

1.0 The use of Enteral Nutrition vs. Parenteral Nutrition

June 28th, 2005

Recommendation:

Based on one level 1 and 12 level 2 studies, when considering nutrition support for critically ill patients, we strongly recommend the use of Enteral Nutrition over Parenteral Nutrition.

Discussion: The committee noted the homogenous results related to the effect of PN on infectious complications across several studies that when aggregated, resulted in a large effect size with narrow confidence intervals. Safety, cost and feasibility considerations favoured the use of EN over PN. The committee noted the results of the subgroup analysis of the studies in which the PN group received more calories and had higher blood sugars than the EN group. The increase in mortality or infections could not be attributed to a higher calorie intake or hyperglycemia. The committee also noted the paucity of data relating to malnourished, gastrointestinal compromised patients.

Values	definition	Score: 0, +, ++, +++
Effect size	magnitude of the absolute risk reduction attributable to the intervention listed--a higher score indicates a larger effect size	3+
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	3+
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+
Homogeneity	similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	3+
Safe	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+
Feasible	ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	3+
Low cost	estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	3+

1.0 Enteral Nutrition vs. Parenteral Nutrition

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Question: Does enteral nutrition compared to parenteral nutrition result in better outcomes in the critically ill adult patient?

Summary of evidence: There were 12 level 2 studies and one level 1 study (Woodcock et al) that were reviewed and meta-analyzed. In the Woodcock study, data from ICU patients only were abstracted and there were 11/38 patients that crossed over between EN and PN group after randomization. The data on mortality and infectious complications from the Moore 1989 study was included in the Moore 1992 meta-analysis whereas data on calorie intake, blood sugars and non septic complications were not and hence appear in the tables for the Moore 1989 study. Apriori, we considered that the harmful effect of PN may be associated with relative overfeeding and hyperglycemia. Accordingly, we conducted a subgroup analysis to determine the effect of excess calories (PN compared to EN) and higher glucose levels (across groups).

Mortality: 12 studies reported on mortality and when these were aggregated, there was no difference in mortality between the groups receiving EN or PN (RR 1.08, 95 % confidence interval 0.70, 1.65, $p = 0.7$) (See page 1-8). When the trials in which the PN group were fed more calories than the EN group were aggregated, EN was associated with a trend towards excess mortality (RR 1.58, 95% CI 0.75, 3.35, $p = 0.2$). When the trials in which the PN and EN groups were fed isocalorically were aggregated, there was no effect seen (RR 1.08, 95% CI 0.56, 2.06, $p = 0.8$). There was not statistical difference across these subgroups ($p=0.34$). Similarly, subgroup analysis comparing studies in which the PN group had higher blood sugars than the EN group to studies in which there was no difference in blood sugars showed that increased mortality in the PN groups could not be explained by hyperglycemia.

Infections: When the 7 studies which reported infectious complications were statistically aggregated, the meta-analysis showed that EN, compared to PN, was associated with a *significant* reduction in the incidence of infectious complications (RR 0.64, 95 % confidence interval 0.47, 0.87 $p = 0.004$) (see page 1-9). Subgroup analysis showed that the increase in infections could not be attributed to higher calories or hyperglycemia.

LOS, Ventilator days: Data not aggregated statistically due to insufficient data. There was no difference found in LOS (Rapp, Adams, Kudsk, Moore 1992) or ventilator days (Rapp, Adams Kudsk, Kalfarentzos) between the groups receiving EN or PN.

Other complications: Of the 11 studies that reported on nutritional intake, 5 found that PN was associated with a higher calorie intake (Rapp, Young, Moore, Kudsk, Woodcock {Blood sugar values in the Woodcock pertain to the entire group, not the ICU population}), the remaining 6 reported no significant difference in intakes between the groups (Adams, Hadley, Cerra, Dunham, Borzotta, Kalfarantzios).

