6.3 Enteral Nutrition (Other): Continuous vs. Other Methods of Administration

Question: Does continuous administration of enteral nutrition compared to other methods of administration result in better outcomes in critically ill patients?

Summary of evidence: There were 5 level 2 studies comparing continuous 24 hour enteral feeding to intermittent or bolus feeds. Four of the studies (Steevens 2002, Serpa 2003, Chen 2006 and MacLeod 2007) gave EN over 15-60 minutes multiple times a day, whereas 1 study (Bonten 1996) gave EN continuously over 18 hours. Given the heterogeneity between Bonten et al and the other 4 studies, Bonten et al was not included in the meta-analysis.

Mortality: Three studies reported on mortality. When two of the studies were meta-analyzed, the method of administering EN had no effect on overall mortality (RR 0.65, 95% CI 0.29, 1.42, p=0.28, heterogeneity I^2 = 0%, figure 1). Bonten et al found no difference in ICU mortality between the groups receiving continuous vs intermittent feeds given over 18 hours (p=0.38).

Infections: Three studies reported on aspiration pneumonia and found a significant increase in incidence in the group receiving continuous feeds (RR 2.90, 95% CI 1.18, 7.14, p=0.02, heterogeneity I^2 = 9%, figure 2). MacLeod et al found no difference between groups (p=0.45) in the incidence of pneumonias. Bonten et al found no difference on the incidence of overall infections between the groups receiving continuous vs. intermittent feeds given over 18 hours (p=1.0).

LOS & Ventilator days: When the two studies (Serpa 2003, MacLeod 2007) that had ICU LOS available in mean and SD were aggregated, there was no difference found between the groups (WMD -0.70, 95% CI -4.89, 3.50, p=0.74, heterogeneity I^2 = 0%, figure 3). Chen et al reported on the number of patients with ICU LOS less than or equal to 21 days and greater than 21 days. They found a trend towards an increase in frequency of ICU LOS >21 days in the group receiving continuous feeds (p=0.15). No studies reported on hospital LOS. No studies reported the duration of mechanical ventilation in mean and standard deviation. Chen et al reported on the number of patients extubated after 21 days and they found a significantly higher number of patients receiving intermittent feeds were free of ventilator support after 21 days (p=0.002). MacLeod 2007 reported on the number of patients extubated prior to day 7 and found no difference between groups (p=0.58).

Other complications: Two studies (Steevens 2002 and MacLeod 2007) reported on total number of patients who developed diarrhea during the study and when the data was aggregated, there was a trend towards reduced diarrhea in the continuously fed group (RR 0.48, 95% CI 0.18, 1.27, p=0.14, heterogeneity I^2=0%; figure 4). Serpa et al reported on the daily occurrence of diarrhea and found no significant differences between groups (p>0.05). Two studies reported on nutritional adequacy but not in mean and standard deviation, therefore, the data could not be aggregated. Both

studies (Steevens 2002 and MacLeod 2007) found no significant difference between groups (p=NS and p>0.05, respectively). Serpa et al reported daily the number of patients with elevated residuals and Chen et al reported the number of patients with residuals >60 ml on day 7. Neither study found a significant difference between groups (Serpa p>0.05, Chen p=0.097). Bonten et al reported on EN reductions due to high gastric residuals but the difference between groups was not significant (p=0.25). Steevens et al reported interruptions to feeds due to elevated residuals and vomiting and found no difference between groups (p=0.36).

Conclusion:

1) Providing EN continuously over 24 hours vs by another method has no effect on mortality in ICU patients.
2) Providing EN continuously over 24 hours vs by another method is associated with increased occurrence of aspiration pneumonia in the critically ill. There is insufficient evidence to comment on the occurrence of other infections.
3) Providing EN continuously over 24 hours vs by another method has no effect on ICU LOS.
4) Providing EN continuously over 24 hours vs by another method may be associated with a reduction in diarrhea occurrence but it has no effect on nutritional adequacy or elevated gastric residual volumes.

