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 6 level 2 studies comparing continuous 24-hour enteral feeding to intermittent or bolus feeds. In the non-continuous EN arm, five of the studies (Steevens 2002, Serpa 2003, Chen 2006, MacLeod 2007 and McNelly 2020) gave boluses of enteral nutrition (EN) over 15-60 minutes multiple times a day, whereas 1 study (Bonten 1996) gave EN continuously over 18 hours.

Mortality: When the four studies reporting mortality were meta-analyzed, continuous feeding was associated with trend towards a reduction in overall mortality compared to intermittent/bolus feeds (RR 0.77, 95% CI 0.53, 1.13, p=0.18, test for heterogeneity I^2 = 0%, figure 1).

Infections: Continuous feeding had no significant effect on pneumonia (RR 1.53, 95% CI 0.59, 3.97, p=0.38, test for heterogeneity I^2=79%, figure 2) or aspiration (RR 0.33, 95% CI 0.04, 2.98, p=0.33, test for heterogeneity I^2 = 0%, figure 3) when compared to intermittent/bolus feeding.

LOS & Ventilator days: When the three studies (Serpa 2003, MacLeod 2007, McNelly 2020) that had ICU LOS available in mean and SD were aggregated, there was no difference found between the groups (WMD -1.17, 95% CI -4.36, 2.02, p=0.47, test for heterogeneity I^2=0%, figure 4). Chen et al reported on the number of patients with ICU LOS less than or equal to 21 days and greater than 21 days and found a trend towards an increase in frequency of ICU LOS >21 days in the group receiving continuous feeds (p=0.15). Only one study reported hospital LOS and duration of mechanical ventilation and there were no differences between the continuously or intermittently fed groups (McNelly 2020, p=0.91 and p=0.25 respectively). Chen et al 2006 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, test for heterogeneity I^2=0%; figure 5). Serpa et al 2003 reported on the daily occurrence of diarrhea and found no significant differences between groups (p>0.05) while McNelly 2020 reported a trend towards a reduction in feeding interruption due to diarrhea in the intermittent fed group compared to the continuous group (p=0.05). When the data from the three studies that reported the number of patents with high gastric volumes were aggregated, there were no significant differences between the two groups (RR 0.64, 95% CI 0.31, 1.31, p=0.22, test for heterogeneity I^2=0%; figure 6). Two other studies reported on varying descriptions of gastric residual volumes with or without vomiting and found no significant differences between continuous or intermittent feedings (Chen 2006 p=0.097 and McNelly 2020 p=0.21). Intermittent feeding resulted in lower incidences of feeding interruption due to nausea and vomiting (p=0.02) but a higher incidence of abdominal distension (p=0.02) as compared to continuous feeding in the McNeely 2020 study.

Three studies reported on percentage goal feeds or calories achieved but not in mean and standard deviation, therefore, the data could not be aggregated. Two studies (Steevens 2002 and MacLeod 2007) found no significant difference between groups (p=NS and p>0.05, respectively) however McNelly 2020 reported that intermittent feeds were associated with achieving a significantly higher percentage of goal calories and protein compared to continuous feeding (p<0.001). In the same study, there were no differences in the preservation of muscle mass between the two groups.

Conclusion:

Compared to intermittent/bolus feedings, providing EN continuously over 24 hours,
1) May be associated with a reduction in overall mortality in ICU patients.
2) Is not associated with a difference in aspiration or pneumonia. There is insufficient evidence to comment on the occurrence of other infections.
3) Is not associated with a difference in ICU LOS.
4) Is inconclusive with respect to its impact on diarrhea.
5) Is not associated with a difference in 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 enteral 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**[1] 5/30 (17)	**VAP**[1] 5/30 (17)
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**[2] 0/9 (0)	**Aspiration**[2] 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)	**Aspiration**[3] 0/14 **Confirmed Pneumonia**[3] 1/14	**Aspiration**[3] 1/14 **Confirmed Pneumonia**[3] 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**[1] 26/51 (61)	**Aspiration pneumonia patch on Xray** 8/56 (14)
5) MacLeod 2007	Trauma patients N=164	C.Random: not sure	Continuous enteral nutrition (started @ 20 ml/hr for 8 hrs and by 20 mls q 8	**ICU** 6/81 (7)	**ICU** 11/79 (14)	**Pneumonia**[1] 33/81 (41)	**Pneumonia** 38/79 (48); p=0.45