5 studies reported on hyperglycemia and in 3 of these, EN was associated with a lower incidences of hyperglycemia compared to PN (Adams $p < 0.001$), (Borzotta $p < 0.05$, Kalfarentzos). Two studies showed no difference in blood sugars between the groups receiving EN and PN (Moore 1989, Rapp). Three studies showed that EN was associated with an increase in diarrhea (Cerra $p < 0.05$, Young, Kudsk $p < 0.01$) while one showed an association with EN and a reduction in diarrhea (Borzotta $p < 0.05$) and one study showed no difference (Adam). EN was also associated with an increase in vomiting (Cerra $p < 0.05$) and a less favourable neurological outcome at 3 months ($p = 0.05$) in brain injured patients (Young $p = 0.05$, this significance disappeared after 6months and 1 year. More overall nutrition related complications were noted in EN vs PN (Dunham).

Cost: Four studies reported a cost savings with the use of EN vs PN (Adams, Cerra, Borzotta and Kalfarentzos)

Conclusions:

- 1) The use of EN compared to PN is not associated with a reduction in mortality in critically ill patients.
- 2) The use of EN compared to PN is associated with a significant reduction in the number of infectious complications in the critically ill.
- 3) No difference found in ventilator days or LOS between groups receiving EN or PN.
- 4) Insufficient data to comment on other complications; hyperglycemia or higher calories not found to result in higher mortality of infections.
- 5) EN is associated with a cost savings when compared to PN.

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 EN vs PN in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				EN	PN	EN	PN
1) Rapp 1983	Head Injured patients n = 38 (<Ideal weight)	C.Random: not sure ITT: no Blinding: no (4)	EN vs PN	9/18 (50)	3/20 (15)	NA	NA
2) Adams 1986	Trauma patients undergoing laporotomy N= 46 36/46 ICU patients	C.Random: not sure ITT: yes Blinding: no (8)	EN vs PN	1/23 (4)	3/23 (13)	15/23 (65)	17/23 (74)
3) Young 1987	Brain injured patients N = 58	C.Random: not sure ITT: no Blinding: no (6)	EN vs PN	10/28 (36)	10/23 (43)	5/28 (18)	4/23 (17)
4) Peterson 1988	Critically ill patients with abdominal trauma N = 59	C.Random: not sure ITT: no Blinding: no (5)	EN vs PN	NA	NA	2/21 (10)	8/25 (32)
5) Cerra 1988	ICU patients post sepsis N = 70 (hypermetabolic patients)	C.Random: not sure ITT: no Blinding: no (2)	EN vs PN	7/31 (22) ICU	8/35 (23) ICU	0	0
6) Moore 1989	Abdominal trauma patients N = 75	C.Random: yes ITT: no Blinding: no (10)	EN vs PN	0	0	5/29 (17)	11/30 (37)

Table 1. (continued) Randomized studies evaluating EN vs. PN in critically ill patients

Study	LOS days		Ventilator days		Cost		Other	
	EN	PN	EN	PN	EN	PN	EN	PN
1) Rapp 1983	49.4 *	52.6*	10.3*	10.4*	NA	NA	Calorie intake (kcal) 685 1750 p = 0.001 Nitrogen intake (gms) 4.0 10.2 p = 0.002 hyperglycemia no difference between groups	
2) Adams 1986	13 ± 11 (19) ICU 30 ± 21 (19) hospital	10 ± 10 ICU 31 ± 29 (17) hospital	12 ± 11 (17)	10 ± 10 (13)	\$ 1346.00/day	\$ 3729.00/day	Calorie intake (kcal) 2088 2572 NS Hyperglycemia (pt. Days) 24/242 (10) 49/220 (22) p < 0.001 line problems 13/9 9/7 diarrhea 3.5 days/patient 3.8 days/patient	
3) Young 1987	NA	NA	NA	NA	NA	NA	Calories ÷ BEE x 1.75 59 % 76 % p = 0.02 protein intake (gm/kg/day) 0.91 ± 0.09 1.35 ± 0.12 p = 0.04 Favourable neurological outcome 3 months 17.9 % 43.5 % diarrhea 23/28 (82) 13/23 (57)	
4) Peterson 1988	13.2 ± 1.6 (21) hospital 3.7 ± 0.8 (21) ICU	14.6 ± 1.9 (24) hospital 4.6 ± 1.0 (25) ICU	NA	NA	NA	NA	Day 5 Calorie Intake (kcal) 2204 ± 173 2548 ± 85 Day 5 Nitrogen Intake (gms) 12.6 ± 1.0 14.8 ± 0.6	
5) Cerra 1988	NA	NA	NA	NA	\$ 228 ± 59 /day	\$ 330 ± 61 /day	Calorie intake 1684 ± 573 2000 ± 20 NS MOSF 7/31 (23) 7/35 (20) diarrhea 25/31 (81) 9/35 (26) vomiting 10/31 (32) 10/35 (6)	
6) Moore 1989	NA	NA	NA	NA	NA	NA	Kcal/kg/day 1847 ± 123 2261 ± 60 p = 0.01 Blood sugars No difference between the groups Non septic complications 6/29 (21) 7/30 (23)	

