7.0 Combination Parenteral Nutrition and Enteral Nutrition

January 31st, 2009

Recommendation:

Based on 5 level 2 studies, for critically ill patients starting on enteral nutrition we recommend that parenteral nutrition not be started at the same time as enteral nutrition. In the patient who is not tolerating adequate enteral nutrition, there are insufficient data to put forward a recommendation about when parenteral nutrition should be initiated. Practitioners will have to weigh the safety and benefits of initiating PN in patients not tolerating EN on an individual case-by-case basis. We recommend that PN not be started in critically ill patients until all strategies to maximize EN delivery (such as small bowel feeding tubes, motility agents) have been attempted.

Discussion: The committee noted that these data pertain to patients with an intact GI tract, not to those who have an absolute indication for parenteral nutrition. The committee reviewed the results of 5 level 2 studies that initiated PN at the same time as starting EN. When aggregated statistically, these studies suggested no benefit. The committee noted that the study results were homogenous and that when the trials in which the combination EN + PN group received more calories than the EN group were compared to those trials that did not, there was no difference in mortality. Given the probability of harm from trials of PN vs. EN in critically ill patients (see section 1.0 En vs. PN) and excess costs associated with the addition of PN when initiating EN, a recommendation against its use was put forward. However, the committee noted the absence of data from randomized trials related to patients not tolerating adequate amounts of EN and when PN should be used in combination in this scenario.

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

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Question: Does the use of parenteral nutrition in combination with enteral nutrition result in better outcomes in the critically ill adult patient?

Summary of evidence:
There were 5 level 2 studies that were reviewed and meta-analysed.

Mortality: All 5 studies reported on mortality. The meta-analysis shows that there was no effect on mortality with the use of combination EN + PN (RR 1.27, 95 % confidence interval 0.82-1.94, p = 0.3) (figure 1). When a sub group analysis was done comparing the trials that overfed to those that did not there was no difference in effect (figures 2,3).

Infections, LOS & ventilator days: Two studies looked at infections, length of stay and ventilator days (Chiarelli 1996 and Bauer 2000). Combination EN + PN was not associated with a higher incidence of infections (RR 1.14, 95 % confidence interval 0.66- 1.96, p = 0.6), had no effect on hospital stay (weighted mean difference {WMD} -2.86, 95 % confidence interval – 10.2, 4.48, p = 0.44) and no effect on ventilator days based on these two studies (WMD 0.58, 95% confidence interval – 1.74, 2.90, p = 0.62) (figures 4, 5, 6).

Other:
Cost: higher with combined group (Chiarelli/Bauer). Blood sugars were significantly higher in the EN + PN group when compared to the EN group but only on Day 7 in one study (Bauer et al) ($p < 0.05$). Chiarelli et al reported no difference in glycemia between the groups although no numbers were reported. None of the other studies reported on blood sugars.

Conclusions:

1) PN in combination with enteral nutrition in critically ill patients provides no added benefit compared to EN alone.
2) PN in combination with enteral nutrition is associated with a higher cost compared to EN alone.

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 combined EN + PN in critically ill patients