[1] Bonten 1996, Chen 2006 and MacLeod 2007: pneumonia confirmed by chest XRay and/or CDC criteria
[2] Steevens 2002: pulmonary aspiration defined as endotracheal tube aspirates with the presence of blue food coloring from EN or visible gastric contents in pulmonary secretions.
[3] Serpa 2003: aspiration recognition was added by dye, pneumonia was affirmed when chest XRay plus symptoms.

		ITT: no Blinding: no (5)	hrs) vs. bolus (100 mls q 4 hrs and by 100 mls q 8 hrs) over 30-60 min per feed.				
6) McNelly 2020	Mechanically ventilated patients with multiorgan failure, expected to be on EN and ICU stay ≥7 days from 8 ICUs N=121	C.Random: not sure ITT: yes Blinding: single (10)	Continuous enteral nutrition as per local feeding protocols vs. intermittent feeding of 60-80 mL every 4 hrs using a syringe over 3-5 minutes.	**ICU** 16/59 (27.1) **Hospital** 19/59 (32.2)	**ICU** 18/62 (29); p=0.17 **Hospital** 23/62 (37.1); p=0.57	NR	NR

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

Study	**LOS days** Continuous	 Other	**Ventilator days** Continuous	 Other	**Other** Continuous Other
1) Bonten 1996	NR	NR	NR	NR	**# patients with decreased feeds due to GRVs** 2/30 (7) vs. 5/30 (17)
2) Steevens 2002	NR	NR	NR	NR	**# patients with diarrhea** 2/9 (22) vs. 5/9 (56) **# patients with interrupted feeds due to high GRVs or vomiting** 3/9 (33) vs. 5/9 (56) **% goal feeds achieved** 87% vs. 86.8%, P=NS

3) Serpa 2003	**ICU** 14.2 ± 10.2 (14)	**ICU** 14.1 ± 9.3 (14); p >0.05	NR	NR	**Days to start of EN** 2.2 ± 1.4 vs. 4.5 ± 5.6 **# patients with High Gastric Residuals, days 1-3** p>0.05 on all three days **# patients with high GRVs (mean of days 1-3)** 5/14 (35.7%) vs 5/15 (35.7%) **Diarrhea and Vomiting, days 1-3** p>0.05 on all three days
4) Chen 2006	**ICU, ≤ 21 days** 36/51 (71) **ICU, >21 days** 15/51 (29)	**ICU, ≤ 21 days** 47/56 (84) **ICU, >21 days** 9/56 (16); p=0.152	**Extubated by day 21** 16/51 (31)	**Extubated by day 21** 34/56 (61); p=0.002	**Feeding Volume on Day 7 >1000 ml** 30/51 vs. 52/56, p<0.001 **Gastric Residual on Day 7 >60 ml** 9/51 vs. 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*	**ICU** 21.2 ± 2 (79) *Mean and SEM* 21.2 ± 17.8 (79)$^+$ p=0.69 *Mean and SD*	**Patients extubated prior to day 7** 7/81 (9)	**Patients extubated prior to day 7** 5/79 (6); p=0.58	**Patients with diarrhea** 3/81 (4) vs. 5/79 (79) **% total calories for 1st 7 days, mean and SEM** 58.3 ± 4 vs. 60.2 ± 4.2, p>0.05

