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Author contact	greet.vandenberghe@med.kuleuven.be + 32 (0)16 344021
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Parenteral nutrition in the critically ill

Jan GUNST, MD, PhD and Greet VAN DEN BERGHE, MD, PhD

Clinical Division and Laboratory of Intensive Care Medicine,
Department of Cellular and Molecular Medicine, KU Leuven,
Herestraat 49, B-3000 Leuven, Belgium

Correspondence to:

Prof Greet Van den Berghe, MD, PhD
Clinical Division and Laboratory of Intensive Care Medicine,
Department of Cellular and Molecular Medicine,
KU Leuven,
Herestraat 49, B-3000 Leuven, Belgium
Phone +32-16-344021
Fax +32-16-344015
e-mail greet.vandenbergh@kuleuven.be

Abstract

Purpose of review: Feeding guidelines have recommended early, full nutritional support in critically ill patients to prevent hypercatabolism and muscle weakness. Early enteral nutrition (EN) was suggested to be superior to early parenteral nutrition (PN). When EN fails to meet nutritional target, it was recommended to administer supplemental PN, albeit with a varying starting point. Sufficient amounts of amino acids were recommended, with addition of glutamine in subgroups. Recently, several large RCTs have yielded important new insights. This review summarizes recent evidence with regard to the indication, timing and dosing of PN in critically ill patients.

Recent findings: One large RCT revealed no difference between early EN and early PN. Two large multicenter RCTs showed harm by early supplementation of insufficient EN with PN, which could be explained by feeding-induced suppression of autophagy. Several RCTs found either no benefit or harm with a higher amino acid or caloric intake, as well as harm by administration of glutamine.

Summary: Although unanswered questions remain, current evidence supports accepting low macronutrient intake during the acute phase of critical illness and does not support use of early PN. The timing when PN can be initiated safely and effectively is unclear.

Keywords: parenteral nutrition, critical illness, intensive care, protein, caloric intake

Introduction

Many critically ill patients develop muscle wasting and weakness, which has been associated with adverse outcome [1-3]. Traditionally, part of the hypercatabolism of critical illness was attributed to anorexia, gastrointestinal dysfunction and the resultant decreased feeding intake that accompanies severe illness [4, 5]. Several observational studies have associated a caloric and/or protein deficit with an increased mortality [6-10]. In healthy volunteers, prolonged starvation leads to a similar degree of muscle wasting, which obviously can be reversed by restarting nutrition [11]. Therefore, feeding guidelines have recommended to prevent caloric and protein underfeeding in critically ill patients and to initiate early, normocaloric enteral nutrition (EN) [12-14]. Association studies, however, do not prove causality, which requires an adequately powered randomized controlled trial (RCT). As EN is often less efficacious in sicker patients, the association of a reduced nutritional intake with poor outcome could also be explained by a higher severity of illness. Recently, several large, adequately powered RCTs have questioned a number of traditional assumptions. In contrast to the expectations, these RCTs commonly found that early, aggressive nutritional support did not deliver the hypothesized clinical benefit and may even be harmful. This review summarizes the most recent evidence with regard to the indication, timing and dosing of parenteral nutrition (PN) for critically ill patients.

Enteral versus parenteral nutrition

When artificial nutrition is indicated, early EN has been recommended over PN [12-14]. Compared to PN, EN has been associated with less infections, may better preserve the integrity of the gastrointestinal epithelium, and is presumably cheaper [15]. However, the association

with infections may partially be explained by overfeeding in older studies and its related complications (among which hyperglycemia). Moreover, early EN often fails to meet the nutritional target because of contraindications and gastrointestinal intolerance [15]. Therefore, some authors have suggested that early PN, while carefully avoiding overfeeding and hyperglycemia, may be preferable to early EN [16**].

Recently, the CALORIES trial investigated this hypothesis (table 1) [16**]. In this large multicenter RCT, 2400 adult critically ill patients who could be fed through either route were randomized to receive early EN or early PN. In contrast to the setup, the achieved caloric intake was similar in both groups. The primary endpoint – mortality at 30 days – was unaffected and also secondary endpoints were largely similar, except for more vomiting by early EN.

A recent meta-analysis including RCTs comparing early EN versus PN also found no mortality difference, but did find a reduction in infectious complications with EN [17*]. However, this difference was explained by the subset of trials in which the PN group received more calories. Moreover, several of these trials were relatively old, with presumably poor blood glucose control. In addition, the meta-analysis revealed substantial publication bias.