Study	Population	Methods (score)	Intervention (both interventions started at same time)	Mortality # (%)† EN + PN	Mortality # (%)† EN	Infections # (%)‡ EN + PN	Infections # (%)‡ EN
1) Herndon 1987	Burns > 50 % TBSA N = 28	C.Random: not sure ITT: yes Blinding: no (6)	EN + PN vs EN EN + PN group received significantly more calories than EN group	8/13 (62)	8/15 (53)	NA	NA
2) Herndon 1989	Burn patients N = 39	C.Randomization: not sure ITT: yes Blinding: no (7)	EN+ PN vs EN EN + PN group received significantly more calories than EN group	10/16 (63) > Day 14	6/23 (26) > Day 14	NA	NA
3) Dunham 1994*	Blunt trauma N = 37	C.Random: not sure ITT: no Blinding: no (8)	EN+ PN vs EN EN + PN group given same calories as EN	3/10 (30)	1/12 (8.3)	NA	NA
4)Chiarelli 1996	ICU patients medical and surgical N = 24	C.Random: not sure ITT: yes Blinding: no (8)	EN+ PN vs EN EN + PN were given 33 kcal/kg/day, EN were given 31 kcals/kg/day	3/12 (25)	4/12 (33)	6/12 (50)	3/12 (25)
5)Bauer 2000	Patients from 2 ICUs N =120 (all degrees of malnutrition)	C.Random: not sure ITT: yes Blinding: double (12)	EN+ PN vs EN + placebo. EN + PN received 24.6 ± 4.9 kcal/kg/day vs. EN group 14.2 ± 6.5 kcal/kg/day (p< 0.0001)	3/60 (5) before day 4 17/60 (28) Day 90	4/60 (6.7) before day 4 18/60 (30) Day 90	39/60 (65)	39/60 (65)

Table 1. Randomized studies evaluating combination parenteral nutrition and enteral nutrition in critically ill patients

Study	LOS days		Ventilator days		Cost		Other	
	EN + PN	EN	EN + PN	EN	EN + PN	EN	EN + PN	EN
1) Herndon 1987	NA	NA	NA	NA	NA	NA	NA	
2) Herndon 1989	NA	NA	NA	NA	NA	NA	NA	
3) Dunham 1994*	NA	NA	NA	NA	NA	NA	Nutrition related complications 5/10 (50)	3/12 (25)
4)Chiarelli 1996	37± 13 (12) hospital	41 ± 23 (12) hospital	19 ± 6 (12)	19 ± 2 (12)	50,000 lira/year more than EN	…	NA	NA
5)Bauer 2000	31.2 ± 18.5 (60) hospital 16.9 ± 11.8 (60) ICU	33.7 ± 27.7 (60) hospital 17.3 ± 12.8 (60) ICU	11 ± 9 (60)	10 ± 8 (60)	204 ± 119 Euro/pt/week	106 ± 47 Euro/pt/week	Glycemia on Day 7 (g/L) 1.16 ± 0.36	1.31 ± 0.49

C.Random: concealed randomization
* Dunham:only looked at data pertaining to EN+PN vs EN (not EN +PN vs PN)
± ( ) : mean ± Standard deviation (number)
ITT: intent to treat; NA: not available
† presumed hospital mortality unless otherwise specified
‡ refers to the # of patients with infections unless specified

