Optimizing energy and protein balance in the ICU

Peter J.M. Weijs\textsuperscript{a,b,c,d} and Paul E. Wischmeyer\textsuperscript{e}

Purpose of review
Perhaps now more than ever, appropriate nutrition delivery in the ICU is a highly debated issue. Nutrition guidelines for ICU patients by European Society for Clinical Nutrition and Metabolism in Europe, The Canadian Nutrition Guidelines, and American Society for Parenteral and Enteral Nutrition in the USA continue to disagree about the need to feed early and how. Most ICU patients around the world appear to be poorly fed.

Recent findings
Most studies have focussed on energy supply by enteral or parenteral nutrition. Some studies suggest that late initiation of energy supply could be beneficial. However, studies still not provide the answer as to when and how to feed the patient. A few studies have now also focussed on protein supply. Studies agree on the importance of adequate protein supply, 1.2–2.0 g/kg, for outcome. In fact, early protein supply might be more important than energy supply; however, limited data are available.

Summary
These findings implicate that optimization of protein balance in ICU patients as well as energy balance will improve outcome. In clinical practice, protein targets for patients should be set and achieved. More research is needed to define when and how to best feed the ICU patient.

Keywords
critical care, energy supply, outcome, protein delivery, protein dosing, protein supply

INTRODUCTION
Perhaps now more then ever, appropriate nutrition delivery in the ICU is a highly debated issue. Our lack of answers in this area is clearly demonstrated by numerous recent publications with conflicting results on the effect of protein/calorie delivery on ICU outcome. Further, there continues to be disagreement in Nutrition guidelines for ICU patients by European Society for Clinical Nutrition and Metabolism (ESPEN) in Europe, The Canadian Nutrition Guidelines, and American Society for Parenteral and Enteral Nutrition (ASPEN) in the USA, as they disagree about the need to feed early and how \cite{1–4}.

WHAT IS THE ULTIMATE GOAL?
The basic reason for feeding the patient is to provide essential nutrients for basic biologic function in sufficient amounts to prevent loss of body mass. It is likely some body mass, mainly fat mass, can be lost without consequences. The importance of fat and fatty acids as a fuel source in critical illness is emphasized by classic ICU patient metabolism studies showing that in severe sepsis and critical illness glucose utilization decreases markedly and free fatty acid (FFA) metabolism increases and becomes a primary energy source \cite{5,6}. However, a study of normal weight versus obese critically ill trauma patients showed that while normal weight patients utilize FFA as the majority of their resting energy expenditure (REE) (61%), obese patients could not mobilize FFAs for REE (39% of REE). These obese patients turned to amino acid metabolism for energy and thus lost existing lean body mass (LBM) much faster then normal weight patients \cite{7}. This has helped lead to consensus recommendations for obese ICU patients to receive 2.0–2.5 g/kg ideal body weight of protein \cite{3} (which no randomized trial of ICU nutrition has achieved to date). Unlike

\textsuperscript{a}Department of Nutrition and Dietetics, Internal Medicine, \textsuperscript{b}Department of Intensive Care Medicine, VU University Medical Center, \textsuperscript{c}Department of Nutrition and Dietetics, Amsterdam University of Applied Sciences, \textsuperscript{d}EMGO+ Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands and \textsuperscript{e}Department of Anesthesiology and Nutrition Therapy Services, University of Colorado School of Medicine, Aurora, Colorado, USA

Correspondence to Dr.ir. Peter J.M. Weijs, PhD, Department of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands. Tel: +31 204443211; e-mail: p.weijs@vumc.nl, p.j.m.weijs@hva.nl

\textit{Curr Opin Clin Nutr Metab Care} 2013, 16:194–201
DOI:10.1097/MCO.0b013e32835bd7e
Again showed an increased mortality with higher energy deficit. These were all small studies (38–57 patients), and none looked at protein delivery or deficit. The results of large randomized trials evaluating evidence-based feeding guidelines have not shown significant effects on mortality [15–17]. These trials were mainly concerned with the implementation of a nutrition policy, not explicit achievement of preset energy and/or protein targets. In fact, energy and protein delivery did not improve much at all. Thus, it is questionable whether this could have impacted mortality to any meaningful extent.

