4.5 Composition of Enteral Nutrition: Strategies for optimizing EN and minimizing risks of EN: Fibre

Question: Do enteral feeds with fibre, compared to standard feeds result in better outcomes in the critically ill adult patient?

Summary of evidence: There were1 level 1 and 9 level 2 studies reviewed. Four studies looked at the effects of soluble fibres (Spapen 2001, Rushdi 2005: hydrolyzed guar; Hart 1988, Heather 1991: psyllium), one study (Dobb 1990) examined the effects of `a formula containing soy polysaccharide (mainly insoluble fibre), two studies (Karakan 2007, Chittawatanarat 2010) looked at the effects of formulas containing both soluble and insoluble fibres, one study (Schultz 2000) looked at the effects of soluble fibre (pectin) and also compared fibre-containing formula to fibre free formula, one study (Xi 2017) looked at soluble fibre (pectin), and one study compared the use of a fibre-containing formula plus soluble fibre supplementation vs. a fibre-containing formula without additional fibre supplementation (Majid 2013).

Mortality: When the data from the 4 studies that reported mortality were aggregated, fibre was associated with a trend towards a reduction in mortality (RR 0.39, 95% CI 0.15, 1.03, p = 0.06, heterogeneity I^2=0%; figure 1).

Infections: When the data from the 3 studies that reported infections (Spapen, Karakan, Xi) were aggregated, no differences were found between the 2 groups (RR 0.79, 95% CI 0.35, 1.79, p = 0.57, heterogeneity I^2=72%; figure 2).

Length of Stay: Five studies reported both hospital and ICU length of stay (Schultz, Karakan, Chittawatanarat, Spapen, Xi), however, data from the Schultz study could not be aggregated since it reported LOS for only its sub-groups and Spapen and Karakan did not report this data as mean±SD. When the data from Xi and Chittawatanarat were aggregated, enteral feeds with fibre were associated with a significant reduction in hospital LOS (RR -8.99, 95% CI -14.37, -3.61, p = 0.001, heterogeneity I^2=0%; figure 3), and ICU LOS 4.5(RR -5.03, 95% CI -8.66, -1.41, p = 0.007, heterogeneity I^2=15%; figure 4).

Ventilator days: Not studied as an outcome

Diarrhea: When the data from the 6 studies reporting on number of patients with diarrhea by group were aggregated, fibre had no effect on diarrhea (RR 0.77, 95% CI 0.50, 1.18, p =0.23, heterogeneity I^2=51%; figure 5). Majid 2013 showed no difference in # patients with diarrhea or the # diarrhea days between the two groups.

Conclusions:

1) Enteral feeds with fibre compared to standard feeds have no effect on diarrhea
2) Enteral feeds with fibre compared to standard feeds may be associated with a reduction in mortality and hospital length of stay.
3) Enteral feeds with fibre compared to standard feeds have no effect on ICU length of stay.

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 enteral feeds with fibre in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)† Fibre	Mortality # (%)† Control	Infections # (%)‡ Fibre	Infections # (%)‡ Control
1. Hart 1988	ICU patients N=68	C.Random: not sure ITT: yes Blinding: single (9)	Standard formula (Osmolite HN) + Fybogel vs. Standard formula (Osmolite HN) + placebo	NR	NR	NR	NR
2. Dobb 1990	ICU patients N=91	C.Random: yes ITT: no Blinding: double (10)	Formula with soy polysaccharide (Enrich) vs Standard (Ensure)	NR	NR	NR	NR
3. Heather 1991	ICU CCU, general wards(ICU 41/49) Nutritionally compromised N=49	C.Random: not sure ITT: no Blinding: no (3)	Standard formula (fibre free) + Hydrocil (psyllium) vs. Standard formula (fibre free)	NR	NR	NR	NR
4. Schultz 2000	Critically ill patients receiving antibiotics N=80	C.Random: yes ITT: no Blinding: double (10)	(A) Fibre (Jevity Plus or Nepro) + pectin vs (B) Fibre free (Osmolite, Promote) + pectin vs (C) Fibre (Jevity Plus or Nepro)+ placebo (D) Fibre free (Osmolite, Promote) + placebo	NR	NR	NR	NR
5. Spapen 2001	Patients with severe sepsis, septic shock, ventilated N=35	C.Random: yes ITT: no Blinding: double (11)	Formula with soluble fibre (partially hydrolyzed guar) vs No fibre (standard)	Hospital 1/13 (8)	Hospital 4/12 (33)	Soluble fibre 13/13 (100)	Standard 12/12 (100)
6. Rushdi 2005	ICU patients N=30	C.Random: yes ITT: no Blinding: double (8)	Standard formula (Sandosource) + soluble Guar gum (Benefibre) vs. Fibre-free formula (Propeptide)	NR	NR	NR	NR