Table 1. (continued) Randomized studies evaluating EN vs. PN in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				EN	PN	EN	PN
7) Kudsk 1992	Abdominal trauma N = 98	C.Random: not sure ITT: no Blinding: single (10)	EN vs PN	1/51 ICU	1/45 ICU	9/51 (16)	18/45 (40)
8) Moore 1992	Meta-analysis High risk surgical patients N = 230	C.Random: NA ITT: NA Blinding: NA (NA)	EN vs PN	6/118 (5) ICU 8/118 (7) 30 day	7/112 (6) ICU 11/112 (10) 30 day	19/118 (16)	39/112 (35)
9) Dunham 1994	Blunt trauma N = 37	C.Random: not sure ITT: no Blinding: no (8)	EN vs PN	1/12 (7)	1/15 (8)	NA	NA
10) Borzotta 1994	Closed head injury N = 59	C.Random: not sure ITT: no Blinding: no (6)	EN vs PN	5/28 (18)	1/21 (5)	51/28 per group	39/21 per group
11) Hadfield 1995	ICU patients, mainly cardiac bypass N = 24	C.Random: not sure ITT: no Blinding: no (7)	EN vs PN	2/13 (15) ICU	6/11 (55) ICU	NA	NA

Table 1. (continued). Randomized studies evaluating EN vs. PN in critically ill patients

Study	LOS days		Ventilator days		Cost		Other	
	EN	PN	EN	PN	EN	PN	EN	PN
7) Kudsk 1992	20.5 ± 19.9 (51)	19.6 ± 18.8 (45)	2.8 ± 4.9 (51)	3.2 ± 6.7 (45)	NA	NA	Calorie intake (Kcal/kg/day) 15.7 ± 4.2 19.1 ± 3.3 p < 0.05 Diarrhea 11/51 7/45	
8) Moore 1992	17.0* hospital 4.4* ICU	22* hospital 7.3* ICU	NA	NA	NA	NA	NA	NA
9) Dunham 1994	NA	NA	NA	NA	NA	NA	Calorie intake No difference between the groups Protein intake No difference between the groups Nutrition related complications 3/12 (25) 2/15 (13)	
10) Borzotta 1994	39 ± 23.1 hospital	36.9 ± 14 hospital	NA	NA	\$ 121,941.00	\$ 112,450.00	Calorie intake No difference between the groups Placement complications 3/28 0/21 aspiration 3/28 0/21 hyperglycemia 12/28 (44) 16/21 (76) diarrhea 30 % 62 %	
11) Hadfield 1995	NA	NA	NA	NA	NA	NA	NA	NA

Table 1. (continued). Randomized studies evaluating EN vs. PN in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				EN	PN	EN	PN
12) Kalfarentzos 1997	Severe acute pancreatitis N = 38	C.Random: not sure ITT: no Blinding: single (9)	EN vs PN	1/18 (6) ICU	2/20 (10) ICU	5/18 (28)	10/20 (50)
13) Woodcock 2001**	Patients needing nutrition support n =562 ICU patients n =38 (all degrees of malnutrition)	C.Random: yes ITT: yes Blinding: single (12)	EN vs PN	9/17 (53)	5/21 (24)	6/16 (38)	11/21 (52)