The first large evaluation of protein intake on outcome is from Alberda et al. [10]. This study evaluated 2772 ICU patients (expected to require mechanical ventilation >72h) from 165 ICUs around the world, and found a significant inverse linear relationship between the odds of mortality and total daily calories received. The key finding of this trial was that increased amounts of calories significantly reduced mortality for patients with a BMI less than 25 and a BMI at least 35 with limited or no benefit of increased calorie intake for patients with BMI 25 to less than 35. Feeding an additional 1000 kcal almost halved the odds of 60-day mortality in patients with a BMI less than 25 or at least 35. Interestingly, similar results were observed for feeding an additional 30 g of protein per day. These data may indicate that nutritional reserve, particularly LBM (or protein) reserve may be vital to the success of nutrition delivery to improve ICU outcome. It is possible, that lean (low BMI < 25) patients and obese patients (BMI > 35, who may have marked sarcopenic obesity) are the patients lacking sufficient LBM (protein) reserves to optimally survive a prolonged ICU stay without more aggressive nutrition and protein provision.

**RECENT CLINICAL TRIALS OF CALORIE DELIVERY IN CRITICAL ILLNESS**

There have been a number of clinical trials recently that have shown conflicting results regarding the benefit of additional calorie delivery on ICU outcome. These studies, including the recent supplemental parenteral nutrition trials, which have recently been discussed elsewhere are summarized in Table 1 [18**].

**THE AMSTERDAM EXPERIENCE**

We have three key challenges in ICU nutrition delivery to consider:

(1) What is the target?
(2) How do we reach the target?
(3) What is the effect on patient outcome?
<table>
<thead>
<tr>
<th>Study</th>
<th>ICU LOS (Median)</th>
<th>Hospital LOS (Median)</th>
<th>Mech. Vent days (Median)</th>
<th>ICU Mortality</th>
<th>Hospital Mortality</th>
<th>Post-discharge Mortality</th>
<th>BMI (Mean, unless indicated)</th>
<th>Protein Delivery</th>
<th>Energy Target</th>
<th>Clinical Benefit of SPN or Additional Calorie-Protein Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPaNIC</td>
<td>3.5 days</td>
<td>15</td>
<td>2</td>
<td>6.2%</td>
<td>10.65%</td>
<td>11.2%</td>
<td>51.6% pts from 25–35</td>
<td>&lt;60 g per day/both groups</td>
<td>Full energy = 54 g per day</td>
<td>-</td>
</tr>
<tr>
<td>TICACOS</td>
<td>12 days</td>
<td>25</td>
<td>10.75</td>
<td>25.4%</td>
<td>38.3%</td>
<td>47%</td>
<td>28.45</td>
<td>Study 76 g per day</td>
<td>Not reported in article</td>
<td>(-) - Mortality</td>
</tr>
<tr>
<td>SWISS</td>
<td>ICU LOS &gt;5 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cont 53 g per day</td>
<td>Full feed = 43.6 g per day</td>
<td>(+) - Infection</td>
</tr>
<tr>
<td>EDEN trial (Pilot 200 points)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Trophic 11 g per day (1st 7 days then ~50 g per day)</td>
<td>Recommended</td>
<td>(+) - Mortality hazard for reaching protein and energy target</td>
</tr>
<tr>
<td>EDEN trial (Full MCT 1000 points)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>~0.8 g/kg per day for both groups after 7 days</td>
<td>Energy target 78 g per day (1.06 g/kg per day)</td>
<td>(+) - Mortality for increased protein delivery</td>
</tr>
<tr>
<td>Arabi trial</td>
<td>13.1</td>
<td></td>
<td>5.6 days (mean vent days in survivors)</td>
<td>19.6</td>
<td>20.4</td>
<td></td>
<td>28.7</td>
<td>(&lt;25, &gt;35 for optimal benefit of calorie delivery)</td>
<td>Mean protein delivery by group:</td>
<td></td>
</tr>
<tr>
<td>Weijis Dutch trial</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allingstrup trial (Danish)</td>
<td>19</td>
<td></td>
<td></td>
<td>34.4%</td>
<td></td>
<td></td>
<td>28.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td></td>
<td></td>
<td>22.5%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

