5.3 Strategies to Optimize Delivery and Minimize Risks of EN: Small Bowel Feeding vs. Gastric May 2015

2015 Recommendation: ***Based on 16 level 2 studies, small bowel feeding compared to gastric feeding may be associated with a reduction in pneumonia in critically ill patients. In units where small bowel access is feasible, we recommend the routine use of small bowel feedings. In units where obtaining access involves more logistical difficulties, small bowel feedings should be considered for patients at high risk for intolerance to EN (on inotropes, continuous infusion of sedatives, or paralytic agents, or patients with high nasogastric drainage) or at high risk for regurgitation and aspiration (nursed in supine position). Finally, where obtaining small bowel access is not feasible (no access to fluoroscopy or endoscopy and blind techniques not reliable), small bowel feedings should be considered for those select patients that repeatedly demonstrate high gastric residuals and are not tolerating adequate amounts of EN intragastrically.***

2015 Discussion: The committee noted that with the inclusion of the data from one new study (Freidman 2015), small bowel feeding was still associated with a significant reduction in pneumonia but had no effect on mortality. There was a similar direction of findings amongst trials as evidenced by the test for heterogeneity. The committee agreed that although the feasibility of placing small bowel feeding tubes has improved considerably over the years, the safety concerns about their placement still exists and there are cost implications that ought to be considered. The committee noted that the new study did not report on nutritional outcomes but there was a strong signal from the existing studies showing small bowel feeding having a favourable effect on optimizing the delivery of calories and protein. The committee agreed to continue making recommendations based on the accessibility of small bowel feeding, consistent with the previous recommendations.

2013 Recommendation: ***Based on 15 level 2 studies, small bowel feeding compared to gastric feeding may be associated with a reduction in pneumonia in critically ill patients. In units where small bowel access is feasible, we recommend the routine use of small bowel feedings. In units where obtaining access involves more logistical difficulties, small bowel feedings should be considered for patients at high risk for intolerance to EN (on inotropes, continuous infusion of sedatives, or paralytic agents, or patients with high nasogastric drainage) or at high risk for regurgitation and aspiration (nursed in supine position). Finally, where obtaining small bowel access is not feasible (no access to fluoroscopy or endoscopy and blind techniques not reliable), small bowel feedings should be considered for those select patients that repeatedly demonstrate high gastric residuals and are not tolerating adequate amounts of EN intragastrically.***

2013 Discussion: the committee noted that there were no changes in the treatment effect on mortality and infections with the inclusion of 5 new RCTs (Hsu 2009, White 2009, Acosta- Escribano 2010, Davies 2012 and Friedman 2015). There was a similar direction of findings amongst trials as evidenced by the test for heterogeneity. The committee agreed that feasibility of placing small bowel feeding tubes has improved considerably over the years while the safety concerns about their placement still exists particularly if it involves transporting the patient to an endoscopy suite. The committee also noted the aggregated data on nutritional outcomes that showed small bowel feeding had a favourable effect on optimizing the delivery of calories and protein.

Semi Quantitative Scoring

	Definition	2009 Score	2013 Score (0,1,2,3)	2015 Score (0,1,2,3)
Effect size	Magnitude of the absolute risk reduction attributable to the intervention listed—a higher score indicates a larger effect size	**2 (pneumonia)**	**2 (pneumonia)**	**2 (pneumonia)**
Confidence interval	95% confidence interval around the point estimate of the absolute risk reduction, or the pooled estimate (if more than one trial)—a higher score indicates a smaller confidence interval	**2 (with Taylor) 1 (without Taylor)**	**2 (with Taylor/Minard) 1 (without Taylor/Minard)**	**2 (with Taylor/Minard) 1 (without Taylor/Minard)**
Validity	Refers to internal validity of the study (or studies) as measured by the presence of concealed randomization, blinded outcome adjudication, an intention to treat analysis, and an explicit definition of outcomes—a higher score indicates presence of more of these features in the trials appraised	**2**	**2**	**2**
Homogeneity or Reproducibility	Similar direction of findings among trials—a higher score indicates greater similarity of direction of findings among trials	**1**	**2**	**2**
Adequacy of control group	Extent to which the control group represented standard of care (large dissimilarities = 1, minor dissimilarities=2, usual care=3)	**3**	**3**	**3**
Biological plausibility	Consistent with understanding of mechanistic and previous clinical work (large inconsistencies =1, minimal inconsistencies =2, very consistent =3)	**3**	**3**	**3**
Generalizability	Likelihood of trial findings being replicated in other settings (low likelihood i.e. single centre =1, moderate likelihood i.e. multicentre with limited patient population or practice setting =2, high likelihood i.e. multicentre, heterogenous patients, diverse practice settings =3.	**2**	**2**	**2**
Low cost	Estimated cost of implementing the intervention listed—a higher score indicates a lower cost to implement the intervention in an average ICU	**2**	**2**	**2**
Feasible	Ease of implementing the intervention listed—a higher score indicates greater ease of implementing the intervention in an average ICU	**1 (depending upon technique)**	**2**	**2**
Safety	Estimated probability of avoiding any significant harm that may be associated with the intervention listed—a higher score indicates a lower probability of harm	**2**	**3 (bedside placement) 2 (other methods)**	**3 (bedside placement) 2 (other methods)**