Study	LOS days		Ventilator days		Cost		Other	
	EN	PN	EN	PN	EN	PN	EN	PN
12)Kalfarentzos 1997	11 (5-21) * ICU 40 (25-83) * hospital	12 (5-24)* ICU 39 (22-73) * hospital	15 (6-16) *	11 (7-31)*	Savings of 70 pounds/day	NA	Calorie intake (kcal/kg/day) 24.1 24.5 NS Protein intake (gm/kg/day) 1.43 1.45 NS hyperglycemia 4/18 (22) 9/20 (45)	
13) Woodcock 2001**	33.2 ± 43 (16)	27.3 ± 18.7 (18)	NA	NA	NA	NA	% target intake achieved 54.1 % 96.7 % p< 0.001 < 80% target intake 62.5 % 6.3 % p < 0.001	

C.Random: concealed randomization

* median/mean values, no standard deviation hence not included in meta-analysis

‡ refers to the # of patients with infections unless specified

** data on ICU patients obtained directly from authors

ITT: intent to treat

NA: not available

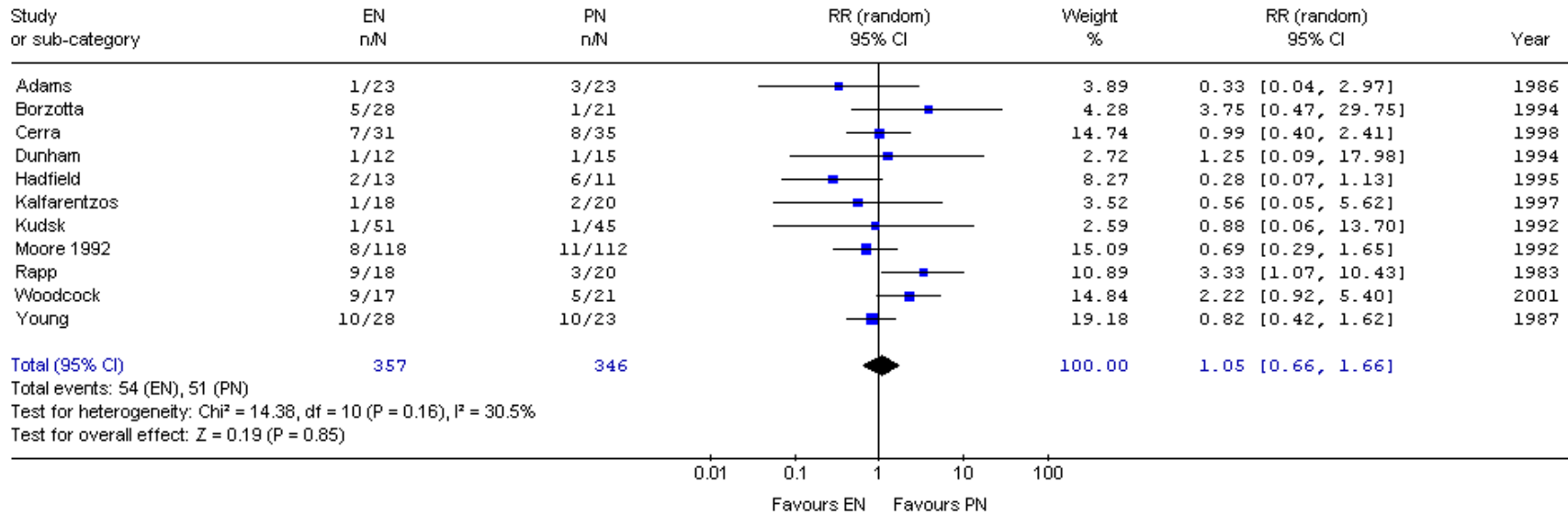
† presumed hospital mortality unless otherwise specified

± () : mean ± Standard deviation (number)