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 continuous enteral nutrition vs. other methods of administration

Study	Population	Methods (score)	Intervention	Mortality # (%) Continuous	Mortality # (%) Other	Infections # (%) Continuous	Infections # (%) Other
1) Bonten 1996	Mixed ICU's Mechanically ventilated N=60	C.Random: not sure ITT: yes Blinding: no (8)	Continuous feeds (24hrs) vs. intermittent feeds (18 hrs)	ICU 6/30 (20)	ICU 9/30 (30)	VAP 5/30 (17)	VAP 5/30 (17)
				RR (CI)*: 0.67 (0.27-1.64) P=0.38		RR (CI)*: 1.00 (0.32-3.10) P=1.0	
2) Steevens 2002	Multiple trauma patients, surgical, medical ICU's N=18	C.Random: not sure ITT: yes Blinding: no (8)	Continuous enteral nutrition (started @ 25 ml/hr and ↑ by 25 mls q 12 hrs)vs bolus (125 mls by gravity over 15 minutes q 4 hrs and ↑ by 125 mls q 12 hrs.	NR	NR	Aspiration 0/9 (0)	Aspiration 1/9 (11)
3) Serpa 2003	Mixed ICU pts requiring EN N=28	C.Random: not sure ITT: yes Blinding: no (7)	Continuous EN vs intermittent EN (8 feeds per 24h, 1h length of feed given 3h apart.	Unknown 3/14 (21)	Unknown 3/14 (21)	Confirmed Aspiration 1/14	Confirmed Aspiration 0/14
4) Chen 2006	ICU pts, APACHE II >15, expected to need EN for ≥ 7 days N=107	C.Random: not sure ITT: yes Blinding: no (7)	Continuous EN using feeding pump vs bolus feed by gravity, 4-6 feeds a day of 350ml or less given over 15-20 minutes	NR	NR	Aspiration pneumonia patch on Xray 26/51 (61)	Aspiration pneumonia patch on Xray 8/56 (14)
3) MacLeod 2007	Trauma patients N=164	C.Random: not sure ITT: no Blinding: no (5)	Continuous enteral nutrition (started @ 20 ml/hr for 8 hrs and ↑ by 20 mls q 8 hrs) vs. bolus (100 mls q 4 hrs and ↑ by 100 mls q 8 hrs) over 30-60 min per feed.	ICU 6/81 (7)	ICU 11/79 (14)	Pneumonia 33/81 (41) P=0.45	Pneumonia 38/79 (48)

Table 1. Randomized studies evaluating continuous enteral nutrition vs. other methods of administration (continued)

Study	LOS days		Ventilator days		Cost		Other	
	Continuous	Other	Continuous	Other	Continuous	Other	Continuous	Other
1) Bonten 1996	NR	NR	NR	NR	NR	NR	# patients with decreased feeds 2/30 (7)	5/30 (17)
2) Steevens 2002	NR	NR	NR	NR	NR	NR	# patients with diarrhea 2/9 (22) # patients with interrupted feeds due to high GRVs or vomiting 3/9 (33) % goal feeds achieved 87%	5/9 (56) 5/9 (56) 86.8%, P=NS
3) Serpa 2003	ICU 14.2 ± 10.2 (14) P >0.05	ICU 14.1 ± 9.3 (14)	NR	NR	NR	NR	Days to start of EN 2.2 ± 1.4 High Gastric Residuals, days 1-3 p>0.05 on all three days Diarrhea and Vomiting, days 1-3 p>0.05 on all three days	4.5 ± 5.6
4) Chen 2006	ICU, ≤ 21 days 36/51 (71) ICU, >21 days 15/51 (29) P=0.152	ICU, ≤ 21 days 47/56 (84) ICU, >21 days 9/56 (16)	Extubated by day 21 16/51 (31) P=0.002	Extubated by day 21 34/56 (61)	NR	NR	Feeding Volume on Day 7 >1000 ml 30/51 Gastric Residue on Day 7 >60 ml 9/51	52/56, p<0.001 4/56, p=0.097
5) MacLeod 2007	ICU 20.1 ± 1.7 (81) *Mean and SEM* 20.1 ± 15.3 (81)+ *Mean and SD* P=0.69	ICU 21.2 ± 2 (79) *Mean and SEM* 21.2 ± 17.8 (79)+ *Mean and SD*	Patients extubated prior to day 7 7/81 (9) P=0.58	Patients extubated prior to day 7 5/79 (6)	NR	NR	Onset of diarrahea 3/81 (4) % total calories for 1st 7 days, mean and SEM 58.3 ± 4	5/79 (79) 60.2 ± 4.2, p>0.05