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: There were sixteen randomized trials that were reviewed, all of which were level 2 studies. In the Taylor et al study, only 34% of the patients achieved small bowel access in this study (large number of protocol violations) and hence the meta-analysis was done with and without this study. Minard et al 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. Meta-analyses on mortality, infections & time dependent variables (LOS) were done with and without the Minard study.

Mortality: Based on the 14 studies that reported on mortality, no significant differences between the groups were found (RR 1.01, 95% CI 0.84, 1.22, p=0.89, heterogeneity I^2=0%; figure 1). When the Taylor et al & Minard studies was excluded, the relative risk did not change (RR 1.03, 95% CI 0.85, 1.24, p=0.77, heterogeneity I^2=0%; figure 2).

Infections (Pneumonia): Based on the 13 studies that reported on pneumonia, the meta-analysis showed that small bowel feeding was associated with a significant reduction in pneumonia when compared to gastric feeding (RR 0.78, 95% CI 0.63, 0.98, p=0.03, heterogeneity I^2=15%; figure 3). When the studies by Taylor et al and Minard et al were removed from the analysis, small bowel feeding was associated with only a trend in the reduction of pneumonia (RR 0.79, 95% CI 0.60, 1.05, p=0.10, heterogeneity I^2=21%; figure 4).

LOS: When all the 9 studies that reported ICU LOS were aggregated, enteral feeding via the small bowel had no effect on ICU length of stay (WMD 0.49, 95% CI -1.36, 2.33, p=0.60, heterogeneity I^2=81%; figure 5). When the Minard study was excluded from the analysis, the signal did not change (WMD 0.04, 95% CI -1.85, 1.93, p=0.97, heterogeneity I^2=82%; figure 6). Based on the aggregation of the 5 studies that reported hospital LOS, enteral feeding via the small bowel had no effect on hospital length of stay (WMD 0.56, 95% CI -3.60, 4.73, p=0.79, heterogeneity I^2=24%; figure 7) when compared to gastric feeding.

Ventilator days: Based on the aggregation of the 6 studies that reported duration of ventilation, enteral feeding via the small bowel compared to gastric feeding had no effect on duration of ventilation (WMD -0.36, 95% CI -2.02, 1.30, p=0.67, heterogeneity I^2=42%; 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, Eatock, Friedman), while other reported a significant improvement in nutritional outcomes in the group fed via small bowel such as better nutrition efficiency (Hsu, Acosta-Escribano), calorie/protein intake & less time to reach goal (Hsu), vomiting (Hsu) and significantly less gastrointestinal tract colonization and high gastric residual volumes

(Acosta Escribano). 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) had fewer major complications and a better neurological outcome at 3 months than the group receiving gastric feeds.

Conclusions:

1) Small bowel feeding, compared to gastric feeding may be associated with a reduction in pneumonia in critically ill patients.
2) No difference in mortality or ventilator days in critically ill patients receiving small bowel vs. gastric feedings.
3) Small bowel feeding improves calorie and protein intake and is associated with less time taken to reach target rate of enteral nutrition when compared to gastric feeding.