Figure 1. Overall Mortality

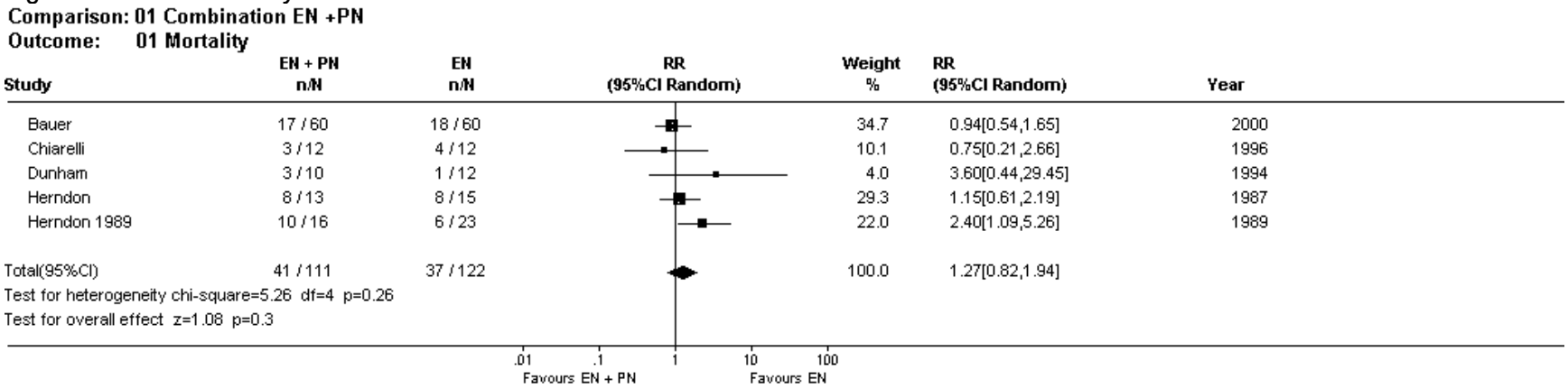


Figure 2. Sub group analysis: Mortality in non-isocaloric trials (where the comb EN + PN group received significantly more calories than the EN group)

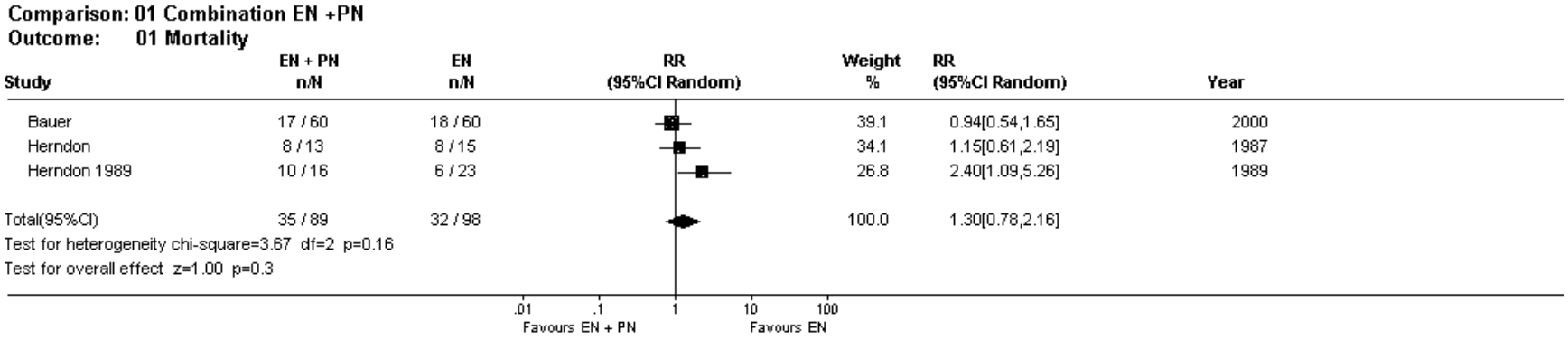


Figure 3. Sub group analysis: Mortality in the isocaloric trials (where the comb EN + PN received similar calories to the EN group)

