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 11 level 2 studies reviewed. Five studies looked at the effects of soluble fibres (Spapen 2001, Rushdi 2005: hydrolyzed guar; Hart 1988, Heather 1991: psyllium and Lu 2018: pectin and water soluble fibre from apple and citrus peel), one study (Dobb 1990) examined the effects of a formula containing soy polysaccharide (mainly insoluble fibre), three studies (Karakan 2007, Chittawatanarat 2010, Freedberg 2020) 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 6 studies that reported mortality were aggregated, fibre was associated with a trend towards a reduction in mortality (RR 0.54, 95% CI 0.26, 1.12, p=0.10, test for heterogeneity I^2=0%; figure 1).

Infections: When the data from the 4 studies that reported infections (Spapen 2001, Karakan 2007, Xi 2017, Freedberg 2020) were aggregated, no differences were found between the 2 groups (RR 0.85, 95% CI 0.48, 1.50, p=0.58, test for heterogeneity I^2=50%; figure 2).

Length of Stay: Six studies reported hospital and/or ICU length of stay, however, data from the Schultz 2000 study could not be aggregated since it reported LOS for only its sub-groups and Spapen 2001 and Karakan 2007 did not report this data as mean±SD. When the data from remaining three studies were aggregated, feeds with fibre had no effect on hospital LOS (WMD -4.09, 95% CI -15.24, 7.06, p=0.47, test for heterogeneity I^2=51%; figure 3) and a trend towards a reduction in ICU LOS (WMD -4.30, 95CI -9.40, 0.81, p=0.10, test for heterogeneity I^2=38%; 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. A fewer number of liquid stools (Rushdi 2005) and firmer stool consistency (p=0.03, Freedberg 2020) were reported in the high fibre groups compared to standard feeds.

Nutritional outcomes: High fibre groups met their target energy needs sooner (Chittawatanarat 2010, Xi 2017, Spapen 2001), met a higher % of target energy needs intakes (Lu 2018, Freedberg 2020), were able to receive higher volumes of feeds (Rushdi 2005) and had less feeding intolerance (Lu 2018) compared to the standard formula fed 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 trend towards a reduction in mortality and ICU length of stay
3) Enteral feeds with fibre compared to standard feeds have no effect on hospital 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 vs. Control	Infections # (%)‡ Fibre vs. 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
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
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
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
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) vs. 4/12 (33)	13/13 (100) vs. 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
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) vs. 4/15 (27)	3/15 (20) vs. 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) vs. 2/17 (12)	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
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 vs. 3/63	**Infectious complication events** 7 (11.3%) vs. 9 (14.3%)
11. Lu 2018	Adult ICU patients with brain/spinal cord injury N=28	C.Random: yes ITT: yes Blinding: single (9)	EN with semi solid nutrients (pectin gel and water soluble fibre from apple and citrus peel)l vs. EN. Both groups EN was given intermittently and started within 48-72 hrs	**30 day** 3/14 (21.4%) vs. 2/14 (14.2%) p =NS	NR
12. Freedberg 2020	Adult Medical ICU patients with sepsis N=22	C.Random: yes ITT: no Blinding: double (9)	EN with 14.3 g/L fibre (Promote 1.0 with Fibre) vs. EN without fibre (Promote 1.0). Both started at same time, similar rates of increase and up to 30 days.	**Hospital** 2/10 (20%) vs. 4/10 (40%)	**Culture proved infections** 3/10 (30%) vs. 3/10 (30%); p=NS

