9.2 Composition of Parenteral Nutrition: Type of lipids

Recommendation:

There are insufficient data to make a recommendation on the type of lipids to be used in critically ill patients receiving parenteral nutrition.

Discussion: The committee noted the variations in the types of lipids used in these small, single-centered studies and although the interventions aimed at reducing the overall omega 6 fatty acid content, there was too much variability in study design to allow for statistical aggregation of all the studies. When they were grouped by the nature of the experimental lipid, there was a lack of a clear signal towards a benefit in clinical outcomes. Only in two small studies using olive oil emulsions was a reduction in ICU length of stay observed; however, the control groups in both studies were different, the studies were small, and did not show any effect on mortality or other clinical parameter. Given this and the concerns around feasibility, potential safety concerns and cost of the varying lipid emulsions, the committee decided that there was not enough evidence to make a recommendation for one type of lipid emulsion over another.

<table>
<thead>
<tr>
<th>Definition</th>
<th>Score (0, 1, 2 or 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect size</td>
<td>0</td>
</tr>
<tr>
<td>Magnitude of the absolute risk reduction attributable to the intervention</td>
<td></td>
</tr>
<tr>
<td>listed--a higher score indicates a larger effect size</td>
<td></td>
</tr>
<tr>
<td>Confidence interval</td>
<td>1</td>
</tr>
<tr>
<td>95% confidence interval around the point estimate of the absolute risk</td>
<td></td>
</tr>
<tr>
<td>reduction, or the pooled estimate (if more than one trial)--a higher</td>
<td></td>
</tr>
<tr>
<td>score indicates a smaller confidence interval</td>
<td></td>
</tr>
<tr>
<td>Validity</td>
<td>2</td>
</tr>
<tr>
<td>Refers to internal validity of the study (or studies) as measured by the</td>
<td></td>
</tr>
<tr>
<td>presence of concealed randomization, blinded outcome adjudication, an</td>
<td></td>
</tr>
<tr>
<td>intention to treat analysis, and an explicit definition of outcomes--a</td>
<td></td>
</tr>
<tr>
<td>higher score indicates presence of more of these features in the trials</td>
<td></td>
</tr>
<tr>
<td>appraised</td>
<td></td>
</tr>
<tr>
<td>Homogeneity or Reproducibility</td>
<td>2</td>
</tr>
<tr>
<td>Similar direction of findings among trials--a higher score indicates</td>
<td></td>
</tr>
<tr>
<td>greater similarity of direction of findings among trials</td>
<td></td>
</tr>
<tr>
<td>Adequacy of control group</td>
<td>2</td>
</tr>
<tr>
<td>Extent to which the control group represented standard of care (large</td>
<td></td>
</tr>
<tr>
<td>dissimilarities = 1, minor dissimilarities=2, usual care=3)</td>
<td></td>
</tr>
<tr>
<td>Biological plausibility</td>
<td>2</td>
</tr>
<tr>
<td>Consistent with understanding of mechanistic and previous clinical work</td>
<td></td>
</tr>
<tr>
<td>(large inconsistencies =1, minimal inconsistencies =2, very consistent</td>
<td></td>
</tr>
<tr>
<td>=3)</td>
<td></td>
</tr>
<tr>
<td>Generalizability</td>
<td>1</td>
</tr>
<tr>
<td>Likelihood of trial findings being replicated in other settings (low</td>
<td></td>
</tr>
<tr>
<td>likelihood i.e. single centre =1, moderate likelihood i.e. multicentre</td>
<td></td>
</tr>
<tr>
<td>with limited patient population or practice setting =2, high likelihood</td>
<td></td>
</tr>
<tr>
<td>i.e. multicentre, heterogenous patients, diverse practice settings =3.</td>
<td></td>
</tr>
<tr>
<td>Low cost</td>
<td>2</td>
</tr>
<tr>
<td>Estimated cost of implementing the intervention listed--a higher score</td>
<td></td>
</tr>
<tr>
<td>indicates a lower cost to implement the intervention in an average ICU</td>
<td></td>
</tr>
<tr>
<td>Feasible</td>
<td>1</td>
</tr>
<tr>
<td>Ease of implementing the intervention listed--a higher score indicates</td>
<td></td>
</tr>
<tr>
<td>greater ease of implementing the intervention in an average ICU</td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>2</td>
</tr>
<tr>
<td>Estimated probability of avoiding any significant harm that may be</td>
<td></td>
</tr>
<tr>
<td>associated with the intervention listed--a higher score indicates a lower</td>
<td></td>
</tr>
<tr>
<td>probability of harm</td>
<td></td>
</tr>
</tbody>
</table>
9.2 Topic: Composition of Parenteral Nutrition: Type of lipids

May 27th 2009

Question: Does the type of lipids in parenteral nutrition affect outcomes in the critically ill adult patient?

