# 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 9 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) and the remaining 4 were in mixed ICU patients.

Mortality: When the data from all the 10 trials that reported on mortality were aggregated, there was no statistically significant difference in mortality between the groups receiving glutamine supplemented EN or not (RR = RR 0.97, 95% CI 0.70, 1.34, p =0.84, test for heterogeneity $I^2$ = 10%) (figure 1). Subgroup analyses of the 5 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 5 studies of burn patients, patient deaths in hospital occurred in 4 studies (Garrel 2003, Zhou 2003, Pattanshetti 2009, Iamsirisaungthong 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 3 level 2 studies and 1 level 1 study 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, 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).

Length of Stay: There were 7 level 2 studies and 1 level 1 study that demonstrated a significant reduction in length of hospital stay (WMD (weighted mean difference) -4.69, 95% CI -8.19, -1.18, p = 0.009, test for heterogeneity $I^2$ = 44%) (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 8) 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 7). Enteral glutamine has no effect on ICU LOS (WMD -1.36, 95% CI -5.51, 2.78, p =0.52, test for heterogeneity $I^2$= 70%) (figure 9) when all studies were aggregated but was associated with a trend towards a reduction in the subgroup of trauma patients (WMD -4.66, 95% CI -9.68, 0.36, p = 0.07, test for heterogeneity $I^2$= 0%) (figure 10).

Mechanical ventilation: Only 2 studies 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 -0.10, 95% CI -0.93, 0.73, p =0.82).

## 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.

*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 glutamine (EN) in critically ill patients

