10.1 Strategies to Optimize Parenteral Nutrition and Minimize Risks: Dose of PN

There are no new randomized controlled trials since the 2015 updates and hence there are no changes to the following summary of evidence.

Question: Does the dose of parenteral nutrition affect the outcome of critically ill patients?

Summary of evidence: Four level 2 studies have evaluated this question. Choban et al looked at low dose feeding in obese patients specifically. In the McCowen and Batistella studies, the control group was also given lipids as a source of calories. Ahrens et al studied the effect of a higher lipid, lower CHO parenteral solution (27 Kcals/kg/day) vs. a higher CHO, lower lipid PN solution (37 Kcal/kg/day)

Mortality: A meta-analysis of all 4 studies showed no effect on mortality (RR 0.61, 95 % CI 0.20,1.85, p = 0.4) (figure 1). This did not change when a sensitivity analysis was done without Ahrens et al (RR = 0.78, 95%CI 0.17, 3.56, p = 0.7) (figure 2) or without McCowen (RR = 0.65, 95% CI 0.10,4.05, p =0.6) (figure 3).

Infections: Three studies reported on the number of patients with infections. Batistella et al found a significant reduction in pneumonia in the low dose PN group ($p < 0.05$) and in the McCowen et al study, low dose PN was associated with a trend towards a reduction in infections (p = 0.2) while Ahrens et al found no significant difference in the number of patients with infectious complications (p = 0.4). When these 3 studies were aggregated, low dose PN has no effect on infectious complications (RR = 0.73, 95%CI 0.41,1.31, p = 0.3) (figure 4). In a sensitivity analysis without the Ahrens, low dose PN was associated with a significant reduction in infectious complications (RR=0.63, 95 % CI-0.42,0.93, p = 0.02) (figure 5).

LOS: A significantly shorter ICU stay (p = 0.02) and hospital stay (p = 0.03) was observed in trauma patients receiving low dose PN (Batistella). No differences in LOS were seen in the other three other studies (McCowen, Choban, Ahrens).

Ventilator days: Were reported in 2 studies. Significantly fewer ventilated days (p = 0.01) were observed in trauma patients receiving low dose PN (no lipids) compared to those receiving higher dose PN (with lipids) (Battistella). No differences were observed between the groups in surgical critically ill patients (Ahrens).

Other complications: Incidence of hypergylcemia was similar in the low dose and standard groups (McCowen), but significantly lower in the Ahrens et al study.

Conclusions:

1) Low dose parenteral nutrition without lipids maybe associated with a reduction in infections in critically ill patients.
2) Insufficient data to comment on the effects of low dose parenteral nutrition in obese 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 Dose of Parenteral Nutrition In Critically Ill Patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡		RR (CI)**
				Low dose	High dose	Low dose	High dose	
1) Ahrens 2003 unpublished	Surgical+ICU patients N=40	C:Random: not sure ITT: no Blinding: no (7)	Low dose PN (lipids/CHO) Pro 1.61g/kg/d±0.13, 27 kcal/kg/d vs. Standard PN, (lipids/CHO) Pro 1.53±0.26g/kg/d 37 kcaL/kg/d	1/20 (5)	3/20 (15)	5/20 (25)	2/20 (10)	2.50 (0.28-2.52)
2) Battistella 1997	Polytrauma patients N=60	C:Random: not sure ITT: no Blinding: no (8)	Lipid-free PN, Pro: 1.6g/kg/d 28.5kcal/kg/d vs. Standard PN (lipids/CHO), Pro 1.6g/kg/d 37kcal/kg/d	2/27 (7)	0/30 (0)	Pneumonia 13/27 (48) Line Sepsis 5/27 (19) Total # infections per group 39/27	Pneumonia 22/30 (73) Line Sepsis 13/30 (43) Total # infections per group 72/30	Pneumonia 0.66 (0.42-1.03) Line Sepsis 0.43 (0.18-1.04)
3) Choban 1997	ICU & hospital obese patients, ICU patients N=13	C: Random: yes ITT: yes Blinding: no (10)	Low dose PN (low lipids/CHO) Pro 2g/kg/d, 22kcal/kg/d vs. Standard PN, (low lipids/CHO) Pro 2 g/kg/d, 36 kcal/kg/d	Hospital 0/6 (0)	Hospital 2/7 (29)	NA	NA	NA
4) McCowen 2000	Probable ICU patients (mostly ventilated) N=48	C:Random: not sure ITT: no Blinding: no (6)	Low dose PN (no lipids), Pro 1.5 g/d, 14 kcal/kg/d vs. Standard PN (lipids,CHO), Pro 1.5 g/d, 18 kcal/kg/d	2/21 (10)	3/19 (16)	6/21 (29)	10/19 (53)	0.54 (0.24-1.21)