More limited data for the Swiss trial due to only abstract data being available. EDEN trials utilized ICU-free, Hospital-free, and Mech. vent-free days as outcome measures so more limited comparison data are available. EPaNIC, Early Parenteral Nutrition Completing Enteral Nutrition in Adult Critically Ill Patients.
During the years preceding the publication of the Dutch Perioperative Feeding Guideline in 2007, discussions about nutritional targets led to the publication by Sauerwein and Strack van Schijndel [19] proposing a definition of optimal nutrition delivery. For ICU patients, they defined optimal nutrition as energy provision according to indirect calorimetry increased by 10% for physical activity. Further, this definition required a protein provision of at least 1.2–1.5 g protein per kg of preadmission body weight. Although the evidence base for nutritional targets is incredibly small, this was used as a working hypothesis for determination of the daily nutrition delivery in local ICU patients.

Setting the target for energy, as well as protein, was the first challenge. The next challenge was to reach both the energy and protein target in all patients. It was clear that one enteral nutrition solution, having a fixed energy to protein ratio, was not sufficient or appropriate. We found at least three different enteral nutrition solutions were required to reach both the energy and the protein targets in most patients. This was in part due to the direct measurement of energy needs (by indirect calorimetry) instead of estimating energy needs by the Harris-Benedict equation, for instance [20]. Indirect calorimetry showed a much broader range of energy needs in patients as compared to estimation of energy needs via formulas. This is likely due to differences in body composition and level of illness. An algorithm was developed in order to calculate the correct enteral nutrition solution per patient and the correct pump speed [21]. Figure 1 shows the central role of this algorithm as part of the standard nutrition policy, which was implemented into the computerized patient management system. This computer algorithm supported assessment of nutritional targets, choice of feeding solutions and daily assessments of achievement of nutrition targets in all patients. Based on daily assessments, this computer program would then send e-mail alerts to nursing staff, intensive care physicians, and the ICU dietician to alert the care team of patients who were not achieving their nutritional targets [22].

Utilizing this computer-assisted nutrition protocol, Strack van Schijndel et al. [23] showed in 2009 that achievement of both the protein and energy target, cumulated over the whole mechanical ventilation period, significantly improved mortality in female ICU patients. This was confirmed and extended to all patients in a larger cohort of 886 patients with measured energy needs [24**]. It was hypothesized that patients with a smaller LBM (or protein mass) may benefit more significantly from adequate provision of protein delivery than patients with a larger LBM. More insight into the role of protein delivery and protein mass of patients is needed in order to confirm this.

Importantly, this increased focus on accurate nutrition delivery via calorimetry did not result in more aggressive feeding during the first days of ICU stay. In most patients it took several days to reach nutritional targets and very often targets were still not reached at all. The mean intake level of $n = 886$ patients was 86% of target (indirect calorimetry + 10%) and 95% of indirect calorimetry (ASPEN targets for energy are without stress factors). Interestingly, in this study there is a small group of patients ($n = 24$) that achieved their protein target but not their energy target, this group in fact showed the lowest mortality rates [24**].

