9.1 Composition of Parenteral Nutrition: Branched Chain Amino Acids (BCAA)

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

Question: Do BCAA in parenteral nutrition affect outcomes in the critically ill adult patient?

Summary of evidence: There were 6 level 2 studies reviewed. One of the studies supplemented IV with BCAA in patients receiving EN and had another experimental group i.e. supplementation with IV glutamine (Ozgultekin 2008) and only the data pertaining to the BCAA group are presented here. Refer to section 9.4 for data on IV glutamine supplementation vs control from Ozgultekin 2008.

Mortality: There were 5 studies that reported on mortality, 4 of these found no significant difference in mortality between the groups receiving higher amounts of BCAA and lower amounts (von Meyenfeldt 1990 ,Vanway 1995, Kuhl 1990, Ozgultekin 2008). Only one study found a significant reduction in mortality ($p<0.03$) in septic patients receiving 45% BCAA vs lower (standard) amounts (Garcia de-Lorenzo). Meta-analysis of these studies showed a trend towards a reduction in mortality in the groups receiving BCAA (RR 0.71, 95% CI 0.42, 1.18, p=0.19, heterogeneity I^2=43%; figure 1). When a sensitivity analysis that excluded the Ozgultekin study was done, BCAA was still associated with a trend towards a reduction in mortality (RR 0.58, 95% CI 0.26, 1.28, p=0.18, heterogeneity I^2=54%; figure 2).

Infections: Two studies reported on infections and found no differences in infections with the use of BCAA (Ott 1988, p=0.68; Kuhl 1990, p=NS).

Length of Stay: Two studies reported on ICU length of stay (Garcia de Lorenzo, Ozgultekin) in which there were no differences between the groups receiving higher amounts of BCAA and standard amounts. The studies could not be aggregated since one study (Garcia de Lorenzo) did not report the standard deviation of the outcome.

Ventilator days: One study reported duration of ventilation and found no differences between the groups (Ozgultekin, p = 0.811).

Other complications: Not reported.

Conclusions:

1) Supplementation with higher amounts of BCAA may be associated with a reduction in mortality when compared to standard amounts of BCAA in ICU patients.
2) Supplementation with higher amounts of BCAA has no effect on infections, LOS or ventilated days in ICU 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 BCAA (PN) in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)		Infections # (%)‡	
1) Ott 1988	Brain injured patients N=20	C.Random: not sure ITT: yes Blinding: no (6)	BCAA (Aminosyn) vs standard PN (travasol)	BCAA NR	Standard NR	BCAA 4/10 (40)	Standard 4/10 (40)
2) Von Meyenfeldt 1990	Septic and traumatized patients N=101	C.Random: not sure ITT: yes Blinding: double (10)	50 % BCAA vs 16% BCAA (standard)	BCAA Hospital 17/49 (35)	Standard Hospital 16/52 (31)	BCAA NR	Standard NR
3) Van Way 1985	Mixed surgical population, severely stressed N=12	C.Random: not sure ITT: yes Blinding: no (7)	45 % BCAA vs 25% BCAA (standard)	BCAA Hospital 1/6 (17)	Standard Hospital 4/6 (67)	BCAA NR	Standard NR
4) Garcia De Lorenzo 1997	Septic patients from 7 ICUs N=69	C.Random: not sure ITT: yes Blinding: no (8)	3 groups: (A) standard BCAA + 1.5 g/kg/day AA (B) 45% BCAA + 1.5 g/kg/day AA (C) 45% BCAA + 1.1 g/kg/day AA Compared (B) + (C) to (A)	(A) ICU 9/22 (41) Hospital 10/22 (46)	(B) (C) 2/25 (8) 5/22 (23) 2/25 (8) 6/22 (27)	NR	
5) Kuhl 1990	Trauma patients requiring PN N=20	C.Random: not sure ITT: yes Blinding: no (8)	46% BCAA vs. 21% BCAA (standard)	BCAA 1/10 (10)	Standard 2/10 (20)	BCAA 9/10 (90)	Standard 9/10 (90)
6) Ozgultekin 2008	CHI & GCS patients, ventilated, sedated, mean APACHE II 18-19 N=60	C.Random: not sure ITT: no Blinding: none (4)	EN + IV BCAA x 10 days vs standard EN	BCAA 30-day 11/20 (55)	Standard 30-day 12/20 (60)	BCAA NR	Standard NR