Summary of evidence: There were 6 level 2 studies and 4 level 1 studies (Lindgren 2001, Grecu 2003, Wang 2008 and Friesecke 2008) reviewed. For most of the studies, the focus of the investigation was on surrogate endpoints but the studies were still included because they did report on mortality or infection. Four studies compared long chain triglycerides (LCTs) plus medium chain triglycerides (MCT) to a LCT emulsion (Nijveldt 1998, Lindgren 2001, Garnacho-Montero 2002 and Iovinelli 2007); 3 studies compared a fish oil containing emulsion (Omegaven) mixed with LCT or LCT/MCT to a LCT or LCT+MCT mixture (Grecu 2003, Wang 2008, Friesecke 2008) while 2 studies compared an olive oil containing emulsion (Clinoleic) to a LCT + MCT mixture (Garcia de-Lorenzo 2005, Huschak 2005). One study compared two different types of LCT emulsions (Kari 1998) In the Friesecke 2008 study, a mixture of LCT/MCT and fish oils (omega 3 fatty acids) was compared to a LCT/MCT mixture while in the Huschak study, a high lipid/low CHO emulsion mixed with olive oil was compared to a lower fat/higher CHO emulsion mixed with soybean oil.

Mortality: A meta-analysis of the studies of LCT+ MCT vs. LCT showed no difference in mortality between the groups (RR = 0.84, 95 % confidence intervals 0.43-1.61, p = 0.59) (figure 1). Similarly, no difference in mortality was seen between the groups of fish oils containing emulsions vs. LCT or LCT+ MCT (RR 0.76, 95 % CI 0.46, 1.26 , p = 0.29) (figure 2) or between the groups receiving the olive oil containing emulsions vs. LCT + MCT (RR 1.34, 95 %CI 0.47, 3.82, p = 0.59) (figure 3). There were no differences in mortality in the single trial that compared Emulsan to Intralipid (both LCT emulsions).

Infections: One study comparing LCT + MCT to MCT reported no differences in the incidences of new infections or positive blood cultures between the groups, however no data was reported (level 1 study Nijveldt 1998). In another study, a higher incidence of infections was observed in the intervention group (Lindgren 2001). When the data from the 3 studies of fish oil emulsions were aggregated, there was no significant effect on infection complications (RR 0.77, 95 % 0.39, 1.49, p =0.43) (figure 4). In the one study of olive oil emulsions (Clinoleic), there were no differences in the number of patients with infections between the two groups (Garcia de Lorenzo 2005) and the other study reported fewer infections in the intervention group (high fat plus Clinoleic) but no data was reported (Huschak 2005).

LOS and Ventilator days: When the data from the two studies comparing LCT+MCT to LCT were aggregated, there were no differences in ICU LOS between the two groups (WMD -1.46, 95 % CI -5.77, 2.85, p = 0.51, significant heterogeneity was present 78%) (figure 5). Similarly, when the data from the three studies of fish oil emulsions were aggregated, no effect on ICU LOS was observed (WMD -2.15, 95 %CI -10.31, 6.01, p = 0.61, significant heterogeneity was present 77%) (figure 6). When the data from the two studies of olive oil emulsions were aggregated, olive oil emulsions were associated with a significant reduction in ICU length of stay (WMD -7.59, 95 % CI -13.09, -2.09, p= 0.007) (figure 7).
Only one study comparing LCT+MCT to LCT reported duration of ventilation and no significant differences were seen between the two groups (Iovinelli 2007). When the data from the studies of fish oils were aggregated, there was no effect on duration of mechanical ventilation (WMD -1.04, 95% CI -5.22, 3.14, p = 0.63) (figure 8) however, the use of olive oil emulsions was associated with a significant reduction in the duration of mechanical ventilation (WMD – 6.47, 95% CI – 11.41, -1.53, p = 0.01), although significant heterogeneity was present (62%) (figure 9).

**Other complications:** A significant improvement in nutritional parameters (i.e. nitrogen balance, retinol binding protein, prealbumin) was observed in the groups receiving LCT + MCT in some of the studies (Garnacho-Montero, Lindgren) and a significant reduction in the time of weaning was seen in one study (Iovinelli 2007). The use of Omegaven was associated with a reduction in the need for surgery due to a subsequent septic episode when compared to LCT (p = 0.010, Grecu 2003).

