

## 4.1c Composition of EN: Glutamine Systematic Review

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### 4.1c Composition of EN: Glutamine

#### Question:

Compared to standard care, does glutamine-supplemented enteral nutrition result in improved clinical outcomes in critically ill patients?

**Summary of Evidence:** There were 13 level 2 studies and 3 level 1 studies, 5 of which were in burn patients (Garrel 2003, Zhou 2003, Peng 2004, Pattanshetti 2009, Iamsirisaengthong 2017), 3 in trauma patients (Houdijk 1998, Brantley 2000 and McQuiggan 2008), 1 in elective cardiac surgery patients (Efremov 2017) and the remaining 7 were in mixed ICU patients. One study of mixed ICU patients also reported on the subgroup of trauma patients (van Zanten 2014).

**Mortality:** When the data from all the 11 trials that reported on 28 day or hospital mortality were aggregated, there was no statistically significant difference in overall hospital mortality between the groups receiving glutamine supplemented EN or not (RR 1.00, 95% CI 0.77, 1.30,  $p=1.00$ , test for heterogeneity  $I^2 = 0\%$ ) (figure 1). Subgroup analyses of the 4 studies of trauma patients showed that glutamine supplemented EN had no significant effect on hospital mortality (RR 1.03, 95% CI 0.54, 1.97,  $p = 0.92$ , test for heterogeneity  $I^2 = 0\%$ ) (figure 2). In the 4 studies of burn patients, patient deaths in hospital were reported in 3 studies (Garrel 2003, Pattanshetti 2009, Iamsirisaengthong 2017) and a significant reduction in hospital mortality was associated with the use of enteral glutamine (RR 0.26, 95% CI 0.08, 0.80,  $p = 0.02$ , test for heterogeneity  $I^2 = 0\%$ ) (figure 3).

**Infections:** Of the 2 level 2 studies and 2 level 1 studies that reported on the total number of patients with infectious complications, there was no statistically significant difference in infectious complications with glutamine supplemented EN (RR 0.93, 95% CI 0.79, 1.10,  $p = 0.39$ , test for heterogeneity  $I^2 = 0\%$ ) (figure 4). In the one study in burn patients that reported on patients with infections (Zhou 2003), glutamine supplemented EN was associated with a significant reduction in infectious complications while in one burn study (Garrel 2003) a significant reduction was seen in the number of positive blood cultures. In the subgroup of trauma patients, based on two studies, there was a trend towards a reduction in infections in the groups that received enteral glutamine (RR 0.85, 95% CI 0.68, 1.06,  $p = 0.15$ , test for heterogeneity  $I^2 = 0\%$ ) (figure 5). In one study in mixed ICU patients, there were no statistically significant differences in the incidence of new severe sepsis between the EN glutamine supplemented group (5.6%, 95% CI; 0–13.9%) and the control group (11.8%, 95% CI, 2.8–23.5%;  $p = 0.309$ , Shariatpanahi 2019).

**Length of Stay:** There were 8 level 2 studies and 1 level 1 study that demonstrated a significant reduction in hospital length of stay (LOS) [WMD (weighted mean difference) -4.13, 95% CI -6.95, -1.30,  $p = 0.004$ , test for heterogeneity  $I^2 = 41\%$ ] (figure 6). A stronger effect was seen in the subgroup of burn patients (WMD -8.18, 95% CI -12.69, -3.67,  $p = 0.0004$ , test for heterogeneity  $I^2 = 30\%$ ) (figure 7) but not seen in the subgroup of trauma patients (WMD -0.54 95% CI -4.40, 3.31,  $p = 0.78$ , test for heterogeneity  $I^2 = 0\%$ ) (figure 8). Enteral glutamine has no effect on ICU LOS (WMD -0.33, 95% CI -2.26, 1.60,  $p = 0.74$ , test for heterogeneity  $I^2 = 69\%$ ) (figure 9) when

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all studies were aggregated but was associated with a trend towards a reduction in the subgroup of trauma patients from two studies (WMD -4.66, 95% CI -9.68, 0.36,  $p = 0.07$ , test for heterogeneity  $I^2 = 0\%$ ) (figure 10).

**Mechanical ventilation:** Only 4 studies, including one in burn patients (Garrel 2003) reported on mechanical ventilation as means and standard deviation and when the data were aggregated, enteral glutamine had no effect on duration of mechanical ventilation (WMD -0.19, 95% CI -0.89, 0.51,  $p = 0.60$ , test for heterogeneity  $I^2 = 0\%$ ) (figure 11).

### Conclusions:

- 1) Glutamine supplemented enteral nutrition is associated with a reduction in mortality in burn patients, but inconclusive in other critically ill patients.
- 2) Glutamine supplemented enteral nutrition may be associated with a reduction in infectious complications in burn and trauma patients.
- 3) Glutamine supplemented enteral nutrition is associated with a reduction in hospital length of stay in burn and other critically ill patients but not in trauma patients and may be associated with a reduction in ICU LOS in trauma patients.
- 4) Glutamine supplemented enteral nutrition has no effect on duration of mechanical ventilation 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

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**Table 1. Randomized studies evaluating glutamine (EN) in critically ill patients**