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)

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 12 ± 2 **Protein (gm/kg/day)** 0.7 ± 0.1 0.4 ± 0.1 **% REE delivered** 69 ± 7 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)	**NA**	**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

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

± ( ) : mean ± Standard deviation (number)
(-) : median (range)
NA: not available
Cost : 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	5	19	5	19	3.1%	1.00 [0.35, 2.90]
Kortbeek	4	37	3	43	1.7%	1.55 [0.37, 6.48]
Taylor	5	41	6	41	2.8%	0.83 [0.28, 2.52]
Kearns	5	21	6	23	3.3%	0.91 [0.33, 2.55]
Minard	1	12	4	15	0.8%	0.31 [0.04, 2.44]
Esparaza	10	27	11	27	7.7%	0.91 [0.47, 1.78]
Boivin	18	39	18	39	15.1%	1.00 [0.62, 1.62]
Davies 2002	4	34	5	39	2.3%	0.92 [0.27, 3.14]
Montejo	19	50	22	51	15.4%	0.88 [0.55, 1.42]
Hsu	26	59	24	62	19.1%	1.14 [0.74, 1.74]
White	11	51	5	57	3.6%	2.46 [0.92, 6.60]
Acosta-Escribano	6	50	9	54	3.8%	0.72 [0.28, 1.88]
Davies 2012	13	91	12	89	6.5%	1.06 [0.51, 2.19]
Friedman	20	54	22	61	14.9%	1.03 [0.63, 1.66]
Total (95% CI)		**585**		**620**	**100.0%**	**1.01 [0.84, 1.22]**
Total events	147		152			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.11$, df = 13 (P = 0.94); $I^2 = 0\%$

Test for overall effect: Z = 0.14 (P = 0.89)

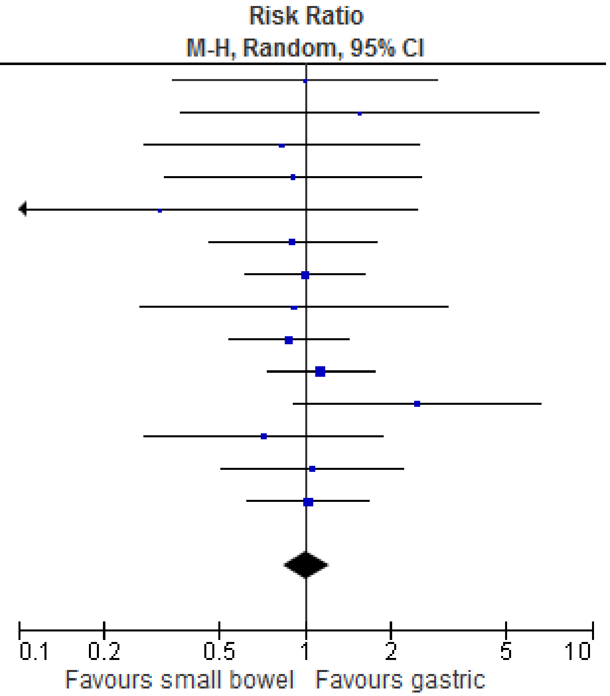

Figure 2. Mortality (excluding Taylor and Minard)

	Small Bowel		Gastric			Risk Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Montecalvo	5	19	5	19	3.2%	1.00 [0.35, 2.90]	1992
Kortbeek	4	37	3	43	1.8%	1.55 [0.37, 6.48]	1999
Kearns	5	21	6	23	3.4%	0.91 [0.33, 2.55]	2000
Esparaza	10	27	11	27	8.0%	0.91 [0.47, 1.78]	2001
Boivin	18	39	18	39	15.6%	1.00 [0.62, 1.62]	2001
Davies 2002	4	34	5	39	2.4%	0.92 [0.27, 3.14]	2002
Montejo	19	50	22	51	16.0%	0.88 [0.55, 1.42]	2002
Hsu	26	59	24	62	19.9%	1.14 [0.74, 1.74]	2009
White	11	51	5	57	3.7%	2.46 [0.92, 6.60]	2010
Acosta-Escribano	6	50	9	54	3.9%	0.72 [0.28, 1.88]	2010
Davies 2012	13	91	12	89	6.8%	1.06 [0.51, 2.19]	2012
Friedman	20	54	22	61	15.4%	1.03 [0.63, 1.66]	2015
Total (95% CI)		**532**		**564**	**100.0%**	**1.03 [0.85, 1.24]**	
Total events	141		142				