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

Study	LOS days		Ventilator days		Cost		Other	
1) Ott 1988	BCAA NR	Standard NR	BCAA NR	Standard NR	BCAA NR	Standard NR	BCAA NR	Standard NR
2) Von Meyenfeldt 1990	BCAA NR	Standard NR	BCAA NR	Standard NR	BCAA NR	Standard NR	BCAA NR	Standard NR
3) Van Way 1995	BCAA NR	Standard NR	BCAA NR	Standard NR	BCAA NR	Standard NR	BCAA NR	Standard NR
4) Garcia De Lorenzo 1997	(A) 18.5	(B) ICU 14.4 / (C) 17.8	NR		NR		NR	
5) Kuhl 1990	BCAA NR	Standard NR	BCAA NR	Standard NR	BCAA NR	Standard NR	BCAA NR	Standard NR
6) Ozgultekin 2008	BCAA ICU 13.6 ± 9.4	Standard ICU 17.3 ± 16.4	BCAA 11.8 ± 8	Standard 14.4 ± 14	BCAA NR	Standard NR	BCAA NR	Standard NR

C.Random: concealed randomization
ITT: intent to treat
BCAA: Branched chain amino acids

NR: not reported
** RR= relative risk, CI= Confidence intervals
‡ number of patients with infections unless specified

LOS: length of stay
ICU: intensive care unit
AA: amino acids

Figure 1. Mortality

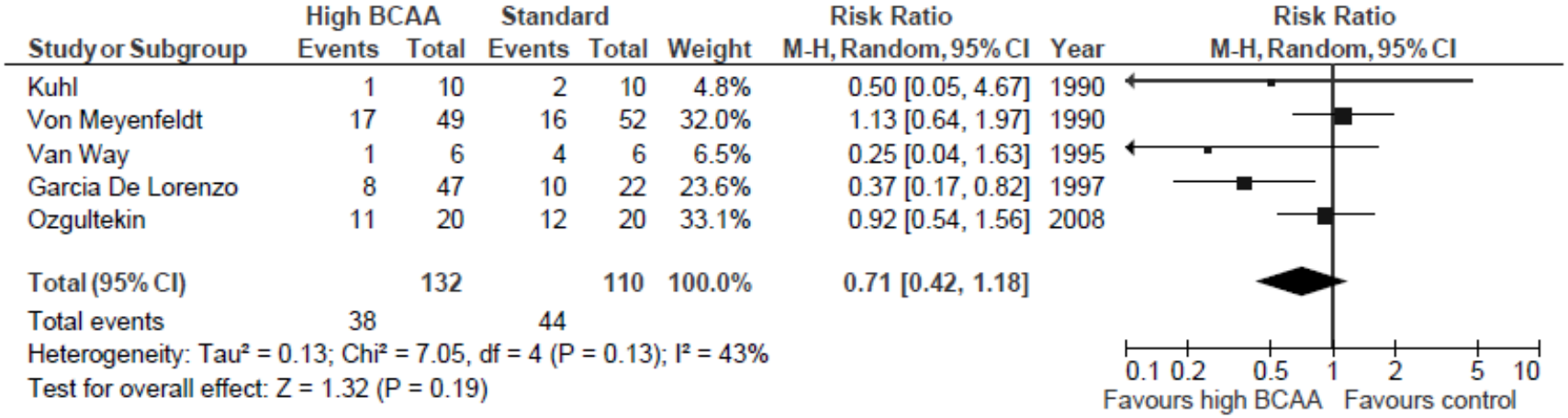

Figure 2. Mortality (excluding Ozgultekin)