6) McNelly 2020	**ICU** 15.52 ± 11.71 **Hospital** 31.8 ± 27.75	**ICU** 17.35 ± 15.67 ; p=0.63 **Hospital** 34.73 ± 33.68 ; p=0.91	9.78 ± 9.74	11.38 ± 9.74; p=0.25	**Nutritional intake mean (95% CI)** **Energy delivered, kcal** 1069 (947.6-1190) vs.1304 (1208-1300); p=0.003 **Protein delivered, kcal** 55.8 (49.1-62.5) vs.63.8 (59.3-68.3); p= 0.048 **% energy targets** 72.5 (69.3-75.7) vs. 82.4 (79.2-85.6); p<0.001 **% protein targets** 69.9 (66.6-73.1) vs. 80.3 (77.3-83.4); p<0.001 **Energy delivered, kcal/kg** 16.8 (15.1-18.5) vs.19.0 (17.5-20.4); p=0.06 **Protein delivered, g/kg** 0.86 (0.77-0.94) vs. 0.90 (0.84-0.96); p=0.40 **Feeding Interruption events due to GRV>300 ml** 24/156 (15.4) vs. 31/157 (19.7); p=0.21 **Feeding Interruption due to Vomiting or Nausea** 16/156 (10.3) vs. 5/157 (3.2); p=0.02 **Feeding Interruption due to Abdominal Distension** 0/156 vs. 5/157 (3.20); p=0.02 **Feeding Interruption due to Diarrhea** 4/156 (2.6) vs. 0/157; p=0.05 **Rectus femoris cross sectional area%, Day 10** -19.8±14.2 vs. -17.4±14.6; p=0.51

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	Continuous EN Total	Other Events	Other Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Bonten	6	30	9	30	17.7%	0.67 [0.27, 1.64]	1996
Serpa	3	14	3	14	7.1%	1.00 [0.24, 4.13]	2003
MacLeod	6	81	11	79	16.0%	0.53 [0.21, 1.37]	2007
McNelly	19	59	23	62	59.2%	0.87 [0.53, 1.42]	2020
Total (95% CI)		**184**		**185**	**100.0%**	**0.77 [0.53, 1.13]**	
Total events	34		46				

Heterogeneity: Tau² = 0.00; Chi² = 1.06, df = 3 (P = 0.79); I² = 0%
Test for overall effect: Z = 1.33 (P = 0.18)

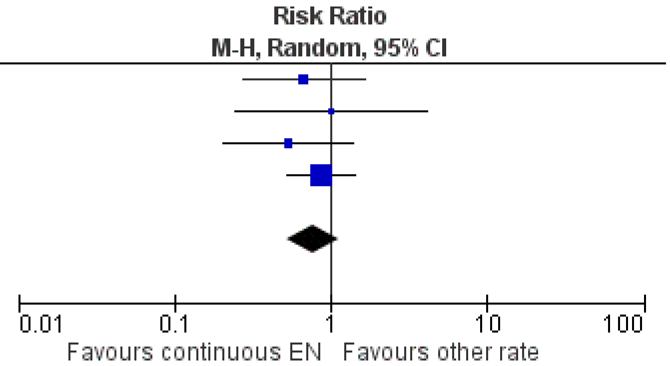


Figure 2. Pneumonia

Study or Subgroup	Continuous EN Events	Continuous EN Total	Other Events	Other Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Bonten	5	30	5	30	24.8%	1.00 [0.32, 3.10]	1996
Serpa	1	14	0	14	7.5%	3.00 [0.13, 67.91]	2003
Chen	26	51	8	56	31.6%	3.57 [1.78, 7.16]	2006
MacLeod	33	81	38	79	36.1%	0.85 [0.60, 1.20]	2007
Total (95% CI)		**176**		**179**	**100.0%**	**1.53 [0.59, 3.97]**	
Total events	65		51				

Heterogeneity: Tau² = 0.63; Chi² = 14.25, df = 3 (P = 0.003); I² = 79%
Test for overall effect: Z = 0.87 (P = 0.38)