Study	Population	Methods (score)	Intervention -Dose (gm/kg/day) or gm/day -Type of feeding	Mortality # (%)†		Infections # (%)‡		Hospital stay (days)		ICU LOS (days)	
				Experimental	Control	Experimental	Control	Experimental	Control	Experimental	Control
<b>1) Houdijk 1998</b>	Critically ill trauma (100%) N = 80	C.Random: Yes ITT: No Blinding: Yes (10) Level: 2	> 0.25 Altira Q (glutamine enriched formula) vs. isonitrogenous control (added amino acids) Same volume of feeding received in both groups	4/41 (9.8)	3/39 (7.7)	20/35 (57.1)	26/37 (70.2)	32.7±17.1 (35)	33.0± 23.8 (37)	NA	NA
<b>2) Jones 1999</b>	Mixed ICU Population (6 burns, 6 trauma, no subgroup analysis) N = 78	C.Random: Yes ITT: No Blinding: Yes (8) Level: 2	0.16 Protina MP + Glutamine (10-15 gm Nitrogen/day) vs. Isonitrogenous Control (11-14 gm Nitrogen/day)	<b>Hospital</b> 10/26 (38.5) <b>ICU</b> 9/26 (35) <b>6 month</b> 12/26 (46)	<b>Hospital</b> 9/24 (37.5) <b>ICU</b> 9/24 (38) <b>6 month</b> 10/24 (42)	NA	NA	NA	NA	11 (4-54)	16.5 (5-66)
<b>3) Brantley 2000</b>	Critically ill trauma (100%) N = 72	C.Random: Not sure ITT: No Blinding: No (4) Level: 2	0.50 Glutamine supplemented Enteral formula vs. standard formula (Isonitrogenous) Protein given 1.5gm/kg/d	NA	NA	NA	NA	19.5±8.8 (31)	20.8±11.5 (41)	11.4	11.1
<b>4) Hall 2003</b>	Mixed ICU Population (mostly trauma, 7 burns) N = 363	C.Random: yes ITT: Yes Blinding: double (13) Level: 1	0.27 Isocal + glutamine (66 gms protein/day) vs. isonitrogenous formula, Isocal + glycine (64 gms protein/day)	<b>6 months</b> 27/179 (15) <b>30 days</b> 26/179 (15) <b>ICU</b> 16/179 (9) <b>Hospital</b> 24/179 (13)	<b>6 months</b> 30/184 (16) <b>30 days</b> 25/184 (14) <b>ICU</b> 14/184 (8) <b>Hospital</b> 23/184 (13)	38/179 (21)	43/184 (23)	25 (16-42)*	30 (19-45)*; p=NS	11(7-19) (excluding deaths)	13 (8-19) (excluding deaths)
	Trauma subgroup			7/76 (9)	6/78 (8)	<b>Sepsis</b> 7/76 (9)	<b>Sepsis</b> 11/78 (14)	NA	NA	NA	NA
<b>5) Garrel 2003</b>	Burns N = 45	C.Random: yes ITT: yes Blinding: double (11) Level: 1	0.28 Sandosource + glutamine (2.15 gm/kg/d protein) vs. Sandosource + amino acids (isonitrogenous), 1.97 gm/kg/day protein	2/21 (10)	12/24 (50)	<b>Positive blood cultures</b> 7/19 (37)	<b>Positive blood cultures</b> 10/22 (45)	33 ±17 (16) **	29 ±17 (19) **	NA	NA
<b>6) Zhou 2003</b>	Severe Burns TSBA 50-80 % N = 41	C.Random: yes ITT: no Blinding: double (8) Level: 2	0.35 Ensure + glutamine vs. Ensure + amino acids (isonitrogenous)	NA	NA	2/20 (10)	6/20 (30)	67 ± 4 (20)	73 ± 6 (20)	NA	NA

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<b>7) Peng 2004</b>	Severe Burns TBSA > 30 % N = 48	C.Random: Not sure ITT: yes Blinding: no (7) Level: 2	0.5 oral glutamine granules vs. placebo (isocaloric, isonitrogenous) 2.0 gm/kg/d protein	NA	NA	NA	NA	46.59 ± 12.98 (25)	55.68 ± 17.36 (23)	NA	NA
<b>8) Luo 2008***</b>	Medical Surgical N=44	C.Random: not sure ITT: no Blinding: double (9) Level: 2	0.32 glutamine + IV saline + vs. Nutren + 15% Clinisol (placebo) (isocaloric, isonitrogenous) 1.7 gm/kg/d protein	<b>28 day</b> 1/12 <b>ICU</b> 1/12	<b>28 day</b> 0/9 <b>ICU</b> 0/9	NA	NA	NA	NA	8.1 ± 0.4 (12)	6.9 ± 0.9 (9)
<b>9) McQuiggan 2008</b>	Shock trauma patients N = 20	C.Random: Not sure ITT: yes Blinding: no (10) Level: 2	0.5 (actual 0.4) Impact + glutasolve via NJ tube (1.3 gm/kg/day protein), bolus with H2O vs. Impact + protein supplements {isonitrogenous, isocaloric, 0.85 gm/kg/day protein}	0/10	2/10 (20)	NA	NA	32 ± 13.6 (10)	39.3 ± 33.6 (10)	4.8 ± 6.7 (10)	10.4 ± 6.2 (10)
<b>10) Pattanshetti 2009</b>	Burn ICU patients N=30	C.Random: Not sure ITT: yes Blinding: single (outcomes) (8) Level: 2	Enteral isonitrogenous mixture + 0.5 g/kg/d EN glutamine supplement + 'regular' nutrition vs Enteral isonitrogenous mixture + 'regular' nutrition	0/15	2/15	NA	NA	22.73 ± 9.13	39.73 ± 18.27	NA	NA
<b>11) van Zanten 2014</b>	Mixed, N= 301	C Random: Yes ITT: Yes Blinding: double (12) Level: 1	Glutamine, omega-3, aox enriched EN (experimental product, Nutriciar) vs high-protein EN (Nutrison Advanced Protison-Nutricia)	<b>Hospital</b> 38/152 (25) <b>ICU</b> 30/152 (20) <b>28 day</b> 31/152 (20) <b>6 month</b> 53/152 (35)	<b>Hospital</b> 33/149 (22) <b>ICU</b> 29/149 (20) <b>28 day</b> 25/149 (17) <b>6 month</b> 42/149 (29)	80/152 (53)	78/149 (52)	38.2 ± 28.9	37.7 ± 27.5	23.7 ± 22.4 (152)	25.6 ± 24.0 (149)
	Trauma subgroup			<b>Hospital</b> 6/55 (11) <b>ICU</b> 5/55 (9) <b>28 day</b> 4/55 (7) <b>6 month</b> 8/55 (15)	<b>Hospital</b> 6/54 (11) <b>ICU</b> 6/54 (11) <b>28 day</b> 2/54 (4) <b>6 month</b> 59/54 (17)	32/55 (58)	36/54 (67)	44.4 ± 31.2	39.8 ± 25.3	31.3 ± 30.3	32.5 ± 27.5