7. Karakan 2007	Patients with severe acute pancreatitis who stopped EN X 48 hrs N=30	C.Random: yes ITT: yes Blinding: double (10)	Standard formula plus a prebiotic multifibre supplement of soluble fibres and insoluble fibres (1.5 gms/100 mls) vs,standard formula alone. Both groups fed via NJ and received peripheral parenteral nutrition	Not specifed 2/15 (13)	Not specifed 4/15 (27)	3/15 (20)	6/15 (40)
8. Chittawatanarat 2010	Surgical ICU, septic patients receiving broad spectrum antibiotics and enteral nutrition N=34	C.Random: no ITT: yes Blinding: double (10)	Standard formula (Nutren fibre), 1.5 gm fibre/L, soluble fibres (FOS, pectin), insoluble fibres (cellulose, lignin, hemicellulose) vs. standard formula without fibre (Nutren Optimum).	Not specifed 1/17 (6)	Not specifed 2/17 (12)	NR	NR
9. Majid 2013	Adult critically ill pts N=47	C.Random: yes ITT: no Blinding: double (10)	Fibre/prebiotic enriched EN formula (Nutrison Multifibre vs. Nutrison protein plus Multifibre – both had 10% oligofructose, 20% inulin, 0.7 g/100ml soluble fibre, 0.8 g/100ml insoluble fibre) + 7 g/d oligofructose/inulin vs same EN formula choices + 7 g/d multidextrin	NR	NR	NR	NR
10. Xi 2017	Adults ICU patients requiring EN N=166	C.Random: yes ITT: no Blinding: no (5)	EN + 6 grams of pectin administered 4h before EN started on days 2 to 6 vs EN only. For both groups: 5% glucose at 25 ml/h started on day 1. EN (Peptisorb) started on day 2, EN advanced to goal slowly with goal to be achieved after day 7. EN given continuously over 20h per day.	30 day 1/62	30 day 3/63	Infectious complication events 7 (11.3%)	Infectious complication events 9 (14.3%)

Table 1. Randomized studies evaluating enteral feeds with fibre in critically ill patients (continued)

Study	LOS days Fibre	 Control	Other

1. Hart 1988	NR		NR		Fybogel Standard # Patients with diarrhea 19/35 (54) 19/33 (58) % Diarrhea days 66/287 (23) 68/297 (23) Mean Volume Received on Day 1 688 ml ± 204 628 ml ± 225 Mean Daily Feeds 1537 ml 1605 ml Total Feeding Days 287 297
2. Dobb 1990	NR		NR		Enrich Standard Diarrhea 16/45 (36) 13/46 (28) Mean Volume Received on Day 1 380 ml ± 172 494 ml ± 265
3. Heather 1991	NR		NR		Psyllium Standard Stool consistency 3.29 2.24 Stool frequency 2.26 2.01
4. Schultz 2000	(A) ICU 22.1 ± 16.4 Hospital 33.8 ± 22.1	(B) ICU 17.3 ± 8.2 Hospital 22.4 ± 9	(C) ICU 20.7 ± 8.5 Hospital 42.8 ± 3.3	(D) ICU 28 ± 14.6 Hospital 34 ± 14.7	Diarrhea* (A) (B) (C) (D) 1/11 (9) 4/11 (36) 6/11 (55) 1/11 (9) Fibre Intake (g) (A) (C) 174 ± 37.8 190 ± 27.2
5. Spapen 2001	Soluble fibre ICU 19 (11-51)		Standard ICU 17 (10-30)		Soluble fibre Standard # Patients with diarrhea 6/13 (46) 11/12 (92) % Diarrhea days 16/148 (11) 46/146 (32) Number of feeding days 148 146 Time to reach ptn/kcal goals (days) 5 ± 3 6 ± 3