The Arabi trial
In a preliminary observational trial, Arabi et al. [25] found ICU patients in the lower tertile of 7-day energy intake experienced the lowest mortality. They then conducted a randomized controlled trial (RCT) with permissive underfeeding (60–70% of energy target, $n = 120$) compared with target feeding (90–100% of energy target; $n = 120$) [26**]. The energy targets were defined by the Harris-Benedict equation with addition of stress factors as appropriate. It is not entirely clear from the study, which period of observation is described, but we assume it is 7 days as in the figures and their previous study [25]. The actual energy intake was 59% (1067 kcal per day) versus 71% (1252 kcal per day) for the two intervention groups. As only a minimal amount of protein was delivered in either group, both groups received a mean of 0.6 g of protein/kg body weight for the study period. The authors observed no difference in ICU, 28-day, and 180-day mortality, and no differences in length of stay and infection rate, but showed significantly reduced hospital mortality with permissive underfeeding. As the RCT comprised a dual intervention with insulin therapy, they analyzed interaction and found significant interaction for 28-day mortality ($P < 0.10$). The difference between energy delivery in the study interventions was rather small (about 10%), based on calculated energy requirements, with equal protein intakes. A significant limitation of this trial was that, in comparison to current ASPEN and ESPEN guidelines, both groups received approximately 50% of recommended protein intake for the entire study period (ASPEN: 1.2–2.0 g/kg per day protein and ESPEN 1.3–1.5 g/kg per day protein).

EDEN trials
In a large ($n = 1000$) randomized trial in acute lung injury patients the effect of initial trophic feeding
Is full EF feasible within 24-48 h?

Severe digestion or absorption disorders? Fluid restriction?

Established nutritional targets: Protein requirements: 1.2-1.5 g/kg/day
Energy requirement
Total energy expenditure (TEE) + HB + 30% or Indirect calorimetry + 10%?

No adequate enteral formula available: consultation nutritional support team for individualized advice

Cut-off point: 19.0-23.8

Promote®
Nutrision protein plus®
Nutrision®

Calculate 'energy/weight-ratio' of patient (TEE/body weight) to choose the optimal enteral formula

Cut-off point: 23.9-30.7

Cut-off point: 30.7-37.5

Calculate the optimal target volume (mL) of the chosen enteral formula: TEE / energy (kcal) of 1 ml of the chosen enteral formula:
Calculate the target pump rate: optimal target volume (mL) / 24 h
Start rate at day 1: 42 mL/h

Perform gastric challenge
Reassess every 6 h

Use prokinetic or consider postpyloric tube

Is gastric retention < 250 mL/h?

Day 2 increase pump rate to target pump rate according to nutritional advice

From day 3 PDMS monitors daily the maximum tolerated enteral nutrition and alerts when not reaching individual energy and protein targets

Nutritional targets reached?

Check reason for failing targets, consider postpyloric tube or TPN
Consider consultation of nutritional support team

