

### 9.3 Composition of Parenteral Nutrition: Zinc (either alone or in combination with other antioxidants) June 28<sup>th</sup>, 2005

**Recommendation:**

*There are insufficient data to make a recommendation regarding IV/PN zinc supplementation in critically ill patients.*

**Discussion:** The committee noted the potentially large treatment effect of zinc enriched PN with respect to a reduction in mortality. The wide confidence intervals weaken this estimate. Safety, cost and feasibility issues were considered to be favourable. The committee noted that in some sub populations of critical illness with high zinc losses (GI fistula, burns, etc) there may be some benefit to zinc supplementation but data are lacking to support a recommendation.

	<b>definition</b>	<b>Score: 0, +, ++, +++</b>
<b>Effect size</b>	magnitude of the absolute risk reduction attributable to the intervention listed--a higher score indicates a larger effect size	<b>3+</b>
<b>Confidence interval</b>	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	<b>2+</b>
<b>Validity</b>	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	<b>3+</b>
<b>Homogeneity</b>	similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials	<b>1+</b>
<b>Safe</b>	estimated probability of avoiding any significant harm that may be associated with the intervention listed--a higher score indicates a lower probability of harm	<b>3+</b>
<b>Feasible</b>	ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	<b>3 +</b>
<b>Cost</b>	estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	<b>3+</b>

### 9.3 Composition of Parenteral Nutrition: Zinc (either alone or in combination with other antioxidants)

June 28<sup>th</sup>, 2005

**Question:** Does zinc supplementation (via IV/PN) given either alone or in combination with other nutrients result in improved outcomes in the critically ill patient?

**Summary of evidence:** There were 3 level 2 studies reviewed, one that compared a higher dose of parenteral zinc to a lower dose in ventilated head injured patients (Porter), both groups progressing to oral zinc (higher vs. lower). The other two studies compared IV zinc in combination with other antioxidants (selenium and  $\alpha$  tocopherol and copper) to placebo.

**Mortality:** When all three studies were aggregated, zinc supplementation was associated with a trend a reduction in mortality (RR = 0.55, 95 % confidence intervals 0.21-1.44, p = 0.2). See figure.

**Infections:** Only reported in two studies, one reported number of infections per patient (Young), hence unable to do a meta-analysis. The other study reported no differences in infectious complications between the two groups (Berger 2001).

**Hospital/ICU length of stay, ventilator days:** There were no statistical differences between the groups.

**Cost, other complications:** Only one study reported the number of patients with organ failure, which was the same in the group receiving zinc supplementation and none (Berger 2001)

#### **Conclusion:**

Zinc supplementation given IV/PN (either alone or in combination with other antioxidants) is associated with a trend towards a reduction in mortality in critically ill patients.

*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 zinc supplementation in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				Experimental	control	Experimental	control
1) ID # 90 Young 1996	Severely head injured patients, ventilated N = 68	C.Random: not sure ITT: yes Blinding: double (12)	12 mg elemental zinc via PN, then progressing to oral zinc vs. 2.5 mg elemental zinc, then progressing to oral placebo	4/33 (12)	9/35 (26)	NA	NA
2) ID # 30 Berger 1998	Burns > 30 % TBSA N = 20	C.Random: not sure ITT: yes Blinding: double blind (11)	IV Copper (40.4 μmol), selenium (2.0 μmol), zinc (406 μmol) + standard trace elements vs. standard trace elements (Copper 20 μmol, selenium 0.4 μmol, zinc 100 μmol) X 8 days, all received early EN	1/10 (10)	0/10 (0)	1.9 ± 0.9 (1-4) per patient	3.1 ± 1.1 (2-5) per patient
3) ID # 73 Berger 2001*	Trauma patients, surgical ICU N = 32	C.Random: not sure ITT: no Blinding: single (7)	IV Selenium + α tocopherol + zinc vs placebo (All groups received enteral nutrition)	0/11 (0)	1/11 (9)	3/11 (27)	3/11 (27)

**Table 2. Randomized studies evaluating zinc in critically ill patients**

Study	LOS days		Ventilator days		Cost		Other	
	Experimental	control	Experimental	control	Experimental	control	Experimental	control
1) ID # 90 Young 1996	NA	NA	NA	NA	NA	NA	NA	NA
2) ID # 30 Berger 1998	30 ± 12 (10) ICU 54 ± 27 (10) hospital	39 ± 13 (10) ICU 66 ± 31 (10) hospital	9 ± 10 (10)	12 ± 9 (10)	NA	NA	NA	NA
3) ID # 73 Berger 2001*	ICU 5.8 ± 4.4 (11) Hospital 60 ± 48 (11)	ICU 6.1 ± 6.0 (11) Hospital 59 ± 37 (11)	4.1 ± 3.6 (11)	4.2 ± 5.2 (11)	NA	NA	Organ failure 3/11 (27)      4/11 (36)	