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<b>12) Koksai 2014****</b>	Septic, malnourished ICU patients N=120	C.Random: yes ITT: other Blinding: single (outcomes) (9) Level: 2	30 g/day EN glutamine (Glutamine resource, Nestle) + EN vs EN, no placebo, no supplemental glutamine	NA	NA	NA	NA	NA	NA	NA	NA
<b>13) Iamsirisaengthong 2017</b>	Major burn patients (>20% TBSA) N=20	C.Random: no ITT: no Blinding: no (3) Level: 2	Neomune (25% protein, gln and arg containing) vs blenderized diet (17% protein). Isocaloric, non-isotonitrogenous.	<b>Hospital</b> 1/10 (10%)	<b>Hospital</b> 1/10 (10%)	<b>Septic complications</b> 4/10 (40%) <b>Wound Healing (days)</b> 32.3 + 14.3	<b>Septic complications</b> 7/10 (70%) <b>Wound Healing (days)</b> 38.3 + 14.9	35.4 ± 15.2	40.4 ± 15.2	NA	NA
<b>14) Efremov 2017</b>	Mechanically ventilated, critically ill patients undergoing elective cardiac surgery N=40	C.Random: yes ITT: yes Blinding: no (10) Level: 2	25 gm/day glutamine (Nutricomp immune-high calorie 1.33 Kcal/mL, 6.7 gm/L protein, 0.2 gm/100 mL omega 3) vs. standard EN (Nutricomp standard-1 Kcal/mL, 3.8 gm/L protein, 0.26 gm/100 mL omega 3). PN used to supplement. Non-isocaloric, non-isotonitrogenous	<b>Hospital</b> 6/20 (30%)	<b>Hospital</b> 4/20 (20%)	NA	NA	<b>Hospital</b> 30 (25-33)*	<b>Hospital</b> 26 (19-21)*	<b>ICU</b> 11 (7-23)*	<b>ICU</b> 9 (7-11)*
<b>15) Shariatpanahi 2019</b>	Mix ICU adult patients Medical (32) Surgical (24) Trauma (14)	C.Random: no ITT: no Blinding: no (6) Level: 2	Glutamine (0.3 grams/kg/d) + EN vs. placebo (maltodextrin) + EN; both 3 times per day	<b>ICU</b> 7/36 19% (95% CI:8-33%)	<b>ICU</b> 4/34 12% (95% CI:3-24%)	<b>New sepsis</b> 5.6% (95% CI; 0-13.9%)	<b>New sepsis</b> 11.8% (95% CI, 2.8-23.5%)	NA	NA	10 (8-20)*	13 (7-29)*
<b>16) Nakamura 2020</b>	Mix ICU population Sepsis (42); Cardiac (20); Stroke (23); Cardiopulmonary arrest (6); Post surgery (13); Respiratory failure (23); trauma (2)	C.Random: Yes ITT: Yes Blinding: single (12) Level: 2	Daily 3grams HMB+14 grams arginine+14 grams of glutamine vs. standard EN	<b>28 days</b> 8.7% (4/45)	<b>28 days</b> 13.6% (6/43)	NA	NA	21.9 ±8.8	24.3 ±7.8	5.4 ±3.5	5.8 ±3.8
	Final Femoral Muscle subgroup analysis SOC (24) vs. Intervention (26)			<b>30-day mortality rate</b> 16.8%	<b>30-day mortality rate</b> 19.3%	NA	NA	20.4 ±10.7	19.8 ±12.5	9.1 ±4.4	8.6 ±5.2
	Femoral Muscle Volume by SOFA subgroup  SOFA <10 (31) vs. SOFA >10 (19)			SOFA<10: 0%	SOFA <10: 0%	NA	NA	<b>SOFA&lt;10</b> 22.7 ±13.1	<b>SOFA&lt;10</b> 19.6 ±9.9	<b>SOFA&lt;10</b> 10.0 ±4.4	<b>SOFA&lt;10</b> 7.3 ±3.7
			SOFA>10: 26.5%	SOFA >10: 25.8%			<b>SOFA&gt;10</b> 17.3 ±7.1	<b>SOFA&gt;10</b> 20.1 ±13.4	<b>SOFA&gt;10</b> 7.9 ±4.4	<b>SOFA&gt;10</b> 11.3 ±6.9	