Hence, recent studies suggest that, in current intensive care unit (ICU) practice, there is no clear difference between enteral and parenteral feeding when an isocaloric and isonitrogenous dose is given. The association of early PN with infectious complications may be dose-related rather than route-related. However, as the enteral route is the easiest and probably cheapest route of providing nutrition, it remains the preferred option if possible [14].

Timing of parenteral nutrition

As early EN often fails to meet the nutritional target because of intolerance or absolute contraindications, the question arises when to initiate supplemental PN. Until recently, due the lack of large RCTs, two opposing strategies existed, which was reflected in divergent guidelines [12, 13]. Proponents of early supplemental PN advocated to supplement failing EN within the first days in ICU, in order to prevent a nutritional deficit [4]. Others advocated to wait at least one week before adding PN, which was based on a presumably increased risk of infections [18]. In the last five years, four multicenter RCTs have investigated the timing of (supplemental) PN in critically ill patients (table 2) [19-22].

In the Early PN trial, 1372 adult patients with a relative contraindication to early EN were randomized to receive early PN versus standard care [19]. In the intervention group, early PN was initiated within 24 hours of ICU admission. There was no difference in mortality at 60 days -the primary endpoint- as was the case in predefined subgroups. The authors suggested a small, possible morbidity benefit by early PN, as days of mechanical ventilation –a tertiary outcome parameter- were slightly reduced (-0.47 days per 10 patient x ICU days). However, the significance of this perceived benefit is questionable, with no meaningful other morbidity benefit and no impact on the ICU length of stay. Moreover, the study suffered some important methodological shortcomings. First, in the standard care group, PN use was not protocolized and more than one third of patients in this group also received PN in the first days in ICU. In addition, the study population is not well defined. Indeed, the number of patients screened for eligibility and the reasons for exclusion are not reported. Likely, the study population represents only a small subset of the total number of potentially eligible patients, as participating centers included on average only 9 patients per year over a period of 5 years. Slow recruitment also led

to premature stopping of the trial, which increases the chance of a false positive result [23]. Finally, parenteral micronutrients were only advised in the intervention group.

In the EPaNIC study, 4640 adult critically ill patients were randomized to early supplementation of insufficient EN with PN versus withholding PN for one week [20**]. In both groups, EN was attempted early if possible, and sufficient intake of micronutrients was ensured to prevent refeeding syndrome. In the early PN group, intravenous glucose was initiated after ICU admission and when EN was still insufficient at day 3, supplemental PN was started. In the late PN group, supplemental PN was only initiated at day 8. More than 90% of potentially eligible patients were included. In contrast to the expectations, early supplemental PN led a prolonged dependency on intensive care with, among others, an increased dependency on vital organ support and an increased incidence of new infections and of muscle weakness [20**, 24]. Withholding PN in the acute phase not only improved clinical outcome, it also was cost-saving [25]. Importantly, the effect of intervention was present in all studied subgroups. Moreover, harm by early PN was even more pronounced in the large subgroup with a contraindication for EN upon admission [20**]. In detailed preplanned secondary analyses, the investigators found that early PN did not counter-act microscopic nor macroscopic muscle wasting [26, 27]. Interestingly, the majority of the extra infused amino acids by early PN was net wasted in ureagenesis [28]. A potential explanation for the harm by early PN is the suppression of autophagy by more aggressive feeding [24, 29-31]. Indeed, autophagy is an important housekeeping process that is strongly inhibited by nutrients. It is crucial for maintaining cellular integrity and is normally activated by cellular stress to remove cellular damage [32].

The harmful impact of early supplemental PN was recently confirmed in a large multicenter RCT in critically ill children (n=1440) [21**]. Indeed, in the PEPaNIC study, early

supplemental PN also led to an increased ICU dependency, with an increased dependency on vital organ support and an increased incidence of new infections. The effect of the intervention was present regardless of baseline risk factors. Moreover, younger children and children with the greatest nutritional risk had most harm from early PN.

Finally, the SPN study enrolled 305 adult critically ill patients with enteral intake below 60% of their energy target at day 3 and who were expected to stay for minimum 5 more days in ICU [22]. Patients were randomized to supplemental PN from day 4 versus no PN before day 9. Although initially, a benefit from early supplemental PN was suggested, with a decreased rate of new infections from day 9 to day 28, this was counteracted by an increased incidence of infections from randomization until day 9 [33]. The impact of the intervention from randomization onward was neutral.