| Study | Population | Methods (score) | Intervention -Dose (gm/kg/day) -Type of feeding | Mortality # (%)† Experimental | Mortality # (%)† Control | Infections # (%)‡ Experimental | Infections # (%)‡ Control | Hospital stay (days) Experimental | Hospital stay (days) Control | ICU LOS (days) Exp | ICU LOS (days) control |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1) Houdijk 1998 | Critically ill trauma (100%) N = 80 | C.Random: Yes ITT: No Blinding: Yes (10) | > 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 |
| 2) Jones 1999 | Mixed ICU Population (6 burns, 6 trauma, no subgroup analysis) N = 78 | C.Random: Yes ITT: No Blinding: Yes (8) | 0.16 Protina MP + Glutamine (10-15 gm Nitrogen/day) vs. Isonitrogenous Control (11-14 gm Nitrogen/day) | Hospital 10/26 (38.5) ICU 9/26 (35) 6 month 12/26 (46) | Hospital 9/24 (37.5) ICU 9/24 (38) 6 month 10/24 (42) | NA | NA | NA | NA | 11 (4–54) | 16.5(5–66) |
| 3) Brantley 2000 | Critically ill trauma (100%) N = 72 | C.Random: Not sure ITT: No Blinding: No (4) | 0.50 Glutamine supplemented Enteral formula vs. standard formula (Isonitrogenous) Protein given 1.5gm/kg/d | 0/31 (0.0) | 0/41 (0.0) | NA | NA | 19.5+/-8.8 (31) | 20.8±11.5 (41) | 11.4 | 11.1 |
| 4) Hall 2003 | Mixed ICU Population (mostly trauma, 7 burns) N = 363 | C.Random: yes ITT: Yes Blinding: Yes ( 13) | 0.27 Isocal + glutamine (66 gms protein/day) vs. isonitrogenous formula, Isocal + glycine (64 gms protein/day) | 6 months 27/179 (15) 30 days 26/179 (15) ICU 16/179 (9) Hospital 24/179 (13) | 6 months 30/184 (16) 30 days 25/184 (14) ICU 14/184 (8) Hospital 23/184 (13) | 38/179 (21) | 43/184 (23) | 25 (16-42)* | 30 (19-45)* | 11(7-19) (excluding deaths) | 13 (8-19) (excluding deaths) |
| | Trauma subgroup | | | 7/76 (9) | 6/78 (8) | Sepsis 7/76 (9) | Sepsis 11/78 (14) | NA | NA | NA | NA |
| 5) Garrel 2003 | Burns N = 45 | C.Random: yes ITT: yes Blinding: yes ( 11 ) | 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) | Positive blood cultures 7/19 (37) | Positive blood cultures 10/22 (45) | 33 ± 17 (16) ** | 29 ± 17 (19) ** | NA | NA |
| 6) Zhou 2003 | Severe Burns TSBA 50-80 % N = 41 | C.Random: yes ITT: no Blinding: double (8) | 0.35 Ensure + glutamine vs. Ensure + amino acids (isonitrogenous) | 0/20 | 0/20 | 2/20 (10) | 6/20 (30) | 67 ± 4 (20) *Mean and SD* | 73 ± 6 (20) *Mean and SD* | NA | NA |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 7) Peng 2004 | Severe Burns TBSA > 30 % N = 48 | C.Random: Not sure ITT: yes Blinding: no (7) | 0.5 oral glutamine granules vs. placebo (isocaoric, isonitrogenous) 2.0 gm/kg/d protein | NA | NA | NA | NA | 46.59 ± 12.98 (25) | 55.68 ± 17.36 (23) | NA | NA |
| 8) Luo 2007*** | Medical Surgical N=44 | C.Random: not sure ITT: no Blinding: double (9) | 0.32 glutamine + IV saline + vs. Nutren + 15% Clinisol (placebo) (isocaoric, isonitrogenous) 1.7 gm/kg/d protein | 28 day 1/12 ICU 1/12 | 28 day 0 /9 ICU 0 /9 | NA | NA | NA | NA | 8.1 ± 0.4 (12) | 6.9 ±0.9 (9) |
| 9) McQuiggan 2008 | Shock trauma patients N = 20 | C.Random: Not sure ITT: yes Blinding: no (10) | 0.5 (actual 0.4 ) Impact + glutasolve via NJ tube (1.3 gm/kg/day protein), bolus with H20 vs. Impact + protein supplements {isonitrogenous,isocaloric, 0.85 gm/kg/day protein} | 0/10 | 2/10 (20) | NA | NA | 32 ± 13.6 (10) *Mean and SD* | 39.3 ± 33.6 (10) *Mean and SD* | 4.8 ± 6.7 (10) *Mean and SD* | 10.4 ± 6.2 (10) *Mean and SD* |
| 10) Pattanshetti 2009 | Burn ICU patients N=30 | C.Random: Not sure ITT: yes Blinding: single (outcomes) (8) | 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 |
| 11) van Zanten 2014 | Mixed, N= 301 | C Random: Yes ITT: Yes Blinding: double (12) | Glutamine,omega-3, aox enriched EN (experimental product, Nutriciar) vs high-protein EN (Nutrison Advanced Protison-Nutricia) | Hospital 38/152 (25) ICU 30/152 (20) 28 day 31/152 (20) 6 month 53/152 (35) | Hospital 33/149 (22) ICU 29/149 (20) 28 day 25/149 (17) 6 month 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 | | | Hospital 6/55 (11) ICU 5/55 (9) 28 day 4/55 (7) 6 month 8/55 (15) | Hospital 6/54 (11) ICU 6/54 (11) 28 day 2/54 (4) 6 month 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 |
| 12) Koksal 2014**** | Septic, malnourished ICU patients | C.Random: yes ITT: other Blinding: single | 30 g/day EN glutamine (Glutamine resource, Nestle) + EN vs EN, no | NA | NA | NA | NA | NA | NA | NA | NA |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N=120 | (outcomes)<br>(9) | placebo, no supplemental glutamine | | | | | | | | |
| 13) Iamsirisaengthong 2017 | Major burn patients (≥20% TBSA)<br>N=20 | C.Random: no<br>ITT: no<br>Blinding: no<br>(3) | Neomune (25% protein, gln and arg containing) vs blenderized diet (17% protein). Isocaloric, non-isonitrogenous. | Hospital<br>1/10 (10%) | Hospital<br>1/10 (10%) | Septic complications<br>4/10 (40%)<br>Wound Healing (days)<br>32.3 ± 14.3 | Septic complications<br>7/10 (70%)<br>Wound Healing (days)<br>38.3 ± 14.9 | 35.4 ± 15.2 | 40.4 ± 15.2 | NA | NA |

C.Random: concealed randomization median (range)
ITT: intent to treat
± ( ) : mean ± Standard deviation (number)
EN: enteral nutrition
TPN: Total parenteral nutrition
† hospital mortality unless otherwise stated
NA: not available
* median and range hence not included in meta analysis (Hall 2003 p = NS)
** data from a subgroup, hence not included in meta-analysis
*** data from PN glutamine group not shown here, appears in PN glutamine section
****Reports on mechanical ventilation