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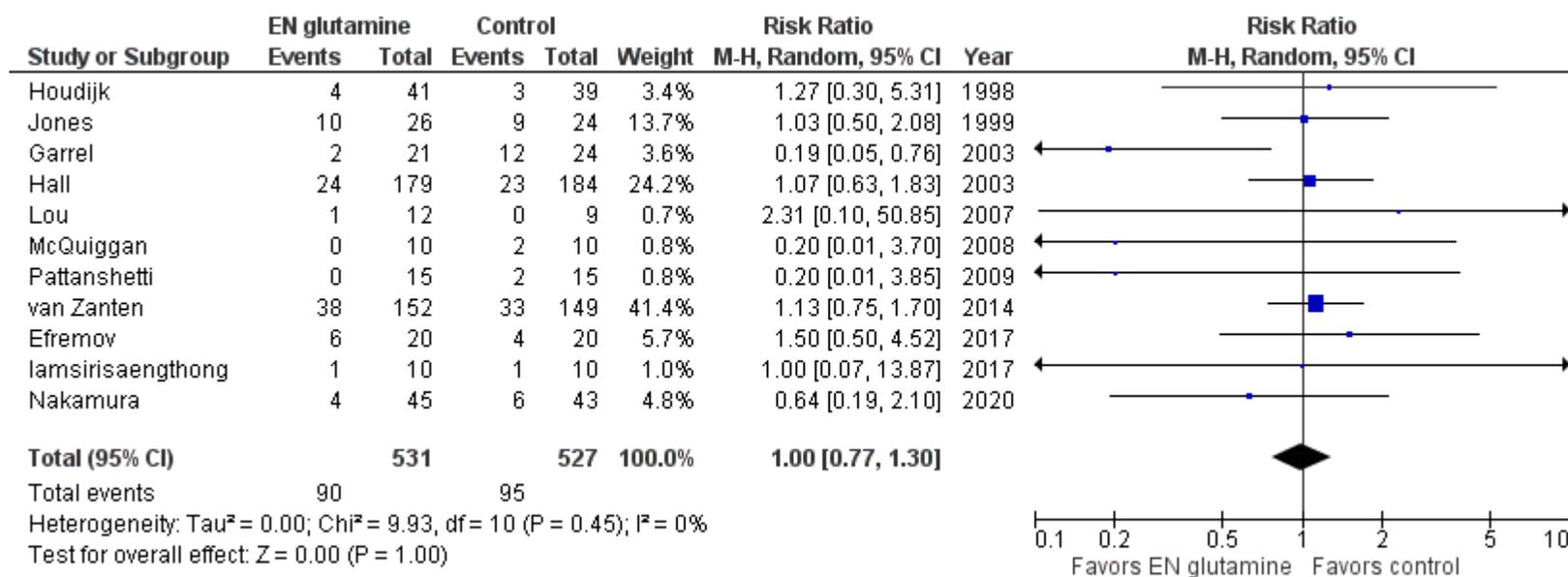
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C.Random: concealed randomization median (range)	EN: enteral nutrition	NA: not available
ITT: intent to treat	TPN: Total parenteral nutrition	
± ( ) : mean ± Standard deviation (number)	† hospital mortality unless otherwise stated	
* median and range hence not included in meta-analyses		
** data from a subgroup, hence not included in meta-analyses		
*** data from PN glutamine group not shown here, appears in PN glutamine section		
****Reports on mechanical ventilation		
28 or 30 day hospital mortality were aggregated as Overall Mortality		
NA: Not available or not reported		

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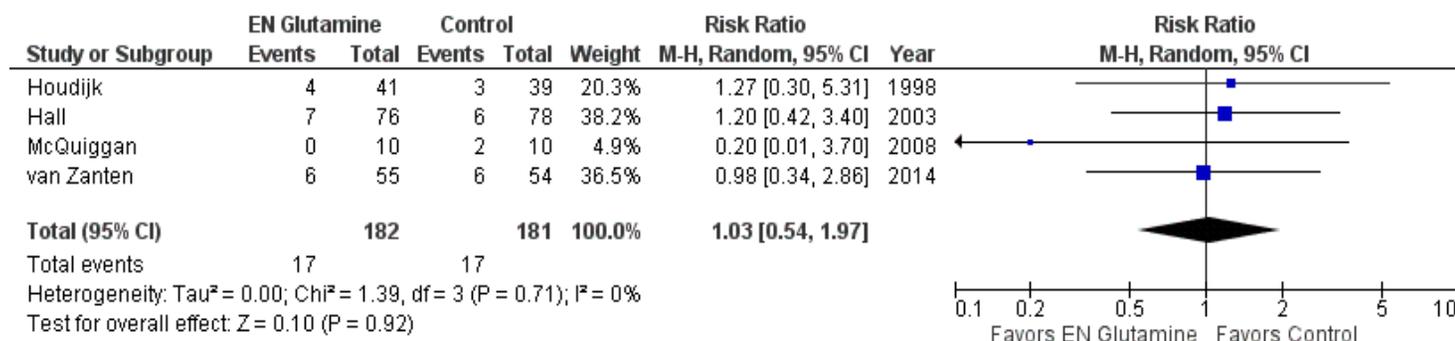
Figure 1. Overall Hospital Mortality



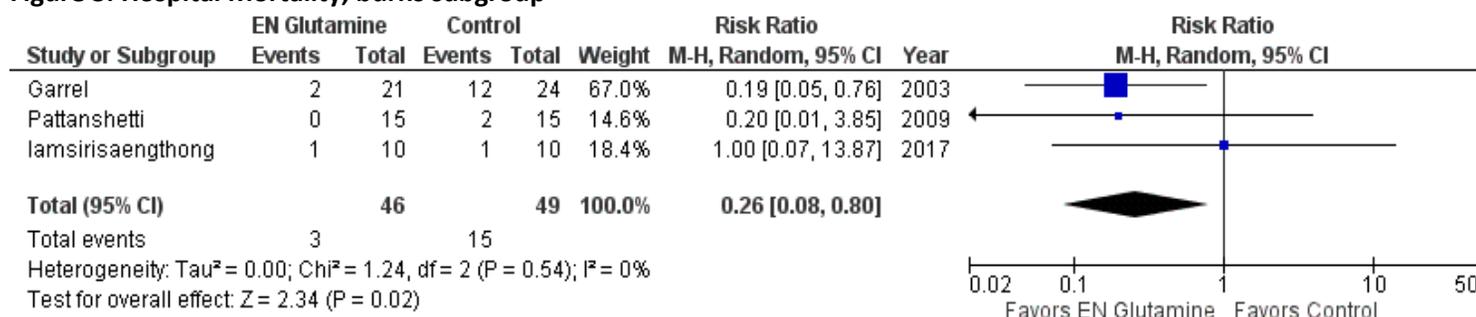
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**Figure 2. Hospital Mortality, trauma subgroup analysis**