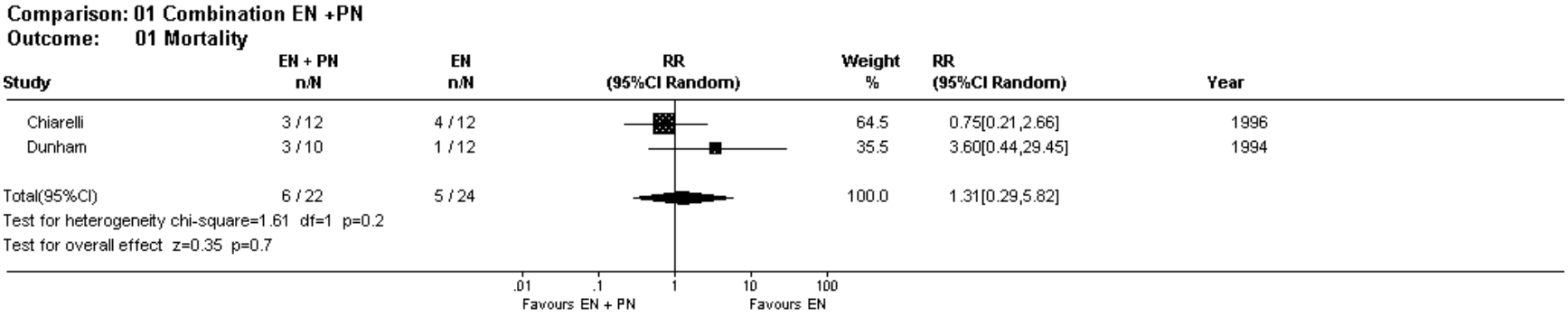


Figure 4.

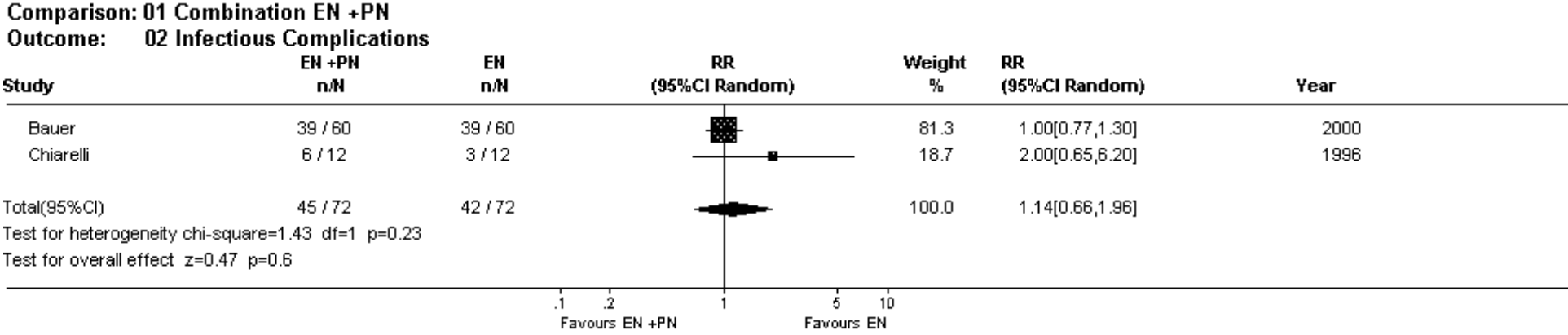


Figure 5.

Review: Supplemental EN +PN
Comparison: 01 Supplemental EN + PN vs. EN
Outcome: 03 Hospital LOS

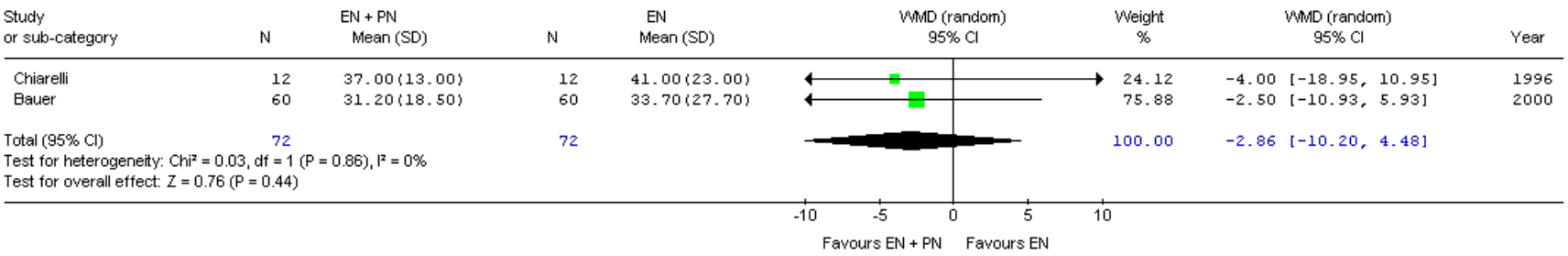
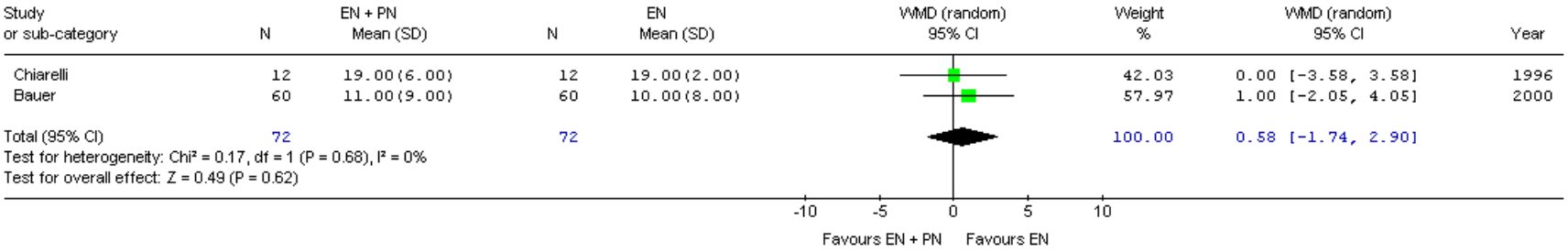