**Figure 1. Overall Mortality**

| | EN glutamine | | Control | | | Risk Ratio | |
|---|---|---|---|---|---|---|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | Year |
| Houdijk | 4 | 41 | 3 | 39 | 4.9% | 1.27 [0.30, 5.31] | 1998 |
| Jones | 10 | 26 | 9 | 24 | 17.5% | 1.03 [0.50, 2.08] | 1999 |
| Brantley | 0 | 31 | 0 | 41 | | Not estimable | 2000 |
| Hall | 24 | 179 | 23 | 184 | 27.5% | 1.07 [0.63, 1.83] | 2003 |
| Zhou | 0 | 20 | 0 | 20 | | Not estimable | 2003 |
| Garrel | 2 | 21 | 12 | 24 | 5.3% | 0.19 [0.05, 0.76] | 2003 |
| Lou | 1 | 12 | 0 | 9 | 1.1% | 2.31 [0.10, 50.85] | 2007 |
| McQuiggan | 0 | 10 | 2 | 10 | 1.2% | 0.20 [0.01, 3.70] | 2008 |
| Pattanshetti | 0 | 15 | 2 | 15 | 1.2% | 0.20 [0.01, 3.85] | 2009 |
| van Zanten | 38 | 152 | 33 | 149 | 39.9% | 1.13 [0.75, 1.70] | 2014 |
| Iamsirisaengthong | 1 | 10 | 1 | 10 | 1.5% | 1.00 [0.07, 13.87] | 2017 |
| **Total (95% CI)** | | **517** | | **525** | **100.0%** | **0.97 [0.70, 1.34]** | |
| Total events | 80 | | 85 | | | | |

Heterogeneity: Tau² = 0.03; Chi² = 8.86, df = 8 (P = 0.35); I² = 10%
Test for overall effect: Z = 0.20 (P = 0.84)

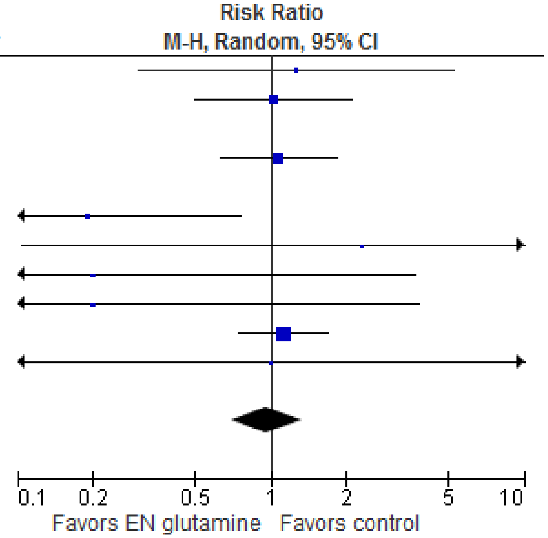



**Figure 2. Hospital Mortality, trauma subgroup analysis**

| | EN Glutamine | | Control | | | Risk Ratio | |
|---|---|---|---|---|---|---|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Random, 95% CI | Year |
| Houdijk | 4 | 41 | 3 | 39 | 20.3% | 1.27 [0.30, 5.31] | 1998 |
| Brantley | 0 | 31 | 0 | 41 | | Not estimable | 2000 |
| Hall | 7 | 76 | 6 | 78 | 38.2% | 1.20 [0.42, 3.40] | 2003 |
| McQuiggan | 0 | 10 | 2 | 10 | 4.9% | 0.20 [0.01, 3.70] | 2008 |
| van Zanten | 6 | 55 | 6 | 54 | 36.5% | 0.98 [0.34, 2.86] | 2014 |
| **Total (95% CI)** | | **213** | | **222** | **100.0%** | **1.03 [0.54, 1.97]** | |
| Total events | 17 | | 17 | | | | |

Heterogeneity: Tau² = 0.00; Chi² = 1.39, df = 3 (P = 0.71); I² = 0%
Test for overall effect: Z = 0.10 (P = 0.92)