**Conclusion:**

1) LCT+MCT, fish oil containing, olive oil containing emulsions have no effect on mortality or infections in critically ill patients.
2) LCT+MCT, fish oil containing emulsions have no effect on ICU LOS, while olive oil containing emulsions may be associated with a reduction in ICU LOS.
3) LCT+MCT, fish oil containing emulsions have no effect on mechanical ventilation, while olive oil containing emulsions may be associated with a reduction in mechanical ventilation.
4) The use of Emulsan (LCT emulsion) over Intralipid (LCT emulsion) has no effect on clinical outcomes 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 type of lipids (PN) in critically ill patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Methods (score)</th>
<th>Intervention</th>
<th>Mortality # (%)*</th>
<th>Infections # (%)+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long Chain Triglyceride (LCT) plus Medium Chain Triglycerides (MCT) vs. LCT</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1) Nijveldt 1998</td>
<td>ICU, septic surgical patients, trauma N = 20</td>
<td>C.Random: not sure ITT: yes Blinding: double (10)</td>
<td>PN + Lipofundin (50% LCT + 50% MCT) vs. PN + Intralipid (100% LCT, soybean)</td>
<td>LCT + MCT ICU 2/12 (17)</td>
<td>LCT ICU 1/8 (13) LCT + MCT NR</td>
</tr>
<tr>
<td>2) Lindgren 2001</td>
<td>ICU patients, sepsis, multi-trauma N = 30</td>
<td>C.Random: yes ITT: yes Blinding: yes (12)</td>
<td>PN + Structolipid (64% LCT + 36% MCT) vs. PN + Intralipid (100% LCT, soybean)</td>
<td>LCT + MCT ICU 1/15 (7)</td>
<td>LCT 0/15 (0) LCT + MCT 6/15 (40)</td>
</tr>
<tr>
<td>3) Garnacho-Montero 2002</td>
<td>Surgical ICU Patients with peritonitis and abdominal sepsis N = 72</td>
<td>C.Random: not sure ITT: no Blinding: no (6)</td>
<td>PN + Lipofundin (50% LCT + 50% MCT) vs. PN with Intralipid (100% LCT, soybean)</td>
<td>LCT + MCT ICU 8/35 (23)</td>
<td>LCT ICU 11/37 (30) LCT + MCT NR</td>
</tr>
<tr>
<td>4) Iovinelli 2007</td>
<td>Patients with COPD requiring ventilation N = 24</td>
<td>C.Random: yes ITT: yes Blinding: no (7)</td>
<td>PN + Lipofundin (50% LCT + 50% MCT) vs. 100% LCT (100% LCT, soybean). In both received 50% of non-protein calories given as lipids</td>
<td>LCT + MCT ICU 2/12 (17)</td>
<td>LCT ICU 3/12 (25) LCT + MCT Catheter-related 1/12 (8)</td>
</tr>
<tr>
<td><strong>Fish oil (ω 3) containing emulsions vs. LCT or LCT+MCT</strong></td>
<td></td>
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</tr>
<tr>
<td>5) Greuc 2003*</td>
<td>Patients with abdominal sepsis N = 54 (15/54 in ICU)</td>
<td>C.Random: yes ITT: yes Blinding: double (12)</td>
<td>PN + Omegaven (10% fish oils) plus LCTs vs. PN with LCT</td>
<td>Omegaven + LCT ICU 2/28 (7)</td>
<td>LCT ICU 3/26 (12) Omegaven VAP 0/8*</td>
</tr>
<tr>
<td>6) Wang 2008</td>
<td>Severe acute pancreatitis patients in ICU N = 40</td>
<td>C.Random: yes ITT: yes Blinding: double (11)</td>
<td>PN + Omegaven (10% fish oils) plus Lipovenos (LCTs, soybean oil) (ω3:ω6 ratio was 1:4) vs. PN with Lipovenos (LCTs, soybean oil). Both received same amounts of lipids (1 gm/kg/day)</td>
<td>Omegaven ICU 0/20</td>
<td>LCT ICU 2/20 (10) Omegaven 3/20 (15)</td>
</tr>
<tr>
<td>7) Friesecke 2008</td>
<td>Medical ICU patients N= 166</td>
<td>C.Random: yes ITT: yes Blinding: double</td>
<td>PN + Lipofundin MCT (50% LCT + 50% MCT) + Omegaven (10% fish oil) vs. Lipofundin MCT (50% LCT + 50% MCT)</td>
<td>LCT + MCT + Fish oil 28 day 18/83 (22)</td>
<td>LCT + MCT 28 day 22/82 (27)</td>
</tr>
<tr>
<td>Study</td>
<td>Population</td>
<td>Methods (score)</td>
<td>Intervention</td>
<td>Mortality # (%)†</td>
<td>Infections # (%)‡</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------------------------------------</td>
<td>----------------------------------</td>
<td>------------------------------------------------------------------------------</td>
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<td>-------------------</td>
</tr>
<tr>
<td>8) Garcia-de-Lorenzo 2005</td>
<td>Severe burn patients, burn severity index ≥ 7, TBSA &gt; 30 % N = 22</td>
<td>C.Random: not sure ITT: yes Blinding: double (10)</td>
<td>PN with ClinOleic 20% (80% olive oil, 20% soybean oil, (63% ω9, 37% ω6= restricted linoleic acid (ω6) content) vs. Lipofundin (50% LCT + 50% MCT).</td>
<td>Clinoleic 4/11 (36)</td>
<td>Lipofundin 4/11 (36)</td>
</tr>
<tr>
<td>9) Huschak 2005**</td>
<td>ICU trauma patients N = 33</td>
<td>C.Random: yes ITT: yes Blinding: None (7)</td>
<td>PN high fat (lipid:glucose 75:25) + Clinoleic (80% olive oil, 20% soybean oil) + EN Glicerina (lipid:glucose 60:40) vs. PN high carbohydrate (lipid:glucose 37.63) + Lipofundin (50% LCT + 50% MCT) + EN Fresubin HP Energy (lipid:glucose 44.56)</td>
<td>High fat + Clinoleic 4/18 (22)</td>
<td>Low fat + LCT + MCT 1/15 (7)</td>
</tr>
<tr>
<td>10) Kari 1998</td>
<td>ICU, severe injury patients N = 20</td>
<td>C.Random: not sure ITT: yes Blinding: no (6)</td>
<td>Two different types of lipids i.e. Emulsan (100% LCT, soybean oil- egg phosphatide) vs Intralipid (100% LCT)</td>
<td>Emulsan 2/10 (20)</td>
<td>Intralipid 2/10 (20)</td>
</tr>
</tbody>
</table>