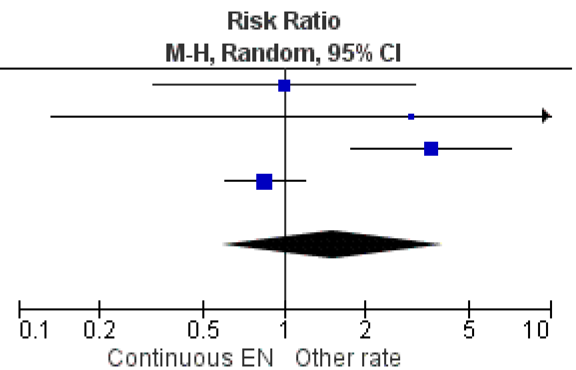


Figure 3. Aspiration

Study or Subgroup	Continuous EN Events	Continuous EN Total	Other Events	Other Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Steevens	0	9	1	9	50.7%	0.33 [0.02, 7.24]	2002
Serpa	0	14	1	14	49.3%	0.33 [0.01, 7.55]	2003
Total (95% CI)		**23**		**23**	**100.0%**	**0.33 [0.04, 2.98]**	
Total events	0		2				

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.98 (P = 0.33)

Risk Ratio
M-H, Random, 95% CI

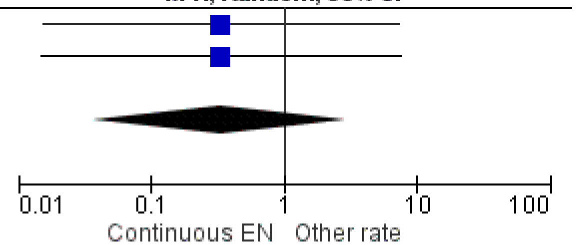


Figure 4. ICU LOS

Study or Subgroup	Continuous EN Mean	Continuous EN SD	Continuous EN Total	Other rate Mean	Other rate SD	Other rate Total	Weight	Mean Difference IV, Random, 95% CI	Year
Serpa	14.2	10.2	14	14.1	9.3	14	19.5%	0.10 [-7.13, 7.33]	2003
MacLeod	20.1	15.3	81	21.2	17.8	79	38.4%	-1.10 [-6.25, 4.05]	2007
McNelly	15.52	11.71	59	17.35	15.67	62	42.1%	-1.83 [-6.74, 3.08]	2020
Total (95% CI)			**154**			**155**	**100.0%**	**-1.17 [-4.36, 2.02]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 2 (P = 0.91); I² = 0%
Test for overall effect: Z = 0.72 (P = 0.47)

Mean Difference
IV, Random, 95% CI

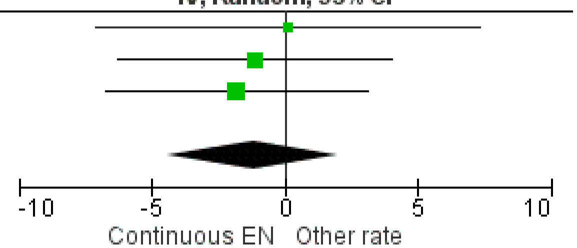


Figure 5. Diarrhea

Study or Subgroup	Continuous EN Events	Continuous EN Total	Other Events	Other Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Steevens	2	9	5	9	51.5%	0.40 [0.10, 1.55]	2002
MacLeod	3	81	5	79	48.5%	0.59 [0.14, 2.37]	2007
Total (95% CI)		**90**		**88**	**100.0%**	**0.48 [0.18, 1.27]**	
Total events	5		10				

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 1.47 (P = 0.14)

Risk Ratio M-H, Random, 95% CI

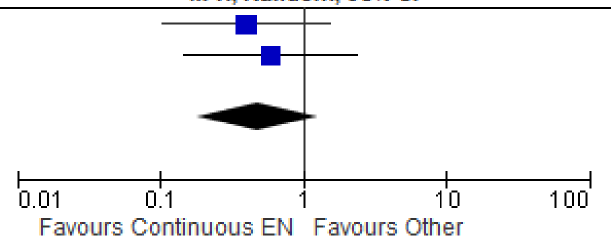
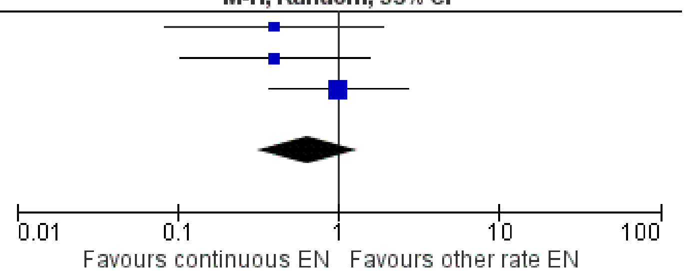