C.Random: concealed randomization NR: not reported * RR = relative risk and confidence intervals ITT: intent to treat +Calculated from the SEM
SEM: Standard error mean SD: Standard deviation

Figure 1. Overall Mortality

Study or Subgroup	Continuous EN Events	Total	Other Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Serpa	3	14	3	14	30.7%	1.00 [0.24, 4.13]	2003
MacLeod	6	81	11	79	69.3%	0.53 [0.21, 1.37]	2007
Total (95% CI)		**95**		**93**	**100.0%**	**0.65 [0.29, 1.42]**	
Total events	9		14				

Heterogeneity: Tau² = 0.00; Chi² = 0.53, df = 1 (P = 0.47); I² = 0%
Test for overall effect: Z = 1.09 (P = 0.28)

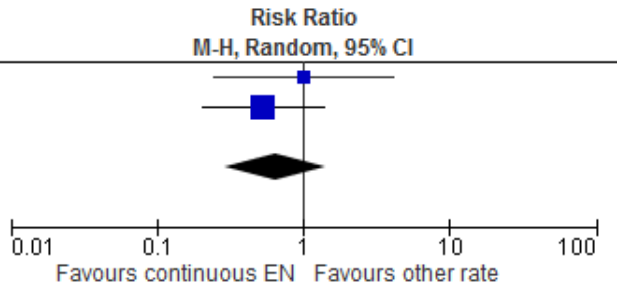

Figure 2. Aspiration pneumonia

Study or Subgroup	Continuous EN Events	Total	Other Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Steevens	0	9	1	9	8.1%	0.33 [0.02, 7.24]	2002
Serpa	1	14	0	14	7.9%	3.00 [0.13, 67.91]	2003
Chen	26	51	8	56	83.9%	3.57 [1.78, 7.16]	2006
Total (95% CI)		**74**		**79**	**100.0%**	**2.90 [1.18, 7.14]**	
Total events	27		9				

Heterogeneity: Tau² = 0.12; Chi² = 2.19, df = 2 (P = 0.34); I² = 9%
Test for overall effect: Z = 2.32 (P = 0.02)

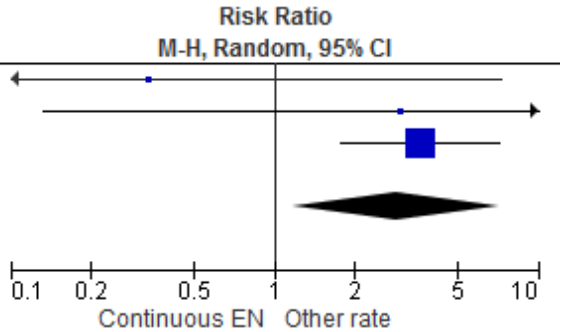

Figure 3. ICU LOS

Study or Subgroup	Early Enhanced EN Mean	SD	Total	Standard EN Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Serpa	14.2	10.2	14	14.1	9.3	14	33.6%	0.10 [-7.13, 7.33]	2003
MacLeod	20.1	15.3	81	21.2	17.8	79	66.4%	-1.10 [-6.25, 4.05]	2007
Total (95% CI)			**95**			**93**	**100.0%**	**-0.70 [-4.89, 3.50]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.79); I² = 0%
Test for overall effect: Z = 0.33 (P = 0.74)