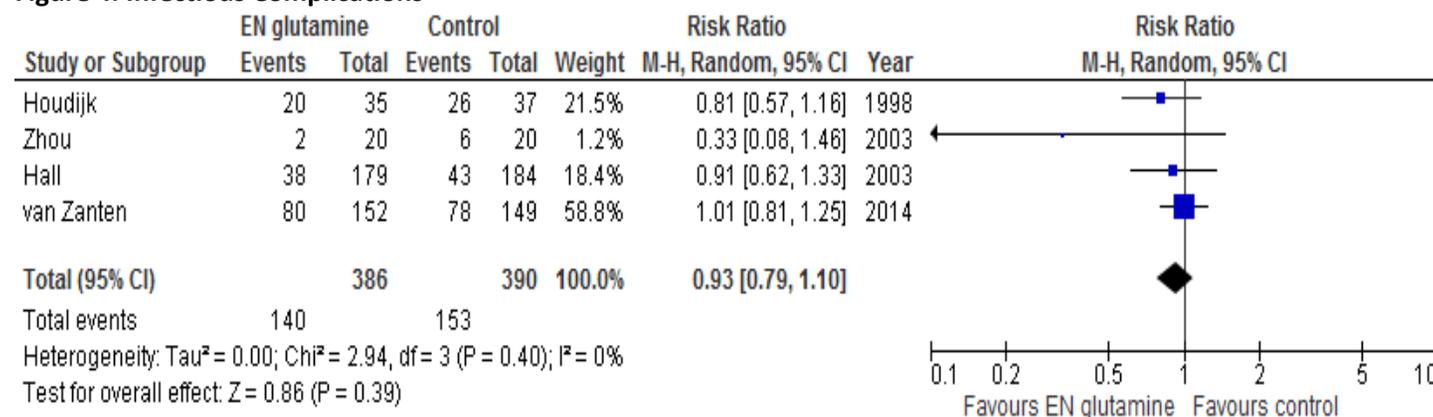
**Figure 3. Hospital Mortality, burns subgroup**



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**Figure 4. Infectious Complications**



