4.5 Composition of Enteral Nutrition: Strategies for optimizing EN and minimizing risks of EN: Fibre May 2015

2015 Recommendation: *There are insufficient data to support the routine use of fibre (soluble or insoluble) in enteral feeding formulas in critically ill patients*.

2013 Discussion: The committee noted that even with the addition of one trial (Majid 2013), the effect of fibre on the incidence of diarrhea was not evident. The committee agreed there was still a paucity of data that suggested fibre was associated with a reduction in mortality or hospital length of stay. The previously raised concerns about how fibre might be associated with some harm in select patients (i.e. hemodynamically unstable, at risk for bowel ischemia, significantly suppressed bowel motility)[1,2] still exists. Despite the low cost and high feasibility, the committee agreed that a recommendation for the use of fibre (soluble or insoluble) could still not be made.

1. Besselink MG et al, Acute Pancreatitis Werkgroep Nederland. [Probiotic prophylaxis in patients with predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial][Article in Dutch]. Ned Tijdschr Geneeskd. 2008 Mar 22;152(12):685-96.
2. Scaife CL, Saffle JR, Morris SE. Intestinal obstruction secondary to enteral feedings in burn trauma patients. *J Trauma*. 1999;47: 859-863

2013 Recommendation: *There are insufficient data to support the routine use of fibre (soluble or insoluble) in enteral feeding formulas in critically ill patients*.

2013 Discussion: The committee noted that with the addition of 2 new trials (Karakan 2007, Chittawatanarat 2010) the data suggesting a reduction in mortality and hospital length of stay with the use of fibre was still sparse. More directly related to fiber, the committee noted that there was no effect on diarrhea. It was also agreed that given our understanding of the physiological function of fibre, some patients, in isolated incidents, may be harmed by its use (i.e. hemodynamically unstable, at risk for bowel ischemia, significantly suppressed bowel motility)[1,2] .Despite the low cost and high feasibility, the committee agreed that a recommendation for the use of fibre (soluble or insoluble) could not be made.

1. Besselink MG et al Acute Pancreatitis Werkgroep Nederland. [Probiotic prophylaxis in patients with predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial][Article in Dutch] Ned Tijdschr Geneeskd. 2008 Mar 22;152(12):685-96.
2. Scaife CL, Saffle JR, Morris SE. Intestinal obstruction secondary to enteral feedings in burn trauma patients. *J Trauma*. 1999;47: 859-863

Semi Quantitative Scoring

Values	Definition	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 (infection) 2 (diarrhea)	2 (infection) 2 (diarrhea)
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	1	1
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
Homogeneity or Reproducibility	Similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	1	1
Adequacy of control group	Extent to which the control group represented standard of care (large dissimilarities = 1, minor dissimilarities=2, usual care=3)	2	2
Biological plausibility	Consistent with understanding of mechanistic and previous clinical work (large inconsistencies =1, minimal inconsistencies =2, very consistent =3)	2	2
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, heterogeneous patients, diverse practice settings =3.	1	1
Cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	3	3
Feasible	Ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	3	3
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	2

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 8 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, , 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 3 studies that reported mortality were aggregated, fibre was associated with a trend towards a reduction in mortality (RR 0.40, 95% CI 0.14, 1.19, p = 0.1, no heterogeneity present, heterogeneity I^2=0%; figure 1).

Infections: When the data from the 2 studies that reported infections (Spapen, Karakan) were aggregated, no differences were found between the 2 groups (RR 0.75, 95% CI 1.18, 3.15, p = 0.69, heterogeneity I^2=83%; figure 2).

Length of Stay: Four studies reported both hospital and ICU length of stay (Schultz, Karakan, Chittawatanarat, Spapen), however, data from the Schultz study could not be aggregated since it reported LOS for only its sub-groups and Spapen did not report this data as mean±SD. When the data from Karakan and Chittawatanarat were aggregated, enteral feeds with fibre were associated with a significant reduction in hospital LOS (RR -5.01, 95% CI -8.56, -1.46, p = 0.006, heterogeneity I^2=0%; figure 3), but had no effect on ICU LOS (RR -3.54, 95% CI -11.92, 4.83, p = 0.41, heterogeneity I^2=78%; figure 4).

