 Nov;25(5):729-35.
2	Not ICU patients	Strong RM, Condon SC, Solinger MR, Namihas BN, Ito-Wong LA, Leuty JE. Equal aspiration rates from postpylorus and intragastric-placed small-bore nasoenteric feeding tubes: a randomized, prospective study. JPEN J Parenter Enteral Nutr. 1992 Jan-Feb;16(1):59-63.
3	No clinical outcomes	Heyland DK, Drover JW, MacDonald S, Novak F, Lam M. Effect of postpyloric feeding on gastroesophageal regurgitation and pulmonary microaspiration: results of a randomized controlled trial. Crit Care Med 2001;29(8):1495-501.
4	Systematic review	Heyland DK, Drover JW, Dhaliwal R, Greenwood J. Optimizing the benefits and minimizing the risks of enteral nutrition in the critically ill: role of small bowel feeding. JPEN J Parenter Enteral Nutr. 2002 Nov-Dec;26(6 Suppl):S51-5; discussion S56-7.
5	Systematic review	Marik PE, Zaloga GP. Gastric versus post-pyloric feeding: a systematic review. Crit Care. 2003 Jun;7(3):R46-51. Epub 2003 May 6.
6	<50% ICU patients	Eatock FC, Chong P, Menezes N, Murray L, McKay CJ, Carter CR, Imrie CW. A randomized study of early nasogastric versus nasojejunal feeding in severe acute pancreatitis. Am J Gastroenterol. 2005 Feb;100(2):432-9.
7	Meta-analysis	Ho KM, Dobb GJ, Webb SA. A comparison of early gastric and post-pyloric feeding in critically ill patients: a meta-analysis. Intensive Care Med. 2006 May;32(5):639-49.
8	Not ICU patients	Kumar A, Singh N, Prakash S, Saraya A, Joshi YK. Early enteral nutrition in severe acute pancreatitis: a prospective randomized controlled trial comparing nasojejunal and nasogastric routes. J Clin Gastroenterol. 2006 May-Jun;40(5):431-4.
9	No clinical outcomes	Zeng R, Jiang F. Comparison of nose jejunal tube and nasogastric tube in providing early enteral nutrition for patients with severe craniocerebral injury. Chinese Journal of Clinical Nutrition. 2010;18(6):355-357.
10	Meta-analyses	Jiyong J, Tiancha H, Huiqin W, Jingfen J. Effect of Gastric Versus Post-pyloric Feeding on the Incidence of Pneumonia in Critically ill Patients: Observations From Traditional and Bayesian Random-Effects meta-analysis. Intensive Care Med. 2013;32(1):8-15
11	Not ICU patients	Singh N, Sharma B, Sharma M, Sachdev V, Bhardwaj P, Mani K, Joshi YK, Saraya A. Evaluation of early enteral feeding through nasogastric and nasojejunal tube in severe acute pancreatitis: a noninferiority randomized controlled trial. Pancreas. 2012 Jan;41(1):153-9.
12	Identical study as Hsu 2009	Huang HH, Chang SJ, Hsu CW, Chang TM, Kang SP, Liu MY. Severity of illness influences the efficacy of enteral feeding route on clinical outcomes in patients with critical illness. Journal of the Academy of Nutrition and Dietetics. 2012.
13	Systematic Review	Deane AM, Dhaliwal R, Day AG, Ridley EJ, Davies AR, Heyland DK. Comparisons between intragastric and small intestinal delivery of enteral nutrition in the critically ill: a systematic review and meta-analysis.Crit Care. 2013 Jun 21;17(3):R125.
14	Meta-analyses	Wang X, Dong Y, Han X, Qi X-Q, Huang C-G, Hou L. (2013) Nutritional Support for Patients Sustaining Traumatic Brain Injury: A Systematic Review and Meta-Analysis of Prospective Studies. PLoS ONE. 8(3): e58838.
15	Meta analyses	Alkhawaja S, Martin C, Butler RJ, Gwadry-Sridhar F. Post-pyloric versus gastric tube feeding for preventing pneumonia and improving nutritional outcomes in critically ill adults. Cochrane Database Syst Rev. 2015 Aug 4;(8):CD008875.
16	Pseudo-randomized	Ge W, Wei W, Shuang P, Yan-Xia Z, Ling L. Nasointestinal Tube in Mechanical Ventilation Patients is More Advantageous. Open Med (Wars). 2019;14:426-430. Published 2019 May 26. doi:10.1515/med-2019-0045