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); p=NS **Days of diarrhea** 3.9 ± 4.1 3.8 ± 3.5; p=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
11. Lu 2018	**ICU** 20.07 ± 25.71 (14) **Hospital** 40.64± 40.87 (14)	**ICU** 14.36 ± 7.59 (14) **Hospital** 26.71± 11.73 (14)	**Pectin** **No Pectin** **3 days caloric intake** 2589.29 ± 844.02 1685.71 ± 388; p<0.01 **Percent prescribed calories received, mean SD** 98% ±6 73% ± 15; p<0.01 **Received target protein, n(%)** 10/14 (71.4%) 9/14 (64%); p=0.5 **Feeding intolerance, n(%)** 2 (14.3) 8(57.1); p=0.046 **Stress hyperglycemia, n(%)** 6/11 (54.5) 8/14 (57.1); p=1.00
12. Freedberg 2020	**NR**	**NR**	**Fibre** **No Fibre** **Number of stools/day, median (IQR)** 1 (0.33-3.33) 1.67 (0.67-2.67); p=0.85 **Stool consistency (5 point likert scale with 0 (most liquid) to 5 (hard)** 1.7 (1.1-2.9) 0.8 (0.43-1.2); p=0.03 **Day 3 % energy needs achieved** 58% (24-84) 33% (2-52); p=0.24

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	12.6%	0.23 [0.03, 1.79]	2001
Karakan	2	15	4	15	22.2%	0.50 [0.11, 2.33]	2007
Chittawatanarat	1	17	2	17	9.9%	0.50 [0.05, 5.01]	2010
Xi	1	62	3	63	10.5%	0.34 [0.04, 3.17]	2017
Lu	3	14	2	14	19.8%	1.50 [0.29, 7.65]	2018
Freedberg	2	10	4	10	24.9%	0.50 [0.12, 2.14]	2020
Total (95% CI)		**131**		**131**	**100.0%**	**0.54 [0.26, 1.12]**	
Total events	10		19				

Heterogeneity: Tau² = 0.00; Chi² = 2.38, df = 5 (P = 0.79); I² = 0%
Test for overall effect: Z = 1.66 (P = 0.10)

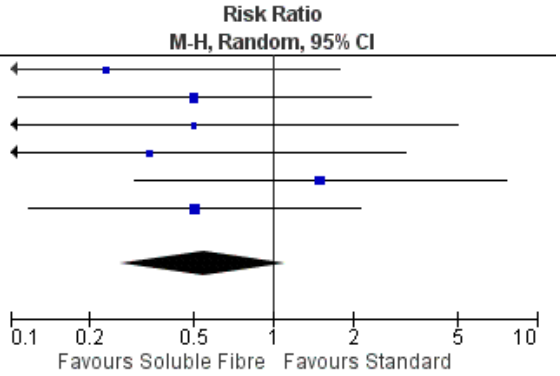


Figure 2. Infections

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	49.3%	1.00 [0.86, 1.16]	2001
Karakan	3	15	6	15	15.8%	0.50 [0.15, 1.64]	2007
Xi	7	62	9	63	21.7%	0.79 [0.31, 1.99]	2017
Freedberg	3	10	3	10	13.3%	1.00 [0.26, 3.81]	2020
Total (95% CI)		**100**		**100**	**100.0%**	**0.85 [0.48, 1.50]**	
Total events	26		30				

Heterogeneity: Tau² = 0.16; Chi² = 5.97, df = 3 (P = 0.11); I² = 50%
Test for overall effect: Z = 0.55 (P = 0.58)

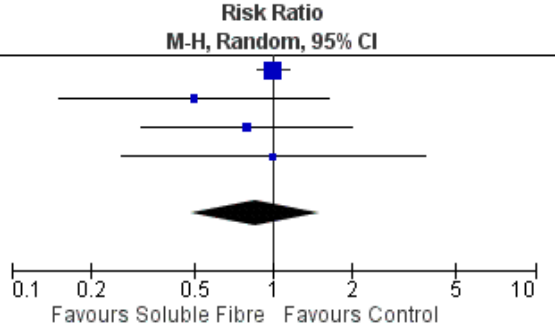


Figure 3. Hospital LOS

	Fibre			Control				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Chittawatanarat	30.9	28	16	36.1	14.8	15	28.1%	-5.20 [-20.83, 10.43]	2010
Xi	23.4	13.2	62	32.9	19	63	54.0%	-9.50 [-15.23, -3.77]	2017
Lu	40.64	40.87	14	26.71	11.73	14	17.9%	13.93 [-8.34, 36.20]	2018
Total (95% CI)			**92**			**92**	**100.0%**	**-4.09 [-15.24, 7.06]**	