In summary, several multicenter RCTs have shown that early initiation of (supplemental) PN is not beneficial and may be harmful, as found in the two largest RCTs [19-22]. Currently, the timing at which PN can be initiated safely and effectively is unclear. Theoretically, harm by early supplemental PN could be explained by the different route or the different nutritional dose. However, the CALORIES trial and a recent meta-analysis suggest that the harm is explained by the higher dose rather than by the different route [16**, 17*]. Several authors have argued that the harm by early PN observed in EPaNIC and PEPaNIC is explained by the specific content of the PN solution, with a lower than recommended amino acid intake in the early PN group [5, 34]. However, a secondary analysis of the EPaNIC study suggested increased harm with a higher achieved amino acid intake [35]. Moreover, over two weeks in ICU, almost two third of the extra amino acid supply by early PN was wasted in urea, which makes it unlikely that an increased amino acid dose would have been beneficial [28]. Of course, these

observational data remain hypothesis-generating. Nevertheless, several recent RCTs investigating different nutritional doses have confirmed these findings to some extent. In the following sections, we will review the RCTs investigating different energy and/or protein targets in critically ill patients, regardless of the route of administration (table 3) [36-41*].

Caloric target

Current feeding guidelines recommend to match caloric intake to 80-100% of estimated or measured energy expenditure (normocaloric feeding) [12-14]. Most often, however, energy expenditure is not measured and feeding targets are calculated based on equations such as the Harris-Benedict formula. In general, feeding targets of 20-30 kcal/kg/day are applied (for adults). However, evidence from RCTs supporting this practice is limited.

In a pilot study, Singer et al. investigated whether indirect calorimetry-based feeding is superior to formula-based feeding (target 25 kcal/kg/day) [36]. Indirect calorimetry was performed throughout ICU stay and was repeated every 48 hours. Although the primary endpoint (hospital mortality) was not statistically different, morbidity was increased in the indirect calorimetry group, which received approximately 600 kcal/day more. Together with the results from the RCTs mentioned above, this may imply that feeding less calories is better in the acute phase of critical illness.

Recently, several RCTs have investigated whether intentional underfeeding is safe or even superior in the acute phase of critical illness. In a single-center study, Rice et al. randomized 200 patients with acute respiratory failure to receive ‘trophic’ or ‘full’ EN for the first 6 days in ICU [37]. Patients in the ‘trophic’ group received low amounts of both calories and protein

(table 3). The intervention did not have an impact on the primary endpoint (ventilator-free days) or other secondary endpoints, except for more gastrointestinal intolerance in the ‘full’ fed group. The EDEN trial, a subsequent multicenter RCT, confirmed these findings in a larger patient population with acute lung injury (n=1200) [38]. In this study, also long-term follow-up did not reveal any impact on physical nor neurocognitive function, nor on mortality up to one year [42, 43].

Arabi et al. investigated whether hypocaloric feeding, while only restricting non-protein calories but maintaining a ‘normal’ amino acid intake, is superior to normocaloric feeding. A pilot single-center study (n=240) found no impact on the primary endpoint (mortality at day 28), but found a significantly lower hospital mortality [39]. However, the difference in caloric intake was very small (approximately 200 kcal/day). Subsequently, the same group designed a multicenter study, which found no impact with a larger difference in caloric intake (approximately 450 kcal/d) [40*]. However, the anticipated mortality reduction of 8% (absolute risk reduction) appears unrealistic, so the study was likely underpowered. Subgroup analyses confirmed a similar effect in patients with the highest nutritional risk score as defined by the NUTRIC score [44*]. Interestingly, however, when nutritional risk was defined according to prealbumin, patients with the lowest prealbumin (who are considered to be at the highest nutritional risk) had a significantly lower mortality with hypocaloric feeding [44*].

A recent meta-analysis including RCTs comparing intentional hypocaloric versus normocaloric feeding found no difference in outcome [45*]. A second meta-analysis, which included all studies in which a significant difference in enteral intake was achieved, found no association of caloric intake with mortality, but associated a lower caloric intake with a lower risk of bloodstream infections and incident renal replacement therapy [46*]. This meta-analysis also

included RCTs in which underfeeding was not intentional, e.g. RCTs on the role of measuring gastric residual volumes. Hence, the resultant heterogeneity warrants caution. Altogether, recent evidence indicates that restricting energy intake during acute critical illness is safe and may be superior.