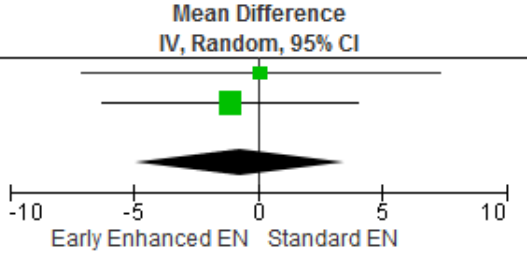

Figure 4. Diarrhea

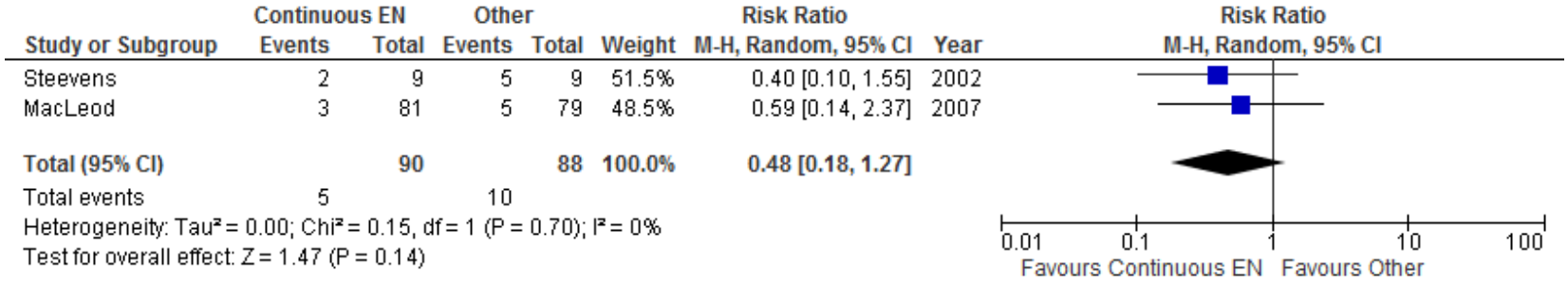

Table 2. Excluded Articles

#	Reason excluded	Citation
1	No clinical outcomes	Hiebert JM, Brown A, Anderson RG, Halfacre S, Rodeheaver GT, Edlich RF. Comparison of continuous vs intermittent tube feedings in adult burn patients. JPEN J Parenter Enteral Nutr 1981;5(1):73-5.
2	No clinical outcomes	Kocan MJ, Hichisch SM. A Comparison of continuous and intermittent enteral nutrition in NICU patients. J Neurosci Nurs 1986;18(6):333-7.
3	Not ICU patients	Ciocon JO, Galindo-Ciocon DJ, Tiessen C, Galindo D. Continuous compared with intermittent tube feeding in the elderly. JPEN J Parenter Enteral Nutr 1992;16(6):525-8.
4	No clinical outcomes	Skiest DJ, Khan N, Feld R, Metersky ML. The role of enteral feeding in gastric colonization: a randomized controlled trial comparing continuous to intermittent enteral feeding in mechanically ventilated patients. Clinical Intensive Care 1996;7:138-143
5	Not ICU patients	Lee JS, Kwok T, Chui PY, Ko FW, Lo WK, Kam WC, Mok HL, Lo R, Woo J. Can continuous pump feeding reduce the incidence of pneumonia in nasogastric tube-fed patients? A randomized controlled trial. Clin Nutr. 2010 Aug;29(4):453-8.
6	No clinical outcomes, both intermittent	Maurya I, Pawar M, Garg R, Kaur M, Sood R. Comparison of respiratory quotient and resting energy expenditure in two regimens of enteral feeding - continuous vs. intermittent in head-injured critically ill patients. Saudi J Anaesth. 2011 Apr;5(2):195-201.
7	Pseudo-randomized	Kadamani I, Itani M, Zahran E, Taha N. Incidence of aspiration and gastrointestinal complications in critically ill patients using continuous versus bolus infusion of enteral nutrition: a pseudo-randomised controlled trial. Aust Crit Care. 2014 Nov;27(4):188-93.
8	No clinically significant outcomes	Evans DC, Forbes R, Jones C, et al. Continuous versus bolus tube feeds: Does the modality affect glycemic variability, tube feeding volume, caloric intake, or insulin utilization? International Journal of Critical Illness and Injury Science. 2016;6(1):9-15. doi:10.4103/2229-5151.177357.
9	No clinically significant outcomes	Nasiri M, Farsi Z, Ahangari M, Dadgari F. Comparison of Intermittent and Bolus Enteral Feeding Methods on Enteral Feeding Intolerance of Patients with Sepsis: A Triple-blind Controlled Trial in Intensive Care Units. Middle East J Dig Dis.2017 Oct;9(4):218-227.