Table 1. continued Randomized studies evaluating type of lipids (PN) in critically ill patients

<table>
<thead>
<tr>
<th>Study</th>
<th>LOS days</th>
<th>Ventilator days</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long Chain Triglyceride (LCT) plus Medium Chain Triglycerides (MCT) vs. LCT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Nijveldt 1998</td>
<td>LCT + MCT</td>
<td>LCT + MCT</td>
<td>LCT + MCT</td>
</tr>
<tr>
<td></td>
<td>13.8 ± 2.9 (12)</td>
<td>17.4 ± 3.0 (8)</td>
<td>NR</td>
</tr>
<tr>
<td>2) Lindgren 2001</td>
<td>LCT + MCT</td>
<td>LCT</td>
<td>LCT + MCT</td>
</tr>
<tr>
<td></td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>3) Garnacho-Montero 2002</td>
<td>LCT + MCT</td>
<td>LCT</td>
<td>LCT + MCT</td>
</tr>
<tr>
<td></td>
<td>ICU 16.6 ± 6.1 (36)</td>
<td>ICU 15.8 ± 7 (37)</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>LCT + MCT</td>
<td>LCT</td>
<td>LCT + MCT</td>
</tr>
<tr>
<td></td>
<td>2.6 ± 5.6 gms</td>
<td>-11.7 ± 4.8 gms</td>
<td>LCT + MCT</td>
</tr>
<tr>
<td></td>
<td>5/15 (33)</td>
<td>4/15 (27)</td>
<td>1.7 ± 1</td>
</tr>
<tr>
<td>Study</td>
<td>LOS days</td>
<td>Ventilator days</td>
<td>Other</td>
</tr>
<tr>
<td>-------</td>
<td>----------</td>
<td>----------------</td>
<td>-------</td>
</tr>
<tr>
<td>4) Iovinelli 2007</td>
<td>LCT + MCT NR</td>
<td>LCT 10.6 ± 3.0 (12)</td>
<td>LCT + MCT LCT Timebefore weaning 52 ± 36 hrs 127 ± 73 hrs</td>
</tr>
<tr>
<td>5) Grecu 2003*</td>
<td>Omegaven ICU 3.32 ± 1.48 (8)</td>
<td>LCT 2.83 ± 1.62 (8)</td>
<td>LCT + MCT LCT Patients undergoing reoperation for septic episode 2/28 (7) 8/26 (31)</td>
</tr>
<tr>
<td>6) Wang 2008</td>
<td>Omegaven ICU 21.4 ± 18.8 (20) Hospital 51.2 ± 32.6 (20)</td>
<td>LCT 23 ± 20 (82)</td>
<td>LCT + MCT LCT Omegaven LCT Duration of CRRT 18 ± 2.3 26 ± 3.4</td>
</tr>
<tr>
<td>7) Friesecke 2008</td>
<td>Fish oil ICU 28 ± 25 (83)</td>
<td>LCT 23 ± 20 (82)</td>
<td>LCT + MCT LCT + MCT + Fish oil Urinary Tract Infections 6/83 (7) 4/82 (5) Catheter-related infections 1/83 (1) 3/83 (4) Total EN Energy Intake (kcal/kg) 22.2 ± 5.5 21.6 ± 5.6</td>
</tr>
<tr>
<td>8) Garcia-de-Lorenzo 2005</td>
<td>Clinoleic ICU 32.9 ± 3.2 (11) Hospital 57.7 ± 4.6 (11)</td>
<td>Lipofundin ICU 41.8 ± 4.9 (11) Hospital 64.9 ± 8.2 (11)</td>
<td>Clinoleic Lipofundin Clinoleic Lipofundin Clinoleic Lipofundin Multiple organ dysfunction score 11.0 ± 3.6 13.0 ± 4.9</td>
</tr>
<tr>
<td>9) Huschak, 2005**</td>
<td>High fat + Clinoleic ICU 17.9 ± 11.2 (18)</td>
<td>Low fat + LCT + MCT ICU 25.1 ± 7.0 (15)</td>
<td>High fat + Clinoleic ICU 13.0 ± 8.9 (18)</td>
</tr>
<tr>
<td>10) Kari 1998</td>
<td>Emulsan NR</td>
<td>Intralipid NR</td>
<td>Emulsan NR</td>
</tr>
</tbody>
</table>