Protein target

Several authors have argued that the disappointing results from the recent nutritional RCTs in ICU are explained by an unfavorable protein-to-energy ratio [5, 47]. Although the energy target was usually met in the group that received most feeding, protein target often was below the recommended target (1.2-1.5 g/kg/day in [12], 1.2-2.0 g/kg/day in [14]).

Until now, only one RCT has adequately studied the impact of administering supplementary amino acids to critically ill patients. In the Nephro-Protective trial, 474 patients were randomized to receive a daily intravenous amino acid supplement versus standard care [41*]. On average, patients in the amino acid group received 1.75 g/kg/day of amino acids, compared to 0.75 g/kg/day in the standard care group. The primary endpoint (duration of renal dysfunction) was unaffected. The intervention led to a small increase in eGFR, with a peak difference of 7.7 ml/min/1.73m². However, as in the EPaNIC study, increased amino acid administration led to substantially increased ureagenesis, with a non-significant trend towards more renal replacement therapy [28, 41*]. There were no data on muscle weakness.

In summary, RCTs comparing different energy or protein targets in the acute phase of critical illness have not found a benefit from administering higher doses and several trials suggested harm. These findings are supported by two cluster RCTs that did not find a clinical benefit by

implementing a protocol that ‘optimizes’ nutritional intake [48, 49]. In addition, one small single-center RCT found greater hospital mortality with an intensified nutrition strategy [50].

Micronutrients and refeeding syndrome

Although restricting nutritional intake in the acute phase of critical illness appears safe and possibly beneficial, a depletion of micronutrients (elektrolytes, trace elements and vitamins) should be avoided to prevent refeeding syndrome [15]. Indeed, rapid reinstitution of feeding in malnourished or starved patients may lead to severe metabolic disturbances resulting in cardiac arrhythmias, respiratory failure, seizures and ultimately death. Hallmark abnormalities of the so-called refeeding syndrome are hypophosphatemia, hypokalemia and thiamine deficiency, which are caused by a substantially increased utilization of these micronutrients in a re-fed state. Doig et al. have shown that, once refeeding syndrome occurs, temporarily restricting feeding intake again may be beneficial [51*]. 339 patients with refeeding syndrome were randomized to temporary restriction of energy intake versus continuation (and even increase) hereof. In the restricted group, caloric intake was reduced to 480 kcal/day for at least 2 days, and thereafter gradually increased. Although the primary endpoint (ICU-free survival days at day 60) was unaffected, the short-term mortality and rate of infections decreased by temporary feeding restriction.

Immunonutrition

Small studies have suggested that certain nutrients with immune-modulating properties may improve outcome of critically ill patients. These include glutamine, omega-3 fatty acids, gamma-linolenic acid and pharmacological amounts of vitamins (vitamin C, vitamin E, beta-

carotene) and trace elements (selenium, zinc). Large multicenter trials, however, have not confirmed these beneficial effects and some suggested harm, especially for glutamine (table 4) [52-57**].

Implications for clinical practice

Although several questions remain unanswered, we recommend to start EN in patients who are not able to resume oral feeding. We initiate EN early after ICU admission, at a low rate, and increase the infusion speed gradually to reach the nutritional target after a few days. In case of a contraindication for EN or gastrointestinal intolerance, we tolerate low intake and do not start PN before day 8. To prevent refeeding syndrome, adequate amounts of micronutrients are provided to all patients and when refeeding syndrome occurs, temporarily restricting nutritional intake can be considered. We do not recommend glutamine administration.

Conclusion

Recently, several large RCTs have yielded important new insights in ICU nutrition. Whereas traditionally, maximizing efforts to maintain a ‘normal’ caloric and protein intake during critical illness was recommended, recent RCTs showed no or a harmful impact of such an approach. Hence, increasing evidence suggests that anorexia, a highly conserved response to severe illness, is adaptive and beneficial, at least in the acute phase of critical illness, in part by stimulation of autophagy. Early PN did not prevent muscle weakness and prolonged ICU dependency. The timing when PN can be instituted safely and effectively is unclear.

Key points

1. In current ICU practice, parenteral nutrition is not clearly associated with more complications than an isocaloric and isonitrogenous dose of enteral nutrition.
2. Withholding parenteral nutrition until one week after ICU admission is clinically superior to early institution of parenteral nutrition.
3. There is no evidence that high amino acid doses are beneficial for critically ill patients.
4. Sufficient amounts of micronutrients should be provided to all patients to prevent refeeding syndrome, and when refeeding syndrome occurs, temporarily restricting nutritional intake may be superior.
5. There is no evidence to support glutamine administration in critically ill patients.