Heterogeneity: Tau² = 0.00; Chi² = 4.73, df = 11 (P = 0.94); I² = 0%
Test for overall effect: Z = 0.30 (P = 0.77)

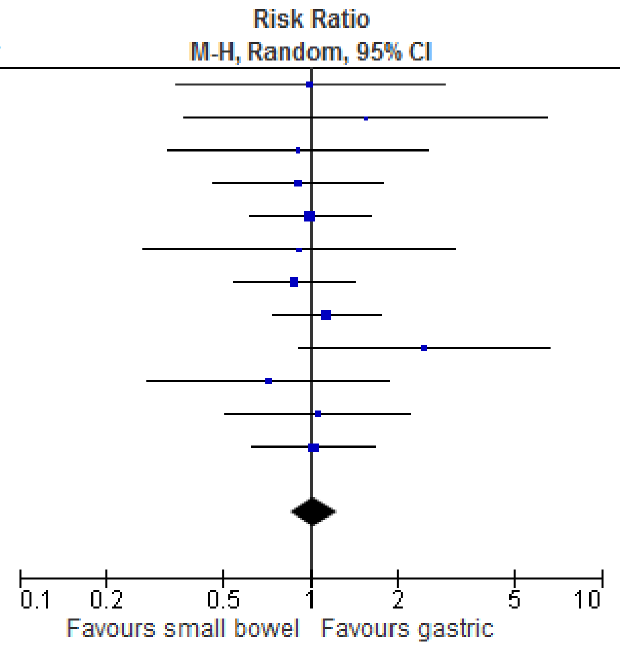

Figure 3. Pneumonia

Study or Subgroup	Small Bowel Events	Small Bowel Total	Gastric Events	Gastric Total	Weight	Risk Ratio M-H, Random, 95% CI
Montecalvo	4	19	6	19	3.7%	0.67 [0.22, 1.99]
Kortbeek	10	37	18	43	9.7%	0.65 [0.34, 1.22]
Taylor	18	41	26	41	18.1%	0.69 [0.46, 1.05]
Kearns	4	21	3	23	2.4%	1.46 [0.37, 5.78]
Minard	6	12	7	15	6.8%	1.07 [0.49, 2.34]
Day	0	14	2	11	0.6%	0.16 [0.01, 3.03]
Davies 2002	2	31	1	35	0.9%	2.26 [0.22, 23.71]
Montejo	16	50	20	51	12.9%	0.82 [0.48, 1.39]
Hsu	5	59	15	62	4.9%	0.35 [0.14, 0.90]
White	11	57	5	51	4.5%	1.97 [0.73, 5.28]
Acosta-Escribano	16	50	31	54	15.6%	0.56 [0.35, 0.89]
Davies 2012	18	91	19	89	11.4%	0.93 [0.52, 1.65]
Friedman	13	54	12	61	8.4%	1.22 [0.61, 2.45]
Total (95% CI)		**536**		**555**	**100.0%**	**0.78 [0.63, 0.98]**
Total events	123		165			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 14.19$, df = 12 (P = 0.29); $I^2 = 15\%$
Test for overall effect: Z = 2.17 (P = 0.03)

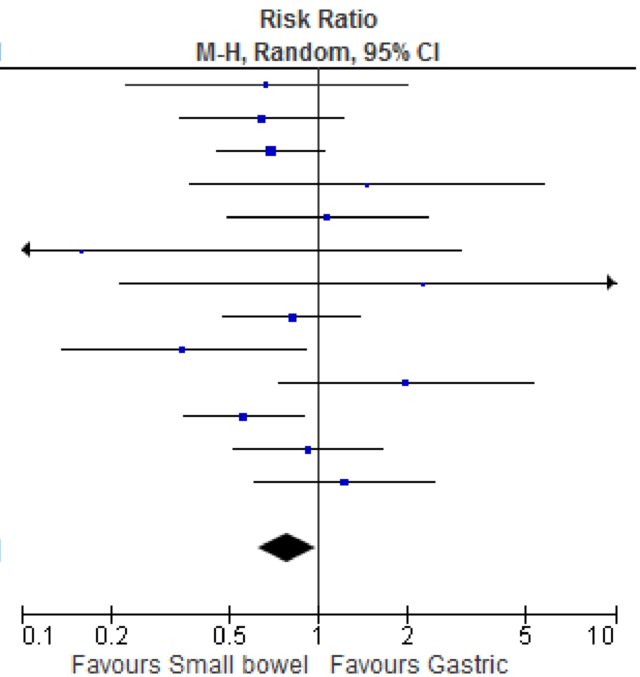

Figure 4. Pneumonia (excluding Taylor and Minard)