C.Random: concealed randomization
ITT: intent to treat
LCT: long chain triglycerides
MCT: medium chain triglycerides
NR: not reported
† hospital mortality unless specified
‡ number of patients with infections unless specified
* data obtained from author, 8 out of 28 in Omegaven and 7 out of 26 in LCT group were in ICU
**intervention includes high fat low CHO PN plus fish oil
**Figure 1. Studies comparing LCT + MCT to LCT**

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>LCT + MCT</th>
<th>LCT</th>
<th>RR (random)</th>
<th>Weight</th>
<th>RR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nijhol et al.</td>
<td>2/12</td>
<td>1/8</td>
<td>8.69</td>
<td></td>
<td>1.33</td>
</tr>
<tr>
<td>Lindgren</td>
<td>1/15</td>
<td>0/15</td>
<td>4.42</td>
<td>3.00</td>
<td>0.12</td>
</tr>
<tr>
<td>Gamache-Mortero</td>
<td>8/35</td>
<td>11/37</td>
<td>70.05</td>
<td>0.77</td>
<td>0.35</td>
</tr>
<tr>
<td>Iovielli</td>
<td>3/12</td>
<td>4/13</td>
<td>16.94</td>
<td>0.66</td>
<td>3.96</td>
</tr>
</tbody>
</table>

Total (95% CI): 74/72

Total events: 13 (LCT + MCT), 15 (LCT)

Test for heterogeneity: $\chi^2 = 0.94$, df = 3 ($P = 0.62$), $I^2 = 0$

Test for overall effect: $Z = 0.53$ ($P = 0.59$)

**Figure 2. Studies comparing Fish oil containing emulsions to LCT or LCT+MCT**

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Fish Oils</th>
<th>LCT, LCT/MCT</th>
<th>RR (random)</th>
<th>Weight</th>
<th>RR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groen</td>
<td>2/12</td>
<td>4/26</td>
<td>8.91</td>
<td>0.62</td>
<td>0.11</td>
</tr>
<tr>
<td>Frieschoe</td>
<td>19/85</td>
<td>22/82</td>
<td>98.15</td>
<td>0.91</td>
<td>0.47</td>
</tr>
<tr>
<td>Wang</td>
<td>0/20</td>
<td>2/20</td>
<td>2.94</td>
<td>0.20</td>
<td>3.92</td>
</tr>
</tbody>
</table>

Total (95% CI): 131/128

Total events: 20 (Fish Oils), 27 (LCT, LCT/MCT)

Test for heterogeneity: $\chi^2 = 0.90$, df = 2 ($P = 0.64$), $I^2 = 0$

Test for overall effect: $Z = 1.07$ ($P = 0.29$)
Figure 3. Studies comparing Olive oil containing emulsions vs. LCT+MCT