**Figure 5. Infectious Complications: trauma**



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Figure 6: Hospital LOS

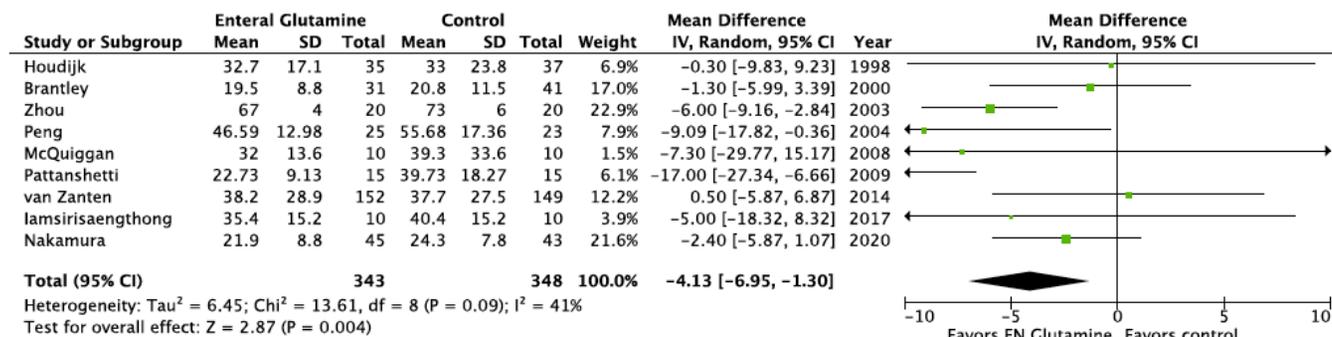


Figure 7. Hospital LOS, burns subgroup analysis

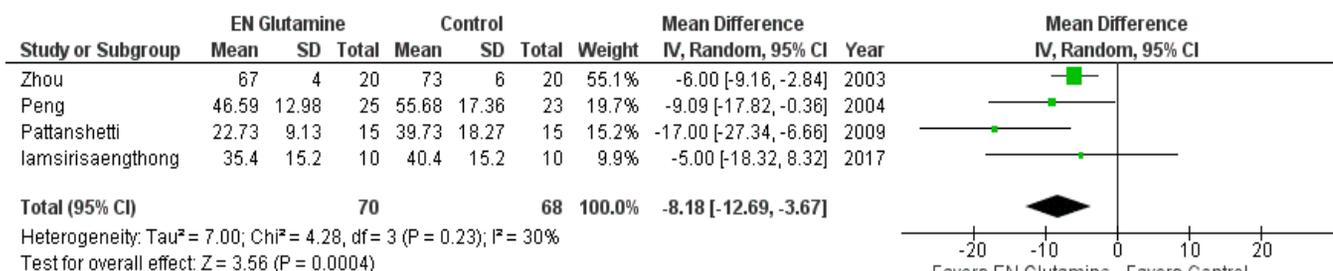


Figure 8. Hospital LOS, trauma subgroup analysis

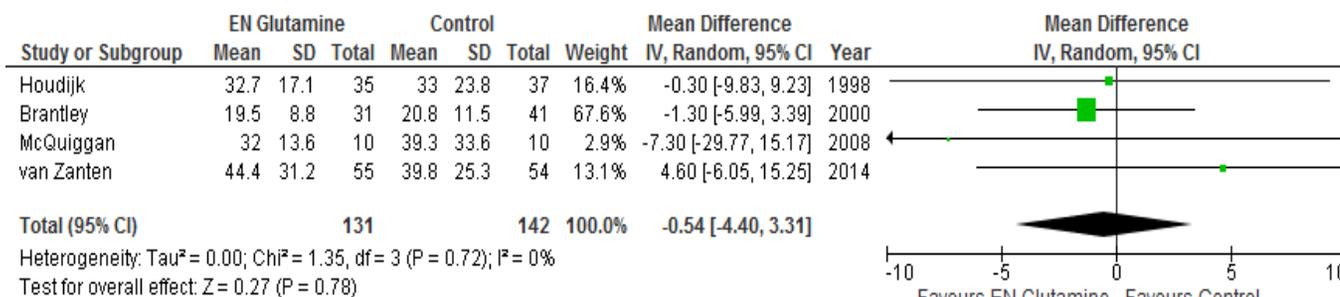


Figure 9. ICU LOS, all studies

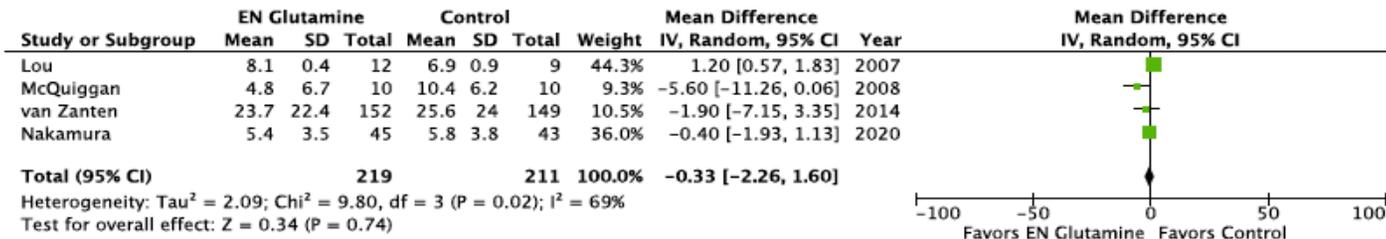
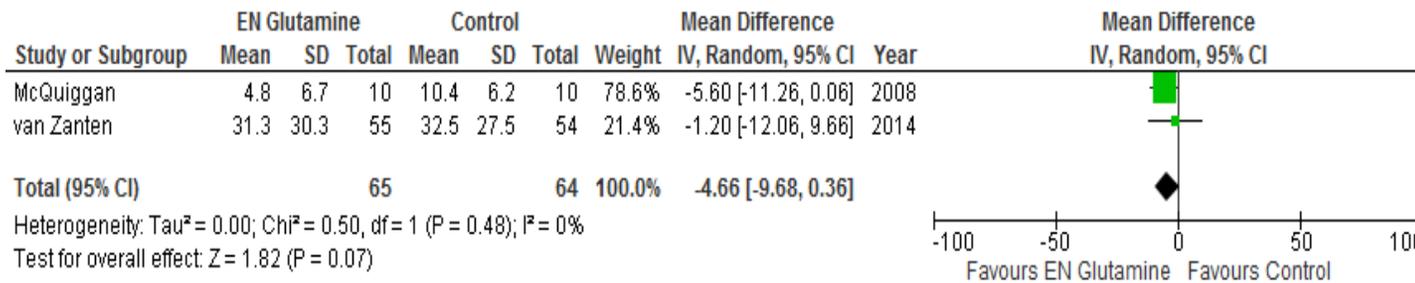
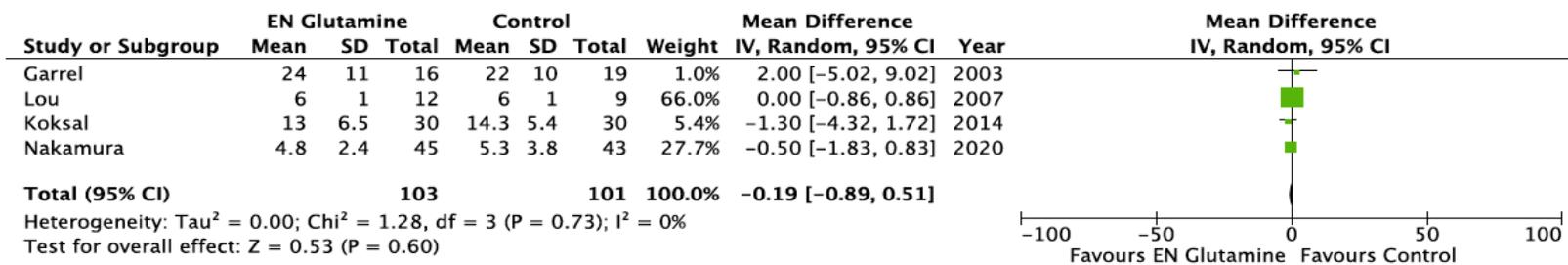


Figure 10. ICU LOS, trauma subgroup analysis



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**Figure 11. Mechanical Ventilation Days**