	Small Bowel		Gastric			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Montecalvo	4	19	6	19	5.6%	0.67 [0.22, 1.99]
Kortbeek	10	37	18	43	13.0%	0.65 [0.34, 1.22]
Kearns	4	21	3	23	3.7%	1.46 [0.37, 5.78]
Day	0	14	2	11	0.9%	0.16 [0.01, 3.03]
Davies 2002	2	31	1	35	1.4%	2.26 [0.22, 23.71]
Montejo	16	50	20	51	16.4%	0.82 [0.48, 1.39]
Hsu	5	59	15	62	7.1%	0.35 [0.14, 0.90]
White	11	57	5	51	6.7%	1.97 [0.73, 5.28]
Acosta-Escribano	16	50	31	54	18.9%	0.56 [0.35, 0.89]
Davies 2012	18	91	19	89	14.8%	0.93 [0.52, 1.65]
Friedman	13	54	12	61	11.5%	1.22 [0.61, 2.45]
Total (95% CI)		**483**		**499**	**100.0%**	**0.79 [0.60, 1.05]**
Total events	99		132			

Heterogeneity: Tau² = 0.05; Chi² = 13.25, df = 10 (P = 0.21); I² = 25%

Test for overall effect: Z = 1.63 (P = 0.10)

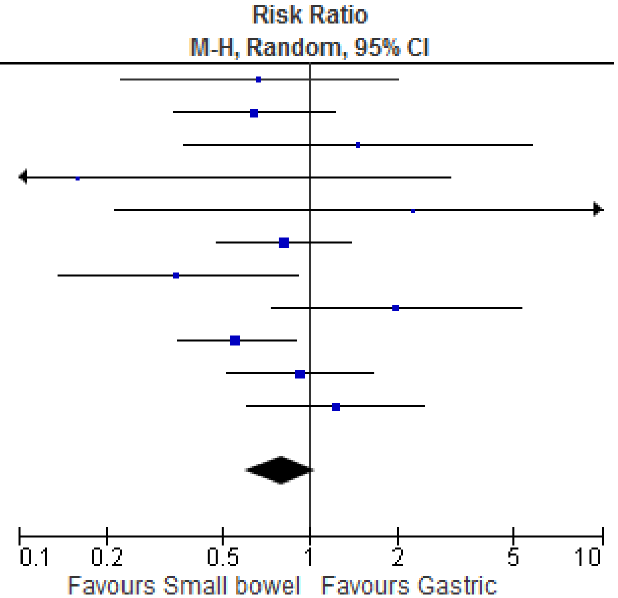

Figure 5. ICU LOS

	Small Bowel			Gastric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Montecalvo	11.7	8.2	19	12.3	10.8	19	6.1%	-0.60 [-6.70, 5.50]	1992
Minard	18.5	8.8	12	11.3	6.1	15	6.4%	7.20 [1.34, 13.06]	2000
Keams	17	2	21	16	2	23	16.7%	1.00 [-0.18, 2.18]	2000
Montejo	15	10	50	18	16	51	7.4%	-3.00 [-8.19, 2.19]	2002
Davies 2002	13.9	1.8	34	10.4	1.2	39	17.5%	3.50 [2.79, 4.21]	2002
Hsu	18.2	11.8	59	18.2	11.2	62	9.5%	0.00 [-4.10, 4.10]	2009
Acosta-Escribano	16	9	50	18	7	54	11.9%	-2.00 [-5.12, 1.12]	2010
White	7.12	6	51	9.1	10.55	55	11.6%	-1.98 [-5.22, 1.26]	2010
Davies 2012	12.5	8.6	91	12.7	9.8	89	13.0%	-0.20 [-2.90, 2.50]	2012
Total (95% CI)			**387**			**407**	**100.0%**	**0.49 [-1.36, 2.33]**	