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Olive Oils n/N</th>
<th>LCT/MCT n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garcia de Lorenzo</td>
<td>4/11</td>
<td>4/11</td>
<td>75.87</td>
<td>1.00</td>
<td>0.30 [0.01, 3.02]</td>
<td>2003</td>
</tr>
<tr>
<td>Huschak</td>
<td>4/18</td>
<td>1/15</td>
<td>24.13</td>
<td>3.33</td>
<td>0.42 [0.26, 0.97]</td>
<td>2008</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>29</td>
<td>26</td>
<td>100.00</td>
<td>1.34</td>
<td>0.47 [0.38, 1.28]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 0.66, df = 2 (P = 0.72), I² = 0%
Test for overall effect: Z = 0.79 (P = 0.43)

Figure 4. Studies comparing Fish oil containing emulsions to LCT or LCT+MCT

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Omega 6 Sparing n/N</th>
<th>LCT n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grecu</td>
<td>0/8</td>
<td>1/7</td>
<td>4.72</td>
<td>0.30</td>
<td>0.01 [0.01, 6.29]</td>
<td>2003</td>
</tr>
<tr>
<td>Friesecke</td>
<td>10/83</td>
<td>11/82</td>
<td>68.81</td>
<td>0.90</td>
<td>0.40 [2.00]</td>
<td>2008</td>
</tr>
<tr>
<td>Wang</td>
<td>3/20</td>
<td>5/20</td>
<td>26.47</td>
<td>0.60</td>
<td>0.17 [2.18]</td>
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</tr>
<tr>
<td>Total (95% CI)</td>
<td>111</td>
<td>109</td>
<td>100.00</td>
<td>0.77</td>
<td>0.39 [1.49]</td>
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</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 0.66, df = 2 (P = 0.72), I² = 0%
Test for overall effect: Z = 0.79 (P = 0.43)
FIGURE 5. Studies comparing LCT + MCT to LCT

<table>
<thead>
<tr>
<th>Study of sub-category</th>
<th>N</th>
<th>LCT+MCT Mean (SD)</th>
<th>LCT Mean (SD)</th>
<th>WMD (random)</th>
<th>Weight %</th>
<th>95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garcia de Lorenzo</td>
<td>12</td>
<td>16.80(2.90)</td>
<td>17.40(2.00)</td>
<td>-0.60 (-2.25, 0.95)</td>
<td>51.45</td>
<td>-6.00 (P = 0.05)</td>
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</tr>
<tr>
<td>Germano-Montero</td>
<td>33</td>
<td>16.60(1.30)</td>
<td>15.80(7.00)</td>
<td>0.80 (-2.23, 3.83)</td>
<td>48.55</td>
<td></td>
<td></td>
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</table>

Total (95% CI) 47 46
Test for heterogeneity: Chi² = 4.58, df = 1 (P = 0.03), I² = 79.2%
Test for overall effect: Z = 2.07 (P = 0.05)

Figure 6. Studies comparing Fish oil containing emulsions to LCT or LCT+MCT

<table>
<thead>
<tr>
<th>Study of sub-category</th>
<th>N</th>
<th>Fish Oil Mean (SD)</th>
<th>LCT, LCT+MCT Mean (SD)</th>
<th>WMD (random)</th>
<th>Weight %</th>
<th>95% CI</th>
<th>Year</th>
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</thead>
<tbody>
<tr>
<td>Greco</td>
<td>8</td>
<td>3.32(1.48)</td>
<td>9.28(3.08)</td>
<td>-5.96 (-8.46, -3.46)</td>
<td>48.91</td>
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<td></td>
</tr>
<tr>
<td>Frieschké</td>
<td>83</td>
<td>28.00(27.60)</td>
<td>23.50(20.60)</td>
<td>5.50 (-1.55, 11.50)</td>
<td>55.04</td>
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<td></td>
</tr>
<tr>
<td>Vergel</td>
<td>25</td>
<td>21.40(13.80)</td>
<td>27.50(25.00)</td>
<td>6.10 (-19.81, 7.61)</td>
<td>28.15</td>
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</tbody>
</table>

Total (95% CI) 111 109
Test for heterogeneity: Chi² = 2.88, df = 2 (P = 0.24), I² = 76.2%
Test for overall effect: Z = 2.52 (P = 0.01)

Figure 7. Studies comparing Olive oil containing emulsions vs. LCT+MCT

<table>
<thead>
<tr>
<th>Study of sub-category</th>
<th>N</th>
<th>Omega 6 Sparing Mean (SD)</th>
<th>LCT Mean (SD)</th>
<th>WMD (random)</th>
<th>Weight %</th>
<th>95% CI</th>
<th>Year</th>
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</thead>
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<tr>
<td>García de Lorenzo</td>
<td>11</td>
<td>32.90(10.60)</td>
<td>41.80(16.30)</td>
<td>-8.90 [-20.39, 2.59]</td>
<td>22.95</td>
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<tr>
<td>Huschak</td>
<td>18</td>
<td>17.90(11.20)</td>
<td>25.10(7.00)</td>
<td>-7.20 [-13.47, -0.93]</td>
<td>77.05</td>
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Total (95% CI) 29 26
Test for heterogeneity: Chi² = 0.06, df = 1 (P = 0.80), I² = 0%
Test for overall effect: Z = 2.70 (P = 0.007)
### Figure 8. Studies comparing Fish oil containing emulsions to LCT or LCT+MCT