Figure 6. Gastric Residual Volumes

Study or Subgroup	Continuous EN Events	Continuous EN Total	Other rate EN Events	Other rate EN Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Bonten	2	30	5	30	20.9%	0.40 [0.08, 1.90]	1996
Steevens	2	9	5	9	27.7%	0.40 [0.10, 1.55]	2002
Serpa	5	14	5	14	51.4%	1.00 [0.37, 2.70]	2003
Total (95% CI)		**53**		**53**	**100.0%**	**0.64 [0.31, 1.31]**	
Total events	9		15				

Heterogeneity: Tau² = 0.00; Chi² = 1.62, df = 2 (P = 0.45); I² = 0%
Test for overall effect: Z = 1.22 (P = 0.22)

Risk Ratio M-H, Random, 95% CI



References

Icluded Studies

1. Bonten MJ, Gaillard CA, van der Hulst R, de Leeuw PW, van der Geest S,Stobberingh EE, Soeters PB. Intermittent enteral feeding: the influence on respiratory and digestive tract colonization in mechanically ventilated intensive-care-unit patients.Am J Respir Crit Care Med. 1996 Aug;154(2 Pt 1):394-9.
2. Steevens EC, Lipscomb AF, Poole GV, Sacks GS. Comparison of continuous vs intermittent nasogastric enteral feeding in trauma patients: perceptions and practice. Nutr Clin Pract. 2002 Apr;17(2):118-22.
3. Serpa LF, Kimura M, Faintuch J, Ceconello I. Effects of continuous versus bolus infusion of enteral nutrition in critical patients. Rev. Hosp. Clin. Fac. Med. S. Paulo 2003 58(1):9-14.
4. Chen Y-C, Chou S-S, Lin L-H, Wu L-F. The effect of intermitten nasogastric feeding on preventing aspiration pneumonia in ventilated critically ill patients. Journal of Nursing Research 2006 14(3):167-179.
5. MacLeod JB, Lefton J, Houghton D, Roland C, Doherty J, Cohn SM, Barquist ES. Prospective randomized control trial of intermittent versus continuous gastric feeds for critically ill trauma patients. J Trauma 2007;63(1):57.61.
6. "Chest. 2020 Apr 2. pii: S0012-3692(20)30584-5. doi: 10.1016/j.chest.2020.03.045. [Epub ahead of print]
Effect of intermittent or continuous feed on muscle wasting in critical illness: A phase II clinical trial."

Excluded Studies

1. 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.	No clinical outcomes
2. Kocan MJ, Hichisch SM. A Comparison of continuous and intermittent enteral nutrition in NICU patients. J Neurosci Nurs 1986;18(6):333-7.	No clinical outcomes
3. 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.	Not ICU patients
4. 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	No clinical outcomes

5. 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. Epub 2009 Nov 12. PubMed PMID: 19910085.	Not ICU patients
6. 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. PubMed PMID: 21804803; PubMed Central PMCID: PMC3139315.	No outcomes, both intermittent
7. 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.	Pseudo-randomized
8. 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.	no clinically significant outcomes
9. 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.	no clinically significant outcomes
10. Nutr Hosp. 2014 Mar 1;29(3):563-7. doi: 10.3305/nh.2014.29.3.7169. Enteral nutrition in critical patients; should the administration be continuous or intermittent? Tavares de Araujo VM1, Gomes PC2, Caporossi C3.	no clinically significant outcomes
11. Zhu, W., Jiang, Y. & Li, J. Intermittent versus continuous tube feeding in patients with hemorrhagic stroke: a randomized controlled clinical trial. Eur J Clin Nutr 74, 1420–1427 (2020). https://doi.org/10.1038/s41430-020-0579-6	No clinical outcomes