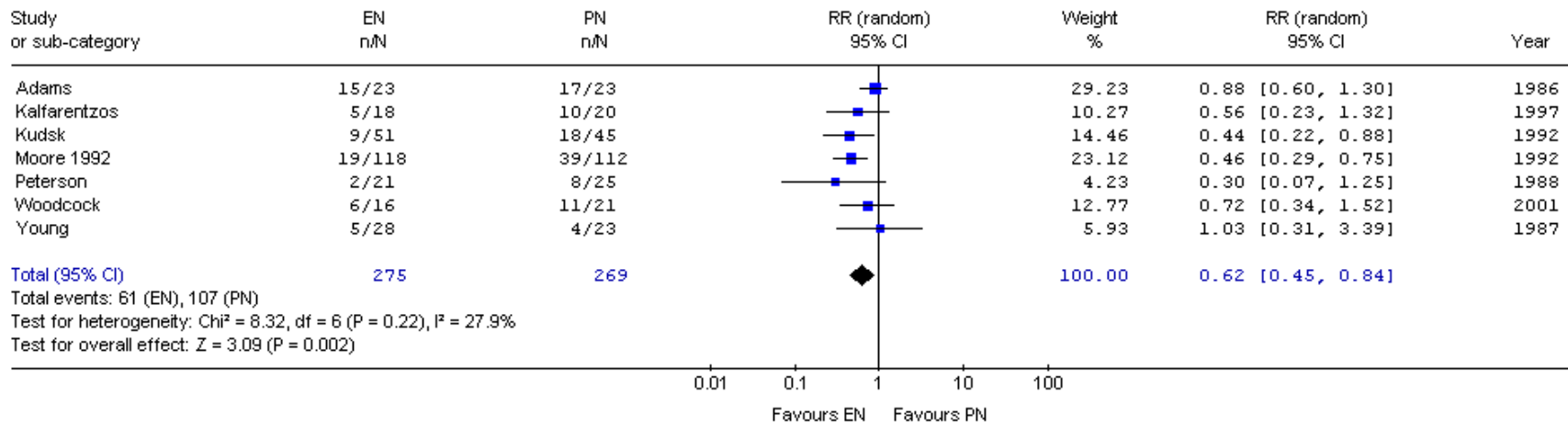
reported data pertaining to ICU patients only

NS = not statistically significant

Review: Enteral Nutrition vs Parenteral Nutrition
 Comparison: 01 EN vs PN
 Outcome: 02 Mortality



Review: Enteral Nutrition vs Parenteral Nutrition
 Comparison: 01 EN vs PN
 Outcome: 01 Infectious complications

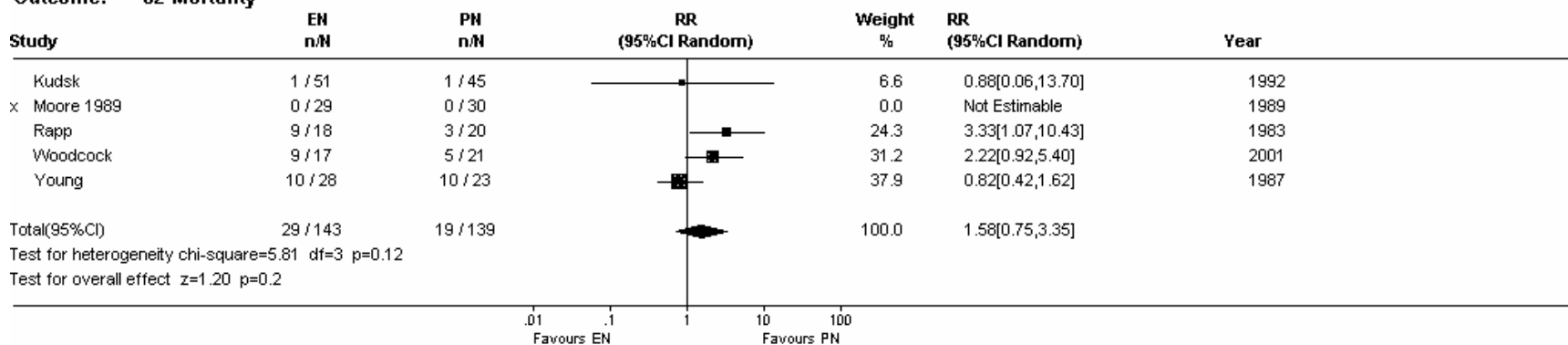


Subgroup analysis EN vs PN

Mortality in non-isocaloric studies (where the PN group received more calories than the EN group)