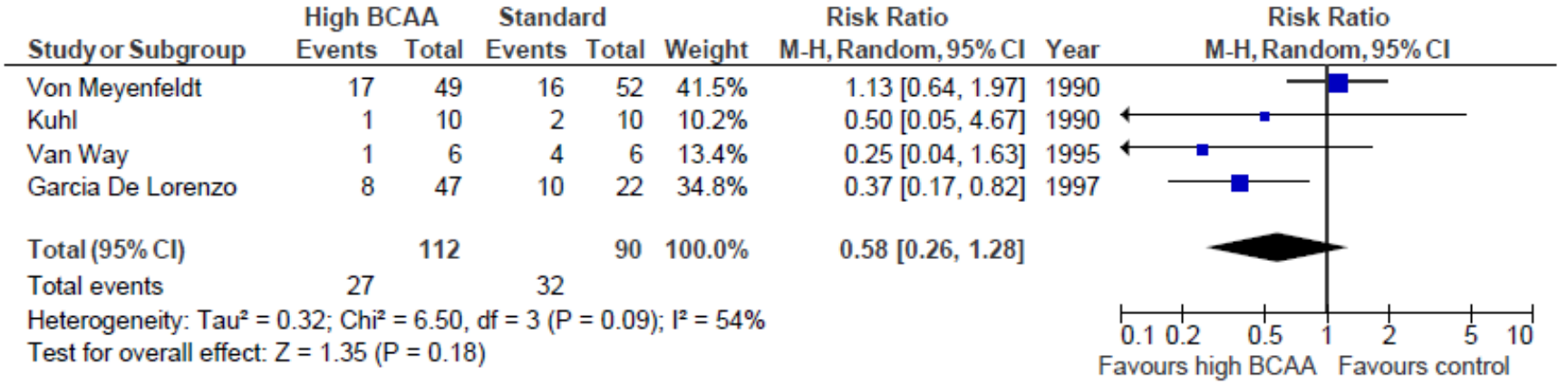

Table 2. Excluded Articles

#	Reason excluded	Citation
1	Not ICU pts	Rossi-Fanelli F, Riggio O, Cancgiano C, Cascino A, De Conciliis D, Merli M, Stortoni M, Giunchi G. Branched-chain amino acids vs lactulose in the treatment of hepatic coma: a controlled study. Digestive Diseases and Sciences. 1982 Oct;27(10):929-935
2	No clinical outcomes	Cerra FB, Mazuski J, Teasley K, Nuwer N, Lysne J, Shronts E, Konstantinides F. Nitrogen retention in critically ill patients is proportional to the branched chain amino acid load. Crit Care Med. 1983 Oct; 11(10): 775-8.
3	Not ICU pts	Wahren J, Denis J, Desurmont P, Eriksson LS, Escoffier JM, Gauthier AP, Hagenfeldt L, Michel H, Opolon P, Paris JC, Veyrac M. Is intravenous administration of branched chain amino acids effective in the treatment of hepatic encephalopathy? A multicenter study. Hepatology. 1983 Jul-Aug;3(4):475-80.
4	Not ICU pts	Cerra FB, Mazuski J, Teasley K, Nuwer N, Lysne J, Shronts E, Konstantinides F. Nitrogen retention in critically ill patients is proportional to the branched chain amino acid load. Crit Care Med. 1983 Oct;11(10):775-8.
5	No clinical outcomes	Iapichino G, Radrizzani D, Bonetti G, Colombo A, Damia G, Della Torre P, Ferro A, Leoni L, Ronzoni G, Scherini A. Parenteral nutrition of injured patients: Effect of manipulation of aminoacid infusion (increasing branched chain while decreasing aromatic and sulphurated aminoacids). Clin Nutr. 1985 Aug;4(3):121-8.
6	No clinical outcomes	Bower RH, Muggia-Sullam M, Vallgren S, Hurst JM, Kern KA, LaFrance R, Fischer JE. Branched chain amino acid-enriched solutions in the septic patient. A randomized, prospective trial. Ann Surg. 1986 Jan; 203(1): 13-20.
7	Crossover RCT	Vander Woude P, Morgan RE, Kosta JM, Davis AT, Scholten DJ, Dean RE. Addition of branched-chain amino acids to parenteral nutrition of stressed critically ill patients. Crit Care Med. 1986 Aug;14(8):685-8.
8	No clinical outcomes	Chiarla C, Siegel JH, Kidd S, Coleman B, Mora R, Tacchino R, Placko R, Gum M, Wiles CE 3rd, Belzberg H, et al. Inhibition of post-traumatic septic proteolysis and ureagenesis and stimulation of hepatic acute-phase protein production by branched-chain amino acid TPN.J Trauma. 1988 Aug; 28(8): 1145-72.
9	Not ICU pts	Naylor CD, O'Rourke K, Detsky AS, Baker JP. Parenteral nutrition with branched-chain amino acids in hepatic encephalopathy. A meta-analysis. Gastroenterology. 1989 Oct; 97(4): 1033-42
10	Pseudorandomized	Jiminez Jiminez JJ, et al. Prospective study on the efficacy of branched chain amino acids in septic patients. JPEN: 15(13):252 1991.
11	No clinical outcomes	Vente JP, Soeters PB, von Meyenfeldt MF, Rouflart MM, van der Linden CJ, Gouma DJ. Prospective randomized double-blind trial of branched chain amino acid enriched versus standard parenteral nutrition solutions in traumatized and septic patients. World J Surg. 1991 Jan-Feb;15(1):128-32; discussion 133.