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### References

#### Included Studies

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Excluded Studies	Reasons
Jebb SA, Marcus R, Elia M. A pilot study of oral glutamine supplementation in patients receiving bone marrow transplants. <i>Clin Nutr.</i> 1995 Jun;14(3):162-5.	Transplant/elective surgery patients
Long CL, Nelson KM, DiRienzo DB, Weis JK, Stahl RD, Broussard TD, Theus WL, Clark JA, Pinson TW, Geiger JW, et al. Glutamine supplementation of enteral nutrition: impact on whole body protein kinetics and glucose metabolism in critically ill patients. <i>J Parenter Enteral Nutr.</i> 1995 Nov-Dec;19(6):470-6.	No clinical outcomes
Jensen GL, Miller RH, Talabiska DG, Fish J, Gianferante L. A double-blind, prospective, randomized study of glutamine-enriched compared with standard peptide-based feeding in critically ill patients. <i>Am J Clin Nutr</i> 1996;64(4):615-21.	No clinical outcomes
Fish J, Sporay G, Beyer K, Jones J, Kihara T, Kennedy A, Apovian C, Jensen GL. A prospective randomized study of glutamine-enriched parenteral compared with enteral feeding in postoperative patients. <i>Am J Clin Nutr.</i> 1997 Apr;65(4):977-83.	Surgical patients
Scolapio JS, Camilleri M, Fleming CR, Oenning LV, Burton DD, Sebo TJ, Batts KP, Kelly DG. Effect of growth hormone, glutamine, and diet on adaptation in short-bowel syndrome: a randomized, controlled study. <i>Gastroenterology.</i> 1997 Oct;113(4):1074-81. Comment in: <i>Gastroenterology.</i> 1997 Oct;113(4):1402-5.	Crossover design
Anderson PM, Ramsay NK, Shu XO, Rydholm N, Rogosheske J, Nicklow R, Weisdorf DJ, Skubitz KM. Effect of low-dose oral glutamine on painful stomatitis during bone marrow transplantation. <i>Bone Marrow Transplant.</i> 1998 Aug;22(4):339-44.	Surgical patients
Anderson PM, Schroeder G, Skubitz KM. Oral glutamine reduces the duration and severity of stomatitis after cytotoxic cancer chemotherapy. <i>Cancer.</i> 1998 Oct 1;83(7):1433-9.	Pediatric patients
Den Hond E, Hiele M, Peeters M, Ghooys Y, Rutgeerts P. Effect of long-term oral glutamine supplements on small intestinal permeability in patients with Crohn's disease <i>JPEN J Parenter Enteral Nutr.</i> 1999 Jan-Feb;23(1):7-11..	Not ICU patients
Schloerb PR, Skikne BS. Oral and parenteral glutamine in bone marrow transplantation: a randomized, double-blind study. <i>JPEN J Parenter Enteral Nutr.</i> 1999 May-Jun;23(3):117-22.	Surgical patients
Scolapio JS. Effect of growth hormone, glutamine, and diet on body composition in short bowel syndrome: a randomized, controlled study. <i>JPEN J Parenter Enteral Nutr.</i> 1999 Nov-Dec;23(6):309-12; discussion 312-3.	Crossover design
Zhou Y, Jiang Z, Sun Y. Gu an zuo an shuang zuo gai shan zhong du shao shang huan zhe chang zhan mo tong tou xing de yan jiu. <i>National Medical Journal of China.</i> 1999;79(11):825.	Earlier study of Zhou 2003 that is included
Jackson NC, Carroll PV, Russell-Jones DL, Sönksen PH, Treacher DF, Umpleby AM. Effects of glutamine supplementation, GH, and IGF-I on glutamine metabolism in critically ill patients. <i>Am J Physiol Endocrinol Metab.</i> 2000 Feb;278(2):E226-33.	Surgical patients; No clinical outcomes
Szkudlarek J, Jeppesen PB, Mortensen PB. Effect of high dose growth hormone with glutamine and no change in diet on intestinal absorption in short bowel patients: a randomised, double blind, crossover, placebo controlled study. <i>Gut.</i> 2000 Aug;47(2):199-205.	Crossover design
Chen G, Xie W, Jiang H. [Clinical observation of the protective effect of oral feeding of glutamine granules on intestinal mucous membrane]. <i>Zhonghua Shao Shang Za Zhi.</i> 2001 Aug;17(4):210-1. Chinese. PubMed PMID: 11876941.	No clinical outcomes
Scolapio JS, McGreevy K, Tennyson GS, Burnett OL. Effect of glutamine in short-bowel syndrome. <i>Clin Nutr.</i> 2001 Aug;20(4):319-23.	Crossover design
Velasco N, Hernandez G, Wainstein C et al. Influence of polymeric enteral nutrition supplemented with different doses of glutamine on gut permeability in critically ill patients. <i>Nutrition</i> 2001;17:907-11.	No clinical outcomes. Duplicate of Houdjik
Boelens PG, Houdijk AP, Fonk JC et al. Glutamine-Enriched Enteral Nutrition Increases HLA-DR Expression on Monocytes of Trauma Patients. <i>J Nutr</i> 2002;2580-6.	No clinical outcomes
Novak F, Heyland DK, Avenell A, Drover JW, Su X. Glutamine supplementation in serious illness: a systematic review of the Evidence. <i>Crit Care Med.</i> 2002 Sep;30(9):2022-9.	Systematic review