6. Rushdi 2005	NR	NR	Benefibre Standard # Liquid stools - Day 1 1.0 1.2 # Liquid stools - Day 4 1.0 2.1 Feed volumes - Day 1 (ml) 1070 n/a Feed volumes - Day 4 (ml) 1775 1070
7. Karakan 2007	Reported as median ICU 6 ± 2 (7), P=NS Hospital 10 ± 4 (15), P<0.05	Reported as median ICU 6 ± 2 (6) Hospital 15 ± 6 (15)	Standard + fibre suppl Standard Median Duration of EN 8 ± 4 10 ± 4
8. Chittawatanarat 2010	ICU 16.8 ± 8.0 (16) Hospital 30.9 ± 28 (16)	ICU 25.5 ± 13.0 (15) Hospital 36.1 ± 14.8 (15)	Nutren Fibre Nutren Optimum # patients with at least 1 day of diarrhea 4/17 (23.5) 8/17 (47) Mean Diarrhea Score 3.6 ± 2.3 6.3 ± 3.6 Day achieved mean kcal intake (1500 kcal) Day 6 Day 8
9. Majid 2013	NR	NR	Oligofructose/Inulin Maltodextrin Pts w ≥ 1 day of diarrhea 11/12 (92) 9/10 (90) NS Days of diarrhea 3.9 ± 4.1 3.8 ± 3.5 NS
10. Xi 2017	ICU 13.8 ± 8.59 (62) Hospital 23.4 ± 13.2 (62)	ICU 17.9 ± 9.72 (63) Hospital 32.9 ± 19.0 (63)	Pectin No Pectin Time to reach full EN (days) 9.99 ± 1.91 13.0 ± 5.12, p=0.05 Vomiting 2 (3.2%) 3 (4.8%), p=0.05 Diarrhea 7 (11.3%) 16 (25.4%), p <0.001 Constipation 2 (3.2%) 7 (11.1%), p <0.001

C.Random: Concealed randomization
† Presumed ICU mortality unless otherwise specified
‡ Refers to the # of patients with infections unless specified** RR= relative risk

ITT: Intent to treat
NR: Not reported
CI: Confidence intervals

* Compared A+B+C to D for effect of fibre and/or pectin to placebo

Figure 1. Mortality

Study or Subgroup	Fibre Events	Fibre Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Spapen	1	13	4	12	22.8%	0.23 [0.03, 1.79]	2001
Karakan	2	15	4	15	40.2%	0.50 [0.11, 2.33]	2007
Chittawatanarat	1	17	2	17	17.9%	0.50 [0.05, 5.01]	2010
Xi	1	62	3	63	19.1%	0.34 [0.04, 3.17]	2017
Total (95% CI)		**107**		**107**	**100.0%**	**0.39 [0.15, 1.03]**	
Total events	5		13				

Heterogeneity: Tau² = 0.00; Chi² = 0.42, df = 3 (P = 0.94); I² = 0%
Test for overall effect: Z = 1.89 (P = 0.06)

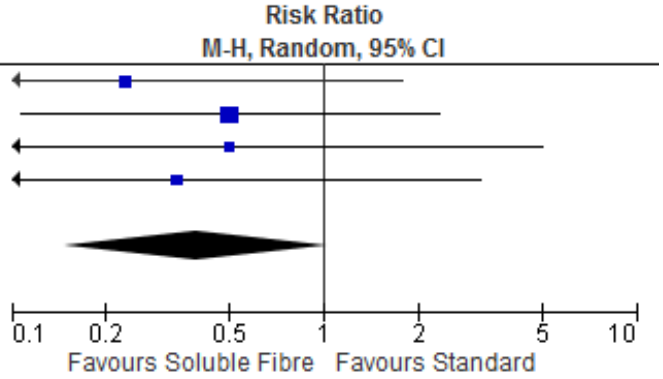

Figure 2. Infections

Study or Subgroup	Fibre Events	Fibre Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Spapen	13	13	12	12	46.7%	1.00 [0.86, 1.16]	2001
Karakan	3	15	6	15	23.7%	0.50 [0.15, 1.64]	2007
Xi	7	62	9	63	29.5%	0.79 [0.31, 1.99]	2017
Total (95% CI)		**90**		**90**	**100.0%**	**0.79 [0.35, 1.79]**	
Total events	23		27				

Heterogeneity: Tau² = 0.37; Chi² = 7.13, df = 2 (P = 0.03); I² = 72%
Test for overall effect: Z = 0.56 (P = 0.57)