**Review:** Type of PN lipids  
**Comparison:** 01 Fish Oils vs. LCT/MCT  
**Outcome:** 04 Mechanical Ventilation

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Omega 6 Sparing</th>
<th>LCT</th>
<th>WMD (random)</th>
<th>Weight</th>
<th>WMD (random)</th>
<th>Year</th>
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<td>N Mean (SD)</td>
<td>95% CI</td>
<td>% 95% CI</td>
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<tr>
<td>Grecu</td>
<td>8 2.83(1.62)</td>
<td>7 5.23(2.80)</td>
<td>70.99  -2.40 [-4.76, -0.04]</td>
<td>2003</td>
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<tr>
<td>Friesecke</td>
<td>83 22.80(22.90)</td>
<td>82 20.50(19.00)</td>
<td>29.01  2.30 [-4.12, 8.72]</td>
<td>2008</td>
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<td>Total (95% CI)</td>
<td>91</td>
<td>89</td>
<td>100.00  -1.04 [-5.22, 3.14]</td>
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**Test for heterogeneity:** Chi² = 1.82, df = 1 (P = 0.18), I² = 44.9%  
**Test for overall effect:** Z = 0.49 (P = 0.63)

### Figure 9. Studies comparing Olive oil containing emulsions vs. LCT+MCT change

**Review:** Type of PN lipids  
**Comparison:** 01 Olive Oils vs. LCT/MCT  
**Outcome:** 04 Mechanical Ventilation

<table>
<thead>
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<th>Study or sub-category</th>
<th>Omega 6 Sparing</th>
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<th>Weight</th>
<th>WMD (random)</th>
<th>Year</th>
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<td></td>
<td>N Mean (SD)</td>
<td>N Mean (SD)</td>
<td>95% CI</td>
<td>% 95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Garcia de Lorenzo</td>
<td>11 11.00(11.93)</td>
<td>11 13.00(16.25)</td>
<td>17.19  -2.00 [-13.91, 9.91]</td>
<td>2005</td>
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<td></td>
</tr>
<tr>
<td>Huschak</td>
<td>18 13.00(8.90)</td>
<td>15 20.40(7.00)</td>
<td>82.81  -7.40 [-12.83, -1.97]</td>
<td>2005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>29</td>
<td>26</td>
<td>100.00  -6.47 [-11.41, -1.53]</td>
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**Test for heterogeneity:** Chi² = 0.65, df = 1 (P = 0.42), I² = 0%  
**Test for overall effect:** Z = 2.57 (P = 0.01)
Overall Omega 6 fatty acid Sparing Strategy (all studies of lower LCT {omega 6 fatty acids} load vs. LCT)

### Mortality

<table>
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<tr>
<th>Study or sub-category</th>
<th>Omega 6 Sparing n/N</th>
<th>LCT n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Year</th>
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<tr>
<td>Lindgren</td>
<td>1/15</td>
<td>0/15</td>
<td>3.69 [0.01, 68.26]</td>
<td>0.20</td>
<td>0.01, 68.26</td>
<td>2001</td>
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<tr>
<td>Carnecho-Mortero</td>
<td>3/15</td>
<td>11/37</td>
<td>0.71 [0.05, 12.37]</td>
<td>2.02</td>
<td>0.05, 12.37</td>
<td>2002</td>
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<tr>
<td>Greco</td>
<td>2/12</td>
<td>3/12</td>
<td>12.35 [0.01, 12.35]</td>
<td>0.62</td>
<td>0.01, 12.35</td>
<td>2003</td>
</tr>
<tr>
<td>Iovirelli</td>
<td>2/12</td>
<td>3/12</td>
<td>14.08 [0.01, 13.30]</td>
<td>0.67</td>
<td>0.01, 13.30</td>
<td>2006</td>
</tr>
<tr>
<td>Wang</td>
<td>0/20</td>
<td>2/20</td>
<td>4.07 [0.01, 2.19]</td>
<td>0.20</td>
<td>0.01, 2.19</td>
<td>2006</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>122</td>
<td>118</td>
<td>1.00 [0.42, 1.39]</td>
<td>0.76</td>
<td>0.42, 1.39</td>
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</table>