FIGURE 1. Nutrition policy for the ICU with a central role for the protein-energy algorithm implemented into the patient management computer system. Introduction of this computer-assisted nutrition policy improved protein targeted feeding from 30 to 60% of patients on the fourth day of admission. Reproduced with permission from [24**].
was tested versus full enteral feeding for the first 6 days of the intervention. The actual energy intake in this trial was 25 versus 80% of energy target, or 400 versus 1300 kcal per day for trophic and full feeding, respectively. These levels were attained at study day 1, but patients were included up to 72 h after intubation. It is not stated in the article what the protein intakes of the two groups were, although it is stated in the online supplement that protein supplementation of the enteral nutrition formula was not allowed. Via discussion with the primary investigator of the EDEN trial (T. Rice, personal communication) the approximate protein delivery was 0.6–0.8 g/kg per day. This delivery is very consistent with protein delivery achieved in the EDEN pilot trial, which delivered 0.6 g/kg per day of protein based on actual body weight or approximately 0.8 g/kg per day based on predicted body weight). There were no differences in outcome, for 60-day mortality, ventilator-free days, or infection rate, although gastrointestinal complaints appeared to be reduced for trophic feeding. This study shows that 25% of energy target during the first 6 days does not change outcome versus achieving 80% of energy target. It is important to note that the patients in this trial were young (mean age 52), well nourished (as severe malnutrition was an exclusion), and on average, obese (average BMI of 30). Existing data from the large observational trial of Alberda et al. would have predicted this group would not have benefited from more aggressive nonprotein calorie delivery versus trophic feeding. As the average BMI in this trial was 30, this was a patient group not likely to be LBM deficient. As was hypothesized recently by Wischmeyer [18**], adequate protein delivery may be a crucial factor for nutrition delivery to improve outcome in the ICU. Most studies to date have been concerned with daily energy needs and adequate or inadequate supply of nonprotein calories, especially during the first week of ICU stay. As shown in Table 1, all recent trials which have achieved a protein delivery of approximately 1.0 g/kg per day or greater have shown a benefit of increased nutrition delivery on ICU outcome. These include the recent TICACOS study [30**], the Swiss SPN study [31], and the Alberda et al. [10] study showing increased survival with increased protein supply. In large part, the other recent (negative) trials have not addressed protein supply, and/or do not relate protein supply to outcome. These data indicate it is possible the energy target may not be the most important nutritional target to be met. Therefore, the widely held discussion of the value of supplemental parenteral nutrition when enteral nutrition goals are not met, maybe hampered by the fact that trials, such as the recent large EPaNIC trial (average protein delivery = ~0.8 g/kg), do not address the protein issue or provide basic guideline recommended protein delivery [32**]. In most studies, it is also not possible to distinguish the effect of energy from protein, as in most cases energy and protein supply are interlinked. When only one nutritional formula is used, there is a fixed ratio between energy and protein. There will also be little difference in statistical variation when energy and protein are evaluated; this may be the case in the Alberda et al. trial [10] with two separate analyses for energy and protein, but not together. In the Weijs et al. trial [24**], the two goals have been combined and an effect is shown on mortality. The limitation of this strategy is that a ‘target-reached’ approach works with cutoffs, and the outcome may then depend on how well the cutoffs (targets) have been chosen. In the Weijs et al. trial, the energy target was preset at indirect calorimetry measurement and 10% for physical activity. However, others would argue that the extra 10% is not needed, and this lower energy target may in fact show better outcomes while with the same protein target achieved.

**Allingstrup et al., Denmark**

In Denmark, an observational study (n = 113) was conducted in critically ill septic patients. In this study both energy and protein requirements were measured on the basis of indirect calorimetry and nitrogen excretion. They divided their cohort into three tertiles of protein intake: 0.8, 1.0, and 1.4 g protein/kg per day. Cox regression analysis and Kaplan–Meier survival curves showed a significant reduction of mortality with increased protein intake, while the level of energy intake did not affect outcome. The authors state that it was not nitrogen balance that was related to the hazard of mortality, but the protein and/or amino acid intake level. This suggests that it is not just preservation of LBM that is of importance to survival when adequate protein delivery is achieved. It is possible that improved protein delivery allows for amino acid delivery vital to other key physiologic processes in critical illness, such as immune cell replication and renal acid clearance.