Table 1. Randomized Studies Evaluating Dose of Parenteral Nutrition In Critically Ill Patients (continued)

Study	LOS days		Ventilator days		Hyperglycemic Episodes	
	Low dose PN	Standard PN				
1) Ahrens 2003 [unpublished]	ICU 14 (10-21) Hospital 15 (11-26)	ICU 14(10-37) Hospital 14(10-37)	10 (4-15)	19 (4-35)	Low dose ≥200 mg/dl: 0 ≥300mg/dl: 0 ≥400mg/dl: 0 # pts with hyperglycemia 5/20 (25 %)	Standard ≥200mg/dl: 33.1%(0-58.4) ≥300mg/dl: 5 % (0-13.8) ≥400 mg/dl: 0% (0-1.5) # pts with hyperglycemia 14/20 (70%)
2) Battistella 1997	ICU 18±12 (27) Hospital 27 ±16 (27)	ICU 29±22 (30) Hospital 39±24 (30)	15 ±12 (27)	27 ± 21 (30)	NA	NA
3) Choban 1997	Hospital 48±30 (6)	Hospital 45±38 (7)	NA	NA	NA	NA
4) McCowen 2000	19±14 (21)	17±15 (19)	NA	NA	20%	26%

C. Random: concealed randomization
ITT: intent to treat
† presumed ICU mortality unless otherwise specified
NA: not applicable
LOS: length of stay
±():mean±Standard deviation (number)
‡ refers to the # of patients with infections
** RR= relative risk, CI=Confidence Intervals
ICU: intensive care unit
PN: parenteral nutrition

Figure 1. Mortality (with Ahrens)

Comparison: 01 Dose of PN
Outcome: 01 mortality

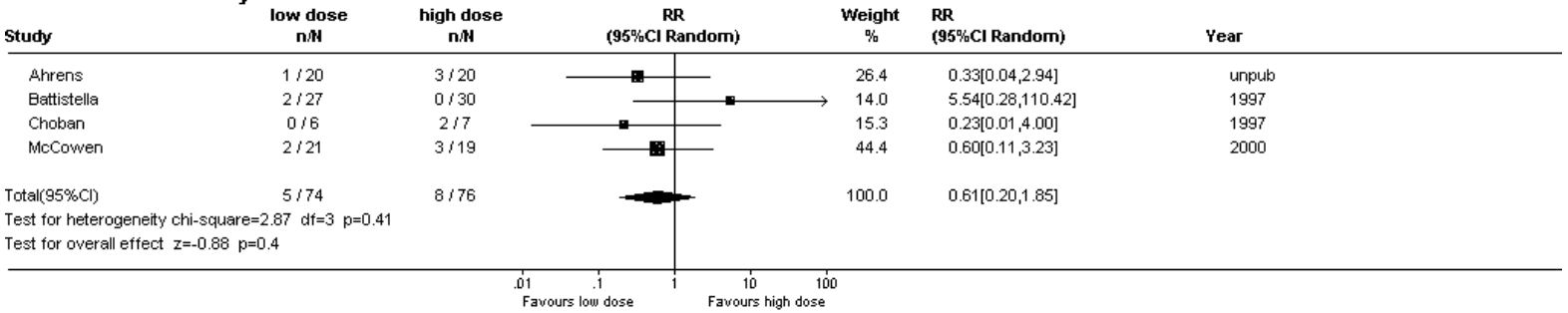

Figure 2. Sensitivity Analysis (Without Ahrens)