Ventilator days: Not studied as an outcome

Diarrhea: Only in one study (Spapen), soluble fibre (hydrolyzed guar) was significantly associated with fewer diarrhea days ($p < 0.001$) and fewer # of patients with diarrhea (RR 0.50, CI 0.27- 0.93). Two studies did not report on the # patients with diarrhea and could not be included in the analysis. When the data from the remaining 4 studies were aggregated, fibre had no effect on diarrhea RR 0.75, 95% CI 0.43, 1.31, p =0.31, heterogeneity I^2=52 %; figure 5). Soy polysaccharide containing formula (Enrich) had no effect on diarrhea (Dobb 1990). 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 had no effect on diarrhea
2) Enteral feeds with fibre compared to standard feeds may be associated with a reduction in mortality, 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 # (%)†		Infections # (%)‡	
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	Fybogel NR	Standard NR	Fybogel NR	Standard NR
2. Dobb 1990	ICU patients N=91	C.Random: yes ITT: no Blinding: double (10)	Formula with soy polysaccharide (Enrich) vs Standard (Ensure)	Enrich NR	Standard NR	Enrich NR	Standard 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)	Psyllium NR	Standard NR	Psyllium NR	Standard 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)	Soluble fibre 1/13 (8)	Standard 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)	Benefibre NR	Standard NR	Benefibre NR	Standard 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	Standard + fibre suppl 2/15 (13)	Standard 4/15 (27)	Standard + fibre suppl 3/15 (20)	Standard 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).	Nutren Fibre 1/17 (6)	Nutren Optimum 2/17 (12)	Nutren Fibre NR	Nutren Optimum 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

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

Study	LOS days		Other
1. Hart 1988	Fybogel NR	Standard 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	Enrich NR		Standard 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	Psyllium NR		Standard 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	Benefibre NR		Standard 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	Standard + fibre suppl ICU 6 ± 2 (7) Hospital 10 ± 4 (15)		Standard ICU 6 ± 2 (6) Hospital 15 ± 6 (15)		Standard + fibre suppl Standard Median Duration of EN 8 ± 4 10 ± 4

8. Chittawatanarat 2010	Nutren Fibre ICU 16.8 ± 8.0 (16) Hospital 30.9 ± 28 (16)	Nutren Optimum 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