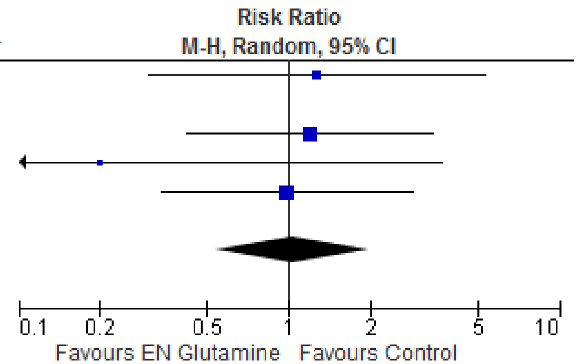


**Figure 3. Hospital Mortality, burns subgroup**

| Study or Subgroup | EN Glutamine Events | EN Glutamine Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Garrel | 2 | 21 | 12 | 24 | 67.0% | 0.19 [0.05, 0.76] | 2003 |
| Zhou | 0 | 20 | 0 | 20 | | Not estimable | 2003 |
| Pattanshetti | 0 | 15 | 2 | 15 | 14.6% | 0.20 [0.01, 3.85] | 2009 |
| Iamsirisaengthong | 1 | 10 | 1 | 10 | 18.4% | 1.00 [0.07, 13.87] | 2017 |
| **Total (95% CI)** | | **66** | | **69** | **100.0%** | **0.26 [0.08, 0.80]** | |
| Total events | 3 | | 15 | | | | |

Heterogeneity: Tau² = 0.00; Chi² = 1.24, df = 2 (P = 0.54); I² = 0%
Test for overall effect: Z = 2.34 (P = 0.02)

Risk Ratio M-H, Random, 95% CI

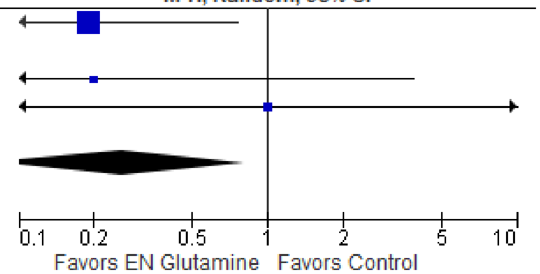



**Figure 4. Infectious Complications**

| Study or Subgroup | EN glutamine Events | EN glutamine Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Houdijk | 20 | 35 | 26 | 37 | 21.5% | 0.81 [0.57, 1.16] | 1998 |
| Zhou | 2 | 20 | 6 | 20 | 1.2% | 0.33 [0.08, 1.46] | 2003 |
| Hall | 38 | 179 | 43 | 184 | 18.4% | 0.91 [0.62, 1.33] | 2003 |
| van Zanten | 80 | 152 | 78 | 149 | 58.8% | 1.01 [0.81, 1.25] | 2014 |
| **Total (95% CI)** | | **386** | | **390** | **100.0%** | **0.93 [0.79, 1.10]** | |
| Total events | 140 | | 153 | | | | |

Heterogeneity: Tau² = 0.00; Chi² = 2.94, df = 3 (P = 0.40); I² = 0%
Test for overall effect: Z = 0.86 (P = 0.39)

Risk Ratio M-H, Random, 95% CI

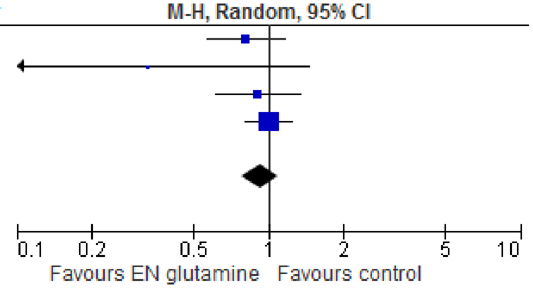



**Figure 5. Infectious Complications: trauma**

| Study or Subgroup | EN glutamine Events | EN glutamine Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| Houdijk | 20 | 35 | 26 | 37 | 40.5% | 0.81 [0.57, 1.16] | 1998 |
| van Zanten | 32 | 55 | 36 | 54 | 59.5% | 0.87 [0.65, 1.17] | 2014 |
| **Total (95% CI)** | | **90** | | **91** | **100.0%** | **0.85 [0.68, 1.06]** | |
| Total events | 52 | | 62 | | | | |

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.43 (P = 0.15)