Figure 6.

Review: Supplemental EN +PN
Comparison: 01 Supplemental EN + PN vs. EN
Outcome: 04 Ventilator Days



TOPIC: 7.0 Combination EN + PN

Article inclusion log

Criteria for study selection

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

	Author	Journal	I	E	Why rejected
1	Hausmann	Int. Care Med 1985		√	Excluded as compares EN + PN to PN, not to EN
2	Herndon	J Trauma 1987	√		
3	Herndon	J Burn Care Rehab 1989	√		
4	Dunham	J Trauma 1994	√		
5	Chiarelli	Minerva Anaesth '96	√		
6	Bauer	Int Care Med 2000	√		
7	Dhaliwal	Int Care Med 2004		√	Systematic review, Individual studies included
8	Thomas	Journal of Nutrition 2005		√	Not ICU pts

I = included, E = excluded

References

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2. Herndon DN, Stein MD, Rutan TC, Abston S, Linares H (1987) Failure of TPN Supplementation to improve liver function, immunity, and mortality in thermally injured patients. J Trauma 27:195-204

3. Herndon DN, Barrow RE, Stein M, Linares H, Rutan TC, Rutan R, Abston S (1989) Increased mortality with intravenous supplemental feeding in severely burned patients. J Burn Care Rehabil 10:309-13

4. Dunham CM, Frankenfield D, Belzberg H, Wiles C, Cushing B, Grant Z (1994) Gut failure-predictor of or contributor to mortality in mechanically ventilated blunt trauma patients? J Trauma 37:30-4

5. Chiarelli AG, Ferrarello S, Piccioli A, Abate A, Chini G, Berioli MB, Peris A, Lippi R (1996) Total enteral nutrition versus mixed enteral and parenteral nutrition in patients in an intensive care unit. Minerva Anestesiol 62:1-7

6. Bauer P, Charpentier C, Bouchet C, Nace L, Raffy F, Gaconnet N (2000) Parenteral with enteral nutrition in the critically ill. Intensive Care Med 26:893-900

7. Dhaliwal R, Jurewitsch B, Harrietha D, Heyland DK. Combination enteral and parenteral nutrition in critically ill patients: harmful or beneficial? A systematic review of the evidence. Intensive Care Med. 2004 Aug;30(8):1666-71. Epub 2004 Jun 8.

8. Thomas DR, Zdrodowski CD, Wilson MM, Conright KC, Diebold M, Morley JE. A prospective, randomized clinical study of adjunctive peripheral parenteral nutrition in adult subacute care patients. J Nutr Health Aging. 2005 Sep-Oct;9(5):321-5.