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Flåring UB, Rooyackers OE, Wernerman J, Hammarqvist F. Glutamine attenuates post-traumatic glutathione depletion in human muscle. <i>Clin Sci (Lond)</i> . 2003 Mar;104(3):275-82	Elective surgery patients
García-de-Lorenzo A, Zarazaga A, García-Luna PP, Gonzalez-Huix F, López-Martínez J, Miján A, Quecedo L, Casimiro C, Usán L, del Llano J. Clinical evidence for enteral nutritional support with glutamine: a systematic review. <i>Nutrition</i> . 2003 Sep;19(9):805-11.	Systematic review
Boelens PG, Houdijk AP, Fonk JC, Puyana JC, Haarman HJ, von Blomberg-van der Flier ME, van Leeuwen PA. Glutamine-enriched enteral nutrition increases in vitro interferon-gamma production but does not influence the in vivo specific antibody response to KLH after severe trauma. A prospective, double blind, randomized clinical study. <i>Clin Nutr</i> . 2004 Jun;23(3):391-400.	Duplicate of Houdijk
Falcao de Arruda IS, de Aguilar-Nascimento JE. Benefits of early enteral nutrition with glutamine and probiotics in brain injury patients. <i>Clin Sci (Lond)</i> 2004;106(3):287-92.	Includes probiotics
Peng X, Yan H, You Z, Wang P, Wang S. Clinical and protein metabolic efficacy of glutamine granules-supplemented enteral nutrition in severely burned patients. <i>Burns</i> 2005;31(3):342-6.	Duplicate of Peng 2004
"Peng X, Yan H, You Z, Wang P, Wang S. Glutamine granule-supplemented enteral nutrition maintains immunological function in severely burned patients. <i>Burns</i> . 2006 Aug;32(5):589-93. Epub 2006 May 24. PubMed PMID: 16725264."	Duplicate of Peng 2004
Guo GH, Deng ZY, Wang YX, Xing JJ, Peng Y, Li GH. [Effects of glutamine enriched enteral feeding on immunoregulation in burn patients]. <i>Zhonghua Shao Shang Za Zhi</i> . 2007 Dec;23(6):406-8. Chinese. PubMed PMID: 18457248.	No clinical outcomes
Kuhls DA, Rathmacher JA, Musngi MD, Frisch DA, Nielson J, Barber A, MacIntyre AD, Coates JE, Fildes JJ. Beta-hydroxy-beta-methylbutyrate supplementation in critically ill trauma patients. <i>J Trauma</i> . 2007 Jan;62(1):125-31; discussion 131-2.	Too many interventions
Spindler-Vesel A, Bengmark S, Vovk I, Cerovic O, Kompan L. Synbiotics, prebiotics, glutamine, or peptide in early enteral nutrition: a randomized study in trauma patients. <i>JPEN J Parenter Enteral Nutr</i> . 2007 Mar-Apr;31(2):119-26.	Too many interventions
Beale RJ, Sherry T, Lei K, Campbell-Stephen L, McCook J, Smith J, Venetz W, Alteheld B, Stehle P, Schneider H. Early enteral supplementation with key pharmac nutrients improves Sequential Organ Failure Assessment score in critically ill patients with sepsis: outcome of a randomized, controlled, double-blind trial. <i>Crit Care Med</i> 2008;36(1):131-44.	Patients received glutamine dipeptides, vit C and E, carotene, selenium, zinc, and butyrate in combination with an immunonutrition formula
Jiang H, Chen W, Hu W, Cai B, Liao RJ. [The impact of glutamine-enhanced enteral nutrition on clinical outcome of patients with critical illness: a systematic review of randomized controlled trials]. <i>Zhonghua Shao Shang Za Zhi</i> . 2009 Oct;25(5):325-30. Review. Chinese. PubMed PMID: 19951553.	Systematic review
Han YY, Lai SL, Ko WJ, Chou CH, Lai HS. Effects of fish oil on inflammatory modulation in surgical intensive care unit patients. <i>Nutr Clin Pract</i> . 2012 Feb;27(1):91-8. Epub 2012 Jan 6. PubMed PMID: 22227725.	Elective surgery patients
Cavalcante AA, Campelo MW, de Vasconcelos MP, Ferreira CM, Guimarães SB, Garcia JH, de Vasconcelos PR. Enteral nutrition supplemented with l-glutamine in patients with systemic inflammatory response syndrome due to pulmonary infection. <i>Nutrition</i> . 2012 Apr;28(4):397-402. Epub 2011 Nov 4. PubMed PMID: 22055478.	No clinical outcomes; Crossover design
Wang X, Dong Y, Han X, Qi X-Q, Huang C-G, Hou L. (2013) Nutritional Support for Patients Sustaining Traumatic Brain Injury: A Systematic Review and Meta-Analysis of Prospective Studies. <i>PLoS ONE</i> . 8(3): e58838.	Meta-analysis
Han W. Sun J. Han R. Wang Y. Yi Q. Hua L. Tian F. Application of enteral nutrition support with different doses of glutamine in elderly critically ill patients. <i>Chin J Clin Nutr</i> 2014;22(3):149-153.	No clinical outcomes
"Kibor DK, Nyaim OE, Wanjeri K. Effects of enteral glutamine supplementation on reduction of infection in adult patients with severe burns. <i>East Afr Med J</i> . 2014 Jan;91(1):33-6."	No clinical outcomes
Han W., Sun J., Han R., Wang Y., Yi Q., Hua L., Tian F. Application of enteral nutrition support with different doses of glutamine in elderly critically ill patients. <i>Chinese Journal of Clinical Nutrition</i> . 2014 Jun;22(3):149-153, 2014.	No clinical outcomes

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Azman M, Mohd Yunus MR, Sulaiman S, Syed Omar SN. Enteral glutamine supplementation in surgical patients with head and neck malignancy: A randomized controlled trial. <i>Head Neck</i> . 2015 Dec;37(12):1799-807. doi: 10.1002/hed.23839.	Surgical patients
Hofman Z, Swinkels S, van Zanten ARH. Glutamine, fish oil and antioxidants in critical illness: MetaPlus trial post hoc safety analysis. <i>Ann Int Care</i> . 2016;6;119.	Post hoc analysis, no new relevant outcomes
Vijey Aanandhi M, John M.R. Enteral oral glutamine supplementation in patients following surgery and accidental injury. <i>Asian J Pharm and Clin Res</i> . 2017 March;10(3):477-479	Surgical patients
Arutla M, Raghunath M, Deepika G, Jakkampudi A, Murthy HVV, Rao GV, Reddy DN, Talukdar R. Efficacy of enteral glutamine supplementation in patients with severe and predicted severe acute pancreatitis- A randomized controlled trial. <i>Indian J Gastroenterol</i> . 2019 Aug;38(4):338-347. doi: 10.1007/s12664-019-00962-7. Epub 2019 Oct 14. PMID: 31612309.	Not ICU patients