Heterogeneity: $Tau^2 = 4.93$; $Chi^2 = 41.62$, df = 8 ($P < 0.00001$); $I^2 = 81\%$
Test for overall effect: Z = 0.52 (P = 0.60)

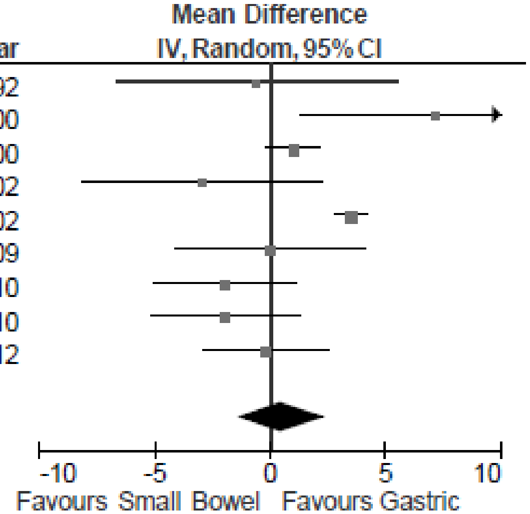

Figure 6. ICU LOS (excluding Minard)

	Small Bowel			Gastric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Montecalvo	11.7	8.2	19	12.3	10.8	19	6.4%	-0.60 [-6.70, 5.50]	1992
Kearns	17	2	21	16	2	23	18.0%	1.00 [-0.18, 2.18]	2000
Montejo	15	10	50	18	16	51	7.8%	-3.00 [-8.19, 2.19]	2002
Davies 2002	13.9	1.8	34	10.4	1.2	39	18.8%	3.50 [2.79, 4.21]	2002
Hsu	18.2	11.8	59	18.2	11.2	62	10.1%	0.00 [-4.10, 4.10]	2009
Acosta-Escribano	16	9	50	18	7	54	12.7%	-2.00 [-5.12, 1.12]	2010
White	7.12	6	51	9.1	10.55	55	12.3%	-1.98 [-5.22, 1.26]	2010
Davies 2012	12.5	8.6	91	12.7	9.8	89	13.9%	-0.20 [-2.90, 2.50]	2012
Total (95% CI)			**375**			**392**	**100.0%**	**0.04 [-1.85, 1.93]**	

Heterogeneity: Tau² = 4.79; Chi² = 38.90, df = 7 (P < 0.00001); I² = 82%
Test for overall effect: Z = 0.04 (P = 0.97)

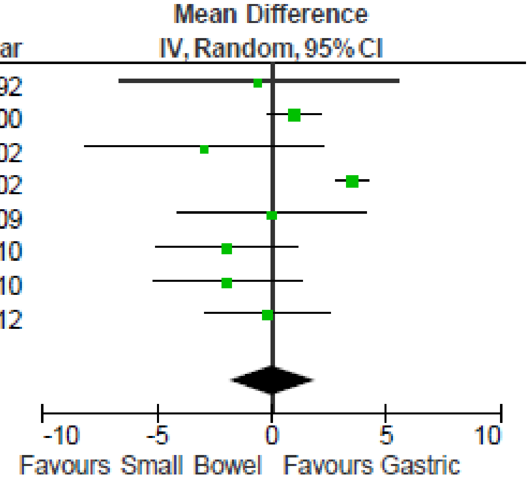

Figure 7. Hospital LOS

	Small Bowel			Gastric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Kearns	39	10	21	43	11	23	29.3%	-4.00 [-10.21, 2.21]	2000
Minard	30	14.7	12	21.3	14.7	12	10.9%	8.70 [-3.06, 20.46]	2000
Hsu	36	24.2	59	31.7	21.1	62	20.1%	4.30 [-3.81, 12.41]	2009
Acosta-Escribano	38	24	50	41	28	54	14.4%	-3.00 [-13.00, 7.00]	2010
Davies 2012	28.8	26.1	91	27.4	21.1	89	25.3%	1.40 [-5.53, 8.33]	2012
Total (95% CI)			**233**			**240**	**100.0%**	**0.56 [-3.60, 4.73]**	