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Conflicts of interest

The authors declare to have no conflict of interest.

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57. Bloos F, Trips E, Nierhaus A *et al.* Effect of Sodium selenite administration and procalcitonin-guided therapy on mortality in patients with severe sepsis or septic shock: a randomized clinical trial. JAMA Intern Med 2016; 176:1266-1276.

* This recent multicenter RCT confirmed a neutral impact of selenium administration in patients with severe sepsis or septic shock.

Table 1: Randomized controlled trials comparing early enteral versus early parenteral nutrition

Study	Year	Setting	Population	N	Age	APACHE-II	Duration of intervention	Energy intake EN ¹	Energy intake PN ¹	Protein intake EN ¹	Protein intake PN ¹	Outcome
CALORIES [16**]	2014	Multi-center	Adult, unplanned admission, expected ICU stay >3 days	2400	63	15	5 days	18.5 kcal/kg/d	21.3 kcal/kg/d	0.6 g/kg/d	0.7 g/kg/d	Primary endpoint unaffected. More gastrointestinal intolerance with EN.

¹ Mean calories, respectively protein received per 24 hours during intervention

APACHE-II: Acute Physiology and Chronic Health Evaluation II; EN: enteral nutrition, PN: parenteral nutrition; ICU: intensive care unit

Table 2: Randomized controlled trials comparing early versus late initiation of supplemental parenteral nutrition

Study	Year	Setting	Population	N	Timing of PN ¹	Age	BMI	APACHE-II (PELOD) ²	Total energy intake early PN group ²	Total protein intake early PN group ³	Outcome in early PN group
Early PN [19]	2013	Multi-center	Adult, mixed ICU, short-term contraindication for EN	1372	Day 1	69	28	21	18 kcal/kg/d	0.7 g/kg/d	Primary endpoint unaffected. Small reduction in ventilator days per 10 patient x ICU days, without meaningful other benefit.
EPaNIC [20**]	2011	Multi-center	Adult, mixed ICU	4640	Day 3	64	26	23	26 kcal/kg/d	0.8 g/kg/d	Increased dependency on intensive care and vital organ support. Increased incidence of new infections. Increased incidence of muscle weakness and hampered recovery herefrom [24]. No difference in mortality.
PEPaNIC [21**]	2016	Multi-center	Pediatric, mixed ICU	1440	Day 1-3	1.5	15	21	75 kcal/kg/d	2.1 g/kg/d	Increased dependency on intensive care and vital organ support. Increased incidence of new infections. No difference in mortality.
SPN [22]	2013	Multi-center	Adult, mixed ICU, <60% target by EN at day 3	305	Day 4	61	26	23	28 kcal/kg/d	1.2 g/kg/d	Neutral

¹ The time at which PN containing minimum two macronutrients was initiated. In the EPaNIC study, supplemental PN containing carbohydrates, amino acids and lipids was started at day 3 (if indicated). In this study, from admission until day 3, the early PN group also received a higher amount of intravenous glucose than the late PN group.

² APACHE-II for the studies in adult patients, PELOD score for the pediatric study

³ The reported energy and protein intake is the mean energy, respectively protein intake achieved after initiation of supplemental PN containing the 3 macronutrients (carbohydrates, lipids and amino acids). For reference 19, these values were reported. For the other studies, the value had to be deducted from the figures. In reference 19, only the total intake is displayed. From this value, a normalized value (per kg) was calculated assuming a mean body weight of 75kg.

BMI: body mass index; APACHE-II: Acute Physiology and Chronic Health Evaluation II; PELOD: Pediatric Logistic Organ Dysfunction; EN: enteral nutrition, PN: parenteral nutrition; ICU: intensive care unit

Table 3: Randomized controlled trials comparing different energy and/or protein doses