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

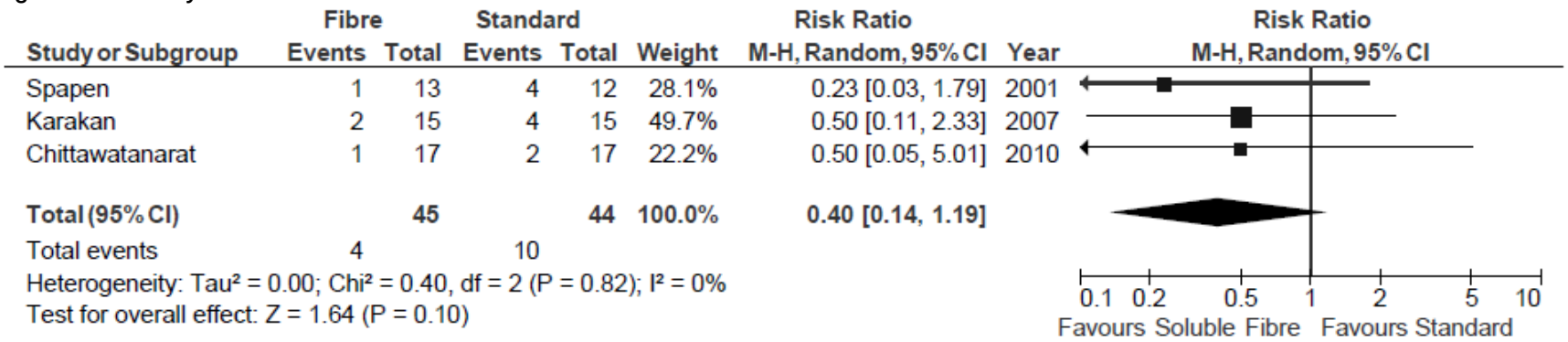

Figure 2. Infections

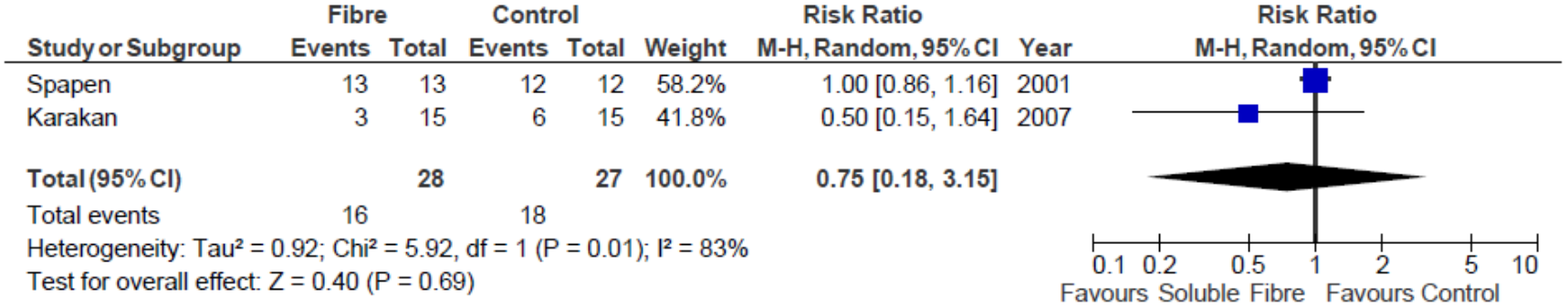

Figure 3. Hospital LOS

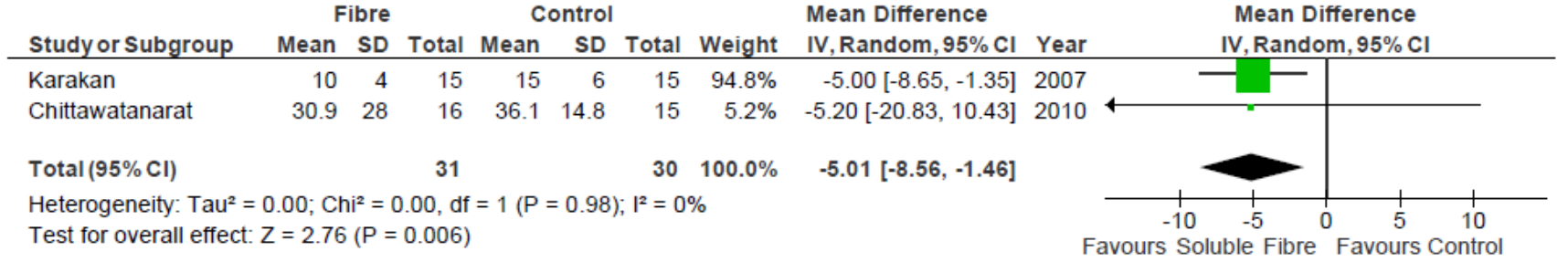

Figure 4. ICU LOS

Study or Subgroup	Fibre Mean	Fibre SD	Fibre Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
Karakan	6	2	7	6	2	6	59.3%	0.00 [-2.18, 2.18]	2007
Chittawatanarat	16.8	8	16	25.5	13	15	40.7%	-8.70 [-16.36, -1.04]	2010
Total (95% CI)			**23**			**21**	**100.0%**	**-3.54 [-11.92, 4.83]**	

Heterogeneity: Tau² = 29.59; Chi² = 4.59, df = 1 (P = 0.03); I² = 78%
Test for overall effect: Z = 0.83 (P = 0.41)

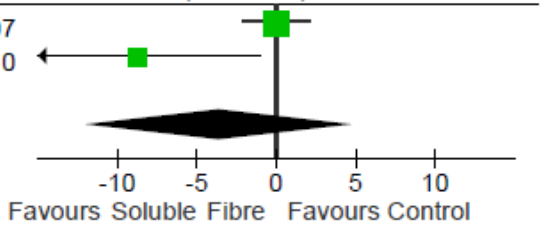

Figure 5. Diarrhea

Study or Subgroup	Fibre Events	Fibre Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Hart	19	35	19	33	40.6%	0.94 [0.62, 1.44]	1988
Schultz	11	33	1	11	7.2%	3.67 [0.53, 25.26]	2000
Spapen	6	13	11	12	32.4%	0.50 [0.27, 0.93]	2001
Chittawatanarat	4	17	8	17	19.8%	0.50 [0.18, 1.35]	2010
Total (95% CI)		**98**		**73**	**100.0%**	**0.75 [0.43, 1.31]**	
Total events	40		39				

Heterogeneity: Tau² = 0.15; Chi² = 6.21, df = 3 (P = 0.10); I² = 52%
Test for overall effect: Z = 1.01 (P = 0.31)