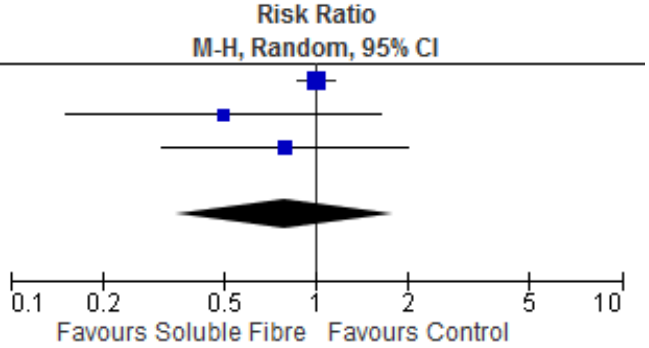

Figure 3. Hospital LOS

Study or Subgroup	Fibre Mean	Fibre SD	Fibre Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
Chittawatanarat	30.9	28	16	36.1	14.8	15	11.8%	-5.20 [-20.83, 10.43]	2010
Xi	23.4	13.2	62	32.9	19	63	88.2%	-9.50 [-15.23, -3.77]	2017
Total (95% CI)			**78**			**78**	**100.0%**	**-8.99 [-14.37, -3.61]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 3.28 (P = 0.001)