Comparison: 01 EN vs PN

Outcome: 02 Mortality

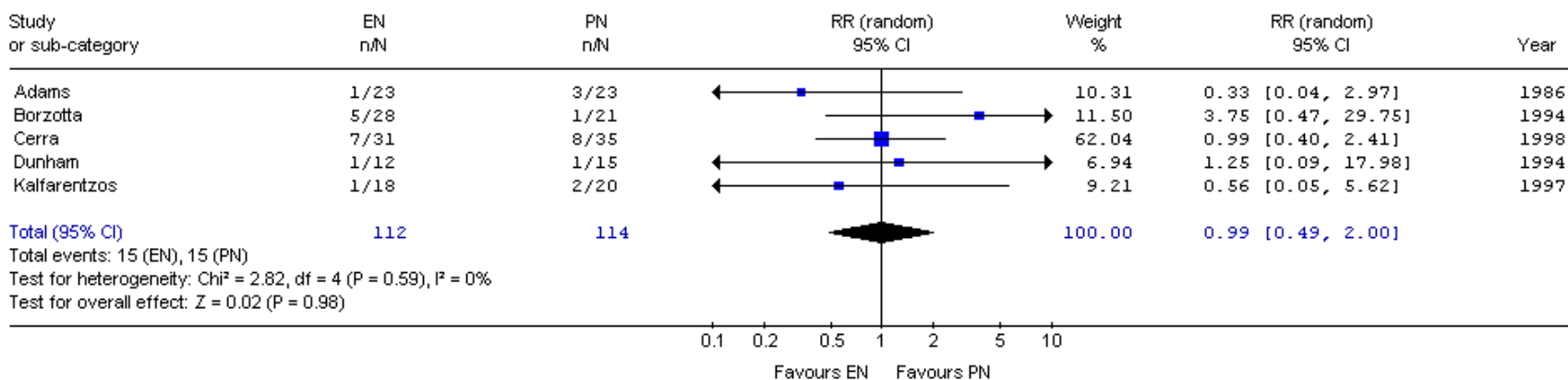


Mortality in isocaloric studies (where the PN group received similar calories to the EN group)

Review: [Enteral Nutrition vs Parenteral Nutrition](#)

Comparison: 01 EN vs PN

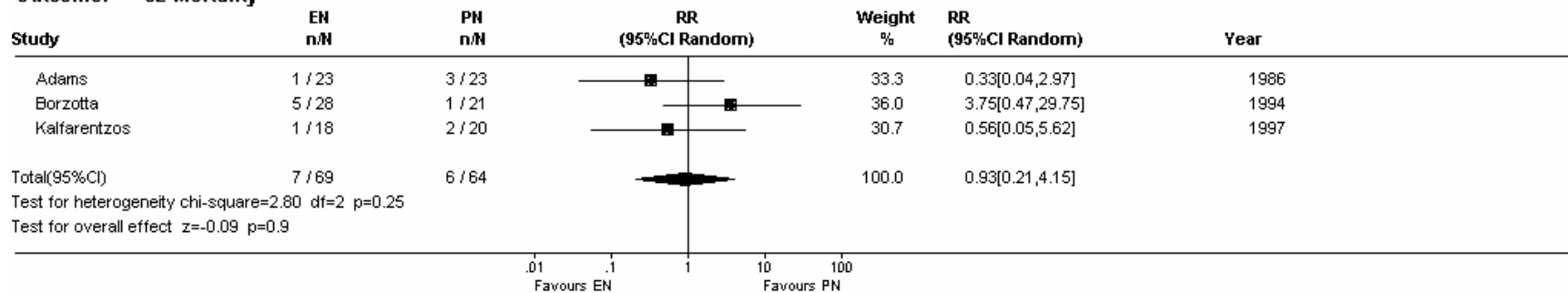
Outcome: 02 Mortality



Mortality in studies with hyperglycemia (where the PN group had higher blood sugars than the EN group)