Heterogeneity: Tau² = 5.40; Chi² = 5.25, df = 4 (P = 0.26); I² = 24%
Test for overall effect: Z = 0.27 (P = 0.79)

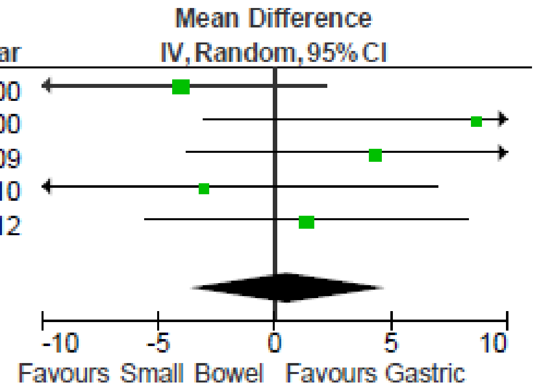

Figure 8. Duration of ventilation

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	Year
Montecalvo	10.2	7.1	19	11.4	10.8	19	6.9%	-1.20 [-7.01, 4.61]	1992
Minard	15.1	7.5	12	10.4	6.1	15	8.2%	4.70 [-0.55, 9.95]	2000
Hsu	28.5	24.9	59	23.8	18.2	62	4.1%	4.70 [-3.10, 12.50]	2009
White	5.73	5.29	51	7.68	9.81	55	18.5%	-1.95 [-4.92, 1.02]	2010
Acosta-Escribano	7.3	4	50	8.9	4	54	32.8%	-1.60 [-3.14, -0.06]	2010
Davies 2012	9.8	6.2	91	9.7	6.3	89	29.4%	0.10 [-1.73, 1.93]	2012
Total (95% CI)			**282**			**294**	**100.0%**	**-0.36 [-2.02, 1.30]**	

Heterogeneity: $Tau^2 = 1.57$; $Chi^2 = 8.67$, $df = 5$ ($P = 0.12$); $I^2 = 42\%$
Test for overall effect: $Z = 0.43$ ($P = 0.67$)

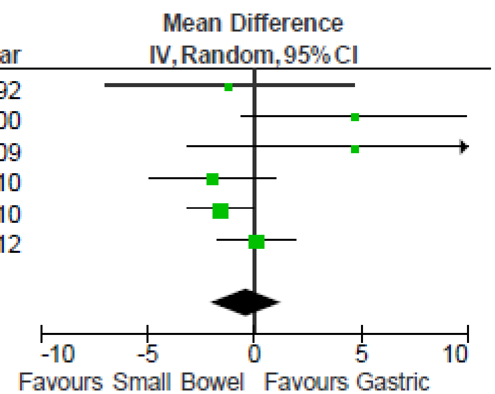

Figure 9. Nutritional efficiency (%)

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	61	17	19	46.9	25.9	19	9.7%	14.10 [0.17, 28.03]	1992
Kearns	69	7	21	47	7	23	19.7%	22.00 [17.86, 26.14]	2000
Montejo	80	28	50	75	30	51	12.0%	5.00 [-6.31, 16.31]	2002
Hsu	95	5	59	83	6	62	21.3%	12.00 [10.04, 13.96]	2009
Acosta-Escribano	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: $Z = 3.56$ ($P = 0.0004$)

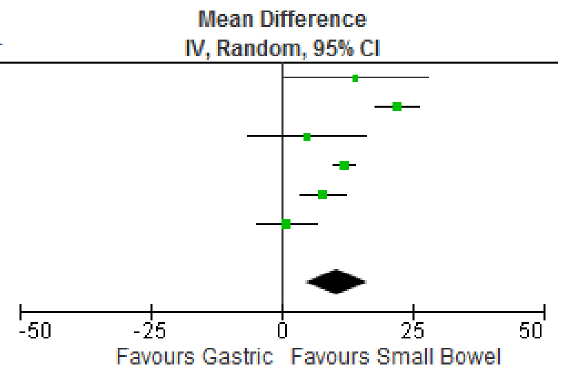

Figure 10. Time to reach EN target

	Small Bowel			Gastric				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Kortbeek	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	43	24.1	30	28.8	15.9	30	23.4%	14.20 [3.87, 24.53]	2002
Hsu	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)