C.Random: concealed randomization

ITT: intent to treat

NA: not available

‡ refers to the # of patients with infections unless specified

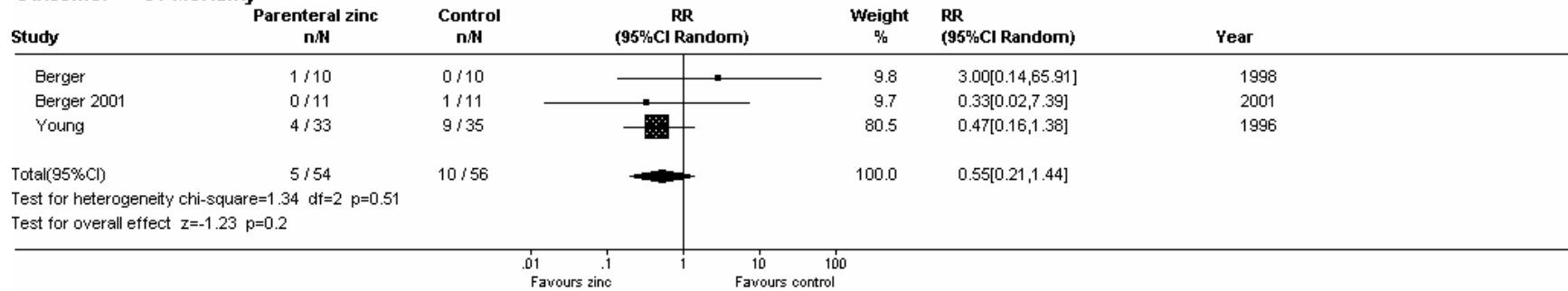
† presumed hospital mortality unless otherwise specified

\* only data pertaining to the selenium + α tocopherol + zinc vs placebo groups reported here

\*\*RR (CI): Relative risk (95 % confidence intervals)

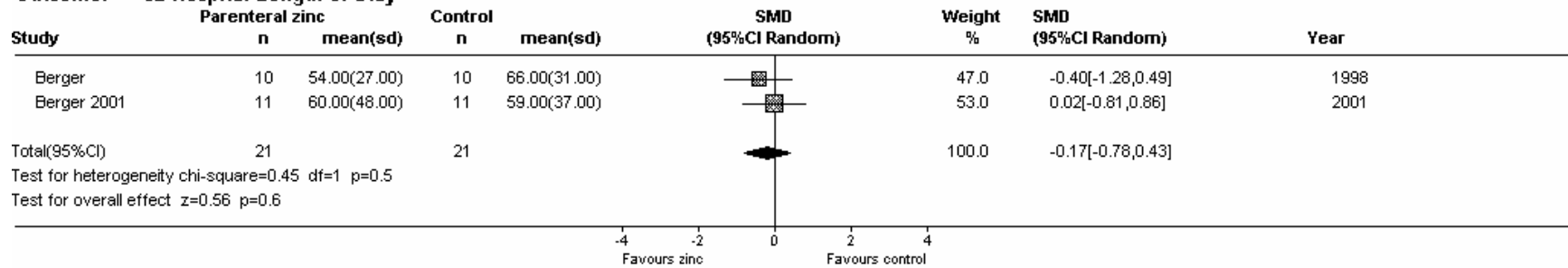
**Comparison: 01 Parenteral Zinc vs control**

**Outcome: 01 Mortality**



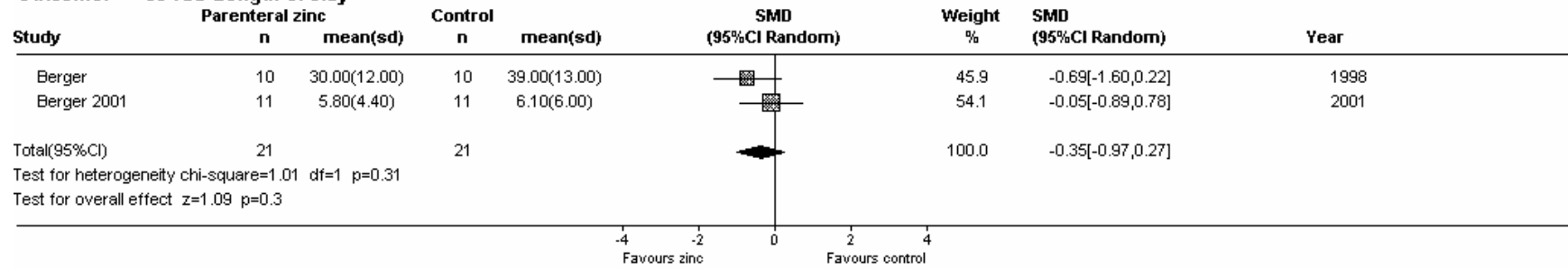
**Comparison: 01 Parenteral Zinc vs control**

**Outcome: 02 Hospital Length of Stay**



**Comparison: 01 Parenteral Zinc vs control**

**Outcome: 03 ICU Length of stay**



TOPIC: PN Composition: Zinc (alone or in combination)  
 (Reviewers: *Ulrich Suchner, Deborah Schroter-Noppe & Carmen Christman*)

Article inclusion log  
 Criteria for study selection

Type of study: RCT or Meta-analysis
Population: critically ill human patients (no elective sx.)
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
90	1.	Young	J of Neurotrauma 1996	√		
30	2.	Berger	Am J Clin Nutr 1998	√		
73	3.	Berger	Int Care Med 2001	√		

I = included, E = excluded