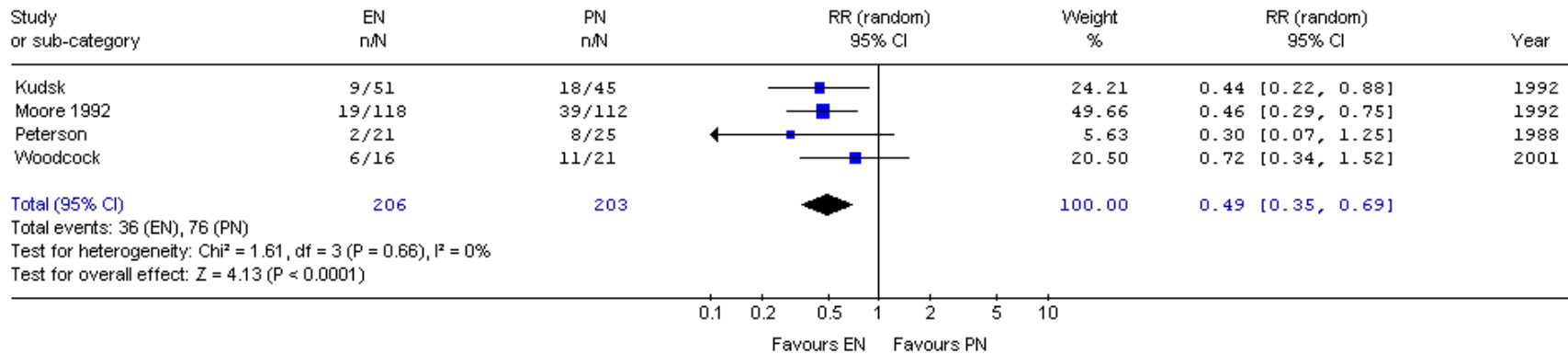
Comparison: 01 EN vs PN

Outcome: 02 Mortality



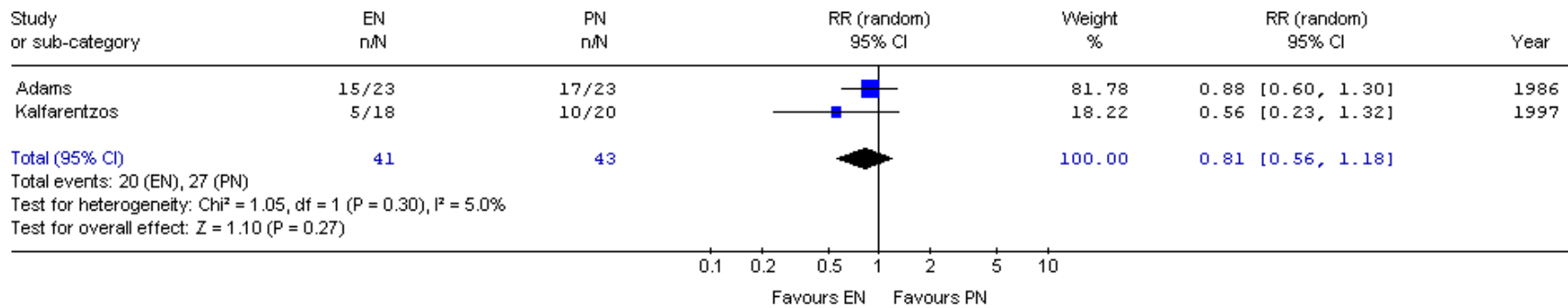
Infections in non-isocaloric studies (where the PN group received more calories than the EN group)

Review: Enteral Nutrition vs Parenteral Nutrition
 Comparison: 01 EN vs PN
 Outcome: 01 Infectious complications



Infections in isocaloric studies (where the PN group received similar calories to the EN group)