Risk Ratio M-H, Random, 95% CI

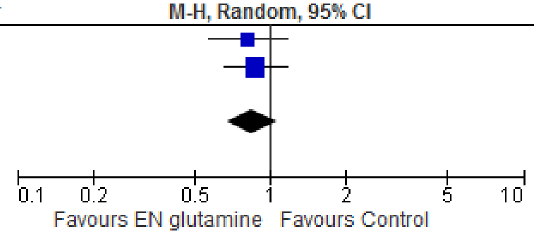


**Figure 6: Hospital LOS**

| | Enteral Glutamine | | | Control | | | | Mean Difference | |
|---|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | Year |
| Houdijk | 32.7 | 17.1 | 35 | 33 | 23.8 | 37 | 9.6% | -0.30 [-9.83, 9.23] | 1998 |
| Brantley | 19.5 | 8.8 | 31 | 20.8 | 11.5 | 41 | 20.9% | -1.30 [-5.99, 3.39] | 2000 |
| Zhou | 67 | 4 | 20 | 73 | 6 | 20 | 26.2% | -6.00 [-9.16, -2.84] | 2003 |
| Peng | 46.59 | 12.98 | 25 | 55.68 | 17.36 | 23 | 10.9% | -9.09 [-17.82, -0.36] | 2004 |
| McQuiggan | 32 | 13.6 | 10 | 39.3 | 33.6 | 10 | 2.3% | -7.30 [-29.77, 15.17] | 2008 |
| Pattanshetti | 22.73 | 9.13 | 15 | 39.73 | 18.27 | 15 | 8.6% | -17.00 [-27.34, -6.66] | 2009 |
| van Zanten | 38.2 | 28.9 | 152 | 37.7 | 27.5 | 149 | 15.9% | 0.50 [-5.87, 6.87] | 2014 |
| Iamsirisaengthong | 35.4 | 15.2 | 10 | 40.4 | 15.2 | 10 | 5.7% | -5.00 [-18.32, 8.32] | 2017 |
| **Total (95% CI)** | | | **298** | | | **305** | **100.0%** | **-4.69 [-8.19, -1.18]** | |

Heterogeneity: Tau² = 9.60; Chi² = 12.50, df = 7 (P = 0.09); I² = 44%
Test for overall effect: Z = 2.62 (P = 0.009)

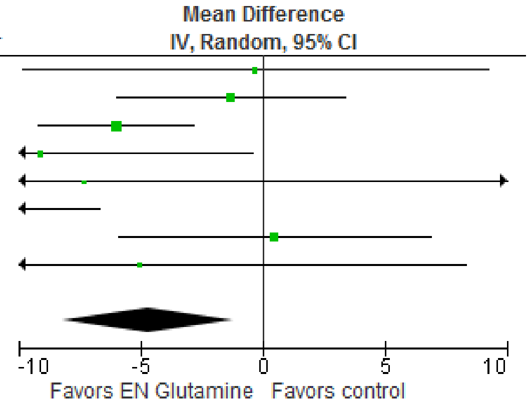
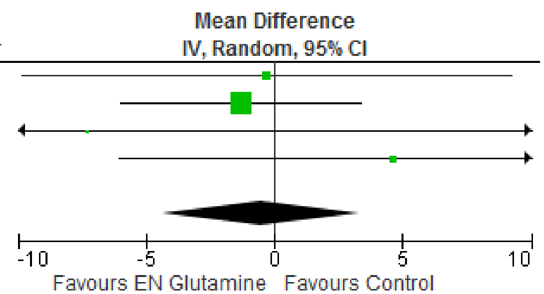



**Figure 7. Hospital LOS, trauma subgroup analysis**

| | EN Glutamine | | | Control | | | | Mean Difference | |
|---|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | Year |
| Houdijk | 32.7 | 17.1 | 35 | 33 | 23.8 | 37 | 16.4% | -0.30 [-9.83, 9.23] | 1998 |
| Brantley | 19.5 | 8.8 | 31 | 20.8 | 11.5 | 41 | 67.6% | -1.30 [-5.99, 3.39] | 2000 |
| McQuiggan | 32 | 13.6 | 10 | 39.3 | 33.6 | 10 | 2.9% | -7.30 [-29.77, 15.17] | 2008 |
| van Zanten | 44.4 | 31.2 | 55 | 39.8 | 25.3 | 54 | 13.1% | 4.60 [-6.05, 15.25] | 2014 |
| **Total (95% CI)** | | | **131** | | | **142** | **100.0%** | **-0.54 [-4.40, 3.31]** | |