**HOW DO THESE NEW STUDIES ADD TO OUR EXISTING KNOWLEDGE?**

As was hypothesized recently by Wischmeyer [18**], adequate protein delivery may be a crucial factor for nutrition delivery to improve outcome in the ICU. Most studies to date have been concerned with daily energy needs and adequate or inadequate supply of nonprotein calories, especially during the first week of ICU stay. As shown in Table 1, all recent trials which have achieved a protein delivery of approximately 1.0 g/kg per day or greater have shown a benefit of increased nutrition delivery on ICU outcome. These include the recent TICACOS study [30**], the Swiss SPN study [31], and the Alberda et al. [10] study showing increased survival with increased protein supply. In large part, the other recent (negative) trials have not addressed protein supply, and/or do not relate protein supply to outcome. These data indicate it is possible the energy target may not be the most important nutritional target to be met. Therefore, the widely held discussion of the value of supplemental parenteral nutrition when enteral nutrition goals are not met, maybe hampered by the fact that trials, such as the recent large EPaNIC trial (average protein delivery = ~0.8 g/kg), do not address the protein issue or provide basic guideline recommended protein delivery [32**]. In most studies, it is also not possible to distinguish the effect of energy from protein, as in most cases energy and protein supply are interlinked. When only one nutritional formula is used, there is a fixed ratio between energy and protein. There will also be little difference in statistical variation when energy and protein are evaluated; this may be the case in the Alberda et al. trial [10] with two separate analyses for energy and protein, but not together. In the Weijs et al. trial [24**], the two goals have been combined and an effect is shown on mortality. The limitation of this strategy is that a ‘target-reached’ approach works with cutoffs, and the outcome may then depend on how well the cutoffs (targets) have been chosen. In the Weijs et al. trial, the energy target was preset at indirect calorimetry measurement and 10% for physical activity. However, others would argue that the extra 10% is not needed, and this lower energy target may in fact show better outcomes while with the same protein target achieved.
In fact, it could be argued that during critical illness, sufficient nonprotein energy substrates are available from endogenous sources for some period after onset of illness. Due to bed rest and physical inactivity, the onset of insulin resistance seems inevitable in mechanically ventilated critically ill patients. The insulin resistance diminishes glucose uptake as well as uptake of FFAs, while not suppressing lipolysis. As stated previously, it is known that in severe sepsis/critical illness glucose utilization decreases markedly and FFA metabolism increases to a limited degree becoming the primary energy source. Throughout this early injury phase endogenous amino acids will be mobilized and utilized for energy metabolism. In the critically ill patient during the early period of ICU stay there may be little to counteract protein loss form the body, other than protein or amino acid supply from outside by enteral or parenteral nutrition supply. For instance the study by Larson et al. in patients with severe trauma the nitrogen balance is highly responsive and becomes less negative, when protein is supplied (in adequate amounts). Further, improved outcome (as defined by mortality) from adequate protein delivery likely involves more than just nitrogen balance, as shown by Allingstrup et al [29**]. As stated, this trial found a statistical reduction in mortality hazard with increasing protein and amino acid intake. This is supported by the Weijs et al. trial, in which the patients who received adequate protein but insufficient energy supply experienced the lowest mortality rate of any studied group, even lower than the group with adequate energy and protein supply. The study by Arabi et al. had no difference in protein supply with both interventions having a suboptimal energy supply. By definition, the lowest energy supply, termed permissive underfeeding, had the highest protein to energy contribution (as energy percentage). As they found significant interaction (28-day mortality) with the insulin therapy intervention, the arms of the study should have been analyzed separately and not adjusted for each other. As was true in the Arabi trial, the EDEN trial appeared to deliver a very low level of protein in both treatment groups. This trial showed no difference in the outcome between two different delivery levels of nonprotein calories only. This suggests that nonprotein energy delivery may not be as relevant to mortality outcomes during the first 6 days of ICU stay in well nourished patients. The hypothesis of aggressive, early nonprotein calorie delivery being detrimental or at least not beneficial in the ICU is perhaps best supported by the results of the Early Parenteral Nutrition Completing Enteral

Nutrition in Adult Critically Ill Patients (EpaNIC) trial. This trial utilized aggressive parenteral nutrition glucose loading in the early-parenteral nutrition group via a low protein parenteral nutrition product leading to a significant nonprotein calorie load (with low protein delivery) versus the late-parenteral nutrition group. This trial showed improved ICU outcomes in patients who did not receive this early, aggressive nonprotein calorie load.

DOES ONE SIZE FIT ALL PATIENTS?