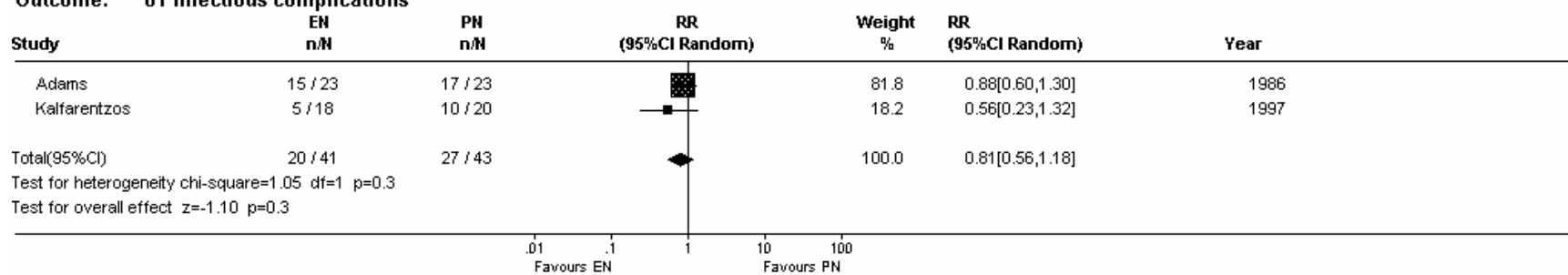
Review: Enteral Nutrition vs Parenteral Nutrition
 Comparison: 01 EN vs PN
 Outcome: 01 Infectious complications



Infections in studies with hyperglycemia (where the PN group had higher blood sugars than the EN group)

Comparison: 01 EN vs PN

Outcome: 01 Infectious complications



TOPIC: Enteral Nutrition vs. Parenteral Nutrition (EN vs. PN)

(Reviewers: Jaime Pinilla and Leah Gramlich)

Article inclusion log

Criteria for study selection

Type of study: RCT or Meta-analysis
Population: critically ill , ventilated patients (no elective surgical patients)
Intervention : TPN and /or EN
Outcomes: mortality, LOS, QOL, functional recovery, complications, cost. Exclude studies with only biochemical, metabolic or nutritional outcomes.

ID #		Author	Journal	I	E	why rejected
10.	1.	Borzotta	J Trauma 1994	√		
11.	2.	Cerra	Surgery 1988	√		
12.	3.	Hadfield	Am J Resp CCM '95	√		
13.	4.	Hadley	Neurosurgery 1986	√		
14.	5.	Kudsk	Annals Sx. 1992	√		
15.	6.	Moore	Annals Sx. 1992	√		
16.	7.	Moore	J Trauma 1989	√		
17.	8.	Woodcock	Nutrition 2001	√		
18.	9.	Dunham	J Trauma 1994	√		
19.	10.	Adams	J Trauma 1986	√		
20.	11.	Rapp	J Neurosurgery 1983	√		
21.	12.	Young	J Neurosurgery 1987	√		
22.	13.	Kalfrantzios	Brit Journal Sx. 1997	√		
42.	14.	Seri	Ital J Surg Sci 1984		√	Excluded April 2002 as not likely ICU patients
	15.	Braunschweig	Am J Clin Nutr 2001		√	Not all ICU patients, ICU studies from this article included.

ID #	Author	Journal	I	E	why rejected
16.	Hamaoui	JPEN 1990		√	Elective surgery pts.
17.	Bower	Archives Surgery '86		√	Elective surgery pts
18.	Kudsk	Gut 1994		√	Duplicate study of # 5
19.	Pacelli	Arch Surgery 2001		√	Elective surgery pts.
20.	Suchner	Nutrition 1996		√	No significant outcomes
21.	Huang	Clinical Nutrition 2000		√	Not RCT
22.	Braga	CCMedicine 2001		√	Elective surgery patients
23.	Bozetti	Lancet 2001		√	Elective surgery patients
24.	Von Meyenfeldt	Clinical Nutrition 1992		√	Elective surgery patients
25.	Fletcher	Surgery 1986		√	Surgery patients
26.	Wicks	Lancet 1994		√	Elective surgery patients
27.	Windsor	Gut 1998		√	Not ICU pts.
28.	Braga	CCMedicine 1998		√	Elective surgery patients
29.	Hernandez-Aranda	Nutr Hosp 1996		√	Not RCT, not ICU patients
30.	Peterson	Surgery 1988		√	No significant outcomes
31.	Young	J Neurosurgery 1987		√	No significant outcomes

I = included, E = excluded

Enteral Nutrition Vs. Parenteral Nutrition

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