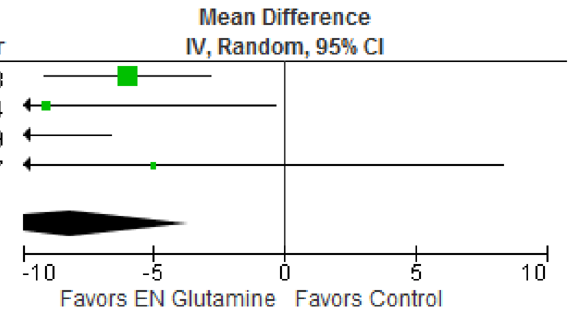
Heterogeneity: Tau² = 0.00; Chi² = 1.35, df = 3 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.27 (P = 0.78)



## Figure 8. Hospital LOS, burns subgroup analysis

| Study or Subgroup | EN Glutamine Mean | EN Glutamine SD | EN Glutamine Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|---|---|
| Zhou | 67 | 4 | 20 | 73 | 6 | 20 | 55.1% | -6.00 [-9.16, -2.84] | 2003 |
| Peng | 46.59 | 12.98 | 25 | 55.68 | 17.36 | 23 | 19.7% | -9.09 [-17.82, -0.36] | 2004 |
| Pattanshetti | 22.73 | 9.13 | 15 | 39.73 | 18.27 | 15 | 15.2% | -17.00 [-27.34, -6.66] | 2009 |
| Iamsirisaengthong | 35.4 | 15.2 | 10 | 40.4 | 15.2 | 10 | 9.9% | -5.00 [-18.32, 8.32] | 2017 |
| **Total (95% CI)** | | | **70** | | | **68** | **100.0%** | **-8.18 [-12.69, -3.67]** | |

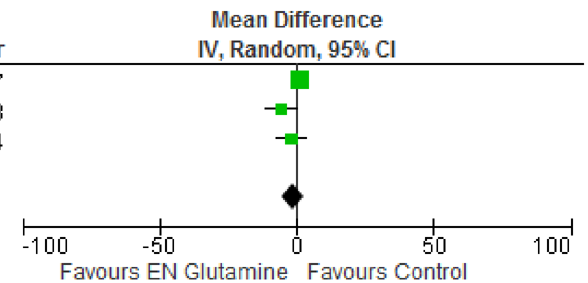
Heterogeneity: Tau² = 7.00; Chi² = 4.28, df = 3 (P = 0.23); I² = 30%
Test for overall effect: Z = 3.56 (P = 0.0004)




## Figure 9. ICU LOS, all studies

| Study or Subgroup | EN Glutamine Mean | EN Glutamine SD | EN Glutamine Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|---|---|
| Lou | 8.1 | 0.4 | 12 | 6.9 | 0.9 | 9 | 47.5% | 1.20 [0.57, 1.83] | 2007 |
| McQuiggan | 4.8 | 6.7 | 10 | 10.4 | 6.2 | 10 | 25.3% | -5.60 [-11.26, 0.06] | 2008 |
| van Zanten | 23.7 | 22.4 | 152 | 25.6 | 24 | 149 | 27.1% | -1.90 [-7.15, 3.35] | 2014 |
| **Total (95% CI)** | | | **174** | | | **168** | **100.0%** | **-1.36 [-5.51, 2.78]** | |

Heterogeneity: Tau² = 9.30; Chi² = 6.73, df = 2 (P = 0.03); I² = 70%
Test for overall effect: Z = 0.65 (P = 0.52)




## Figure 10. ICU LOS, trauma subgroup analysis

| Study or Subgroup | EN Glutamine Mean | EN Glutamine SD | EN Glutamine Total | Control Mean | Control SD | Control Total | Weight | Mean Difference IV, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|---|---|
| McQuiggan | 4.8 | 6.7 | 10 | 10.4 | 6.2 | 10 | 78.6% | -5.60 [-11.26, 0.06] | 2008 |
| van Zanten | 31.3 | 30.3 | 55 | 32.5 | 27.5 | 54 | 21.4% | -1.20 [-12.06, 9.66] | 2014 |
| **Total (95% CI)** | | | **65** | | | **64** | **100.0%** | **-4.66 [-9.68, 0.36]** | |

Heterogeneity: Tau² = 0.00; Chi² = 0.50, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 1.82 (P = 0.07)