Comparison: 01 Dose of PN
Outcome: 01 mortality

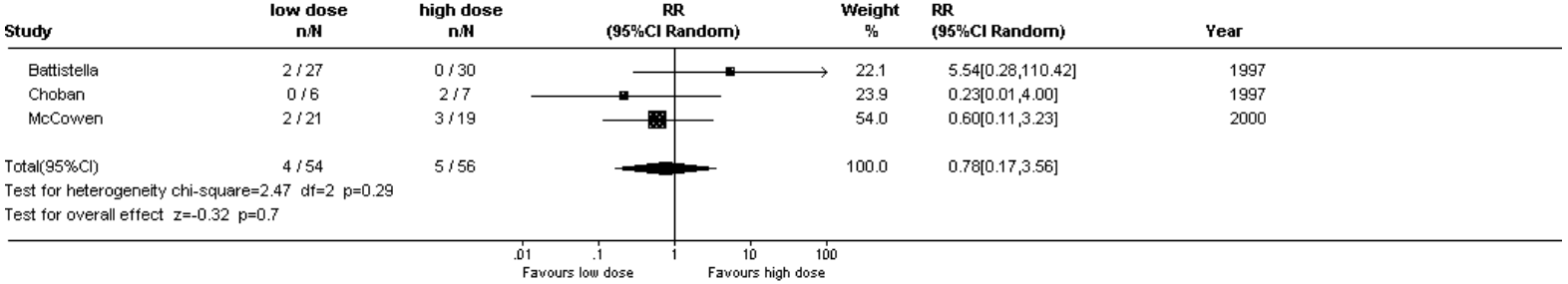

Figure 3. Sensitivity Analysis (without McCowen)

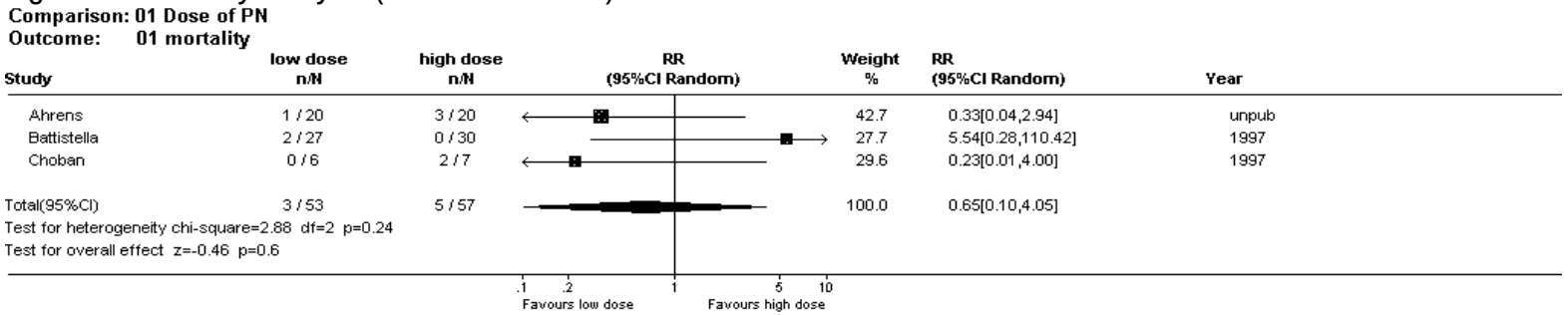

Figure 4.