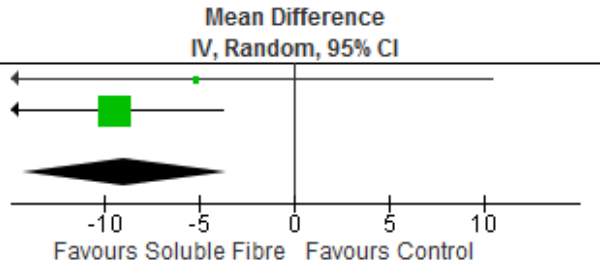

Figure 4. ICU LOS

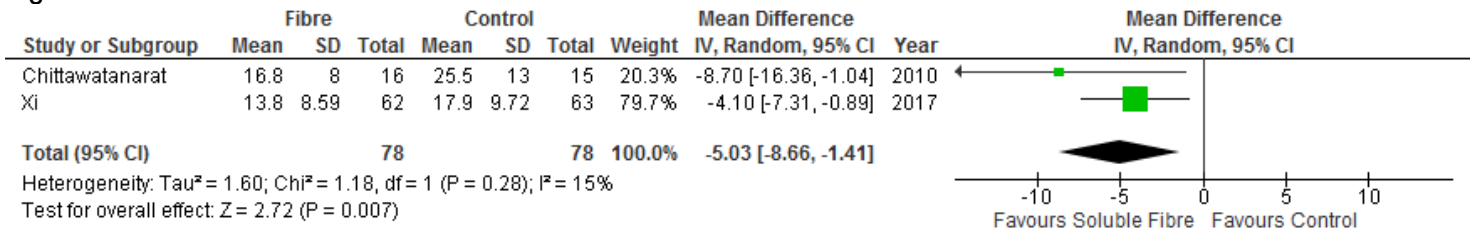

Figure 5. Diarrhea

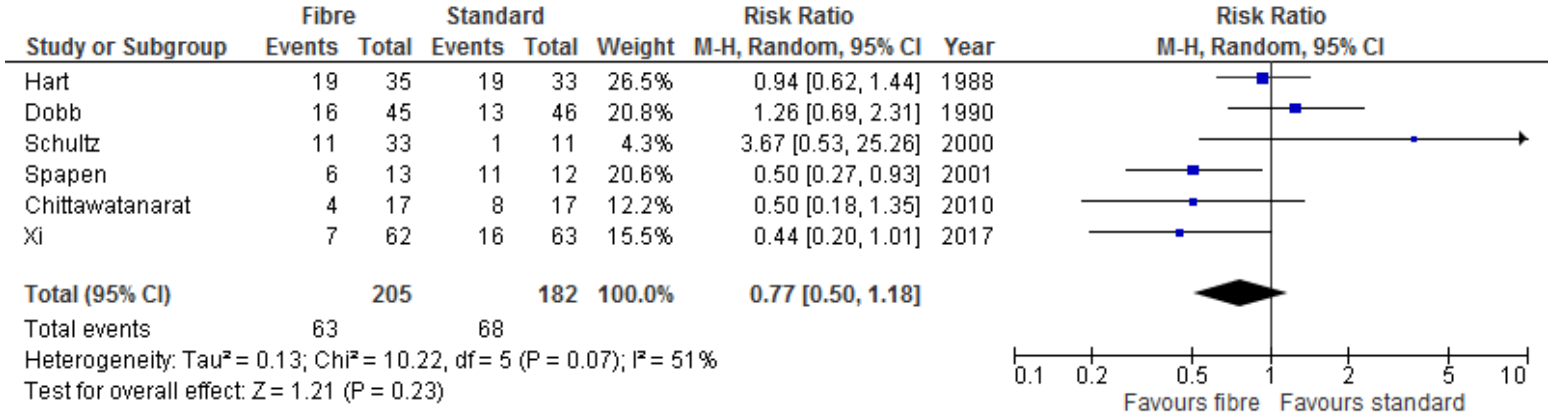

Table 2. Excluded Articles

#	Reason excluded	Citation
1	Crossover RCT	Frankenfield DC, Beyer PL. Soy-polysaccharide fiber: effect on diarrhea in tube-fed, head-injured patients. Am J Clin Nutr 1989;50(3):533-8.
2	Elective surgery pts	Borlase BC, Bell SJ, Lewis E, Swails W, Bistrian BR, Forse A, Blackburn GL. Tolerance to enteral tube feeding diets in hypoalbuminemic critically ill, geriatric patients. Surgery, Gyn Obs 1992;174:181-188.
3	No clinical outcomes	Levinson M, Bryce A. Enteral feeding, gastric colonisation and diarrhoea in the critically ill patient: is there a relationship? Anaesth Intensive Care. 1993 Feb;21(1):85-8.
4	Not ICU pts	Homann HH, Kemen M, Fuessenich C, Senkal M, Zumtobel V. Reduction in diarrhea incidence by soluble fiber in patients receiving total or supplemental enteral nutrition. JPEN J Parenter Enteral Nutr 1994;18(6):486-490.
5	Not ICU pts	Khalil L, Ho KH, Png D, Ong CL. The effect of enteral fibre-containing feeds on stool parameters in the post-surgical period. Singapore Med J. 1998 Apr;39(4):156-9.
6	Elective surgery pts	Rayes N, Hansen S, Seehofer D, Müller AR, Serke S, Bengmark S, Neuhaus P. Early enteral supply of fiber and Lactobacilli versus conventional nutrition: a controlled trial in patients with major abdominal surgery. Nutrition. 2002 Jul-Aug;18(7-8):609-15.
7	Elective surgery pts	Rayes N, Seehofer D, Hansen S, Boucsein K, Müller AR, Serke S, Bengmark S, Neuhaus P. Early enteral supply of lactobacillus and fiber versus selective bowel decontamination: a controlled trial in liver transplant recipients. Transplantation. 2002 Jul 15;74(1):123-7.
8	Only 30% were ICU patients (according to author)	Homann HH, Senkal M, Kemen M, Lehnhardt M. The beneficial effects of PHGG in enteral nutrition in medical and surgical patients. Clin Nutr Suppl 2004;1:59-62.
9	Meta-analysis	Yang G, Wu XT, Zhou Y, Wang YL. Application of dietary fiber in clinical enteral nutrition: A meta-analysis of randomized controlled trials.j World J Gastroenteral 2005;11(25):3935-3938.
10	Crossover study	Schneider SM, Girard-Pipau F, Anty R, van der Linde E et al. Effects of total enteral nutrition supplemented with a multi-fibre mix on faecal short-chain fatty acids and microbiota. Clin Nutr 2006;25:82-90.
11	Not ICU pts, only 15% ventilated	Plaudis H, Pupelis G, Zeiza K, Boka V. Early low volume oral synbiotic/prebiotic supplemented enteral stimulation of the gut in patients with severe acute pancreatitis: a prospective feasibility study. Acta Chir Belg. 2012 Mar-Apr;112(2):131-8.
12	Not ICU pts	Jakobsen LH, Wirth R, Smoliner C, Klebach M, Hofman Z, Kondrup J. Gastrointestinal tolerance and plasma status of carotenoids, EPA and DHA with a fiber-enriched tube feed in hospitalized patients initiated on tube nutrition: Randomized controlled trial. Clin Nutr. 2017 Apr;36(2):380-388.
13	Not ICU pts	Tabei I.; Tsuchida S.; Akashi T.; Ookubo K.; Hosoda S.; Furukawa Y.; Tanabe Y.; Tamura Y. Effects of a novel method for enteral nutrition infusion involving a viscosity-regulating pectin solution: A multicenter randomized controlled trial. Clin Nutr ESPEN. 2017.
14	Pseudo randomized	Tuncay P, Arpaci F, Doganay M, Erdem D, Sahna A, Ergun H, Atabey D. Use of standard enteral formula versus enteric formula with prebiotic content in nutrition therapy: A randomized controlled study among neuro-critical care patients. Clin Nutr ESPEN. 2018 Jun;25:26-36.