Heterogeneity: Tau² = 51.44; Chi² = 4.10, df = 2 (P = 0.13); I² = 51%
Test for overall effect: Z = 0.72 (P = 0.47)

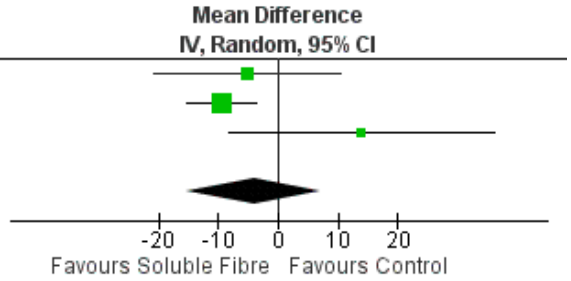


Figure 4. ICU LOS

	Fibre			Control				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Chittawatanarat	16.8	8	16	25.5	13	15	28.5%	-8.70 [-16.36, -1.04]	2010
Xi	13.8	8.59	62	17.9	9.72	63	60.2%	-4.10 [-7.31, -0.89]	2017
Lu	20.07	25.71	14	14.36	7.59	14	11.3%	5.71 [-8.33, 19.75]	2018
Total (95% CI)			**92**			**92**	**100.0%**	**-4.30 [-9.40, 0.81]**	

Heterogeneity: Tau² = 8.58; Chi² = 3.23, df = 2 (P = 0.20); I² = 38%
Test for overall effect: Z = 1.65 (P = 0.10)

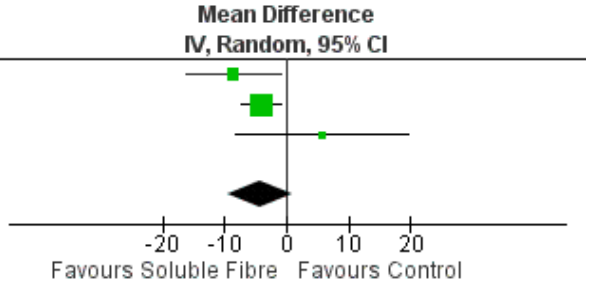
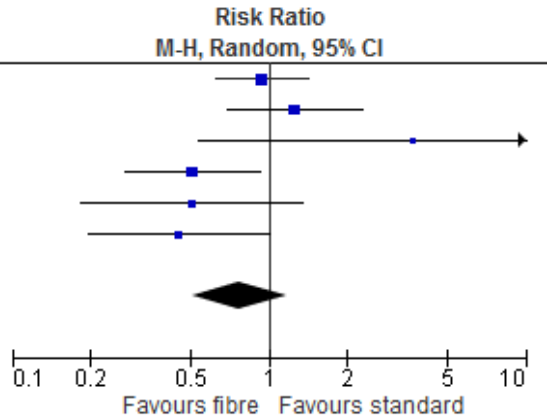


Figure 5. Diarrhea

	Fibre		Standard			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Hart	19	35	19	33	26.5%	0.94 [0.62, 1.44]	1988
Dobb	16	45	13	46	20.8%	1.26 [0.69, 2.31]	1990
Schultz	11	33	1	11	4.3%	3.67 [0.53, 25.26]	2000
Spapen	6	13	11	12	20.6%	0.50 [0.27, 0.93]	2001
Chittawatanarat	4	17	8	17	12.2%	0.50 [0.18, 1.35]	2010
Xi	7	62	16	63	15.5%	0.44 [0.20, 1.01]	2017
Total (95% CI)		**205**		**182**	**100.0%**	**0.77 [0.50, 1.18]**	
Total events	63		68				

Heterogeneity: Tau² = 0.13; Chi² = 10.22, df = 5 (P = 0.07); I² = 51%
Test for overall effect: Z = 1.21 (P = 0.23)



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