Total events: 16 (Omega 6 Sparing), 20 (LCT)
Test for heterogeneity: $\chi^2 = 1.61$, df = 5 (P = 0.67), $I^2 = 0$
Test for overall effect: $Z = 3.00$ (P = 0.05)

### Infections

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Omega 6 Sparing n/N</th>
<th>LCT n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lindgren</td>
<td>5/15</td>
<td>4/15</td>
<td>56.43 [1.53, 4.26]</td>
<td>1.50</td>
<td>0.53, 4.26</td>
<td>2001</td>
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<tr>
<td>Greco</td>
<td>0/8</td>
<td>1/7</td>
<td>6.59 [0.01, 6.29]</td>
<td>0.30</td>
<td>0.01, 6.29</td>
<td>2003</td>
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<tr>
<td>Wang</td>
<td>0/20</td>
<td>5/20</td>
<td>36.90 [0.01, 2.10]</td>
<td>0.60</td>
<td>0.01, 2.10</td>
<td>2006</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td>43</td>
<td>42</td>
<td>1.00 [0.44, 2.11]</td>
<td>0.96</td>
<td>0.44, 2.11</td>
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Total events: 9 (Omega 6 Sparing), 11 (LCT)
Test for heterogeneity: $\chi^2 = 1.61$, df = 4 (P = 0.40), $I^2 = 0$
Test for overall effect: $Z = 3.10$ (P = 0.05)
### Review: Type of PN lipids

**Comparison:** 01 Omega 6 Sparing vs. LCT  
**Outcome:** 04 Mechanical Ventilation

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Omega 6 Sparing</th>
<th>LCT</th>
<th>WMD (random)</th>
<th>Weight</th>
<th>KMD (random)</th>
<th>Year</th>
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<tbody>
<tr>
<td></td>
<td>N</td>
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<td>N</td>
<td>Mean (SD)</td>
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<td>%</td>
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<tr>
<td>Grecu</td>
<td>12</td>
<td>13.88 (2.92)</td>
<td>8</td>
<td>17.42 (3.00)</td>
<td>95.01</td>
<td>68.20 (2.40)</td>
</tr>
<tr>
<td>Iovinelli</td>
<td>25</td>
<td>15.49 (6.10)</td>
<td>27</td>
<td>15.85 (7.00)</td>
<td>95.01</td>
<td>68.20 (2.40)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Omega 6 Sparing</th>
<th>LCT</th>
<th>WMD (random)</th>
<th>Weight</th>
<th>KMD (random)</th>
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<tbody>
<tr>
<td></td>
<td>N</td>
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<td>%</td>
</tr>
<tr>
<td>Grecu</td>
<td>12</td>
<td>2.83 (1.62)</td>
<td>7</td>
<td>5.23 (2.80)</td>
<td>95.01</td>
<td>68.20 (2.40)</td>
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<tr>
<td>Iovinelli</td>
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<td>10.60 (3.00)</td>
<td>12</td>
<td>13.40 (3.50)</td>
<td>95.01</td>
<td>68.20 (2.40)</td>
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</tbody>
</table>

**Total (95% CI):**  
Test for heterogeneity: Chi² = 11.50, df = 3 (P = 0.008), I² = 74.1%  
Test for overall effect: Z = 2.89 (P = 0.004)

---

**Review: Type of PN lipids**  
**Comparison:** 01 Omega 6 Sparing vs. LCT  
**Outcome:** 04 ICU LOS

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Omega 6 Sparing</th>
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<th>WMD (random)</th>
<th>Weight</th>
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<th>Study or sub-category</th>
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<th>Weight</th>
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<td>68.20 (2.40)</td>
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**Total (95% CI):**  
Test for heterogeneity: Chi² = 0.05, df = 1 (P = 0.82), I² = 0%  
Test for overall effect: Z = 2.89 (P = 0.004)
TOPIC: 9.2 Composition of PN: Type of lipids

Article inclusion log
Criteria for study selection

Type of study: RCT or Meta-analysis
Population: critically ill ventilated patients (no elective surgery patients)
Intervention: TPN
Outcomes: mortality, LOS, QOL, functional recovery, complications, cost. Exclude studies with only biochemical, metabolic or nutritional outcomes.

Included articles

LCT + MCT vs. LCT

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Fish Oil containing emulsions

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Olive Oil containing emulsions

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LCT vs. LCT

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I = included, E = excluded
References

**LCT + MCT vs. LCT**


**Fish Oil containing emulsions**


**Olive Oil containing emulsions**


LCT vs. LCT


Excluded References


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