As the evidence base for protein recommendations for specific patient groups is very limited, most guidelines are also rather ‘general’ in their description. It is quite likely that patients with a low LBM, or loss of LBM due to a chronic illness, may clearly benefit most from adequate protein supply. Especially, because the early LBM loss during ICU stay (day 1–4) may have a much more dramatic impact on subsequent survival and long-term physical function. On the contrary, it is possible that a larger LBM would need a larger dose of protein to be maintained properly. The best indicator of protein mass is likely to be LBM. A recent analysis of Weijs et al. suggests that BMI cutoffs of 20 and 30 could be used for calculation of protein provision [33**]. At a BMI less than 20, the weight of each patient is recalculated to BMI 20; and above BMI 30 the weight of each patient is recalculated to BMI 27.5. Although this suggestion needs further confirmation in outcome studies, these data show that using these calculations for protein provision complies rather well with a chosen reference intake of 1.5 g/kg LBM as measured by Ishibashi et al. [8]. This is a suggestion for clinical practice that may improve protein provision for individual needs.

CONCLUSION

The recent trials of calorie delivery in the ICU present a number of new hypotheses, which need to be investigated in well designed multicenter randomized controlled trials (RCTs). These include the possibility that in well nourished patients (BMI of 25–35), reduced nonprotein calorie delivery coupled with adequate protein delivery early in ICU care may be optimal. More importantly, large trials examining the effect of nutrition delivery with adequate protein delivery (1.2–2.0 g/kg per day) on outcome are needed, these data do not currently exist. Finally, better methods by which to evaluate patients nutrition status and LBM are needed. These include easily accessible bedside methods such as the ultrasound LBM technique currently being
tested in the TOP-UP trial of supplemental parenteral nutrition (ClinicalTrials.gov Identifier: NCT01206166). Also, the analysis of computed tomography scans for LBMM is currently being investigated in the TOP-UP trial, as well as by other investigators (Weijs). Improved nutrition evaluation methods may finally allow us to better target patients at risk for malnutrition and reduced LBMM, so we provide more aggressive nutrition delivery to those who are the most nutritionally ‘at-risk’.

Acknowledgements
None.

Conflicts of interest
P.J.M.W. serves as a member of the Protein Advisory Board of Baxter. P.J.M.W. has received funding from Danone.
P.E.W. has served as a consultant to Baxter Inc and Fresnens Inc on the subject of appropriate Parenteral Nutrition use in the ICU setting. P.E.W. receives funding from the National Institutes of Health, US Department of Defense, and the American Burn Association.

REFERENCES AND RECOMMENDED READING
Papers of particular interest, published within the annual period of review, have been highlighted as:
• of special interest
•• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 226–237).

8. This is a comprehensive review article examining latest evidence for determination of energy needs and optimal feeding in critically ill obese patients.
20. This is a comprehensive review article examining latest trials in parenteral nutrition and calorie delivery in critically ill patients. Examines roles of acuity of illness, protein delivery, and metabolic cart utilization in recently published data.
27. This examines relationship between protein and energy goal directed feeding and mortality as outcome, based on measured indirect calorimetry. While at similar energy target intake, patients also achieving protein target intake had lower mortality rate compared with patients not achieving protein target intake.
30. This is an RCT of ‘permissive underfeeding’ with ‘target feeding’ a very small difference in calorie delivery (60 versus 70% of target) and no difference in protein delivery. One out of six outcome measures was significantly different.
33. A randomized trial with a large difference in energy delivery, with inadequate protein delivery in both groups and no effect on mortality.
35. An observational study that, for the first time, shows a dose–response relationship between protein delivery and mortality.
37. A randomized trial with targeted feeding achieved with supplemental parenteral nutrition showing lower mortality rate, but higher infection rate, compared with unsupplemented group.
40. A randomized trial showing no mortality difference between early and late supplemental feeding with parenteral nutrition. Heavily debated study, with low protein intake and estimated energy requirement.
42. Suggestions for improvement of protein delivery in clinical practice by considering weight category of patient, as current guidelines have not considered this issue yet.