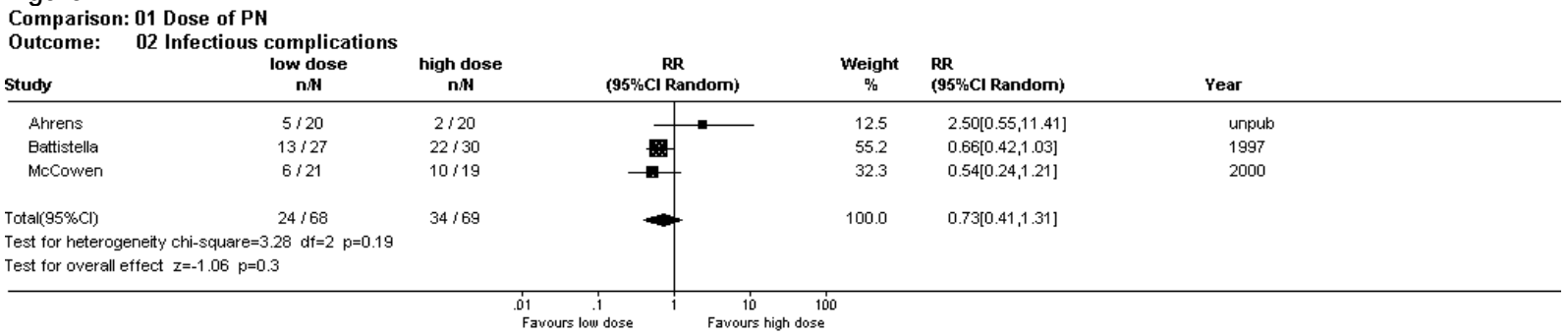

Figure 5. Sensitivity Analysis (without Ahrens)

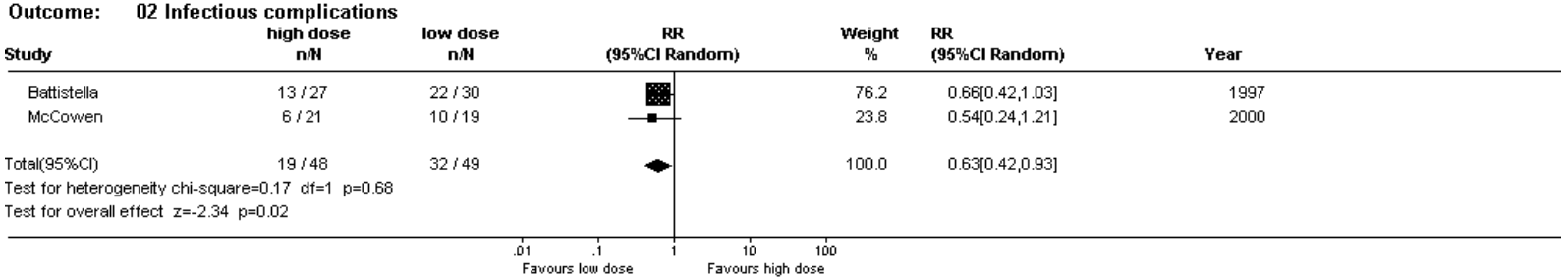

Table 2. Excluded Articles

#	Reason excluded	Citation
1	Not RCT, not ICU pts	Dickerson RN, Rosato EF, Mullen JL. Net protein anabolism with hypocaloric parenteral nutrition in obese stressed patients. Am J Clin Nutr. 1986 Dec; 44(6): 747-55.
2	Crossover trial and no significant outcomes	De Chalain TM, Michell WL, O'Keefe SJ, Ogden JM. The effect of fuel source on amino acid metabolism in critically ill patients. Surg Res. 1992 Feb; 52(2): 167-76.
3	Not ICU pts	Burge JC, Goon A, Choban PS, Flancbaum L. Efficacy of hypocaloric total parenteral nutrition in hospitalized obese patients: a prospective, double-blind randomized trial. JPEN J Parenter Enteral Nutr. 1994 May-Jun; 18(3): 203-7.
4	Elective surgery pts	Jiménez Jiménez FJ, Leyba CO, Jiménez Jiménez LM, Valdecasas MS, Montero JG. Study of hypocaloric peripheral parenteral nutrition in postoperative patients(European project). Clin Nutr. 1995 Apr;14(2):88-96.
5	Elective surgery pts	Schricker T, Meterissian S, Lattermann R, Adegoke OA, Marliss EB, Mazza L, Eberhart L, Carli F, Nitschman E, Wykes L. Anticatabolic effects of avoiding preoperative fasting by intravenous hypocaloric nutrition: a randomized clinical trial. Ann Surg. 2008 Dec;248(6):1051-9.
6	Elective surgery pts	Marton S, Ghosh S, Papp A, Bogar L, Koszegi T, Juhasz V, Cseke L, Horvath PO. Effect of glutamine in patients with esophagus resection. Dis Esophagus. 2010 Feb;23(2):106-11. Epub 2009 Aug 28.