Study	Year	Setting	Population	N	Age	BMI	APACHE-II	Duration of intervention	Energy intake higher target ¹	Energy intake lower target ²	Protein intake higher target ¹	Protein intake lower target ²	Outcome in group receiving more calories and/or protein
Indirect calorimetry versus formula-based feeding													
TICACOS [36]	2011	Single center	Adult, MV, expected ICU stay >3 days	130	61	28	22	ICU stay	2086 kcal/d	1480 kcal/d	76 g/d	53 g/d	Primary endpoint unaffected. More infections, longer duration of mechanical ventilation and ICU stay.
Intentional hypocaloric feeding (including protein restriction) versus normocaloric feeding													
Rice [37]	2011	Single center	Adult, ARF, expected MV >3 days, receiving EN	200	54	29	27	6 days	1418 kcal/d	300 kcal/d	54 g/d	11 g/d	Primary endpoint unaffected. More gastrointestinal intolerance.
EDEN [38]	2012	Multi-center	Adult, ALI requiring MV and EN	1000	52	30	NA	6 days	1300 kcal/d	400 kcal/d	NA	NA	Primary endpoint unaffected. More gastrointestinal intolerance
Intentional hypocaloric feeding (with protein supplements) versus isonitrogenous normocaloric feeding													
Arabi [39]	2011	Single center	Adult, expected ICU ≥2 days, receiving EN	240	51	29	25	ICU stay	1252 kcal/d	1067 kcal/d	44 g/d	48 g/d	Primary endpoint unaffected. Increased mortality.
PermiT [40*]	2015	Multi-center	Adult, expected ICU ≥3 days, receiving EN	894	51	29	21	ICU stay or until day 14	1299 kcal/d	835 kcal/d	59 g/d	57 g/d	Neutral.
Amino acid supplementation versus regular (low) dose of amino acids													
Nephro-Protective [41*]	2015	Multi-center	Adult, expected ICU >2 days	474	63	29	21	ICU stay	1350 kcal/d ³	1100 kcal/d ³	1.75 g/kg/d ³	0.75 g/kg/d ³	Primary endpoint unaffected. Small increase in eGFR, but more ureagenesis and trend towards more RRT.

¹ The intake achieved during the intervention window in the group receiving most energy or proteins. In the TICACOS study, the indirect calorimetry-fed group received most calories and proteins.

² The intake achieved during the intervention window in the group receiving least energy or proteins. For the TICACOS study, this corresponds to the group receiving formula-based feeding.

³ The value was deducted from the figures.

BMI: body mass index; APACHE-II: Acute Physiology and Chronic Health Evaluation II; ICU: intensive care unit; ARF: acute respiratory failure; MV: mechanical ventilation; ALI: acute lung injury; EN: enteral nutrition; NA: not available; eGFR: estimated glomerular filtration rate; RRT: renal replacement therapy

Table 4: Randomized controlled trials on immunonutrition

Study	Year	Immunonutrient studied ¹	Setting	Population	N	Age	BMI	APACHE-II	Duration of intervention	Outcome in study group (intention to treat)
SIGNET [52]	2011	2x2 factorial design	Multi-center	Adult, expected ICU stay ≥ 2 days and requiring PN	502	64	NA	20	ICU stay, max 7 days	
		Glutamine								Neutral
		Selenium								Neutral
OMEGA [53]	2011	n-3 fatty acids, γ -linolenic acid, vitamin C, vitamin E, beta-carotene, zinc, selenium, L-carnitine, taurine	Multi-center	Adult, ALI requiring MV and EN	272	54	NA	NA	ICU stay	Fewer ventilator-free days. Increased dependency on ICU care. More days with organ failure. Trend towards increased mortality
Scandinavian glutamine study [54]	2011	Glutamine	Multi-center	Adult, APACHE-II ≥ 10 , requiring artificial nutrition	413	62	NA	22	ICU stay	Neutral
REDOXS [55**]	2013	2x2 factorial design	Multi-center	Adult, requiring MV, ≥ 2 organ failures	1223	63	30	26	ICU stay, max 28 days	
		Glutamine								Increased mortality Increased ureagenesis
		Selenium, zinc beta-carotene, vitamin E, vitamin C								Neutral
METAPLUS [56]	2014	Glutamine, n-3 fatty acids, vitamin C, vitamin E, selenium, zinc	Multi-center	Adult, Expected MV > 3 days and requiring EN	301	58	26	22	ICU stay, max 28 days	Primary endpoint unaffected. Increased adjusted mortality.
SISPCT [57*]	2016	Selenium	Multi-center	Adults, severe sepsis or septic shock	1089	66	28	24	ICU stay, max 21 days	Neutral

¹ When vitamins or trace elements are included in the study feed, pharmacological amounts were administered, i.e. higher than the dose usually administered.

BMI: body mass index; APACHE-II: Acute Physiology and Chronic Health Evaluation II; ICU: intensive care unit; PN: parenteral nutrition; MV: mechanical ventilation; ALI: acute lung injury; NA: not available; EN: enteral nutrition